

RECONSTRUCTIVE SURGERY IN BREAST CANCER

Honorary Editors: Claudio Angrigiani, Kimito Yamada,
Peter G. Cordeiro
Editors: Jiong Wu, Peirong Yu



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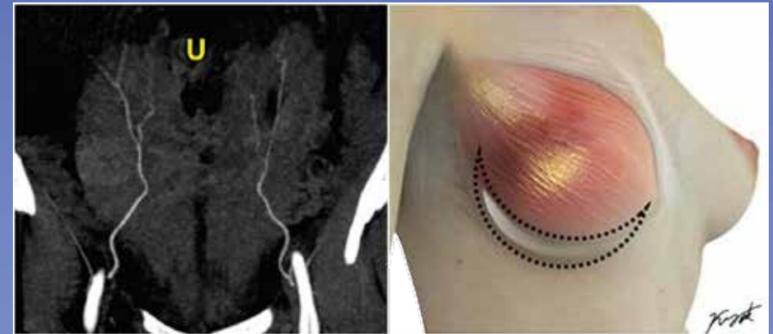


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I am honored to participate as an Honorary Editor of this new book “*Reconstructive Surgery in Breast Cancer*” together with Dr. Jiong Wu (Fudan University Shanghai Cancer Center, China), and Dr. Peirong Yu (MD Anderson Cancer Center, USA)

In the last two decades, there have been many innovations in breast cancer treatment and reconstruction following partial or total mastectomy. These advancements have focused on improving technology, surgical expertise, outcomes and reducing complications.

Breast reconstruction has become an aesthetic and reconstructive procedure. Some of the advancements include better devices and techniques that optimize breast shape, and new technologies that have facilitated our understanding of anatomy, physiology, perfusion, and monitoring.

Our objective with this book is to join the most experienced surgeons that have lately contributed to medical literature in this field. By editing this book, surgeons, residents and students will have access to high quality, current, state-of-the-art, and up-to-date information on planning, & performing autologous, prosthetic, and oncoplastic procedures for breast reconstruction following mastectomy or conservative treatment.

In summary, we hope that this book on breast reconstruction will prove to be a valuable resource to the practitioner. I would like to thank the staff of AME Publishing Company for their valuable assistance in preparing this material, which is open access and indexed in PubMed. I would also like to thank all the authors that took time away from their busy schedules to prepare all the manuscripts.

Claudio Angrigiani, M.D.

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It is a great privilege for me to participate as an Honorary Editor of this new book *Reconstructive Surgery in Breast Cancer*.

Recently, this field has been getting attention in Japan. We have established Japan Oncoplastic Breast Surgery Society in 2008, which accelerated the medical insurance coverage of reconstructive surgical procedures with silicone implants. We are now excited to start collaborating with plastic surgeons and realizing new methodologies being developed for reconstructing the breast, particularly after breast cancer surgery.

However, we are now facing new problems. The rate of breast-conserving surgery is reported to be decreasing, while that of mastectomy increasing. Hopefully, this is partly because we are becoming not to perform breast-conserving surgery without cosmetic satisfaction. Quality of breast reconstruction is the biggest concern at present. For example, we have to be cautious on the improper usage and mismanagement of silicone implants, which clearly deteriorate cosmetic results.

Lastly, I hope that this book will help breast surgeons, plastic surgeons and surgical staffs to learn the up-to-date technologies as well as information and improve the quality of breast cancer surgery in each institution.

Kimito Yamada, MD, PhD

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Many breast reconstruction books are currently available, some are comprehensive textbooks with topics ranging from basic theories to various surgical techniques whereas some focus on certain aspects of breast reconstruction, such as autologous breast reconstruction and reoperative breast surgery for complications and asymmetry.

AME invited us to compile a book about oncologic breast reconstruction and provided numerous articles recently published in the journal of *Gland Surgery*. These valuable reviews and original articles were written by renowned experts from various parts of the world. They can provide not only novel ideas and technology, but also allow readers to understand the development of breast reconstruction in these regions.

Although these papers are independent publications, we find that they can also be organized into certain categories, from anatomy to preoperative evaluation, surgical approaches, and the state-of-art breast reconstructive technologies in a systematic fashion. At the same time, this book also covers oncoplastic surgery in the era of breast conservation and conservative mastectomy in the treatment of breast cancer. Therefore, we believe that this will be a welcome book for breast surgeons and plastic surgeons alike.

In this book, we try to use a novel compilation method to make it rather unique and different from other monographs with the same topic. Apart from the academic authority of this book, developmental characteristics are also reflected, which is a unique feature of breast reconstructive surgery. We sincerely hope that readers can benefit from the variety of technologies and concepts in this book and appreciate the aesthetic value of the operations and the humane care for breast cancer patients. With this purpose, we anticipate that this book be updated regularly in the future.

Peirong Yu

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Table of Contents

Preface

- i Claudio Angrigiani
- ii Kimito Yamada
- iii Peirong Yu, Jiong Wu

Local/Regional Anatomy in Reconstructive Breast Surgery

- 1 The venous anatomy of the abdominal wall for Deep Inferior Epigastric Artery (DIEP) flaps in breast reconstruction
Warren M. Rozen, Mark W. Ashton
- 20 Anatomy relevant to conservative mastectomy
Rachel L. O'Connell, Jennifer E. Rusby
- 28 Anatomic and physiological fundamentals for autologous breast reconstruction
Anita T. Moban, Michel Saint-Cyr
- 46 Anatomy of the nipple and breast ducts
Gustavo Zucca-Matthes, Cícero Urban, André Vallejo

Preoperative Evaluation

- 51 Essential elements of the preoperative breast reconstruction evaluation
Angela Cheng, Albert Losken
- 55 Preoperative digital mammography imaging in conservative mastectomy and immediate reconstruction
Alberto Rancati, Claudio Angrigiani, Dennis Hammond, Maurizio Nava, Eduardo Gonzalez, Roman Rostagno, Gustavo Gercovich

Conservative Mastectomies—SSM, NSM and Mastopexy w/wo Reduction

- 61 Nipple areola complex sparing mastectomy
Camilla Rossi, Matteo Mingozzi, Annalisa Curcio, Federico Buggi, Secondo Folli
- 74 How to perform a NAC sparing mastectomy using an ADM and an implant
Gudjon Leifur Gunnarsson, Mikkel Børsen-Koch, Peter Wamberg, Jørn Bo Thomsen
- 80 Using intraoperative laser angiography to safeguard nipple perfusion in nipple-sparing mastectomies
Monica M. Dua, Danielle M. Bertoni, Dung Nguyen, Shannon Meyer, Geoffrey C. Gurtner, Irene L. Wapnir
- 89 The evolution of mastectomies in the oncoplastic breast surgery era
Gustavo Zucca-Matthes, Andrea Manconi, Rene Aloísio da Costa Viera, Rodrigo Augusto Depieri Michelli, Angelo do Carmo Silva Matthes

- 94 **Oncological safety of prophylactic breast surgery: skin-sparing and nipple-sparing versus total mastectomy**
Victorien M. T. van Verschuer, Marike C. Maijers, Carolien H. M. van Deurzen, Linetta B. Koppert
- 103 **Oncologic safety of conservative mastectomy in the therapeutic setting**
John R. Benson, Dorin Dumitru, Charles M. Malata
- 113 **Introduction to conservative mastectomies**
Alberto Rancati, F. Gustavo Gercovich
- 116 **Skin-sparing mastectomy**
Eduardo G. González, Alberto O. Rancati
- 129 **Surgical decision making in conservative mastectomies**
Giuseppe Catanuto, Nicola Rocco, Maurizio Bruno Nava
- 135 **Conservative mastectomies: an overview**
Maurizio Bruno Nava, Nicola Rocco, Giuseppe Catanuto
- 139 **What is the evidence behind conservative mastectomies?**
Nicola Rocco, Giuseppe Catanuto, Maurizio Bruno Nava

Oncoplastic Breast Surgery-Strategy, Techniques and Training

- 152 **Training the oncoplastic breast surgeon—current and future perspectives**
Sue K. Down, Jerome H. Pereira, Sam Leinster, Andrew Simpson
- 154 **Evaluating the feasibility of extended partial mastectomy and immediate reduction mammoplasty reconstruction as an alternative to mastectomy**
Kimito Yamada, Norio Kobno
- 157 **Oncoplastic breast surgery: indications, techniques and perspectives**
Alexandre Mendonça Munhoz, Eduardo Montag, Rolf Gemperli
- 172 **Oncoplastic breast conserving surgery**
Lucy Mansfield, Avi Agrawal, Ramsey I. Cutress
- 177 **Oncoplastic options in breast conservative surgery**
Alberto Rancati, Eduardo Gonzalez, Claudio Angrigiani, Gustavo Gercovich, Ernesto Gil Deza, Julio Dorr
- 184 **An example of lumpectomy for lower inner quadrant breast cancer with 1st level oncoplastic reconstruction by glandular splitting**
Pier Carlo Rassu, Alberto Serventi, Eliana Giaminardi, Maurizia Bocchio, Paolo Tava
- 187 **Oncoplastic breast surgery for centrally located breast cancer: a case series**
Yuko Kijima, Heiji Yoshinaka, Yoshiaki Shinden, Munetsugu Hirata, Akibiro Nakajo, Hideo Arima, Hiroshi Okumura, Hiroshi Kurahara, Sumiya Isbigami, Shoji Natsugoe
- 199 **Oncoplastic technique in breast conservative surgery for locally advanced breast cancer**
Prakasit Chirappapha, Youwanush Kongdan, Wichai Vassanasiri, Kampol Ratchaworapong, Thongchai Sukarayothin, Chairat Supsamutchai, Phatarachate Klaiklern, Monchai Leesombatpaiboon, Alaa Hamza, Stefano Zurrida

- 205 **Oncoplastic breast surgery in Australia and New Zealand—2014 and beyond**
Michael Yunaev, Guy Hingston
- 209 **Oncoplastic volume replacement techniques according to the excised volume and tumor location in small- to moderate-sized breasts**
Jeong Woo Lee, Min Chul Kim, Ho Yong Park, Jung Dug Yang
- 217 **International oncoplastic breast surgery training**
Supakorn Rojananin, Visnu Lobsirawat
- 220 **Oncoplastic breast surgery: current strategies**
Merisa Piper, Anne Warren Peled, Hani Sbitany
- 230 **Immediate breast volume replacement using a free dermal fat graft after breast cancer surgery: multi-institutional joint research of short-term outcomes in 262 Japanese patients**
Yuko Kijima, Chihaya Koriyama, Terubiko Fujii, Kouichi Hirokaga, Kiyoshi Ishigure, Tomoyo Kaneko, Shuji Kayano, Sachio Miyamoto, Yasuaki Sagara, Takashi Sakurai, Teruhisa Sakurai, Keiichi Sotome, Hiroaki Ueo, Kazuyuki Wakita, Masabiro Watatani
- 246 **Oncoplastic volume replacement technique for the upper inner quadrant using the omental flap**
Hisamitsu Zaba
- 253 **Oncoplastic techniques in breast surgery for special therapeutic problems**
Prakasit Chirappapha, Panuwat Lertsithichai, Thongchai Sukarayothin, Monchai Leesombatpaiboon, Chairat Supsamutchai, Youwanush Kongdan

Implant Breast Reconstruction and Alloplastic Adjuncts

- 261 **Direct-to-implant breast reconstruction**
Amy S. Colwell
- 264 **Alloplastic adjuncts in breast reconstruction**
Miguel S. Cabalag, Marie Rostek, George S. Miller, Michael P. Chae, Tam Quinn, Warren M. Rozen, David J. Hunter-Smith
- 280 **Prosthetic breast reconstruction: indications and update**
Tam T. Quinn, George S. Miller, Marie Rostek, Miguel S. Cabalag, Warren M. Rozen, David J. Hunter-Smith
- 293 **The biplanar oncoplastic technique case series: a 2-year review**
Alexander J. Kaminsky, Ketan M. Patel, Costanza Cocilovo, Maurice Y. Nababedian, Reza Miraliakbari
- 299 **Evolution and update on current devices for prosthetic breast reconstruction**
Kristina O'Shaughnessy
- 313 **Current strategies with 1-stage prosthetic breast reconstruction**
Amy S. Colwell
- 318 **Current opinions on indications and algorithms for acellular dermal matrix use in primary prosthetic breast reconstruction**
Michael M. Vu, John Y. S. Kim
- 327 **Current strategies with 2-staged prosthetic breast reconstruction**
Christin Harless, Steven R. Jacobson

- 335 **Conservative mastectomies and immediate reconstruction with the use of ADMs**
Alexander Govsbievich, Ron B. Somogyi, Mitchell H. Brown
- 345 **Risk-reducing, conservative mastectomy—analysis of surgical outcome and quality of life in 272 implant-based reconstructions using TiLoop® Bra versus autologous corial flaps**
Mabdi Rezai, Stefanie Strauß, Rainer Kimmig, Peter Kern
- 353 **Implant-based breast reconstruction following conservative mastectomy: one-stage vs. two-stage approach**
Maurice Y. Nababedian

Autologous Breast Reconstruction

LDF and Evolving Related Tissue Flaps

- 361 **The evolving breast reconstruction: from latissimus dorsi musculocutaneous flap to a propeller thoracodorsal fasciocutaneous flap**
Jørn Bo Thomsen, Gudjon Leifur Gunnarsson
- 365 **Propeller thoracodorsal artery perforator flap for breast reconstruction**
Claudio Angrigiani, Alberto Rancati, Ezequiel Escudero, Guillermo Artero, Gustavo Gercovich, Ernesto Gil Deza
- 372 **Use of latissimus dorsi muscle onlay patch alternative to acellular dermal matrix in implant-based breast reconstruction**
Jeeyeon Lee, Youngtae Bae
- 379 **Extended thoracodorsal artery perforator flap for breast reconstruction**
Claudio Angrigiani, Alberto Rancati, Ezequiel Escudero, Guillermo Artero

Free Abdominal Perforator Flap—Preoperative Imaging Evaluation and Surgical Techniques

- 388 **Magnetic resonance angiography in perforator flap breast reconstruction**
Julie V. Vasile, Joshua L. Levine
- 403 **Preoperative computed tomography angiography for planning DIEP flap breast reconstruction reduces operative time and overall complications**
Edmund Fitzgerald O'Connor, Warren Matthew Rozen, Muhammad Chowdbry, Bassam Band, Venkat V. Ramakrishnan, Matthew Griffiths
- 409 **Comparative study of software techniques for 3D mapping of perforators in deep inferior epigastric artery perforator flap planning**
Michael P. Chae, David J. Hunter-Smith, Warren Matthew Rozen
- 417 **Three routine free flaps per day in a single operating theatre: principles of a process mapping approach to improving surgical efficiency**
Dan Marsh, Nakul Gamanlal Patel, Warren Matthew Rozen, Muhammed Chowdbry, Hrsikesa Sharma, Venkat V. Ramakrishnan
- 425 **Increasing options in autologous microsurgical breast reconstruction: four free flaps for ‘stacked’ bilateral breast reconstruction**
Warren Matthew Rozen, Nakul Gamanlal Patel, Venkat V. Ramakrishnan

- 431 **The microvascular anastomotic coupler for venous anastomoses in free flap breast reconstruction improves outcomes**
Edmund Fitzgerald O'Connor, Warren Matthew Rozen, Muhammad Chowdhry, Nakul Gamanlal Patel, Whitney T.H. Chow, Matthew Griffiths, Venkat V. Ramakrishnan
- 436 **Nipple-areola complex reconstruction**
Anongporn Nimboriboonporn, Suebwong Chuthapisith
- 444 **Bilateral breast reconstruction with bipedicle transverse rectus abdominis myocutaneous (TRAM) flap for simultaneous delayed and immediate breast reconstruction after therapeutic modified radical mastectomy and prophylactic nipple sparing mastectomy**
Ajaree Sattaratnamai, Visnu Lohsirivat
- 447 **Achieving ideal breast aesthetics with autologous reconstruction**
Maurice Y. Nababedian
- 458 **Abdominal perforator vs. muscle sparing flaps for breast reconstruction**
Paris D. Butler, Liza C. Wu
- 468 **Comparative analysis of fluorescent angiography, computed tomographic angiography and magnetic resonance angiography for planning autologous breast reconstruction**
Michael P. Chae, David J. Hunter-Smith, Warren Matthew Rozen
- 483 **Conservative mastectomies and Immediate-DElayed AutoLogous (IDEAL) breast reconstruction: the DIEP flap**
Maximilian Otte, Carolin Nestle-Krämling, Sonia Fertsch, Mazen Hagouan, Beatrix Munder, Philip Richrath, Peter Stambera, Alina Abu-Ghazaleh, Christoph Andree

Radiation Therapy, the Influence on Reconstructive Breast Surgery and Vice-versa

- 491 **Radiotherapy and breast reconstruction: oncology, cosmesis and complications**
Warren M Rozen, Mark W Ashton
- 500 **Immediate breast reconstruction: does the pathology affect the reconstruction?**
Alaa Mostafa Hamza, Mario Rietjens
- 502 **Minimizing incisional dehiscence following 2-stage prosthetic breast reconstruction in the setting of radiation therapy**
Maurice Y. Nababedian
- 505 **Current perspectives on radiation therapy in autologous and prosthetic breast reconstruction**
Mark W. Clemens, Steven J. Kronowitz

Complications and its Management in Breast Reconstructive Surgery

- 515 **Achieving ideal donor site aesthetics with autologous breast reconstruction**
Maurice Y. Nababedian
- 524 **Does immediate reconstruction increase postmastectomy surgical site infection?**
Salvatore Carlucci, Filippo Montemurro, Riccardo Ponzzone

- 526 **The role of the physiotherapy in the plastic surgery patients after oncological breast surgery**
Luiz Felipe Nevola Teixeira, Fabio Sandrin
- 531 **Metabolic syndrome and outcome after breast reconstruction**
Areerat Oumbasuttiyanon, Visnu Lobsirawat
- 534 **A multiple logistic regression analysis of complications following microsurgical breast reconstruction**
Samir Rao, Ellen C. Stolle, Sarah Sber, Chun-Wang Lin, Babram Momen, Maurice Y. Nababedian
- 540 **Lymphatic mapping and lymphedema surgery in the breast cancer patient**
Ketan M. Patel, Oscar Manrique, Michael Sosin, Mahjabeen Aftab Hashmi, Poysophon Poysophon, Robert Henderson
- 553 **Breast reconstruction following conservative mastectomies: predictors of complications and outcomes**
Sophocles H. Voineskos, Simon G. Frank, Peter G. Cordeiro

An Update and Forecast in Reconstructive Breast Surgery—Fat Grafting and Tissue Engineering

- 566 **Stem cell and tissue engineering in breast reconstruction**
Tanasit Techanukul, Visnu Lobsirawat
- 573 **Fat grafting and breast reconstruction: tips for ensuring predictability**
Allen Gabriel, Manish C. Champaneria, G. Patrick Maxwell

Comparison of Breast Reconstruction between Chinese and American Cancer Centers

- 585 **Current status of breast reconstruction in China: an experience of 951 breast reconstructions from a single institute**
Nai-Si Huang, Chen-Lian Quan, Lin-Xiao-Xi Ma, Jing Si, Jia-Jian Chen, Ben-Long Yang, Xiao-Yan Huang, Guang-Yu Liu, Zhen-Zhou Shen, Zhi-Min Shao, Jiong Wu
- 594 **Breast reconstruction at the MD Anderson Cancer Center**
Peirong Yu

The venous anatomy of the abdominal wall for Deep Inferior Epigastric Artery (DIEP) flaps in breast reconstruction

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Background: Despite improving outcomes, venous problems in the harvest of deep inferior epigastric artery perforator (DIEP) flaps remain the more common vascular complications. However, it is apparent that the venous anatomy of the anterior abdominal wall has not been described to the same extent as the arterial anatomy. Cadaveric dissection studies of venous anatomy frequently lack the detail of their arterial counterparts. Venous valves complicate retrograde injection, resulting in poor quality studies with limited anatomical information.

Methods: The current manuscript comprises a review of the literature, highlighting key features of the anatomy of the venous drainage of the abdominal wall integument, with particular pertinence to DIEP flaps. Both cadaveric and clinical studies are included in this review. Our own cadaveric and *in-vivo* studies were undertaken and included in detail in this manuscript, with the cadaveric component utilizing direct catheter venography and the *in-vivo* studies were undertaken using preoperative computed tomographic angiography (CTA), mapping *in-vivo* venous flow.

Results: Several key features of the venous anatomy of the abdominal wall render it different to other regions, and are of particular importance to DIEP flap transfer.

Conclusions: The cause of venous compromise is multi-factorial, with perforator diameter, midline crossover, and deep-superficial venous communications all important. Venous cadaveric studies as well as clinical CTA preoperatively can identify these anomalies.

Keywords: Abdominal wall; Deep inferior epigastric artery perforator flap; DIEA perforator flap; venous drainage; abdomen; vein

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Introduction

The venous anatomy of the anterior abdominal wall differs from its arterial counterpart, with a dominant superficial venous drainage despite a dominant deep arterial supply. This inherent conundrum has had profound influences on the fate of flaps based on the abdominal wall integument, such as the deep inferior epigastric artery perforator (DIEP) flap, the transverse rectus abdominus myocutaneous (TRAM) flap and the superficial inferior epigastric artery (SIEA) flap. In two previous studies of the venous system of the DIEP flap for breast reconstruction, we were able

to highlight the importance of the venous anatomy in flap success (1,2). In one of these studies, the clinical importance of considering both the superficial and deep venous drainage systems of the abdominal wall was highlighted (*Figure 1*) (2). In the other study, a cadaveric study was used to demonstrate the venous anatomy of the abdominal wall, and this led the way to clinical studies for highlighting this anatomy *in-vivo* (*Figures 2,3,4*) (1). The current review, including all of the clinical context, is based on that cadaveric study (1), and we offer a further review of the literature to highlight additions to our knowledge, including advanced imaging modalities with computed tomographic

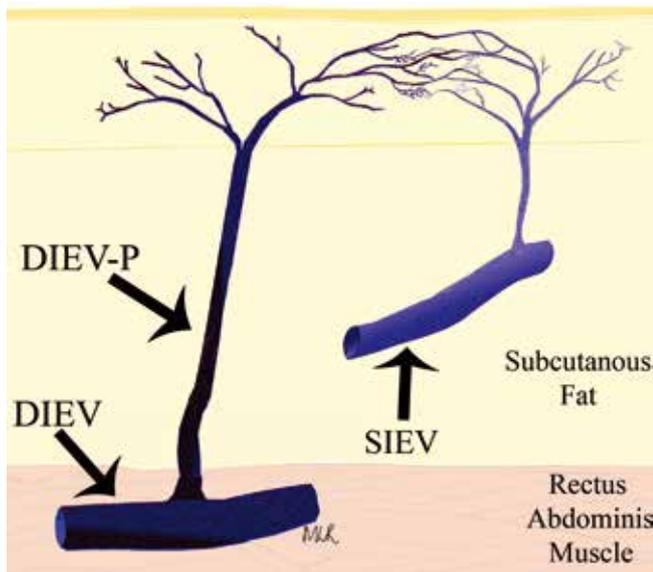


Figure 1 Representation of the venous anatomy of the anterior abdominal wall, with the subcutaneous tissues drained by both superficial and deep venous systems, the superficial inferior epigastric vein (SIEV) and the deep inferior epigastric vein (DIEV) respectively, through DIEV perforators (DIEV-P) (Reproduced with permission from: Enajat M, Rozen WM, Whitaker IS, *et al.* A single center comparison of one versus two venous anastomoses in 564 consecutive DIEP flaps: investigating the effect on venous congestion and flap survival. *Microsurgery* 2010;30:185-91)

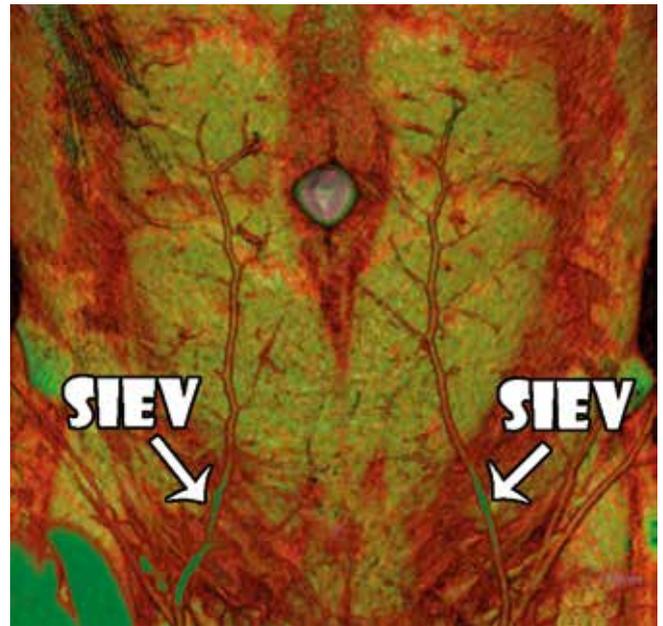


Figure 2 Computed tomographic angiogram (CTA) performed preoperatively, with volume-rendered reconstruction demonstrating the superficial inferior epigastric veins (SIEVs) and their branches bilaterally. (Reproduced with permission from: Rozen WM, Pan WR, Le Roux CM, *et al.* The venous anatomy of the anterior abdominal wall: an anatomical and clinical study. *Plast Reconstr Surg* 2009;124:848-53)

angiography (CTA) and magnetic resonance angiography (MRA), as well as clinical findings of anatomical variations in the venous anatomy.

The importance of this venous anatomy to this flap, the deep inferior epigastric artery (DIEA) perforator flap, is essential. The DIEP flap has been widely shown to have a low incidence of complications, contributing to its popularization for use in breast reconstruction (3-6). While the arterial anatomy of the abdominal wall forming the basis for supply to this flap has been widely described in the literature, the venous anatomy has not received an equal appraisal (7,8). Despite this, venous problems continue to be the more frequently encountered vascular complications seen, with Blondeel (9) reporting a series of DIEA perforator flaps with insufficient venous drainage requiring re-operation, and this having been echoed in subsequent studies (9-11).

Many authors have since offered varying means to augmenting or supercharging the venous drainage of

congested or compromised flaps. The methods used to augment this venous drainage have included the use of additional venae comitantes of the ipsilateral DIEA (12,13), the venae comitantes of the contralateral DIEA (14), through the ipsilateral superficial inferior epigastric vein (SIEV) (10,11,15), and the contralateral SIEV (16). In understanding the cause for venous problems in these flaps, Carramenha e Costa *et al.* undertook an anatomical study using corrosion casts and dye injection to describe the venous architecture of the abdominal wall integument, and demonstrated venous drainage through both superficial and deep venous systems (17). Subsequent studies have explored the use of plain-film angiography to evaluate this anatomy (18-20), and a recent anatomical study utilized cadaveric computed tomographic angiography (CTA) to evaluate the venous anatomy (21). With the increasing use of preoperative CTA, the ability to analyse the *in-vivo* venous architecture of the abdominal wall has become possible.

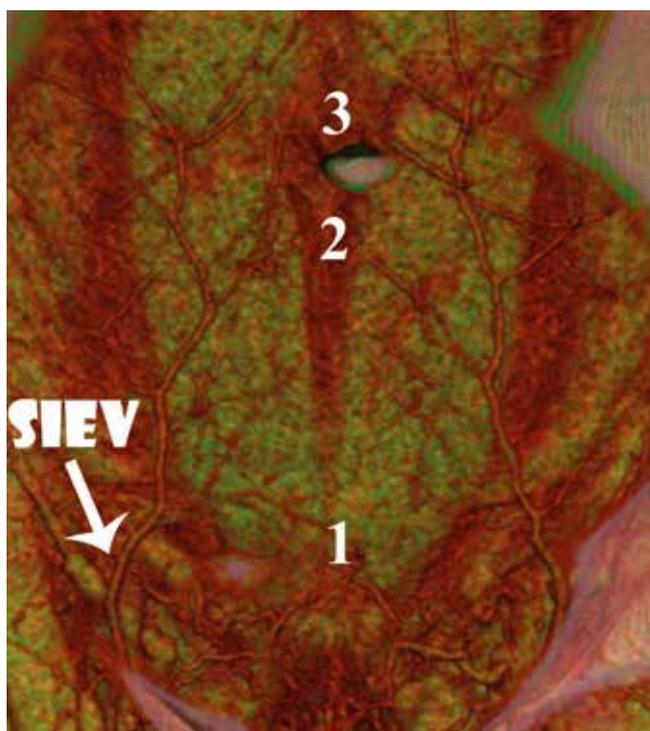


Figure 3 Preoperative computed tomographic angiogram (CTA) with volume-rendered reconstruction demonstrating the superficial inferior epigastric veins (SIEVs) and their multiple points of crossover, in this case at the arcuate line, immediately infraumbilically, and immediately supraumbilically (Reproduced with permission from: Rozen WM, Pan WR, Le Roux CM, *et al.* The venous anatomy of the anterior abdominal wall: an anatomical and clinical study. *Plast Reconstr Surg* 2009;124:848-53)

Previous cadaveric anatomical studies

In our previous cadaveric anatomical studies, we undertook contrast venography and dissection studies on 8 whole fresh cadaveric abdominal wall specimens. The cadavers spanned a wide range of body habitus types, and the cadaveric age ranged from age 50-85. No cadavers had undergone previous abdominal surgery. Six of these specimens were archival studies, utilized in previous studies of the venosomes of the body (20,22). In each case (both current and archival studies), the abdominal wall integument was harvested from its respective cadaver, in anticipation of contrast radiographic studies. A contrast mixture was made, comprising heated normal saline (to 50 °C), 10% w/v of commercial grade (96% pure) lead oxide as an orange powder and 10% w/v gelatine injection (23). The

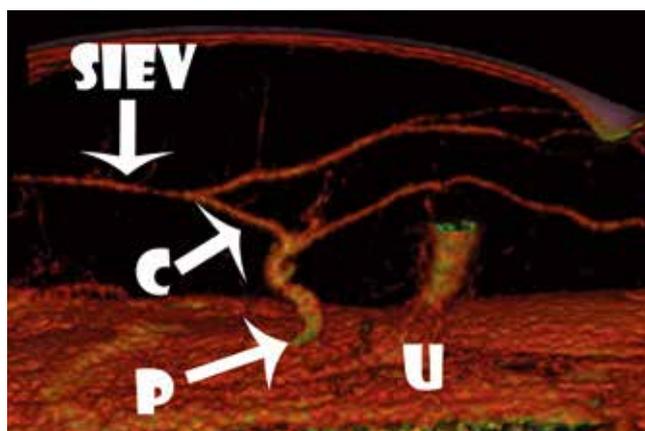


Figure 4 Preoperative computed tomographic angiogram (CTA) with volume-rendered reconstruction demonstrating the superficial inferior epigastric vein (SIEV) and its communication (C) with a venous perforator (P). U = umbilicus (Reproduced with permission from: Rozen WM, Pan WR, Le Roux CM, *et al.* The venous anatomy of the anterior abdominal wall: an anatomical and clinical study. *Plast Reconstr Surg* 2009;124:848-53)

deep inferior epigastric vein (DIEV) and SIEV were then identified and cannulated, with each vessel injected with the contrast media. Each specimen underwent venography with plain-film radiography (Fuji Computed Radiography Processor, Model CR-IR 357, Fuji Film Corporation, Tokyo, Japan). In two specimens, periumbilical dissection was undertaken in order to identify veins for cannulation, with a view to filling veins that may have not filled with contrast initially due to the presence of valves. In these cases, repeat venography was undertaken.

We identified that the SIEV was found to consistently lie superficial to Scarpa's fascia (all 16 sides), to have a single (87.5% of sides) or bifurcating (12.5% of sides) trunk below the umbilicus, and to routinely overlie the rectus abdominis muscle at the level of the arcuate line. A large (>1 mm) medial branch was distributed that crossed the midline in 15 of 16 sides. While this crossover point was routinely at the level of the arcuate line, in some cases there were additional midline cross-over points seen: immediately infraumbilically and immediately supraumbilically (*Figure 5*). Inferiorly, the SIEV coursed through the superficial inguinal lymph nodes to drain into either the superficial femoral vein (62.5% of sides), the long saphenous vein (12.5% of sides) or the saphenous bulb (25% of sides). The mean diameter of the SIEV at its termination was 2.3 mm (range, 1.8-3.3 mm). It received tributaries throughout its course, including the superficial

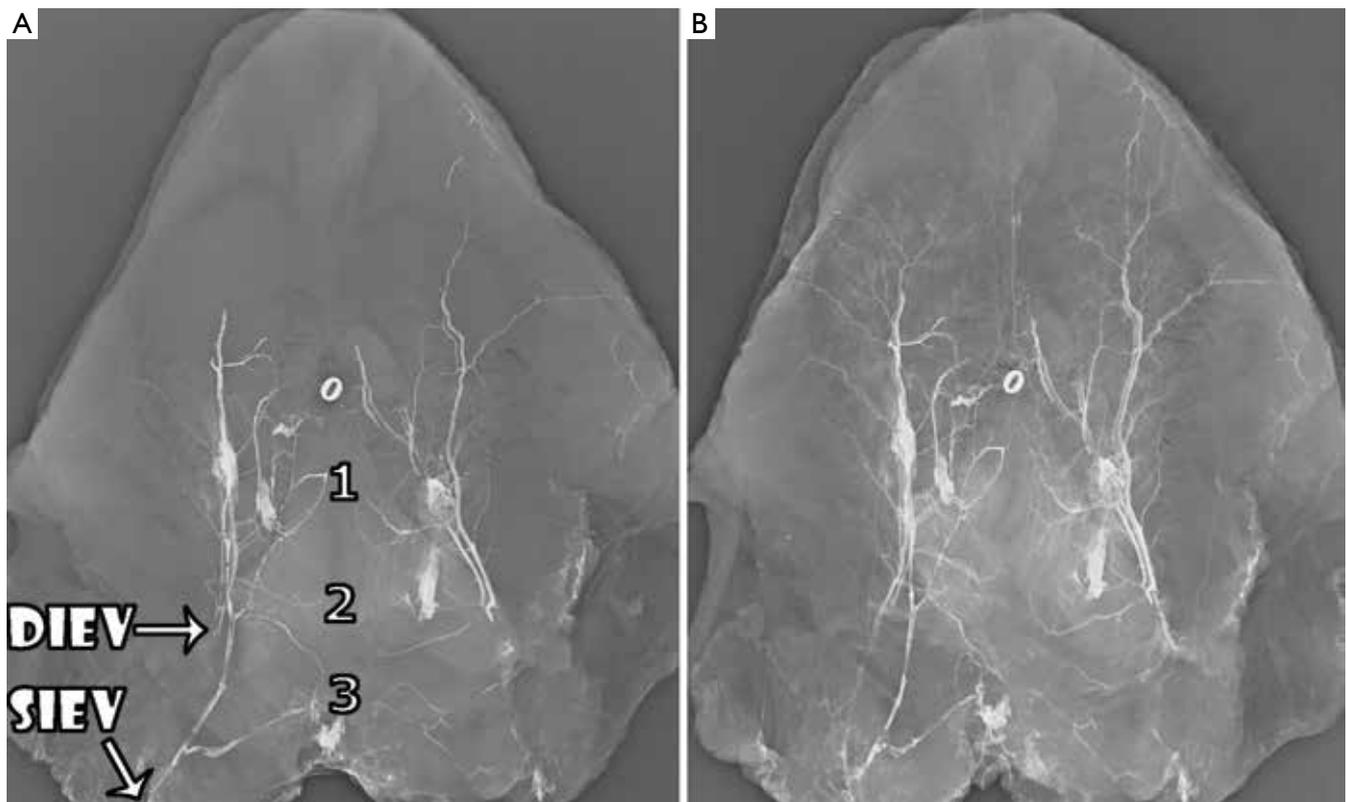


Figure 5 A. Plain film venogram of the anterior abdominal wall, with deep inferior epigastric vein (DIEV) and superficial inferior epigastric vein (SIEV) and periumbilical communicating veins all injected with contrast. Three points of midline crossover in this specimen are highlighted; B. The deep inferior epigastric artery (DIEA) is also injected in the same specimen, confirming that the left image is a venogram, and demonstrating the concomitant nature of the veins. O = umbilicus (Reproduced with permission from: Rozen WM, Pan WR, Le Roux CM, *et al.* The venous anatomy of the anterior abdominal wall: an anatomical and clinical study. *Plast Reconstr Surg* 2009;124:848-53)

circumflex iliac vein (SCIV) and/or the superficial external pudendal vein (SEPV). The SIEV distributed multiple deep branches throughout its course, which comprised the venae comitantes of DIEA perforators. These perforator veins were numerous, and primarily showed a periumbilical distribution. They perforated the anterior rectus sheath to drain into the venae comitantes of the DIEA.

The venae comitantes of the DIEA ran alongside the major branches of the DIEA within or deep to the rectus abdominis muscle. Communications between the two venae comitantes were evident throughout their course, and below the arcuate line, the DIEA and its venae comitantes turned laterally to encroach upon the femoral vein, and the venae comitantes united to form a single DIEV. The mean diameter of the DIEV at its termination was 3.2 mm (range, 2.3-3.9 mm). Of note, the mean distance between

the SIEV and the superficial inferior epigastric artery (SIEA) at the level of the inguinal ligament was 2.9 cm, while the mean distance between the DIEA and DIEV at this level and throughout their course was <0.5 cm.

During radiographic studies, both the SIEV and DIEV were incompletely filled with contrast upon direct injection at their terminations, suggesting the presence of valves orientated toward a caudal venous flow in both systems. In two of the eight cadaveric specimens, microsurgical dissection was undertaken to identify a periumbilical venous perforator, which was injected with contrast bidirectionally with a small calibre injecting needle. In these cases, contrast was seen both macroscopically and radiographically to flow into the deep system but not the superficial system, demonstrating the presence of valves in these perforators directing flow from superficial to deep.

In-vivo (clinical) anatomical studies

We undertook further anatomical studies in the clinical setting, with a cohort of 100 patients (200 hemi-abdominal walls) undergoing DIEP flaps for breast reconstruction included in the study. All imaging was performed between July 2006 and October 2008. Patients were recruited at a single institution, with institutional ethics approval, and no patients were excluded from the study. Patients were all female, were of a range of body habitus types, and were between 35-68 years of age. All imaging was performed at a single institution, using a 64 slice multi-detector row CT scanner (Siemens Medical Solutions, Erlangen, Germany), with 100 mL of intravenous contrast (Omnipaque 350; Amersham Health, Princeton, USA). CTA images were reformatted into maximum intensity projection (MIP) and 3-dimensional volume rendered technique (VRT) images using commercially available software (Siemens Syngo InSpace; Version: InSpace2004A_PRE_19, Pennsylvania, USA). Thin axial slices were used for all vessel measurements, with calibre measurements given as internal diameters. The location, size and course of the DIEV, SIEV and their communications were recorded.

We found that the superficial venous system and its communications with the deep venous system were readily demonstrated on CTA imaging (*Figure 2*), with characteristics of the venous system able to be recorded as with the cadaveric study. In all cases, the SIEV was found to consistently lie superficial to Scarpa's fascia (all cases), to have a single (82% of sides), bifurcating (17% of sides) or trifurcating (1%) trunk below the umbilicus, and to supply a large (>1 mm) medial branch that crossed the midline in 86% of cases. This medial branch routinely crossed below the level of the arcuate line. In some cases, there were additional midline cross-over points seen: immediately infraumbilically and immediately supraumbilically (*Figure 3*). The SIEV drained into either the superficial femoral vein (41% of sides), the long saphenous vein (9% of sides), the saphenous bulb (49% of sides) or the SEPV (1%). The mean diameter of the SIEV at its termination was 2.5 mm (range, 1.8-5.2 mm). It was seen to receive numerous tributaries, including the superficial circumflex iliac vein (SCIV) and/or the superficial external pudendal vein (SEPV).

While the SIEV was shown to distribute deep branches which perforated the anterior rectus sheath to drain into the venae comitantes of the DIEA, these were not visible in all cases or for all perforators. This communication between deep and superficial venous systems was thus often too

small to see with CTA. A communication between the SIEV and individual perforator veins was only identified in 90% of cases, and for only 1-3 perforators per patient amongst these patients (*Figure 4*).

Clinical outcome studies of venous drainage

In order to assess the role of dominance between the deep and superficial venous systems, as well as to assess the need for single versus double venous outflow routes in DIEP flaps, we undertook a retrospective study for patients having undergone DIEP flap breast reconstructions during the period of January 2000 to September 2008. This was a consecutive series, with all operations undertaken by a single reconstructive surgical unit, of four core surgeons. The only exclusion criterion was flaps that were supplied by more than one artery (stacked or bipediced flaps). All flaps were fasciocutaneous, included no rectus muscle, and were raised on a single DIEA. Recorded data comprised patient demographics, operation details, complications, implementation of secondary venous outflow routes and details of the vascular basis for flap supply and drainage. Patients were stratified into two groups according to the number of veins used for venous drainage (one versus two). The decision to use an alternative (secondary) source of venous drainage was made based upon individual surgeon preference, with factors influencing this decision including a good match of two donor and recipient veins, the presence of a subjectively enlarged (greater than 1.5 mm) SIEV, a subjectively engorged (tense and dilated) SIEV, or in the presence of frank venous congestion during flap harvest or flap inseting (where pedicle flow continuity was confirmed to be present). The donor vessel of choice was the SIEV, in order to achieve venous flow through both deep and superficial venous territories, with a second DIEV (DIEA concomitant vein) as an alternative option. The contralateral SIEV was the preferred choice of vessel (97% of cases), however where inappropriate (inadequate size or absent vessel, or in bilateral reconstructions), the ipsilateral SIEV was used (3% of cases). Where an SIEV was used, the cephalic vein was used as the recipient vessel of choice, harvested through a small incision in an anterior axillary skin crease with minimal operative time or scarring (*Figures 6, 7, 8*). The full description of the technique is in the sub-section below. The use of the cephalic vein as a recipient vessel as described, and the use of anastomotic devices that achieve fast anastomotic times (either 'Anastoclip' Vascular Closure Staples (VCS) micro-

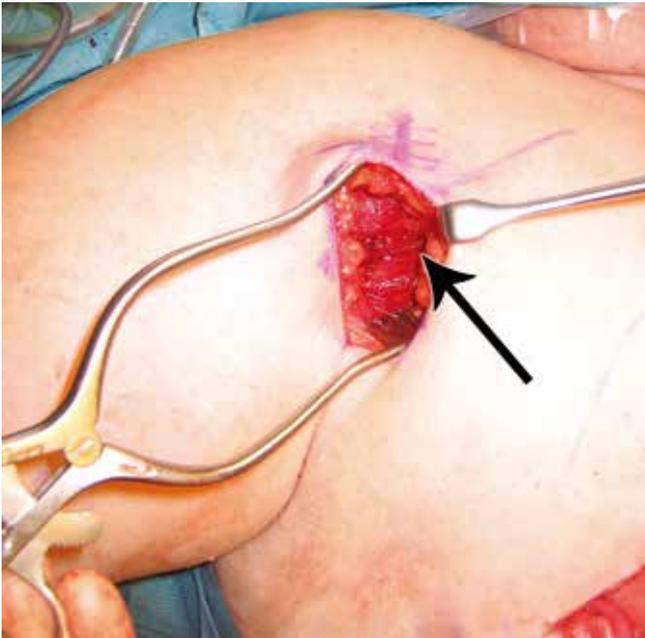


Figure 6 Intraoperative photograph during cephalic vein harvest, highlighting an anterior axillary skin crease incision, exposing the cephalic vein (black arrow) (Reproduced with permission from: Audolfsson T, Rozen WM, Wagstaff MJ, *et al.* A reliable and aesthetic technique for cephalic vein harvest in DIEP flap surgery. *J Reconstr Microsurg* 2009;25:319-21)

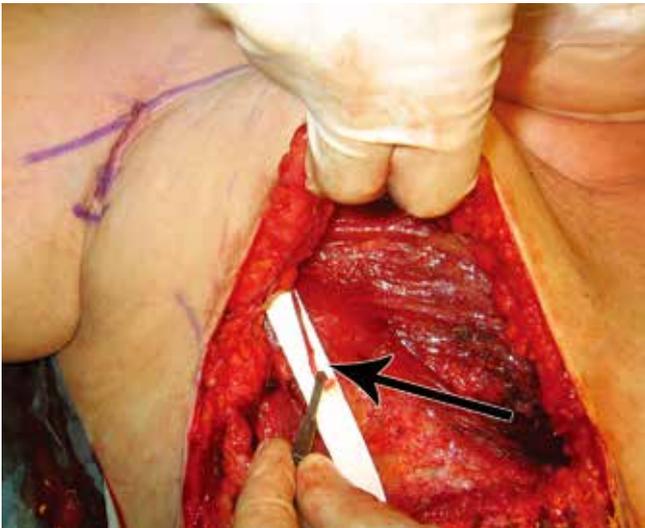


Figure 7 Cephalic vein (black arrow) transposed into the chest wall with good length (Reproduced with permission from: Audolfsson T, Rozen WM, Wagstaff MJ, *et al.* A reliable and aesthetic technique for cephalic vein harvest in DIEP flap surgery. *J Reconstr Microsurg* 2009;25:319-21)



Figure 8 Cephalic vein harvest site closed, with the wound concealed in an anterior axillary line skin crease and wound less than 4 cm long (Reproduced with permission from: Audolfsson T, Rozen WM, Wagstaff MJ, *et al.* A reliable and aesthetic technique for cephalic vein harvest in DIEP flap surgery. *J Reconstr Microsurg* 2009;25:319-21)

staple clips or a microvascular anastomotic coupling device, allowed us to perform a second venous anastomosis with no increase in operative time. Our use of these anastomotic procedures has been described previously (24), and it should be noted that these occurred more frequently in the latter part of the series, and thus a learning curve is certainly an important consideration in evaluating surgical times.

Venous anastomoses were performed with anastomotic devices that achieve fast anastomotic times: either ‘Anastoclip’ Vascular Closure Staples (VCS) micro-staple clips (AnastoClip Vessel Closure System, Le Maitre Vascular Inc, Sulzbach, Germany) or a microvascular anastomotic coupling device (Microvascular Anastomotic Coupling System, Synovis Micro Companies Alliance Inc, St Paul, Minnesota, USA), advanced anastomotic devices have been developed to aid arterial and venous anastomosis, with the use of staples and the ‘anastomotic ring coupler’ being the more widely discussed modern techniques. A recent article by Camara *et al.* described the use of anastomotic couplers for use in free deep inferior epigastric artery perforator (DIEP) flap surgery (25), which demonstrated the utility of the anastomotic coupler in 12 free flaps, and we have now utilized these devices in over 1,000 free flaps. Our experience is described in a subsequent subsection below.

In this series, a total of 564 DIEP flap breast reconstructions were performed in 501 patients, with 438 unilateral and 63 bilateral reconstructions. Of these, 273 breast reconstructions were performed in which only a single venous outflow route was implemented, and 291 cases had two veins used primarily for venous outflow. The DIEV was the primary source of venous drainage in all cases, and for secondary venous drainage, the SIEV was used most commonly (92.1%), followed by a second DIEV (7.9%). In the vast majority of cases where an SIEV was used, the cephalic vein was harvested as the recipient vein for these anastomoses (82.8% overall). There were no differences in outcomes when each of these venous outflow routes were compared for venous congestion (0 cases in either group). Of note, the use of a secondary vein did not result in any increase in operative time (385 *vs.* 383 minutes, $P=0.57$).

Of the 273 flaps in which a single vein was used, 7 flaps demonstrated venous congestion on clinical examination postoperatively. Of the other 291 flaps, which received an additional vein during initial breast reconstruction, no flaps demonstrated any signs of venous congestion. This decrease in the rate of venous congestion with the use of 2 veins was statistically significant, $P=0.006$. Of the 7 congested flaps, 5 were due to venous thrombosis and 2 were due to relative venous congestion with no pedicle compromise. All cases of venous congestion were taken back to theatre for re-exploration, and all cases of pedicle compromise were taken back to theatre for re-exploration, with the ultimate cause for compromise identified in theatre. Other complications were statistically similar between the groups, including complete flap failures (due to either arterial or venous thrombosis), partial flap losses, arterial or venous complications and overall take-backs.

Notably, while there were 5 cases of venous thrombosis in each group, all cases in which venous thrombosis did occur in the one vein group resulted in global venous congestion identified on examination (5/5=100%), however in the two vein group, venous thrombosis in a single vein (identified with the implantable Doppler probe) did not result in any clinical suggestion of venous congestion in any cases (0/5=0). There were no cases in which venous thrombosis occurred in both veins in the two vein group. In the two vein group, venous thrombosis was identified with the implantable Doppler probe and findings at theatre, rather than the clinical manifestations of venous failure. Of the cases of venous thrombosis, one case of venous thrombosis resulted in complete flap failure in the one vein group (1/5=20%), while no cases resulted in complete flap

failure in the two vein group (0/5=0%). All other cases of complete failure flap were due to arterial thrombosis. This study demonstrated that by prospectively embarking on a second venous anastomosis, the venous drainage of a free flap can be significantly improved, reducing the incidence of venous congestion. The study also demonstrated that this can be readily achieved, without any demonstrable increase in operative times if planned effectively. In our series of over 500 DIEP flaps, we reduced our venous congestion rate to zero if a secondary vein was performed.

Use of the cephalic vein for secondary venous drainage

Given the clinically significant benefit in using a secondary route for venous drainage in the DIEP flap, the cephalic vein lends itself to a readily accessible option with minimal donor site morbidity (24). In preparing the patient, the arm is placed on an arm-board that enables abduction and draped appropriately. The delto-pectoral groove is marked and this line is extended out onto the arm as the cranial-most limit of the incision. An anterior axillary skin crease is identified where it meets the delto-pectoral groove (at the drawn line), and a line is drawn caudally along this crease for two to four centimeters to mark the line of incision. The subcutis is incised until the muscular fascia is reached. The dissection is continued in the cranial part of the wound until the fat pad between the deltoid and pectoralis major is identified. The fascia covering the fat is opened and the cephalic vein should be easily exposed (*Figure 6*).

Blunt dissection is then performed with a finger to expose the path of the vein, following the cephalic vein laterally along the arm. The vein is then harvested medially, ligating and dividing small branches, usually followed until it dives towards the subclavian vein. The dissection is then continued laterally, isolating the vein as far as can be reached with long scissors and long DeBakey forceps. If a longer vein is needed, this can easily be achieved by following the vein through small incisions distally on the arm. A headlamp or a lighted retractor can be used to aid vision. The vein is then clamped with vascular clips and divided. A subcutaneous tunnel from the flap recipient site (chest wall) to the delto-pectoral groove is created, and the vein delivered through it (*Figure 7*). We have observed a good size match between the SIEV and cephalic vein in all of our cases, and have had no harvest-site morbidity, with a scar less than 4cm long in all cases (*Figure 8*).

With the ease and speed of performing cephalic vein harvest as described, we perform a secondary venous

anastomosis *prospectively*, before venous complications arise, and have had no venous compromise in any of our flaps using this technique. Our choice is based on the assessment of the dominance of the SIEV for venous drainage: if the diameter is large on preoperative imaging or intraoperatively, or if there is a distended or high pressure SIEV upon venous pressure measurements after cannulation, we will prospectively perform a second anastomosis.

Venous anastomoses

Advanced anastomotic devices have been developed to aid venous anastomosis, given the importance of venous drainage to flap survival. While suturing has been the traditional mainstay, staples and the 'anastomotic ring coupler' have been the more widely discussed modern techniques. Our cohort study comprised 1,000 consecutive patients undergoing a range of reconstructive procedures, recruited through a single institution (26). This comprised breast reconstructive cases (600 cases), extremity reconstruction (150 cases) and head and neck cases (250 cases). Three modes of vascular anastomosis were performed: standard sutures, the 'Anastoclip' Vascular Closure Staples (VCS) micro-staple clips (AnastoClip Vessel Closure System, Le Maitre Vascular Inc, Sulzbach, Germany) and a microvascular anastomotic coupling device (Microvascular Anastomotic Coupling System, Synovis Micro Companies Alliance Inc, St Paul, MN, USA). Our preliminary use of these anastomotic procedures has been described (27).

The devices were applied intraoperatively by the primary surgeon in each case, with decision to use the particular device at the discretion of the surgeon. There were no particular intraoperative criteria for selection of a particular anastomotic technique. For the ring coupler, vessel wall eversion was achieved with the device itself, while for stapled anastomoses eversion was achieved with a combination of stay sutures and everting forceps in order to achieve ideal intima-to-intima apposition. Two main outcome parameters were assessed: anastomotic time and anastomotic failure. Anastomotic times were recorded by the scout nurse in each case, and anastomotic failure was confirmed in theatre at revision surgery. Data were analysed statistically with the Fisher exact test, with a P-value of less than 0.05 considered as having statistical significance. In 1,000 reconstructive cases, 2,500 vascular anastomoses were performed, of which 1,400 comprised the use of either of

the two adjunctive anastomotic devices. These devices were thus used in 80% of all venous anastomoses and 10% of all arterial anastomoses, with the anastomotic ring coupler used in 1,000 cases and staples in 400 cases. In cases of sutured anastomoses, mean anastomotic time was 22 minutes, compared to 15 minutes with staples and 4 minutes for the ring coupler, a significant reduction in anastomotic times with the use of these devices ($P < 0.01$). In terms of anastomotic failures, there were 90 failures overall, of which 12 were arterial failures and 78 were venous failures. Of these, all arterial failures were sutured (no stapled or coupled arterial anastomoses failed), and of the venous failures, 29 were sutured, 20 were stapled and 29 were coupled ($P > 0.05$). In 1,000 free flaps in which we used the anastomotic coupler, the mean reduction in time with the use of a ring coupled anastomosis was 15 minutes as compared to sutured anastomosis ($P < 0.001$). The surgical anastomosis itself is just one of several aspects of microvascular surgery that have reaped the reward of technological advances in the field: The ability to preoperatively select the optimal vessels of choice for inclusion in the vascular pedicle has been shown to improve a range of operative outcomes, with techniques that have now been established comprising color duplex ultrasound (28), computed tomographic angiography (29), and magnetic resonance angiography (30); developing and future techniques include the use of 'virtual' image-guided stereotactic navigation pre- and intra-operatively (31); intraoperative mapping of vasculature have been shown to accurately map the vascular territories of selected vessels, enabling improved flap design and harvest (32); and vascular monitoring postoperatively has also been revolutionized with the use of pedicle monitoring techniques such as the implantable Doppler probe (see subsection below), which has been shown to rapidly identify vascular complications (such as thrombosis, compression or kinking) and potentiate rapid return to theatre and flap salvage (33).

Postoperative venous monitoring

The Cook-Swartz implantable Doppler probe has become increasingly recognized as a useful tool for the postoperative monitoring of free flaps (33-39). With the potential for either flap salvage or flap loss, prompt and effective postoperative evaluation of flap viability is essential, and may potentiate early intervention. While the no-reflow phenomenon will still mean that flaps are lost regardless of the experience of the microsurgeon, optimal methods for post-operative monitoring of free flaps have become increasingly sought.



Figure 9 Immediate postoperative photograph of a deep inferior epigastric artery perforator (DIEP) flap, being monitored with clinical monitoring alone (Reproduced with permission from: Whitaker IS, Rozen WM, Chubb D, *et al.* Postoperative monitoring of free flaps in autologous breast reconstruction: a multicenter comparison of 398 flaps using clinical monitoring, microdialysis, and the implantable Doppler probe. *J Reconstr Microsurg* 2010;26:409-16)



Figure 11 Photograph of a deep inferior epigastric artery perforator (DIEP) flap being monitored with microdialysis. The photograph is taken at the end of a re-exploration performed on the 3rd postoperative day based on microdialysis values (Reproduced with permission from: Whitaker IS, Rozen WM, Chubb D, *et al.* Postoperative monitoring of free flaps in autologous breast reconstruction: a multicenter comparison of 398 flaps using clinical monitoring, microdialysis, and the implantable Doppler probe. *J Reconstr Microsurg* 2010;26:409-16)



Figure 10 Immediate postoperative photograph of a deep inferior epigastric artery perforator (DIEP) flap, being monitored with the Cook-Swartz implantable Doppler probe (Reproduced with permission from: Whitaker IS, Rozen WM, Chubb D, *et al.* Postoperative monitoring of free flaps in autologous breast reconstruction: a multicenter comparison of 398 flaps using clinical monitoring, microdialysis, and the implantable Doppler probe. *J Reconstr Microsurg* 2010;26:409-16)

A broad range of different technologies have been discussed for post-operative monitoring, however there is little evidence for any single technique. This is reflected in the wide variety of techniques currently used in this role: clinical monitoring alone, pulse oximetry, near infra-red spectroscopy (NIRS), perfusion photoplethysmography, surface temperature measurement, fluorometry, microdialysis, ultrasound, the hand-held Doppler probe, implanted (Cook-Swartz) Doppler probes, laser Doppler flowmetry, impedance plethysmography, confocal microscopy, nuclear medicine, subcutaneous pH measurement, hydrogen clearance, externalisation of part of a buried flap and white light spectrometry.

We have used three established monitoring techniques in a recent and comparable cohort of patients. Three different techniques were utilised as the primary mode for postoperative monitoring: the implantable Cook-Swartz Doppler probe, microdialysis and clinical monitoring alone, all techniques which have been previously shown to accurately predict the onset and existence of flap compromise (*Figures 9,10,11*). Clinical monitoring alone, the implantable Doppler probe and microdialysis all showed statistically similar rates of flap salvage, however there was a statistically significant increase in false positive alarms

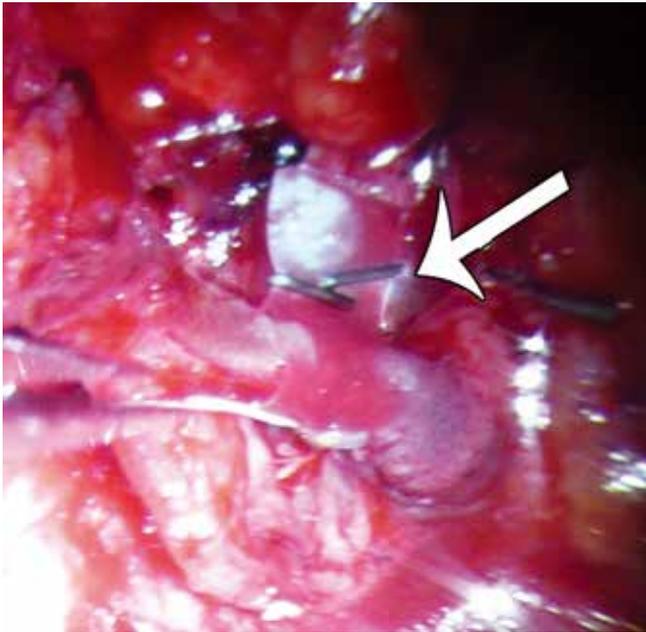


Figure 12 Implantable Doppler probe silicon cuff secured to the venous pedicle with the use of micro-clips (Reproduced with permission from: Rozen WM, Ang GG, McDonald AH, *et al.* Sutured attachment of the implantable Doppler probe cuff for large or complex pedicles in free tissue transfer. *J Reconstr Microsurg* 2011;27:99-102)

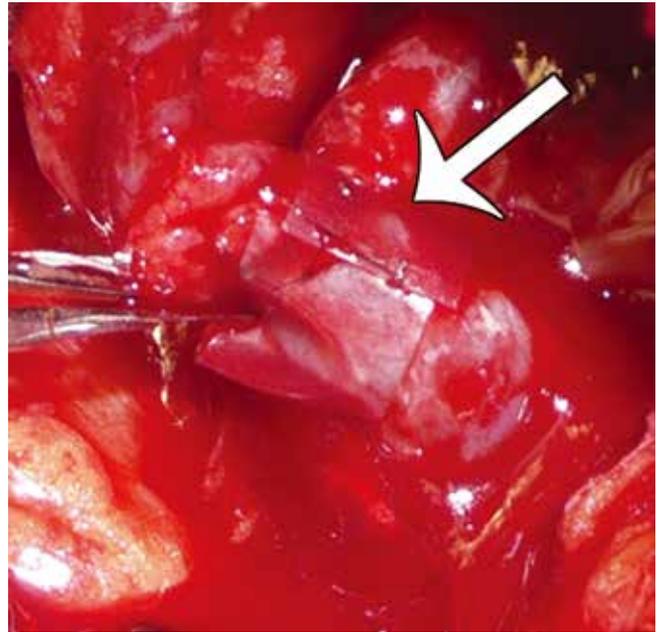


Figure 13 Implantable Doppler probe silicon cuff secured to a large venous pedicle with the use of suturing (Reproduced with permission from: Rozen WM, Ang GG, McDonald AH, *et al.* Sutured attachment of the implantable Doppler probe cuff for large or complex pedicles in free tissue transfer. *J Reconstr Microsurg* 2011;27:99-102)

causing needless take-backs to theatre in the microdialysis and implantable Doppler arms, finding no technique superior to clinical monitoring alone.

In using the implantable Doppler probe, our preference of the adjunct techniques available, the probe cuff is placed around the venous pedicle following successful venous anastomosis, and monitoring of the venous pedicle proceeds during flap inseting and throughout the early postoperative period (40). The Cook-Swartz implantable Doppler probe is either left unattached around the venous pedicle or is secured. In our combined experience with over 300 such applications of the Cook-Swartz implantable probe (Cook Medical®, Cook Ireland Ltd, Limerick, Ireland), we typically secure the silicone cuff with two small micro-clips as described previously (38). An alternative technique for attachment is to glue the cuff with the use of fibrin glue (41). These techniques require redundant silicone cuff for apposition, however we have encountered some vessels that are of sufficiently large diameter as to not provide enough cuff to employ these methods. The Cook-Swartz venous Doppler probe is adherent to a silicone cuff that is wrapped around the

selected vessel. As per the manufacturer and literature, the probe is always used on the venous pedicle (as arterial compromise causes venous changes within minutes). The tension of the silicone cuff is highly important, as placement of a tight cuff may obstruct venous outflow, while placement of a loose cuff may result in loss of the Doppler signal or cause migration of the cuff. Metallic micro-clips are easily applicable for cuff attachment, achieved by opposing the redundant ends of the cuff before careful placement of the clips (*Figure 12*). In some cases vessel diameter or anatomy is such that after placement of the silicone cuff, there is no redundancy to the cuff ends and clips and/or glue are not able to be used. Placement without cuff attachment would increase the chance of false positive results, and thus we use two techniques in this setting to aid attachment. The first is to apply two interrupted sutures through the cuff ends to mimic the technique of micro-clips (*Figure 13*). The sutures can be tightened to the desired tension, and can be used in cases where the cuff ends are not in direct apposition. A second technique is to excise a segment of silicone cuff and either clip or suture the excised segment to the cuff ends,

effectively elongating the cuff diameter.

In our experience (over 300 cases) of using all four techniques (non-attachment, micro-clip fixation, suture fixation, silicone cuff elongation), no complications have been encountered as a consequence of the use of the implantable Doppler probe or as a consequence of the technique selected. In the first 300 of our cases, the breakdown of fixation techniques were as follows: 270 cases using micro-clips, 20 cases using suturing, 8 cases without fixation (early in our experience) and 2 cases using silicone cuff elongation. Of note, the technique of non-attachment was associated with an increased rate of false positive results, as migration away from the vessel being monitored was postulated to have occurred. The other three methods were not associated with any unique problems. In terms of outcome measures from the use of the implantable Doppler probe, there has been shown to be a strong trend toward improved salvage rates with the implantable Doppler probe compared with clinical monitoring (80% *vs.* 66%), and a meta-analysis has shown this to be statistically significant ($P < 0.01$) (34). There was no statistical difference in false-positive rates in these series. In addition to the absence of complications in the application of the silicone cuff, we have similarly not encountered any complications as a result of probe removal. The probes are removed at the end of the monitoring period (typically at the end of the first postoperative week) by simply applying a minimal amount of traction on the wire where it exits the wound. This force detaches the wire from the silicone cuff, leaving the cuff in-situ. According to the manufacturers specifications, a force of only 50 grams is required to achieve detachment, and in cases where there is any resistance to traction, we cut the wire at the level of the skin and leave the internal length of wire in-situ. In all cases thus far, we have not encountered any complications during probe removal.

Through direct monitoring of the vascular pedicle, the implantable Doppler probe is an immediate reflection of impaired flow (42,43). The signal itself can be highly variable and can be associated with a substantial learning curve for interpretation. This is largely due to *in-vivo* changes in venous flow and offer a fascinating insight into venous anatomy and physiology. Despite an increased reporting of the use of this technique for monitoring flaps, there has not been a discussion of the bedside techniques available to aid interpretation of the audible Doppler signal (44).

It is important for medical and nursing staff to

recognize that despite the probe always being applied to the venous pedicle, there are two main Doppler waveforms that are possible: venous and arterial. Venous flow is typically low-pitch and constant, resembling a humming sound or the sound of the ocean (Supplementary *Video 1, 2*). The arterial waveform can often predominate when the arterial pedicle is in close proximity to the vein, and is both louder than its venous counterpart and is pulsatile. Often a combination of each of these waveforms is heard, and in many cases there can be interchange between the predominant waveform during the postoperative period. The implantable Doppler signal can vary substantially in volume, pitch and quality throughout the postoperative period in any one patient. Significant changes often warrant re-exploration, but in equivocal cases, we have found several bedside tests can help to reassure the presence of pedicle flow. Such bedside tests can aid in both identification of the presence of an otherwise equivocal Doppler signal, and confirm appropriate flap flow after a Doppler signal change.

Respiratory variation

Respiratory variation in Doppler flow is particularly useful for flaps based on recipient vessels in the thorax, such as those for breast reconstruction. Respiratory action causes changes in intra-thoracic pressure which cause resultant increases and decreases in pedicle flow. These flow changes result in audible changes in volume and pitch, and confirm pedicle patency (Supplementary *Video 1*).

Flap compression

Manual compression of a flap (whether a cutaneous or muscle flap) causes an artificial increase in venous outflow by emptying intra-flap veins, resulting in an audible increase in the volume and pitch of the Doppler signal (Supplementary *Video 2*). This too confirms pedicle patency.

Elevation/dependency

Changes in Doppler signal occur with relative changes in the dependency of the recipient site, and this is particularly useful for lower limb recipient sites. By lowering and raising a limb, there are gravitational changes in venous outflow from a flap, with the resultant changes in Doppler signal confirming pedicle patency.

With a range of bedside clinical manoeuvres, reliability in interpreting the implantable Doppler signal can be improved, with the potential for a decrease in needless take-backs to theatre or missed pedicle compromise.



Video 1 Respiratory variation. Demonstration of the postoperative monitoring of a free deep inferior epigastric artery perforator (DIEP) flap for breast reconstruction using the Cook-Swartz implantable Doppler probe. The venous flow signal and changes with respiratory variation are demonstrated (Reproduced with permission from: Rozen WM, Ang GG, Acosta R, *et al.* Bedside manoeuvres and waveform changes in the interpretation of the implantable Doppler probe signal for free-flap monitoring. *Microsurgery* 2010;30:670-1)



Video 2 Flap compression. Demonstration of the postoperative monitoring of a free deep inferior epigastric artery perforator (DIEP) flap for breast reconstruction using the Cook-Swartz implantable Doppler probe. The venous flow signal and changes with flap compression are demonstrated (Reproduced with permission from: Rozen WM, Ang GG, Acosta R, *et al.* Bedside manoeuvres and waveform changes in the interpretation of the implantable Doppler probe signal for free-flap monitoring. *Microsurgery* 2010;30:670-1)

Venous anomalies and clinical cases

Dual SIEV trunks

While the SIEV is classically considered to drain via a single trunk, two SIEVs draining into separate venous trunks was identified (45). While venous anatomy is known to be variable, this variant of normal anatomy had not been described previously, with clinical implications clearly warranting a review. Preoperative computed tomographic angiogram (CTA) to assess the vasculature of the anterior abdominal wall for flap planning was undertaken, and as shown in *Figure 14*, there was found to be a paucity of DIEA perforators, and rather dominant SIEAs bilaterally were identified. Large SIEVs were also seen adjacent to the SIEAs, which were considered suitable for donor venous drainage. The differentiation between the superficial arterial and venous systems was based upon careful three-dimensional, multi-planar analysis of the CTA, rather than a single image (as seen in *Figure 14*), tracing the vessels to their origins and destinations. As was our routine practise (and as described in the broader literature to date), the scan was carefully analysed in terms of arterial vasculature, while the venous anatomy was analysed only in terms of

its presence and location. The branching pattern of the SIEV was not primarily considered in the process of flap planning. As such, the patient underwent an abdominal wall flap based on the right SIEA. The right hemiabdominal flap (to the midline) was raised on the right SIEA and SIEV. The SIEA (2.2 mm at its origin) and SIEV (2.5 mm) were anastomosed to the internal mammary artery and vein, with relatively good size match (2.9 and 3.0 mm respectively). The anastomoses were both sutured with interrupted nylon sutures, and there was good pedicle flow upon removal of the clamps.

While perfusion was good throughout the length of the operation, relative venous congestion to half the flap was noted progressively throughout the early postoperative period. Of particular note was the clear demarcation of the congestion to half the flap only (*Figure 15*). The lack of global venous congestion highlighted that this was not a pedicle problem, but rather a territorial issue related to relative venous congestion. Rather than warranting immediate exploration, this suggested an expectant approach. While consideration of re-exploration was certainly given, we reviewed the patient's preoperative

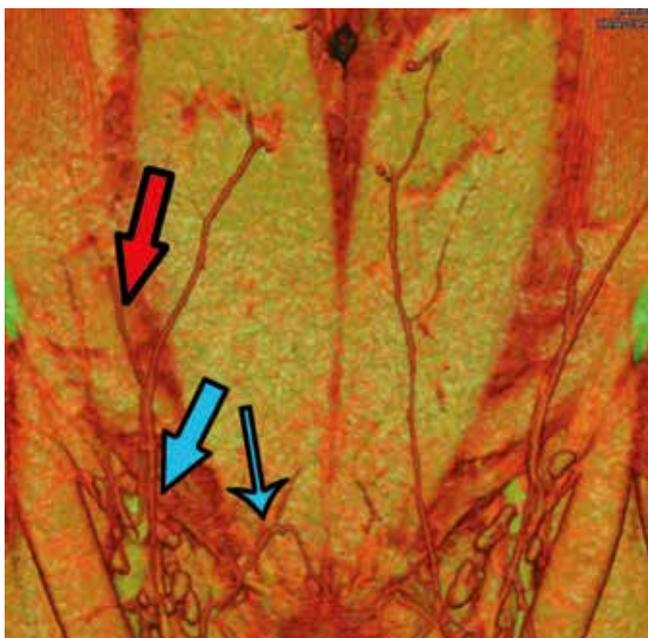


Figure 14 Computed tomographic angiogram of the anterior abdominal wall, with a dominant superficial inferior epigastric artery (SIEA; red arrow) highlighted, and the presence of both a medial superficial inferior epigastric vein (SIEV; thin blue arrow) and a lateral SIEV (thick blue arrow). The differentiation between the superficial arterial and venous systems was based upon careful three-dimensional, multi-planar analysis of the CTA, rather than a single image, tracing the vessels to their origins and destinations. This anatomical variant in which there are two separate SIEVs is present in 40% of hemiabdominal walls (Reproduced with permission from: Rozen WM, Chubb D, Whitaker IS, *et al.* The importance of the superficial venous anatomy of the abdominal wall in planning a superficial inferior epigastric artery (SIEA) flap: case report and clinical study. *Microsurgery* 2011; 31:454-7)

CTA in order to explore any potential reasons for the area of venous compromise. Retrospective review of her CTA highlighted an interesting feature of her SIEV - there were two separate SIEV trunks on the right side, with only one (the lateral trunk) used to drain the flap (*Figure 14*). While clear that an additional venous anastomosis of the medial trunk is what would have been required in this case, this trunk was not prophylactically dissected for any substantial length, and thus was not a clinical option. This understanding of the cause of the congestion contributed to the decision for expectant management. Over the course of the postoperative period, the congestion gradually improved



Figure 15 Postoperative photograph following left breast reconstruction with a superficial inferior epigastric artery (SIEA) flap and the lateral superficial inferior epigastric vein (SIEV) shown in *Figure 6*. The medial half of the reconstructed breast (that drained by the medial SIEV) showed venous congestion postoperatively (blue arrow), while the lateral half of the flap did not (white arrow) (Reproduced with permission from: Rozen WM, Chubb D, Whitaker IS, *et al.* The importance of the superficial venous anatomy of the abdominal wall in planning a superficial inferior epigastric artery (SIEA) flap: case report and clinical study. *Microsurgery* 2011;31:454-7)

and ultimately a small area of fat necrosis was treated conservatively, with no reoperation performed.

The 'Perforating' SIEV

With the use of preoperative CTA, a unique anomaly has been identified in which there is no superficial inferior epigastric vein (SIEV) entering the abdominal wall integument below the inguinal ligament, and instead arises from the DIEA itself and perforates the rectus abdominis muscle as a musculocutaneous perforator at a more proximal origin (46). This anomalous 'perforating' SIEV is a new anatomical variant detected with preoperative CTA. With an increasing detection of anatomical variation, the benefits of preoperative imaging before abdominal wall free flaps are further highlighted. A clinical study of 145 patients undergoing preoperative CTA for consecutive DIEA perforator flaps for breast reconstruction was undertaken. Scans were reviewed for the incidence of the 'perforating' SIEV, with anatomical features recorded. In five cases (3.4% of overall cases), the perforating SIEV variant was identified. In all cases there was no caudal SIEV originating from an inguinal vein (superficial femoral vein, saphenous bulb or long saphenous vein). Instead, a large SIEV originated

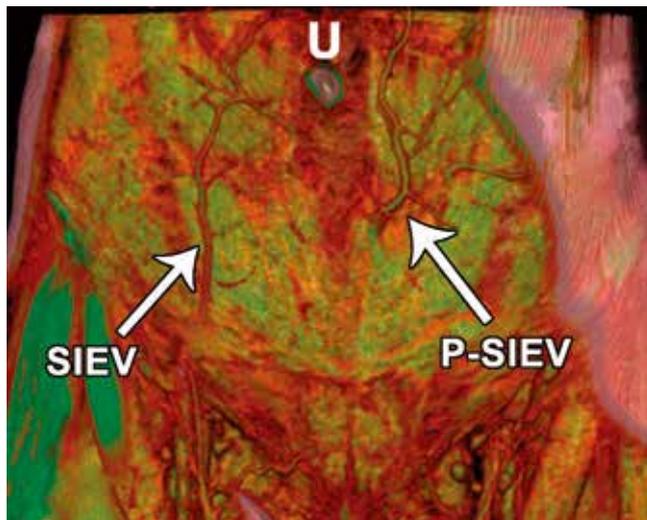


Figure 16 Computed tomography angiogram (CTA) volume-rendered technique reconstruction of the anterior abdominal wall vasculature (anterior view), demonstrating a normal superficial inferior epigastric vein (SIEV) on the right and an anomalous 'perforating' SIEV (P-SIEV) on the left. U=Umbilicus (Reproduced with permission from: Rozen WM, Grinsell D, Ashton MW. The perforating superficial inferior epigastric vein: a new anatomical variant detected with computed tomographic angiography. *Plast Reconstr Surg* 2010;125:119e-20e)

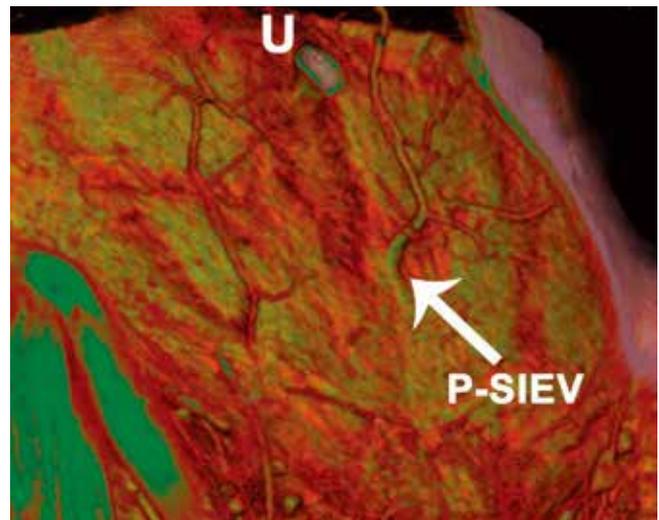


Figure 17 Computed tomography angiogram (CTA) volume-rendered technique reconstruction of the anterior abdominal wall vasculature (oblique view), demonstrating the anomalous 'perforating' superficial inferior epigastric vein (P-SIEV) on the left. U=Umbilicus (Reproduced with permission from: Rozen WM, Grinsell D, Ashton MW. The perforating superficial inferior epigastric vein: a new anatomical variant detected with computed tomographic angiography. *Plast Reconstr Surg* 2010;125:119e-20e)

from the DIEA and traversed the rectus abdominis muscle as a very large (>3 mm) musculocutaneous perforator. In all 5 cases, this originated from the medial branch of the DIEA as a medial row perforator, and perforated the rectus sheath approximately midway between the umbilicus and the arcuate line. In all cases, this perforator (combined artery and vein) was the largest perforator for the entire abdominal wall. Upon emerging from the anterior rectus sheath, the SIEV traversed the cutaneous tissues cranially (*Figures 16,17*).

Macrovascular arterio-venous shunts

We have been able to identify large shunts between arterial perforators and the superficial venous system (47). While we have until now highlighted the venous 'half' of the abdominal wall circulation, in which circulation from the heart, through arteries and arterioles to capillaries, and returning through venules and veins is well established. Alternative bypass networks are known to occur however, with 'arteriovenous anastomoses' (AVAs) well described anatomical structures which appear to be common throughout the circulatory system (48) with a few known exceptions. They are most easily defined as normally

occurring, pre-capillary communications between the arterial and venous sides of the circulation, with most studies on this topic demonstrating their pre-capillary positioning. The term 'shunt' has been used interchangeably with AVA, as the function of these structures is to allow a bypass circuit around capillary beds. All of the literature on these structures have described AVAs of a usual calibre of 0.05-0.15 mm in diameter (48) with the largest described AVA being 0.5 mm (49), and all intimately associated with capillary beds.

While all previous studies on the topic have utilized techniques such as histology, and pharmacological and/or physiological manipulation, the use of advanced imaging technologies such as computed tomographic angiography (CTA) has provided a new modality for investigating increasingly small calibre vessels. We have been able to identify radiological evidence of such as vessel: the macrovascular arteriovenous shunt (MAS). As shown in *Figure 18*, a 1mm communication is clearly identifiable between a DIEA perforator and the SIEV, with a schematic of this anatomy shown in *Figure 19*. We have further evaluated the anatomical features of these shunts clinically



Figure 18 Axial slice of an arterial phase computed tomographic angiogram (CTA), demonstrating the presence of a 1 mm macrovascular arteriovenous shunt (MAS) between a large deep inferior epigastric artery perforator (DIEAP) and the superficial inferior epigastric vein (SIEV) (Reproduced with permission from: Rozen WM, Chubb D, Ashton MW, *et al.* Macrovascular arteriovenous shunts (MAS): a newly identified structure in the abdominal wall with implications for thermoregulation and free tissue transfer. *J Plast Reconstr Aesthet Surg* 2010;63:1294-9)

and histologically (50). In *Figure 20*, the structure is seen *in-vivo* at high-power magnification, demonstrating the MAS communication between a DIEA perforator (DIEA-P) and the SIEV (*Figure 20*). Upon excision of this structure, the anatomy has been displayed *ex-vivo* (*Figure 21*). *Figure 22* demonstrates the histology of the MAS, with ‘arterial’ features on the arterial side of the shunt and ‘venous’ features on the venous side (*Figure 22*).

These MAS provide vascular shunting prior to capillary filling and have potentially profound clinical implications and therapeutic possibilities in a range of medical and surgical conditions. An understanding of the autonomic supply to these shunts and potential role for pharmaceutical manipulation in free flap surgery offer an important field of future research.

Discussion

The implications of inadequate venous drainage of DIEA perforator flaps are great, with the potential for partial or complete flap loss (1). However, the cause for venous compromise in individual cases is difficult to either predict

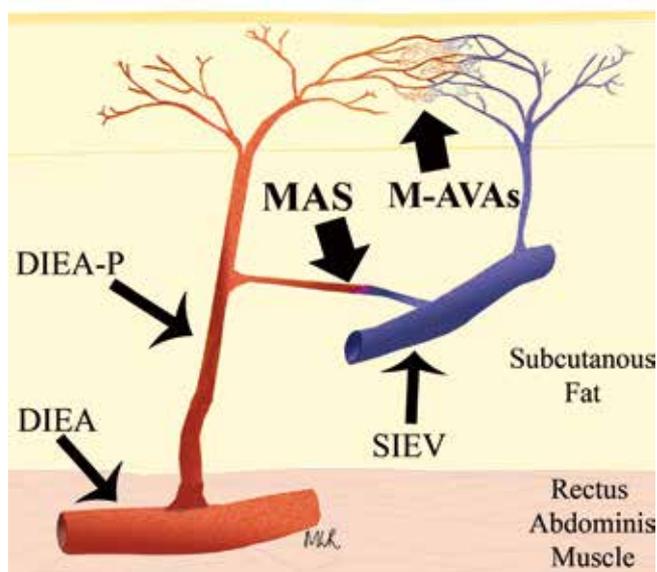


Figure 19 Schematic diagram of the macrovascular arteriovenous shunt (MAS) between a deep inferior epigastric artery (DIEA) perforator (DIEA-P) and the superficial inferior epigastric vein (SIEV). This shunt occurs within the deeper subcutaneous fat, unlike small-vessel microvascular arteriovenous anastomoses (M-AVAs), which occur more superficially at a precapillary level (Reproduced with permission from: Rozen WM, Chubb D, Ashton MW, *et al.* Macrovascular arteriovenous shunts (MAS): a newly identified structure in the abdominal wall with implications for thermoregulation and free tissue transfer. *J Plast Reconstr Aesthet Surg* 2010;63:1294-9)

preoperatively or select intraoperatively. By identifying the features of draining veins that optimize venous drainage, selection of those perforating veins with optimal anatomy or selection of using the superficial venous system can be made preoperatively for inclusion in the flap.

Previous anatomical studies have indeed sought to achieve this, using cadaveric or excisional specimen models to assess the direction of venous flow past valves (10,17-20). A limitation of these techniques includes the *ex-vivo* changes in vascular anatomy that may influence findings. In addition, early studies focused their observations on the implications for pedicled abdominal wall flaps, such as pedicled transverse rectus abdominis myocutaneous (TRAM) flaps, with limited application to the DIEP flap, in which only 1-3 perforators are included in the venous drainage of the flap. Despite these limitations, these studies were able to demonstrate that the direction of venous flow

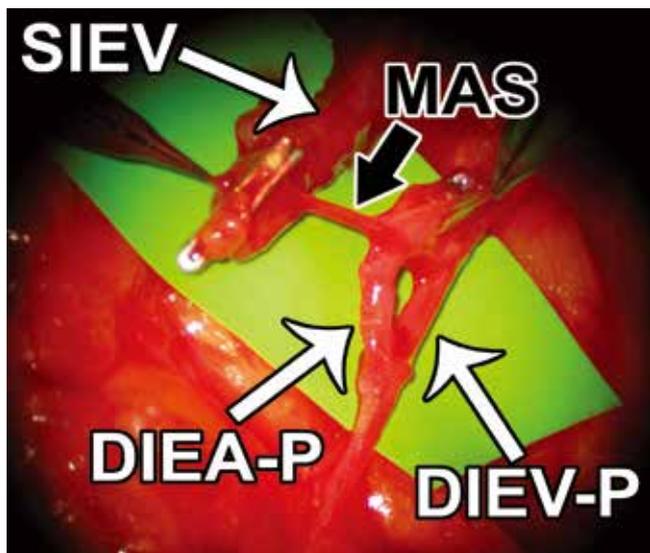


Figure 20 A macrovascular arteriovenous shunt (MAS) is shown in-vivo through a high-power (10-times magnification) microscope, demonstrating the MAS communication between a DIEA perforator (DIEA-P) and the SIEV, and an adjacent deep inferior epigastric vein perforator (DIEV-P) is also seen (Reproduced with permission from: Rozen WM, Chubb D, Ashton MW, *et al.* Images in plastic surgery: the anatomy of macrovascular arteriovenous shunts and implications for abdominal wall free flaps. *Ann Plast Surg* 2011;67:99-100)



Figure 21 The macrovascular arteriovenous shunt (MAS) is shown *ex-vivo*, after excision of the structure. Again, the MAS communication between a DIEA perforator (DIEA-P) and the SIEV is demonstrated, with an adjacent deep inferior epigastric vein perforator (DIEV-P) (Reproduced with permission from: Rozen WM, Chubb D, Ashton MW, *et al.* Images in plastic surgery: the anatomy of macrovascular arteriovenous shunts and implications for abdominal wall free flaps. *Ann Plast Surg* 2011;67:99-100)

is preferentially from the superficial venous system to the deep venous system, through a series of perforating veins. This direction of flow, and the dominance of the superficial venous system in the drainage of the abdominal wall, is a finding confirmed in the current study.

As a DIEP flap is not drained by the dominant drainage system, and relies upon 1-3 perforating veins to drain an entire flap, factors relating to the venous anatomy have been postulated in the pathogenesis of venous problems in the raising of a DIEP flap. In these previous studies, the size of venous perforators has been highlighted as a significant contributing factor. Cases have been identified where there have been no suitable perforating veins in an entire hemiabdominal wall, with the proposition that venous compromise is “probably due to the sacrifice of a critical number of venous perforators” (17). This hypothesis, that the calibre of perforating veins is the limiting factor to venous drainage, has been shown experimentally to be true (51,52), and has been echoed more recently in a clinical study of the DIEA perforator flap (11).

In addition to the size of perforators, an additional factor implicated in the causality of venous compromise has been the degree of midline crossover by the SIEV (10,21). While a single perforator may be of sufficient calibre to drain the flap, its communication with veins of each side of the abdominal wall is also essential. Blondeel *et al.* found a lack of midline crossover by the SIEV in 36% of specimens, while Schaverien *et al.* identified a case without midline crossover. Both these studies postulated this midline crossover as a cause of venous problems. In our series, there was no midline crossover in 1/16 cadaveric specimens and in 14/100 clinical cases (13% of cases overall).

In addition to these factors, there may be a further anatomical factor in the pathogenesis of venous compromise in DIEP flaps. The communication between the perforating vein and the SIEV is not uniform, and frequently this communication is of substantially smaller calibre than either the SIEV or the perforating veins themselves. These communications, described as oscillating veins between the adjacent venous territories (20), may be the

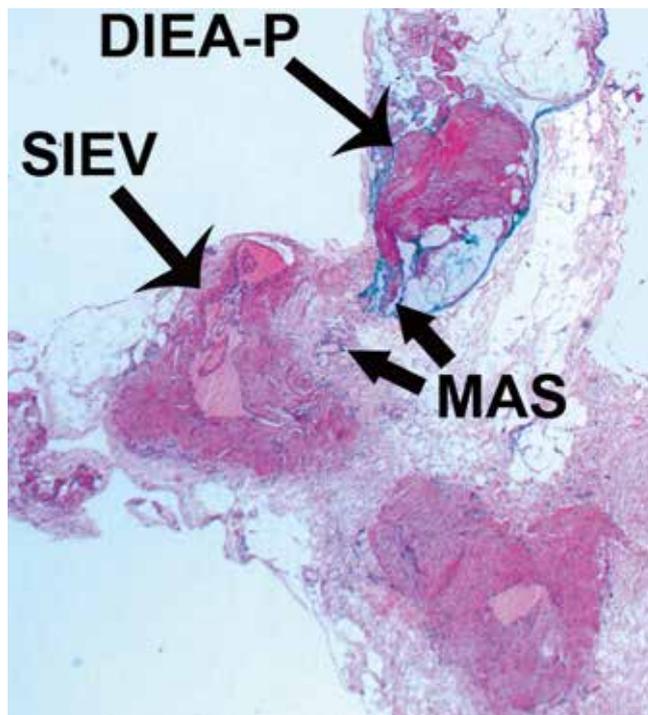


Figure 22 Histological analysis with Hematoxylin and Eosin (H and E) stain of a transverse section through the macrovascular arteriovenous shunt (MAS) shown in Figures 1A and 1B. ‘Arterial’ features are seen on the arterial side of the shunt, with a thicker wall, particularly the media and thinner lumen, while ‘venous’ features on the venous side, with thinner wall and wider lumen. Scale as shown (30 times magnification) (Reproduced with permission from: Rozen WM, Chubb D, Ashton MW, *et al.* Images in plastic surgery: the anatomy of macrovascular arteriovenous shunts and implications for abdominal wall free flaps. *Ann Plast Surg* 2011;67:99-100)

limiting factor to venous flow in many cases. With the use of CTA in the current study, the presence and calibre of these communications are readily identifiable and can be identified preoperatively. The use of identification of the presence and calibre of this communication in selecting the optimal perforators for inclusion in the vascular supply of the flap has been described, and shown to be a useful tool for aiding perforator selection and for maximizing venous outflow (53). Throughout our previous anatomical and clinical studies, we have identified the anatomical basis for this, and confirmed the utility of CTA in evaluating this anatomy. With this anatomy essential to flap survival in DIEP flap surgery, and continuing evolution in our understanding of this anatomy, future research will no

doubt further improve our appreciation of this intricate anatomy.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Anatomy relevant to conservative mastectomy

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Abstract: Knowledge of the anatomy of the nipple and breast skin is fundamental to any surgeon practicing conservative mastectomies. In this paper, the relevant clinical anatomy will be described, mainly focusing on the anatomy of the “oncoplastic plane”, the ducts and the vasculature. We will also cover more briefly the nerve supply and the arrangement of smooth muscle of the nipple. Finally the lymphatic drainage of the nipple and areola will be described. An appreciation of the relevant anatomy, together with meticulous surgical technique may minimise local recurrence and ischaemic complications.

Keywords: Anatomy; nipple; conservative mastectomy; nipple-sparing

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Introduction

The detailed surgical anatomy of the breast was of almost no consequence during the Halsteadian era when the standard treatment was a radical mastectomy. The resurgence of interest in preservation of the skin and nipple with a view to optimizing aesthetic outcome, so called “conservative mastectomy”, has led researchers to attempt to build upon the seminal work of Sir Astley Cooper (1).

The anatomy of the breast, in particular the nipple, is highly relevant to surgeons considering conservative mastectomy. This paper will describe the clinical anatomy of the ducts as this pertains to the margins of a conservative mastectomy, but also the vascular anatomy of the breast skin and nipple as this has implications for the risk of ischaemic complications. An understanding of the anatomy, together with careful surgical technique may minimise these. We will briefly consider the nerve supply to the nipple and the arrangement of smooth muscle in of the nipple as these are relevant to residual function of the nipple after conservative mastectomy. While the detailed lobar anatomy of the breast (2-5) is of interest in optimising breast conservation it is not relevant in the case of mastectomy so will not be covered here.

Embryological development of the nipple and ducts

Paired mammary ridges, also known as milk lines develop

on the ventral surface of the embryo. These extend from the axilla to the inguinal region, however much of each line atrophies leaving only the part overlying the pectoral region (6). The ectoderm is responsible for the formation of the ducts and alveoli and the mesenchyme is responsible for the connective tissue and the vasculature of the breast. The ectodermal thickening of the mammary primordium grows downwards into the dermis (7) producing solid cords of ectodermal cells growing within the underlying mesoderm. These buds become canalized and later form the lactiferous ducts and alveoli. When the foetus is near term the nipple becomes everted and ready to accept the lactiferous ducts. Developmental abnormalities in this process in a minority of foetuses result in congenital abnormalities such as amastia (absence of one or both breasts), athelia (absence of one or both nipples) and polythelia (more than two nipples).

Anatomy for skin-sparing mastectomy

From a surgical perspective, there is a clear compromise between completeness of excision of at-risk ducts and likelihood of damaging the blood supply of the skin and nipple. Thus skin-sparing mastectomy requires careful surgical technique, as described in subsequent chapters (on skin-sparing and skin-reducing mastectomy).

The development of the breast from ectoderm and mesenchyme may explain the presence of an “oncoplastic

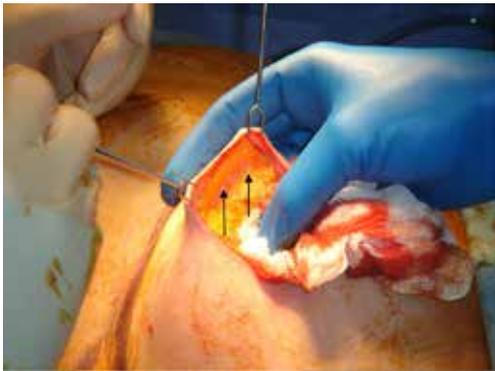


Figure 1 Operative image to show the “oncoplastic plane” with white connective tissue between subcutaneous fat and parenchymal fat shown by black arrows.

plane”, seen by surgeons between the subcutaneous fat, and the fat of the breast itself (see *Figure 1*). Named, like the discipline of oncoplastic surgery, to reflect the marriage of ablative oncological surgery, with aesthetic plastic surgery, this is the key to an oncologically-sound skin-sparing mastectomy.

The breast tissue lies deep to this plane and the blood vessels, upon which the skin depends, run in the subdermal layer and are preserved with the skin, enhancing the aesthetic outcome of reconstruction. Failure to preserve the blood supply of the skin may result in necrosis of the skin flap, requiring debridement and possibly skin-grafting and risking infection and implant loss. Surgeons must, therefore, seek this plane, but in some patients it is easily found, and in others, more difficult. Anatomical (histological) studies shed some light on the reasons for this:

Beer *et al.* presented a histological study of thickness of the skin flap (i.e., depth of the oncoplastic plane) and showed great variability (8). Furthermore, they discovered that the fascial plane was not histologically distinguishable in 44% of resection specimens, and in some cases breast tissue came to within 0.4 mm of the surface of the skin. Larson *et al.* (9) also carried out histological examination of 76 breast specimens from 38 women undergoing reduction mammoplasty. The median subcutaneous tissue thickness (deep dermis to most superficial breast tissue) was 10 mm but with a wide range of 0-29 mm. The interquartile range was 6-17 mm. There was no correlation between the thickness of this subcutaneous tissue and body mass index, patient age, breast specimen weight, or dermis-to-breast thickness of the contralateral breast. Technical considerations (sampling and preservation of specimens) may partially explain these findings, but it is

not uncommon, surgically, to find that the plane lies quite superficially in some patients and deeper in others, and indeed there may be variation within a patient in different quadrants. Hence no optimum mastectomy skin flap thickness can be recommended (10). Rather, the surgeon must be observant and careful when developing the plane.

Anatomy of the ducts

In addition to careful adherence to the oncoplastic plane, nipple-sparing mastectomy requires an understanding of the anatomy of ducts, their position within the nipple and their relationship to the vasculature and to the overall nipple shape. Again, surgical techniques for best managing this compromise will be discussed in later chapters. Here we present the relevant anatomy.

Number of ducts

In Sir Astley Cooper’s book “On the anatomy of the Breast”, he stated “The greatest number of lactiferous tubes I have been able to inject, has been twelve, and more frequently from seven to ten. But the greatest number of orifices I have been able to reckon has been twenty-two; however, some of these might be been follicles only, and not open ducts” (1). The variable results according to technique used, is reflected in the 21st century literature.

Going and Moffat (11) examined a single coronal section through the base of 72 nipples and found a median of 27 (IQR 21-30) collecting ducts. Similarly, Rusby *et al.* (12) studied 129 nipples and found the median number of ducts was 23 (IQR 19-28). Taneri *et al.* (13) sampled 226 mastectomy nipples histologically and found a mean of 17 (range, 18-30) ducts. Other techniques tend to result in smaller estimates of the number of ducts. For example, Ramsay *et al.* (14) used ultrasound to study 21 lactating women and found a mean of 9.6 ducts beneath the nipple of the left breast and 9.2 on the right. However, the equipment had insufficient resolution to identify ducts of less than 0.5 mm in diameter. Love and Barsky (15) employed several approaches to the study of ductal openings. Using serial sectioning and cytokeratin immunocytochemistry of ten nipples they identified 5-9 duct openings per nipple. They noted a mean of 5 duct openings by direct in vivo observations of lactating women and 6-8 openings by observation of passive conduction of lymphazurin from a subareolar injection to the nipple tip in mastectomy specimens. These findings are restricted to the number

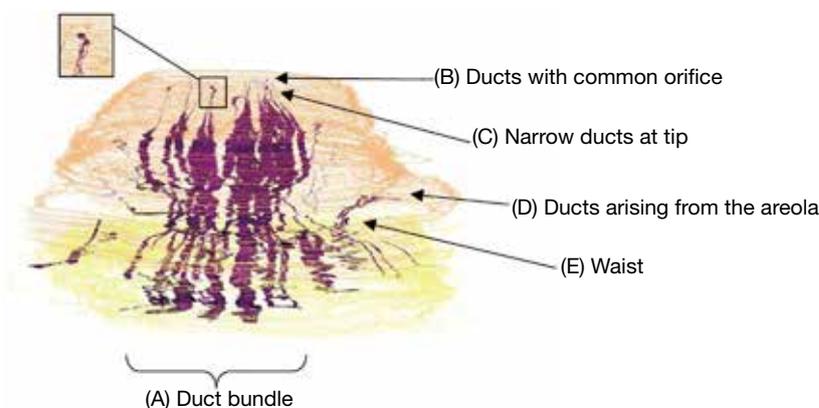


Figure 2 Three-dimensional reconstruction of a nipple. Skin in tan, cut edge in yellow and ducts in purple. Reproduced with permission from ref (12).

of ductal openings and do not establish the number of underlying ducts or their interconnections.

Relationship between ducts and openings

Four groups using histological techniques have noted the discrepancy between duct number and opening number and postulated that duct branching may be responsible (11,13,15). Going and Mohun (4) tried to elucidate the path of the 19 identifiable ducts in a 2.2 mm thick block at the tip of a nipple using episcopic fluorescence image capture (EFIC). However, they found that EFIC has insufficient resolution to discriminate reliably between keratin plugging and discontinuity between the duct and the skin surface. Using hematoxylin and eosin staining (H&E) sections from an entire nipple-tip, Rusby *et al.* showed that several ducts arose in the same cleft of the nipple (12), accounting for the discrepancy between the number of ducts in the nipple and the number of openings that can be counted externally.

Duct diameter

Estimating diameter at different levels has shown that most ducts are very narrow at the tip of the nipple with only a few ducts of a size that could be cannulated. At 1 and 1.5 mm beneath the tip the average duct diameter was 0.06 mm, and this increased to 0.7 mm at 3 mm deep (12).

Position of the ducts within the nipple

For conservative mastectomy, the exact number and size of the ducts is less relevant than their position and

relationships to other structures in the nipple. The surgical community is divided over whether it is necessary to attempt to excise all of the ducts (potentially compromising blood supply) and it certainly might seem unnecessary to remove the duct core in prophylactic mastectomy since most tumours develop in the terminal ductal lobular units. However, it has been reported that 9-17% of nipples do contain lobular tissue (16,17), thus, potentially carrying the risk of *de novo* cancer formation within the nipple in high-risk women.

Duct arrangement is best seen in a three-dimensional image of a reconstructed nipple (12) (*Figure 2*).

This shows:

- (A) The ducts are arranged in a central bundle with a peripheral duct-free rim;
- (B) The bundle narrows to a “waist” just beneath the skin, possibly at the level of the superficial fascia;
- (C) Some ducts originate on the areola or part way up the nipple;
- (D) Most ducts are very narrow as they approach the tip of the nipple;
- (E) Many of the ducts originate within a smaller number of openings on the nipple surface.

The finding that the majority of ducts form a central bundle that occupies 21-67% of the cross-sectional area of the papilla (12) suggests that near-complete surgical excision of the central duct bundle is feasible if it is deemed advisable. The changing cross-sectional area of the duct bundle forms a “waist” as shown in the three-dimensional reconstructions (12,18). This may have a developmental origin as sagittal sections illustrate that the narrowest point of the duct bundle occurs at the level of the superficial

fascia, perhaps indicating that in-growing ducts pierce this fascia together before dispersing into the developing breast. The waist may also correspond to the operative finding that the plane between breast and subcutaneous fat becomes more fibrous at the border of the nipple and this must be freed before the nipple can be inverted.

Going and Moffat (11) classified nipple ducts into three categories, ducts with a wide lumen, ducts with a minute lumen at the origin in the vicinity of the apex of the nipple and a minor duct population which arise from around the base of the papilla. Similar findings have been reproduced in other three-dimensional studies as well as identifying ducts originating in the areola (12). Going and Moffat's hypothesis that larger ducts might be connected to larger duct systems were not confirmed in the aforementioned study by Rusby *et al.* as there was no organized relationship between size of duct and whether it terminated within the nipple or passed deeper into the breast.

Vascular anatomy of the nipple

Nipple necrosis after nipple-sparing mastectomy may result in a requirement for excision of the nipple. Nipple necrosis can also occur following surgery to correct inversion, for mammary duct fistula, and after Hadfield's major duct excision. An understanding of the vascular anatomy is, therefore, clinically-relevant beyond nipple-sparing mastectomy.

Much of the available anatomical information about vascular anatomy within the breast and about supply to the nipple-areola complex is found in literature on breast reduction, where nipple viability is of key importance. Several studies have demonstrated that the blood supply of the breast is from the external and internal thoracic arteries, the intercostal, and the thoracoacromial arteries (19-22). Many of these studies were carried out in a small number of cadavers, which may account for discrepancies in comments on predominant supply to the nipple-areola complex.

Würinger (23) described two main sources of neurovascular supply to the nipple: a central and a superficial network. The central supply travels in a ligamentous septum originating from pectoralis fascia at the level of the 5th rib and inferior border of pectoralis major. Branches of the thoracoacromial, lateral thoracic and intercostal arteries and the deep branch of the 4th intercostal nerve passed within this septum. Würinger also described a medial ligament arising from the sternum and guiding blood vessels of the internal thoracic artery and anterior cutaneous intercostal nerve branches. A lateral ligament attached to the lateral border of

pectoralis minor guides branches of the lateral thoracic and lateral cutaneous intercostal nerves. These ligaments merge and carry a blood supply to the superficial fascia.

O'Dey *et al.* (22) found that the lateral thoracic artery supplied up to three separate branches to the nipple-areola complex during its descending course. However, these passed through deep breast tissue before ascending towards the nipple-areola complex to reach the superolateral edge. While important in breast reduction, these branches would be divided during a mastectomy. O'Dey concluded that the internal thoracic artery, in particular, supplies the nipple-areola complex. 86% of cases studied had one or two perforating vessels usually emerging in the 2nd or 4th intercostal spaces. These vessels had a curved course with superior convexity and arrived at the supero-medial border of the nipple-areola complex. These are described as traversing the subcutaneous tissue, converging on the nipple-areola complex at a depth of 1.5 ± 0.4 cm.

These studies all report that there is a superficial and a deep blood supply: the deep blood supply to the nipple shown in whole breast anatomical studies runs either through breast parenchyma (22) or in a ligamentous septum (24) and will be excised with the mastectomy specimen. If, according to O'Dey *et al.*, the "superficial" supply runs approximately 1.5 cm deep to the skin surface it, too, is unlikely to be preserved during a good oncological mastectomy as it is unusual to leave skin flaps that are 1.5 cm thick (as described above). Furthermore, this implies that despite leaving 0.5 cm thickness of glandular tissue beneath the nipple as advocated by some surgeons, the most important vessels are likely to have been severed. Nakajima *et al.* (19) described branches of the external and internal mammary arteries travelling in the subcutaneous tissue and communicating with one another above and below the areola. Small branches derived from the communicating vessels were found running toward the nipple-areola complex. These small vessels reached the base of the nipple, giving off fine vessels to the areolar skin, and ascended in the nipple in a circular fashion. Nakajima found that these arborised in the upper and middle thirds of the nipple. The close proximity of these vessels to the ducts implies that any technique in which the nipple core is excised will result in disruption of the major neurovascular supply within the nipple. A subsidiary part of Nakajima's work involved angiograms of breast skin specimens in which mammary glands and subcutaneous tissue had been resected. These showed rather sparse dermal and subdermal plexuses around the nipple-areola complex. It appears to be these plexuses upon which the survival of the nipple-areola complex depends if complete duct excision is

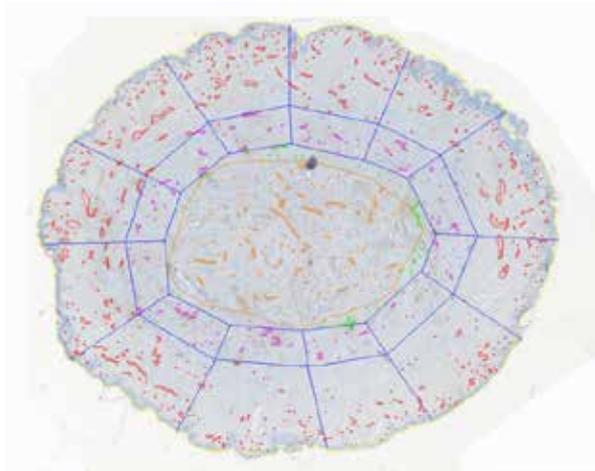


Figure 3 Coronal section of a nipple with nipple outline, duct bundle and peripheral 2 and 3 mm rims marked. Vessels stained with anti-factor VIII antibody to vascular endothelium have been highlighted and counted. Ducts are faintly visible within the central duct bundle. In this example, leaving either a 2 or 3 mm rim would have removed all ductal tissue. Reproduced with permission from ref (29).

attempted in nipple-sparing mastectomy.

Thus the two conflicting challenges of nipple preservation, ensuring oncological safety and maintaining nipple viability, are dependent on the underlying anatomy and on surgical technique and are inextricably linked through surgical judgment about the value of excising as much duct tissue as possible. Clinical series reporting necrosis rates often do not report in sufficient detail on surgical technique to allow readers to evaluate the trade-off being made.

Incision placement, however, is usually reported and many different incisions have been described for the conservative mastectomy with some high quality retrospective studies addressing this. A review of 48 studies by Munhoz *et al.* (25) demonstrated that the most common incision was the radial, followed by periareolar, inframammary, mastopexy and transareolar. Wijayanayagam *et al.* (18) found that the radial incision had the greatest likelihood of avoiding ischaemia of the nipple-areola complex in a series of 64 conservative mastectomies. However the scar from this incision is prominent. Colwell *et al.* (26) reviewed 500 nipple-sparing mastectomy procedures and found that a periareolar incision was an independent predictor of complications on multivariate analysis and the inferolateral inframammary fold incision was associated with a decreased risk of total and ischaemic complications. Similar results for the periareolar incision have been found in another study (27). Garwood

et al. (28) found on logistic regression analysis that using an incision that was more than one third of the circumference of the nipple-areola complex was an independent risk factor for complete or partial nipple loss and skin flap necrosis. It can be assumed that if the sparse dermal and subdermal plexuses around the nipple-areola complex are disturbed in addition to division of the deeper vessels during the mastectomy, the risk of ischaemic complications is higher.

A study to investigate the microanatomy of the un-irradiated nipple vasculature used anti-factor VIII antibody to highlight blood vessels in sections from coronal 3 mm thick blocks of resected nipples. Within a 2 mm rim of peripheral nipple tissue 50% of the vessels were contained, and within a 3 mm rim, 66%. Only 29% of the vessels were located within the duct bundle (Figure 3). However, in terms of density, the mean microvascular density was 16 per mm² in the duct bundle and 9 per mm² in the peripheral tissue (29). The proportion of vessels in the duct bundle and the microvessel density was unchanged by radiation. These data are of anatomical interest, though it is difficult to apply these microscopic findings to improve surgical practice.

Anatomy of retained function

Opatt *et al.* (30) argue that sparing the nipple serves little purpose if the nipple is insensate. However, there is some evidence that nipple sensation and erection can be regained after nipple-sparing mastectomy (31-35).

The sensory innervation of the breasts comes from the lateral and anterior cutaneous branches of intercostal nerves (36,37). Controversies as to which intercostal nerves are relevant and their course are likely to be due to difficulty in dissecting thin nerves and the small number of cadavers in each study. Schlenz *et al.* (38) undertook an anatomic study of 28 female cadavers. They found that the nipple and areola were always innervated by the lateral and cutaneous branches of the 3rd, 4th and 5th intercostal nerves with the most constant innervation pattern being from the 4th lateral cutaneous branch. The anterior cutaneous branches took a superficial course within the subcutaneous tissues of the medial breast and terminated at the medial areolar border. The lateral cutaneous branches took a deep course within the pectoral fascia and reached the nipple via the breast parenchyma and pierced the nipple via its posterior surface. Montagne and Macpherson (39) demonstrated that the neural elements are concentrated at the base of the nipple with few at the side of the nipple and even fewer in the areolar. Therefore it is unsurprising that the nipple is

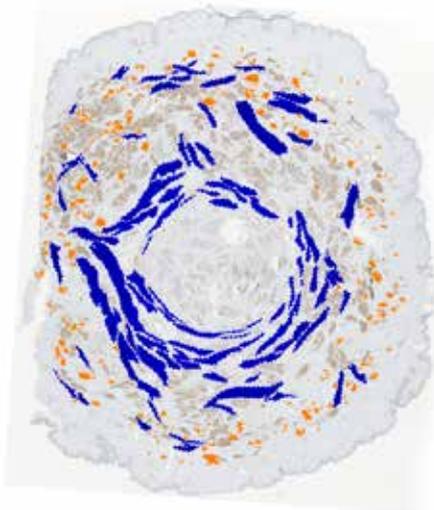


Figure 4 Section with muscle fibres. Circular fibres highlighted in blue, longitudinal fibres in orange. Reproduced with permission from ref (40).

largely insensate after nipple-sparing mastectomy due to injury of the anterior cutaneous nerves as the anatomical plane between the subcutaneous fat and breast parenchyma is developed and the lateral cutaneous nerves are divided as the breast parenchyma is separated from the pectoral fascia.

Although most authors report that sensation is lost, some preserved nipples remain erectile and therefore behave more naturally than a reconstructed nipple.

The arrangement of smooth muscle highlighted in *Figure 4* (40) is reminiscent of the concentric muscle layers of the gastrointestinal tract or of a sphincter. At the base of the papilla the circular smooth muscle is particularly prominent around the duct bundle suggesting that contraction of this muscle could lead to erection of the nipple and possibly occlusion of the ducts. Conversely, towards the tip of the nipple, the concentrations of muscle fibres surround individual ducts as they narrow and unite close to the tip of the nipple.

Anatomy of lymphatic drainage

Sappey first described the anatomical basis of the breast lymphatics in the 1870s (41). He demonstrated a subareolar plexus of lymphatics and a small number of large lymphatic vessels draining into the axillary lymph nodes. Sappey concluded that the lymphatics of the breast collected in a subareolar plexus and then drained towards the axilla.

Many of his observations contributed significantly to the development of breast lymphatic mapping and sentinel lymph node biopsy. In 1959 Turner-Warwick (42) studied the lymphatics and concluded that lymphatic pathways passed directly from the tumour injection site to the axillary lymph nodes without passing through the subareolar plexus. He suggested Sappey had mistaken mammary ducts for a lymphatic vessel, therefore overemphasizing the importance of the subareolar plexus. Whether or not the subareolar plexus drains the breast tissues and then lymph then drains towards the sentinel lymph node is still controversial and calls into question the optimal location of dye or radioisotope for sentinel lymph node biopsy. Suami *et al.* (43) undertook lymphatic mapping of 14 cadavers using hydrogen peroxide and injecting with a lead oxide mixture and then imaging the specimens. Similarly to Sappey they found the lymphatics deep to the nipple and areola were a dense network of lymph capillaries, however they favoured the Turner-Warwick findings that suggested a direct pathway from the injection site to the axilla, not via the subareolar plexus.

Conclusions

Together with careful surgical technique, a good working knowledge of the blood supply of the skin and nipple of the breast contributes to the avoidance of ischaemic complications in conservative mastectomy. Similarly, an understanding of the spatial relationships of ducts and blood vessels within the nipple will help surgeons make decisions on the relative benefits of removing or preserving the nipple core, and optimising technique to do so should this be deemed necessary.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Anatomic and physiological fundamentals for autologous breast reconstruction

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Abstract: The success of autologous tissue transfer is reliant on adequate blood supply and as we endeavour to tailor our reconstructive options through our flap choices and design. Autologous breast reconstruction has made substantial progress over the years and the evolution of refinements over the last 30 years has allowed flaps to be based on specific perforators. The ultimate goal of breast reconstruction following mastectomy is to match optimal tissue replacement with minimal donor-site expenditure. In parallel surgeons will seek ways to ensure safe flap design and harvest while maintaining predictability and reliable tissue perfusion. Better understanding of the vascular anatomy and physiology of the cutaneous circulation of soft tissues, and that of patterns of blood flow from individual perforator has provided insight to advance perforator flap harvest and modifications in flap design. The aim of this article is to review the principles of blood supply and flap design exemplified through common flaps used in autologous breast reconstructive surgery, to better understand approaches for safe flap harvest and transfer of well perfused tissue.

Keywords: Autologous reconstruction; anatomy; blood supply; flap design; vascular territory; perforasome; perforator flaps; free flaps; pedicled flaps; breast reconstruction

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Introduction

Breast reconstruction has become an important consideration for women after mastectomy. The goal is to re-create a breast mound that is naturally soft, durable, looks and feels like a normal breast, and can mature and naturally change with the patient over time. Women undergoing breast cancer surgery have become younger over the years and so reconstructive options ought to place greater emphasis on longevity. Documented trends include changes in patient demands and expectations; the disadvantages of implant reconstruction being better understood and the results through autologous reconstruction being more widely recognized (1,2).

Although the use of autologous tissue is less commonly performed compared to implant-based reconstruction it is still seen as a preferable choice in circumstances and has gained increasing popularity over the years. Autologous

tissue can behave very much like normal breast tissue, however the surgery is considered to be more complex and lengthy in comparison to prosthetic based reconstruction. However, the advancement of microsurgical and reconstructive techniques and incorporation of enhanced recovery protocols has significantly reduced the associated morbidity with autologous breast reconstruction.

The success of autologous tissue transfer is reliant on adequate blood supply and as we endeavour to tailor our reconstructive options through our flap choices and design. Autologous breast reconstruction has made substantial progress over the years and the evolution of refinements over the last 30 years has allowed flaps to be based on specific perforators. This revolutionary concept can preserve underlying muscle, reduce donor site morbidity and ability to tailor the flap to reconstruct exactly the tissues that are missing at the recipient site. The ultimate goal of breast reconstruction following mastectomy is to

Table 1 “Perforasome theory” summarized key concepts

“Perforasome theory” key concepts

One vascular territory defined by injection of one perforator is called a perforasome
Direct linking vessels are direct vascular branches connecting a perforasome to an adjacent perforator territory
Indirect linking vessels are constituted by the subdermal plexus
Communicating branches exist between direct and indirect linking vessels
Skin paddle designs should consider the orientation of dominant linking vessels and axially of flow

match optimal tissue replacement with minimal donor-site expenditure. In parallel surgeons will seek ways to ensure safe flap design and harvest while maintaining predictability and reliable tissue perfusion.

The mantra of Sir Harold Gillies that surgeons are “faced with a constant battle between vascular supply and beauty,” is a reflection of the challenges and goals of the reconstructive breast surgeon. The foundations of our vascular anatomical knowledge stems from pioneering works including that of Manhot, Salmon, Cormack and Lamberty, and Taylor and Palmer (3-5). Better understanding of the vascular anatomy and physiology of the cutaneous circulation of soft tissues, and that of patterns of blood flow from individual perforator has provided insight to advance perforator flap harvest and modifications in flap design.

The aim of this article is to review the principles of blood supply and flap design exemplified through common flaps used in autologous breast reconstructive surgery, to better understand approaches for safe flap harvest and transfer of well perfused tissue.

The perforasome theory

The angiosome theory defined by Taylor and Palmer in 1987 characterized the vasculature of the human body as organized into “Angiosomes” (5). Each angiosome refers to a block of tissue supplied by a source vessel and linked to each other via “choke vessels” in the subdermal plexus, named due to their relatively small calibre. The increasing use of perforator flaps advocated a critical need to better assess vascular architecture. Saint-Cyr *et al.* focused on the perforator itself and not the source vessel through a series of anatomical studies, to define individual vascular territories through 3D and 4D computed tomographic angiography (CTA). The “Perforasome” concept, coined by Saint-Cyr *et al.* in their original article, described how each cutaneous perforator had its own unique vascular arterial territory (6), and this has been referred to in other texts as a “perforator angiosome” (7) or “cutaneous

angiosome” (8). Large filling pressures through a single dominant perforator can allow for large perforator flap harvest based on linking vessels that may connect multiple perforasomes to one another (9). Some key principles of the perforasome theory are summarized in *Table 1*.

First principle

Each perforasome is linked with adjacent perforasomes by means of two main mechanisms that include both direct and indirect linking vessels. Direct linking vessels are large vessels which allow flow from one perforator to the next and allow capture of adjacent perforasomes through an inter-perforator flow mechanism. Perforasomes are also linked to one another by indirect linking vessels or recurrent flow via the subdermal plexus (*Figure 1*). These vessels are similar to choke vessels described by Taylor *et al.* (10).

Second principle

Flap design and skin paddle orientation should be based on the direction of the linking vessels, which is axial in the extremities and perpendicular to the midline in the trunk. Orientation of the linking vessels corresponds to the orientation of maximal blood flow, and flap axis should ideally be designed with this consideration (*Figure 2*).

Third principle

Preferential vascular filling patterns occur within perforators of the same source artery first, followed by the perforators of other adjacent source arteries. The linking vessels then emanate from this main perforasome to perforasomes of adjacent vascular territories from other source arteries.

Fourth principle

Mass vascularity of a perforator found adjacent to an

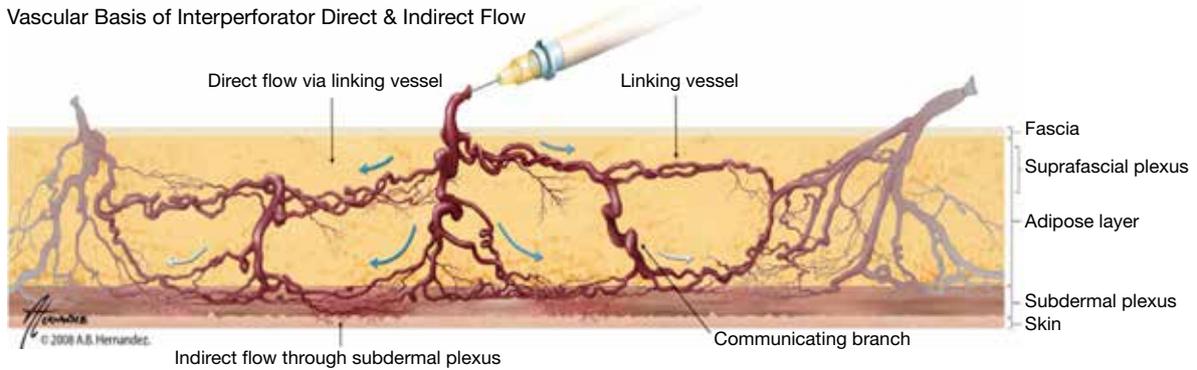


Figure 1 Communication between adjacent perforators through direct linking vessels and indirect communications via the subdermal plexus. (Permissions requested for Re-print) (6).

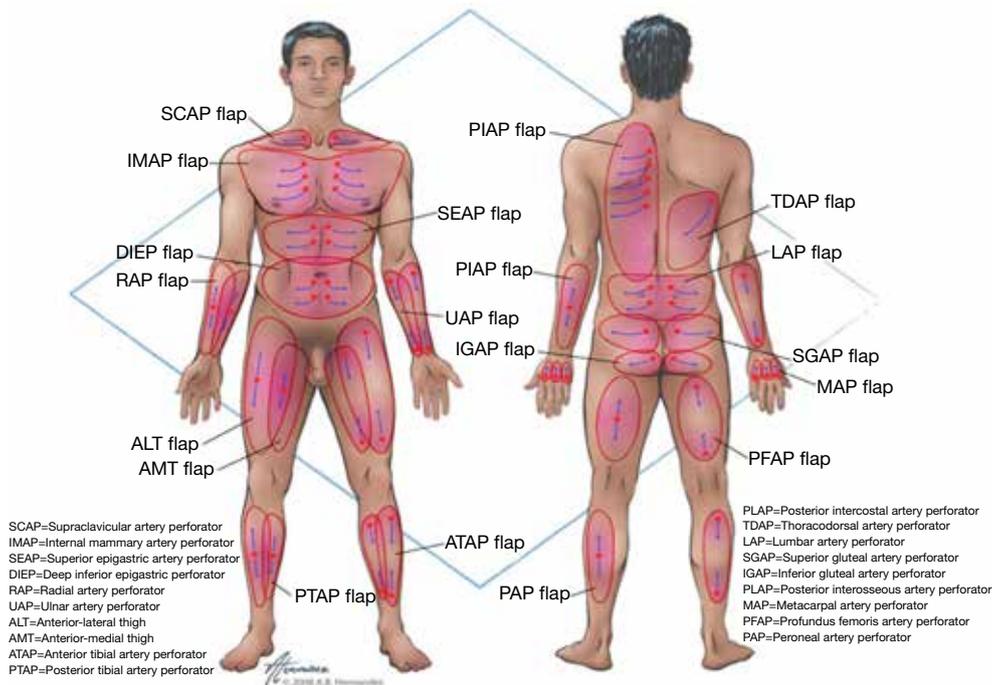


Figure 2 Illustration to demonstrate the direction of principal linking vessels and the axially of flow from perforators dependent on anatomical site. (Permissions requested for Re-print) (6).

articulation is directed away from the same articulation. Whereas perforators found at a midpoint between two articulations or midpoint of the trunk has a multidirectional flow distribution. Therefore flap design should take into consideration the perforator location.

Successful autologous reconstruction relies on robust blood supply. We discuss the principles of vascular anatomy and flap design for autologous flaps for reconstructive breast

surgery. A comprehensive understanding of the vascular anatomy is critical to evidence-based perforator selection and optimizing flap design.

Deep inferior epigastric perforator (DIEP) flap

The use of abdominal tissue for autologous breast reconstruction has been long and widely practiced, with

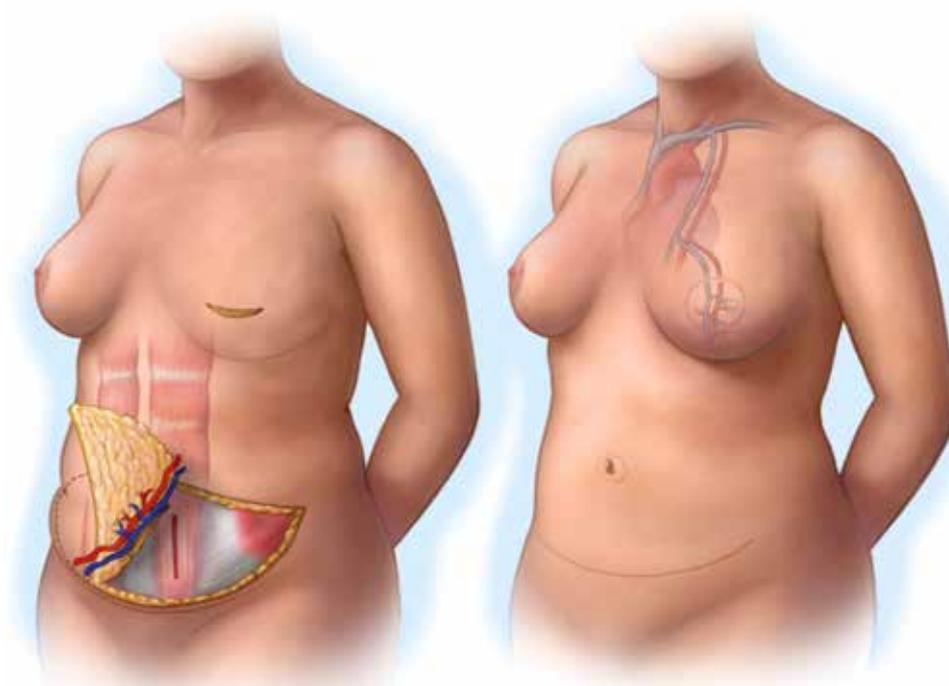


Figure 3 Illustrative example of DIEP flap for breast reconstruction, with preservation of the underlying rectus muscle and postoperative reconstruction following inset and anastomosis to the internal mammary vessels. DIEP, deep inferior epigastric perforator.

similar characteristics to breast tissue and an aesthetic donor site scar. The DIEP flap had evolved from the traditional transverse rectus abdominis myocutaneous (TRAM) flap that was used for pedicled breast reconstruction based on the superior epigastric artery (11). However, the inferior epigastric artery plays the dominant role in abdominal tissue transfer in autologous reconstruction (12). Koshima and Soeda first described the DIEP flap in 1989 (13) and Allen and Treece popularized its use in breast reconstruction in 1994 (14). This flap has been studied extensively and is a safe reliable option in breast reconstruction with low morbidity (*Figure 3*).

The artery arises from the external iliac artery and approaches the rectus muscle on its lateral edge and travels towards the arcuate line on its deep surface. At this level the main artery will form one of three typical branching patterns (15). The commonest branching pattern is a type II (57-89%), which is a simple bifurcation and perforators arising from the medial or lateral row of the DIEA. Type I vascular pattern involves a single inferior vessel (27-29%) and type III pattern (14-16%) is a trifurcating pattern above the arcuate line (16). Variations in anatomy include absent unilateral DIEA (17), duplicate systems and intra-

abdominal origin of the DIEA (16). The perforators may take an intramuscular course, which can be short (most common), perpendicular or a long oblique course, or they may have a completely extra-muscular course. After exiting the rectus muscle, the perforators may directly pierce the anterior rectus sheath or travel a short distance in the sub-fascial plane before penetrating the anterior rectus sheath. In a systematic review by Ireton *et al.* [2014] the course of these perforators had described a considerable anatomical variation in that 20% up to 67% had a direct course on exiting the fascia, and around 33% and 50% may have a sub-fascial course between 0.5 up to 3 cm from the collated studies. Perforators that had a more direct course were found usually within 3 cm of the umbilicus, and those lower in the abdomen were more likely to have a longer sub-fascial course (16,18).

In the subcutaneous layer, lateral row perforators have a more oblique course through this layer, whilst the medial row perforators a more direct path. Once the perforators reach the subcutaneous and dermal layers, there is a considerable branching and anastomoses, with midline perforators presenting with a high degree of midline crossover, in contrast to the lateral row perforators that

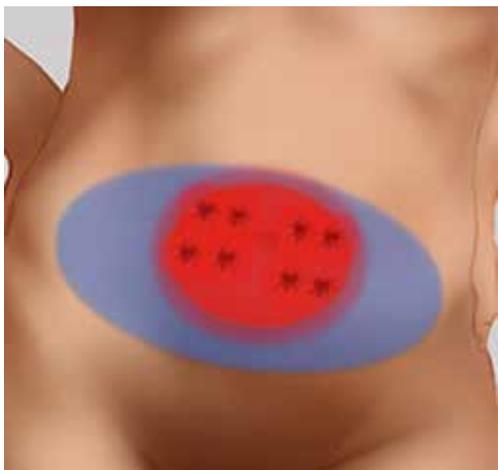


Figure 4 Location of dominant perforators in DIEP flap harvest, identified as a “hot spot” in the lower abdomen. DIEP, deep inferior epigastric perforator.

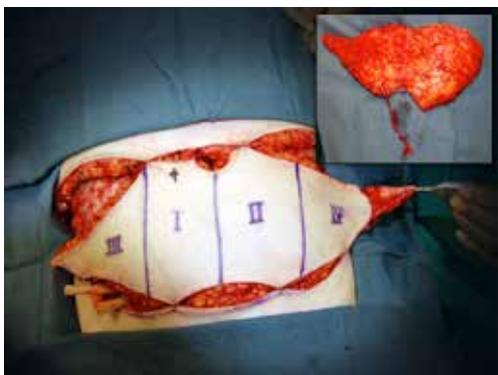


Figure 5 Representation of the traditional Hartrampf zones of perfusion for TRAM flaps which has still been used with reference to DIEP flap harvest. TRAM, transverse rectus abdominis myocutaneous; DIEP, deep inferior epigastric perforator.

have little midline crossover of their vascular territories which has been demonstrated on cadaveric anatomical studies (7,19). Larger dominant perforators are typically seen in the medial row, and within 3-5 cm of the umbilicus, representing a “hot spot” of dominant perforators in DIEP flap harvest (Figure 4). There has been a considerable degree of anatomical, radiological and clinical studies using a variety of intraoperative technologies, to determine the perfusion patterns of perforators following DIEP flap harvest. In the harvest of the TRAM flap, where most of the DIEP perforators are included, it has been accepted that

the perfusion of the flap integument occurs in zones. Four zones have been typically described for vascular perfusion of the lower abdominal wall, with sequential filling of each zone (11,20-22). The first zone universally represents the highest degree of perfusion found on the ipsilateral side of the DIEA perforator. The Hartrampf zones of perfusion (I to IV) are familiar to most plastic surgeons (Figure 5). The Hartrampf zones II and III were shown reversed by Holm *et al.* using intraoperative fluorescence imaging (22). There is contention in the literature of the characteristics of these zones and the application of these traditional zones to perforator flaps based on a single dominant perforator. It is recognized that lateral and medial row perforator have different vascular perfusion patterns through clinical, radiological and cadaveric anatomical studies (7,22-24).

Medial row perforators generally are larger in calibre, with more extensive branching patterns and greater perfusion patterns compared to lateral row perforators (7,12,19,23,24). The medial row perforators can reliably perfuse across the midline and provide a robust vascularity to flaps raised on a single dominant perforator in the central two zones (19). The perforators are found to have a more direct course through the anterior rectus sheath (16) and to Scarpa’s fascia compared to lateral row perforators. The medial row perforasome can be classified using the traditional zone concepts and through anatomical studies have demonstrated perfusion patterns similar to Hartrampf zones of perfusion. In contrast, the lateral row perforasome is more representative of Holm’s zones of perfusion (23).

For unilateral reconstruction, the medial row perforators perfuse more medially and lateral perforators perfuse laterally, that is more concentrated to a hemi-abdomen (7), and they share a similar territory to the ipsilateral superficial inferior epigastric artery (SIEA) (23). The DIEP flap’s vascular territory could be potentially augmented with the inclusion of a second perforator. The lateral branches of the DIEA during flap harvest were frequently dominant and run a more rectilinear course which would permit an easier dissection (25). However, if the medial row perforators were dominant, it would be recommended to harvest a flap based on a dominant medial row perforator, particularly if a larger flap is being required (as an alternative to muscle-sparing TRAM flap). Although in the past it was advocated that if a flap was reconstructed with only a hemi-abdominal flap, a lateral row perforator DIEA or SIEA could be considered. However, perfusion territories can vary between medial and lateral row, the decision for perforator choice should be based on the largest and dominant perforator in the hemi-

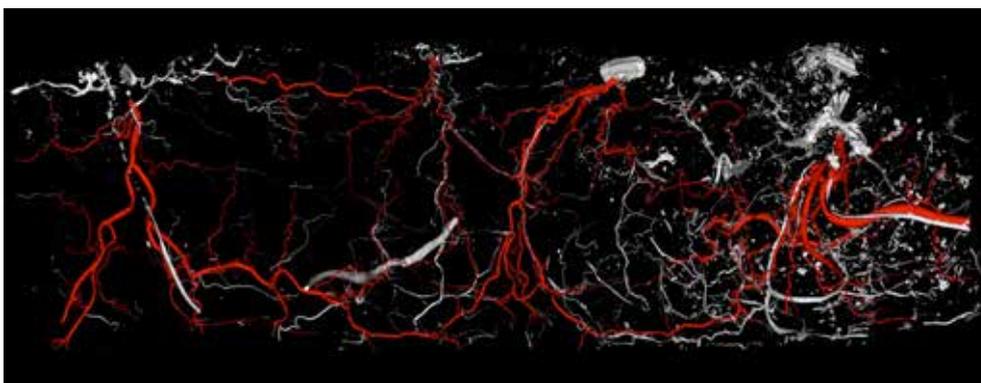


Figure 6 Micro computed tomographic studies following a single perforator injection to demonstrate the presence of direct linking vessels in a DIEP flap and recurrent flow via the subdermal plexus, with communication with adjacent perforators. DIEP, deep inferior epigastric perforator.

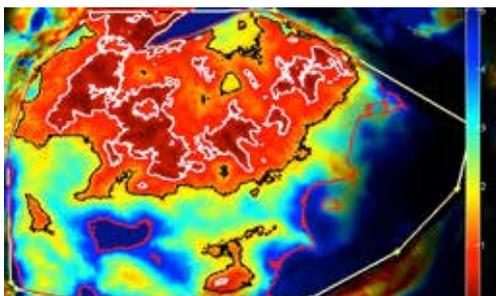


Figure 7 Intraoperative use of indocyanine green fluorescence laser angiography and quantitative analysis of flap physiology in a left hemi-DIEP flap. Marker to show position of medial row perforator and colour map overlay applied. DIEP, deep inferior epigastric perforator.

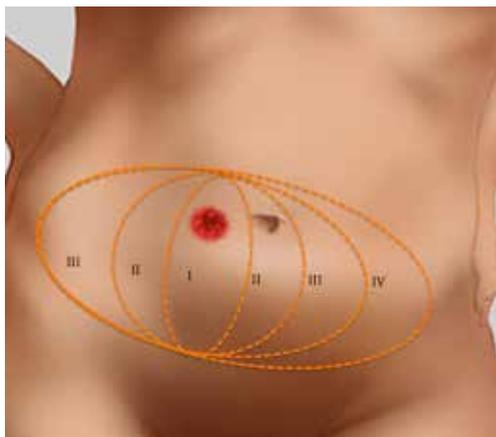


Figure 8 Alternative perforator zones of perfusion territories based on a medial row perforator in the lower abdomen in DIEP flap harvest. DIEP, deep inferior epigastric perforator.

abdomen, regardless of row.

In the hemi-abdomen the medial and lateral row are connected by direct linking vessels and indirect linking vessels via the subdermal plexus (*Figure 6*). For medial row perforators, there are large linking vessels, which connect with the lateral row and additional intra-row perforators; linkage with the contralateral medial row perforators across the midline is obtained via the subdermal plexus. These linking vessels are similar to the choke vessels described by Taylor. The use of preoperative CTA can be used preoperatively, to review the presence of dominant perforators and linking vessels, and the course of the dominant perforators to plan the dissection and flap harvest (26,27). The addition of intraoperative use of indocyanine green laser fluorescence angiography has provided a useful tool for an early assessment of flap perfusion and micro-anastomotic flow (*Figure 7*).

A newer model proposed for perforator perfusion is centred on the dominant perforator and perfusion falls sequentially between adjacent perforasomes (7,9). For example, zone I supplied by an ipsilateral medial row DIEA perforator, the immediate adjacent perforasome zone II is captured by the ipsilateral lateral row DIEA and contralateral medial row DIEA; zone III, refers to the second captured perforasome of the contralateral lateral row and ipsilateral SIEA territory, and Zone IV refers to the contralateral SIEA territory (6,9) (*Figure 8*).

Linking vessels in the trunk are commonly directed perpendicular to the midline and follow an oblique transverse direction, parallel to the cutaneous dermatomes. Flow from these perforator angiosomes can be multidirectional and cross the midline in many cases, but

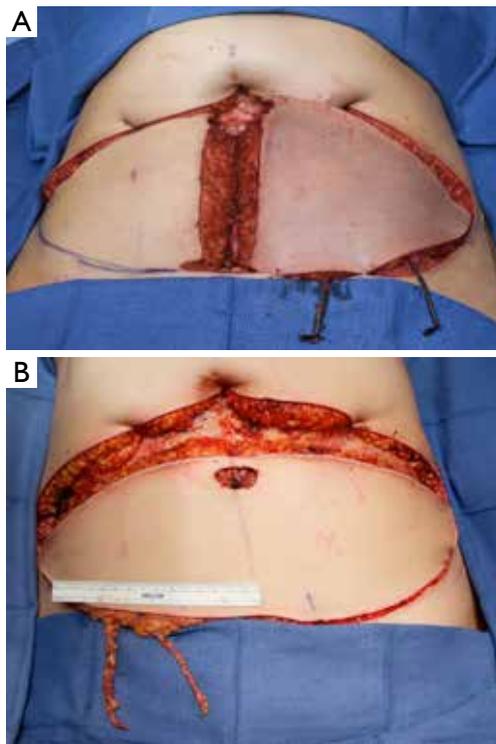


Figure 9 (A) Intraoperative clinical recognition of venous congestion following hemi-DIEP flap harvest prior to flap transfer, provides a good indication to augment venous drainage with the SIEV or the MSIEV, which have both been dissected out; (B) dissection of the SIEV and MSIEV during DIEP flap harvest. DIEP, deep inferior epigastric perforator; SIEV, superficial inferior epigastric vein; MSIEV, medial superficial inferior epigastric vein.

preferential flow is normally directed away from the midline to maintain adequate blood supply to adjacent regions, which are populated with fewer perforators (*Figure 2*).

Venous outflow can be the limiting factor in DIEP reconstruction leading to flap failure (28), but although venous compromise is multifactorial, the physiology of venous outflow is still poorly understood. The incidence of venous congestion in DIEP flaps has ranged from 3 to 27 percent in the literature, and the higher rates are usually recognized intra-operatively (*Figure 9A*) (29). Proposed mechanisms include the perforator being too small, absence of midline crossover veins except for indirect linking vessels at the subdermal plexus level found in up to 36% of cases in anatomical studies (30), connections between the superficial and deep systems (28,31). Although arterial inflow from DIEA is often reliable the DIEV may be inadequate and therefore augmentation of venous drainage may be required.

A variety of approaches have been adopted to supercharge or augment the venous drainage of the DIEP flap. These approaches generally incorporate the use of a “lifeboat” option during DIEP flap harvest, including dissecting out the superficial inferior epigastric vein (SIEV), a medial branch of the SIEV (MSIEV) or additional perforator (*Figure 9B*). Additional venous anastomoses include using both venae comitantes, connection of the SIEV intrinsically within the flap (to a deep perforator venae comitante) or extrinsically (e.g., antegrade or retrograde to the internal mammary vein) (29).

The diameters of the DIEA, DIEV, perforator veins and arteries have been correlated but independent of the SIEV in cadaveric studies (31-33). Cadaveric injection studies by Carramenha e Costa *et al.* first described that venous drainage of abdominal wall was dominated by the superficial system, but this still warrants further investigation (32). In anatomical studies carried out by Schaverien *et al.* [2008] (24), superficial and deep venous drainage systems were connected by the venae comitantes of the perforators of the DIEA and injection studies of either revealed similar venous filling patterns, including those of adjacent venae comitantes. Adjacent superficial epigastric vein filling patterns crossed the midline at the level of the subdermal plexus (30).

Dominant perforators of the deep system concentrate around the periumbilical area (32) and flap design should include perforating veins at the level of the umbilicus. However, inadequate communication between the chosen perforator venae comitantes and the SIEV system can be responsible for diffuse venous congestion seen in some DIEP flaps (30). Schaverien *et al.* [2010] reviewed venous anatomy on preoperative magnetic resonance angiography (MRA) and identified that venae comitantes with direct venous connections to the SIEV were significantly more likely to be found in the medial row, demonstrating that medial row perforators may provide more adequate venous drainage to a DIEP flap (30). It is important to highlight that the sensitivity of detecting small communicating vessels between the deep and superficial systems can be limited in CTA and MRA for very small vessels. However, Rozen *et al.* [2012] have described the presence macrovascular shunts identified on preoperative CTA (a direct communicating vessel between a DIEA and SIEV territory), which warrants further investigation (34).

In addition to flap harvest for breast reconstruction, we have adopted a conservative approach to the dissection of the abdominoplasty flap for donor site closure. This

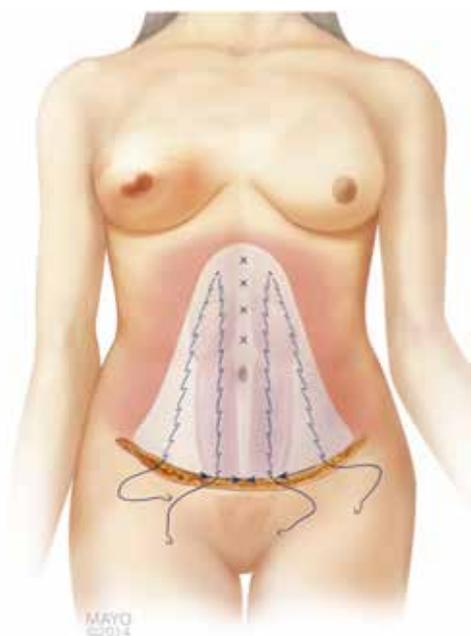


Figure 10 DIEP donor site closure using progressive tension sutures and limited dissection of the abdominoplasty to preserve the lateral perforators of the anterior abdominal wall. DIEP, deep inferior epigastric perforator.

technique involves a limited lateral dissection to preserve lateral perforators to the abdominoplasty skin flap, and a central dissection that proceeds to the xiphoid process (*Figure 10*) (35,36).

A better understanding of vascular anatomy and zones of perfusion of perforators in DIEP flap harvest for breast reconstruction will help to improve the predictability and reliability of flap harvest, and decrease flap-related complications, such as fat necrosis, and partial flap loss. Linking vessels are a key component to understand the full potential of vascular territories of individual perforators and the overlap with vascular territories of other source arteries. Anatomical, radiological and intraoperative imaging studies have provided fundamental knowledge base to our understanding of vascular anatomy, although there are many areas that warrant going research for DIEP breast reconstruction.

Key points of DIEP anatomy for flap design

- (I) Flaps should be raised on the largest and dominant perforator regardless of row. Dominant perforators

are usually found in a “hot spot” within 3–5 cm of the umbilicus;

- (II) Lateral perforators commonly have a more rectilinear course and perfusion is concentrated more to the hemi-abdomen;
- (III) Medial row perforators exhibit a greater degree of branching and larger calibre direct and indirect linking vessels via the subdermal plexus, which provides more robust vascularity across the midline, in contrast to lateral row perforators;
- (IV) When a large amount of tissue is required, either a dominant medial row perforator or muscle-sparing TRAM should be preferentially chosen for flap harvest;
- (V) The use of preoperative CTA can identify the largest perforators in the lower abdomen, their course, and the presence of large linking vessels intra-row and inter-row, which can provide some inference to overall flap vascularity;
- (VI) Venous systems can be assessed to a certain degree with preoperative imaging and connections between the superficial and deep systems. However, lifeboat options should be considered and incorporated in the flap harvest e.g., inclusion of the SIEV routinely within the flap;
- (VII) Intraoperative imaging including fluorescence laser angiography is gaining popularity in reconstructive surgery as an intraoperative adjunct to assess flap perfusion and venous congestion for early identification of perfusion changes.

Transverse myocutaneous upper gracilis flap

The transverse myocutaneous gracilis, also known as the transverse upper gracilis (TUG) flap, has been utilized in breast reconstruction since its anatomical description in 1992 (37–42). It can be used in bilateral reconstruction or stacked for a unilateral reconstruction. A perceived disadvantage with the flap is the low volume of harvested tissue compared with abdominal and gluteal flaps, which has traditionally limited this technique to small and to mid-size breasts. Medial thigh tissue correlates well with body mass index, and therefore a good option if abdominal or alternative donor sites are not available. Harvesting tissue from a more posterior location is a modification we have adopted to take opportunity of the bulkier posterior thigh tissue (39–41) allowing further recruitment of tissue into the flap. We discuss the basic anatomy and these modifications

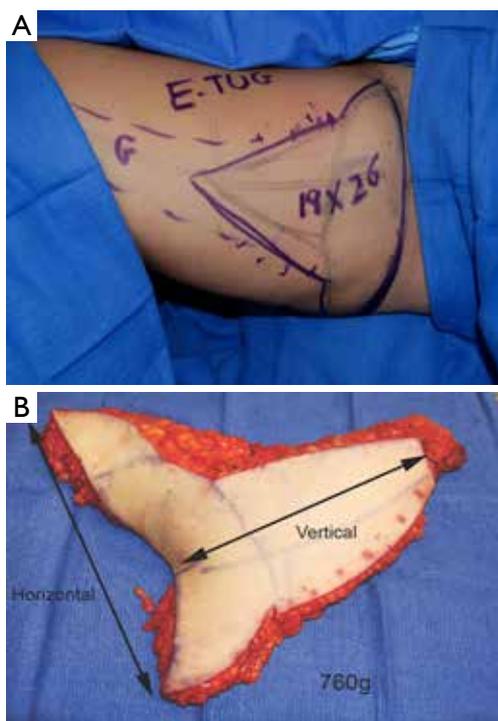


Figure 11 (A,B) Intraoperative preoperative marking of a “tri-lobed” skin paddle design in TUG myocutaneous flap for breast reconstruction. TUG, transverse upper gracilis.



Figure 12 Preoperative marking of “S” shaped skin paddle design for TUG myocutaneous flap in breast reconstruction. TUG, transverse upper gracilis.

described as the extended TUG flap. Saint-Cyr *et al.* have shown this surgical approach to be appropriate to gain size without increased morbidity (43).

The gracilis is a flat type II (Mathes and Nahai) muscle flap of the medial thigh and in the presence of adductor longus and magnus it is expendable. The dominant pedicle arises from the ascending branch of the medial circumflex

artery or directly from the profunda femoris and enters the muscle belly on its deep surface in the upper third, at 9-12 cm inferior to the pubic tubercle. Usually two or three vascular pedicles enter the muscle, the most proximal usually being the dominant pedicle. The dominant pedicle can provide up to 6-7 cm in the length and on entering the muscle it divides into an ascending, descending, transverse branches running in parallel with the longitudinal muscle fibres and commonly anastomosing with the second vascular pedicle. The dominant pedicle provides musculocutaneous perforators to the overlying skin in the proximal third of the muscle and direct fasciocutaneous vessels from the medial circumflex artery, or superficial femoral artery in the distal portions of the muscle.

The skin paddle was traditionally designed longitudinally with variable distal perfusion, however Yousif *et al.* showed that perforators had a tendency to travel in a horizontal direction with perforators posterior to the gracilis muscle and this led to re-design of the skin paddle (37). The potential skin territory is thought to extend from the rectus femoris to the biceps femoris and selective angiographic studies of the dominant pedicles have demonstrated vascular cutaneous territories of up to 400 cm², with the perfusion territory extending posteriorly to the gracilis muscle (44).

The skin paddle superior border is roughly 1-2 cm below the upper thigh crease concealing the donor TUG flap specifically, skin paddles can be raised up to approximately 16.5 cm × 11 cm or more, but dependent on skin laxity. The maximal anterior extension of the horizontal skin paddle is approximately 1-2 cm anterior to the lateral edge of adductor longus to avoid disruption the lymphatic basin or create a noticeable scar. Variations of the skin paddle design include combination with a vertical skin paddle, to create a tri-lobed (*Figure 11*), “L” shaped skin paddle, or “S” shaped design (*Figure 12*). When designing the tri-lobed pattern, it is important to keep the base of each lobe relatively broad which would result in an oval shape at the centre of the flap (*Figure 11A*). When wanting to incorporate horizontal and transverse laxity, the senior author would prefer the “S” design to avoid the problematic T-junction at the donor site resultant from the tri-lobed design. The vertical incision should be placed at the anterior border of the gracilis and stopped at mid-thigh level to avoid the unreliable perfusion zone of the distal gracilis territory. Fattah *et al.* have described undermining of the inferior skin incision in a bevelled fashion to recruit subcutaneous fat over the gracilis muscle and posteriorly to add flap volume, but it is restricted in the widest portion of the flap to avoid wound

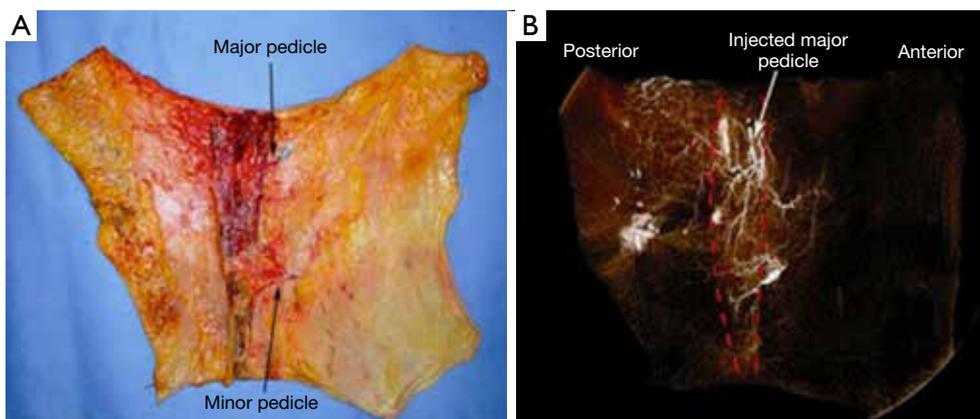


Figure 13 Cadaveric injection study of the perforator territory of the dominant pedicle of the gracilis myocutaneous flap. (A) Medial thigh flap harvest from a fresh frozen cadaver and demonstration of dominant pedicle; (B) iodinated contrast injection study demonstrating the cutaneous vascular territory of the main pedicle extends more posteriorly in the thigh.



Figure 14 (A) Donor site resultant scar at 6 weeks post procedure following TUG flap for breast reconstruction using a transverse skin paddle; (B) preoperative (left) and postoperative (right) results following TUG breast reconstruction. TUG, transversus upper gracilis.

closure with undue tension (39).

A dominant blood supply of the extended TUG flap is concentrated posteriorly (Figure 13). Therefore the posterior extension of the flap is carried out midway between the medial mid-axial line and posterior thigh midline. Any extension beyond this point may increase the risk of fat necrosis, damage to posterior cutaneous nerves, and flap-related complications. The extended transverse upper gracilis flap has consistent vascular reliability, with enough tissue for reconstruction of small to moderate sized breasts. In a retrospective study of 12 extended transverse gracilis flaps, the average flap weight was 386 grams, yielding up to 750 grams on the large size (7). The approaches described for skin paddle modifications, incorporate knowledge of potential perfusion territories, and methods to reliably maximize volume without

additional morbidity (Figure 14A,B).

Key points of vascular anatomy for TUG flap design

- (I) Reconstruct small to medium breasts;
- (II) The dominant blood supply extends posteriorly and over the proximal medial thigh (distal skin perfusion is unreliable) which must be considered when designing the skin paddle;
- (III) The extended TUG flap can optimize recruitment of posterior and medial thigh subcutaneous tissue;
- (IV) Subcutaneous tissue recruitment should be concentrated over the gracilis muscle and posteriorly only;
- (V) Limit anterior extension of the skin paddle, as this less reliably perfused and limited anterior dissection will.

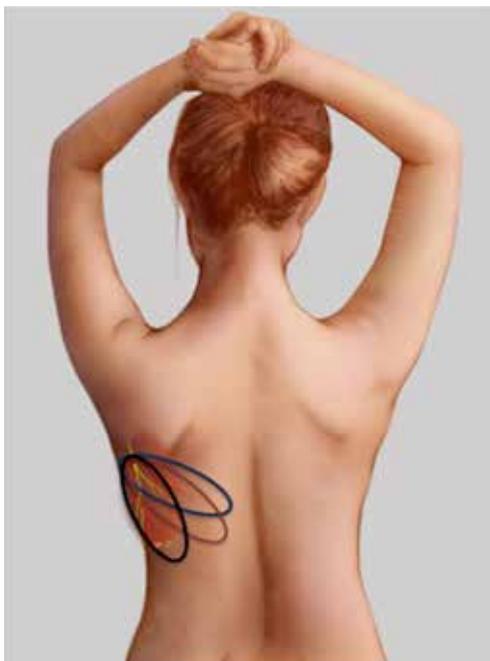


Figure 15 Potential orientation of skin paddles in a muscle sparing LD flap reconstruction based on the descending branch of the thoracodorsal artery. LD, latissimus dorsi.

Thoracodorsal artery perforator (TDAP) flap

The thoracodorsal artery perforator (TDAP) flap was first described by Angrigiani and colleagues (45) in which the cutaneous island of latissimus dorsi (LD) musculocutaneous flap was raised on one perforator without the LD muscle included. This flap is not as commonly used in autologous breast reconstruction thought to have anatomic consistencies of the perforators compared to other autologous perforator flap options. However the donor site is aesthetically acceptable and permits the preservation of the underlying LD muscle without seroma formation.

The perforating branching of the TDAP originate from the descending and transverse branches of the thoracodorsal artery, with the most dominant reliable perforators arising from the descending branch which courses along a parallel line 2 cm from the anterior edge of the latissimus muscle (46). There are around 2-3 cutaneous perforators along this course, with the proximal perforator, which is usually the largest, found approximately 8 cm below the posterior axillary fold or at the angle of the inferior angle of the scapula. This proximal perforator is usually close to the hilum of the thoracodorsal artery and nerves. In a study by Schaverien *et al.* [2010] the incidence of distal perforators along the

course of the descending branch decreased in 15 anatomical cadaveric dissections (47). In this study it was also noted that in 53% of the dissections a direct extramuscular branch from the thoracodorsal artery was observed coursing over the lateral edge of the muscle and arising as a septocutaneous perforator. In this study, CTA injection studies demonstrated the perfusion of these flaps occurred through direct and indirect linking vessels in a similar manner to DIEP flaps.

Muscle-sparing latissimus dorsi (MSLD) flap

Following on from the previous description of the TDAP flap, the MSLD flap can be used for pedicled breast reconstruction without or without combined tissue expander. In this form of autologous breast reconstruction, only the anterior portion of the LD muscle is harvested with the skin paddle. The cutaneous skin paddle of this flap and preoperative markings are based on the anatomy of perforating branches of the descending branch of the thoracodorsal artery previously described (*Figure 15*). Advantages over its thoracodorsal perforator-based counterpart includes: simple technical dissection, versatility in flap design irrespective of adequately sized perforator location, and better neurovascular pedicle protection due to the small muscle cuff retained (48,49). In the presence of a previously irradiated bed, our preferential reconstruction would be an extended LD myocutaneous flap incorporating the entire muscle.

The thoracodorsal artery provides the dominant blood supply to the LD muscle in addition to segmental perforating branches from the intercostal and lumbar arteries (Mathes and Nahai type V circulatory pattern). The thoracodorsal artery pierces the LD muscle 10-11 cm distal to the origin of its insertion (50) and bifurcates into the transverse and descending branches, with significant overlap of vascular territories via cross-linking vessels (51,52). The average distance from the axillary artery, the subscapular artery and posterior axillary fold to the bifurcation is approximately 8, 4, and 5 cm respectively (51). The mean length of the descending branch is around 15 cm (48). The descending branch musculocutaneous perfusion territory covers around 87 percent relative to the thoracodorsal artery perfusion (51). The area of greater perforator density can be found between 9 to 15 cm from the posterior axillary fold and within 4 cm from the lateral edge of the latissimus muscle (47). The descending branch of the thoracodorsal artery can then be identified coursing along the under surface of the muscle. A 3-4 cm pedicle width of muscle from the anterior border is usually harvested.

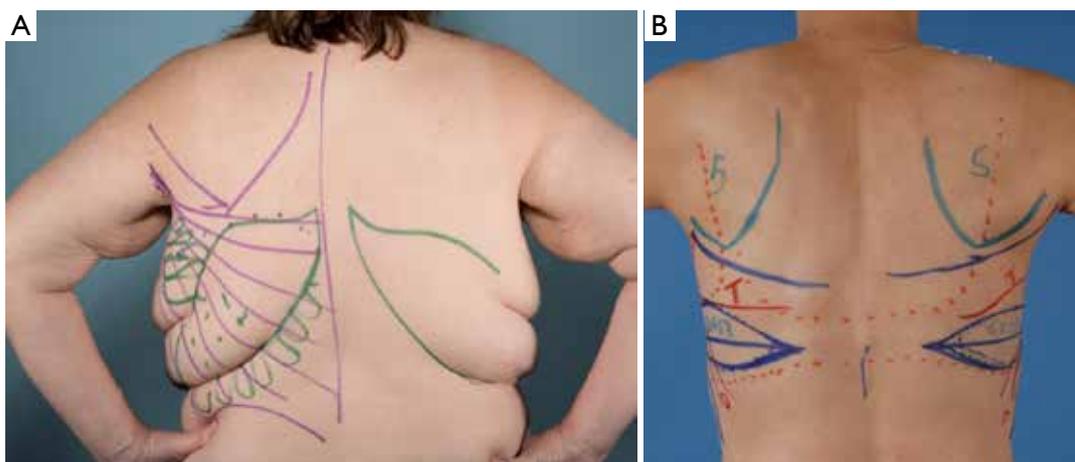


Figure 16 Preoperative planning for LD breast reconstruction and orientation of the skin paddle along natural skin tension lines and maximal size designed following the pinch test in a high pinch BMI patient (A) and a slim patient (B). LD, latissimus dorsi.

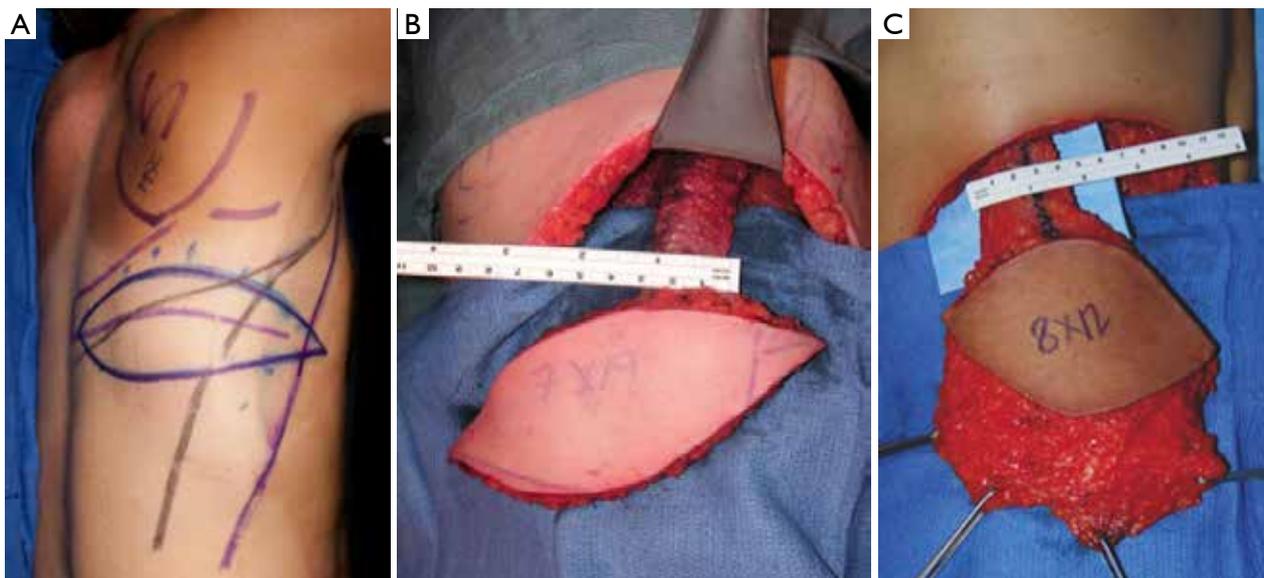


Figure 17 (A,B) Illustration of surface anatomy of MSLD flap and design of skin paddle, and flap harvest; (C) intraoperative photograph following MSLD flap harvest prior to flap transfer and inset. MSLD, muscle sparing latissimus dorsi.

Unlike the thoracodorsal artery perforator flap, the skin paddle for the descending branch muscle-sparing LD flap is not dependant on a specific perforator. The skin paddle location is designed irrespective of perforator location and can be positioned at any level along the axis of the descending branch of the thoracodorsal artery. The skin paddle, if required, is oriented transversely or slightly oblique along one of the natural adipose tissue rolls of the lower back to maximize flap dimension, place the donor scar along a natural skin crease (*Figure 16*). Skin paddle perfusion

can be optimized by centring it over the LD muscle cuff harvested along the descending branch, and consideration of perforator density in the area described above (47,51). The most lateral edge of the skin paddle should be 1-2 cm anterior to the muscle border to optimize perforators captured and therefore flap perfusion (*Figure 17A-C*) (53). Positioning the skin paddle lower in the back will provide a longer pedicle with a greater amount of freedom in the arc of rotation. The skin paddle can be raised off the muscle outside the limits of the planned muscle pedicle width.

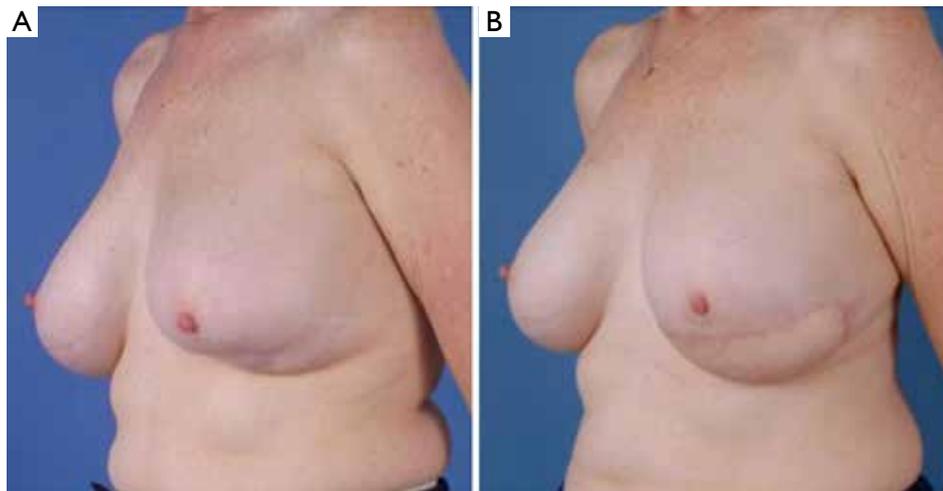


Figure 18 (A) Preoperative and (B) postoperative following MSLD for a lumpectomy contour defect of the left breast. MSLD, muscle sparing latissimus dorsi.

A large arc of rotation is made possible by two flap pivot points that are located at the flap muscle juncture and at the proximal bifurcation point (*Figure 18*) (53).

Key points of vascular anatomy for MSLD flap design

- (I) Based on dominant large perforators arising from the descending branch of the thoracodorsal artery, with usually 3-4 cutaneous perforators identified along its course;
- (II) The largest perforators are usually found proximally at the level of the inframammary fold or inferior angle of the scapula;
- (III) The skin paddle is not designed over a specific perforator unlike the TDAP flap;
- (IV) A 4-cm anterior muscle pedicle is raised with a skin paddle, which can be dissected off the latissimus muscle, except over the planned muscle pedicle. This creates a two point pivot intrinsic to the flap and adds further versatility for inset.

Profunda artery perforator (PAP) flaps

The PAP flap is a relatively newer fasciocutaneous option used in autologous breast reconstruction based on musculocutaneous perforators of the posteromedial thigh. The donor site can be conspicuous and scar well-hidden.

The medial and posterior aspects of the thigh have abundant skin and excess subcutaneous tissue. Angrigiani *et al.* [2001] described the adductor flap based on the

medial and posterior aspects of the thigh based on the musculocutaneous perforator from the first medial branch of the profunda femoris artery (54). The largest part of the posterior skin territory is supplied by the profunda femoris artery, mostly by the first and second PAPs (55). Smaller areas supplied by the adjacent vascular territories from the superficial femoral artery and inferior gluteal artery (56,57).

The proximal cutaneous perforator of the adductor magnus muscle is a major contributor to the vascular perfusion of the medial and posterior thigh skin and one of the largest musculocutaneous perforators of the body (58,59). This flap has been used as a free transfer with a transverse skin paddle for breast reconstruction when a gracilis flap or cutaneous branch of the medial circumflex artery was not appropriate (*Figure 19*) (60). Cormack and Lamberty identified a consistent proximal cutaneous perforator of the adductor magnus which is consistently located 2 cm posterior to the posterior border of the gracilis and 8 cm inferior to the groin crease. The second medial branch of the profunda femoris artery originates at approximately the same level as the second lateral perforating branch and distributes perforators to the semimembranosus and semitendinosus, and pierces the mass of the adductor muscle (61). In previous study by Saad *et al.* [2012] the dominant perforator for this flap was consistently found within 5 cm of the inferior gluteal crease and on average 6.2 cm from the posterior midline (60) and average pedicle length of 10.6 cm. Skin paddles are traditionally orientated transversely for breast reconstruction, with a maximal width of 8 cm to ensure direct closure however,

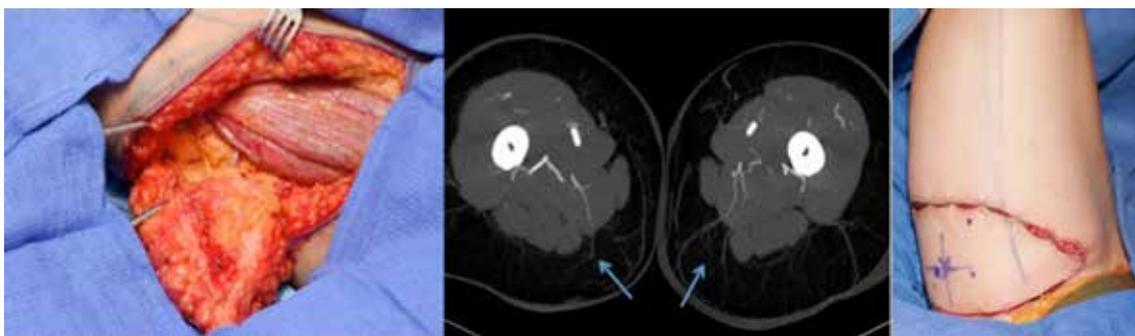


Figure 19 The intraoperative dissection of the PAP flap for breast reconstruction (left image) and the identification of large perforators on preoperative imaging (center image); intraoperative picture of the flap raised but not transferred, demonstrating the posterior position of the donor site scar. PAP, profunda artery perforator.

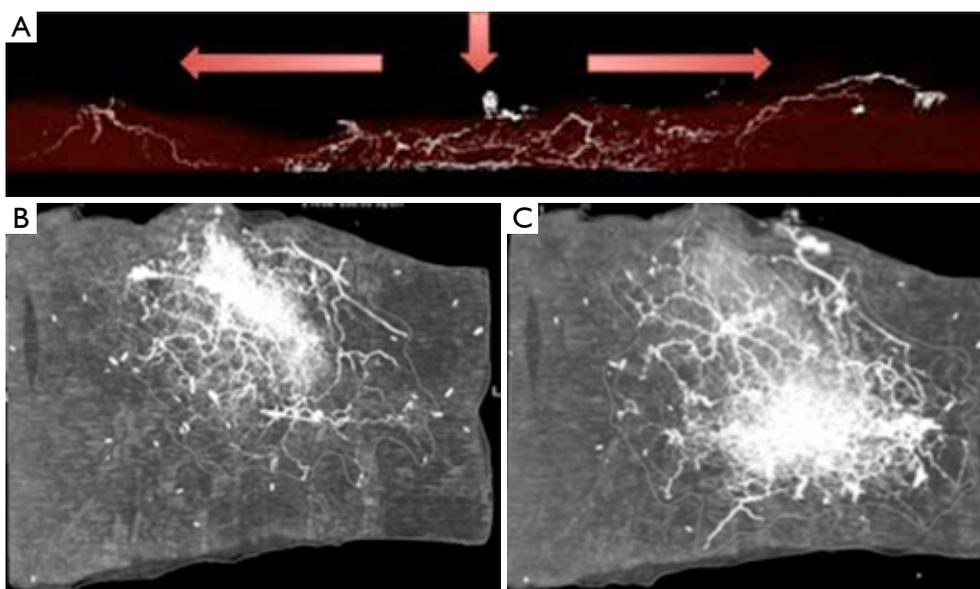


Figure 20 (A) High resolution CTA following injection of a posterior midline perforator of the PAP and demonstration of bi-directional flow to the medial and lateral aspects of the upper posterior thigh flap in cadaveric studies; (B) CT imaging of a posterior thigh flap with a proximal profunda artery perforator injected with iodinated contrast and demonstration of the individual perforator vascular territory; (C) a perforator injected in the posterior midline of the thigh with an extended territory towards the lateral thigh. CTA, computed tomographic angiography; PAP, profunda artery perforator.

as with the TUG flap, variations on design can be adapted with consideration of the tissue laxity. In our cadaveric study, the dominant proximal perforator was musculocutaneous 70% of the time, however, sometimes it did arise between the adductor magnus and semitendinosus. The mean pedicle length harvested was 10.4 cm, mean diameter of the vessels of 3.5 mm at the origin and average perforator injection territory was 265 cm². The largest concentration of perforators was located in the upper medial posterior thigh region, which is relevant

to autologous breast reconstruction. Large linking vessels were seen traversing from medial to lateral within the upper posterior thigh, and perforators that arose and travelled more obliquely towards the posterior midline of the thigh, had a bidirectional axi-ality of flow (*Figure 20*).

Superior (SGAP) and inferior gluteal artery perforator (IGAP) flaps

The superior and inferior gluteal myocutaneous flaps have

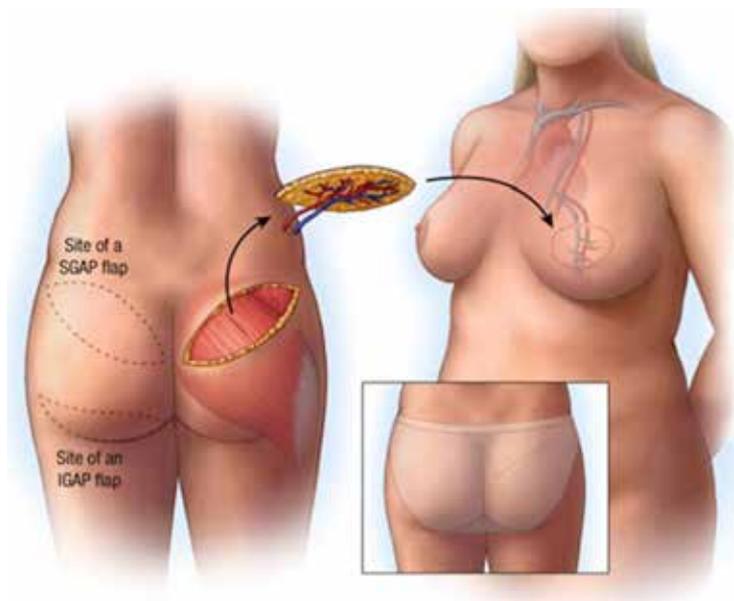


Figure 21 Illustration of anatomical landmarks of the superior gluteal perforator flap for autologous breast reconstruction. SGAP, superior gluteal artery perforator; IGAP, inferior gluteal artery perforator.

been described in breast reconstruction in 1975 and 1978 respectively (62,63). Koshima *et al.* described its use as a perforator flap, however its use in breast reconstruction as a SGAP flap was described by Allen and Tucker in 1993 (64,65). The IGAP flap is the first line alternative for autologous breast reconstruction for some surgeons when the lower abdominal donor site is of insufficient volume. As perforator flaps, the advantages of these flaps include a hidden scar and low donor-site tissue, good volume of tissue can usually be ascertained which has a similar feel to breast tissue (*Figure 21*). There may be an abundance of donor tissue in this area even in slim patients.

The superior and inferior gluteal arteries are terminal branches of the internal iliac artery, exiting the greater sciatic foramen superior and inferiorly to the piriformis muscle. The inferior pedicle is accompanied by the posterior cutaneous nerve of the thigh and greater sciatic nerve. The SGAP cutaneous territory will have around three perforators, whilst the IGAP territory has 2-4 perforators on average. The pedicle length of the IGAP is usually longer at around 7-10 cm, as it courses more obliquely through the gluteus maximus muscle, compared to the 3-8 cm pedicle length of the SGAP. The vascular territory of an individual perforator can reliably perfuse the whole region of the flap, and perfusion extends to adjacent perforator territories through direct linking vessels and recurrent flow via the subdermal plexus of the flap (66).

Conclusions

Blood supply is critical to successful autologous breast reconstruction. A fundamental appreciation of the vascular anatomy and integrity of flap designs used in breast reconstruction provides the foundation knowledge to ensure safe, more predictable flap harvest and provides scope for further modifications whilst maintaining a robust blood supply.

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Footnote

Conflicts of Interest: Dr. Saint-Cyr is a Consultant for Allergan, Mentor and Lifecell. The other author has no conflicts of interest to declare.

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Anatomy of the nipple and breast ducts

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Abstract: Over time, variations of mastectomy came up and started allowing the oncological safety and the possibility of an immediate breast reconstruction. Nipple sparing mastectomy (NSM) procedures have strongly increased in frequency and have become one of the best alternatives to treat breast cancer, also improving overall aesthetic outcomes and the achievement of contralateral breast symmetry. The nipple areola-complex (NAC) must be considered the identity of the breast concerning self-esteem of patients. This paper will remind the main anatomical topics around the nipple and breast ducts.

Keywords: Breast; breast conserving treatment; mastectomy; mammoplasty; nipple; anatomy; breast cancer

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Introduction

Over time, variations of mastectomy came up and led to enhance the oncological safety and the possibility of an immediate breast reconstruction. Those techniques permit the conservation of skin, inframammary fold and specially the nipple areola complex (NAC) to achieve better outcomes.

Nowadays the number of publications describing a nipple sparing mastectomy (NSM) has strongly increased. Regarding self-esteem the nipple must be considered the identity of the breast. Therefore, in order to increasing safe indications of sparing NAC this paper will revise the main anatomical topics around the nipple and breast ducts.

History of the anatomy (1)

Several important remarks on the NAC anatomy were made by Sir Astley Cooper [1840]. Over the last 160 years some of the anatomy knowledge acquired has changed (2) since Cooper's original work. For example, the glandular tissue is depicted as 15-20 lobes radiating out from the nipple,

whereas Cooper stated that he observed up to 22 ducts leading to the nipple but considered that many of these ducts were not functional and that there were normally fewer than 12 patent ducts opening at the nipple.

Actually, the breast is described as being composed of glandular and adipose tissue held together by a loose framework of fibers called Cooper's ligaments. Histological studies demonstrate that the lobes are composed of lobules, which consist of clusters of alveoli containing mammary secretory epithelial cells (3). The alveoli are connected to very small ducts that join to form larger ducts draining the lobules. These larger ducts finally merge to a unique duct for each lobe. Under the areola, this single duct is depicted as widening into a lactiferous sinus before narrowing at the base of the nipple and terminating at its orifice on the surface of the nipple (1,4). Adipose tissue of the breast is situated between lobes rather than within lobules.

Embryology (5)

The beginning of mastogenesis occurs around the sixth

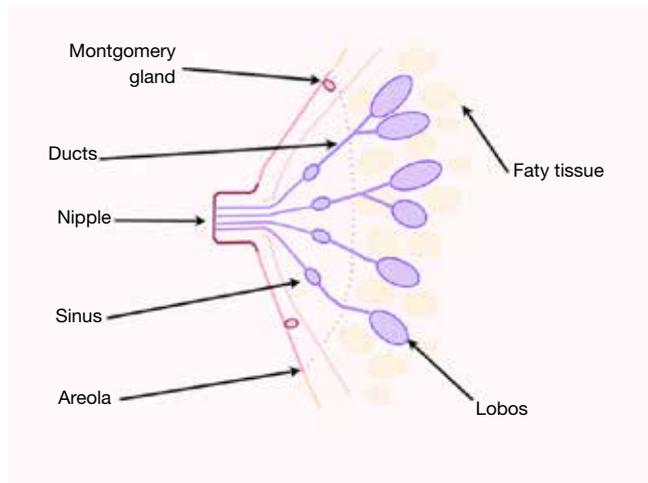


Figure 1 Schematic view of nipple areola-complex (NAC).

week of development. At 9 months there is a clear linear elevation, called “milk line”. By the eighth week, the mammary gland is formed from the thickening located in the epidermic “milk line” in the area of the final breast. There is a proliferation of basal cells that invade the underlying mesoderm and at the same time, it will occur a regression of mammary segment, yielding papillary primordium. After the 31st week of intrauterine life, papillary bag suffer occlusion, forming the NAC. The nipple will appear at time of birth.

The areola is recognized by forming a circular area free of hair sketches, also appearing branched glands around (Montgomery).

Nipple abnormality

These anomalies could be classified into multiple conditions.

- (I) Accessory nipple. One to five percent of the population, equal incidence in male and females. Usually found in the inframammary region, and are prone to the same diseases as normal nipples. Excision is only indicated for cosmetic purposes, discomfort during menstruation, anxiety, pain, or restriction of arm movement (6).
- (II) Athelia is characterized by the congenital absence of the nipple areolar complex with the presence of breast tissue (7). This condition can be inherited by autosomal dominant inheritance, or as a part of a syndrome (e.g., Poland’s).
- (III) Amastia is the complete absence of breast structures.
- (IV) Amasia is the absence of breast tissue with

preservation of the NAC.

- (V) Inverted nipple is a condition where the nipple, instead of pointing outward, is retracted into the breast. In some cases, the nipple will be temporarily protruded if stimulated, but in others, the inversion remains regardless of stimulus. Women and men can have inverted nipples. Most common nipple variations that women are born with are caused by short ducts or a wide areola muscle sphincter (8).

Anatomy of NAC (1,5)

The NAC comprises two basic structures: the areola and the nipple (*Figure 1*).

The areola has a round shape and a varying size, on average 3 to 6 centimeters, normally situated around the fourth rib level. It has sebaceous glands that make projections on its surface, forming tubercle of morgani, or areolar glands, which during pregnancy become enlarged giving rise to tubercles of Montgomery.

Some authors believe that such structures represent accessory mammary glands and it has been observed milk secretion output with manual expression of these tubers (this supposition leads some surgeons to prefer the use of the skin sparing mastectomy instead of nipple or areola sparing mastectomies because of oncological concerns).

In the center of the areola emerges a papillar cylindrical formation varying in size, averaging 10 to 12 millimeters (mm) wide by 9 to 10 mm in height. Its skin is similar to the areola, but has no sebaceous glands. It has 10 to 20 corresponding pores as the output of the milk ducts.

The NAC has no subcutaneous tissue. The skin of the nipple rests on a thin layer of smooth muscle, areolar muscle fibers which are distributed in two directions: radial and circular. The muscle of Sappey responsible for circular fibers and the muscle of Meyerholz, formed by the radial fibers.

The areolar muscle is continued in the papilla with longitudinal and circular fibers surrounding the milk ducts along with connective tissue support. Its contraction is responsible for the ejection of secretion in the milk sinuses and for the telotism of the papilla, “mimicking an erection”.

Below the areolar muscle there is a thin layer of fat which disappears as it approaches the papilla. In this pre-mammary fat tissue layer vessels are found running on radiated sense.

Blood supply

The NAC is mainly supplied by internal mammary artery,

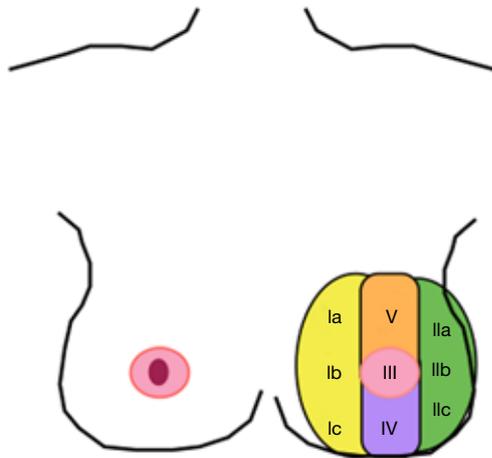


Figure 2 Schematic view of blood supply of NAC by “NACsomes” (Type I yellow—medial, Type II green—lateral, Type III pink—central, Type IV purple—inferior and Type V orange—superior).

also known as internal thoracic artery, which is branch of the subclavian artery. Internal mammary artery sends perforating branches along the first, second, third and fourth intercostal spaces, crossing the pectoralis major and irrigating the inner half of the breast, including the NAC. The intercostal arteries, which are branch of the aorta, also cross the pectoralis major and irrigate the deep surface of the breast, complementing the arterial vascularization of the NAC.

Venous drainage of breast is divided into two systems: superficial and deep. The superficial veins run along the anterior surface of the fascia, following the path of areola under the NAC, called venous plexus of Haller.

Recently the use of breast MRIs have become increasingly common in breast cancer work-up. Previously obtained breast MRIs may facilitate oncoplastic surgery by delineating the blood supply to the NAC. Seitz *et al.* (9) retrospectively reviewed 52 breasts underwent to breast MRI over 1-year period. Blood supply to the NAC was classified into five anatomic zones (“NACsomes”): medial (type I), lateral (type II), central (type III), inferior (type IV) and superior (type V). Twenty-eight breasts had type I only blood supply, 22 breasts had multi-zone blood supply (type I + II, n=20; type I + III, n=2), one breast had type II only blood supply, and a single breast had type III only blood supply. Anatomic symmetry was observed in 96% of patients. Superomedial source vessels supplying the NAC were predominant (*Figure 2*).

Innervation

The skin surface of the breast is innervated by the first to sixth intercostal nerves and a supraclavicular branch of the superficial cervical plexus. The nipple is innervated by the fourth intercostal nerve. Objective investigations about the real impact of breast size on NAC sensibility threshold should be better clarified. Longo *et al.* (10) suggested that large and heavy breasts may potentially produce a chronic nerve traction injury, causing an inverse relationship between breast volume and sensibility. Concerning mammoplasty, the fibrotic scar at the areolar edges could be responsible for the progressive sensibility worsening over time 6 to 48 months. Another interesting mentioned phenomenon is neural organization in the somatosensory system after reduction mammoplasty. Phantom sensations are reported after partial and total breast amputation for cancer, possibly due to both rearranging of peripheral nerves and remapping on different subcortical and cortical somatosensory areas.

Lymphatic drainage

The lymphatic drainage of the breast is carried through superficial and deep plexus. Superficially, there are the areolar plexus and the subareolar plexus of Sappey. The subareolar plexus receives the glandular lymph vessels and they continue towards the papilla and the areolar plexus, finally reaching the lymph nodes into the axilla.

Nipple areola-complex (NAC) by ultrasound

Ramsay *et al.* used ultrasound imaging to re-investigate the anatomy of the lactating breast. They showed that the mean number of main ducts at base of nipple was 9.6 (range, 6-18) and 9.2 (range, 4-14) for the left breast and right breast, respectively, which was not significantly different. The common sac-like appearance of lactiferous sinuses under the areola was not observed during scanning. The mean number of ducts and the diameter of main ducts were not related to nipple diameter, areola radius or milk production for individual breasts (2).

Nipple and breast feeding

Characteristics of nipple are an important factor in the success of breast feeding. Minimum nipple length of seven millimeters has shown to be specific for a highly successful

rate of breastfeeding (11). Short, flat, or inverted nipples can be related to physical and psychological negative effects for the breastfeeding mother.

Nipple-sparing mastectomy (NSM)

It is clear that when a total mastectomy is performed, the removal of the NAC increases the sensation of mutilation, and the risk of tumor involvement should be considered within the spectrum of lumpectomy, skin-sparing mastectomy, and modified-radical mastectomy. Controlled-trials have clearly demonstrated the oncologic equivalence of modified-radical and skin-sparing mastectomies, where the risk of future breast cancer occurrence is low but not zero (12,13).

Current reports on NSM are most common to single-institution series. However the number of NSM procedures has increased over the past years. Tumor involvement is reported in over 35% of the patients when tumor size is more than 2 cm, especially when the tumor is situated in the subareolar area (14). NSM can be performed for prophylactic mastectomy and the treatment of selected breast cancer with oncologic safety. The risk of skin and nipple necrosis is a frequent complication of NSM procedure, and it is usually related to the volume of breast removed (15).

Despite varying indications and surgical protocols reports of the development of cancer in the NAC following NSM are remarkably rare. Different aspects should be considered to be a selection criteria for NSM indication as well as primary tumors located outside the areola margins, no nipple retraction or bloody discharge from the nipple, no retro areolar microcalcifications, no inflammatory signs and no retro areolar tumor infiltration at the frozen section (13,16,17). In our experience the most important aspect to allow the indication for a NSM is the negative frozen subareolar biopsy area during the surgery. The rate of a positive subareolar biopsy ranges between 2.2% to 12% (13,18).

Tumoral aspects will be important to take into account when considering the indication of adjuvant therapies. Overall, NSM is associated with high patient satisfaction rates (19-22).

Tips

The NAC may host benign pathologies, especially during pregnancy and puerperium. In addition, it has an important role in breast surgery when tumors can be resected through an incision that circles the areola (periareolar or “round block technique”). This technique can be used in numerous

types of breast surgery. It allows the scar to go up to the periareolar circle which is in itself generally inconspicuous. In cases of tumoral excision, the round block produces a discreet scar and a more regular breast contour (23). Scar in this region maintains good aesthetic. It is recommended that the incisions are made just outside the areola in darker-skinned patients and immediately inside the areola in lighter-skinned patients. This is because the lighter shade of scar tissue.

Conclusions

Development of the current practice depends on a solid knowledge. Consistent knowledge of the anatomy of the NAC allows surgeons to perform better surgical procedures decreasing the sensation of mutilation without decreasing the chance of cure. The NAC is undoubtedly the identity of the breast.

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Footnote

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Essential elements of the preoperative breast reconstruction evaluation

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Abstract: A plethora of options exist for breast reconstruction and preoperative evaluation must be thorough to lead to a successful outcome. We review multiple components of the preoperative assessment including the patient's history, goals, imaging, and key elements of the physical exam. Consideration for tumor biology, staging, need or response to chemotherapy or radiation therapy is important in deciding on immediate versus delayed reconstruction. It is also important to consider the patient's anatomy, breast size and whether the reconstruction will be unilateral or bilateral. The reconstructive surgeon must accommodate all these factors to consider partial or complete mastectomy defects and guide the patient to the most appropriate reconstructive technique whether it be an oncoplastic reduction mammoplasty, expander-based reconstruction, immediate implant reconstruction, or immediate versus delayed autologous tissue reconstruction such as the deep inferior epigastric artery perforator (DIEP)/transverse rectus abdominis muscle (TRAM), latissimus, transverse upper gracilis (TUG)/profunda femoris artery perforator (PAP), or gluteal artery perforator (GAP) flaps.

Keywords: Breast reconstruction; consultation; risk factors; breast cancer; screening; motivations

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Introduction

Pre-operative planning for breast reconstruction patients is one of the most important aspects of the process and is often overlooked. Appropriate alignment of the patient's desires and the surgeon's abilities is critical to ensure realistic expectations and will contribute significantly to the patients overall satisfaction with the process, their surgeon and their final aesthetic result. We will discuss these factors based on our personal experience as well as highlight current literature regarding breast reconstruction.

Preoperative consultation

A proper initial consultation for breast reconstruction is obviously important in the road to a successful reconstruction process. This is often not a quick process and not only involves understanding the patient's medical

history and doing a physical examination, but also involves getting to know the patient from a personal and psychological perspective. A thorough evaluation of multiple factors in the patient's medical history, physical examination, consideration of psychosocial factors and imaging is necessary to select the appropriate reconstructive technique. Level of education and socio-economic status may be useful as predictors of compliance and ability to successfully complete the reconstructive process. It is important to have an idea of the driving forces and motivations behind why patients are here discussing breast reconstruction (1). If the patient is only in the office because she was sent by her breast surgeon, or her significant other is forcing her to be there, then perhaps a more educational approach should be taken to allow the patient to make her own decision.

Most patients have been referred from an oncologic surgeon with a known diagnosis and a definitive plan for

surgery and/or adjuvant therapy. It is important to review the pathological diagnosis to understand the tumor biology beyond simple benign versus malignant potential. Ductal carcinoma *in situ* behaves differently from lobular carcinoma *in situ* in contralateral risk. Some “benign” tumors (i.e., Phyllodes) have a high likelihood of locoregional recurrence and reconstruction may be best delayed. The plastic surgeon must consider the possible need for additional surgery (axillary lymph node dissection) and/or chemotherapy or radiation therapy. Patients with diffuse disease or large aggressive tumors (triple negative) may have positive margins despite mastectomy and need postoperative radiation. Lobular carcinoma and patients with BRCA mutation may benefit from bilateral mastectomy. Many surgeons prefer to delay reconstruction if postoperative radiation therapy is definitely indicated. Autologous reconstructions for example are often deferred until completion of radiation therapy and the decision on whether an expander or temporary reconstruction will be performed depends on the surgeon’s preferences, patient’s desires and also breast size/shape. If the patient has already had radiation therapy then this also directly impacts the decision process since prosthetic based reconstructions might be less preferable due to a higher complication rate (2). The reconstructive surgeon must consider individual tumor biology and staging prior to recommending reconstructive options.

A thorough review of the patient’s co-morbidities is crucial to understanding the possible risks of surgery and complications. A history of tobacco use is another important aspect of the preoperative evaluation that needs to be addressed. While smoking is not an absolute contraindication, the rate of mastectomy flap necrosis increases significantly in active smokers. Active heavy smokers with compromised vascularity of the mastectomy flap(s) may benefit from delayed reconstruction. The importance of preoperative smoking cessation is critical and even with being off cigarettes for at least a month prior to the procedure, there are certain procedures that would be less desirable in patients even with a remote history of smoking (3-5). Coagulopathy screening may be indicated in patients with significant family history or a personal history of embolic disease, deep venous thrombosis (DVT), and/or spontaneous abortions. Obesity alone is associated with higher complication rates including wound, medical, infection, major surgical, graft and prosthesis loss, and return to the operating room (6). Older age, smoking, obesity and BMI contribute to delayed wound healing in patients undergoing free tissue reconstruction (7). Patients with multiple co-morbidities are at higher risk for

complications associated with increased length of surgery associated with complex autologous reconstruction. While it is often not feasible to have patients lose weight prior to the procedure if immediate reconstruction is planned, it is important to discuss the risk of potential complications with the patient and if deemed to be risky, delay reconstruction to allow for weight loss.

Physical exam

Examination of the patient’s breast size, shape and body habitus is obviously one of the more important parts of the preoperative evaluation. The surgeon needs to determine what they are trying to match if it is a unilateral reconstruction and what options the patient has for autologous reconstruction. The current breast size and desired postoperative breast size must be noted with equal importance. Patients may not have initially considered contralateral procedure for symmetry via mastopexy, augmentation, or reduction, however, this is important since it is often not possible to match a significantly ptotic, large or even small breast. Adjusting the opposite breast will often improve the ability to provide symmetry and needs to be discussed with the patient. It is important that the surgeon guide the patient in terms of breast size. Laterality is also important in determining the most appropriate reconstructive procedure. Some patients may adamantly refuse procedures on the contralateral breast and therefore the goal will be to match the native breast, and realistic expectations need to be presented. In patients with macromastia, reconstruction is often not possible without significant reduction on both sides. Patients desiring reduction in size and have smaller tumors may be amenable to oncoplastic approach (8). Most commonly patients desire matching breast size and therefore selection of implant versus tissue will depend on the volume of tissue available. Patient should be counseled that contralateral symmetry procedures are performed either simultaneously or in a delayed fashion (9).

During the examination attention should be focused on the patient’s breasts to note overall size and shape, location and size of masses in the breast/axilla, the position of the inframammary fold and nipple (grade of ptosis), nipple deformity (i.e., inversion), location of the biopsy scar, any chest wall deformity (i.e., pectus), skin changes (peau d’orange or radiation fibrosis) and any asymmetries. Measurements of the sternum to nipple, nipple to fold, and base diameter are taken to aid in selection of implants.

For patients considering autologous tissue reconstruction,

Table 1 Proposed checklist in pre-operative evaluation

The workup
Tumor stage, size, type, ER/PR/Her2neu
Surgical plan or history (lumpectomy vs. mastectomy, immediate vs. delayed)
Chemotherapy or radiation therapy plan or history
Current size, desired size
Family history (breast disease and coagulopathy)
Contralateral breast imaging/pathology
Prior surgical history (donor site)
Smoking
Patient expectations/goals and compliance
Comorbid conditions (HTN, DM, CAD, obesity, hypercoagulable disorders)
Examination
BMI
Size and location of tumor or mastectomy defect
Breast size (base diameter, volume, shape), ptosis
Skin quality (radiation changes, scar)
Nipple areolar position (ptosis)
Contralateral breast (size, shape, projection, ptosis)
Donor site (abdomen, back, thighs, buttocks)
Imaging
Mammogram
Ultrasound
MRI breast
PET scan
CT angiography
MR angiography

the possible donor sites with adequate volume must be thoroughly examined. The abdomen is commonly used and should be noted for any previous surgical scars which may have damaged the vascularity or caused hernias. The Pfannenstiel scar is commonly encountered nowadays following Caesarian sections or hysterectomy but does not necessarily preclude the use of the abdominal tissue (10). Patients with subcostal scars are at slightly higher risk for abdominal wound healing complications (11). Approaches can be modified in such patients to minimize donor and flap morbidity utilizing preoperative imaging (12). While the back may lack adequate volume in a thinner patient, it may be ideal in obese patients with ample tissue (13). Alternatively if the abdominal donor site and back are not suitable, the inner thigh region can be considered for a transverse upper gracilis

(TUG) flap (14) or profunda femoris artery perforator (PAP) flap (15). Also, the gluteal region is available in women using the superior or inferior gluteal artery perforator (SGAP/IGAP) flap (16). Some women may find these specific donor sites less culturally acceptable.

Pre-operative imaging

Any concern for disease in the contralateral breast requires complete evaluation with imaging and or biopsy prior to intervention to avoid missing any pathology. A review of preoperative imaging such as mammogram, ultrasound and MRI studies is useful to understanding tumor size and location. Additional preoperative imaging may be ordered by the reconstructive surgeon in mapping perforator anatomy to expedite surgery (17,18). Both CT angiography (CTA) and MR angiography require specific protocols for obtaining useful mapping of the perforator location (19,20). Preoperative CTA prior to deep inferior epigastric artery perforator (DIEP) flaps demonstrate good correlation between perforator locations to reduce operative time. However, clinical judgment at the time of dissection is still important in final perforator selection and successful flap harvest since the imaging may be inadequate. Keys *et al.* noted only 62 or 76 planned perforators were ultimately selected, with 23/52 flaps involving intraoperative changes based on clinical findings not apparent on preoperative imaging (21). For patients with prior extensive abdominal surgery, preoperative imaging can confirm the viability of perforators for abdominal based flaps. Preoperative imaging can also improve the chances of successful DIEP versus transverse rectus abdominis muscle (TRAM) flap harvest and decrease partial flap failure (22). The disadvantages include increased preoperative costs, radiation exposure, risk of contrast nephropathy, and a small risk of incidental findings requiring additional intervention. Nonetheless, several studies demonstrate reduced surgeon stress, decreased donor and recipient site complications, and improved operative time (23). Ultimately, the surgeon must use his/her best judgment in utilizing preoperative imaging appropriately to facilitate perforator flap breast reconstruction.

Conclusions

Preoperative evaluation of breast reconstruction is a complex process involving multiple components (*Table 1*). A successful relationship should be established after thorough

evaluation of each individual patient history, imaging, physical exam, goals, and discussion of options to decide on the optimal reconstructive technique.

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Footnote

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Preoperative digital mammography imaging in conservative mastectomy and immediate reconstruction

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Background: Digital mammography clearly distinguishes gland tissue density from the overlying non-glandular breast tissue coverage, which corresponds to the existing tissue between the skin and the Cooper's ligaments surrounding the gland (i.e., dermis and subcutaneous fat). Preoperative digital imaging can determine the thickness of this breast tissue coverage, thus facilitating planning of the most adequate surgical techniques and reconstructive procedures for each case.

Methods: This study aimed to describe the results of a retrospective study of 352 digital mammograms in 176 patients with different breast volumes who underwent preoperative conservative mastectomies. The breast tissue coverage thickness and its relationship with the breast volume were evaluated.

Results: The breast tissue coverage thickness ranged from 0.233 to 4.423 cm, with a mean value of 1.952 cm. A comparison of tissue coverage and breast volume revealed a non-direct relationship between these factors.

Conclusions: Preoperative planning should not depend only on breast volume. Flap evaluations based on preoperative imaging measurements might be helpful when planning a conservative mastectomy. Accordingly, we propose a breast tissue coverage classification (BTCC).

Keywords: Breast tissue coverage; conservative mastectomy; digital mammography

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Introduction

Oncoplastic surgery, which combines oncologic and reconstructive surgery, has become increasingly popular (1-3). Conservative mastectomy, including skin sparing mastectomy (SSM), nipple sparing mastectomy (NSM), and skin reducing mastectomy (SRM) (1), is a well-established, validated (4), and widely used procedure for breast cancer treatment; in such cases, immediate breast reconstruction is the current standard (1,4).

Ideally, oncoplastic surgery will provide aesthetically pleasing results while achieving appropriate oncologic safety (5). However, a potential pitfall of these oncoplastic techniques is uncertainty regarding the blood supply to the remaining flaps and the nipple-areola complex (NAC) (2,3). Post-procedural nipple and skin necrosis rates as high as 38% have been reported (5). Patients with a large cup size or a previous history of surgery or radiation are considered high risk for nipple-sparing mastectomies

because these factors are associated with even higher rates of complications (2).

Currently, standard film mammograms do not allow the clear identification and measurement of non-glandular

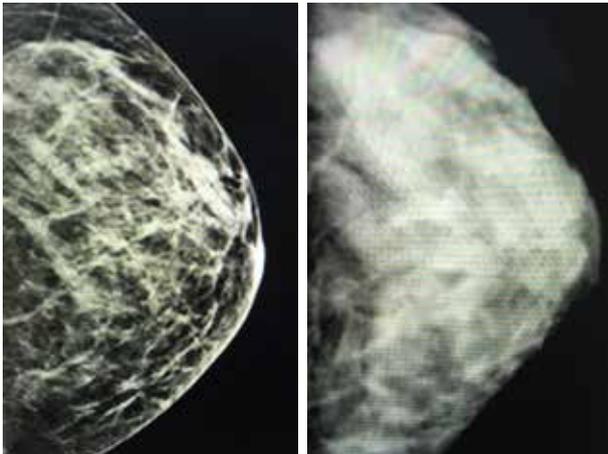


Figure 1 Difference of density between digital and standard (film) mammograms of a same patient.

breast tissue coverage. In contrast, digital mammography clearly distinguishes gland tissue density from tegument and fat coverage; accordingly, this preoperative imaging modality can determine the coverage thickness (6,7) (i.e., distance between the breast skin and Cooper’s ligaments surrounding the gland; *Figures 1,2*). As incision planning, treatment selection, surgical technique, and reconstructive procedures are usually related to the breast volume, tumor characteristics, and surgeons’ and patients’ preferences, preoperative information regarding the breast tissue coverage thickness might highlight the likelihood of post-mastectomy flap issues and assist with the planning process, rather than relying on breast volume alone as a guideline (2).

Methods

A total of 176 Caucasian women were stratified into five groups according to the Laldardie and Jouglard (8) classification of breast volume. Descriptive statistics regarding data from each group are summarized in *Table 1*.

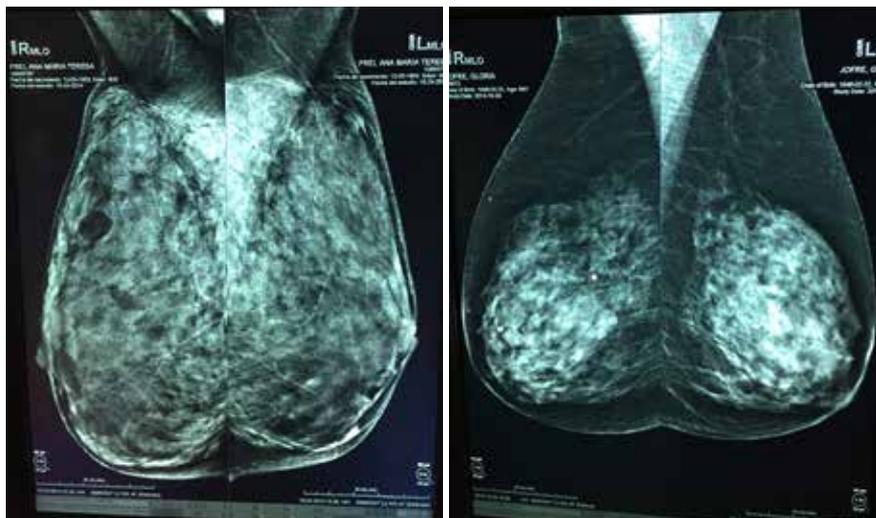


Figure 2 Pre operation. Digital mammograms, Group D. Breast volume between 801 and 1,000 cc, showing different thickness in breast tissue coverage on two different large breast patients.

Table 1 Descriptive patient data					
Breast volume	Group A 200-400 cc	Group B 401-600 cc	Group C 601-800 cc	Group D 801-1,000 cc	Group E 1,001-1,500 cc
Number of patients	30	42	35	36	33
Breast volume (cm ³) median value	292	459	652	936	1,263
Breast coverage median value (cm)	1.02	2.43	2.62	1.68	1.7

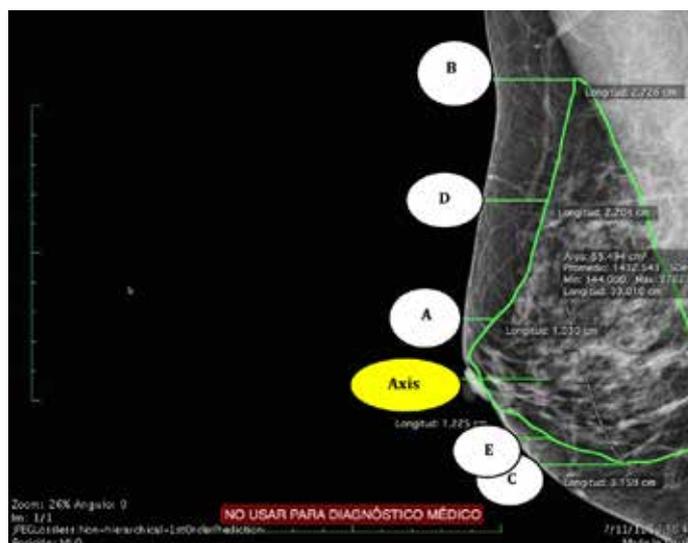


Figure 3 Measurements over digital mammogram with OSIRIX software on Dicom format.

Classification	Size (cm)	Coverage
Type 1	<1	Poor
Type 2	1-2	Medium
Type 3	>2	Good

Initially, 200 patients who underwent preoperative digital mammography for conservative mastectomy at our institution between January 2013 and February 2015 were selected randomly. Twenty-four cases were excluded. The exclusion criteria were severe breast asymmetry (>20% difference in size between breasts) and previous breast surgery. A total of 352 preoperative digital mammograms corresponding to the 176 remaining patients were retrospectively reviewed. The subject ages ranged from 33 to 70 years (mean: 49 years).

Breast volume was assessed using the BREAST-V (9), a free simple tool for IOS and Android devices (available from the Apple Store and Google Play Store, respectively) based on a mathematical algorithm that allows estimations of breast volume using direct measurements of three anthropomorphic values. Patients were stratified into groups as described above. All digital mammographic studies were performed on a 3D Selenia Dimensions Full Field Digital Mammograph (Hologic, Bedford, MA, USA). A single evaluator obtained all measurements with OSIRIX Software (available at www.osirix-viewer.com) from DICOM-format

digital mammogram files with a lateral medium oblique incidence and angulation between 40° and 50°.

Breast tissue coverage measurements were reported in cm and mm. For each mammogram, measurements were taken at five different points (*Figure 3*) as follows:

With the axis corresponding to the nipple line:

- A: Parallel to and 2 cm above the nipple (Axis);
- B: Parallel to the superior border of the gland;
- C: Parallel to the inferior border of the gland;
- D: Parallel to and at a midpoint between A and B;
- E: Parallel to and at a midpoint between the Axis and C.

For each image, average tissue coverage was obtained and correlated with the corresponding breast volume group (A to E; *Table 1*).

Statistical analyses were performed using R software (version 2.14.2) (10). As 95% of our sample fell within approximately two standard deviations of the mean, we obtained mean tissue cover thickness measures to establish reference intervals for our breast tissue cover classification. As a result, breast tissue coverage was coded as poor (type 1), medium (type 2), and good (type 3) according to the mean standard deviations of the overall values (*Table 2*).

Results

Differences between two directly consecutive breast volume groups were not statistically significant; however, there was a trend toward a flap thickness increase when comparing groups with greater differences in breast volume. Breast

Table 3 Numbers of patients by volume (A-B-C-D-E), clustered in three different groups according to breast soft tissue coverage

Group	N	Type 1 (<1 cm)	Type 2 (1 to 2 cm)	Type 3 (>2 cm)
A	30	19	9	2
B	42	12	20	10
C	35	8	15	12
D	36	6	14	16
E	33	7	13	13
Coverage		Poor	Medium	Good

tissue coverage varied from 0.2 to 4.4 mm, with an average of 1.952 cm (*Table 1*). The median values for measurements A, B, C, D, and E were 1.02, 2.43, 2.62, 1.68, and 1.71 cm, respectively.

In our analysis of breast tissue coverage and breast volume (*Table 3*), we observed the following. In group A (30 patients with breast volumes of 200-400 cm³), 19 patients had tissue coverage of 0.1-1 cm, 9 had tissue coverage of 1.1-2 cm, and 2 had tissue coverage exceeding 2 cm. In group B (42 patients with breast volumes of 401-600 cm³), 12 patients had tissue coverage of 0.1-1 cm, 20 had tissue coverage of 1.1-2 cm, and 10 had tissue coverage exceeding 2 cm. In group C (35 patients with breast volumes of 601-800 cm³), 8 patients had tissue coverage of 0.1-1 cm, 15 had tissue coverage of 1.1-2 cm, and 12 had tissue coverage exceeding 2 cm. In group D (36 patients with breast volumes of 801-1,000 cm³), 6 patients had tissue coverage of 0.1-1 cm, 14 had tissue coverage of 1.1-2 cm, and 16 had tissue coverage exceeding 2 cm. In group E (33 patients with breast volumes of 1,001-1,500 cm³) 7 patients had tissue coverage of 0.1-1 cm, 13 had tissue coverage of 1.1-2 cm, and 13 had tissue coverage exceeding 2 cm.

Discussion

To our knowledge, no reports have previously addressed the relationship between breast tissue coverage and breast volume. However, adequate fat tissue coverage thickness is one of the most important independent factors in immediate breast reconstruction and flap survival (11-13). Anatomically, the vascular network that ensures flap survival and NAC runs between Cooper's ligaments and the skin (14). Compression of this vascular network by implant insertion, surgical damage, tissue tension at closure, or extremely thin flaps might endanger vascularization, and such events have

been shown to cause tissue damage in the distal parts of flaps (8-21). Consideration must therefore be given to this preoperative breast tissue coverage measure as an important factor in immediate reconstruction.

Preoperative evaluation of gland coverage can help to predict the viability of the remaining flaps after conservative mastectomies and to select the optimal immediate reconstructive procedure to diminish post-operative coverage complications. Additionally, the use of surgical materials may be evaluated according to this coverage measure. According to our classification, for patients in the Poor coverage group (type 1), it would be helpful to add supplementary coverage for the reconstruction, such as ADM, retropectoral implant placement, and delayed fat grafting. In the medium coverage group (type 2), a 2-stage reconstruction should be suggested to avoid tension at the flap closure, whereas in the good coverage group (type 3), single-stage reconstruction with implants could be performed.

One of the most important factors for vascularization of the remaining post-mastectomy flaps is preservation of the skin perforators and flap thickness (11,12,17,18). The remaining skin flap thickness after gland resection during conservative mastectomy plays an important role in flap integrity and NAC vitality. Cooper's ligaments separate the mammary gland from the superficial fat and skin tissue layers that contain the vascular plexus, of which the mastectomy flaps are composed (13). The vascularization and, therefore, the viability of the remaining flaps may be compromised after gland resection if this flap tissue coverage is too thin and/or closure tension is forced. Preoperative information regarding this tissue coverage is therefore of the utmost importance to avoid complications associated with immediate reconstruction procedures (11,16,17).

The selection of mastectomy and reconstruction procedures should be made jointly by the oncologic and plastic surgeon based on objective pre-operative information (12,18,19). In this study, we observed that breast tissue coverage and breast volume are independent factors (*Table 1*). This finding suggests that a preoperative measurement of the breast tissue coverage thickness is important for surgical decisions.

For large breasts, conservative mastectomy is usually designed according to the Wise pattern for skin reduction, shape, and projection. This procedure is considered suitable for single-stage reconstruction with implants (4). Regardless of breast volume, however, a preoperative evaluation of

tissue coverage is crucial for surgical planning by both the oncologic and plastic surgeon as this factor is directly related to flap and NAC ischemia/necrosis. Thin flaps can lead to ischemic complications following mastectomies and reconstructive procedures (11,17). Preoperative digital mammography is therefore potentially useful not only for tumor detection, but as an objective tool for predicting the resulting flap thickness, thus improving patient safety.

Flap damage after mastectomy is a serious complication during immediate breast reconstruction (22-24). Preoperative breast tissue coverage and flap thickness evaluations via digital mammography should be considered during surgical planning, and the proposed classification may help to identify patients at high risk for flap ischemia and necrosis. Digital mammography offers the possibility of preoperative measurements and better predictions of flap thickness and vitality after mastectomy (6,7), thus improving patient safety (13,14,20,25,26).

Based on the obtained range of coverage values, we propose a 3-stage breast tissue coverage classification (BTCC) as follows: type 1, ≤ 1 cm (poor coverage); type 2, 1-2 cm (medium coverage); and type 3, > 2 cm (good coverage; *Table 2*). This classification may inform the rational use of materials for individual patients rather than according to breast volume, surgeon's experience, or comfort (21,27). As a result, preoperative communication between the reconstructive and oncologic surgeons regarding the incision choice and integumentary preservation according to digital mammogram findings might lead to improved outcomes with a decreased rate of complications.

This study has generated normative data for breast tissue coverage measurements in different breast volumes to provide three thickness classification levels. This information may be useful as a reference for future investigations of various breast surgical procedures and for the rational use of materials in conservative mastectomies and immediate reconstruction. Our study is limited, however, by the lack of validation of the BREAST-V tool against standard 3D virtual techniques; nevertheless, this tool underwent a strict development process that included internal and cross-validation of the model to verify the reliability of the algorithm (9,19). A comparison of the predictive performances of BREAST-V with a previous published formula demonstrated higher accuracy when evaluating breast volumes on new breasts (i.e., those not used to derive the formula). These considerations highlight the reliability of this tool.

Conclusions

This report provides a complete data bank of normative non-glandular breast tissue coverage measurements from digital mammograms across a wide range of breast volumes, and suggests that breast volume and flap thickness are independent factors; in other words, large breasts, (C, D, and E volume categories) can have poor tissue coverage, whereas small breasts (A and B categories) can have good tissue coverage.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Nipple areola complex sparing mastectomy

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Abstract: Breast conservative therapy (BCT) is established as a safe option for most women with early breast cancer (BC). The best conservative mastectomy that can be performed, when mastectomy is unavoidable, is nipple-areola-complex sparing mastectomy (NSM), which allows the complete glandular dissection preserving the skin envelope and the nipple areola complex. In the treatment of BC, the cosmetic outcomes have become fundamental goals, as well as oncologic control. NSM is nowadays considered an alternative technique to improve the overall quality of life for women allowing excellent cosmetic results because it provides a natural appearing breast. The breast surgeon must pay attention to details and skin incision must be planned to minimize vascular impairment to the skin and the nipple. Preservation of the blood supply to the nipple is one of the most important concern during NSM because nipple or areolar necrosis is a well-described complication of this surgery. Another issue associated with the nipple preservation and the surgical technique is oncological safety related to nipple-areola-complex (NAC) involvement in patients with invasive BC. The authors present their experience on 252 NSM performed in the Breast Surgery Unit in Forlì. Careful selection of patients for this surgical procedure is imperative and many patients are not ideal candidates for this procedure because of concerns about nipple-areolar viability as women with significant large/ptotic breast, pre-existing breast scars and history of active cigarette smoking. To extend the benefits of nipple preservation to patients who are perceived to be at higher risk for nipple necrosis the authors describe technical modifications of NSM to allow nipple preservation and obtain good cosmetic outcomes.

Keywords: Breast cancer (BC); breast conservation; breast surgery; mastectomy; outcome

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Introduction

Breast conservative therapy (BCT) is the gold standard in the treatment of the majority of women with early breast cancer (BC) (1). BCT provides long-term survival rates equivalent to those of total mastectomy while preserving the breast (2).

However, approximately one-third of women still require a mastectomy, because of their own preference or because a breast-conserving therapy would not be compatible with the distribution of the disease and the tumor size (with respect to the breast size), either from the oncological or aesthetic point of view.

Nowadays oncological breast surgery has to be

performed sparing no effort in maximizing also cosmetic results, and even mastectomies, when unavoidable, should conform to acceptable aesthetic results (3).

Respecting these concepts, today we have on tap the so-called “conservative mastectomies” which entail the removal of all the breast parenchyma together with the tumour, while saving the skin envelope of the mammary gland and therefore leaving the patient with a normal breast appearance after the reconstruction procedure (4).

The most conservative procedure is nipple-areola-complex sparing mastectomy (NSM), which involves the complete glandular dissection and preserves the whole skin mantle, including the nipple-areola-complex (NAC). It is of course an invasive procedure, but safeguarding the integrity

of the NAC, which removal is recognized as a factor that exacerbates the patient's feeling of mutilation (5), offers acceptable cosmetic results.

There have been some controversies regarding the oncologic safety of this procedure, and the NSM has also introduced a set of complications that were not a concern with total mastectomy, such as nipple and areolar necrosis (6).

Indications

The overarching principle guiding surgical management of women with BC remains oncological safety.

Careful selection of candidates to NSM is imperative and requires a combination of good clinical assessment with modern imaging techniques.

NSM may be indicated in order to treat extensive or multicentric DCIS and LCIS, multifocal/multicentric invasive ductal or lobular carcinomas (more than 2 cm distant from nipple, without skin involvement and/or pathologic discharge from the nipple) and BRCA1/2 mutation carriers. Beyond the oncological indications, the conventional NSM procedure is suitable for small-medium breasts only (NAC-inframammary fold distance <8 cm), when breast conserving surgery is likely to result in unsatisfactory cosmetic results or when in keeping with patient's preference (7).

Conversely, carcinoma infiltrating the skin and/or NAC (cancer within 2 cm from the base of the nipple), inflammatory carcinoma, pathologic discharge from the nipple (C4-C5) and nipple Paget's disease are considered absolute contraindications to NSM.

Previous radiotherapy, active smoking, diabetes, obesity, recent peri/subareolar surgery, large and ptotic breasts (NAC-inframammary fold distance >8 cm, NAC below the infra-mammary crease and suprasternal notch to nipple distance of 26 cm or more) and extensive lympho-vascular invasion are considered relative contraindications. Patients with large breasts or with grade 3-ptosis are not encouraged to have this procedure because of the increased risk of nipple necrosis and asymmetries.

Surgical technique

The current nipple-sparing mastectomy technique is a feasible procedure with a low rate of postoperative complications.

The goal of the breast surgeon is to remove the breast glandular tissue while maintaining a viable skin envelope.

All patients undergo a preoperative clinical and instrumental evaluation consisting in anamnesis, physical examination, mammography, ultrasonography and, when available, magnetic resonance images (MRI) which appears essential to determine nipple and retroareolar morphology.

Skin incisions

The choice of incision appears to affect cosmesis, technical ease in performing the operation and vascular viability of the nipple.

Sacchini *et al.* (8) described four different types of skin incisions for NSM. The periareolar incision with lateral extension can be performed on the inferior or superior areolar edge. This allows excellent exposure for the dissection of the retroareolar ducts and lateral breast tissue and bleeding can be easily controlled. The lateral extension can extend up to 7 cm, facilitating dissection of the lateral margin of the pectoral muscle for implant placement. This incision, however, may compromise blood supply at the periphery of the skin flaps and areola, and can cause ischemia of the areola. This kind of incision is no longer practically used. The transareolar incision with peri-nipple and lateral-medial extension may reduce the risk of ischemia to the lower portion of the areola. The possible sequelae of this incision is downward nipple projection caused by the peri-nipple scar formation. The trans-areolar and trans-nipple incision with medial and lateral extension involves bivalving the nipple. This incision does not compromise the vascularity of the nipple or areola and provides the best exposure to the retro-areolar ducts. The mammary crease incision can be performed inferiorly or laterally for a length of 8-10 cm (9). With this incision, the scar is the least evident, and the vascularization of the skin flap is preserved by the superior and medial vessels. However, access to the breast parenchyma in the parasternal and subclavicular regions is limited, and adequate removal of tissue in these regions may be compromised. The italic S incision extends from 1 cm out of the lateral edge of the areola to the external equatorial line and allows for easy access to all breast quadrants and also permits an access to axillary lymph nodes (*Figure 1*).

Rawlani *et al.* (10) investigated the effect of incision choice on nipple necrosis and outcomes of NSM; periareolar incision resulted in significantly more cases of nipple necrosis compared with the lateral or infra-mammary incisions (31.8% *vs.* 6.25%) and in 23.8% of cases nipple necrosis was complete.

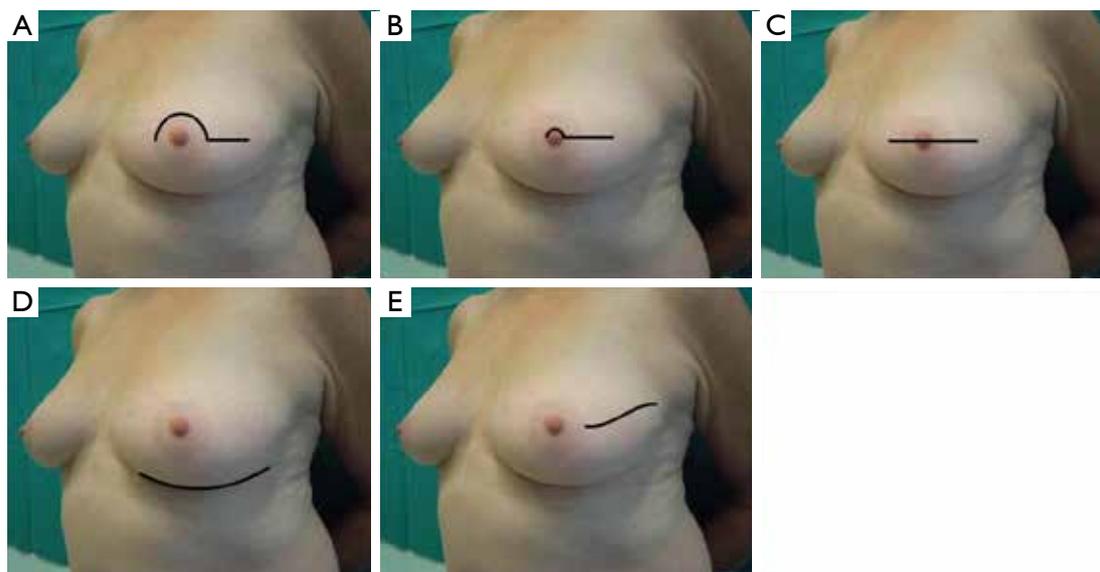


Figure 1 Skin incisions. (A) Periareolar with lateral extension; (B) transareolar with lateral extension; (C) transareolar/transnipple; (D) infra-mammary crease; (E) italic S.



Figure 2 Hydrodissection of the areola.

Glandular dissection

Following incision, skin flaps are raised in most instances using electrocautery. It is recommended to find the plane between the subcutaneous fat and the breast glandular tissue, to detach the superior part of the breast by dissecting the Cooper ligaments first and then remove the mammary gland along the pectoralis major fascia (9). The dissection should preserve, whenever it is possible, the subcutaneous fat layer and its blood vessels (11). Under the NAC, the breast glandular tissue closely adheres to the overlying dermis with little or no fat interposed.

The NAC is elevated just beneath the level of the deep dermis. Following breast removal, by nipple eversion the central ducts are transected at the base of the nipple. Dissection of the ducts should be performed with scissors rather than with electrocautery to avoid thermal damage to the subdermal vascular network of the NAC.

In our surgical practice NAC isolation is performed by hydrodissection of the areola: a 20 cc saline solution containing 2.5 mcg/mL of adrenaline is injected into the deep sub-areolar dermis to obtain complete detachment of the skin (*Figure 2*), then the areola is isolated by dissecting the swollen plane with scissors and the nipple may be cored without increasing the risk of ischemic complications (12) (*Figure 3*).

Hydrodissection causes swelling and widening of the virtual spaces among connective tissue fibers in the subdermal plane. As nipples survive on the blood supply from dermal vessels (13), NAC isolation along a plane that extends deep into the dermis is thought to cause minimal vascular injury to the nipple, thus maintaining its viability; adrenaline is commonly used in surgical practice to keep bleeding to a minimum, a procedure that eliminated the need to use the cautery which, in itself, could damage the dermal vessels of the nipple.

Retroareolar tissue specimen is sent for intra-operative frozen section biopsies or evaluated with permanent histology. If the tissue results positive for carcinoma the NAC is removed.

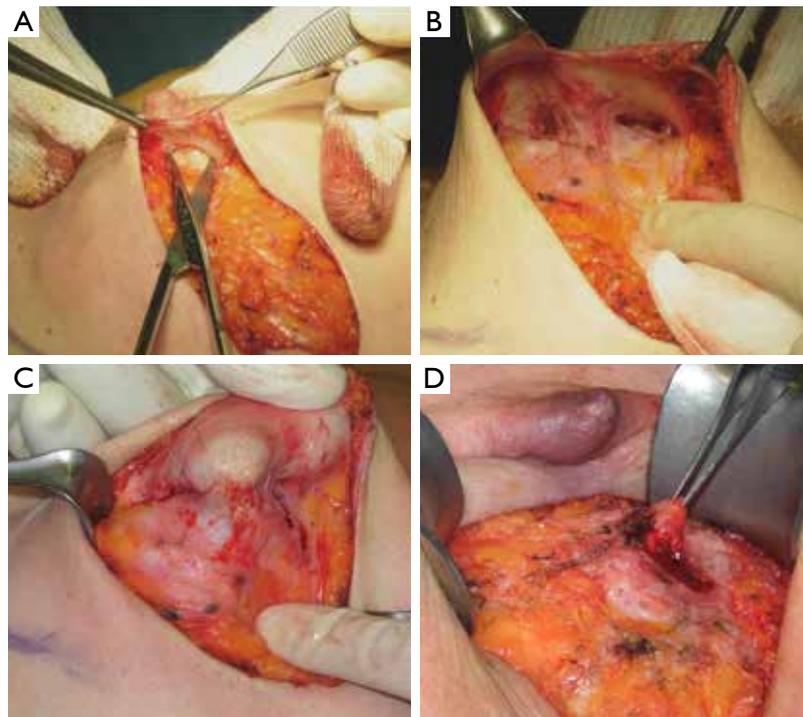


Figure 3 Nipple-areola-complex isolation. (A,B) Duct bundle dissection; (C) nipple eversion; (D) nipple coring.

Breast reconstruction

The preservation of the whole skin envelope and the NAC implies the necessity of immediate breast reconstruction, either with a tissue expander/permanent implant in a submuscular pocket, or with autologous flaps (DIEP, GAP, TRAM).

If a prosthetic reconstruction is chosen, a direct-to-implant procedure is normally performed for small sized breasts because it is likely that minimal expansion of the subpectoral pocket is required. A two-stage reconstruction is otherwise performed in medium-sized breasts because the pocket tissue has to be expanded by a temporary expander before inserting a large prosthesis (14).

Schneider *et al.* demonstrated that NSM and free-flap breast reconstruction can be safely and reliably performed also in selected patients with large ptotic breasts (15).

In order to cover and support the inferior aspect of the breast pocket and optimize aesthetic results, acellular dermal matrix (ADM) is increasingly being used in implant-based breast reconstruction; however, its use has not yet gained universal acceptance because of reported postoperative infection and seroma formation rates (16).

Controversial aspects

Nowadays, as quoted by Rusby *et al.* (17), the three main issues associated with NSM are oncological safety, nipple viability and aesthetic outcome.

Oncological safety

Routine removal of the nipple in mastectomies has been performed on the base of the risk of occult nipple involvement. Studies have shown that occult NAC involvement in BC patients with invasive carcinoma varies from 0% to 58% (18).

Parks (19), Jensen and Wellings (20) and Wellings (21) demonstrated that breast ductal and lobular cancer arises in terminal duct lobular units (TDLUs).

Stolier *et al.* (22) reviewed 32 nipple specimens obtained from mastectomy, detecting the presence of TDLUs in only 3 (9%) of the nipples examined and all TDLUs were located at the base of the papilla. No TDLUs were found in the tip of the nipple. Stolier's results showed that the infrequent occurrence of TDLUs in the nipple papilla consequently renders the development of a primary cancer

in this area unusual.

Vlajcic and colleagues (23) identified prognostic factors predictive of NAC involvement by cancer. According to their analysis, the NAC could be safely preserved with tumor size <2.5 cm and tumor-to-nipple distance >4 cm.

Larger tumours have higher rates of occult nipple malignancy: the overall incidence of nipple involvement in tumours smaller than 2 cm is 9.8%; 2 to 5 cm, 13.3%; and greater than 5 cm, 31.8% (24-26).

Simmons *et al.* (27) identified tumor location as a variable that reliably predicts nipple involvement. In their study, the overall frequency of nipple involvement was 10.6% (23 of 217 cases). When the tumor was located in central or retroareolar regions, the nipple was involved in 27.3%, when located in the other quadrants it was in 6.4%.

Kissin and Kark detected an higher nipple involvement in patients with central tumors located within 2 cm from the areolar margin and in women with four or more positive axillary nodes (28).

There is strong evidence to suggest that reduced tumor to nipple distance (<2 cm), lymph node metastasis, lymphovascular invasion (LVI), presence of an extensive intraductal component, HER2 amplification, multicentricity and retroareolar location increase the incidence of occult nipple malignancy (29).

Recently Caffrey *et al.* carried out the first study to evaluate whether pathological features on preoperative core biopsy could predict retroareolar involvement. Ninety-three cases of NSM with available biopsy slides were retrieved; the overall rate of retroareolar malignancy was 11.8% (11/93). They observed a correlation between preoperative identification of LVI on core biopsy and positive retroareolar margin and this should contribute significantly to surgical decision making in combination with current radiological and clinical criteria (30).

Patients undergoing mastectomy are usually those with the most extensive disease and attention to the oncological safety is paramount; namely, complete removal of the gland including the axillary tail must be warranted. Conservative mastectomies offer to the surgeons poorer exposure as compared to conventional mastectomy and consequently patients are at increased risk for close or positive margins with reported rates as high as 28.8-68.8% (31-33).

NSM is considered a safe option for women with BC and does not seem to increase recurrence or diminish survival. Loco-regional recurrence (LRR) rates in patients after NSM have proven to be equivalent to those seen with other procedures (34), and recurrence at the nipple is very rare (35).

In 2009, Gerber *et al.* (36) compared three groups of patients who underwent either modified radical mastectomy (MRM), skin sparing mastectomy (SSM), or NSM and provided almost 10 years of extended follow-up data. The overall local recurrence rates amounted to 10.4% (SSM), 11.7% (NSM) and 11.5% (MRM). There were no significant differences between subgroups and NSM was deemed an oncologically safe procedure.

Likewise, Kim and co-workers (37) noted no differences in local recurrence and overall survival comparing the same three groups of patients as Gerber, after a follow-up of 101 months.

Benediktsson and colleague (38) reported a series of 216 patients who underwent conservative mastectomy with a long follow-up (median 13 years). The 10-year frequency of LRR was 20.8% and they attributed this high rate to the lack of radiotherapy in many cases that later would have received it according to international guidelines. The LRR rate in irradiated patients was 8.5%.

At the European Institute of Oncology (39), from March 2002 to December 2007, 934 women underwent NSM: 772 patients with invasive carcinoma (group A) and 162 with intraepithelial neoplasm (group B). Median follow-up was of 50 months. In group A were reported 28 (3.6%) local recurrences in the breast at 5-year cumulative incidence and 6 (0.8%) were observed on the NAC. In group B 9 (4.9%) recurrences were noticed in the breast and 5 (2.9%) on the NAC. The 5-year overall survival was 95.5% for the invasive group and 96.4% for the total series of 934 patients. The LRR, distant recurrence and death rates reported in this study are consistent with the results of the literature after radical mastectomy or SSM.

Poruk *et al.* (40) performed a chart review on patients who underwent NSM compared to SSM for BC treatment and prophylaxis over a 6-year period evaluating the outcomes including recurrence and survival and they found no significant differences.

Low rate of local recurrence in most series, and 5-year survival rates of more than 95%, are reassuring for both patient and surgeons.

Nipple viability

Preservation of the blood supply to the nipple and areola is the most important concern during NSM. Nipple or areolar necrosis is a well described complication of this operation and presents an increased risk of implant loss (41).

The reported incidence of necrosis following NAC

preservation ranges from 0 to 20 per cent in the literature, with higher rates in patients receiving radiation.

It is likely that nipple necrosis is influenced by patient factors and surgical technique. Komorowski *et al.* (42) showed that age over 45 years has a significant impact on the risk of necrosis and Garwood and co-workers (33) reported smoking to be a risk factor due to direct skin vasoconstrictor effects of nicotine.

Garwood *et al.* (33) also showed that incisions extending around more than 30 per cent of the areolar circumference are an independent risk factor for necrosis. They also investigated the impact of reconstruction type: immediate reconstruction with a fixed-volume implant may result in immediate tension on the skin flaps and thus affect the blood supply to the nipple causing nipple necrosis, so they increased the use of tissue expanders. The use of tissue expanders helps to reduce surgical complications preventing ischemia and necrosis of the preserved NAC through a progressive stretching of the skin.

In fact, viability of the NAC relies on preservation of the blood supply to the nipple, ducts, and the surrounding skin.

Rusby and colleagues (43) conducted a microanatomical study of nipple microvessels and their position relative to lactiferous ducts in 48 mastectomy specimens. The peripheral 2-mm layer of a non-irradiated nipple tissue was found to contain 50% of the blood vessels in cross-section, whereas 66% of the blood vessels were identified in 3-mm of the periphery. According to their study, leaving a peripheral rim of 2-mm of nipple skin and subcutaneous tissue resulted in complete excision of the duct bundle in 96% of cases, while a thicker peripheral rim of 3-mm would lead to complete excision in 87% of cases only, with a consequent higher risk of leaving residual duct tissue in place.

Stolier *et al.* (44) reported 82 consecutive cases of NSM in which a 2-mm rim of tissue was left in place at the tip of the nipple with no skin loss affecting the NAC.

When performing NSMs, Petit *et al.* (45) prefer to leave a 5-mm thick layer of tissue in place under the areola with the aim of preserving NAC microscopic circulation. However, such a procedure requires intra or post-operative radiotherapy to decrease the risk of local recurrences and this, in turn, exposes the nipple to ischaemic damages with an increased risk of NAC necrosis.

Nipple necrosis can be partial and does not always result in complete skin loss. Sacchini *et al.* (8) reported a nipple necrosis rate of 11%, but 59% of these cases involved less

than one third of the nipple.

Van Deventer noted that the small vessels feeding the NAC are in turn fed by much larger vessels, the most prominent of which are the internal mammary artery (internal thoracic) and the lateral thoracic artery (46). Based on the work of van Deventer as well as Palmer and Taylor, it would appear that the 2nd intercostal perforator off the internal mammary artery is the main vessel supplying the NAC; it is the principal perforator in 85% of cases (47) and it should be spared whenever possible.

The 2nd intercostal perforator exits the pectoralis major muscle outside of the breast parenchyma and it is easily damaged as skin flaps are developed, therefore elevating skin flaps over the medial breast should be done carefully. This vessel can be also used for free flap vascularization. Other perforating vessels which emerge from the 3rd and 4th interspaces off the internal mammary artery are also important in NAC vascularization. Those that arise more medially into the substance of the breast are sacrificed to achieve complete breast removal.

It is likely that NAC necrosis cannot be entirely avoided. However, to limit these complications, the breast surgeon must pay attention to details and incisions must be planned to minimize vascular impairment to the skin and NAC. It could be helpful to carefully review breast imaging prior to surgery, not just to evaluate the extent of disease but also to help define the appropriate anatomic planes of dissection (48). In fact, patients expect not only adequate oncological outcomes but also good cosmetic results and, aside from the flap failure or loss of a synthetic implant, nothing affects the cosmetic outcome more than skin or nipple necrosis.

Cosmetic outcomes

It is generally accepted that NSM provides better cosmetic results than MRM and the importance of NAC preservation within the context of a woman's body image has been addressed in several studies.

In a study by Gerber *et al.* (34), patients and surgeons evaluated aesthetic results of SSM versus NSM 12 months after surgery. Patients expressed similar satisfaction with SSM and NSM and most aesthetic outcomes were reported as good or excellent. However, the surgeons reported 74% of NSM as excellent result and 26% as good, while only 59% of SSM were rated excellent, 22% good, and 20% fair.

Didier *et al.* reported that patients expressed a very high level of satisfaction with nipple preservation and perceived NSM as helpful to better cope with the traumatic

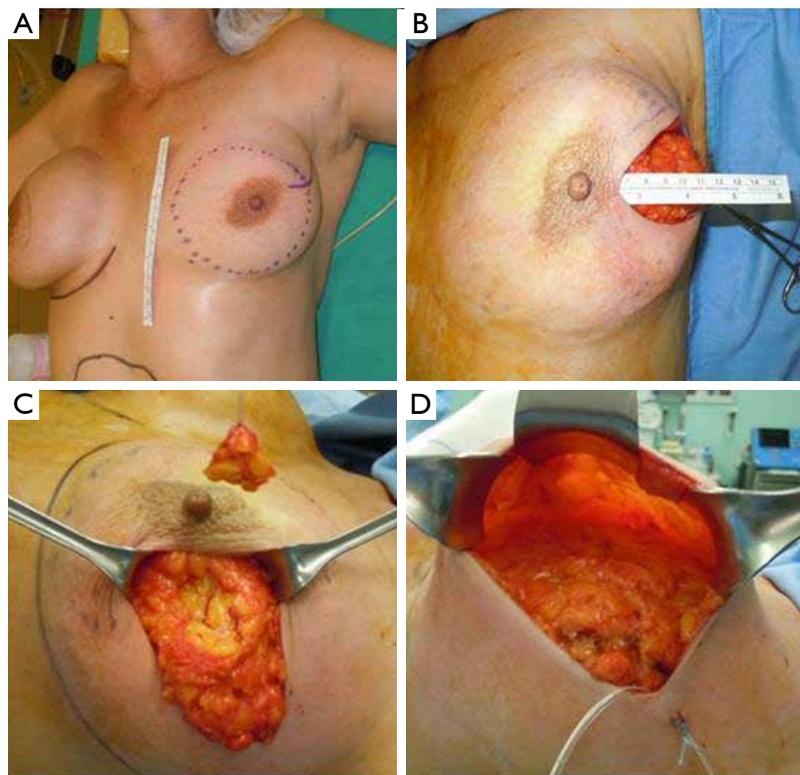


Figure 4 Surgical delay procedure. (A) Preoperative drawing: area of dissection; (B) preparation of the retroareolar and periareolar skin flap; (C) retroareolar biopsy; (D) skin flap.

experience of BC and loss of a breast (49). Their study focused on patient satisfaction with body image, sexuality, cosmetic results, and psychological adjustment. Patients with NSM were more willing to see themselves or be seen naked, and had significantly lower ratings for feelings of mutilation. Patients who underwent NSM as compared to SSM reported significantly greater satisfaction with cosmetic results. NSM was judged good/excellent from 78.6% of patients, and 42.9% of them retained nipple sensation (50).

Adjuvant radiotherapy decreases the aesthetic results even after a long period of time; if the need for post-operative radiation therapy is known, a delayed reconstruction is preferable (36).

NSM has evolved as an oncologically safe technique to improve the overall quality of life for women providing excellent cosmetic outcomes. NSM grants a natural appearing nipple and enables the patient to have a truer sensation of having her own breast. In addition, the procedure spares the patient from operations associated with nipple reconstruction, decreasing the anxiety and costs.

Alternative surgical techniques

Many patients are not ideal candidates for NSM because of concerns about nipple-areolar viability. Significant large/ptotic breast (defined by location of the NAC below the infra-mammary crease and suprasternal notch to nipple distance of 26 cm or more), pre-existing breast scars and history of active cigarette smoking are considered risk factors to nipple necrosis following NSM (51).

In order to extend the benefits of nipple preservation to patients who are perceived to be at higher risk for nipple necrosis, a surgical delay procedure 7-21 days prior to mastectomy aimed at improving nipple viability was proposed by Jensen *et al.* (52).

The skin flap is elevated in the plane of a therapeutic mastectomy beneath the nipple-areolar complex and surrounding mastectomy skin, so that the surgical wound stimulates an improved blood supply to the areola; approximately 4-5 cm of surrounding skin is undermined (*Figure 4*).

The incision is vertical from the edge of the areola toward

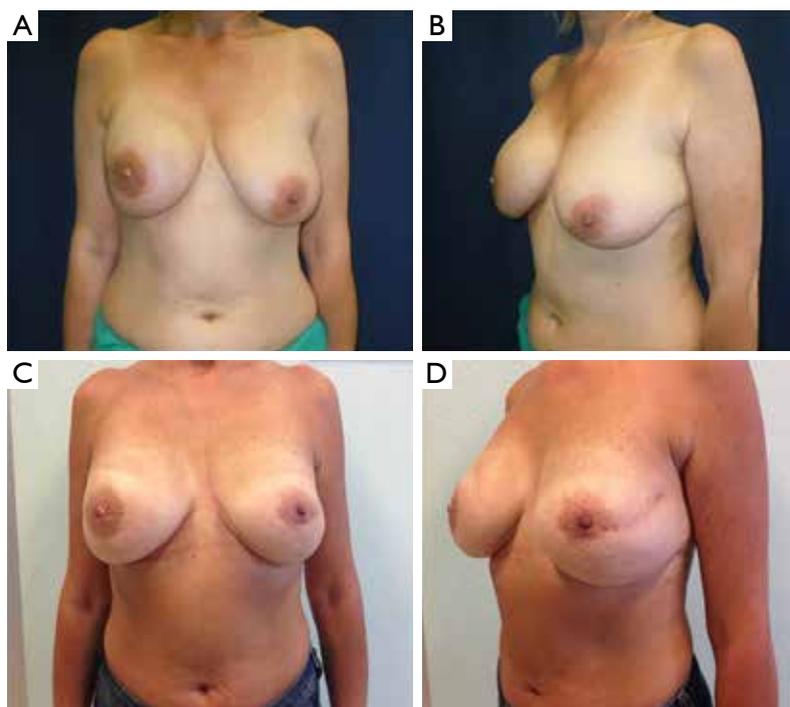


Figure 5 Surgical delay procedure: our experience. (A,B) Preoperative; (C,D) post-surgical delay and nipple sparing mastectomy.

the infra-mammary crease or lateral to the NAC extending toward the axilla. Attention is paid to the concept of “degrees of perfusion” of the nipple areola complex (53). In patients who have had previous circumareolar or periareolar incisions, special attention is directed at maintaining the existing blood supply through the scar tissue by not using the previous incision around the NAC.

Alternatively, a “hemi-batwing” procedure can be performed in patients with breast ptosis; the skin within the hemi-batwing pattern remains undisturbed during the delay procedure and will be removed with the underlying breast gland at the time of mastectomy.

After this delay procedure, blood supply for the retained NAC is maintained for 360° of perfusion if a linear incision is chosen, or it is limited to 180° of perfusion through the inferior mastectomy flap if a hemi-batwing pattern is used.

Special attention is paid to the transection of the ducts connecting the breast gland to the nipple.

A 1-cm thick biopsy of this ductal tissue (directly beneath the nipple) is submitted for permanent section pathology. If it is positive for tumor the NAC is removed at the time of mastectomy. Similarly, sentinel node biopsy can be brought forward, and in case of positivity on permanent section, an axillary dissection can be made at the time of mastectomy,

7-21 days later according to the traditional technique.

Jensen *et al.* (52) performed the nipple-areolar delay procedure on 31 nipples and all of them survived.

Palmieri *et al.* (54) recruited 18 women with T1 cancer, 2.5 cm from the NAC and 1.5 cm from the skin and pectoralis fascia. The procedure was divided into two different phases: NAC vascular autonomization using local tumescent anesthesia with electrified laparoscopic scissor; and delayed nipple sparing modified subcutaneous mastectomy plus subpectoralis textured silicone breast implant 3 weeks later using general anesthesia. No NAC necrosis was observed.

The surgical delay is a safe, simple and effective technique used to enhance vascularization of the skin flaps and the NAC. The ischemic insult induced in the first stage surgery leads to hypertrophy of the vessels and/or the development of new blood vessels. This procedure performed 7-21 days before NSM allows safe preservation of the nipple-areolar-complex in patients who generally would not be considered candidates for NAC sparing mastectomy and it can provide a better planning of surgery (*Figure 5*).

Recently our group published a technical modification of NSM that is performed through an inverted-T mastopexy,

designed with the purpose to allow nipple preservation in large and ptotic breasts (55). Sixteen procedures in 13 patients were performed, with no cases of complete necrosis requiring removal of NAC; however, this early experience has not yet received a formal outcome assessment.

The G.B. Morgagni hospital experience

The surgical technique we use for NSM (including immediate reconstruction) is similar to that described by Regolo *et al.* (9), Sacchini *et al.* (8) and Garwood *et al.* (33), and involves making an italic S incision that extends from the lateral edge of the areola to the external equatorial line, which also permits access to axillary lymph nodes. NAC isolation is performed by hydrodissection of the areola, as previously described (12).

Once mastectomy has been completed and the breast excised, a 3-5 mm thick layer of tissue is removed from the retroareolar area of the specimen and submitted for subareolar margin evaluation on frozen sections. If neoplastic tissue is detected, the NAC is removed and the procedure is converted to a SSM. All the retroareolar specimens undergo a definitive histological evaluation; if it confirms as negative for neoplasia we suggest follow up. If the definitive evaluation results positive we can consider the removal of NAC, radiotherapy or follow-up depending on histological examinations and patient preferences.

In a period between December 2006 and September 2014, in the Breast Surgery Unit of Morgagni hospital in Forlì, 252 NSM were planned: 53 (21%) procedures were converted to SSM because of intraoperative findings of cancer in retro areolar tissue and 199 (79%) NSM were performed. Histological examination of removed NACs showed the presence of 9 (17%) invasive cancer, 38 (72%) *in situ* carcinoma and 6 (11%) LIN III.

All the intraoperative biopsies of the retroareolar specimen were confirmed at the definitive histological evaluation.

Indications for surgery were risk reducing mastectomy (RRM) with prophylactic purpose in 23 cases (9.1%), *in situ* carcinoma in 83 (33%), invasive carcinoma in 127 (50.4%) and C5 pre-operative cytology in 19 (7.5%).

Among 178 patients (199 procedures) who underwent NSM and breast reconstruction, 21 had a bilateral procedure and 157 a monolateral one. Mean age of the patients was 49±8 (range, 27-74) years. The mean distance between the tumor and the nipple was 35 mm (SD: ±20; range: 5-80 mm). Multicentric tumour localization was

detected in 71 cases.

We performed 168 intraoperative sentinel lymph node (SNL) biopsies and 25 of these were positive with subsequent axillary lymph node dissection (ALND).

The post operative histological reports showed 110 (55.2%) invasive cancer (DCI and LCI), 51 (25.6%) *in situ* carcinoma (DCIS and LCIS), 14 (7%) DIN-LIN, 7 (3.6%) other histotype and 17 (8.6%) absence of neoplasia. Median follow-up was 43 months (range, 2-94 months).

In our cases we had two immediate post-operative major complications, one case of infection of the prosthesis requiring its removal and one case of severe bleeding requiring re operation to evacuate the hematoma. No complete necrosis of the NAC was identified. We observed 25 partial transient ischemia of the NAC with epidermolysis, NAC dystopia in six patients, flattening of the nipple in nine, small size of the areola in four and retraction or lateral deviation of the NAC in two cases. Nipple sensitivity and erectile capacity of the nipple appeared insufficient in most of our patients. Baker grade IV capsular contracture was noticed in one patient and grade II or III in six. The capsular contracture was subsequent to radiotherapy in three cases and in those patients we performed lipofillings.

Local recurrence developed in one patient in the subcutaneous tissue corresponding to the former tumor site (upper inner quadrant), 14 months after the initial procedure. None of our patients had recurrences in the NAC after NSM. Distant metastasis occurred in six patients (3%); two in the bones, one in the lung, one in the axilla, one in the liver and one in the ovary.

All our patients underwent immediate reconstruction with prosthesis or tissue expander, only a woman did not accept the prosthesis and we reconstructed her breast performing three lipofillings. Immediate reconstruction with subpectoral permanent implant was performed in 43 procedures (21.6%) and 156 (78.4%) were a two-stage reconstruction with a subpectoral tissue expander (*Figure 6*). The breast reconstruction has been completed with the second stage in 119 patients and 53 (68.9%) implant augmentation, 18 (23.4%) mastopexy, 5 (6.4%) mastopexy with prosthesis and 1 (1.3%) reductive mastopexy were performed to obtain symmetry of the contralateral breast.

Overall aesthetic and functional results of the post-NSM reconstructed breasts were judged by the patients and surgeons as poor (1%), good (67%) and very good (32%) results (*Figure 7*). The morphology of the contralateral breasts was considered good (65%) and very good (35%). Level of satisfaction with cosmetic results was high at the

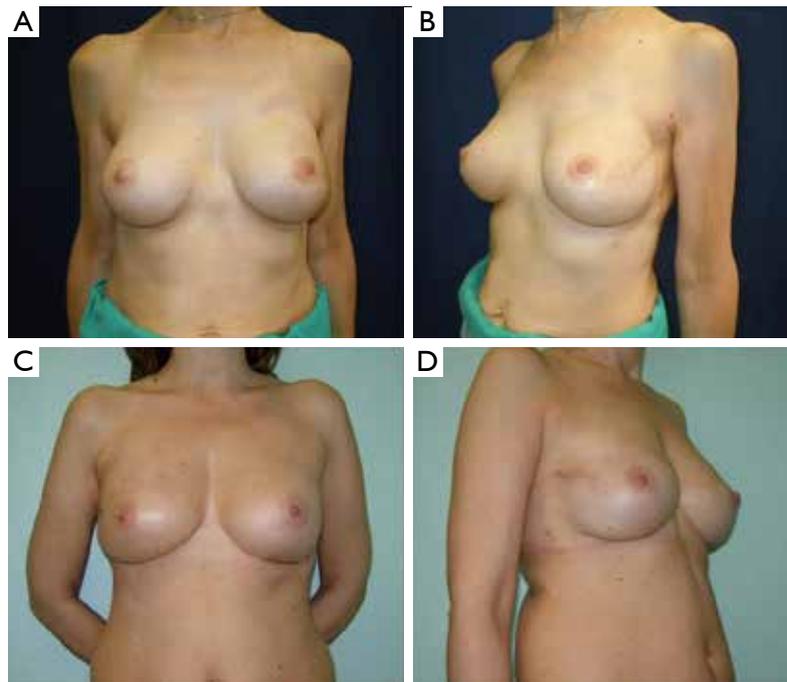


Figure 6 Monolateral nipple sparing mastectomy. (A,B) Left nipple sparing mastectomy and right implant augmentation; (C,D) right nipple sparing mastectomy and left implant augmentation.

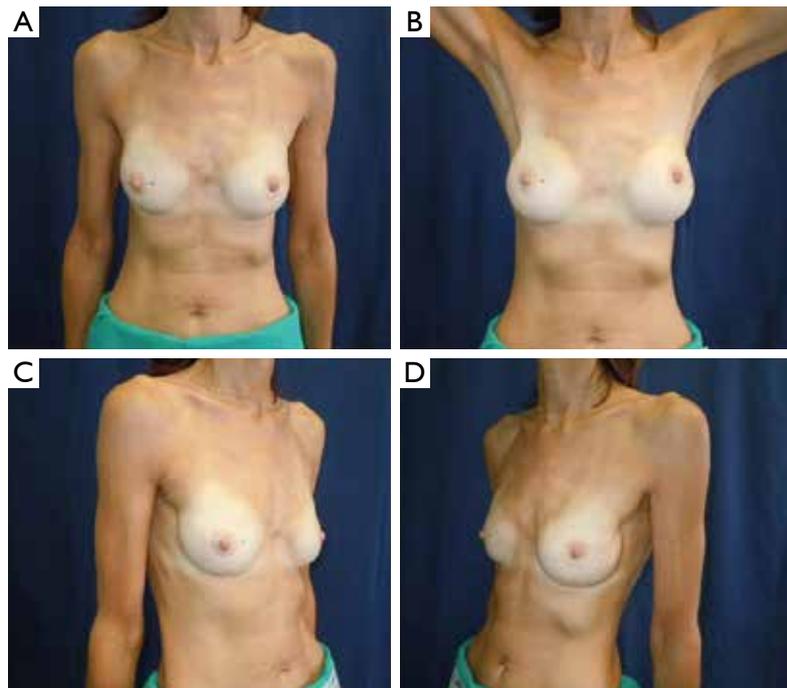


Figure 7 Bilateral nipple sparing mastectomy and immediate reconstruction with prosthesis.

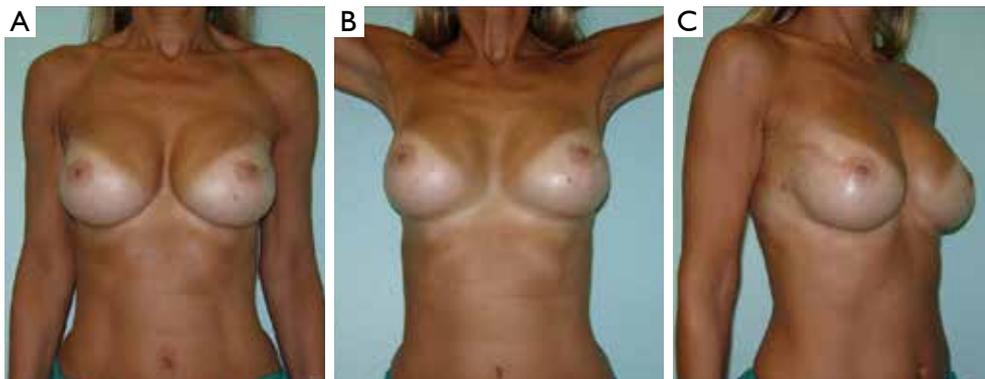


Figure 8 Bilateral nipple sparing mastectomy and a two-stage reconstruction.

end of the reconstruction process and similar between prophylactic and therapeutic procedures (*Figure 8*).

Conclusions

Nowadays NSM can be considered the best surgical option for BC treatment when the mastectomy becomes inevitable. NSM is also assessed as an elective indication in risk reduction mastectomy. This surgery allows for an excellent cosmetic results ensuring, at the same time, a correct and complete oncological radicality.

The preservation of the entire skin envelope makes this surgical procedure less traumatic from the psychological point of view of the patient and the reconstruction becomes better and more physiological. The commitment of the scientific community should aim to experiment and explore new surgical techniques that can extend the application of this procedure to an increasing number of patients.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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How to perform a NAC sparing mastectomy using an ADM and an implant

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Background: Preservation of the nipple areolar complex (NAC) provides the optimal conditions for immediate breast reconstruction (IBR). Growing evidence suggests the oncological safety of nipple sparing mastectomy (NSM) when neither NAC nor skin is affected by tumor. This paper presents our initial experience performing NSM and IBR in a selected group of patients through the inframammary incision assisted by hydrodissection.

Material and methods: The study includes 20 healthy women, aged 23-53, and referred for bilateral risk-reducing mastectomy. NSM was carried out using inframammary crease incision assisted by hydrodissection followed by IBR with an acellular dermal matrix (ADM) and an implant as presented in the attached video. Exclusions criteria were hypertension, diabetes, active smoking and previous chest radiation therapy. Data was collected retrospectively.

Results: We achieved the reconstructive goal for all 40 breasts (100%). There were no cases of NAC necrosis. Minor complications were registered in two reconstructions (5%), including one case of small partial necrosis and one case of wound dehiscence. The median follow-up was 13 months (range, 1-32 months).

Conclusions: Bilateral risk-reducing NSM and IBR can be successfully achieved through an inframammary crease incision assisted by hydrodissection. Patient selection is the key to a successful outcome.

Keywords: Nipple sparing; mastectomy; reconstruction; acellular dermal matrix (ADM); implant

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Introduction

Breast cancer treatment has changed over the last decade from radical mastectomy towards a more conservative surgical approach favoring skin sparing mastectomy (SSM) (1). Patients are more reluctant to accept a loss of their breast when other options exist and are increasingly requesting a combined ablative and reconstructive surgical procedure. Hence, SSM and more recently a nipple-areola sparing mastectomy (NSM) together with immediate breast reconstruction (IBR) are becoming a popular choice when

indicated (1-3).

The preservation of the nipple areolar complex (NAC) provides optimal conditions for IBR as opposed to SSM, where the NAC has to be reconstructed in a secondary, often challenging procedure which tends to result in a flattened and dissatisfying appearance of the breast mound (4,5). Growing evidence suggests that NSM is safe to perform when the NAC and skin is not affected by tumor (5-10). We have regularly performed NSM and IBR for the past 4 years on oncologic as well as risk reducing indication.



Figure 1 How to perform a NAC sparing mastectomy using an ADM and an implant (11). NAC, nipple areolar complex; ADM, acellular dermal matrix.

Available online: <http://www.asvide.com/articles/363>

We present our initial experience performing NSM on a selected group of patients using hydrodissection in combination with an inframammary incision and illustrate the technical aspects of the procedure performed as presented in the attached video (*Figure 1*).

Material and methods

The study population consisted of 20 women aged 23-53 who were referred after genetic consultation for bilateral risk-reducing mastectomy. Included patients had NSM and IBR using the same method, presented in this paper, at Vejle Hospital in Denmark and Telemark Hospital in Norway between September 2012 and July 2014.

The patients consented to surgery after oral and written information. Patient selection criteria were based on previously reported findings (12), including only healthy patients without major comorbidity. The exclusion criteria were hypertension, diabetes, active smoking and previous chest radiation therapy. Data was collected retrospectively by revision of charts and supplemented by patient interviews when the information was insufficient or ambiguous.

Pre-operative marking

The breast footprint was marked using a permanent marker with the patient in the upright position. The planned inframammary crease incision was then drawn below the nipple extending 8-9 cm laterally. The expected projection of the planned breast reconstruction was estimated from measurements of the breast, degree of ptosis and laxity of the skin.

Surgical technique

The surgical technique is illustrated in the video: “How to perform a NAC sparing mastectomy with an ADM and an implant”.

A preoperative dose of intra venous antibiotics was given as a standard. Following application of local anesthesia, the skin was incised at the inframammary crease marking. The breast gland was dissected of the pectoralis major muscle and thoracic wall in the subglandular plane using a monopolar cautery. The subglandular cavity was subsequently palpated to ensure that this level had been reached in the entire breast circumference. The breast was then infiltrated with a solution of 1 liter NaCl/ 1 mL epinephrine using a blunt tip cannula immediately below the subcutaneous fascia. The non-dominant hand was used to palpate the movement of the cannula ensuring infiltration in the correct plane.

Correct infiltration is paramount and the cannula should slide freely without resistance as this may indicate displacement of the tip into the wrong dissection plane. However the regions lateral and cranial to the NAC contain more fibrous tissue connecting the cutis and subcutis, and can be challenging to infuse correctly.

The dissection of the glandular tissue commenced at the level of the subcutaneous fascia using combined blunt and sharp scissor dissection. The tissue beneath the NAC as well as the fibrous adhesions laterally to the NAC were cut by careful, sharp dissection removing the entire glandular tissue en bloc through the inframammary incision, and marking it for pathologic evaluation in a standard manner.

The cavity was inspected and palpated to ensure that the ablative surgery had been performed correctly and any excess tissue underneath the subcutaneous fascia was removed, guided by vision. A subdermal, avascular dissection plane is readily found beneath the areola. The underside of the NAC was checked by eversion through the inframammary crease to make sure that no glandular tissue remnants were left behind. In all cases, the underside of the nipple was biopsied for separate histopathology and finally the cavity was checked for sufficient hemostasis.

The skin quality and viability was evaluated prior to reconstruction. The pectoralis major muscle insertion was released inferomedially using a monopolar cautery, as for a dual-plane breast augmentation, to allow partial muscular coverage of the implant.

Extended implant coverage was created using a hammock of acellular dermal matrix (ADM) (12,13). The ADM was



Figure 2 Before and after direct NSM and immediate breast reconstruction. NSM, nipple sparing mastectomy.

sutured to the inferior edge of the muscle and the desired position of the inframammary crease. Implant selection was based on breast footprint measurements, skin quality, as well as the patient's wishes for size and projection. Two drains were placed, one at the inframammary crease and the other pointing towards the axilla. The reconstruction was finalized suturing the skin in two layers using absorbable 3-0 sutures.

Drains were removed when the daily output was less than 20 mL. Oral antibiotics were administered until all drains were removed. After discharge, patient follow-up was conducted in the outpatient clinic.

Results

We achieved the reconstructive goal for all 40 breasts (100%) (Figure 2). There were no cases of NAC necrosis, neither partial nor complete. Minor complications were registered in two reconstructions (5%), one case of small partial necrosis and one case of wound dehiscence.

The ADMs used were 8×16 cm in 24 breasts and 8×20 cm in 14 breasts according to the size needed for the selected implant (Figure 3). Permanent silicone implants were used in most patients 18/20 (90%). In the remaining cases we used

expander implants 2/20 (10%). The mean implant size at the time of reconstruction was 450 cc (range, 225-700 cc).

Four women in this series (20%) had either a great degree of ptosis or macromastia too large for IBR. They received a reduction mammoplasty 3 months prior to the subsequent NSM and IBR. The combined pre-reduction mammoplasties and subsequent NSM and IBR were all achieved without complications (Figure 4).

The median follow-up was 13 months (range, 1-32 months).

Discussion

We have performed risk-reducing NSM and IBR since 2011 using hydrodissection in combination with different incisions and approaches. In this series focusing on the inframammary crease approach, reconstructive goals were achieved in all of the planned cases without any major complications. Two minor complications occurred; in the first case, ADM's were not available and the reconstruction was achieved using silicone implants and marionette suture fixation of the pectoralis muscle over the implant upper pole, as previously described by Spear *et al.* (14) (Table 1).



Figure 3 Before and after direct NSM and immediate breast reconstruction showing that the reconstructed breast is often bigger than prior to surgery because the skin envelope has to be filled out by the implant to create a correct NAC placement. NSM, nipple sparing mastectomy.



Figure 4 Before and after NSM and immediate breast reconstruction in a woman with phylloides tumors previously undergoing seven surgical procedures. A breast reduction was performed 3 months prior to a subsequent successful. NSM and immediate breast reconstruction NSM, nipple sparing mastectomy.

The patient suffered compression necrosis of the lower pole due to the tight bandage covering the sutures. She made an uneventful recovery in 3 weeks. In the other case the patient developed a blister due to wound dehiscence at the inframammary crease. The wound margins were revised under sterile conditions and the patient made a full and uneventful recovery.

We prefer the inframammary crease approach which in our experience results in a more optimal reconstruction. This technique may appear challenging at first, however, plastic surgeons are familiar with both the inframammary approach and the subglandular dissection. Consequently, the

procedure is a joint team effort performed simultaneously by a breast surgeon and a plastic surgeon. This teamwork leads to an ongoing and important discussion about skin thickness, trying to balance ablative and reconstructive surgery in a way which ensures removal of sufficient tissue, and at the same time sustaining blood supply for the remaining skin flaps for reconstruction. When we are able to identify the superficial fascia, we use this as our dissection plane. However, as described recently in a review by Robertson *et al.*, the superficial fascia is readily identified in just 56% of patients (15). When the fascia is not well identified the dissection plane is based on team experience. We have not measured the thickness

Table 1 Bilateral risk reducing NSM using hydrodissection in women with no co-morbidity

Patient	Age (years)	Hammock type	Hammock size	Implant type	Implant size (cc)	Drain days	Complications minor/major	Outcome achieved	Follow up months
1	28	None	-	Silicone	300	14	Mi	Y	32
2	39	ADM	8×16	Silicone	300	13	None	Y	31
3	30	ADM	8×16	Silicone	550	12	None	Y	30
4	49	ADM	8×16	Becker50/50	400	14	None	Y	21
5	49	ADM	8×16	Silicone	225	15	None	Y	20
6	46*	ADM	8×20	Silicone	475	14	None	Y	16
7	45	ADM	8×20	Expander	550	21	None	Y	15
8	41	ADM	8×16	Silicone	440	21	None	Y	12
9	53	ADM	8×20	Silicone	555	12	None	Y	11
10	49	ADM	8×20	Silicone	475	11	Mi	Y	10
11	40	ADM	8×16	Silicone	475	14	None	Y	9
12	38	ADM	8×16	Silicone	325	12	None	Y	8
13	45*	ADM	8×16	Silicone	420	15	None	Y	8
14	34	ADM	8×16	Silicone	440	11	None	Y	7
15	32	ADM	8×16	Silicone	420	7	None	Y	6
16	38*	ADM	8×20	Silicone	590	12	None	Y	5
17	43	ADM	8×20	Silicone	515	9	None	Y	3
18	42	ADM	8×16	Silicone	440	14	None	Y	3
19	47*	ADM	8×16	Silicone	440	14	None	Y	2
20	50	ADM	8×20	Silicone	700	11	None	Y	1

*, pre-reduction 3 months prior to NSM. NSM, nipple sparing mastectomy; ADM, acellular dermal matrix.

of the skin flaps of the studied patients. However, we found that the skin flaps varied between patients and we estimate the variation was between 4 to 8 mm.

The most recent and largest reported series on NSM by Colwell *et al.* based on 500 procedures supports our findings stating the importance of patient selection and that inframammary crease incision persistently produces better results and fewer complications (16). A lateral inframammary crease incision in combination with hydrodissection, similar to our technique, has been described earlier by Blechman *et al.* (17). Our incision is more medially placed and the patient sample more homogenous.

It seems that skin and nipple survival can be optimized by correct patient selection and lower the risk of reconstructive failure and cancer recurrence (9,12,18,19). Oncological safety is an important issue when performing NSM and IBR. However, risk-reducing NSM and IBR can be regarded oncologically safe (6,8). Reported evidence, after 5-15 years follow-up, shows that there does not seem to be an increased risk of recurrence in patients treated by the

nipple sparing technique compared to other approaches. Thus the procedure does not seem to increase the risk of tumor recurrence or decreased survival compared to other ablative methods (6-10). The use of ADM in primary breast reconstruction is well established and as in other techniques, patient selection is a key element to a successful result (12,13). The most important selection criteria are breast size and comorbidity as described above. A large ptotic breast cannot be reconstructed using this NSM technique in a satisfactory manner. Pre-shaping or the pre-reduction/mastopexia can be offered to patients undergoing risk-reducing procedures as a safe alternative as described by Spear *et al.* (20). Pre-shaping seems to cause a delayed effect by increasing the dermal vascularity of the NAC, which increases the chance of survival after the subsequent mastectomy and reconstruction (21).

Conclusions

Bilateral risk-reducing NSM and IBR can be performed

successfully through an inframammary crease incision in combination with hydrodissection. Critical patient selection is the key to a successful outcome.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Using intraoperative laser angiography to safeguard nipple perfusion in nipple-sparing mastectomies

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Abstract: The superior aesthetic outcomes of nipple-sparing mastectomies (NSM) explain their increased use and rising popularity. Fortunately, cancer recurrences involving the nipple-areolar complex (NAC) have been reassuringly low in the range of 1%. Technical considerations and challenges of this procedure are centered on nipple ischemia and necrosis. Patient selection, reconstructive strategies and incision placement have lowered ischemic complications. In this context, rates of full NAC necrosis are 3% or less. The emergence of noninvasive tissue angiography provides surgeons with a practical tool to assess real-time breast skin and NAC perfusion. Herein, we review our classification system of NAC perfusion patterns defined as V1 (from subjacent breast), V2 (surrounding skin), and V3 (combination of V1 + V2). Additionally, we describe the benefits of a first stage operation to devascularize the NAC as a means of improving blood flow to the NAC in preparation for NSM, helping extend the use of NSM to more women. Intraoperative evaluation of skin perfusion allows surgeons to detect ischemia and modify the operative approach to optimize outcomes.

Keywords: Nipple-sparing mastectomy (NSM); ischemia; perfusion; skin necrosis; breast

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The superior cosmetic results of nipple-sparing mastectomies (NSM) account for the steady increase in use of these operations. Cancer recurrences involving the nipple-areolar complex (NAC) have been reassuringly low. Wang *et al.* reviewed 981 cases of total skin-sparing mastectomy (TSSM) and immediate breast reconstruction, reporting an overall 5-year locoregional recurrence of 3% and no recurrences in the NAC (1). Similarly, others have reported equally low rates of NAC recurrences, less than 1%, thus counterbalancing some of the high rates of occult involvement of the nipple with tumor as discussed below (2-5). The oncologic safety of this procedure is further demonstrated in BRCA-positive patients who are at higher risk for developing breast cancer and in patients after neoadjuvant chemotherapy (6).

Preservation of the NAC gives way to the possibility of recurrence therein and especially of a Paget's type of recurrence. Boneti and coauthors reported comparable local recurrence rates among 227 patients undergoing SSM and 281 NSM, 6% and 5% (P=0.89), respectively (7). Lohsiriwat *et al.* reported 7 (0.8%) of 36 local recurrences were Paget's disease among 861 NSM with electron beam intraoperative radiotherapy (8). The average time interval to Paget's recurrence was 32 months (range, 12-49 months). Risk factors for this type of recurrence included invasive ductal carcinoma with extensive *in situ* component, negative hormonal receptor status, high grade, and HER2-positive subtype.

Contraindications to nipple-sparing mastectomy are straightforward, namely Paget's disease, nipple retraction or

direct involvement by tumor (9). However, in the absence of clinical changes, occult involvement of the NAC remains a concern. Tumor extension to the NAC has ranged widely, from as low as 6% to 38%, if only studies with 100 or more patients are considered (2,10-13). Clinically occult nipple involvement has been related to retroareolar location or distance of index lesion, size of primary tumor, lymph node metastases, lymphovascular invasion and HER-2 overexpression (4,14). Brachtel *et al.* found that invasive ductal histology with DCIS had the highest association with nipple involvement, while age, multifocality, BRCA positive status and neoadjuvant chemotherapy did not (2). Moreover, this group found that the absence of carcinoma in retroareolar sampled tissue correlated with the absence of carcinoma in the nipple, a sensitivity of 0.8 and a negative predictive value of 0.96. Recently, Eisenberg *et al.* reported their experience regarding occult nipple involvement in 325 NSM performed at Weill-Cornell Medical Center (15). Biopsies taken from the base of the nipple were free of tumor in 117 prophylactic mastectomies while 14% of 208 therapeutic mastectomies showed tumor cells, including five cases of LCIS. Central location of tumor and four or more positive nodes were the only two factors associated with nipple margin status. The intraoperative positive frozen section rate was considerably lower, 4.8%, a practical point to consider, as these assessments are preliminary and may require nipple resection once permanent sections are finalized. Interestingly, another 12 cases underwent nipple resection based on other considerations (cosmetic, close margin or technical reasons), finding malignant cells in an additional two cases.

Evaluation of skin perfusion

Skin flap ischemia is the most common postoperative complication affecting all skin sparing mastectomies (7). The rates for skin-sparing and NSM are 6.2% *vs.* 7.1%, respectively. The work by Chirappapha and colleagues underscore the risk of skin and NAC necrosis occurring in patients with larger breasts (16). They suggest a protocol of slow expansion with tissue expanders or the use of autologous musculocutaneous flap to prevent ischemic complications.

Visual inspection and bleeding along skin flap edges have been the traditional methods used to judge adequate skin perfusion in the operating room. Surgeons typically excise discolored, cyanotic-appearing skin or trim skin to a bleeding edge. Visual inspection can be deceptive

leading to underestimation or overestimation of ischemia. A case in point is shown in *Figure 1*, where it is likely that the presence of vascularized autologous tissue beneath the area of ischemia lessened the severity of evolving skin necrosis. Reversible conditions such as vasospasm, cooling, or low circulating volume, may affect the appearance of skin flaps. Consequently, many plastic surgeons avoid being overly aggressive in resecting areas with seemingly marginal perfusion. Beyond visual inspection, Doppler devices, tissue oxymetry, and fluorescein have been used to evaluate perfusion but have not been shown to be completely reliable in clinical practice (17). Fluorescein dye angiography has more significant side effects, 15-minute delay to visualization, and longer half-life (18). Moreover, although less expensive, it has the added disadvantage of not providing quantitative information and single use per operation.

Objective evaluation of skin perfusion is critical to the recognition of tissues with poor blood flow. Intraoperative angiography can provide real-time information on tissue perfusion, complementing visual assessments and clinical decisions (17,19). Indocyanine green (IC-GREEN™, ICG) (Pulsion Medical Systems SE, Germany; 2.5 gm/mL) is a fluorescent dye approved in the US for injectable use with reported rare allergic side effects have (20). The SPY *Elite*™ imaging system (Novadaq Technologies, Inc., Ontario, Canada) utilizes an infrared camera to capture the inflow of blood, which is visualized within seconds after intravenous administration on computer screen. The early iterations of this system monitored flow continuously for only a 60-second segment, while the upgraded equipment extends imaging over 270 seconds. This technology is being used in many centers to assess breast, mastectomy skin or myocutaneous flap perfusion in order to guide skin resection, resulting in a decrease of ischemic complications (21). Phillips *et al.* prospectively compared the fluorescein angiography to an older version of ICG-based angiography (18). The sensitivity of the two methods was similar but SPY imaging was superior in terms of specificity, as well as positive and negative predictive values. In their study, fluorescein was more likely to overestimate areas of skin flap necrosis than SPY imaging.

Evaluation of skin perfusion during mastectomy operations continues to be received with some skepticism. The sequence of events shown in *Figure 2*, illustrate the utility of SPY imaging as an intraoperative tool in a case of immediate post-mastectomy reconstruction. Compromised



Figure 1 Postoperative changes after unilateral nipple-sparing mastectomy with immediate DIEP flap reconstruction resulting from nipple-areola ischemia. Serial pictures demonstrate skin demarcation within the native NAC above island of DIEP skin at 4 days; eschar at 14 days; tissue loss involving tip of nipple and inferior aspect of areola at 40 days; and 1 year later healed with slight discoloration of lower areola and loss of nipple height. NAC, nipple-areolar complex.

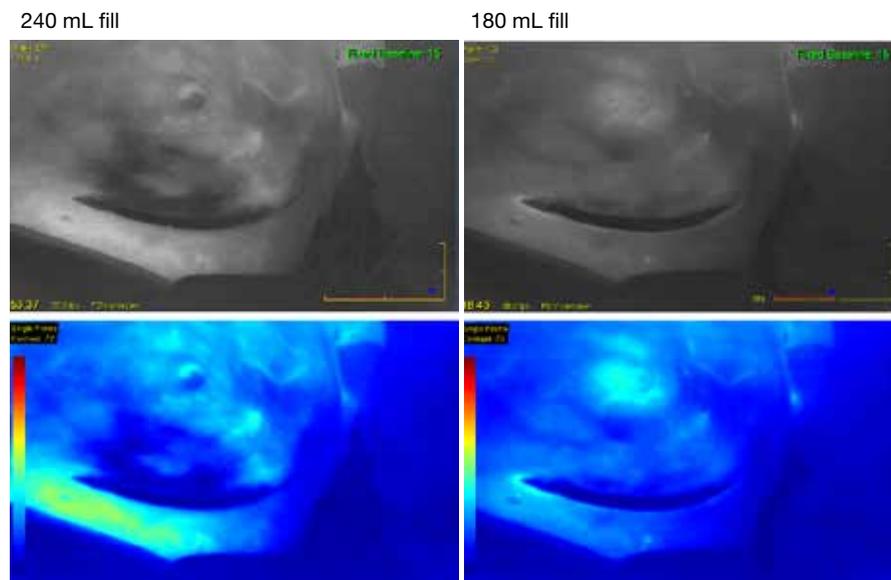


Figure 2 Intraoperative assessment of mastectomy flap ischemia. Effects of tissue expander filling on skin perfusion in nipple-sparing mastectomy. Operation was performed via an infra-mammary fold incision. Removal of 60 mL volume decreased pressure on skin flaps and restored perfusion to the areas (black) devoid of blood flow in left panels.



Figure 3 Chronic ischemic changes after NSM. Depigmentation occurring after partial ischemia and epidermolysis. NSM, nipple-sparing mastectomies.

perfusion involving part of the areola and inferior mastectomy flap can be identified on the photograph associated with 240 mL volume in the tissue expander. Removal of 60 mL, restored adequate blood flow to those areas. Accordingly no ischemic complications were noted clinically during the postoperative course. More recently, Duggal and colleagues demonstrated that ICG angiography significantly lowered reoperation rates (14.1% *vs.* 5.9%) and skin necrosis (23.4% *vs.* 13.0%) in their experience on 184 skin-sparing but non-nipple sparing, mastectomies (19). Moreover, they demonstrated a cost-benefit advantage to the use of this technology when considering overall hospitalization and reoperation charges.

Nipple-areola ischemia

Dissection of involved or at-risk breast tissue along the subdermal plane is standard practice in mastectomy operations. The primary goal in NSM is removal of all the breast tissue in the same manner without compromising the oncologic safety of the more aesthetic operation. Technically, NSM are more challenging and the larger skin envelopes more prone to ischemic complications. Impaired perfusion leads to discoloration, and partial or complete nipple necrosis (*Figures 1,3*). Thin skin flaps and pressure exerted by prosthetic reconstruction, can add to the compromise of skin blood flow in the post-operative period (1). Groups that knowingly leave breast tissue below the base of the nipple add intraoperative radiotherapy target the NAC (22). Alternatively and more commonly in the United States, the practice of coring out nipple ducts for NSM has been adopted in order to address concerns about the potential hazards of leaving breast tissue at risk in

association with the NAC.

Rusby *et al.* studied the cross-sectional anatomy of the nipple to investigate the distribution of terminal ducts coursing through (23). By leaving a 2 mm rim of nipple skin, they calculated that 96% of the total number of ducts would be excised, while a 3 mm peripheral rim would only excise 87% of ducts. In addition, they demonstrated the viability of the nipple by staining vascular endothelium and assessing blood vessels. About 50% of the nipple vessels on cross-section were preserved with as little as a 2 mm rim of nipple skin. Their observations provide useful anatomic information indicating that excision of the duct bundle should not compromise the arteriolar blood supply of nipple dermis.

The incidence of ischemic complications involving the NAC vary from study to study. Less than complete NAC necrosis affected 37.5% of women in this series with 14 of 15 of these cases healing simply with local wound care and only one requiring nipple reconstruction (24). While tissue loss is a major complication of nipple-areolar ischemia, reversible ischemia or transient ischemia that results in epidermolysis and epidermal sloughing can result in permanent discoloration of the nipple and areola (*Figure 3*).

Partial and full nipple necrosis was reported by Mallon *et al.* as 6.3% and 2.9%, respectively (4). A study from University of California San Francisco presented a lower overall rate of partial nipple necrosis, 2.0%, with only ten cases (1.5%) out of the total 657 NSM complicated by complete NAC necrosis and loss. Limiting the extent of periareolar incisions to 30% of the areolar circumference and, using a superior areolar and inframammary incisions were helpful changes in their intraoperative technique for the remaining 557 cases. This was reflected in a reduction in rates of nipple necrosis from 13% to 1.8% ($P < 0.0001$) when comparing earlier with later cohorts of patients (25,26). In a recent update, the same group reported full nipple necrosis in 1% and superficial necrosis or epidermolysis in 3.5% (1). Minimizing pressure on skin flaps via the use of tissue expanders and optimizing coverage of prosthetics with acellular dermal matrix or muscle led to improvements in outcomes.

Incisions and nipple perfusion

The location of incision for NSM is influenced by the breast volume and ptosis, the distance between the NAC and inframammary fold, the presence of prior scars and the type of reconstruction. However, patient and physician

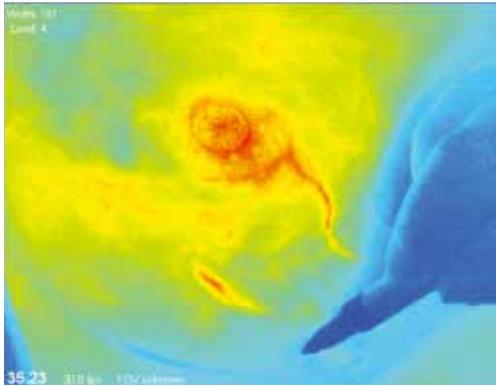


Figure 4 Intraoperative pre-incision evaluation of skin perfusion in nipple-sparing mastectomy. Mapping of baseline skin perfusion pattern depicting arterial inflow in order to guide placement of incision.

preference and desire to maximally camouflage the incisions also play a role. From a technical standpoint, in order to resect all the breast tissue extending from the clavicle and beyond the anterior axillary line, an infra-mammary fold incision must be made sufficiently wide to allow access. As such, many surgeons favor the radial-lateral or inferior vertical-radial incisions, including partial but limited extension around the areola. Recently, in a pooled analysis Endara *et al.* described, NAC necrosis of 8.8% for radial and 9.1% for inframammary incisions compared to 17.8% for periareolar and 81.8% for transareolar incisions (27). Based on these results the inframammary fold or the radial approaches were recommended.

Garwood and colleagues were able to reduce NAC complications by limiting the extent of periareolar incisions to less than one-third of the circumference of the areola or by avoiding the NAC entirely (28). In this study, two cohorts of two sequential time periods were analyzed. Nipple survival rates rose from 80% to 95% ($P=0.003$) and necrotic complications decreased from 30% to 13% ($P=0.01$). Here too, incisions involving $>30\%$ of the NAC were an independent risk factor for skin necrosis. They noted that improved NAC viability with limited periareolar incisions is consistent with not disrupting the subdermal vascular plexus that supplies the nipple. Most of their subsequent cases since their early experience have been performed through inframammary or limited superior areolar incisions, with a subsequent reduction of NAC complications to 1.8% in their 2012 series (26).

Our group at Stanford uses SPY *Elite*TM imaging

intraoperatively to perform baseline assessments of the skin circulatory anatomy, with the aim of avoiding injury to critical skin vessels before making an incision in nipple or skin-sparing mastectomies. Moreover, we have incorporated this technology in other challenging situations where a breast lumpectomy for cancer is combined with a reduction mammoplasty procedure. *Figure 4* shows a pre-incision sequence depicting arterial inflow to the NAC at the 5 o'clock position. Perfusion to the NAC would have been significantly compromised if an inferior-based periareolar incision were used. Instead, the real time obtained images altered the surgical approach and guided the surgeon to employ an inframammary incision.

Nipple perfusion patterns

We have been using SPY *Elite*TM imaging as an adjunct to breast cancer operations combined with reconstructive surgery. One of the ways this technology is helpful, is by informing surgeons in real-time, the circulatory anatomy of the NAC. Intraoperative post-mastectomy imaging revealed absent perfusion in the area of the NAC (*Figure 5*). The arterial ingress pattern demonstrated filling from the underlying breast tissue without any seeming contribution from surrounding cutaneous blood vessels. These observations led to a more extensive examination of NAC perfusion.

Three patterns of arterial-arteriolar filling were defined qualitatively: V1, underlying breast tissue; V2, surrounding skin; and V3, dual or V1 and V2 (29). Among the 39 cases initially reported, 7 of 39 (18%) breasts demonstrated a V1 perfusion pattern in the NAC, 18 (46%) a V2 pattern and 14 (36%) a V3 pattern. The proportion of cases in each category at baseline remained similar in a larger cohort with 93 breasts as shown in *Table 1*. Specifically, the majority or 48%, demonstrate a V2 pattern while 20% have V1. In our original series of 39 breasts, 71% with a V1 pattern underwent NAC removal based on intraoperative ischemic changes *vs.* 11% for the V2 group. The differences in rates of NAC loss by perfusion classification were significant ($P=0.0003$). We now report an additional 15 breasts undergoing a one-stage NSM (*Table 2*). In this combined analysis, 56% of breasts with a V1 pattern had intraoperative nipple resection compared to 3.4% with V2 patterns. Postoperative loss of the NAC has been lowered to 2%, excluding those removed intraoperatively. With a larger sample size, interactions with other factors such as type of incision may further our understanding and our ability to

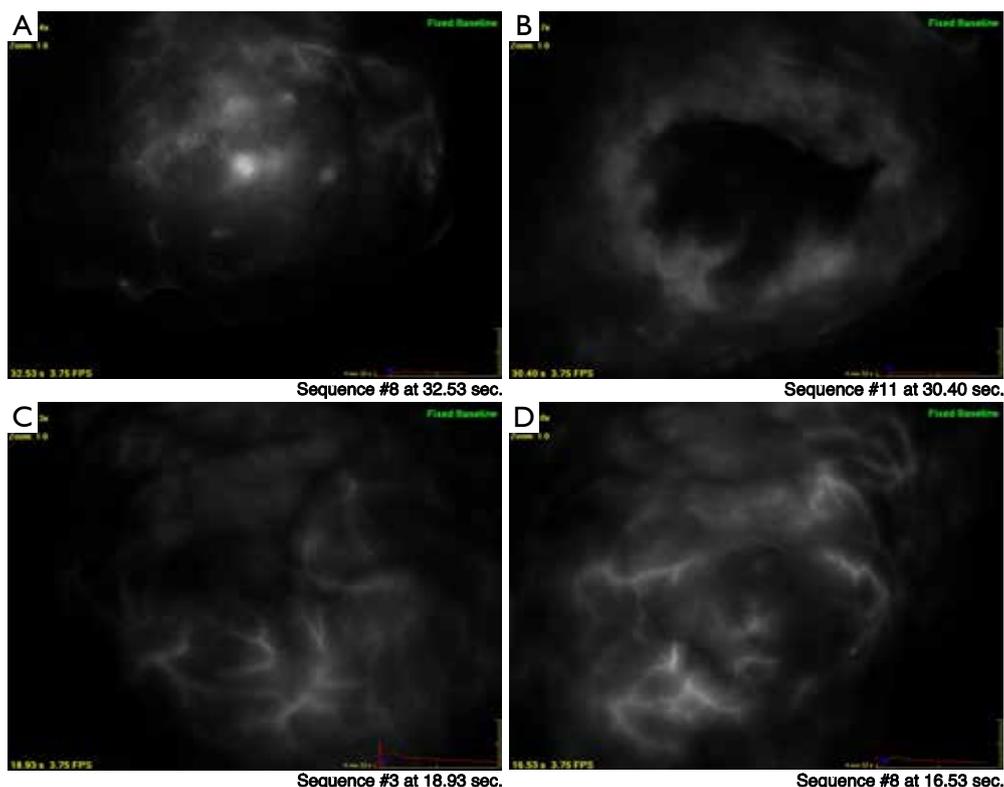


Figure 5 Intraoperative assessment of skin and nipple-areolar perfusion. Changes in perfusion patterns before and after mastectomy: (A) V1 pattern showing filling of NAC/periareolar area from underlying breast tissue, and corresponding post-mastectomy image; (B) taken at the same time point demonstrating a large filling defect that progressively filled in over the next 120 seconds (not shown); (C) another case illustrating V2 pattern with arterial inflow from surrounding skin and (D) immediate post-mastectomy images showing intact perfusion; inframammary fold incision. NAC, nipple-areolar complex.

Table 1 Baseline patterns of perfusion in the nipple areolar complex	
Baseline pattern	N=93 [%]
V1= underlying breast tissue	19 [20]
V2= surrounding skin	45 [48]
V3= mixed (V1 + V2)	29 [31]

predict ischemic complications. In summary, preservation of adequate NAC perfusion in NSMs is likely dependent on a confluence of factors ranging from breast volume, ptosis, location and type of incision as well as circulatory anatomy. The latter is evaluable and unique in every individual.

Staged devascularization of the NAC

Ischemic complications and skin loss detract from

the cosmetic goals of NSM. Women with larger or ptotic breasts seeking NSM, experience more ischemic complications (14,30). Devascularization or vascular delay has been used in surgery for many years as a means of improving blood flow through tissues via hypertrophy of existing vessels or the formation of new collaterals (31). Jensen *et al.* have ingeniously applied a two-stage approach for women at higher risk of developing ischemia based on ptosis, previous scars, and active cigarette smoking (32). The first stage entails undermining the NAC with some surrounding skin along the mastectomy plane. A subnipple biopsy is also included at this time to confirm the absence of tumor involving the NAC. Seven to 21 days later, the mastectomy is completed. During this timeframe, it is presumed that the surgical wound enhances blood flow. In their study of 20 patients, none of the 28 tumor free NAC that were devascularized were lost and only two patients experienced superficial ischemia or epidermolysis after

Baseline pattern	N=54 [^] [%]	Intraoperative nipple resection N=19 [%]	Post-operative epidermolysis	Post-operative partial necrosis/loss NAC
V1	9 [17]	5 [56]	4 [44]	0
V2	29 [54]	1 [3.4]	11 [38]	1 (3.4)
V3	16 [30]	0	4 [25]	0

[^], breasts; NAC, nipple-areolar complex.

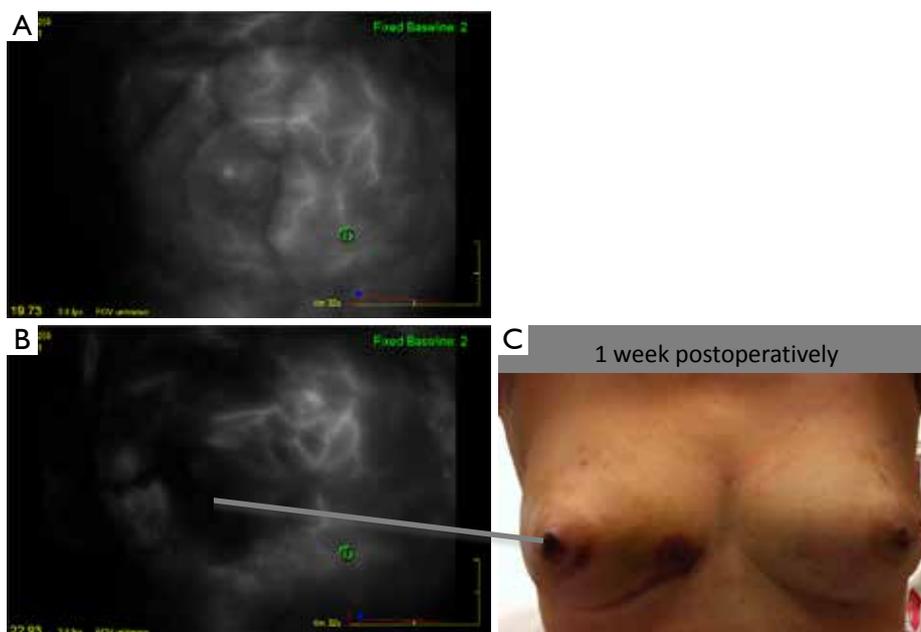


Figure 6 Devascularization of nipple-areolar complex. First stage devascularization of the nipple-areolar complex prior to delayed mastectomy. (A) Baseline V3 perfusion pattern; (B) image shows a central perfusion defect in the skin at the 22 second sequence immediately following the undermining of this area along the mastectomy plane; (C) one week later, epidermolysis is apparent in the overlying nipple skin.

the delay procedure. A variation on this technique was published by Palmieri and colleagues (33). They advocate the use of tumescence and endoscopic cauterization along the subareolar plane during a first operative procedure.

We have adopted a similar approach and are studying the changes in patterns of perfusion that occur in the course of this two-stage vascular delay approach. Using intraoperative ICG-based SPY *Elite*TM imaging, recovery of deficits in skin perfusion can be observed. Slow filling areas recover over 3 to 4 weeks either due to hypertrophy and vasodilatation of existing dermal blood vessels or neovascularization. *Figure 6* illustrates a woman with a BMI of 33 who underwent a two-stage NSM. The baseline images demonstrated areas of hypoperfusion affecting the NAC and correlate with zones of epidermolysis on the 1-week post-devascularization clinical examination, that healed completely over the

following weeks. This approach will surely facilitate the use of NSM for more patients and minimize ischemic complications and reoperations.

Reconstruction and NSM

Immediate reconstruction has certainly gained favored over the last two decades, with a preference in many centers toward a two-stage procedure whereby a tissue expander is placed at the time of ablative surgery, with the advantage of gauging the pressure exerted on the skin flap. Plastic surgeons face greater challenges when performing NSM. The larger skin envelopes predispose patients to more ischemic complications. Acellular dermal products are used to enlarge the limited cover provided by the pectoralis major muscle, forcing parts of the NAC and skin flaps to be in direct

contact with non-perfused tissue. Clearly, the greater demand for NSMs challenges the surgical community to conduct this type of operation for patients previously considered poor candidates. The adoption of periareolar pexy in women with moderately ptotic breasts is an added example of how these technical problems can be resolved (30).

Conclusions

Technological advances have made it possible to evaluate tissue perfusion in real time. This is extremely useful in the case of NSM where preservation of blood flow is most critical. The challenge before us is to extend the benefits of natural appearing NSM to women with prior breast surgery, large and ptotic breasts.

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Footnote

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The evolution of mastectomies in the oncoplastic breast surgery era

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Abstract: Over time, surgical techniques have advanced to the point where oncological safety and aesthetic outcomes are the pillars of contemporary breast surgery. Variations of mastectomy came up and started allowing the oncological safety and the possibility of an immediate breast reconstruction. Nowadays the association between plastic surgical techniques and mastectomy with immediate breast reconstruction is one of the best alternatives to treat breast cancer and also improved overall aesthetic outcomes and favors the achievement of contralateral breast symmetry. “Oncoplastic mastectomy” is a feasible term and can be routinely used.

Keywords: Breast cancer; breast conserving treatment; reconstructive surgical procedure; mastectomy; mammoplasty

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Introduction

Over time, surgical techniques have advanced to the point where oncological safety and aesthetic outcomes are the pillars of contemporary breast surgery. Although can a mastectomy be considered an oncoplastic surgical procedure? Can this procedure be called “oncoplastic mastectomy”? Can it be included in the arsenal against breast cancer? To answer those questions it is important to understand part of the evolution of breast cancer surgical treatment.

The partial evolution of treatment

Oncoplastic surgery

By the early 90's Audretsch (1) suggested the integration of plastic surgery techniques with breast-conserving treatment (BCT) for breast cancer. Conceptually, this approach was referred as “oncoplastic surgery”, which aims at providing safe oncologic treatment through careful pre-

operative planning and the incorporation of plastic surgery techniques in order to obtain good oncologic control with favorable cosmetic results in cases of large breast volume and large tumors. Subsequently the concept was accorded the term tumour specific immediate reconstruction. Moreover, oncoplastic surgery very often offers improved overall aesthetic outcomes and favors the achievement of contralateral breast symmetry (2).

The american plastic surgeon John Bostwick III in 1996, suggested that the term Oncoplastic Breast Surgery (OBS) includes not only techniques preventing the consequences of conservative treatment but also a whole range of techniques involving partial or total immediate post-mastectomy reconstruction (immediate breast reconstruction), correction of their consequences (delayed breast reconstruction), and immediate repair of the surgical treatment of locally advanced tumours and recurrences in the chest wall. Nowadays, following a period of uncertainty in the nomenclature, the term OBS is uniformly associated in the medical community with the classification system of

Table 1 Bostwick III classification for oncoplastic breast surgery (3)

Post-mastectomy breast reconstruction

(I) Immediate breast reconstruction. This is done when the tumor is resected. Depending on whether the skin of the breast or the nipple-areola complex (NAC) is resected, IBM may be classified in turn as:

- (i) Conventional or no skin sparing mastectomy, when the cutaneous layer is resected without leaving excessive breast skin behind;
- (ii) Skin sparing mastectomy (SSM), when as much of the cutaneous layer as possible and the sub-mammary fold are preserved, but with resection of the NAC and prior biopsy incisions and/or diagnostic percutaneous biopsy scarring;

SSM may in turn be subdivided into five groups:

- (a) Periareolar or lozenge resection of the NAC, sparing the skin of the breast;
- (b) Resection of the NAC with a medial or lateral extension resecting previous biopsy scarring;
- (c) Periareolar resection of the NAC and separate incision resecting previous biopsy scarring;
- (d) Border lozenge resection of skin including the NAC, in an attempt to reduce ptosis (indicated for ptotic and hypertrophic breasts);
- (e) Resection of the skin and NAC in an inverted T shape (ptotic and hypertrophic breasts).

(iii) Skin and areola sparing mastectomy (ASM), when the entire cutaneous cover, areola, and sub-mammary fold preserved, but the nipple and incision from previous biopsies and/or scarring from diagnostic percutaneous biopsies are resected;

(iv) Nipple sparing mastectomy (NSM), when the entire cutaneous layer, areola, nipple, and sub-mammary fold are preserved, as well as incisions from previous biopsies and/or scarring from diagnostic percutaneous biopsies

(II) Delayed breast reconstruction. The period of time in which is done varies after the mastectomy;

Conservative post-surgery reconstruction

(III) Immediate breast reconstruction. This is done at the time of the partial tumour resection from the breast to prevent the consequences of resection and of subsequent radiotherapy;

(IV) Delayed breast reconstruction. The period of time in which is done varies after the conservative treatment to correct the consequences of surgery and radiotherapy

Reconstruction of defects in the chest wall and in soft tissues, secondary to surgical treatment of locally advanced breast cancer and of extensive local recurrences

John Bostwick III (*Table 1*), in both Latin and Anglo-Saxon publications (3). It is important to clarify that the term OBS also encompasses the techniques developed for preventive surgery in high-risk patients (risk reduction mastectomies).

Skin sparing mastectomy

Down this same path, the mastectomy has changed and Toth & Lappert (4) described the Skin Sparing Mastectomy technique (SSM) in association with the removal of malignant tumors. It allowed the conservation of a large part of the skin and mammary fold in favor of immediate breast reconstruction (IBR).

Carlson *et al.* (5) considered four different types of incisions for SSM (*Figure 1*). The incision type IV is an example of using a plastic surgery technique to perform mastectomy. It is called Wise-pattern skin sparing mastectomy (WPM) which enabled excellent results as IBR in heavy and pendulous-breasted patients who

require a conspicuous reduction of the skin envelope and a contralateral reduction or mastopexy. However, the side undergoing the WPM, the skin flaps are thin and wound healing problems are well described, particularly skin necrosis at the “T” as frequent as 27%, predisposing to prosthesis exposure and therefore limiting its utility. Thus, Nava *et al.* (6) described a modification of this last type of skin-sparing mastectomy, that he called skin-reducing mastectomy. In that case the mammary reconstruction in selected patients is performed in a single-stage in which an anatomical silicone gel implant is placed in a dermal muscle flap pocket. It also allows the achievement of contralateral breast symmetry (*Figures 2,3*).

Nipple sparing mastectomy (NSM)

Other variations of mastectomy came up and started allowing the oncological safety and the possibility of an IBR. Defending the idea of IBR performed by breast surgeons



Figure 1 Skin sparing mastectomy: types of incisions.



Figure 2 Preoperative drawings for an “oncoplastic mastectomy”.

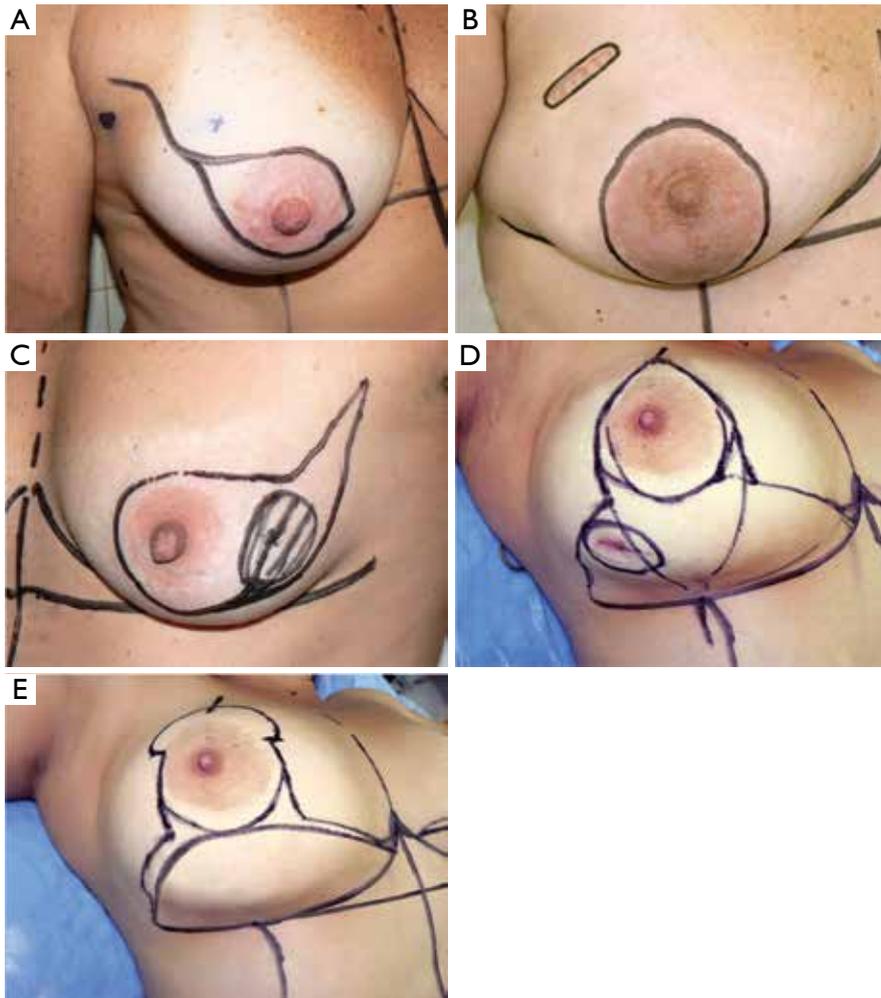


Figure 3 Post operative “oncoplastic mastectomy”: skin-sparing mastectomy and immediate symmetrization.

trained in oncoplastic surgery or by dedicated teams of breast surgeons and reconstructive surgeons, Petit *et al.* (7), described the nipple-sparing mastectomy as an option for patients with small invasive and non-invasive cancer located far from the nipple-areola complex. The principle of complete removal of breast gland with preservation of skin and also nipple-areola complex was maintained. At the beginning it was indicated in small breast women with multicentric disease, extensive intraductal carcinoma and especially when there was an unfavorable relation between breast volume and tumor size and also for women at high risk.

Risk-reducing mastectomy (RRM)

It is important to mention the prophylactic mastectomy or RRM responsible for sparing the most part of skin and nipple areola-complex but it is indicated for benign treatment or for reducing cancer risk. It has been largely performed for patients displaying the following oncologic risk factors: a positive family history, BRCA-1 and -2 gene mutation, atypic ductal hyperplasia, intensive lobular carcinoma in situ, and ductal carcinoma in situ and still when an extreme fear of breast cancer is manifested. RRM has been performed increasingly due to either patient demand or oncologic surgeon proposal. Sparing of the nipple-areola complex is extremely important for aesthetic results and patient satisfaction in both early-stage breast cancer and high-risk groups.

Conservative mastectomy

Nowadays the principle of oncoplastic surgery is amplified and was incorporated to the idea of an IBR. Recently Veronesi *et al.* (8) published the term conservative surgery regarding a surgical technique demanding on an oncological treatment by removing the breast parenchyma and trying to spare as much skin envelope as possible, including nipple areolar complex. In other words to remove breast glandular tissue without disruption of the breast appearance. It allows an IBR and the contralateral symmetric approach. It also boosts the patient's self-esteem and quality of life.

Conclusions

There are no doubts that mastectomy remains the most common choice of treatment for breast cancer around the world. More often the patients, especially young women,

are looking for a safety oncological treatment warranted by the benefits of breast reconstruction. The breast surgical procedures were updated and the mastectomy too. Those modalities of mastectomy are safe techniques providing better cosmetic outcome without compromising oncological safety as per the current evidence (9). They have allowed the approach of large tumors with an IBR something regarded as unthinkable in the past (10). Moreover the recent literature showed that IBR is a feasible and safe option for women undergoing mastectomies for their breast cancer (9). Today it is important to individualize each case, listen to the patient, clarify her doubts and try to provide the best option for each situation. It is also important to explain the risks of complications and delays to adjuvant therapy. Although radiotherapy does not represent a contraindication to IBR there is no consensus about the adjuvant treatment.

In short, the mastectomy with IBR is one of the best alternatives to treat breast cancer and also the most suitable solution to the relevant points of body image if well indicated. This manuscript does not defend the indiscriminate use of mastectomy but the idea to create and use the term "oncoplastic mastectomy" to the different kinds of sparing mastectomies. It can definitely be used as an evolutionary weapon against breast cancer.

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Footnote

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Oncological safety of prophylactic breast surgery: skin-sparing and nipple-sparing versus total mastectomy

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Abstract: Women with a *BRCA1/2* gene mutation and others with a high breast cancer risk may opt for bilateral prophylactic mastectomy. To allow for immediate breast reconstruction the skin envelope is left *in situ* with or without the nipple-areola complex (NAC). Although possibly leading to a more natural aesthetic outcome than the conventional total mastectomy, so-called skin-sparing mastectomies (SSM) and nipple-sparing mastectomies (NSM) may leave some breast glandular tissue *in situ*. The oncological risk associated with remaining breast glandular tissue is unclear. We present a case of primary breast cancer after prophylactic mastectomy followed by a review of the literature on remaining breast glandular tissue after various mastectomy techniques and oncological safety of prophylactic mastectomies.

Keywords: Risk-reduction; skin-sparing mastectomy (SSM); nipple-sparing mastectomy (NSM); total mastectomy; primary breast cancer; breast glandular tissue; terminal duct lobular units

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Introduction

BRCA1/2 mutation carriers have a cumulative lifetime breast cancer risk of 55-85% by the age of 70 (1-5). As an alternative to surveillance, *BRCA1* and *BRCA2* mutation carriers and other women with a high breast cancer risk may choose to undergo bilateral prophylactic mastectomy, reducing breast cancer risks by 90-100% after 3-13 years of follow-up (6-10). The prophylactic character of the bilateral mastectomy emphasizes the importance of a natural aesthetic outcome (11), which can be achieved by various immediate autologous and implant breast reconstruction techniques. Instead of the conventional total mastectomy, to allow for an immediate breast reconstruction and to achieve a natural aesthetic outcome so-called conservative mastectomies are increasingly performed for risk reduction. In conservative mastectomies, all breast glandular tissue is removed while leaving the skin envelope and, if spared, the nipple-areola complex (NAC) *in situ* [skin-sparing mastectomy (SSM) and nipple-sparing mastectomy (NSM), respectively].

Safety of conservative mastectomies in women at high breast cancer risk is subject to an ongoing debate. The presumed oncological risk of the conservative technique lies in potential remaining breast glandular tissue with the skin flap and, if spared, with the NAC. Smaller incisions that are tailored to individual reconstruction wishes, however, may result in a technically difficult surgical approach. Therefore, the oncological safety of the conservative mastectomy remains a challenge for the oncological surgeon. We present a case of primary breast cancer developed after prophylactic conservative mastectomy. Further, we provide a review of the literature on the oncological safety of prophylactic conservative mastectomies.

Case: a 43-year-old woman with primary breast cancer in the prophylactic mastectomy scar

In 2011, a 43-year-old woman presented a lesion clinically suspicious of breast cancer. In 1982, at the age of 15, she had been successfully treated for stage IIa Hodgkin's disease

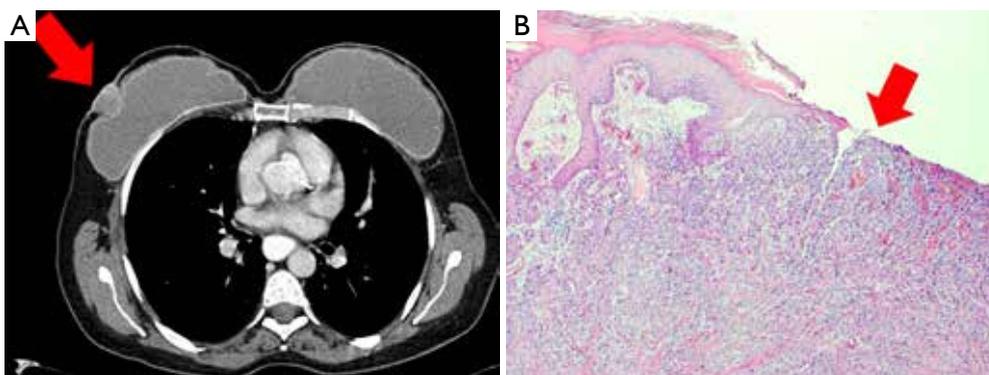


Figure 1 A 43-year-old woman presented with a primary, ulcerous breast cancer in the right prophylactic mastectomy scar. Eight years before presentation she had undergone prophylactic mastectomy and immediate breast implant reconstruction because of a history of Mantle field radiation at the age of 15. Histology of the mastectomy specimens showed no (*in situ*) malignancy. (A) Computer-assisted Tomography (CT) scan of the thorax shows the tumor of 2.1×2.7 cm² that invades the skin and causes dimpling of the subpectoral implant; (B) microscopic examination showed a grade 3 invasive ductal carcinoma with skin involvement, indicated by the arrowhead. Haematoxylin and eosin stained (H&E); 4× objective.

in her neck and mediastinum with 40 Gy mantle field radiation. After 10 years there were no signs of recurrence and she was discharged from follow-up.

In 1998, a mammography—performed because of a wish for breast reduction—revealed suspect microcalcifications in the left breast. The suspect lesion was excised by upper outer quadrantectomy. Pathological examination of the lumpectomy specimen showed grade 2 ductal carcinoma *in situ*. No adjuvant radiotherapy was administered due to the history of mantle field radiation. Initially, physicians and patient agreed to frequent radiological screening instead of a completing mastectomy. However, after several additional diagnostic procedures due to suspect lesions of the left breast, in 2001, the patient chose to undergo a SSM and immediate implant reconstruction. In 2003, this was followed by a prophylactic SSM of the right breast and bilateral implant reconstruction. In both cases, histologic investigation showed no (*in situ*) malignancy.

In 2011, she returned with an ulcerous lesion in the right mastectomy scar. On CT-scan a superficial tumor of 21×27 mm² was seen (*Figure 1A*). Ultrasonography of the axilla did not show pathological lymph nodes. A wide local excision with axillary lymph node dissection was performed and the implants were removed. Histological examination of the excised specimen showed an invasive ductal carcinoma with a diameter of 2.4 cm, Bloom Richardson grade 3, estrogen receptor (ER) positive, progesterone receptor (PR) and human epithelial growth factor-2 receptor (HER2 receptor) negative (*Figure 1B*). Adjacent to the tumor,

normal glandular breast tissue was found. One out of eight dissected axillary nodes showed a metastasis. According to our national protocol, she received adjuvant chemotherapy, hormonal therapy and re-irradiation with hyperthermia of the chest wall. At the time of writing the patient is alive without breast cancer recurrence.

Surgical techniques of conservative mastectomies: SSM and NSM

Examples of conservative mastectomies include SSM and NSM. In SSM, a periareolar incision is used with caudal or lateral extension if necessary (“racquet” incision). The skin envelope is created by subcutaneously excising the breast glandular tissue while preserving a thin subcutaneous layer to support skin vascularization. Nipple-papilla and surrounding pigmented areola (NAC) are removed. In NSM, the skin envelope is created through a semicircular periareolar or an inframammary incision. The NAC is dissected as thin as possible by macroscopically removing all breast glandular tissue while preserving vascularization. The nipple-papilla is “cored” by inverting it and excising residual breast glandular tissue. The NAC is then left *in situ* adherent to the skin envelope. A breast reconstruction is performed during the same procedure. The oncological safety of SSM in the prophylactic setting is generally acknowledged, whereas safety of NSM is still subject to debate.

In the last two decades of the past century it was

common to perform a so-called subcutaneous mastectomy. Although subcutaneous mastectomy encompassed a skin- and nipple-sparing technique as well, it is likely that this was not comparable to current NSM and SSM techniques. A description of the 'state of the art' subcutaneous mastectomy in 1983 mentions that a plaque of one centimeter of breast glandular tissue should be left *in situ* with the areola (12). In contrast, current NSM and SSM techniques aim for skin flaps <5 mm and NACs of 2-3 mm thickness (13).

Breast glandular tissue or terminal duct lobular units (TDLUs): residuals after mastectomy

The hazard of remaining breast glandular tissue after mastectomy for development or recurrence of breast cancer has been a recurring subject to debate since more than half of a century. Anatomically the NAC is a continuation of the mammary gland and therefore should be removed when pursuing a complete mastectomy. Therefore, especially sparing of nipple and areola in NSM has been a controversial topic. However, the growing ability of more specifically identifying women at high breast cancer risk and the consequently increasing interest in prophylactic mastectomies has revived the discussion. Breast cancer is thought to originate in TDLUs, defined as a terminal duct combined with an associated lobule (14-16). Consequently, theoretically any remaining TDLUs may represent a lifelong potential breast cancer hazard. To estimate the remaining risk after prophylactic mastectomy, some authors have studied whether TDLUs are left *in situ*. Several others have simply examined the presence of remaining ductal or lobular structures or more non-specifically the presence of glandular tissue.

Residual breast glandular tissue after total mastectomies

The first study to investigate the amount of glandular tissue left *in situ* after a conventional total mastectomy was already in 1940 by Hicken *et al.* (17). The authors had been triggered by two cases of women who developed breast cancer and mastitis of residual axillary breast tissue 15 and 10 years, respectively, after an ipsilateral mastectomy for a benign indication. Mammographies of 385 breasts using intraductal contrast showed that mammary ducts frequently extend beyond regular mastectomy resection planes. In 95%, mammary ducts extended into the axillary fossa, in 15% downward into the epigastric region, in 2% beyond the lateral limits of the latissimus dorsi muscle and in two cases

even past the midsternal line to the contralateral side (17). A histological analysis of 17 total mastectomies was performed in the same study by preoperatively injecting methylene blue dye into the ducts of the nipple-papilla. Any resection plane that colored blue during surgery meant that ducts had been cut and the resection site was defined as 'irradical' (17). Results showed that breast glandular tissue had been excised irradically underneath the skin flap in 94% of cases, in 12% the axillary tail had been removed irradically, in 23% the ducts had been cut in the sternal region and in 11% in the epigastric region (17). The authors therefore concluded that, even when it is intended to perform a total mastectomy, it is seldom accomplished (17).

In 1991, a small study was performed in ten total mastectomies in five women (18). Frozen sections of skin flaps, pectoral muscle and axillary tail were examined. Similar to the results of Hicken, residual breast glandular tissue was found in caudal skin flaps, the axillary tail and even in the pectoral fascia (18). Another small study separately resected specimens specifically of the inframammary fold (IMF) and encountered small amounts of residual breast tissue in 13/24 IMF specimens (with breast glandular tissue volume/IMF specimen volume rates of 0.04%) (19).

In 2013, Griepsma *et al.* studied the superficial dissection planes of 206—mostly total—mastectomy specimens (20). Per mastectomy 36 biopsies were obtained from standardized locations of the subcutaneously dissected part of the total mastectomy specimens. In 76% of mastectomies, one or more biopsies contained breast glandular tissue at the resection plane. Areas of predilection were the lower outer quadrant (15% positive biopsies) and halfway the subcutaneous dissection plane between the peripheral pectoral muscle margin and central skin margin (12% positive biopsies) (20).

Residual breast glandular tissue after conservative mastectomy: SSM and NSM

Three decades after the first report on total mastectomies by Hicken *et al.*, Goldman and Goldwyn picked up on the issue of conservative prophylactic mastectomy by performing 12 subcutaneous (skin- and nipple-sparing) mastectomies in six cadavers through an inframammary incision (21). Biopsies of post-mastectomy skin flaps, resection planes and any fibrous or adipose tissue remaining elsewhere showed residual breast glandular tissue after 83% of mastectomies (21). In all cases even, residual breast glandular tissue was

found behind the spared NAC. However, the authors do not describe which biopsy sites were positive for breast glandular tissue, nor the surgical technique used for dissection of the NAC (21).

Aiming to investigate the potential value of NSM in the treatment of lobular carcinoma in situ (LCIS), Rosen and Tench (22) vertically sectioned 101 nipples in conventional mastectomies performed for breast cancer. In 17% of the nipples lobules were found and in 13% (*in situ*) carcinoma was encountered. The authors propose that “coring” of the nipple-papilla in NSM, which had been described before (23), is necessary to remove as much glandular tissue as possible. The NAC was further examined in 1993 (24). By inverting the projected center of the NAC—the nipple-papilla—and grossly removing all glandular tissue inside the papilla, the nipple was cored. Despite nipple-coring the authors did encounter mammary ducts in the areolar dermis (24).

In 1991, Barton *et al.* compared 27 conservative mastectomies with 28 modified radical mastectomies (25). Post-mastectomy biopsies were taken at the inframammary fold, parasternal region, infraclavicular chest wall, latissimus dorsi muscle border, anterior lower axilla and skin flaps. The NAC was not examined. No differences were found between the number of biopsies containing residual breast glandular tissue after conservative mastectomy (22%) and after total mastectomy (21%) (25). After conservative mastectomy, most positive biopsies (50%) originated in the skin flap. In contrary, after total mastectomy, most positive biopsies (38%) originated at the latissimus dorsi border (25).

The skin flap after conservative mastectomy was further examined in 1998 (26). The authors removed 114 small ($0.5 \times 2.0 \text{ cm}^2$) strips of skin from the remaining skin flap in 32 patients for complete histological examination. In none of the strips ductal breast tissue was encountered (26), however, regarding the size of the strips, this negative finding may be due to a sampling error. Somewhat larger skin flaps have been examined in a more recent study (27). In 66 SSMs, skin specimens that had been removed additionally to the SSM specimen to facilitate reconstruction were examined for residual glandular tissue. Skin specimens had a mean volume of 93.9 cm^3 and in specimens of only four patients (6%) residual breast tissue was found (27). However, since only a minimum of three sites per skin specimen was analyzed, again in this study a sampling error cannot be ruled out. A study of 168 SSMs for therapeutic indication analyzed the superficial margin to the dermis just above the tumor that would have been left *in situ* otherwise. In contrast with the two studies described above, in 89 (53%) of the cases benign breast ducts

were present in the superficial margin specimen (28).

Residual TDLUs after conservative mastectomy: SSM and NSM

Several studies have more specifically studied whether TDLUs remain after SSM or NSM (22,29-31). The only study on SSM was by Torresan *et al.* in 2005 (32). In 42 total mastectomies, they resected the skin flap that would have been left *in situ* if it were a SSM and submitted 80 slides per skin specimen for examination. In contrary to the two studies mentioned earlier, they found TDLUs in 60% of the skin flaps (32). The risk of finding TDLUs strongly increased for skin flaps thicker than 5 mm (32).

The other five studies focus on NSM. Stolier *et al.* examined the nipple-papilla for presence of TDLUs in 2008 (29). During mastectomies, 32 nipple-papillas were transected at the junction of papilla and areola. Nipple-papilla's were sectioned, entirely embedded and examined microscopically for presence of TDLUs. Only in three out of 32 nipple-papilla TDLUs were found. Therefore, it was concluded that TDLUs are scarce in the nipple-papilla (29). Reynolds *et al.* collected 62 mastectomy specimens from 33 *BRCA1/2* mutation carriers and excised the NAC for histologic evaluation (30). In 24% of the NACs, TDLUs were found; only 8% was located in the papilla (30). Similarly, Kryvenko *et al.* studied 105 NACs from mastectomy specimens (31). Sixty-five NACs were entirely embedded for examination of presence of TDLUs; of 40 NACs only one vertical section was examined. TDLUs were found in 26% of NACs but most frequently were located in the papilla (31)—in contrast to the results of Reynolds and Stolier (29,30). It has been suggested that an areola-sparing mastectomy rather than a NAC-sparing mastectomy should be performed for risk reduction. Removing the nipple-papilla might further reduce any remaining breast cancer risk. However, this is not supported by the abovementioned studies since two of the three show a higher incidence of TDLUs in the areola versus the nipple-papilla.

Recently, our own group compared presence and numbers of TDLUs between skin flap and NAC (33). In 105 total mastectomies, the NAC and an adjacent skin-island were dissected as if an NSM was performed, and the papilla was cored. TDLUs were found in 61% of the NACs *vs.* 24% of the skin islands (33). Also after adjustment for volume of the excised specimens, density of TDLUs was significantly higher in the NACs as compared with the skin. Further, risk factors for presence of TDLUs were

younger age and parity (*vs.* nulliparity) (33). We concluded that NACs, as well as skin flaps might harbor a risk for developing breast cancer, albeit very small.

Oncological safety of prophylactic mastectomy: clinical studies

In addition to the histopathological studies, we assessed whether there are any oncological consequences of the residual glandular tissue. We performed a systematic PubMed search using the term “prophylactic mastectomy [Title/Abstract] OR skin-sparing mastectomy [Title/Abstract] OR nipple-sparing mastectomy [Title/Abstract] OR subcutaneous mastectomy [Title/Abstract] OR conservative mastectomy [Title/Abstract] OR risk-reducing mastectomy [Title/Abstract] AND breast cancer [Title/Abstract]”, yielding 680 titles. Titles and abstracts were checked for relevance. Reviews and case reports were excluded, as were articles that were not in English. Also excluded were: studies that focused: (I) on merely therapeutic mastectomy and/or comprised <20 prophylactic mastectomies and/or did not report clinical follow-up outcome of prophylactic mastectomies; (II) on survival benefits of contralateral prophylactic mastectomy or oophorectomy; (III) on uptake, counseling and decision-making of prophylactic surgery.

Twenty-four studies from 1976-2014 met our criteria and are summarized in *Table 1*. All are observational studies describing prospective or retrospective cohorts or a case-control series. In 24 studies, 7,173 mastectomies are described of which 1,392 were for therapeutic indications and which were not considered in further analysis. Most prophylactic mastectomies were performed in *BRCA1/2* gene mutation carriers and other women at high breast cancer risk. Average follow-up periods range from 10.4-168 months. Most recent studies focus on NSM rather than SSM; while in older studies conservative mastectomies are defined as ‘subcutaneous mastectomy’, suggesting that the NAC is—partly—spared. However, as described above, it is likely that in subcutaneous mastectomy the NAC and skin are not dissected as thin as modern NSM or SSM techniques dictate.

As reported by the 24 studies in *Table 1*, grossly, 21 primary breast cancers occurred after 6,044 prophylactic mastectomies. Of these, three occurred after a total mastectomy (0.6% of all total mastectomies), 17 occurred after a conservative mastectomy (0.3% of all subcutaneous mastectomies, NSM or SSM) and for one breast cancer

the prophylactic mastectomy technique was not specified. Besides, four patients presented with distant metastases with unknown primary site. Most prophylactic mastectomies included in these studies, as well as the ones in which a primary breast cancer developed, were subcutaneous mastectomies, NSM or SSM. Nonetheless, the majority of primary breast cancers did not originate near the NAC or skin flap. Of the 21 breast cancers that developed after prophylactic mastectomy, five were encountered at the chest wall, four in the axilla, (two in the axillary tail, one in an axillary lymph node, one in an unknown location), one in the outer quadrant, one in the nipple and one “above the areola” (not further specified). In nine cases the location was unclear or not reported.

The 21 loco-regional primary breast cancers correspond with an incidence of 0.7% per woman who undergoes bilateral prophylactic mastectomy (0.35% per mastectomy). Most breast cancers that developed after conservative mastectomy were found at the chest wall or in the axilla. Although the chest wall and the axilla may be at risk in total mastectomy as well, two things should be considered: First, the origin of the breast cancer may have been the skin flap, even though it was described as ‘chest wall’. Most breast implants in immediate breast reconstruction are placed underneath the pectoral muscle. Consequently, skin-flap and chest wall are in direct contact. Therefore, although we have no information on the reconstruction techniques used in these studies, it is possible that the breast cancers developing at the chest wall actually did originate in the skin flap. Second, as mentioned before, the surgical technique of SSM and NSM using small peri-areolar or inframammary incisions can be challenging. A suboptimal exposure may impede thorough removal of remaining breast glandular tissue in all quadrants and in the axillary tail.

In four cases, breast cancer presented as metastatic disease and the primary tumor site was never found. Pathological findings specific for breast cancers, the high a priori breast cancer risk of the patient and elimination of other potential first sites because of negative radiological examinations may all have led to the conclusion that the metastatic disease most probably originated from breast cancer. The possibility that the primary tumor already may have been present in the prophylactic mastectomy specimen emphasizes the importance of standardized pathological examination of the excised specimen, and—even more—thorough radiological screening by MRI before prophylactic mastectomy.

In conclusion, the incidence of primary breast cancers

Table 1 Primary breast cancers after prophylactic total mastectomy, nipple-sparing and skin-sparing mastectomies: an overview of studies (6-9,13,34-52)

First author, year	Study population	Mast		Therapeutic mastectomy not taken into account		Prophylactic mastectomy (PM)		Follow-up after PM		Primary BC after PM n (% of all PM)	Distant metastases after PM	Location primary breast cancer after PM
		n	n	n	n	Total PM		Months (range)	n			
						SSM	Conservative PM					
de Alcantara Filho, 2011	125 unknown; 36 BRCA1/2+; 39 non-BRCA1/2	353	157	—	196	—	—	10.4 (0-109)	0	0	—	0
Anver, 2011	129 BRCA1/2+; 94 non-BRCA1/2 or unknown	446	—	100	338 ¹	8	—	79.2 (25.2-168.0)	0	1 metastatic disease 9 yrs after PM (0.2%)	—	Distant metastases
Colwell, 2014	285 patients	482	222	—	260	—	—	26.0 (10.8-71.0)	0	—	—	N/A
Contant, 2002	63 BRCA1+; 13 BRCA2+; 36 non-BRCA1/2 or unknown	207	—	193	—	14	—	30.0 (12.0-70.8)	0	—	—	N/A
Evans, 2009	202 BRCA1/2+; 348 non-BRCA1/2>25% BC risk	864	—	346 ²	200 ²	—	—	73.2 (range NR)	0	—	—	N/A
Garcia-Etienne, 2009	25 patients	42	7	—	34	—	—	10.5 (0.4-56.4)	0	—	—	N/A
Hagen, 2014	267 BRCA1/2+; 104 history of BC	449	—	166 ³	49 ³	5 ²	—	35 (3-336)	—	1 primary BC 6.6 yrs after subcutaneous PM (0.2%)	—	NR
Harness, 2011	6 BRCA1/2+; 37 non-BRCA1/2 or unknown	60	40	—	20	—	—	18.5 (6-62)	0	—	—	N/A
Hartmann, 1999 and 2001	26 BRCA1/2+; 150 non-BRCA1/2 high risk; 38 not tested; 425 moderate risk	1,278	—	1,146 ³	132	—	—	168 (range NR)	—	6 primary BC; 2, 3, 5, 6, 15 and 25 yrs after subcutaneous PM (0.5%)	—	2 yrs: chest wall; 3 yrs: lateral side chest wall; 5 yrs: left breast "above areola"; 6 yrs: left nipple; 15 yrs: left breast; 25 yrs: chest wall
Heerskerk-Gerritsen, 2013	156 BRCA1+; 56 BRCA2+	424	—	384	40	—	—	75.6 (1.2-208.8)	0	1 metastatic disease 3.5 yrs after prophylactic SSM (0.1%)	—	N/A
Jensen, 2010	99 patients	149	99	—	50	—	—	60.2 [12-144]	0	—	—	N/A
Kaas, 2010	179 BRCA1+; 75 BRCA2+	401	—	NR (Majority)	NR	NR	—	Bilateral: 63.5; Unilateral: 65.0; (ranges NR)	—	1 primary BC 2 yrs after PM (history of contralateral BC) (0.2%)	—	Axillary tail which was incompletely removed
Meijers-Heijboer, 2001	64 BRCA1+; 12 BRCA2+	152	—	148	—	4	—	33.6 (1.2-68.4)	0	—	—	N/A
Munhoz, 2013	158 patients genetic status unknown	233	114	—	119	—	—	65.6 (6-130)	0	—	—	N/A
Peled, 2014	53 BRCA1/2+; 53 non-BRCA1/2	212	108	—	104	—	—	51 (8.3-132.8)	0	—	—	N/A
de la Peña-Salcedo, 2011	52 patients	64	64	—	42	22	—	144 (range NR)	0	—	—	N/A
Pernisi, 1976	1244 patients	NR	64 ²	—	1,160 ^{3,4}	—	—	84 (range NR)	—	6 primary BC after subcutaneous mastectomy	—	—
Rebbeck, 2004	105 BRCA1/2+	210	—	56 ^{3,4}	100 ⁴	—	—	66 (0-373)	—	2 BC 2 and 9 yrs after subcutaneous mastectomy in BRCA2+ and BRCA1+, respectively (1.0%)	—	—
Sacchini, 2006	3 BRCA1/2+; 1 non-BRCA1/2; 119 unknown	219	68	—	151	—	—	24.6 (2.1-570.4)	—	2 BC 2 and 5 yrs after prophylactic NSM (1.3%)	—	1 in the axillary tail; 1 in the upper-outer quadrant
Skytte, 2011	67 BRCA1+; 29 BRCA2+	192	—	NR	NR	NR	—	47.3 (range NR)	—	3 BC in BRCA1+; 2, 5 and 7 yrs after total mastectomy (1.6%)	—	2 at the thoracic wall; 1 in the axilla (lymph node metastasis or ectopic breast tissue)
Spears, 2011	22 BRCA1/2+; 79 non-BRCA1/2 or unknown	162	49	—	113	—	—	43 [5-246]	0	1 metastatic disease of unknown primary after 9 yrs (0.9%)	—	N/A
Wagner, 2012	7 BRCA1/2+; 3 BRCA1/2-; 23 unknown; 33 patients	54	17	—	37	—	—	15.0 [1-29]	0	—	—	N/A
Warren Peled, 2012	19 BRCA1/2+; 411 non-BRCA1/2 or unknown	657	412	—	245	—	—	28	0	—	—	N/A
Wilayanagarn, 2008	43 patients; partly BRCA1/2+ Total numbers of primary BC after conservative and total PM:	75	35	—	29	11	—	NR	0	17 BC after conservative PM (0.3%); 3 BC after total PM (0.6%); 1 BC after unknown PM technique	—	N/A

¹, ², ³, ⁴ of 338 NSM concerned SSM with retransplantation of the nipple but removal of the areola; ², women with unilateral and bilateral mastectomies; exact numbers of mastectomies not reported and are analyzed as one mastectomy per woman; ³, conservative mastectomy = subcutaneous mastectomy; ⁴, of 26 patients (62 mastectomies) mastectomy techniques were unknown. Abbreviations: BC, breast cancer; Mas, mastectomies; SSM, skin-sparing mastectomy; NSM, nipple-sparing mastectomy; NR, not reported; N/A, not applicable; BRCA1/2+, female BRCA1/2 gene mutation carrier; BC1, breast conserving therapy.

after prophylactic mastectomy is very low after total as well as after conservative mastectomies. However, theoretically, according to these data, approximately one out of 140 women undergoing bilateral prophylactic mastectomy for breast cancer prevention will develop a primary breast cancer over time. Oncological surgeons should be aware of this risk and may minimize it by putting extra care in dissecting all glandular tissue, especially in the axillary tail and chest wall, and by dissecting skin flaps and NAC as thin as possible. More studies are warranted that further assess long-term oncological safety. Further, it is important to more specifically study patient satisfaction after NSM and SSM and potential differences in patient expectations. Ultimately, surgeons and patients may be able to balance any remaining oncological risk against expected benefits of NSM or SSM.

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Footnote

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Oncologic safety of conservative mastectomy in the therapeutic setting

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Abstract: Conservative mastectomy is a form of nipple-sparing mastectomy which is emerging as a surgical option for selected breast cancer patients. This technique differs from subcutaneous mastectomy which is well established as a technique for risk reduction but leaves behind a finite remnant of retro-areolar breast tissue. Clinical trials have confirmed the efficacy and safety of breast conservation therapy for smaller localised breast tumors whereby a variable amount of surrounding normal tissue is excised with administration of breast radiotherapy post-operatively. Conservative mastectomy aims to remove all breast tissue with dissection continued into the core of the nipple. However, the indication for conservative mastectomy remains to be defined but generally includes tumors of modest size located at least 2 cm away from the nipple. Patients undergoing conservative mastectomy do not necessarily receive adjuvant radiotherapy and this may only be intra-operative irradiation of the nipple-areola complex (NAC). Preservation of the NAC as part of a skin-sparing mastectomy in patients who might otherwise require standard mastectomy is of unproven safety from an oncologic perspective but is associated with enhanced cosmetic outcomes and quality-of-life. The advent of conservative mastectomy has coincided with a trend for “maximal surgery” with bilateral extirpation of all breast tissue in conjunction with immediate breast reconstruction. It is essential there is no compromise of local recurrence and survival in terms of ipsilateral breast cancer treatment. Further studies are required to clarify the indications for conservative mastectomy and confirm oncologic equivalence to either wide local excision and breast irradiation or conventional/skin-sparing mastectomy with sacrifice of the nipple areola complex.

Keywords: Nipple preservation; mastectomy; recurrence; safety

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Introduction

The term ‘conservative mastectomy’ has been formalised in recent years by Veronesi and colleagues from the European Institute of Oncology in Milan who accrued evidence in favour of nipple-preserving skin-sparing mastectomy procedures for early stage breast cancers of modest size and located away from the nipple-areola complex (NAC) (1). Nonetheless, the term conservative mastectomy has previously appeared in the literature but can be confusing *prima facie* due to the widespread use of the term conservative or conservation surgery for those

procedures which aim to remove a localised tumour and a variable margin of normal surrounding breast tissue. In a sense, the term conservative mastectomy might be considered appropriate in the sense that this implies an extreme form of ‘breast conservation’ in which the wide excision is extended to include the whole breast parenchyma but leaves the skin envelope including the NAC intact. So in some respects this is a form of breast conservation, but at the same time is a type of mastectomy in terms of extirpation of all breast parenchyma. A distinction should be made between conservative mastectomy and other forms

of nipple preserving mastectomy such as subcutaneous mastectomy which is often employed in the context of surgical prophylaxis (2). The latter aims are to preserve a thin sliver of breast tissue in order to ensure viability of the nipple-areolar complex. This operation is often undertaken in younger women with dense breast tissue which can be difficult to dissect off the under-surface of the NAC without compromise of vascular supply. By contrast, conservative mastectomy is a potentially curative procedure for established malignancy within the breast and aims for extirpation of all glandular tissue—it should be noted that these patients will not routinely receive adjuvant radiotherapy to the chest wall tissues which might otherwise treat any residual foci of breast tissue. It is imperative that conservative mastectomy is safe from an oncological perspective and not associated with higher rates of local recurrence compared with conventional or skin-sparing mastectomy without nipple preservation. Seminal breast conservation therapy trials have confirmed that preservation of the NAC as part of breast conserving surgery does not compromise overall survival and rates of local recurrence are acceptable when the remaining breast tissue is irradiated.

The aesthetic advantages of conservative mastectomy are well documented and recent data has emerged on psychological issues and other aspects of quality of life in women undergoing this type of mastectomy. However, the indications for conservative mastectomy remain to be defined and this procedure may not be appropriate for some women with larger breasts in whom reduction of the breast skin envelope is necessary. Preservation of the NAC as part of a skin-sparing mastectomy in patients for whom a mastectomy is otherwise indicated is of unproven safety and only practiced selectively for some patients with relatively small tumours located some distance from the NAC. Under these circumstances it might be reasonable to perform a conventional wide excision and oncoplastic glandular readjustment. The emergence of the conservative mastectomy has coincided with some important trends in surgical choice amongst breast cancer patients.

Breast conserving surgery

Breast conservation surgery has been established over the past 30 years as the preferred standard of surgical management for women with early stage breast cancer (3). Longer term follow-up data from several prospective randomized controlled trials have demonstrated survival equivalence for breast conservation therapy compared

with radical or modified radical mastectomy (MRM/RM) (4-7). An update of National Surgical Adjuvant Breast and Bowel Project (NSABP) B-06 trial with 20 years follow-up confirms that post-operative irradiation improves local recurrence-free survival with similar distant disease-free and overall survival for MRM, wide local excision and radiotherapy or wide local excision alone (8). These findings suggest that residual cancer cells are a determinant of local failure but not distant disease. There is a finite rate of ipsilateral breast tumor recurrence (IBTR) for patients undergoing breast conservation therapy with recent estimates of between 3.5% and 6.5% at 10 years (9). Moreover, systemic therapies reduce rates of IBTR by approximately one-third and are halved with anti-HER2 directed therapies. Breast conservation surgery represents a balance between oncological mandates and cosmetic outcomes and aims to excise tumor with 'negative' margins and acceptable cosmesis. Rates of in breast recurrence are determined by negative margin status, but no direct relationship exists between margin width and IBTR (10). A consensus statement has decreed that an adequate margin exists when tumor is not touching ink and recommends this as the standard definition for invasive cancer (11). A negative margin does not imply absence of residual disease within remaining breast tissue but implies a residual burden of tumor sufficiently low to be controlled with adjuvant treatments (radiotherapy and chemo/hormonal therapies). Although histological examination of mastectomy specimens reveals that many tumors are multifocal with additional tumor foci beyond the index lesion, contemporary rates of IBTR after breast conserving therapy are very low. Local surgery does not completely eliminate residual disease burden with local recurrence determined by a combination of surgery, tumor biology, radiation and systemic therapies (9).

Changing trends in breast surgery

Increasing numbers of women are opting for 'maximal surgery' which implies removal not only of the ipsilateral breast but also the contralateral breast (even when otherwise suitable for breast conservation surgery for a unilateral breast cancer). In some instances contralateral prophylactic mastectomy (CPM) can be justified, such as for patients with carriage of BRCA gene mutations, but otherwise there is no widespread evidence to support CPM. In recent years there have been divergent trends—some women seek 'maximal surgery' whilst others prefer minimal surgical intervention with a desperate desire to preserve as much breast tissue

as possible and avoid even unilateral mastectomy. Rates of CPM increased 150% between 1998 and 2003 (4% to 11%) and continue to do so with a doubling of CPM rates in the past 10 years (12). Furthermore, total mastectomy rates are decreasing in the USA but rates of breast conserving surgery have stabilized (13). With more women choosing 'maximal surgery', unilateral mastectomy has become a less commonly performed operation, but unilateral mastectomy rates are driving increased CPM rates. These trends are age dependent with dramatic increases in CPM amongst women <40 years of age (14). Nonetheless, increasing use of bilateral mastectomy is seen across all age groups, but is most pronounced for women <40 years. More women are choosing to undergo immediate breast reconstruction and requesting simultaneous CPM with breast reconstruction. The annual hazard rate for death from contralateral breast cancer has been decreasing since 1985 due to widespread use of adjuvant systemic treatment (15). Contemporaneous rates for development of contralateral breast cancer are about 0.2% per year and higher for those with BRCA mutations. Therefore rates of CPM are increasing, but paradoxically rates of contralateral breast cancer are decreasing.

This has to some extent been prompted by improvements in the availability and cosmetic outcomes of immediate breast reconstruction. Furthermore, many women chose implant-based reconstruction and it has been suggested that a desire to have matching breasts may be a driver for increased rates of CPM (simultaneous bilateral implant-based reconstruction) (16). Interestingly, patient satisfaction with bilateral implant-based reconstruction is higher than for unilateral reconstruction. The advent of nipple-sparing forms of mastectomy improves cosmetic outcome and may further increase rates of CPM. Long term outcomes from implant-based reconstruction are excellent and this desire to have matching breasts is relevant to increased rates of CPM. However, there may be surgical reasons for recommending mastectomy in more patients due to widespread use of pre-operative MRI for assessment of potential multifocality and confirmation of tumour size in patients who are otherwise considered suitable for conventional wide local excision *ab initio*. The indications for pre-operative MRI remain controversial and undoubtedly this modality of investigation is over-used and may have inadvertently led to increased rates of mastectomy—perhaps unnecessarily. Several studies have now assessed the effects of pre-operative MRI on either clinical (IBTR) or surgical (rates of re-operation) endpoints. In a retrospective study, Solin and colleagues

examined rates of IBTR amongst a group of 756 patients, half of whom underwent breast conserving therapy based on conventional modes of staging whilst half had additional pre-operative MRI. Rates of IBTR were similar at 8 years for patients undergoing pre-operative MRI compared with those who did not (3% versus 4%) with no differences in contralateral breast cancer, breast cancer specific survival or overall survival (17). Likewise, a similar study of pre-operative MRI found that rates of IBTR were independent of whether this investigation was carried out or not (1.8% versus 2.5%) (18). MRI is highly sensitive for detection of cancer (lower specificity) and a meta-analysis found that additional tumor foci were identified in 20% of newly diagnosed breast cancer patients (16% in the ipsilateral and 4% in the contralateral breast) (19,20). Moreover, this actually led to a change in surgical therapy in between 8% and 33% of patients which was usually a change from breast conservation surgery to mastectomy. However, many of these additional foci were not confirmed on second biopsies and the incidence of additional foci is higher than the long term rates of IBTR. Indeed, some patients forewent additional biopsies of these MRI detected lesions because of perceived delays in final surgery (which was likely to be mastectomy with immediate breast reconstruction) (21). Furthermore, the randomised Comparative Effectiveness of Magnetic Resonance Imaging (COMICE) trial failed to show that use of pre-operative MRI (dedicated breast coil) in addition to imaging with mammography and ultrasound led to any reduction in rates of re-excision for those patients undergoing pre-operative MRI (22). Furthermore, as previously emphasized, there is no evidence for any reduction in rates of IBTR from routine pre-operative MRI examination which can detect additional tumor foci. This implies that many of these additional foci have no clinical significance and will be adequately treated with adjuvant therapies such as breast radiotherapy and chemo-hormonal therapies (9). It is therefore questionable whether there is an increasing need to perform total glandular excision on the basis of pre-operative MRI findings *per se* (1). Additional tumor foci, especially in different quadrants of the breast should be confirmed with biopsy—guided either by ultrasound or MRI if sonographically occult. A retrospective study involving more than 5,000 patients treated at the Mayo Clinic found that women who had pre-operative MRI were more likely to undergo mastectomy than those who did not have MRI (54% versus 36%; $P < 0.0001$) (23). Though there is no causal relationship, this study did provide evidence for a link between increased

usage of MRI and increased mastectomy rates.

Women often overestimate their risk of developing contralateral breast cancer but fail to appreciate that removal of the other breast will not improve overall survival which is usually determined by prognostic features of the ipsilateral cancer (4). Increased genetic testing (for BRCA-1 and BRCA-2) has strengthened the indications for bilateral prophylactic mastectomy and unilateral therapeutic mastectomy with CPM in patients with a strong family history of breast cancer. For these patients preservation of the NAC along with the entire breast skin envelope may be appropriate and should be aimed for in the context of risk-reducing procedures. However, this group constitutes only a small proportion of all breast cancer (5-10% at most) and is certainly not an explanation for increased rates of mastectomy in some units.

Oncological and technical aspects of nipple preservation

Oncological aspects

Although it is feasible to dissect the skin and subcutaneous tissues from the breast parenchyma without risk of leaving remnant breast tissue, this is not the case for the NAC; the main lactiferous ducts converge upon the nipple and breast tissue and are inextricably linked with the tissues of the nipple itself. The areola can be readily dissected off the underlying breast tissue but in younger women with dense breasts this can be technically challenging and sometimes a thin layer of breast tissue must be retained to ensure viability of the NAC. With a conservative mastectomy, excision of the retro-areolar tissue is a particularly important manoeuvre and a balance must be achieved between complete excision of the duct system and preservation of blood supply to the NAC. The ducts are usually cored out of the nipple, although micro-anatomical studies suggest that breast tissue within the nipple contains no terminal duct lobular units. There are two histological issues to consider with preservation of the NAC; firstly, leaving behind residual, but normal breast tissue and secondly the potential problem of leaving cancerous tissue/cells when surgery is performed as a therapeutic procedure for a known breast cancer. The proximal bundle of ducts can be examined pathologically using a frozen section specimen and the NAC removed when cancer cells are present. Sometimes mastectomy is the preferred surgical option on the basis of tumour size and not proximity to the NAC. There is no reason to suppose that

tumors located away from the nipple would be associated with residual malignancy in the event of NAC preservation. In a retrospective pathological study of resected mastectomy specimens, malignant involvement of the nipple was found in 10.6% of cases. Moreover, cancer cells were found in the region of the nipple in only 6.7% of cases where the index lesion was a small (<2 cm) peripherally located tumor with no documented evidence of multi-focal lesions pre-operatively (24).

Despite these intuitive concerns about nipple sparing mastectomy for breast cancer, several groups have explored this procedure for smaller peripheral tumors situated more than 2 cm from the NAC. Enthusiasm for these approaches has been spurred on by reassuring reports about the oncological safety of skin-sparing mastectomy (25). Pioneering work from the European Institute of Oncology in Milan provided the foundations for the concept of conservative mastectomy (26). Between 2002 and 2007, just over 1,000 patients underwent nipple-sparing mastectomy for invasive ductal carcinoma (82%) or ductal carcinoma *in situ* (18%). All tumors were located away from the NAC at a minimum distance of 2 cm therefrom. Frozen section examination was undertaken in all patients at the time of surgery but there was a significant false negative rate associated with this procedure (8.6%). Moreover, 80% of patients received intra-operative radiotherapy (IORT) to the NAC with a single dose of 21 Gy from electron beams (ELIOT). In 20% of cases, radiotherapy was delayed due to ischaemic changes of the NAC intra-operatively (these patients subsequently received a fractionated dose of 16 Gy from a linear accelerator). There was a finite rate of partial (5.5%) and total (3.5%) nipple necrosis which necessitated removal of the nipple in 5% of cases. Patients with larger breasts were more susceptible to skin necrosis. An interim analysis at a median of 20 months follow-up (range, 1-69 months), revealed a very low rate of local recurrence (1.4%) and none of the relapsed cases involved the NAC directly. These very low rates of local recurrence with IORT prompt the question of whether acceptable rates of local recurrence for nipple-sparing mastectomy could be achieved without the use of radiotherapy. The Milan group have now published results from this cohort of patients at 50 months follow-up (27). A total of 11 (1.2%) patients have developed recurrence at the NAC [7 with DCIS (Paget's disease); 4 with invasive carcinoma] with an overall survival of 96.4% at 5 years. Patients with local recurrence underwent complete excision of the NAC with no evidence of further recurrence at a median follow-up of 33 months.

Interestingly, amongst the 8.6% of patients with a false negative frozen section, none have developed recurrence in the region of the NAC but half these cases were associated with local recurrence away from the NAC. Patients with widespread DCIS prompting mastectomy or invasive tumor with an extensive intraductal component were at higher risk of recurrence involving the NAC (DCIS is known to spread along ducts towards the nipple which may not be evident radiologically as microcalcification). Gerber and colleagues reported rates of local recurrence amongst a group of almost 300 patients for whom pre-operative investigations revealed a localised tumor more than 2 cm from the NAC without any extensive intraduct component (28). Patients underwent either skin-sparing mastectomy (51 patients), nipple-sparing mastectomy (61 patients) or conventional mastectomy (134 patients) with local recurrence rates of 10.4%, 11.7% and 11.5% respectively ($P=0.974$). Therefore no significant differences were noted for rates of local recurrence according to mastectomy type when patients were selected appropriately (small peripheral tumours without extensive DCIS and unlikely to require chest wall radiotherapy). One should be wary about nipple-preserving procedure in patients for whom mastectomy would be indicated on surgical grounds, such as biopsy proven multifocal disease, larger primary tumours (>4 cm), location in more central parts of the breast and associated DCIS. In these circumstances, there is a risk of potential nipple involvement and rates of local recurrence may be increased in the future. Age, tumour size, nodal status and distance between tumour and NAC are crucial factors in selection of patients and minimising local recurrence. However, there is no clear association between tumor-NAC distance and rates of recurrence (29,30) with freedom from NAC recurrence reported in several studies where tumor-NAC distance was only 1 cm (27,31). Key questions to address for conservative mastectomy include the following:

- (I) Is there an absolute upper size limit above which rates of local recurrence are unacceptable?
- (II) What minimum distance between tumor and nipple should be stipulated?
- (III) Should this distance be modulated by tumor size and is it best measured with MRI?
- (IV) Can conservative mastectomy be safely recommended for a small tumor (≤ 1 cm) which lies just outwith the NAC?

Paradoxically, these tumours can be managed with a central excision in large breasted patients, but no attempt is made to preserve the nipple which is excised en bloc

with the tumor. In a comprehensive review of the available literature, Mallon and colleagues examined the incidence of occult nipple malignancy when nipple-sparing mastectomy was undertaken for primary breast cancer and found an overall incidence of 11.5% (32). Nipple involvement was statistically more likely ($P<0.05$) when associated with the following tumor characteristics (i) location <2 cm from the NAC; (ii) presence of nodal metastases; (iii) lymphovascular invasion; (iv) HER2 positivity; (v) negative hormone receptor status and (vi) size >5 cm. In addition, there was a greater chance of cancer within the NAC when tumors were multifocal and situated more centrally within the breast. The authors reported a nipple recurrence rate of 0.9% and concluded that nipple-sparing mastectomy for breast cancer was safe when patients were appropriately selected, namely with unifocal or well-circumscribed multifocal node negative, grade I or II, ER positive, HER2 negative tumors. Murthy and Chamberlain have further reviewed the evidence base for nipple sparing mastectomy and consider this a “reasonable alternative” for risk-reducing procedures and selected breast cancer patients. They emphasize the importance of pre-operative investigations and careful evaluation of MRI and mammographic features together with intra-operative frozen section examination. Moreover, standardization of pre-operative work up, intra-operative assessment and surgical technique is essential with clarification of radiotherapy delivery systems (intra-operative versus post-operative external beam) (33).

Technical aspects

Attention to surgical technique is especially important in the context of nipple-sparing mastectomy where careful and meticulous dissection deep to the NAC is essential to ensure both complete excision of ductal tissue with preservation of nipple vascularization. Skin-sparing mastectomy with sacrifice of the NAC is usually undertaken using a periareolar incision. This can be modified/extended if indicated to encompass skin overlying any tumor adjacent to the NAC and associated with skin tethering from involvement of the suspensory ligaments. By contrast, incisions must be adjusted accordingly when the NAC is preserved in order to retain a vascular supply from the adjacent mastectomy skin flaps via dermal vessels. Skin incisions can be placed around part of the NAC circumference with a lateral extension, but incisions placed remote from the NAC are preferred. These include the sub-mammary fold, a radial incision in the upper outer quadrant



Figure 1 Preoperative assessment of a 24-year-old patient with BRCA 1 mutation carrier.



Figure 2 Two years follow-up post bilateral nipple sparing mastectomies using a hemi-Y incision and immediate breast reconstruction with implant and acellular dermal matrix.



Figure 3 A 42-year-old patient 8 months post wise pattern mastectomy and nipple preservation for BRCA 2 mutation carrier (frontal view).

(which facilitates axillary surgery) or possibly a mid-axillary line incision when endoscopic-assistance is employed (34–38). Radial incisions have been popularised by the Milan group but may be less advantageous in the post-Z11 era when fewer patients undergo completion axillary lymph node dissection after a positive sentinel lymph node



Figure 4 A 42 years old patient 8 months post wise pattern mastectomy and nipple preservation for BRCA 2 mutation carrier (lateral view).

biopsy (the axilla should ideally be accessed through the breast incision and not a separate counter axillary incision) (39–41). Nonetheless, periareolar incisions are more likely to be associated with nipple necrosis and another alternative is the omega pexy incision (34). An interesting surgical manoeuvre is to dissect the retro-areolar tissue under local anaesthesia in advance of definitive surgery in order to ‘pre-condition’ the blood supply of the NAC by stimulating inflow of blood from the adjacent peripheral skin (42,43). The skin flaps for a conservative mastectomy are dissected in a similar manner to skin-sparing mastectomy with dissection along the cleavage or ‘oncological’ plane which lies between the subcutaneous fat layer and the superficial fascia of the breast. It is particularly important to maintain adequate thickness of the flaps in patients with larger breasts for whom the flaps will be proportionately longer and at higher risk of ischaemia. In some circumstances reduction of the breast skin envelope leads to malpositioning of the NAC which must then be sacrificed and subsequently reconstructed. Most surgeons prefer to preserve the pectoralis major fascia which assists with creation of an intact sub-pectoral pocket for implant-based reconstruction (44) (Figures 1–4). Another issue with conservative mastectomy is reduction of the skin envelope to achieve optimal shape of the breast with good ptosis—especially larger breasts. Hence, despite preservation of the NAC, some of the skin is sacrificed and no longer can it be claimed that there is ‘no disruption to the appearance of the breast’. Many surgeons do not preserve the NAC even when performing prophylactic mastectomy because of malpositioning in the reconstructed breast which may necessitate shift of the NAC at a later date. Likewise, immediate nipple reconstruction at the time of mastectomy and reconstruction for malignancy can lead to asymmetry

with respect to the NAC.

Immediate breast reconstruction after conservative mastectomy can be undertaken using either implant-based or flap-based techniques for small/moderate and larger sized breasts respectively. Patient satisfaction with bilateral implant-based reconstruction is higher than for unilateral reconstruction. Long-term outcomes from implant-based reconstruction are excellent and a desire to have matching breasts may be relevant to increased rates of CPM. However, there is evidence that unilateral implant-based reconstruction is worse than unilateral flap based reconstruction after 10 years in terms of maintenance of breast symmetry (16). Both expanders and fixed-volume implants can be used for reconstruction after conservative mastectomy and increasingly acellular dermal matrix is being used as an adjuvant material to reinforce the pocket and provide maximal implant coverage (45).

Cosmetic outcomes and quality of life

Cosmesis

Amongst the aforementioned group of 1,000 patients treated at the European Institute of Oncology in Milan, 414 were evaluated from an aesthetic perspective using a 10-point scale (1 worse; 10 best results). Overall score for both surgeons and patients was 8/10 with poorer scores relating to reduced sensitivity of the NAC rather than appearance of the reconstructed breast. Most patients underwent implant-based reconstruction with no significant differences in cosmetic outcome between expander and fixed-volume implants. Other groups have also reported favorable outcomes from conservative mastectomy in conjunction with implant-based immediate breast reconstruction (46,47). For patients undergoing autologous flap-based reconstruction, Gerber and colleagues reported notable decreases in cosmetic scores between the 5th and 9th years post-operatively whilst Denewer and Farouk observed excellent aesthetic outcomes in 82.9% of patients reconstructed with a modified extended latissimus dorsi muscular flap after conservative mastectomy (48). In addition, more than 90% of these patients experienced some nipple sensation post-operatively.

Psychological aspects

Using a specially developed patient questionnaire, researchers in Milan have examined the impact of conservative

mastectomy on global health-related quality-of-life (49). Several key domains were evaluated including emotional status, anxiety levels, sexual functioning and body image amongst a group of well-educated women with an average age of 46 years. Women who underwent conservative mastectomy felt more comfortable viewing their own naked body and being seen by their partners compared with women who had reconstruction of the NAC after skin-sparing mastectomy. The sense of mutilation was significantly less, and cosmetic satisfaction significantly higher for conservative mastectomy patients who considered preservation of the NAC important in coming to terms with a cancer diagnosis and perception of a normal body image. Of note, these psychological benefits were not offset by an increased fear of recurrence due to retention of the NAC. A further analysis has revealed that a majority of women chose conservative mastectomy believing that nipple preservation will reduce psychological stress, enhance body image and improve overall satisfaction with results of breast surgery (50).

Conclusions

The procedure of 'conservative mastectomy' is appropriate for those patients who would otherwise be suitable for conventional wide excision with preservation of the NAC but who (for one reason or another) request mastectomy from personal choice. These patients are not recommended mastectomy from a surgical point of view and indications for conservative mastectomy remain to be defined. Where there is biopsy proven evidence of multicentricity which does not involve nor encroach upon the NAC radiologically, then conservative mastectomy may be indicated from a surgical perspective. There is currently no evidence that women should undergo 'maximal' surgery based on MRI findings of multicentric cancer. An important issue is post-mastectomy irradiation and demonstration of low rates of recurrence for NAC irradiation following nipple-preserving mastectomy begs the question of whether radiotherapy can be selectively omitted for this group of patients.

Further data are required to prove the oncological safety of conservative mastectomy and to define both selection criteria and the need for irradiation of the NAC. On the basis of evidence to date, it seems reasonable to exclude conservative mastectomy in those cases with evidence of extensive DCIS and multifocality—particularly when additional foci lie in the central zone of the breast. These questions demand further high quality studies before conservative mastectomy is widely adopted for localised

cancers in patients without a confirmed BRCA gene mutation or strong family history of breast cancer. Limited conclusions can be drawn from small mono-institutional studies where much heterogeneity in practice exists (51). Rates of IBTR after breast conserving surgery have reduced dramatically in recent years and therefore conservative mastectomy has less potential for any oncological benefit in the absence of any overall survival gain. The main advantages of this procedure are likely to derive from its psychological and cosmetic benefits compared to oncoplastic breast conserving surgery. Nonetheless, “rigorous scientific scrutiny” (33) of this technique is mandatory to confirm oncological equivalence with skin-sparing mastectomy for breast cancer patients.

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Footnote

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Introduction to conservative mastectomies

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Abstract: Conservative mastectomy (CM) has become an established alternative in the treatment of breast cancer, offering by different techniques a good cosmetic outcome, as well as oncologic control. The different options to achieve these goals are presented. Oncoplastic treatment of breast cancer needs planning and knowledge of well-established plastic surgery techniques.

Keywords: Skin-sparing mastectomy (SSM); nipple-sparing mastectomy (NSM); skin-reducing mastectomy (SRM)

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The definition of conservative mastectomies was first introduced in the medical literature by Dr. Nava *et al.*, of the Istituto Nazionale dei Tumori Milano, Italy (1).

Nowadays, the aesthetic result for primary treatment of breast cancer patients is as important as oncological safety and must be the actual goal of the breast surgeon. In this context, new surgical procedures emerged as “conservative mastectomies”, expanding the concept of a better outcome for breast conservation procedures.

In the last 50 years, breast surgery evolved from maximum tolerable treatment with aggressive and mutilating interventions, like radical mastectomy, to minimum effective treatment, and from an anatomical concept of cancer spread to a biological concept.

Conservative mastectomies incorporate the advantage of tumor and total gland excision, as in a traditional total mastectomy, with improvement in the esthetic result through conservation of the skin envelope and the nipple areolar complex (NAC). The use of anatomical expanders and high cohesive silicone implants ensures high quality immediate reconstruction in these patients, but autologous tissue can also be used to fill the empty skin pocket after gland resection.

At first glance, conservative mastectomy (CM) may appear similar to subcutaneous mastectomy, which was first described by Freeman (2), and it's still used for risk reduction.

However, there are two significant differences: the thickness of the skin flaps and the presence of retroareolar tissue.

As a curative procedure, CM incorporates the entire breast parenchyma, sparing only the skin, or in selected cases utilizing NAC preservation (3).

NAC ischemia and necrosis are some of the expected complications; however, solutions for these are technically simple. The issues relevant to the technique are oncological safety and long-term follow-up.

Three different techniques for CM that have been oncologically validated are:

- skin-sparing mastectomy (SSM) (4);
- nipple-sparing mastectomy (NSM) (5);
- skin-reducing mastectomy (SRM) (6).

CM by using any of these three techniques is indicated when mastectomy is unavoidable, or when the patient prefers a mastectomy instead of breast conservation surgery (BCS). CM is also indicated for small breasts, when more than 30% of the breast volume must be resected and the cosmetic result after radiotherapy (RT) will be poor.

Preserving skin, NAC, and the inframammary fold (IMF) enables improved immediate reconstruction with both implants and autologous tissue (*Tables 1-6*).

The difference in terminology between these approaches to breast cancer is important.

Table 1 Indications for SSM

DCIS
Stage I-II infiltrating breast carcinomas (Union for International Cancer Control-American Joint Committee on Cancer), and in very selected stage III cases (7,8)
Positive retroareolar frozen section during NSM
SSM, skin-sparing mastectomy; DCIS, ductal carcinoma in situ; NSM, nipple-sparing mastectomy.

Table 2 Contraindications for SSM

Inflammatory carcinoma
Skin involvement
Locally advanced carcinomas
Smoking (relative contraindication)
SSM, skin-sparing mastectomy.

Table 3 Indications for NSM

Large or multicentric DCIS
Invasive carcinoma 2 cm from nipple without skin involvement
Multifocal multicentric invasive carcinoma (ductal intraepithelial neoplasia grades 1, 2, and 3)
BCS with an expected poor esthetic result (more than 30% resection)
<i>BRCA</i> genes 1 and 2
Medium or small breast with <8 cm NAC-IMF distance
Negative retroareolar frozen section
Patient preference (if completely informed of its advantages and disadvantages)
NSM, nipple-sparing mastectomy; DCIS, ductal carcinoma in situ; BCS, breast conservation surgery; NAC-IMF, nipple areolar complex-inframammary fold.

Table 4 Contraindications for NSM

Absolute
Inflammatory carcinoma
Skin involvement
Pathologic NAC secretion
Relative
Previous RT, smoking, DBT
Large, ptotic breasts
Recent peri- or subareolar surgery
NSM, nipple-sparing mastectomy; NAC, nipple areolar complex; RT, radiotherapy; DBT, diabetes.

Table 5 Indications for SRM

Unicentric or invasive carcinoma without skin involvement
Large breasts, at least 8 cm from NAC to IMF
Multifocal multicentric invasive carcinoma
Large or multicentric DCIS or LCIS
<i>BRCA</i> genes 1 and 2
Patient preference
BCS with expected unsatisfactory result
Contraindication for RT
SRM, skin-reducing mastectomy; NAC, nipple areolar complex; IMF, inframammary fold; DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ; BCS, breast conservation surgery; RT, radiotherapy.

Table 6 Contraindications for SRM

Absolute
Inflammatory carcinoma, skin involvement
Relative
Previous RT, smoking, DBT
Tumor in lower quadrants
SRM, skin-reducing mastectomy; RT, radiotherapy; DBT, diabetes.

BCS with Previous RT has been accepted since the 1980s as a standard therapeutic modality for low-grade breast cancer.

This is a partial breast resection that includes lumpectomy (removal of the lump), quadrantectomy (removal of one quarter, or quadrant, of the breast), and segmental mastectomy (removal of the cancer, some of the breast tissue around the tumor, and the lining over the chest muscles beneath the tumor). A universally accepted basic oncological priority is to maximize disease control and obtain a satisfactory cosmetic outcome.

Different oncoplastic planning approaches and techniques can be used to improve the final cosmetic result in BCS (9,10), with rigorous selection of candidates. In addition to a complete history and physical examination, the most important guideline includes preoperative diagnostic imaging, including magnetic resonance imaging (MRI) (Tables 7,8).

Desirable cosmetic result in BCS and in CM is mandatory and a key factor in selecting an approach, when oncologic safety is guaranteed with either modality (11).

Different CM techniques appear to combine oncological safety with high quality cosmetic outcomes (12,13), and this

Table 7 Indications for BCS

Small, unicentric tumors
Medium-sized or large breasts
Favorable physical factors
Likely good cosmetic outcome
Patient compliance
BCS, breast conservation surgery.

Table 8 Contraindications for BCS

Locally widespread disease
Multicentricity
Diffuse (malignant) microcalcifications
First or second pregnancy trimester
Patients with mutations of <i>BRCA1</i> and <i>2</i> genes
Previously irradiated thoracic wall
BCS, breast conservation surgery.

procedures are an extending concept of breast preservation. Cooperation between breast and reconstructive surgical teams is still necessary, and both teams must be aware of the oncological and plastic surgery approaches and oncoplastic technique for each case (14). CM offers today an important psychological benefit and oncological safety for a large group of breast cancer patients.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Skin-sparing mastectomy

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Abstract: The surgical treatment of breast cancer has evolved rapidly in recent decades. Conservative treatment was adopted in the late 1970s, with rates above 70%, and this was followed by a period during which the indications for surgical intervention were expanded to those patients at high risk for *BRC1*, *BRC2* mutations, and also due to new staging standards and use of nuclear magnetic resonance. This increase in the indications for mastectomy coincided with the availability of immediate breast reconstruction as an oncologically safe and important surgical procedure for prevention of sequelae. Immediate reconstruction was first aimed at correcting the consequences of treatment, and almost immediately, the challenge of the technique became the achievement of a satisfactory breast appearance and shape, as well as normal consistency. The skin-sparing mastectomy (SSM) in conservation first and nipple-areola complex (NAC) later was a result of this shift that occurred from the early 1990s to the present. The objective of this review is to present all these developments specifically in relation to SSM and analyze our personal experience as well as the experience of surgeons worldwide with an emphasis on the fundamental aspects, indications, surgical technique, complications, oncological safety, and cosmetic results of this procedure.

Keywords: Breast cancer; oncologic breast surgery; oncoplastic breast surgery; skin-sparing mastectomy (SSM)

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Introduction

Our post-mastectomy breast reconstruction experience has taught us that it is necessary to accurately define surgical sequelae to prevent problems in reconstruction and to design it according to the individual characteristics of each patient. Techniques involving autologous procedures such as dorsi flap, TRAM flap (TF), DIEP flap, and lipotransfer, among others, and heterologous procedures such as tissue expanders and prosthetic devices have proven to be excellent for the restoration of breast volume. These techniques were introduced in the 1980s (1,2), when delayed breast reconstruction was popular, and outcomes improved with the increased experience of involved surgeons and advances in the prosthetic materials used for these procedures.

Incorporating immediate reconstruction as an oncologically safe surgical procedure (3-5) not only improved patients' physical and psychological perspectives but also forced surgeons to refine their techniques. Skin-sparing mastectomy (SSM) was later introduced to optimize the cosmetic outcomes of smaller incisions and to preserve breast anatomy. As a result of these conceptual changes, the following new questions arose:

- Does immediate reconstruction complicate or modify the course of the disease?
- In cases where the surgeon can select the incision location and length, can this procedure improve the outcome of reconstruction?
- Does conserving more skin and mammary structure have a direct impact on the final aesthetic result?

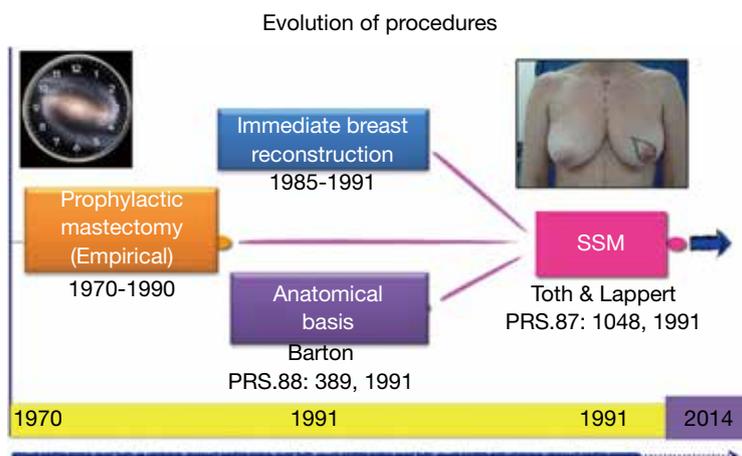


Figure 1 Evolution of the procedures (I) that generated the skin sparing mastectomy. SSM, skin-sparing mastectomy.

- Do aesthetic and conservative incisions have implications for the control of local and/or distant disease?

For the second time since the advent of radical conservative surgery, its applicability in the surgical treatment of breast cancer has been questioned. In this article, we discuss the origin of mastectomy with preserved skin, its fundamental aspects, indications, technique, complications, oncological safety, and finally cosmetic outcomes.

Overview

In June 1991, Toth and Lappert (6) first used the term “skin-sparing mastectomy” for immediate reconstruction, and around the same time, Kroll *et al.* (7) published the MD Anderson experience in 100 cases using the same technique. These reports led to the start of an interesting discussion on the improvement of cosmetic results and parallel doubts regarding local disease control.

But this story actually begins here, but before and serendipity. Barton *et al.* (8) has a job where I wanted to test the hypothesis insecurity of prophylactic mastectomies [retaining skin and nipple areola complex (NAC)] with the assumption that these glandular residue left over that year. A comparison with conventional cancer mastectomies (without skin sparing) performed by trained surgeons of the same institution revealed persistent gland flaps, sub-mammary furrow, and axillary extension, taking these samples to independent surgeons who conducted the primary resection. Contrary to expectations, the rates of glandular residue were similar between the two groups (21% with therapeutic

mastectomy versus 22% with prophylactic surgery), which raised questions as to the value of prophylactic surgery and the effectiveness of conventional radical methods. This experience, in parallel with the first publication on immediate breast reconstruction mastectomies, marked the start of the SSM era, and a new horizon had been set for good cosmetic results and oncological safety (*Figure 1*).

With the discovery of mutations to *BCRA1* (9) and *BRCA2* (10) oncogenes in 1994 and 1995, respectively, and their association with high breast cancer risk, new preventative measures were advocated for high-risk patients. Stefanek *et al.* (11) redefined the term “risk reduction surgery” for prophylactic mastectomies, which was the start of another new chapter in breast cancer surgery. First, preventative and therapeutic indications were postulated in an attempt to not only retain the skin but also the NAC (12,13). This therapeutic approach is the subject of ongoing controversy, as indicated in previously published research protocols (*Figure 2*).

Definitions and classifications

SSM is defined as a simple or radical surgery with modified minimal incisions that retain the widest possible coverage and sub-cutaneous breast groove but dry the NAC, flaws of previous biopsies and/or scarring caused by diagnostic percutaneous biopsies. Access to the armpit for a possible sentinel-node biopsy or axillary dissection is obtained through the same incision. An additional incision may be necessary to perform the reconstructive procedure (e.g., microsurgical axillary anastomosis). SSM is classified into

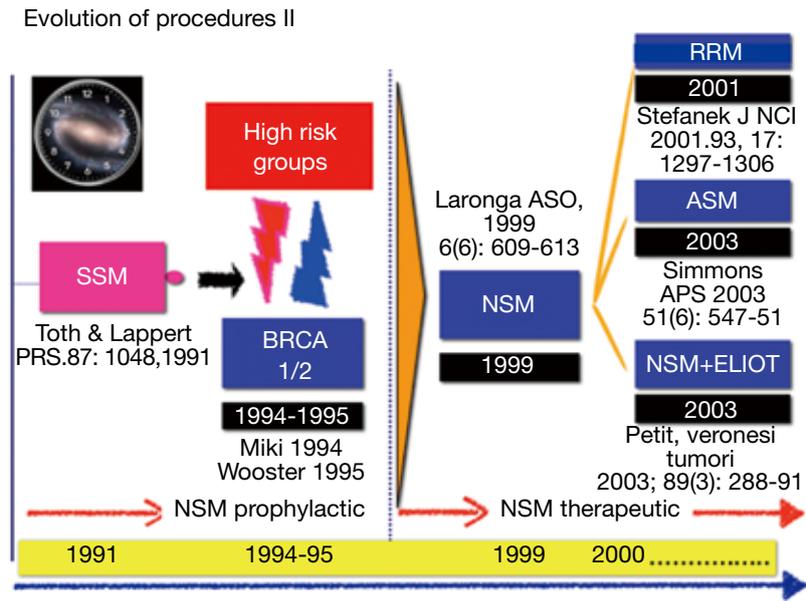


Figure 2 Evolution of the procedures (II) of the SSM to Nipple Sparing Mastectomies (risk reduction and therapeutic). SSM, skin-sparing mastectomy; NSM, nipple sparing mastectomy; ASM, areola sparing mastectomy; ELIOT, intraoperative radiotherapy with electrons.

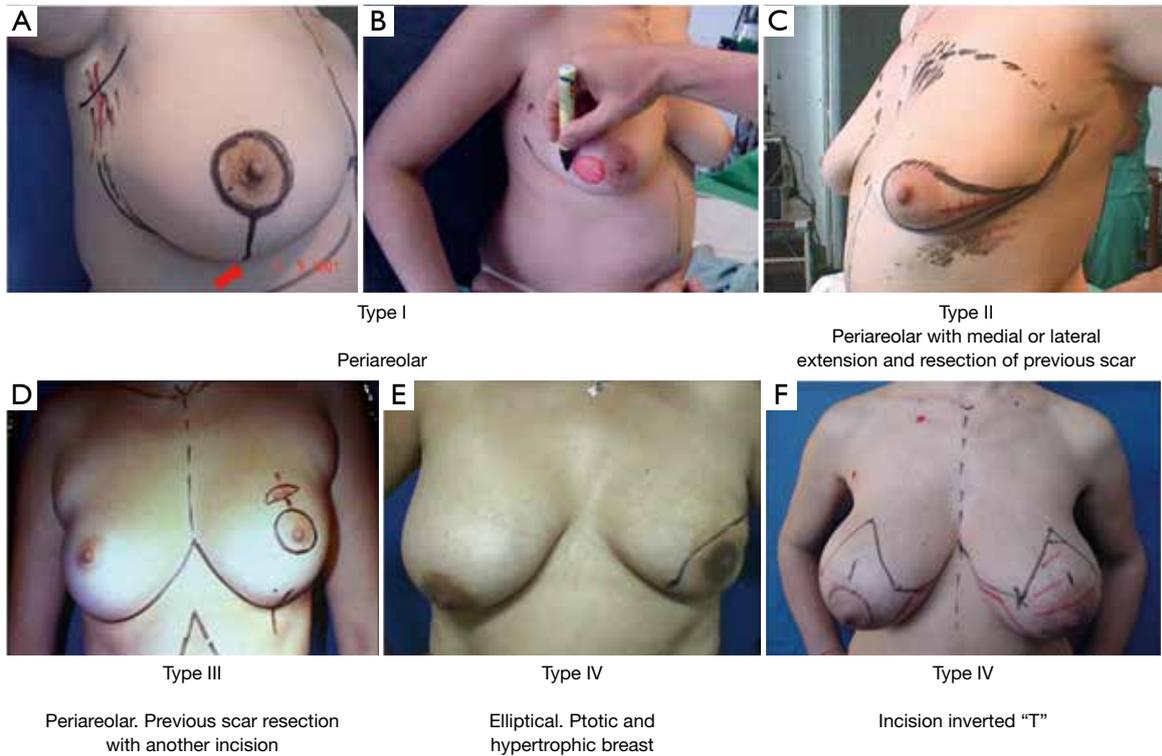


Figure 3 Skin sparing mastectomies. Classification: (A,B) Incision type I; (C) incision type II; (D) incision type III; (E) incision type IV; (F) incision type IV.

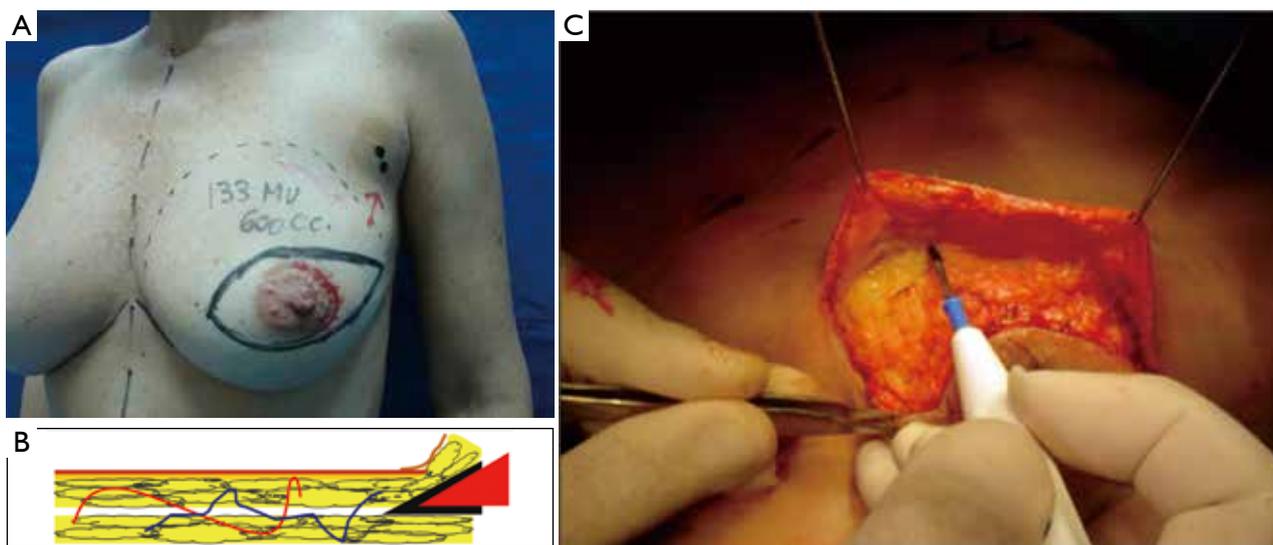


Figure 4 (A) Skin sparing mastectomy design; (B,C) dissection of the flaps in the plane of the superficialis fascia. Careful management of mastectomy flap to prevent vascular complications.

the following five types (6,14,15), as shown in *Figure 3*:

- (I) NAC peri-areolar resection or losangic resection of breast skin;
- (II) Resection of the NAC with medial or lateral extension and previous biopsy scar resection;
- (III) NAC peri-areolar resection and incision for resection of previous biopsy scar;
- (IV) Elliptical, wider resection of skin including the NAC aimed at reducing ptosis (indicated in ptotic and hypertrophic breasts);
- (V) Resection of skin and CAP with inverted T pattern (indicated in ptotic and hypertrophic breasts).

Indications

SSM can be performed in patients requiring mastectomy for: ductal carcinoma *in situ*; stage I-II infiltrating breast carcinomas [the Union for International Cancer Control and American Joint Committee on Cancer (UICC-AJCC)], and in much selected cases, stage III (16); and local recurrences (LRs) after conservative treatment, when the skin has a slight heating sequel (17). Contraindications for SSM include: inflammatory carcinomas, locally advanced carcinomas, and smoking (relative contraindication).

Surgical technique

For good outcomes with a low complication rate, it is

necessary to consider the fundamental aspects of this technique. First, the incision must be designed depending on the presence or absence of scars after excisional biopsy or puncture, as well as breast volume and ptosis (*Figure 3*).

In type I SSM, a 5-mm incision is made from the edge of the NAC with its surroundings marked, and a second transverse axillary incision can be made for axillary dissection or a possible microsurgical anastomosis. Some situations may require the peri-areolar incision to be extended into the armpit or to the 6 o'clock position to facilitate performance of the reconstruction technique. In type II, contemplates inclusion in NAC incision and scar prior continuity being designed in particular according to the present scar. In type III SSM, the incisions for NAC resection and previous scar are designed separately, to allow a “bridge” between both cutaneous non-small margins and avoid possible loss of vitality. Types IV and V are for ptotic breasts, when correction of the asymmetry of the opposite breast is considered, and can be used with elliptical skin resection or incision techniques such as the inverted “T” resection performed bilaterally for the NAC.

The dissected mastectomy flaps require a more detailed explanation as they are the key factors in this surgery from the oncological as well as postoperative vitality perspectives. The dissection must be meticulous, and the flaps must be of uniform thickness to avoid trauma with spacers. Very thin flaps do not increase oncological safety and are associated with a higher incidence of skin necrosis (*Figure 4*) (18).

Previous anatomical studies have shown that only 56% of patients have superficial layer of the superficial fascia, which facilitates dissection, but the remaining 44% is difficult to perform this surgical technique. Moreover, in both cases, there may be a mammary gland near the dermis, making it virtually impossible to complete removal of the breast tissue without compromising the vitality of the flaps (19) (Figure 5).

Breast resection is performed using conventional techniques such as axillary dissection or sentinel-node biopsy, which preserve the structure and the sub-groove (groove in the sub-mammary gland) where occurrence of disease is rare (Figures 6 and 7) (20).

The resected tissue should be examined by a pathologist in the operating room, orient, make a mammography,

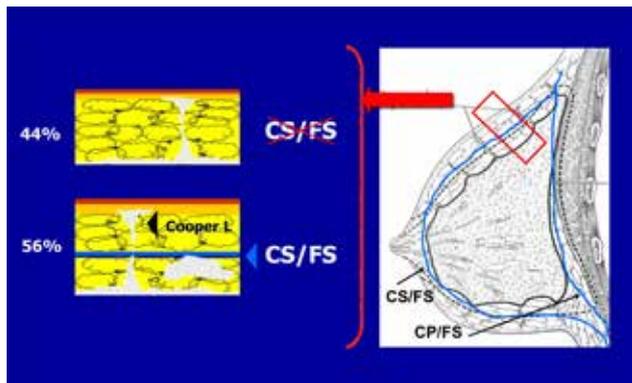


Figure 5 Anatomical variations of the mastectomy flaps in the presence surface sheet—superficialis fascia (CS/FS) or absence and location of the mammary gland in relation to the dermis (19).

especially in the breast tissue surrounding the tumor and confirm that it is free of disease. Otherwise the surgeon should expand the cutaneous resection. This examination is especially important for *in situ* carcinomas, and it decreases the risk of LR (Figure 8) (21).

The four primary reconstruction techniques used are: TF, pedicled or a microsurgical flap such as the DIEP flap; temporary or definitive anatomical expanders, with prosthesis indicated exceptionally; extended latissimus dorsi flap; latissimus dorsi flap over prosthesis or expander.

Complications

Necrosis of the mastectomy flaps is an important complication and requires extensive care. Avoiding necrosis is crucial for the final cosmetic result, especially if the reconstruction is performed with an expander and/or prosthesis, where this complication may cause extrusion and failure of the procedure. Necrosis is prevented with meticulous preparation of the mastectomy flaps, which is necessary to optimize the outcomes of the surgical technique. The flaps must be of a uniform thickness to prevent devitalization.

In patients in whom SSM and placement of expanders are indicated, especially in those with an increased risk of necrosis due to special circumstances such as tobacco use (22), it is important to cover the implant with a complete muscular pocket or use acellular dermis to minimize the consequences of a skin complication



Figure 6 Skin-sparing mastectomy type I (periareolar) and axillary dissection. (A) Conservation of cutaneous pocket and the submammary fold, preserving the anatomical limits; (B) mastectomy and axillary dissection specimen.



Figure 7 Skin-sparing mastectomy type I (periareolar) and sentinel node biopsy through the same incision detected by Gamaprobe. Excision of skin percutaneous biopsy scar.

(*Figure 9*) (23). If necrosis occurs, whether or not muscular coverage was provided, further surgical exploration is indicated to prevent the loss of the implant.

According to a protocol described in recent publications (24,25) we are making pockets with pectoralis major on the inner upper region of the breast, sutured to a mesh silk (SERI™ Surgical Scaffold, Allergan, California, USA) in the outer lower region achieving full coverage of the expander and evaluate whether this technique provides the same results in terms of complications and aesthetics, which completely muscular pocket (*Figure 10*).

The patient's smoking status must also be assessed with regard to the reduction of necrosis. Nicotine is a direct vasoconstrictor that affects the skin; it has an indirect effect on the production of capillary flow by inhibiting release of catecholamines. Non-smoking status is therefore preferred (relative contraindication).

Radiotherapy influences various aspects of surgical planning and outcome. When performed before surgery, it can negatively influence the final aesthetic result and increase

the rate of complications (necrosis of skin flaps). When used as an adjuvant treatment or for a LR, it can worsen the aesthetic result according to the type of reconstructive technique employed (26). Therefore, in general, in patients who have undergone previous irradiation and SSM, reconstruction techniques such as DIEP flap and TF are preferred to improve outcomes and favorably influence the preserved skin by preventing necrosis, as these minor procedures help maintain the cosmetic results (*Figure 11*).

In previous publications, flap necrosis has been reported in 5.6-8% (27) of conventional mastectomies. In SSM, it has been reported in 3-15% of cases depending on the series (28). In our experience, the incidence of flap necrosis was relatively low, at 5.6% (26), possibly related to the care taken in patient selection and optimization of the surgical technique.

Oncological safety

The big question that this technique was in its infancy was his relationship to the risk of higher rates of LR.

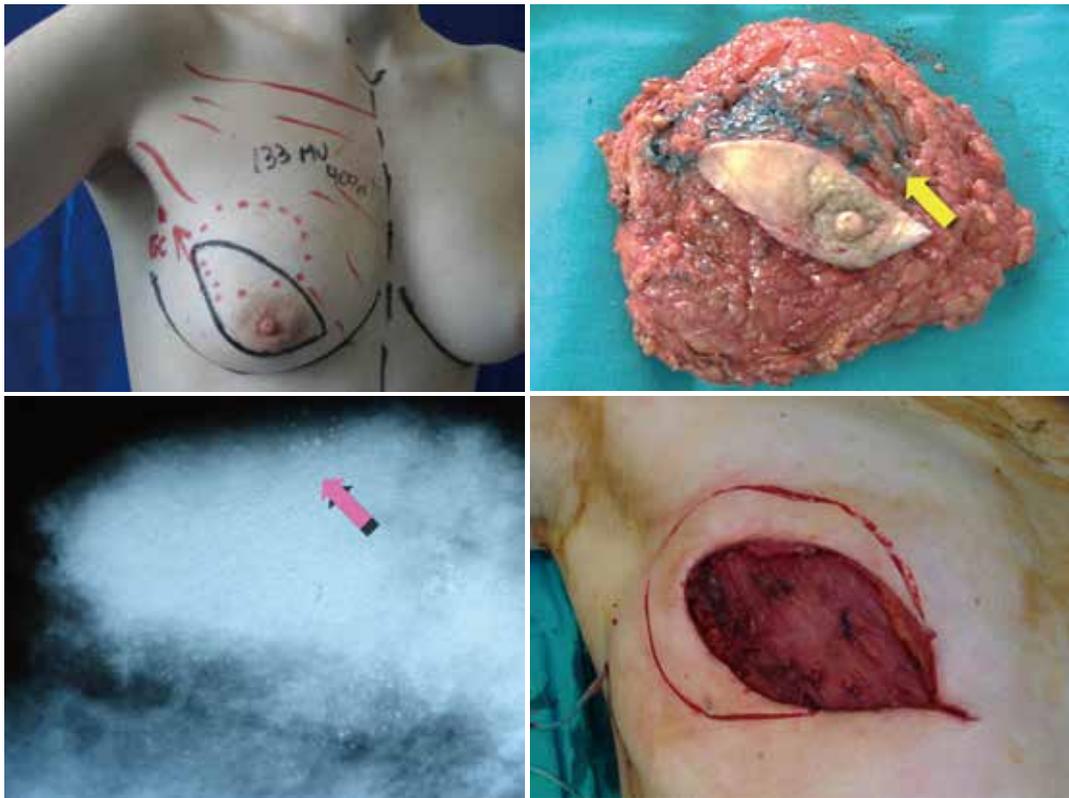


Figure 8 Skin-sparing mastectomy with suspicious microcalcifications near the dermis (Mammogram). Mastectomy specimen stained with ink. Margins were insufficient in the frozen section. Bottom-right: extension of cutaneous resection.



Figure 9 Skin-sparing mastectomy and reconstruction with expander. Prevention of complications. A complete muscle dissection pocket covering the implant in its entirety. The risk of extrusion and loss of the prosthesis to a possible skin necrosis decreases.

As is known histological examination of the RL, rarely shows identifiable breast tissue. Traditional literature, in the past associate LR with inadequate surgical technique, determining that recurrences, might result from residual tumor remnants of the intervention.

However, despite the technical variations, LR rates have remained similar over the years (29,30). Therefore, it is

clear that there are other predictive factors of LR.

The significance of the LR these findings is not well understood. Current concepts of tumor biology and post-mastectomy LR have pointed to these LRs as “risk markers” of distant metastases (31). Over 90% of LR is detected within 5 years of initial treatment, and 30-60% is associated with simultaneous systemic disease. The prognosis may be more



Figure 10 Skin-sparing mastectomy and reconstruction with expander. Prevention of complications. Dissection of the pectoralis major muscle and realization of a full pocket coverage of the expander, with the help of a mesh of silk. Outcome at 1 month after surgery.



Figure 11 Skin-sparing mastectomy and reconstruction with free tram flap in a local recurrence of conservative treatment. Patient irradiated and smoking. Extensive skin necrosis. Local expectation and toilette. Autoshaping sequel and secondary scar correction. Final result.

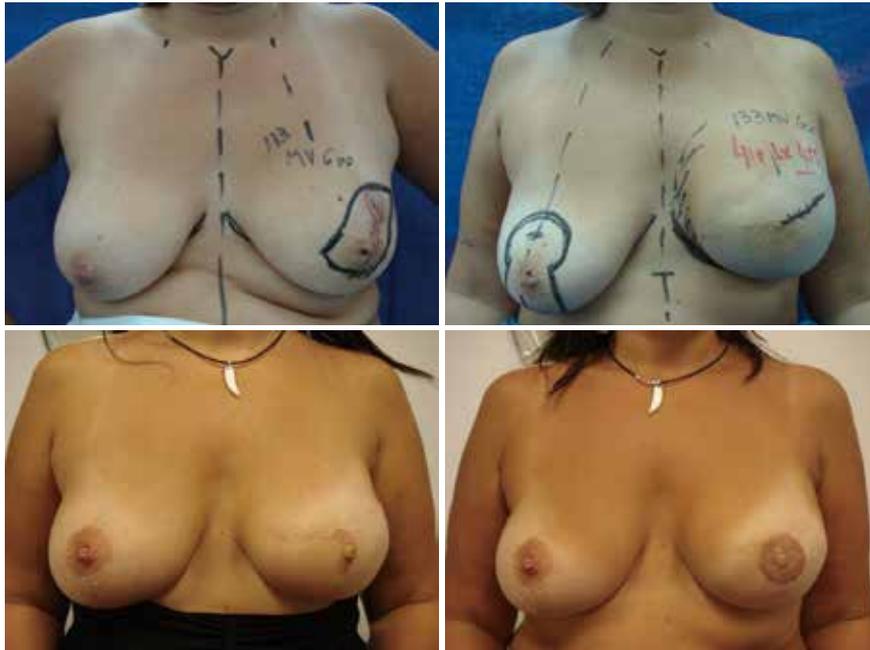


Figure 12 Skin-sparing mastectomy type II axillary dissection, and immediate breast reconstruction with anatomical expander. Top right: planning the second time to change expander for definitive prosthesis and reduction of the opposite breast. Down: satisfactory end result, then the reconstruction of the nipple and areola tattoo.

favorable in cases of isolated LR.

Retrospective studies published since the description of the surgical technique by Toth and Lappert in 1991 (6) have analyzed the rate of local relapse.

Kroll *et al.* (7) reported the first statistical results of the MD Anderson Cancer Center Institute as an LR rate of 1.2%, with a mean of 23.1 months. Following this, several groups published their retrospective experience with mastectomies without skin sparing comparing them with SSM and found no significant differences in the rate of LR, as reported by Cunnick and Mokbel (32).

In our experience, a comparison of the two procedures did not reveal a statistically significant difference in LR rates. With a mean of 68 months, LRs were observed in 5.4% in the SSM group versus 5.1% in the group of not SSM (33).

When we analyze the LR rate of patients who underwent SSM and compare it with the rates reported in randomized prospective studies of mastectomies without reconstruction (31), relapses were found to occur in 2-10% of patients with a follow-up of 6-10 years; these figures are comparable to those of reconstructive procedures that retain skin.

Although, to date, no prospective, randomized study with a control group has been conducted, after more than 20 years of the use of SSM, its LR rates have remained

similar, as shown in a meta-analysis conducted by Lanitis *et al.* (34).

Cosmetic outcome

It is difficult to scientifically address questions on the aesthetic advantages of SSM. We, like other authors (26), are convinced that this technique helps improve reconstruction outcomes by preserving the sub-mammary and skin coverage. This effect has been previously demonstrated by Kroll and colleagues (35,36), who compared immediately BR and delayed BR and highlighted the influence of SSM on outcomes. Correction of symmetry is also influenced by the conservation of skin, as demonstrated in a previous report (37) that compared the TF with expander reconstructions, with and without SSM. It was found that 94% of TF-SSM *vs.* 50% of TF-NO-SSM cases did not require correction of the opposite breast, and correction was not needed in 12% of the expander-SSM group *vs.* 4% of the expander-NO-SSM group. We believe that demonstrating the results of the procedure on the basis of the reconstruction and symmetry it achieves is the best evidence for the aesthetic advantages of this procedure (Figures 12-15).

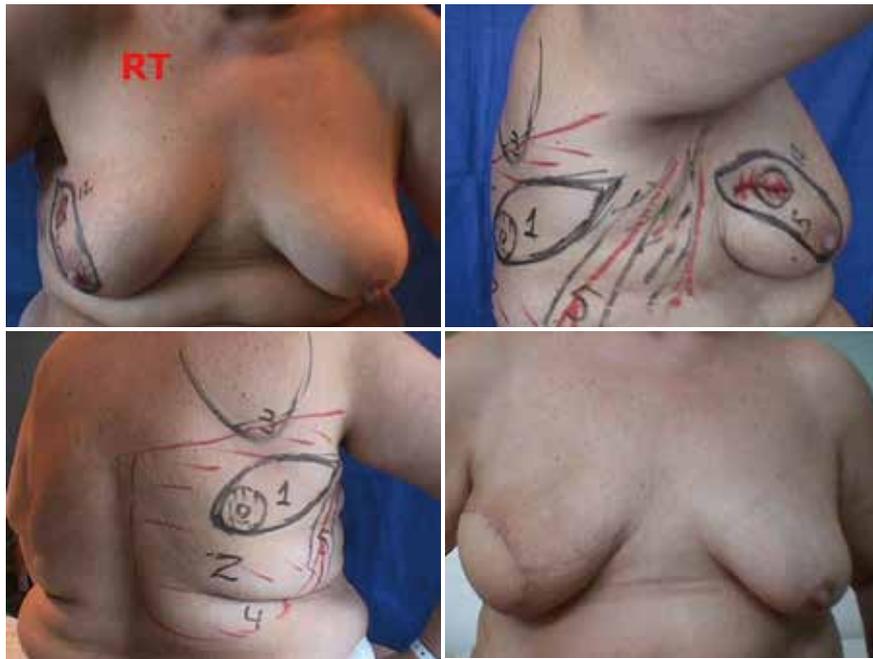


Figure 13 Skin-sparing mastectomy and reconstruction with extended latissimus dorsi flap. Local recurrence of conservative treatment in an irradiated breast. Bottom left five zones of adipose tissue that will rotate back with the flap to give volume is. Final result. Good result of the reconstructed breast and symmetry.



Figure 14 Skin-sparing mastectomy type I and free tram flap reconstruction. Immediate and mediate result. Final result after reconstruction of the NAC. Good result of the reconstructed breast and symmetry. NAC, nipple-areola complex.

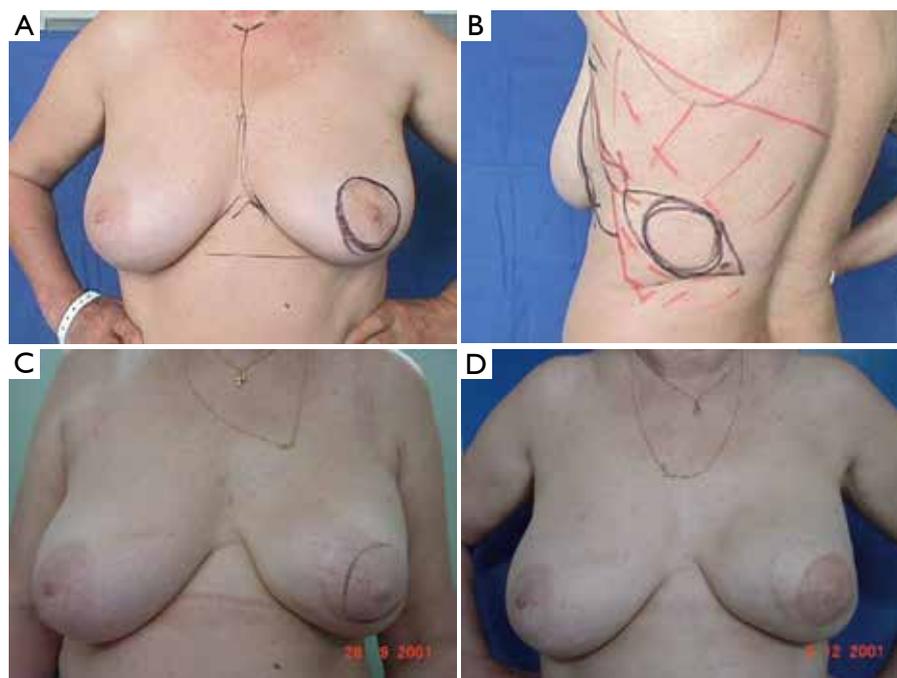


Figure 15 (A,B) Skin-sparing mastectomy and reconstruction with latissimus dorsi flap to repair the central cutaneous defect, and definitive expander placement to replace the volume; (C) reconstruction ended after reconstruction of the NAC; (D) good result of the reconstructed breast and symmetry. NAC, nipple-areola complex.

Conclusions

As outlined in the Guidelines of the National Comprehensive Cancer Network (NCCN-2014) (38), SSM is a safe procedure that provides good cosmetic results with good local cancer control. However, the following four prerequisites must be met: experienced surgical team, multidisciplinary evaluation, proper patient selection, and obtaining appropriate margins.

In skin-sparing mastectomy, the choice of location and type of incision, preservation of cutaneous pocket and submammary fold, allows the surgeon to replace the glandular defect with different procedures with the advantage of getting a better aesthetic result, enabling fewer procedures in both the reconstructed breast as in the opposite breast, for symmetry conservation.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Surgical decision making in conservative mastectomies

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Abstract: We present some clinical advice to drive the decision process in performing conservative mastectomies. Several factors are taken into consideration to indicate these techniques. First of all, we need to identify patients who need a mastectomy due to the extension of the disease. In this case we suggest assessing patients anthropometric characteristics (breast volume—ptosis), and personal preferences regarding the extension of surgical treatment. Small, medium size, without ptosis or with moderate ptosis can be better served by standard nipple-sparing mastectomy. Large and ptotic breast can be removed and reconstructed performing a skin-reducing mastectomy. Mastectomies cannot replace breast conservation and should be discouraged whenever breast-conserving surgery can be performed with good results. However, in some selected cases, and especially in patients with small breast, conservative mastectomies with contralateral reshape can yield favourable results.

Keywords: Nipple-sparing mastectomy; oncoplastic breast surgery; breast cancer

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Background

It is well known that the choice between breast conservation and mastectomy has become rather complex over the years, especially once the equivalence in terms of oncological control between breast conservation followed by radiotherapy and mastectomy has been solidly demonstrated (1-6). Thanks to great advancements in breast reconstruction, nowadays we can offer preservation or demolition of the gland obtaining similar results also in terms of quality of life (7). These results were obtained thanks to new kinds of mastectomies that allowed the preservation of the breast envelope possibly including the nipple areola complex (NAC). We named these techniques “conservative mastectomies” (8-10) and we are going to propose indications and techniques to perform envelope preservation safely. Notably we tried to embed elements in our decision-making derived from validated models, such as a quantitative assessment of breast volume and ptosis, an algorithm able to anticipate the risk of complications after breast reconstruction and finally a very advanced calculator of

risk of positive margins with breast conservation (11-14).

We candidate all patients with early stage breast cancer (ESBC) to implant based reconstructions irrespective of breast size and shape. We inform all patients in this subset regarding the stability of results with this technique (15). We use autologous flaps only in delayed reconstructions after radiation treatment for locally advanced breast cancer, or immediately after salvage mastectomies for recurrence after breast conservation. Autologous flaps can be a good option also in young women diagnosed affected by primary localized extensive disease with a very good prognosis. In view of an expected long-term survival, these women may obtain the maximum benefit from sophisticated techniques based on microsurgery with muscle preservation that we normally recommend.

Clinical elements to be investigated before deciding to candidate patients to conservative mastectomies

Although some oncoplastic techniques have broadened the

Table 1 Volume subgroups

Volume (cc)
Minimal: $V < 200$
Medium: $200 < V < 500$
Large: $500 < V < 700$
Very large: $V > 700$

Table 2 Classification of breast ptosis (12)

None
Minor
Moderate
Major

Table 3 Immediate Breast Reconstruction Risk Assessment Scale Score based on the ACS-NSQIP database (14)

Low [0-2]
Intermediate [3-4]
High [5-7]
Very High [8-9]

indication to breast conservation, clinical conditions exist in which the total removal of the mammary gland is still mandatory. This happens in patients affected by ESBC with extensive ductal carcinoma in situ (DCIS) with or without an infiltrating component, multi-centric disease and of course in locally advanced breast cancer (LABC) requiring multimodality treatment. Some more patients with ESBC may lie in a borderline condition in which it is more difficult to decide between mastectomy and breast conservation.

The decision to perform a mastectomy in patients affected by localized cancer is based on a combination of clinical, histological and biological characteristics. We added to this the personal preferences of the patient regarding final appearance, breast shape and volume in order to perform maximum reshape or reduce surgical aggressiveness.

These are normally acquired during the first consultation after a referral for a suspicious lump or infra-clinical disease. The morphological characteristic (breast volume and ptosis) of the patients are acquired either in a visual or in a quantitative way. More specifically, we study the breast volume using a model described by Longo *et al.* (11) and we create five categories as described in (Table 1). We use a further model to describe ptosis in a reliable

and reproducible way (12) with the definition of four subcategories (Table 2). During clinical examination and assessment of imaging we also evaluate the location of the disease in the breast segmented in four areas radial areas and a central one, clearly certain cases may include double or multiple locations (multifocal or multicentric carcinoma). Before surgical treatment, all our patients undergo a core biopsy in order to reach a pre-operative diagnosis. Combined with other information summarized in Table 3, it can be introduced into a validated model named breast conservation (13), in order to get information regarding the risk of positive margins.

Investigation of patients' preferences

We refuse a paternalistic approach to clinical decisions and therefore we tend to share this process with patients (16). This is not always easy, as some patients do not fully understand complex medical languages (17). For this reason, we enhanced the information process using booklets, video of results or surgical operation, videos and photographs of previous patients regarding each possible surgical technique to be employed. Normally this was done after the second consultation once a diagnosis is already known and a cluster of possible surgical options has been already offered. We ask patients that can be treated by either conservation or demolition to express their preference regarding the surgical technique according to three possible sub-categories:

- (I) Mastectomy;
- (II) Minimal aggressiveness;
- (III) Maximum reshape.

Those who are inevitably candidate to mastectomy can indicate their wish between the last two subcategories (minimal aggressiveness-maximum reshape).

The three subcategories of patients' wishes are created to include all possible surgical techniques that a patient may require.

Regarding the subgroup indicating "mastectomy" we include in this all women that can be candidate either to breast preservation or mastectomy who after a thorough information of possible cosmetic results, risks and benefits of radiotherapy, limitations and impact of breast reconstruction still prefer to undergo breast removal. Patients whose single option was mastectomy cannot be included in this category.

The second subgroup named "minimal aggressiveness" includes women who prefer to receive simple operations with minimal residual deformities without contralateral

adjustments if breast conservation is indicated. For patients invariably candidate to mastectomy this subgroup includes women who wish to receive skin or nipple sparing mastectomies with the simplest technique without contralateral reshape possibly in one stage.

Finally, the third subgroup denominated “maximum reshape” includes patients who require bilateral operations to reach the best cosmetic results with minimal asymmetries. If they can be candidated only to mastectomy this will mean that they wish to have contralateral adjustment concurrently with breast reconstruction.

Indication to conservative mastectomies

We offer conservative mastectomies in all patients affected by unifocal breast cancer located in the inner quadrants, or in the central quadrant of a small to medium size breast. In this setting of patient, we tend not to perform breast conservation, unless specifically requested, as this could yield poor cosmetic results. We also encourage the decision to remove the breast in all patients with small gland specifically requiring a mastectomy. This may reduce the need for second operations if positive margins occur, and is especially recommended in case of a demonstrated high risk of leaving residual disease. We also offer a mastectomy to patients with small to medium size breast with moderate or no ptosis affected by unifocal breast cancer located in the lower outer quadrant if specifically requested by the patient after proper consultation.

Multi-centric breast cancers or multifocal breast cancers that are not suitable for breast preservation are always candidate to mastectomy.

We indicate conservative mastectomies in selected cases of LABCs who had very good response to pre-operative systemic treatment with significant reduction of the breast mass and resolution of edema (18-20).

Nipple or skin preservation?

We perform nipple preservation in all cases where the absence of disease is demonstrated by multiple intra-operative biopsies of the retro-areolar ducts. However, nipple preservation is more a technical challenge rather than an oncologic one (18,21-24). The impact on local control of nipple preservation has been demonstrated by several studies, none of which has shown an exceeding risk of local recurrence. However, total preservation of the envelope in large and ptotic breast can create long and ischemic flaps

with possible necrotic complications (25).

Skin preservation in ESBC (no infiltration of the skin by definition) can be performed in a large majority of the cases. We discourage preservation of the mammary cutaneous mantle in patients with a high risk score of complications (14).

Surgical techniques in patients with small and medium sized breast and minimal/no ptosis

Patients with small/medium breast and minimal to moderate ptosis (12,13) can safely preserve the breast envelope. The nipple will be removed only in case of presence of neoplastic cells in the major ducts. The reconstruction will be performed according to patients’ preferences either in one stage with permanent implants (possibly with acellular dermal matrices) or in two stages. Depending on patients wishes (“maximum reshape”) a contralateral adjustment can be performed in a single stage or at the second stage with contralateral breast augmentation with or without mastopexy. The mastectomy should be performed through an S-italic incision starting 2-3 cm laterally of the nipple towards the upper-outer quadrants (photo of incision plan). The contralateral adjustment will usually require an augmentation (with implants placed in a dual plane/sub-pectoral/sub glandular position according to the characteristics of the skin, upper pole fullness and of course patients preferences). In selected cases with minor to moderate ptosis, a contralateral mastopexy with autoptosis could be offered with very natural results. Some patients wishing minimal aggressiveness may require a unilateral procedure possibly in one stage that can be performed once the patient has been clearly informed regarding possible asymmetric results.

Patients with large breast with or without ptosis

These patients may undergo a novel technique described by Nava *et al.* (8,10,26) named skin reducing mastectomy. This is a modification of type IV skin sparing mastectomies as described by Carlson *et al.* (27) that uses a de-epithelialized dermal adipose flap sutured to the pectoralis major and the fascia of the serratus anterior as a component of a compound pouch in which a permanent implant could be easily allocated. The final inverted T scars will look symmetric to that of a breast reduction or mastopexy that can be performed on the contralateral side. This operation offers a good chance to have breast reconstruction in one stage with permanent implants in patients in which

Table 4 Clinical elements to be assessed before final decision
Tumor size/extension in the breast
T >2 cm
T <2 cm
T <2 cm + surrounding DCIS <4 cm
Extensive DCIS
LABC
Multicentric
Location
Central
Upper outer
Upper inner
Lower outer
Lower inner
Volume
Minimal
Medium
Large
Very large
Ptosis
None
Minor
Moderate
Major
Risk of margin positive
High
Intermediate
Low
Patient wishes
Mastectomy
Max. reshape
Min. aggressiveness
Risk of surgical morbidity after reconstruction
Low
Intermediate
High
Very high
DCIS, ductal carcinoma in situ; LABC, locally advanced breast cancer.

skin preservation is a non-sense and therefore there is no point to undergo expansion and a second stage operation. Sometimes, as reported in some studies (8) the presence of extra-projection implants may create tension and ischemia

of the mastectomy flaps with a little bit higher complication rate. For this reason in selected patients at high risk of complication, we advise to undergo a two-stage skin-reducing mastectomy in order to minimize the tension on critical residual mastectomy flaps. The contralateral adjustment will be performed in the second surgical stage of the operation.

Nipple sparing skin reducing mastectomies are indicated in patients with large breast, but still moderate ptosis. The nipple preservation can be performed in cases in which the nipple to sternal notch distance does not exceed 2-3 cm. In these cases, the NAC can be held on very thin superior dermal flap, if a very radical ablation of the major ducts is performed.

Patients with unifocal breast cancer suitable for breast conservation requiring a mastectomy are discouraged to undergo this operation and diverted to easier techniques of preservation. Depending on tumour size and location, this may include bilateral therapeutic mammoplasties that may generate very good final cosmetic results.

Conclusions

In this paper, we provide some clinical advice to drive the decision process in performing conservative mastectomies. Several factors should be taken into consideration to indicate these techniques (*Table 4*). First of all, we need to identify patients who need a mastectomy for the extension of the disease. These women cannot be offered breast conservation at any time. In this case we suggest assessing patients' anthropometric characteristics (breast volume—ptosis), and personal preferences regarding the extension of surgical treatment (*Figure 1*). Small, medium size, without ptosis or with moderate ptosis can be better served by standard nipple sparing mastectomy if oncological requirements are fulfilled. Large and ptotic breast can be removed and reconstructed in one stage with a proper reshape of the breast envelope. Some patients in this subgroup are at high risk of complication and may be better served by a two-stage procedure with tissue expansion. Mastectomies cannot replace breast conservation and should be discouraged whenever breast-conserving surgery can be performed with good results. However, in some selected cases, especially in patients with small breast, conservative mastectomies with contralateral reshape can yield favourable results.

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None.

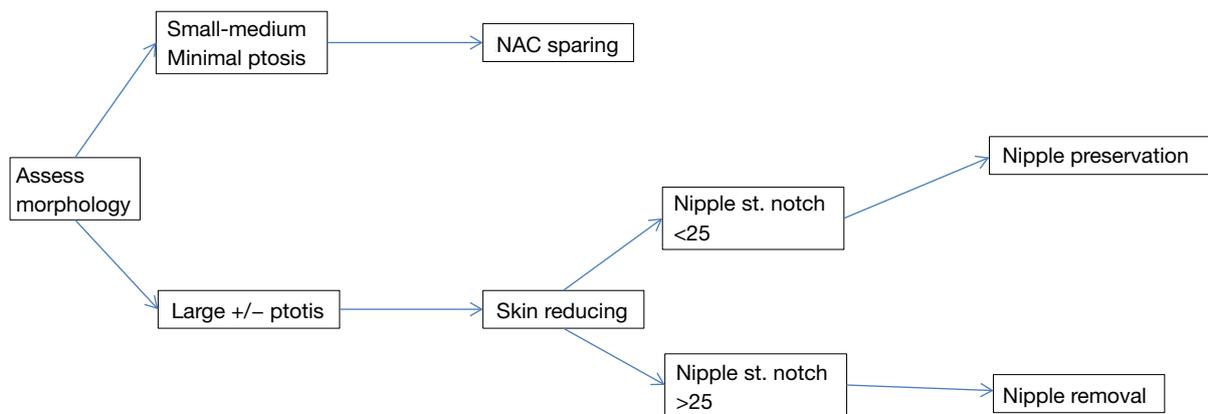


Figure 1 Simplified algorithm for decision making in conservative mastectomies. NAC, nipple areola complex.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Conservative mastectomies: an overview

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Abstract: Conservative mastectomies provide removal of the entire breast parenchyma, saving the outer covering of the mammary gland with the possibility of performing an immediate reconstruction preserving women body image. We rationalised and systematically organized our reconstructive algorithms giving a new different light to mastectomies, the so-called “conservative mastectomies”, an oxymoron indicating skin-sparing mastectomies (SSM), nipple-areola complex-sparing mastectomies (NSM) and skin-reducing mastectomies (SRM). Eventhough randomized controlled trials comparing conservative mastectomies with traditional mastectomy and breast conserving surgery would be auspicious in order to achieve higher levels of evidence, we could confidently conclude that conservative mastectomies offer the psychological advantages of good cosmesis and maintenance of woman body image without compromising the oncological safety of mastectomy.

Keywords: Skin-sparing mastectomy (SSM); nipple-sparing mastectomy (NSM); breast cancer

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Eighties saw the flames of Halsted mastectomy's hell to extinguish (1), showing the heaven of Fisher lumpectomy (2) and Veronesi quadrantectomy (3).

In the late 1990's the two separate worlds of mastectomy and breast conserving surgery started to work together with the development of oncoplastic breast surgery: breast reconstruction became a standard procedure and a huge range of surgical techniques with a progressive reduction of aggressiveness have been offered to women facing the diagnosis of breast cancer, achieving optimal oncological and reconstructive results.

In the XXI century breast cancer surgery did not represent a dichotomous choice anymore. Higher sensitivity of diagnostic imaging, new genetics investigations and opportunity for risk reducing procedures led to a renewed increase of mastectomy rates during the first decade of 2000's (4,5) that are continuing to grow (6).

A higher percentage of women well informed about the equivalence in terms of survival between breast conserving treatments (BCT) and mastectomy starts to

prefer undergoing a mastectomy followed by immediate reconstruction.

We rationalised and systematically organized our reconstructive algorithms giving a new different light to mastectomies, the so-called “conservative mastectomies” (7), an oxymoron indicating skin-sparing mastectomies (SSM), nipple-areola complex-sparing mastectomies (NSM) and skin-reducing mastectomies (SRM).

Conservative mastectomies provide removal of the entire breast parenchyma, saving the outer covering of the mammary gland [subcutaneous fat, skin and nipple (if oncologically safe)] with the possibility of performing an immediate 1- or 2-stage implant-based reconstruction or an immediate autologous tissue reconstruction, preserving women body image.

SSM was first described in 1991 by Toth and Lappert as an effort to maximize skin preservation to improve cosmetic outcome and facilitate reconstruction (8).

Mastectomy with preservation of the skin and the nipple-areola complex (NAC) was first described even before than

SSM: Rice and Stickler in 1951 presented the “adenomammectomy” for benign diseases (9) and Freeman in 1962 introduced the term “subcutaneous mastectomy” (10).

Other authors in the last 15 years used the terms “total skin-sparing mastectomy”, “nipple-sparing mastectomy” or “NAC-sparing mastectomy”.

NSM is similar to SSM for the dissection of skin flaps, but also consider the respect of the NAC.

Obviously the additional preservation of the NAC makes the procedure more technically demanding, with the need of complete removal of the retroareolar ducts and preservation of nipple vascularisation.

Some authors recommend the nipple eversion during surgery and the use of sharp dissection instead of electrocautery to limit thermal injury and increase NAC preservation rates (11). We recently proposed the use of hydrodissection in order to facilitate the sub-areolar breast tissue removal (12).

Some authors attempted to precondition the NAC by dissecting it under local anesthesia from the underlying breast tissues several days before the mastectomy to stimulate blood flow from the peripheral skin (13,14). Performing this approach, the authors present the advantage of retroareolar biopsy before mastectomy and the biopsy specimen could be submitted to permanent histological analysis.

Usually, the retroareolar tissues are removed at the time of the conservative mastectomy and the specimen is analyzed by frozen section.

Other authors used intraoperative radiotherapy of the NAC when the frozen section of retroareolar tissue is negative, as a risk-reducing technique for local recurrence (15).

An appropriate incision for NSM should ease both the mastectomy and the reconstruction, preserve the NAC blood flow and guarantee a good cosmetic result.

Several incisions have been proposed to achieve these goals: periareolar/circumareolar (+/- inferolateral or superolateral extension or omega), radial (straight, lateral or vertical), inframammary, inverted-T and transareolar (16-19).

Trans-areolar and periareolar/circumareolar incisions present the highest risk of NAC necrosis, while lateral radial incision ease the glandular dissection and the access to the axilla for sentinel lymph node biopsy, leaving the NAC untouched (15,20,21).

When an envelope reduction is required, in large and ptotic breasts, we advice a “Wise Pattern” access. Such an approach was criticized in the past for the high complication rate due to the risk of skin necrosis (22). We

developed and presented in 2006 a technical modification of “Wise Pattern” mastectomies, we called “skin reducing mastectomy (SRM)” (23), expanding the implant-based breast reconstructive opportunities and choices and achieving good oncological and cosmetic results (24,25).

Some surgeons also presented minimally-invasive video-assisted techniques through a mid-axillary skin incision (26-28).

Survival of the NAC is one of the most important issues when performing a NSM. Complete necrosis of the nipple rates range from 0% to 60% (17,29). Factors affecting NAC vascularisation are smoking habit, young age and type of skin incision (30).

Other common complications are capsular contracture following implant-based reconstruction and skin flap ischaemia.

Implant-based reconstruction is extensively used in association with conservative mastectomies, both 1-stage (direct-to-implant) and 2-stage (expander to implant).

Two-stage reconstruction is preferred in case of compromised blood supply reducing the retroareolar pressure, skin tension and flap ischaemia in the immediate postoperative days (31).

The implant is always positioned under a muscular pocket created by the pectoralis major and the serratus muscles. Human acellular dermal matrices and synthetic meshes could provide lower pole coverage allowing a direct-to-implant reconstruction (32,33).

When post-operative radiation is required on the basis of nodal status and a 2-stage expander-to-implant reconstruction has been performed, we prefer to deliver radiation soon after the replacement of the expander with the permanent implant (34).

We consider autologous myocutaneous flaps reconstruction [deep inferior epigastric perforator (DIEP)] only for previously irradiated patients, as we presented with our “extra-projected surgical model” for breast reconstruction (35).

Our pathway of research and development is actually moving through advancements in biomaterials together with enhanced fat grafting techniques, achieving the next step of reconstruction: the “hybrid reconstruction”, that will allow immediate breast reconstruction combining the use of fat and implants, a safe approach also for radiotreated patients.

Conservative mastectomies provide a better quality of life for women with breast cancer. The preservation of the nipple-areola complex in particular offers the possibility of

preserving the woman body image.

Even if the studies indagating conservative mastectomies are low-evidenced, the low rates of local recurrence reported in several large retrospective series and prospective cohorts with 5-year survival rates of more than 95% reassure both patients and surgeons.

Eventhough randomized controlled trials comparing conservative mastectomies with traditional mastectomy and breast conserving surgery would be auspicable in order to achieve higher levels of evidence to answer to many open questions (the minimum distance between tumor and nipple, maximum tumor size, best skin incision, type of reconstruction), we could confidently conclude that conservative mastectomies offer the psychological advantages of good cosmesis and maintenance of woman body image without compromising the oncological safety of mastectomy.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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What is the evidence behind conservative mastectomies?

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Introduction: Besides the diffusion of breast reconstructive techniques, several “conservative” approaches in mastectomy have been developed, in order to perform an immediate reconstruction with better aesthetic results: the skin-sparing mastectomy (SSM), the nipple-areola complex (NAC)-sparing mastectomy (NSM) and the skin-reducing mastectomy (SRM). During the last decade, SSMs and NSMs have gained widespread acceptance and are currently considered standard treatment for early breast cancer. We would like to investigate the evidence behind this radical shift towards conservative mastectomies, where there has been a renewed interest worldwide.

Methods: We reviewed English literature by consulting the following databases: Medline, Embase, Cochrane Register of Controlled Trials, the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) search portal and Clinicaltrials.gov. The objective is to include any randomized controlled trial (RCT) comparing a “conservative mastectomy” technique to breast conservative surgery or modified radical mastectomy (MRM) for the treatment of early-stage breast cancer. In the absence of randomized trials, we took into account prospective cohorts and retrospective series for a narrative description of available evidence.

Results: Our review included 58 studies [19 prospective cohorts (34%) and 39 retrospective series (66%)] considering NSM and immediate reconstruction and ten studies [1 prospective cohort (10%) and 9 (90%) retrospective series] considering SSM and immediate reconstruction. In the NSM group, 29 studies reported data about complication rates and 42 studies presented data on NAC partial or complete necrosis. In the NSM group 45 studies and all the studies in the SSM group presented data on local and NAC recurrence.

Conclusions: In order to achieve higher levels of evidence, RCTs comparing conservative mastectomies to traditional mastectomy and breast conservative surgery would be desirable. However we can conclude that conservative mastectomies offer the psychological advantages of good cosmetics and maintenance of woman body image without compromising the oncological safety of mastectomy.

Keywords: Skin-sparing mastectomy (SSM); nipple-sparing mastectomy (NSM); breast cancer

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Introduction

The Copernican revolution has been validated by the historical randomized controlled trials (RCTs) by Veronesi *et al.* and Fisher *et al.* (1,2) leading to breast conservative surgery definition as standard treatment for early breast cancer.

Thanks to breast cancer screening programs and higher levels of breast cancer awareness, breast conservation rates have increased up to 75% (3).

Today mastectomy cannot be avoided for multicentric disease or after local recurrence (LR) following breast conservative treatments. Moreover the wider diffusion of risk-reducing procedures for women identified to be

at higher breast cancer risk who have predisposing gene mutations find in mastectomy the best treatment.

All women undergoing mastectomy can take advantage of the many options available for breast reconstruction.

Together with the diffusion of breast reconstructive techniques, several “conservative” approaches in mastectomy have been developed, in order to allow an immediate reconstruction with better aesthetic results.

The modified radical mastectomy (MRM) or non-skin-sparing mastectomy (NSSM) was described by Madden in 1965 (4) and consists in the removal of all breast tissue, preserving both pectoralis muscles, together with the dissection of level I and II axillary lymph nodes.

The SSM was first described by Toth and Lappert in 1991 (5) with the aim of removing the entire parenchymal breast tissue while preserving the overlying skin of the breast envelope and the natural inframammary fold (6).

The traditional SSM also takes into account the excision of the skin overlying superficial tumors as well as previous biopsy entry sites. However, this is not routinely performed by all surgeons (7).

From the concept of SSM the natural evolution was the nipple-areola complex-sparing (NAC-sparing) mastectomy (NSM), requiring removal of nipple-areolar ducts (8,9). Skin flaps should only be 2-3 mm in thickness at the NAC. The technique could be facilitated by hydro dissection (10) and sharp dissection instead of electrocauterization to limit thermal injury and increase NAC preservation rates (9).

The nipple-areolar ducts are commonly sent for frozen section examination of the NAC for residual cancer suggesting removal of the entire NAC (conversion to SSM) if the frozen section is positive to the disease (11,12). Other authors wait for permanent sections and return to the operating room for the removal of the NAC if final pathology results positive (13). Some other groups recommend the use of intraoperative radiotherapy in association with the NSM (14).

Multiple techniques and skin incisions have been described for NSM in order to prevent NAC necrosis that can be a complication of NSM due to the close dissection under the NAC.

During the last decade, SSMs and NSMs have gained widespread acceptance and are currently considered standard treatment for early breast cancer.

We would like to investigate the evidence behind this radical shift towards conservative mastectomies, where there has been a renewed interest worldwide (15).

NAC-sparing mastectomy would appear to be the

most ideal mastectomy alternative, but are we sure it achieves oncological equivalent outcomes when compared to traditional (modified radical) mastectomy and breast conserving approaches? Are women asking for a conservative mastectomy well-informed about the risks and potential adverse outcomes?

Methods

Any RCT comparing a “conservative mastectomy” technique to breast conservative surgery or MRM for the treatment of early-stage breast cancer was considered for inclusion.

In the absence of randomized trials, we considered cohort or case control studies for a narrative description of available evidence.

Our primary outcomes were oncological ones LR and patient-reported outcomes (post-operative quality of life or satisfaction level) as measured by BREAST-Q, EORTC QLQ-BR23 and SF-36. We also considered as secondary outcomes, post-operative short-term complications (infection, hematoma, seroma, skin flaps or NAC necrosis), re-intervention and long-term complication rates and cosmetic outcomes not reported by participants (i.e., evaluation of reconstructive outcomes by the operating surgeon or other uninvolved clinicians).

We performed a review of the English literature by consulting the following databases: Medline, Embase, Cochrane Register of Controlled Trials, the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) search portal and Clinicaltrials.gov.

We tried to identify further studies by reviewing reference lists of relevant trials or reviews. A copy of the full article for each reference reporting a potentially eligible study was obtained. When this was not possible, attempts were made to contact study authors to request additional information.

All abstracts identified by the search strategies were screened for duplicates and assessed by two independent review authors to exclude studies that did not meet the inclusion criteria. Disagreements were solved through discussion between two review authors; in cases of persistent disagreement, a third review author was consulted. The full publications of all potentially relevant abstracts were obtained and formally assessed for inclusion. Review authors were not blinded to the names of the study authors, their corresponding institutions and the journal of publication.

A tailored data extraction form was developed to record

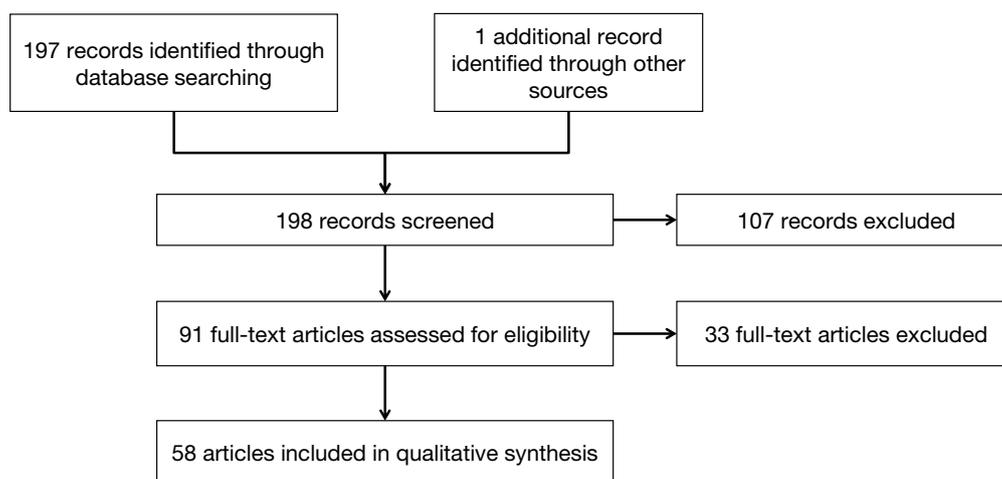


Figure 1 Flow diagram for included studies—nipple-sparing mastectomy.

the details of the studies.

Data was extracted independently by two review authors; differences of opinion between review authors were solved through discussion with a third author. Missing or updated information was obtained by contacting the study authors.

Quantitative data from studies with more than one publication was extracted from the latest source; this was considered as the primary reference.

Results

The search was launched in November 2014. No RCTs comparing NSSM or breast conserving surgery (BCS) versus skin- and NAC-sparing mastectomy (SSM-NSM) were found in literature.

Therefore we only analyzed retrospective series and prospective cohorts (that is level of evidence III and IV) presenting data on LR, post-operative complications and patient satisfaction level.

The high level of heterogeneity between the studies design, stage of disease, tumor characteristics, additional therapies (chemotherapy or radiation therapy), surgical technique, type of reconstruction and follow-up time made it impossible to perform a meta-analysis of the included studies according to LRs, post-operative complications or aesthetic outcomes.

We could only carry out a narrative review of the existing literature, achieving a level III of evidence according to Oxford Classification.

Our review included 58 studies [19 prospective cohorts (34%) and 39 retrospective series (66%)] considering

NSM and immediate reconstruction (*Figure 1, Table 1*) and ten studies [1 prospective cohort (10%) and 9 (90%) retrospective series] considering SSM and immediate reconstruction (70-79) (*Table 2*).

The indications for NSM included invasive cancer, carcinoma *in situ* and risk-reduction. SSM was performed for carcinoma *in situ* and invasive breast cancer.

There was high heterogeneity in the inclusion criteria between NSM studies (risk-reducing mastectomy, no NAC involvement confirmed with MRI, no NAC involvement confirmed with intraoperative frozen section, no nipple retraction, bloody discharge or retro areolar microcalcifications, tumor size <3-5 cm, tumor located >1-2 cm from nipple, no skin involvement, no Paget disease, no axillary involvement, BMI <40, no history of collagen vascular disease, small or medium breast size, minimal ptosis, no preoperative irradiation or chemotherapy, no smoking).

Most studies (78%) on NSM were conducted after 2008, confirming that this type of procedure became more popular in the last decade.

Twenty-nine studies in the NSM group reported data on complication rates and 42 studies presented data on NAC partial or complete necrosis (*Table 1*).

In the NSM group 45 studies and all the studies in the SSM group presented data on LR (*Table 2*).

Fifty-three studies reported data on methods of reconstruction following NSM. Forty-seven percent of reconstructions following NSMs were two-stage procedures (expander to implant), 41% were one-stage (direct-to-implant) and 12% were autologous reconstructions.

Table 1 Skin-sparing mastectomy and characteristics of included studies					
Study ID	Study design	N of patients	N of procedures	Complications (%)	Nipple necrosis (%)
Verheyden 1998 (16)	Retrospective	20	30	24 (80.0)	11 (36.0)
Sufi et al. 2000 (17)	Retrospective	12	12	–	–
Mustonen et al. 2004 (18)	Retrospective	34	34	23 (67.6)	6 (17.6)
Dao and Verheyden 2005 (19)	Retrospective	16	32	12 (37.5)	0 (0)
Margulies et al. 2005 (20)	Retrospective	31	50	9 (18.0)	7 (14.0)
Palmieri et al. 2005 (21)	Retrospective	18	25	1 (4.0)	1 (4.0)
Bistoni et al. 2006 (22)	Retrospective	14	18	–	–
Caruso et al. 2006 (23)	Prospective	50	51	4 (8.0)	2 (4.0)
Komorowski et al. 2006 (24)	Retrospective	38	38	–	5 (13.1)
Nahabedian and Tsangaris 2006 (25)	Retrospective	12	14	4 (28.6)	0 (0)
Sacchini et al. 2006 (8)	Retrospective	192	192	–	4 (7.0)
Denewer 2007 (26)	Retrospective	41	41	11 (26.8)	1 (2.4)
Mosahebi 2007 (27)	Retrospective	71	71	–	–
Benediktsson and Perbeck 2008 (28)	Prospective	272	272	–	–
Crowe et al. 2008 (29)	Prospective	110	149	–	2 (1.5)
Regolo et al. 2008 (30)	Retrospective	70	102	–	61 (60.0)
Sookhan et al. 2008 (31)	Retrospective	20	20	3 (15.0)	2 (10.0)
Stolier et al. 2008 (32)	Prospective	58	82	10 (17.2)	0 (0)
Voltura et al. 2008 (33)	Retrospective	36	51	–	–
Wijayanayagam et al. 2008 (13)	Prospective	43	64	23 (36.0)	3 (4.7)
Chen et al. 2009 (34)	Retrospective	66	115	–	25 (21.7)
Didier et al. 2009 (35)	Retrospective	310	310	–	–
Garcia-Etienne et al. 2009 (36)	Retrospective	25	42	6 (14.0)	3 (7.1)
Garwood et al. 2009 (37)	Prospective	72	106	–	17 (10.4)
Gerber et al. 2009 (38)	Retrospective	60	60	–	–
Munhoz et al. 2009 (39)	Retrospective	18	22	–	–
Paepke et al. 2009 (11)	Prospective	96	109	–	27 (25.0)
Petit et al. 2009 (14)	Prospective	1,001	1,001	358 (35.8)	90 (9.0)
Sakamoto et al. 2009 (40)	Retrospective	87	89	–	–
Yueh et al. 2009 (41)	Prospective	10	17	12 (70.6)	3 (17.6)
Babiera and Simmons 2010 (42)	Retrospective	54	55	–	–
Colwell et al. 2010 (43)	Retrospective	8	14	1 (12.5)	0 (0)
Kim et al. 2010 (44)	Prospective	152	152	40 (22.6)	40 (22.6)
Luo et al. 2010 (45)	Retrospective	52	52	–	–
Radovanovic et al. 2010 (46)	Prospective	205	214	35 (16.0)	9 (4.5)
Rusby and Gui 2010 (47)	Retrospective	11	18	–	–
Salgarello et al. 2010 (48)	Retrospective	33	42	10 (23.8)	4 (9.5)
Boneti et al. 2011 (49)	Retrospective	–	281	20 (7.1)	–
de Alcantara Filho et al. 2011 (50)	Retrospective	200	353	90 (25.5)	12 (3.3)
Harness et al. 2011 (51)	Retrospective	43	60	12 (20.0)	5 (8.3)
Jensen et al. 2011(52)	Prospective	99	149	9 (6.0)	8 (6.3)

Table 1 (continued)

Table 1 (continued)

Study ID	Study design	N of patients	N of procedures	Complications (%)	Nipple necrosis (%)
Maxwell <i>et al.</i> 2011 (53)	Retrospective	98	186	–	–
Rawlani <i>et al.</i> 2011 (54)	Retrospective	20	37	16 (43.2)	9 (24.3)
Spear <i>et al.</i> 2011 (55)	Retrospective	101	162	46 (28.4)	7 (4.3)
Algaithy <i>et al.</i> 2012 (56)	Prospective	45	50	–	13 (25.0)
Jensen <i>et al.</i> 2012 (57)	Prospective	200	313	–	–
Kneubil <i>et al.</i> 2012 (58)	Retrospective	–	–	–	–
Moyer <i>et al.</i> 2012 (59)	Retrospective	26	40	16 (61.5)	15 (37.5)
Peled <i>et al.</i> 2012 (60)	Prospective	288	450	252 (56.0)	4 (0.9)
Schneider <i>et al.</i> 2012 (61)	Retrospective	19	34	2 (5.8)	1 (2.9)
Spear <i>et al.</i> 2012 (62)	Retrospective	15	24	10 (41.6)	7 (29.0)
Wagner <i>et al.</i> 2012 (63)	Prospective	33	54	–	16 (29.6)
Warren Peled <i>et al.</i> 2012 (64)	Prospective	428	657	–	23 (3.5)
Yang <i>et al.</i> 2012 (65)	Prospective	92	92	–	12 (13.0)
Blechman <i>et al.</i> 2013 (66)	Retrospective	29	55	–	3 (6.0)
Lohsiriwat <i>et al.</i> 2013 (67)	Retrospective	934	934	–	40 (4.3)
Tanna <i>et al.</i> 2013 (68)	Retrospective	51	85	–	11 (12.9)
Sahin <i>et al.</i> 2013 (69)	Retrospective	21	41	8 (19.0)	0 (0)

N, number.

Table 2 Skin-sparing mastectomy and characteristics of included studies

Study ID	Study design	N of patients	LR rate (%)	Follow-up (months)
Newman <i>et al.</i> 1998 (70)	Retrospective	372	6.2	26
Slavin <i>et al.</i> 1998 (77)	Retrospective	26	0	45
Kroll and Khoo 1999 (74)	Retrospective	114	7	72
Rubio <i>et al.</i> 2000 (76)	Retrospective	95	3	44.4
Foster <i>et al.</i> 2002 (78)	Prospective	25	4	49.2
Spiegel and Butler 2003 (72)	Retrospective	44	0	117.6
Downes <i>et al.</i> 2005 (79)	Retrospective	38	2.6	52.9
Greenway <i>et al.</i> 2005 (75)	Retrospective	28	0	49
Carlson <i>et al.</i> 2007 (71)	Retrospective	539	5.5	65
Lim <i>et al.</i> 2010 (73)	Retrospective	87	4.6	60

N, number; LR, local recurrence.

Fifty-five out of 58 included studies in the NSM group described the mastectomy incision used.

Fifteen different incisions were described. In 36 studies (64.3%) more than one type of incision was performed. The various incisions were classified in five categories: the most common incision types were radial, followed by periareolar/circumareolar, inframammary, inverted-T and trans-areolar. Trans-areolar approaches resulted in the highest rate of nipple necrosis. LR in relation to incision location was not

reported in any study.

Stolier and colleague performed 82 NSMs without NAC necrosis using a six-o'clock radial incision or a lateral incision if excising a biopsy or breast conserving therapy (BCT) scar (32). The authors also stressed the importance of lighting, use of headlamps, blended current cautery used only for pinpoint hemostasis and the utility of bipolar dissecting scissors.

Other authors also preferred radial or lateral incisions,

noting that medial incisions could compromise blood flow (8,29). Paepke and colleague (11) reported only a 1% NAC loss with a periareolar incision, while Regolo and colleague (30) reported a 60% NAC loss with periareolar incision.

Skin-sparing mastectomy (SSM)

Oncological safety

SSM leaves behind more tissue than NSSM. The surgeon leaves superior and inferior skin flaps to preserve the natural skin envelope, removing as much breast tissue as possible, carrying out a dissection above the superficial fascia, leaving in situ only epidermis, dermis and a small amount of subcutaneous fat. Obviously the procedure is more technically demanding when compared to NSSM. Some reports investigating the histological characteristics of skin flaps specimens doubt the oncological safety and equivalence of SSM with NSSM regarding local control of the disease (70,80).

Some authors analyzed skin flap specimens after SSM looking at the amount of residual breast tissue and they found 59.5% of specimens containing residual breast tissue and 9.5% of skin flaps with residual disease, concluding that skin flaps thicker than 5 mm were associated with the presence of residual disease (81,82). Other authors found 23% of skin flaps after SSM involved by residual tumor, in particular at the level of the skin projection of the tumor (83).

Although several studies did not show any statistical difference between NSSM and SSM in terms of LR, other authors showed SSM as an independent predictor of close or positive margins (81-84).

No randomized controlled clinical trials comparing SSM with NSSM have been conducted, but several retrospective series and some prospective cohorts over the past two decades presented data demonstrating the equivalence of SSM and NSSM in terms of LR (71-74,85-88).

The LR rates after NSSM in tumors up to 4 cm was shown to be 10% after 20 years of follow-up (1,2) and our review of the literature found LR rates following SSM to range from 0% to 7% (75-79).

As expected, LR rates after SSM were lower for smaller and low stage tumors with less aggressive characteristics. LR rates after NSSM for DCIS in most series range between 1% and 3% (89-92) and similarly Slavin and colleague showed no recurrences at a follow-up of 45 months after SSM for DCIS (77). Carlson and colleague also presented only one LR after 65 months of follow-up following SSM for

DCIS (85) (Table 2).

Newman and colleague presented a 6.2% recurrence rate at a mean follow-up time of 26 months after SSM for T1 and T2 tumors (70). These findings are in line with those of Kroll and Khoo who reported a 7% LR rate at a mean follow-up time of 6 years after SSM (74). Carlson and colleague studied 539 patients undergoing SSM with a mean follow-up time of 65 months and found tumor size, nodal status and lymphovascular invasion to be significant predictors of recurrence, with LR rates of 3%, 10% and 11% for T1, T2 and T3 tumors respectively (85).

Other authors also reported that tumor size, stage, lymph node involvement and poor tumor differentiation were risk factors for LR, showing a LR rate after SSM at a median follow-up of 73 months of 4.5% (83). Spiegel and Butler reported a 5.6% LR rate at 9.8 years in 117 patients treated with SSM (72).

Some authors investigated the use of SSM in small populations of high-risk patients (stage IIB and III) showing promising results, with recurrence rates ranging between 2.6% and 4.6% (73,78,79).

Nipple-sparing mastectomy (NSM)

Oncological safety

Incidence of occult involvement of the nipple by tumor

Many studies reported data on the pathological involvement of the nipple, with the incidence ranging from 0% to 58% (93-109). Excluding small series (less than 100 patients) the range narrows down to 5.6% to 31%.

Obviously patient selection, definition of nipple involvement and pathological methods affect the reported incidence. Many historical studies only included women with small-volume disease. Moreover mastectomy has today become a common procedure for extensive DCIS, while older series excluded DCIS.

Three landmark studies investigating the incidence of microscopic tumor involvement in the NAC presented conflicting results.

Laronga and colleague (105) in 1999 reported that 5.6% of NAC in SSM specimens were positive for occult tumor involvement, concluding that NAC involvement was not an indicator of increased LR or breast cancer specific survival. They reported that central tumor location, multicentricity and positive lymph nodes determine an increased risk of NAC involvement.

In 2001, Cense and colleague (110) reported that

up to 58% of mastectomy specimens presented NAC involvement, correlating tumor size, distance from the NAC (<4-5 cm) and positive lymph nodes. They discouraged the use of NSM, recommending patients to undergo BCT, with the benefit of additional radiotherapy.

In 2002 Simmons and colleague (106) studied NAC involvement from mastectomy specimens, finding only 0.9%.

Local recurrence (LR)

No randomized controlled clinical trials comparing NSM versus NSSM or BCT have been found in literature. Evidence deriving from retrospective series and prospective cohorts showed a LR rate after NSM ranging between 0% and 24.1% with high heterogeneity in inclusion criteria, surgical technique and follow-up times.

Benediktsson and colleague (28) performed NSM in patients who were poor BCT candidates, including patients with large and multicentric tumors. They reported a LR rate of 20.8% at a mean follow-up time of 13 years. Despite high LR rates, they reported 0% recurrences at the NAC. They found a statistically significant reduction in the LR rate of 8.5% when adding post-mastectomy radiotherapy (PMRT) to NSM.

Petit *et al.* (14) and Sookhan *et al.* (31) reported 0% of NAC LR at short follow-up periods respectively 19 and 10.8 months, thanks to the use of preoperative breast magnetic resonance imaging.

In 2009, Gerber *et al.* provided (38) data at a follow-up of 10 years, finding only one NAC recurrence out of 112 NSMs performed, without statistical significance in overall LR between NSM and MRM.

In 2012, Petit *et al.* (111) reported 10% of NAC specimens to be positive after frozen section, but a long-term recurrence rate of 1.18% thanks to the use of intraoperative radiotherapy.

Postoperative complications

NAC necrosis

Nipple-areolar complex necrosis (either partial or complete) was reported in 42 studies (Table 1). The reported rates of NAC necrosis (either partial or complete) ranged from 0% to 60%.

Mastectomy skin flap necrosis

The definition of skin flap necrosis was very variable, with some studies only reporting cases requiring re-interventions

and other including all cases of partial or full-thickness necrosis.

Patient satisfaction

Nahabedian and Tsangaris (25) reported good or excellent satisfaction with 11 of 14 reconstructed breasts following NSM. Yueh *et al.* (41) reported that six out of nine patients were satisfied. The limit of these series is that they did not compare patient satisfaction with patients without NAC preservation.

Gerber and colleague (38) presented the evaluation of aesthetic results of SSM versus NSM after 12 months assessed by patients and surgeons. Patients rated satisfaction with SSM and NSM similarly, with the majority defining the aesthetic outcome as good or excellent. The surgeons rated 74% of NSM as excellent and 26% as good, while rating only 59% of SSM excellent, 22% good and 20% fair (P=0.001).

Didier and colleague (35) studied patient satisfaction with body image, sexuality, cosmetic results and psychological adjustment in two cohorts of patients who underwent NSM and SSM. They did not find any difference in feelings of sexuality, but patients who underwent NSM were more willing to see themselves or be seen naked and had significantly lower ratings for feelings of mutilation. Patients who underwent NSM as compared to SSM reported significantly greater satisfaction with cosmetic results.

Discussion

Despite being commonly offered as an alternative to NSSM, indications for NSM have typically been identical to those for BCT (9,50,112).

Even if no high level evidence is available in literature, NSM has been considered safe in women with small, peripherally located tumors, without multicentricity or risk-reducing mastectomy (50).

While there is data supporting the safety of SSM for larger tumors and more advanced stages, there is less applied to NSM and additional studies, preferably RCTs comparing NSM with NSSM, should be performed.

Schechter and colleague developed (113) an image based model using mammography that helps providing a NAC involvement score (NACIS) based on tumor-nipple distance, pathologic stage and tumor size with 92% sensitivity, 77% specificity and 93% negative predictive value.

Breast MRI can also be considered a useful tool to determine nipple and retroareolar morphology prior to consideration of NSM.

Friedman and colleague (114) correlated preoperative MRI appearance of the nipple in 35 patients with breast cancer undergoing mastectomy with histological results and predicted NAC involvement with 99.5% sensitivity and 100% specificity. They concluded that breast MRI could not only identify retro areolar tumors with or without nipple involvement but also differentiate normal from abnormal nipple.

The literature regarding margins for NSM deeply focuses on the margin at the NAC, but the surgeon should always remember that superficial and deep margins apply too, and this has not been sufficiently studied.

Preoperative counseling for all patients potentially eligible for a NSM is fundamental, discussing potential risks of NAC recurrence but also partial or total NAC necrosis and loss of nipple sensation. Moreover, in case of an intraoperative positive frozen section or complication, patient consent to remove the NAC is mandatory.

RCTs are needed to address almost all questions regarding NSM. However the actual best available evidence deriving from level of evidence III and IV studies provide some characteristics of the patients who can be a candidate for NSM.

The optimal tumor-to-nipple distance has not been defined yet and various prediction models to aid in selection of patients for NSM using preoperative tumor-to-nipple distance values have been proposed; however the total number of mastectomies analyzed in these studies is small and requires validation with larger studies (34,44,109,113).

Although no consensus regarding the oncologic selection criteria exist, general trends include tumor size up to 3 cm and tumor-to-nipple distance greater or equal to 2 cm (28,46,55).

There is no clear consensus regarding whether clinically negative axillary nodes should be required as a selection criteria for NSM, even though axillary nodal status has not been found to influence nipple involvement (14,36,55).

Some authors consider preoperative irradiation as a contraindication for NSM, but no studies validated this assumption (29,66). Several studies included patients who underwent radiation therapy before or after a NSM and reconstruction. Nipple necrosis varied among those studies, ranging from 0% to 54.5%. No meta-analysis could be performed due to the high level of heterogeneity between the studies in terms of irradiation protocols and timing of

the treatment.

NSM is not recommended in patients with extensive lymphovascular invasion, estrogen/progesterone receptor-negative tumors and inflammatory carcinomas (33,36).

Risk-reducing NSM may be considered in anatomically appropriate patients (23,36,55).

According to these selection criteria, NSM could be considered an oncologically safe procedure. Because of variable inclusion criteria among included studies, we are not able to assess which selection criteria are more important for overall outcomes.

Numerous incision types have been reported in order to ease the mastectomy and the reconstruction, to preserve the NAC blood flow and to obtain good aesthetic results.

However, there is no one ideal incision choice. However, according to the data presented in the included studies we can conclude that higher rates of NAC necrosis are reported with periareolar/circumareolar patterns and mostly with the transareolar approach (36,43).

NSM can be performed in association with immediate one-stage or two-stage reconstruction.

The direct-to-implant technique decreases costs and seems to lower complication rates, while the two-stage technique allows to improve symmetry, to better define the inframammary fold and optimize the perfusion of the mastectomy skin flaps (34,46).

The incidence of NAC necrosis slightly increases with one-stage reconstruction but the overall complication rate is higher with the two-stage technique.

NSM has been reported also in association with autologous reconstruction [free and pedicled transverse abdominis musculocutaneous (TRAM), deep inferior epigastric perforator (DIEP), superficial inferior epigastric artery (SIEA), latissimus dorsi (LD) and transverse upper gracilis (TUG) flap] (19,44,57,61,65), but due to the high level of heterogeneity between studies and limited patient numbers, it was not possible to draw any conclusion about autologous flaps and their relation to NAC and LR.

In the majority of the included studies, subareolar tissue was sent as a frozen section or as a permanent pathologic specimen or both, with a high level of heterogeneity among studies.

The sensitivity and specificity of frozen section subareolar biopsy for occult malignancy has been shown to be 91% and 98%, respectively (28). Some surgeons however send subareolar tissue for permanent section only and in these cases the NAC can be resected at the second stage of reconstruction.

However the rate of occult carcinoma within the NAC (most often DCIS) has been shown to be low, ranging from 1.2% to 5.9% (55).

There is no consensus regarding intraoperative or delayed radiation therapy on the NAC.

Reported LR rates after NSM vary very widely across studies (from 0% to 24.1%). The high level of heterogeneity among studies may be attributed to several factors, including the variability and inadequacy of follow-up length (10 months to 15 years), the variability in the tumor stage considered and the variability in additional treatments.

This review presents the great limitation of including only retrospective series and some prospective cohorts, having high heterogeneity in the characteristics of included patients, additional treatments received, surgical technique and reported methods of outcome.

NSM is generally considered oncologically safe in selected patients, but the decision to proceed with a NSM should always take into account oncological and anatomical selection criteria with the selection of the most appropriate skin incision and the best reconstructive option, always performing accurate subareolar tissue sampling (115-118).

The level of the evidence behind conservative mastectomies appears to be low and RCTs comparing BCT and MRM with skin-sparing techniques would be advisable in order to obtain higher levels of evidence on oncological and reconstructive outcomes.

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Footnote

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Training the oncoplastic breast surgeon – current and future perspectives

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Abstract: Oncoplastic breast surgery has evolved to become a distinct subspecialty within the field of general surgery. The oncoplastic breast surgeon requires comprehensive knowledge and understanding of all aspects of breast oncology, in addition to technical proficiency in operative procedures to remodel and reconstruct the breast. This article describes current educational resources available for the training of oncoplastic breast surgeons both within the UK and internationally. A recent development is the online Master of Surgery degree in Oncoplastic Breast Surgery, based at the University of East Anglia in the UK. This innovative course combines delivery of clinical knowledge using interactive problem-based forum discussions with assessment of operative and decision making skills. The degree is facilitated and assessed by an expert specialist breast faculty, and requires students to achieve standards expected of a first year practising UK oncoplastic breast consultant. Future international developments using this blended educational model are discussed.

Keywords: Oncoplastic; breast; e-learning; Masters; education

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UK background

Oncoplastic breast surgery has evolved as a distinct specialty over the last 10 years. This approach entails a single surgeon performing both the oncological procedure and subsequent reconstruction, thus providing a comprehensive oncoplastic approach. Although breast surgery remains under the auspices of general surgery in the UK, the new intercollegiate training curriculum recognises the wide range of oncoplastic procedures in which trainees must gain competency before the award of a certificate of specialist training required for a substantive consultant post.

International background

Traditionally, the majority of breast surgery is performed by a general surgeon in the United States and Australasia, or by a gynaecologist in European countries. The subsequent reconstruction is then undertaken by a plastic surgeon.

However, this approach has limitations as it requires co-ordination of surgeon availability which may delay primary operative treatment, and geographic inequalities exist in accessing reconstructive services. Increasingly, the oncoplastic single surgeon model is gaining popularity internationally.

Current UK educational resources

UK trainees currently undertake oncoplastic breast surgery training during their last three years of specialty rotations. This practical experience is provided by local breast units, and can be supplemented by a one year fellowship, either as one of the highly competitive National Training Interface Group posts, of which there are only 9 per year, or as an independent fellowship post which usually includes an element of service provision.

In addition, the UK Royal Surgical Colleges provide a range of optional specialist courses in oncoplastic

theory and practice, including legal aspects of surgical practice. Other available educational resources include industry sponsored events which address specific practical techniques such as the use of acellular dermal matrices and lipomodelling. Specialist conferences such as Oncoplastic and Reconstructive Breast Surgery (ORBS) are a chance to update practice and disseminate current information in a rapidly evolving specialty. The Association of Breast Surgery offers a subsidised annual trainees conference which includes a large element of oncoplastic surgery, and further educational events are organised by trainee groups such as the Mammary Fold and Plasta.

Online resources

The use of blended e-learning is gaining in popularity as an effective educational approach for postgraduate specialist medical training. The introduction of the European Working Time Directive to the UK has reduced clinical training hours and decreased trainees' exposure to training opportunities. Virtual learning environments allow trainees to access teaching materials at any time to suit their work schedule.

A Master of Surgery degree (MS) in Oncoplastic Breast Surgery was launched by the University of East Anglia in January 2011. This course blends online problem based learning forums with face-to-face lectures and summative examinations, and is open on a competitive basis to all UK breast surgeons of grade ST5 and upwards. In addition to theoretical knowledge, it includes assessment of practical skills including decision making and operative competence. The standard required for the award of the degree is that expected of a first year practising UK oncoplastic breast consultant, as judged by an expert faculty panel.

In addition to compulsory modules which cover benign breast disease and breast oncology, a full range of oncoplastic techniques is taught, including level I breast conserving surgery approaches, implant-based and flap-based breast reconstruction. Topics are taught using a range of clinical scenarios which are discussed by students in an online forum moderated by experienced senior clinicians. Students are able to assess their own progress using formative tools such as MCQs and script concordance tests. Each module is introduced with a face-to-face lecture session, and concludes with a written examination. There is an annual OSCE to assess practical skills and

communication.

The MS in oncoplastic breast surgery is now in its third year. Approximately 18 students have enrolled each year, and the first cohort is due to graduate in 2014. Anonymised student feedback has been generally excellent, and the course content and delivery is constantly reviewed and refined based on suggestions received from both students and faculty members. Following the success of this model, further MS degrees are now being delivered in regional anaesthesia and coloproctology, with programmes in both knee and hepatobiliary surgery also currently under development.

Future directions

As previously mentioned, there is growing interest in developing the specialty of oncoplastic breast surgery from countries outside the UK. The challenge will be to deliver accessible quality training in this new area of clinical practice. The established online MS degree in oncoplastic breast surgery is one potential mode of delivering high quality theoretical and practical training which will be globally accessible, but which can also be tailored to meet local educational needs. Various potential models exist, but there is an opportunity to provide a higher qualification which is widely accessible and recognised internationally.

At present the MS degree is open to UK residents, with European applicants considered on a case-by-case basis but the possibility of wider international dissemination is being explored. Further information is available by contacting andrew.d.simpson@uea.ac.uk.

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Footnote

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Evaluating the feasibility of extended partial mastectomy and immediate reduction mammoplasty reconstruction as an alternative to mastectomy

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The surgical strategy for breast cancer has been drastically changed from “maximum tolerable treatment” in the 1970s to “minimum effective treatment” in the 2000s. The results of efficacy studies of breast conserving therapy (BCT) combined with radiotherapy as an alternative to mastectomy, introduced and presented by Veronesi *et al.* and Fisher *et al.*, brought about a sensational movement worldwide (1-4). This major shift was realized owing to the development and progression of systemic drug therapy, including chemotherapy, endocrine therapy and molecular targeting therapy. We now recognize that prognostic factors for breast cancer are determined by not only tumor size and nodal status, but also biological factors such as ER status, HER2 status, and Ki-67 index. This indicates that systemic therapy is more significant than local therapy for the prognosis of breast cancer patients.

Oncoplastic breast surgery requires both cure of the breast cancer and cosmesis (5-8). The need to obtain negative margins often results in severe defects that are disfiguring and which compromise not only the aesthetic outcome, but also the patients’ psychological well-being. In such circumstances, patients often select mastectomy, with or without reconstruction (9-11).

Song *et al.* reported the importance of stricter patient selection and improved confirmation of negative margins for minimizing the need for either re-excisions or completion mastectomy and reconstruction (12-18). The article by Chang *et al.* in the June 2012 issue of *Annals of Surgery* reported the efficacy of using concurrent partial mastectomy and reduction mammoplasty for the resection of a wide range of tumor sizes. They compared oncologic outcomes

and postoperative complications on the basis of tumor size. As their study background, they stated that although tumor size greater than 4 cm has been considered an indication for undergoing a mastectomy, this dictum may not apply in women with breast hypertrophy, where the ratio of tumor size to breast size may still permit breast conservation. They proposed the use of an approach combining extended partial mastectomy with simultaneous reconstruction using breast reduction techniques in large-breasted women as a means of improving aesthetic outcomes while still maintaining excellent oncologic and surgical outcomes.

In this study, 79 patients who underwent simultaneous partial mastectomy and bilateral reduction mammoplasty (comprising a total of 85 cases, including 2 cases of phyllodes tumor) between January 2000 and December 2009 were included. The median follow-up was 39 months (range, 10-130 months). The average patient age at the time of reduction mammoplasty was 53.6 years. Twenty-five of 85 tumors (29.4%) were larger than 4 cm. In 56 cases, the tumors were estrogen-receptor-positive, 44 tumors were progesterone-receptor-positive, and 17 tumors were HER2/neu-positive. Eleven patients had positive lymph nodes on sentinel node biopsy, all of whom subsequently underwent completion axillary node dissection. Seventy-five of 79 patients were treated with adjuvant radiation therapy and 49 patients received chemotherapy. All patients with hormone-receptor-positive invasive breast cancer received adjuvant endocrine therapy.

Only 2 patients had local recurrence during the follow-up period, one of whom had a tumor smaller than 4 cm and the other had a tumor larger than 4 cm, which was not

significantly different between groups ($P=0.50$). Kaplan-Meier analysis demonstrated a 5-year local recurrence-free survival of 97.7%. The overall 5-year survival was 98.7% and the disease-free survival was 94.8%. The overall complication rate was 14.1% (12 cases), which included 4 major complications. All of the major complications occurred in the early postoperative period, prior to the start of adjuvant radiation therapy. Major complication rates were not significantly different between patients with tumors larger than 4 cm compared with those with smaller tumors ($P=0.58$).

Their results suggested that the ratio of tumor size to breast tissue may be the more important determinant of BCT feasibility rather than tumor size. In addition, in the era of modern systemic therapy, the major issue significantly impacting overall outcomes and guiding treatment decisions is distant disease rather than local disease.

In this study, the data presented provided initial evidence to support the safety and efficacy of treating tumors, even those larger than 4 cm, with an extended partial mastectomy and reduction mammoplasty in large-breasted women.

In summary, attempts at salvage of a woman's breast in the surgical management of breast cancer can greatly impact a woman's self-image and overall health and well-being. This procedure can further improve aesthetic outcomes and patient satisfaction, providing a cosmetic way to resect a large amount of breast tissue, depending on breast size, breast shape, and tumor location.

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Oncoplastic breast surgery: indications, techniques and perspectives

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Abstract: Breast-conservation surgery (BCS) is established as a safe option for most women with early breast cancer. Recently, advances in oncoplastic techniques have reduced surgical trauma and thus are capable of preserving the breast form and quality of life. In spite of the most BCS defects can be managed with primary closure, the aesthetic outcome may be unpredictable. Oncoplastic reconstruction may begin at the time of BCS (immediate), weeks (delayed-immediate) or months to years afterwards (delayed). With immediate reconstruction, the surgical process is smooth, since both procedures can be associated in one operative setting. Additionally, it permits wider excision of the tumor, with a superior mean volume of the specimen and potentially reducing the incidence of margin involvement. The oncoplastic techniques are related to volume displacement or replacement procedures including local flaps, latissimus dorsi myocutaneous flap and reduction mammoplasty/masthoplexy. Regardless of the fact that there is no consensus concerning the best approach, the criteria are determined by the surgeon's experience and the size of the defect in relation to the size of the remaining breast. On the basis of our 15-year experience, it is possible to identify trends in types of breast defects and to develop an algorithm for immediate BCS reconstruction on the basis of the initial breast volume, the extent/location of glandular tissue resection and the remaining available breast tissue. The main advantages of the technique utilized should include reproducibility, low interference with the oncologic treatment and long-term results. Surgical planning should include the patients's preferences, and chiefly addressing individual reconstructive requirements, enabling each patient to receive an individual "custom-made" reconstruction.

Keywords: Breast reconstruction; conservative breast surgery; partial mastectomy; oncoplastic; reduction mammoplasty; local flaps; outcome; complications

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Introduction

Breast-conservation surgery (BCS) is established as a safe option for most women with early breast cancer (1). In fact, the 5-year survival of BCS with radiation is not statistically different when compared with mastectomy alone in patients with Stage I or II breast cancer (2). Habitually, these procedures include quadrantectomy and lumpectomy. In quadrantectomy, a wide excision is usually performed, including skin and underlying muscle fascia. In lumpectomy,

the objective is tumor excision without skin resection and with negative surgical margins (2).

In spite of the acceptance that most BCS defects can be managed with primary closure, the aesthetic outcome may be unpredictable and frequently achieve an unsatisfactory outcome (2-10). In fact, approximately 10% to 30% of patients submitted to BCS are not satisfied with the aesthetic outcome. The main reasons are related to the tumour resection which can produce asymmetry, retraction,

and volume changes in the breast. In addition, radiation can also have a negative effect on the native breast. The main clinical aspects are related to skin pigmentation changes, telangiectasia, and skin fibrosis. In the glandular tissue, local radiation causes fibrosis and retraction (2,6).

Recently, increasing attention has been focused on oncoplastic procedures since the immediate application of plastic breast surgery techniques provide a wider local excision while still achieving the goals of a better breast shape and symmetry (6-18). In fact, the modern oncoplastic breast surgery combines principles of oncologic and plastic surgery techniques to obtain oncologically sound and aesthetically pleasing results. Thus, by means of customized techniques the surgeon ensures that oncologic principles are not jeopardized while meeting the needs of the patient from an aesthetic point of view (3).

In general, the oncoplastic techniques are related to volume displacement or replacement procedures and sometimes include contra-lateral breast surgery. Among the procedures available, local flaps, latissimus dorsi myocutaneous flap and reduction mammoplasty/masthoxey techniques are the most commonly employed (11). Additionally, oncoplastic approach may begin at the time of BCS (immediate), weeks (delayed-immediate) or months to years afterwards (delayed). Regardless of the fact that there is no consensus concerning the best approach, the criteria are determined by the surgeon's experience and the size of the defect in relation to the size of the remaining breast (9-11). The main advantages of the technique utilized should include reproducibility, low interference with the oncologic treatment and long-term results. Probably, all these goals are not achieved by any single procedure and each technique has advantages and limitations (11).

Indications

Timing

Surgical planning and timing of reconstruction should include breast volume, tumor location, the extent of glandular tissue resected, enabling each patient to receive an individual "custom-made" reconstruction. With immediate oncoplastic approach, the surgical process is smooth since oncological and reconstructive surgery can be associated in one operative setting. Additionally, because there is no scar and fibrosis tissue, breast reshaping is easier, and the aesthetic is improved (6,8,9,11,12,19). In fact, Papp *et al.* (12) observed that the aesthetic results

showed a higher success rate in the immediate group when compared with delayed reconstruction patients. Similarly, Kronowitz *et al.* (9) observed that immediate repair is preferable to delayed because of a decreased incidence of complications. In our previous experience utilizing reduction mammoplasty techniques for BCS reconstruction, we observe that our post-radiation complication rate (delayed BCS reconstruction) was higher than that expected for mammoplasty without radiotherapy (20). After adjusting for other risk factors, the probability of complications tends to be higher for delayed reconstruction group. This finding is similar to published reports that suggest that delayed BCS reconstruction has a significantly higher complication rate compared with immediate procedures (8,9).

In terms of oncological benefits and adjuvant treatment, immediate oncoplastic reconstruction can be advantageous. Some clinical series have observed that patients with large volume breasts present more radiation related complications than patients with normal volume breasts (21-23). Additionally, some authors suggested that there is an increased fat content in large breasts, and the fatty tissue results in more fibrosis after radiotherapy than glandular tissue. Thus, Gray *et al.* (23), in a clinical series, observed that there was more retraction and asymmetry in the large-breasted versus the small-breasted group. Thus, breast reduction can increase the eligibility of large-breasted patients for BCS since it can reduce the difficulty of providing radiation therapy (15-17,21,24).

Another aspect is the possibility of accomplishing negative resection margin. In fact, the immediate reconstruction allows for wider local tumor excision, potentially reducing the incidence of margin involvement (15-17,24,25). Kaur *et al.* (25) compared patients submitted to oncoplastic procedures and to BCS. The oncoplastic approaches permitted larger resections, with a superior mean volume of the specimen and negative margins.

In spite of the benefits, the immediate reconstruction presents limitations. The surgical time can be lengthened, it can be time consuming, and require specialist training to learn and properly apply these procedures (2,3,15). Thus, delayed reconstruction can be advantageous in some specific group of patients. In fact, in some cases the final contour of the breast cannot be predicted at the time of the BCS (24). In addition, it is well accepted that radiation usually involves some degree of fibrosis and shrinkage. Some authors observed that although the aesthetic outcome can be satisfactory, the appearance of the radiated breast is occasionally less pleasing than the nonradiated one (5-8,24).

Thus, in delayed reconstruction the plastic surgeon waits until the postoperative changes in the deformed breast stabilize. Another important point is related to the postoperative recovery. In theory some complications of the immediate reconstructions can unfavorably defer the adjuvant therapy. With delayed oncoplastic reconstruction, operative time is shortened and the surgical process is less extensive than an immediate. However, our previous experience (11,14-17), and of others (8,18,24), has shown that immediate reconstruction does not compromise the start of radio and chemotherapy in the overall treatment of breast cancer.

Partial breast defects classification

Several classification schemes have been developed to characterize breast deformity and proposed reconstructive techniques (2,7-9,26-30). It has been our impression that a number of classifications have been described involving primary closure, breast reshaping, local and distant flaps, yet some of these techniques address late repair. Some of them are related to delayed reconstruction based on tissue deficiency and the presence of radiotherapy effects. Additionally, most articles include them within a broader category of complex breast defects and up to now, there are few clinical series that describe a systematic approach or propose an algorithm for reconstruction on an immediate basis.

In delayed reconstructions (29,30), Clough *et al.* classified the breast defects and oncoplastic procedures according to the response to reconstruction (30). Thus, patients with a type-I breast deformity have a normal-appearing breast with no deformity. However, there is asymmetry in the volume or shape between breasts and were managed by a contralateral breast surgery. Type-II patients have deformed breasts, however, is treated by an ipsilateral breast surgery or flap reconstruction. Type-III patients have either major deformity with fibrosis and were treated with total mastectomy and reconstruction.

Berrino *et al.* emphasized the importance of analyzing the etiology of the breast defect (29). In type I, the breast defect results from fibrosis and scar contracture. In type II, there is a localized deficiency of tissue including skin, or breast tissue, or both). Type III has a more advanced breast retraction with normal overlying skin. This is most frequently secondary to radiation in patients with large and grade III-IV of ptosis. Lastly, type-IV defects results from severe distortion and asymmetry. There is significant breast

tissue retraction, and the skin has local radiation-induced changes.

Recently, Hamdi *et al.* proposed a classification based on the size and location of the expected tumor resection and the ratio of breast volume to resection volume (2). Tumors involving the lower pole are most treated because this region is removed during most reduction mammoplasty. Other regions of tumor resection, can also be repaired using a combination of mammoplasty and glandular flaps to fill the breast defect. According to Hamdi's classification one of the relative contraindications for rearrangement breast surgery (glandular flaps and reduction mammoplasty) is a large tumor/breast ratio (2). Thus, smaller breasts require different methods of reconstruction and a large-volume tumor resection, the recruitment of local flaps is required. A small lateral defect can be reconstructed with a skin rotation flap or lateral thoracic axial skin flap. If these flaps become unavailable due to axillary lymph-node dissection, the lateral breast defects can be reconstructed using a flap based on the thoracodorsal system. The latissimus dorsi musculocutaneous flap is the most commonly used, however it is possible to use a similar skin paddle raised on perforators either from the thoracodorsal (TDAP) or intercostal vessels. In fact, the authors reported the use of the lateral intercostal artery perforator (LICAP) in BCS reconstruction within a clinical algorithm based on the location of the defect and the availability of these perforators. Both flaps are good alternative for lateral and inferior breast defects, however, the TDAP has a longer pedicle, thus enabling the flap to reach most of the breast. Medial defects are more complex to repair. In small lower-pole defects an epigastric rotation flap can be utilized, however, donor-site closure may distort the inframammary fold (IMF) contour once this flap is based on tissue directly below this anatomic area.

On the basis of our 15-year experience, it is possible to identify trends in types of breast defects and to develop an algorithm for immediate BCS reconstruction on the basis of the initial breast volume, the extent/location of glandular tissue resection and the remaining available breast tissue (11). Each defect has its own special reconstructive necessities varying expectations for aesthetic outcome. To make possible development of a BCS reconstructive algorithm, immediate partial breast defects are classified into one of three types (*Figure 1*).

Type I

Defects include tissue resection in smaller breast without

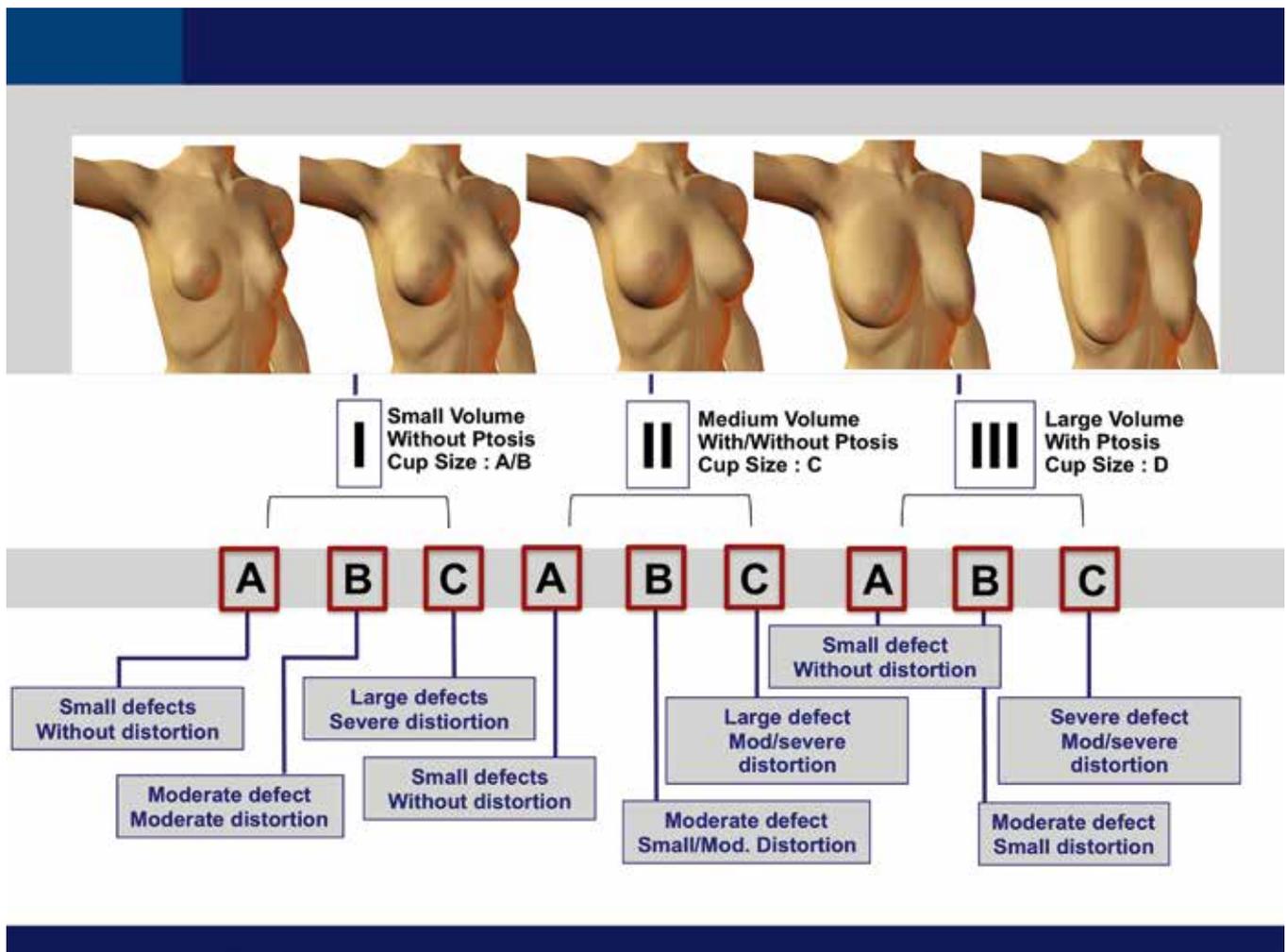


Figure 1 Algorithm for immediate conservative breast surgery reconstruction based on the type of breast and extent of defect.

ptosis. Type IA defects involve minimal defects that do not cause volume alteration/distortion in the breast shape and the tissue resected is less than 10-15 percent of the total breast volume. Initial tumor exposure is achieved through a periareolar approach in cases where the tumor is located deeply. In patients where the tumor is located close to the skin, a separate incision is planned directly over the region to be resected. Type IB defects involve moderate defects that do originate moderate volume alteration/distortion in the breast shape or symmetry and the tissue resected is between 15 and 40 percent of the total volume. Usually, the skin above the tumor is resected with the tumor. Type IC defects involve large defects that do cause significant volume alteration/distortion in the breast shape and symmetry and the tissue resected is more than 40 percent of the total breast volume.

Type II

This group includes tissue resection in medium sized breasts with/without ptosis. Type IIA involves small defects that do not cause enough volume alteration/distortion in the breast shape. Type IIB defects involve moderate defects that cause minor/moderate volume alteration in the breast shape. Type IIC defects involve large defects that cause moderate/large volume variations in the breast shape and symmetry.

Type III

This group includes tissue resection in large sized breasts with ptosis. Type IIIA involves small defects that do not cause enough aesthetic deformity. Type IIIB defects involve moderate defects that originate minor/moderate volume alterations in the breast shape or symmetry. Type IIIC defects involve large defects that cause significant volume

alteration in the breast.

Oncoplastic techniques

Partial breast defects represent an anatomic variety that ranges from small defects that may repair with primary closure and to large defects that involve skin, NAC and a significant amount of glandular tissue. It has been our impression that a number of procedures have been described involving primary closure, breast reshaping, local and distant flaps, yet some of these techniques address late repair (11). In addition, some classifications have been described to evaluate the extent of resection, which has consequently created wide-range of surgical options with different indications (7-9,26-28). We believe that an algorithm gives the surgeon guidelines for management of immediate BCS defects. Partial mastectomy defects can be scored and classified according to the proposed classification. The application of this system to the spectrum of cases demonstrated that the algorithm works well and classifies patients in a useful system. Surgical planning should include the breast volume, tumor location, the extent of glandular tissue resected, and chiefly addressing individual reconstructive requirements, enabling each patient to receive an individual “custom-made” reconstruction. Evaluation of BCS reconstruction must subsequently consider these important points and, only then should the proper technique or a combination of procedures be chosen. In our experience, the majority of reconstruction techniques are performed with one of six surgical options: breast tissue advancement flaps (BAF), lateral thoracodorsal flap (LTDF), bilateral mastopexy (BM), bilateral reduction mammoplasty (BRM), latissimus dorsi myocutaneous flap (LDMF) and abdominal flaps. Concerning the use of distant flaps (pedicled and free) in CBS reconstruction, there is no consensus about the indication and the more appropriate technique. In terms of benefits and morbidity, the abdominal wall area as donor site has some positive aspects. In fact, it has been our experience that the abdominal area provides the ideal volume for a partial and total breast reconstruction, even in large-breasts patients or in patients who undergo bilateral mastectomy. Thus, it is possible to utilize the mono-pedicled or bipedicled TRAM flap in CBS reconstruction. The establishment of microsurgery techniques led to the development of the free TRAM flap because of its increased vascularity and decreased rectus abdominis resection. Recently, the muscle-sparing free TRAM, DIEP, and SIEA

flap techniques followed in an effort to reduce donor site morbidity by decreasing damage to the rectus abdominis muscle and fascia. However, a significant number of patients with positive postoperative tumor margins after immediate CBS reconstruction underwent a completion mastectomy with immediate abdominal flap breast reconstruction (31). This observation demonstrates the importance of not using the abdominal area (TRAM, DIEP or SIEA flaps) for immediate CBS reconstruction. In addition, our experience indicate that the great part of patients who develop a local recurrence and have a completion mastectomy will desire breast reconstruction with a abdominal flap. Again, and similar as pointed out by other authors (2,9), this stresses the importance of preservation of reconstructive options, especially the abdominal wall area.

Surgical planning should include breast characteristics, extent of breast tissue resected, and chiefly addressing individual reconstructive requirements. Additionally, the decision is usually determined by the surgeon’s preferences and the size of the defect in relation to the size of the remaining breast. In fact, it is important to identify trends in types of breast defects on the basis of the initial breast volume, the extent/location of glandular tissue resection and the remaining available breast tissue.

Types IA, IIA and IIIA

Defects are usually repaired with BAF in which the defect created is usually spherical or rectangular. The breast tissue is advanced along the chest wall or beneath the breast skin flap to fill the tumor defect. In order to achieve a better aesthetic outcome without significant skin retraction, superficial undermining between the breast tissue and the skin flap can be performed, preserving the skin blood supply. In the situation of simultaneous superficial and deeper undermining of the breast tissue, the blood supply of the BAF can be decreased, especially in obese patients with fatty breasts. Thus, care must be taken in this group of patients in order to avoid late fat necrosis. Usually, in these patients no contralateral breast procedure is performed (*Figure 2*).

Type IB

In patients with lateral defects the LTDF is performed. Previously described elsewhere (14), this local flap is planned as a wedge-shaped triangle located entirely on the lateral aspect of the thorax and then rotated to the

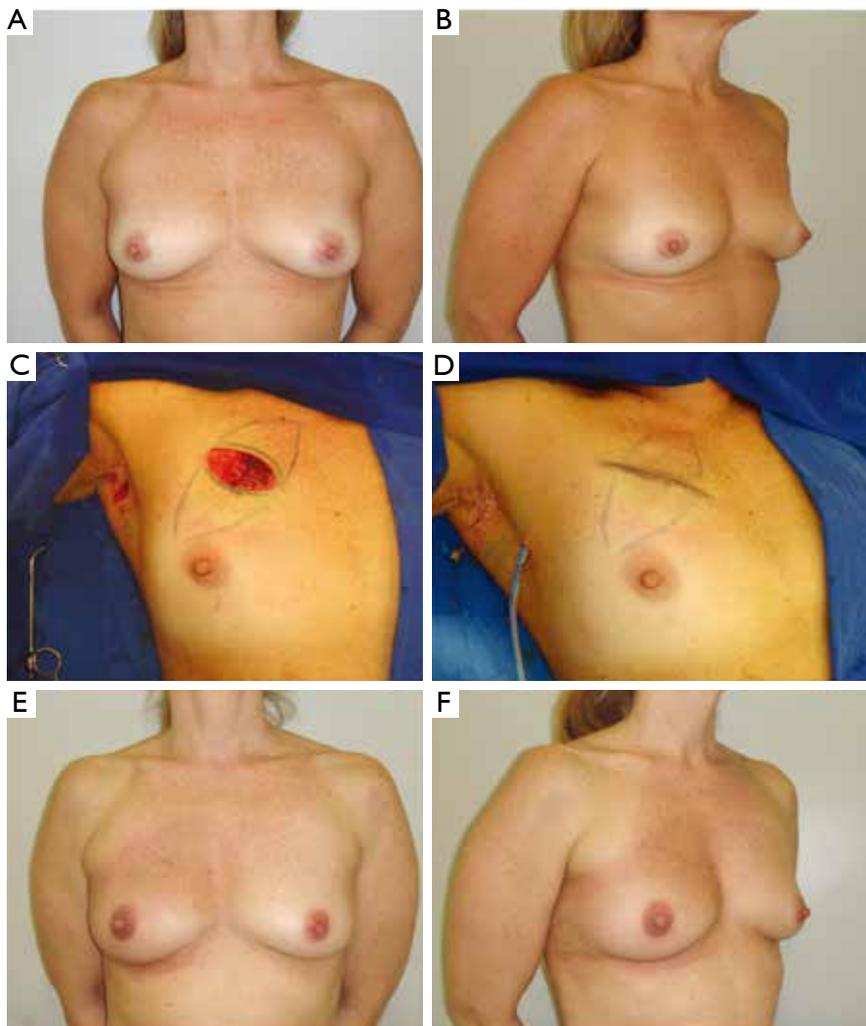


Figure 2 A 42-year-old patient with invasive ductal carcinoma (1.3 cm) of the right breast (A,B. above left and right). The patient underwent a right superior lumpectomy and sentinel lymph node biopsy, immediately followed by a breast advancement glandular flaps (BAF) reconstruction; a total of 65 g was removed from the right breast (C,D. center left and right). One year postoperative appearance after the radiotherapy (E,F. below left and right).

lateral breast defect. Introduced as a fasciocutaneous flap, the LTDF is a well-described technique for delayed breast reconstruction following radical surgery (32). In conservative breast surgery, Clough *et al.* (30) utilized the subaxillary area as a transposition flap with satisfactory results in lateral breast defects. According to the authors, if the defect is located in the superior pole of the breast, a superiorly based flap can be applied with the same principles. Similarly, Kroll *et al.* (33) transferred the subaxillary skin and subcutaneous fat as a composite and rotation flap to reconstruct a lateral breast defect. Although additional scars are created, they will be placed

in the lateral region and therefore will not interfere with the wearing of clothing. In our experience, raising the LTDF provides a very wide access to the axilla which greatly facilitates lymph node dissection which was performed without excessive traction or injury to the structures in the axilla. When indicated the glandular tissue is dissected of the pectoral muscle in order to improve and reshaping of the breast. The defect margins are sutured to the margins of the flap and the donor site is closed primarily in layers (*Figure 3*). In patients with central and medial tumors, the LDMF can be utilized (11,13). The flap is designed into a horizontal position

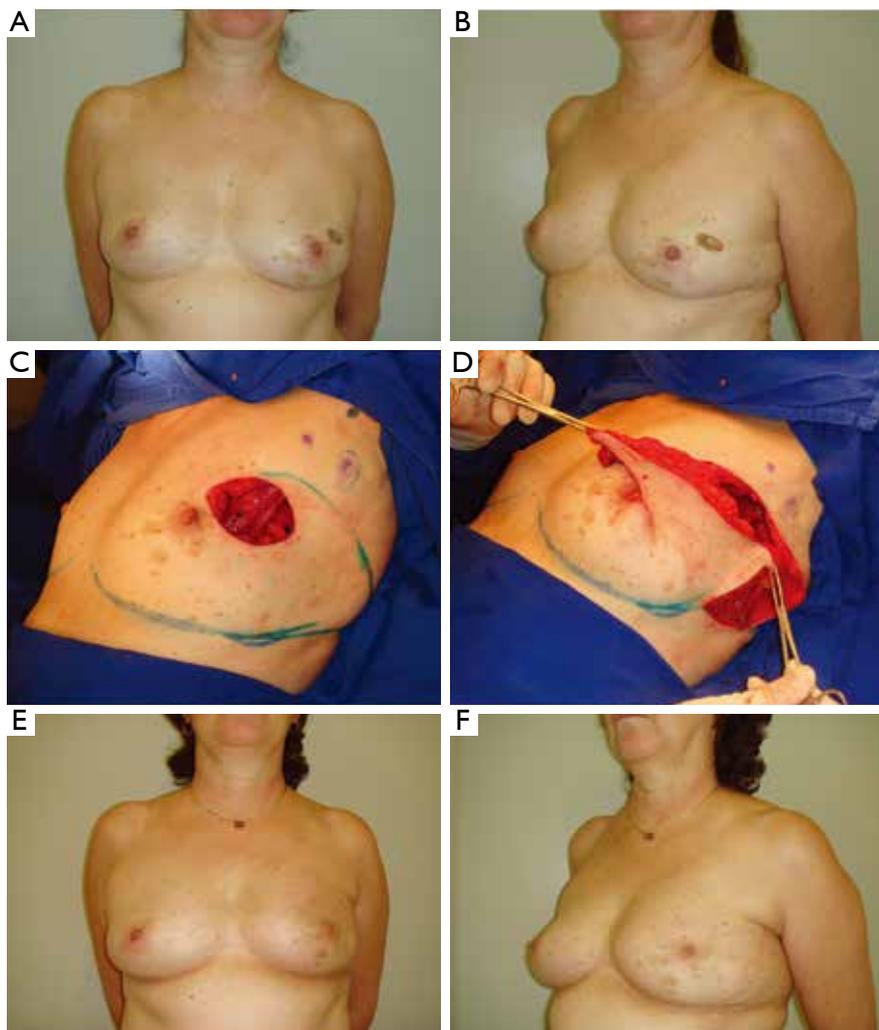


Figure 3 A 58-year-old patient with invasive ductal carcinoma (3.7 cm) of the lateral quadrant of the left breast (A,B. above left and right). The patient underwent a left superior-lateral quadrantectomy and sentinel lymph node biopsy, immediately followed by a Lateral Thoracodorsal Flap (LTDF) reconstruction; a total of 225 g was removed from the left breast (C,D. center left and right). Two years postoperative appearance after the radiotherapy with a very good outcome (E,F. below left and right).

and the width of the paddle is measured according to the skin previously resected. The inferior and superior flap extension is subjectively estimated to match the volume of glandular tissue removed. Local flaps and specially the LTDF are useful techniques for upper outer or lower outer defects. Using tissue next to defect will provide matching color and texture to the breast. The technique provides wide access to the axilla when the flap incision is made in continuity with that of axillary incision.

In our previous experience, the LDME is used to replace skin and glandular tissue resected during oncologic surgery (13). It is frequently indicated for severe defects

where there is not enough breast tissue to perform the reconstruction. In addition, the most common use for BCS reconstruction has been in patients who underwent extensive breast tissue resection because of large tumors or compromised breast margins (13,34). These included patients with small or medium-volume breasts without ptosis that precludes the use of mammoplasty techniques. Comparing the LTDF with LDME, local flaps are easy to perform, less time consuming, no special positioning, and no loss of muscle function (11). Additionally, LTDF when used as alternative to LDME will spare the muscle as a potential reserve for future use in case of local recurrence.

Type IC

Defects are converted to a skin-sparing mastectomy (SSM) and reconstructed with an appropriate technique. In patients with enough abdominal tissue, an abdominal flap (pedicled/free TRAM or DIEP) can be an option according to the surgeon's preference. In patients without an adequate abdomen, a LD MF associated with an implant can be performed.

Type IIB

Defects are frequently reconstructed with BM techniques when there is sufficient breast tissue to perform the reconstruction. It has been our experience that BM for BCS reconstruction have aesthetic, functional and oncological advantages (15-17,19). The preoperative appearance can be improved, having smaller and more proportional breasts. Patients can obtain potentially less back and shoulder pain and the bilateral procedure allows us to examine the contralateral breast tissue for occult breast lesions (15,35). In terms of local control and adjuvant therapy, the added removal of a substantial volume of breast tissue could add a significant amount of safety in terms of surgical margins (24,25). In addition, the technique reduces the difficulty of providing radiation therapy to the remained breast tissues with acceptably low complication rates (21-23).

In previous reports (15,18), there is no consensus regarding the best BM technique for immediate BCS reconstruction. Possibly an ideal procedure does not exist and each case should be planned individually. The main advantages of the BM technique utilized should include reproducibility, safety and long-term results. As any surgical technique, all these goals are probably not met by any single procedure and it is supported by the large number of RM techniques available (15,36,37). Each presents particular advantages for their indications, tumor location limitations, vascular pedicle, additional skin and glandular resections due to compromised margins, and resultant scar. Because of rich breast tissue vascularization, the majority of techniques have based their planning on preserving the pedicle of the NAC after tumor removal. For tumors located in the lower region, the tumor resection can be incorporated into the sector of breast tissue removed as part of a superior pedicle mammoplasty (15,16). For upper region tumors, the lower breast tissue may be moved into the defect as a glandular flap and an inferior pedicle mammoplasty can be utilized (17). For inner and outer region tumors, the

reduction pattern can be rotated and a superior-lateral or a superior-medial pedicle mammoplasty can be done (15) (*Figure 4*). The opposite breast surgery is usually performed to match the appropriate symmetry, particularly in breasts with severe ptosis. With a well-trained surgical team, the procedure can be conducted on both sides at the same time, consequently reducing the operative time. When performing symmetrization, the surgeon can use this opportunity to resect any suspicious breast lesion that may have been revealed by a preoperative exams (15,35).

Type IIC

Defects are analyzed individually according to the size of the breast defect in relation to the remaining breast tissue available. For this purpose, the patient is positioned upright to assess the amount of the remaining glandular tissue. Thus, the type IIC can be subclassified into favorable and unfavorable defects. If there is enough tissue to perform an adequate breast mound shaping the defect is classified as favorable. For the lateral defects, the extended LTDF is most commonly employed where the inferior and superior limits are designed more obliquely with curved borders to incorporate a large amount of subcutaneous tissue from the lateral and posterior region of the thorax. In patients with central and medial defects, the extended LD MF can be utilized (13). Conversely, if not enough breast tissue remains, the breast defect is classified as unfavorable and a SSM and total reconstruction is indicated.

Type IIIB

Defects are frequently reconstructed with BRM techniques when the patient presents large volume breasts and there is a sufficient amount of breast tissue (*Figure 2*). The most favorable tumor location is in the lower breast pole where a conventional superior pedicle or superior-medial technique can be utilized (15,16). In patients with central tumors, an inferior pedicle is used to carry parenchyma and skin into the central defect (17) (*Figure 5*).

Type IIIC

Breast defects are analyzed individually. When the defect is favorable the deficiency is most frequently reconstructed with BRM. A marked reshaping of the breast with available tissue and a similar contralateral breast reduction is then performed. In patients in which the relation is not favorable

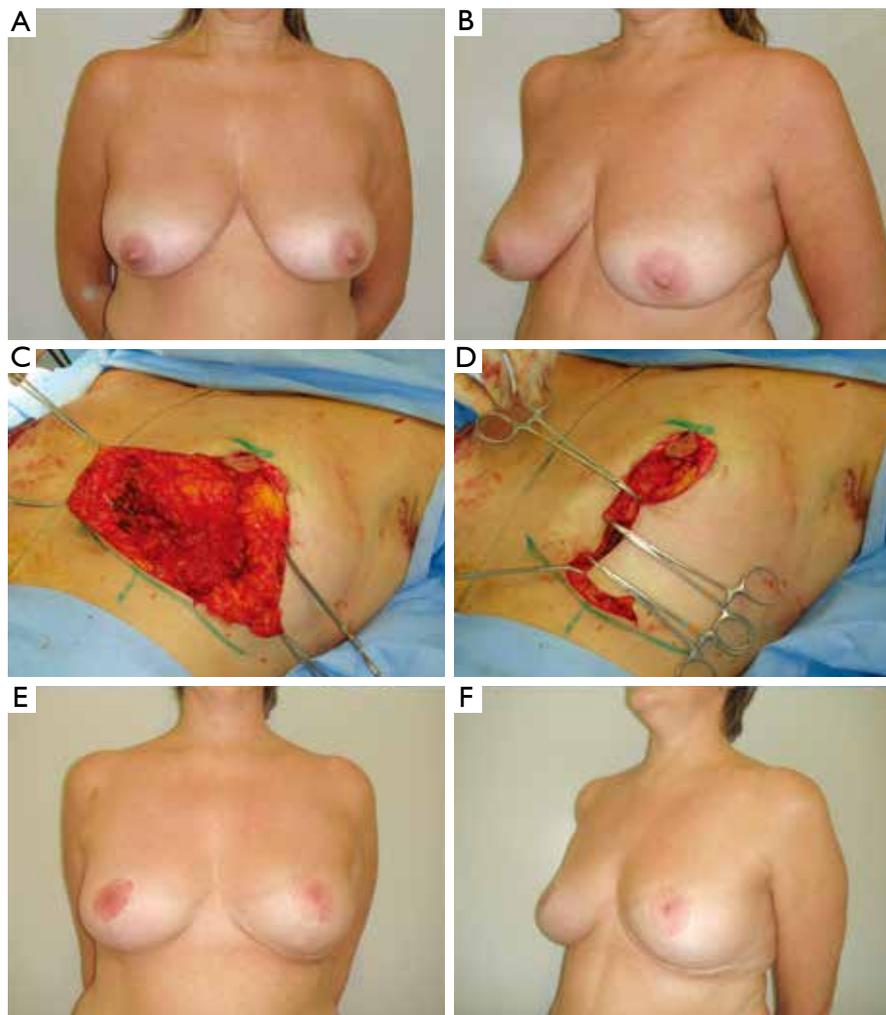


Figure 4 A 48-year-old patient with invasive ductal carcinoma (2.7 cm) of the inferior quadrant of the left breast (A,B. above left and right). The patient underwent an inferior left quadrantectomy and sentinel lymph node biopsy, immediately followed by a mastopexy reconstruction; a total of 125 g was removed from the left breast (C,D. center left and right). Four years postoperative appearance after the radiotherapy with a very good outcome (E,F. below left and right).

a skin-sparing mastectomy and total breast reconstruction with an appropriate technique can be indicated.

Clinical results of oncoplastic breast surgery

Immediate BCS reconstruction is challenging for oncological and plastic surgeons, demanding understanding of the breast anatomy, ability in reconstructive techniques and a sense of volume, shaping techniques and symmetry. It has been our impression that this approach has evident advantages, and there is no doubt that this concept will become more widely available and possibly become standard practice in the future (3). At the present time, optimal

treatment should be correct, adequate and preventive by performing immediate reconstruction, before radiotherapy (9,19,26). However, to date there is limited evidence in the plastic and breast surgery literature on the safety and aesthetic clinical results of the oncoplastic techniques (8-10,19,20,26,31,38). In fact, the great part of these clinical series are retrospective studies, generally based on a limited number of patients and sometimes only a single surgeon's experience. In addition, there are a small number of data on its impact on local recurrences, distant metastasis and overall survival (9,25). Kronowitz *et al.* (9) in a review of 69 patients observed local recurrence in 2% of immediate oncoplastic reconstructions and in 16 percent

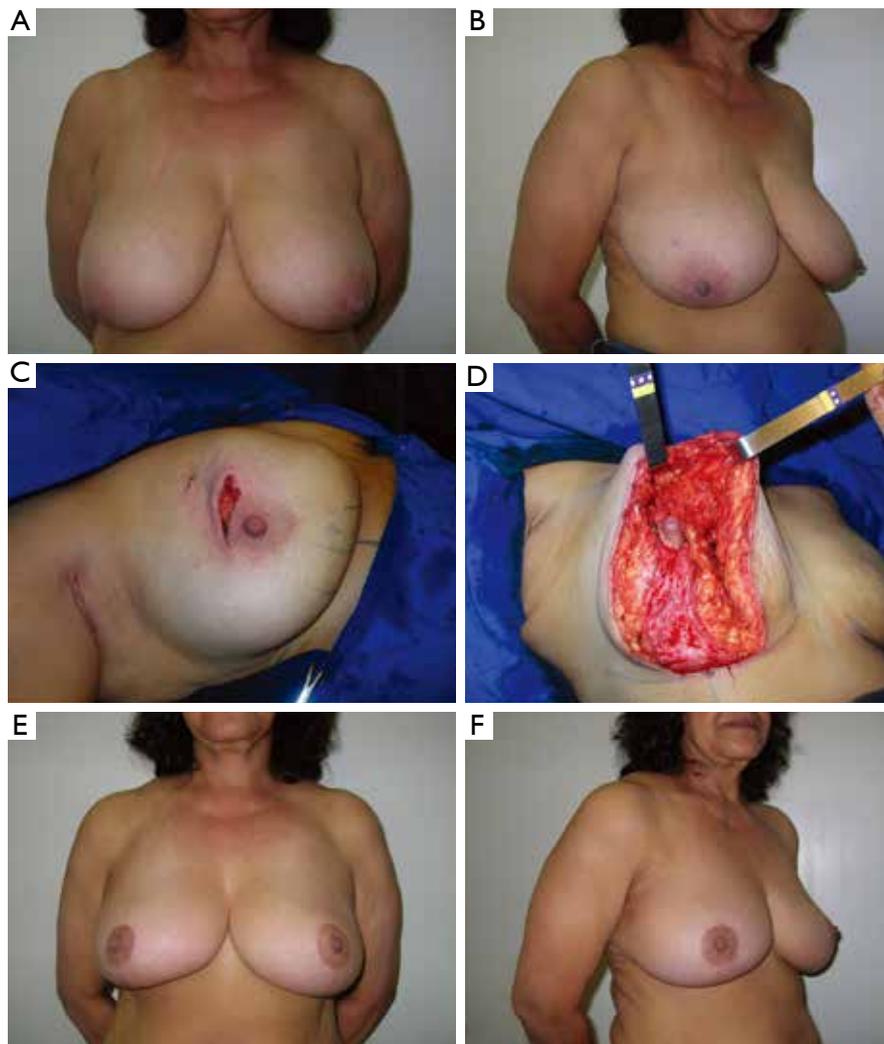


Figure 5 A 61-year-old patient with invasive ductal carcinoma (3.9 cm) of the superior quadrant of the right breast (A,B. above left and right). The patient underwent a superior right quadrantectomy and sentinel lymph node biopsy, immediately followed by a reduction mammoplasty reconstruction (inferior pedicle); a total of 325 g was removed from the right breast (C,D. center left and right). Two years postoperative appearance after the radiotherapy with a very good outcome (E,F. below left and right).

of delayed ($P=0.06$). The difference observed between the two groups can be explained by the advanced tumor stage for the patients who had a delayed reconstruction. Similarly, Clough *et al.* (38) with a median follow-up of 46 months reported 101 patients who were underwent BCS and oncoplastic reconstruction. Local recurrence developed in 11 cases (5-year local recurrence rate was 9.4%). Thirteen patients developed metastases and eight died of their disease (5-year metastasis-free survival of 82.8% and an overall survival rate of 95.7%). Recently, Rietgens *et al.* (20) reported the long-term oncological results of the oncoplastic reconstruction in a series of 148 patients. With a

median follow-up of 74 months, 3% developed an ipsilateral breast cancer recurrence 13% developed distant metastasis. According to the authors the rate of local recurrence after 5 years was low in their series when compared with the 14.3% of cumulative incidence in the NSABP trial, the 9.4% after 5 years in the Institut Curie study and the 0.5% after 5 years in the Milan I trial. Consequently, the oncoplastic approach associated with BCS can be considered as safe as mastectomy in tumours less than 2 cm and possibly safer than the BCS.

Concerning the aesthetic results there is limited evidence of the oncoplastic procedures. In addition, the methods of aesthetic evaluation vary significantly (9,10).

Some authors reported that the amount of glandular and skin tissue resection is directly associated to the aesthetic outcome (39-41). Olivotto *et al.* (39) and Mills *et al.* (40) have documented that excision of a volume greater than 70 cm³ in medium-size breasts often leads to unsatisfactory aesthetic results. Gendy *et al.* (28), retrospectively compared the aesthetic outcomes of 106 patients. Although the panel scored the cosmetic outcome quite high, the cosmetic failure rate was 18% on breast retraction assessments. The authors demonstrated an advantage for the BCS reconstruction with regard to the incidence of complications (8% versus 14%), additional surgery (12% versus 79%), and restricted activities (54% versus 73%). Clough *et al.* (38) in a panel of three assessed cosmetic results at 2 and 5 years. At 2 years 88% and at 5 years 82% of patients had a fair to excellent outcome. A significantly worse aesthetic outcome was observed in the 13 patients that received pre-operative radiotherapy compared to the remainder which were given radiotherapy postoperatively (poor outcome 42.9 *vs.* 12.7%, $P < 0.02$). Recognizing that there is a small risk for local recurrence and based on clinical series previously published, we believe that immediate application of oncoplastic procedures could be a reasonable and safe option for early-breast-cancer patients who desire BCS.

Limitations of oncoplastic breast surgery

Complications rates, adjuvant treatment and surveillance

One of the limitations concerning the BCS reconstruction at the time of oncological surgery is that the additional procedure would result in complications and delay adjuvant therapy. In a recent published meta-analysis, the average complication rate in the oncoplastic reduction mammoplasty group was 16%, and in the oncoplastic flap reconstruction group was 14% (42). However, there was no delay in the initiation of adjuvant therapy. According to the authors, it does not seem that complications in the oncoplastic groups, although potentially higher, have any negative impact on patient care from an oncologic point of view. In fact, adequate technique and patient selection is crucial in order to minimize morbidity when this oncoplastic techniques are selected (42,43).

Concerning late complications, the most common event is related to fat necrosis. In our previous experience comparing immediate and delayed BCS reconstruction with reduction mammoplasty techniques, this complication was significantly higher in the delayed group (19). It has been

our impression that radiation therapy played a significant role and contributed to development of fat necrosis. One might surmise that in delayed reconstructions, a slower reestablishment of a local blood supply to rearranged breast tissues from the underlying irradiated chest wall can be observed. In addition, previous breast tissue scarring and local effects of radiotherapy can also disrupt the local blood supply and the ability to create a safe parenchymal pedicle (9,19). Thus, in these patients a careful surveillance is prudent since the risk of local recurrence is always possible. According to Losken *et al.* (26), postoperative surveillance is not impaired by simultaneous BM. In some cases, calcifications and fat necrosis can simulate tumor recurrence; however, these aspects can be distinguished on mammogram or core biopsy (15-17,26).

Opposite breast (OB) surgery

Another important issue is related to the OB surgery. In our previous experiences, all patients submitted to reduction mammoplasty reconstruction had bilateral procedures (15-17), and almost 40% of patients submitted to volume replacement underwent a contra-lateral breast surgery in order to achieve a satisfactory outcome (13,14). In fact, Kronowitz *et al.* (44) observed a significant relationship existing between the reconstructive technique and the need for an OB reduction. This aspect can be viewed as a negative point, however it also has the advantages of allowing for sampling of glandular tissue (15-17,19,21,35,44). In our previous study (19), we report our experience with surgical management and outcome in BCS reconstruction with BM techniques with regard to whether immediate or delayed reconstruction is better in terms of complication rates. In this series, in three patients (2.8 percent) an unexpected cancer in the OB was observed in immediate reconstruction. Although the diagnosis of occult cancer is not a reason to perform an OB reduction, this procedure can be advantageous for high-risk patients and especially for patients with previous breast cancer (19).

Postoperative radiation and boost therapy planning

All immediate techniques that involve rearrangement of glandular tissue may jeopardize the boost radiation dose delivery since the target area for the radiation is defined as the site of the tumor (15,45). For this reason, a coordinated planning with the multidisciplinary team, especially with the radiotherapy group is crucial since

Table 1 Intra and posoperative assessment of margins × surgical management

Margins × surgical management	No. (%)
Intraoperative (initial margin)	
Free (negative)	151 (72.2%)
Positive (re-excision)	48 (23%)
Positive (SSM)	10 (4.7%)
Permanent paraffin (final margin)	
Positive	12 (5.7%)
Re-excision w/o reconstruction	5 (2.3%)
Re-excision + local reconstruction	3 (1.4%)
SSM + total reconstruction	4 (1.9%)

SSM, skin-sparing mastectomy; W/O, without.

some oncoplastic techniques alter the normal architecture of the breast (15,16). To locate the original tumor area we recommend orienting the tumor site by skin markings and also placing surgical clips at the tumor margins. It has been our impression and similar as observed by a other authors (45-47) that identification of the original tumor bed based only on physical exam, without precise imaging information, can result in missing the primary tumor bed in a substantial percentage of patients. In our previous experience (15-17), surgical clips have not interfered with mammography, and, actually, have helped recognize areas at risk for recurrence. Additionally, clips have not been mentioned as interfering with physical examination or cosmesis or to have added to any morbidity related to the reconstructive procedure (45).

Another important issue is related to delayed reconstruction following radiotherapy. Frequently, the appearance of the radiated breast is less pleasing than the nonradiated one and total dose, the boost therapy and the number of radiation fields may be involved (19,21,23,24). Losken *et al.* (24), emphasized that when radiation is expected, the possibility of fibrosis/atrophy should be taken into account in an attempt to preserve symmetry. The authors suggested a less aggressive reductions on the ipsilateral breast to accommodate for any additional size distortion. Additionally, some authors advocated that oncoplastic reconstruction with radiation is best achieved using autologous, nonirradiated flaps (6,9,11,19).

Final surgical margins assessment and immediate reconstruction

Techniques that involve rearrangement of glandular tissue

make reexcision difficult in cases where close or positive margins are observed (31). This fact could make it difficult to locate the residual tumor and to perform margin reexcision. In our previous studies (14-17), intraoperative margin evaluation was assessed by pathological monitoring, which is based on radiological, macroscopic, and histological examination of frozen sections. In our previous experience, positive margins discovered on permanent pathology in a previously negative margin patient were observed in 5.5 percent (31) (*Table 1*). Previous studies have been investigating the risk factors to identify patients with a high probability of having positive margins following CBS (26,31,48-53). In fact, younger age (26,31,52,53), histopathologic characteristics (in situ carcinoma) (26,52-54), and larger tumor size (31,53) have all been associated with positive margins. Our results were comparable to those of the previous studies with young patients and larger tumor size as more likely to have positive margins (31). Our data suggest that patients with those characteristics require more meticulous intraoperative margins evaluation to avoid the need for re-operation. Concerning the reoperative rates, Olson *et al.* (49) observed that 11.3% of patients submitted to CBS require second operations to achieve negative margins. Weinberg *et al.* (55) observed that 6.2% had later re-excisions and Cendán *et al.* (56), reported that 19.6% of subjects required additional operations to clear surgical margins. In spite of these aspects, the positive margins can be effectively managed with either re-excision with/without reconstruction or with skin-sparing mastectomy and total reconstruction, depending on the extention of tissue resection, preference, and pathology. The decision to re-operate depends on the extent of tumor involvement, whether the dissection had already been extended to the chest wall or skin, or whether the patient had opted to proceed with a total reconstruction. It has been our impression that re-operation was not a disadvantage in these patients and the negative aspect of a more extensive surgery is negligible. However, it is important that the patient should be appropriately informed about the risk of further positive margins and the requirement of an additional surgery (31). Thus, intraoperative assessment of surgical margins require multidisciplinary cooperation among oncological and plastic surgeons and pathologists. Diverse techniques have been described, depending on the tumor type, size, the CBS technique, and whether or not the tumor is palpable (31,49,54). Unfortunately, all techniques can present some limitations and as with any other test, there is an inherent false-negative rate (31). According to Losken

et al. (26), all patients should be informed preoperatively on the potential need for a delayed-immediate approach. Additionally, these high-risk patients can be better managed by staged procedures and confirmation of negative margins prior to CBS reconstruction (26,31).

Delayed BCS reconstruction and outcome

Another important issue is related to the complication rates and the timing of reconstruction. In our previous series, delayed reconstruction complication rates have been shown to be higher than immediate reconstruction (31 versus 22 percent respectively) (19). However, this aspect was not significant ($P=0.275$). Thus, our results indicate that timing of reconstruction is not a significant predictor of complications following BCS reconstruction with BM. This finding is contradictory to published reports that suggest that delayed BCS reconstruction has a significantly higher complication rate compared with immediate procedures (9,38). In fact, Kronowitz *et al.* (9) observed that delayed reconstruction was associated with a complication rate almost twice that of immediate. In our study, the relatively small number of patients and especially the small number of obese patients in the delayed group (21.7 versus 10.5 percent) may have influenced this comparison. Thus, a large number of patients and a prospective and controlled sample are necessary for definitive conclusions.

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Footnote

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Oncoplastic breast conserving surgery

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Abstract: Oncoplastic breast conserving surgery is a fundamental component of the repertoire for the management of breast cancer. It facilitates removal of large volumes of breast tissue, and can improve cosmetic outcomes and patient satisfaction whilst maintaining good oncological principles, reducing re-excision and mastectomy rates and assisting in adjuvant radiotherapy planning. We review the various techniques for oncoplastic breast conserving surgery that have emerged over recent years and describe their utilisation in excising tumours from various locations within the breast, and the pertinent patient specific factors that must be considered in technique selection. Finally complications and the evidence for the oncological safety specific to this type of surgery are discussed.

Keywords: Oncoplastic; breast; breast cancer; breast surgery; breast conservation

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Introduction

Breast conservation surgery with adjuvant radiotherapy is widely accepted as a treatment modality for women with early stage breast cancer. Prospective, randomised trials, with 20 years outcome reported in some studies, have reported no difference in breast cancer mortality and overall survival when compared to women treated with mastectomy (1-4).

Breast conservation success is based around the principles of complete removal of the tumour with adequate surgical margins whilst preserving the natural shape and appearance of the breast. Historically, breast conservation has not always achieved a good cosmetic result, which has had the resultant sequelae of negative patient reported outcome scores, for example body image and quality of life. The deformities caused by poorly planned breast conservation surgery are often severe and difficult to manage with high levels of complications and dissatisfaction (5).

Oncoplastic breast conserving surgery techniques have emerged over recent years, facilitating the achievement of better cosmetic results whilst maintaining good oncological principles. The term “oncoplastic”, is a Greek derived word which literally translated means “moulding of tumour”. It

first appeared in the literature in 1996 (6). Audretsch (7), considered by some as the father of oncoplastic surgery, described the technique of reconstructing a partial mastectomy defect in 1998 as a further refinement of breast conservation avoiding mastectomy. Since its introduction, oncoplastic breast surgery has enabled surgeons to remove greater volumes of tissue successfully, and thus reducing mastectomy and re-excision rates. The breast oncoplastic service is now a core component of the breast multidisciplinary team. Here we review various strategies for oncoplastic breast reconstruction and discuss the oncological principles.

The decision making process

When considering a patient for an oncoplastic breast conserving procedure, the following points must be considered:

- ❖ volume of tissue to be excised;
- ❖ tumour location;
- ❖ breast size and glandular density;
- ❖ patient related risk factors, particularly smoking, obesity, diabetes, previous surgery;

❖ adjuvant therapies.

Excision volume is the single, most predictive factor for breast deformity (8). It is reported in the literature that there is a substantial risk of deformity once over 20% of the breast is excised (9).

Tumour location is another important consideration. Excision of tumours from the upper inner quadrant and lower pole of the breast are at particular risk of leaving a severe deformity. For example, excision of tumours from the lower pole carries the risk of a “bird’s beak” deformity (10).

Breast conservation is contraindicated when clear margins cannot be assured without performing a mastectomy, in patients with T4 tumours, or in the setting of extensive multicentric disease, extensive malignant microcalcification or inflammatory breast cancer (11).

Pre-operative and successive post-operative views should be taken for consenting patients undergoing oncoplastic breast conserving surgery with a standard set of views acquired in a studio setting. There should be a full and tiered consent process for this that must be followed with each patient (12).

Technique selection

Clough *et al.* (8) have described the use of a bi-level classification system in selecting the most appropriate technique of oncoplastic breast conservation surgery. If less than 20% of the breast volume is to be excised then they advocate the use of a level I procedure encompassing the following steps:

- ❖ skin incision;
- ❖ extensive skin undermining following the mastectomy plane to facilitate both tumour resection and glandular redistribution once the tumour has been removed;
- ❖ nipple areola complex (NAC) undermining;
- ❖ full thickness glandular excision;
- ❖ glandular defect closed with tissue reapproximation;
- ❖ if required, an area in the shape of a crescent bordering the areola is de-epithelised and the NAC repositioned.

Should more than 20% of the breast need to be excised, more complex procedures, requiring specific training in oncoplastic breast surgery should be employed. Patients should be counselled thoroughly in the pre-operative setting regarding resultant scars using oncoplastic techniques and the potential requirement for symmetrisation procedures.

These techniques can be broadly categorised into volume displacement and volume replacement techniques.

Volume displacement

Volume displacement involves the principle of mobilising local glandular or dermoglandular flaps and transposing them into the resection defect. This employs predominantly mammoplasty techniques. The result is a net loss of breast volume from which arises the potential requirement for contralateral symmetrisation procedures. Type I procedures, as described by Clough *et al.* (8) also employ the use of glandular remodelling as part of volume displacement, but with lesser volume excisions than type II procedures.

There are a range of mammoplasty techniques which can be utilised. The tumour location will influence both Selection of the most appropriate skin incision/excision pattern, and where appropriate pedicle utilised for nipple repositioning. A range of approaches have been advocated, and in general divide the breast into quadrants or “zones” for planning the surgical approach (8,13). Schematically rotating the nipple areola pedicle opposite the site of tumour excision allows the application of these techniques for a variety of tumour locations (8).

Skin excision pattern

Wise pattern type

These allow extensive excision of lower outer or lower inner quadrant tumours. In addition, modifications of the Wise pattern technique have been described (14). These techniques as described by Cutress *et al.*, facilitate excision of a tumour outside the standard Wise pattern markings. This is particularly useful for tumours within the upper outer quadrant or upper inner quadrants of the breast. Through modification of the skin incision, the skin overlying the tumour can also be removed en bloc.

Vertical scar/Lejour type

For inferior pole or retroareola tumours. This technique allows a similar location and volume of tissue to be excised as seen with the superior pedicle mammoplasty techniques, but avoids the scar running along the inframammary fold (15).

Nipple areolar complex pedicle

Inferior pedicle

For tumours located within the superior aspect of the breast (11-1 o’clock). Traditional Wise pattern incisions can be used with this mammoplasty technique. The blood supply to the nipple-areola complex is maintained through

its inferior and posterior glandular attachments as the tumour resection involves the upper pole. The inferior pedicle is deepithelised and advanced upwards and into the glandular defect left from the tumour resection. Resection of glandular tissue from the inner and outer lower breast quadrants is performed in sufficient volume to allow closure and optimisation of breast shape (8). The resultant scars are periareolar with an inverted T, as traditionally seen in breast reduction patients.

Superior pedicle

For tumours located within the inferior aspect of the breast (4–8 o'clock). This mammoplasty technique uses a similar pattern of incisions as the inferior pedicle technique and results in a similar set of scars. The nipple-areola complex can however be dissected away from the surrounding breast tissue and maintained on a superior dermoglandular pedicle.

Round block/Benelli technique

For upper pole tumours, in particular those located in the 12 o'clock position. This technique utilises a periareolar incision, and begins by making two concentric incisions around the areola. The intervening skin is then deepithelised. The outer edge of the deepithelisation is then incised and the skin envelope is undermined in the mastectomy plane. The nipple-areola complex maintains its blood supply through the posterior glandular base. Wide excision of the tumour is then performed onto the pectoralis fascia. The medial and lateral glandular flaps are then mobilised off the pectoralis muscle and approximated. The two periareolar skin incisions are then sutured together for closure.

Grisotti flaps

For central tumours, requiring excision of the nipple-areola complex (16). In addition to maintaining the desirable breast shape, this technique also aids the reconstruction of a nipple-areola complex through preservation of a skin island on an advancement flap (17).

Volume replacement

Using these techniques, autologous tissue is harvested and transferred from a remote site into the resection defect. This can be performed as either a pedicled or free flap. Traditionally this has involved the use of latissimus dorsi flaps (18). However newer techniques are evolving, for

example, lateral intercostal artery perforator flaps which are based on intercostal perforators arising from the costal groove (19). These confer an advantage over thoracodorsal artery perforator flaps (TDAP) and latissimus dorsi miniflaps by enabling preservation of the thoracodorsal pedicle should a mastectomy and latissimus dorsi flap breast reconstruction be required in the future.

Complications of oncoplastic breast conserving surgery

Glandular necrosis is a pertinent issue affecting volume displacement techniques, and are more likely to occur with type I procedures than with excision alone due to the greater glandular mobilisation. This is a particular problem when the breast is predominantly made up of fatty rather than glandular tissue and there is extensive mobilisation of the tissue with wide areas of skin undermining and dissection of the gland from pectoralis major (8). Areas of fat necrosis may ultimately become infected, leading to post-operative healing problems and potentially delays in adjuvant therapies.

In order to reduce the risk of glandular necrosis, as mentioned previously an assessment of glandular density as part of the pre-operative surgical planning is particularly important. Patients can then be offered appropriate procedures on an individual by individual basis.

Where volume displacement is performed using breast reduction or type II techniques, all complications associated with the reduction technique used may additionally occur. Finally complications specific to volume replacement techniques include donor site morbidity and the risk of flap loss.

Oncological safety

It remains a standard of care to use adjuvant radiotherapy in all patients undergoing breast conserving surgery regardless of technique. There is an established body of evidence within the literature from randomised controlled trials that reports significantly lower rates of local recurrence and better oncological outcomes if breast conserving surgery is used in combination with adjuvant radiotherapy compared to surgery alone (20).

To date, the published literature supports the use of oncoplastic breast conserving surgery, in comparison to historical standard techniques. Clough *et al.*, have reported a prospective analysis of a 100-patient series undergoing the

more complex type of oncoplastic breast surgery, with 5-year overall and disease-free survival rates of 95.7% and 82.8% respectively (21). Rietjens *et al.*, have reported an overall local recurrence rate of 3% in their series involving similar surgical techniques (22). A systematic review of studies of oncoplastic breast conserving surgery demonstrated higher rates of complications, but these did not impact on delays in adjuvant therapies or oncological outcomes (23).

Indeed, there is increasing evidence that reduction mammoplasty techniques, within the setting of oncoplastic breast conserving surgery, can result in excision of the tumour with wider surgical margins and more effective radiotherapy planning (21,24,25). It has been reported that patients with large, pendulous breasts treated with standard breast conserving surgery receive a much higher radiotherapy dose and hence demonstrates the advantage to a reduction in breast size achieved with reduction mammoplasty techniques (26).

Conclusions

Oncoplastic breast conservation surgery is a significant advancement in the surgical management of breast cancer. It facilitates the removal of large volumes of breast tissue with significantly improved cosmetic outcomes and patient satisfaction whilst maintaining good oncological principles, potentially reducing re-excision rates (27) and mastectomy rates and assisting in adjuvant radiotherapy planning. Within the UK there are now clear good practice guidelines for the provision of an oncoplastic breast surgery service (12).

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Footnote

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Oncoplastic options in breast conservative surgery

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Abstract: Conservative surgery has become the primary alternative in the treatment of breast cancer, and cosmetic outcome fundamental goal, as well as oncologic control. Different options to achieve these goals are presented. Oncoplastic treatment of breast cancer needs planning and knowledge of well-established plastic surgery techniques.

Keywords: Conservative surgery; oncoplastic

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Conservative surgery has become the elective alternative in the treatment of breast cancer. However, to achieve tumor-free margins and to reduce the risk of local recurrence, in case of large lesions, small breasts, or more than 30% of breast volume resection, the procedure can often compromise the aesthetic result. To overpass this situations, different surgical procedures, called oncoplastic techniques have been described to optimize the efficacy of conservative surgery, both in terms of local control and cosmetic results. Indications, advantages, and limitations of different oncoplastic approaches, and their results are discussed.

Surgical treatment of breast cancer has been modified during the past decades. The long-term results of several studies conducted worldwide have definitely confirmed that conservative surgery (CS) and radical mastectomy have similar survival rates, endorsing the CS as the gold standard of therapy for most women with breast cancer (1,2).

The long-term success of the CS can be measured by two variables:

- (I) Local control rate;
- (II) Cosmetic outcome of the conserved breast.

Sometimes, in CS it can be difficult for the surgeon to adequately meet these two points, especially when trying to resect large lesions or in small breasts.

The extent of parenchymal removal and the skin resection is directly correlated with the cosmetic result: the higher volumes of tissue are removed, the risk of a poor outcome cosmetic increases. Olivotto *et al.* (3) and Mills *et al.* (4)

have reported that the cleavage of a volume greater than 70 cm³ parenchyma in medium sized breasts often leads to unsatisfactory aesthetic results. The Rochefordiere *et al.* (5) and Taylor *et al.* (6) have documented a lower cosmetic outcome in patients who had a volume of removed tissue greater than 86 and 100 cm³ respectively.

Cochrane *et al.* (7) demonstrated that the cosmetic result is impaired when the weight of the piece: breast volume ratio is greater than 10%.

This unfavorable correlation explains why some surgeons have favored more limited resections, describing techniques such as lumpectomy (primary tumor excision with margins of healthy breast tissue less than 1 cm), as opposed to classical proposed quadrantectomy Veronesi *et al.* (8) (“a large quadrant resection of primary carcinoma house with at least 2 cm of healthy tissue surrounding the tumor and including removal block a large portion of the overlying skin en bloc to the pectoralis major muscle fascia”).

The magnitude of parenchymal excision is also directly correlated with the rate of local control of cancer. Therefore, with use of more limited resections, results in an increased risk of local relapse. Many studies have confirmed this hypothesis. In Phase II Trial Milano 1,705 patients with tumors up to 2.5 cm in diameter were randomly selected to receive (I) lumpectomy (excision near the tumor) or (II) quadrantectomy (excision of tumors with macroscopically apparent margins 2 cm) including the skin and pectoral fascia.

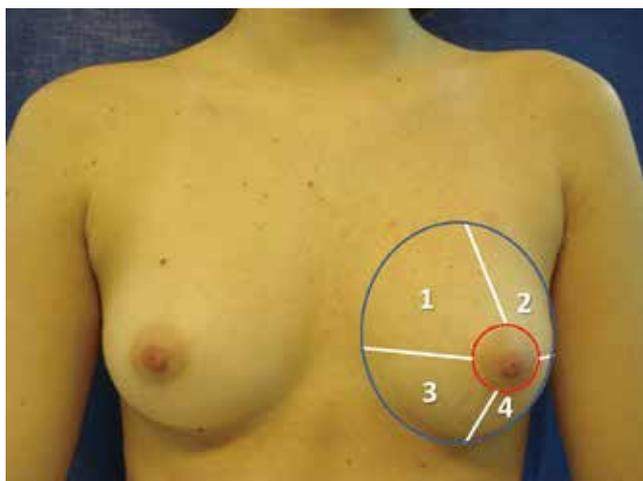


Figure 1 Breast quadrants.

Although the overall survival rate was not different in the two groups, the local recurrence rate at 5 years was much higher in the lumpectomy group (7.0% vs.2.2%).

Holland *et al.* demonstrated that the risk of leaving the engaged margins operated breast was inversely related to the degree of local control of the disease. Resecting the tumor healthy tissue around 1 cm range, the likelihood of residual cancer foci was about 59% whereas with 3 cm removed, decreases to 17% (9).

Technological advances in diagnosis, mammography and MRI, as well as greater use of punctures preoperative neoadjuvant systemic treatments have expanded the indications, arriving today in Argentina usage rates of this procedure to 70-80% of patients with breast cancer. However, in USA is below 50% (10) and 58% in Italy (11). Among the factors that may explain this under CC are the concerns of the patient and the surgeon for control of the disease in terms of local recurrence or poor outcome.

In an attempt to optimize the balance between the risk of local recurrence and cosmetic results in DC, new surgical procedures that combine the principles of surgical oncology and plastic surgery have been introduced in recent years (12-15). These new techniques, called “oncoplastic” may allow resection of a greater amount of breast tissue and safer margins without compromising the aesthetic result.

Oncoplastic procedures are technically more demanding, requiring training and planning, and sometimes more time consuming.

These procedures are usually done in one surgical time, and the patient leaves the operating room with minimum asymmetry or deformity.

When designing an oncoplastic procedure, steps must be met: careful planning of skin incisions, parenchymal resections in block up to the pectoral fascia, metal clip placement in the resection margins, proper gland remodeling after parenchymal resection, repositioning of the nipple-areola complex (CAP) in the center of the breast, and the correction of the contralateral breast for better symmetry.

Depending on the location of the lesion in the breast (*Figure 1*), different oncoplastic techniques can be used (16,17).

Quadrantectomy with round block or Benelli technique

This oncoplastic procedure has its best application in periareolar lesions treatment in the upper quadrants, specially, in breasts, with moderate ptosis or hypertrophy. It is based on the mammary modelling technique described by Louis Benelli.

In this technique, two concentric rings of different diameters are marked and designed around the nipple areolar complex. It allows resect, repair, model and lift the NAC. The skin between the two circles is excised (*Figure 2A,B,C,D*). This incision allows convenient access to the region through a periareolar incision, which is wider compared with traditional conservative techniques.

Ideal for:

- ❖ Ptotic breasts, large or medium size;
- ❖ Raising the NAC;
- ❖ Reducing the areola;
- ❖ Breast modeling;
- ❖ You can flatten the breast (advantage or disadvantage);
- ❖ Superior Quadrants tumors resection around areola.

The remodeling of the breast is performed with the residual gland, dissecting above the pectoralis major muscle with the use of electrocautery. Care must be taken in dissecting major vascular pedicles perforators' vessels between pectoral muscle and the preserved breast, to minimize the risk of NAC ischemia, residual glandular tissue necrosis and to minimize the risk of hematoma. The larger circle diameter is reduced by a circular suture around the new areolar margin.

Axillary dissection is usually performed through a separate incision, but on rare occasions may be performed through the same periareolar incision. If the two are concentric circles, the NAC is not elevated. If the outer circle is centered around a point above the existing

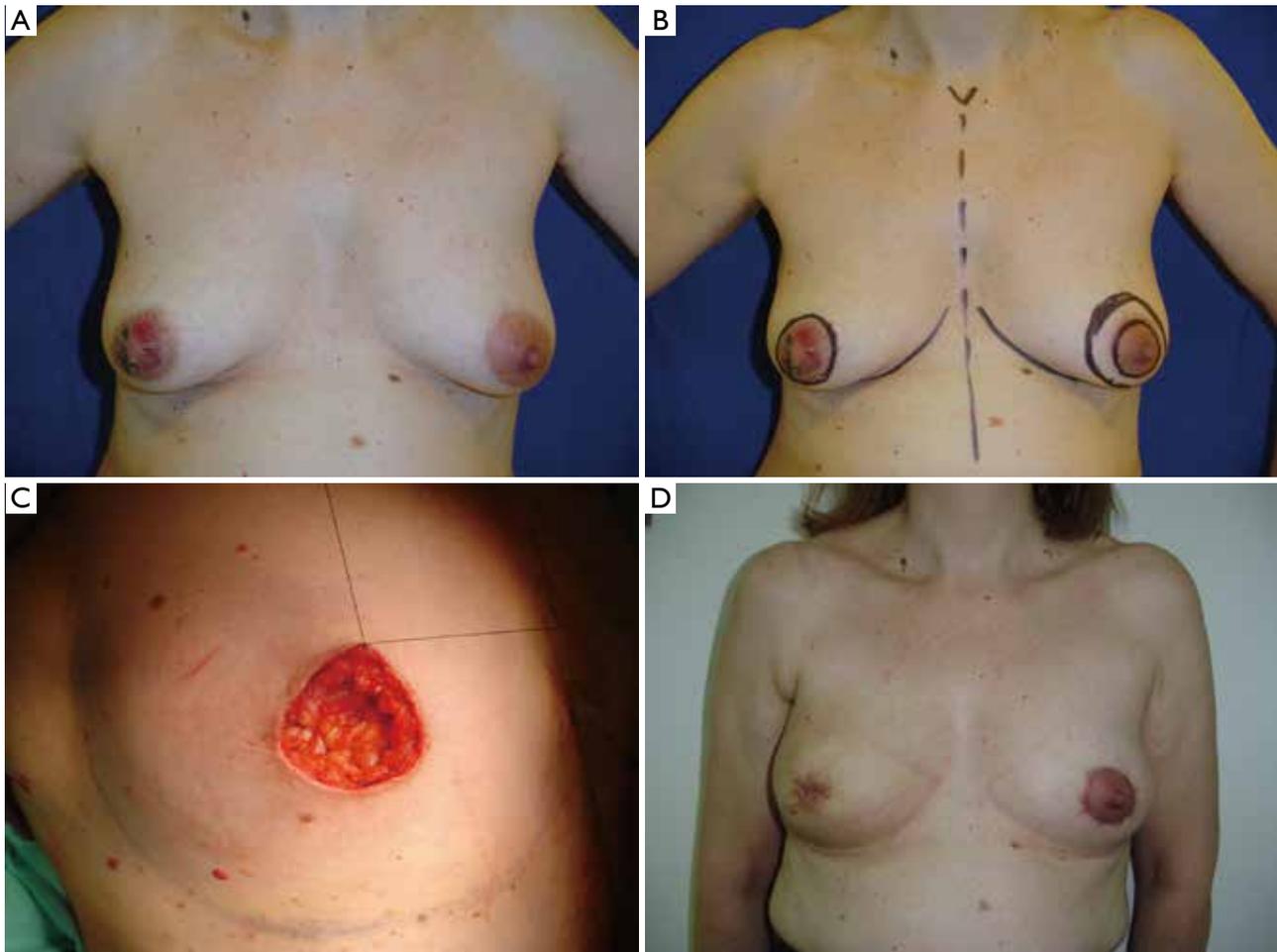


Figure 2 Block round quadrantectomy. A. Marking concentric; B. Periareolar tumor resection; C. Immediate closure; D. Post op result.

NAC, this may be rise, and a little pseudoptosis can be simultaneously corrected. Regarding the diameter of the inner and outer part of the oval design, the later must not exceed that of the existing areola diameter of 20-25 mm more toward lateral or medial, making an oval, to prevent distention of the circumareolar scar or excessive flattening of the breast.

Central quadrantectomy with a skin-glandular flap or Grisotti technique

This technique is used in oncoplástic designs for subareolar lesions and Paget's disease. These tumors often tend to be excluded from conservative surgery techniques due to oncologic concerns about multicentricity or multifocality association, and were treated with mastectomy due to bad cosmetic result, associated with NAC amputation.

This simple technique allows conservative treatment for retroareolar tumors or in Paget disease, with oncologic safety and excellent aesthetic results (*Figure 3A,B,C*). Resection is performed including a NAC cylinder and the parenchyma up to the pectoral fascia. The creation of a new NAC is achieved by a dermo-glandular flap, mobilized from residual gland in the lower breast pole. The flap is deepithelized, except a circular area of skin near the defect which will replace the NAC resected area by rotation.

The flap is incised medially, up to the pectoral fascia. It is very important to accurately separate the fascia flap to allow better rotation and advancement. The flap is mobilized and sutured to the gland superiorly in order to provide adequate projection and prevent dead spaces. If desired by the patient, the nipple can be reconstructed at a later stage. Consideration should be given to flap vascularization, in order to minimize the risk of ischemic injury.



Figure 3 Paget disease case A. Preop. Image B. Planning; C. Result.



Figure 4 Lower region tumor, V resection, vertical closure. For lesions located in the upper quadrants, the keyhole design includes the tumor, and the new NAC position covers the resection site.

Therapeutic reductions

This oncoplastic techniques can be used for tumors located in the upper or lower quadrants in the periareolar region, and are particularly indicated in patients with macromastia. This therapeutic reductions can be based on V design (Figure 4A,B,C) or over a wise keyhole inverted T pattern. The areola can be moved as necessary to change the position of the NAC, and the lesion is included within the resection area (Figure 5A,B,C,D,E).

For tumors located in inferomedial or inferolateral quadrants, the keyhole pattern may rotate slightly and allows lateral or medial excision. NAC is mobilized in the opposite direction of the surgical defect, leaving an inverted T scar.

Using techniques of reduction mammoplasty, tumors can be resected easily with large safety margins, even in small breasts, avoiding major cosmetic defects. These techniques can also facilitate the completion of radiation therapy in the postoperative period, particularly in women with macromastia (Figure 6A,B,C,D,E).

Reducing the size of the breast by mastoplasty techniques, significantly reduces the risk of retraction,

without affecting adjuvant therapies or clinical and radiological follow-up (18,19).

The resection should be full thickness and glandular tissue must be advanced to close the defect (20).

While performing symmetrization procedures in the contralateral breast, the surgeon should take the opportunity to remove any suspicious tissue that may have been revealed by a preoperative mammogram. Oncoplastic surgery techniques can expand the indications for CS, but since oncoplastic techniques have been introduced recently, little data are available to measure results (21).

In a prospective study to evaluate cosmetic and oncologic results after performing oncoplastic techniques, Clough *et al.* (22) collected data from 101 patients with breast cancer with a median size of 32 mm. The most common surgical procedure was breast reduction with keyhole pattern (83% of cases). The average weight of the resected specimen after oncoplastic procedures was significantly higher (220 g) compared with the average weight of a lumpectomy specimen in the same institution (40 g). After a follow-up of 3.8 years, the rate of complications after oncoplastic surgery (fat necrosis, fibrosis and hypertrophic scarring) was 10% and the cosmetic

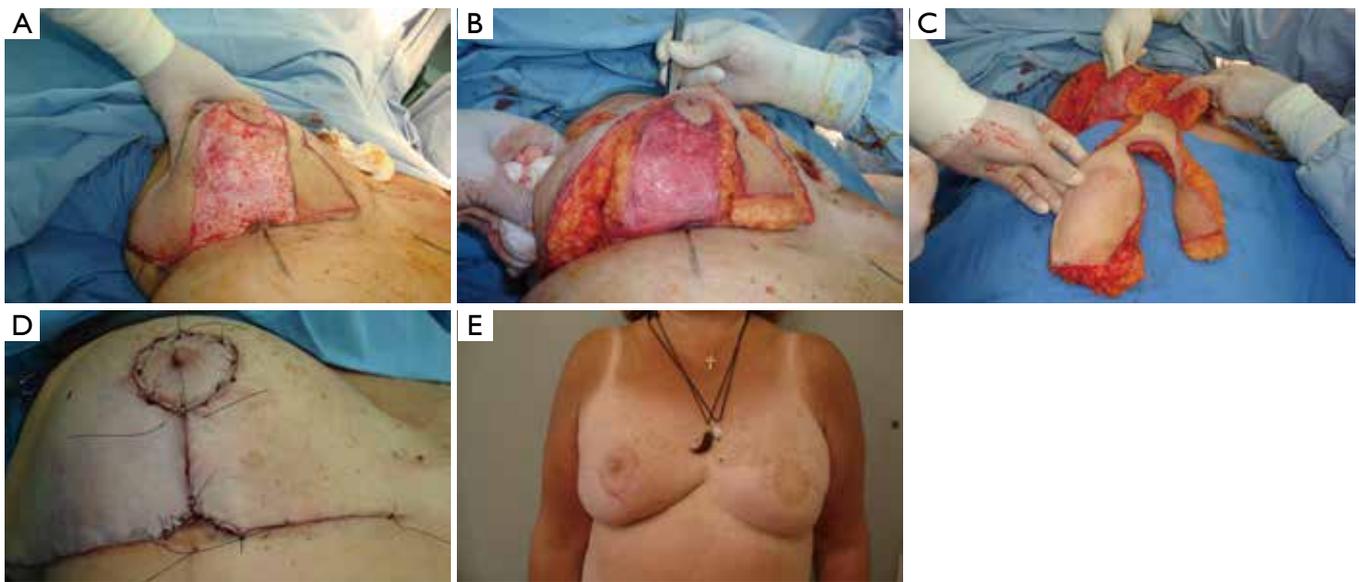


Figure 5 Left supra areolar lesion, marking with the lesion included in the pattern, inverted T closure.

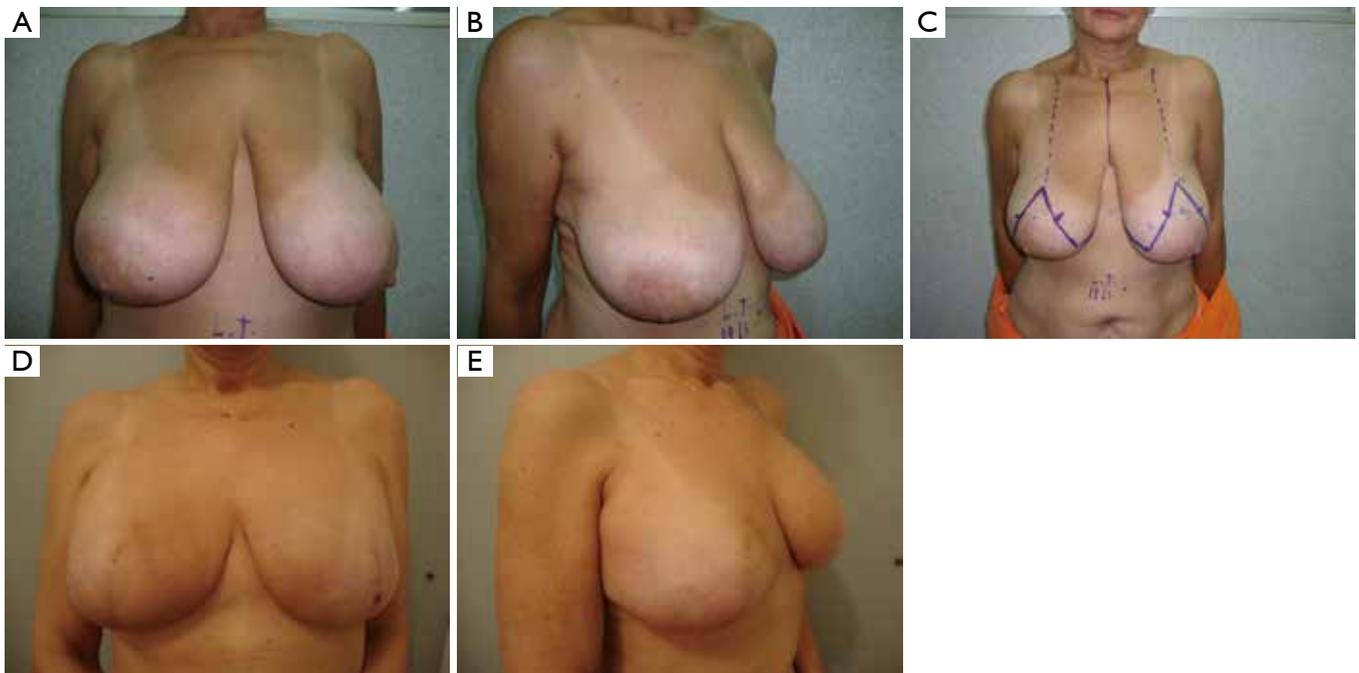


Figure 6 By allowing the wide removal of the skin overlying the lesion, this procedure may improve local control in tumors located superficially. Patients with hypertrophic and pendulous breasts are particularly eligible for this procedure, which can also be applied to the contralateral breast to achieve symmetry.

result was acceptable (excellent, good or fair) in 88% of cases. The local recurrence rate at 5 years was 9.4% and the overall survival rate was 82.8%, which compares favorably with most CS studies (22).

In a recent study, we prospectively studied 30 consecutive patients with breast cancer undergoing oncoplastic procedures (group 1) and 30 patients undergoing traditional lumpectomy (group 2).

Oncologic evaluated stage, surgical procedures, the volume of breast tissue removed, and histopathology of the tumors, with specific details on the surgical margins. Patients in group 1 were younger than patients who had a classic lumpectomy.

Oncoplastic approach allowed large resections, with an average volume of 200 cm³ sample, compared with 117 cm³ in the quadrantectomy group. Surgical margins were negative in 25 of the 30 cases (83%) in group 1, and 17 of 30 cases (56%) in group 2, the average length of the surgical wound was 8.5 mm in group 1 and 6.5 mm in group 2, although the difference was not statistically significant (23).

As Masetti *et al.* observed several studies and world experience suggest that oncoplastic techniques can optimize cancer treatment with oncological safety and good cosmetic results in CS.

Surgeons with interest in the surgical treatment of breast cancer, should seek appropriate training in oncoplastic surgery in order to offer these procedures to their patients (24).

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Footnote

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An example of lumpectomy for lower inner quadrant breast cancer with 1st level oncoplastic reconstruction by glandular splitting

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Abstract: Oncoplastic techniques extend the scope for breast conserving surgery by combining an extensive local excision with a simultaneous reconstruction of the defect to avoid local deformity. If less than 20% of the breast volume is excised a level I procedure is adequate and can be performed by breast surgeon without specific training in plastic surgery. For breast cancer is possible to fill the defect of the lower inner lumpectomy by splitting the upper inner quadrant. The Authors describe a novel technique in giant breast.

Keywords: Oncoplastic breast surgery; breast surgery; breast conserving surgery; oxidized regenerated cellulose polymer

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Introduction

Oncoplastic breast surgery allows a more radical local tumour excision which potentially reduces margin involvement and hence local recurrence. Usually breast reshaping decreases the risk of a localized defect although there are zones that are at high risk of deformity and cosmetic failure (1). With the application of oncoplastic techniques, the surgery has become complex in terms of preoperative drawings, intra-operative set-up in order to get an aesthetically pleasing result (2).

Operative techniques

The authors describe the case of a woman of 63 years old suffering from a metabolic syndrome with a BMI >30 and breast cancer of lower inner quadrant identified with mammography. The ultrasound and fine needle aspiration cytology have confirmed the malignancy. Preoperative skin planning is based on the principle that an acceptable breast shape should be conserved by filling the defect of the lower inner quadrant after lumpectomy using the remaining gland body (*Figure 1*). After oncologic resection the advancement flap is prepared by detaching the whole gland body from the pectoralis major muscle. The upper inner quadrant is

cut horizontally in the middle between the skin and pectoral muscle and medially detached to mobilize the flap as necessary. After medial detachment the flap is still supplied by internal thoracic artery and pectoral branch of thoracoacromial artery. The pectoral part of the upper inner quadrant is pulled down and placed into the tumor cavity and attached with 3 or 4 stitches to the inframammary fold (*Figure 2A,B*). To improve the shape, volume and symmetry of the breast is also described the use of oxidized regenerated cellulose polymer into the space between the gland and the pectoral muscle.

Discussion

The application of oncoplastic techniques in breast conserving surgery combine the oncologic local excision with simultaneous reconstruction to avoid local deformity. If less than 20% of the breast volume is excised a level I procedure is adequate and can be performed by breast surgeon without specific training in plastic surgery. For excisions which exceed 20-50% of breast volume will require a level II procedure that are based upon mammoplasty techniques and require specific training (3). The authors describe a novel application of the 1th level oncoplastic technique in a case of lower inner quadrant



Figure 1 Preoperative drawing in the upright position.

cancer in a woman with giant breasts. The lower inner quadrant reshaping is quick, safe and has a good cosmetic result in giant and ptotic breasts. This technique provides first the gland detachment from the pectoralis major muscle, then the upper inner quadrant gland is splitted parallel to the thoracic wall exactly in the middle. The inferior layer of the gland body can be placed into tumor bed as a flap that can be sutured to the inframammary fold with 3 or 4 absorbable stitches. The technique leads to a quick and acceptable filling of the defect and avoids nipple deviation even after a large lumpectomy like in this case (160 gr), so that the breast shape can be preserved and the original size is being only marginally reduced also after radiotherapy (Figure 3A,B). Usually the large resection may lead to hematoma and seroma formation which can result in unpredictable long-term cosmetic results. The excision

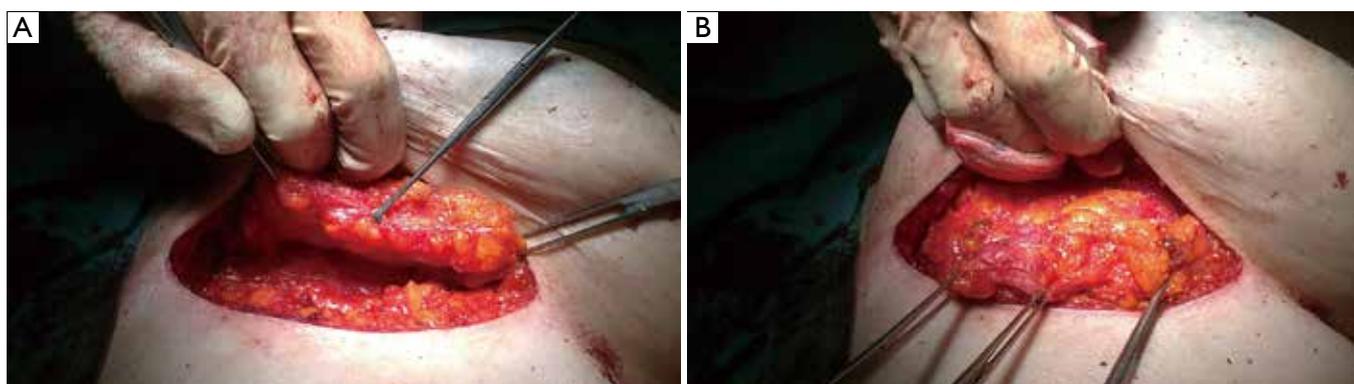


Figure 2 Mobilization of the pectoral part of the upper inner quadrant.



Figure 3 Cosmetic result 18 months later surgery and radiotherapy.

cavity becomes prominent due to fibrosis and retraction of the surrounding tissue creating a noticeable defect. In oncoplastic breast surgery the oxidized regenerated cellulose by preventing the hematoma, can promote dermal fibroblasts proliferation and cell migration playing a role in adjustment of the shape, volume and symmetry of the breast and reducing skin retraction (1,4). In oncoplastic literature a similar method is described only by Rageth (5), while Takeda uses an advancement flap obtained from the lateral tissue adjacent to the breast (6). Apart Rageth and Takeda we did not find any reports of similar techniques in the literature.

Conclusions

Oncoplastic surgery extend the indications of breast conserving surgery allowing oncologic resections and, with the application of some surgical plastic techniques, can achieve the best possible aesthetic result. The creation of an advancement flap with the upper inner quadrant can have a role in reconstruction of the lower inner quadrant defect.

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Footnote

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Oncoplastic breast surgery for centrally located breast cancer: a case series

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Abstract: Oncoplastic breast surgery (OBS), which combines the concepts of oncologic and plastic surgery, is becoming more common worldwide. We herein report the results of OBS in Japanese patients with centrally located breast cancer (CLBC) and Paget's disease. We performed OBS combining partial mastectomy and immediate volume replacement on patients with non-ptotic and/or small breasts, and volume reduction surgery for patients with ptotic breasts, as reported in Western countries. Japanese encounters are described in this report as a case series.

Keywords: Breast cancer; oncoplastic surgery; Paget's disease; skin-glandular flap; cosmesis; free dermal fat graft (FDFG)

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Introduction

Oncoplastic breast surgery (OBS), which combines the concepts of oncologic and plastic surgery, is becoming more common, especially in Western countries (1-6). At present, there are many different oncoplastic surgical techniques such as careful planning of skin and parenchymal excisions, reshaping of the gland following parenchymal excisions, and repositioning of the nipple areola complex (NAC) to the center of the breast mound with or without a correction in the contralateral breast to achieve better symmetry (7). The concept of OBS combining partial mastectomy with the breast reduction technique has become more popular; however, few studies have been conducted by Japanese institutions (8-11).

We previously reported that resection of partial deformities followed by immediate volume replacement using a local flap or distant autologous graft resulted in good outcomes for patients with non-ptotic breasts (12-19).

We herein report OBS performed on patients with centrally located breast cancer (CLBC) or Paget's disease

in our institution. Immediate breast reshaping using a latissimus dorsi mini flap (20), free dermal fat graft (FDFG) (15-17,19), and key hole-shaped skin glandular flap (21) were selected for patients with non-ptotic breasts, whereas OBS using the Grisotti flap (22,23) and amputation and free-NAC grafting (24) were selected for patients with CLBC in ptotic and/or large breasts, respectively.

Patients and diagnosis

Four Japanese patients were diagnosed with Paget's disease (cases 3, 4, 5, and 6), one with centrally located invasive ductal carcinoma (IDC) (case 7), and three with ductal carcinoma and ductal spread to the nipple (cases 1, 2, and 8) in our institution between February 2006 and April 2012. None of these patients received preoperative systemic chemotherapy or endocrine therapy. They were examined preoperatively and diagnosed with adequate disease for breast conserving surgery by mammography (MMG), ultrasonography (US), computed tomography (CT), and magnetic resonance image (MRI) systems and histological

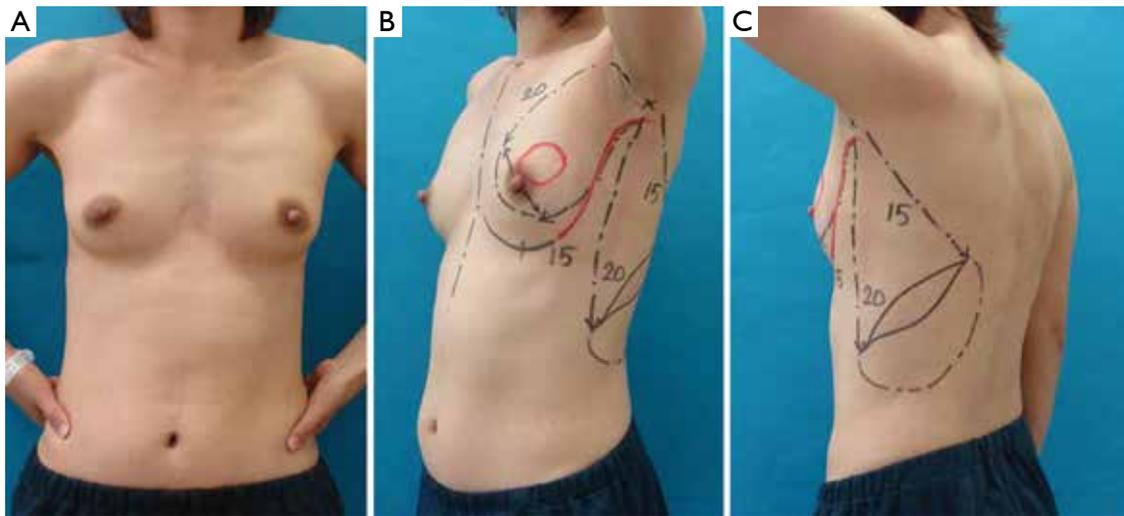


Figure 1 Case 1. A 37-year-old patient with non-ptotic breasts. (A) Preoperative findings of cancer in the left breast; (B,C) Red circle shows the cancerous area. Partial mastectomy with axillary lymphadenectomy and immediate volume replacement using a latissimus dorsi myocutaneous flap via an anterior axillary incision (red line) were planned.

findings. According to the spread of intramammary lesions and the distance between the lesions and the NAC, we preoperatively decided whether the NAC should be resected or not. Sentinel lymph node (SLN) biopsy using the radioisotope (RI) and dye method was performed to avoid axillary lymphadenectomy in six patients, while axillary lymphadenectomy was performed on two patients with IDC (cases 1 and 7) according to the indication for axillary preservation at that time. Neither local nor distant recurrence was observed in any patients within a median observation period of 46.6 months.

Case presentation

Latissimus dorsi mini flap (case 1) (20)

A 37-year-old patient with a slim body and non-ptotic breasts was diagnosed with a T1 cancerous tumor on the upper-outer quadrant area of the left breast. She wanted to undergo partial mastectomy and immediate volume replacement using autologous tissue, but not an implant. We planned, designed, and drew the resected area and latissimus dorsi myocutaneous flap (case 1, *Figure 1*). During surgery, several margins were examined histologically and revealed to be cancer-free; however, the edge toward the NAC was positive for ductal spread. The NAC was completely removed (*Figure 2A*) and the latissimus dorsi flap with ellipse-shaped skin was raised and passed from an anatomically

normal position toward the anterior deformity via an incision line on the anterior axillary line (*Figure 2A,B*). The latissimus dorsi flap was sutured to some edges of the remnant gland following trimming such as rolling and gathering until the treated breast shape was the same as that of the contralateral breast (*Figure 2C*). The deformity after removal of the NAC was restored by trimming the skin in a circle (*Figure 2D*). Five years after surgery, she was diagnosed with primary breast cancer in the contralateral right breast (*Figure 3A*). We performed partial mastectomy and immediate volume replacement using a FDFG from the lateral abdomen according to a previous report (18). The NAC for the left breast was reconstructed during surgery (*Figure 3B,C*). Free grafts from the bilateral groins and half of the nipple from the right breast, following an intraoperative histological examination to confirm that this tissue was cancer-free, were used to reconstruct the left NAC (*Figure 4*). The nipple graft bolster was removed on postoperative day 7. Excellent symmetry was obtained six months after radiation therapy to the right breast (*Figure 5*).

Free dermal fat graft (FDFG) (cases 2 and 3) (15-17)

A 57-year-old Japanese female had an operation scar on her lower abdomen in a cranio-caudal direction due to a gynecological disorder (case 2, *Figure 6A*). A histological examination of erosion on the right nipple revealed

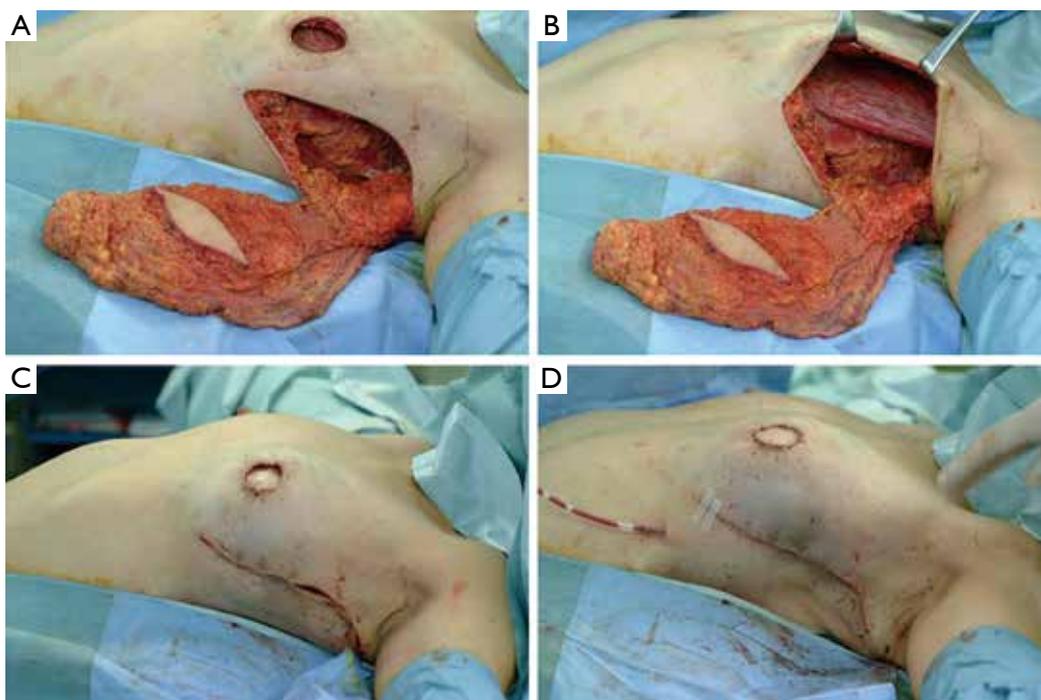


Figure 2 Operation procedure of case 1. (A) The nipple areola complex (NAC) was removed after a histological examination showed that it had a positive margin. The latissimus dorsi muscle was raised with an ellipse-shaped island of skin on the back; (B) At the end of partial mastectomy; (C,D) Partial defects in the breast and the center hole were repaired.

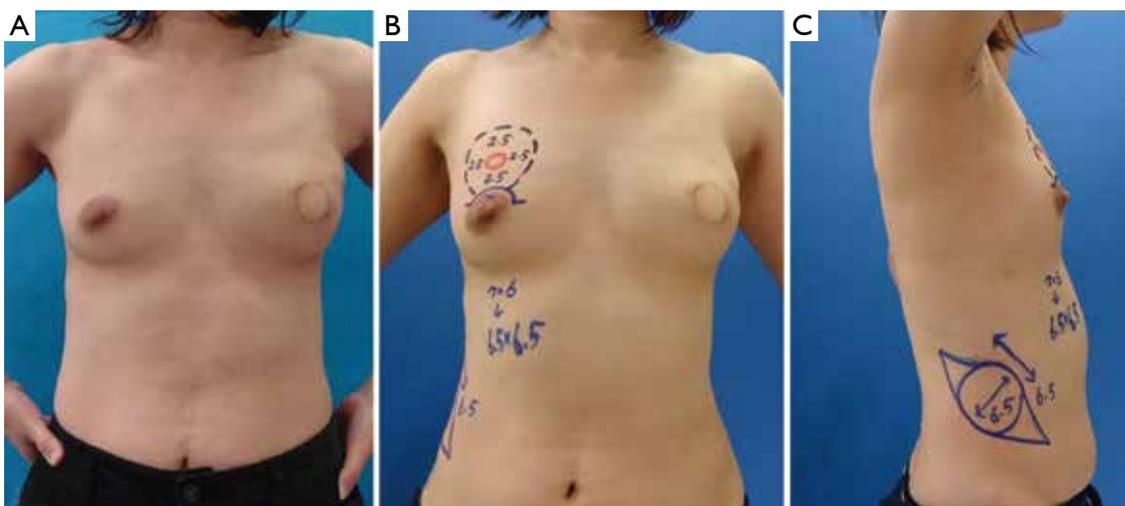


Figure 3 Five years after surgery in case 1. (A) Reconstructed left breast showed good shape and volume although NAC has not been reconstructed yet; (B,C) The design for partial mastectomy of the cancer lesion on the upper area of the right breast. Immediate volume replacement using a free dermal fat graft (FDFG) from the lateral abdomen (18) was planned.

that she has Paget’s disease in her right breast. Partial mastectomy with the whole nipple, but not the areola via a horizontal incision and SLN biopsy via another incision

were performed. A cylinder-shaped piece of breast tissue was removed and the partial defect on the central area of the breast was repaired using a FDFG from the lower



Figure 4 Reconstruction of the left nipple areola complex (NAC) in case 1. (A) De-epithelialization was performed on the left breast. Half of the right nipple was sutured into the center of the circle; (B,C) Skin grafts from the bilateral groins were peripherally sutured; (D,E) Tie-over was added at the end of the operation.

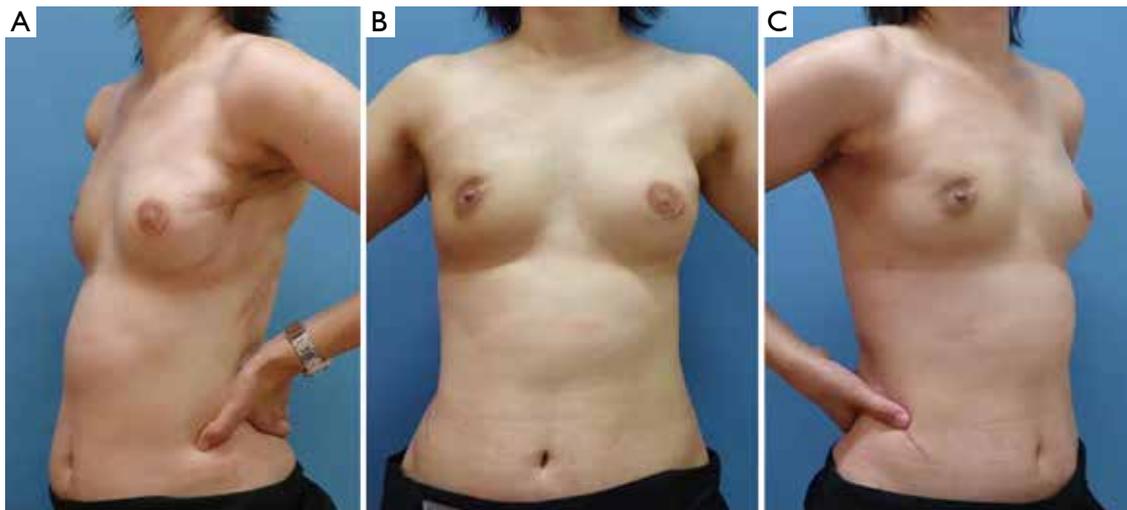


Figure 5 The findings of case 1 seven months after surgery for cancer in the right breast. Good symmetry was obtained, although a different OBS technique was selected for metachronous, bilateral breast cancer.

abdomen (15,16) (*Figure 6B*). Although she did not want to reconstruct the right nipple, the cosmetic results achieved were excellent four years after surgery (*Figure 6C*).

A 58-year-old patient was diagnosed with Paget's disease with an intraductal component restricted to just under the central area of the right breast (case 3). A 3-mm erosive lesion was found in the center of the right nipple (*Figure 7*). Complete resection of the top and internal ductal component of the nipple, but not of the areola or lateral surface of the nipple was planned (*Figures 7B,8A-D*). Immediate volume replacement using a FDFG from the lower abdomen followed by repair of the left nipple were performed. Lateral colored skin following resection of

the ductal component was sutured, resulting in a smaller nipple than the original one (*Figure 8E,F*). The Paget's lesion and ductal spread via the nipple to the breast tissue were completely resected, and 60 g of breast tissue with the nipple was resected (*Figure 9*). After *in situ* de-epithelialization, sharp dissection, and trimming, 80 g of the FDFG was implanted into the defect with the dermis facing the surface of the pectoralis major muscle (15). The dermis of the FDFG was peripherally sutured to the edge of the fascia of the major pectoral muscle using 3-0 Vicryl sutures. Good symmetry was maintained seven years after surgery; however, the operated nipple was smaller than that of the contralateral healthy one (*Figure 7C*).

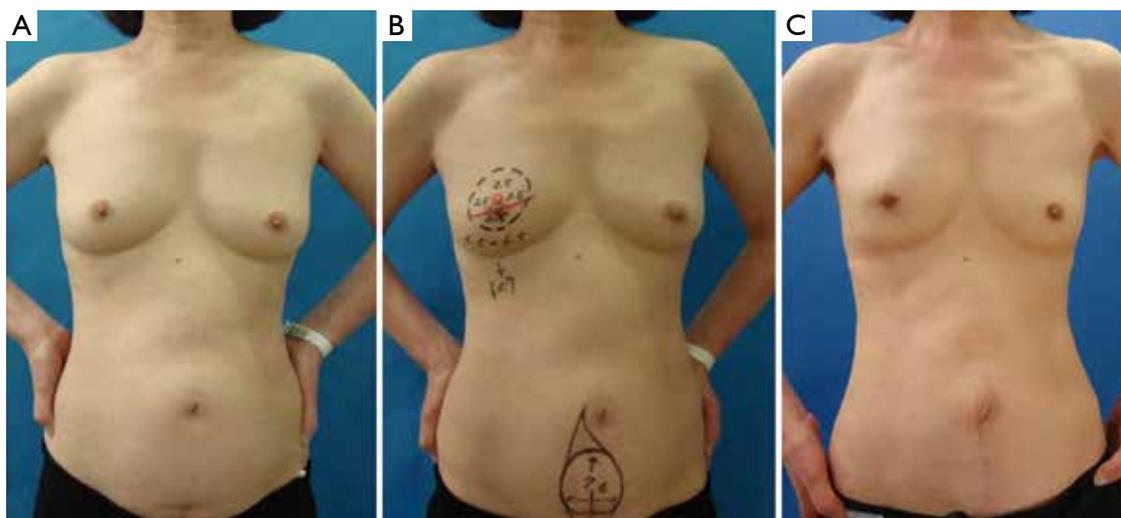


Figure 6 A 57-year-old patient with a slim body and non-ptotic breasts (case 2). (A) Preoperative findings; (B) An incision line was drawn in red across the nipple. A free dermal fat graft (FDFG) from the lower abdomen was implanted in the cylinder-shaped deformity in the central breast; (C) Four years after surgery.

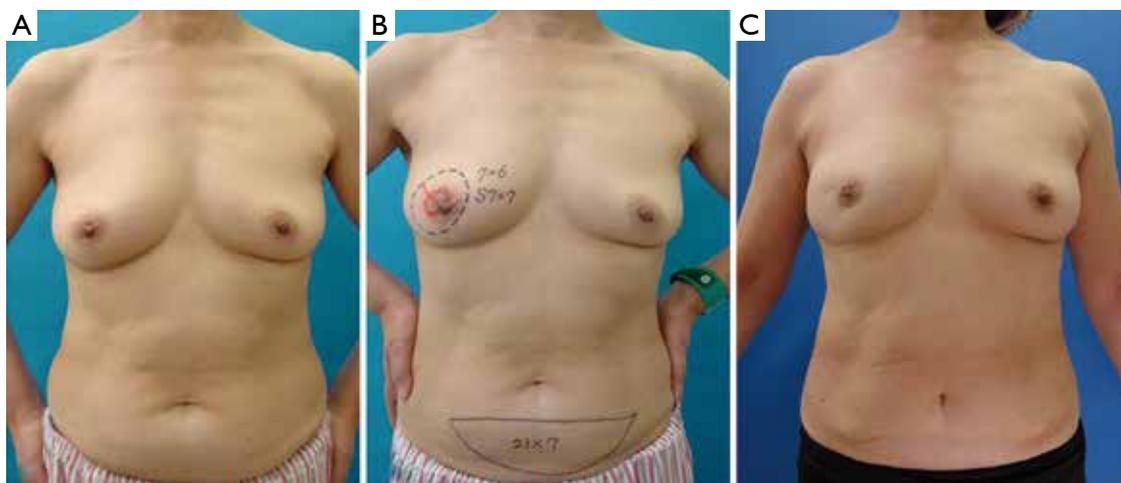


Figure 7 A 58-year-old patient with Paget's disease in the right breast (case 3). (A) Preoperative findings; (B) An incision line was drawn in red. The nipple, but not the areola was removed together with the breast tissue. A free dermal fat graft (FDFG) from the lower abdomen was harvested for implantation into the breast defect (15,16); (C) Seven years after surgery.

Key hole-shaped skin glandular flap for patients with non-ptotic breasts (cases 4 and 5) (18)

A 65-year-old Japanese patient with non-ptotic breasts was diagnosed with Paget's disease in her left breast. Preoperative US, CT, and MRI showed that intraductal spread to the breast tissue was restricted to just under the areola (case 4). Both breasts were placed into the operative field to allow the surgeon to observe the size, projection,

and level of the inframammary line of the healthy contralateral breast for the maintenance of symmetry. We removed a cylinder-shaped piece of gland with surface and bottom circles of 50 and 55 mm in diameter, and 15 mm of normal skin around the cancerous lesion on the NAC, which was 23 mm × 21 mm in diameter. The fascia of the major pectoral muscle was removed at the same time. Several surgical margins were histologically

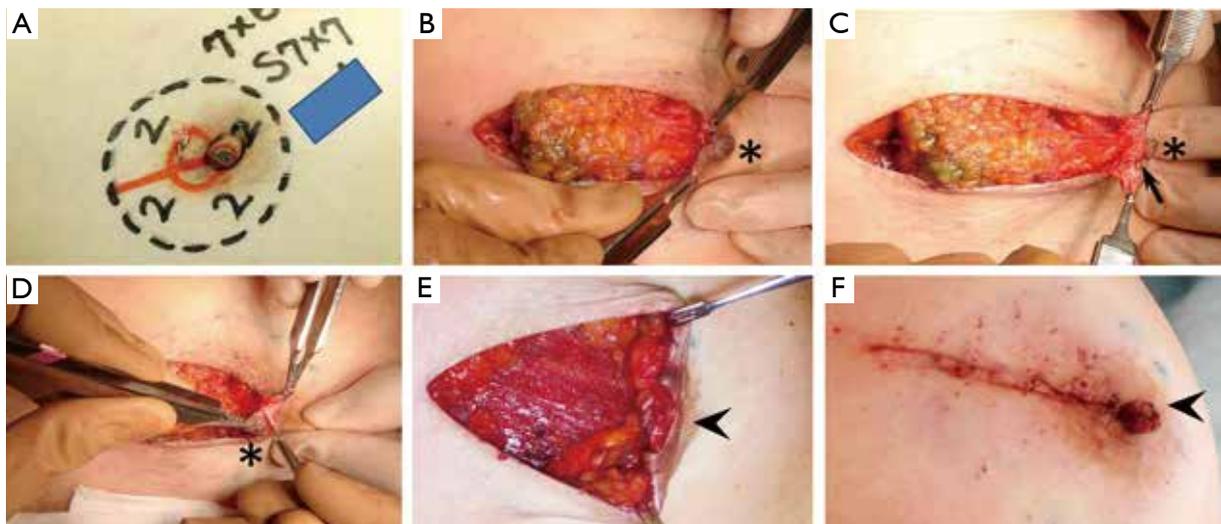


Figure 8 Case 3. (A) Paget's lesion was seen on the top of the right nipple; however, it did not invade the lateral surface of the nipple; (B) With a skin incision directed to 10 o'clock, the top on the nipple (*) was removed together with a cylinder-shaped piece of breast tissue from the central area; (C) The ductal component inside the nipple (arrow) was separated from the skin of the nipple; (D) The top of the nipple was removed; (E) After the removal of breast tissue with part of the nipple. Only the areola and lateral wall of the nipple were preserved (arrow head); (F) A free dermal fat graft (FDG) was implanted and the nipple was reshaped after suturing the remnant pigmented skin of the nipple.



Figure 9 Resected tissue in case 3. Ductal components (arrow) and the top surface of the nipple (*) were removed.

examined during the operation to ensure that the cancerous lesions were completely removed. A keyhole-shaped skin glandular flap was raised according to the marked lines (*Figure 10*). Perforators were reserved as much as possible. An inframammary line was drawn on the parenchymal tissue containing the perforator and fascia of the anterior serratus muscle to maintain symmetry with the contralateral healthy breast. We moved the flap to the cranial side. A new inframammary line was drawn on the surface of the skin located at the bottom of the keyhole. Suturing with 3-0 Vicryl fixed the two lines drawn on the parenchymal tissue and skin as an inframammary line, and a new inframammary fold reappeared.

The postoperative findings one year after surgery of case 5 without ptotic breasts were shown in *Figure 11*.

Grisotti flap (cases 6 and 7) (22,23)

An 82-year-old patient with ptotic breasts was diagnosed with Paget's disease in her left breast (case 6). A preoperative study using MMG, US, histological examinations (core needle biopsy or wedge biopsy of nipple erosion), bone scintigraphy, and MRI was performed. The cancerous lesion had both an erosive lesion on the NAC and intraductal components restricted to the retroareolar area (*Figure 12A*).

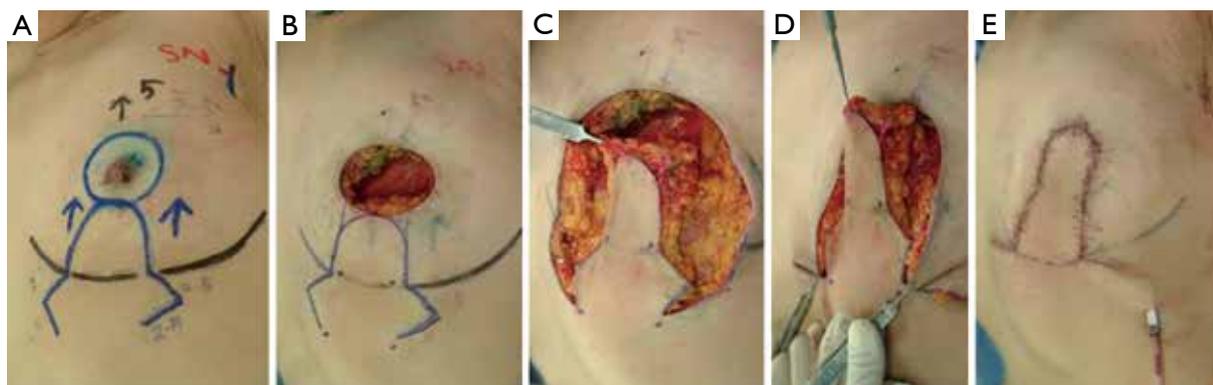


Figure 10 Case 4. A 65-year-old patient with Paget's disease in the left breast; areolar erosion was seen as a 23 mm × 21 mm circle. Preoperative findings (18). (A) One centimeter surgical margins from the erosive lesion were obtained (blue circle). Two zigzag lines were drawn from the edge of the inverted U on the upper abdominal area. One side of the zigzag was 25 mm in length so that the total zigzag length of 5 cm agreed with the craniocaudal length of the circular defect in the central breast area; (B) A cylinder-shaped piece of gland, with surface and bottom circles of 50 and 55 mm in diameter attached with normal skin, around the cancerous lesion was removed; (C-E) A keyhole-shaped flap was raised according to the marked lines.

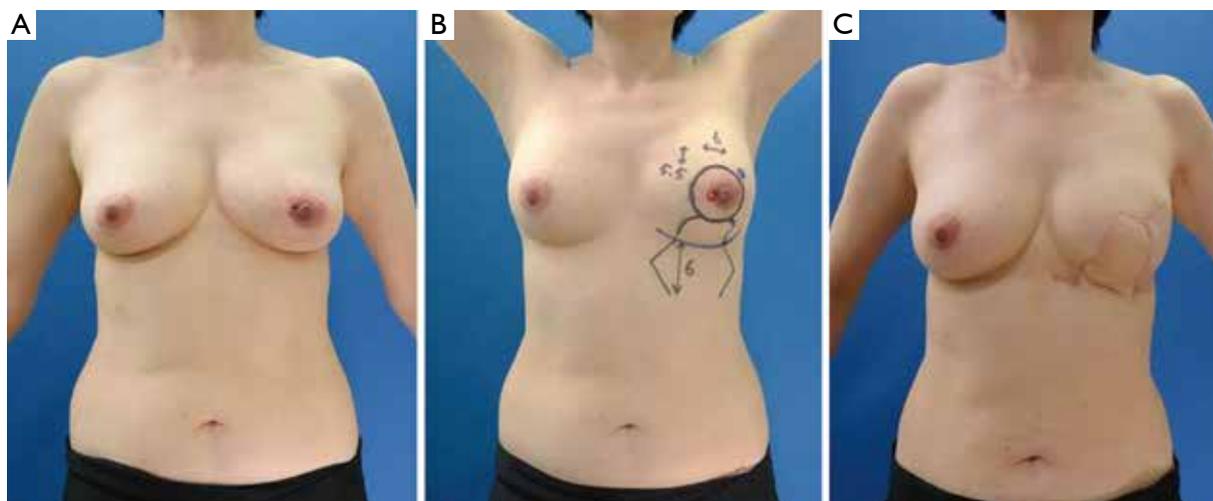


Figure 11 Case 5. A 52-year-old patient with Paget's disease in the left breast. (A,B) Preoperative findings. The nipple areola complex (NAC) with cylinder-shaped resection of the gland (black circle) followed by immediate breast reshaping using a key hole-shaped skin-glandular flap was planned; (C) One year after surgery.

With the patient in a standing position, we ensured that the nipple was located below the inframammary line and the softness and amount of skin was sufficient enough for the Grisotti flap. With the patient in a supine position, the edge of the tumor was determined by US and marks were placed on the skin surface. The partial mastectomy line was then marked in the form of a circular line using permanent ink 2 cm beyond the area of skin erosion. A curvilinear flap and neonipple line were marked on the breast with the patient

in a standing position (*Figure 12B,C*).

The cylinder-shaped piece of gland and NAC with surgical margins were removed (*Figure 13A,B*). During the operation, several surgical margins were histologically examined to ensure that the cancerous lesion was completely removed. A curvilinear flap was obtained inferior to the defect (*Figure 13C*). The flap was then de-epithelialized, except for a circular area of skin close to the defect, which was lifted intact in order to form the neonipple, with blood

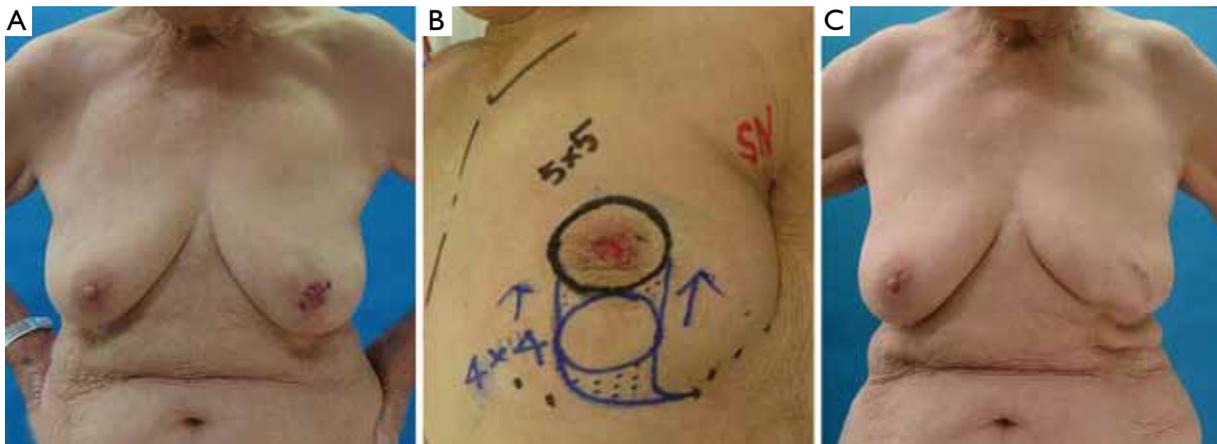


Figure 12 Case 6. An 82-year-old patient with Paget's disease in the left breast. (A) Preoperative findings. Her breasts were ptotic. An erosive nipple lesion with a clear margin was found; (B) A surgical margin of 15 mm from the edge of the erosion was drawn on the skin using black ink. The neo-nipple was drawn using blue ink; (C) Two-year postoperative findings.

being supplied from a lateral pedicle (*Figure 13D-F*). The flap was incised medially and along the inframammary fold down to the pectoralis fascia, before being undermined laterally from the fascia to allow rotation and advancement of the flap to fill the defect. The skin-glandular flap was then rotated into the central quadrantectomy defect, and its deep part was sutured to the deep aspect of the breast defect with two to three 3-0 Vicryl sutures to fill the empty space around the defect and ensure adequate projection to the tip of the breast mound (*Figure 13G-I*). The tumor was removed, with a favorable esthetic outcome (*Figure 12C*).

We performed partial mastectomy and immediate breast reshaping using the Grisotti method on an invasive lesion just under the right NAC and axillary lymphadenectomy in case 7. Five years after surgery, excellent symmetry was obtained even though the patient had no NAC (case 7, *Figure 14*).

Amputation and NAC grafting for ptotic breasts (case 8) (24)

A 65-year-old Japanese woman with a past history of abdominal surgery was referred to us for an investigation of grouped calcification on the MMG of her left breast. US and MRI revealed ductal carcinoma *in situ*, which was restricted to the lower quadrant of the left breast, but was positive for ductal spread toward the left nipple. Oncologically, partial mastectomy of the left breast together with the left nipple was possible; however, difficulties achieving a good symmetrical outcome were anticipated due to the degree of ptosis. We decided on OBS combining amputation and

NAC grafting (25,26). The incision line was drawn in black (*Figure 15*). We performed partial mastectomy with SLN biopsy. Excessive skin and parenchymal tissue, including the nipple, were removed with the fasciae of the pectoralis major muscle and serratus muscle. An intraoperative histological examination revealed that the three surgical margins were cancer-free and negative for metastasis in one SLN (*Figure 16A-C*). The healthy nipple of the right breast was taken and divided into two pieces for the new nipples (*Figure 16D*). The bilateral areolas were preserved prior to amputation of the breasts. After marking the NAC site, it was de-epithelialized, and a piece of the right nipple was sutured to the center of the de-epithelialized NAC site (*Figure 16E*). The free areola graft was then sutured to the site with interrupted and circumareolar sutures, before 4-0 Nylon bolster ties were sutured through the graft and the skin edge at eight circumferential points. A tie-over bolster of gauze and cotton was secured with 4-0 silk bolster ties (*Figure 16F,G*).

The nipple position, size, and degree of projection of the bilateral nipple were symmetrical four years after surgery (*Figure 17*).

Discussion

Patients with CLBC account for 5% to 20% of breast cancer cases and, for a long time, they have been denied breast conservation surgery (BCS) and instead been conventionally treated with mastectomy (27). The high incidence of NAC involvement associated with these tumors

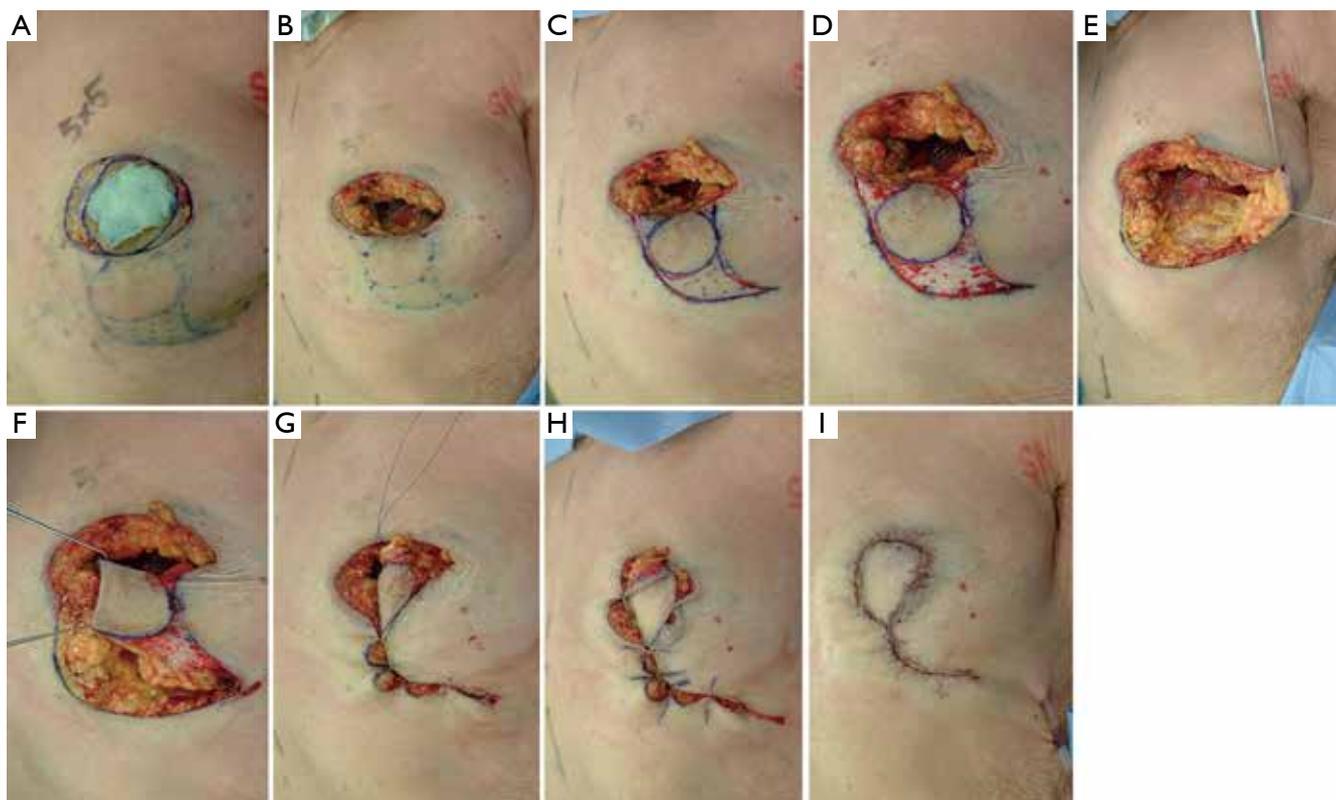


Figure 13 Case 6. (A,B) A cylinder-shaped piece of gland with the nipple areola complex (NAC) and normal skin was removed; (C) A curvilinear flap was obtained inferior to the defect. The flap was de-epithelialized, except for a circular area of skin, which was lifted intact in order to form the neo-nipple; (D-F) The flap was incised medially along the inframammary fold down to the pectoralis fascia, before being undermined laterally from the fascia to allow rotation and advancement of the flap to fill the defect. The skin-glandular flap was rotated into the central quadrantectomy defect; (G,H) A deep section was sutured into the deep aspect of the breast defect using two to three 3-0 Vicryl sutures to fill the empty space; (I) After closure.

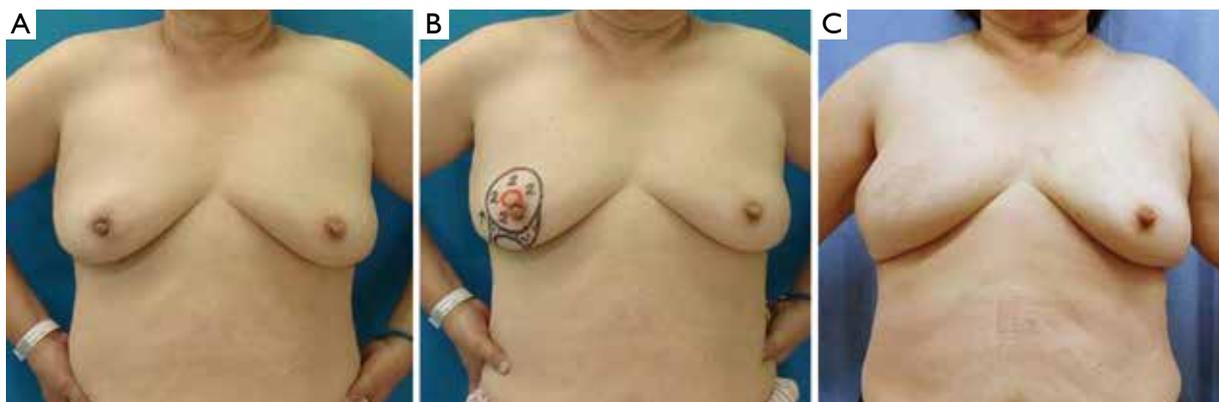


Figure 14 Case 7. A 60-year-old patient with cancer in the right breast. (A,B) Preoperative findings; (C) Five years after surgery using the Grisotti flap (22,23).



Figure 15 Case 8. A 65-year-old patient with ptotic breasts. (A,B) An invasive lesion (red circle) and non-invasive lesion (dotted red circle) toward the left nipple were observed on the left ptotic breast; (C) Over half of the breast with the nipple areola complex (NAC) was removed along the black line. X was planned as the position of the neo-NAC (24).

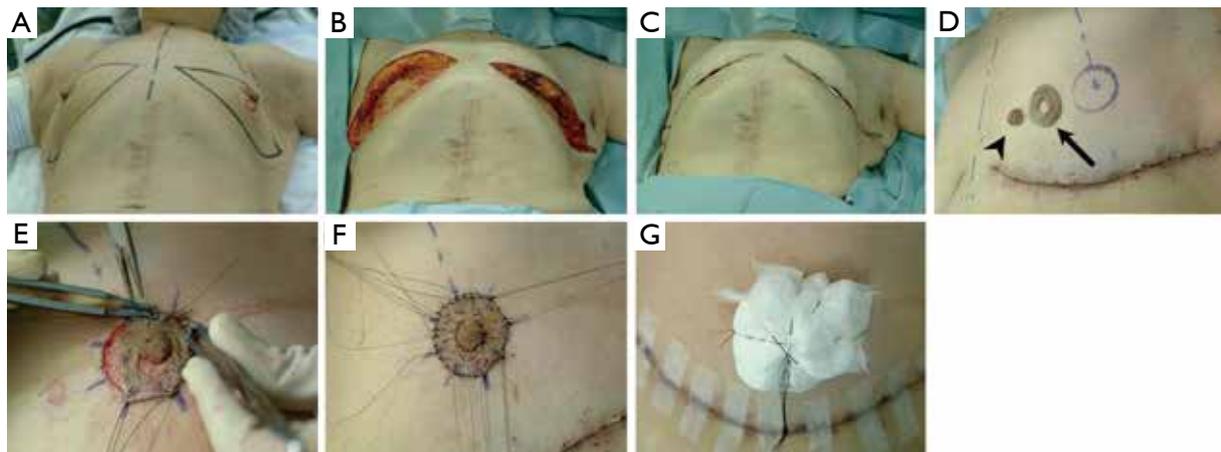


Figure 16 Case 8. Operative findings of oncoplastic breast surgery (OBS) using amputation (24). (A-C) Amputation was performed bilaterally; (D) The bilateral areola was preserved (arrow). The healthy right nipple was divided into two pieces for new bilateral nipples (arrow head); (E,F) The round skin was de-epithelialized for the neo-NAC; (G) A bolster made of gauze and soaked cotton was secured with 3-0 Nylon.

necessitates nipple and areola resection together with an adequate safety margin around the tumor, which has yielded acceptable cosmetic results and oncological control (28). Although Paget's disease of the nipple has been extensively studied, its optimal treatment remains the subject of controversy. In 1991, Dixon *et al.* (29) reported the results obtained from 48 cases of Paget's disease without a palpable lump that had undergone either simple mastectomy or cone excision of the NAC. They condemned conservation surgery in these cases because locoregional recurrence was found in 40% of cases after cone excision and in only 5.4% of cases after mastectomy. On the other hand, other reports

concluded that BCT could safely be proposed to patients with Paget's disease (14,29-32). Simple closure of the central defect, both vertically and horizontally, gave the breast a particular shape, which appeared as if the breast had been amputated at the tip (23). Central quadrantectomy including NAC resection through an elliptical incision was advocated by Pezzi *et al.* (33) and yielded satisfactory results without reconstruction. Clough *et al.* (34) advocated immediate breast repair after central tumor resection, and declared that cosmetic results were poor following simple lumpectomy and that secondary reconstruction in the breast was very difficult.

We performed OBS involving partial mastectomy with

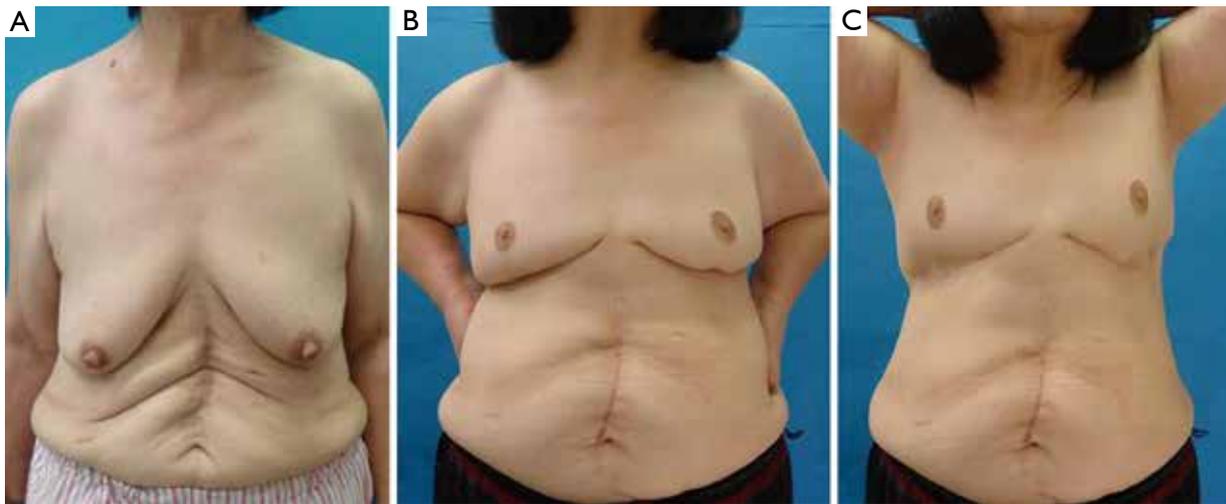


Figure 17 Case 8. (A) preoperative findings; (B,C) four years after surgery.

immediate breast reshaping using volume replacement or volume displacement for Paget's disease or CLBC in Japanese patients in this series. According to previous reports, we selected OBS based on the size and shape of the breast in the standing position; volume replacement for patients with non-ptotic breasts, volume displacement using a skin-glandular flap or amputation for patients with ptotic breasts. All procedures were successfully performed both cosmetically and oncologically.

The number of cases in this series was not large, and the follow-up period was short; however, we demonstrated that OBS for Paget's disease or CLBC produced good cosmetic results in Asian as well as in Western females.

Conclusions

Oncoplastic surgery combining partial mastectomy with immediate breast reshaping using a keyhole-shaped skin glandular flap was successfully performed in patients with Paget's disease. Partial mastectomy, but not total mastectomy or immediate breast reconstruction can be selected. This surgery is expected to become more popular for the treatment of patients without large and ptotic breasts.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Oncoplastic technique in breast conservative surgery for locally advanced breast cancer

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Abstract: Locally advanced breast cancer (LABC) should be taken into decision making when planning breast conservative surgery, but this procedure should be done on the principle of oncologic safety in order to achieve negative surgical margin and maintain aesthetic result. This procedure should be offered as the choice of treatment in selected patients.

Keywords: Breast conservative surgery; locally advanced breast cancer (LABC); neoadjuvant chemotherapy

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Introduction

Breast-conservation therapy (BCT) is a valuable component of breast cancer surgery in patients who need to preserve the breast and the data show that it has an equivalent survival benefit compared with the conventional mastectomy (1). The lumpectomy and oncoplastic resection are different conceptually. Lumpectomy usually requires a margin of a few millimeters whereas oncoplastic resection usually includes a margin of a few centimeters. Resection of large tumors and locally advanced breast cancer (LABC) can be challenging, in view of the breast conservation surgery (BCS). For making the BCS effective and oncologically safe, there is a need to completely remove all foci of the cancers with an adequate surgical margin width giving enough histological normal tissue and maintaining the cosmetic result of the breast and there are no deformity sequelae.

Inclusion criteria for BCT

The BCT is generally reserved for patients with T1 and T2

tumor. However, the ratio between size of the tumor and the breast is important because the surgeon will plan to remove the tumor with adequate margin and good cosmetic result.

In patients with LABC, giving of neoadjuvant chemotherapy can down stage the tumor for BCS but the surgeon must realize that there are three types of patterns of response after receiving chemotherapy. The first pattern is pathologic complete response in that the gross tumor has totally disappeared. The second pattern is concentric shrinkage in that the tumor has shrunk to a small volume and there is no residual nodule in the peripheral area. The third pattern is mosaic pattern (multifocal residual) in that the tumor has shrunk to small volume like the concentric pattern but it has still many small nodules in the edge of the tumor.

In this condition, BCS is not proper to perform due to high incidence of local recurrence although the tumors will respond well as shown in *Figure 1*. The total mastectomy is the good procedure for the third pattern of response. When the mastectomy has been done in the mosaic pattern, the margin of resection is crucial because the surgeon can archive the negative margin in two conditions. The first



Figure 1 Patient presented with LABC and plan to give neoadjuvant chemotherapy. (A) T4b lesion at right breast before giving neoadjuvant chemotherapy; (B) The tumor has shrunk to small volume after receiving six cycles of FAC regimen (the types of patterns of response can't be assessed whether concentric shrinkage or mosaic pattern. However, we can't see whether there are still many small nodules outside the edge of the tumor or not).

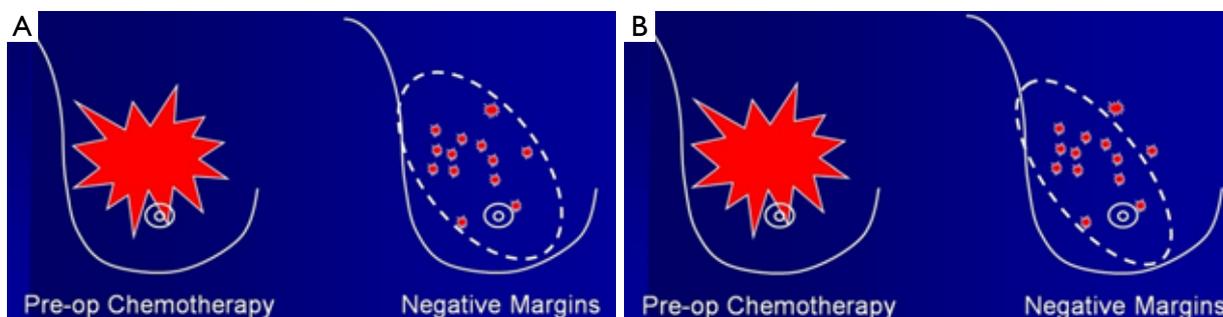


Figure 2 The third pattern of response is mosaic pattern (multifocal residual). (A) This is the real negative margin after removing tumor in mosaic pattern; (B) There are still many small nodules outside the edge of skin incision after finishing the operation but the surgeon can't identify these nodules and the pathological result shows negative margin.

condition is the exact negative margin and there is no residual tumor in the chest wall (*Figure 2A*). The second one is the presence of foci of tumors outside the skin incision (*Figure 2B*) but pathological report is also negative margin. The third response can be evaluated by physical examination, mammogram, breast ultrasound and magnetic resonance imaging (MRI). In the patient considering to receive neoadjuvant chemotherapy, photographs and measurement are useful in recording the extent of initial skin lesions such as the small nodules around the primary lesion or area of skin metastases (*Figure 3A*) because these nodules sometimes disappear after responding to chemotherapy (*Figure 3B*). Using a radio-opaque marker or tattooing the skin of the breast is another method for identifying the tumor location.

Mammography and ultrasound have been used to evaluate the tumor response after giving neoadjuvant chemotherapy but both techniques cannot differentiate the mass density due to fibrotic lesion of the dead tumor from the viable tumor. The false-positive rates of mammography and breast ultrasound may be 50% or higher (2).

MRI can improve the assessment of neoadjuvant chemotherapy response with sensitivity ranging from 70% to 100% and 50-100% specificity when the tumors respond to chemotherapy, MRI can show the loss of enhancement and MRI is related with pathologic response of residual disease 36-96%. However, MRI cannot detect the absence of residual tumors foci and underestimate the residual noninvasive lesion in the breast following neoadjuvant chemotherapy (3).

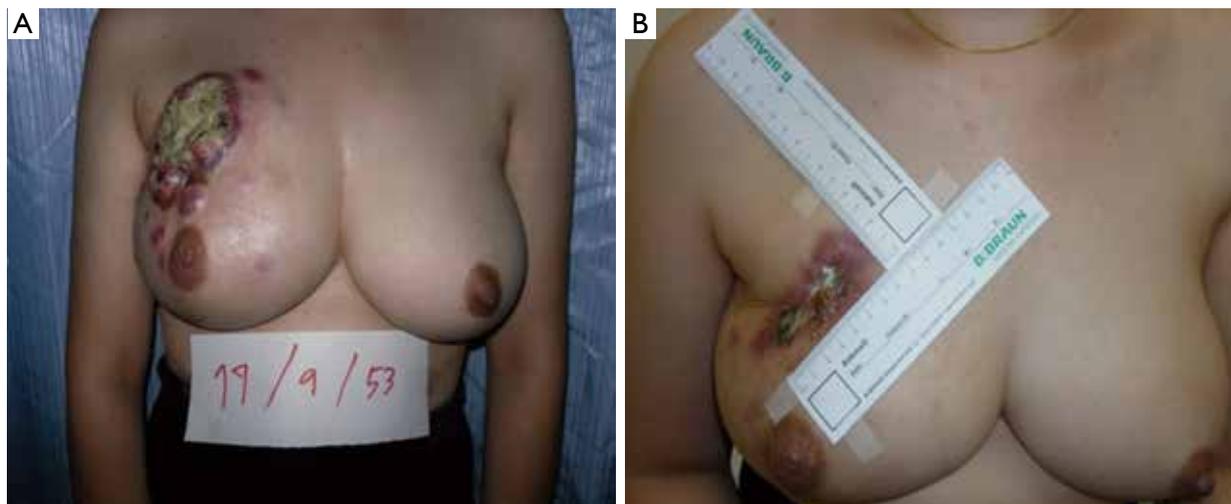


Figure 3 Photographs and measurement in planning neoadjuvant chemotherapy. (A) There are many skin nodules or shin metastases before giving neoadjuvant chemotherapy; (B) The tumor has shrunk to small volume after receiving six cycles of PACS-01 regimen and the previous skin nodules can't be seen if the photographs have not recorded these lesions.

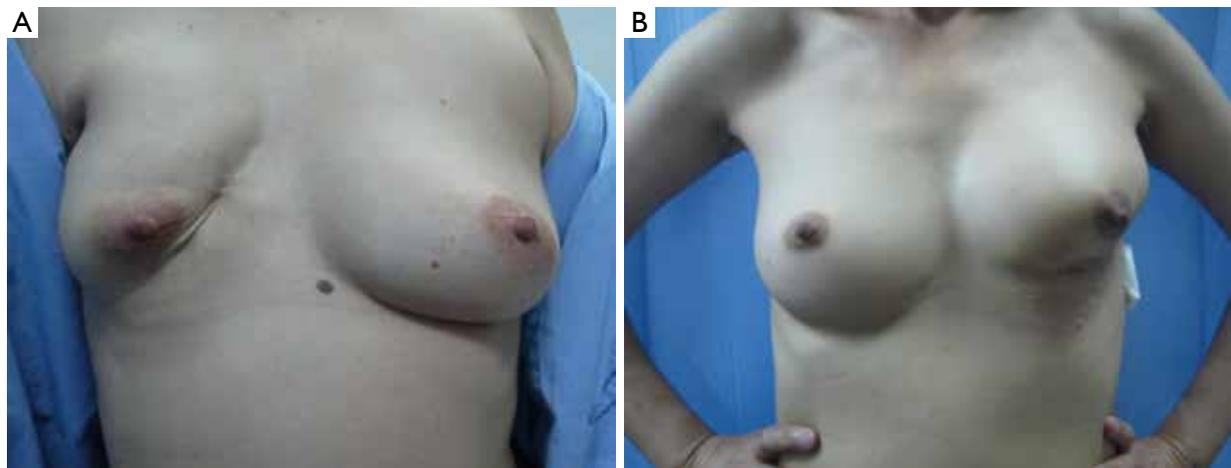


Figure 4 Cosmetic sequelae after breast conservative surgery. Type II, deformity of the breast after BCS, compatible with partial reconstruction and breast conservation.

The following are selective criteria for selecting candidates for breast-conserving surgery after neoadjuvant chemotherapy (4):

- ❖ Complete resolution of skin edema;
- ❖ Residual tumor size <5 cm;
- ❖ No evidence of multicentric lesion;
- ❖ Absence of extensive intramammary lymphatic invasion/extensive microcalcification.

Cosmetic sequelae after BCS can occur in patients with large tumors and there is a need to remove the large volume of breast tissue. There are three types of cosmetic sequelae after BCS. Type I is asymmetrical breasts with no deformity

of the treated breast. Type II is deformity of the treated breast, compatible with partial reconstruction and breast conservation. Type III is major deformity of the breast, requiring mastectomy (5).

If 20-50% of breast volume resection can be estimated after finishing the operation, cosmetic sequelae type II deformity can occur (*Figure 4*) (5). Reshaping the breast by using oncoplastic technique such as the latissimus dorsi flap is required to fill the defect after removing large volume of the breast from BCS (6). This oncoplastic technique can prevent and correct the deformity with a good cosmetic outcome (*Figure 5*).

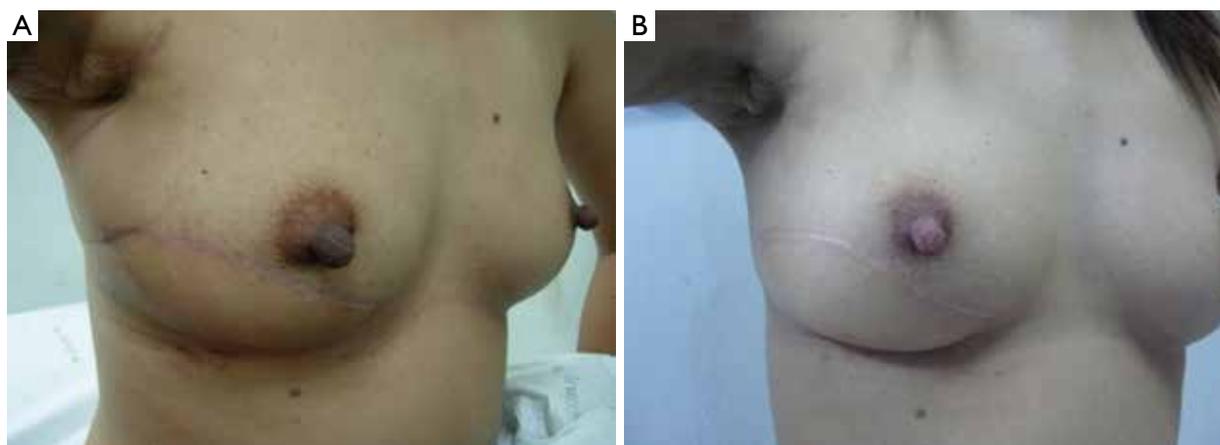


Figure 5 In the patient with 50% of breast volume resection in lower quadrant, reconstructing the breast by using oncoplastic technique such as the latissimus dorsi flap is needed to fill the defect after removing large volume of the breast from BCS.

Absolute contraindication of breast conserving therapy

Absolute contraindications for BCT are as follows (7):

- ❖ Diffuse suspicious or malignant appearing microcalcifications on mammography;
- ❖ Extensive disease that cannot be removed by local excision through a single incision that gets the negative margins with good cosmetic result;
- ❖ Positive pathologic margin;
- ❖ Patients who have received previous radiation to the breast or chest wall;
- ❖ Pregnant women who plan to give the radiation therapy during pregnancy.

The patients who develop breast cancer during pregnancy must avoid radiation therapy due to the internal scatter of the radiation from treatment reaching to the fetus.

Relative contraindication of breast conserving therapy

The following can be considered as relative contraindications of the BCT:

- ❖ Active connective tissue disease especially scleroderma and lupus;
- ❖ Tumor greater than 5 cm in diameter;
- ❖ Focally positive pathologic margins after BCS;
- ❖ Patients ≤ 35 yr. or patients with a known BRCA1/2 mutation gene.

Patients with systemic lupus erythematosus and scleroderma are significant risk for breast fibrosis with pain

and chest wall necrosis.

In patients with LABC in which the tumor to breast size ratio is unfavorable is crucial. After removing the tumor in the patients with large breasts, the breast parenchyma defect can be repaired with tissue rearrangement. Reduction mammoplasty techniques can be done at the opposite breast due to symmetry of both sides (*Figure 6*). This procedure can achieve the greatest benefit from radiation therapy due to reducing the size of the breasts and the patients have a greater degree of dose homogeneity with standard two-dimensional dose compensation techniques.

Margin status in BCS for LABC after neoadjuvant chemotherapy

The studies showed BCS for LABC after neoadjuvant chemotherapy is feasible and safe and associated with acceptable local recurrence rates (8-12). As with oncologically breast cancer procedure, the primary goal is to remove the tumor with negative margins. Surgical excision doesn't attempt to remove the whole previous neoadjuvant volume of lesion because the goal of wide excision is to remove any residual lesion with 1 cm of clear margins. If the lesion after responding to neoadjuvant chemotherapy can be observed in mammography such as microcalcification or spiculated lesion, specimen mammography should be sent to confirm that the whole lesion is removed (*Figure 7*). If there is no detectable residual lesion in the patient who achieve a clinical complete response, a 2-cm specimen with the metallic marker in the center is suggested (13).

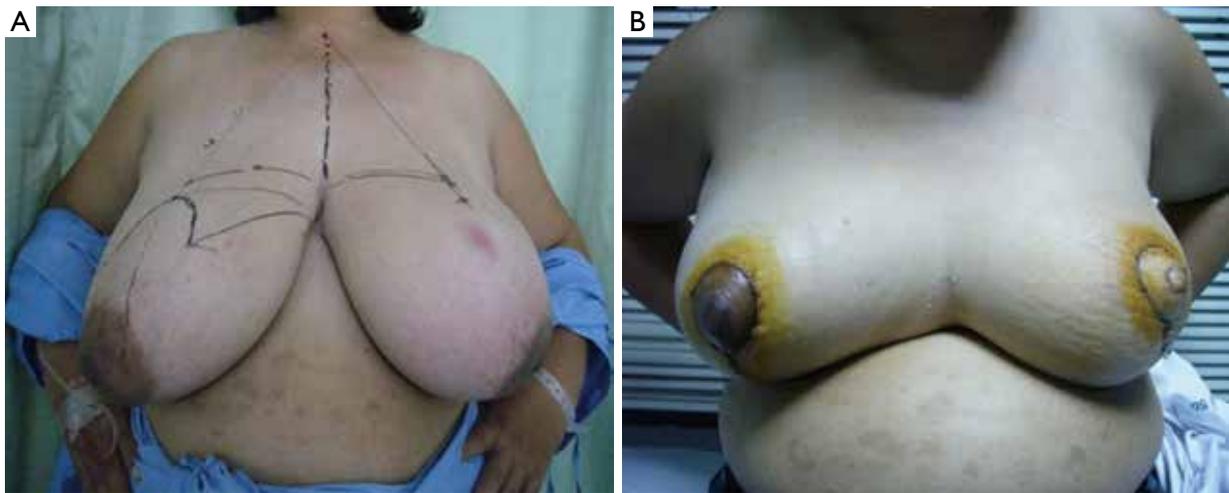


Figure 6 The patient presenting with LABC at left breast and had the large breasts with severe ptosis of both breasts. (A) Preoperative, quadrantectomy for left breast; (B) Postoperative, quadrantectomy with tissue rearrangement at left breast and reduction mammoplasty techniques was done at the opposite breast due to symmetry of both sides.



Figure 7 Specimen mammography showed incomplete wide excision of the spiculated lesion after giving neoadjuvant chemotherapy.

Conclusions

For selected LABC patients (adequate reduction in the tumor size and no evidence of residual nodules in the peripheral area after giving chemotherapy), BCS can be an appropriate local treatment option with acceptable local recurrence rates. Oncoplastic surgery for LABC is safe and effective. Using oncoplastic technique in patients who need

to remove the large volume of breast tissue, can prevent and correct the deformity with a good cosmetic outcome.

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Footnote

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Oncoplastic breast surgery in Australia and New Zealand—2014 and beyond

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Abstract: Oncoplastic breast surgery (OBS) is an established field of surgery bringing together oncological and reconstructive principles to the surgical management of breast disease, which is yet to make inroads into some areas of Australia and New Zealand (A&NZ). Both patients and medical fraternity are supportive of these approaches and improved quality of life and aesthetic outcomes resulting from their application. Oncological outcomes have been shown to be no different when these oncoplastic approaches are utilised. There is a broad interest amongst breast surgeons regarding OBS and development of their own skills. However a new and improved method of training the current and the next generation of breast surgeons is required. This has already begun in some countries such as the UK, but is slower in A&NZ region. Some of the obstacles in training of OBS to the next generation of surgeons are discussed and highlighted. This year first steps in formalised training approaches are being made. The future of breast surgery is likely to involve OBS as part of mainstream surgical management of breast disease.

Keywords: Breast reconstruction; oncoplastic surgery; training

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Oncoplastic breast surgery (OBS) is an amalgamation of extirpative oncological surgical techniques and plastic/cosmetic reconstructive techniques to produce a significantly improved aesthetic outcome for the breast cancer patient, whilst not compromising oncological treatment. It includes breast reshaping/remodelling and implant/autologous reconstructive techniques.

In this article we aim to identify the key features that led to the development of OBS and to focus on the current training in this discipline, highlighting the current problems facing surgeons wishing to gain qualification in OBS.

History

This branch of surgery has come about from the multiple preceding improvements in breast surgery, particularly the development of breast conservation therapy (BCS), but also from improved breast cancer screening/diagnosis and adjuvant therapy.

Consumer advocacy has also aided the promotion of

OBS. With significant numbers of women missing out on reconstruction opportunities or alternatively acknowledging their dissatisfaction with more traditional surgical treatment outcomes, the OBS approach has been developed.

There are many studies examining the psychological benefit of breast conservation surgery and breast reconstruction in breast cancer patients, with evidence of significant positive impact in the lives of these women (1). Expectantly, women undergoing breast conservation surgery and breast reconstruction procedures post mastectomy as a group, have higher satisfaction rates post surgery with respect to their body image, self-esteem and sexuality, compared with those undergoing mastectomy alone (1). However, breast conservation surgery can create significant breast asymmetry or disfigurement at times [particularly with the addition of radiotherapy (RXT)]. This is where OBS and reconstructive techniques can be superior to standard BCS approaches.

OBS in Australia and New Zealand (A&NZ) has had a presence for almost 30 years, being introduced and pioneered in The Royal Adelaide Breast Unit. It has become

widespread across the world in the last 15 years, becoming mainstream in some units. However, despite its pioneering days in A&NZ, it has yet to become the standard of care across our region.

Since the early days, OBS has been shown to be a safe and oncologically sound approach to the treatment of breast cancer. Fitoussi *et al.* (2) showed no difference in local recurrence or survival between BCS patients and OBS patients for tumours both high in volume and difficult in position.

Follow up for breast cancer local recurrence after OBS has also been shown to be unaffected by mammoplasty procedures, with similar mammographic findings noted in both BCS and OBS patients in a study by Losken *et al.* (3).

Importantly, OBS offers a way of achieving clear margins whilst providing an acceptable cosmetic outcome by trying to achieve the most natural breast shape and appearance. However, surgical competence and proficiency are important in achieving these outcomes.

Who should be performing OBS?

In A&NZ, public reconstructive waiting lists for plastic surgeons tend to be lengthy (particularly in the delayed setting) and Health Insurance cover or Medicare rebates are low (or absent if these are considered to be cosmetic procedures), leaving most patients significantly out of pocket (4). This can act as a deterrent to at least some of the women who may benefit from OBS and reconstruction. The system has worked better in the immediate breast reconstruction setting in some tertiary hospitals, however even here issues of coordinating multiple teams and provision of adequate theatre time tend to hinder the process (4).

Therefore an opportunity to expand the scope of practice of a breast surgeon to include OBS and breast reconstruction would benefit these patients in need of these procedures. A lot of OBS techniques are simple and easy to learn, whilst others are complex and require extended mentoring. Acquiring the necessary armamentarium, however, is not straightforward. Most of the breast surgeons performing these procedures have developed their skills by working with an experienced plastic surgeon, or alternatively in a few breast units where OBS procedures are performed. Other breast surgeons have also attended various courses or visited overseas units who perform these OBS techniques.

Are the aesthetic results as good as those achieved by plastic surgeons? This has been shown to be comparable

for some of the oncoplastic procedures such as breast reductions, but little studies have been performed on more complex procedures. For instance, Krysander *et al.* (5) examined outcomes in reduction mammoplasties between breast and plastic surgeons. They found no difference in outcomes examined in the two groups. This indicates that breast surgeons can have similar results to plastic surgeons, at least with respect to some procedures after adequate training and mentoring and therefore once competent should be encouraged to expand their practice.

It should also be noted that there are units across A&NZ, where a two-team approach has been established, refined and works very well and their importance in provision of service to the public should not be underestimated. The need for an oncoplastic breast surgeon may be less apparent in these settings. Regardless of the setting, more complex reconstructive procedures should always have the benefit of input, guidance and mentoring from a more experienced colleague be they oncoplastic breast surgeons or plastic surgeons if available.

Worldwide interest in OBS

The interest in OBS continues to grow worldwide. This has been shown by a simple analysis of the number of publications over the last ten years, which has grown six times over the preceding 20 years. This has come from more diverse regions of the world, indicating its increased popularity and momentum (6). In 2008 Kollias *et al.* (7) examined their breast surgical oncology practice and found that 28% of all cancer related procedures between 2001 and 2005 in public and private setting were related to OBS procedures, thus indicating that the proportion of reconstructive and oncoplastic techniques being used were quite significant for that established unit.

The initial expansion of breast surgeons into the field of OBS has been met with variable support. Malycha and Gough (8) noted that there were around 1,200 general surgeons in Australia in 2007, most of whom offered some form of breast surgical service, with those exclusively practicing breast surgery numbering around 20, 10 of which offered OBS. Since then these numbers have increased but not as dramatically as one might have hoped.

OBS training

Currently appropriate training is a rate-limiting factor in A&NZ for dissemination of OBS. How has the rest of the

world dealt with this same issue?

The 7th Portuguese Senology congress in 2009 (9) looked at OBS services and training in several countries. Portugal, Spain, Brazil and the UK all presented findings of significant interest in oncoplastic surgery in their countries and in accelerated development in the last ten years. However, only the UK has formalised training in OBS since 2002, with the establishment of nine oncoplastic breast surgical fellowships. These are open to surgeons trained in either general or plastic surgery. These training fellowships were set up within the context of large tertiary units with multidisciplinary inputs to management of breast cancer.

More recently, Brazilians have also established a formalised post-fellowship 2-year oncoplastic training program and have recently published excellent results in the development of skills in this cohort (10).

Furthermore, in 2007, the British Association of Surgical Oncology (BASO) and the British Association of Plastic Surgeons (BAPS) via the Training Interface Group of Surgery put together the 'Guide to Good Practice' for OBS (11). This document stresses many aspects, but the training and experience of the oncoplastic surgeon both in the setting up and delivery of an oncoplastic breast service is emphasised. The European society of breast cancer specialists (EUSOMA) also published independent training guidelines, which again emphasized experience in OBS and reconstructive techniques (12).

The above guidelines stress experience of the trainee/fellow in a number of different settings, with exposure to broad range of oncoplastic and reconstructive techniques with adequate opportunity for training in complex techniques and tissue handling, under supervision of experienced breast and plastic surgeons.

To address this issue in A&NZ, the recently established BreastSurgANZ society has embarked on a process of formalising post fellowship training in breast surgery. It has set up an Oncoplastic Subcommittee to monitor post fellowship training in OBS by accrediting appropriate units and is currently setting up a centralised application process for the A&NZ region. This has come about from experience gathered from the early cohort of fellows reporting on their fellowship posts and the experience gathered. In the future, this information will likely guide the fellowship placement process by matching the fellow's interests to the experience provided by the unit.

Importantly, there is no reason that most of the OBS (perhaps short of free flap reconstructive techniques) can't be performed in regional/rural and metropolitan units,

assuming that the oncoplastic surgeons and their supporting teams are adequately trained and there is a multidisciplinary input to surgical management as well as adjuvant treatment. This is key to the provision of adequate services across a geographically vast and diverse region.

Finally, it is essential for the plastic surgeon to remain an important part of the team. The work of an oncoplastic surgeon is not designed to diminish the role of the plastic surgeon, but rather to supplement and focus it. A breast unit utilising both an oncoplastic breast surgeon and a plastic surgeon is one that can offer all of the options to the patient and to deal with most potential complications that may arise, as supported and promoted by the BASO guidelines (11).

Conclusions

It is clear that OBS and the improvements that will flow on from its utilization are the next step forward in surgically managing breast disease. There is widespread acceptance of its principles and benefits. The next challenge is contained in dissemination of the necessary skills and refashioning the way surgeons approach the breast. This is the task for overseeing training committees, promoting the development of this subspecialty as well as its uptake within the surgical community.

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Footnote

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Oncoplastic volume replacement techniques according to the excised volume and tumor location in small- to moderate-sized breasts

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Background: In the treatment of cancer patients with small breasts, breast-conserving surgery (BCS) with adjuvant radiotherapy has become popular. In Korean women, many of whom have small- to moderate-sized breasts, the removal of an adequate volume of tissue during breast cancer surgery may compromise the cosmetic outcome and sometimes cause unpleasant results. In such cases, oncoplastic volume replacement techniques can be valuable.

Methods: Between January 2007 and December 2013, 213 women underwent 216 BCSs with various oncoplastic volume replacement techniques selected according to the volume of breast tissue excised. When the excised volume was <150 g, regional flaps such as a lateral thoracodorsal or thoracoepigastric flap, or perforator flaps such as an intercostal artery perforator (ICAP) flap or a thoracodorsal artery perforator (TDAP) flap were used. When the excised volume was >150 g, a latissimus dorsi (LD) myocutaneous flap was used.

Results: The mean age was 45.7 years, and the mean follow-up interval was 11.3 months. The mean excised volume was 148.4 g. The oncoplastic volume replacement techniques used included 22 lateral thoracodorsal flaps, 8 thoracoepigastric flaps, 29 ICAP flaps, 20 TDAP flaps, and 137 LD myocutaneous flaps. Postsurgical complications occurred in 30 cases, including 1 case of congestion and 26 cases of seroma in LD myocutaneous flaps, and 3 cases of fat necrosis in ICAP flaps. Most of the patients were satisfied with the cosmetic outcome.

Conclusions: Oncoplastic volume replacement techniques according to the excised volume and tumor location are reliable and useful for the correction of breast deformity after BCS, especially in patients with small- to moderate-sized breasts.

Keywords: Breast neoplasms; breast reconstruction; mammoplasty; surgical flaps

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Introduction

Early-stage breast cancers are increasingly being detected with the advancements in diagnostic tools for breast cancer and the increasing number of women who undergo periodic medical examinations, improving the prognosis of patients with breast cancer. Therefore, breast-conserving surgery (BCS), which aims to minimize postoperative breast deformity after partial mastectomy without compromising

tumor resection and allowing optimal oncological control, has become more common. Oncoplastic surgery, which is the expanded concept of BCS, was first attempted by Audretsch *et al.* in 1998 and included consideration of breast cancer and aesthetics (1). Two techniques are currently used in oncoplastic surgery according to the excised volume of the breast (2): the volume displacement technique based on glandular reshaping or reduction mammoplasty, and

the volume replacement technique, which uses autologous tissue for different types of flaps.

Breast size and the excised volume are important considerations in oncoplastic surgery. In patients with relatively large breasts, the residual tissue is sufficient to obtain satisfactory cosmetic outcomes using the volume displacement technique. In patients with relatively small breasts, the volume displacement technique can be performed after the removal of a small-sized defect. However, if the defect is moderate or large, satisfactory cosmetic outcomes can only be obtained using volume replacement techniques. The tumor location should also be considered in the selection of an appropriate oncoplastic volume replacement technique.

In the present study, patients with small- to moderate-sized breasts who underwent BCS with different oncoplastic volume replacement techniques were evaluated and a comprehensive overview of the different types of volume replacement techniques was performed, including a lateral thoracodorsal flap, a thoracoepigastric flap, or perforator flaps such as an intercostal artery perforator (ICAP) flap or a thoracodorsal artery perforator (TDAP) flap, and a latissimus dorsi (LD) myocutaneous flap.

Methods

This study was performed at the Kyungpook National University Hospital and Kyungpook National University Medical Center, Daegu, Republic of Korea, and was approved by the institutional review board. Between January 2007 and December 2013, 213 patients with small- to moderate-sized breasts who underwent 216 oncoplastic volume replacement techniques after BCS by the senior author (J.D.Y.) were enrolled in this study.

Under general anesthesia, a wide excision (approximately 2 cm from the initial tumor margin) was performed by the general surgeon and tumor invasion at the resection margin was evaluated in the operating room using frozen sections. In patients with confirmed tumor invasion by sentinel node biopsy, axillary lymph node dissection was performed at level I and II nodes. The oncoplastic volume replacement technique was selected according to the excised volume. When the excised volume was <150 g, regional flaps were used, such as a lateral thoracodorsal flap, a thoracoepigastric flap, or perforator flaps such as an ICAP flap or a TDAP flap. When the excised volume was >150 g, a LD myocutaneous flap was used.

The tumor location was also considered in the selection of an appropriate oncoplastic volume replacement

technique. When the tumor is located in the lateral aspect of the breast (upper outer or lower outer quadrant), a lateral thoracodorsal flap can be used. When the tumor is located in the lower pole of the breast (lower inner or lower outer quadrant), a thoracoepigastric flap can be used. An ICAP flap can be an alternative choice for lateral and inferior aspects. A TDAP flap can be also used for lateral and inferior quadrants and even for the upper inner quadrant (*Figure 1*).

The medical charts of all the patients were retrospectively reviewed, including history of radiotherapy and chemotherapy, and operative results such as excised volume, tumor location, type of oncoplastic volume replacement technique used, and postoperative complications.

To evaluate the satisfaction of the patients with the general and aesthetic outcomes of the oncoplastic surgeries, KNUH breast reconstruction satisfaction questionnaire was conducted six months after surgery (*Table 1*). Each question was graded on a 5-point Likert scale ranging from “very satisfied [5]” to “very dissatisfied [1].” Then, each questionnaire was divided into two groups, with a rating of “satisfied” for mean scores >4 and “dissatisfied” for all other scores.

To evaluate the aesthetic outcomes by the surgeon, three blinded plastic surgeons reviewed preoperative and 6-month postoperative photographs with frontal and bilateral oblique views for each patient. The surgeons scored the results on a 5-point Likert scale ranging from “excellent [5]” to “poor [1].”

Results

A total of 213 patients underwent 216 oncoplastic volume replacement techniques after BCS. The mean age was 45.7 years (range, 23-65 years), and the mean follow-up interval was 11.3 months (range, 4-23 months).

The characteristics of the breast cancers are shown in *Table 2*, including the tumor location, pathological report, tumor node metastasis stage, and history of radiotherapy and chemotherapy. The largest number of the pathologic report was invasive ductal carcinoma.

The mean excised volume was 148.4 g (range, 50-408 g). The tumor location in relation to the surgical technique used is shown in *Table 3*. Eighteen of 22 lateral thoracodorsal flaps (*Figure 2*) were used for tumors located in the upper outer quadrant of the breast; 5 of 8 thoracoepigastric flaps were used in the lower inner quadrant; and 20 of 29 ICAP flaps (*Figure 3*), 11 of 20 TDAP flaps, and 74 of 137 LD myocutaneous flaps (*Figure 4*) were used in the upper outer

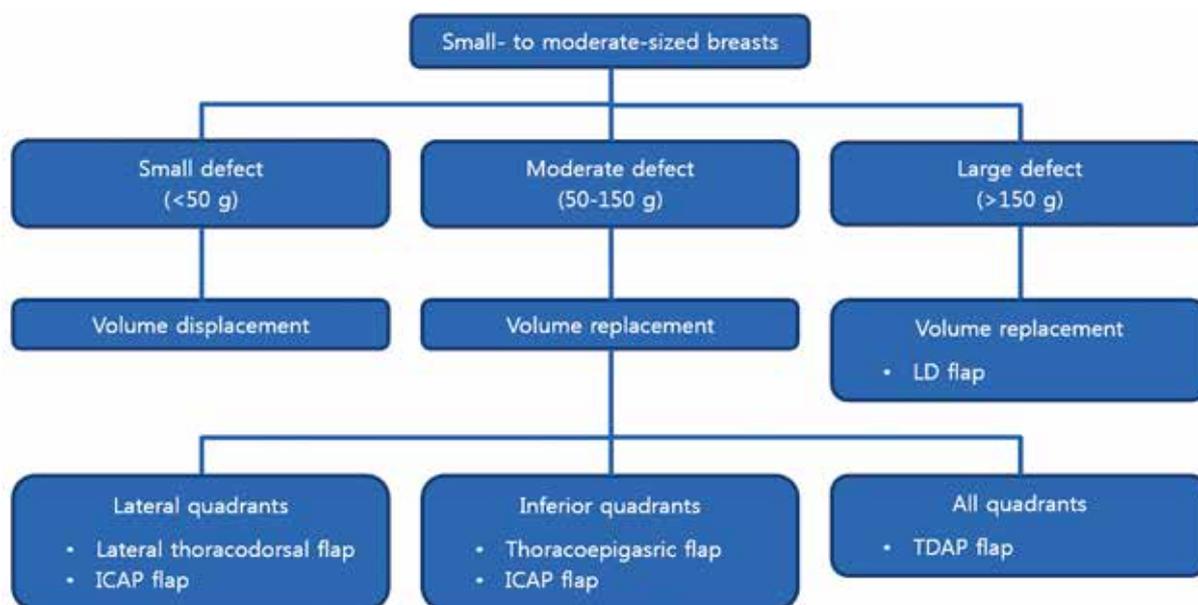


Figure 1 Algorithm of partial breast reconstruction with oncoplastic techniques in small to moderate-sized breasts. LD, latissimus dorsi; ICAP, intercostal artery perforator; TDAP, thoracodorsal artery perforator.

Table 1 KNUH breast reconstruction satisfaction questionnaire

Question	Very satisfied		→	Very dissatisfied	
Q1. Overall satisfaction with my breast reconstruction	5	4	3	2	1
Q2. Symmetry of my breasts	5	4	3	2	1
Q3. Size of my reconstructed breast	5	4	3	2	1
Q4. Shape of my reconstructed breast	5	4	3	2	1
Q5. Feel to touch my reconstructed breast	5	4	3	2	1
Q6. Pain in my reconstructed breast	5	4	3	2	1
Q7. Scar of my reconstructed breast	5	4	3	2	1
Q8. Donor site pain	5	4	3	2	1
Q9. Donor site scar	5	4	3	2	1
Q10. Self-confidence	5	4	3	2	1
Q11. Sexual attractiveness	5	4	3	2	1

quadrant.

No postoperative complications such as flap necrosis or wound infection were observed. One case of congestion was observed in a LD myocutaneous flap, and three cases of fat necrosis occurred in ICAP flaps. There were 26 cases (19.0%) of seroma at the donor site of LD myocutaneous flaps that were resolved using regular needle aspiration in the outpatient clinic.

The results of patient satisfaction surveys are shown in *Figure 5*. A total of 178 patients (82.3%) were satisfied with the general and aesthetic outcomes. LD myocutaneous flap

ranked highest among the other types of flaps regarding general and aesthetic satisfaction. The score of the aesthetic analysis by the plastic surgeon was 4.13. These results indicate that the cosmetic outcomes were considered satisfactory by most of the patients.

Discussion

In 1981, Veronesi *et al.* reported no significant difference in the survival rates between quadrantectomy with axillary dissection followed by radiotherapy and modified radical

Characteristics	n	%
Location 1 (Total =213)		
Right	112	52.6
Left	98	46.0
Both	3	1.4
Location 2 (Total =216)		
Upper outer quadrant	124	57.4
Upper inner quadrant	20	18.1
Lower outer quadrant	28	13.0
Lower inner quadrant	19	8.8
Whole breast	6	2.8
Pathology		
Adenocarcinoma	1	0.5
Ductal carcinoma <i>in situ</i> (DCIS)	58	26.9
Intraductal papilloma	2	0.9
Invasive ductal carcinoma (IDC)	153	70.8
Invasive mixed ductal and mucinous carcinoma	1	0.5
Mucinous carcinoma	1	0.5
Tumor node metastasis stage		
0	18	8.3
I	98	45.4
IIA	62	28.7
IIB	24	11.1
IIIA	11	5.1
IIIB	0	0.0
IIIC	1	0.5
IV	2	0.9
Radiotherapy		
Preoperative	5	2.3
Postoperative	137	64.3
None	71	33.3
Chemotherapy		
Yes	165	77.5
No	48	22.5

mastectomy in patients with breast cancer <2 cm in diameter and negative axillary lymph nodes (3). In 1985, Fisher *et al.* reported no significant differences in local recurrence and survival rates between modified radical mastectomy and BCS followed by radiotherapy in patients with breast cancer <4 cm (4). Since then, BCS has been accepted as the primary treatment modality in patients with stage I and II breast cancer, unless specifically contraindicated (5). However, the unfavorable cosmetic results of BCS are a major drawback (6).

In oncoplastic surgery, an expanded concept of BCS, the breast is reconstructed by plastic surgery techniques using the remaining breast tissue after tumor excision or using autologous tissue flaps (7,8). The advantages of oncoplastic surgery as compared with BCS are wider free margins and better cosmetic results (9,10). Disadvantages of oncoplastic surgery as compared with BCS include longer operation times, morbidity and scarring of the donor site, and the need for an experienced surgeon.

There are two types of oncoplastic surgery techniques according to the volume of the excised breast tissue (2). One is the volume displacement technique, in which the remaining breast tissue is rearranged using glandular reshaping or reduction mammoplasty techniques, thus minimizing the deformity of the breast after tumor excision. The other is the volume replacement technique, in which the excised breast tissue volume is replaced with autologous tissue in various types of flaps.

Breast size and excised volume are important considerations in oncoplastic surgery. In patients with relatively large breasts, especially in the Western population, the residual tissue is sufficient to reconstruct the breast after tumor excision. In these patients, satisfactory cosmetic outcomes can be obtained using glandular reshaping for relatively small

Type of reconstruction	n	%	Tumor location (n)					Mean excised volume (g)
			UOQ	UIQ	LOQ	LIQ	Whole	
Lateral thoracodorsal flap	22	10.2	18	0	4	0	0	74.2
Thoracoepigastric flap	8	3.7	1	0	2	5	0	95.4
ICAP flap	29	13.4	20	0	5	4	0	98.8
TDAP flap	20	9.3	11	5	3	0	1	99.2
LD myocutaneous flap	137	63.4	74	34	14	10	5	181.0
Total	216		124	39	28	19	6	148.4

UOQ, upper outer quadrant; UIQ, upper inner quadrant; LOQ, lower outer quadrant; LIQ, lower inner quadrant; ICAP, intercostal artery perforator; TDAP, thoracodorsal artery perforator; LD, latissimus dorsi.

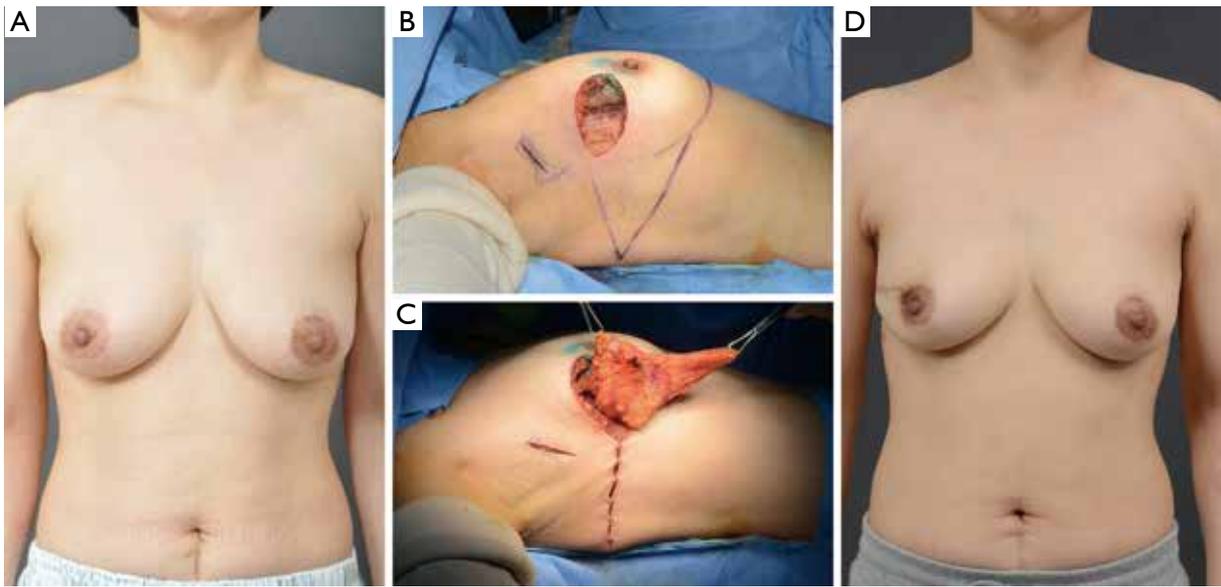


Figure 2 Case of a lateral thoracodorsal flap. A 45-year-old woman with invasive ductal carcinoma of the right breast. (A) preoperative view; (B) intraoperative view of the designed lateral thoracodorsal flap after partial mastectomy; (C) intraoperative view of the elevated flap; (D) 4-month postoperative outcome.

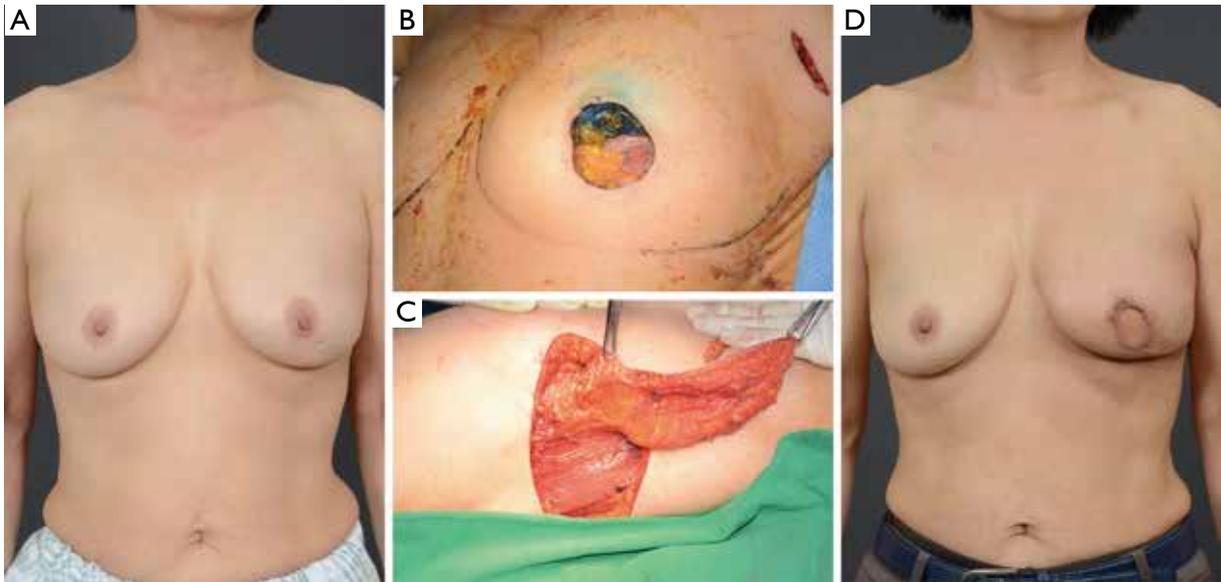


Figure 3 Case of an intercostal artery perforator (ICAP) flap. A 60-year-old woman with invasive ductal carcinoma of the left breast. (A) preoperative view; (B) intraoperative view after partial mastectomy; (C) intraoperative view of the elevated ICAP flap; (D) 8-month postoperative outcome.

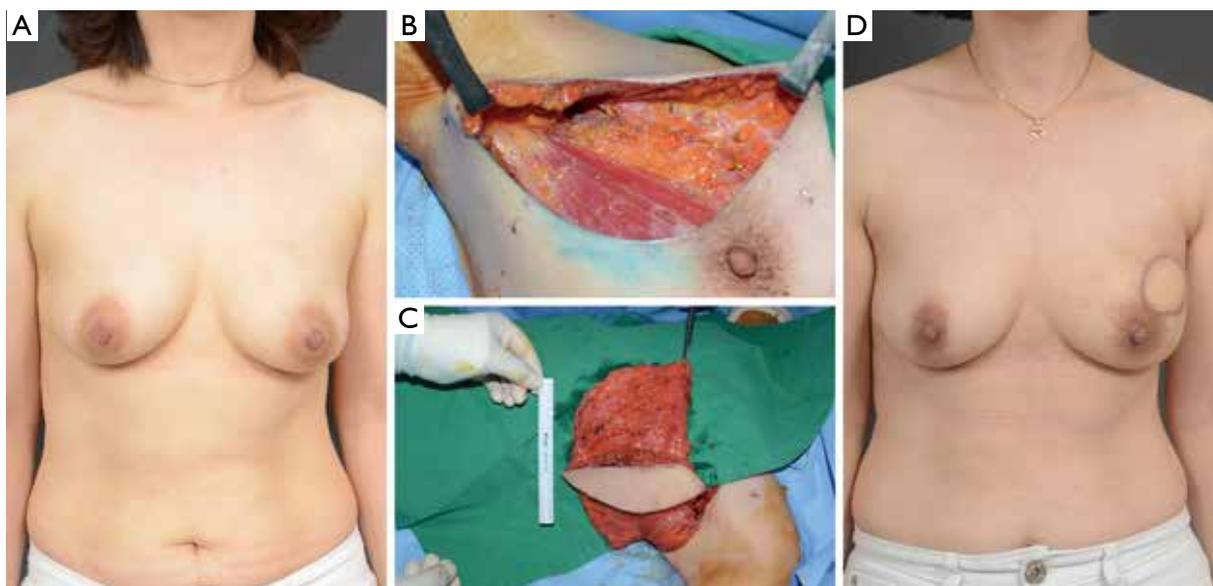


Figure 4 Case of a latissimus dorsi (LD) myocutaneous flap. A 40-year-old woman with invasive ductal carcinoma of the left breast. (A) preoperative view; (B) intraoperative view after partial mastectomy; (C) intraoperative view of the elevated LD myocutaneous flap; (D) 3-month postoperative outcome.

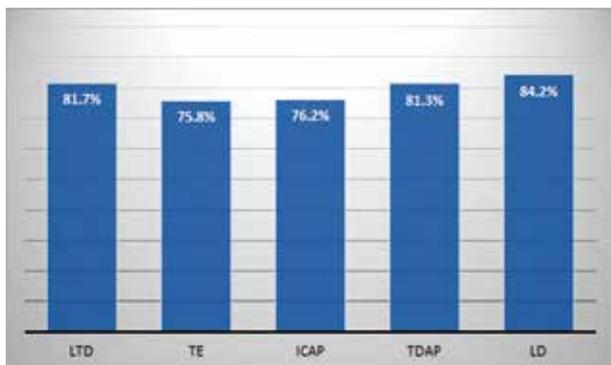


Figure 5 The results of patient satisfaction surveys according to various types of flap. LTD, lateral thoracodorsal flap; TE, thoracoepigastric flap; ICAP, intercostal artery perforator flap; TDAP, thoracodorsal artery perforator flap; LD, latissimus dorsi myocutaneous flap.

defects or reduction mammoplasty for moderate or large defects. In patients with relatively small breasts, especially in the Asian population, the volume displacement technique can be performed after the removal of a small-sized defect. However, in patients with moderate or large defects after tumor excision, satisfactory cosmetic outcomes are difficult to achieve using the volume displacement technique. In these cases, satisfactory cosmetic outcomes can only be obtained using a volume replacement technique with

autologous tissue in various types of flaps.

The tumor location should be also considered when selecting oncoplastic surgery. Each flap has a favorable arc of rotation necessary to reach the defect. Consequently, surgeons need to consider the excised volume and tumor location before performing oncoplastic surgery. In the present study, the senior author used five different volume replacement procedures. For cases in which the excised volume was <150 g, four regional flaps were used according to the tumor location. For tumors located in the lateral aspect of the breast, a lateral thoracodorsal flap can be useful, whereas tumors located in the lower pole of the breast can be treated using a thoracoepigastric flap. An ICAP flap can also be used for the lateral and inferior aspects. A TDAP flap can be used for the lateral and inferior quadrants, and even for the upper inner quadrant. For cases in which the excised volume was >150 g, a LD myocutaneous flap was used (11).

A lateral thoracodorsal flap is a wedge-shaped fasciocutaneous transposition flap with an axis along the lateral and dorsal extensions of the inframammary fold (12). The superior border of this flap starts at the medial to anterior axillary fold and extends laterally, with a curved inferior border extending to the anterior axillary line. The pinch test is useful to estimate the available volume of the lateral chest wall. During flap elevation, inclusion of the fascia of the LD and anterior serratus muscles under the

flap is important, as they provide a reliable vascular supply derived from the lateral intercostal perforators, muscular fascia, and lateral perforators of the intercostal arteries. After flap is inset, the donor site is closed primarily. This flap is indicated when the tumor is located in the lateral aspect of the breast and when abundant skin and tissue of the lateral chest wall are available, which are good sources for reconstruction. However, a history of surgery to the lateral chest wall is a contraindication. This flap has certain advantages, including excellent skin and tissue matching with the breast, an inconspicuous scar positioned under the arm and brassiere, minimal donor site morbidity and preservation of the muscle under the flap (13).

A thoracoepigastric flap is a transposition flap based on the perforators derived from intercostal or superior epigastric vessels through the rectus abdominis or external oblique muscles (14,15). The superior border of this flap is at the inframammary fold, and the inferior border is determined after the pedicle is located using Doppler tracing. The flap consists of skin and subcutaneous tissue, and can be raised with or without the fascia of the rectus and external oblique muscles under the flap. The flap can be inset through the subcutaneous tunnel. The donor site is closed primarily. This flap is indicated in patients with sufficient skin and subcutaneous tissue under the breast and in tumors located in the lower pole of the breast. A history of previous surgery to the ipsilateral upper abdomen is a contraindication (16). The scar at the donor site can be easily concealed because it is located at the inframammary fold.

An ICAP flap is a fasciocutaneous transposition flap based on the perforators of the costal segment on the lateral aspect of the thorax (lateral ICAP, located 3 to 4.5 cm from the anterior border of the LD muscle) or from the muscular segment (anterior ICAP, located between the 6th and 7th intercostal spaces). Doppler tracing is useful to determine the location of the perforators, and the flap is located over the perforators. This flap provides excellent skin and tissue matching with the breast. The scar at the donor site can be easily concealed because the flap axis is located at the inframammary fold. This flap is suitable for tumors located at the lateral or inferior breast and for patients with sufficient skin and subcutaneous tissue on the lateral chest wall or under the breast (17).

A TDAP flap is an adipocutaneous flap based on the perforators (first perforators, approximately 8 cm below the posterior axillary fold and 2-3 cm posterior to the lateral border of the muscle; second perforators, 2-4 cm distal to the origin of the first perforator) from the thoracodorsal

artery derived from the subscapular artery (18,19). This flap is similar to the LD flap (harvesting a similar skin paddle is possible), although the LD muscle can be spared; therefore, the morbidity of the donor site can be reduced. This flap can be used for defects in the lateral or central, and even medial breast.

A pedicled LD myocutaneous flap for breast reconstruction was first introduced by Schneider *et al.* (20). This safe and reliable flap is based on the thoracodorsal artery as the pedicle, and it provides muscle and subcutaneous tissue for the repair of glandular defects and skin for cutaneous defects. However, it has disadvantages compared with the other flaps, including a difficult surgical procedure, long surgical time, and morbidity of the donor site such as a wide scar, which can be concealed by the brassiere, limited range of shoulder motion, and seroma.

In patients with relatively small breasts, the volume displacement technique can be used to treat small defects; however, when the defect is moderate or large, there are some limitations in achieving a satisfactory cosmetic outcome using the volume displacement technique. In conclusion, in these cases, selection of the appropriate volume replacement technique considering the excised volume and tumor location is important for the patient's satisfaction with the cosmetic outcome.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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International oncoplastic breast surgery training

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Abstract: Breast cancer mortality is being dramatically reduced in past decades. Breast cancer survivors are seeking their quality of lives after treatment along with effective and curative oncological control. Surgical options both on ablative and reconstructive purpose procedures are more widely performed in different techniques, making the breast cancer surgery becoming an individualized or tailoring surgery. Multidisciplinary team approach in breast cancer is becoming a standard practice. Training in oncoplastic breast surgery will improve the quality of breast cancer patient care. International program should be established to develop collaboration in academic and science all over the globe.

Keywords: Surgical education; surgical training; oncoplastic breast surgery; breast surgery; breast reconstruction

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During the past twenty years until recently, medical technology and public awareness on health are emerging developed. Consequently, breast cancer among women can be more early detected with a far more increasing in number of patients around the world.

In developing countries with national screening program, over 50% of breast cancer patients are found in stage 0 and stage I which are basically curable in majority of cases. These breast cancer survivors are seeking their quality of lives after treatment.

In accordance with new technology for earlier breast cancer detection, new procedures are developed to handle those asymptomatic diseases both in diagnostic and therapeutic purposes, such as, stereotactic or ultrasound guided biopsy, needle localization and surgical removal of diseases, etc.

To fulfill the quality of life among survivors, two surgical options are usually advised; that is mastectomy or breast conservation surgery (BCS). In some institutes, BCS are carried out more than 75% of cases. Oncoplastic breast surgery plays more roles to restore the breast shape and symmetry. In addition, wider margins on lumpectomy can be performed without compromising breast deformity (1).

For those who still need mastectomy, immediate total

breast reconstruction with autologous tissue flap transfer or implantation or combination of both can be offered (2,3).

Axillary management is still a part of definitive surgery for breast cancer; sentinel lymph node biopsy is routinely performed as initial assessment followed by axillary clearance for positive metastasis (4). The outcome of this approach is promising and could spare more than half of cases from a routine axillary clearance. It reduces the subsequent arm lymphedema in a number of cases as well as shoulder dysfunction from surgery.

With the advance in DNA and gene mutation detection, potentially developed hereditary breast cancer among risk population can be accurately predicted (5,6). As the Angelina Jolie effect, risk reduction surgery in these specific individuals is becoming more popularized. The nipple sparing mastectomy with immediate reconstruction could reduce the individual risk of cancer in over 90% without or minimal impact on the quality of life (7).

Surgical options both on ablative and reconstructive purpose procedures are more widely performed in different techniques, making the breast cancer surgery becoming an individualized or tailoring surgery (8). Surgeons should instruct the patients on surgical options that are appropriate to their tumor characteristics on presentation, facility of

Risk reduction mastectomy + reconstruction



Surgical treatment for breast cancer

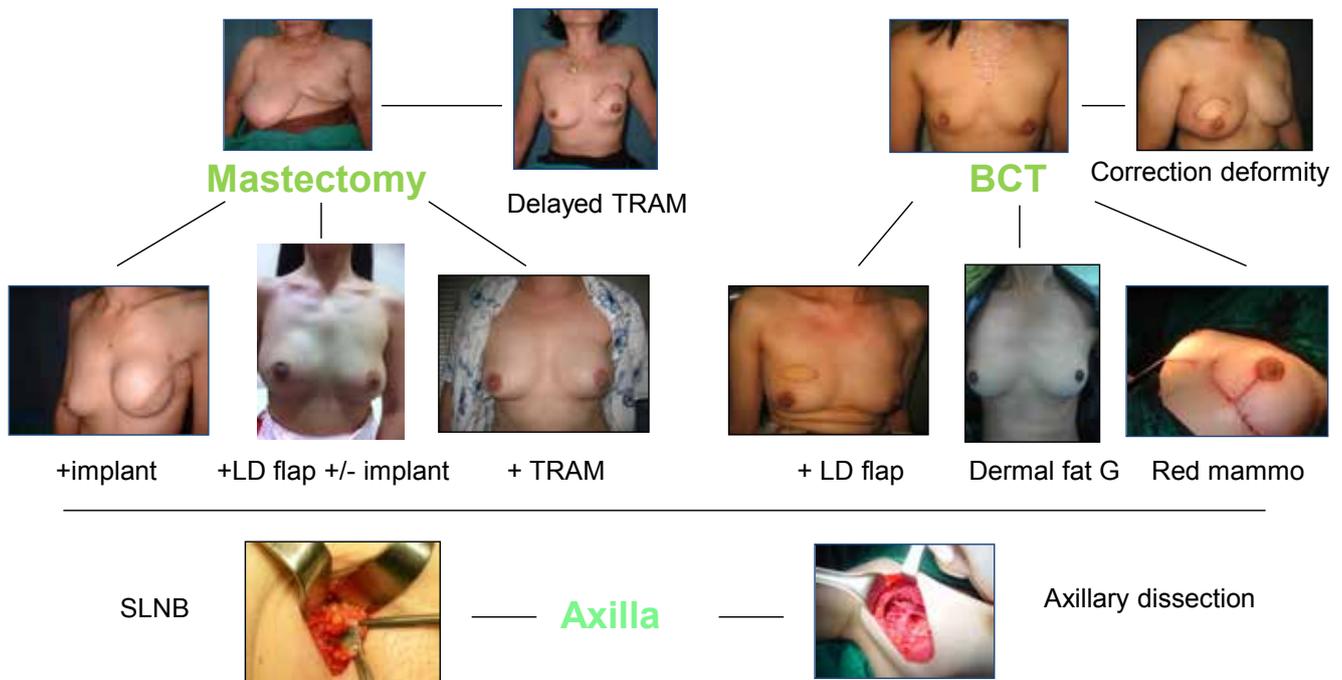


Figure 1 Surgical options for breast cancer.

the hospital and surgeon, and patient preference (*Figure 1*). Multidisciplinary team approach in breast cancer is becoming a standard practice. Surgeons play a major role in local disease control. However, we need to understand and keen on other basic principles in oncology, nature of disease, and be competent on breast imaging and diagnostic procedures as well as radiation therapy and systemic therapy, etc.

Training in oncoplastic breast surgery will improve the quality of breast cancer patient care. All specialties are keen and well trained with more collaboration. Tumor registration, risk management and quality improvement are all included as part of the curriculum for better outcome and learning. Apart from competency in surgical procedures (*Figure 2*), the objectives for trainees will include:

(I) To understand the principle of oncology and nature of breast cancer;

- (II) To make clinical decision for breast cancer in standard and up to date fashion;
- (III) To participate all varieties of surgical procedure for breast cancer;
- (IV) To be familiar with multidisciplinary approach such as radiographic diagnosis, radiation therapy, systemic therapy, cancer epidemiology, patients and family support.

Over the years I have been visited many countries in the regions. The experience has been truly educational and perspective widening. It made me realize that there are huge gaps in our community, not only in economic status but also in the quality and accessibility of health care, especially in surgical problems. There are lots of surgical diseases that are still quite a major problem in one place while quite rare in others. Even in some organ specific cancers, such as breast cancer; the incidence and

Competency of surgical oncologists on breast cancer procedures

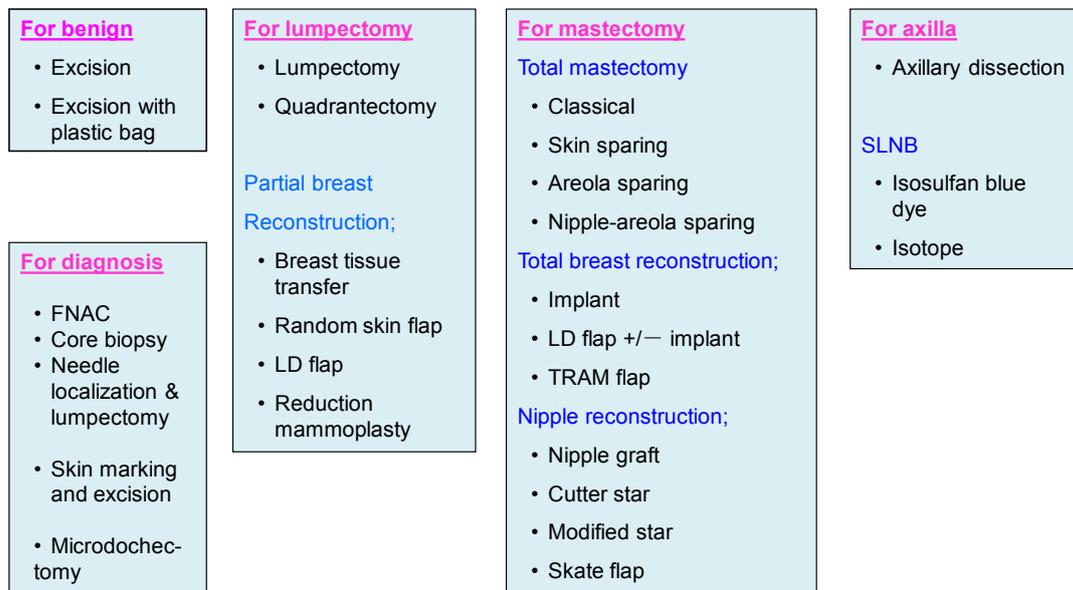


Figure 2 Common procedures for breast diseases.

clinical presentations and cure rates are somewhat totally different, not to mention the facility, technology, quality of service and culture of patient safety, all of which are incomparable in some regions.

Disparities in surgical care are still a major problem. Early detection of breast cancer and public education is a priority concern and should be considered in parallel to the training program. International program should be established to assist other countries with less opportunity. If we consider surgery as being something without boundary, it is about time for us to join hands and solve all these matters together.

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Footnote

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Oncoplastic breast surgery: current strategies

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Abstract: The surgical management of breast cancer has dramatically evolved over the past 20 years, with oncoplastic surgery gaining increased popularity. This field of breast surgery allows for complete resection of tumor, preservation of normal parenchyma tissue, and the use of local or regional tissue for immediate breast reconstruction at the time of partial mastectomy. These techniques extend the options for breast conservation surgery, improve aesthetic outcomes, have high patient satisfaction and result in better control of tumor margins. This article will detail the approach to evaluating and treating patients undergoing oncoplastic reconstruction. Different oncoplastic approaches will be described and applied to an oncoplastic reconstructive algorithm. Surgical complications, oncologic outcomes and aesthetic outcomes are reviewed.

Keywords: Breast reconstruction; oncoplastic surgery; partial mastectomy; reduction mammoplasty; mastopexy

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Introduction

Surgical management of breast cancer has evolved significantly over the years, trending away from radical procedures, and moving towards those with complete resection of tumor while preserving normal parenchyma tissue thereby decreasing patient morbidity. This shift has allowed for improved aesthetic outcomes and quality-of-life for patients, while maintaining equivalent oncologic safety (1,2).

A more recent innovation to further enhance aesthetic outcomes has been the development of “oncoplastic” surgery, which broadly refers to reconstruction of partial mastectomy defects. A variety of techniques have been described for partial mastectomy reconstruction, including local tissue rearrangement, reconstruction through reduction mammoplasty or mastopexy approaches, and transfer of local-regional flaps.

The rapidly expanding body of literature on outcomes following oncoplastic surgery has shown numerous benefits to this reconstructive approach, including improved aesthetic outcomes (3,4), better control of tumor margins (5), high patient satisfaction (6-8), and the ability to extend the option of breast conservation (9-11).

This review will describe a comprehensive approach

to evaluating and treating patients with oncoplastic reconstruction as well as summarize the different approaches and outcomes for the various techniques.

Pre-operative evaluation

In the patient who is a candidate for oncoplastic breast surgery, it is necessary to have a multidisciplinary preoperative evaluation with the breast oncologic surgeon and plastic surgeon. The breast oncologic surgeon will determine the volume and location of breast to be resected thereby providing information as to the anticipated defect that will be reconstructed, and whether or not the patient is a candidate for breast conservation therapy. Preoperative planning affords surgeons increased flexibility in terms of incision design and pedicle selection. Some patients with locally advanced breast cancer may be candidates for neoadjuvant chemotherapy. Tumor shrinkage through this preoperative treatment, resulting in tumor downstaging, may then allow these patients to become candidates for breast conserving surgery (12-16). The option of significant tissue rearrangement through oncoplastic techniques can facilitate the removal of larger tumors, which can potentially extend the option of breast conservation to patients

who would have traditionally required mastectomy (9). It is particularly important to consider the combination of neoadjuvant chemotherapy for tumor shrinkage followed by oncoplastic surgery in patients who will require post-operative radiation therapy even if they have a mastectomy, given the high rates of complications following post-mastectomy breast reconstruction and subsequent post-mastectomy radiation therapy (11,17). It is also important to establish expectations both of the patient and the surgeons during the preoperative period.

The preoperative evaluation should include examination for degree of ptosis, overall skin quality, evidence of prior radiation, and overall breast size. The reconstructive options available are primarily determined by the size of the breast and the tumor to breast ratio. In the smaller breasted woman, there is less glandular tissue available to perform local tissue rearrangement, and therefore these patients are more likely to need regionally-based flaps. Mastectomy with reconstruction may provide a more aesthetically pleasing result than breast conservation surgery in the small to moderate-breasted woman with a large tumor (on average, a resection size to breast size ratio greater than 1:5). Larger breasted women have more options available for reconstruction, whether it is local tissue rearrangement, local or regional flaps, or reduction mammoplasty/mastopexy. In the oncoplastic breast reduction, tumor location will dictate the reduction technique used and the design of the nipple/areolar pedicle.

Given that the majority of women with breast cancer are older than 50, and with aging there is inferolateral descent of the breast and nipple-areolar complex (NAC), there will often be contralateral breast asymmetry following resection and reconstruction of the affected breast. Many women desire symmetry-achieving surgery following oncoplastic breast surgery. Both breasts play equal roles in the “aesthetic triangle”, therefore the contralateral breast’s appearance is vital in the overall aesthetic outcome. Relocation of the NAC and achieving volumetric symmetry greatly improve the overall result. However, controversy exists over timing of symmetry-achieving surgery. Some institutions perform synchronous surgery with the affected breast, while others delay symmetry surgery given the potential effects of hormonal therapy, chemotherapy and radiation therapy on morbidity, and on further changing the shape and appearance of the effected breast (18-20). There have been reports as to the timing of these procedures in post-mastectomy reconstruction, with excellent aesthetic outcomes reported for synchronous procedures.

Furthermore, several studies have reported uncovering occult malignancies in the contralateral breast, with an overall rate ranging from 0.16-5% (21-24). Additionally, there is evidence that breast reduction significantly reduces breast cancer incidence in women over the age of 50 (25). Therefore, the benefits of symmetry surgery on the non-disease breast may be more than just producing an improved aesthetic outcome.

Oncoplastic techniques

Oncoplastic breast surgery entails complete tumor extirpation, partial reconstruction of wide local excisions, and symmetrizing surgery for the contralateral breast (26). The technique used for reconstruction depends on a number of factors, most importantly tumor location and size, tumor to breast size ratio, and patient desires.

Local tissue rearrangement

Local tissue rearrangement is an essential component of many oncoplastic techniques. It is most commonly used in women with moderate-sized breasts, small tumors and grade 1 ptosis. This technique may shift the defect to a less conspicuous location by taking advantage of subcutaneous fat and skin elsewhere (see *Figure 1*). These approaches often involve raising of skin/subcutaneous flaps to allow for mobilization of the underlying glandular tissue to fill the glandular defect. Glandular flaps may allow defects in all areas of the breast to be filled, even in the difficult-to-repair upper inner quadrant defects, provided there is sufficient tissue (see *Figure 2*).

If there is insufficient tissue for local tissue rearrangement because the defect is too large, local or regional flaps provide viable options for reconstruction. Local flaps from the subaxillary region are useful for moderate defects in the smaller breast. More lateral defects may be reconstructed with a transposition or rotational flap, moving skin and subcutaneous fat that is lateral to the breast (28) into defects in the outer quadrants of the breast. The latissimus dorsi flap provides enough volume to correct almost any partial mastectomy defect, is technically simple and has relatively low morbidity (29,30). Because of the different skin color and texture with this flap, it is better to replace an entire aesthetic unit during latissimus dorsi reconstruction. This is ideally done by having one edge of the skin paddle form the inframammary fold, the lateral breast border, or both (28). However, this flap can still be used if no skin is missing by

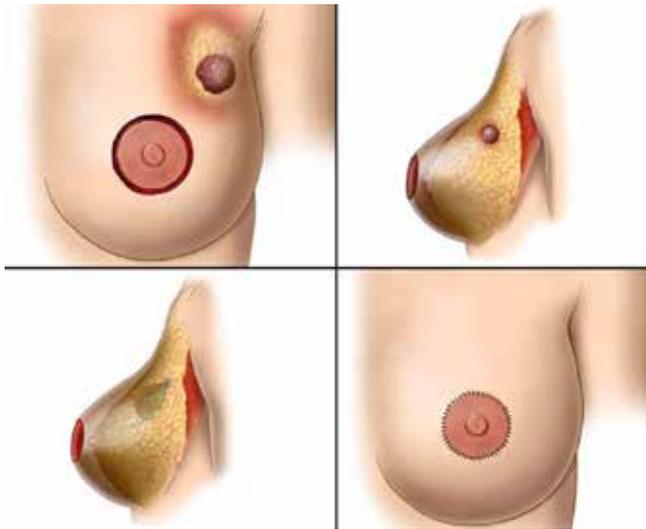


Figure 1 Schematic of local tissue rearrangement to fill defect following upper pole tumor resection [printed with permission from reference (27)].



Figure 2 Example of local tissue rearrangement following tumor resection.

transferring the muscle alone.

Mastopexy approaches

Mastopexy techniques are good options for patients with significant ptosis and adequate breast volume, as well as larger breasted patients (31). These procedures, in conjunction with partial mastectomy, help maintain an aesthetically pleasing breast shape following large tumor resections (see *Figure 3*). Benelli's 'round block' technique is ideal for upper pole tumors close to the areola in mildly ptotic breasts that would benefit from mastopexy (32). This technique involves de-epithelialization of the peri-areolar area with the NAC supplied by a central glandular pedicle. Local parenchymal remodeling with wide skin undermining is performed after tumor excision. The same technique may be used on the contralateral breast at the same time or following radiotherapy to achieve symmetry (33). The omega-plasty, or 'batwing' mastopexy is another good option for tumors of the upper pole (31). It involves wide en bloc resection of superior peri-areolar skin, gland and tumor to the pre-pectoral plane, with the shape of the final resected skin and glandular specimen having a 'batwing' type appearance. Wound closure is performed in a layered fashion, which allows for elevation of the inferior quadrants and NAC, thereby correcting ptosis (33).

Oncoplastic reduction mammoplasty

Bilateral reduction mammoplasty is an ideal treatment option for breast cancer in women with preoperative macromastia (21,34,35). Based on tumor location, a skin pattern and NAC pedicle are designed pre-operatively to allow for resection of the tumor within the typical resection pattern for the specific reduction technique chosen, and filling of the planned tumor defect with the remaining breast tissue (see *Figures 4* and *5*). Once the amount of required tissue resection is determined on the ipsilateral side, the contralateral breast is reduced to match (36). This technique can also be applied to tumors in other areas of the breast by shifting tissue and rotating the reduction pattern (28).

The most commonly employed oncoplastic technique is the Wise pattern with inferior pedicle reduction mammoplasty (33). This technique combines wide upper

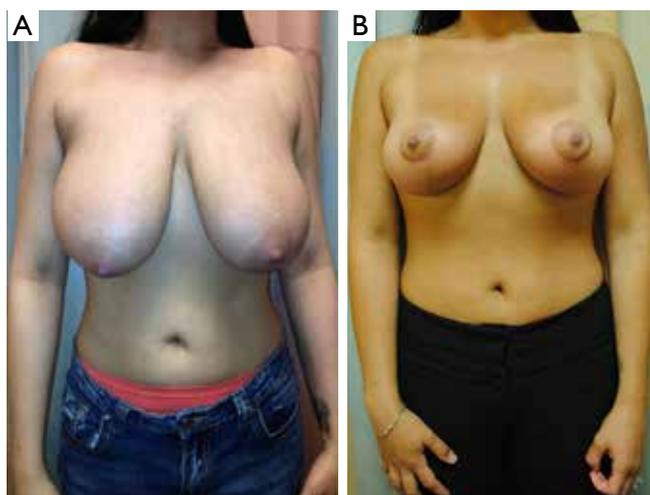


Figure 3 Example of large-breasted patient with significant ptosis before (A) and after (B) tumor resection and mastopexy.



Figure 4 Example of bilateral reduction mammoplasty following upper pole tumor resection in large-breasted, ptotic patient.

pole tumor excision with excess gland resection, resulting in an improved aesthetic for the large or ptotic breast. The incision pattern maintains viability of the skin flaps while providing adequate access and exposure for the partial mastectomy to be performed. The dermo-glandular pedicle



Figure 5 Example of bilateral reduction mammoplasty.

vascularizes the NAC, thus keeping it well perfused and viable. This technique can also be used for peri-areolar and central tumors.

The vertical scar technique is ideal for inferior pole tumors and central subareolar tumors as they may be widely excised within the boundaries of the standard markings. It was first described by Lassus (37), then popularized by Lejour (38) for aesthetic breast surgery. The advantages of this technique include shorter skin incisions, straightforward glandular resection, and a shorter pedicle which offers reliable blood supply to the NAC for a variety of breast sizes (39). Use of this approach in oncoplastic reconstruction has become increasingly popular, with recent studies demonstrating good cosmetic and oncologic outcomes, and high patient satisfaction (6).

Lateral pole tumors are well suited for lateral mammoplasty. This technique combines wide tumor excision with supero-medial NAC repositioning on a dermo-glandular pedicle, thereby counteracting lateral axial scar contraction and breast ptosis. Good or excellent outcomes have been reported in the majority of reconstructions performed with this technique (40). Additionally, the incision may be extended superiorly

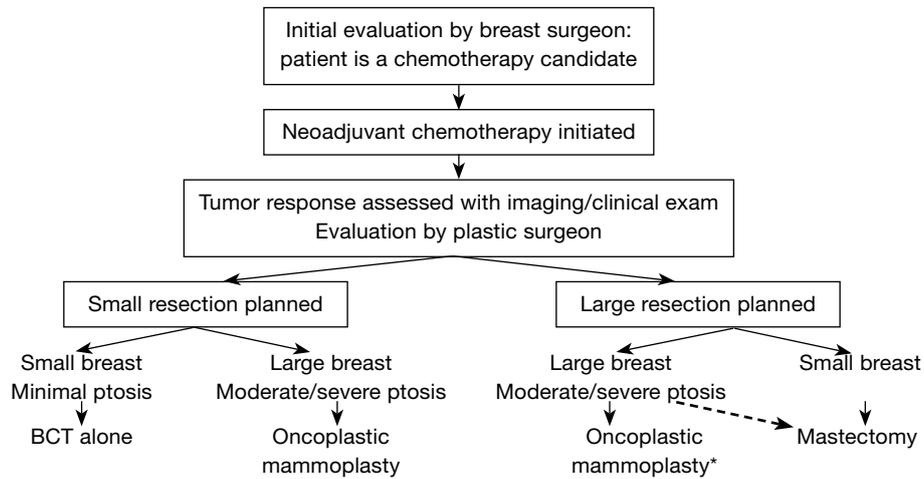


Figure 6 Algorithm for method of oncoplastic reconstruction [printed with permission from reference (11)]. *, preferred.

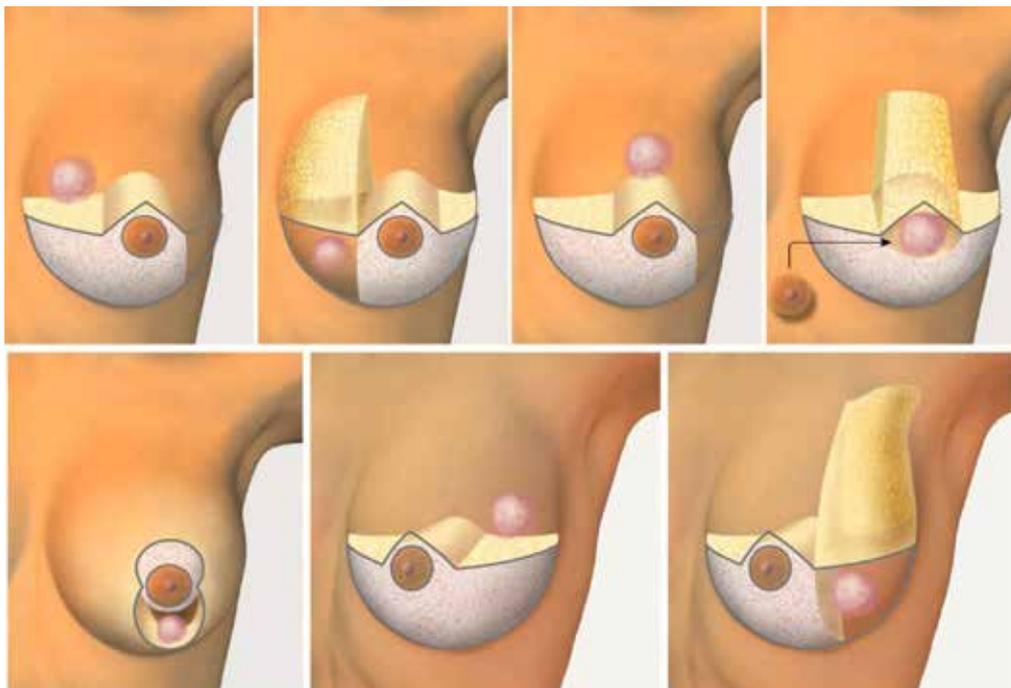


Figure 7 Division of breast into seven zones based on tumor location, and respective oncoplastic reconstruction [printed with permission from reference (27)].

to access the axilla for node dissections without having to make a separate incision. Medial mammoplasty, used for medial tumors, is almost the mirror image of lateral mammoplasty. The NAC pedicle is de-epithelialized to allow its repositioning on the breast mound. For larger volume resections, extending the incision along the medial IMF allows for parenchymal rotation flaps to be used.

Oncoplastic reconstructive algorithm

A number of studies have been published describing oncoplastic technique algorithms based on tumor location (see *Figure 6*) (27). Berry *et al.* described ten oncoplastic techniques based on tumor location (33). In a similar manner, Iwuchukhu *et al.* divided the breast into seven zones (see *Figure 7*), and each zone corresponded with

several suggested mammoplasty techniques (41). Overall, tumor location can be divided into the upper or lower pole, and then whether it lies medially, laterally or centrally.

The majority of breast cancers are found in the upper outer or lower outer quadrants. Most of these tumors may be treated with the inferior pedicle technique (42,43), which is the most common form of breast reduction. This technique allows for removal of additional breast tissue, maintains nipple perfusion, and achieves an aesthetic and symmetric reconstruction. Upper outer tumors can also be treated using a superior-medial extended pedicle through a Wise incision (44,45).

Lower pole tumors can be excised using a superior or superior-medial based pedicle using the Wise pattern skin envelope or vertical mammoplasty technique. Good or very good cosmetic outcomes have been reported in the majority of these patients (46-48).

Upper pole tumors are more difficult to reconstruct given the difficulty of maintaining upper pole breast volume following wide local excision. The inferior pedicle approach (44), round block technique (49) and “batwing” design (31) are all suitable techniques. Tumors of the upper inner quadrant are especially difficult to reconstruct given their more visible location post-operatively. Various approaches have been reported, including an extended superior-lateral pedicle (35,50), extended inferior pole pedicle that would normally be discarded as part of the reduction mammoplasty (28,42), and lateral pedicle with up-rotation of the whole breast (51) all with good cosmetic results.

Medial tumors can be easily access via a Wise pattern skin incision with an extended superior pedicle flap. A supero-lateral nipple pedicle can be extended inferiorly and then rotating the inferior pole upwards to fill the defect, thereby negating the increased risk of fat necrosis associated with two pedicles. Local rotation of breast parenchyma is also suitable for this zone (44).

Lateral tumors can be resected via a Wise incision or inverted “T” pattern incision and filled using a superior-medial pedicle (52). The Wise pattern skin incision affords better access for tumor resection, as well as allows for axillary surgery through the tail of the incision (44). Several other techniques have been described to repair this defect, including rotation of adjacent breast tissue (32), lateral thoracic rotation flap (53,54), latissimus dorsi myocutaneous rotational flap (28) and matrix rotation flap (55).

Central tumors present a unique challenge in that they may or may not require resection of the NAC. If the nipple

is left in place, a standard Wise or vertical mammoplasty incision can be used with an inferior, medial or lateral pedicle. Fitzal *et al.* suggested that a medio-inferior pedicle technique may preserve nipple sensation better than either superior or inferior pedicles (51). A simple approach is excision via the inverted “T” closing wedge or melon slice mammoplasty, which does not require a planned NAC pedicle (56). Therefore, the risk of fat necrosis and pedicle necrosis are decreased making this a more appealing option for high risk patients. If NAC removal is required, a Wise pattern incision with an inferior pedicle to fill the central defect has been demonstrated to have good outcomes (57). Nipple reconstruction can either be performed at the time of initial reconstruction, or delayed. Options for immediate nipple reconstruction include creation on an advanced skin paddle (44), as well as reconstruction using a full thickness skin graft (58).

Outcomes

Complications

Overall complication rates for oncoplastic reconstruction range from 15-30% and have been well-documented (11,59-61). The complications unique to this type of surgery include skin/flap necrosis, nipple and nipple areola complex necrosis, seroma, hematoma, infection, wound dehiscence and fat necrosis. The most common complication in Wise pattern/inverted “T” techniques is delayed healing of the “T” junctions (the areas where perpendicular scars meet. This is due to reduced vascular perfusion. While wound healing complications may delay time to adjuvant radiotherapy, this is a rare occurrence in all series reported to date. These procedures do have longer operating times than wide local excision alone, which should be taken into consideration when evaluating patients to ensure they are appropriate candidates for oncoplastic reconstruction.

Oncologic outcomes

Recurrence

With oncoplastic reconstruction, concern exists that local tissue rearrangement may impact local recurrences and the ability to detect them. However, numerous studies have demonstrated that oncoplastic techniques have low local recurrence rates when compared with breast conserving therapy alone (62). Reijtens *et al.* found that local recurrence rates were low over long-term follow-up, with a 3% rate at

5 years and no recurrences seen in those tumors smaller than 2 cm (24). This was echoed by Caruso *et al.*, who reported a 1.5% local recurrence rate when evaluating 63 women who had undergone bilateral reduction mammoplasty (43). This was similar to the 2.5% recurrence rate Chang *et al.* found in an evaluation of 79 patients who underwent simultaneous partial mastectomy and reduction mammoplasty (9). In a prospective cohort study of patients with locally advanced breast cancer undergoing oncoplastic surgery, Bogusevicius *et al.* reported a local regional recurrence rate of 10%, at 86 months (63). However, these patients had larger tumors and longer follow-up than the previously mentioned studies. Additionally, excision of multifocal tumors within the same quadrant has been shown to be oncologically safe with the wide margins that can be taken with oncoplastic procedures (64).

Positive margins

While oncoplastic techniques allow for wider resections, the tissue rearrangement performed in reconstruction may complicate management of positive margins. Positive margins have been reported between 2.7-22% (9,20,62,63) and have been associated with higher stage, positive nodes, positive lymphovascular invasion, use of neoadjuvant chemotherapy, larger initial "T" stage, positive estrogen receptor and younger age (20,51,65). Many oncoplastic techniques utilize dermo-glandular rotational flaps, which transpose tissue from one area of the breast to another. If a second surgical stage is needed for presence of disease at the edges of the specimen, this can become challenging due to the displacement of the glandular tissue, thereby making further excision very difficult (41). Although re-excision is possible, more often these patients undergo completion mastectomy. Additionally, since most mammoplasty techniques rely on a unipedicle or bipedicle, subsequent need for surgery risks pedicle compromise thereby restricting future therapeutic options. However, it has been demonstrated that patients undergoing oncoplastic surgery are more likely to have negative margins compared to partial mastectomy alone (5,66). This is likely due to the more aggressive resection afforded to the surgical oncologist, with the knowledge that the oncoplastic reduction will limit the aesthetic detriment following this procedure. Giacalone *et al.* found that patients who underwent oncoplastic surgery were more likely to achieve 5 or 10 mm free margins in a significantly higher percentage of cases compared with patients who underwent quadrantectomies (67).

Intraoperative frozen section has been evaluated as a means to combat positive margins. Rusby *et al.* used frozen

section as a diagnostic technique to evaluate margins in patients undergoing latissimus dorsi mini-flaps at the time of partial mastectomy. One third of patients had positive frozen sections with a sensitivity of 83% and accuracy of 96% when compared with paraffin sections. Overall, local recurrence rate was 0.9% with a median follow-up of 41.4 months (68). Caruso *et al.* evaluated the utility of intraoperative frozen section in patients undergoing therapeutic mammoplasty. They found that 8/52 patients (3 false positives, 5 true positives) had positive frozen sections, with a sensitivity of 83% and accuracy of 94%. Based on their findings, they advocated for intra-operative assessment of margins as a means of improving local control in a single stage, thereby reducing the need for secondary re-excisions or mastectomies (none in their study) (69).

Need for completion mastectomy

Although large long-term follow-up studies are lacking for oncoplastic breast surgery, published studies have described low rates of completion mastectomy. Reported rates have ranged from 5% to 10% (9,21,24,33). These low rates have been demonstrated despite inclusion of patients with tumors greater than 4 cm in size (9).

Aesthetic outcomes/patient satisfaction

Overall, oncoplastic breast reconstruction results in better aesthetic outcomes and higher patient satisfaction relative to breast conserving oncologic surgery without reconstruction. Bogusevicius *et al.* found that 87.2% of patients had good to excellent aesthetic outcomes in patients with locally advanced breast cancer undergoing oncoplastic surgery (63). The vast majority of patients (>80%) who underwent therapeutic mammoplasty over mastectomy or lumpectomy would make the same choice if given that choice again (21,34). Veiga *et al.* found that patients who underwent reduction mammoplasty following partial mastectomy had improved self-esteem and mental health when compared with patients who did not undergo reconstruction following partial mastectomy (4). However, patients undertaking oncoplastic procedures have higher expectations compared with classic conservative treatment (70). This most likely explains why between 5-14% of patients undergoing oncoplastic surgery reportedly have a poor cosmetic outcome (10,21,34,35,49,50,71-73).

Conclusions

Oncoplastic breast reconstruction at the time of partial

mastectomy, either through local tissue rearrangement or mastopexy/reduction mammoplasty technique, is an extremely valuable tool in comprehensive oncologic treatment. These techniques leave patients with minimal breast deformities following proper treatment, without compromising oncologic safety. These are procedures that all reconstructive breast surgeons should be familiar with and offer their patients at the time of breast conserving surgery for breast cancer.

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Footnote

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Immediate breast volume replacement using a free dermal fat graft after breast cancer surgery: multi-institutional joint research of short-term outcomes in 262 Japanese patients

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Background: Immediate volume replacement using a free dermal fat graft (FDFG) has been proven safe with early postoperative benefits. The aims of the present study were to clarify adequate indications and risk factors associated with operative morbidity.

Patients and methods: A multi-institutional analysis of partial mastectomy with immediate volume replacement with FDFG was undertaken in 14 hospitals specializing in breast cancer treatment. Clinical and oncological variables were analyzed to identify factors associated with postoperative complications.

Results: A total of 262 cases were analyzed. Considering the observation period and overlap of patients, 13 (5.4%) out of 242 patients had complications within 1 month of surgery while 7 (4.6%) out of 151 patients developed complications 1-12 months after surgery. Two hundred and eleven out of 242 patients were statistically examined using a multivariate analysis, which revealed that the weight of resected breast tissue, size of implanted FDFG (cranio-caudal length), and weight of implanted FDFG were associated with a higher likelihood of postoperative complications.

Conclusions: Immediate breast volume replacement using a FDFG after breast cancer surgery should be done for selected patients with breast cancer to avoid postoperative complications. The prospective and larger investigations are warranted for the establishment of appropriate guidelines.

Keywords: Breast cancer; breast conservative surgery; cosmetic outcome; immediate breast reconstruction; free dermal fat graft (FDFG); oncoplastic surgery

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Introduction

In the 1980s, breast-conserving surgery (BCS) rapidly became the first-line procedure for early-stage breast cancer as it ensured local control and produced acceptable cosmetic results (1-4). Many factors are known to influence cosmetic outcomes (5-7), such as the tumor size and location in the breast parenchyma. Poor cosmetic results are related to larger tumors, especially relative to breast size, and to inner quadrant tumors. A previous study identified the factors influencing cosmetic outcomes after breast-conserving therapy (BCT) for breast cancer and suggested the importance of both tumor-related and treatment-related factors (8). Studies on oncoplastic surgery combining partial mastectomy with immediate volume replacement have been conducted in Japan, and some simple cosmetic techniques for repairing partial defects in various locations can be performed during BCT and have achieved excellent results (9-12). Since 2003, Kijima *et al.* has reported oncoplastic breast surgery (OBS) combining partial mastectomy and immediate volume replacement using a free dermal fat graft (FDFG). They performed a wide excision for cancer lesions in the upper inner quadrant and immediate reconstruction using FDFG from the lower abdomen with/without axillary lymphadenectomy. The early experiences of this surgical method were reported in detail and it was concluded to be useful for the immediate reconstruction of partial defects during BCT (13). Reconstructions using an autologous FDFG were easy to perform and produced excellent cosmetic results (14). However, guidelines to recommend which quadrant should be repaired by this method, references to the size of FDFG, and how often postoperative complications occur currently do not exist. Therefore, we examined a large multi-institutional data set of patients undergoing partial mastectomy or total mastectomy followed by immediate breast reconstruction using FDFG in order to determine what the risk factors for complications were and identify preoperative clinical factors associated with postoperative outcomes. We hypothesized that factors associated with complications may occur at a frequency that varies according to factors associated with the patient and also the surgeon, in addition to oncological findings such as the tumor location, size of partial mastectomy, as well as the existence of systemic diseases such as diabetes mellitus, a smoking habit, experience of the surgeon, case numbers in one institution, and details for surgery. The purpose of this study is to clarify the cause of postoperative complications after breast cancer surgery with

immediate volume replacement using FDFG routinely done in Japan and whether the indication should be determined.

Patients and methods

Patients

A retrospective analysis of a prospectively maintained database of patients undergoing BCS and immediate breast reconstruction using FDFG from 14 hospitals in Japan was performed with Institutional Review Board approval. Operative cases performed between October 2003 and December 2010 comprised the data set for this analysis. All patients underwent radical and curative resections. Fellowship-trained breast surgeons or plastic surgeons performed operative procedures at each institution. Each institution provided specified preoperative, operative, and postoperative data elements using a common menu-derived database file that incorporated precise coding instructions and dropdown menu options where appropriate. Patient selection, surgical procedures such as partial mastectomy (Bp), quadrantectomy (Bq), or total mastectomy (Bt), resection of the fascia of the major pectoralis muscle, and the choice of neo-adjuvant, adjuvant systemic, and postoperative radiation therapies were determined by the individual surgeon. The surgical period was recorded and included the waiting period for a pathological examination of surgical margins and/or sentinel lymph nodes. A data sheet was retrospectively collected as a questionnaire from each institution.

Surgical technique

Partial mastectomy or total mastectomy and immediate reconstruction using FDFG were basically carried out using a previously reported method (13). The operative defect was measured pre- and intra-operatively to decide the size of FDFG. Each surgeon/plastic surgeon chose the donor sites of FDFG freely (lower abdomen, lateral abdomen, inguinal region, and femoral region). After *in situ* de-epithelialization and sharp dissection, FDFG was harvested as a columnar-shaped specimen. Some surgeons used a knife for de-epithelialization, while others used scissors or a dermatome. We intraoperatively measured the defect size of the breast as the horizontal and cranio-caudal lengths and thickness of the resected gland. We trimmed the size of FDFG (horizontal and craniocaudal lengths, and cranial and caudal thicknesses) based on these measured

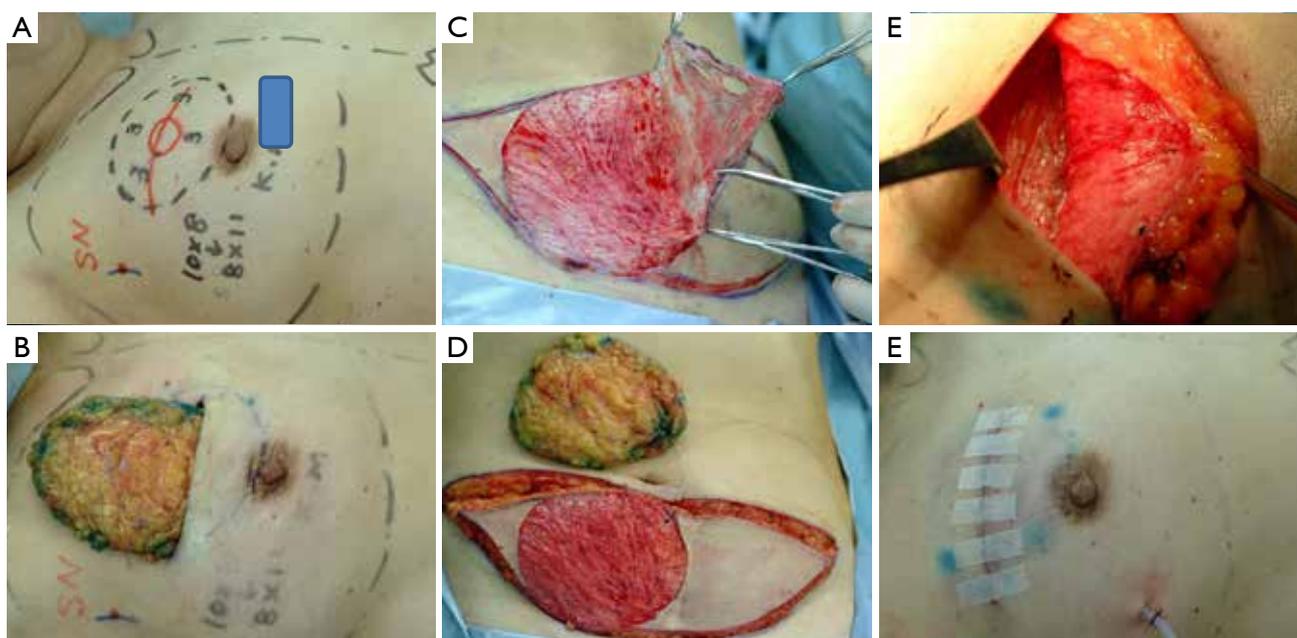


Figure 1 (A) Macroscopic findings of the breast and donor site with the patient in the operative position; (B) a cylindrical area of breast tissue including the fascia of the pectoralis major muscle was removed. Pathological examinations of three points along the surgical margin performed during the operation were negative; (C) de-epithelialization was then performed according to the conventional technique; (D) cylindrical free dermal fat graft (FDFG) composed of a de-epithelialized dermis and subdermal fatty tissue was harvested; (E) FDFG was turned over and implanted into the breast deformity facing the dermis and the surface of the pectoral major muscle; (F) findings at the end of the operation.

values. FDFG was inserted in an ideal direction that fit the dermis and irregular defects with the dermis facing the surface of the pectoralis major muscle (*Figure 1*). Details were recorded in *Table 1*.

Follow-up

Data were collected until June 2011. Postoperative complications were recorded until the latest time distinguishable by each surgeon (*Figures 2-4*).

Postoperative outcomes

Complications occurring within 1 month, 1 to 12 months, and over 12 months were recorded and included the following; skin necrosis, delayed wound healing, outflow of fat, and infection.

Patient selection

Two hundred and sixty-two data sheets were collected from 14 institutions for this retrospective study. To investigate

postoperative complications, we first excluded 20 patients because of a shorter observation period than 1 month or the lack of complete answers regarding postoperative complications. Two hundred and forty-two and 151 patients were analyzed to determine the incidence of postoperative complications within 1 month and 1 to 12 months, respectively. Before performing statistical analyses for postoperative risk factors, we furthermore excluded 31 and 13 patients from each phase for the following reasons: (I) patients without information on resected breast tissue, and (II) patients without information on implanted FDFG.

Patients, surgery, and oncological variables were analyzed to identify factors associated with postoperative complications for these two study periods: (I) within the first month and (II) 1 to 12 months after surgery. Thus, the numbers of cases used in the statistical analyses were 211 and 124 for the first and second study periods, respectively (*Figure 5*).

Statistics

A comparison of the distribution of categorical variables

Table 1 Patient characteristics			
Characteristics	All, n=262	Follow-up (1 month), n=211	Follow-up (1-12 months), n=124
Median age: years [range]	49.5 [26-75]	49 [26-74]	49 [26-74]
Median BMI [range]	22.4 [16.7-36.8]	21.8 [16.8-36]	21.4 [16.8-36]
Smoking [%]			
Yes	19 [7]	12 [6]	6 [5]
PAST	3 [1]	3 [1]	1 [1]
No	221 [84]	185 [88]	114 [92]
NA	19 [7]	11 [5]	3 [2]
Systemic diseases [%]			
None	229 [87]	184 [87]	110 [89]
DM	4 [2]	2 [1]	1 [1]
Hyperlipidemia	3 [1]	3 [1]	3 [2]
Others	14 [5]	14 [7]	6 [5]
Multiple	4 [2]	2 [1]	1 [1]
NA	8 [3]	6 [3]	3 [2]
Tumor location [%]			
Upper-inner	77 [29]	61 [29]	32 [26]
Upper-outer	32 [12]	21 [10]	14 [11]
Upper	29 [11]	27 [13]	18 [15]
Lower-inner	22 [8]	19 [9]	11 [9]
Lower-outer	34 [13]	26 [12]	14 [11]
Lower	15 [6]	13 [6]	7 [6]
Inner	20 [8]	17 [8]	10 [8]
Outer	15 [6]	15 [7]	9 [7]
Central	10 [4]	9 [4]	7 [6]
All areas	5 [2]	2 [1]	1 [1]
NA	3 [1]	1 [0.5]	1 [1]
Preoperative treatment [%]			
Chemotherapy	11 [4]	7 [3]	2 [2]
Endocrine therapy	3 [1]	2 [1]	0 [0]
Biopsy	3 [1]	2 [1]	2 [2]
None	245 [94]	200 [95]	120 [97]
Preoperative clinical T stage [%]			
T0 Tis	41 [16]		
T1	124 [47]		
T2	85 [3]		
T3	4 [1]		
NA	8 [3]		

Table 1 (continued)

Table 1 (continued)			
Characteristics	All, n=262	Follow-up (1 month), n=211	Follow-up (1-12 months), n=124
Preoperative clinical N stage [%]			
N0	218 [83]		
N1	32 [12]		
N2	2 [0.7]		
NA	21 [8]		
Preoperative clinical M stage [%]			
M0	251 [96]		
M1	0 [0]		
NA	11 [4]		
Type of mastectomy [%]			
Bp	199 [76]	174 [82]	116 [94]
Bq	52 [20]	37 [18]	8 [6]
Bt	11 [4]	0 [0]	0 [0]
Resection of the fascia of Mj [%]			
Yes	109 [42]	75 [36]	27 [22]
No	151 [58]	136 [64]	97 [78]
NA	2 [1]	0 [0]	0 [0]
Thickness of skin above the resected area [%]			
0-5 mm	75 [29]	66 [31]	25 [20]
-10 mm	20 [8]	14 [7]	10 [8]
-20 mm	10 [4]	5 [2]	5 [4]
21 mm-	132 [50]	120 [57]	82 [66]
Unknown	13 [5]	4 [2]	1 [1]
NA	12 [5]	2 [1]	1 [1]
Axillary dissection [%]			
Yes	59 [23]		
SNB	190 [73]		
No	4 [1]		
NA	9 [3]		
Median size of resected breast tissue: cm [range]			
Horizontally	7.8 [3-19.5]	7.5 [3-19.5]	7.5 [3-17]
Vertically	7.0 [3-17.5]	7.0 [3-17]	6.8 [3.5-17]
Median thickness of resected breast tissue: cm [range]			
	2.0 [0.3-6.5]	2.0 [0.3-8.0]	2.0 [0.7-8]
Median amount of resected breast tissue: g [range]			
	63 [14-230]	62 [14-230]	54 [14-230]
Instruments for denuding [%]			
Knife	247 [94]	201 [95]	120 [97]
Scissors	12 [5]	10 [5]	4 [3]
Dermatome	3 [1]	0 [0]	0 [0]

Table 1 (continued)

Table 1 (continued)

Characteristics	All, n=262	Follow-up (1 month), n=211	Follow-up (1-12 months), n=124
Preparation of FDFG [%]			
Denuding first	242 [92]	195 [92]	117 [94]
Harvesting first	14 [5]	12 [6]	6 [5]
NA	6 [2]	4 [2]	1 [1]
Median size of FDFG: cm [range]			
Horizontally	7.0 [3-22]	7.0 [3-20]	7.0 [3-17]
Vertically	6.0 [3-19]	6.0 [3-19]	6.0 [3-19]
Median thickness of FDFG: cm [range]	2 [0.8-8.0]	2.0 [0.8-8]	2.0 [0.8-8]
Median amount of implanted FDFG: g [range]	54.5 [10-215]	55 [10-215]	50 [12-215]
Placement of a drain into the implanted area [%]			
Closed suction drain	210 [80]	187 [89]	114 [92]
No	45 [17]	21 [10]	9 [7]
Open drain	3 [1]	3 [1]	1 [1]
NA	4 [2]	0 [0]	0 [0]
Placement of a drain into the donor site [%]			
Yes	71 [27]	55 [26]	26 [21]
No	176 [67]	149 [71]	94 [76]
NA	15 [6]	7 [3]	4 [3]
Median total surgical period: minutes [range]	150 [65-500]	150 [65-311]	155 [94-300]
Median total plastic period: minutes [range]	60 [19-167]	60 [19-167]	60 [28-100]
Bleeding: median [range]	73 [0-630]	71 [0-630]	69 [0-400]
Postoperative systemic therapy [%]			
Chemotherapy*	33 [13]	21 [10]	12 [10]
Endocrine therapy**	135 [52]	122 [58]	68 [55]
Chemo and endocrine therapy	33 [13]	25 [12]	18 [15]
No	42 [16]	33 [16]	19 [15]
NA	19 [7]	10 [5]	7 [6]
Radiation therapy [%]			
Yes	177 [68]	154 [73]	94 [76]
No	71 [27]	49 [23]	29 [23]
NA	14 [5]	8 [4]	1 [1]
Median postoperative period of radiation therapy: months [range]	16 [2-52]	16 [4-52]	23 [5-52]
Median exposure dose: Gray [range]	50 [46-60]	50 [46-60]	50 [46-50]

*, FEC, CE, Taxane, TC, AC, UFT, Trastuzumab, GEM, CMF; **, AI, TAM, LH-RH ag, tremifen. Abbreviations: Bp, partial mastectomy; Bq, quadrantectomy; Bt, total mastectomy; BMI, body mass index; DM, diabetes mellitus; NA, not available; SNB, sentinel lymph node biopsy.

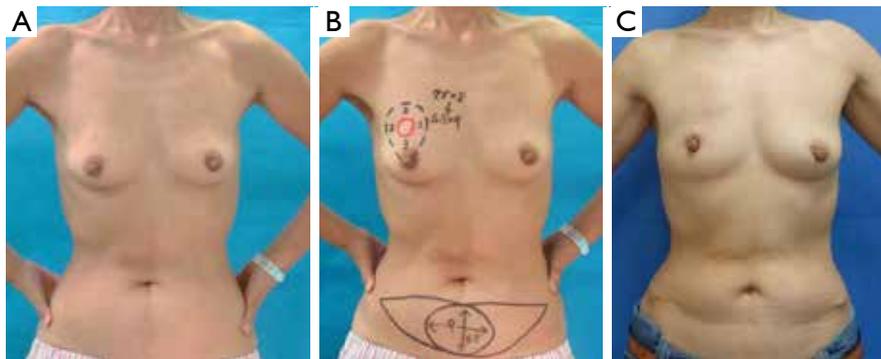


Figure 2 (A) Preoperative findings of a 52-year-old patient with right breast cancer; (B) preoperative designs of the breast and donor site (lower abdomen). The resected area of the breast was marked in the supine position with a black dotted line (black dotted line) with a gross margin of 2-3 cm from the cancer lesion (red circle). The resected size and weight of the breast were $7.5 \times 8 \times 1.5 \text{ cm}^3$ and 83 g, respectively. The partial defect was replaced immediately with FDFG from the lower abdomen; $6.5 \times 9 \times 1.5 \text{ cm}^3$, 55 g; (C) gross findings of the patient 5 years postoperatively.

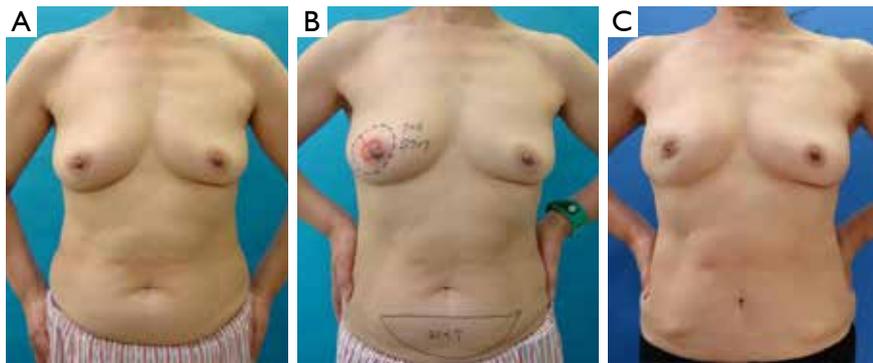


Figure 3 (A) Preoperative findings of a 58-year-old patient with right breast cancer; (B) preoperative designs of the breast and donor site (lower abdomen). The resected area of the breast was marked in the supine position with a black dotted line (black dotted line) with a gross margin of 2 cm from the cancer lesion (red circle). The resected size and weight of the breast were $7 \times 7 \times 1.5 \text{ cm}^3$ and 60 g, respectively. The partial defect was replaced immediately with FDFG from the lower abdomen; $7 \times 7 \times 1.5 \text{ cm}^3$, 80 g; (C) gross findings of the patient 6 years postoperatively.

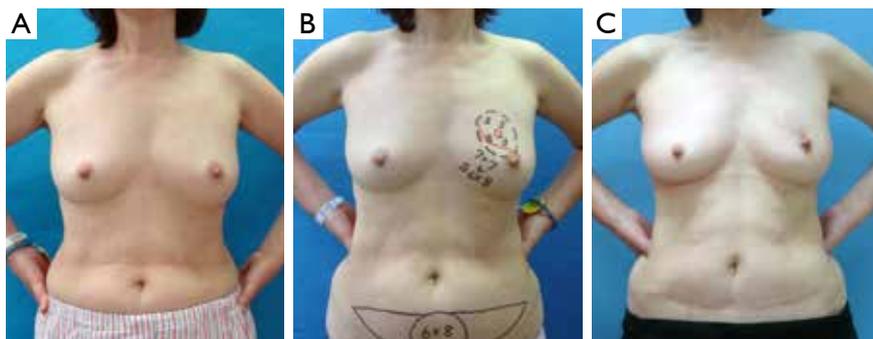


Figure 4 (A) Preoperative findings of a 56-year-old patient with right breast cancer; (B) preoperative designs of the breast and donor site (lower abdomen). The resected area of the breast was marked in the supine position with a black dotted line (black dotted line) with a gross margin of 3 cm from the cancer lesion (red circle). The resected size and weight of the breast were $7 \times 7 \times 1.5 \text{ cm}^3$ and 94 g, respectively. The partial defect was replaced immediately with FDFG from the lower abdomen; $6 \times 8 \times 2.5 \text{ cm}^3$, 80 g; (C) gross findings of the patient 6 years postoperatively.

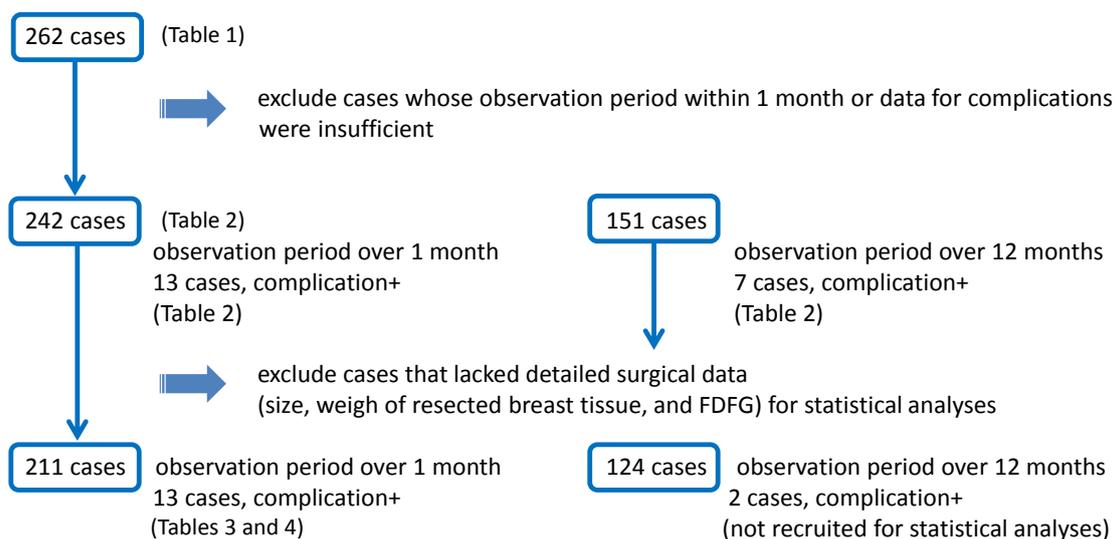


Figure 5 Case numbers analyzed in this study.

between patients with and without complications was performed using the chi-square test. The Mann-Whitney U test was used for continuous variables. In addition, these variables were categorized into two or three groups and analyzed by the chi-square test. Variables with $P < 0.05$ on either the chi-square test or Mann-Whitney U test were applied for further analyses to estimate odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) using a logistic regression model in adjusting for the effect of the experience of the surgeon/plastic surgeon. The risk of postoperative complications with changes in continuous variables was examined by the likelihood ratio test. Significance was defined as $P < 0.05$. All P values are two-sided.

Results

Background and surgical procedure (Table 1)

Between October 2003 and December 2010, 262 patients underwent partial/total mastectomy followed by immediate breast reconstruction using FDFG at 14 institutions in Japan. Over that period, 251 patients underwent partial mastectomy and 11 underwent total mastectomy. The indication for this treatment depended on each institution and individual surgeon. The indications for BCS using FDFG were as follows: all patients who were selected to undergo partial mastectomy in 0 institutions; tumor locations in three; for research in one; size and shape of the

breast in three; and others in four institutions, respectively.

The median age and median body mass index (BMI) of patients were 49.5 (range, 26–75) years and 22.4 (range, 16.7–36.8) years, respectively. The clinical, preoperative, and oncological data of patients are listed in *Tables 1* and *2*. Twenty-two patients had a history of smoking. Systemic diseases such as diabetes mellitus, hyperlipidemia, and others, were identified in 5, 10, and 14 patients, respectively. Cancer lesions were located in the upper-inner quadrant area in 77 patients, upper-outer in 32, upper (upper-inner and upper-outer) in 29, lower-inner in 22, lower-outer in 34, lower in 15, inner in 20, outer (upper-outer and inner-outer) in 15, central in 10, and all areas in 5, respectively. Preoperative systemic therapy involving chemotherapy and endocrine therapy was administered to 11 and 3 patients, respectively. Incisional biopsy for diagnosis was performed in 4 patients.

Partial mastectomy was performed in 199 patients, quadrantectomy in 52, and total mastectomy in 11. Sentinel lymph node biopsy and axillary lymph node dissection were performed in 190 and 59 patients, respectively. The fascia of the major pectoralis muscle was completely removed in 109 patients. The thickness of the skin above the resected area was 0–5 mm in 75 patients, 6–10 mm in 20, 11–20 mm in 10, and over 21 mm in 132. The median size of resected breast tissue was 7.8 (range, 3.0–19.5) cm horizontally and 7.0 (range, 3.0–17.5) cm vertically. The median thickness and weight of resected breast tissue were 2.0 (range, 0.3–6.5) cm and 63 (range, 14–230) g, respectively.

Table 2 Postoperative complications

Complications	Observation period	
	(<1 month) n=242	(1-12 months) n=151
Postoperative complications		
No	198	110
Yes	13*	14**
Skin necrosis	3	3
Bleeding	0	0
Wound delay	2	4
Outflow of fat	8	8
Infection	3	7
Complications in the donor site (during the observation period)		
No		
Glad [new body image]	38	13
Acceptable	70	19
Yes		
Unacceptable	0	0
Others	4	1
NA	130	119

*, Three patients developed multiple complications; **, Seven patients continuously exhibited complications from one month after surgery. NA, not available.

In the plastic procedures performed, denuding was achieved with a knife in 247 patients, scissors in 12, and dermatome in 3, respectively. Concerning the preparation of FDFG, denuding was performed ahead of harvesting in 237 patients whereas harvesting was conducted ahead of denuding in 14 patients, respectively. The median size of FDFG was 7.0 (range, 3.0-22.0) cm horizontally and 6.0 (range, 3.0-19.0) cm vertically. The median thickness and weight of FDFG were 2.0 (range, 0.8-8.0) cm and 54.5 (10-215) g, respectively. A closed suction drain or open drain was placed in the implanted area in 210 and 45 patients, respectively.

The median total surgical period and total plastic period were 150 (range, 65-500) minutes and 60 (range, 19-167) minutes, respectively. Median bleeding was 73 (range, 0-630) g.

Chemotherapy was administered as postoperative systemic therapy to 33 patients, endocrine therapy to 135, chemotherapy followed by endocrine therapy to 33, and no treatment in 42, respectively (*Table 1*). The chemotherapy regime and endocrine therapy were FEC (fluorouracil,

epirubicin and cyclophosphamide), CE (epirubicin and cyclophosphamide), Taxane (docetaxel or paclitaxel), TC (docetaxel and cyclophosphamide), AC (doxorubicin and cyclophosphamide), UFT (uracil-tegafur), GEM (gemcitabine), CMF (cyclophosphamide, methotrexate and fluorouracil), Trastuzumab, and AI (aromatase inhibitor: anastrozole or letrozole), TAM (tamoxifen), LH-RH ag (goserelin acetate implant or leuprorelin acetate), tremifen.

Prior to performed analyses, we excluded 20 cases with observation periods within 1 month or incomplete data for postoperative complications (*Figure 5*).

Postoperative complications (*Table 2*)

Complications occurred in 13 patients within 1 month of surgery, with skin necrosis in 4, delayed wound healing in 3, outflow of fat in 4, and infections in 2 multiple complications were observed in 3 patients.

Fourteen patients developed postoperative complications between 1 to 12 months after surgery while seven patients continuously exhibited complications from 1 month after surgery as 22 events. Skin necrosis occurred in 3 patients, delayed wound healing in 4, outflow of fat in 8, and infections in 7 patients. Multiple complications were observed in 4 patients.

Fatty melting and wound healing delay were observed in one patient over 12 months after surgery.

All complications were managed conservatively with antibiotics and/or prolonged drainage and/or debridement. Regarding the relationship between follow-up and the overlap of patients with complications, 13 (5.7%) out of 242 patients developed complications within one month of surgery, 7 (4.6%) out of 151 patients between 1 and 12 months after surgery, and one (1.4%) out of 72 patients over 12 months after surgery, respectively. We then examined the relationship between postoperative complications and clinical and technical factors within 1 month and 1-12 months postoperatively. According to the exclusion of insufficient cases (*Figure 2*), 13 and two patients who developed postoperative complications within 1 month and 1-12 months, respectively, were recruited for further statistical analysis, while the total numbers of patients in each period were 211 and 124, respectively. Two cases were considered to be inappropriate for inclusion in an analysis of the relationship between postoperative complications and clinical factors; therefore, we analyzed 13 out of 211 patients who had postoperative complications between 1 to 12 months after surgery.

Complication rates in 14 institutions

The number of complication-positive cases ranged between 0 and 5 (55.6%). Postoperative complications were not observed in any patients in nine institutions.

Postoperative complications in the donor site (Table 2)

Complications in the donor site were observed in 114 cases only. Thirty-nine patients (14.9%) felt comfortable or good with their new body image, 71 (27.1%) felt that their appearance was acceptable, and 4 (1.5%) felt that it was unacceptable at the donor site.

Univariate cox-regression analysis for postoperative complications

We excluded some cases as insufficient because they lacked detailed surgical data for statistical analyses such as the size and weight of resected breast tissue and implanted FDFG. Two hundred and eleven and 124 cases were examined. The number of surgeries performed at each institution, the experience of the surgeon, smoking habit, systemic diseases, plastic period, intraoperative bleeding, resection of the fascia of the major pectoralis muscle, thickness of the skin paddle, size of resected breast tissue (cranio-caudal length of tissue), weight of resected breast tissue, size of implanted FDFG (cranio-caudal length), weight of implanted FDFG, and avoidance of postoperative radiation for remnant glands were risk factors for within one month (Table 3).

Multivariate cox-regression analysis for complications within one month of surgery

Variables showing a correlation with postoperative complications within one month on either the chi-square test or Mann-Whitney U test were applied to further analyses using a multivariate logistic regression model adjusting for the effect of the experience of the surgeon/plastic surgeon. Further analyses for postoperative complications 1-12 months after surgery were not carried out as there were only two patients with complications during that period. A multivariate analysis revealed that the weight of resected breast tissue, size of implanted FDFG (cranio-caudal length), and weight of implanted FDFG were associated with a higher likelihood of postoperative complications after OBS combining partial mastectomy with immediate volume replacement using FDFG (Table 4).

Discussion

BCT has rapidly become the first-line procedure for early-stage breast cancer, ensures local control, and produces acceptable cosmetic results (1,2). Cosmetic results have been associated with psychological morbidity in patients who have undergone BC (2-4). OBS, which combines the concepts of both oncologic and plastic surgeries, is becoming more common, especially in Western countries (15,16). Many different techniques are performed in OBS, one of which involves the careful planning of skin and parenchymal excisions, reshaping of the gland after parenchymal excision, and repositioning of the nipple areola complex to the center of the breast mound with or without a correction to the contralateral breast for better symmetry (17). According to Hoffmann's classification of OBS, there are four categories in BCT due to technical complexity and difficulty. They recommended that an oncoplastic procedure should be performed for cosmetic reasons if the breast defect after partial mastectomy was over 25% of the total size of the breast (18).

Autologous FDFG has been used sporadically for soft tissue augmentation. Previous studies reported that an ideal reconstructive technique in the field of the surgical treatment of head and neck diseases would be easy, inexpensive, single-stage, and autologous (19,20). BCS and immediate reconstruction using FDFG were shown to be effective for selected patients with small breasts and a slim body in a retrospective study at a single institution (13,21). A study has not yet been conducted to compare other breast reconstruction methods using vascularized flaps and fat injections with this method (14). In a previous study, the operative procedure and cosmetic results were retrospectively compared among three groups according to the reconstructive procedure that was used for the defect following partial mastectomy. Patients receiving immediate volume replacement using a mini flap of the latissimus dorsi (LD group) achieved better cosmetic results than those receiving only rotation and fixation of the parenchymal adipose tissue or gland to repair the defect. Disadvantages observed in the LD group over the FDFG group were longer operation durations, more bleeding, higher rates of postoperative complications, and longer hospital stays. Fat injections represent a complementary technique that is ideal for autologous reconstruction using the LD flap because its muscle and fat act as an ideal recipient site for fatty tissue grafts (22). It is an excellent technique that can be applied to all patients, except those with no potential fat deposits.

Table 3 Analysis of variables associated with postoperative complications

Variable	Complications (<1month)		Complications (1-12 months)	
	P value*	P value**	P value*	P value**
Number of patients in an institution	<0.001		0.001	
Experience of the surgeon/plastic surgeon		<0.001		0.003
Age		NS		NS
BMI		NS		NS
Smoking habit	0.006		NS	
Systemic diseases	0.007		0.014	
Tumor location	NS		NS	
Preoperative systemic treatment	NS		NS	
Surgical period		NS		NS
Plastic period		0.014		NS
Intraoperative bleeding		0.040		NS
Type of partial mastectomy	NS		NS	
Resection of the fascia of the major pectoralis muscle	<0.001		<0.001	
Thickness of the skin paddle (<20 mm)	<0.001		<0.001	
Size of the resected breast; medial-lateral length		NS		NS
Size of the resected breast; cranio-caudal length		0.009		NS
Thickness of resected breast tissue		NS		NS
Weight of resected breast tissue		0.011		0.029
Size of implanted FDFG; medial-lateral length		NS		NS
Size of implanted FDFG; cranio-caudal length		<0.001		0.005
Thickness of implanted FDFG		NS		NS
Weight of implanted FDFG		<0.001		0.004
Suction drainage to the implanted area	NS		NS	
Avoidance of postoperative radiation therapy	0.004		0.002	
Systemic adjuvant therapy	NS		NS	

*, P values were obtained by the chi-square test; **, P values obtained by the Mann-Whitney U test. Abbreviations: Bp, columnar-shaped partial mastectomy; Bq, quadrantectomy; NS, not significant; DM, diabetes mellitus; HT, hypertension; NA, not available.

Fat injections can also be used for implant reconstruction, replacement of an implant, and revision after a vascularized flap. Lipofilling and adipose tissue containing flap (e.g., TRAM, DIEP) have been well known as vascular-rich and oncologically safe grafts to repair a defect after partial and total mastectomy. Unfortunately there is no literature in which the clinical and basic results were compared between those techniques and the immediate volume replacement using FDFG. To compare the results and discuss the differences between them, the further research should be needed. Only one literature used a rat model implanted FDFG reported the histological findings of implanted

FDFG, the vascularity and apoptotic resistance (23). From their conclusion, we presume that the implanted FDFG in the clinical case is maintained by the vascularization of a certain degree.

Immediate volume repair for the partial defect after BCS in each institution was as follows; OBS using FDFG was selected for all patients who were indicated for BCS in 0 institution; the other volume replacement technique using autologous tissue such as a latissimus dorsi muscle flap or local tissue flap was selected in two institutions; volume displacement using parenchymal breast tissue was selected in nine institutions; no volume replacement or displacement

Table 4 The results of a logistic regression analysis of the variables associated with postoperative complications within 1 month

Variable	With complications (N=13)	Without complications (N=198)	Adjusted odds ratio* (95% confidence interval)
Number of patients in an institution			
<10	7	28	5.6 (1.7-19)
10-	6	170	1.0
Experience of the surgeon/plastic surgeon (P for trend =0.004**)			
<10 years	1	8	3.9 (1.2-13)
10-20 years	6	38	3.1 (0.3-29)
>21 years	6	50	1.0
Smoking habit			
No	7	178	1.0
Yes	3	12	8.3 (1.6-43)
Systemic diseases			
No	8	176	1.0
DM, HT, others	4	17	5.7 (1.5-22)
Plastic period (minutes) (P for trend =0.339**)			
<60	2	64	1.0
60-	9	110	0.4 (0.1-1.9)
90-	2	14	0.4 (0.04-2.9)
Intraoperative bleeding (mL) (P for trend =0.015)			
<100	12	12	1.0
100-	1	67	7.8 (1.0-62)
Resection of the fascia of the major pectoralis muscle			
No	0	136	1.0
Yes	13	62	NA
Thickness of the skin paddle (mm)			
<20	12	73	1.0
20-	0	120	NA
Size of the resected breast; cranio-caudal length (cm) (P for trend =0.023)			
<8	5	135	1.0
8-	3	31	2.3 (0.5-10)
9-	5	26	4.6 (1.2-18)
Weight of resected breast tissue (g) (P for trend =0.017**)			
<100	5	156	1.0
100-	4	28	3.4 (0.8-14)
Size of implanted FDFG; cranio-caudal length (cm) (P for trend =0.022**)			
<6	2	110	1.0
6-	2	27	3.8 (0.5-29)
7-	9	34	11 (2.0-55)
Weight of implanted FDFG (g) (P for trend =0.003)			
<80	2	134	1.0
80-	7	44	7.5 (1.4-39)

Table 4 (continued)

Table 4 (continued)

Variable	With complications (N=13)	Without complications (N=198)	Adjusted odds ratio* (95% confidence interval)
Postoperative radiation therapy			
No	7	42	1.0
Yes	5	149	0.3 (0.1-1.2)

*, Adjusted odds ratios and corresponding 95% confidence intervals were obtained by a logistic regression analysis to adjust for the effect of the experience of surgeon/plastic surgeon; **, P values for trends were obtained by the likelihood ratio test. Abbreviations: DM, diabetes mellitus; HT, hypertension; NA, not available.

was selected in two institutions.

The relationship between postoperative complications and clinical and technical factors after surgery was assessed using a univariate cox-regression analysis and the results obtained identified the number of patients in each institution, the experience of the surgeon/plastic surgeon, BMI, smoking habit, resection of the fascia of the major pectoralis muscle, thinner (<20 mm) skin envelope, larger FDFG in the cranio-caudal length (>6 cm), and devices used for denuding as significant risk factors for postoperative complications. A multivariate cox-regression analysis revealed that the experience of the surgeon/plastic surgeon, heavier breast tissue (>100 g), larger FDFG in the cranio-caudal length (6 cm), and thicker FDFG (>3 cm) were significant risk factors for postoperative complications. No significant differences were observed in postoperative complications or oncological factors such as the tumor size, location, and preoperative and postoperative therapy for cancer control. The number of complication-positive cases ranged between 0 and 5 (55.6%) in 14 institutions. No postoperative complications were observed in any patients in 9 institutions, whereas the incidence of these complications was high in one institution (55.6%). Although a learning curve or skill in avoiding postoperative complications may exist, no significant difference was noted between postoperative complications and the experience of the breast surgeon or plastic surgeon by a multivariate cox-regression analysis; however, since this study was retrospective, not prospective, bias may exist that should be taken into consideration. Over 50% of all tumors were located in the upper-inner, upper-outer, or upper area. Although partial mastectomy with immediate breast reshaping using FDFG provided excellent results for patients with a slim body and diagnosed early with breast cancer in the upper-inner quadrant area (13), it currently remains unknown whether partial mastectomy can be safely

performed in this area in a patient with slim body and small breasts. The results to avoid postoperative complication in this study maybe introduce rather than contra-indication on such cases.

In the upper areas (A or C), we trimmed the thickness of FDFG so that it easily fit the defect. FDFG was made thinner to replace the upper portion of the breast, and thicker to replace the area under the nipple-areolar complex. In the lower areas (B or D), we could not repair the defect to adjust the thickness of FDFG and resected breast tissue because of a limitation in the thickness of the donor site of FDFG. This procedure was originally performed on and indicated for slim patients with early breast cancer in the upper areas of small breasts (13). However, this study revealed that this procedure could be performed on patients with lower lesions (72 cases) and for patients with a BMI over 25 (46 cases). Furthermore, these were not risk factors for postoperative complications.

The BMI of our patients ranged between 16.7 and 36.8 with an average of 22.4. Therefore, we cannot currently confirm that OBS is adequate for Western women with higher BMI. We can only state that even patients with high BMI were able to undergo BCS with immediate volume replacement using FDFG if their resected breasts had a cranio-caudal length of under 8 cm, a weight under 100 g, implanted FDFG had a cranio-caudal length of under 6 cm, the weight of implanted FDFG was under 80 g, and postoperative radiation therapy was administered. Under these conditions, early breast cancer without widely spreading intraductal components that is located in the upper-inner quadrant area in which breast thickness is relatively thin in any patient with high or low BMI may be good indications in Western women.

In this study, the percentage of irradiation at each institution ranged between 0% (two institutions that enrolled four and five patients to this study, respectively)

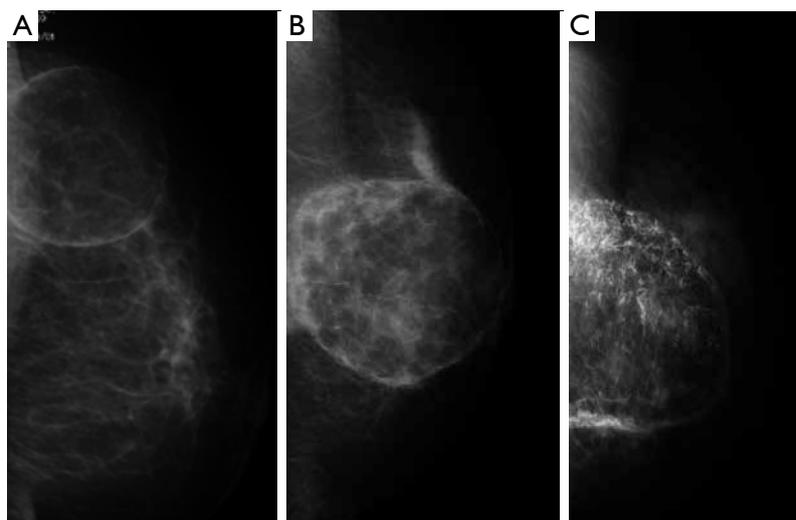


Figure 6 Mammography findings. According to implanted FDFG findings, there were three patterns. (A) Same density as fatty tissue; (B) Higher density than fatty tissue; (C) with coarse calcifications.

and 100%. A reverse correlation was observed between postoperative radiation therapy and postoperative complications. Although the rate of complications was predicted to be high in the irradiation group, the reverse was observed. The prolonged development of postoperative complications may account for why postoperative radiation therapy was not administered adequately. To resolve this question, further studies should be planned prospectively with particular indications for surgical, systemic, and radiological treatments. Adverse results to control tumor progression should also be analyzed individually in the next step of this study.

A disadvantage of this procedure is the horizontal scar on the lower abdomen (13). Although 161 patients left the answer box blank, 39 answered that they were happy with the results, 71 said they were acceptable, and 4 were not happy. Middle-aged to elderly Japanese women are not in the habit of wearing bikinis, and sunbathing and swimming in the sea are not popular activities. Therefore, this may explain the low complication rate regarding the donor site.

This study had important limitations. It was a retrospective study and data was collected from several institutions retrospectively. A prospective study needs to be conducted in order to demonstrate that OBS combining partial mastectomy with immediate volume replacement using autologous FDFG is a feasible procedure for selected cases. In addition, there was a lack of cosmetic evaluations. Although one institution reported cosmetic advantages over other techniques for selected patients, we did not

examine this point. Further prospective or randomized and larger analyses are needed regarding cosmetic results. In the present study, data were collected without any pilot study for the protocol used or training for this procedure; therefore, the quality of the technique and skill set were completely dependent on the surgeon. This is the first study to describe this procedure in multiple institutions.

Fat necrosis can typically develop within 2-3 years of surgery or longer. Therefore, the relationship between the extent of fat necrosis and worse cosmetic results needs to be determined over a longer observation period. Implanted FDFG had three patterns on mammography; a mass with lower density than fatty tissue; a mass with the same density as parenchymal tissue; and a mass with coarse calcifications (*Figure 6*). After analyzing the questionnaire of this study, we were unable to detect any difference in the hardness of FDFG between the radiated and irradiated groups. Appropriate guidelines should be established for this technique in order to reduce postoperative complications. A longer follow-up period of 5 years is also essential for assessing the delayed development of complications and cosmetic results. A previous study conducted in one institution, showed that postoperative cosmetic problems and fibrous degeneration of FDFG are associated with this procedure (13,21). In the present study, postoperative breast form was excluded from the postoperative complications examined. We should have clarified postoperative complications based on the experience of the surgeon, techniques used, procedures performed, and

treatment-related factors by collecting data from non-selected institutions. We are aware of the necessity of a further study to objectively evaluate the hardness of the breast and cosmetic results. In the present study, we could not differentiate fat necrosis from degenerated FDFG using ultrasonography or other objective findings. Image evaluations by central judgments and histopathological analysis of implanted FDFG are also required. The experience of the included institutions with this procedure varied widely, and may have impacted on the results obtained. Future studies should involve a larger sample size and longer follow-up, and also examined the various clinical applications of our technique.

Conclusions

OBS combining partial mastectomy and immediate volume replacement using FDFG can be performed safely with a low incidence of postoperative complications; however, the complete avoidance of postoperative complications is essential. A learning curve under an experienced surgeon may be necessary for young breast surgeons or plastic surgeons. Immediate breast volume replacement using a FDFG after breast cancer surgery should be done for selected patients, and also the prospective and larger investigations are warranted for the establishment of appropriate guidelines.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Oncoplastic volume replacement technique for the upper inner quadrant using the omental flap

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Background: In breast-conserving surgery (BCS), a large defects in the upper inner quadrant (UIQ) named the no man's land of the breast will cause shift the nipple in an unnatural upward or medial fashion. We have developed oncoplastic volume replacement techniques using a laparoscopically harvested omental flap (OF). This paper presents our experiences performing partial breast reconstruction for the defect in the UIQ using the OF.

Methods: A wide excision (>20% of the breast tissue) was performed mainly through a periareolar incision. The pedicled OF was harvested laparoscopically. A small incision was made along the medical inframammary fold and a subcutaneous tunnel was created towards the xyphoid process. The OF was extracted through the tunnel, and used to fill the defect in the UIQ.

Results: Thirty patients were included in this study. The median resected breast volume was 142 g. A donor-site complication was only one ventral hernia. The surgical margins were positive in one patient (3.3%), and neither local nor systemic recurrence has occurred during medial follow-up periods of 64 months. Cosmetic outcomes were mostly satisfactory with negligible donor-site scars, and more than 80% of the patients scored excellent or good.

Conclusions: The OF is a useful volume replacement technique for the UIQ which is the most difficult quadrant for the other distant flaps.

Keywords: Omental flap (OF); oncoplastic surgery; volume replacement; upper inner quadrant (UIQ)

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Introduction

Oncoplastic breast-conserving surgery (BCS) can be classified as volume displacement or volume replacement. Many local and distant flaps have been developed for volume replacement. The LD flap plays a major role in volume replacement (1,2), but has the major disadvantages of donor site morbidity and deformity such as postoperative seroma formation and impairment of shoulder function (3,4).

Lateral chest wall perforator flaps have been described to minimize these problems, including use of the thoracodorsal artery perforator (TDAP) flap, and the lateral intercostal artery perforator (LICAP) flap (5). However, it is generally difficult to utilize these perforator flaps in partial breast

reconstruction for medial located tumors because adequate mobilization and a longer pedicle are needed to reach and replace the distant defect of the breast tissue (6,7).

Defects in the lower inner quadrant can be addressed using the abdominal adipofascial flap (8,9) and the anterior intercostal artery perforator (AICAP) flap (10). However, it is still difficult to utilize these flaps for the upper inner quadrant (UIQ) which constitutes a major part of a no man's land of the breast.

Since April 2002, we have performed more than 170 cases of immediate breast reconstruction with a laparoscopically harvested omental flap (OF) (11,12), and previously reported the results of partial reconstruction for the lower inner quadrant (13). Here, we present the

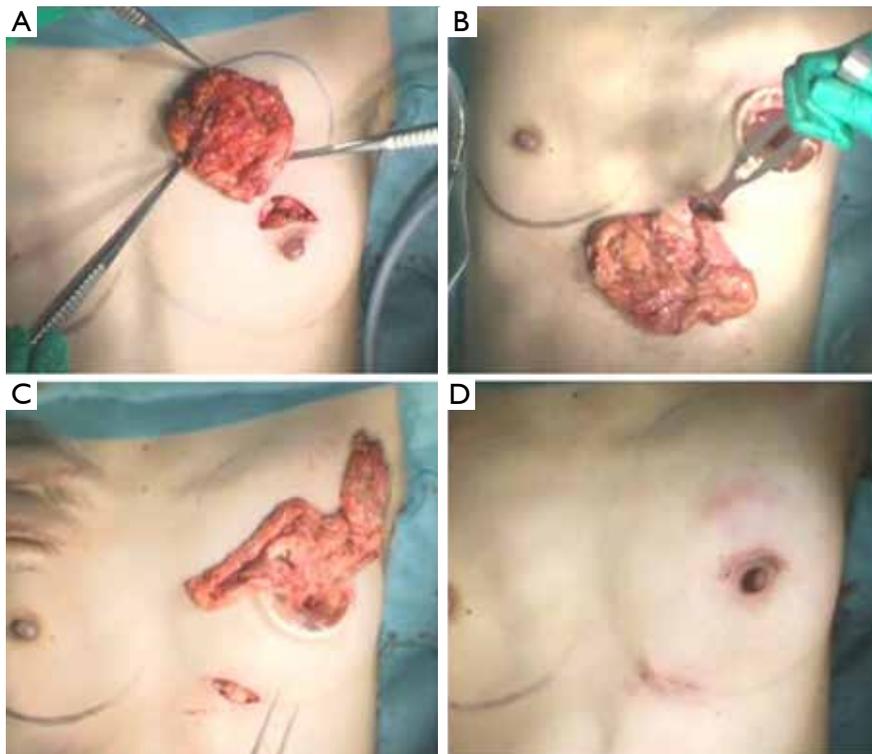


Figure 1 (A) A periareolar incision was made and wide excision was completed; (B) a small incision was made along the medial inframammary fold, and a pedicled omental flap was extracted through the subcutaneous tunnel; (C) the omental flap was passed under the subglandular tunnel, and filled the defect in the upper inner quadrant; (D) a closed suction drain was inserted over the OF and the incision was closed in two layers.

oncological and cosmetic outcomes in a series of 30 of partial breast reconstruction with the OF for the most difficult quadrant; the UIQ of the breast.

Materials and methods

Between April 2002 and December 2013, immediate partial breast reconstruction with the OF was performed for 30 patients with a tumor in the UIQ of the breast. All the tumors were evaluated preoperatively using mammography, ultrasound, and magnetic resonance imaging. Wide excisions (>20% of the breast tissue) were planned to achieve negative margins. The procedure was not performed in patients with a history of intraabdominal malignancy or upper abdominal laparotomy. However, patients with a history of laparoscopic surgery such as laparoscopic cholecystectomy or lower abdominal surgery such as Caesarean section were not excluded from the indication. Patients with a body mass index (BMI) ≥ 35 kg/m² were also excluded. The study was approved by the hospital ethics committee and all patients

provided written informed consent.

Surgery was performed in a supine position with the ipsilateral arm rested at 90° abduction. A periareolar incision was the first choice (*Figures 1,2*), however, when the skin over the tumor needed to be resected for an oncological reason, an elliptical radial or a transverse skin incision was chosen (*Figure 3*). The skin flap around the UIQ was then widely elevated to the lateral wedge of the sternum medially, and to the subclavicle cranially. A partial mastectomy was carried out, excising the tumor with a margin of at least 2 cm of normal breast tissue (*Figures 1A,2A,3A*). A 2- to 6-cm skin incision was made along the axillary skin crease and sentinel lymph node biopsy or axillary dissection was performed.

Laparoscopy for harvesting the OF was then performed, as described in detail elsewhere (12). First, the omentum was dissected from the transverse colon, and advanced leftward, and the left gastroepiploic vessels were divided near the spleen. The gastric branches of the gastroepiploic vessels were divided close to the stomach wall. The omentum



Figure 2 (A) Periareolar incision was made and wide excision including the entire no man's land was completed; (B) a small incision was made along the medial inframammary fold, and a pedicled omental flap was extracted through the subcutaneous tunnel; (C) postoperative result two months after postoperative radiation therapy.



Figure 3 (A) Wide excision was performed with an elliptical radial incision to remove the skin over the tumor; (B) a pedicled omental; (C) postoperative result two years after surgery and radiation therapy.

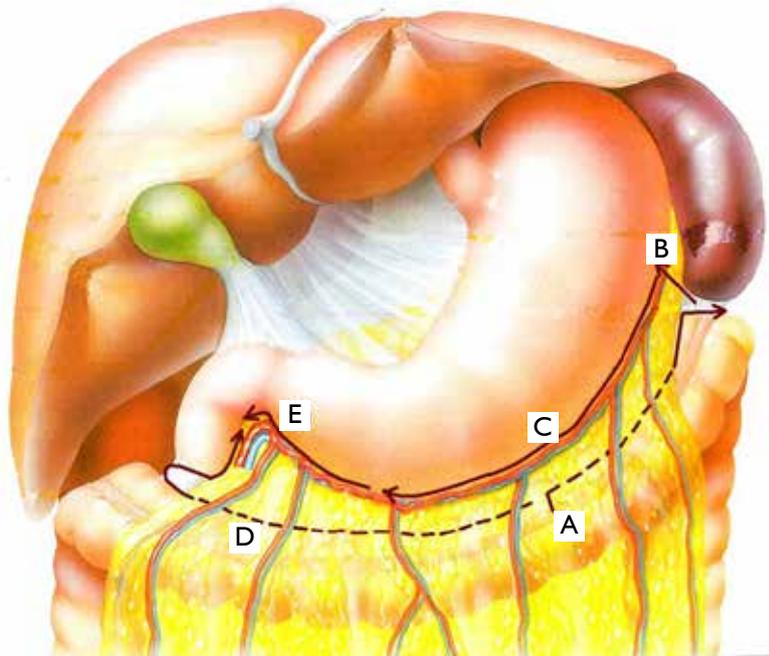


Figure 4 Laparoscopic procedures. (A) entering the omental bursa and the dissection from the left side of the transverse colon; (B) transection of the left side of the omentum which includes the left gastroepiploic vessels; (C) division of the gastric branches of the gastroepiploic vessels at a site as close to the stomach wall as possible; (D) dissection from the right side of the transverse colon and confirmation of the root of the right gastroepiploic vessels; (E) dissection from the stomach across the pyloric ring.

Table 1 Patient characteristics and operative data

Characters	Operative data
Number of patients	30
Age (yrs)	48.5 [33-58]*
Median follow-up periods (months)	64 [7-136]*
Tumor size (cm)	2.8 (1.0-4.2)**
T staging	
pT0	6
pT1	10
pT2	14
Node positivity	
pN0	23
pN1	4
pN2	1
pN3	2
Resected volume (g)	142 [75-330]*
Operative time (min)	250 [210-380]*
Complications	3 (10.0%)
Positive margin	1 (3.3%)
Local recurrence	0 (0.0%)

*, values are median (range); **, non-invasive carcinomas were excluded.

was dissected till passing the pyloric ring (*Figure 4*). Roots of the gastroepiploic vessels were preserved as a pedicle and the OF was harvested in about one hour.

An additional 4 cm skin incision was made along the medial inframammary fold, and an approximately 2-finger wide subcutaneous tunnel was prepared toward the xyphoid process. When the tunnel reached the white line, a 2-finger wide longitudinal incision was made to communicate with the abdominal cavity. This was facilitated by intraabdominal resection of the white line. The forceps or fingers were inserted into the abdominal cavity via the tunnel and the pedicled OF was carefully withdrawn with avoidance of twisting (*Figures 1B,2B,3B*).

A subglandular tunnel which passed under the lower inner quadrant was also created between the inframammary incision and the partial mastectomy defect in the UIQ. After hemostasis was completed, the OF was pulled out and filled the defect (*Figure 1C*).

It was usually unnecessary to fix the OF to the chest wall. A closed suction drain was inserted over the OF and the incision was closed in two layers (*Figure 1D*). When

the laparotomy incision was wider than 2-finger width, the wound was semi-closed to avoid postoperative ventral hernia. The pedicle of the flap was made as slim as possible by careful defatting, and the subcutaneous fat tissue around the tunnel was excised to avoid postoperative bulging. An entrance of the subcutaneous tunnel was also semi-closed for appropriate recreation of a medial site of the inframammary fold. The reconstructed OF was usually monitored with Doppler sonographic examination for a day or two days postoperatively.

Cosmetic results were evaluated using a cosmetic score (14) assessed by three health professionals and BCCT.core which is 2D computer software as excellent, good, fair, or poor (15).

Results

The characteristics of the 30 patients who underwent immediate volume replacement with the OF after resection of the UIQ of the breast are shown in *Table 1*. The mean pathological tumor size was 2.8 cm, and two patients had internal lymph node metastasis. The median resected breast tissue volume was 142 g. The OFs were harvested laparoscopically in about 1 hour without conversion to a laparotomy in all cases. The complication rate (including short- and long-term events) was 10.0%. They were two cases of partial flap necrosis and one case of ventral hernia. Partial flap necrosis could be treated conservatively, but caused prolonged necrotic drain discharge which resulted in loss of nearly a half of the volume and lately formed a hard nodule in the reconstructed breast because of calcified fat necrosis. Ventral hernia in infra-xyphoid area occurred in one patient 5 years after surgery, and repaired by laparoscopic herniorrhaphy with a mesh.

The surgical margins, defined negative as no ink on tumor were positive in one patient (3.3%) and the patient underwent re-excision (*Table 1*).

Neither local nor systemic recurrence has occurred to date in any patients during medial follow-up periods of 64 months (*Table 1*).

Cosmetic outcomes were mostly satisfactory with negligible donor-site scars (*Figures 3,5*). The scars on the medial inframammary fold were usually hidden by the breast and became unobvious because of positive effect of postoperative radiation therapy to avoid hypertrophic scar formation. More than 80% of the patients scored excellent or good both with panel assessment and BCCT.core (*Table 2*). Compared with the panel assessment, fewer patients were scored as excellent. No size reduction of the OF was noted

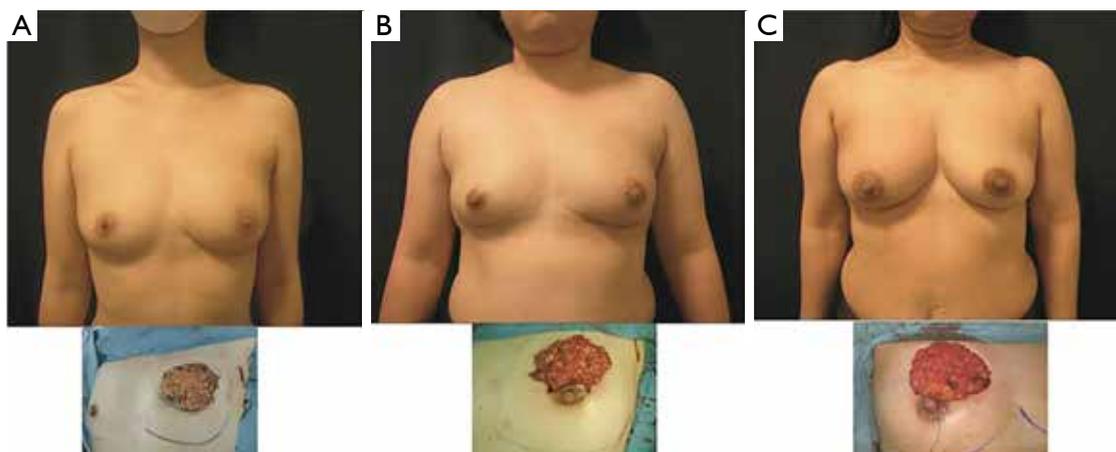


Figure 5 (A) Postoperative result two years after surgery for the left upper inner quadrant; (B) postoperative result one year after surgery for the left upper inner quadrant; (C) postoperative result one year after surgery for the right upper inner quadrant.

Table 2 Cosmetic results

Cosmetic score	Panel assessment (n, %)	BCCT.core (n, %)
Excellent	20 (66.7)	13 (43.3)
Good	6 (20.0)	13 (43.3)
Fair	1 (3.3)	4 (13.3)
Poor	3 (10.0)	0 (0.0)

Values in parentheses are percentages; a value is mean (range).

during follow-up except in cases of partial flap necrosis, even after radiation therapy.

Discussion

Cosmetic outcome after BCS is negatively influenced by many factors, and medial tumor location is one of the reasons. Grisotti *et al.* defines the no man's land that is the area upward to a line drawn on the inferior border of the pectoralis, around the areolar at a superior distance of 16 cm from the sternal notch and 7 cm medially (16), and the no man's land is mainly constituted with the UIQ. A large skin resection in this area followed by dermoglandular flap advancement including the nipple-areolar complex will shift the nipple in an upward or medial fashion that would look highly unnatural in location (16). Defects in the UIQ are more likely to cause patient dissatisfaction (17,18). Patient outcomes following surgery can be enhanced by restoring volume and minimizing scars in the UIQ. For the patients whose breasts are large, several volume displacement techniques have been developed and well standardized to solve the problem (19). However, for the patients whose

breasts are small, volume replacement technique is the only key to solve the problem.

The LD flap has been played a major role in volume replacement (1,2), but has the disadvantages of donor-site scar and morbidities (3,4). Recent advances in chest wall perforator flaps can minimize these problems; however, perforator flaps generally tend to have less range (20), although the TDAP flap replacement of volume is reported in all quadrants (21). The superior epigastric artery perforator (SEAP) flap can also reach and fill the defect in the UIQ, but usually results in very visible donor-site scarring (22).

We have already reported on partial reconstruction using the OF for the lower inner quadrant. The UIQ is also comfortable field for the OF which can easily reach any quadrants of the breasts (13). Although two separate incisions are needed for partial reconstruction for the UIQ, the small incision along the medial inframammary fold to extract the OF is usually invisible. When the volume of the OF is large, the subglangular tunnel should be wider by resecting breast and fat tissue around the tunnel to avoid bulging in the lower inner quadrant.

The big advantages of the OF are minimal donor-site scar and morbidities because the flap can be harvested laparoscopically (12). The scars in the abdomen are just like those of laparoscopic cholecystectomy. The short- and long-term laparoscopy-associated complication rates are very low and acceptable (12). Because the OF is very soft due to abundance of fat and has a long pedicle, it is easy to replace an irregular-shaped defect after BCS (13). A volume replacement procedure can be completed even through

a small periareolar incision by which a visible scar in the no man's land can be avoided. If the surrounding residual breast parenchyma and the inframammary fold are not dissected from the underlying muscles, a fixation of the OF is unnecessary and the OF naturally fits and fills the defect.

The most important disadvantage of the OF is an impossibility of preoperative volume estimation of the flap (11,13). When the resected volume is larger than 100g or the patient is slim, the volume of the OF may be inadequate. On the other hand, the volume of the OF may be very large enough for total reconstruction, however, it is usually difficult to extract an extremely large sized OF through the small subcutaneous tunnel, which might cause a trauma of small vessels of the flap and partial flap necrosis. Then a mid-line abdominal skin incision would be needed in such a case, which negatively affects donor-site cosmesis. Therefore when the volume of the OF is large, a free flap is better choice because a large sized OF can be easily extracted from the umbilical incision (23).

Cosmetic results were mostly satisfactory with natural soft tactile feeling of the reconstructed breast. However, compared with the panel assessment, fewer patients were scored as excellent in this study. One of reasons might be poor quality of our photographs because of lack of adequate lightning and standardization in taking photographs which are the necessary conditions for evaluating cosmetic outcome using BCCT.core (15).

The OF is strong against radiation therapy and less atrophic than the muscle flap, and the LD flap and the lower abdominal wall flap such as the transverse rectus abdominis myocutaneous (TRAM) flap and the deep inferior epigastric artery perforator (DIEP) flap can be completely preserved for total reconstructions in case. In conclusion, the OF is attractive for partial reconstruction after BCS for the UIQ; a part of the no man's land of the breast.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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Oncoplastic techniques in breast surgery for special therapeutic problems

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Abstract: Resection of large tumors can be challenging, from the view point of breast preservation. Oncoplastic techniques are a valuable component of breast surgery in patients with large breast tumors who desire breast preservation. These techniques have been shown to be oncologically safe, while maintaining acceptable breast cosmesis. For locally advanced or recurrent breast cancers, the goals of surgery include local disease control and palliation of clinical symptoms. Oncoplastic surgery is also effective and oncologically safe in these situations. The need to completely remove all foci of cancers with adequate surgical margins often requires the displacement of adjacent or distant skin and soft tissue to cover the resulting soft tissue defect. Sometimes doing so can be cosmetically pleasing as well. In this article we present three special therapeutic problems in three distinct conditions, all resolved with oncoplastic techniques: the benign breast condition, malignant breast condition, and the palliative setting.

Keywords: Breast conservative treatment (BCT); oncoplastic technique; breast reconstruction; phyllodes tumor; giant fibroadenoma; breast flap; random skin flap; salvage mastectomy; stage IV breast cancer

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Special therapeutic problems in benign breast conditions

Benign proliferative breast lesions are most frequently observed in women 30 to 40 years of age, sometime causing significant breast asymmetry because of the large size. The differential diagnoses for these lesions include pseudoangiomatous stromal hyperplasia (PASH), benign phyllodes tumors, juvenile fibroadenoma, and giant fibroadenoma with increased stromal cellularity. The principles of surgical treatment are different for each diagnostic category. The crucial steps in management consist of preoperative tissue diagnosis and surgical techniques for breast reconstruction after removal of the tumor.

Core needle biopsy (CNB) is preferable to fine needle aspiration for preoperative tissue diagnosis, because fibroadenomas and phyllodes tumors have similar cytologic features. Clinical findings that could increase the suspicion

of phyllodes tumors include older patient age, larger tumor size, and history of rapid growth (1). The major pathological feature that distinguishes a phyllodes tumor from a giant fibroadenoma is the cellularity of the stromal component in the former (2). However, the histologic features of benign phyllodes tumors can be difficult to distinguish from those of fibroadenomas on CNB.

It is common for a CNB of either a phyllodes tumor or fibroadenoma to be interpreted as a “fibroepithelial lesion”, hence a phyllodes tumor cannot be ruled out in such a situation. The clinical challenge for the surgeon is to decide whether to remove the entire lesion for management, as is done for a typical fibroadenoma, or to excise the lesion with wide margins, as is therapeutically indicated for phyllodes tumors. If large benign phyllodes tumors are excised with narrow or no margin, reexcision should be performed. Several publications advocated margins of at least 1 cm as adequate (3,4).



Figure 1 Presentation and management of a giant fibroadenoma. A 40-year-old woman presented with a palpable mass at the right middle inner quadrant, which had grown from 2.4 to 10 cm over 2 years. Imaging and core needle sampling at first presentation were interpreted as “fibroadenoma”. The final pathology on excision was a giant fibroadenoma. (A) Preoperative presentation with bulging mass apparent on inspection; (B) intraoperative view showing the large tumor and planned skin excision (outer de-epithelized line), which is drawn immediately superficial to the mass; (C) postoperative view after the “round block” mastopexy technique with 325 cc subglandular implant.

Appropriate techniques for breast reconstruction are crucial after removal of a large benign tumor. Lesions with microscopic appearance of a conventional fibroadenoma, however large, should still be classified as fibroadenomas and may be managed adequately by enucleation. Cosmetic sequelae after enucleation of large tumors are common. If an estimated 20% to 50% of breast volume has been resection, a type II breast deformity can occur (5). Reshaping the breast by using a “round block” technique such as the periareolar Benelli mastopexy is required to correct the defect after removing a large volume of the tumor (*Figure 1A-C*) (6). If total mastectomy is considered for a large benign phyllodes tumor, then a free flap or a pedicled flap such as a pedicled transverse rectus abdominis (TRAM) flap can be used to reconstruct the breast (*Figure 2A,B*).

Special therapeutic problems in malignant conditions

In patients with a CNB result interpreted as “malignant phyllodes tumor”, the crucial information is whether the tumor to breast size ratio is favourable (e.g., a low ratio) or not. A pseudocapsule of dense, compressed, normal tissue, often containing microscopic malignant cells, surrounds malignant phyllodes tumors. As a result, more tissue typically needs to be removed to achieve adequate margins (7). Simple mastectomy without axillary dissection has been recommended for malignant phyllodes tumors with high tumor to breast

size ratio. Margins can be typically wider than 1 cm, but a width greater than 2 cm is associated with the lowest risk of recurrence (8). After removing the tumor with negative margins, a large skin and soft tissue defect can be covered with a pedicled TRAM flap reconstruction (*Figure 3A-D*). In a patient who presented with local recurrence (LR) after performing left breast conservative treatment (BCT) for a malignant phyllodes tumor, and who also had large breasts with severe ptosis, we performed a restaging work-up to rule out distant metastases. The majority of such patients with LR after BCT are treated with mastectomy, although the use of repeat breast conservation surgery for LR has been reported (9). In the case of our patient, after a restaging work up ruled out distant metastasis, we performed a left mastectomy, and a reduction mammoplasty of the opposite breast to reduce breast weight, with a good cosmetic result (*Figure 4A,B*) (10). A reduction mammoplasty in the present setting can help relieve back pain and achieve good body balance, with only one remaining but smaller breast.

Special therapeutic problems in the palliative setting

Breast cancer patients who have concurrent distant metastases (stage IV disease) are primarily treated by palliative systemic therapy. Surgical removal of the breast tumor does not provide survival benefit. On occasion the primary tumor is removed in these patients for palliative reasons, such as for



Figure 2 Presentation and resection of a large benign phyllodes tumor. A 39-year-old woman presented with a large mass in the left breast. Core needle biopsy (CNB) was reported as “benign phyllodes tumor”. (A) Preoperative presentation with bulging mass apparent on inspection; (B) postoperative view after performing a pedicled transverse rectus abdominis (TRAM) flap.



Figure 3 Presentation and management of a malignant phyllodes tumor. A 44-year-old woman presented with a large mass in the left breast. CNB was reported as “malignant phyllodes tumor”. (A) Preoperative presentation with a bulging mass apparent on inspection; (B) intraoperative view after simple mastectomy with 3 cm lateral margins of surrounding soft tissue; (C) the defect was covered with a pedicle TRAM flap; (D) postoperative view 2 weeks after surgery. CNB, core needle biopsy; TRAM, transverse rectus abdominis.

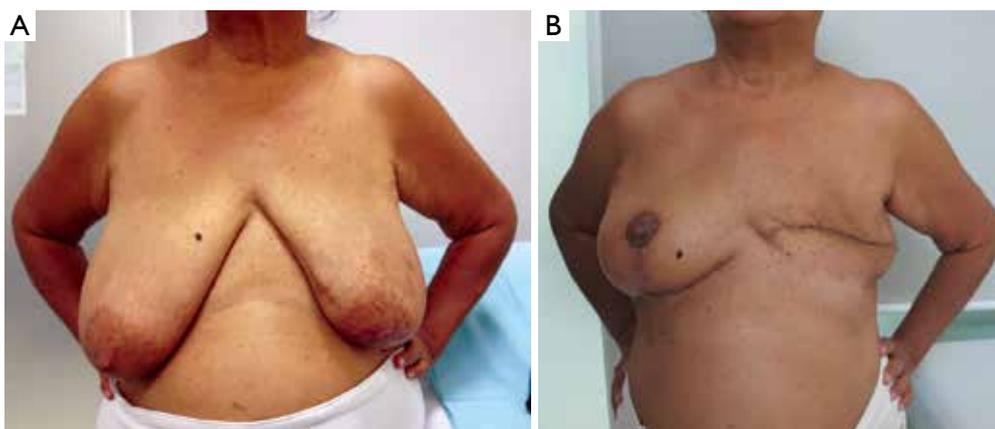


Figure 4 Presentation of local recurrence (LR) after left BCT for a malignant phyllodes tumor. Large breasts with severe ptosis can be seen. An assessment for metastatic disease showed no lesion on computed tomography of the chest and abdomen, bone scan and combined positron emission tomography-computed tomography. (A) Preoperative view in preparation for an inverted T inferior-pedicle breast reduction; (B) anterior view of the results at 6 weeks after performing left mastectomy and reduction mammoplasty of the opposite breast. BCT, breast conservative treatment.

disabling pain, infection, ulceration or bleeding. Nonetheless, these patients should be initiated on systemic therapy as the first-line treatment. Patients who respond to systemic therapy, or have persistent but non-progressive metastatic diseases, with good performance status, may be considered for palliative or salvage surgery for quality of life (QoL) reasons. The QoL benefits have been highlighted in a recent study (11). A salvage resection is defined as the resection of all visible lesions, extending to the surrounding skin with a safety margin of at least 2 cm (12). Closure or reconstruction of the soft tissue defect of the chest wall can be performed using skin grafts or different types of vascularized pedicled musculo-cutaneous flaps.

The choice of closure or reconstruction methods depend on the location and size of the defect, availability of the local and pedicled flaps, previous surgery or radiotherapy at the donor and recipient site, and the general condition of the patient. Direct simple closure is possible for small lesions. Skin grafts can be used for superficial chest wall defects involving only the soft tissue. Previous or post-operative radiation therapy may compromise the healing of skin grafts.

Local flaps

Breast flap

The breast parenchyma can be used as a flap to cover defects

located predominantly in the midline (*Figure 5A-D*). This flap is suitable for elderly patients with associated comorbidities, because of the short operative time required. The blood supply of breast flap is good, but the cosmetic outcome is rather poor (13).

Random skin flap from the lateral chest wall

This flap can cover small and moderate sized defect on the anterior and lateral aspects of the chest wall, and can be used in combination with the other flaps (*Figure 6A-E*). It is also suitable for the elderly, or for patients with poor functional status, due to the short operative time. The weakness of this method is a lack of sufficient volume to cover large defect.

Pedicled flaps

The regional pedicled musculocutaneous flaps available for reconstruction include the latissimus dorsi (LD) flap or TRAM flap. We prefer the use of the LD flap when available, and it is usually large enough to cover most defects (*Figure 7A,B*). The LD flap can be rotated widely, is easy to harvest, and can be tailored to cover the anterior, lateral, and posterior regions of the chest wall. In addition, this technique can be performed within a relatively short period of time, and patients experience fewer postoperative complications afterwards.

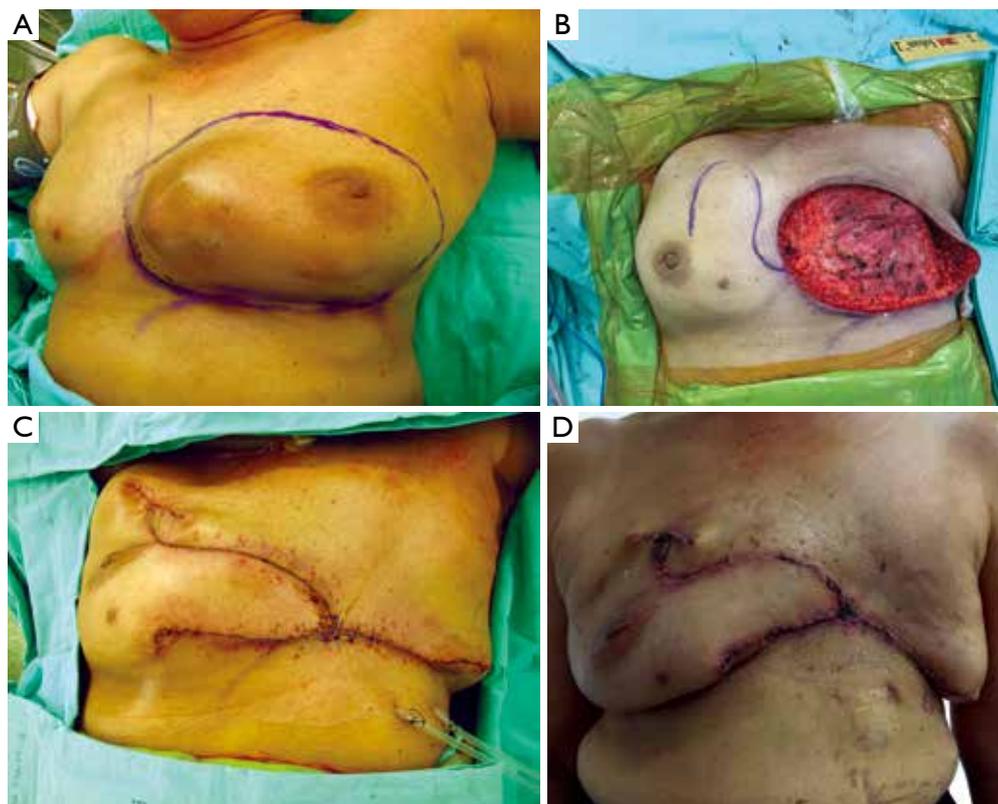


Figure 5 Presentation and management of invasive ductal carcinoma at left breast with stable bone metastasis. A 65-year-old woman presented with a large mass at the left breast. CNB was reported as “invasive ductal carcinoma”. An assessment for metastatic disease showed no lesion on computed tomography of the chest and abdomen, but multiple bone metastases were found on radionuclide scintigraphy. She received systemic endocrine therapy and her bone metastases stabilized. (A) Preoperative presentation with large mass apparent on left breast; (B) intraoperative view of medial chest wall defect after salvage mastectomy; (C) the defect was covered with a right breast flap; (D) anterior view of the results at 6 weeks after performing right breast flap. CNB, core needle biopsy.

Complications of oncoplastic surgery after radiation

Previous studies suggested that the surgeon should be more cautious in performing oncoplastic surgery in patients with irradiated breasts. The study by Losken *et al.* suggested that radiation therapy might decrease compliance of the covering soft tissue (14). Our results demonstrate that oncoplastic surgery is a simple and reliable technique to correct nipple areola complex (NAC) malposition after previous breast procedures, even in those patients who previously underwent locoregional radiotherapy that could negatively affect wound healing and graft intake (15).

In previously irradiated patient, our experience showed a mastectomy skin flap necrosis occurred after performing nipple sparing mastectomy (NSM) with LD flap plus implant reconstruction (*Figure 8A-D*). This finding may due

to the individual surgeon’s technique. The surgeon must carefully make the dissection of the gland more precisely and the preservation of the subdermal vessel network to the cutaneous flaps. To reduce severity of necrotic complications, the reconstruction should be performed with autologous flap (LD flap, TRAM flap) with the use of an additional implant. When mastectomy skin flap or NAC necrosis occurred, we sometimes performed only skin flap debridement with or without NAC and we did not remove implant because the flap could protect and cover it.

Conclusions

Breast reconstruction techniques are of crucial importance after removal of large benign proliferative lesions with an adequate margin. For large phyllodes tumors, oncoplastic surgery can

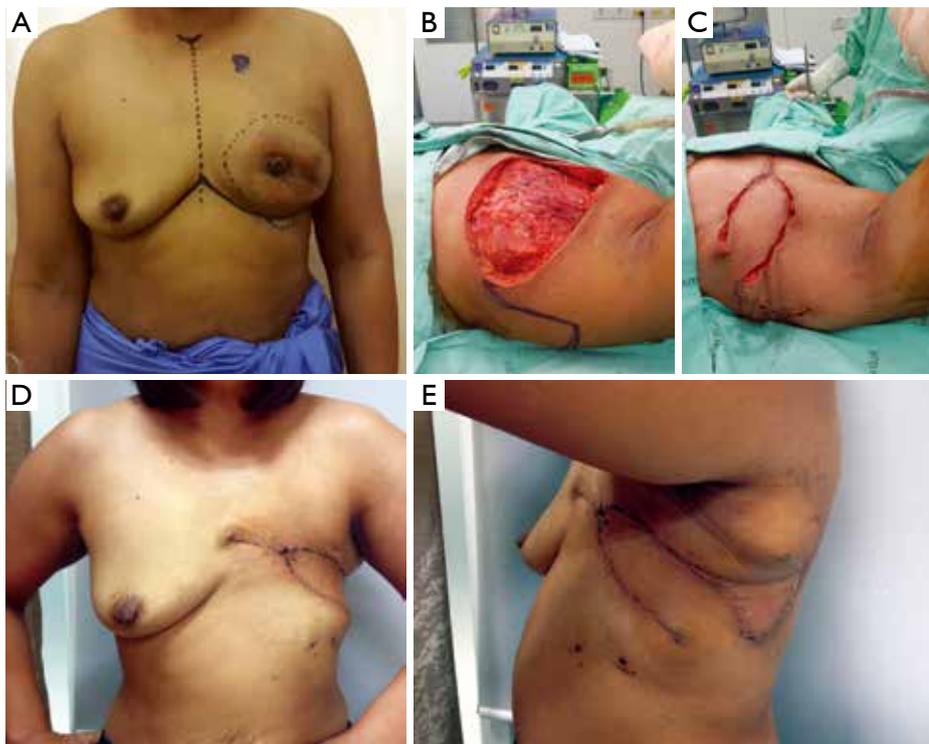


Figure 6 Presentation and management of invasive ductal carcinoma at left breast with stable bone metastasis. A 60-year-old woman presented with a large mass at the left breast. CNB was reported as “invasive ductal carcinoma”. An assessment for metastatic disease showed no lesion on computed tomography of the chest and abdomen, but bone metastases were found on radionuclide scintigraphy. She received systemic therapy for stage IV disease until her bone metastases stabilized. The large tumor was partially responsiveness to systemic treatment. The patient requested tumor removal because of pain. (A) Preoperative presentation with large mass apparent at left breast; (B) intraoperative view of the chest wall defect after salvage mastectomy; (C) the defect was covered with a random skin flap from lateral chest wall; (D) anterior view of the results at 6 weeks after surgery; (E) lateral view of the results at 6 weeks after surgery. CNB, core needle biopsy.



Figure 7 Presentation and management of invasive ductal carcinoma at right breast with stable bone metastasis. A 64-year-old woman presented with a tumor at the right breast. Skin involvement can be seen. CNB was reported as “invasive ductal carcinoma”. An assessment for metastatic disease showed no lesion on computed tomography of the chest and abdomen, but bone metastases was found on radionuclide scintigraphy. She received systemic endocrine therapy until bone metastases were stabilized. (A) Preoperative presentation with skin involvement; (B) anterior view of the results at 6 weeks after performing right LD flap closure of defect. CNB, core needle biopsy; LD, latissimus dorsi.



Figure 8 Presentation and management of a mastectomy skin flap necrosis occurred after performing NSM with LD flap plus implant reconstruction. A 46-year-old woman presented with recurrent tumor at the left breast. She had previously undergone a left lumpectomy with whole breast radiation. We performed NSM and immediate breast reconstruction with LD flap plus implant. (A) NAC necrosis with mastectomy skin flap necrosis around NAC. The necrosis occupied mostly in the superior outer quadrant and incision is supero-lateral radial incision; (B) we performed only skin flap debridement with NAC; (C) resuture mastectomy skin flap was performed with nylon 4-0; (D) postoperative view of the results at 6 weeks after debridement and nipple reconstruction. NSM, nipple sparing mastectomy; LD, latissimus dorsi; NAC, nipple areola complex.

prevent and correct breast deformities after adequate removal with wide margins, resulting in a good cosmetic outcome. Larger soft tissue and skin defects can be closed using oncoplastic methods. Salvage mastectomy and reconstruction for stage IV breast cancer is a feasible procedure, providing adequate local disease control and excellent palliation of very disabling symptoms in selected patients.

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Footnote

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Direct-to-implant breast reconstruction

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Introduction

Implant-based breast reconstruction is the most common means to restore the breast following mastectomy for breast cancer treatment or risk reduction. Many patients chose implant reconstruction secondary to the advantages of a shorter operative time, lack of donor-site morbidity, and quicker return to normal life activities. A single-stage direct-to-implant (DTI) breast reconstruction offers an ideal reconstructive choice in select patients by replacing loss of the breast at the time of the mastectomy in a single operation. In the past, DTI reconstruction was largely abandoned secondary to issues with pectoralis muscle retraction, implant malposition, and contracture. The advent of acellular dermal matrix products (ADM) offered a solution to these problems by holding the released pectoralis muscle on stretch and forming a complete pocket around the implant in the desired position (1). By off-loading stress on the inferior skin envelope, and by changing the interface of the skin envelope with the implant, it is thought that ADM-assisted reconstruction may be associated with lower contracture rates than reconstructions without ADM. A DTI procedure has obvious appeal to patient and surgeon alike, but not everyone is a candidate for single-stage reconstruction. The key to success is in patient selection, technique, and intraoperative decision-making (2).

Indications

Patient selection begins at the initial consultation. The history assesses the overall health of the patient and treatment plan, previous surgeries and co-morbidities, current medications, and smoking status. The ideal

candidate for DTI reconstruction is an otherwise healthy non-smoker with a small to moderate sized breast, and who desires to be a similar breast size. If a patient wishes to be significantly larger in size, this is typically more safely done in two stages with tissue expander-implant reconstruction. Patients who have advanced disease or multiple medical co-morbidities that increase the complication risk may be better served with delayed reconstruction. Active smoking and pre-existing scars on the breast adversely affect skin perfusion and thus DTI may not be possible. Skin of the large breast may also pose challenges as it tends to become more ischemic than the skin of smaller breasts with mastectomy. Therefore, even though there is often an excess amount of skin available to use, reconstruction may need to be done in two stages or it may even need to be delayed. If the patient meets the above criteria, she is a candidate for DTI reconstruction. However, the final decision on DTI is made in the operating room based on the health and perfusion of the mastectomy skin envelope, and the surgeon should be prepared to do a tissue expander reconstruction if required.

Technique

The patient is marked preoperatively while sitting or standing. Important landmarks include the inframammary fold (IMF), the relation of the inframammary fold on one side to the other side, and the lateral borders of the breast. The optimal incision is determined with the breast oncologic surgeon. For nipple-sparing mastectomies, I find the inferolateral inframammary fold incision provides the best aesthetics while the straight lateral scar without a superior or inferior periareolar extension is the safest (3).

The patient is given a muscle relaxant to facilitate subpectoral dissection. A plane is created from lateral to medial in the fine areolar tissue beneath the pectoralis muscle to the sternal attachment of the muscle. To facilitate implant positioning, the inferior origin of the muscle is divided to the 4 o'clock or 8 o'clock position on the chest wall (1). Once the muscle is released, an acellular dermal matrix (ADM) is used as the inferior and lateral borders of the implant. In my own practice, I have the most experience with human ADM (Alloderm, Lifecell).

The ADM is sewn to the IMF inferiorly if intact or to the chest wall to create the desired IMF position. Care is taken to allow some horizontal laxity medially to accommodate the implant. Laterally, the ADM is sewn to the chest wall to create the lateral border of the breast pocket. If the ADM size is insufficient for the breast base diameter, a serratus flap may be raised laterally to gain length. A sizer is placed into the pocket and sewn into place. The skin is temporarily stapled shut and the patient is sat upright to assess pocket size and dimensions. Increasing volumes are added to the sizer while the skin is observed for signs of ischemia to help determine implant volume. The final implant is chosen based on the diameter of the breast pocket and the volume that did not induce significant ischemia. The pocket is closed over the implant. Two closed suction drains are placed with one inside the pocket along the inframammary fold (IMF) and the other outside the pocket in the axillary region. The mastectomy skin is trimmed to freshen the edges and closed in two layers. Incisions are dressed with a surgical glue (Dermabond, Ethicon) and a clear semipermeable dressing (Tegaderm, 3M) over the incision. I currently use a chlorhexidine impregnated sponge (Biopatch, Ethicon) around the drains. The implants are stabilized using microfoam tape at the lateral and inferior borders and a loose-fitting surgical bra is placed prior to discharge from the hospital in 1-2 days.

The patient is followed weekly until the drains are removed. Criteria for drain removal includes output less than 30 cc for a 24 hour time period. Activity is limited for the first six weeks to facilitate wound healing and minimize chances of implant malposition.

Outcomes

Our published institutional experience at Massachusetts General Hospital shows favorable outcomes in ADM-assisted DTI reconstruction with low total complication rates and an explant rate of 1.5% (2). There is a learning

curve with the technique of DTI reconstruction that is primarily related to the ability of surgeons to determine the volume of implant the skin will be able to tolerate. If the limits of perfusion are surpassed, skin necrosis ensues. Clinical experience with the technique and in working with the oncologic surgeons yields fewer complications. Novel techniques quantifying skin perfusion (Indocyanine green perfusion imaging, laser Doppler) have the potential to shorten the learning curve for surgeons who are just starting to perform DTI reconstruction or who do so infrequently.

Although there are a number of reports associating ADM with an increased risk of infections and complications, there are also numerous studies showing no increase in complication rates, including our own paper (1,3-12). The reason for the discrepancy may reflect the learning curve in using a new product and technique. It is very important to drain the spaces adequately to prevent seroma and to limit excessive stress on the skin envelope to help prevent skin necrosis.

Patient satisfaction with DTI reconstruction is high and similar to two-stage tissue expander-implant reconstruction (unpublished data) (*Figure 1*).

The costs associated with ADM are a frequent topic of discussion, and cost alone may be prohibitive to the availability of ADM in select regions and countries. We have shown that the cost of ADM is offset by doing the reconstruction in a single setting compared to the two surgeries required for tissue expander-implant reconstruction (2). The availability of ADM may also be limited in certain regions secondary to restrictions on the use of human or animal products. As novel matrix materials are generated and tested, their usage may become more universal.

Conclusions

Direct-to-implant breast reconstruction in properly selected patients offers excellent outcomes and patient satisfaction. The complication rate is low and improves with experience of the surgeon. If the skin envelope is determined to be healthy and sufficient at the time of the mastectomy and the patient desires a similar or smaller-sized breast, this may be the procedure of choice.

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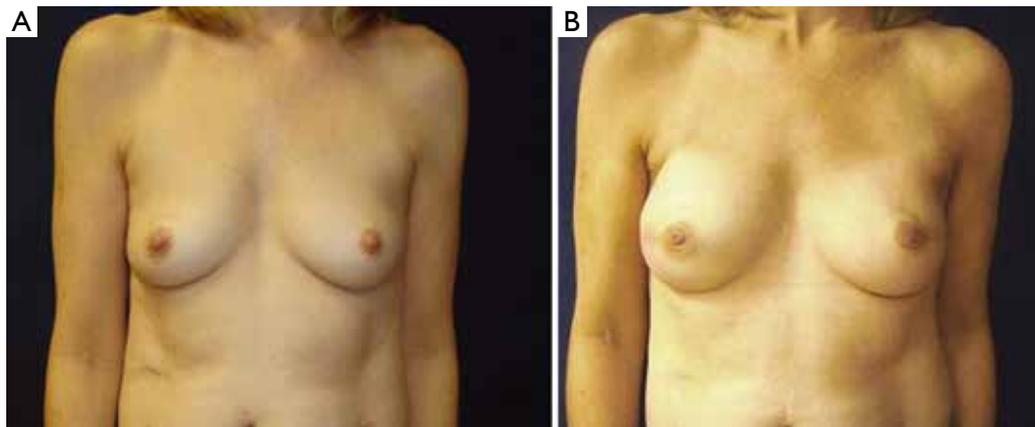


Figure 1 This 42 year-old female had a strong family history of breast cancer and tested positive for the BRCA gene (Preoperative photo, A). She had pre-existing incisions on both breasts. The patient wanted to stay a similar breast size and desired a single-stage procedure. She had bilateral nipple-sparing mastectomies through lateral radial scars without a periareolar extension to maximize blood flow to the nipples. The patient had immediate single-stage direct-to-implant reconstruction using silicone cohesive gel implants (Postoperative photo, B)

Footnote

Conflicts of Interest: Amy S. Colwell M.D. is a consultant for Allergan and Lifecell. She is also a clinical investigator for a study using the AirXpander in two-stage breast reconstruction.

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Alloplastic adjuncts in breast reconstruction

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Background: There has been an increasing role of acellular dermal matrices (ADMs) and synthetic meshes in both single- and two-stage implant/expander breast reconstruction. Numerous alloplastic adjuncts exist, and these vary in material type, processing, storage, surgical preparation, level of sterility, available sizes and cost. However, there is little published data on most, posing a significant challenge to the reconstructive surgeon trying to compare and select the most suitable product. The aims of this systematic review were to identify, summarize and evaluate the outcomes of studies describing the use of alloplastic adjuncts for post-mastectomy breast reconstruction. The secondary aims were to determine their cost-effectiveness and analyze outcomes in patients who also underwent radiotherapy.

Methods: Using the PRSIMA 2009 statement, a systematic review was conducted to find articles reporting on the outcomes on the use of alloplastic adjuncts in post-mastectomy breast reconstruction. Multiple databases were searched independently by three authors (Cablag MS, Miller GS and Chae MP), including: Ovid MEDLINE (1950 to present), Embase (1980 to 2015), PubMed and Cochrane Database of Systematic Reviews.

Results: Current published literature on available alloplastic adjuncts are predominantly centered on ADMs, both allogeneic and xenogeneic, with few outcome studies available for synthetic meshes. Outcomes on the 89 articles, which met the inclusion criteria, were summarized and analyzed. The reported outcomes on alloplastic adjunct-assisted breast reconstruction were varied, with most data available on the use of ADMs, particularly AlloDerm[®] (LifeCell, Branchburg, New Jersey, USA). The use of ADMs in single-stage direct-to-implant breast reconstruction resulted in lower complication rates (infection, seroma, implant loss and late revision), and was more cost effective when compared to non-ADM, two-stage reconstruction. The majority of studies demonstrated inferior outcomes in ADM assisted, two-stage expander-to-implant reconstruction compared to non-ADM use. Multiple studies suggest that the use of ADMs results in a reduction of capsular contracture rates. Additionally, the reported beneficial effects of ADM use in irradiated tissue were varied.

Conclusions: ADM assisted two-stage breast reconstruction was associated with inferior outcomes when compared to non-ADM use. However, alloplastic adjuncts may have a role in single stage, direct-to-implant breast reconstruction. Published evidence comparing the long-term outcomes between the different types of adjuncts is lacking, and further level one studies are required to identify the ideal product.

Keywords: Breast reconstruction; breast implants; alloplastic implants; acellular dermal matrices (ADMs)

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Introduction

Breast cancer is the most common cancer in women, accounting for 29% of newly diagnosed cancers, and with a lifetime risk of one in eight for females in the United States (1). Numerous options and technical variations exist for post-mastectomy breast reconstruction, and can be categorized into autologous versus alloplastic, immediate versus delayed, as well as single versus two-staged. An estimated one-half to two-thirds of women who undergo a mastectomy will proceed to have an alloplastic reconstruction (2).

Acellular dermal matrices (ADMs) have been used since the 1990s in the areas of burns, head and neck, abdominal wall, hand, nasal as well as lower extremity reconstruction (3-10). These materials are allegedly immunologically inert, and act as biological scaffolds for re-epithelialization, neovascularization and fibroblast infiltration. Duncan first published the use of ADMs in breast surgery in 2001, in which AlloDerm® was utilized in revisional aesthetic surgery to correct implant rippling (11). However, it first used in breast reconstruction in 2005, where Breuing and Warren described the use of AlloDerm® as an inferior sling in single stage (direct to implant) post-mastectomy reconstructions (5). In the same year, Rietjens *et al.* described the use of a synthetic non-absorbable mesh (Mersilene), to recruit upper abdominal skin for additional soft-tissue coverage of the implant, as well as to recreate the infra-mammary fold (12). Since then, the types and number of alloplastic adjuncts have increased, including ADMs derived from human, bovine and porcine dermis, as well as synthetic meshes. These products vary significantly in their processing, level of sterility, biomechanical properties, thickness, preparation methods and cost (13-15). The use of ADMs in breast reconstruction has gained increasing popularity since its introduction, with an estimated 25% to 75% of tissue expander reconstructions utilizing ADMs (16-19).

Numerous advantages have been proposed with the use of alloplastic adjuncts, including: facilitating immediate implant reconstruction, improved implant positioning via better definition of the infra- and lateral mammary folds, shorter expansion times in tissue-expander reconstructions, improved capsular contracture rates, masking implant rippling, providing an additional layer between the prosthesis and overlying mastectomy skin, reduced rates of implant/expander migration, reduced discomfort during post-operative expansion, and protective effects in patients undergoing radiotherapy (5,20-24). However, there are also concerns regarding potential increased risks of infection, inflammatory reaction, seroma, masking tumour recurrence and significant costs (25-29).

Numerous alloplastic adjuncts exist, and these vary in material type, processing, storage, surgical preparation, level of sterility, available sizes and cost. However, there is little published data on most, posing a significant challenge to the reconstructive surgeon trying to compare and select the most suitable product. The aims of this systematic review were to identify, summarize and evaluate the outcomes of studies describing the use of alloplastic adjuncts for post-mastectomy breast reconstruction. The secondary aims were to determine their cost-effectiveness and to analyze outcomes in patients who also underwent radiotherapy.

Methods

Study identification

Multiple databases were searched independently by three authors (Cablag MS, Miller GS and Chae MP), including: Ovid MEDLINE (1950 to present), Embase (1980 to 2015), PubMed and Cochrane Database of Systematic Reviews.

The following search terms and Boolean operators were used: (I) (“breast reconstruction” OR “post mastectomy” OR “implant reconstruction” OR “tissue expander” OR “alloplastic”) AND (II) (“acellular dermal matrix” OR “acellular dermal matrices” OR “mesh” OR “synthetic mesh” OR “biological matrix”). Additional searches were conducted using (I) AND (II) AND (“radiotherapy” OR “irradiated”), as well as (I) AND (II) AND (“cost” OR “cost-effectiveness” OR “cost analysis”).

Inclusion criteria

Inclusion criteria for studies reviewed included: (I) meta-analyses or review articles; (II) adult patients aged 18 years or over undergoing post-mastectomy breast reconstruction; (III) alloplastic breast reconstruction (i.e., tissue-expander and/or implant-based) performed using adjuncts (ADMs and/or synthetic meshes); (IV) studies including outcome measures; (V) case series with more than ten patients; and (VI) English language.

Data extraction

A systematic review was conducted using the PRISMA 2009 statement (30). Data was extracted by three authors (Cablag MS, Miller GS and Chae MP), and included author, year, journal, study design, level of evidence, outcome details, number of patients (if applicable), and follow-up period. Differences in data extraction were corrected via discussion.

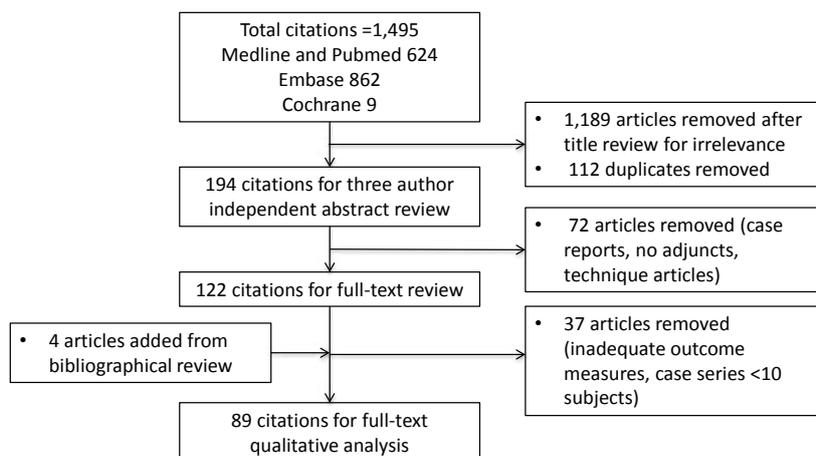


Figure 1 Summary of the literature review process.

Table 1 Summary of recommendations

Key points
1. The overall quality of studies was low, with the majority being of level III to IV evidence (i.e., case series or cohort studies). Additional level I to II evidence are required to validate the use of alloplastic adjuncts
2. Evidence for the use of ADMs in irradiated tissue is varied and inconsistent. However, synthetic mesh should be avoided in patients undergoing radiotherapy
3. Benefits of ADM use include: facilitating single stage, direct-to-implant breast reconstructions; improved cosmesis with better control of the inframammary fold; and shorter expansion times in tissue-expander reconstructions
4. ADM-assisted two stage, expander-to-implant reconstruction led to inferior outcomes when compared to traditional, two-stage submuscular techniques
5. ADM-assisted single stage, direct-to-implant reconstruction resulted in lower overall complication rates (infection, seroma, implant loss and late revision), compared to traditional, two-stage submuscular techniques. However, it was associated with an increased rate of mastectomy skin flap necrosis
6. Cost-analysis studies suggest a cost advantage in ADM-assisted, direct-to-implant reconstruction, compared to non-ADM, two-stage reconstructions
7. The use of ADMs was associated with decreased rates of capsular contracture
8. More studies comparing the long-term outcomes between different alloplastic adjuncts are required to select the best material ADMs, acellular dermal matrices.

Results

The search was conducted on April 4, 2015, resulting in 1,495 articles, managed using Endnote X7™ (Thomson Reuters, Philadelphia, PA, USA). A summary of the literature review process is shown in *Figure 1*. After the authors independently assessed the titles for relevance, a total of 1,189 articles were excluded, and 112 duplicates were removed. The abstracts for the remaining articles were then reviewed based on the inclusion criteria, leaving

a total of 122 articles for full review. A further four articles were added based on review of bibliographies. Thirty-seven studies were eliminated after full review (inadequate outcome measures, case series <10 subjects). After full text review, analysis and data extraction was conducted for a total of 89 articles. The recommendations of this review are summarized in *Table 1*. *Tables S1-S4* are a summary of the: systematic reviews and meta-analyses; levels III and IV studies; cost-analyzing studies; and studies focusing on synthetic meshes respectively.

Table 2 List of alloplastic adjuncts

ADMs
Allograft
AlloDerm® (LifeCell Corp., Branchburg, New Jersey, USA)
AlloDerm® Ready to Use (LifeCell Corp., Branchburg, New Jersey, USA)
FlexHD® (MTF/Ethicon, Somerville, New Jersey, USA)
AlloMax™ (Bard, Warwick, Rhode Island, USA)
DermaMatrix® (MTF/Synthes, West Chester, Pennsylvania, USA)
DermaCell® (Lifenet, Virginia Beach, Virginia, USA)
Xenograft
Porcine
PermaColl™ (Covidien, Boulder, Colorado, USA)
Strattice™ (Lifecell, Branchburg, New Jersey, USA)
Protexa (Tecnos, Mestre, Italy)
Fetal bovine
SurgiMend® PRS (TEI Biosciences, Boston, Massachusetts, USA)
Tutomech® (RTI Biologics, Alachua, Florida, USA)
Synthetic mesh
TiLOOP® Bra (PFM Medical, Cologne, Germany)
TIGR® Matrix Surgical Mesh (Novus Scientific Pte Ltd, Singapore)
Knitted Vicryl Mesh (Vicryl, Ethicon, Somerville, New Jersey, USA)
ADMs, acellular dermal matrices.

Types of alloplastic adjuncts available

The types of alloplastic adjuncts in breast reconstruction described in the literature are listed in *Table 2* and summarized in *Table 3* (14). In summary, they comprise of either ADMs or synthetic meshes. Within ADMs, there are either allografts, derived from cadaveric human skin, or xenografts. There is significantly less published literature on the use of synthetic meshes in post-mastectomy reconstruction.

Allogeneic ADMs

AlloDerm® (LifeCell Corp., Branchburg, New Jersey, USA)

First introduced in 1994, AlloDerm was the first human dermis product available, and was initially used for burns reconstruction. It is a cadaveric split-thickness skin graft, in which the epidermis and cells are removed from the skin to reduce its antigenicity. It now comes in two forms: an aseptic, freeze-dried version requiring refrigerated storage and rehydration prior to use; and a newer, sterile, ready to use product. It was first used as an infero-lateral sling in breast reconstruction in 2005, but now also has a role

in tissue-expander based as well as nipple reconstructions (5,31,32). Of note, AlloDerm has two distinct surfaces, and thus requires specific orientation during implantation. The dermal side of the product, characterized by the dull, rough texture, is placed against the vascularized wound bed (i.e., the mastectomy skin flaps). AlloDerm is the most extensively studied ADM in breast reconstruction, with 135 references in the PubMed database as of April 2015. Histological studies have demonstrated AlloDerm to be partially integrated into host tissue within 7 days of implantation (33).

FlexHD® (MTF/Ethicon, Somerville, New Jersey, USA)

FlexHD is a pre-hydrated, aseptic, cadaveric dermal matrix, which, similar to AlloDerm is orientation-specific. Rawlani *et al.* studied the use of FlexHD in 121 breast reconstructions, with complications occurring in 20 breasts (two seromas, eight partial mastectomy flap necroses and nine infections). Furthermore, when compared to the non-irradiated group, the irradiated cohort had a higher rate of complications (13.7% *vs.* 30.8% respectively) (34).

Allomax™ (Bard, Warwick, Rhode Island, USA)

Previously known as NeoForm®, Allomax™ is a sterile,

Table 3 Types of alloplastic adjuncts in breast reconstruction

Alloplastic adjunct	Product name	Material	Sterility	Use	Contraindications	Other
Acellular dermal matrix						
Allograft	AlloDerm® (LifeCell Corp, Branchburg, New Jersey, USA); AlloDerm® Ready to Use (LifeCell Corp., Branchburg, New Jersey, USA)	Cadaveric	Non-sterile, aseptic; Terminally sterilized	<ul style="list-style-type: none"> • Freeze dried or pre-hydrated; • Orientation specific; • Infero-lateral sling; • Immediate implant or expander based reconstruction; • Nipple reconstruction; • Shelf life 2 years 	<ul style="list-style-type: none"> • Potential allergen—multiple antibiotics are used in product processing 	<ul style="list-style-type: none"> • Most documented in literature
	FlexHD® (MTF/ Ethicon, Somerville, New Jersey, USA)	Cadaveric	Non-sterile, aseptic	<ul style="list-style-type: none"> • Pre-hydrated; • Orientation specific; • Mainly used for abdominal reconstruction; • Shelf life 3 years 	<ul style="list-style-type: none"> • No information available (NIA) 	
	DermaMatrix® (MTF/ Synthes, West Chester, Pennsylvania, USA)	Cadaveric	Non-sterile, aseptic	<ul style="list-style-type: none"> • Freeze dried; • Orientation specific; • Immediate implant or expander based reconstruction; • Shelf life 3 years 	<ul style="list-style-type: none"> • Not recommended in patients with autoimmune connective tissue disease 	
	AlloMax™ (Bard, Warwick, Rhode Island, USA)	Cadaveric	Terminally sterilized	<ul style="list-style-type: none"> • Freeze dried; • Not orientation specific; • Immediate implant or expander based reconstruction; • Shelf life 5 years 	<ul style="list-style-type: none"> • NIA 	
	DermaCell® (Lifenet, Virginia Beach, Virginia, USA)	Cadaveric	Non-sterile, aseptic	<ul style="list-style-type: none"> • Ready to use; • Orientation specific; • Nipple reconstruction; • Shelf life 2 years 	<ul style="list-style-type: none"> • Sensitivities to gentamicin and vancomycin 	
Xenograft	PermaColl™ (Covidien, Boulder, Colorado, USA)	Porcine	Terminally sterilized	<ul style="list-style-type: none"> • Pre-hydrated; • Not orientation specific; • Mainly used for abdominal reconstruction; • Not recommended for breast reconstruction due to inadequate laxity 	<ul style="list-style-type: none"> • Sensitivities to porcine tissue 	
	Strattice™ (Lifecell, Branchburg, New Jersey, USA)	Porcine	Terminally sterilized	<ul style="list-style-type: none"> • Pre-hydrated; • Not orientation specific; • Mainly used for abdominal reconstruction; • Shelf life 18 months 	<ul style="list-style-type: none"> • Sensitivities to porcine tissue 	<ul style="list-style-type: none"> • Highest stiffness and tensile strength of all the acellular dermal matrices (ADMs)

Table 3 (continued)

Table 3 (continued)

Alloplastic adjunct	Product name	Material	Sterility	Use	Contraindications	Other
	SurgiMend® PRS (TEI Biosciences, Boston, Massachusetts, USA)	Fetal Bovine	Terminally sterilized	<ul style="list-style-type: none"> • Pre-hydrated; • Not orientation specific; • Shelf life 3 years 	<ul style="list-style-type: none"> • Sensitivities to bovine tissue 	
Synthetic mesh	TiLOOP® Bra (PFM Medical, Cologne, Germany)	Titanium coated polypropylene mesh	Terminally sterilized	<ul style="list-style-type: none"> • Infra-mammary fold like shape; • Comes in three sizes; • Mainly available in Europe— not yet approved in the United States as of July 2013 	<ul style="list-style-type: none"> • Not suitable for revision surgery 	
	TIGR Matrix Surgical Mesh (Novus Scientific Pte Ltd, Singapore)	Fast-degrading (copolymer of glycolide and trimethylene carbonate) and slow-degrading (copolymer of lactide and trimethylene carbonate) fibers	Terminally sterilized	<ul style="list-style-type: none"> • Long term, absorbable, macroporous knitted mesh; • Retains mechanics for up to 9 months; • Totally hydrolysed by 3 years 	<ul style="list-style-type: none"> • Higher complication rates in irradiated patients 	
	Knitted Vicryl Mesh (Vicryl, Ethicon, Somerville, New Jersey, USA)	Polyglactin 910	Terminally sterilized	<ul style="list-style-type: none"> • Absorbable; • Ready to use; • Cheap and widely available; • Minimum inflammatory response and non-allergenic 	<ul style="list-style-type: none"> • Higher complication rates in irradiated patients 	

cadaveric dermal matrix, which is non-orientation specific. Losken *et al.* published a study involving 22 patients and 31 breast reconstructions, reporting no cases of infection, seroma or foreign body reaction (35).

DermaMatrix® (MTF/Synthes, West Chester, Pennsylvania, USA)

DermaMatrix® is an aseptic, freeze-dried, orientation specific cadaveric allograft. Becker *et al.* compared DermaMatrix® with AlloDerm® in 30 patients (50 breasts) who underwent immediate expander-based breast reconstruction, in which the only statistically significant difference was a shorter duration in which the drains remained in-situ for AlloDerm® *vs.* DermaMatrix® (11 *vs.* 13 days) (36). No significant differences in complication rates (4%) were noted.

DermaCell® (Lifenet, Virginia Beach, Virginia, USA)

DermaCell® is a prehydrated, ready to use cadaveric dermal matrix, which can be stored at room temperature. The literature search revealed three articles on the use of DermaCell® in breast reconstruction, which suggested a relatively low rate of post-operative complications

(14,37,38). In a recent case series of ten patients, Bullocks reported two cases of failed tissue-expander reconstructions due to chronic seromas and infection (37). In another recent case series of nine patients, Vashi *et al.* reported only one patient with bilateral post-mastectomy reconstruction who subsequently developed seromas and infection (38).

Xenogenic ADMs

Strattice™ (Lifecell, Branchburg, New Jersey, USA)

Strattice™ is a pre-hydrated, terminally sterilized, porcine-derived dermal matrix.

Permacol™ (Covidien, Boulder, Colorado, USA)

Permacol™ is a pre-hydrated, terminally sterilized, porcine-derived dermal matrix. Of note, it is not recommended for breast reconstruction as it lacks adequate laxity to produce natural, ptotic lower pole coverage.

Surgimend® PRS (TEI Biosciences, Boston, Massachusetts, USA)

Surgimend® is the only product comprised of fetal bovine dermal collagen, and is terminally sterilized.

Synthetic mesh

Knitted Vicryl Mesh (Ethicon, Somerville, New Jersey, USA)

Comprised of polyglactin 910, Knitted Vicryl Mesh is cheap, ready to use and widely available. It also exhibits minimal inflammatory reaction, is non-allergenic and resistant to bacteria biofilm formation (39,40).

TiLOOP® Bra (PFM Medical, Cologne, Germany)

TiLOOP Bra is a lightweight, non-absorbable, titanium-coated polypropylene mesh, first approved for use in breast reconstruction in Europe in 2008. It is the most commonly used synthetic mesh in Germany (15). It consists of a monofilament structure and is available in three different bra-like sizes. The mesh comes in an infra-mammary fold like shape, helping to define the lower pole and preventing the implant from bottoming out. Both animal and human studies have demonstrated improved biocompatibility compared to non-titanium coated meshes, with histological evidence of incorporation during the time of expander-implant exchange (41,42). In Europe, the mesh costs €400 (43).

TIGR® Matrix Surgical Mesh (Novus Scientific Pte Ltd, Singapore)

TIGR® Matrix Surgical Mesh is a long-term, absorbable synthetic mesh. It is a macroporous mesh knitted from both a fast- (copolymer of glycolide and trimethylene carbonate) and slow-degrading (copolymer of lactide and trimethylene carbonate) fibers. After 2 weeks post implantation, the mesh will become noticeably softer and flexible, with due to the degradation of the fast fibers, which becomes totally resorbed within 4 months. The slow-degrading fibers keep their mechanics for up to 9 months, and are totally hydrolysed after 3 years (13). A 10 cm × 15 cm sheet of TIGR® mesh costs USD \$900. A preclinical study has demonstrated that the mesh is rapidly vascularized, demonstrates minimal inflammatory response, and is replaced by well-organized connective tissue over time (44).

Use of ADMs in post-mastectomy breast reconstruction and outcomes compared to non-ADM reconstruction

Currently, ADMs are used in both primary and revisional alloplastic breast reconstructive and aesthetic surgery. Techniques include: (I) expansion of the submuscular pocket to allow for direct-to-implant breast reconstruction (5); (II) expansion of the submuscular pocket to improve two-stage expander-to-implant breast reconstruction (31); (III) providing an interface when performing capsulotomies or

capsulectomies for capsular contracture; (IV) correction of symmastia (45); (V) aid in the masking surface irregularities and rippling (23); and (VI) prevention or correction of inframammary fold malposition and 'bottoming out' (46).

Use of alloplastic adjuncts in single stage, direct-to-implant reconstruction

Breuing and Warren first described the use of AlloDerm® as an inferior sling in immediate, direct-to-implant post-mastectomy reconstruction (5). The technique re-establishes the lower pole of the pectoralis major muscle, creating a subpectoral-sub-AlloDerm pocket that encloses the implant. The advantages of this method include the ability for a single stage, direct-to-implant reconstruction and its associated cost benefits, the ability to control lower pole fullness by adjusting the width of the sling and providing an additional layer of tissue between skin and implant. In a recent review by Macadam and Lennox, the use of ADMs (AlloDerm®) in direct-to-implant breast reconstruction, when compared to no ADM use in two-stage reconstructions (the Mentor and Allergan core studies) (47-51), resulted in lower rates of capsular contracture (0.3% vs. 8.3-17.1%), seroma (1.2% vs. 4.9%), infection (1.4% vs. 3.2-5.7%), late revisions (8.5% vs. 27-53.3%) and implant loss (1.5% vs. 5.7-7.7%). However, a higher rate of skin flap necrosis was observed (4.7% vs. 2.3%), which may be attributable to increased skin tension due to placement of the implant (52). Of note, the rate of skin flap necrosis is comparable to expander-to-implant reconstructions without the use of ADM published in previous studies (range, 2-6%) (53-56). Similarly, Salzberg *et al.* demonstrated a low overall complication rate (3.9%) in a retrospective analysis of 260 patients (466 breasts) who underwent single-stage reconstruction with AlloDerm®, with a mean follow up of 29 months (57). Specific complication rates included implant loss (1.3%), flap necrosis (1.1%), hematoma (1.1%), ADM exposure (0.6%), capsular contracture (0.4%) and infection (0.2%). Irradiated breasts had a fourfold higher rate of complications. The low complication rates are also projected long-term, with no complications seen in 354 breasts with more than 1 year of follow-up. A systematic review by Jansen and Macadam further reaffirms the comparable complication rates between AlloDerm®-assisted single stage and non-ADM, two-stage reconstructions (58). Of note, to validate these findings, Zhong *et al.* are currently conducting a randomized controlled trial comparing direct-to-implant reconstruction with ADM to traditional two-stage non-ADM reconstruction (59).

In contrast, a meta-analysis conducted by Ho *et al.* revealed higher odds of infection [odds ratio (OR), 2.7; 95 percent confidence interval (95% CI), 1.1-6.4], seroma (OR, 3.9; 95% CI, 2.4-6.2) and reconstructive failure (OR, 3.0; 95% CI, 1.3-6.8) in ADM compared to non-ADM breast reconstructions. However, ADM use was associated with lower rates of capsular contracture. The meta-analysis reviewed a total of 16 studies, most of which did not differentiate between single- or two-stage reconstruction. The most common complication associated with ADM use was skin flap necrosis (10.9%; 95% CI, 8.7-13.5%), followed by seroma (6.9%; 95% CI, 5.3-8.8%), infection (5.7%; 95% CI, 4.3-7.3%), reconstructive failure (5.1%; 95% CI, 3.8-6.7%), cellulitis (2.0%; 95% CI, 1.2-3.1%), hematoma (1.3%; 95% CI, 0.6-2.4%) and capsular contracture (0.6%; 95% CI, 0.1-1.7%).

Vicryl mesh has also been used in immediate single stage reconstructions with favorable results. In a retrospective analysis by Tessler *et al.*, 50 consecutive patients (76 reconstructions) underwent immediate implant-based reconstruction using knitted Vicryl mesh as an inferolateral sling. The overall complication rate was 6.6%, with one case (1.3%) of infection, two cases (2.6%) of mastectomy skin flap necrosis, one case (1.3%) of capsule contracture requiring revision (postradiation), one case (1.3%) of implant failure, and one case of a delayed type IV hypersensitivity reaction. Reported contour and implant positioning were excellent, with a revision rate of 3.9% (three breasts) for size enlargement. Additionally, Garganese *et al.* have used TiLOOP Bras in immediate implant-based reconstruction in ten patients, reporting no early complications and minimal post-operative pain (60). Klein *et al.* reported higher complication rates with the use of TiLOOP Bras in immediate reconstruction, with an infection, hematoma and seroma rate of 10.3%, 17.2% and 9.2% respectively (61).

Use of alloplastic adjuncts in two stage, expander-to-implant reconstruction

In 2007, Bindingnave *et al.* first described the use of ADMs in a two-stage expander-to-implant reconstructions (31). Alleged advantages include increased intra-operative expansion volumes and thus reduced post-operative expansion time, avoiding the need to raise serratus anterior muscle for lateral prosthesis coverage leading to reduced post-operative pain with expansion, as well as more precise placement of the expander resulting in better lower pole projection and improved aesthetics. However, multiple

studies have expressed concern regarding the increased morbidity associated with the use of ADM in two-stage reconstructions. In a series of 283 patients (415 breasts), Chun *et al.* demonstrated that the use of ADMs increased the odds of seroma by 4.24 times (P=0.018) and infection by 5.37 times (P=0.006), when compared to the non-ADM group (26). This was further confirmed in a meta-analysis performed by Kim *et al.* comparing the use of ADM (19 studies, n=2,037) and no ADM (35 studies, n=12,847) in two-stage breast reconstruction, reporting inferior outcomes in the ADM group. There were higher rates of seroma (4.8% *vs.* 3.5%), infection (5.3% *vs.* 4.7%) and mastectomy flap necrosis (6.9% *vs.* 4.9%) in the ADM group (62). However, the rate of reconstructive failure was comparable (3.8%). These findings were reinforced by a weighted analysis conducted by Macadam and Lennox for two-stage reconstructions using ADMs, compared to no ADMs, revealing higher rates of seroma (5.8% *vs.* 4.9%), infection (5.3% *vs.* 3.2-5.7%), and mastectomy flap necrosis (7.6% *vs.* 2.3%). However, there were lower rates of capsular contracture (2.6% *vs.* 8.3-17.1%), and late revisions (10.7% *vs.* 27-53%). The rate of implant extrusion was comparable (4.9% *vs.* 5.7-7.7%). Additionally, a meta-analysis by Hoppe *et al.*, consisting of eight studies comparing the use of AlloDerm® in expander-implant reconstruction to traditional submuscular techniques, demonstrated a three-fold increase in the odds seroma formation (OR, 3.00; 95% CI, 1.96-4.61) and a two-fold increase in the odds of infection in the ADM group (OR, 2.33; 95% CI, 1.55-3.49) (63).

In contrast, a systematic review by Sbitany and Serletti comparing the use of ADMs in two-stage reconstruction to standard subpectoral coverage techniques revealed a comparable complication profile, but more rapid reconstruction in the ADM group. There was a significantly higher rate of seroma formation in the ADM group (8.4% *vs.* 4.3%, P=0.03), but the rate of infection resulting in explantation was similar (3.4% *vs.* 3.2%, P=0.18, in the ADM and submuscular group respectively). There were also slightly higher rates of hematoma (2.0% *vs.* 1.2%, P=0.09) and partial mastectomy flap necrosis (9.3% *vs.* 7.2%, P=0.08) in the ADM compared to the submuscular group, none of which were statistically significant. The ADM group demonstrated higher intra-operative fill volumes (mean of 68.5% of final total volume *vs.* 24.2%, P=0.01) and a shorter post-operative expansion period (mean of 2.4 fills to achieve final volume *vs.* 5.1, P=0.03) (64).

Furthermore, a multicenter, blinded randomized, controlled trial comparing the use of ADM in two-stage

breast reconstruction showed no significant difference in adverse outcomes (hematoma, seroma and infection) between the ADM and non-ADM group (17% vs. 15% respectively, $P=1.00$) (65). Furthermore, there were no significant differences in immediate post-operative pain, pain during expansion phase, or the rate of post-operative expansion between the two groups.

A titanium-coated polypropylene mesh, TiLOOP Bra (PFM Medical, Cologne, Germany) is a widely used synthetic adjunct for post-mastectomy reconstruction in Europe. In a retrospective, multicenter analysis by Dieterich *et al.*, 207 patients (231 breasts) underwent either single- or two-stage reconstruction using TiLOOP Bra. The overall complication rate was 29%, with major complications occurring in 13.4% of the cases requiring operative intervention. The rate of mesh removal and implant loss was 7.8% and 8.7% respectively (43). Becker *et al.* used TIGR® mesh in 11 patients (19 breasts) undergoing two-stage reconstruction, reporting an overall complication rate of 47.3% (one case of flap necrosis, two cases of seroma, three cases of infection/extrusion, one case of rippling, and two cases of asymmetry requiring revision) (13).

Furthermore, Haynes and Kreithen reported on the use of Vicryl mesh in 38 patients (46 breasts) who underwent two-stage reconstructions. The results suggest that Vicryl mesh may be a suitable alternative to ADMs, with an overall complication rate of 15.2% (7 breasts): 3 cases (6.5%) of infections leading to expander removal, 1 case (2.2%) of expander exposure requiring removal in a patient undergoing radiotherapy, 2 cases (4.3%) of mastectomy skin flap necrosis, and 1 case (2.2%) of seroma. However, when analyzing the non-irradiated cohort (38 breasts), the overall complication rate was 10.5% (one case of infection leading to removal of the expander, two cases of mastectomy skin flap necrosis and one case of seroma). The revision rate was 16.2% in the non-irradiated group (two for size change, three for malposition and one for capsular contracture).

Comparison of outcomes between different ADMs

With the great diversity of alloplastic adjuncts available in the market, one of the main challenges faced by reconstructive surgeons is choosing the ideal product. The ideal adjunct would be terminally sterilized, able to be stored without refrigeration, have a long shelf life, not require any preparation (e.g., rehydration or rinsing), result in minimal inflammatory reaction, not require orientation, offer good long-term durability, available in multiple sizes

and thickness, as well as be affordable. The majority of published studies focus on AlloDerm®, as it was the first widely available ADM used for breast reconstruction.

Currently, Mendenhall *et al.* are conducting the largest prospective randomized trial comparing the outcomes after using AlloDerm® versus DermaMatrix® as an inferolateral sling in two stage expander-implant breast reconstruction in 128 patients (199 breasts). Preliminary results demonstrate a significant overall complication rate of 36.2%, with similar rates between the two groups (33.6% in the AlloDerm® and 38.8% in the DermaMatrix® group, $P=0.52$). In both the AlloDerm® and DermaMatrix® groups, the majority of complications were due to skin necrosis (17.8% vs. 21.4% respectively, $P=0.66$) and infections (13.9% vs. 16.3% respectively, $P=0.29$), both of which led to tissue expander losses (5% vs. 11.2% respectively, $P=0.11$). Of note, the rates of infection and skin necrosis are considerably higher compared to those previously reported (62,64). Complication rates (specifically infection and tissue expander loss) were significantly higher in obese patients, with the authors suggesting that ADM use should be avoided in such patients. Patients reconstructed with AlloDerm® had significantly faster expansion times (42 vs. 70 days, $P<0.001$).

The use of sterile AlloDerm® Ready to Use, when compared to aseptic AlloDerm®, led to reduced rates of mastectomy skin flap necrosis, seroma and infection (66,67). In contrast, although limited by sample size, a retrospective analysis comparing AlloDerm® (aseptic) with AlloDerm® Ready to Use (sterile) in implant based reconstructions, showed a higher seroma rate with the latter (68). Similarly, in a comparison between AlloDerm® and Stratice for alloplastic breast reconstruction, Glasberg and Light showed a significantly higher seroma rate with the use of AlloDerm® (21.4% vs. 6.3%, $P=0.0003$). All other complications were similar between the two groups (69). Other studies have shown AlloDerm® has comparable outcomes with DermMatrix, Stratice, SurgiMend, FlexHD, AlloMax and AlloDerm Ready to Use (70-75). Furthermore, Seth *et al.* showed no significant differences in complication rates between the use of cryopreserved or prehydrated human ADMs (PHADMs) (76).

Furthermore, Mofid *et al.* conducted a retrospective analysis on the use of Veritas®, a bovine pericardium xenograft, in immediate tissue expander/implant-based breast reconstructions. The overall complication rate was found to be similar, if not lower, compared to the use of AlloDerm® in previous studies (77).

Role of ADM in preventing capsular contracture

Capsular contracture is one of the most common complications in reconstructive breast surgery, with cumulative risks reported to be 12% after 1 year, and increasing to 30% at 5 years post-operatively (78). The aetiology remains unclear, although a common inflammatory pathway has been postulated, leading to increased deposition of collagen around the implant and myofibroblast migration (79-82). The use of ADMs appears to reduce the rate of capsular contracture. A meta-analysis conducted by Ho *et al.* revealed a pooled capsular contracture rate of 0.6%, significantly lower compared to the 3-18% rate reported in traditional two-stage reconstructions (22,23,83-85). Vardanian *et al.* studied the use of ADMs in immediate implant based reconstruction, and found a significantly lower rate, and risk of capsular contracture in the ADM group versus the non-ADM group (3.8% *vs.* 19.4% respectively; OR, 0.18; 95% CI, 0.08-0.43) (24). Basu *et al.* have also shown the protective effects of ADMs histologically, with intra-operative biopsies of human breast capsules and associated ADM at the time of implant exchange demonstrating decreased capsular fibrosis and fibroblast cellularity relative to controls (86). Multiple other studies have similarly demonstrated a low capsular contracture rate in patients undergoing both single- and two-stage breast reconstruction with ADM, ranging from 0-3.8% (5,24,31,34,57,87,88). Interestingly, in a primate model, Stump *et al.* have demonstrated the role of AlloDerm® in preventing capsular formation (89). However, further long-term follow up is necessary as the rate of capsular contracture may increase with time.

Role of ADMs in irradiated tissue

There have been mixed reports on the role of ADMs in irradiated tissue. In a study where two AlloDerm implants were placed in the backs of 41 rats that were irradiated, Komorowska-Timek *et al.* demonstrated that the use of AlloDerm decreased radiation-related inflammation and potentially delayed capsular formation and contraction, with the protective effects still present at 12 weeks (90). Similarly, in a retrospective review of 417 consecutive patients (592 breasts), Seth *et al.* demonstrated a decreased risk of all complications in irradiated breast tissue reconstructed with ADM, versus the non-ADM group (91). Non-ADM patients who received post-mastectomy radiation therapy were almost three times as likely to have a complication

compared to non-irradiated patients (OR, 2.63; P=0.002). Conversely, ADM patients who received radiotherapy did not show a significant increase in the risk of complications compared to the non-irradiated group (OR, 1.90; P=0.10). Additionally, Mitchell suggested a protective effect of ADM in irradiated tissue, in a retrospective series of 103 patients (158 breasts) who underwent ADM assisted reconstruction using Strattice™ (92). Interestingly, no complications occurred in patients who received radiotherapy post reconstruction.

In contrast, Spear *et al.* investigated the use of AlloDerm in a prospective series of 58 immediate expander-based breast reconstructions, and found that the use of AlloDerm did not protect against the effects of radiotherapy, with an overall complication rate of 71.4% (46). Additionally, Nahabedian found a minor increase in the rates of infection, seroma and wound dehiscence in irradiated versus the non-irradiated groups (21). Twenty-three out of 100 breasts reconstructed with AlloDerm received radiotherapy, and complications included: seroma (13%), infection (8.7%), skin necroses (0%) and dehiscence (13%) versus the non-irradiated AlloDerm group: seroma (2.6%), infection (3.9%), dehiscence (1.3%) and skin necrosis (3.9%). The lack of protective effects in ADM assisted breast reconstruction is further strengthened by a recent meta-analysis conducted by Valdatta *et al.* (93).

Costs

Conducting cost-benefit analyzes for procedures is complex, as it requires not only the immediate costs of the procedure to be calculated, but also any additional costs that may be incurred post-operatively. Most of the cost analysis studies on the use of ADM have taken into account some, if not all of the significant outcomes associated with breast reconstruction: no complication, seroma, infection, hematoma, capsular contracture, implant exposure with loss, implant exposure with salvage, and skin flap necrosis. The majority of these studies highlight a cost advantage in conducting single stage, direct-to-implant breast reconstructions using ADMs. Using a calculator based on immediate operative costs and expected outcomes, Macadam and Lennox estimated that direct-to-implant reconstruction using ADM was cheaper than two-stage reconstruction without ADM (\$11,072 *vs.* \$15,049) (52). Similarly, de Blacam *et al.* estimated that direct-to-implant reconstruction with ADM was more cost-effective compared to expander-to-implant with ADM, and expander-to-

implant with no ADM reconstruction (\$5,432.02 vs. \$11,255 vs. \$10,934 respectively).

Additionally, costs will vary depending on the type and size of alloplastic adjunct used, as well as the country of interest. An inquiry in August 2011 by Cheng *et al.* revealed that the price of ADMs ranged from approximately USD \$21.63-34.76 per centimeter squared (14). However, these prices do not reflect the charges to the patient, and some are still considered experimental and thus are not covered by insurance.

The cost of synthetic meshes is considerably cheaper, with Vicryl mesh costing under USD \$200 per breast. With the use of Vicryl mesh in 76 reconstructions, Tessler *et al.* have reported a saving of USD \$172,112 in direct material costs over 10 months (40).

Discussion

First introduced in 1995 for reconstructive burns surgery, ADMs are extracellular matrix grafts which provide a scaffold upon which the patient's own cells can repopulate and revascularise the implanted tissue (94). Since its introduction for post-mastectomy breast reconstruction in 2005, multiple studies have detailed varied and inconsistent outcomes on the use of alloplastic adjuncts. To date, they can be classified into two main categories, ADMs that are derived from either allogeneic or xenogeneic dermis, as well as synthetic meshes. To date, there are over ten different products available (*Table S1*). The absence of comparative data between these products makes choosing the ideal material a significant challenge to the reconstructive surgeon. The primary aim of this systematic review was to summarize the published data available for these alloplastic adjuncts, including analyzing outcome data which available, with particular interest in its role in irradiated tissue and cost-effectiveness. Importantly, most of the published data available are on AlloDerm®.

Despite the majority of systematic reviews and meta-analyses demonstrating inferior outcomes in ADM-assisted breast reconstructions, Macadam and Lennox suggested superior outcomes with the use of ADMs in single stage, direct-to-implant reconstructions, compared to traditional two-stage reconstructions. Reduced rates of seroma, infection, late revisions, implant loss and capsular contracture were observed (52). The direct placement of an implant may lead to a better match in the volumes of the overlying mastectomy skin flap and implant, leading to reduced rates of seroma. However, this needs to be balanced

by the higher risk of skin necrosis. The use of the ADM as an inferolateral sling may allow better control of the inframammary fold, leading to improved cosmesis and lower rates of late revision. The reduced frequency of infection may be a consequence of the reduced seroma rate, as well as avoiding the need for repeated expander manipulation for filling and a second surgery for expander-implant exchange.

Based on the available systematic reviews and meta-analyses, skin flap necrosis was the most common complication post ADM-assisted breast reconstruction, ranging from 1.1-10.9% (52,62-64,84). This is higher when compared to traditional submuscular techniques (range, 2-6%) (53-56). This increased incidence may be attributable to a number of factors, including a higher intra-operative expander fill volume leading to excessive skin tension, and inappropriate preservation of post-mastectomy skin with ADM use. However, a delicate balance needs to be achieved between adequate expander filling to maximize incorporation of the ADM to the mastectomy skin flap, without creating excessive tension. This outcome may potentially improve with increased surgeon experience. More recently, to address this issue, ADMs have been used in staged, immediate (direct-to-implant) breast reconstruction. In patients at high risk of skin flap necrosis, reconstruction using an implant and ADM sling was performed 2 weeks after the initial mastectomy, without the use of interval expanders. Initial results are promising, with no infectious or bleeding complications, and no cases of nipple malposition (95).

One of the main concerns regarding the use of ADMs is the increased risk of infection, as some are 'aseptic', and not terminally sterilized (i.e., a sterility assurance level of 10^{-6}). The majority of published evidence confirms this concern, with three meta-analyses and a systematic review pointing to increased rates of infection in ADM-assisted breast reconstruction compared to standard submuscular techniques (62,63,84,96). A possible explanation for this is that prior to being revascularised, which takes approximately 2 weeks to occur, ADMs may act as a nidus for infection (33). However, there are numerous potential confounding factors that may affect the rate of infection [e.g., patient age, smoking status, diabetes body mass index (BMI), radio- or chemotherapy]. Studies have shown that a higher BMI, higher age, larger breasts (>600 grams), presence of axillary dissection and chemo-radiation are significant risk factors for infection (26,93,97,98). Furthermore, studies may have varying definitions of infection, with a number of studies having both 'infection', and 'cellulitis', as outcomes of

interest, terminally sterilized human ADMs have recently been introduced, including AlloMax and AlloDerm Ready to Use, and xenogeneic ADMs (e.g., Strattice and SurgiMend PRS) are also terminally sterilized, which may theoretically improve the infection rate. Importantly, the red breast syndrome is associated with ADM use, and may be mistaken for infection in some cases. This typically manifests as erythema limited to the region overlying the ADM, and is often self-limiting and not responsive to antibiotics. The underlying aetiology remains unclear, but may represent a delayed hypersensitivity reaction (66,99).

Furthermore, multiple studies have demonstrated a higher rate of seroma in the ADM versus the non-ADM group (62,63,84). This may be a result of a mismatch between the size of the overlying skin envelope and the underlying tissue expander volume. Additionally, seromas are also more likely to form prior to revascularization of the ADM. Further confounding factors, including surgical technique, concomitant axillary node dissection, placement and number of drains may also affect risk of seroma formation.

The use of synthetic mesh, particularly Vicryl mesh, appears to show promising outcomes as a comparable, but cheaper alternative to ADMs. However, one of the major concerns of using absorbable mesh as an inferolateral sling is implant malposition or 'bottoming out', in the long-term, as Vicryl mesh is normally resorbed by 3 to 4 weeks (40). The introduction of TIGR[®] mesh was meant to address this, but published data is scarce and despite a small sample size (19 breasts), demonstrated inferior outcomes (13). Furthermore, the use of TIGR[®] and Vicryl mesh may be limited to non-irradiated tissue, as the complication rate was significantly higher in irradiated patients (13,100). Further higher powered, long-term studies on the use of these synthetic meshes are needed.

Limitations

Direct comparison between alloplastic adjuncts is challenging, as there are distinct differences between ADMs and synthetic meshes, and also between different types of ADMs themselves. The definition of outcome measures in the included studies may also differ, making direct comparison challenging. For example, seromas may be classified into those that require drainage, or those that are simply observed. Additionally, a limitation inherent in most surgical outcome studies is accounting for the heterogeneity in surgeon skill and technique, which may be an important

confounding factor. Related to this is the type of mastectomy performed (simple, skin sparing, nipple sparing, modified radical), and initial fill volumes in tissue expander reconstructions, as these will influence the rate of skin flap necrosis and subsequent complications. Importantly, a significant number of studies did not differentiate between single- and two-stage reconstructions, which may affect the results as these two techniques have different complication profiles. Due to the retrospective nature of the majority of included studies, the number of complications reported may be underestimated. Furthermore, there may be an element of publication bias as researchers are less likely to publish unfavorable results.

Conclusions

The majority of systematic reviews and plural of meta-analysis demonstrate increased complication rates in ADM-assisted expander-implant reconstruction compared to traditional submuscular techniques. However, the potential benefits, including superior outcomes in single-stage direct-to-implant surgery, improved cosmesis, lower costs and reduced incidences of capsular contracture, must also be considered. The reported protective effects of ADMs in irradiated tissue are inconsistent. Additionally, due to the diversity of available products, one of the main challenges is selecting the ideal material. There remains a paucity of literature comparing the long-term outcomes between the different types of alloplastic adjuncts and further studies are required to identify the superior adjunct.

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Footnote

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Prosthetic breast reconstruction: indications and update

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Background: Despite 82% of patients reporting psychosocial improvement following breast reconstruction, only 33% patients choose to undergo surgery. Implant reconstruction outnumbers autologous reconstruction in many centres.

Methods: A systematic review of the literature was undertaken. Inclusion required: (I) Meta-analyses or review articles; (II) adult patients aged 18 years or over undergoing alloplastic breast reconstruction; (III) studies including outcome measures; (IV) case series with more than 10 patients; (V) English language; and (VI) publication after 1st January, 2000.

Results: After full text review, analysis and data extraction was conducted for a total of 63 articles. Definitive reconstruction with an implant can be immediate or delayed. Older patients have similar or even lower complication rates to younger patients. Complications include capsular contracture, hematoma and infection. Obesity, smoking, large breasts, diabetes and higher grade tumors are associated with increased risk of wound problems and reconstructive failure. Silicone implant patients have higher capsular contracture rates but have higher physical and psychosocial function. There were no associations made between silicone implants and cancer or systemic disease. There were no differences in outcomes or complications between round and shaped implants. Textured implants have a lower risk of capsular contracture than smooth implants. Smooth implants are more likely to be displaced as well as having higher rates of infection. Immediate breast reconstruction (IBR) gives the best aesthetic outcome if radiotherapy is not required but has a higher rate of capsular contracture and implant failure. Delayed-immediate reconstruction patients can achieve similar aesthetic results to IBR whilst preserving the breast skin if radiotherapy is required. Delayed breast reconstruction (DBR) patients have fewer complications than IBR patients.

Conclusions: Implant reconstruction is a safe and popular mode of post-mastectomy reconstruction. Evidence exists for the settings in which complications are more likely, and we can now more reliably predict outcomes of reconstruction on an individual basis and assess patient suitability.

Keywords: Breast cancer; breast implant; prosthesis; reconstruction; tissue expander; alloplastic

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Introduction

In 2010, breast cancer was the most common cancer amongst Australian women, with 14,181 new diagnoses (1). Breast cancer comprises 28% of all new cancers in women and the risk of developing breast cancer before the age of 85 is 1 in 8 (1). Approximately 35–40% of women diagnosed with breast cancer undergo a total mastectomy, a trend which is increasing (2). Fewer than 33% of those who are suitable undergo breast reconstruction (2) despite 82% of women reporting psychosocial improvement following reconstruction (3).

Although reconstruction using a transverse rectus abdominis musculocutaneous (TRAM) flap or a deep inferior epigastric artery perforator (DIEP) flap offers women the option of autologous reconstruction, prosthetic reconstruction is still widely used. Data from the United States indicate that between 1998 and 2008, there was an 11% increase in the use of implants per year, whereas autologous reconstruction rates remained stable (4,5). Indeed, the data shows that prior to 2002, autologous reconstructions were the more frequently chosen method of reconstruction compared with the use of prostheses. However, after 2002, this relationship was reversed and in 2008 implants outnumbered autologous reconstructions by a ratio of 2:1 (258 *vs.* 120 per 1,000 mastectomies) (4). Albornoz *et al.* (4) suggests a number of reasons behind this change in trend; the longer time it takes to perform autologous reconstruction, a cultural shift towards acceptance of breast implants, and the way in which reconstruction is funded. In the US Medicare funding for autologous implants decreased between 1998 and 2008. Also private insurance companies increased payment for implant reconstruction by 64%, while reimbursement for autologous reconstruction was unchanged (4).

In the 1960s silicone breast implants were introduced, launching the era of modern breast reconstruction. Radovan (6) pioneered the use of tissue expanders in the early 1980s which has allowed for further reconstructive options. Since then, there have been great advances in the both the technique of expander/implant breast reconstruction and in the prostheses themselves (7).

The decision for autologous *vs.* prosthetic reconstruction is a decision that requires a long discussion between the patient and surgeon which must take into account many factors. There are many advantages and disadvantages that autologous reconstruction has over prosthetic reconstruction which is outside the scope of this article. Once the decision has been made to pursue prosthetic

breast reconstruction, the aim of this article is to provide a summary of the current data to assist the clinician in the complex decision making process that follows.

In considering prosthetic breast reconstruction, a number of factors need to be considered by both surgeon and patient. The indications and selection of patients for prosthetic reconstruction will be discussed as will the timing of reconstruction following mastectomy. Integral to this is determining whether or not adjunctive therapy is required as this can greatly affect the outcome of prosthetic reconstruction.

Methods

The current study comprises a systematic review of the literature focusing on the evidence for prosthetic breast reconstruction.

Study identification

Multiple databases were searched independently by two authors (TQ and GM), including: Ovid Medline (1950 to present), EMBASE (1980 to 2015), PubMed and Cochrane Database of Systematic Reviews.

The following search terms and Boolean operators were used: (I) “breast reconstruction” or “breast neoplasm,” or “breast implants” or “breast” and (II) “alloplastic” or “prosthesis” or “implants”. Additional searches were conducted using (I) and (II) and “tissue expansion devices” or tissue expander”; (I) and (II) and “surgical flaps” or “mammoplasty” or “mastectomy” as well as (I) and (II) and “reconstructive surgical procedure”.

Inclusion criteria

Inclusion criteria for studies reviewed included: (I) meta-analyses or review articles; (II) adult patients aged 18 years or over undergoing post-mastectomy alloplastic breast reconstruction (i.e., tissue expander or implant based); (III) studies including outcome measures; (IV) case series with more than 10 patients; (V) published since 1 January 2000; and (VI) English language.

Data extraction

A systematic review was conducted using the PRISMA 2009 statement. Data was extracted by two authors (TQ and GM), and included author, year, journal, study design, level of evidence, outcome details, number of patients

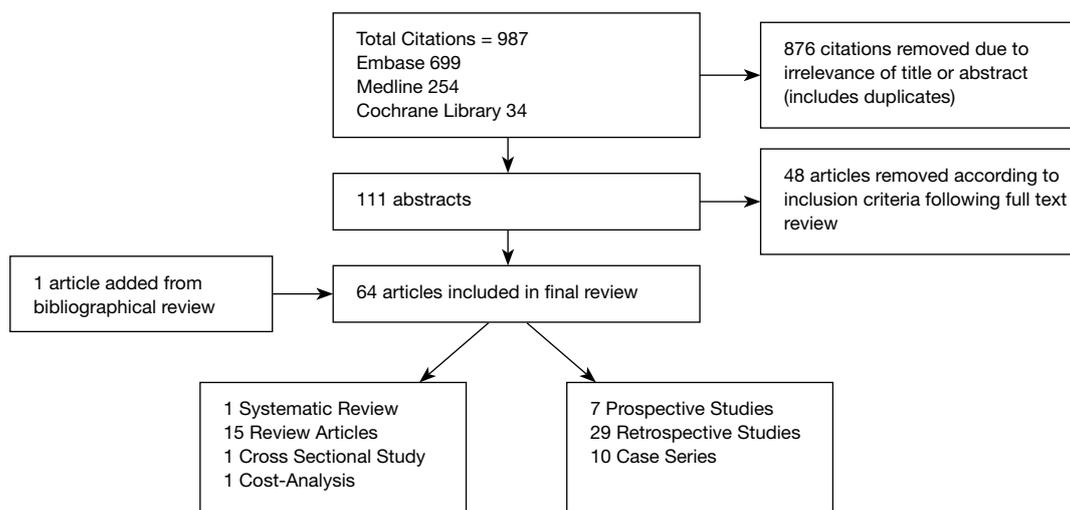


Figure 1 Article selection.

(if applicable), and follow up period. Differences in data extraction were corrected via discussion.

Literature search results

The search was conducted on April 10, 2015, resulting in 987 articles, managed using Endnote X7™ (Thomson Reuters, Philadelphia, PA). A summary of the literature review process is shown in *Figure 1*. After the authors independently assessed the titles a total of 876 articles were removed for irrelevance or duplication. The abstracts for the remaining articles were then reviewed based on the inclusion criteria, leaving a total of 111 articles for full review. A further one article was added based on review of bibliographies. Fifty studies were eliminated after full review (due to publication date prior to the year 2000, inadequate outcome measures, and case series fewer than 10 patients). After full text review, analysis and data extraction was conducted for a total of 62 articles, summarized in *Table S1*.

Outcomes on the 62 articles that met the inclusion criteria were summarized and analyzed. The breakdown of the types of articles included was 1 systematic review, 14 reviews, 7 prospective studies, 26 retrospective studies, 10 case series, 1 cost-analysis, and 3 cross-sectional studies).

Discussion

Indications and patient selection

Most patients who undergo mastectomy for breast cancers

are candidates for prosthetic reconstruction. There are factors that limit a patient's ability to undergo autologous reconstruction. This may include general medical health, an unsuitable donor site, lifestyle factors and availability of resources. Prosthetic breast reconstruction, however, can be a safe and viable option, even for older patients. Indeed, Hershman *et al.* [2012] reported that the immediate in-hospital complication rate was significantly higher in patients who underwent autologous reconstruction when compared to those who had prosthetic reconstruction (8).

The choice of whether or not to undergo reconstruction can be a complex. This has been studied by Reaby *et al.* [1998] (9) and by Ng *et al.* [2014] (10). Many patients choose not to undergo reconstruction. This may be because they lack information about the procedures, do not feel that it was necessary for their physical or emotional well-being or that due to fears that it would mask cancer recurrence (9). Of the approximately 33% (2), however that do choose reconstruction, they report that they did so because they could get rid of external prostheses, be able to wear many types of clothing, regain their femininity and to feel "whole" again after the surviving breast cancer (9). In the areas of social functioning and emotional wellbeing, it has been reported that patients who underwent reconstruction did better than those who did not have reconstruction (11). Some patients may have unclear and potentially inaccurate expectations of the appearance of, and physical sensation, in particular the "unnatural feel", firmness and lack of movement, associated with prosthetic breast reconstruction which can lead to dissatisfaction with the outcome (12).

Definitive reconstruction with an implant can be done either at the time of the mastectomy, referred to in this article as immediate breast reconstruction (IBR), or as a two-stage reconstruction with a tissue expander followed by a permanent implant and most of the time with intervening (13) adjuvant therapy, a process referred to in this article as delayed breast reconstruction (DBR). Clinicopathological features which are considered when making decision regarding the type of reconstruction include cancer stage, status of the sentinel node, smoking, body habitus, pre-existing scars and prior radio or chemotherapy (14).

Immediate reconstruction is preferred where possible because of the psychological and physical benefits attained from restoration of mammary volume and shape (15) and is associated with a high level of patient satisfaction (16). Prosthetic breast reconstruction has the advantages of shorter procedure time, hospital stay and recovery as well as being lower cost (17) and not having an additional donor site associated with an autologous reconstruction (18). Unfortunately, having prosthetic IBR is associated with requiring unplanned surgery in the future to revise the reconstruction (19,20) and a higher complication rate related to prosthesis failure (21). Patients with small, minimally ptotic breasts are ideal candidates for single-stage reconstruction (22) as are patients who have a good cancer prognosis, who are sentinel node negative and therefore do not require axillary surgery and have late local recurrence (LR) in a previously treated breast (23). Patients with larger and/or ptotic breasts are not ideal candidates for IBR as they often need contralateral balancing procedures to achieve symmetry which can be difficult to judge at the time of immediate reconstruction (24).

Delayed or two-stage reconstruction with a tissue expander followed by a permanent implant is an alternative pathway for prosthetic reconstruction. Tissue expansion is simple, safe and allows for preservation of the skin envelope and allows for better matched color, texture and hair-bearing qualities of the skin (25). It also allows for implantation of synthetic materials underneath the expanded tissue as the skin flaps are vascularized (25). Tissue expansion is recommended in patients who require adjuvant radiotherapy as radiotherapy can adversely affect the aesthetic outcome, and tissue expanders can impede effective and safe radiation delivery to the internal mammary and axillary lymph nodes (26).

Breast reconstruction in the elderly

Despite the recent increase in the rate of immediate

reconstruction, many older women choose not to undergo breast reconstruction following mastectomy due to the fear of complications and the perception that they are “too old” for the procedure (9).

The literature indicates that older patients tolerate breast reconstruction well. Walton *et al.* [2011] reports similar complication rates in older compared to younger patients but that autologous reconstruction result in better outcomes than implant reconstruction (11). August *et al.* [1994] reported, in a patient cohort of 242, that there were significantly fewer complications in women over the age of 60 following both IBR and DBR. It was also noted that older women tended to require fewer operations to achieve the final results compared to their younger counterparts (27).

Risks and complications of prosthetic reconstruction

The most common complications associated with prosthetic reconstruction include capsular contracture, hematoma and infection (28). The complication rate was significantly lower when implants were inserted for cosmetic reasons (6.5% at 1 year and 12% at 5 years) compared to those who had expanders inserted either following prophylactic mastectomy (17.3% at 1 year and 30.4% at 5 years) or mastectomy for cancer (21.8% at 1 year and 34% at 5 years) (28). In a systematic review of 14 observational studies, which included more than 3,000 breasts, Tsoi *et al.* [2014] concluded that reconstructive failure and surgical site infection was higher in patients who had prosthetic reconstruction compared to those who underwent autologous reconstruction (29).

Wound complications are associated with large breast volume (greater than 750 g) and sternal notch to nipple length of greater than 26 cm (30). Significant risk factors for reconstructive failure include smoking (31), obesity (32), incomplete muscle coverage (31), implant volume >400 mL (31), type 2 diabetes mellitus (32), higher grade tumors and nodal involvement (33). Although not a statistically significant risk factors for complications, older age was associated with a borderline increased risk of complications in both IBR and DBR (31). Tamoxifen, an oestrogen receptor antagonist use is associated with a borderline risk of complications but a significant risk of reconstructive failure in patients who undergo expander/implant reconstruction (34).

Capsular contracture

Capsular contracture development is multifactorial.

Numerous potential aetiologies and contributing factors have been described including bacterial colonization, the type and texture of the implant, the placement of the implant and the use of radiotherapy (35). Overall incidence of significant capsular contracture (Baker classification III or IV) ranges from 10.4% (36) to 29% (37). Capsular contracture rates in immediate reconstruction has been reported as being between 20% (38) to 40.4% (39) and rates for delayed reconstruction range from 17% (39) to 26.4% (38). Smoking, use of smooth implants (40) and hematoma increased the risk of developing contractures, as does the duration of implantation (41).

Staphylococcus epidermidis is the bacteria most implicated in capsular contracture. It exists in the ductal system in the breast and has been cultured from breast milk, nipple secretions and biopsied from breast parenchyma (42). Bacterial etiology is a likely major contributor of capsular contracture. Bacteria adhere easily to silicone and form a biofilm comprised of extracellular polysaccharides and glycoprotein. Virden *et al.* (42) cultured 55 silicone implants at the time of removal. Bacterial growth was detected in 56% of implants surrounded by contracted capsules compared to 18% of implants without contracted capsules, a significant difference. Patients who undergo radiotherapy are at significant risk of developing capsular contracture. Patani *et al.* [2008] reports a rate of capsular contracture requiring capsulotomy as a staggering 87%, compared to 13% in those who did not have radiotherapy (43). Of the 71% of patients receiving radiotherapy who developed capsular contracture in the study conducted by Ringberg *et al.* [1999], 8% had Baker classification III and IV contractures (44). The use of a flap with the implant seems to mitigate capsular contracture, reducing the risk of capsular contracture to 6.8% compared to a rate of 25% of those who had implants alone (41).

In a series of 326 tissue expanders, Rheingold *et al.* [1994] reported an overall contracture rate of 78.5% Baker I, 12% Baker II, 8.6% Baker III and 0.9% Baker IV contractures (45). Holmes *et al.* [1989] reported that neither the speed of expansion, nor the degree of over-expansion influenced the onset of contracture. However, patients with Baker I contractures had a significantly longer interval been full expansion and definitive recon than did those who developed Baker III contractures (37).

Types of prostheses

Silicone vs. saline implants

Gylbert *et al.* [1990] reported a higher capsular contracture rate in silicone implants (50%) compared to 16% of saline

implants. However, 16% of the saline implants deflated. Despite the higher contracture rates amongst the silicone implant group, 85% of the patients in this study reported that they were satisfied with the reconstruction (46). Both Macadam *et al.* [2010] (47) and McCarthy *et al.* [2010] (48) report that patients who have silicone implants have higher quality of life and satisfaction scores than those with saline implants. There is also a statistically significant difference in overall physical function (silicone implants performed better) and systemic side effects (higher in patents with saline implants).

Despite concerns, there has been no associations found between silicone implants and cancer, immunological or systemic disease (49).

A prospective review from 1990 to 1997 by Spear *et al.* [2000] reviewed 40 consecutive patients with saline implants (50). Almost half (47.5%) of irradiated breasts with saline implants required revision or replacement by a flap (compared to 10% of control group who required revision with a flap but none required replacement). Patients with saline implants also had higher contracture rate of 32.5%

One type of implant containing hydrogel filler (polyvinylpyrrolidone and guar gum) was reported as having similar contracture rates to saline implants but twice the rupture rate. This was subsequently withdrawn from use in the United Kingdom market in 2000 (51).

Round vs. anatomic implants

The consensus is that there is no difference seen between round and shaped implants including rippling, overall satisfaction with breast and outcome (52).

Cohesive gel implants are comprised of a textured silicone elastomer shell filled with cohesive silicone gel. There is increased number of cross links between gel molecules which results in better shape retention and less likely to collapse (53). Highly cohesive shaped devices have been reported to be firmer than the less cohesive round implants. In addition, because of the added cohesivity of the shaped implant, there may be less rippling (52). In cases that involve reconstructing an upper pole deficiency of the breast an anatomic implant is favoured. Round implants are usually favoured when there is no appreciable upper pole deficiency. Nahabedian *et al.* [2014] reported similar complication rates between the two strategies (54).

Textured vs. smooth implants

Textured implants form thinner and more pliable capsules that are less likely to contract than smooth implants. In a

review of 16 randomized control trials and two retrospective trials, Liu *et al.* [2015] found that smooth implants were more likely to be associated with capsular contracture than textured implants (55). About 96% of textured implants were reported to have a satisfactory (Baker classification Grade II or better) result compared to 72% of patients who had a smooth implant inserted (56).

The contracture rate reported by Embrey *et al.* [1999] was 58% for smooth implants compared to 8% for textured implants (35). Hakelius *et al.* [1992] performed bilateral, subglandular implant insertion in 25 patients for mammary hypoplasia. In each case one smooth and one textured implant was inserted. It was found that at 1 year, the textured implant was less likely to develop contractures (57). Longer-term follow up at 10 years found a reduced rate of contractures in textured implants compared to smooth implants (58) with a reported contracture rate of 65% in smooth implants *vs.* 11% in textured implants (40). Not only are smooth implants associated with significant capsular contracture they also are more likely to be displaced as well as having higher rates of infection and pain on expansion (59). Textured implants, in contrast, maintained their position and expanded easily with minimal pain (59).

Integrated port *vs.* distant port tissue expanders

The Becker Expander, (TM) a textured tissue expander produced by Mentor, which has a distant port, offers the advantage of single-stage reconstruction. The expander is filled until the desired volume is reached prior to the ports being removed under local anesthetic and the expanders being left in-situ as implants. Large series have reported good outcomes at 3 years. However at 5 years Chew *et al.* [2010] found that 68% were removed due to complications (poor aesthetics, capsular contracture, infection). The congenital hypoplasia group had better retention rates (67% at 10 years) than oncological (2%) or risk reducing mastectomy (5%) groups (60).

Spear *et al.* [1998] performed 171 consecutive reconstructions using textured, integrated valve expanders. All were two-stage reconstructions. Four percent deflated over 7 years, 2 were removed for infection and 1 electively. About 98% of a subgroup of 42 patients were satisfied with their reconstructions (61). Yanko-Arzi *et al.* [2009] found more complications with integrated-valve expanders compared to those with distant inflation ports (62).

Timing of reconstruction with prostheses

Albornoz *et al.* [2013] reports that from 1998 to 2008, there

was a 78% increase in the rate of IBR from 20.8% to 37.8%, an average of 5% per year (4). IBR gives the best aesthetic outcome if radiotherapy is not required (63), and patients who received IBR had better physical and psychosocial scores than those undergoing DBR (64). As mastectomy defects can result in the loss of body integrity and femininity, patients who have IBR have higher satisfaction levels than those who have delayed reconstructions (32). Factors associated with an increase likelihood of IBR included large hospital size with a high number of patients requiring IBR and surgeons who perform IBR regularly. Decreased likelihood was associated with increased age, black race, patients who were married, patients from rural locations and patients with increased comorbidities (8).

The early complication rate ranges from 9.2% (65) to 16% (66) and include skin flap necrosis, infection, sarcoma, hematoma and a 1.7% risk of explantation (65). Late complication rates have been reported to be as high as 23% (65). Unfortunately the cosmetic outcome following IBR diminished over time from 86% acceptable cosmetic appearance at 2 years to 54% acceptable cosmetic appearance at 5 years, independent of radiotherapy, type of implant, volume of implant, age of the patient or the type of mastectomy incision used (65).

There is a reported revisional surgery rate of 30.2% following IBR (65). Fifty seven percent of IBR required revision compared to 27% of DBR (67), although the two groups had similar complication rates and failure rates. Patients undergoing IBR also need more capsular intervention procedures which leads to greater expense but they can obtain good results due to revisional surgery (68). The risk of requiring revision is higher if the patient has undergone radiotherapy, is D-cup size or larger, or has grade 2 or 3 ptosis of the breast (67).

The rate of complications is higher in patients who have IBR compared to the DBR group (69), with capsular contracture being the most significant complication (40.4% *vs.* 17%) (39). The negative effect of radiotherapy is more significant with IBR than DBR groups (70). The rate of implant loss has been reported from 1.7% (65) to 18% (31). IBR is reported to have a higher overall complication and implant failure rate than DBR (71).

Delayed-immediate reconstruction

Patients who are anticipated to require radiotherapy who desire breast reconstruction are considered candidate for delayed-IBR (63). Using the delayed-immediate protocol enables surgeons to provide the near optimal reconstruction

despite whether radiotherapy eventuates or not. Those patients who do not end up needing radiotherapy achieve aesthetic results comparable to patients who undergo IBR. For the patients who do end up receiving radiotherapy, the aesthetic problems usually associated with radiotherapy following IBR are avoided (30). This protocol of breast reconstruction also allows for skin-preserving DBR after radiotherapy for patients in whom radiotherapy only becomes apparent after review of the pathological sections post mastectomy. Preserving the breast skin envelope in patients who have undergone radiotherapy allows for the direct placement of an implant and decreases the need for addition of autologous flaps or at least minimizes the dimensions of the skin island required from an autologous flap.

In stage 1 of a delayed-immediate reconstruction, patients undergo a skin sparing mastectomy plus the insertion of an expander, with or without the addition of an acellular dermal matrix (ADM). The expander is then filled to the required volume intraoperatively. The pathology is subsequently examined and the patient discussed at a multidisciplinary team (MDT) meeting. If radiotherapy is not required, the patient proceeds to have definitive reconstruction (stage 2) with an autologous flap, flap plus implant or implant alone. If radiotherapy is required, however, the expander is deflated following the course of chemotherapy (if the patient is having it) and prior to radiotherapy planning. She then undergoes radiotherapy, has the expander re-expanded then completes stage 2 of the reconstruction three months after radiotherapy is completed.

Delayed breast reconstruction (DBR)

DBR is significantly more common in the USA than elsewhere in the world (72). A two-stage reconstruction gives a more predictable result as it can be adjusted at the second operation (24). Multiple authors have suggested that patients who undergo DBR have fewer complications than patients who have IBR. Francel *et al.* [1993] found that patients who had DBR were less likely to require surgery to correct capsular contracture (67). Cosmetic results in patients who have DBR 6 weeks after radiotherapy were found to be superior when compared to those who had IBR (73). The timing of reconstruction after radiotherapy is also important. Lentz *et al.* [2013] studied patients who had reconstruction within 4 months following compared to patients who had reconstruction greater than 4 months after radiotherapy. The former group had a non-significant trend towards increased infection whilst the latter tended to have a higher capsular contracture rate (74).

The concept of “delayed-delayed” prosthetic reconstruction is described by Kronowitz *et al.* [2015] (26). Neoadjuvant chemotherapy and radiotherapy in conjunction with skin sparing mastectomy in patients who have locally advanced breast cancer is increasingly resulting in good long-term disease control and survival (26). Following neoadjuvant chemotherapy, which decreases the need to resect skin at the time of mastectomy, patients with locally advanced breast cancer are discussed at an MDT and eligibility for skin sparing DBR is decided. For those that are deemed suitable, they undergo a skin-sparing mastectomy with insertion of a tissue expander with or without ADM. The expander is filled intra-operatively but then is partially deflated immediately prior to planning for radiotherapy. After the resolution of any radiation induced skin desquamation the expander is re-inflated to the pre-deflation volume and 3 months after radiotherapy and re-inflation, the definitive reconstruction is performed. The aim of this protocol is to improve aesthetic outcome, decrease complications and reduce psychological disadvantages associated with DBR after radiotherapy.

Radiotherapy and prosthetic breast reconstruction

More centers globally are recommending radiotherapy for patients with breast cancer, including early breast cancer, which increases the complexity of reconstructive planning (26). The USA has been reported to have higher rates of reconstruction prior to radiotherapy than elsewhere in the world (72). Chen *et al.* [2013] found that 57% of 358 surveyed radiation oncologists felt that breast reconstruction challenged their ability to deliver effective radiation. Sixty percent preferred a moderately inflated expander (150-250 CC) compared to completely deflated (13%) or completely inflated (28%) (72).

In a review article by Fodor *et al.* [2003] the most common type of complication associated with radiotherapy was significant capsular contracture (Grade III or IV) (69). Rates of capsular contracture varied from 29% (75) to 68% (76) in patients who had radiotherapy compared to 10% (77) to 40% (34) of those who did not have radiotherapy. The risk of significant capsular contracture (Baker Grade III or IV) was also higher in irradiated breasts (33). Patients who had moderate skin changes and no induration had similar aesthetic outcomes to non-irradiated chest walls. However those who developed induration or severe post-radiotherapy skin changes had a greater chance of Baker IV contracture (78). Capsular contracture was also found to

be associated with a significant increase in persistent pain 2 years following surgery (79).

The risk of overall complications was also found to be significantly higher in patients who had radiotherapy (80). Fodor *et al.* [2003] reports that 0-64% of IBR patients and 22-55% of DBR developed complications compared to 0-12% of IBR patients and 13-34% of DBR who did not have radiotherapy (70). Radiotherapy is also associated with significantly higher rates of reconstruction failure with rates varying from 22.7% (33) to 37% (34). As such, radiotherapy significantly increases the number of secondary procedures required in both unilateral and bilateral reconstruction (81,82). Reconstruction with prostheses following radiotherapy was found to be much more reliable when used in conjunction with a flap (83,84). Overall, patients who have radiotherapy have significantly lower satisfaction with their physical and psychosocial outcomes compared with non-irradiated patients when adjusted for other treatment factors (85).

Outcomes

Satisfaction rates following prosthetic breast reconstruction is up to 85% (16,44). Lifestyle and social relations had improved in 82% and 53% of patients respectively post reconstruction (3). Klit *et al.* [2013] reported that there was no significant difference in the reported levels of pain experienced by patients who had prosthetic reconstruction compared to those who did not. Also, the timing of the reconstruction (immediate *vs.* delayed) did not associated

with a significant difference in pain (86). Although 60% of reconstructions resulted in some complication or complaint, patients feel more balanced and whole, are less depressed and were glad they had the reconstruction (87).

The patient's acceptance of cosmesis was found to be better if she could see photos or have a discussion with patients who had previously undergone similar process (88). Having bilateral (*vs.* unilateral) and not having radiotherapy were significant predictors in good cosmetic outcomes (36). Understandably, failure of the reconstruction was associated with significantly decreased aesthetic satisfaction (34).

In order to give all eligible patients equal opportunity to have the best possible outcomes with breast reconstruction, treatment should be centralized in hospitals with a MDT team comprising of, amongst others, an oncological breast surgeon, pathologist, radiologist, oncologists and plastic surgeons (89).

Conclusions

Implant reconstruction following mastectomy has increased at a steady rate since 1998 and is now utilized more frequently than autologous reconstruction. This trend can be attributed to the increased understanding of indications and patient selection for implant reconstruction. This understanding is derived from evidence regarding common and long-term complications, as well as evidence regarding type of prostheses; timing options for reconstruction; and the adjuvant use of radiotherapy (*Table 1*). We can now more reliably predict outcomes of reconstruction on

Table 1 Key points

Incidence of breast cancer 1 in 8 in Australia

Only 33% choose to have reconstruction despite an 82% psychosocial improvement

Implant use has increased by 11% per year from 1998-2008 and now exceeds autologous reconstruction

Indication and patient selection

Most patients are candidates for prosthetic reconstruction

Consider clinicopathological features when making decision

Patients with small, minimally ptotic breasts are suitable for immediate reconstruction

Patients with large, ptotic breasts or who need radiotherapy are better suited to delayed reconstruction

Breast reconstruction in the elderly

Older patients tolerate reconstruction well and can have fewer complications

Risks and complications

Common complications-capsular contracture, hematoma and infection

Risks for complications-smoking, obesity, large breast volume, diabetes, higher grade tumors

Table 1 (*continued*)

Table 1 (continued)

Capsular contracture
Multifactorial-bacterial colonization, type/texture/placement of implant and radiotherapy
Incidence of significant capsular contracture up to 209%
Types of prostheses
Silicone vs. saline
Higher capsular contracture rate in silicone
Higher satisfaction and quality of life scores for silicone
Silicone not associated with cancer, immunological or systemic disease
Round vs. anatomic
No significant difference
Anatomic implants may feel firmer and have less rippling
Textured vs. smooth
Textured have lower risk of capsular contracture
Smooth more likely to be displaced and cause more pain on expansion
Integrated vs. distant port
No significant difference
Timing of reconstruction
Immediate
Best aesthetic outcomes if no radiotherapy needed
Higher rate of complications, capsular contracture, implant failure and revision surgery
Delayed-immediate
Achieve similar aesthetic results to immediate reconstruction
Preserves the breast skin if radiotherapy required
Delayed
Fewer complications than immediate reconstruction
Better aesthetic results if radiotherapy required compared to immediate reconstruction
“Delayed-delayed”-for locally advanced breast cancer patients requiring neoadjuvant chemotherapy. Improves aesthetics and reduces psychological disadvantages associated with DBR
Radiotherapy
Increases risk of capsular contracture-occurs in 68% of irradiated breasts
Higher risk of complications and reconstruction failure
More likely to need revision surgery
Lower patient satisfaction with outcome
Outcomes
High satisfaction rates with prosthetic reconstruction
Cosmesis better accepted if patient better informed
Better aesthetic outcomes associated with having bilateral reconstruction and not having radiotherapy
Patients receive best treatment in hospitals with multidisciplinary breast team
DBR, delayed breast reconstruction.

an individual basis and assess patient suitability to many different reconstructive options.

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Footnote

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The biplanar oncoplastic technique case series: a 2-year review

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Background: Oncoplastic techniques for breast reconstruction following partial mastectomy are now commonly included in the armamentarium of most reconstructive plastic surgeons. These techniques have been frequently used for women with large breast volume and less frequently used for women with small to moderate breast volume. Most women with smaller breast volumes have been typically considered for mastectomy. As an alternative to mastectomy, the biplanar technique was designed and described as an oncoplastic option. The purpose of this manuscript is to review our 2-year experience using this technique in a series of women with small to moderate breast volume.

Methods: A retrospective review of patients who underwent oncoplastic surgery from 2011-2012 by the senior authors (RM and MYN) was completed. Ten patients were identified that had the biplanar technique involving glandular tissue rearrangement in conjunction with the immediate placement of a submuscular implant or tissue expander. Patient demographics, perioperative details, and post-operative outcomes were evaluated.

Results: The mean age and BMI of the ten patients in the study was 56 years (range, 40-68 years) and 24.1 years (range, 20.3-28.6 years) respectively. The mean resection volume was 76.5 g (range, 25-164 g). Eight patients had placement of a permanent implant and two patients had placement of a tissue expander. The average volume of the implanted devices was 138 cc (range, 90-300 cc). In eight patients, a sheet of acellular dermal matrix was used. Immediate biplanar reconstruction was performed in seven patients and a staged-immediate biplanar reconstruction was performed in three patients. Complications included a positive margin on final pathology requiring mastectomy (n=1), infection (n=1), incisional dehiscence following radiation (n=1), and loss of nipple sensation (n=2). Follow-up ranged from 4.5-27 months (mean of 19.5 months).

Conclusions: The biplanar oncoplastic technique may represent a valuable option in women with small to moderate breast volumes that choose to have breast conservation therapy (BCT). This technique has demonstrated success with minimizing contour irregularities and maintaining breast volume. Based on our early experience, patient satisfaction is favorable.

Keywords: Breast; breast reconstruction; lumpectomy; lumpectomy; oncoplasty; partial mastectomy

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Introduction

Breast conservation therapy (BCT) has evolved with the intent of removing a localized breast cancer while preserving the natural contour of the breast. The oncologic safety of this procedure has been well demonstrated and documented in numerous clinical studies with follow-up that now exceeds 20 years (1,2). Oncoplastic surgery

has evolved with the intent of removing larger segments of the breast in order to ensure clear margins in patients where a lumpectomy may not be feasible (3,4). Various oncoplastic techniques have evolved in order to minimize or completely eliminate any contour deformity that may occur with such resections (5-8). The common reconstructive options for oncoplasty include volume displacement and

Table 1 Patient demographics and perioperative details

Variables	Data (n=10) [range]
Average age (years)	56 [40-68]
Average BMI	24 [20.3-28.6]
Smoker (%)	33
Diabetic (%)	0
Sentinel lymph node biopsy	6
Average lumpectomy weight (g)	76.5 [25-164]
Immediate reconstruction	7
Immediate delayed reconstruction	3
Reconstructive pattern	
Wise	4
Circumvertical	4
IMF	2
Average implant size (cc)	138 [90-300]
ADM used	8
Average follow up (months)	19.5 [4.5-27]

volume replacement procedures. Volume displacement techniques include reduction mammoplasty, mastopexy, and glandular rearrangement and are typically reserved for women with larger breast volumes. Volume replacement techniques include the use of local or remote flaps that are typically used for women that are not candidates for volume displacement because of smaller breast volumes.

The biplanar technique was recently described as an option for women with small to moderate breast volume that were not candidates for a single modality of volume displacement, lacked sufficient remote tissue, or did not desire autologous volume replacement, and who did not want to have a mastectomy (9). The biplanar technique is a simultaneous combination of volume displacement and volume replacement method utilizing techniques of tissue rearrangement and device reconstruction. Although several studies have previously reported poor outcomes in the setting of breast radiation and delayed implant reconstruction, this technique differs in that the device is placed before radiation for the purpose of partial breast reconstruction (10,11).

The purpose of this study is to review our 2-year outcomes using this technique. Factors for review include patient selection, surgical technique, complications, and outcomes.

Methods

An IRB-approved retrospective review of patients who

underwent oncoplastic surgery by the senior authors (RM and MYN) from 2011–2012 was performed. All patients that had the biplanar approach were included in the review. Patient demographics and perioperative details are included in *Table 1*. Patient selection criteria was based on the criteria mentioned previously: women with small to moderate breast volume that were not candidates for a single modality of volume displacement, lacked sufficient remote tissue, or did not desire autologous volume replacement, and who did not want to have a mastectomy.

The biplanar technique has been previously described. The basic principles of this technique include simultaneous volume displacement and replacement using tissue rearrangement and devices, respectively. The tissue rearrangement was always in the form of a mastopexy. The incision pattern was circumvertical in four cases, a wise pattern in four cases and an inframammary fold incision in two cases. The partial mastectomy was performed by the ablative surgeon using the delineated pattern. Patients were given the option for immediate reconstruction based on intraoperative frozen section pathology or staged immediate reconstruction as defined as reconstruction prior to radiation, but after final pathology assessments. The skin flaps were elevated and the glandular resection completed. The reconstructive surgeon then performed the glandular rearrangement paying strict attention to the vascular anatomy in order to prevent devascularization of the remaining parenchyma and the nipple areolar complex. The surgical plan was to use inferior or lateral breast tissue to reconstruct the partial mastectomy defects. The subpectoral plane was entered and either a permanent silicone cohesive gel implant or a tissue expander was inserted. Acellular dermal matrix was used to support the lower pole tissues. A closed suction drain was inserted in all patients (*Figure 1*).

Results

Ten patients met the study criteria. The average patient age was 56 years (range, 40–68 years) and average BMI was 24.1 kg/m² (range, 20.3–28.6 kg/m²) respectively. Average ablative resection weight was 76.5 grams (range, 25–164 g). The average ablative specimen volume was 95 cm³ (range, 35–411 cm³). Three patients had a final pathology of ductal carcinoma *in situ*, one had a pathology of ductal carcinoma *in situ* and invasive ductal adenocarcinoma, one patient had a pathology of ductal carcinoma *in situ* and lobular carcinoma *in situ*, three patients had pathology of invasive ductal adenocarcinoma, one patient had a pathology of invasive ductal adenocarcinoma and lobular



Figure 1 58F after right breast biplanar oncoplasty technique with central/lateral lumpectomy of 40 g, circumvertical incision with utilization of medial pedicle (marked “flap”), staged immediate implant of 240 cc, ADM was used.



Figure 2 A 48 F with Central/inferior lumpectomy, inframammary incision with utilization of medial pedicle and immediate implant of 100 cc, No ADM used. The patient later requested a contralateral symmetry procedure. From left to right Pre-operative, post-operative 2 months follow-up, post-operative 8 months follow-up.

carcinoma *in situ* and one patient had a pathology of invasive ductal adenocarcinoma with pleomorphic lobular carcinoma. A permanent implant was used in eight patients and a tissue expander was used in two patients. Acellular dermal matrix was used in nine patients. Immediate reconstruction was performed in seven patients, and three patients were reconstructed using the staged-immediate protocol to ensure clear tumor margins.

Ablative resection site was in the upper outer quadrant in two patients, upper inner quadrant in three patients, lower outer quadrant in two patients and central location in three patients. Location of the pedicle for glandular rearrangement was lateral in two patients, superior in two patients, medial in four patients, inferior in one patient and central in one patient. Nine of the ten patients underwent radiation treatment, one patient had her radiation performed at a location outside of the author's home institution and her records were unobtainable. The average days of radiation treatment was 32 days (range, 22-45 days), and the average number of fractions was 22 (range, 16-28). All radiation was administered with tangential fields with a boost to the affected breast. The average total dosage was 5,563 cGy (range, 4,770-6,200 cGy) with the average boost of 1,193 cGy (range, 530-1,800 cGy).

Following the glandular rearrangement, an implant was placed in the subpectoral space to replace the volume displaced from lateral and inferior quadrants. Average implanted volume was 138 cc (range, 90-300 cc). In general, ADM was used when the devices volume exceeded 125 cc and was not used when less than 125 cc. Tissue expanders were used in cases where the patient desired to have slightly larger breasts postoperatively (n=2). Both of these patients underwent contralateral augmentation postoperatively. Nipple sensation was maintained in 9 of 10 patients (complete loss of sensation was reported by one patient who underwent subsequent a mastectomy for positive margins). Follow-up ranged from 4.5-27 months (mean of 19.5 months) (Figure 2).

Complications were infrequent following this procedure. One patient developed a post-operative infection, prior to radiation, requiring explantation and a subsequent latissimus dorsi flap (prior staged immediate reconstruction). One patient developed a late complication occurred related to radiation-induced wound dehiscence resulting in implant exchange. One patient, who underwent an immediate reconstruction, had a positive margin requiring a completion mastectomy.

A basic satisfaction survey was conducted of all the patients. Five questions on the survey inquired about overall satisfaction, likelihood of doing the surgery again, recommending the procedure, perceived symmetry, and desiring further surgery. The responses were graded from 1 (least) to 5 (most). The results are stated in the Table 2.

Discussion

Breast preserving procedures have become mainstay surgery for many women seeking therapeutic oncologic management.

Table 2 Satisfaction survey results

Post-operative survey questions	Average response
How satisfied are you with the outcome of your surgery	4
Would you undergo this procedure again?	4
Would you recommend this procedure to other breast cancer patients?	4.3
Rate your breast symmetry: 1 (asymmetric) to 5 (symmetric)	3.1
Rate your nipple sensation: 1 (none) to 5 (same as pre-surgery)	3.6

It has been estimated that 70% of patients diagnosed with breast cancer will be candidates for some type of BCT. The advantages of a partial mastectomy or quadrantectomy (>2 cm margin) over lumpectomy (<1 cm margin) are well understood (4). The benefits of immediate or staged immediate reconstruction are well appreciated and designed to be completed prior to the initiation of radiation therapy (12). Thus, the challenge to obtain reasonable cosmetic outcomes has been achieved with the various oncoplastic techniques are our disposal.

The experience with immediate oncoplastic breast surgery has been universally demonstrated to be safe and effective in properly selected patients (12-14). The benefits of performing an immediate contralateral symmetry procedure (when advisable) has also been evaluated (15). This has been effectively performed when placing permanent implants in the ipsilateral breast undergoing the oncoplastic procedure. A contralateral implant can be placed immediately based on the preoperative symmetry measurements, the volume of resected tissue on the opposite side, and the volume of the permanent implant on the opposite side.

The biplanar technique for oncoplastic reconstruction is relatively new and as such is not described in any textbook on this subject. Historically speaking, most attempts at volume restoration with implants were described using devices following radiation. This resulted in an unacceptable rate of capsular contracture, asymmetry, and other adverse events (16,17).

Partial breast reconstruction with prosthetic devices has been addressed either directly or indirectly in a number of studies. Petit *et al.* (18) looked at 111 cases of BCT and immediate reconstruction performed at institute of oncology in Milan. These included 11% that underwent immediate implant reconstruction. This technique resulted in a good result in 58% but with a complication rate of

75%. Mean follow-up was 21 months. The implants were used in larger reconstructions where local tissue use would not have been adequate. The location of the implant, either subpectoral or subcutaneous was not mentioned, nor if there were any other complementary reconstructive procedures performed.

Schaverien *et al.* (19) reviewed their experience with 23 delayed subglandular implant reconstruction after completions of BCT. Radiotherapy to implant time ranged 7-150 months. Follow-up after implant reconstruction was 8-101 months. They reported high satisfaction rates of all respondents to their questionnaire (all above an 8 out of 10 point scale). It is unclear what immediate local measures were taken to address the partial mastectomy defect, if any. They did state that four patients underwent a “mini latissimus dorsi” flap reconstruction.

Rietjens *et al.* (20) reported a series of patients having immediate reconstruction with placement of a subpectoral breast implant, glandular reapproximation, and intraoperative radiation (IORT). They report good outcomes at 1-year follow-up from an oncologic as well as an aesthetic standpoint. They also report that a prospective study evaluating BCT patients comparing IORT and conventional radiotherapy is underway. This study will also look at long term outcome immediate reconstruction after IORT.

Thomas *et al.* (8) reported on 59 patients who underwent a partial mastectomy and immediate placement of an implant in the lumpectomy pocket. Radiotherapy was performed in 64% of the patients. The explantation rate was 18.6% (11/59). Baker grade III/IV contractures were noted in 48%. Of those surveyed, 58% expressed satisfactory results.

The evolution of the biplanar technique was based on the concepts of breast conservation and avoidance of mastectomy in women with localized breast cancer who had small to moderate breast volumes. Traditional oncoplastic techniques for women with small to moderate breast volume were to use a local flap such as a latissimus dorsi or a thoracodorsal artery perforator flap (TDAP). However, some women lack sufficient tissue or do not want any additional scars so an alternative other than mastectomy was needed. The biplanar technique provides this option for women in this category. The concept behind this surgical plan was to reconstruct the partial mastectomy pocket with local breast tissue rearrangement techniques and then to augment the inferior or inferolateral pole (the more common sites of glandular tissue donor site) with the subpectoral implant. The placement of a prosthetic device in this setting is similar to that of a total mastectomy

defect that undergoes reconstruction with immediate reconstruction. Patients with macromastia and severe micromastia are usually not candidates for this technique.

At the time of this preparation, the follow-up for these patients was less than 27 months. The number of patients is small but this partly due to the fact that there are few women that meet the criteria for inclusion. Most women have the expectation that contralateral procedure will be avoided. Some surgeons may have issue with this procedure based on the historic data related to implants and radiation in the setting of BCT and the reality is that this procedure will only be indicated in a few patients. The main benefit is avoiding a mastectomy as well as placement of additional scars on the body. With our current understanding of radiation therapy and device based reconstruction, studies have demonstrated acceptable results as long as the device is placed prior to the radiation. Although capsular contracture is a known and persistent risk, most women will have an acceptable outcome. Patients who have undergone the biplanar oncoplasty reconstruction have similar satisfaction rates as our other oncoplasty patients. We are looking forward to obtaining a long term (5 and 10 years) follow-up to assess the oncologic safety as well as the aesthetic outcome of these patients.

Our study has several shortcomings. Although retrospective in nature, it still provides insight as to the benefits of this technique and provides the groundwork for future investigation. The method of assessing patient satisfaction was not validated; however, moving forward, more sophisticated methods using the Breast-Q or the SF-36 can be implemented. The number of patients in this series is low; however, as we continue to follow these patients and modify our techniques, more patients can be considered and results may be more predictable. The purpose and goal of this study was to establish the technical feasibility of this technique and provide 2-year follow-up that was accomplished.

A combined submuscular implant-tissue rearrangement reconstruction may represent a valuable option in properly selected patients considering oncoplastic breast surgery. In addition to minimizing the incidence of contour irregularities, volume restoration was successfully restored and sometimes enhanced using this technique. A detailed discussion of risk and benefits is a prerequisite prior to offering this option to certain patients. Based on our early experience, patient satisfaction is high and long-term evaluations will determine if sustainable reconstructive outcomes are possible.

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Footnote

Conflicts of Interest: Dr. Nahabedian is a consultant for LifeCell Corp, Branchburg, New Jersey and Sientra Corp, Santa Barbara, CA. The other authors have no conflicts of interest to declare.

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Evolution and update on current devices for prosthetic breast reconstruction

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Abstract: Over the past decade, the leading breast reconstruction modality has shifted from autologous tissue to implants. This trend reversal is multi-factorial but includes increasing bilateral mastectomies and the more widespread acceptance of implants due to stringent quality and safety regulatory surveillance by the US Food and Drug Administration (FDA). Since 2012, the US FDA has approved several new implant styles, shapes and textures, increasing the choices for patients and surgeons. Predictable, superior aesthetic results after prosthetic breast reconstruction are attainable, but require thoughtful planning, precise surgical technique and appropriate device selection based on several different patient and surgeon parameters, such as patient desires, body mass index, breast shape, mastectomy flap quality and tissue based bio-dimensional assessment. This article briefly reviews historic devices used in prosthetic breast reconstruction beginning in the 1960s through the modern generation devices used today. We reflect on the rigorous hurdles endured over the last several decades leading to the approval of silicone gel devices, along with their well-established safety and efficacy. The various implant characteristics can affect feel and performance of the device. The many different styles and features of implants and expanders are described emphasizing surgical indications, advantages and disadvantages of each device.

Keywords: Breast reconstruction; review; implant; device; shaped; cohesive; textured

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Introduction

The predominant modality for breast reconstruction has shifted from autologous to implant-based techniques with an over 2-fold increase since 1998 (1). As of 2010, 83% of breast reconstructions in the United States were performed with devices either in one or two stages (2). The reasons are multi-factorial, including greater awareness, overall patient preferences, changes in reimbursement, shorter operations and hospital stays and diminished relative contraindications for reconstruction in high-risk surgical and oncologic patients. One of the predominant reasons is increasing bilateral mastectomies (1,3). Qualitative studies point to physician recommendation, patient concern about recurrence, genetic susceptibility to breast cancer, increased use of breast magnetic resonance imaging, and desire for

symmetry as the primary reasons women undergo bilateral mastectomy (4-6). Rise in implant-based reconstruction over the last decade is also concurrent with improvements in breast implant safety, quality, performance, and manufacturing. The Food and Drug Administration (FDA) has approved new implant styles, shapes and textures in just the last few years. As our choices in expanders and implants grow, so does our need for information surrounding safety, efficacy and outcomes data.

Modern generation breast implants can be divided into categories based on fill (saline versus silicone), shape (anatomic versus round) and surface structure (textured versus non-textured). Silicone gel implants can be further categorized by the degree and viscosity of gel fill and gel-shell interaction. Because each of these implant characteristics can affect feel and performance of the device,

selection is dependent on the specific surgical indication along with patient and surgeon preferences. Various implant dimensions (height/width, projection and volume) allow individualization for each patient depending on the patient's tissue quality/quantity and tissue-based bio-dimensional assessment. Breast device manufacturing and design spans several generations of refinements and advances in technology. The following review will journey through the evolution of various device characteristics leading up to the modern generation devices available today. We will further provide understanding into the safety and efficacy of current devices, highlighting the rigorous FDA hurdles surrounding their approval. We will discuss the advantages, disadvantages and indications for current generation device use as well as surgical advances that have enhanced device-based reconstruction.

Historic silicone gel devices

Silicone is a synthetic polymer made up of silicon, oxygen, carbon and hydrogen. The most common form is polydimethylsiloxane (PDMS), which contains a repeating SiO backbone with organic CH₃ groups attached to the silicon atom (CH₃)₂SiO. Silicone fluids are composed of mostly PDMS straight chains. Silicone gels are polymeric networks of cross-linked PDMS swollen with silicone fluids. The extent of cross-linking and amount of fluid added to the gel accounts for the wide variety of viscosities and cohesivities of various generation silicone gel implants. Silicone elastomers that make up the implant shells are structured similar to gels but with much greater cross-linking, very little fluid and the addition of amorphous silica for strength. Barrier layer elastomers in modern generation implants contain either phenyl or trifluoropropyl to protect from gel bleed. Beneficial physical properties of silicone include stability across varying temperatures, low reactivity to other chemicals and low surface tension (7).

Since the introduction of silicone gel implants in the 1960s, their manufacturing and design have continued to evolve. Five main generations of silicone breast implants have been introduced to the United States market over the last 50 years (8). Originally implanted in 1962 for breast augmentation and reported by Cronin in 1963, the first generation silicone gel implants were introduced as new "natural feel" gel devices manufactured by Dow Corning Corporation (Midland, Michigan). A few years later, Cronin published his experience using these implants for single stage breast reconstruction after mastectomy (9). The initial design

consisted of a thick elastomeric silicone outer shell (0.75 mm) and a thick, firm gel that together created an anatomically shaped device. Because the shell was smooth, Dacron (DuPont, USA) patches posteriorly were used to anchor the implant *in situ*. In 1969, Dow Corning began manufacturing the implants with a mandrel that was dip-coated which eliminated the peripheral seam (10). Capsular contractures were a common complication of these first generation devices, which were available from 1963 through 1972.

In an effort to create softer, natural feeling breasts, second-generation implants were developed with thinner more pliable shells and softer, less cohesive gels. The gel was composed mostly of low molecular weight chains instead of highly cross-linked silicone, which created a thin, less viscous gel. Contained in a shell only 0.2 mm thick, the thin silicone was able to diffuse across the intact shell causing silicone "bleed". Despite gel bleed and shell failures, the second-generation implants were used into the mid 1980s. For thirteen years, breast implants were unregulated by the government. It wasn't until 1976 that the FDA had authority to review and approve the safety and effectiveness data of new medical devices, including breast implants, under the Medical Devices Amendment to the Federal Food, Drug and Cosmetic Act. Existing devices, such as breast implants, were "grandfathered" in and allowed to remain on the market (11).

Concerns about silicone gel bleed, migration and possible systemic effects began to surface, so the third-generation silicone gel implants were designed to improve the shell strength and permeability. Multi-lumen implants were also introduced for the same reason, including the Becker implant, a permanent round expandable saline-gel device with a remote port (12). Previous silicone gel implant designs were improved by creating thicker silicone shells, up to 0.35 mm, and a protective barrier layer to prevent silicone gel bleed. Although the new designs were more durable with less shell failure (13), public concerns continued to escalate leading to classification of silicone gel implants as Class III devices by the US FDA in the 1980s. During this time, Dow Corning's rat studies generated public warnings on the dangers of silicone implants and their possibility of causing cancer. Although the FDA panels could not find evidence to ban implants, they required pre-market approval (PMA) applications from all implant manufacturers. In addition, a national registry of women with breast implants was created to evaluate the possible association of implants with cancer and other systemic disease. In 1992, the FDA determined that the PMA

applications for silicone gel implants were insufficient, citing the absence of data on safety and efficacy (14). By this time, Mentor Corporation and McGhan Medical Corporation were the only implant manufacturers who had not withdrawn from the US market. On January 5th, 1992, the US FDA announced a moratorium on the use of silicone gel filled breast implants with restricted use to participants in a clinical observational study, mostly for reconstructive purposes.

Current silicone gel devices

Despite access to silicone devices for breast reconstruction, many plastic surgeons switched to saline devices for all types of breast surgery during the silicone gel moratorium from 1992-2006. The smooth and textured round silicone gel fourth generation implants currently available today were developed in the early 1990s under strict quality, safety and performance standards. The new gel devices were filled with a more viscous, higher cross-linked gel and termed “cohesive”. In essence, all previous generations of silicone gel implants had some degree of cross-linking and therefore some degree of cohesion, but these devices were developed with more intended cross-linking than their predecessors. Both the fourth and fifth generation implants are generally referred to collectively as “cohesive implants”, manufactured with gel that is increasingly cohesive through these two generations correlating with increasing form stability and better maintenance of shape. Fourth generation round silicone gel implants were originally manufactured by Mentor Corp. (Santa Barbara, Calif) and McGhan/Inamed (now Allergan) Medical Corp (Santa Barbara, Calif). Both companies offer a portfolio of round smooth and textured devices in various widths and projections. Each manufacturer participated and submitted data from large-scale, prospective, multicenter trials evaluating preclinical safety and efficacy. In 2006, the US FDA approved marketing of implants from both Mentor (MemoryGel round implant) and Allergan (Natrell round implant).

The Allergan 10-year Core Study, which began in 2000, is a prospective, multicenter, US FDA regulated clinical trial. Its purpose was to evaluate safety and efficacy of Natrell round cohesive gel implants in women undergoing augmentation, reconstruction and revision surgery. Published results are available from both the 6- and 10-year data points. Of 715 subjects implanted with Natrell round devices, 98 were post-mastectomy reconstruction patients

and 15 were revision-reconstruction patients. At 10 years, 71.5% of reconstruction patients underwent reoperation most commonly for implant malposition followed by asymmetry. For all cohorts, the overall rupture rate was 7.7% for implants in subjects undergoing serial MRI. Capsular contracture rates were 24.6% for reconstruction and implant texture was not considered significant. Assessment of feel improved from 21.2% at baseline to 75.8% at 10 years with an overall satisfaction rate of 90.7%. Results of the core study demonstrate safety; efficacy and a high level of patient satisfaction with Natrell round fourth generation silicone smooth and textured devices (15).

The Mentor 10-year Core Study, which began in 2000, is a prospective, multicenter, non-randomized, open label trial. Its purpose was to evaluate safety and efficacy of Mentor’s round silicone gel implants in women undergoing augmentation, reconstruction and revision surgery. Data from multiple time points have been published (16,17). Of 1,008 subjects, 251 patients were implanted at primary reconstruction and 60 patients were implanted at revision-reconstruction. The overall rupture rate for augmentation and reconstruction patients, including the MRI cohort, at 6 years was 2.6% for implants. However, when combined with the premarket approval longer-term data, implant rupture rate at 12 years was 9% (16), similar to the 7.7% rate at 10 years in the Allergan core study. Data from 6-year follow-up is the latest published time point to date. The Grade III/IV capsular contracture rate in primary breast reconstruction was 13.7%. Patient satisfaction with implant surgery was high with 97.8% of patients indicating they would have surgery again. In the reconstruction group, the re-operation rate for any reason was 33.9%, most commonly for asymmetry, followed by capsular contracture. Results of the core study established safety and efficacy of the Mentor MemoryGel implants. Further published reports are anticipated regarding the 10-year follow-up data (17).

The manufacturer-sponsored core studies adequately demonstrated safety as well as efficacy of the fourth generation round devices we use today. However, it’s important to realize that the core studies have many non-standardized variables in regards to surgeon skill, operative technique, post-operative management and adjuvant therapies. Therefore further investigation of long-term outcomes, specifically evaluating complications, reoperations and patient satisfaction with these devices is necessary. Capsular contracture is reportedly higher in reconstructive procedures compared to augmentation, and risk is progressively cumulative, increasing with time from implantation and just slightly less, although not significantly



Figure 1 Sientra's shaped devices are available in three different base shapes: classic, round and oval.

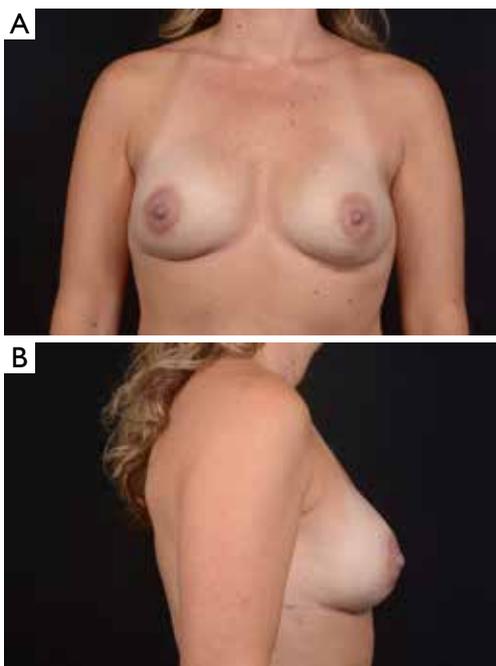


Figure 2 Patient with a history of right breast cancer 2 years after bilateral two-stage prosthetic breast reconstruction with round base shaped Sientra devices.

so, with textured devices (18). Future studies will need to re-evaluate these findings since the incidence of capsular contracture seems to be decreasing with use of biologics in first stage and revision reconstruction (19,20). Despite complications and re-operations, reconstructive patients with implants have high levels of satisfaction (18).

Fifth generation implants are generally considered cohesive form stable devices that retain their anatomic shape despite pressure from surrounding tissue. Most devices are

textured to maintain proper positioning and orientation. The exception is Sientra's round breast implant, which is the only FDA-approved (March, 2012) fifth generation round device, filled with high-strength cohesive (HSC) gel, available in both smooth and TRUE texture surfacing (21). All other fifth generation devices are shaped and textured. After 20 years of restricting use of shaped devices, the FDA-approved (March, 2012) Sientra's High-Strength Cohesive (HSC*) filled device with TRUE texture surfacing. Shortly thereafter, in 2013, the US FDA approved marketing of both MemoryShape (Mentor, Santa Barbara, Calif.) and Natrelle 410 (Allergan, Irvine, Calif) form stable shaped devices.

Sientra's silicone gel breast implants are manufactured by Silimed and composed of a silicone elastomer shell with a barrier coat designed to minimize gel bleed. Every implant is filled with HSC silicone gel, a specifically formulated gel material manufactured by Applied Silicone Corporation (Santa Paula, Calif) and exclusive to Sientra's breast implants (21). The Sientra fifth generation device portfolio includes round and shaped implants divided into categories based on profile, base shape and projection. The round devices are available in both smooth and TRUE texture surfacing. The smooth round devices have four different projection styles: moderate, moderate plus, moderate high and high whereas the textured devices are available in three different projection styles: low, moderate and high. Sientra offers five different styles of shaped form stable devices with three different base shapes (*Figure 1*): the classic-base moderate-projection, the round-base high projection, and the oval-base low, medium and high projection. The base shape is chosen based on the patient's vertical and horizontal breast dimensions, taking into account the amount of projection needed. The classic base is used in women with vertically dominant dimensions, but does not offer as much projection as the other two available shapes. The round base is designed to optimize projection in women with similar vertical and horizontal breast measurements (*Figure 2*). The oval base can also optimize projection and provides increased breast width in reconstruction patients who have increased horizontal over vertical breast dimensions (22).

The Natrelle Style 410 matrix consists of 12 categories or cells of implants based on implant height (low-L, medium-M and full-F) and projection (low-L, medium-M, full-F and extra full-X). In February of 2013, the FDA approved four specific cells of Allergan's form stable fifth generation silicone implants (Style 410 medium height,

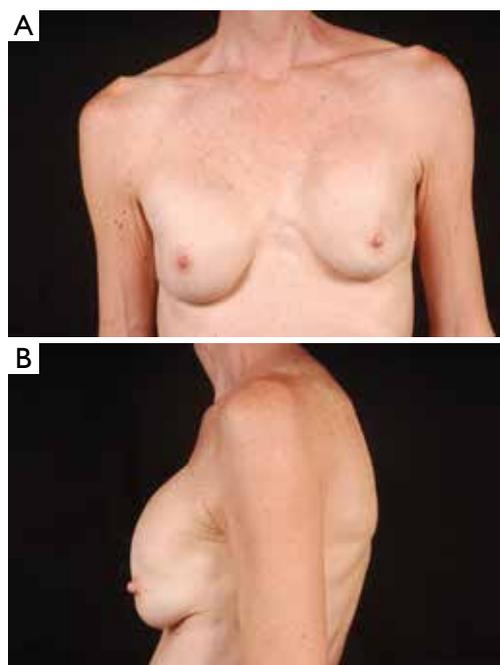


Figure 3 The above patient has a history of previous breast augmentation and left breast cancer treated with lumpectomy and radiation therapy. She subsequently developed bilateral, left greater than right, capsular contracture.

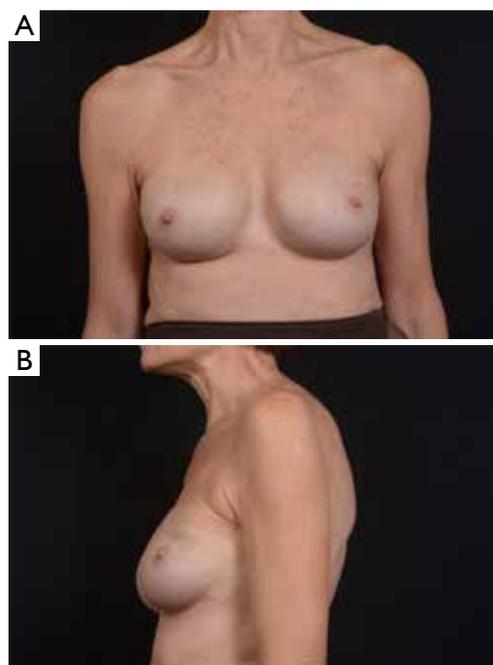


Figure 4 Due to high risk and a suspicious breast mass, she underwent bilateral mastectomies and two-stage prosthetic breast reconstruction with Natrelle 410 shaped devices.

medium projection-MM, medium height, full projection-MF, full height, medium projection-FM and Style 410 full height, full projection-FF devices) for use in breast augmentation or reconstruction. The low and extra projection devices were only available to investigators in research studies through December of 2014, but were just approved by the FDA for unrestricted use in November of 2014. The wide variety of implant dimensions allows reconstruction of almost any breast footprint (*Figures 3,4*). The additional X projection devices provide patients with increased projection, even for larger volume breasts.

The Mentor MemoryShape breast implant was formerly known as the Contour Profile Gel or CPG device when used in U.S. research studies from 2000 to 2014. The only Mentor form stable device (MemoryShape) approved by the FDA in June of 2013 was the medium height, moderate projection implant. In September 2014, the FDA approved four additional styles of the Mentor MemoryShape devices: the low height, moderate plus projection implant, the medium height, moderate plus projection implant, the medium height, high projection implant and the tall height, moderate plus projection implant. Similar to Allergan

devices, the Mentor MemoryShape devices offer a variety of sizes and are categorized based on their height (low, medium and high) and projection (moderate, moderate plus and high).

Use of shaped devices in breast reconstruction is safe and efficacious with predictable and reproducible results (23-26). Advantages include the ability to control breast shape, position and contour with good to excellent outcomes achievable in the majority of patients (22,27). Each manufacturer's implant portfolio has characteristics that differ slightly but affect performance and satisfy a variety of patient desires and expectations. As for the degree of cohesivity, Allergan 410 implants are the most form stable, followed by Mentor MemoryShape implants and Sientra HSC devices, respectively (28). Increases in cross-linking and form stability correlate with increased shape retention but also increasing firmness of the device (*Figure 5*). However, firmness does not necessary correlate with increased strength, which is also dependent on gel/shell integration (28). Each form stable device is manufactured with circumferentially textured proprietary surfacing, differing in pore size to assist in positional stability and



Figure 5 Increased gel cross-linking creates form stability and maintenance of implant shape. Natrelle 410 device gel is considered the most cohesive.



Figure 6 Precise pocket creation, judicious drain use and adherence to post operative protocols, such as compressive bras and bands are important in preventing rotation with shaped devices.

avoid rotation in the breast pocket. Reviewing studies with at least 5-year follow-up, capsular contracture and infection are low, ranging from 5-10% and 1-5%, respectively (24,25,29). The ability to avoid rotation with shaped devices is dependent on surgical technique with creation of a tight pocket, using capsulorrhaphies if necessary, and protocols such as judicious drain use and compressive bras or garments to prevent fluid accumulation in the periprosthetic space (*Figure 6*). Device malposition or rotation requiring

reoperation ranges from 4-12%. Overall reoperation for any reason rates range from 43-45%.

Shaped vs. round silicone devices

Widespread consensus is lacking regarding the indications, advantages and disadvantages of shaped versus round silicone filled breast implants. Few studies have evaluated long-term performance and patient satisfaction comparing the two devices in breast reconstruction partly because shaped devices have only been on the US market a few years (30-32). Shaped devices have complication profiles similar to those of round implants and also have low rates of rotation in both aesthetic and reconstructive breast surgery (31). A recent study comparing round and shaped devices found lower rates of rupture and capsular contracture with shaped implants but the cumulative incidence of reoperation through nine years was similar (30).

In breast reconstruction, shaped implants can create a more naturally shaped breast mound with a gentle sloping upper pole and optimal lower pole breast projection. Because of the high cohesivity, the form stable devices tend to withstand deformational tensile forces (28) and are therefore a good option to correct deformities such as rippling or wrinkling. They can be especially useful in low body mass index patients or those with thin mastectomy flaps and deficient upper pole subcutaneous tissue. Technical considerations, such as precise breast pocket creation are paramount in avoiding rotation. For example, at the first stage of breast reconstruction, expansion is limited to avoid over-expansion of the pocket. Later, an equal or larger shaped device is placed with specific attention to pocket dimensions (*Figure 7*). This is in contrast to round gel implants that tolerate a larger pocket. Since rotation is not an issue, round implants may be more appropriate in difficult revision cases where many variables can affect the size and shape of the pocket. In general, round implants are felt to provide a softer, more natural breast feel. Patients will have movement of the implant within the breast pocket and are more likely to visualize and palpate wrinkling of the device. Therefore, the round devices are a good choice for women who have adequate upper pole tissue and who desire a soft natural feeling breast (30,31). A recent study detected no statistically significant difference in overall satisfaction with reconstruction when comparing shaped versus round silicone gel implants. Although patients reconstructed with the shaped devices reported firmer breasts, they were just as satisfied which could be because the implant chosen for each

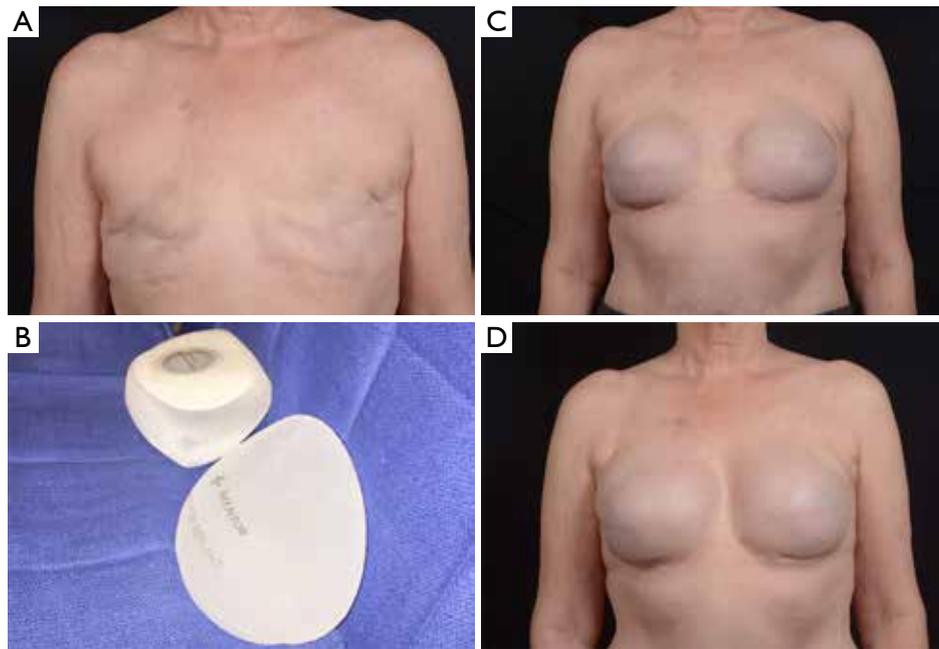


Figure 7 (A,B) Delayed breast reconstruction is commonly performed with a two-stage technique. The expander is chosen based on the final implant dimensions and the patient's chest wall width. (C,D) It is important when using shaped devices (in this case MemoryShape) to use an expander that is the same or smaller dimensions than the planned device.

patient specifically suited the type of patient receiving it (32).

All manufacturers have a range of smooth and textured cohesive round and shaped implants with varying widths and projections. The recent additions of ultrahigh and extra projecting devices from each company have further increased options for reconstructive surgeons and allow creation of more projecting breast mounds (*Figure 8*). Breast reconstruction patients frequently rely on the expertise and advice of their surgeon when deciding on their final implant size and shape. The ability to convey various device characteristics and match them to the patient desires for feel and contour help surgeons choose the best device for each patient. Other factors to take into account include the upper breast pole soft tissue quality, bio-dimensional analysis, body mass index, and laterality of the reconstruction. Future outcome and satisfaction studies will continue to enhance our communication with patients and optimize our reconstructive results.

Inflatable breast implants: (saline)

Like the silicone gel filled implants, inflatable implants evolved through several generations of design and

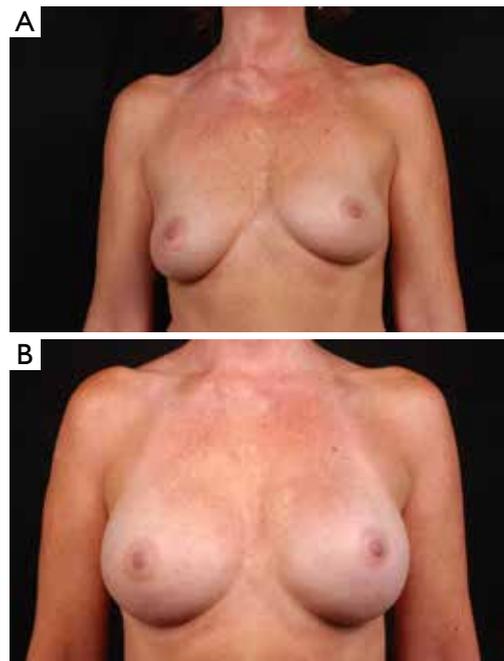


Figure 8 This patient is 3 years status post bilateral prophylactic mastectomy and two-stage prosthetic breast reconstruction with extra projection (Natrelle style 45) devices.

manufacturing. Only a few years after the first silicone gel breast augmentation in 1962, Dr. Henri Arion of France introduced the first inflatable breast implant. Over the next few decades, several renditions of inflatable designs were introduced, including the shaped saline device with optional Dacron patches. Unfortunately, these initial designs struggled with high spontaneous deflation rates due to seam and valve issues, which were eventually solved with seamless, diaphragm-valve implants. Additionally, focus on appropriate fill volumes avoided the leaks from fold flaw cracking (33,34). The silicone moratorium in 1992 generated widespread use of saline filled breast implants for both breast augmentation and reconstruction. During this time of rigorous data collection for confirmation of safety and efficacy of devices, the US FDA examined evidence from both Mentor and McGhan Medical Corporation determining that saline-filled breast implants were safe and did not cause any major disease (35,36).

Few studies have evaluated the effect of implant fill type on patient perception of outcome after breast reconstruction. Overall patient satisfaction is high after breast reconstruction, whether they receive a silicone or saline implant (18). In 2010, Macadam studied the effect of saline versus silicone prosthetic breast reconstruction on patients' postoperative satisfaction and found satisfaction was higher among those who received silicone implants compared with those who received saline implants (37). This finding was confirmed in a subsequent large multicenter cross sectional study (38).

Surface structure

The development of surface texturing resulted from discouraging high rates of capsular contracture with smooth walled implants in the 1960s. Ashley *et al.* published their initial experience using the first textured anatomic shaped silicone gel breast implant in 1970, which they developed and patented in 1968 (Natural-Y Prosthesis) (39). The texturing consisted of a 1 to 2 mm, fine cell polyurethane (PU) shell covering that allowed total tissue-implant fixation of the device. Several PU-coated implants were subsequently manufactured by different companies in a response to gaining popularity for the device's ability to reduce capsular contracture rates (40,41). Early follow up of PU coated implants in immediate one stage breast reconstruction, even when placed subcutaneously, created soft, compressible breasts in most patients with low capsular contracture rates. The improved results were satisfying to both surgeons and

patients (40). Reduced capsular contracture rates were due to in-growth of surrounding tissue into the fine cell PU, creating foreign body reaction. The chronic inflammation prevented circumferential linear fibrosis associated with the spherical contractile forces of capsular contracture (42,43). Unfortunately, the initial enthusiasm with early PU coated devices did not last at long term follow up as many women developed capsular contractures many years after implantation (44,45). In addition, explantation was difficult due to extensive in-growth of surrounding tissue (45). The delayed capsular contracture was thought to be due to progressive hydrolysis of the PU causing it to biodegrade, leaving behind a smooth walled implant. The uncoated device then acted as a smooth surface implant and likewise, developed capsular contracture at similar rates of other smooth wall devices of this era. One study reported the capsular contracture rate after implantation with PU coated devices at 6 to 10 years after implantation to be almost 60% (46). The situation worsened when animal studies linked one of the breakdown products of PU, 2,4-toluenediamine (TDA), to carcinogenesis (47). Therefore, in April 1991, PU coated implants were voluntarily removed from the US Market. Later, research concluded the lifetime risk of developing cancer from the PU metabolite, TDA, to be approximately one in one million and that there was no significant risk of cancer (48). Use of PU coated devices continued in several other countries with modifications including increased gel cohesivity and replacement of adhesive fixation with vulcanized thinner PU coating. Now once the PU disappears, the elastomere retains the imprint of the foam so the implant behaves as a textured device. Over 10-year long-term follow up of these devices (Silimed, Rio de Janeiro, Brazil) in 1,257 patients has revealed a very low capsular contracture rate of 1% (49).

Because the PU surface structure effectively decreased capsular contracture, there was strong enthusiasm to develop a similar textured silicone surface that would produce the same favorable response. The Biocell textured surface was designed in the late 1980s to promote tissue in-growth in an attempt to disrupt and prevent the circumferential linear fibrosis associated with capsular contracture around traditional smooth silicone surfaces (42). Each of the three current implant manufacturers retains proprietary texturing methods. The types of texturing include the Biocell surface texture by Allergan (Irvine, Calif), the Siltex surface texture by Mentor (Santa Barbara, Calif) and the TRUE texture by Sientra (Santa Barbara, Calif). Preventing peri-implant pathologic fibrosis was the original intent of new surface texture design. Indeed,

each manufacturer's textured devices share similar surface morphologies that disrupt regular capsule alignment and longitudinal contraction vectors resulting clinically in low capsular contracture rates (29,50-53).

Smooth surface implants are usually manufactured by repeatedly dipping mandrels in silicone and curing in a laminar flow oven. For textured implants, there is an intermediate step to allow texturing. The Biocell surface is manufactured by a "salt-loss" technique. Salt crystals are added to the dipped silicone mandrel before curing and then washed from the surface leaving behind a pitted appearance with randomly arranged cube indentations (53). The Siltex surface is created by pressing the dipped silicone mandrel into PU foam, a process termed negative contact imprinting. The resulting texture pore size, with a diameter of 70-150 μm (54), is meant to mimic the PU foam. TRUE texture is designed to promote tissue in-growth and is created neither by salt-loss, sugar, soak/scrub or imprinting, but a proprietary process that leaves behind smooth hollow pores with thin cell webbing that reduces particle formation (29,55).

Surface texture is an important implant characteristic for device stability, preventing rotation of form stable devices and migration of anatomic tissue expanders used in breast reconstruction. It has been postulated that the texture pore size correlates with tissue adherence and implant stability (54). Biocell texture with a pore diameter of 600-800 μm and depth of 150-200 μm (54) has been termed "aggressive" in that the capsule will grow into the pores creating a Velcro like effect between the device and the surrounding tissues (56). However, implant stability is also related to friction between the implant and the surrounding capsule, so despite the lack of tissue in-growth with Siltex, these form stable devices maintain proper position (56). Qualitatively, the TRUE texture is a hybrid of the other textures, more aggressive than Siltex but less aggressive than Biocell.

There are few disadvantages of textured breast implants when used in properly selected patients. Long-term outcomes studies show higher propensity of visible rippling and wrinkling and higher rates of saline implant deflation with textured devices (18). Double capsule formation, described as two layer capsular adherence, both to the device and to the adherent tissue, has been seen most commonly around textured devices but are of unknown clinical significance (57,58). Seromas may present as fluid collects between the two layers. These rare double capsules, reported at less than 1% in the literature (57), may form because of shear, trauma, infection, bio-films or large implant pockets limiting tissue-device adherence (58-61).

Safety of breast implants

Over the last several decades, breast implant safety has been studied more extensively than any other medical device. Concerns surrounding links to cancer, connective tissue disease and other systemic illnesses have been addressed in large epidemiological studies. In 1992, the same year of the silicone breast implant moratorium, two studies published evidence that women with implants are not at increased risk of developing cancer (62-64). Since this time, there has been overwhelming data confirming this claim as well as additional evidence that implants do not increase risk of recurrence when used in breast reconstruction nor do they cause non-breast tumors (65,66). Controlled epidemiologic studies have failed to find a causal association between silicone breast implants and connective tissue diseases or symptoms (67-69). The American College of Rheumatology released a statement endorsing the evidence and conclusions from these reports (70,71). In 1999, after a comprehensive assessment of silicone implants, the Institute of Medicine concluded that there was no evidence of a causal association between silicone-gel filled implants and connective tissue disease, rheumatic disease, neurological disease or cancer (72).

Implant associated anaplastic large cell lymphoma (ALCL) is a rare form of non-Hodgkin T cell lymphoma that has been reported in augmented and reconstructed women with saline and silicone implants. Primary lymphomas of the breast are rare and account for only 0.4-1% of all malignant breast neoplasms (73). Furthermore, ALCL only occurs in 0.1 per 100,000 women with or without implants (74). Although the US FDA in 2011 concluded there is a possible association between breast implants and ALCL, the rarity of the disease makes formulating epidemiologic studies and proving causality quite difficult. Extensive research is currently devoted to ALCL and its relationship to breast implants along with a registry of patients to facilitate data collection and a better understanding of the disease.

Tissue expanders

Although there is a place for single stage breast reconstruction with implants, two-stage implant based breast reconstruction using tissue expanders is currently the most commonly performed post-mastectomy breast reconstruction modality (75). A temporary device is placed at the time of mastectomy or at the first stage in a delayed breast reconstruction. After appropriate expansion and after adjuvant treatments, the expander is exchanged for a



Figure 9 Current generation expanders are anatomic shaped with integrated valves and optional suture tabs.

permanent implant.

The history of two-stage breast reconstruction dates back to the late 1970s when Birnbaum described two-stage breast reconstruction in a series of patients with an inflatable implant later exchanged for a custom silicone device (76). Around this same time, Radovan described using smooth walled temporary saline filled tissue expanders for breast reconstruction as an alternative to single stage silicone gel implant reconstruction (77). Expanders allowed for non-operative serial volume adjustments of the device to slowly stretch and mould the breast. Early expanders were burdened with complications such as infection, valve dysfunction, device failures, extrusion, malposition, capsular contracture, pain on expansion, and chest wall compression (78-80). However, many of these early concerns were alleviated with improvements in expander design as well as advances in surgical techniques.

Expanders were redesigned with integrated valves to decrease infection rates and resolve remote valve issues such as valve flipping, pain and tube kinking (81). Capsular contractures around smooth expanders caused expander displacement and resistance to expansion with chest wall pain and compression. Biocell texturing of expanders created surrounding tissue adherence, which caused immobility of the device, but also reduced capsular contracture with progressive softening several weeks after expansion (42). Clinically, compliance allowed for further expansion with less pain and chest wall morbidity while immobility fostered ease of expansion in the desired location. At the time of tissue expander removal, the capsule and soft tissue cover were soft and pliable facilitating second stage reconstruction with a permanent implant without removal

of the capsule (80). Anatomic shaped tissue expanders were introduced to produce a more natural breast appearance and to accommodate shaped devices at the second stage. The geometry of the device allowed for differential expansion, maximized in the lower pole of the breast (82,83).

The improved integrated-valve, textured, anatomic expanders produced low complication rates clinically. In 1998, Spear published his results using these devices in 171 immediate two-stage breast reconstructions with a Baker class III/IV capsular contracture rate of 3%, infection rate of 1.2%, overall deflation rate of 1.8% and no valve dysfunctions (81). Consistent, reproducible results were achieved with a 2004 follow up study with the same devices, but improved breast aesthetics due to change in device positioning from a total submuscular location to a partial subpectoral location allowing further lower pole expansion of the breast and accentuation of the inframammary fold, as well as a change from saline to silicone devices (84). Modern day tissue expanders are quite sophisticated with acceptable complication rates and high levels of overall patient satisfaction (85-88). In a recent report by Cordiero, 88% of patients had good to excellent aesthetic results following two-stage implant reconstruction (89).

The integrated-valve, textured, anatomic expanders are currently available today with the additional option of suture tabs (*Figure 9*). This optional refinement allows fixation of the device to the chest wall to further ensure stability, to prevent migration during expansion, to better control the anatomic boundaries of the breast pocket, thereby creating a more precise breast mound with less pocket modification at the second stage. With increasing use of acellular dermal matrix in the inferior breast pole at immediate breast reconstruction, the tabbed expander may allow for less variability and more reliance on the device to shape the breast mound. The outcome is more predictable at the second stage since the device is optimally placed on initial insertion with creation of more appropriate breast pocket dimensions (90).

All three US implant manufacturers also have a portfolio of available tissue expanders with varying widths, heights, projections and volumes to match the patient's bio-dimensional assessment. Many of the expanders are developed to match the corresponding manufacturer's implant portfolio. Often, it is best to choose the desired implant first and then select an expander that is the same or smaller in dimensions than the anticipated implant. This is especially important for the shaped implants that require a precise pocket in order to avoid rotational deformity.

Sientra's tissue expander product line consists of the

Table 1 Current gel implants and expanders

Device characteristics	Allergan	Mentor	Sientra
Gel round (smooth and textured)	Natrelle®	MemoryGel®	High strength cohesive (HSC)
Texture surface	Biocell™	Siltex™	TRUE texture™
Shaped	Natrelle® 410	MemoryShape®	HSC+
Main expander	Natrelle® 133 series	Contour Profile® CPX3/CPX4	Anatomical Controlled® ACX

Source: www.natrelle.com 2014, www.mentorwwllc.com 2014, www.sientra.com 2014.

ACX (Anatomical Controlled Tissue Expansion) matrix, which are either double chamber or single chamber (low, moderate and full height) devices, as well as round and crescent smooth and textured expanders with remote or integrated ports. The ACX devices have integrated ports, an orientation mark, TRUE texture surfacing and four suture tabs at the 4-, 8-, 10- and 2-o'clock positions for optimal stability. Sientra has the only double chamber breast tissue expander on the market and boasts differential expansion with optimal control.

Mentor's Contour Profile (CPX) Expander portfolio consists of CPX3 and CPX4 devices. The previous CPX2 expander had an anatomic shape, SILTEX surface texturing, and an integrated injection dome with surrounding buffer zone with self-sealing technology and was available in low, medium and tall heights. The CPX3 expander matrix replaced this device and has all the same features of the CPX2 style with the addition of three suture tabs for stability at the 3-, 6-, and 9-o'clock positions. The slightly modified CPX4 tissue expander has a stronger magnet than the original contour profile device, an enhanced buffer zone self-sealing-patch around the integrated port which is now flush without a palpable ring and a posterior Dacron patch to focus the expansion at the lower pole of the breast. Mentor also offers both a textured and smooth expandable implant with remote port (Spectra).

Allergan's Natrelle 133 tissue expander is available in 84 sizes with variable projection in the low, short, moderate and full height devices as well as extra projection in the short, moderate and full height devices. Additionally, they are anatomically shaped, with integrated magnetic ports, Biocell texturing and are available with optional suture tabs at the 4-, 8- and 12-o'clock positions (*Table 1*).

Conclusions

Rates of implant-based reconstruction are increasing steadily. The current generation devices have been

extensively studied and are deemed safe and efficacious with good aesthetic outcomes and acceptable complication and reoperation rates. Development of different styles of silicone gel implants, including more projecting devices and form-stable shaped devices increase choices for both surgeons and patients undergoing reconstruction. Introduction of acellular dermal matrices and improved surgical techniques further optimize reconstructive results. There is no one perfect implant, but with continuing research, development and long-term outcomes data, surgeons will be armed with the most up to date technology, along with the knowledge and expertise to provide the best possible prosthetic reconstructions.

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Footnote

Conflicts of Interest: The author is a speaker and consultant for Lifecell and Allergan; the author has equity ownership in Strathspey Crown Holdings, LLC (parent company of ALPHAEON Corporation).

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Current strategies with 1-stage prosthetic breast reconstruction

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Background: 1-stage prosthetic breast reconstruction is gaining traction as a preferred method of breast reconstruction in select patients who undergo mastectomy for cancer or prevention.

Methods: Critical elements to the procedure including patient selection, technique, surgical judgment, and postoperative care were reviewed.

Results: Outcomes series reveal that in properly selected patients, direct-to-implant (DTI) reconstruction has similar low rates of complications and high rates of patient satisfaction compared to traditional 2-stage reconstruction.

Conclusions: 1-stage prosthetic breast reconstruction may be the procedure of choice in select patients undergoing mastectomy. Advantages include the potential for the entire reconstructive process to be complete in one surgery, the quick return to normal activities, and lack of donor site morbidity.

Keywords: Breast reconstruction; breast implants; direct-to-implant (DTI) reconstruction; acellular dermal matrix (ADM)

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Introduction

Breast cancer is a leading cause of morbidity and mortality in women of all ages (1). An increasing number of these women and those who have the breast cancer gene are choosing unilateral or bilateral mastectomy to treat or prevent breast cancer (2). The etiology of this interesting trend is multifactorial, but it is likely influenced by improved techniques in mastectomy and reconstruction. The evolution of mastectomy to skin-sparing and nipple-sparing procedures has offered an opportunity to create natural breast reconstructions, and it has increased the number of patients eligible for 1-stage direct-to-implant (DTI) reconstruction (3). Our ability to obtain excellent cosmetic results with implants adds to the known advantages of implant-based reconstruction including a shorter operative time, lack of donor-site morbidity, and quicker return to normal life activities. This in turn has decreased the number of patients who now seek autologous reconstruction in the United States (4).

DTI breast reconstruction has appeal to patient and surgeon alike. For the patient, a DTI reconstruction allows

the potential for completion of the entire reconstruction process in a single surgery, which avoids extra office visits and a second surgery to exchange the tissue expander to a permanent implant. However, not all patients are candidates for 1-stage prosthetic breast reconstruction. This article reviews patient selection, technical pearls, postoperative management, complications, and outcomes in DTI breast reconstruction.

Patient selection

The ideal candidate for 1-stage breast reconstruction is a healthy patient who desires to stay about the same breast size (*Figures 1,2*). Nipple-sparing mastectomy procedures offer more skin to accommodate a full size implant; however, skin-sparing mastectomies offer more of an uplift for the woman with large breasts looking to decrease her size (*Figure 3A,B*). If the patient has significant co-morbidities such as uncontrolled diabetes, a history of transplantation, or active smoking, a 2-stage or delayed reconstruction is often advised. Advancing age, obesity, radiation, and prior breast

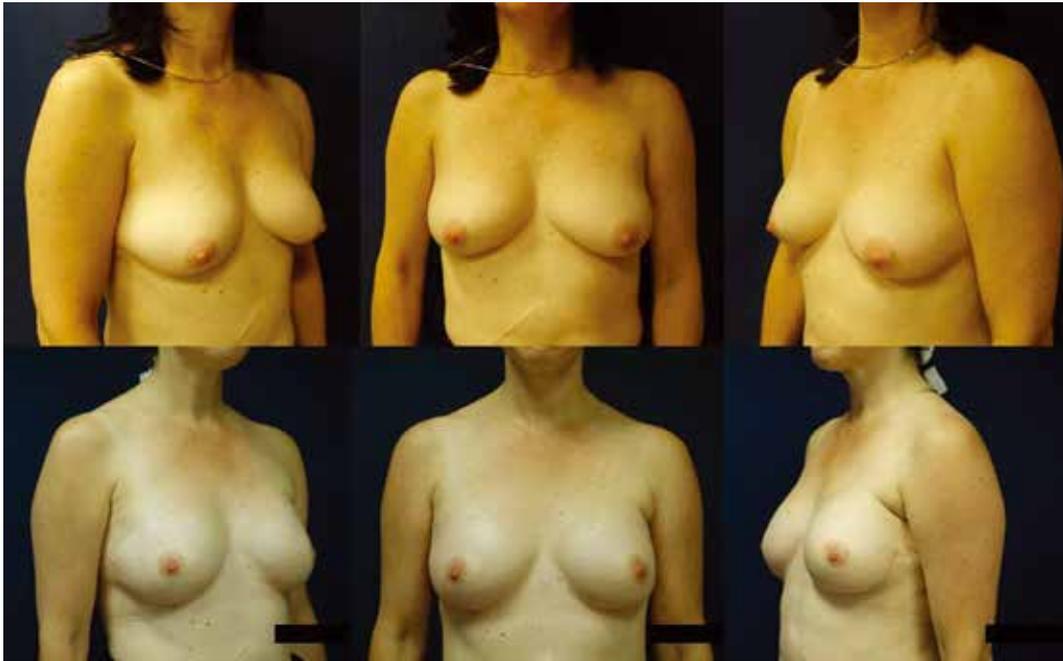


Figure 1 This 52 years old female had the *BRCA1* gene and was high risk for developing breast cancer (upper photos). She underwent bilateral nipple-sparing mastectomy using inferolateral inframammary incisions with 1-stage prosthetic breast reconstruction using round cohesive moderate plus profile 400 cc silicone gel implants (lower photos).



Figure 2 This 37 years old female developed left-sided DCIS (ductal-carcinoma in-situ) and had bilateral NSM for treatment and prevention. She desired to stay about the same size and had implants placed in 1-stage using inframammary (IMF) incisions.

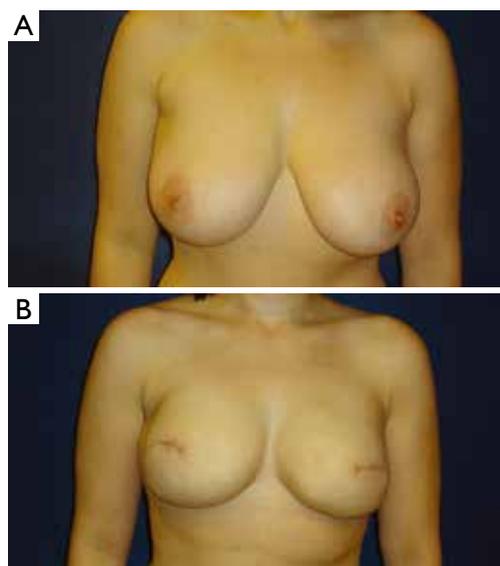


Figure 3 This 36 years old female tested positive for the *BRCA1* gene (A). She desired a slightly smaller size breast with more of an uplifted appearance. She had bilateral skin-sparing mastectomies with immediate implant reconstruction (B).

surgery are not contraindications to 1-stage reconstruction, but patients need to be considered on an individual basis (3,5-7). With skin-sparing or skin-reducing mastectomies it is possible to make the patient much smaller in size in one surgery, whereas significant size reduction with nipple-sparing mastectomies is more challenging. If the mastectomy skin envelope is ideal, it is sometimes possible to make the patient larger in size than their natural breast. However, significant size enhancements are more safely done with a 2-stage tissue expander-implant reconstruction.

Technical pearls

Preoperative Planning: In the initial consultation, an assessment of patient size goals and native breast symmetry is noted. The breast diameter is measured and the volume approximated to ensure the right implants are available on the day of surgery. It is important to discuss asymmetries and plan for differences in inframammary fold location. A paravertebral block is given for perioperative pain control.

Marking: The inframammary folds and lateral borders of the breasts are marked with the patient in the sitting or standing position. Incision placement is determined with the breast oncologic surgeon. A decision is made on a skin-reducing, skin-sparing, or nipple-sparing approach. For



Figure 4 An inferolateral inframammary (IMF) incision is often chosen for the nipple-sparing mastectomy approach. The muscle is released to approximately the 4 or 8 o'clock position on the chest wall to allow medial implant positioning and partial muscle coverage. When performing bilateral procedures, it is important to assess the position of the inframammary folds for asymmetry.

nipple-sparing mastectomies, an inferolateral incision allows excellent access for mastectomy, lymph node sampling, and reconstruction (*Figure 4*) (8). However, a radial incision maximizes blood flow and should be considered when the blood supply to the nipple or skin may be compromised, such as in cases where thin mastectomy skin flaps are anticipated and in cases with scars on the breast.

Preparation: The skin is prepped with a betadine or chlorhexidine scrub. Once the mastectomies are finished, the skin is prepped once again and new sterile drapes are placed on top of the original drapes. The arms are angled approximately 75 degrees from the operating table on arm boards. A muscle relaxant is given to facilitate partial subpectoral implant placement.

Procedure: The pectoralis muscle is elevated from lateral to medial and the inferior attachment is released with electrocautery to approximately 4 or 8 o'clock. A piece of acellular dermal matrix (ADM) or mesh is sewn to the inframammary fold or chest wall inferiorly and to the chest wall (or serratus flap) laterally (*Figure 5*). Care is taken to leave some laxity medially to allow the implant to assume a medial position. Simple interrupted sutures are used inferiorly and horizontal mattress sutures are used laterally to the chest wall. Alternatively the ADM or mesh can first be sewn to the pectoralis muscle and the inferior/lateral suturing can then be performed after placement of the implant. A sizer is placed inside the newly created pocket and sewn in place. The patient is sat upright and the sizer is inflated to check for proper pocket placement and to determine size. An implant is chosen that best matches the width of the pocket

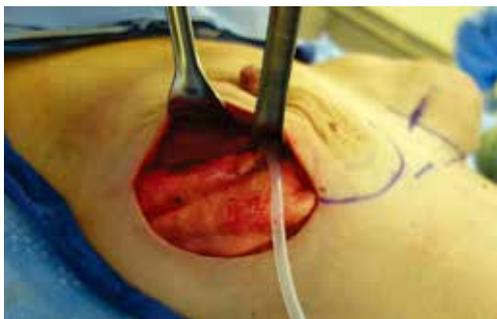


Figure 5 The pectoralis major muscle is released from its inferior attachment using electrocautery. An acellular dermal matrix or mesh is used to recreate the inferior and lateral boundaries for the implant, and to create a complete pocket around the implant with the pectoralis muscle. A sizer is placed into the pocket to assess pocket dimensions and volume for the implant.

and the volume determined by the sizer. Anatomic/shaped implants are often preferred for unilateral reconstructions and patients with thin skin. Round implants offer more upper pole volume and mobility making them more attractive to younger patients. Prior to implant placement, the pocket is irrigated with a triple antibiotic solution containing Cefazolin, Gentamycin, and Bacitracin. One drain is placed inside the pocket along the inframammary fold and another drain is placed laterally outside the pocket and travels over the superior surface of the muscle. Care is taken to make a separate stab incision for drain exit and to tunnel 1-2 cm within the tissue prior to exiting. The surgeon's gloves are changed and the implant is placed. The pocket is closed using horizontal mattress or figure-of-eight sutures from the muscle to the ADM (*Figure 6*). The skin edges are trimmed and the skin is closed in layers. The skin is then sealed with Dermabond and covered with Tegaderm. Biopatches and tegaderm are placed around the drains. Microfoam tape is placed to stabilize implant position. The tape is covered with Tegaderm to allow postoperative showering (3,9).

Postoperative management

The patient stays in the hospital one or two nights. No bra is placed for the first 12 hours. Prior to discharge from the hospital a loose-fitting surgical bra is placed to help support the implants. A tight compressive bra or wrap is avoided as it may compromise blood flow to the breast skin. Drains are removed when output is less than 30 cc for 24 hours. Typically one drain is removed from each side one



Figure 6 The implant is placed into the submuscular-subADM pocket and the pocket is sutured closed using absorbable sutures.

week after surgery and the other two drains are removed two weeks after surgery. Patients are maintained on oral antibiotics until the drains are removed. If Tegaderm is covering the incisions, patients may shower and let water run over the Tegaderm dressing. Activity is limited for 4-6 weeks after surgery. A patient may not lift more than 10 pounds during this time. At 4 weeks, the patient is instructed to start implant massage. This is particularly important for smooth round implants to help avoid contracture.

Complications and management

Skin necrosis: ischemic injury to the breast skin may occur during the mastectomy if the skin flaps are made too thin or if there is excessive traction on the skin flaps. This is often seen as exposed dermis on the undersurface of the flap and/or a red/blue discoloration to the skin immediately after the mastectomy, or with inflation of a sizer. If significant ischemic injury is observed at the time of surgery, it is best to do a 2-stage or delayed breast reconstruction. Ischemic injury may also occur during reconstruction as placement of an implant can put direct stress on the skin flaps limiting perfusion. Ischemic injury may result in skin necrosis. If skin necrosis ensues, it is best managed aggressively. Skin edge necrosis (2-5 mm) can often be managed with debridement and closure under local anesthesia. If the necrosis is more severe, the implant may need to be downsized or changed to a tissue expander.

Infection: following mastectomy, the skin inevitably experiences some element of reduced blood supply making it more susceptible to infections. An infection presents as redness of the skin (cellulitis), fever, increased pain, swelling, or a combination of the above. The initial step in management is antibiotics (10). For patients presenting with redness of the skin without other symptoms or comorbidities, oral antibiotics are administered. If other

symptoms are present, or if the redness does not improve with oral antibiotics, the patient is placed on intravenous antibiotics. Failure to respond to intravenous antibiotics results in an operation for implant exchange or removal (explant). If the inside pocket appears clean without evidence of infection, consideration can be made to pocket irrigation and implant replacement. If there is evidence of periprosthetic infection inside the pocket, the implant is removed and the incision is closed over a drain.

Seroma: fluid may accumulate inside the breast pocket if it is not adequately drained or if the drains are removed before the body can reabsorb the lymphatic fluid. Seromas are managed with percutaneous or operative drainage.

Other complications: potential complications include bleeding, hypertrophic scar, capsular contracture, asymmetry, implant rupture, and contour deformity.

Outcomes

A single institution study examined outcomes of 1-stage prosthetic breast reconstruction with ADM compared to 2-stage reconstruction without ADM (3). In this series of 331 DTI reconstructions, there was no difference in overall or individual complications compared to 2-stage reconstruction. There was a learning curve in complication rates with fewer complications observed as the surgeons gained experience with the technique. Patients with preoperative or postoperative radiation had an increase in complications. Patient satisfaction was assessed retrospectively with the Breast-Q. Survey results showed a similar high degree of satisfaction in 1-stage compared to 2-stage reconstruction (unpublished data).

In another large series of 260 patients and 466 breasts, the complication rate was low at 3.9% and the explant rate was 1.3% (11). The authors conclude DTI reconstruction with ADM is safe and reliable.

Conclusions

1-stage prosthetic breast reconstruction is a safe, reliable way to reconstruct the breast. With proper patient selection and surgical judgment, an aesthetically pleasing breast can be created in one surgery combined with the mastectomy and achieve results similar to traditional 2-stage surgery.

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None.

Footnote

Conflicts of Interest: Amy S. Colwell, MD, is a consultant for Lifecell and Allergan.

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Current opinions on indications and algorithms for acellular dermal matrix use in primary prosthetic breast reconstruction

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Abstract: Acellular dermal matrix (ADM) is widely used in primary prosthetic breast reconstruction. Many indications and contraindications to use ADM have been reported in the literature, and their use varies by institution and surgeon. Developing rational, tested algorithms to determine when ADM is appropriate can significantly improve surgical outcomes and reduce costs associated with ADM use. We review the important indications and contraindications, and discuss the algorithms that have been put forth so far. Further research into algorithmic decision-making for ADM use will allow optimized balancing of cost with risk and benefit.

Keywords: Breast reconstruction; acellular dermal matrix (ADM); algorithm

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Introduction

Since Salzberg's first description (1) and Breuing's subsequent publication (2) of the use of human acellular dermis as an adjunct to traditional prosthetic breast reconstruction, there has been a surge of interest in this technique. Today, acellular dermal matrix (ADM) is used in nearly 60 percent of the 50,000 prosthetic-based breast reconstructions that are performed annually (3). Users have cited numerous benefits of ADM in prosthetic breast reconstruction, ranging from better control of anatomic placement (1,4-10) increased definition of the inframammary fold (1,4-10) reduced capsular contracture (5,7-17) faster and fewer expansions especially of the lower pole (1,4,7-10,12,14,16-22) and overall improved aesthetic outcomes (6,23-26).

Nonetheless, important concerns have arisen surrounding ADM use, most notably including increased cost and heightened complication rates (3,8,9,27-31). Among the literature there is a very high variation in many of the reported outcomes for ADM compared to traditional non-ADM techniques (32,33). A literature review by Kim *et al.* revealed reported complication rates from ADM-assisted reconstruction ranging from as low as 8.6% to as

high as 19.5% (28). In that study, the complication rate with ADM use had a pooled average of 15.4%, slightly but statistically significantly higher than the non-ADM pooled average of 14.0%. Certainly, rigorous randomized controlled trials (RCTs) investigating complication rates would be enlightening, but unfortunately only one has been completed to our knowledge; it showed equal outcomes between ADM use and traditional, no-ADM breast reconstruction (30), although the conclusions of this study may be limited by its use of an older, now-disfavored size of ADM sheet (34). The Multi Center Canadian Acellular Dermal Matrix Trial (MCCAT) promises to provide further RCT data to answer this question (35), which is reassuring because clearly, more data from RCTs can help to sharpen our understanding of ADM's effects on surgical outcomes.

Even so, some have posited that at least some of the disparity in reported complication rates with and without ADM is actually due to the lack of clear indications and contraindications to use (36). The disparate complication rates we are seeing in the literature may be caused by implicit variations in patient selection. Careful and rational patient selection is critical to maximize reconstructive

Table 1 Various literature-reported indications and contraindications for acellular dermal matrix use in primary breast reconstruction

Indications	Contraindications
Nipple-sparing or direct to implant procedure (37-41)	Obese (42-45)
Large breasts (46,47)	Large breasts (43,48,49)
Anticipated post-operative radiation (43,50,51)	Pre-operative radiation (39,42,43,48,52)
Non-ptotic breasts (46)	Smoker (43,44)
Compromised or small pectoralis major (31,43,53-55)	Thin skin flaps (43)
Skin excess (56)	Poor flap vascularity (36,39,43,57)

outcomes (9). The literature is rife with associations between certain patient parameters and better or worse outcomes (*Table 1*). For example, a recent publication by Mendenhall *et al.* (42) studying the difference between two different ADMs notably found that radiation therapy, larger tissue expander size, and obesity were all predictors of a longer time spent with drains, which itself was associated with a greater number of complications.

When surgical decision-making relies on many factors, it is common and helpful to develop rational algorithms to help guide decisions. For example, the decision to choose a particular breast reconstruction modality, i.e., prosthetic versus autologous reconstruction, has enjoyed significant discourse that explores rational algorithms (37). Yet until very recently, there has been a paucity of literature on whether selective use of ADM is even possible, let alone specific proposals for algorithms governing ADM use. We believe that the body of literature surrounding ADM indications and contraindications in primary prosthetic breast reconstruction has matured sufficiently to where a discussion of selective ADM algorithms is both now possible and necessary. Therefore, we wish to review the literature's current opinion on those various indications and contraindications, and discuss the few algorithms that have thus far been proposed.

Pre-operative indications and contraindications

Surgical technique: direct-to-implant and nipple-sparing surgical techniques

The advent of ADM has made major impacts on breast

reconstruction, one of the most notable of these being the expanded use of the direct-to-implant reconstructive modality (37,38). These single-stage techniques avoid the need for the expansion visits necessary for tissue expander reconstructions. Because there is no planned expansion of the skin envelope, maximal placement of volume must be achieved at the time of prosthesis insertion. However, the patient's pectoralis major muscle will likely be insufficient to accommodate the prosthesis, so ADM emerges as an obvious choice to allow the release and augmentation of the existing pectoralis (39).

A similar situation arises in the setting of a nipple-sparing mastectomy (NSM) and total-skin-sparing mastectomy (TSSM). In these cases, there will be maximal skin remaining since the surgeon has taken none; hence the discordance between the inner pectoralis lamellae and the outer lamellae of the skin envelope will be high. Proper alignment between these two lamellae improves the overall outcome and aesthetics of the reconstruction (36) (*Figure 1*). Like in the case of direct-to-implant reconstructions, NSM and TSSM techniques may benefit from releasing the pectoralis muscle and using ADM as a sling augmenting the inner tissue plane (40,41).

Body mass index and breast size

The relationship between body mass index and breast size can affect the concordance between the reconstructive outer lamella and the reconstructive inner lamella. When patients with high body mass index also have large, ptotic breasts, the available pectoralis major muscle may not accommodate the redundant skin hosted by the outer lamella. Therefore, in these patients ADM can be useful in providing the needed inner lamellar surface area, resulting in better contact between the skin flap and the underlying pectoralis muscle layer and ultimately reduced dead space (*Figure 1*). The ability to manipulate the ADM also confers control over the projection vector of the lower so that it better replicates the shape of the pre-mastectomy breast (46,47). ADM may also be used advantageously in high body mass patients to reduce the risk of seroma and other complications when it is employed as a tool to define the lateral and inferior edges of the prosthetic pocket (36).

On the other hand, it has also been noted that patients with high body mass index and large breasts may be at increased risk of poor wound healing due to the long flaps of skin which become prone to ischemia (43). Some studies have identified obesity as a risk factor for breast reconstruction using ADM (48,49). This conflict in the

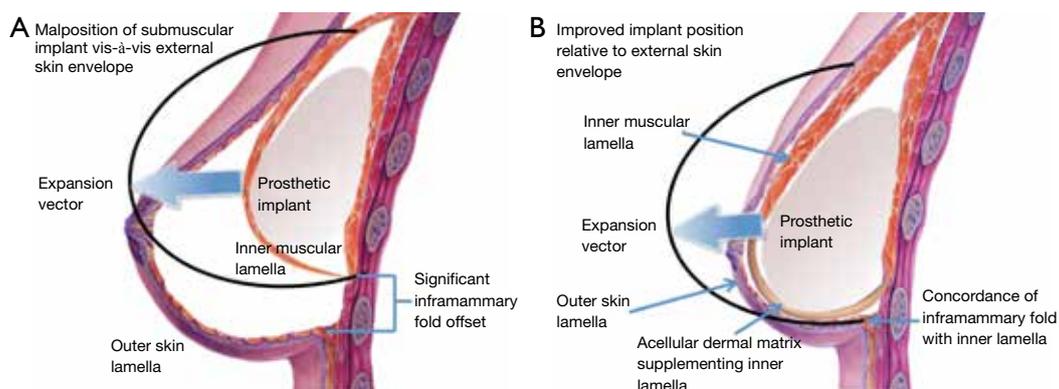


Figure 1 The relationship between the outer lamella, or skin envelope, and the inner lamella, or pectoralis-acellular dermal matrix plane. (A) A discordant alignment between the inframammary fold and the inferior border of the pectoralis major produces a vertical offset that causes unwanted ptosis; (B) the inner layer is augmented with acellular dermal matrix to resolve the disparity between the pectoralis and the outer skin flap, improving the expansion vector of the lower pole.

literature is reflected in *Table 1*. Therefore, while the use of ADM may help protect the reconstruction in the case of an ischemic complication, a surgeon will likely have to weigh the option of a delayed reconstruction in high body mass index patients with large breasts.

Pre-operative radiation therapy and expectation of post-operative radiation

Pre-operative radiation exposure has been tenuously linked to poor outcomes, most likely due to the observation that irradiation compromises tissue microvasculature by provoking fibrosis (43,58-60). Additionally, fibroblast infiltration into the ADM disrupts its usual incorporation into surrounding tissue. Consequently, the integration of the ADM is threatened by serious complications such as infection, seroma, infection, explantation, and poor aesthetic outcomes because it begins to act as a foreign body (60-62).

But while pre-operative radiation contraindicates the use of ADM, preliminary evidence in conjunction with our own clinical experience suggest that ADM can accelerate expansion of the prosthetic pocket before the start of post-operative radiotherapy and provide protection against the risk of skin flap necrosis induced by post-operative radiation (50). Moreover, when the inferior border of the pectoralis major is released during the course of breast reconstruction with ADM, pectoralis tightness due to post-operative radiation-induced fibrosis is alleviated. For example, post-operatively irradiation was shown to reduce rates of explantation in a study of 428 breasts undergoing two-stage prosthetic breast reconstruction using ADM, compared to historically

reported values (62). Likewise, another study reported that postmastectomy radiation therapy without the use of ADM during reconstruction resulted in a 2.63-fold increase in complications, compared to a similar cohort who received ADM during reconstruction (63). In contrast, ADM has not demonstrated any benefits when used on breasts that have undergone pre-operative radiotherapy (39,43,64,65). Therefore, when post-operative radiotherapy is expected, the surgeon should consider using ADM during the breast reconstruction.

Intra-operative indications and contraindications

Pectoralis major anatomy

Surgeons conducting breast reconstruction must continuously assess the integrity and tautness of the pectoralis major as it is being manipulated. During the operation, the pectoralis, serratus fascia, or rectus fascia may be subject to iatrogenic damage that compromises their ability to house the reconstructive pocket. In these cases, ADM is used as an interpositional graft (31,43,47,53,54). On a similar note, expansion of the inferior pole is restricted when the pectoralis muscle is too tight, a situation that can arise when the muscle is too narrow or sits high on the chest wall; therefore, in these cases the pectoralis is released inferiorly and its coverage augmented with ADM in order to close the gap between the inframammary fold and the inferior border of the muscle. Indeed, Madsen *et al.* reported that 72 percent of patients have pectoralis that is either too high or too narrow (55).

While it is true that these cases may be handled simply

with elevation of the serratus and rectus fascial flaps, use of ADM often provides more powerful control over the breast mound. It permits full expansion of the lower pole and limits iatrogenic damage to the serratus anterior and rectus abdominus fascia that would otherwise endanger the definition of the inframammary fold.

Flap vascularity and skin excess

Flap vascularity is a critical prerequisite for expedient wound healing. In the face of numerous, often-conflicting indications and contraindications (*Table 1*), flap vascularity is in general the most important factor and ought to take precedence in the event of a conflict between different decision-points (36). Skin flaps are inherently hypovascular, which renders them vulnerable to incisional breakdown and prosthetic exposure if they are not managed properly (57). A number of patient comorbidities, notably smoking, peripheral vascular disease, and hypertension have been shown to compromise flap vascularity (57,66,67). The surgeon must observe flap vascularity intra-operatively to assess the degree of perfusion that the flap will be capable of providing. Compromised skin edges must be trimmed for optimal healing. If the flap is significantly devascularized, the subdermal vascular plexus damaged, or the flap itself is too thin, use of ADM is contraindicated due to the probability that it will not integrate (39,43).

If vascularity is deemed sufficient, the decision to use ADM rests on an intra-operative determination of relative skin excess. The goal of the operation is to match the length of the outer skin to the length of the muscle layer underneath, maximizing contact between the two layers. If the pectoralis muscle and the outer skin flap are mismatched, the skin flap may experience tension that can harm the natural aesthetic of the breast as well as disrupt perfusion to the nipple, causing nipple necrosis (56).

Sentinel-node status

As mentioned previously, the expectation of post-operative radiation is a good indicator for ADM use in breast reconstruction because of its beneficial effects on capsular constriction elicited by radiation. From an intra-operative finding of positive lymph node status, the surgeon can infer that the patient will likely undergo post-operative radiation therapy. Therefore such a finding is also a good indicator for the surgeon to use ADM (36).

Previously proposed algorithms

Presently, algorithms that assist surgeons to decide whether ADM is appropriate have not been well investigated, and specific proposals of such algorithms in the literature are sparse. Most such algorithms proposed so far have been one- or two-factor decision tools. For example, Colwell *et al.* suggested using a focused algorithm for ADM use that centered on the evaluation of skin flap vascularity (39). According to this algorithm, patients with thin or devascularized skin flaps would be reconstructed using total muscular coverage while thick and well-vascularized skin flaps would be reconstructed with ADM using a direct-to-implant technique.

Dupin *et al.* has also formulated a strategy that helps to identify scenarios where ADM is appropriate (68). In their algorithm, reconstruction assisted by ADM is favored for patients who have small breasts. Patients with large breasts, or those who smoke or are obese, may still be reconstructed with ADM at the surgeon's discretion, but the algorithm recommends against it if the mastectomy is associated with radiation.

Peled *et al.* (50) went further by formally assessing their simple algorithm, which selected the use of ADM for patients undergoing total skin-sparing mastectomies whose skin flaps weren't substantial enough to adequately fill tissue-expanders. Compared to not using ADM at all, which had an infection rate of 27.8%, and compared to indiscriminant ADM use, which had an infection rate of 20%, implementation of their selection algorithm significantly reduced infection rates to 15.8%.

Finally, we have previously published our own algorithm (36) designed to account for a multitude of patient factors and help generate a decision about whether reconstruction should be assisted by ADM. Our algorithm considered patient body mass index, pectoralis anatomy, flap vascularity, skin excess, and pre- and post-operative radiation therapy including sentinel-node status as a predictor of radiation. By deploying the algorithm for consistent use in our practice, we demonstrated a reduction in ADM usage without compromising safety or aesthetic outcomes.

The promises of well-designed algorithms to help ADM decision-making

Cost reductions

Rapidly mounting costs of health care alongside changes brought by the Affordable Care Act are forcing physicians

to reevaluate cost-benefit analysis of many procedures, as even the smallest inefficiencies will likely come under close scrutiny. Surgical decision-making should not only include consideration of utility and complications, but must also be sensitive to the economic consequences of the decisions. The economics of ADM use have been hotly debated in the literature, yielding various viewpoints and conclusions. Besides improving outcomes, one benefit of introducing algorithms for ADM use to surgical practice may be a reduction in healthcare costs as a direct result of more selective and therefore less frequent ADM use. Because ADM is instrumental in direct to implant reconstructions, which obviate the second operation of a two-stage reconstruction, ADM makes available a significantly cost-saving option (39,69-72). Even when patients elect to perform further aesthetic procedures after a direct to implant ADM-assisted breast reconstruction, the total cost may still lie below that of traditional non-ADM two-stage techniques (71). de Blacam *et al.* (69) published a cost-minimization analysis in the United States healthcare setting that estimated the cost of direct to implant reconstruction with ADM to be \$5,423.02 versus \$10,934 for the traditional non-ADM two-stage technique. This finding makes suggests that algorithms should include surgical technique, such as direct-to-implant, as a relevant factor in deciding ADM appropriateness.

Of course, not every patient is a candidate for a single-stage breast reconstruction, and the more challenging question is whether ADM use in two-stage techniques is still economically sound compared to similar non-ADM two-stage techniques. As an example of the divergent views in the existing literature, de Blacam *et al.*'s analysis (69) reported that ADM use in two-stage reconstructions cost \$11,255, compared to \$10,934 for a similar non-ADM option; Krishnan *et al.* arrived at a similar result, estimating a \$362 cost increase when ADM is used. Both of these reported price differences could be described as negligible. In contrast, Bank *et al.* (73) found a \$3,047 increase when ADM was used in two-stage reconstruction, nearly ten times greater than de Blacam's or Krishnan's estimation. Some authors have also argued that alternatives to ADM such as dermal allografts provide the same benefits at a reduced price (74-76).

There are many variables that may help or harm the cost-effectiveness of ADM in two-stage reconstruction. ADM use in tissue-expander surgery can cut the number of post-operative expansion visits required because larger intraoperative fill volumes can be attained; in that respect,

they have a cost-saving advantage versus a similar non-ADM-assisted technique (71-73). Specifically Bank *et al.* (73) argued that the cost of breast reconstruction rises in part due to the number of expansion visits needed, and that ADM use in large breasts (over 500 mL) was particularly effective at reducing costs. This analysis seems to support the inclusion of breast size in an ADM-use algorithm, as previously discussed, large breasts also come with countervailing effects that may warrant a delayed reconstruction in such breasts instead (*Table 1*). But likely the source of uncertainty in the costs of ADM use is driven by its aforementioned variance in reported complication rates (69,77). If ADM's complication rates are and severities are truly high, the overall cost of using them will obviously increase. Thus, an algorithm whose rational selection of ADM use can successfully reduce complication rates will likely improve the cost-effectiveness of ADM.

Despite these differences and uncertainties, Bank *et al.* and Krishnan *et al.* both have suggested that in reality, material costs are the largest factor driving ADM cost-utility analyses (73,75). Presently the market price of a 6 cm × 16 cm sheet of ADM is approximately \$3,100. With these assumptions, we reported that our algorithm could save on material costs by \$150,000 over a year of 100 prosthetic breast reconstructions, given that our algorithm reduced ADM use from 84% to 36% (36). If material costs truly represent the majority of the economic burden of ADM-use in breast reconstruction, an algorithm that can be more selective in choosing patients for whom to use ADM would represent a substantial improvement in cost-effective surgical practice.

Aesthetic outcomes and complication rates

ADM used in breast reconstruction effectively acts as a supporting hammock for the prosthetic in order to recreate natural breast morphology (47), and many authors have supported claims that it produces better aesthetic outcomes. Vardanian *et al.* (11) showed ADM can improve the surgeon's control over and definition of the inframammary fold, boosting aesthetic outcomes. Nguyen *et al.* (78) comparably demonstrated improved breast mound volume, breast mound placement, and inframammary fold definition with the use of ADM compared to non-ADM-assisted reconstructions. More recently, Forsberg *et al.* (26) found that ADM resulted in better aesthetic scores in the naturalness of the contour, the symmetry of shape and size, the position on the chest wall, and the overall aesthetic of the reconstructed breast. With all of the positive reports,

it is natural to suppose that a mature, honed algorithm can improve reconstruction aesthetic outcomes if it is able to accurately select patients that will benefit most from ADM.

Likewise, such an algorithm can reduce complication rates by allowing surgeons to judiciously decide whether ADM is appropriate given a particular patient's individual factors. Peled *et al.* was able to lower complication rates using their basic ADM algorithm for TSSM reconstructions (50), which is an encouraging finding for those interested in further developing more complex algorithms.

The challenge, of course, is developing and refining the right algorithm. For any of these promises to be realized, much greater effort must be applied toward the development and assessment of sophisticated algorithms—ones that account for the many factors the field has identified as indications and contraindications. Furthermore, long-term outcomes such as capsular contracture, as well as detailed aesthetic outcomes, have been insufficiently assessed in ADM algorithms including our own. In order to discover what parameters the surgeon can leverage to make good ADM decisions, researchers must be prepared to conduct long-term studies to assess complications, as well as test for aesthetic end-points in sophisticated manners.

Finally, we wish to stress that it is not our intention to lock surgical decision-making into a rigid decision-making protocol. Obviously, the clinical experiences of different surgical practices may conflict with our algorithm. Furthermore, many situations cannot be perfectly captured by an uncompromising decision algorithm; additional judgment extending past our simple algorithm must also contribute to the decisions in such cases. Rather, the purpose of this algorithm is to stimulate a shift away from the previously indiscriminate use of ADM in breast reconstruction, and encourage discussion about rational selection criteria for patients who would most benefit from ADM.

Conclusions

Surgical decision-making with ADM in primary prosthetic breast reconstruction continues to evolve. We have reviewed some important indications and contraindications for the use of ADM, as well as the few algorithms that have been thus far proposed to assist in the decision of whether ADM is appropriate. This approach can reduce costs and improve aesthetic outcomes and complication rates. We encourage plastics practices to further develop and evaluate their own decision-making tools for ADM use.

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Footnote

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Current strategies with 2-staged prosthetic breast reconstruction

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Abstract: Over the last decade, prosthetic-based breast reconstruction has been revolutionized with technological advancements. Reconstructive surgeons now have a multitude of prosthetic devices and tissue expanders, tools for intraoperative perfusion analysis, implantable bioprosthetic materials and a technique for autoaugmentation within their armamentarium to reconstruct natural breasts today like never before.

Keywords: Breast reconstruction; implant-based breast reconstruction; prosthetic-based breast reconstruction; breast implants; acellular dermal matrix (ADM); fat grafting; laser-assisted indocyanine green angiography

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In conjunction with the passing of the Women's Health and Cancer Right Act in 1998, and the increase in breast cancer awareness, the rates of breast reconstruction have increased dramatically. Nearly 1 in 8 women will develop breast cancer over her lifetime; an estimated 232,670 new cases of invasive breast cancer were expected to be diagnosed in women in the USA in 2014 (1). It was estimated that in 2014 alone, nearly 102,215 reconstructive procedures were performed for breast reconstruction (2). Post-mastectomy reconstruction has innumerable benefits to a woman's sense of sexuality, body image, self-esteem and quality of life (3,4).

Breast reconstruction can be performed through a multitude of pathways: autologous (use of one's own tissues), prosthetic (implant-based), or a hybrid of the two. The most common pathway for implant-based reconstruction is a 2-staged process where the first stage involves placement of a tissue expander and a second stage where the tissue expander is exchanged for a prosthetic breast implant (5). Nearly 70% of all breast reconstructions are prosthetic-based (6,7). Based on the Nationwide Inpatient Sample database from 1998 to 2008 there was an overall 78% increase in immediate breast reconstruction with a 203% rise in implant use (7). This trend continues today as advancements in technology continue to be made.

As oncologic principles and therapies have evolved so too have reconstructive tools and principles. Over the past 20 years, strides have been made in developing and refining tissue expanders, prosthetic breast implant devices, tools for intraoperative perfusion assessment, bioprosthetic materials for construction of internal support, and combining prosthetic reconstruction with autologous augmentation through fat grafting. All these advances allow reconstructive surgeons to take a once morbid and disfiguring procedure and make it a visually imperceptible defect.

Breast cancer management requires a multidisciplinary approach involving medical oncologists, radiation oncologists, pathologists, oncological surgeons and plastic surgeons. Ongoing communication amongst all parties involved during the planning stages allows for avoidance of potential postoperative complications and provides the best possible outcome for the patient. "A good reconstruction always begins with a good mastectomy" (8). It is imperative for reconstructive surgeon to be aware of the extent of resection and necessity for neoadjuvant and/or adjuvant therapies the patient may require such that the reconstructive timeline may be tailored to the individual patient.

Since introduction of the Halstead radical mastectomy

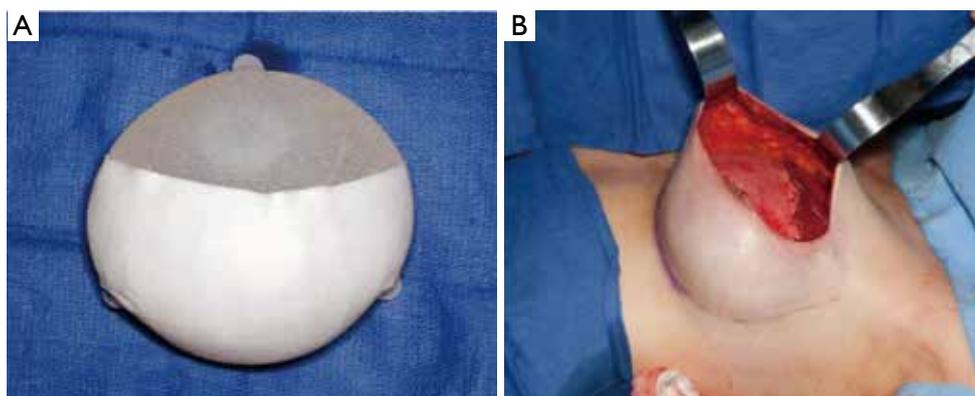


Figure 1 (A) Standard tissue expander device with partial ADM coverage. Note textured surface, tabs and incorporation of filling port. (B) In a standard 2-staged reconstruction, this device is placed in the subpectoral plane with the superior aspect being covered with the pectoralis major.

in 1882, the extirpative surgery has evolved from a radical approach to a more conservative one where by the skin and/or nipple are spared (9,10). By maintaining the native breast envelope and inframammary fold, reconstruction of a natural, cosmetically appealing breast is possible at the time of mastectomy (11,12). While initial critics of the evolution raised concerns regarding compromising oncologic safety and potential increase in locoregional recurrence these well intentioned concerns have not been scientifically validated (13,14).

Once the glandular tissue has been removed, the reconstructive process commences. A 2-staged implant-based approach is begun through first placing a tissue expander to first save the natural breast footprint (inframammary fold, shape, width, and projection) and secondly to allow for expansion of the skin envelope to desired volume. At the second stage the expander is replaced with a long-lasting prosthetic device and refinements are made to the breast pocket and mound to achieve the desired aesthetic shape.

The concept of tissue expansion through placement of a subcutaneous balloon was first described by Neumann in 1957 to reconstruct an auricle (15). However, it was not until after 1982 when Radovan (16) published his experience with placing a deflated silicone expander with an external reservoir dome for reconstruction of the breast when 2-staged prosthetic breast reconstruction gained acceptance. The initial tissue expanders used by Radovan were round and dome-shaped with non-expandable bases and had external filling ports. The subsequent evolution included incorporation of the filling port into the device itself as

to eliminate the need for dissection outside of the breast footprint and thereby reduce risks of lateral migration of the implant. In the late 1990s, McGhan Medical (Allergan) began production of variable height and variable projection devices which allowed for preferential expansion of the lower pole of the breast for a natural appearing breast (17). This was followed shortly thereafter with the incorporation of a textured surface and tabs to precisely control placement of the device and prevent any malpositioning and rotation of the device (18) (*Figure 1*). As tissue expanders have evolved so too have permanent prosthetic implants. Throughout history, there has been a desire for breast augmentation. In the 1800's, there were reports of injecting various synthetic materials into breast including beeswax, petroleum jelly, and various epoxy resins (19). However, it was not until 1962 when Cronin and Gerow developed implants consisting of a thick silicone shell with a less viscous silicone filling which led to the modern era of breast implants. Unfortunately, in the 1970s the original generation implants had high failure rates with silicone leakage, high degree of capsular contracture and subsequent deformities which ultimately led to the temporary Federal Drug Administration's (FDA's) moratorium on silicone gel implants in 1992 (20). During the temporary embargo, silicone implants were utilized in clinical trials. Finally, in 2006, after multiple studies reported safety of the device, the FDA reversed the ban. Subsequent generations of breast implants have focused on creation of a higher fidelity shell to prevent silicone bleed, textured surfaces to prevent implant migration, cohesive silicone gels for a more natural feel, and anatomically shaped implants for a more



Figure 2 Silicone breast implants. A round, smooth-textured implant on the left. A textured, anatomic implant on the right.

natural appearance. Today's implants, although made of similar material, are fundamentally different than previous generations.

While silicone implants have had a rocky history, saline-filled implants have remained on the market throughout the temporary silicone implant moratorium. However, these are not without faults. Initially described in France in 1965 by Arion, these devices were developed to allow for smaller incisions and versatility in adjusting volume and a soft, natural feel. Clinical trials in the 1970s showed high rates of deflation secondary to weak silicone shells and valve failures. Subsequent design modifications have resulted in deflation rates of 5.5% at 6 years (21). While saline breast implants are presently used in a fraction of primary cosmetic breast augmentation, they do not perform as well in the reconstructive realm; it is exceedingly difficult to achieve a natural appearing reconstruction with the use of saline implants. This is not just surgeon bias; this has been shown through patient reported outcomes. A study utilizing the BREAST-Q, a validated questionnaire measuring postsurgical body image and quality of life in the breast reconstruction, showed higher overall satisfaction with breast reconstruction, higher psychological well-being, higher sexual well-being, and higher satisfaction with surgeon for silicone implant recipients compared to saline implant recipients (22) (*Figure 2*).

The primary benefit of a 2-staged prosthetic approach is the placement of a partial deflated implant to preserve the breast footprint while not stressing the perfusion of the remaining mastectomy skin to prevent contracture of the wound while healing ensues. The nature of a mastectomy is inherently an ischemic process relative to the skin envelope. The perfusion of the breast arises from several sources including the internal mammary artery, lateral thoracic artery, thoracoacromial artery, and anterior/

posterior branches of the intercostal arteries. The process of removing the glandular tissue eliminates the perfusion from the thoracoacromial artery and potentially from the other sources, particularly when the boundaries of the natural breast are violated. Skin necrosis, which was reported to occur in up to 25% of reconstructions, was plaguing complication early in the evolution of breast reconstruction, particularly in the immediate setting (23).

Accurate intraoperative prediction of skin flap viability with clinical judgement is a challenging task that often relies on subjective parameters including: color, capillary refill, and dermal edge bleeding. Assessment of skin flap perfusion with intraoperative LA-ICGA (laser-assisted indocyanine green fluorescent angiography) allows for real-time visualization of skin perfusion, providing the surgeon with an objective marker to facilitate surgical decision-making. The utility of LA-ICGA in predicting necrosis was illustrated in an article by Newman *et al.*, in 2010 where LA-ICGA was performed on 20 consecutive mastectomy flaps showing a 95% correlation between intraoperative imaging and clinical course with 100% sensitivity and 91% specificity (24). A prospective trial of 51 implant based breast reconstruction LA-ICGA correctly predicted necrosis in 19 of 21 cases where clinical judgment failed (25). The Mayo Clinic adopted the technology in 2011 since has dropped the rate of skin necrosis in immediate breast reconstruction by 83% (26). Furthermore, when immediate implant-based reconstruction is to immediately follow the oncologic procedure, LA-ICGA allows for maximal fill volume without compromising perfusion of the mastectomy flap (*Figure 3*).

Traditionally, the prosthetic device has been placed in the sub-muscular plane with total submuscular coverage utilizing the pectoralis major and serratus anterior. The interposition of well vascularized muscular tissue between the skin and prosthetic device helped reduce the visibility of the implant under the skin and minimize the step-off between the device and chest wall (27). Conventionally, this involved elevation of the pectoralis major and serratus anterior fascia, however, this resulted in difficulty with inframammary fold definition, lateral deviation of the breast mound, failure to develop lower pole fullness, loss of a naturally ptotic appearing breast and a painful, prolonged expansion process. Furthermore, the submuscular pocket was taut while the overlying mastectomy was redundant resulting in contraction of the mastectomy flaps while the muscular pocket is slowly expanded. This resulted in disunion between the device and overlying skin envelope.

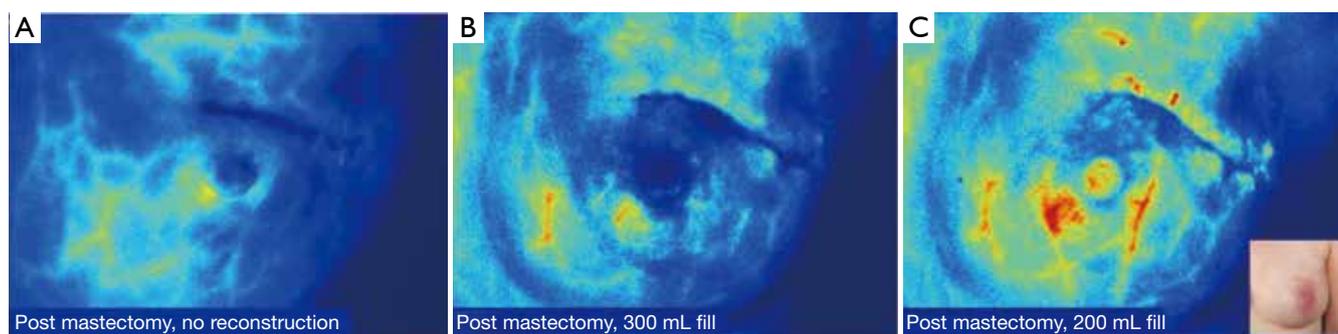


Figure 3 (A) Prior to beginning the reconstruction, post-mastectomy intraoperative LA-ICGA revealed adequate perfusion to the nipple-areolar complex; (B) 550 mL tissue expanders filled to 300 mL, were placed in the partial subpectoral pocket with the lower pole reinforced with ADM. Repeat LA-ICGA showed compromised perfusion to the left upper outer quadrant; (C) the left tissue expander was partially deflated and repeat LA-ICGA revealed adequate perfusion. LA-ICGA, laser-assisted indocyanine green fluorescent angiography; ADM, acellular dermal matrix.



Figure 4 Incorporated ADM showing revascularization at time of second stage from tissue expander to implant (3 months). ADM, acellular dermal matrix.

These drawbacks of total submuscular coverage led to the use of acellular dermal matrices (ADMs) in breast reconstruction. ADMs are decellularized dermal matrices that provide a scaffold for the patient's tissues to incorporate into through revascularization and repopulation. Breuing and Warren were the first to report use of ADM as an inferolateral dermal sling resulting in a partial subpectoral, partial sub-ADM pocket resulting in precise control of the lower pole and lateral mammary fold as well as reduced time to full expansion (28) (*Figure 4*).

ADMs have since revolutionized prosthetic breast reconstruction. Acting as internal support for the device, they provide precise control of the inframammary and lateral mammary folds, prevention of “window-shading” or retraction of the pectoralis muscle cephalad, shorter expansion times, reduction in implant visibility and rippling,

and protective effects against radiation changes and capsular contracture (29-33). A diverse array of regenerative matrices are available; varying with respect to tissue source, processing, preparation, sizes, cost, and performance (34). ADMs have disrupted the dogma of total muscular coverage with the current technique of partial-muscular, partial-ADM coverage being routinely used. The door has now opened for total-ADM covered devices in the subcutaneous (pre-pectoral) plane. While the evolution from total muscular coverage to subcutaneous breast reconstruction is at the forefront of breast reconstruction with promising aesthetic outcomes, long-term results and complications are not yet available (27) (*Table 1*).

Historically, a consistent problem restricting the aesthetic outcome for prosthetic-based breast reconstruction was implant visibility and contour deformities; placement of an implant beneath an inherently thin skin envelope consistently generated an unnatural, conically shaped mound with obvious step-off between the implant and chest wall and lack of a naturally ptotic, tear-shaped breast. Currently, the solution to this problem is transplantation of fat from remote areas to the breast. This concept was first reported by Czerny in 1895 when he transplanted a lipoma to a breast after a partial mastectomy for fibrocystic disease (35). It was not until the 1980s with the advent of liposuction that fat grafting gained popularity as surgeons were now able to take a small aliquot of fat and inject it to fill contour deformities (36).

The general concept of modern fat grafting includes lipoaspiration at sites of excess adiposity (typically flanks, abdomen and/or thighs). This is done with a small 3- to

Table 1 Strengths and limitations of plane of implant placement

	Total submuscular coverage	Dual plane—subpectoral + ADM sling	Pre-pectoral—subcutaneous + full ADM coverage
Preservation of natural breast shape	+	++	+++
Muscle spasm	+++	++	–
Animation deformity	+++	+++	–
Postoperative pain	+++	++	+
Cost	–	++	+++
Operative time	++	++	+
Initial fill volume	+	++	+++
Number of fills (time to complete expansion)	Many	Few	Fewest
Indications	Thin mastectomy flaps with near complete resection of skin envelope; mastectomy flaps with questionable perfusion	Healthy mastectomy flaps without areas concerning for ischemia	Healthy, thick mastectomy flaps with excellent perfusion

ADM, acellular dermal matrix; –, none; +, some; ++, more; +++, most.

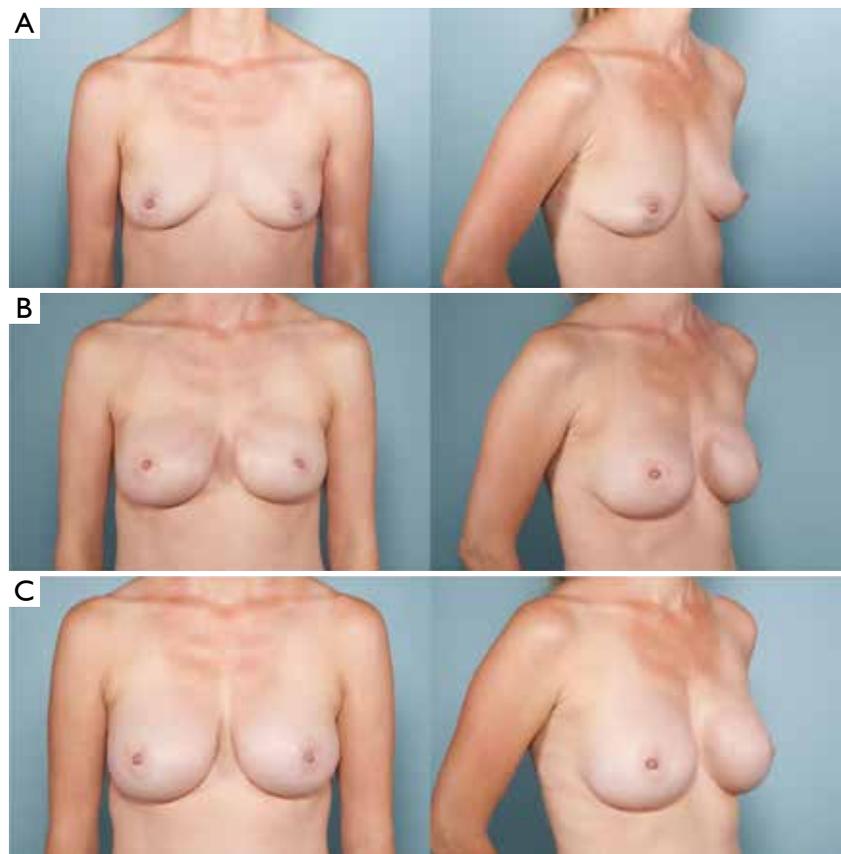


Figure 5 (A) Preoperative photographs of a patient with right breast cancer; (B) after undergoing bilateral nipple-sparing mastectomies with immediate tissue expander placement in the subcutaneous plane through an inframammary fold approach; (C) final reconstruction after exchange of tissue expander for anatomic silicone breast implants and fat grafting.

4-mm blunt cannula and negative pressure suction with a collection system between the suction device and cannula. The fat aspirated is then separated from the excess fluid and supernatant oils. The pure fat is then injected into the skin envelop in the subcutaneous plane between the dermis and underlying ADM capsule and/or muscle (*Figure 5*).

Early in the application of this technique to breast reconstruction, concerns were raised regarding not only the efficacy and long-term results but also oncologic safety. Science has yet to identify any association between autologous fat grafting and increased breast cancer recurrence (37-40). Furthermore, current studies have reported excellent aesthetic outcomes, a high degree of patient and surgeon satisfaction and overall a low rate of complications (38,41). More than just filling contour defects, autologous fat grafting fundamentally changes the quality of the overlying skin envelope especially in setting of radiation (42). Pre-clinical studies have shown reversal of radiation-induced dermal fibrosis and hypovascularity (43). Autologous fat grafting has proven to be a valued tool in breast reconstruction, which has revolutionized surgeons' abilities to camouflage the prosthetic devices allowing for reconstruction of a natural breast.

Radiation therapy has become a mainstay in breast cancer treatment with more women being offer radiation treatment as studies have proven a survival benefit (44,45). This poses a challenge for reconstructive surgeons. Historically, prosthetic-based reconstruction was discouraged in the setting of post-mastectomy radiation due to the high rate of wound healing problems, implant malposition, capsular contracture, infection, extrusion of implants, and poor aesthetic outcome (46,47). However, with the adjuvant tools available including ADMs, anatomic breast implants, and fat grafting, successful prosthetic based reconstructions are now possible (48-51).

Breast reconstruction over the past decade has been completely revolutionized by the technical advances in oncologic management of breast cancer, development of anatomically shaped prosthetic devices, and application of bioprosthetic materials, intraoperative perfusion technology, and autologous fat grafting. Today's breast reconstruction is nearly visually imperceptible, something that was a significant challenge with previous generations of technology, devices and techniques.

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Footnote

Conflicts of Interest: Dr. Jacobson is a consultant for LifeCell, Allergan, Sientra, and Mentor. The other author has no conflicts of interest to declare.

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Conservative mastectomies and immediate reconstruction with the use of ADMs

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Background: In recent years, a novel approach to immediate breast reconstruction has been introduced with the advent of acellular dermal matrix (ADM). In the setting of conservative mastectomies where the native skin envelope is preserved, placement of ADM at the lower pole in continuity with the pectoralis major muscle (PMM) provides additional support, allowing direct-to-implant breast reconstruction. The following manuscript presents the senior author's experience with ADM-assisted reconstruction and provides a detailed description of surgical technique along with a comprehensive discussion of patient selection and potential complications.

Methods: A retrospective chart review of patients undergoing direct-to-implant breast reconstruction following skin sparing or nipple sparing mastectomy with the use of ADM (AlloDerm; LifeCell Corp., Branchburg, USA) was conducted at Women's College Hospital in Toronto over a 5-year period [2008-2013]. Demographic data, previous radiation therapy and post-operative complications were recorded.

Results: A total of 72 patients representing 119 breasts were identified. Average follow-up was 16 months (range, 3-51 months). Twenty-seven complications were recorded for a complication rate of 22.7% (27/119). Complications included six cases of capsular contracture (Baker III/IV), five cases of red skin syndrome, four cases of rippling, three cases of dehiscence and two cases of seroma. Overall, direct-to-implant reconstruction was successfully completed in 97.5% of breasts (116/119). One case of infection was treated with explantation and conversion to autogenous reconstruction. Two breasts with tissue necrosis or dehiscence had the implants removed and replaced with tissue expanders. Overall reoperation rate was 9.7% (7/72 patients).

Conclusions: ADM assisted direct-to-implant breast reconstruction has been shown to be a safe option for women who are candidates for skin sparing or nipple sparing mastectomies. Judicious patient selection, effective collaboration between the oncologic and reconstructive surgeon, careful evaluation of post-mastectomy skin flaps and precise surgical technique are paramount to the success of this technique.

Keywords: Acellular dermis; breast reconstruction; conservative mastectomy; implant-based; direct to implant

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Introduction

In the last several decades, significant advancements have been made in the surgical management of breast cancer. Nipple-sparing mastectomies (NSM) and skin-sparing mastectomies (SSM) followed by immediate alloplastic breast reconstruction have emerged as oncologically safe treatment options yielding excellent cosmetic results. These techniques minimize breast deformity and optimize aesthetic outcome through preservation of the native skin envelope and restoration of a naturally looking breast mound using tissue similar in color, texture and sensation.

Traditionally, immediate implant-based breast reconstruction is performed in two stages using tissue expander/implant (TE/I) technique. Following mastectomy, the inferior border of the pectoralis major is released and a partially filled expander is placed in the submuscular pocket, often with inferior pole coverage provided by a thin serratus muscle/fascia flap. As such, sufficient coverage of the prosthesis is ensured and stress to the thin and vulnerable mastectomy skin flap is minimized. Post-operatively, serial expansions are followed by exchange of expander to implant once the desired breast size is achieved.

To eliminate delayed return to normal body image and minimize the burden of serial expansions and additional surgery associated with TE/I technique, a novel approach to immediate breast reconstruction has been introduced with the advent of acellular dermal matrix (ADM). ADM is an immunologically inert biomaterial prepared from xenoplastic or alloplastic cadaveric dermis devoid of cellular elements. It provides structurally intact tissue matrix that serves as a biological scaffold necessary for tissue ingrowth, angiogenesis and regeneration (1). In the setting of SSM or NSM where the entire native skin envelope is preserved, placement of ADM at the lower pole in continuity with the pectoralis major allows complete coverage of the prosthesis and provides additional support. The inferiorly placed ADM hammock suspends the prosthesis thus offloading mechanical stress from the overlying skin flap. Based on the quality of the skin envelope as well as surgeon preference, a decision can be made to either insert the permanent implant or alternatively insert a tissue expander.

Utilization of ADM confers several additional advantages including improved control over placement of the inframammary (IMF) and lateral mammary folds (LMF), preventing mechanical shift of the implant and stabilizing the pectoral muscle to minimize superior migration or window shading (2). Together, these can contribute to superior

aesthetic outcomes of the reconstructed breast. Further, inferior placement of a dermal matrix may reduce rippling, visibility, palpability, bottoming-out and exposure of the implant (3,4). Reduced incidence of capsular contracture has also been reported (3).

The following manuscript presents the senior author's 5-year experience with ADM in the setting of direct-to-implant breast reconstruction following SSM or NSM. A detailed description of surgical technique is provided along with a comprehensive discussion of patient selection and potential complications.

Materials and methods

Patients

A retrospective chart review of patients undergoing direct-to-implant breast reconstruction with the use of ADM (AlloDerm; LifeCell Corp., Branchburg, USA) was conducted at the Women's College Hospital (Toronto, Ontario, Canada) over a 5-year period [2008-2013]. All operations were performed by the senior author using similar operative technique. Demographic data, previous radiation therapy and post-operative complications were recorded.

Candidates for direct to implant breast reconstruction are determined based on the indication for mastectomy, breast size and shape, BMI, patient co morbidities, patient preference as well as surgeon preference. Ideal candidates should be small breasted (A or B cup), with minimal ptosis and a nipple complex that requires minimal elevation on the breast mound. Generally direct to implant reconstruction is offered to women undergoing prophylactic mastectomy or mastectomy for pre-invasive disease. In some centers, patients with small invasive tumors are also offered single stage reconstruction. Patients should have a low or normal BMI (maximum BMI of 30), should be non-smokers and should not have undergone previous breast radiation.

Surgical technique

Prior to surgery, all patients receive a combination of medications that have been shown to assist in rapid recovery with minimal use of narcotics (5). This "cocktail" includes celebrex, acetaminophen and gabapentin. Intravenous antibiotics and a single dose of dexamethasone are administered in the operating room. Patients are positioned supine with arms abducted at 90 degrees.

Incision options for NSM

- IMF
- LMF
- Lateral breast
- PA
- Sickle
 - Lower areola
 - Upper areola
- Mastopexy pattern



Figure 1 Incision options for nipple sparing mastectomy. NSM, nipple-sparing mastectomies; IMF, infra-mammary fold; LMF, lateral mammary fold.

Various incisions have been described for both NSM and SSM (*Figure 1*). The choice of incision is based on the preference of the oncologic surgeon, the size of the breast and the location of existing pathology or previous scars. When performing a NSM, it is the author's preference to use an IMF incision. In larger breasts, a mid breast incision extending from the areola may be used to allow easier access to the upper pole and the lateral breast tissue. It is important for the oncologic surgeon and the reconstructive surgeon to work collaboratively. As the mastectomy is started, the ADM is placed in a saline bath. The bath is changed every 15 minutes until the ADM is inserted. This assists with the removal of any preservatives that may be present from the processing of the material.

Following the mastectomy, the defect is carefully assessed. It is important to evaluate the quality of the skin envelope as well as the viability of the breast skin and the nipple areola complex. Assessment is performed clinically although various new technologies including the SPY Elite® System (LifeCell Corporation, Branchburg, USA) may be helpful in assessing tissue perfusion. The pectoral muscle as well as the serratus fascia is also assessed, as occasionally the muscle may be attenuated or damaged at the time of mastectomy. Prior to beginning muscle dissection, the pocket is irrigated vigorously to remove any loose tissue and fatty remnants. This is important to minimize infection and decrease the incidence of seroma formation.

Muscle elevation is performed with electro-cautery and begins along the IMF (*Figure 2*). This incision is carried laterally to include the serratus muscle fascia. Adding the fascia improves lateral implant stability and assists in

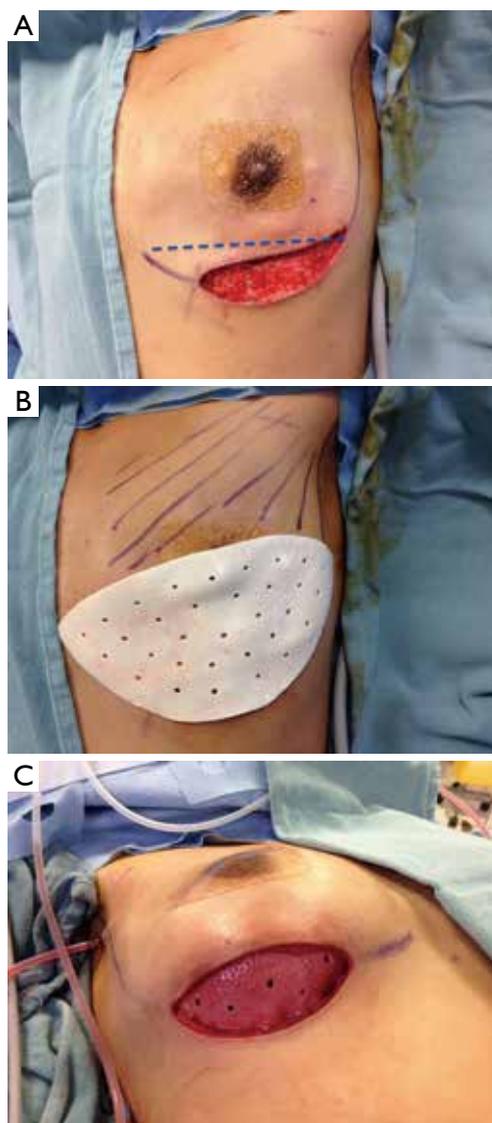


Figure 2 (A) Following completion of the mastectomy, the pectoral muscle is released along the IMF and raised in continuity with the serratus fascia; (B) a perforated contour piece of ADM ready for insertion; (C) implant inserted and ADM secured to pectoral muscle followed by the IMF. ADM, acellular dermal matrix; IMF, infra-mammary fold.

defining the lateral mammary fold. The sub-pectoral pocket is dissected in a similar fashion to a breast augmentation, with pocket dimensions determined by the choice of a round or a shaped implant. The ADM is placed in the lower pole of the breast and oriented with the deep dermal side towards the breast skin. The ADM is secured to the inferior edge of the elevated muscle using interrupted and

running absorbable suture. Several sutures are placed near the medial/inferior border. A sizer is inserted and several sutures are placed in the medial and lateral IMF. The bed is flexed to 90 degrees and the breasts are assessed for size, symmetry and fold position. The final implant is selected and the patient is returned to a supine position.

Two closed suction drains are inserted, one superficial and one deep to the ADM. Some surgeons chose to use one drain only, placed superficial to the ADM. The pocket is irrigated with antibiotic solution and the implant is inserted using a minimal or no touch technique. The ADM is then advanced inferiorly over the implant in order to secure a tight pocket for the implant. When a mid-breast incision is used, it is important to advance the ADM inferiorly to ensure that the pectoral muscle is sitting under the incision. The ADM is then secured to the IMF with a running absorbable suture.

Following skin closure, the skin and the nipple areola complex are again checked for color and perfusion. A light dressing and a supportive sports bra are applied. Drains remain in place until they are draining less than 30 cc per day for 2 consecutive days. Patients are kept on antibiotics during this time period. Several case examples are shown in *Figures 3-6*.

Results

Patient demographics

A total of 72 patients representing 119 breasts were identified. Mean patient age at time of surgery was 41.7 years (range, 28-62 years). Forty-seven patients underwent bilateral direct to implant reconstruction and 25 patients underwent unilateral direct to implant reconstruction. Among breasts operated, 45 (38%) cases were oncologic and 74 (62%) cases were prophylactic. Eighteen breasts (15.1%) undergoing reconstruction had a history of radiation to the reconstructed breast. Average follow-up was 16 months (range, 3-51 months).

There were approximately equal numbers of skin sparing and nipple sparing mastectomies (52% SSM, 48% NSM), however the percentage of nipple sparing mastectomies steadily increased during the period of study. All implants were silicone gel filled devices with the majority being shaped form stable implants (62% shaped 38% round).

Post-operative outcomes and complications

Overall, a total of 27 complications were recorded for a complication rate of 22.7% (27/119). Of the 119 breasts

operated on, 116 successfully completed direct to implant reconstruction. One patient had an infection, which was treated with explantation and conversion to autogenous reconstruction. Two breasts with tissue necrosis or dehiscence had the implants removed and replaced with tissue expanders. These patients went on to successful reconstruction with an implant. Complications occurred in 23 out of the 72 patients (32%). The most common complication was capsular contracture (Baker III/IV), identified in six breasts. It should be noted that 4 of the 6 breasts with capsular contracture occurred in the 18 breasts that had undergone radiation therapy. Other complications included five cases of red skin syndrome, four cases of rippling, three cases of dehiscence and two cases of seroma (*Figure 7*). Most complications were treated non-surgically. Overall reoperation rate was 9.7% (7/72 patients). All red skin syndrome patients resolved with antibiotics and anti-inflammatories. Infection was recorded in two cases. Of these, one patient underwent removal of the implant and was subsequently treated with autologous reconstruction. The other case of infection was managed conservatively with oral antibiotics. Hematoma occurred in one patient. Partial NAC necrosis was noted in two breasts (1.7%). A list of complications appears in *Table 1*.

Discussion

Since the late 1990's, a steady increase in implant-based breast reconstructions has caused a paradigm shift away from autologous tissue techniques. In 2008, alloplastic breast reconstruction comprised 68% of all reconstructive procedures performed in the United States (6). The 2-stage tissue expander to implant approach is the current gold standard for prosthetic breast reconstruction in North America. When compared to autologous reconstruction, it requires shorter operative times, eliminates donor site morbidity and allows for a more rapid convalescence (7,8). Notwithstanding, traditional implant-based breast reconstruction necessitates a series of visits for tissue expansion, a second surgical procedure and the eventual insertion of a permanent prosthesis, which will require ongoing maintenance and reoperations.

Since its introduction into reconstructive breast surgery by Breuing *et al.*, ADM has gained acceptance as a safe and effective adjunct to surgery, permitting direct-to-implant reconstruction where the native skin envelope is preserved (9). In patients undergoing NSM or SSM, reconstruction with ADM provides internal support that stabilizes the implant

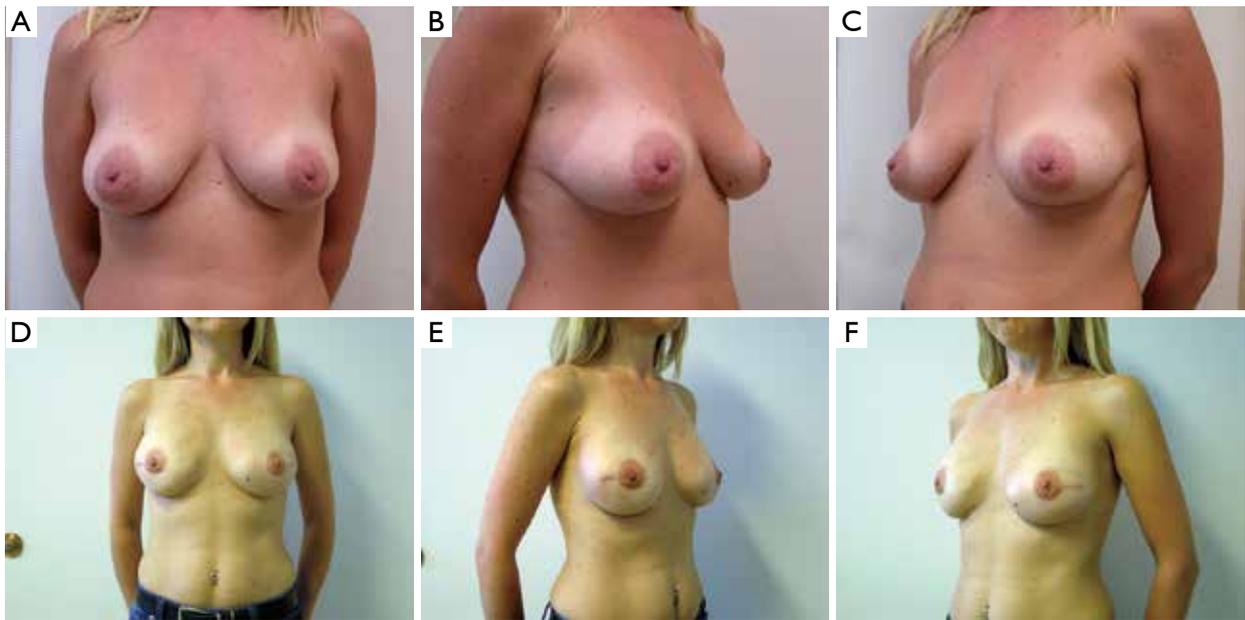


Figure 3 (A-C) Preoperation photos of patient with BRCA1 for prophylactic NSM through periareola incision with lateral extension. Reconstructed with MF420 shaped implant and ADM; (D-F) results at 2 years. NSM, nipple-sparing mastectomies; ADM, acellular dermal matrix.

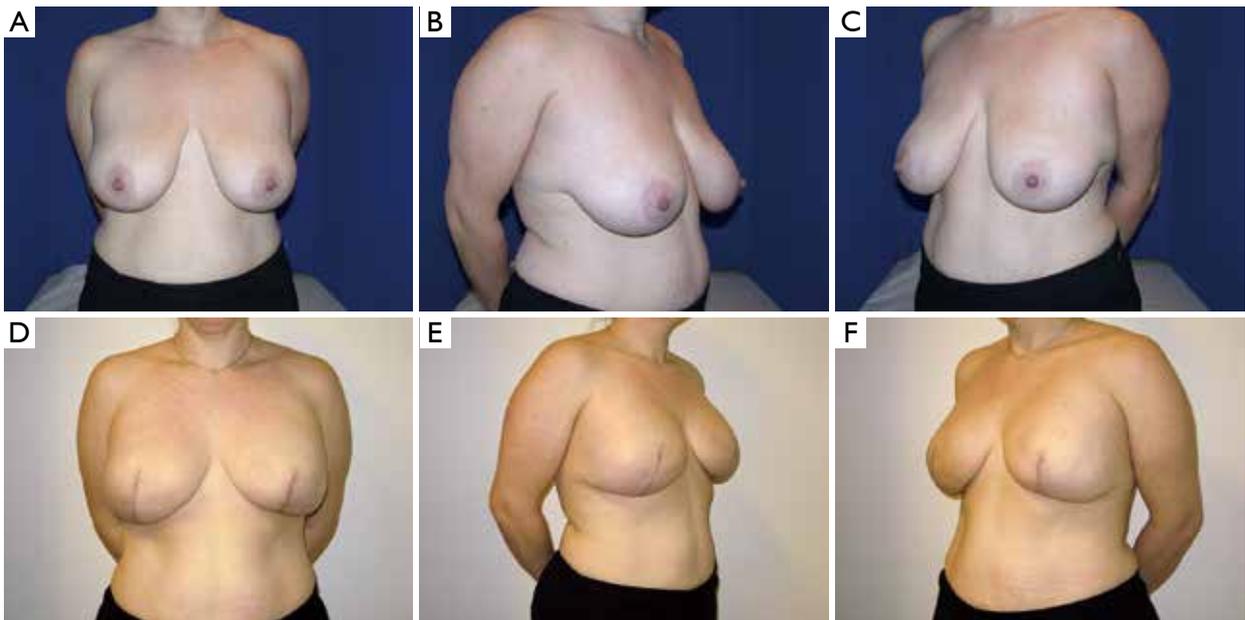


Figure 4 (A-C) Preoperation photos of patient for prophylactic skin reduction pattern mastectomy using an inverted T pattern. Direct to implant with round 500 cc implants and ADM; (D-F) results at 6 months prior to NAC reconstruction. ADM, acellular dermal matrix.

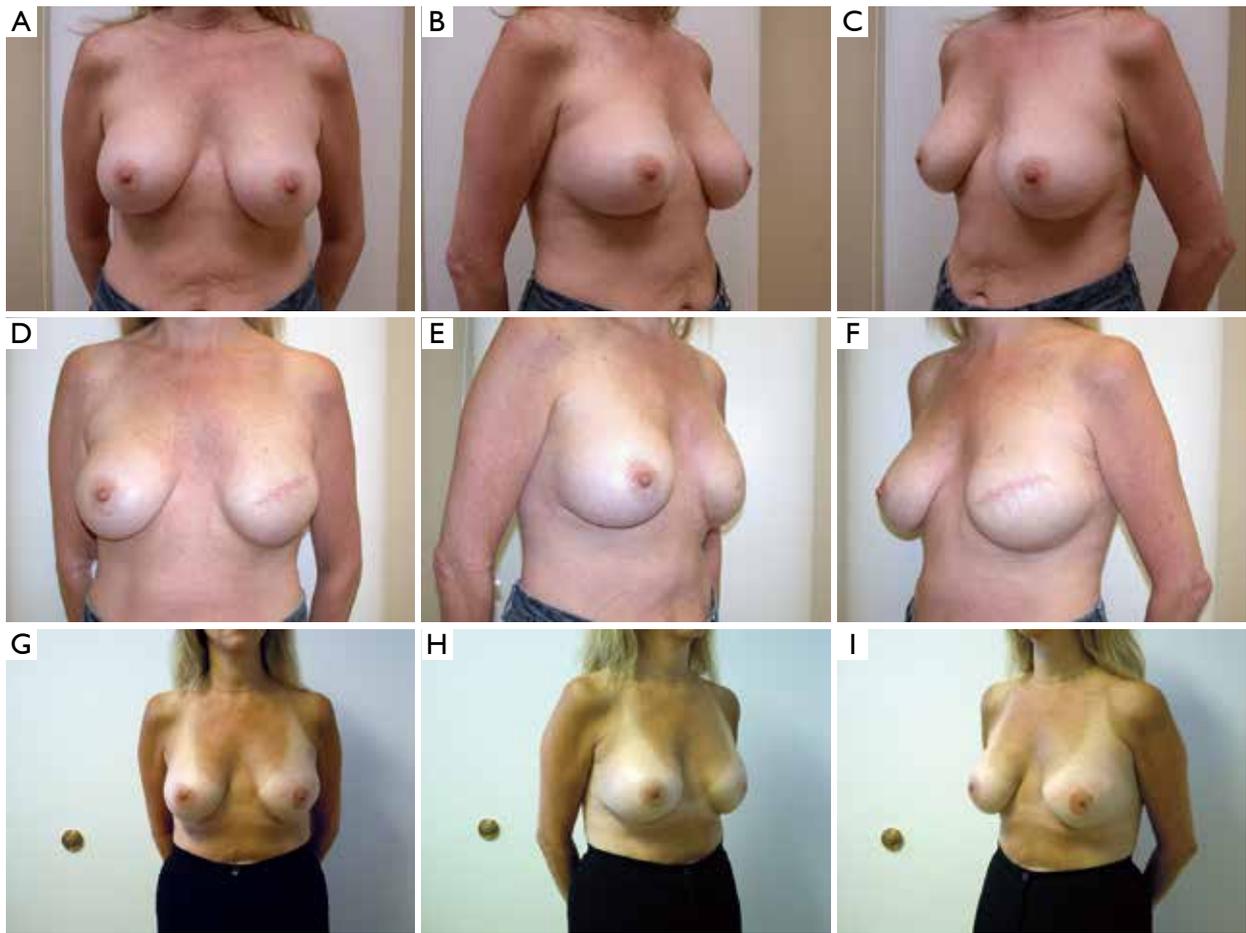


Figure 5 (A-C) Preoperation photos of patient with small left invasive cancer undergoing SSM and reconstruction with round 400 cc implant and ADM; (D-F) results at 4 months; (G-I) results at 15 months following NAC reconstruction. SSM, skin-sparing mastectomies; ADM, acellular dermal matrix.

position and minimizes pressure on the overlying skin flap. Placement of ADM at the lower pole in continuity with the sub-pectoral plane also confers the ability to control the inferior and lateral mammary folds, regardless of their potential violation during the mastectomy.

Additionally, supplementary coverage of the lower pole has been shown to decrease the incidence of rippling, bottoming out and implant migration when compared to non-ADM breast reconstructions (3). Other advantages of ADM-assisted direct-to-implant technique include reduced incidence of capsular contracture (Baker III/IV) and support of the pectoral muscle to minimize superior migration or window shading (3,10).

A wide assortment of alloplastic or xenoplastic dermal matrices have been used in breast reconstruction. Bovine-derived matrices include Tutomesh® (Novomedics GmbH,

Bahnhofstrasse, Zürich) (11), Veritas® (Synovis, Minnesota, USA) (2) and SurgiMend® (TEI Biosciences, South Boston, USA) (12). Porcine-derived matrices include Strattice™ (LifeCell) (13,14) and Protexa® (Tencoss) (15). Finally, cadaveric ADM options include Flex HD® (Ethicon) (16), DermaMatrix® (Synthes) (17), NeoForm® (Mentor) (18) and AlloDerm® (Lifecell). The latter is commonly reported in the literature and represents the ADM used in this series.

The reported frequency of complications in direct to implant, ADM assisted breast reconstruction ranges from 3.9% (19) to 69.5% (20). Implant loss was reported from 0% to 17.4% of cases (21). With regard to specific major post-operative complications, seroma formation has the highest reported incidence, occurring in up to 17.8% of operated breasts (11). In our patient population, seroma was recorded in two breasts (1.7%). Multiple reports exist in the literature

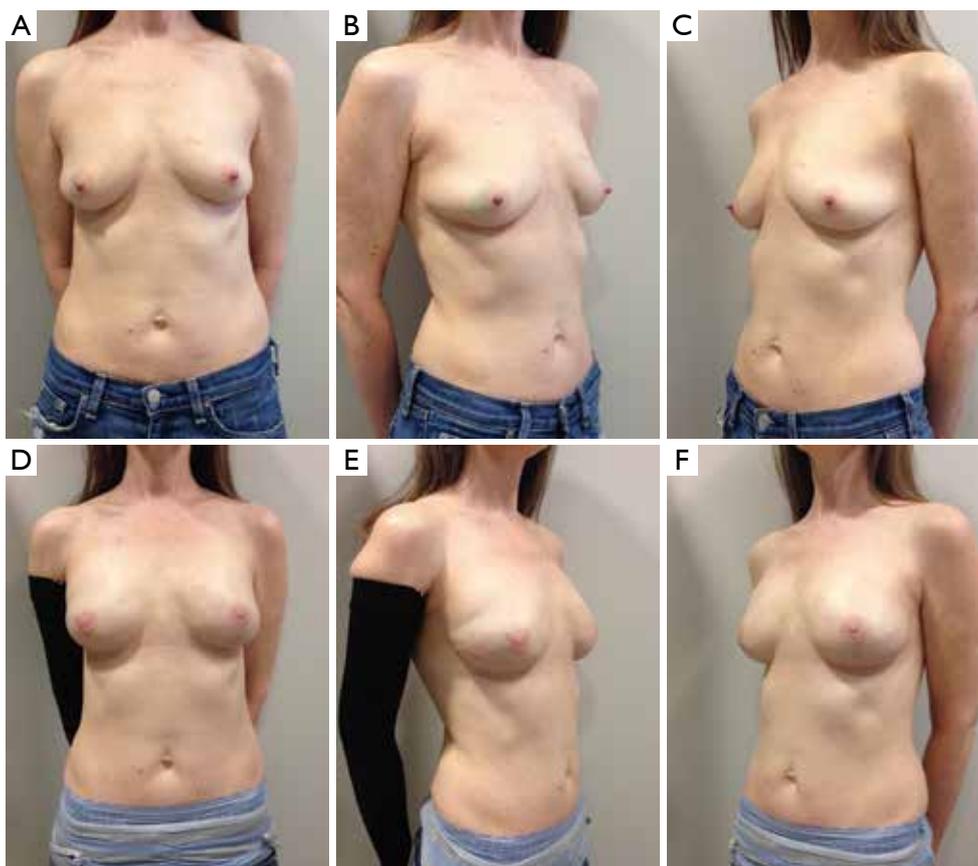


Figure 6 (A-C) Preoperation photos of patient with BRCA1 for bilateral areola sparing mastectomy through IMF incision with additional circular excision around base of nipple. Reconstructed with shaped MF295 implants and ADM; (D-F) results at 6 months. Note the slight prominence at the site of the nipple which was closed with a purse string suture. IMF, infra-mammary fold; ADM, acellular dermal matrix.



Figure 7 Red breast syndrome 3 weeks following skin reduction mastectomy and reconstruction with tissue expanders and ADM. Note that the redness is primarily over the location of the ADM. ADM, acellular dermal matrix.

Table 1 Post-operative complications following single-stage direct-to-implant breast reconstruction with ADM

Complications	Immediate breast reconstruction with ADM (119 breasts) (%)
Seroma	2 (1.7)
Hematoma	1 (0.9)
Infection	2 (1.7)
Dehiscence	3 (2.6)
Red skin syndrome	5 (4.3)
Capsular contracture	6 (5.1)
Rippling	4 (3.4)
NAC necrosis (partial)	2 (1.7)
Implant malposition	1 (0.9)
Implant loss [†]	1 (0.9)
Total	27 (22.7)

[†], not included in total complication rate as direct result of another complication. ADM, acellular dermal matrix.

suggesting higher rates of seroma associated with the use of ADM. However, conflicting information exists. In a study of 415 immediate implant-based breast reconstructions performed with or without the use of ADM (269 ADM, 146 non-ADM), Chun *et al.* demonstrated a 4-fold increase in the rate of seroma formation (22). Conversely, in a study comparing 330 single-stage reconstructions with ADM to 148 two-stage TE/I reconstructions without ADM, Colwell *et al.* showed a low overall complication rate that was similar between both groups (14.8% for single-stage ADM *vs.* 19.6% for two-stage non-ADM, $P=0.18$). In their series, post-operative seroma was recorded in 1.5% *vs.* 1.9% of breasts reconstructed with or without ADM, respectively ($P=0.81$) (8). They suggested that in patients with a healthy skin envelope, ADM does not appear to increase the risk of complications and constitutes an important factor in the patient selection algorithm. Salzberg has also emphasized the importance of a healthy, well-vascularized and good quality skin flap in the clinical decision making process proceeding direct to implant breast reconstruction with ADM (4). Given contradictory evidence and lack of consensus, several technical precautions have been suggested to minimize the risk of seroma. These include placement of both sub-mastectomy and sub-ADM drains, decreased drain removal threshold (<20 cc/24 h) and post-operative use of a soft compression dressing and bra (23). It is also the author's approach to vigorously irrigate the mastectomy pocket prior to ADM insertion to remove any residual fat from the pocket. Avascular fat has been shown to increase local inflammation and may predispose to a higher rate of seroma formation.

Infection leading to implant loss was the second most common major complication in our review of the literature; occurring in up to 13.0% of cases (21). Cellulitis managed conservatively was reported in up to 6.1% of breasts (20). Concern has been expressed in the literature regarding the "aseptic" and non-"sterile" nature of some ADMs available today and several studies suggest that these grafts are associated with higher infection rates. Chun *et al.* demonstrated a 5-fold increase in infection rate in ADM compared to non-ADM TE/I immediate breast reconstructions (269 ADM, 146 non-ADM) (22). Lanier *et al.* found a statistically significant higher rate of infection in the ADM group when comparing 75 ADM *vs.* 52 non-ADM TE/I breast reconstructions (28.9% *vs.* 12.0%, $P=0.022$) (24). Similarly, Liu *et al.* also demonstrated a statistically significant increase in overall wound infection rate in the ADM group compared with the non-ADM

group in a cohort of 470 immediate TE/I reconstructions (6.8% *vs.* 2.5%, $P=0.031$) (16). However, as with seroma formation, literature is conflicting and numerous studies demonstrating no increased infection risk exist. A recent systematic review by Sbitany *et al.* comparing morbidity in ADM-assisted *vs.* non-ADM TE/I reconstruction illustrated similar rates of infection leading to explantation (3.2% for sub-muscular and 3.4% for ADM, $P=0.18$) and cellulitis/wound infection not requiring surgical intervention (2.8% *vs.* 3.4%, $P=0.09$) (25). In our series, a low overall infection rate was recorded (two cases) for a total infection rate of 1.7%. Of these, infection resulted in implant loss in one case (0.9%). In our institution, several preventative measures are employed to help minimize risk of infection during direct-to-implant reconstruction. The ADM is bathed 3 times for 10 minutes each in bacitracin and saline solution to remove any preservatives that may exist in the material. Further, utilization of new gloves for handling the ADM, copious irrigation of the ADM-pectoral pocket with bacitracin solution and minimal touch technique for manipulation of the final implant are used. Drains are inserted through separate incisions distant from the mastectomy incision and covered with sterile, waterproof dressings. Lastly, patients are continued on oral antibiotics until the drains are removed.

Mastectomy skin flap necrosis or skin breakdown requiring operative revision has been reported in up to 9.1% of cases (8). Minor skin flap necrosis or superficial epidermolysis managed conservatively was more frequent, reported in up to 28.7% of breasts (20). In our present study, wound dehiscence was recorded in three breasts (2.6%) and partial NAC necrosis in two others (1.7%). Several authors have suggested that larger pre-operative breast size and more significant breast ptosis are associated with higher likelihood of complications and failure in direct-to-implant reconstruction (20,26). Gdalevitch *et al.* demonstrated significantly higher mastectomy flap necrosis in D-cup breasts (OR, 6.25; $P=0.027$) and Roostaeian *et al.* showed higher revision rates in patients with D-cup breast size or greater ($P=0.018$) and grade two ptosis or greater ($P=0.017$) (20,26). As with any reconstructive procedure, patient selection is paramount and should include optimization of co-morbidities and identification of risk factors including large breast size, ptosis, smoking history, radiation as well as existence of previous breast scars.

In summary, ADM assisted direct-to-implant breast reconstruction has been shown to be a safe option for women who are candidates for nipple sparing or skin

sparing mastectomies. The ability to preserve the breast envelope and restore volume with an implant that is supported in position by ADM can result in excellent aesthetic outcomes for the patient. It eliminates the need for frequent expansions and obviates the need for a planned secondary expander to implant exchange. This may assist in decreasing the physical and psychological impact of mastectomy and accelerate a return to normal life with a restored body image and improved quality of life. Judicious patient selection, careful evaluation of post-mastectomy skin flaps and consideration of possible risk factors for complications such as pre-operative breast size and ptosis are paramount to the success of this technique. Future studies including the ongoing Canadian Multi-Center Randomized Controlled Trial (MCCAT) will offer a rigorous comprehensive assessment of the direct to implant ADM-assisted approach and help to better define its future role in the field of reconstructive breast surgery (7).

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Risk-reducing, conservative mastectomy – analysis of surgical outcome and quality of life in 272 implant-based reconstructions using TiLoop® Bra versus autologous corial flaps

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Background: Different approaches have evolved for conservative mastectomies, mostly according to surgeon's preference. Patients' perspective was not always in the primary focus. BRCA status has drawn much attention and therapeutic as well as prophylactic mastectomies are rising. However, knowledge on quality of life (QoL) thereafter is limited. We investigated the surgical and patient reported outcome of conservative mastectomies with implants and TiLoop® Bra *vs.* corial flaps.

Methods: Conservative mastectomies were analyzed from a prospectively maintained database in a unicentric study of consecutive 272 reconstructions from 2000-2014. We used four validated QoL questionnaires: FACT-G, EORTC C-30, EORTC B-23 and Breast Cancer Treatment Outcome Scale (BCTOS). The use of TiLoop® Bra, a titanized polypropylene mesh, for lower breast pole coverage was compared to autologous corial flaps.

Results: A total of 217 patients with 272 conservative mastectomies (55 bilateral) were included. Median follow-up was 3.5 years (range, 0-14 years). Skin-sparing mastectomy (SSM) was performed in 131 patients and subcutaneous mastectomy (SCM) in 86 patients. Invasive breast-cancer was the indication for surgery in 106 patients, non-invasive breast cancer (DCIS) in 80 patients, prophylactic indication (BRCA1/2-mutation) in 30 patients and contralateral alignment in 1 patient. TiLoop® Bra was used in 78 and corial flap in 79 patients. Response to questionnaires was 70%. TiLoop® Bra improved aesthetic results ($P=0.049$) and prevented implant dislocation ($P=0.009$). All patients expressed their adherence to the decision for surgery. Patients with SCM expressed their satisfaction even to a higher extent than those with SSM, particularly with regard to symmetry ($P=0.018$) and scars ($P=0.037$).

Conclusions: QoL after conservative mastectomies is demonstrated as excellent in several validated QoL-instruments. Double-plane technique for coverage of the implant yields good results with autologous corial flaps and TiLoop® Bra, favouring the latter in terms of aesthetics and prevention of implant dislocation.

Keywords: TiLoop® Bra; corial flap; conservative mastectomy; skin-sparing mastectomy (SSM); subcutaneous mastectomy (SCM); quality of life (QoL)

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Introduction

Breast cancer requires mastectomy in—at least—one out of four women, and the possibility to prevent breast cancer in families with known genetic inheritance by prophylactic surgery increases the demand for this procedure (1,2). If breast conservation (BCT) is not an option, the question arises which type of mastectomy shall be applied. The evolution of surgical techniques for removal of the mammary gland started from Rotter-Halsted's radical mastectomy (3) to Patey's modified mastectomy (4) of the last millennium up to modern concepts with preservation of the skin envelope by skin-sparing mastectomy (SSM), subcutaneous mastectomy (SCM) or nipple-(areola) sparing mastectomy (NSM/NASM) which are considered as oncologically safe (5). Different approaches and incision patterns have been developed for these surgical procedures such as tennis-racket incision pattern, reduction mammoplasty technique as inverted T- or J-incision, up to total or partial periareolar incision. These techniques have been applied mostly according to the surgeons' preference. The patients' perspective was not always in the primary focus. BRCA-mutational status has attracted much attention in the last years when individuals of public interest submitted themselves to prophylactic mastectomy in cases of a positive BRCA1/2-mutational status (1). We investigated the patient's view on these procedures with validated measurements of quality of life (QoL) and explored the surgical safety and acceptance of these surgical procedures.

Patients and methods

A consecutive cohort of a prospectively maintained database in a single-institution experience at European Breast Center Düsseldorf was analyzed for this study. All patients were eligible who were treated with an immediate implant-reconstruction after mastectomy for prophylactic and therapeutic indications between 2000 and 2014. Inclusion criteria were infeasibility of BCT and no necessity of post-mastectomy radiation as by pre-surgical assessment. Exclusion criteria were inflammatory breast cancer, skin infiltration/fixation and previous radiation. All autologous reconstructions were excluded from this study. Data was retrieved from patient charts and multiple detailed questionnaires. We used four validated QoL-questionnaires to evaluate patients reported outcome (PRO) and QoL: EORTC C-30 (6), EORTC B-23 (7), FACT-G (8) and Breast Cancer Treatment Outcome Scale (BCTOS) (9) and also

a customized, study-specific questionnaire. Questionnaires were repeatedly sent by regular mail (thrice). We analyzed the surgical outcome with regard to the safety and the complication of the methods, as well as PRO regarding the volume, symmetry and aesthetic result including the evaluation of scars. Early complications were defined as first presentation of sequelae before 6 months after surgery and late complications as occurring beyond 6 months after surgery. In particular, we compared the use of a TiLoop® Bra for coverage of the lower pole of the breast with the coverage of the same region with an autologous corial fat flap. This study was approved by the Institutional Review Board (IRB) and complied with the declaration of Helsinki.

Reconstruction techniques

Reconstruction mode 1: technique developed for normal breast size (non-ptotic)—coverage with a titanized polypropylene mesh (TiLoop® Bra) (Figure 1A-C)

The glandular tissue is removed via a reduction mammoplasty pattern and the Musculus pectoralis (M. pectoralis) major incised at its insertion and with cautious mobilisation of the M. serratus in the lateral part and the titanized mesh is sutured to the edge of the M. pectoralis major to cover the lower pole and wrapped around the implant without attaching it to the chest wall (double-plane).

Reconstruction mode 2: technique developed for hypertrophic and ptotic breasts—coverage with a corial-fat flap (Figure 2A-C)

Initially, when the skin incision is performed in the sense of a reduction mammoplasty (inverted T), the skin of the lower hemisphere of the breast is de-epithelialized and the corium is separated from the glandula. The glandular tissue is removed and the M. pectoralis major incised at its insertion and a subpectoral pouch has been formed with cautious mobilisation of the M. serratus in the lateral part. The corial flap is then sutured to the edge of the M. pectoralis major to cover the lower pole of the implant (double-plane).

Results

We included 217 patients with 272 mastectomies (55 bilateral cases) and immediate breast reconstructions (IBR) in our study. Median follow-up was 3.5 years (range, 0-14 years). SSM was the most frequently performed procedure with 131 patients, whereas SCM was performed in 86 patients.

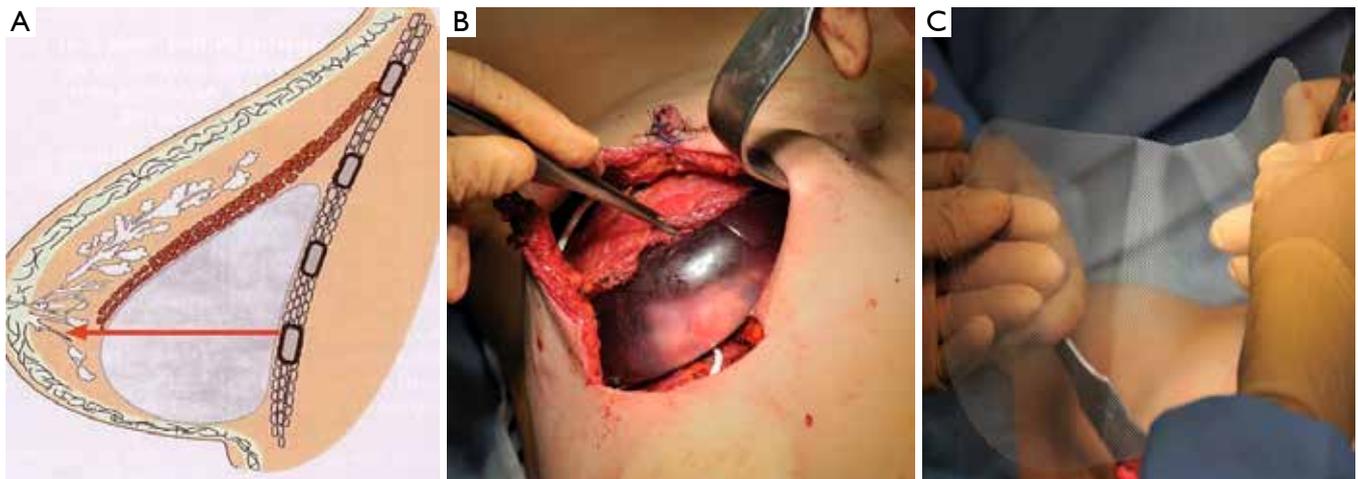


Figure 1 Coverage of the lower implant pole with a titanized polypropylene mesh. (A) Lateral projection; (B) edge of musculus pectoralis (*M. pectoralis*); (C) titanized polypropylene mesh.



Figure 2 Coverage of the lower implant pole with a corial-fat flap. (A) Reverse side—corial flap; (B) outer side—corial flap; (C) corial flap at musculus pectoralis (*M. pectoralis*).

Invasive breast-cancer was the indication for surgery in 106 patients, non-invasive breast cancer (DCIS) in 80 patients, prophylactic indication (BRCA1/2-mutation) in 30 patients and contralateral alignment in 1 patient. Comparing the two groups of coverage of the lower pole of the implant, groups were well balanced with 78 patients with a titanized, polypropylene mesh TiLoop® Bra and 79 cases with a corial fat flap. For evaluation of patient reported outcome, we were able to refer to a final questionnaire response rate of 70%.

Sequelae of surgery

Early complications

Early complications—defined as surgical sequelae occurring

before 6 months after surgery—were low in our cohort: We registered 6 scar insufficiencies, 7 infections, 10 seroma, and 17 hematomas with the necessity of a wound revision. Seventeen patients had hypertrophic scars (keloid). A comparably frequent complication was the loss of sensitivity in any part of the breast or dysaesthesia, reported by 78 patients, which was due to skin incisions.

Late complications

Late complications were low in our cohort: 15 patients developed a capsula fibrosis. In none of these cases implant loss occurred. We recorded an implant rotation in three cases which did not necessitate surgery again. Seven patients reported any kind of dislocation of the implant. There was a significant correlation with the occurrence of an implant

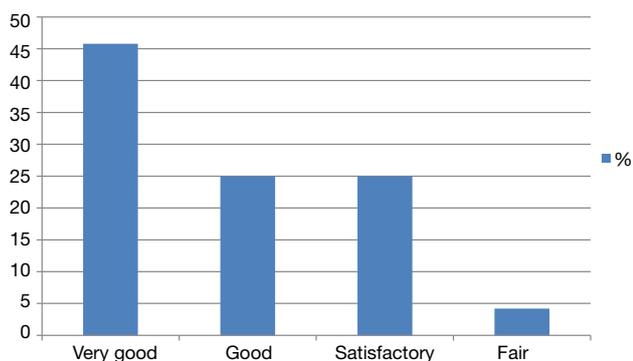


Figure 3 Satisfaction with symmetry after conservative mastectomy.

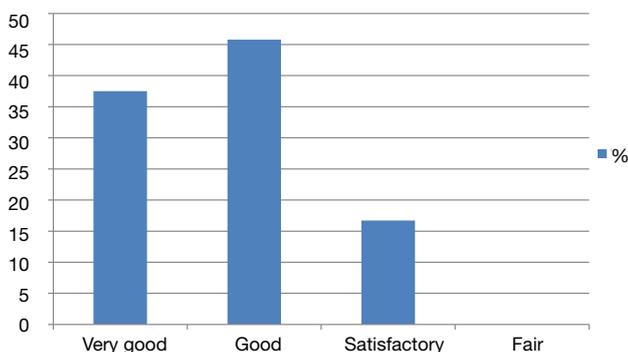


Figure 4 Satisfaction with volume after conservative mastectomy.

dislocation and the mode of coverage of the lower pole of the implant: all implant dislocations occurred in the group of corial-fat flaps, and none in the group of TiLoop® Bra meshes ($P=0.01$).

A rupture of implants was seen in one case only. A removal of implants was necessary in two cases. An exchange of implants was performed in 17 cases. Restrictions of movement were denoted by 22 patients and only six recurrences were seen in this large cohort.

Symmetry

Patients were satisfied with symmetry after both SSM/SCM and immediate reconstruction, even though the reconstruction of the contralateral side was eventually performed as a two-point time procedure. As much as 45.8% rated the symmetry as very good, 25% as good and 25% as satisfactory. Thus, almost 96% of patients were satisfied with the symmetric result of the procedure; only 4.2% rated the result as “fair” (Figure 3). Patient reported outcome was best when the procedure was performed bilaterally ($P=0.007$).

Volume

Satisfaction with volume was high with 37.5% rating “very good”, 45.8% as “good” and 16.7% as “satisfactory”. Thus all patients were satisfied with reconstruction volume (Figure 4).

Adherence to the decision

All patients in the corial-flap group and all patients in the TiLoop® Bra group considered the operation as the right choice and thus demonstrated adherence to the decision for this type of surgery.

Influencing factors on overall aesthetic result

We found a significant improvement by use of titanized polypropylen meshes in the aesthetic results ($P=0.049$) as well as in the prevention of implant dislocation ($P=0.009$).

Patients with SCM expressed their satisfaction even to a higher extent than those with SSM. This referred particularly to satisfaction with symmetry ($P=0.018$) and satisfaction with scars ($P=0.037$).

Of note, genetic screening for BRCA1/2 mutation did not have an impact on partner interaction ($P=0.200$). Interestingly, radiotherapy—performed in 23 patients—was neither detrimental on cosmetic outcome ($P=0.754$) nor on body image ($P=0.660$). Smoking, however, was associated with a significant deterioration of the aesthetic outcome ($P=0.007$).

Quality of life (QoL) and implant reconstruction mode

QoL was good after both SSM and SCM, and rating of the result was best when the procedure was performed bilaterally. There was no difference in QoL depending on the use of either corial-flap or mesh-reconstruction ($P=0.757$), also no significant difference in perception of pain after surgery ($P=0.237$) with either of the two modes of coverage of the lower breast pole, however—as stated above—implant rotation and displacement was less often when meshes were used, which influences QoL strongly.

Discussion

This study provides evidence on the surgical outcome and the patient reported QoL after risk reducing surgery of the breast with SSM and SCM. In our study, we analyzed skin-sparing and subcutaneous mastectomies, all combined with

immediate BR and evaluated both the physical as well as the psychological well-being after these surgical procedures. This is of major importance, as the demand for this type of surgery increases. As a recent publication indicated referrals to genetics services showed a rise from May 2013 onwards, with almost 2.5-fold quantity, in a consortium of over 30 UK breast cancer family history clinics and ten more genetics centres, when film actress Angelina Jolie decided to make public that she underwent BRCA testing and subsequent prophylactic mastectomy and salpingo-oophorectomy. This trend was perceived world-wide and is apparently long-lasting (1).

Quality of life (QoL) instruments

To analyze QoL and surgical outcome after these surgical procedures, as much as 272 reconstructions in 217 patients were analyzed retrieving data from patient charts, customized questionnaires and validated instruments of measurement of QoL in our study.

So far, these surgical procedures have not been evaluated with several QoL instruments at a time: We used EORTC C-30 (6), EORTC-BR23 (7), FACT-G (8) and BCTOS (9). These instruments focus on the self-reporting of patients concerning the following items: functional restrictions, disease symptoms, and global perception of QoL. For validation of surgical techniques by patients, BCTOS has been demonstrated to be a reliable instrument for functional and aesthetic assessment (9). Kanatas *et al.* also described these instruments as validated instruments of measuring QoL specifically for breast cancer patients (10). Furthermore, we developed a study-specific questionnaire which was comparable to similar studies (11,12). The design of our customized questionnaire put emphasis on individually perceived QoL under distress of the risk of breast cancer as well as measurements of surgical outcomes. We were able to retrieve information of these questionnaires by as much as 70% of all patients with three emissions by regular mail.

Breast cancer is a threat to life of patients, and the primary aim of breast cancer therapy is the risk reduction by local and systemic treatment. However, the side effects of either of the therapies affect the physical and psychological well-being of the patients. With views on the surgical therapy, surgeons need to be aware of the best surgical options for their patients and their physical and psychological effects. Physical, psychological and social well-being builds the dimensions of QoL and all

three refer to each other (13). Psychological well-being is deteriorated massively by the diagnosis of breast cancer as every individual is confronted with the anticipated risk of mortality. When the probability of survival is higher, aspects of an unimpaired body image regain importance as the breast is a symbol of female identity and sexual attraction. Chen *et al.* (14) performed a systematic literature review to identify breast-surgery-specific PRO measures and reported significant shortcomings in terms of formal development and psychometric evaluation.

A systematic review conducted by Pusic *et al.* (15) found that only 1 out of 223 PRO measures used in breast surgery studies had psychometric evidence to support their use in the breast cancer population. The reviews by Chen *et al.* (14) and Pusic *et al.* (15) are limited to breast cancer surgery-specific instruments. We included both breast-cancer-surgery specific and general instruments of measurement of QoL.

The techniques analyzed in this study, subcutaneous and SSM and the latter with two different modes of coverage of the lower breast pole were examined with detailed questionnaires.

Patients satisfaction, body image

We detected a high grade of patient satisfaction with volume (99.8%), symmetry (96%) and scars in both forms of mastectomy and immediate reconstruction. Ueda *et al.* (16) found a smaller cohort of 74 patients that the median score for patient satisfaction including social activity, physical aspects and general condition, were the same in the three groups of BCT, mastectomy and mastectomy with immediate reconstruction. For body image however, BCS and IBR scored higher than with mastectomy only ($P < 0.05$). Ueda's study group included a scoring by four external reviewers for cosmetic outcome—which we did not apply to our study population to avoid subjective bias—and there was no difference in the estimated cosmetic outcome between BCT and IBR ($P = 0.20$) nor between the SSM and NSM subgroups ($P = 0.09$). Scores referring to pain perception and sexuality were better in the BCT than in the mastectomy group; however there was no difference between BCT and IBR regarding these items.

Adherence to decision and body image after surgery

We focussed primarily on satisfaction and QoL with SCM and SSM, and particularly on the mode of reconstruction of the lower pole of the breast in skin sparing mastectomy, with

and without the use of meshes and corial flaps. So far, this item was not analyzed in a direct comparison in literature. All patients of our study expressed their conviction from the aesthetical viewpoint that this type of surgery was the right decision (100% adherence to the decision). The majority of patients rated their satisfaction with symmetry, volume and scars with “good” and “very good”.

We detected a higher satisfaction in patients with reconstructions which were performed bilaterally. Nano *et al.* (17) analyzed the psychological impact and cosmetic outcome in 123 BR compared with 109 BCT and 78 mastectomies. QoL was similar in all groups, but the BCT group and patients with reconstruction had higher body image scores than patients with a mastectomy. Patient satisfaction was higher in the reconstruction group than the breast conservation group, while aesthetic outcome was similar in both groups. The authors concluded that the high satisfaction and cosmesis scores in the BR group were indicating the superior results that can be achieved with BR.

Corial flap

A study with a lower caseload of 27 patients (34 reconstructions) with mastectomy according to a modified Wise pattern with a tissue expander also used a fasciocutaneous flap for coverage of the lower pole of the breast in women with macromastia while the upper part of the breast was covered by the M. pectoralis major (18). The authors reported a fairly high unplanned re-operation rate of 15%, rate of post-surgical complications of 37%, including seroma of 18% which we did not see in our study. Ladizinsky *et al.* (19) report on a cohort of 60 patients with a de-epithelialized corial flap with a complication rate of 24% (i.e., skin necrosis, hematoma and infection) and analyzed risk factors for these events and found that overall complications were associated with a body mass index (BMI) greater than 35 ($P=0.035$) and prior smoking ($P=0.0001$). The most frequent complication in their study was mastectomy flap skin necrosis (30%). This correlated with placement of a permanent implant ($P=0.029$) and any history of smoking ($P=0.0001$). Skin necrosis led to implant loss in 1.2% in their study. In our study, we did not detect a correlation between implant loss and BMI ($P=0.262$) or history of smoking ($P=0.363$), however we detected that a higher BMI was a predictor for skin dehiscence (without implant loss) ($P=0.043$) whereas smoking exerted a negative impact on aesthetic outcome ($P=0.007$).

TiLoop® Bra

A recent study with a smaller cohort of 34 TiLoop® Bra meshes in the submuscular pocket than in our study compared this surgical approach with 39 TiLoop® Bra meshes with a prepectoral use (20). In their cohort, complications were very low, with two skin flap infections and one wound dehiscence only. No implant loss was recorded. The study group found that TiLoop® Bra was safe and effective in a short-term analysis, both for a retropectoral and a totally subcutaneous implant placement. Contrary to our study, follow-up of this study however was short with 13 months (range, 3-27 months) in the group of TiLoop® Bra mesh, whereas our study had a longer follow-up 3.5 years (range, 0-13 years). Also, inclusion criteria were strict in this study with normal BMI, no large and very ptotic breasts, no history of smoking, no diabetes, and no previous radiotherapy. In our study, we included all patients of any BMI, with large and ptotic breasts, smokers and patients with diabetes, however radiotherapy was allowed after, but also not before surgery. On this background, complication rates were low with no implant loss in the TiLoop® Bra group and only 7 infections, 6 scar insufficiencies, 10 seroma and 17 hematomas in this large cohort of 272 reconstructions. Casella's study did not report on dysaesthesia which we recorded in our study: 78 patients declared to have experienced these sequelae.

Limitations of our study were that we did not randomize patients to each of the modes of reconstruction—like almost all other studies related to breast surgery—but used size and ptosis as criteria to choose the respective method. Questionnaires were sent to the patients by our own institution, however participation was voluntarily and patients were already discharged from hospital and no influence was exerted on the patients.

Conclusions

In our study, we saw the highest scores for aesthetic results in patient reported outcome with the use of titanized polypropylene meshes (TiLoop® Bra) compared with corial flap which was significantly differing. QoL in general was good in both modes of reconstruction and coverage of the lower breast pole.

We found a significant improvement by use of titanized polypropylene meshes in the aesthetic results as well as in the prevention of implant dislocation. All patients expressed their adherence to the decision for this type of surgery, with

highest score with SCM, particularly to satisfaction with symmetry with scars.

Genetic screening for BRCA1/2 mutation did not have an impact on partner interaction and radiotherapy was neither detrimental on cosmetic outcome nor on body image. Smoking, however, was associated with a significant deterioration of the aesthetic outcome.

Dual-plane reconstruction with TiLoop® Bra in normal breasts size and corial flaps in ptotic breasts produces stable results with low complication rates and high levels of QoL in conservative mastectomies.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Implant-based breast reconstruction following conservative mastectomy: one-stage vs. two-stage approach

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Abstract: Conservative mastectomy with preservation of the nipple areolar complex is now considered a safe and effective technique in properly selected patients. Good candidates for this procedure include women with small to moderate breast volume having therapeutic or prophylactic mastectomy. Both autologous and prosthetic options are available; however prosthetic techniques are performed more frequently. Prosthetic approaches include immediate 1-stage (direct to implant) or 2-stage (tissue expander/implant) techniques. Delayed prosthetic reconstruction is also possible with conservative mastectomy. This manuscript will review the 1-stage and 2-stage methods with an emphasis on indication, surgical techniques, and outcomes.

Keywords: Breast reconstruction; nipple sparing mastectomy; conservative mastectomy; breast implants; tissue expanders

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Conservative mastectomy has become the newest option in the armamentarium of oncoplastic surgery. Conservative mastectomy is defined as preservation of the entire skin envelope including the nipple areolar complex. Other commonly referred to names for this procedure include nipple sparing mastectomy and total skin sparing mastectomy. This can be performed for therapeutic as well as prophylactic indications (1,2). The benefit of this approach is that reconstructive outcomes are optimized as breast volume, contour, and appearance are usually maintained or enhanced. Reconstruction can be performed using prosthetic devices or autologous tissues. In the United States, approximately 80% of reconstructions are performed using prosthetic devices, with the vast majority performed immediately at the time of mastectomy (3,4).

One of the controversies associated with prosthetic reconstruction is whether to perform the reconstruction in 1 stage (direct to implant) or 2 stages (tissue expander/implant). Advocates for the 1 stage technique emphasize a low revision rate, fewer operations, reduced overall cost, and excellent patient outcomes (5-8). Advocates for the 2 stage technique emphasize improved patient outcomes

based on recontouring and selecting an ideal device for the second stage, reduced capsular contracture in the setting of post mastectomy radiation, a lower unplanned revision rate, and excellent patient outcomes (9,10). Success with either technique is ultimately based on proper patient selection, surgical technique, and surgeon experience.

In a multi-institutional study evaluating short-term outcomes following 1,528 1 stage and 9,033 2 stage reconstructions, Davila *et al.* demonstrated a higher incidence of complications following 1 stage (6.8% vs. 5.4%, P=0.02) and higher failure following 1 stage (1.4% vs. 0.8%, P=0.04) (11). There were no differences between 1 and 2 stage reconstructions with regard to surgical site infections (3.9% vs. 3.4%, P=0.34) or reoperation (7.5% vs. 6.9%, P=0.4) rates. Roostaieian *et al.* in review of a single institutions experience comparing outcomes following 1- and 2-stage prosthetic reconstruction demonstrated no differences with respect to complication rates, need for revision, and aesthetic outcomes (12). One stage reconstruction did result in fewer office visits and less time to completion.

In a large single institution study, the differences in complications between conservative and skin sparing

mastectomy were evaluated in 233 cases (13). Nipple sparing mastectomy was performed in 113 cases and skin-sparing mastectomy was performed in 120 cases. The overall complication rate was 28% following nipple sparing and 27% following skin sparing. Of interest, in patients that had risk-reducing mastectomy (without axillary procedures), the complication rate was higher in the nipple-sparing cohort (26% *vs.* 9%, $P=0.06$) compared to the skin-sparing cohort.

Patient selection

Patient selection is an important factor when considering nipple sparing mastectomy, prosthetic reconstruction, and 1 or 2 stage techniques (14). In general, conservative mastectomy is considered for women with smaller tumors (<3 cm in diameter) that are more than 3 cm from the nipple areolar complex. Conservative mastectomy is also dependent upon breast size. Women with larger breasts are often not considered suitable candidates for conservative mastectomy because the vascularity to the nipple areolar complex may be compromised and may become necrotic.

Prosthetic reconstruction can be considered in the majority of women having skin or nipple sparing mastectomy. Ideal patients for prosthetic reconstruction include women of virtually any size breast, unilateral or bilateral cases, as well as women considering immediate or delayed reconstruction. Poor candidates for prosthetic reconstruction often include women that have had prior radiation therapy, morbidly obese patients, and patient that are actively smoking tobacco products. The decision regarding skin *vs.* nipple sparing mastectomy is dependent on patient selection with larger volumes usually having skin sparing techniques. The ability to achieve symmetry is another important consideration. Secondary procedures are more common following prosthetic reconstruction and may involve the ipsilateral or contralateral breast (15). In the setting of bilateral reconstruction, the specific characteristics of the breast are less important because the two reconstructed breasts will be very similar.

Immediate 1-stage reconstruction following conservative mastectomy

The staging of prosthetic reconstruction as a 1-stage or 2-stage procedure in the setting of conservative mastectomy depends on patient and breast characteristics as well as the quality of the mastectomy. Direct to implant reconstruction

is sometimes considered in women with small to moderate breast volume with a cup size ranging from A-C (16). With these patients, the mastectomy should meet certain specifications that include adequate thickness of the skin flaps, no to minimal undermining of the regions outside the breast, and retention of a meniscus of fat along the medial and inframammary folds. These maneuvers will increase the likelihood of natural shape and contour without clefts or folds in the breast.

The technique of 1-stage reconstruction in the setting of conservative mastectomy has been previously described in detail (6,17). The salient points will be reviewed in this section. Mastectomy incisions can be created lateral to the areola, periareolar, along the inframammary fold, and via an inverted T approach. Munhoz *et al.* has demonstrated that complications related to delay healing are increased in patients having hemiareolar and inverted T incisional patterns (18). Regardless of the incisional pattern, the length of the incision should be adequate to perform a complete mastectomy. Suboptimal mastectomy in the setting of conservative mastectomy can increase the incidence of local recurrence (19). Sentinel lymph node biopsy can be performed through a separate incision near the axilla or via the laterally based incision if used. A subareolar biopsy is usually obtained. The permanent implant is selected based on the external and internal base diameter of the breast as well as mastectomy weight. Round or shaped devices can be used based on the breast and patient characteristics as well as patient desire (20). The selected devices are usually silicone gel, but saline devices can also be considered. The device can be placed in a variety of locations that include prepectoral, total subpectoral or partial subpectoral. Acellular dermal matrices are often used for prepectoral and partial subpectoral but are not usually necessary for subpectoral. Adequate compartmentalization of the device is necessary to ensure that the device does not migrate laterally or inferiorly. With shaped devices, proper orientation and compartmentalization is critical to ensure that the device does not rotate. Once the device has been properly positioned and secured, the mastectomy skin envelope is carefully redraped in order to prevent malposition of the nipple areolar complex. A closed suction drain is used in all cases. *Figures 1-4* demonstrate a woman that had immediate direct to implant reconstruction following conservative mastectomy.

Outcomes following 1-stage reconstruction in the setting of conservative mastectomy have been favorable; however the unplanned secondary revision rate may be



Figure 1 Preoperative photograph of a patient with left breast cancer scheduled for unilateral conservative mastectomy.



Figure 2 Intraoperative photograph of the lateral and periareolar incision with a 300 cc permanent implant and acellular dermal matrix.

higher when compared to the two-stage technique. Over an 8-year follow-up period, Salzberg *et al.* has demonstrated consistently low complications rates with excellent aesthetic outcomes in the majority of patients (5). In 466 breasts reconstructed in a single stage, the overall complication rate was 3.9% that included explanation in 1.3%, delayed healing in 1.1%, infection in 0.2%, and capsular contracture in 0.4%. Although many of these patients had conservative mastectomy, the percentage was not quantified. Colwell *et al.* studied 331 reconstructed breasts that had immediate 1-stage prosthetic breast reconstruction of which 66 (20%) were in the setting of conservative mastectomy (6). The overall complication rate following immediate single-stage implant reconstruction was 14.8% that included ten infections (3%), five seromas (1.5%), and delayed



Figure 3 Preoperative photograph following permanent implant placement. The plan is for right augmentation with a 100 cc device and exchange of the left implant for a 350 cc device.



Figure 4 Postoperative photograph demonstrating excellent volume and contour symmetry at 1 year follow-up.

healing in 30 (9.1%). There was no difference in the complication rate following skin sparing and nipple sparing techniques. Dent *et al.* have evaluated nipple areolar ischemia following conservative mastectomy in the setting of 1-stage reconstruction (21). They reviewed 318 nipple-sparing mastectomies that were performed through an inframammary incision and demonstrated partial thickness nipple-areolar necrosis in 44 breasts (13.8%) and full thickness nipple-areolar necrosis in 21 breasts (6.6%). Operative debridement was not performed following partial thickness necrosis and in four cases of full thickness necrosis. Factors associated with nipple areolar ischemia included advanced age, higher body mass index (BMI), greater breast volume, tobacco use, ADM use, and 1-stage reconstruction.

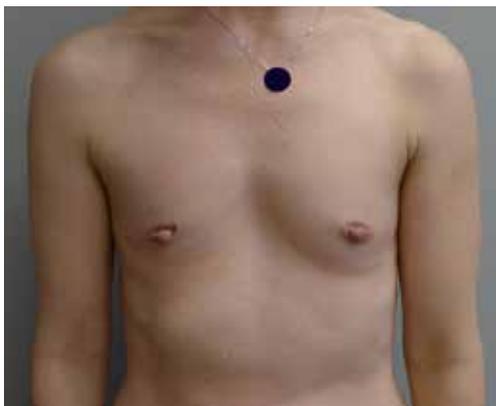


Figure 5 Preoperative photograph of a patient scheduled for bilateral risk reduction conservative mastectomy.



Figure 6 Early postoperative photograph following bilateral breast reconstruction with tissue expanders.

Immediate 2-stage reconstruction following conservative mastectomy

With larger breast volume and increasing BMI or in the event of surgeon preference, the 2-stage reconstruction can be considered (10). Other indications for a 2-stage approach would be excessively thin mastectomy skin flaps, excessive undermining beyond the breast borders, need for postoperative radiation, a large quantity of skin with random blood supply, or evidence of poor skin and questionable nipple vascularity. The second stage provides a planned opportunity to improve the position of the inframammary and lateral mammary fold, perform a capsulotomy to improve contour, perform a capsulorrhaphy to minimize device migration, select an optimal permanent implant to achieve symmetry and projection, and to perform

a contralateral symmetry procedure if needed (9). These are the reasons why most surgeons in the United States prefer the 2-stage technique.

The technique of 2-stage reconstruction in the setting of skin sparing mastectomy is well described (9,22,23); however, the technique of 2-stage reconstruction in the setting of conservative mastectomy is not. Nipple sparing mastectomy is usually performed through an inframammary or laterally based breast incision. The incision can traverse through the areola or can extend around the edge superiorly or inferiorly. Following the mastectomy, the inferior edge of the pectoralis major muscle is usually elevated and the subpectoral space is created. A tabbed tissue expander is usually used and secured with absorbable sutures placed along the inframammary fold to firmly secure the device. Anterior coverage of the device can be achieved using the pectoralis major muscle completely or partially. In the setting of partial muscle coverage, an acellular dermal matrix is usually used and sutured first to the inferior edge of the pectoralis major muscle and then to the fascia along the desired inframammary fold. The tissue expander is usually filled to 40-60% of capacity to minimize pressure on the mastectomy skin flaps and the nipple areolar complex. The periprosthetic space is copiously irrigated with an antibiotic solution. One or two closed suction drains are inserted. The mastectomy skin flap is carefully redraped over the reconstructed breast mound to minimize malposition of the nipple areola complex. The incisions are closed with resorbable sutures. Patients are seen in the office weekly for expansion until complete.

The second stage usually occurs 3 months later; however, this may be extended depending on the timing of chemotherapy and radiation therapy (24). The prior incision is usually used for access. The tissue expander is removed and a capsulotomy is usually performed along the upper pole and sometimes medially or inferiorly as needed for optimal positioning of the permanent implant. In the event of lateral or inferior device migration, a capsulorrhaphy is performed to compartmentalize the permanent implant. Device sizers are usually used to determine the optimal shape and volume of the permanent implant. A shaped or round silicone gel implant can be selected based on the breast parameters. Closed suction drains are rarely used at the time of device exchange unless there is a specific indication for them. *Figures 5-10* highlight a woman that had immediate 2-stage prosthetic reconstruction following conservative mastectomy.

Outcomes following 2-stage reconstruction in the

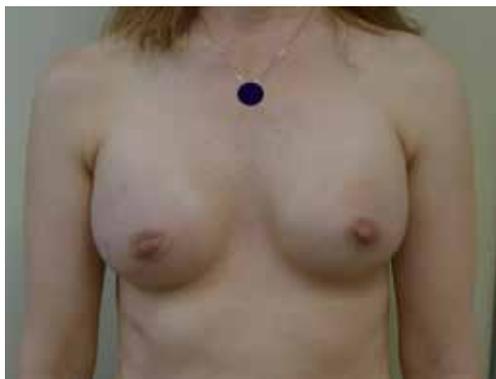


Figure 7 Preoperative photograph with fully inflated tissue expanders.



Figure 8 Postoperative photograph with bilateral 400 cc silicone gel implants demonstrating excellent volume and contour symmetry.

setting of conservative mastectomy have also been favorable. Sbitany *et al.* reviewed 122 patients and 202 breasts following 2-stage prosthetic reconstruction in the setting of total skin sparing mastectomy (25). Total pectoralis major coverage was used in 113 breasts and partial pectoral coverage with an ADM was used in 89 breasts. Intraoperative fill volume was greater in the partial muscle coverage group (205 *vs.* 52 cc). The postoperative complication profile with regard to delayed healing, seroma, and infection was similar for the two cohorts. Final nipple position was better controlled with the partial muscle coverage technique. Chen *et al.* reviewed a series of 115 nipple-sparing mastectomies performed in 66 patients that had immediate 2-stage reconstruction using a total muscle coverage technique (26). The most common incisional pattern was periareolar and radial (n=61) followed



Figure 9 Right lateral view demonstrating excellent contour.



Figure 10 Left lateral view demonstrating excellent contour.

by inframammary (n=25), omega (n=14), prior incision (n=10), and trans areolar (n=5). Of the 115 conservative mastectomies, six were removed because of cancer (5.2%) and four were removed because of delayed healing (3.5%).

Delayed 2-stage reconstruction following conservative mastectomy

A delayed approach to prosthetic reconstruction is sometimes considered following conservative mastectomy. This is usually in the setting of thin mastectomy skin flaps,

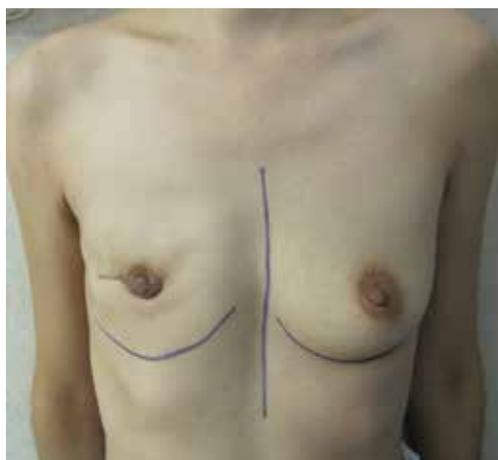


Figure 11 Preoperative photograph of a woman following right conservative mastectomy scheduled for delayed 2-stage prosthetic reconstruction.



Figure 12 The lateral and infra-areolar incisions are opened and the tissue expander and acellular dermal matrix are placed.

questionable viability for the nipple areolar complex, or to minimize the incidence of adverse events in patients at increased risk due to tobacco use or poorly controlled diabetes mellitus (9,27). The rationale is that placement of a tissue expander or implant in this setting would pose an unnecessary risk for reconstructive failure.

The technique of delayed reconstruction following conservative mastectomy requires special considerations in order to ensure optimal positioning of the nipple areolar complex. This is especially true in the setting of unilateral



Figure 13 Preoperative photograph demonstrating an over inflated tissue expander scheduled for exchange and contralateral augmentation for symmetry.

mastectomy because achieving breast symmetry will be more challenging. The timing can be as soon as 4 weeks following the mastectomy or years later. It is usually not considered when there has been prior radiation therapy of the natural breast or the mastectomy defect. The 2-stage technique is preferred in the setting of delayed reconstruction because a moderate to severe degree of skin contracture has usually occurred that will require reexpansion. Relevation of the mastectomy skin flaps can sometimes recreate the mastectomy defect and allow for the same 2-stage technique that was described above. An alternative technique in the setting of subpectoral placement of the tissue expander is to leave the upper mastectomy skin flap attached to the pectoralis major muscle. Acellular dermal matrices are sometimes considered especially when the mastectomy defect has been recreated. Subpectoral placement of the tissue expander is usually considered although prepectoral placement can be considered in the uncommon scenario of thick mastectomy skin flaps. Tabbed tissue expanders are less important with delayed prosthetic reconstruction because the periprosthetic space has been carefully created. Intraoperative fill volumes are usually less compared to immediate reconstruction because of the skin contraction. The proper positioning of the nipple areolar complex usually requires some degree of mobility of the upper mastectomy skin flap in order to properly drape the skin envelope to match the opposite breast. In unilateral cases, patients are told that contralateral procedures such as mastopexy or reduction mammoplasty may be necessary to achieve symmetry. This is less of a consideration with bilateral cases. *Figures 11-14* illustrate a patient having



Figure 14 Postoperative photograph demonstrating excellent volume and contour symmetry at 6 months follow-up.

delayed 2-stage prosthetic reconstruction following conservative mastectomy.

Outcomes following delayed prosthetic reconstruction have been favorable (27,28). Sullivan *et al.* have demonstrated fewer complications following delayed prosthetic reconstruction compared to immediate ($P=0.008$) (27). Capsular contracture occurred significantly more often following immediate reconstruction compared to delayed reconstruction (40.4% *vs.* 17%, $P=0.001$). This is partially explained because of higher degree of wound contamination during immediate reconstruction, compromised vascularity of the mastectomy skin flaps, and fewer infections following delayed reconstruction compared to immediate (2.4% *vs.* 5.4%, $P=0.26$). Alderman *et al.* have demonstrated that immediate reconstruction is associated with an increased total and major complication rate compared to delayed reconstruction regardless of the type of reconstruction ($P=0.011$ and 0.005 , respectively) (28).

Conclusions

Conservative mastectomy can be safely and effectively performed with a variety of reconstructive techniques using prosthetic devices. The reconstruction can be performed immediately at the time of mastectomy or on a delayed basis. The 1-stage and 2-stage techniques can be used and provide excellent aesthetic and surgical outcomes. Considerations regarding the location of mastectomy incisions, use of ADM, and device location are important and will contribute to the outcome. Adverse events can

occur and often related to skin and nipple vascularity, infection, and symmetry.

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The evolving breast reconstruction: from latissimus dorsi musculocutaneous flap to a propeller thoracodorsal fasciocutaneous flap

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Abstract: The aim of this editorial is to give an update on the use of the propeller thoracodorsal artery perforator flap (TAP/TDAP-flap) within the field of breast reconstruction. The TAP-flap can be dissected by a combined use of a monopolar cautery and a scalpel. Microsurgical instruments are generally not needed. The propeller TAP-flap can be designed in different ways, three of these have been published: (I) an oblique upwards design; (II) a horizontal design; (III) an oblique downward design. The latissimus dorsi-flap is a good and reliable option for breast reconstruction, but has been criticized for morbidity and complications. The TAP-flap does not seem to impair the function of the shoulder or arm and the morbidity appears to be scarce. However, an implant is often needed in combination with the TAP-flap, which results in implant related morbidity over time. The TAP-flap seems to be a promising tool for oncoplastic and reconstructive breast surgery and will certainly become an invaluable addition to breast reconstructive methods.

Keywords: Breast reconstruction; thoracodorsal; perforator; latissimus; flap; imaging

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Background

The publication of the *Latissimus dorsi musculocutaneous flap without muscle* by Angrigiani *et al.* in 1995 (1) was in fact the first thoracodorsal artery perforator flap (TAP/TDAP-flap) and represented a new way of thinking in autologous flap design based on the angiosome concept previously presented by Taylor and Palmer in 1987 (2). The TAP or TDAP-flap concept within breast surgery has since been developed further by Hamdi *et al.* for both oncoplastic breast surgery as well as for breast reconstruction (3,4) and a muscle sparing variation of the technique in combination with an implant was subsequently published by Brackley *et al.* (5).

In 2013 the concept was taken a step further, when the propeller TAP-flap was combined with the hammock technique using an ADM and an implant for a one stage breast reconstruction (6). In this issue of GS, Angrigiani

et al. show that the propeller TAP-flap can be designed in an oblique upwards design, enabling a flap length of more than 30 cm, and furthermore that the dominating perforator, in some instances runs anterior to the latissimus dorsi muscle straight to the subcutis (7). The applicability of the propeller TAP-flap in reconstructive breast surgery is thus expanding and includes an array of indications from corrective oncoplastic breast procedures to one stage breast reconstruction. The aim of this editorial is to give an update on the use of the propeller TAP-flap within the field of breast reconstruction. To emphasize its simplicity and applicability focus will be on the planning and surgical technique, as well as the debate on LD *vs.* TAP and future perspectives.

Preoperative planning and surgical technique

TAP perforators are quite predictably localized in up to

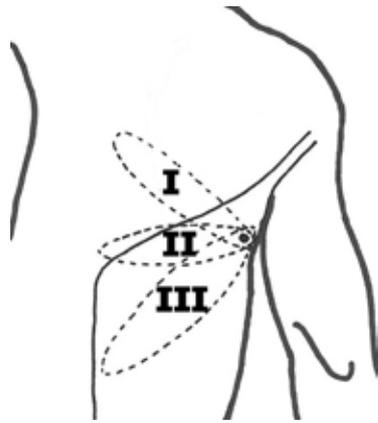


Figure 1 Three different TAP-flap skin paddle designs: (I) Oblique upwards; (II) Horizontal; (III) Oblique downwards. TAP-flap, thoracodorsal artery perforator flap.

80% of patients approximately 8 cm from the top of the axilla and close to the anterior edge of the LD muscle (1,3-7). In general perforators can reliably be localized based on anatomical knowledge and intraoperative exploration (8). This also applies for the thoracodorsal perforator, however, pre-operative identification is recommended by most authors using either a Doppler probe, color Doppler ultrasonography or CT-angiography (6,9,10). The Doppler probe enables identification of the location of the perforators, but does not give any additional information other than an estimation of the relative size of the perforators based on the volume of sound. In contrast Color Doppler ultrasonography and CT-angiography not only visualize the location of the perforators, but also provides an estimate of the vessel diameter for each perforator as well as information about topography and direction of their branches (6,10). This information increases the surgeons comfort level and speeds up the dissection (10,11). The advantage of color Doppler ultrasonography in particular is that it can be performed either immediately before or during surgery. The disadvantage is that it requires some experience to perform. CT-angiography has been shown to reduce procedure time (10,11). However it is time consuming, costly and requires dedicated radiologists. The simplest and most optimal setup seems to be a well trained surgeon experienced with use of either a Doppler probe or color Doppler ultrasonography to identify the perforators before surgery (6).

The location of the perforators is variable and it seems that in 1/15 patients the dominant perforator originates from the horizontal branch of the thoracodorsal vessel. When this is the case, the perforator is approximately

4-5 cm behind the anterior edge of the LD muscle and dissection of the perforator is necessary and in some instances the horizontal branch needs to be divided to gain sufficient length (6). Another variation that calls for an alternative muscle-sparing design is the case with several small perforators instead of 1-3 larger vessels.

The TAP-flap can be dissected by a combined use of a monopolar cautery and a scalpel. Microsurgical instruments are generally not needed. Loop-magnification can be an advantage for perforator dissection but is usually not required when the perforator location is mapped prior to surgery. Bipolar cautery can be used to peel off the muscle fibers from around the perforator if necessary.

Flap design variations

The propeller TAP-flap skin paddle can be designed in many different ways, but three designs have been published: (I) an oblique upwards design in a cranial direction ending medially to the scapula (7); (II) a horizontal design (3,4); (III) an oblique downward design in a caudal direction, where the skin paddle is designed within the boundaries of the LD muscle following the upper edge of the muscle (6) (*Figure 1*).

All of these designs leave a satisfying donor site scarring, which can be hidden by clothing. However, there seems to be a significant difference in terms of the complexity of perforator dissection required according to the description of the three different designs. Design I and II require a longer axis of rotation of 180 degrees or more, whereas design III generally makes the angle less than 135 degrees. Thus, designs I and II requires dissection of the perforator to the TD-vessels to gain sufficient laxity when rotating the perforator, whereas identification of the perforator at the fascia level is usually sufficient to allow the required rotation when the oblique downwards design III is used. The disadvantage of the limited dissection in this design is, however an occasional lateral bulkiness in the axilla, easily corrected by liposuction along with a secondary procedure. The dissection of the oblique downward design III is quick, easy, and simple and vascular compromise is seldom a problem. However, dissection of the perforator can be argued to be advantageous for better shaping of the reconstruction.

LD versus TAP-flap

The Latissimus dorsi-flap (LD-flap) is a good and reliable option for breast reconstruction, either combined with

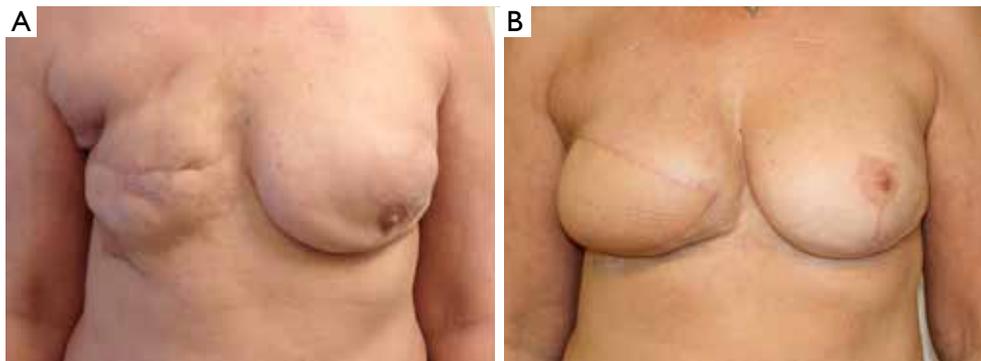


Figure 2 (A) Result after unsuccessful attempted immediate breast reconstruction; (B) Result after TAP-flap breast reconstruction with an implant.

an implant or alone as an extended flap (12-14). LD-reconstructions have been criticized for the morbidity of the muscle loss and alleged high rate of complications. Most commonly reported are seroma formation at the donor site, postoperative shoulder dysfunction, and/or pain in the affected upper extremity (14-16). The long term morbidity has been and will continue to be debated in literature (17). Surgeons seem to adapt to two different view-points, one stating that there are no problems in regard to donor site morbidity as long as the patient, guided by physiotherapist continue to use the remaining muscles of the shoulder cuff. The other group is reluctant to use the LD-flap as a reconstructive option stating that the morbidity is too high for the use to be justified. It is probably true that patients can achieve a fairly normal function of their muscle and arm with sufficiently guided rehabilitation. However, in our experience, LD reconstructed patients report some impairment of shoulder and arm function when asked at 5 or 10 years follow-up. Furthermore, when inspected, the spine seems to curve towards the non-operated side in many of these patients.

The TAP-flap does not impair the function of the shoulder or arm as opposed to the LD-flap, since the muscle and neural innervations are totally spared (18). The morbidity, both perioperative and long term, seem to be very low regarding back seroma formation and function of the affected upper extremity. In select cases reconstruction can be achieved by the TAP-flap alone or in combination with fat grafting with the flap working as a vascular matrix (19). In most cases an implant is needed to achieve the reconstructive goals (6) (*Figure 2*). The use of implants is not without morbidity and implant exchange and re-operation related to capsular contracture are to be expected. The experience is limited so far, but rates will probably be similar to those of an

LD in combination with an implant (20).

The paper by Angrigiani *et al.* in this issue of GS is yet another step toward a better understanding of the potentials and limitations of the use of the TAP-flap for breast reconstruction (7).

Future aspects

The TAP-flap seems to be a promising tool for oncoplastic and reconstructive breast surgery and will certainly become an invaluable addition to breast reconstructive methods. Reports of its use by several different surgeons provide us with the diversity of opinions needed for objective evaluation. Experience is still limited and long term results are awaited. How does it affect the patients in terms of long term aesthetic satisfaction, quality of life, shoulder and arm functionality? A constantly changing environment of breast surgery calls for plasticity and diversity. A prospective randomized trial is needed to evaluate the true impact of the TAP-flap in context of other reconstructive methods.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Propeller thoracodorsal artery perforator flap for breast reconstruction

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Background: The thoracodorsal artery perforator (TDAP) flap has been described for breast reconstruction. This flap requires intramuscular dissection of the pedicle. A modification of the conventional TDAP surgical technique for breast reconstruction is described, utilizing instead a propeller TDAP flap. The authors present their clinical experience with the propeller TDAP flap in breast reconstruction alone or in combination with expanders or permanent implants.

Methods: From January 2009 to February 2013, sixteen patients had breast reconstruction utilizing a propeller TDAP flap. Retrospective analysis of patient characteristics, clinical indications, procedure and outcomes were performed. The follow-up period ranged from 4 to 48 months.

Results: Sixteen patients had breast reconstruction using a TDAP flap with or without simultaneous insertion of an expander or implant. All flaps survived, while two cases required minimal resection due to distal flap necrosis, healing by second intention. There were not donor-site seromas, while minimal wound dehiscence was detected in two cases.

Conclusions: The propeller TDAP flap appears to be safe and effective for breast reconstruction, resulting in minimal donor site morbidity. The use of this propeller flap emerges as a true alternative to the traditional TDAP flap.

Keywords: Thoracodorsal artery perforator (TDAP); propeller flap; breast reconstruction

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Introduction

Our group first described the thoracodorsal artery perforator flap (TDAP) in 1995, in an attempt to minimize donor-site complications related to the latissimus dorsi muscle cutaneous flap (1). Since then, several studies have demonstrated that the use of muscle-sparing latissimus dorsi flap is feasible and ensures excellent objective and subjective aesthetic outcomes without contour defect (2-4). Like the conventional muscle cutaneous flap, TDAP requires intramuscular dissection of the arterial perforator, and thus, it is more complex and time-consuming, entailing an additional learning curve for the surgeon.

In order to simplify breast reconstruction using a TDAP flap, we have modified the surgical technique by rotating

the flap 180 degrees over the pedicle, to the mastectomy area (propeller technique), which eliminates the need for intramuscular pedicle dissection. In this report, we describe our clinical experience with the propeller TDAP flap during breast reconstructions.

Patients and methods

We performed a retrospective analysis to examine the outcomes associated with 17 patients who underwent propeller-shaped TDAP flaps (without intramuscular pedicle dissection) for breast reconstruction from January 2009 to February 2013. The ages of the patients ranged from 38 to 57 years. In 7 cases, the TDAP flap was designed in a horizontally, and the rest were created in an oblique

Table 1 Procedural characteristics

Case	Age	Indication	Timing of reconstruction	Flap design	Flap size	Complication
1	52	Coverage & Volume	Immediate	Oblique	35×7	None
2	70	Coverage	Delayed	Oblique	32×8	None
3	59	Coverage	Delayed	Horizontal	28×7	None
4	47	Coverage	Immediate	Horizontal	28×9	None
5	52	Coverage	Immediate	Oblique	27×8	None
6	53	Coverage & Volume	Delayed	Oblique	32×9	None
7	48	Coverage & Volume	Immediate	Horizontal	30×10	None
8	65	Coverage & Volume	Delayed	Oblique	32×10	None
9	63	Coverage & Volume	Delayed	Horizontal	28×10	None
10	45	Coverage	Immediate	Oblique	32×8	None
11	55	Coverage	Delayed	Horizontal	33×9	None
12	42	Coverage & Volume	Immediate	Horizontal	35×9	None
13	66	Coverage & Volume	Delayed	Oblique	30×8	None
14	62	Coverage & Volume	Delayed	Oblique	34×8	Distal necrosis—3 cm
15	48	Coverage	Immediate	Horizontal	25×8	None
16	50	Volume	Delayed	Oblique	38×8	Distal necrosis—2 cm
17	60	Volume	Delayed	Oblique	36×8	None

upward position, using a Hammond-banana design (*Table 1, Figures 1-3*). Flap length ranged from 25-38 cm and width 8-10 cm (*Table 1*). In 15 cases this cutaneous branch was observed as a true muscular perforator of the latissimus dorsi muscle (83%) and in 3 cases (17%) there was a direct cutaneous branch coming from the descending branch. Operative time ranged 90-100 minutes. The flaps covered 90-95% of the width of the back. All flaps were vascularized by the proximal perforator of the descending branch of the thoracodorsal artery. The follow-up period ranged from 4 to 48 months. We collected data prospectively regarding demographics along with peri-operative, and postoperative outcomes. Prior to surgery, 14 patients underwent some type of chemotherapy, while four of them had also received breast radiation. Two patients had a bilateral reconstruction, one was immediate (patient with adenomastectomy for siliconomas), while the other was delayed (patient with prior mastectomy and radiotherapy). The rest (n=14) underwent a unilateral reconstruction. Indications for TDAP flaps (per breast) were as follows: skin reconstructions in 12 cases, skin reconstruction and volume enhancement in 5 and reconstructive volume enhancement in 1 (*Table 1*). In all cases, the indications for TDAP flaps were equally appropriate for latissimus dorsi flaps. The results were evaluated based on the survival of the flap and the associated donor site morbidity.

Technique

The flaps were designed with the patient in standing position, arms at the sides with the hands on the waist. Each patient was asked to actively contract her back muscles, with a cutaneous mark being made to represent the leading edge of the Latissimus dorsi muscle contraction. A point is marked on that line, 8 cm below the axillary fold. The descending branch of the proximal perforator artery runs parallel to that line, 2 cm lateral, approximately. The proximal perforator branch of the descending branch of the thoracodorsal artery pierces the muscle in the line of the descending branch at 8cm from the axillary fold or more. However, in 20% of the cases, a direct cutaneous branch from the descending branch of the thoracodorsal artery is the most important cutaneous branch (considering its diameter). This direct cutaneous branch does not pierce the muscle; it passes immediately anterior to the muscle lateral border. Thus, the design of the flap must exceed the edge of the muscle to assure the presence of this branch in the raised flap. The width of the flap is designed according to the possibility of direct closing of the donor site. The skin and the associated subcutaneous tissue are pinched with the thumb and index finger in order to mark the desired width. The flap's length extends across the width of the back when the design is horizontal or across the superior inferior angle

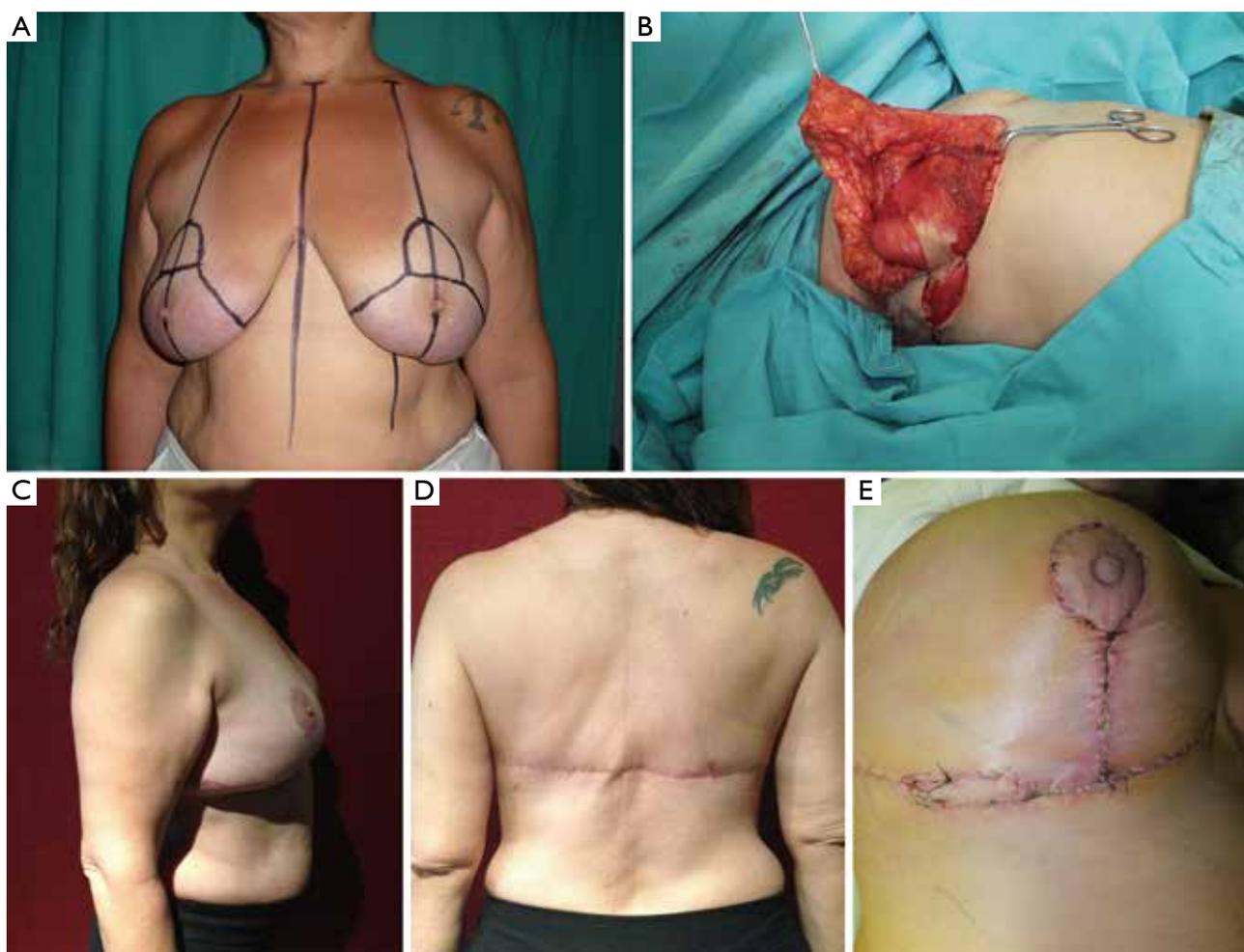


Figure 1 Preoperative (A) marks. Thoracodorsal artery perforator flap dissected and deepithelialized (B). Postoperative anterior view (C) shows optimal evolution of the cutaneous flap island. Lateral (D) and posterior (E) follow-up view at 6 months after breast reconstruction revealing vitality of the flap islet and a scar at the donor site.

of the scapula when the design is made obliquely upward. We prefer the oblique, upward design because the thickness of the adipose tissue in the parascapular area provides more volume. The final choice, however, rests with each patient.

The location of the perforators is ideally determined using preoperative angiography and color Doppler ultrasonography. When these techniques are not available, the surgeon must rely on anatomical knowledge and clinical experience with the use of the flap, to locate these vessels that, in most cases, are in an area 8-cm below the axillary folds.

The flap is raised from distal to proximal direction, superficial to the deep fascia, while observing the fascia of the latissimus dorsi. The perforator arteries are carefully

observed, using 4× magnifications, to detect any bleeding from the tip of the flap. The continuous and progressive control of the bleeding quality from the end portion of the flap represents an excellent way of monitoring the presence of a good perforator. If the flap has excellent perfusion by the time that it is half separated from the dorsal muscle, the perforator is likely to be adequate (diameter >0.5 mm). On the other hand, if a marked decrease in perfusion is detected when the flap is half raised and the intercostal perforators sectioned, we prefer to defer the procedure. Such a situation was not observed in this series. Dissection continues along the suprafascial plane to the anterior border of the muscle and it proceeds superiorly up to the perforator entrance point.

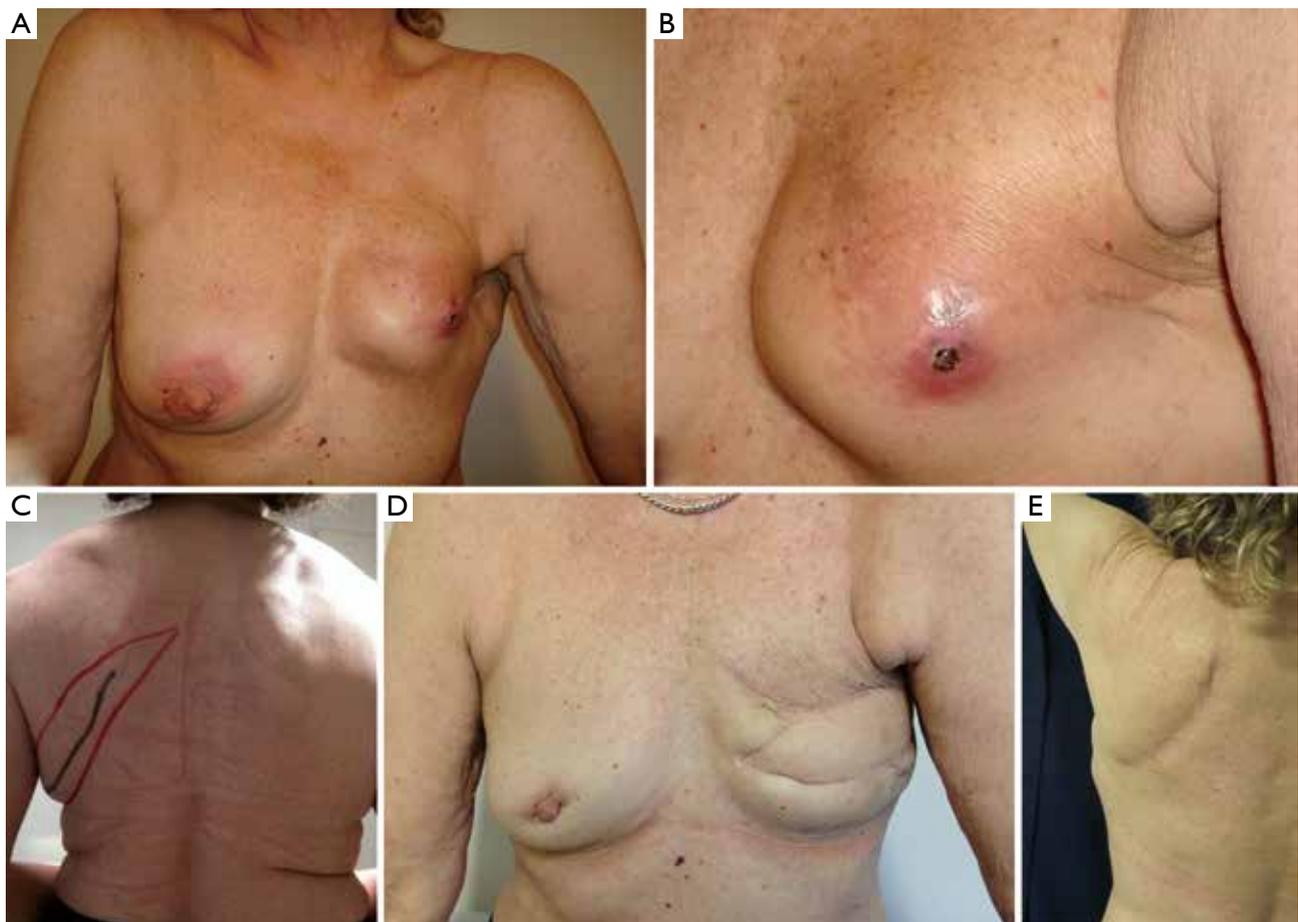


Figure 2 Preoperative anterior (A) and lateral magnified (B) views. The outlines of the designed TDAP flap (C). The skin ellipse is designed in an oblique fashion. Postoperative anterior view (D) shows optimal healing of the flap. Donor site (E) at two months follow-up. TDAP, thoracodorsal artery perforator.

Locating the lateral edge of the muscle is important because the descending branch of the thoracodorsal artery runs parallel to that edge, at a distance of $\leq 2-4$ cm. Therefore, the proximal perforator is found at approximately the same distance from the edge. In cases involving a direct cutaneous branch, this level is at the edge surrounding the muscle.

The proximal perforator artery also has an accompanying vein. Once this artery has been located, we perform complete dissection of the skin around the island itself. The dissection around the perforating artery is minimal, and serves to release the muscle and allow rotation of the flap along this axis, creating the “flap helix” (propeller) (5).

In cases of mastectomy sequelae, we release the scar and leave a gap to place the flap. In these cases, the previous scar incision is made in continuity with the flap incision. In the case of an immediate reconstruction, when performing

skin sparing mastectomy or when no scar at the breast side is present, the flap is deepithelized and tunneled, remaining under the skin below the tunnel. Donor site closure is performed in two planes. A suction drain is placed and removed 48-72 hours after surgery.

Results

There were no donor-site seromas, and minimal wound dehiscence was detected in two cases. Minor skin paddle tip necrosis occurred in two flaps (34×8 and 38×8) which required tip resection. Both cases healed by second intention.

We found that tissular volume achievement with the TDAP flap is enough for symmetrization of the contralateral breast when facing a “A or B size cup”.

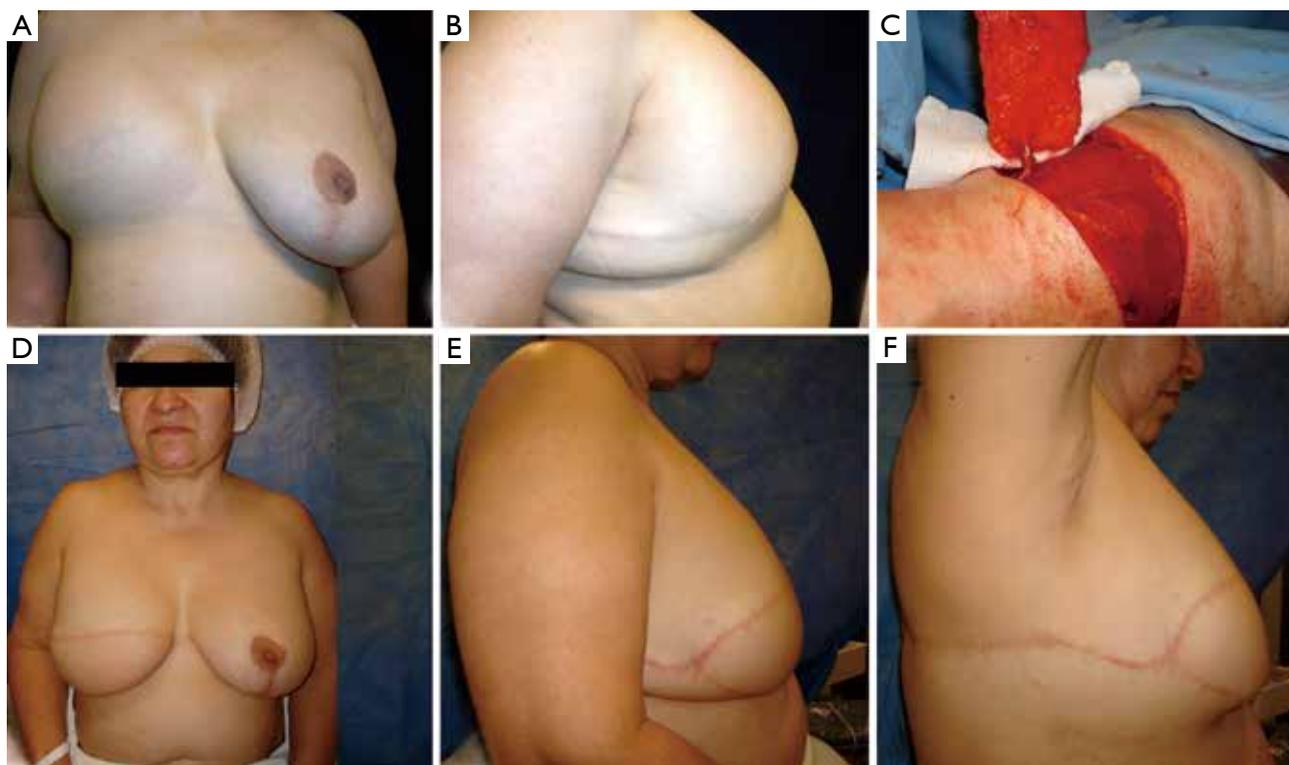


Figure 3 Preoperative anterior (A) and (B) lateral views demonstrating volume deficit in the breast. Intraoperative (C) view with the TDAP flap elevated. Postoperative anterior (D) and lateral views (E and F) three months after reconstruction. TDAP, thoracodorsal artery perforator.

Case examples

Case 1: a 48-year-old patient with multiple breast nodules and skin ulceration following 250 cc liquid silicone injection for breast augmentation in both breast (*Figure 1A*). We performed a staged bilateral adeno mastectomy with a Strombeck approach, utilizing two propeller TDAP flaps for breast reconstruction (*Figure 1B,C*). Note the final aesthetic results at 6 months (*Figure 1D,E*).

Case 2: a 68-year-old patient had immediate breast reconstruction with a 200 cc expander following simple mastectomy for the treatment of multicentric carcinoma. After the procedure, the patient received radiotherapy, which resulted into extrusion of the expander (*Figure 2A,B*). We removed the deflated expander and repaired the defect with a propeller TDAP flap with (*Figure 2C,D*) excellent results at two-month visit (*Figure 2E*).

Case 3: a 53-year-old patient referred after suboptimal breast reconstruction with expander and ultimately prosthesis implantation. There was a deficit in the breast envelope (*Figures 3 A,B*). We decided to provide breast area

coverage with a propeller TDAP flap (*Figure 3C*) without changing prosthesis volume. Note the aesthetic results at three months follow-up (*Figure 3D,E*).

Discussion

Over the past two decades, the ability for breast reconstruction has improved substantially. At first, musculocutaneous flaps (i.e., latissimus dorsi and TRAM, transverse rectus abdomino muscle cutaneous flap) remained the workhorse for coverage of most skin defects of the breast, but were progressively replaced by muscle-sparing flaps, owed to their lower morbidity at the donor-site and their greater precision during breast reconstruction (6-11). Specifically, the TDAP flap represents an extremely versatile muscle-sparing flap that possesses a reliable cutaneous blood supply arising from the lateral branch of the thoracodorsal artery (1,4). If needed, TDAP flaps can be rather large with a long pedicle length (up to 23 cm), which provides an extensive arc of rotation for pedicle transfers. Several reports have shown aesthetically pleasing donor site

results following breast reconstruction with this flap-type, in part due to harvesting from a natural skin fold produced on lateral flexion without damaging the axillary silhouette (2,4). Consequently, donor site scars can usually be concealed underneath the arm or in the underwear. TDAP flaps have a thin subcutaneous fat tissue (commonly encountered at the back region), thus, providing a thin skin for precise breast reconstruction. Although there are other potentially useful muscle-sparing flaps with similar skin texture like the scapular and parascapular flaps, pedicles are shorter and hence, freedom is limited when compared to TDAP flaps.

The use of TDAP flaps is indicated for:

- (I) Partial breast reconstructions;
- (II) Combined with an expander or implant during complete breast reconstruction or;
- (III) For further refinements when additional volume is required for reconstruction of the nipple-areola complex area.

Despite all advantages, harvesting TDAP flaps involves intramuscular dissection of the pedicle, a step that is particularly time-consuming. In an attempt to simplify this technique, we used TDAP propeller flaps, thus eliminating the need for intramuscular pedicle dissection.

According to the Tokyo Consensus, the term “propeller flap” describes a flap, based on a random subcutaneous pedicle, with a skin island of a length largely exceeding its width, made of two portions (the blades of the propeller), one at each side of the pedicle (12). Several authors have reported the application of the perforator propeller concept to the reconstruction of soft-tissue defects in different areas of the body (13-15).

In the current study, harvesting the TDAP propeller flaps was simple, feasible and safe. Donor-site aesthetic results were acceptable with minor complications and no long-term sequelae. Propeller flaps are expected to have the same complications as any other perforator flap. Venous congestion with necrosis at the flap tip, and distal flap tissue suffering for insufficient irrigation are the most frequent complication. This sign must not be interpreted as a venous congestion: it is produced by pressure decrease in the vascular system, slowing of blood flow and, thus, inappropriate capillary perfusion. Even though it looks like venous congestion, it can be solved by additional incorporation of arterial inflow and not by additional venous drainage. It is the distal limit of a possible flap designed with a determined pedicle. In this case, it is the distal limit of the TDAP.

Ischemia can be caused by an insufficient flow in the

perforating vessel or by inadequate release of the fascial adhesions around the vascular pedicle and especially around the vein. In the present study, we identified minor necrosis at the tip of skin paddle in two excessively long flaps. Nowadays we refrain from harvesting flaps >30 cm in length.

Noteworthy, a propeller TDAP flap reach is shorter than conventional ones, as the pedicle length is restricted. Therefore, care should be taken when calculating the flap length. Although a propeller flap can usually be converted to a conventional perforator flap if needed, such surgical maneuver requires significant operator dexterity.

Conclusions

This preliminary study has demonstrated the feasibility and clinical versatility of the TDAP propeller flap in breast reconstruction. This flap is simple to harvest; it is associated with minimal donor site morbidity and emerges as optimal alternative during reconstructive breast surgery.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Use of latissimus dorsi muscle onlay patch alternative to acellular dermal matrix in implant-based breast reconstruction

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Background: An acellular dermal matrix (ADM) is applied to release the surrounding muscles and prevent dislocation or rippling of the implant. We compared implant-based breast reconstruction using the latissimus dorsi (LD) muscle, referred to as an “LD muscle onlay patch,” with using an ADM.

Method: A total of 56 patients (60 breasts) underwent nipple sparing mastectomy with implant-based breast reconstruction using an ADM or LD muscle onlay patch. Cosmetic outcomes were assessed 4 weeks after chemotherapy or radiotherapy, and statistical analyses were performed.

Results: Mean surgical time and hospital stay were significantly longer in the LD muscle onlay patch group than the ADM group. However, there were no statistically significant differences between groups in postoperative complications. Cosmetic outcomes for breast symmetry and shape were higher in the LD muscle onlay patch group.

Conclusions: Implant-based breast reconstruction with an LD muscle onlay patch would be a feasible alternative to using an ADM.

Keywords: Breast; latissimus dorsi muscle; reconstruction

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Introduction

Implant-based breast reconstruction is the most frequently utilized surgical technique. The breast volume can be adjusted based on remained breast tissue and volume of inserted implant. Usually, the implant is inserted underneath the pectoralis muscle. However, a displacement or rippling of the implant can occur, because the chest wall and pectoralis muscle has strong tension which makes limited space between them (1). In addition, the capsular contracture after radiotherapy sometimes may result in respiratory discomfort (2,3).

Acellular dermal matrix (ADM) has been used to cover and support the inferior aspect of the breast pocket, and prevent capsular contracture or dislocation of the implant. Although ADM allowed the reconstructed breast to maintain its natural contour and shape (4-7), it has some

complications, such as infection and postoperative seroma (8-14). There are some reports that autologous tissue has been used for full muscle coverage instead of an ADM (15). When implant-based breast reconstruction is performed with a latissimus dorsi (LD) muscle flap, the additional coverage by the LD muscle will thicken the overlying flap which might be positive to the appearance and feeling of the breast.

This study was undertaken to compare immediate implant-based breast reconstruction using a LD muscle flap, which is referred as “LD muscle onlay patch,” and implant-based breast reconstruction using an ADM.

Methods

We reviewed a database of patients with breast tumors between January 2009 and December 2011. Fifty-six

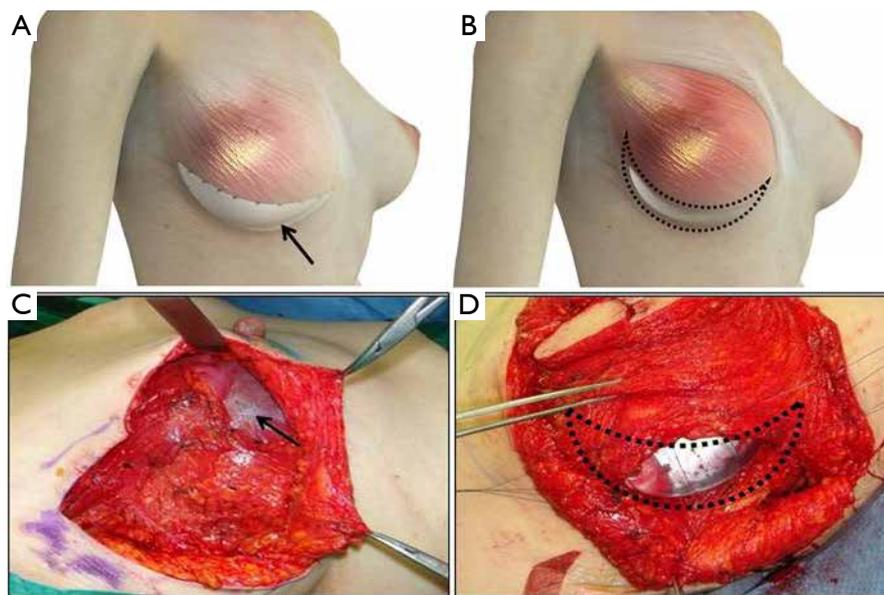


Figure 1 Implant-based breast reconstruction. (A,C) An acellular dermal matrix (black arrow) and (B,D) the latissimus dorsi muscle (dots) are used to cover the triangular window.

patients (60 breasts) underwent implant-based breast reconstruction using either the ADM (n=28) or LD muscle only patch (n=32).

All data were collected and analyzed retrospectively, and included clinicopathologic characteristics, volumes of the resected breast and implant, treatment modalities, complications, and cosmetic outcomes. The questionnaire survey for cosmetic outcomes was conducted by patients and physicians after 4 weeks from radiotherapy based on a 4-point scoring system, which included the following items: overall satisfaction, breast symmetry, shape, softness, and tension with movement.

Both groups underwent nipple sparing mastectomy with implant-based breast reconstruction. After the breast tumor was removed with safety margin, the pectoralis major muscle was dissected from the chest wall from the lateral to the medial and inferior margins of the muscle. A triangular window composed of the lateral margins of pectoralis, anterior serratus muscle, and the lateral side of inframammary line was covered with the ADM or LD muscle only patch (*Figure 1*). In the ADM group, the implant was inserted into the breast pocket and the window was covered with ADM (Surgimend®, TEI Biosciences Inc. Boston, MA, USA). And in the LD only patch group, the window was enveloped with the LD muscle after an appropriate volume of the implant was positioned. The extent of the patch is decided after considering the volume

of the breast prosthesis. Then, anchoring sutures were inserted to fix the muscle and prevent displacement of the implant. Anchoring sutures should be inserted at 1-cm intervals to prevent the escape of the implant and to avoid damaging the vasculature of the LD muscle. These sutures should avoid the vascular structures of the LD muscle, because damage to the vascularity may cause necrosis or stiffness of the flap (*Figure 2*).

Statistical analyses were performed using SPSS ver. 12 (SPSS, Inc., Chicago, Ill, USA). For comparisons of the ADM and LD muscle only patch groups, Pearson's chi-square test, Fisher's exact test, and the Wilcoxon-Mann-Whitney test were performed. The chi-square and Fisher's exact tests were applied for unadjusted categorical variables, and the Mann-Whitney test was used for nonparametric categorical variables. Continuous data were described as the mean \pm the standard deviation (SD), and P value less than 0.05 was considered statistically significant.

Results

The mean age of the patients was 46 years (range, 24-64 years), and the mean body mass index was 21.8 kg/m² (range, 16.4-30.6 kg/m²). The mean follow-up period was 35.5 months (range, 18.7-53.5 months), and the mean interval period between surgery and chemotherapy or radiotherapy was 21.3 days (range, 15-32 days).

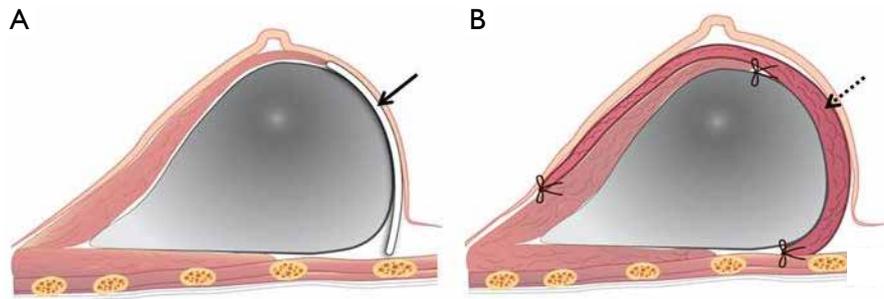


Figure 2 Transverse views of a completed implant-based breast reconstruction. (A) An acellular dermal matrix (black arrow) is placed between the inferior border of pectoralis muscle and the inframammary line; (B) the latissimus dorsi muscle onlay patch (dot arrow) is fixed with anchoring sutures on the inferior border of the pectoralis muscle and the chest wall at the inframammary line.

Table 1 Comparison of patient characteristics between using acellular dermal matrix group and latissimus dorsi muscle onlay patch group

Characteristics	ADM* (n=28)	LD [†] muscle onlay patch (n=32)	P value
Age (years, SD)	36.8±11.31	45.8±11.99	0.284
Body mass index (kg/m ² , SD)	19.0±2.76	23.4±3.43	0.065
Volume loss (g, SD)	153.9±120.29	299.7±116.03	0.275
Implant volume (cc, SD)	194.5±49.50	155.2±74.25	0.022
OP time (minutes, SD)	198.0±86.06	342.5±54.7	0.003
Hospital stay (days, SD)	6.9±1.52	8.7±1.56	0.010
Follow-up period (mo, SD)	36.2±8.48	34.9±8.60	0.244
Interval period (days, SD)	19.9±6.24	27.9±7.58	0.992
Chemotherapy, n (%)	16 (57.1)	25 (78.1)	0.167
Radiotherapy, n (%)	23 (82.1)	31 (96.9)	0.454
Complication, n (%)	4 (14.3)	1 (3.1)	0.175

*, acellular dermal matrix; [†], latissimus dorsi.

Clinical characteristics are listed in *Table 1*; there were statistically significant differences between groups in terms of implant volume ($P=0.022$), surgical time ($P=0.003$), and hospital stay ($P=0.010$). However, the mean volume loss of the breast and incidence of complications were not statistically different between groups.

Pathological characteristics were analyzed with regard to tumor size, type, multicentricity, overall stage, microcalcification of the tumor, differentiation of tumor cells, perineural and lymphovascular invasion of tumor cells, and hormone receptor status. No tumor characteristics showed a significant difference between groups (*Table 2*).

The postoperative complications occurred in four out of 28 in the ADM group and one out of 32 in the LD muscle onlay patch group. A severe infection of the ADM occurred in the ADM group. We removed both the cohesive gel implant and ADM immediately, because methicillin-

resistant staphylococcus aureus (MRSA) was detected in tissue culture. Other complications were capsular contracture after radiotherapy, inflammation, and seroma of the implant cavity, which were confirmed by breast MRI. In the LD muscle onlay patch group, only one seroma of the implant cavity was detected by breast MRI (*Table 3*). The patient, who was diagnosed the second degree of capsular contracture in MRI, had no previous surgical history or radiotherapy. This contracture occurred on 4 months after surgery and 3 months after radiotherapy.

The scores of each item for cosmetic outcomes are shown in *Table 4* and *Figure 3*. The LD muscle onlay patch group had a greater degree of satisfactory than the ADM group in terms of breast symmetry ($P<0.001$) and breast shape ($P=0.008$). However, in terms of overall satisfaction, breast softness and tension with movement were similar between groups.

Table 2 Comparison of clinicopathologic characteristics between using acellular dermal matrix group and latissimus dorsi muscle onlay patch group

Characteristics	ADM* (n=28)	LD [†] muscle onlay patch (n=32)	P value
Mean tumor size (cm, SD)	2.0±1.43	3.8±2.27	0.483
Tumor type, n (%)			0.095
Atypical ductal hyperplasia	4 (14.3)	0	
Carcinoma <i>in situ</i>	6 (21.4)	7 (21.9)	
Invasive carcinoma	18 (64.3)	25 (78.1)	
Multicentricity, n (%)	3 (10.7)	1 (3.1)	0.331
Stage, n (%)			0.673
0	6 (21.4)	7 (21.9)	
I	3 (10.7)	0	
IIA	7 (25.0)	9 (28.1)	
IIB	6 (21.4)	10 (31.3)	
IIIA	2 (7.1)	2 (6.3)	
IIIB	0	4 (12.5)	
Microcalcification on mammography, n (%)	2 (7.1)	3 (9.4)	0.982
Differentiation, n (%)			0.378
Well	7 (25.0)	3 (9.4)	
Moderately	9 (32.1)	16 (50.0)	
Poorly	2 (7.1)	6 (18.8)	
Perineural invasion, n (%)			0.736
Positive	1 (3.6)	1 (3.1)	
Negative	17 (60.7)	24 (75.0)	
Lymphovascular invasion, n (%)			0.637
Positive	1 (3.6)	3 (9.4)	
Negative	17 (60.7)	22 (68.8)	
Estrogen receptor, n (%)			0.754
Positive	15 (53.6)	21 (65.6)	
Negative	9 (32.1)	11 (34.4)	
Progesterone receptor, n (%)			0.126
Positive	13 (46.4)	15 (46.9)	
Negative	11 (39.3)	17 (53.1)	
c-erbB2 protein, n (%)			0.446
Positive	5 (17.9)	7 (21.9)	
Negative	19 (67.9)	25 (78.1)	
Triple negative, n (%)	1 (3.6)	3 (9.4)	0.387

*, acellular dermal matrix; †, latissimus dorsi.

Table 3 Comparison of the incidence of postoperative complications between using acellular dermal matrix group and latissimus dorsi muscle onlay patch group

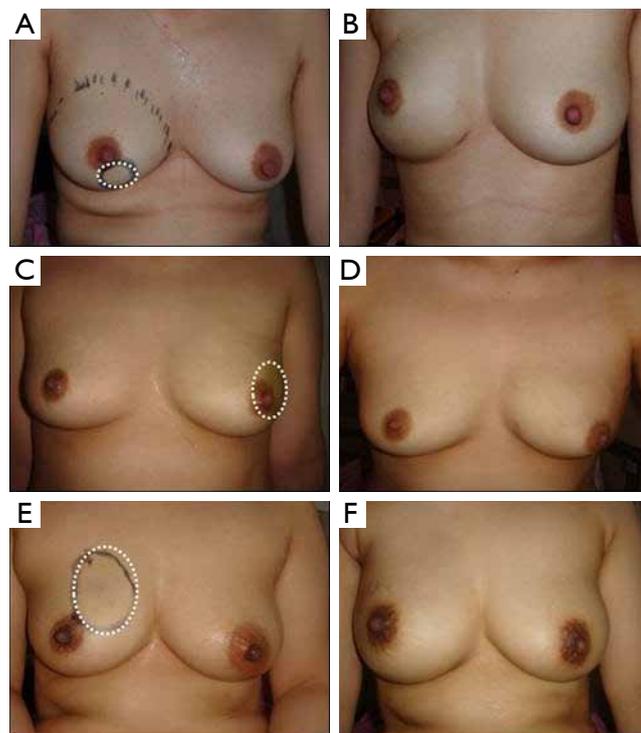
Postoperative complications, n (%)	ADM* (n=28)	LD [†] muscle onlay patch (n=32)
Inflammation in cavity	1 (3.6)	0
Seroma in cavity	1 (3.6)	1 (3.1)
Capsular contracture (grade II)	1 (3.6)	0
Severe infection of covering material	1 (3.6)	0

*, acellular dermal matrix; †, latissimus dorsi.

Table 4 Comparison of cosmetic outcomes between using acellular dermal matrix group and latissimus dorsi muscle onlay patch group

	ADM* (n=28) (%)				LD [†] muscle onlay patch (n=32) (%)				P value
	Excellent	Good	Fair	Poor	Excellent	Good	Fair	Poor	
Overall satisfaction	9 (32.1)	15 (53.6)	2 (7.1)	2 (7.1)	16 (50.0)	11 (34.4)	5 (15.6)	0	0.429
Breast symmetry	5 (17.9)	14 (50.0)	9 (32.1)	0	20 (62.5)	11 (34.4)	1 (3.1)	0	<0.001
Breast shape	9 (21.1)	13 (46.4)	6 (21.4)	0	16 (50.0)	13 (40.6)	3 (9.4)	0	0.008
Breast softness	7 (25.0)	16 (57.1)	4 (14.3)	1 (3.6)	13 (40.6)	15 (46.9)	3 (9.4)	1 (3.1)	0.217
Tension with movement	17 (60.7)	8 (28.6)	2 (7.1)	1 (3.6)	24 (75.0)	5 (15.6)	3 (9.4)	0	0.450

*, acellular dermal matrix; † latissimus dorsi.

**Figure 3** Cosmetic outcomes after implant-based breast reconstruction. (A,C,E) Pre- and (B,D,F) post-operative views after implant-based breast reconstruction with latissimus dorsi muscle onlay patch.

Discussion

Oncoplastic breast surgery has been performed with autologous flaps or artificial implants. In cases of breast reconstruction after mastectomy or nipple sparing mastectomy, implant-based breast reconstruction is primarily performed. Because an excessive movement or displacement of the implant can occur when the implant is put into the breast cavity, the implant should be inserted under the muscle in a fixed position. However, the full muscle coverage for the implant does not only limit the space for the implant but is usually not possible to be achieved, because the pectoralis muscle anatomically does not reach so far down to cover the lower lateral part of the implant. Even with additional intraoperative lifting of the serratus muscle a full coverage in the lower lateral aspect of the breast is hardly to achieve. Thus, breast surgeons have used an ADM to cover and support the lateral and inferior aspects of the cavity, allowing expansion of the space and prevention for displacement of implant (1,7,10,14).

A single stage reconstruction is beneficial regarding postoperative capsule fibrosis then this could also be achieved with an implant only reconstruction straight underneath the skin too, or with a reconstruction with the use of LD muscle flap (3,11,16). Implant-based breast reconstruction with ADM allows a natural breast contour with the formation of a neo-inframammary fold. However, postoperative seroma or infection is the most frequent complication (10). When, a severe infection occurred, the ADM or prosthesis should be removed immediately. In our study, there was one case of methicillin-resistant staphylococcus aureus infection of the ADM. We removed the ADM and prosthesis immediately and delayed breast reconstruction was planned after chemotherapy and radiotherapy. Although this complication arose before adjuvant treatment in our study, we might expect the higher incidence of infection in patients who received chemotherapy or radiotherapy.

When breast symmetry cannot be achieved with an autologous flap, such as using a transversus rectus abdominis myocutaneous flap, or is impossible because of old age or underlying disease, implant-based breast reconstruction can be planned. However, breast symmetry would not be acceptable only with large volume of implant in ptotic breasts, because the reconstructed breast would be firm and elastic compared to the contralateral breast (17). To obtain high-quality of breast symmetry and shape, breast reconstruction should be performed with an autologous

flap and any insufficient breast volume can be filled with the implant. In implant-based breast reconstruction using an LD muscle flap, a triangular window can be covered with a LD muscle flap instead of an ADM. And it is able to reduce the incidence of postoperative infection, even in patients who received chemotherapy or radiotherapy. And because the LD muscle onlay patch is thicker than ADMs, it can also prevent radiotherapy-induced capsular contracture, which tends to occur when the implant is close to the skin (2,15).

In performing breast reconstruction using an LD muscle onlay patch, there are some limitations. Breast reconstruction using an LD muscle needs an additional surgery which takes a relatively long time, and it can cause donor site morbidity (18). And flap necrosis can occur when the anchoring suture to fix as patch type. However, the surgical technique is quite easy and provides excellent cosmetic outcomes (19). In a recent study, we verified that using the LD muscle onlay patch method is not inferior to the ADM method. Although the surgical time and hospital stay for the LD muscle onlay patch group were both significantly longer than that of the ADM group, this method was not harmful to the patients. Additionally, the incidence of postoperative complications was lower in the LD muscle onlay patch group, even if this decrease did not show statistical significance. Furthermore, satisfaction with regard to breast symmetry and shape was significantly higher in the LD muscle onlay patch group.

The surgeons should strive to achieve satisfactory cosmetic outcomes with regard to breast volume, breast symmetry, and breast shape. Implant-based breast reconstruction using a concurrent autologous tissue flap would achieve some of these outcomes. In conclusion, the implant-based breast reconstruction using an LD muscle onlay patch is a feasible surgical technique achieving good cosmetic outcomes as well as fewer postoperative complications compared to the using ADM method.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest

to declare.

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Extended thoracodorsal artery perforator flap for breast reconstruction

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Abstract: A total of 45 patients underwent partial or total autologous breast reconstruction after skin-sparing mastectomy, skin-reducing mastectomy, and quadrantectomy using a thoracodorsal artery perforator (TDAP) flap. The detailed surgical technique with its variations is explained in this report. The propeller, flip-over, conventional perforator, and muscle-sparing flaps have been described and evaluated. The flaps were partially or completely de-epithelialized. The conventional TDAP can be enlarged or “extended” as the traditional latissimus dorsi musculocutaneous (LD-MC) flap by incorporating the superior and inferior fat compartments. It can be referred to as the “extended TDAP flap”. This technique augments the flap volume. In addition, this flap can serve as a scaffold for lipofilling to obtain autologous breast reconstruction in medium to large cases. There were two complete failures due to technical errors during flap elevation. Distal partial tissue suffering was observed in four flaps. These flaps were longer than usual; they reached the midline of the back. It is advisable to discard the distal medial quarter of the flap when it is designed up to the midline to avoid steatonecrosis or fibrosis. A retrospective analysis of the 39 flaps that survived completely revealed a satisfactory result in 82% of the cases. The main disadvantage of this procedure is the final scar. The TDAP flap is a reliable and safe method for partial or total breast autologous reconstruction.

Keywords: Extended thoracodorsal artery perforator (TDAP); breast reconstruction; perforator flap

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Introduction

Conservative mastectomies lead to varying amounts of volume deficit depending on the dimensions of the resected tissue. De-epithelialized flaps from the lateral thoracic wall and the back can be transposed to the anterior thorax for breast mound reconstruction using the thoracodorsal artery perforator (TDAP) flap or the lateral intercostal artery perforator (LICAP) flap.

The TDAP flap was originally described in 1992 (1) as a method of harvesting the skin and subcutaneous island of the traditional latissimus dorsi musculocutaneous (LD-MC) flap without the muscle. It was reported as a possible breast reconstruction method in 1996 (2), and Hamdi published its first clinical use for breast reconstruction in 2004 (3). Several studies have demonstrated that the TDAP flap is a

reliable and safe technique (4-6).

The TDAP flap is irrigated by the proximal perforator of the descending branch of the thoracodorsal artery (*Figure 1*). This branch is consistently present, according to several anatomical studies (7-13). The superior (scapular) and inferior (lumbar) fat compartments can be partially captured and irrigated by this proximal muscle perforator in the same manner as in the extended LD-MC flap (14) when additional volume is needed without the muscle (Angrigiani 2010 “TDAP Flap” presented at 13th International Perforator Flap Course Mexico 2010). We have named this variation “the extended TDAP flap” (*Figure 2*).

With this method, sufficient volume to reconstruct a B-cup sized breast can be obtained using a totally or partially de-epithelialized flap.

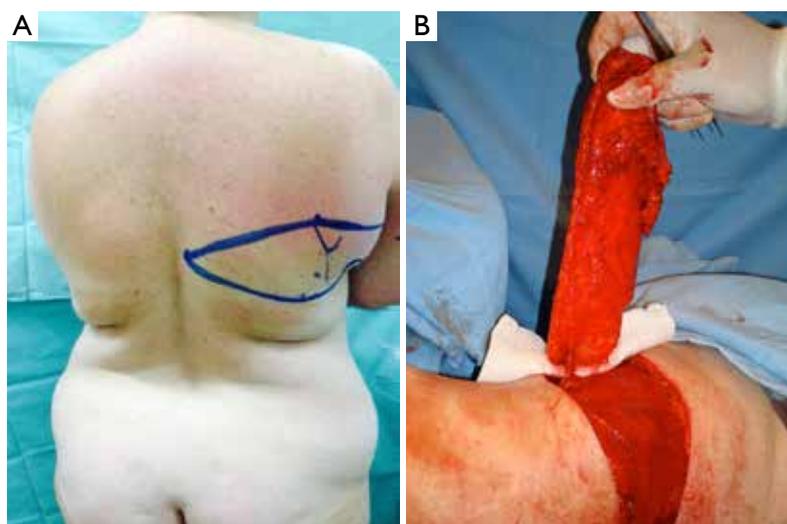


Figure 1 (A) Horizontal design of the thoracodorsal artery perforator flap (TDAP); (B) the flap is elevated and the cutaneous perforator is seen.

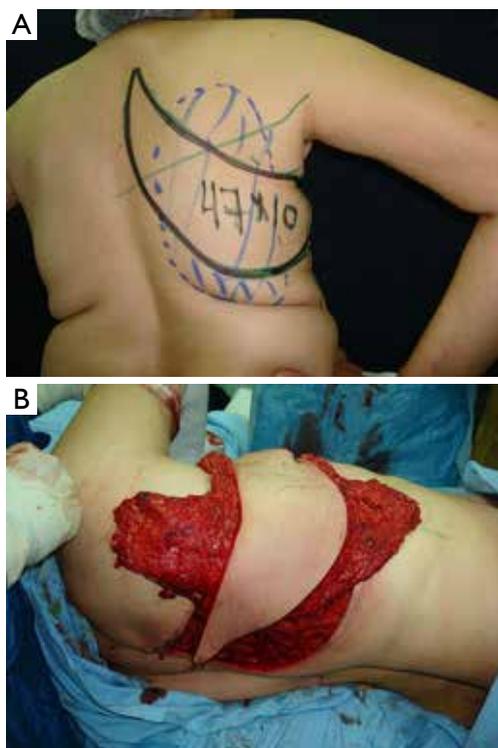


Figure 2 (A) Extended thoracodorsal artery perforator flap (extended TDAP) ascending oblique flap design; (B) the flap is elevated with the harvested scapular and lumbar fat compartments.

Additional fat grafting may be performed to increase volume in the same procedure with the use of the TDAP flap as a scaffold by lipofilling (*Figure 3*).

Surgical technique

Evaluation of volume deficit and location

The best way to evaluate needed volume need is to weight or measure the resected tissue. In secondary or delayed reconstruction, however, the volume is frequently underestimated as the retracted tissue may mislead the calculation. Intraoperative evaluation after releasing the retractive scar exposes the true volume deficit. Contralateral comparison, if possible, may provide a good approximation.

Flap indication

The indications for the TDAP flap, which are similar to those of the LD-MC flap, are as follows: primary or additional volume for breast reconstruction; salvage procedure for exposed implants; primary or additional surface (envelop) reconstruction; and combined implant autologous tissue reconstruction. Selection of a regular LD-MC flap or a TDAP flap must be done prior to designing the flap. There are some differences in the designs of these two flaps; these are described in the next paragraph. The LD flap involves muscle harvesting, is easier to perform, and requires shorter operating time. The TDAP flap involves a more complex technique but preserves the muscle and is associated with less seroma in the donor area.

Once the volume deficit is known, possible donor areas must be evaluated. A pinch test gives an approximate idea of the amount of subcutaneous tissue available for transfer as an island flap. It is important to measure the middle back; the

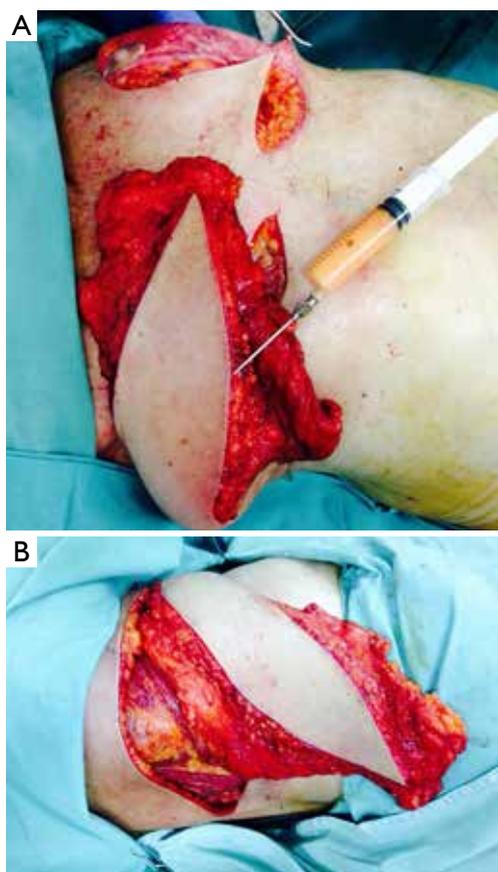


Figure 3 (A) Extended thoracodorsal artery perforator flap (TDAP) plus immediate lipofilling for volume enhancement; (B) The flap is lipofilled with saline 100 cc.

lumbar and subscapular fat pads can be transferred partially. Of the available fat flap volume, 50% may be safely added by lipotransfer, using the flap as a scaffold for flap survival.

The volume of the back should be compared with that of the lateral thoracic wall. In cases with available volume in the lateral thoracic area, an intercostal perforator flap should be considered, although the same area can be safely harvested with the TDAP flap.

Flap design

The flap is designed with the patient in the standing position, with the arms at the sides and the hands on the waist. The patient is asked to actively contract her back muscles, at which time the anterior lateral border of the LD muscle appears clearly under the skin and is marked with a line. The absence of this obvious contraction in mastectomy

sequelae cases is highly suspicious of a neurovascular muscle pedicle lesion. Although representative of only a nerve lesion, it is frequently associated with a vascular lesion. The possibility of raising a LD-MC flap with “compensatory” irrigation has been reported, but we prefer to utilize other options to avoid the possible risk of flap loss.

A point “A” is marked on the anterolateral muscle line, 8 cm below the axillary fold. The descending branch of the proximal perforator artery runs parallel and approximately 2 cm lateral to that line. The proximal perforator branch of the descending thoracodorsal artery pierces the muscle in the line of the descending branch, at 8 cm or more from the axillary fold. However, in 20% of the cases, a direct cutaneous branch from the descending branch of the thoracodorsal artery is the most important cutaneous branch (based on diameter). This direct cutaneous branch does not pierce the muscle; instead, it passes immediately anterior to the lateral border of the muscle. Thus, the design of the flap must exceed the edge of the muscle to assure the presence of this branch in the raised flap. This is the main difference with the LD-MC flap; the skin island of the LD may be designed more posterior or inferior without including point “A” within the flap design. It can be safely nourished by other muscle perforators of the thoracodorsal artery, resulting in a more posteriorly placed final scar.

The piercing point of the perforator (or cutaneous branch) must be included in the flap design as its irrigation is necessary. The flap length reaches the union of the lateral 3/4 with the most medial quarter of the back. Achieving the maximum possible length can improve inset in the breast mound. Clinical criterion is important for resection of the distal, under irrigated part of the flap, when it is fully elevated. No method has been reported previously for assessing this distal area. In addition, in our experience, it varies greatly across patients. The dimension of this distal under-perfused area is not related to only the perforator diameter; the subcutaneous vascular network status might also play an important role in the functional and physiological irrigation of the flap.

The flap width is designed according to the possibility of direct closing of the donor site. The skin and the associated subcutaneous tissue are pinched with the thumb and index finger to mark the desired width. It is preferable to achieve a fine aesthetically acceptable scar than a skin graft in the donor area. The flap length extends across the width of the back when the design is horizontal or across the superoinferior angle of the scapula when the design is made obliquely upward. We prefer the oblique design because the thickness

of the adipose tissue in the parascapular area provides more volume. However, many patients prefer the horizontal design. The final choice depends on the patient's decision.

The location of the perforators is ideally determined using preoperative angiography and color Doppler ultrasonography. When these techniques are not available, the surgeon must rely on anatomical knowledge and clinical experience in using the flap to locate these vessels, which in most cases, are in an area 8-cm below the axillary fold.

Single and double flap harvesting

De-epithelialized TDAP may be applied in unilateral or bilateral cases, with variations in surgical technique depending on the case. In unilateral cases, the patient is placed in contralateral decubitus, with the arm prepared free hold by an assistant. This position allows easy access to the pedicle origin and direct transfer of the flap to the anterior thorax. In bilateral cases, the patient is placed in ventral decubitus, and the procedure is performed by two teams simultaneously.

The flap is raised in the distal to proximal direction, superficial to the deep fascia, while observing the fascia of the LD muscle. The perforator arteries are carefully observed, under 4× magnifications. Continuous and progressive control of the bleeding quality from the end of the flap is an excellent way to monitor the presence of a good perforator. If the flap has excellent perfusion by the time it is half separated from the LD muscle, the perforator is likely to be adequate (diameter >0.5 mm). By contrast, if the perfusion markedly decreases when the flap is half-raised and the medial intercostal perforators are sectioned, we would prefer to postpone the procedure. Such a situation was not observed in this series.

When an "extended TDAP" is planned, the subcutaneous tissues superior and inferior to the skin incision are harvested. Lipofilling of this flap may supplement the final volume. We usually add 150 cc.

Dissection continues along the suprafascial plane to the anterior border of the muscle and proceeds superiorly up to the perforator entrance point. Locating the lateral edge of the muscle is important because the descending thoracodorsal artery branch runs parallel to that edge, at a distance of $\leq 2-4$ cm. Therefore, the proximal perforator is found at approximately the same distance from the edge. In cases involving a direct cutaneous branch, this level is at the edge surrounding the muscle.

The proximal perforator artery also has an accompanying

vein. Once this artery has been located, we perform complete dissection of the skin around the island itself. If the flap has good vascularization (bleeding from the skin edges and skin refilling), and no perforator is apparent when the lateral anterior border of the muscle is completely exposed, the direct cutaneous branch of the thoracodorsal artery should be carefully looked for. If it is not present, or is of a small diameter, then the lateral intercostal perforator must be present and is the main irrigating source of this flap. This rationale should be applied if the flap is well vascularized after passing the anterolateral border of the LD muscle. Neighboring cutaneous arteries may be of different calibers: if one has a large diameter, the other one is smaller, or vice versa, to compensate for the necessary blood flow of the skin. This was originally described by the French anatomist Dubreuil Chamardell, reported by Salmon (15). If the flap turns white or bluish, suggesting sluggish circulation, presence of a lesion of the muscle perforators must be assumed, and the flap should be discarded.

Once the perforator is completely exposed, there are several possibilities for continuing the surgical procedure, as described below:

(I) Propeller flap. The dissection around the perforating artery is minimal and serves to release the muscle and allow flap rotation along this axis, creating the "flap helix" (propeller) (16,17). The procedure is simple and quick. A special dissection technique is not required. The main disadvantage is its shorter length. The flap does not reach the midline of the anterior chest wall. A substantial portion of the flap remains in the subaxillary area, where it is not necessary, while the medial portion of the breast does not receive adequate volume. If a longer flap is harvested to reach the medial part of the breast, tissue suffering as well as steatonecrosis might be observed.

In cases of mastectomy sequelae, we release the scar and leave a gap to place the flap. The previous scar incision is made continuous with the flap incision. In immediate reconstructions, when performing skin-sparing mastectomy or when no scar at the breast side is present, the flap is de-epithelialized and tunneled, remaining under the skin below the tunnel. Donor site closure is performed in two planes. A suction drain is placed and removed 48-72 hours after surgery.

(II) Flip-over flap. The flap is raised in the same conventional manner, from distal to proximal. Once the muscle perforators corresponding to the descending branch of the thoracodorsal artery are

visualized, the dissection is discontinued. The flap is de-epithelialized and turned over the anterior part of the thorax. This “turn over” or “flip-over” flap is very simple to harvest. There is an important portion of the flap volume that remains under the axillary area and lateral to the breast. It provides a good volume for reconstruction of a medium-sized breast or complements a partial mastectomy repair.

- (III) Muscle-sparing flap. The flap is raised in the distal to proximal direction; once the lateral border of the LD is approached and the perforators of the descending branch are visualized, the muscle containing the perforators is sectioned-muscle sparing technique (18); the flap can be turned over or rotated to the breast area. This technique is a variation of the propeller but it partially damages the muscle innervation and has a reduced reaching point. It is used for partial volume deficit reconstruction on the lateral aspect of the breast.
- (IV) Conventional TDAP flap. In this procedure, the perforator is dissected free from the muscle, and the flap is tunneled under the most lateral muscle fibers to completely preserve the muscle innervation. Although this is a somewhat more cumbersome and difficult procedure, it affords the greatest pedicle length. The flap reaches the thoracic anterior midline, allowing better flap inseting and positioning of the fat volume. The main disadvantage of this method is the necessity for magnification and specialized instruments. The flap is then deepithelialized. We frequently leave a small cutaneous island to monitor flap viability.

Treatment of donor area

The donor area is closed directly in two layers. Vicryl and monocryl internal sutures are utilized for approximation of wound edges, and interrupted 4-0 nylon is used for the skin. Suction drainage is usually applied for 24-48 hours, but we leave them in place as long as necessary. They are removed when there is no more drainage. As the LD is not mobilized in this technique, wound drainage is generally moderate. It is greater in the cases of “extended TDAP” than in regular TDAP, as there is less undermining of the wound flaps.

Flap transference

In unilateral cases, the flap is transferred directly. When

the flap incision is not in continuity with the breast wound, a tunnel is performed under the lateral breast mound and lateral thoracic wall for passage. The flap is left without final inseting; the back wound is covered, and the patient is turned to dorsal decubitus position, at which time the anterior area is prepared again.

Inseting

The flap is distributed under the breast, enveloped and fixed at the borders with interrupted absorbable sutures. If the nipple-areolar complex must be reconstructed, a round skin island, 6 cm in diameter, is left in the flap. In cases of adenomastectomy sequelae, when the nipple-areolar complex has been preserved, a small skin island is preserved to monitor the flap viability. It is usually placed in the breast submammary sulcus and is eventually removed during a complementary procedure.

Clinical experience

A total of 45 patients underwent partial or complete autologous tissue breast reconstruction from 1996 to 2014 with a TDAP. There were two cases of complete failure due to technical errors and four cases of partial distal tissue suffering or necrosis due to exaggerated flap length. These four cases required partial flap resection, or eventually, complete resection and reconstruction with a new flap. Of the total flaps, 39 survived completely. A simple satisfaction level survey of these patients indicated that 32 of these patients were satisfied with the procedure (82%).

Clinical examples

Case 1 (*Figure 4*): a 43-year-old female patient was scheduled for skin-sparing mastectomy of the left breast. She had previously undergone a lumpectomy on the superolateral quadrant and lymph node biopsy. Autologous tissue reconstruction was performed with a partially de-epithelialized TDAP flap, harvested with an ascending oblique design. This design is similar to the Hammond-type design used for conventional LD-MC flaps. The patient was dissatisfied with the final scar in the donor area but considered the result of the breast shape and volume to be very good. Patient did not continue treatment for nipple-areolar reconstruction or possible complementary aesthetic procedures.

Case 2 (*Figure 5*): a 42-year-old female patient was scheduled for skin sparing mastectomy (SSM) with

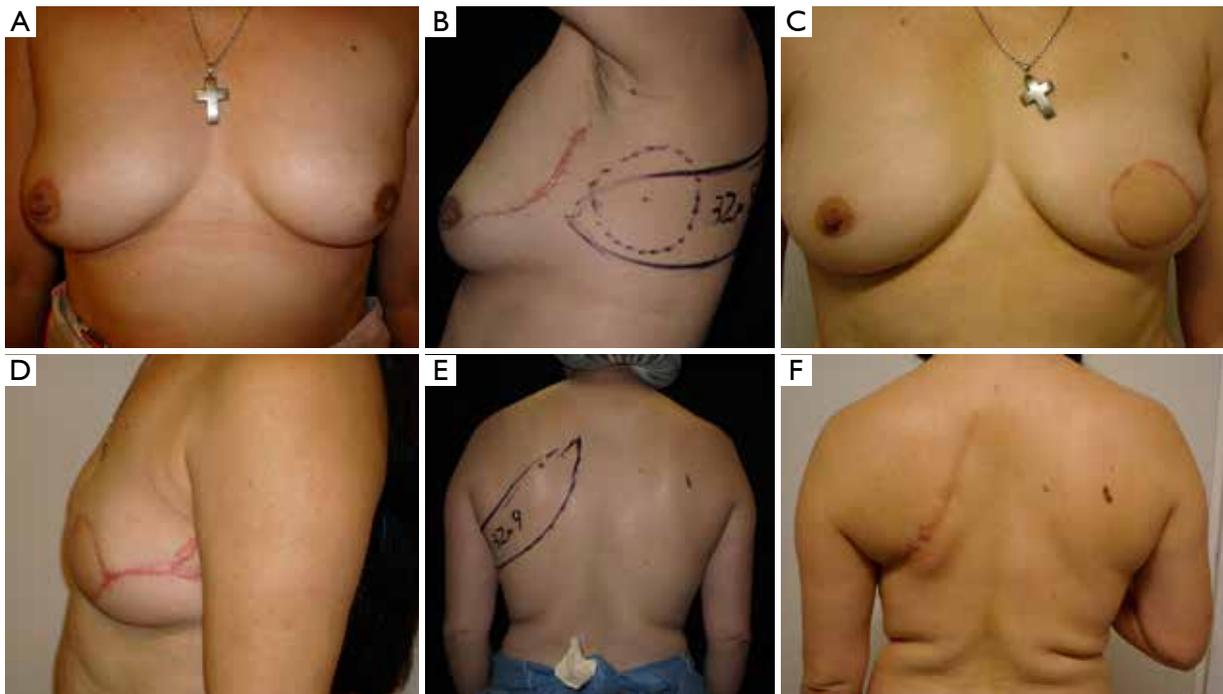


Figure 4 Clinical case 1. (A) Preoperative frontal view; (B) lateral view; (C) postoperative frontal view; (D) lateral view; (E) donor area preoperative view; (F) postoperative view.

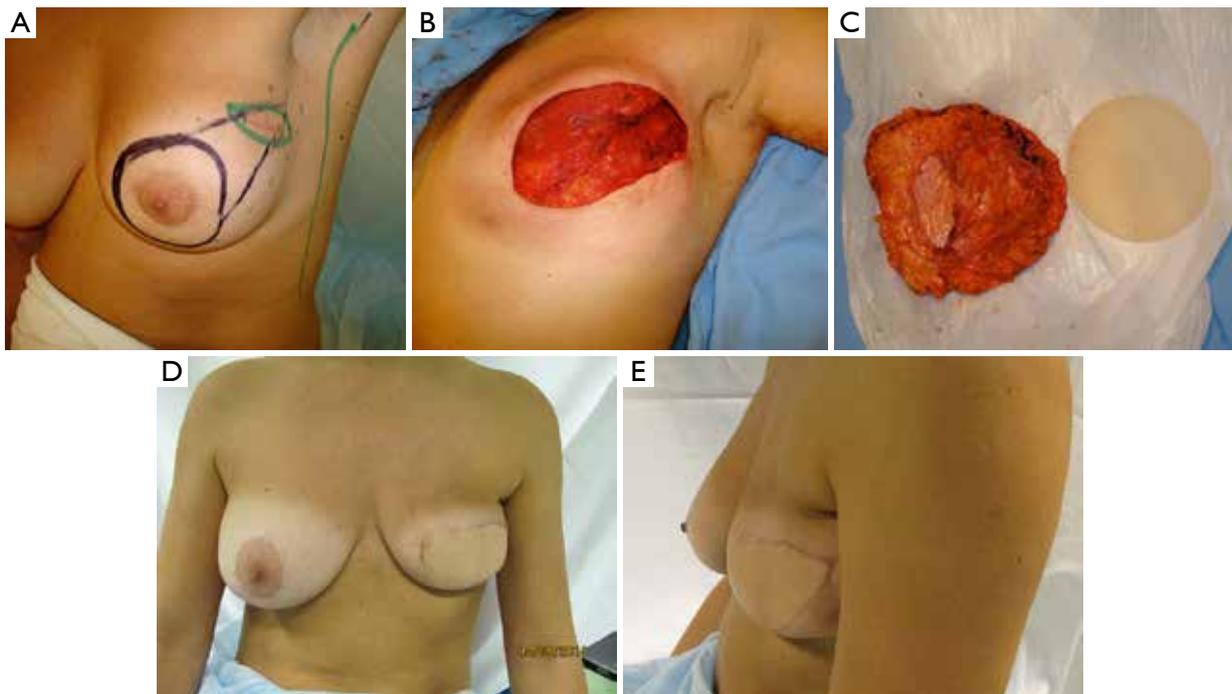


Figure 5 Clinical case 2. (A) Preoperative view: design of the SSM with extension to the upper lateral quadrant to incorporate the biopsy entrance point; (B) mastectomy defect; (C) gland and implant resection; (D) postoperative frontal view; (E) lateral view. SSM, skin sparing mastectomy.

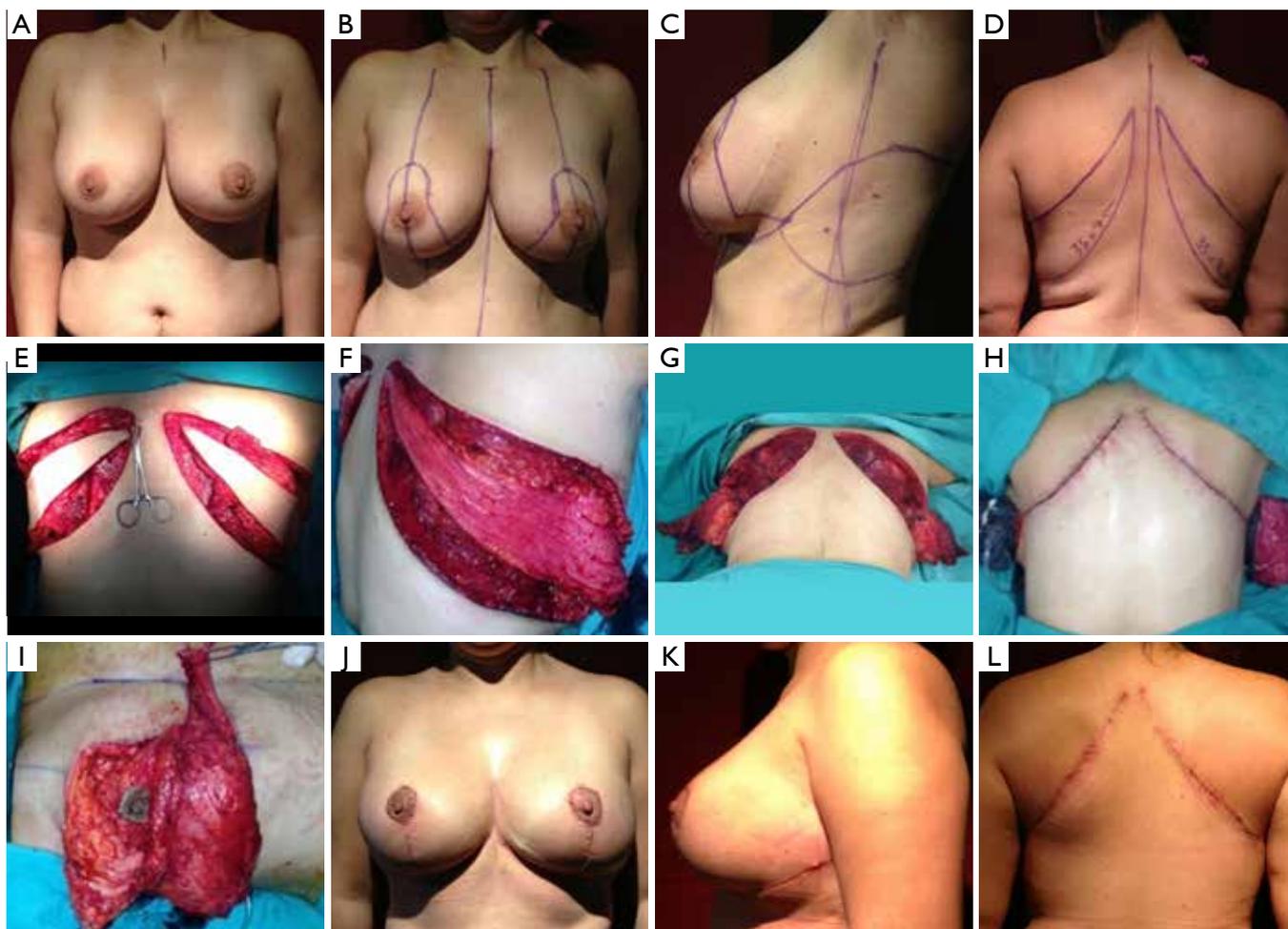


Figure 6 Clinical case 3. (A) Preoperative frontal view; (B) design of SRM; (C) lateral view of the extended TDAP; (D) posterior view; (E) flap elevation; (F) flap de-epithelialization; (G) flaps are turned over; (H) closure donor area; (I) flap is placed inferior to the SRM; (J) postoperative frontal view; (K) postoperative lateral view; (L) donor area. TDAP, thoracodorsal artery perforator flap.

extension to the superolateral pole to involve the biopsy area within the resection. The patient had 275 cc silicone implants placed several years prior, which were explanted at the same procedure. The contralateral right implant was left in place. An immediate reconstruction was performed with an extended TDAP, partially de-epithelialized, with no implant. It is possible to compare the final immediate volume obtained with the contralateral side that still has a 275 cc implant. The patient was satisfied with the result. She eventually underwent explantation of the contralateral implant, as advised by the oncologist.

Case 4 (*Figure 6*): a 41-year-old female patient was scheduled for a bilateral siliconoma resection. A skin-reducing mastectomy was planned with an inverted T pattern and an inferior pedicle. A bilateral de-epithelialized

TDAP flap with an ascending oblique design was performed for volume replacement. The flaps were elevated simultaneously by two operating teams that reduced the operating time significantly. The flap was transferred with a flip-over technique (19). The patient was completely satisfied with the final result and the donor area.

Discussion

Autologous tissue breast reconstruction is considered a reliable surgical technique. The LD-MC flap has been the “workhorse” for treating difficult or complicated cases as well as for primary reconstruction. Lipotransference to the conventional LD-MC flap has been reported to increase its initial volume and improve autologous breast reconstruction (20,21). Morbidity

of the donor area might be considered a disadvantage, albeit to a minimal extent, for this procedure. Muscle harvesting remains controversial, with conflicting favorable and negative reports on the technique. As mentioned above, the final scar of the LD flap may be placed more posteriorly with an adequate horizontal design. The TDAP design must incorporate the first perforator resulting in a more anteriorly placed final scar.

The incorporation of the TDAP flap, a derivation of the perforator flap era and which was initially described as “the LD-MC flap without muscle”, permits harvesting of the same skin and subcutaneous tissue area normally obtained with the conventional LD-MC flap without the muscle, thereby avoiding the possible morbidities of this procedure. The presence of the muscle might be considered important considering the necessity of volume for the reconstruction. However, the most voluminous part of the muscle remains under the axilla after transferring the flap to the anterior area. The muscle transferred to the breast mound is quite thin, with minimal volume contribution.

The incidence of seroma is almost none in regular TDAP; it is slightly higher in extended TDAP due to the necessary undermining of the donor area but lower compared to the LD flap. In addition, it is not associated with any impairment of shoulder motion. No aesthetic sequelae at the anterolateral border of the muscle on the lateral side are evident in normal-weight women. Steatonecrosis, distal tissue necrosis, and distal tissue suffering are the most common complications. They can be avoided by adequate resection of the distal part of the flap until healthy red bleeding is observed from the dermis. Medial breast volume reconstruction requires a conventional thoracodorsal perforator flap with full dissection of the pedicle in order to reach the midline with well-irrigated tissue.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Magnetic resonance angiography in perforator flap breast reconstruction

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Abstract: Magnetic resonance angiography (MRA) is an extremely useful preoperative imaging test for evaluation of the vasculature of donor tissue to be used in autologous breast reconstruction. MRA has sufficient spatial resolution to reliably visualize 1 mm perforating vessels and to accurately locate vessels in reference to a patient's anatomic landmarks without exposing patients to ionizing radiation or iodinated contrast. The use of a blood pool contrast agent and the lack of radiation exposure allow multiple studies of multiple anatomic regions in one examination. The following article is a detailed description of our MRA protocol developed with our radiologists with examples that illustrate the utility of MRA in perforator flap breast reconstruction.

Keywords: Perforator flap breast reconstruction; magnetic resonance angiography (MRA); imaging; deep inferior epigastric perforators (DIEP); superficial inferior epigastric artery (SIEA); deep circumflex iliac perforator flap (DCIP); profunda artery perforator (PAP); gluteal artery perforator (GAP); lumbar artery perforator (LAP); thoracodorsal artery perforator (TDAP); septocutaneous tensor fasciae latae (scTFL)

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Introduction

Preoperative anatomic imaging of vasculature markedly enhances the ability of a surgeon to devise a surgical strategy before going to the operating room. Prior to the era of preoperative perforator imaging, a surgeon had little knowledge of an individual patient's vascular anatomy until surgery was well underway. As a result, perforator selection could be a tedious and stressful decision process that occurred in the operating room at the expense of operating time and general anesthetic requirement.

Doppler

As technology has advanced, surgeons explored various modalities for preoperative imaging. Initially, a handheld Doppler ultrasound was solely used to attempt to locate

perforating vessels. A Doppler ultrasound is portable and simple to use but cannot differentiate perforating vessels from superficial and deep axial vessels, large perforators from small ones. It cannot accurately determine the location that perforators exit the fascia, or provide information on the anatomic course of a vessel (1,2). In comparison, color Duplex sonography provides more detailed information about the anatomy of the vessels, but requires highly trained technicians with knowledge of perforator anatomy and is time-consuming (2). The technique's most crucial drawback is an inability to produce anatomic images in a format that a surgeon can easily and independently view.

Computed tomographic angiography (CTA)

CTA is a modality that can demonstrate vessel anatomy,

assess vessel caliber, accurately locate perforators, and produce anatomic images in a format that a surgeon can easily and independently view. Although CTA can be performed quickly in as little as 15 min (1,2), it requires that patients must be exposed to ionizing radiation. Radiation exposure precludes multiple repeated imaging studies in one examination. CTA may expose patients to excessive and potentially unnecessary radiation (3-6). Patients with breast cancer may have a heightened concern for any factor that can potentially increase the risk of developing a second cancer and may perceive the risks of radiation exposure even more negatively. Patients with breast cancer gene (BRCA) mutations, which confer an increased risk of developing both breast and ovarian cancer, are especially concerned about receiving radiation to the abdomen. Also, iodinated contrast to enhance vessels for CTA can be associated with small, but real risks of anaphylaxis and nephrotoxicity (7,8).

Magnetic resonance angiography (MRA)

Magnetic resonance imaging (MRI) uses a magnetic field to uniformly align the spin of hydrogen atoms in tissue. The subsequent application of a radiofrequency pulse results in release of energy as hydrogen atoms return to their relaxed state. MRI coils detect the released energy, and computer software processes the data into anatomic images. Exposure to a magnetic field or radiofrequency pulse with MRI has not been linked to the development of cancer (9). A paramagnetic contrast agent (gadolinium-containing) is injected to enhance vessels. Our previous papers demonstrated that MRA accurately locates perforating vessel branches and shows vessel anatomy in a format that is easily viewed by a surgeon (10-13). However, because MRI does not use radiation, this modality has an important advantage over CTA of allowing multiple series of images to be obtained.

Disadvantages of MRA are contraindication to use with a cardiac pacemaker or very claustrophobic patients. Most patients with claustrophobia can tolerate a MRI with an anxiolytic. Continuing advances in MRA have decreased the procedure time for a single donor site to as little as 20 min, and decreased the actual acquisition scan time to 20 s (11,13-15). However, the examination time could be 40 min for multiple donor site studies.

MRA contrast agents

Gadolinium-containing contrast agents used for MRA have several distinct advantages over iodinated contrast agents

used for CTA. The incidence of an acute allergic reaction to iodinated contrast is 3%, which is much higher than the 0.07% incidence of allergic reaction to gadolinium contrast (7,16). Unlike gadolinium contrast agents, iodinated CT contrast agents can induce renal insufficiency even in patients with normal renal function (8,17). Gadolinium contrast agents can potentially induce nephrogenic systemic fibrosis (NSF), also called nephrogenic fibrosing dermopathy. However, reports of NSF have been limited to patients with impaired renal function (18-20). Patients with an acute kidney injury or chronic severe renal disease (glomerular filtration rate <30 mL/min/1.73 m²) are considered most at risk (18). NSF is a very rare disease with about 380 cases reported worldwide (19,20). Although, patients undergoing elective microsurgical free flap are generally healthy and thus are not at significant risk for developing NSF, a creatinine level is drawn preoperatively in patients with a history of hypertension, diabetes, renal disease or any other indication that renal function may be impaired.

Advances in gadolinium contrast agents with blood pool contrast agents have resulted in a decreased amount of contrast required, improved MR images, and increased even further the number of donor sites that can be imaged in one study. The MRA protocol developed with our radiologists uses 10 mL of gadofosveset trisodium, a blood pool MRI contrast agent. Prior to using this blood pool agent, 20 mL (instead of 10 mL) of gadolinium contrast (gadobenate dimeglumine) was required. Gadofosveset trisodium is a gadolinium chelate that reversibly binds to serum albumin with ~90% binding fraction, and effectively stays within the blood pool with a redistribution half-life of 28 min (21). It also demonstrates greater T1 relaxivity that allows administration of a 4-fold lower molecular dose while still conferring greater vascular enhancement compared to most other gadolinium chelates. This virtually eliminates the risk of NSF (22).

Gadofosveset improves vessel-to-muscle contrast ratio and vessel sharpness, mainly due to preferential enhancement of vessels compared to muscle derived from blood pool distribution of gadofosveset (23). This results in significantly improved images of the intramuscular course of perforating vessels, which gives valuable information for choosing the best perforating vessel and planning the intramuscular dissection.

Because blood pool contrast agents are bound to albumin, with a redistribution half-life of 28 min, there is a significantly increased amount of time to acquire images (24). This affords the opportunity to assess many

donor sites for autologous breast reconstruction in a single examination. A patient has time to turn from the prone to supine positions to image the posterior (thigh, buttock, back) and anterior (abdomen) donor sites, respectively. In addition, flap volume estimates can be more accurately determined at both anterior and posterior donor sites because the imaging is acquired with the patient in the supine and prone positions, respectively, so that the tissue is not compressed. For example, buttock flap volumes are calculated with the patient in the prone position and abdominal deep inferior epigastric perforators (DIEP) flap volumes are calculated with the patient in the supine position. Knowledge of the vessels and flap volume at each donor site assists with discussion with breast reconstruction candidates on selecting the most suitable flap donor sites. Moreover, a patient who is found to not be a candidate for an abdominal perforator flap based on imaging findings, or suddenly changes her preference of donor site, or has a flap failure and requires another perforator flap reconstruction does not require further studies.

MRA protocol

MRA is performed on a long-bore, self-shielded 1.5T scanner (GE Signa 14.0, Waukesha, WI) using an eight channel phased array coil. The field of view is individualized, but usually extends from 5 cm above the umbilicus to the upper thigh, and transversely is set to match the width of the patient. After acquiring a three plane localizer, axial and coronal T2-weighted single shot fast spin echo images are acquired to screen for unexpected pathology and to help characterize any lesions detected on post gadolinium scans. Most of these patients have history of breast cancer, and metastatic disease is detected occasionally. This sequence is also helpful to confirm the central position of umbilicus in prone position. A transverse pre and post contrast arterial phase 3D liver accelerated volume acquisition (LAVA) sequence is acquired with imaging parameters of: TR/TE/flip =3.9/1.9/15, bandwidth =125 kHz, slice thickness =3 mm reconstructed at 1.5 mm intervals using 2-fold zero interpolation (ZIP2), matrix =512×[128-256], parallel acceleration factor =2. Pre-contrast imaging is important to determine adequacy of fat suppression. Central frequency and shim field of view can be adjusted as necessary to ensure effective fat suppression over the subcutaneous tissues of interest if Dixon fat-water separation is not available. The arterial phase imaging is bolus tracked by automated triggering (Smartprep) and scanning is initiated after

arrival of contrast in the suprarenal aorta. Totally 10 mL of gadofosveset trisodium blood pool MRI contrast agent is injected, followed by 20 mL of normal saline at a rate of 1 mL/s. Hand injection is preferred, especially if there is a tenuous IV, because approximately 1/3 of patients may experience some sensation at the injection site or in the pelvis related to the ionic contrast agent (24). K-space is mapped sequentially with the absolute center of k-space collected in the middle of the scan, which is about 20 s after bolus detection for a 35-s scan duration with a 5-s pause for breath holding instruction. This is important to provide time for the contrast to reach and fill perforating arteries. However, only the largest perforator arterial/vein bundles are adequately seen on this sequence. This is followed by equilibrium phase transverse 3D LAVA at higher resolution without parallel imaging using following parameters: TR/TE/flip =4/1.9/15, matrix =512×512×[172-240], bandwidth =125 kHz, slice thickness =3 mm reconstructed at 1.5 mm intervals using ZIP2. Phase encoding is set to the right-left direction. This is the primary sequence utilized to generate reconstructions and create reports and also serves as a reference for the plastic surgeons. It is acquired with free breathing and typically requires 3-5 min acquisition duration with 0.9×0.9×3 mm³ acquired voxel dimension and 0.9×0.9×1.5 mm³ reconstructed voxel dimensions. Thereafter, a lower resolution coronal and sagittal plane LAVA is acquired with acquisition matrix of 512×256 and 512×224 respectively, in a single breath hold and parallel acceleration factor of two to evaluate internal organs.

First, the planned donor site is imaged, followed by a single high spatial resolution equilibrium phase imaging of other potential donor sites using free breathing 3D LAVA sequence described above. A typical complete perforator flap MR examination, including abdomen, buttocks and upper thigh, can be 45 min.

After screening axial and coronal single shot fast spin echo images for unexpected pathologies, the arterial phase images are reviewed to determine number of perforators available and to look for any enhancing lesions. High spatial resolution equilibrium phase images are used for final perforator evaluation, as perforators are best visualized on these images. The equilibrium phase series is loaded on a computer workstation (GE Advantage Windows 4.4, Milwaukee, WI) for post-processing. Coronal, sagittal and surface rendered reformatted images are generated. The reference point and each candidate perforator artery/vein bundle are identified. The diameter and perforator exit location at the point where the vessel pierces the superficial



Figure 1 Coronal MIP MRA abdomen (25). (A) Type 1 deep inferior epigastric branching pattern; (B) type 2 deep inferior epigastric branching pattern on both sides of the abdomen with a medial and lateral branch denoted by 1 and 2; (C) type 3 deep inferior epigastric branching pattern with 1, 2, 3 denoting multiple branches from the left deep inferior epigastric. MIP, minimum intensity projection; MRA, magnetic resonance angiography; SIEA, superficial inferior epigastric artery.

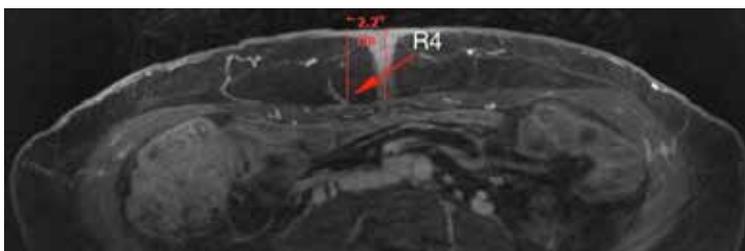


Figure 2 Axial MRA abdomen (25). DIEP location measured at the anterior rectus fascia in relation to the center of the umbilicus at the fascia level. MRA, magnetic resonance angiography; DIEP, deep inferior epigastric perforators.

fascia and enters into subcutaneous fat are noted. The cephalad/caudal and right/left distances of each perforator exit site relative to the reference point are calculated to create a perforator location coordinate. The intramuscular course and length of each perforator is measured to predict vascular pedicle length. Finally, a predicted flap volume is calculated on the same workstation assuming an elliptical geometry on a slice by slice basis.

Coordinates identifying the location of the perforating arteries on the axial images are superimposed and displayed on volume rendered 3D reconstructed images and coronal 3D minimum intensity projection (MIP) images. These images are especially helpful to locate the perforator vessels during preoperative surface marking and then intraoperatively.

Discussion on the finer points of MRA and perforator selection

Vessel caliber in conjunction with a centralized location on

the flap is the most important factors for optimal perforator selection at every donor site. Caliber measurements are uniformly performed at the point where a vessel exits the superficial fascia to perfuse the flap tissue. Location measurements are performed in reference to a landmark at each donor site. Specific considerations regarding each donor site are presented below.

Abdomen

First, the deep inferior epigastric vessel branching pattern is identified on each hemiabdomen. A coronal MIP image (*Figure 1*) best illustrates the branching pattern and is included in the report. This image is helpful for confirming vessel patency, and for planning when a double flap used in combination to reconstruct one breast is anticipated. Next, the location of the largest DIEP are identified at the point of exit from the anterior rectus fascia, and is measured in reference to the center of the base of the umbilical stalk as seen in *Figure 2*. Vessel caliber measurements are also

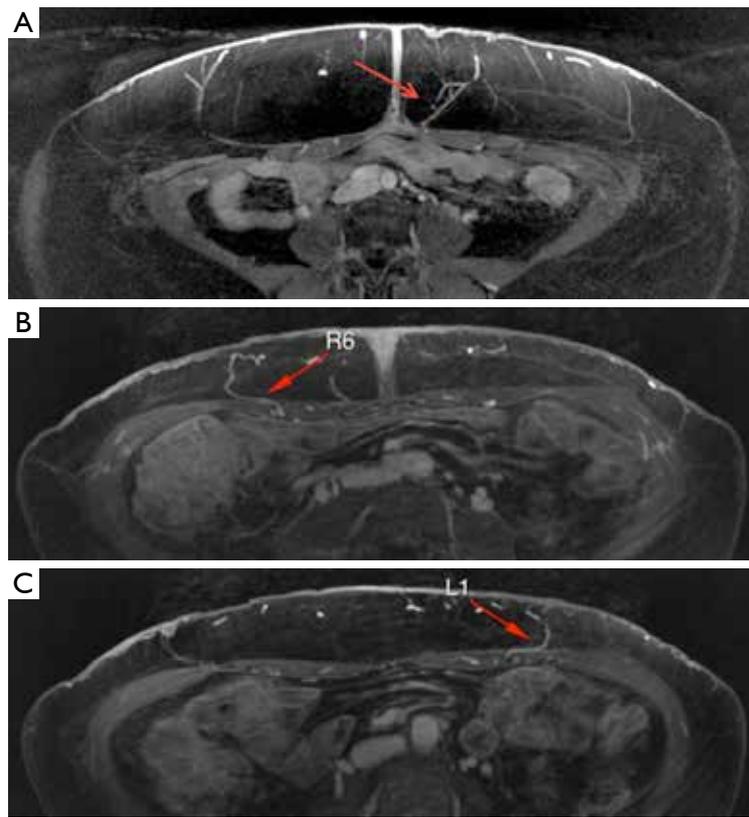


Figure 3 Axial MRA abdomen (25). (A) Arrow pointing to left paramuscular (septocutaneous) DIEP; (B) arrow pointing to right DIEP with short IM course; (C) arrow pointing to DIEP with a longer intramuscular course, and MRA provides helpful information that the perforator has a medial course before it courses caudal. MRA, magnetic resonance angiography; DIEP, deep inferior epigastric perforators.

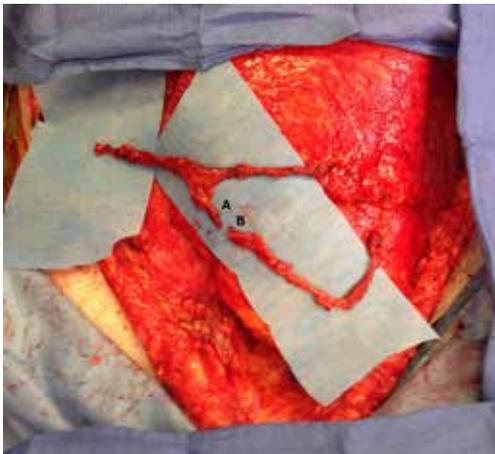


Figure 4 Photograph of a DIEP pedicle lateral branch (marked as A) adjacent to the origin of a second DIEP pedicle (marked as B) in preparation for microsurgical anastomosis, in which one DIEP flap will perfuse the second DIEP flap (flow-through flap) (25). DIEP, deep inferior epigastric perforators.

performed just above the anterior fascia level.

Finally, the intramuscular course or paramuscular (septocutaneous) course is examined, as seen in *Figure 3*. The vessel course provides information for a surgeon to anticipate a tedious or straight-forward dissection. The improved visualization of intramuscular perforator course on MRA allows for preoperative decision making on harvesting more than one perforator (e.g., whether muscle transection will be required and if the pedicle has a large caliber to facilitate pedicle reanastomosis to avoid muscle transection to harvest two perforators). It also enhances the ability of a surgeon to plan for double flaps used together to make one breast, in which one flap vessel pedicle can be connected to a second flap vessel pedicle at a branching point or at the cephalad continuation of the pedicle beyond the perforator (*Figure 4*).

The location of the largest deep circumflex iliac perforators may also be identified and are measured in reference to the umbilicus (*Figure 5*). The perforator

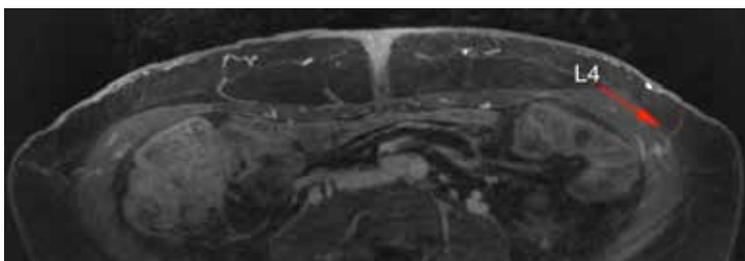


Figure 5 Axial MRA abdomen (25). Arrow points to left DCIP. MRA, magnetic resonance angiography; DIEP, deep inferior epigastric perforators.

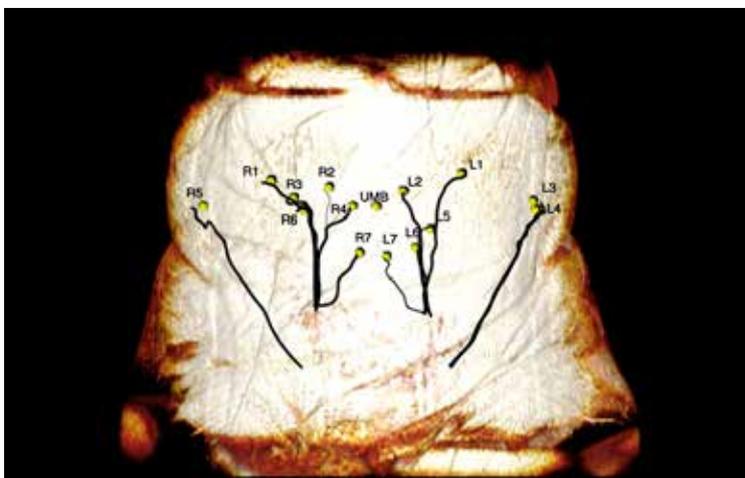


Figure 6 3D volume rendered MRA abdomen with DIEP, DCIP, and umbilicus locations, and vessel courses superimposed (25). MRA, magnetic resonance angiography; DIEP, deep inferior epigastric perforators.

locations and course are then superimposed onto a volume rendered 3D reconstructed image, and this image is included in the report (*Figure 6*).

The superficial inferior epigastric artery (SIEA) is evaluated and noted in the radiology report whether the SIEA shares a common origin with the superficial circumflex iliac vessels, as this will result in a larger caliber vessel for anastomosis.

A clinical example of the utility of MRA in planning bilateral breast reconstruction using an abdominal perforator flap in a patient with a midline and two right paramedian scars from several bowel surgery operations is shown in *Figure 7*.

Spiral imaging may be employed by the radiologist to subtract venous flow to only view the SIEA (*Figure 8*), but this is not routinely done. The largest superficial inferior epigastric vein (SIEV) is identified on each hemiabdomen, and the location is measured from the umbilicus at 12 cm

inferior to the umbilicus.

The branching pattern of the perforating vessels within the subcutaneous fat is also evaluated. The two point Dixon methods for fat/water signal separation at 1.5 T and LAVA Flex at 3T are methods used by radiologists to suppress the fat signal, resulting in clearer images of DIEP arborization into the fat (*Figure 9*). In a unilateral reconstruction, it is helpful to see a medial row DIEP with branches crossing into the subcutaneous fat on the contralateral abdomen because zone III is more likely to be well-perfused, as seen in *Figure 10*. *Figure 11* shows a DIEP with a very lateral course into the subcutaneous fat and a corresponding photograph of a patient with inadequate venous drainage of the medial tissue. A different perforator selection and/or indocyanine green injection would have prevented this. Usually DIEP branches can be visualized in close proximity with superficial inferior epigastric venous branches, which may theoretically provide improved venous drainage

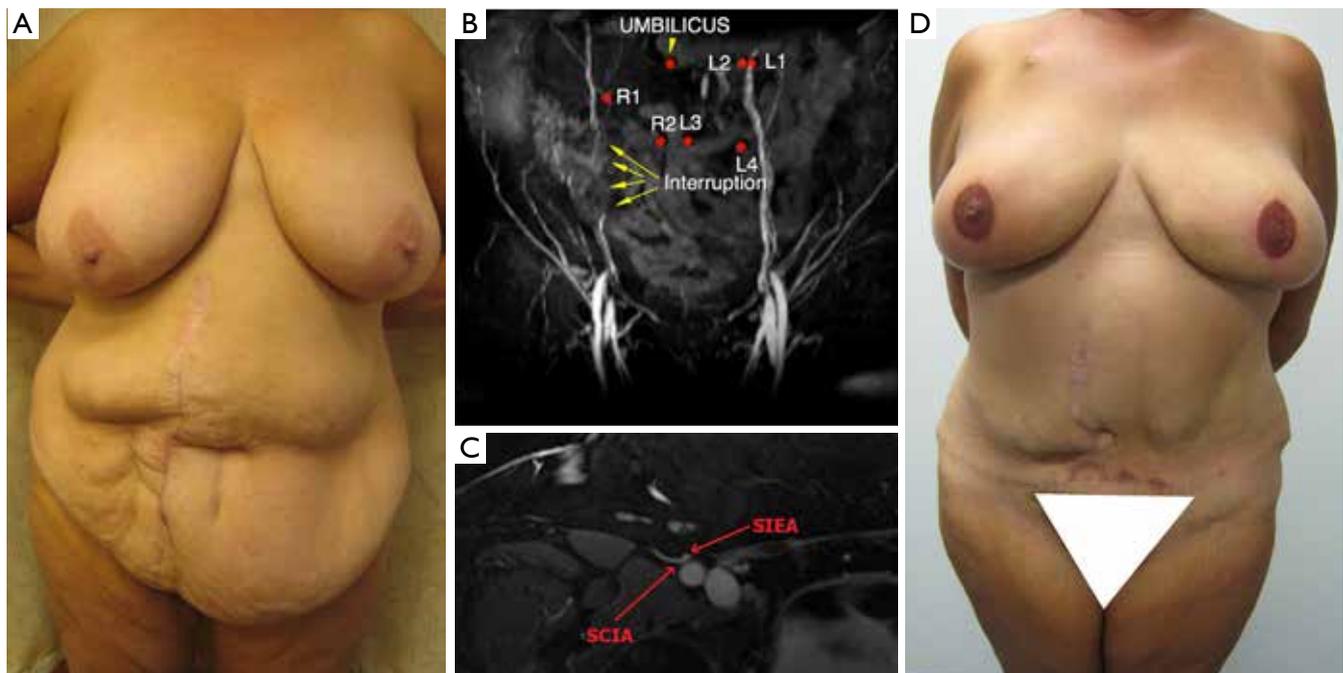


Figure 7 (A) Photograph of patient for bilateral breast reconstruction with a midline and two right paramedian scars from several bowel surgery operations, who desired abdomen as donor site. The estimated hemi-abdominal flap volume was 1,000 g and estimated thigh flap volume was 325 g. (B) Coronal MRA abdomen. Arrows point to interruption in contrast in right DIEP pedicle secondary to previous abdominal surgery. (C) MRA abdomen. Common origin of SIEA and SCIA measuring 2.2 mm. (D) Postoperative photograph of patient with successful bilateral reconstruction with abdominal tissue (left breast SIEA flap and right breast DIEP flap) Adopted from (25). MRA, magnetic resonance angiography; DIEP, deep inferior epigastric perforators; SIEA, superficial inferior epigastric artery.

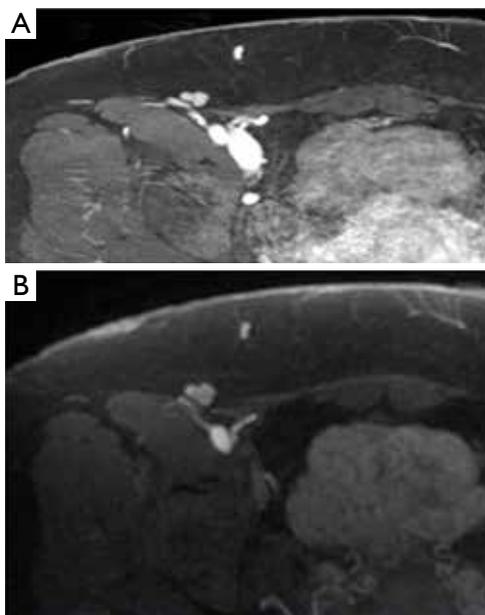


Figure 8 MRA abdomen (25). (A) Arterial and venous vessels enhanced; (B) venous vessel enhancement subtracted. MRA, magnetic resonance angiography.

through connections (*Figure 12*).

Post-processing software is used by the radiologist to calculate projected abdominal flap volume (*Figure 13*). To increase accuracy of the estimated flap volume, a radiologist must first be educated in the typical markings and dimensions of an abdominal flap.

Buttock

A vitamin E capsule is placed on the skin surface at the top of the gluteal crease as a reference point from which the perforator locations are measured. The largest perforators from the superior gluteal artery perforator (SGAP) and inferior gluteal artery perforator (IGAP) are identified. The locations of the perforators are calculated at the point of exiting the superficial fascia and this point is transposed on to the skin surface. Then, the distance of the perforator from the reference point is measured along the curved skin contour of the buttock (*Figure 14*). These measurements are taken with the patient in the prone position for increased accuracy because of the compliance of the gluteal tissue. Finally the

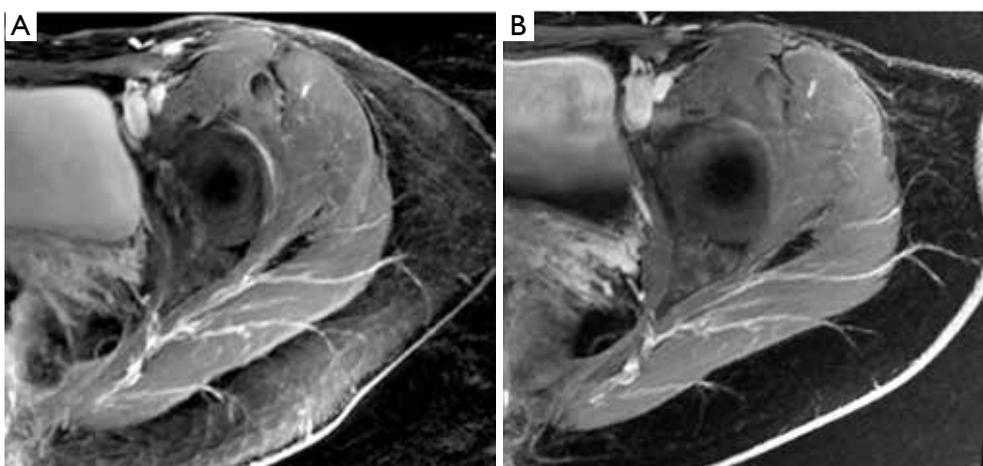


Figure 9 Axial MRA abdomen (25). (A) Inhomogenous fat suppression; (B) LAVA Flex used on a 3T resulting in improved visualization of DIEP arborization into the fat. MRA, magnetic resonance angiography; DIEP, deep inferior epigastric perforators.

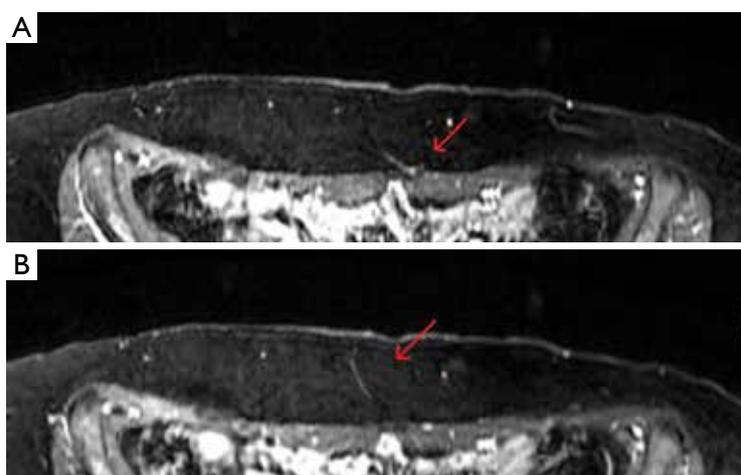


Figure 10 Axial MRA abdomen (25). Arrow pointing to left DIEP that has large branch crossing the midline to perfuse the contralateral abdominal tissue. MRA, magnetic resonance angiography; DIEP, deep inferior epigastric perforators.

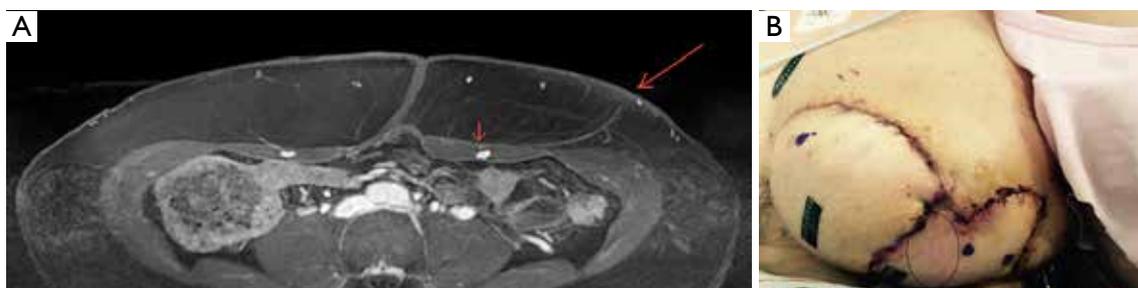


Figure 11 Axial MRA abdomen (25). (A) Short arrow points to location of DIEP exiting anterior rectus fascia. Long arrow points to approximate location that DIEP arborizes into the subdermal plexus. Note the very oblique course laterally. (B) Photograph postoperative day 5 after double DIEP flap in patient with midline abdominal scar. Circle is on medial flap that has decreased venous drainage. A lateral DIEP with very oblique lateral arborization was used. MRA, magnetic resonance angiography; DIEP, deep inferior epigastric perforators.

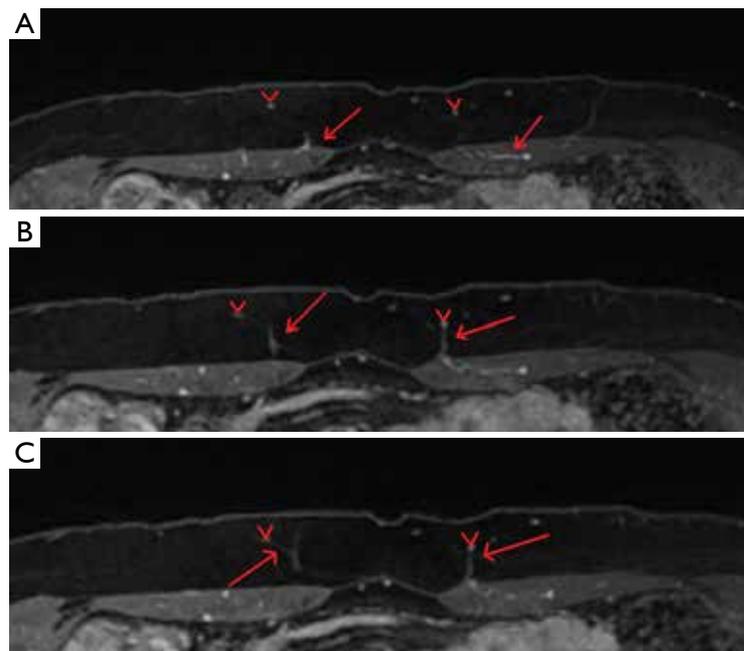


Figure 12 Axial MRA abdomen (25). “V” denotes SIEV, Arrows pointing to bilateral DIEPs. (A) Axial MRA; (B) left DIEP meeting SIEV; (C) right DIEP branch also meeting SIEV. MRA, magnetic resonance angiography; DIEP, deep inferior epigastric perforators; SIEV, superficial inferior epigastric vein.

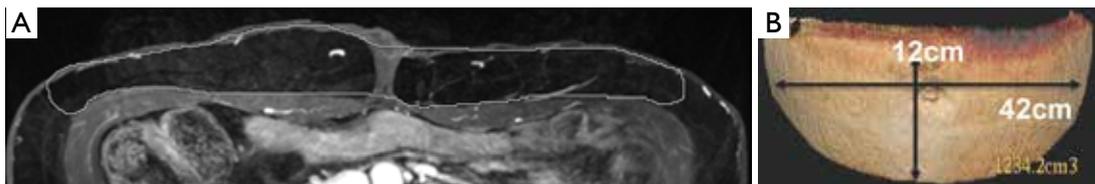


Figure 13 (A) Axial MRA abdomen with subcutaneous fat manually outlined to calculate abdominal flap volume; (B) 3D volume rendered abdominal flap. MRA, magnetic resonance angiography (25).

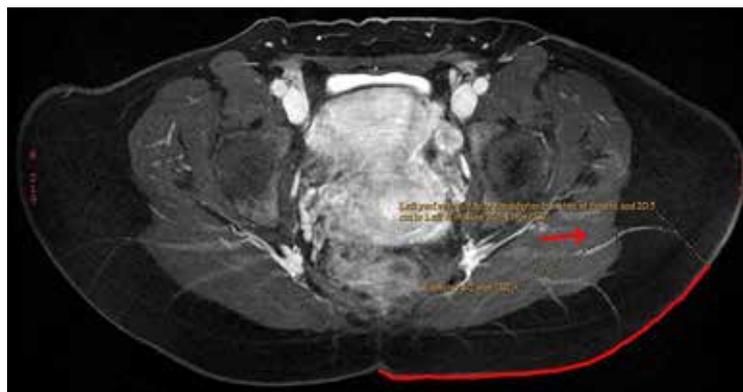


Figure 14 Axial MRA buttock with arrow pointing to gluteal perforator (25). Distance from midline reference point is calculated by measuring the distance along the curved skin surface with patient in the prone position to increase accuracy. Vessel caliber is calculated at superficial fascia exit point. MRA, magnetic resonance angiography.

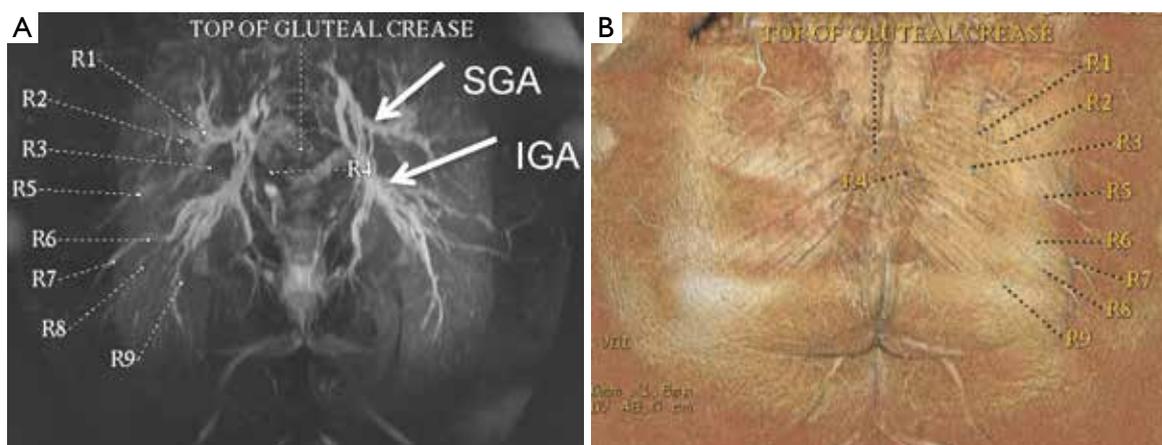


Figure 15 (A) Coronal MRA buttock with SGAP and IGAP locations and reference point location marked; (B) 3D volume rendered MRA buttock with perforator locations and reference point superimposed (25). MRA, magnetic resonance angiography; SGAP, superior gluteal artery perforator; IGAP, inferior gluteal artery perforator.

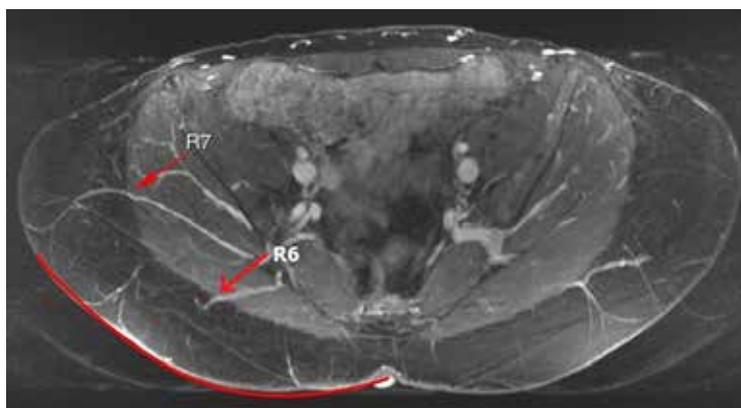


Figure 16 Axial MRA buttock showing two superior gluteal perforators (25). R7 is located more lateral than R6 and has a longer intramuscular course, yielding a longer pedicle. MRA, magnetic resonance angiography.

perforator locations and reference point are superimposed onto a volume rendered 3D reconstruction of the buttock in the prone position so that the perforator location markings can be replicated preoperatively (*Figure 15*).

The placement of the buttock flap skin paddle is significantly influenced by optimal perforator location. The goal is to design a flap that incorporates the optimal perforator and a back-up option. Because there are usually many large caliber perforator options in the buttock, vessel location is an important determining factor in selecting the optimal vessel, taking scar location into account. Laterally positioned perforators will result in a longer pedicle, which is advantageous for flap inseting (*Figure 16*). In addition, more lateral flaps that may spare the central aesthetic unit in

superior buttock flaps or the medial cushioning fat in lower buttock flaps. In bilateral flaps, an attempt is made to design flaps that will result in symmetrical scars by locating large perforators at a similar position bilaterally. As the familiarity of the radiologist increases with typical flap dimensions, the radiologist may calculate predicted upper and buttock flap volumes. Generally, an elliptical designed pattern measuring 6 cm in vertical dimension \times 20 cm in transverse dimension is used by the radiologist.

Thigh

The upper thigh is imaged from the mid gluteal region to the mid-thigh [about 12 cm caudal to the inferior gluteal

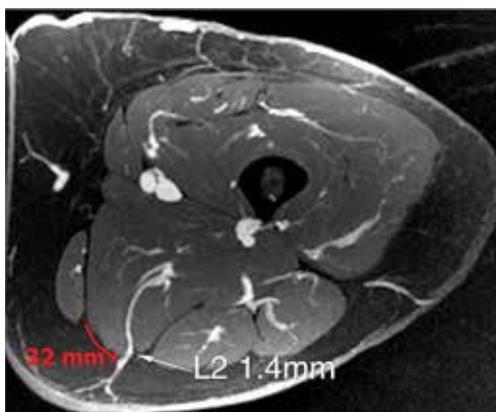


Figure 17 Axial MRA thigh with arrow pointing to profunda femoral artery perforator and distance from the posterior edge of the gracilius muscle (G) is measured (25). MRA, magnetic resonance angiography.

crease (IGC)]. A transversely-oriented upper thigh flap is designed from medial to predominantly posterior thigh tissue to avoid the more anteriorly located lymphatic channels. A typical elliptical flap design for calculating thigh volume is 6 cm × 20 cm. The reference point from which the perforator locations are measured is the skin surface along the midline at the bottom of the gluteal crease. The locations of profunda artery perforators (PAP) flap are calculated at the point of exiting the superficial fascia. The perforators are also located in reference to the distance to the posterior edge of the gracilis muscle, to facilitate intraoperative identification of the perforator (*Figure 17*). Similar to gluteal artery perforators, the best PAP have an oblique course through the adductor magnus to yield a longer pedicle. Perforators that course more laterally adjacent to the femoral bone and then course cephalad into the gluteal vessels may be mistaken for PAP. As the patients are operated in the supine position, these gluteal perforators result in a difficult dissection with difficult exposure to yield adequate caliber and length pedicles. Occasionally, there is a large medial circumflex vessel perforating through the gracilis muscle or a paramuscular (septocutaneous) medial circumflex vessel that courses around the gracilis muscle (*Figure 18*). Perforator locations and courses and reference point are transposed onto the skin surface (*Figure 19*).

Sometimes, the lateral upper thigh (LTP flap) has a favorable fat deposition. A septocutaneous (paramuscular) lateral circumflex femoral artery perforators coursing around the tensor fasciae latae is measured in reference to the umbilicus and pubic tubercle (*Figure 20*). The anterior

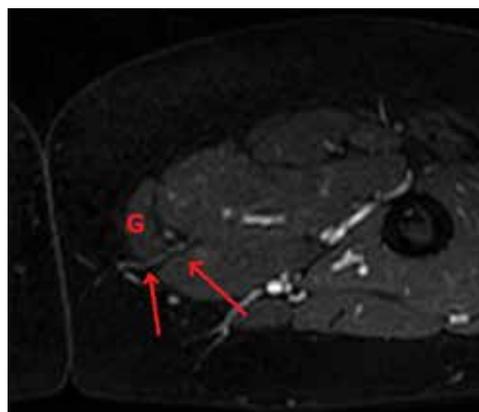


Figure 18 Axial MRA with arrows pointing to a septocutaneous medial circumflex femoral perforator that courses around the gracilis muscle (25). MRA, magnetic resonance angiography.

superior iliac spine (ASIS) was initially used as a reference point, but the ASIS can be difficult to palpate on some patients and lead to inaccuracies.

Lower back

Lumbar artery perforators (LAP flap) are measured in reference to the midline upper gluteal crease. The limiting factor of this flap is the short pedicle length (*Figure 21*). Sometimes, LAP has an oblique course to yield a slightly longer pedicle. In general, these flaps are used as a back up option when the abdomen cannot be used, and the body habitus is not favorable for thigh or buttock flaps.

Upper back

The chest is initially imaged with the patient in the supine position and the arms abducted to avoid compression of the lateral chest soft tissue. In patients with large body mass imaging for bilateral reconstruction, each side can be imaged separately so that one arm can be abducted at a time. It may be necessary for patients with a greater volume of upper arm fat to raise their arms and rest their hands on their head. Images should also be obtained of patients in the lateral decubitus position with the arm raised. Most radiology technicians are not aware that patients are positioned in the lateral decubitus position for the surgical reconstruction and part of the preoperative marking, and are not accustomed to scanning patients in this position. Measurements change significantly with

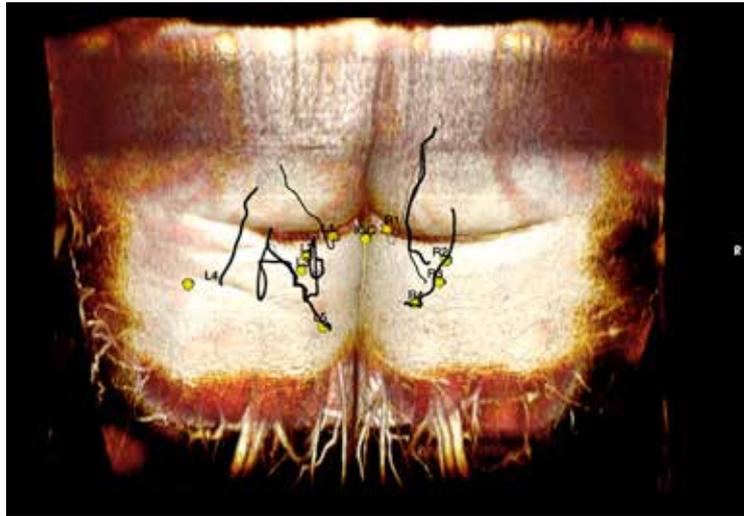


Figure 19 3D volume rendered MRA thigh with perforator locations and course and reference point at the IGC superimposed (25). MRA, magnetic resonance angiography; IGC, inferior gluteal crease.

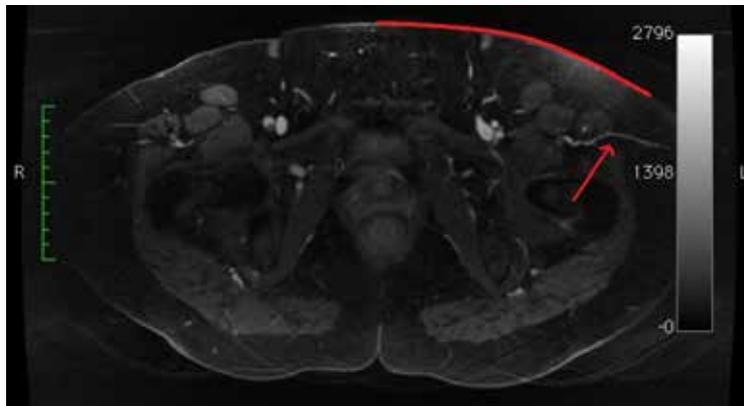


Figure 20 Axial MRA thigh. Arrow pointing to left septocutaneous lateral circumflex femoral perforator (25). MRA, magnetic resonance angiography.



Figure 21 Axial MRA back. Arrow pointing to right lumbar perforator (25). MRA, magnetic resonance angiography.



Figure 22 Axial MRA chest in a patient with a radiated open left chest wound. Arrow points to large thoracodorsal artery perforator (25). MRA, magnetic resonance angiography.

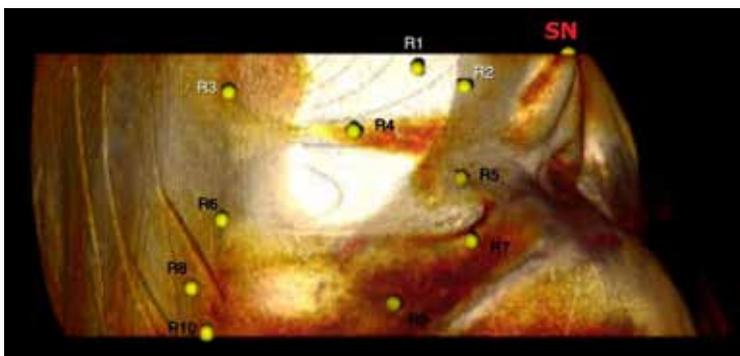


Figure 23 3D volume rendered MRA chest lateral decubitus with perforator locations and reference point at the sternal notch (SN) marked (25). MRA, magnetic resonance angiography.

the patient's position and arm position. Thus, it is crucial for the radiologist to communicate the patient's position in the series that the measurements are taken from. The radiologist should be aware that preoperatively a patient may need to be turned to the lateral decubitus position to mark posteriorly located perforators, and thus this series should be used for posteriorly located perforator measurements. The reference point is the skin surface at the sternal notch. The locations of thoracodorsal and internal mammary artery perforators are measured from a reference point at the sternal notch skin surface (*Figure 22*) and transposed onto the skin surface (*Figure 23*). Thoracodorsal artery perforators (TDAP) usually yield a longer pedicle, which is advantageous for inseting the flap.

Conclusions

The tremendous anatomic variability in the vascular system can make perforator flap breast reconstruction challenging for surgeons at all experience levels. Accurate preoperative anatomic vascular imaging enables optimal perforator selection and improves flap design. Shifting the brunt of the perforator selection process preoperatively improves operating efficiency, which can result in reduced operating time, reduced general anesthesia requirements, and potentially increased flap success (10,11,13). MRA is in our view the preoperative method of choice due to the absence of radiation exposure or iodinated contrast agents, and the ability for serial imaging acquisitions to visualize multiple donor sites with the patient in different positions in one examination.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Preoperative computed tomography angiography for planning DIEP flap breast reconstruction reduces operative time and overall complications

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Background: The approach and operative techniques associated with breast reconstruction have steadily been refined since its inception, with abdominal perforator-based flaps becoming the gold standard reconstructive option for women undergoing breast cancer surgery. The current study comprises a cohort of 632 patients, in whom specific operative times are recorded by a blinded observer, and aims to address the potential benefits seen with the use of computer tomography (CT) scanning preoperatively on operative outcomes, complications and surgical times.

Methods: A prospectively recorded, retrospective review was undertaken of patients undergoing autologous breast reconstruction with a DIEP flap at the St Andrews Centre over a 4-year period from 2010 to 2014. Computed tomography angiography (CTA) scanning of patients began in September 2012 and thus 2 time periods were compared: 2 years prior to the use of CTA scans and 2 years afterwards. For all patients, key variables were collected including patient demographics, operative times, flap harvest time, pedicle length, surgeon experience and complications.

Results: In group 1, comprising patients within the period prior to CTA scans, 265 patients underwent 312 flaps; whilst in group 2, the immediately following 2 years, 275 patients had 320 flaps. The use of preoperative CTA scans demonstrated a significant reduction in flap harvest time of 13 minutes ($P < 0.013$). This significant time saving was seen in all flap modifications: unilateral, bilateral and bipedicle DIEP flaps. The greatest time saving was seen in bipedicle flaps, with a 35-minute time saving. The return to theatre rate significantly dropped from 11.2% to 6.9% following the use of CTA scans, but there was no difference in the total failure rate.

Conclusions: The study has demonstrated both a benefit to flap harvest time as well as overall operative times when using preoperative CTA. The use of CTA was associated with a significant reduction in complications requiring a return to theatre in the immediate postoperative period. Modern scanners and techniques can reduce the level of ionising radiation, facilitating patients being able to benefit from the advantages that this preoperative planning can convey.

Keywords: Computer tomography (CT); microsurgery; microvascular; free flap

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Introduction

The approach and operative techniques associated with breast reconstruction have steadily been refined since its inception, with abdominal perforator-based flaps becoming the gold standard reconstructive option for women undergoing breast cancer surgery. Surgeons continue to look for ways to improve operative outcomes and minimise complications in this surgery, and preoperative planning has offered a means to achieving these outcomes. The decisions made by the surgeon at every stage of planning and raising of a free flap has the potential to affect the success of the operation, and as such techniques and technologies to help surgeons in this decision making process, has led to a gradual refinement in this decision making.

Perforating vessels arising from the deep inferior epigastric artery are anatomically highly variable in regards to their location, course and calibre. Objective measurements can then provide a road-map of these variables prior to surgery starting has been sought, with computed tomography angiography (CTA) becoming the first such objective imaging modality in this role. CTA of abdominal perforators has been demonstrated to be highly sensitive and specific in the identification of perforator site and calibre (1-3). When compared to the technologies that had been previously used, such as the hand-held Doppler probe and duplex sonography, CTA has been demonstrated to have a far greater level of accuracy and objectivity in its findings (4). The use of CTA imaging in deep inferior epigastric perforator (DIEP) flap planning has since been shown to significantly reduce overall operation time, donor site morbidity and increase flap survival (5,6). However these benefits need to be tempered with the obvious disadvantage of exposure to ionising radiation.

In a resource finite healthcare environment the benefit of a preoperative planning tool which has been shown to reduce complications and operative time, should be assessed as to its net cost benefit or disadvantage. However, studies to date have been limited either in power (number of included patients) or in the level of detail in recording times, focusing on those aspects of surgery most likely to be affected by improved planning. The current study thus comprises a cohort of 632 patients, in whom specific operative times (including flap raise time specifically) are recorded and aims to address the potential benefits seen with the use of CT scanning preoperatively on operative outcomes, complications and surgical times.

Methods

A prospectively recorded, retrospective review was undertaken of patients undergoing autologous breast reconstruction with a DIEP flap at the St Andrews Centre over a 4-year period from 2010 to 2014. Patients operated on by one of the two senior authors were identified during this period. CTA scanning of patients began in September 2012 and thus two time periods were compared: 2 years prior to the use of CTA scans and 2 years afterwards. All patients in both time periods had preoperative hand-held Doppler marking either as primary planning or as an adjunct to CTA, and those patients in the second time period underwent CTA imaging and consultant radiologist-led analysis of suitable perforators. Perforator anatomy was described in respect to vessel location, calibre, and length of intramuscular course, with the operating surgeon able to independently decide which perforator was the primary target for flap perfusion. For all patients, key variables were collected including patient demographics, operative times, flap harvest time, pedicle length, surgeon experience and complications. Statistical analysis was undertaken using SPSS (SPSS Inc., IBM Armonk, NY, USA) statistical software. Primary outcomes assessed comprised flap survival, and complications requiring a return to theatre. Data regarding costs were taken directly from the hospital finance department.

Results

In group 1, comprising patients within the period prior to CTA scans, 265 patients underwent 312 flaps; whilst in group 2, the immediately following 2 years, 275 patients had 320 flaps (*Table 1*). The majority of flaps undertaken in both time periods were unilateral reconstructions, accounting for 63% of all reconstructions prior to CTA scans and 67% of reconstructions after. The use of preoperative CTA scans demonstrated a significant reduction in flap harvest time of 13 minutes ($P < 0.013$). This significant time saving was seen in all flap modifications: unilateral, bilateral and bipedicle DIEP flaps. The greatest time saving was seen in bipedicle flaps, with a 35-minute time saving (*Table 2*). There was no difference found in the average pedicle lengths raised between the two groups, ruled out as a confounder. The return to theatre rate significantly dropped from 11.2% to 6.9% following the use of CTA scans, but there was no difference in the total failure rate (*Table 3*). When looking

Table 1 Total number of flaps and patients

Flap type	Before CT		After CT	
	Patients	Flaps	Patients	Flaps
Unilateral	197	197	216	216
Bilateral	36	72	29	58
Unilateral bipedicle	21	21	14	14
Unilateral stacked	11	22	16	32
Total	265	312	275	320

at surgeon grade, there was no difference in flap raise time with the use of CTA between levels of experience, however fellows and registrars demonstrated a significant reduction in complication rates from 4.2% to 0.9%. Two flaps were lost over the entire 4-year period, which was a 0.31% flap loss rate.

Discussion

Since the advent of preoperative imaging with CTA

Table 2 Time for flap harvest

Variables assessed	Flap raise time (mins)			Pedicle length		
	Without CTA	With CTA	Student <i>t</i> -test	Without CTA	With CTA	Student <i>t</i> -test
Reconstruction type ^a						
Unilateral	134	122	0.05*	11.6	10.3	0.067
Bilateral	124	102	0.03*	11.98	9.4	0.021*
Unilateral bipedicle	161	126	0.046*	12.8	11.3	0.068
Unilateral stacked	127	144	0.463	10	8	0.313
Mean	136.5	123.5	0.013*	11.5	9.75	0.515
Grade of surgeon ^b						
Consultant	109	110	0.93	10.9	10.3	0.233
Fellow/registrar	143	139	0.71	12.1	9.8	0.001**
Consultant & fellow	142	143	0.98	11.3	10.25	0.172

*, $P \leq 0.05$; **, $P < 0.001$; ^a, by flap type; ^b, by grade of surgeon; CTA, computed tomography angiography.

Table 3 Clinical outcomes for computed tomographic angiography (CTA) versus no CTA for flap planning

Variables assessed	Complication rate			Flap loss		
	Without CTA	With CTA	Student <i>t</i> -test	Without CTA	With CTA	Student <i>t</i> -test
Reconstruction type ^a						
Unilateral	14.0%	6.2%	0.032*	1.0%	0	0.276
Bilateral	8.3%	8.6%	0.74	0.0%	0	0
Unilateral bipedicle	10.0%	14.0%	0.713	0.0%	0	0
Unilateral stacked	40.0%	13.0%	0.114	10.0%	0	0.212
Mean	11.2	6.9	0.023*	0.64%	0	0.136
Grade of surgeon ^b						
Consultant	3.5%	4.7%	0.069	0.0%	0	0
Fellow/registrar	4.2%	0.9%	0.004*	0.3%	0	0.219
Consultant & fellow	3.5%	1.3%	0.158	0.3%	0	0.32
Total	11.2%	6.9%	0.023*	0.64%	0	0.136

*, $P \leq 0.05$; ^a, by flap type; ^b, by grade of surgeon; CTA, computed tomography angiography.



Figure 1 Preoperative computed tomographic angiogram, with volume rendered technique reconstruction, demonstrating an overview of the major abdominal wall perforators for deep inferior epigastric artery (DIEA) perforator flap planning.

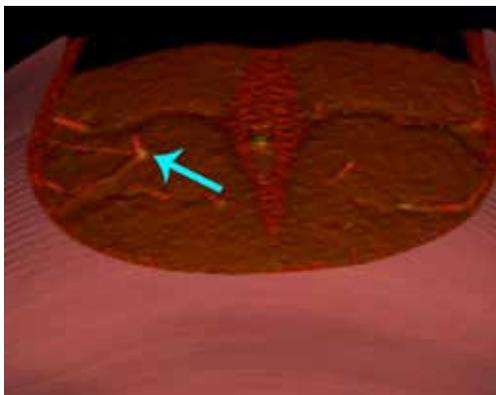


Figure 2 Preoperative computed tomographic angiogram, demonstrating the precise location of emergence of a deep inferior epigastric artery (DIEA) perforator from the anterior rectus sheath.

scanning for DIEP flap planning (7), there have been a number of studies demonstrating both the benefits but also the drawbacks of using this technology in flap planning. Our study is commensurate with the literature with respect to demonstrating a reduction in overall operative time and complication rates (5). We found that with preoperative CTA scans, flap raise was 13 minutes quicker and overall operative time was 44 minutes shorter. The time saved was made even more apparent when looking at the more complex reconstructive cases. Bilateral DIEP flaps were

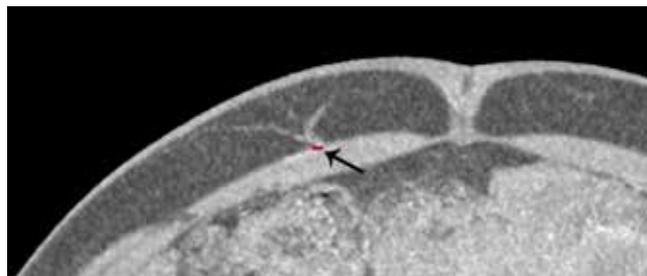


Figure 3 Preoperative computed tomographic angiogram, demonstrating the measurement of luminal calibre of a deep inferior epigastric artery (DIEA) perforator.

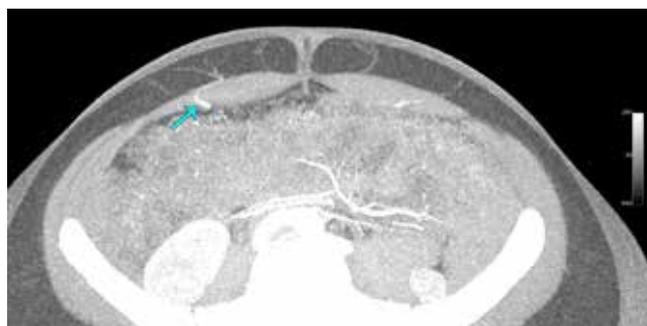


Figure 4 Preoperative computed tomographic angiogram, demonstrating the intramuscular course of a deep inferior epigastric artery (DIEA) perforator.

raised 22 minutes faster and bipediced flaps were raised 35 minutes faster. This decrease in flap raise time has been seen in other published cohorts (6). The ability to plan incisions and plan which perforator to target can be seen to reduce the intraoperative decision making which would otherwise slow down the process (*Figures 1,2*). Given that there was no difference in pedicle length in both groups, this was able to demonstrate that pedicle length was not being sacrificed as a time saving technique (*Figures 3,4*). However, the presence of a road map does not suggest that one should follow it at all costs. Clinical judgement must be used to decide a change of course when necessary. One study of 52 DIEP flaps demonstrated 44% involved intraoperative changes due to features not appreciated on the CTA scans (8). Time saving during surgery is associated with decrease morbidity, furthermore using CTA scans have also been shown to reduce a surgeons operative stress which may well have a causal relationship with the decrease morbidity (9).

The greatest disadvantage to preoperative scanning

with CTA is the exposure to ionising radiation. A CTA of the abdominal wall is estimated to expose the recipient to between 6 and 10 millisieverts (10). There are adjustments and refinements in the literature which can reduce this exposure to 2 millisieverts and still get accurate information, but such modifications can never remove the potential to induce cancer entirely (11). There is clearly a cost-benefit analysis in assessing this risk, and certainly this risk needs to be assessed in a cumulative fashion rather than assessing only the single dose amount each patient would receive from a single scan. Patients diagnosed with cancer who are offered a breast reconstruction will often have already had a number of exposures to ionising radiation, thus accumulating a conferred additional risk with each further investigation (12). Patient factors such as high body mass index will have an impact on the amount of ionising radiation required to undertake a planning CTA. However, the use of CTA could be similarly seen as a useful surveillance tool at the time of reconstruction for delayed cases, with concurrent scan analysis able to identify other pathologies (13). Often patients complete their entire course of cancer treatment and wait 1 to 2 years for reconstruction, and may even be discharged from oncologic surveillance. The use of CTA in this setting provides a reassuring snap shot into the patients' preoperative risk of regional or distant recurrence. In our cohort of 275 women, none were found to have tumour recurrence at the time of surgery; however other incidental findings requiring further investigation did occur. Evidence of recurrent of disease has been reported in the literature (13).

There are options for preoperative imaging with scans that do not yield ionising radiation, with these including colour duplex sonography and magnetic resonance imaging (MRI). These options are useful, but have substantial limitations. A systematic review of CTA and contrast enhanced MRA demonstrated no difference in the modalities' ability to localise perforators preoperatively (14), however resolution of images, availability and cost have made this modality less widely adopted. When comparing colour duplex ultrasonography, many authors have demonstrated this as an operator dependent imaging modality, with highly variable sensitivity (15).

Our data demonstrates that outcomes can be improved, alongside time savings with preoperative CTA scanning. Patients who underwent a pre-operative CTA had 4.3% fewer complications requiring a return to theatre while an inpatient, compared to those who did not undergo a CTA. A significant difference was seen also in the subgroup analysis

of flaps raised by fellow or registrar grade surgeons. This would indicate that a road-map provides a greater resource for guidance to a training surgeon than a consultant. In the 275 patients operated on with a CTA scan, there were no flap losses. Although not significant, given that the previous group only had 2 out of 312 flaps lost, it does demonstrate that stepwise technological and process advancements will continue to lead improvements in outcomes.

When assessing the reduction in time and reduction in complications, the use of preoperative CTA can be seen as potential cost saving process. This is essential, given that in a resource finite healthcare environment cost savings need to be considered. Within our operating theatre, the fixed costs of operating were calculated to be £14 GBP/min. This can be calculated to conclude that using a CTA would save £616 per operation. The isolated cost of the CTA is £500, suggesting that the use of CTA is essentially cost neutral. Although this is far from a formal cost analysis, this can be further expanded to included complications and their costs, given that a take-back to theatre places a significant increase on the overall cost of surgery (16). One study demonstrated that staffing costs accounted for 73% of the total cost of DIEP surgery. If the take back rates can be reduced in addition to the overall costs, savings will build.

In conclusion, this is one of the largest series in the literature to compare CTA scanned patients for DIEP flap breast reconstruction with an equivalent non-scanned cohort. The study has demonstrated both a benefit to flap harvest time as well as overall operative times when using preoperative CTA. The use of CTA was associated with a significant reduction in complications requiring a return to theatre in the immediate postoperative period. Modern scanners and techniques can reduce the level of ionising radiation, facilitating patients being able to benefit from the advantages that this preoperative planning can convey.

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Footnote

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Comparative study of software techniques for 3D mapping of perforators in deep inferior epigastric artery perforator flap planning

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Background: Computed tomographic (CT) angiography (CTA) is widely considered the gold standard imaging modality for preoperative planning autologous breast reconstruction with deep inferior epigastric artery (DIEA) perforator (DIEP) flap. Improved anatomical understanding from CTA has translated to enhanced clinical outcomes. To achieve this, the use of appropriate CT hardware and software is vital. Various CT scanners and contrast materials have been demonstrated to consistently produce adequate scan data. However, the availability of affordable and easily accessible imaging software capable of generating 3D volume-rendered perforator images to clinically useful quality has been lacking. Osirix (Pixmeo, Geneva, Switzerland) is a free, readily available medical image processing software that shows promise. We have previously demonstrated in a case report the usefulness of Osirix in localizing perforators and their course.

Methods: In the current case series of 50 consecutive CTA scans, we compare the accuracy of Osirix to a commonly used proprietary 3D imaging software, Siemens Syngo InSpace 4D (Siemens, Erlangen, Germany), in identifying perforator number and location. Moreover, we compared both programs to intraoperative findings.

Results: We report a high rate of concordance with Osirix and Siemens Syngo InSpace 4D (99.6%). Both programs correlated closely with operative findings (92.2%). Most of the discrepancies were found in the lateral row perforators (90%).

Conclusions: In the current study, we report the accuracy of Osirix that is comparable to Siemens Syngo InSpace 4D, a proprietary software, in mapping perforators. However, it provides an added advantage of being free, easy-to-use, portable, and potentially a superior quality of 3D reconstructed image.

Keywords: Computed tomographic angiography (CTA); perforator imaging; Osirix; Siemens; accuracy

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Introduction

Currently, computed tomographic (CT) angiography (CTA) is widely considered the gold standard perforator imaging technique for preoperative planning an autologous breast reconstruction with deep inferior epigastric artery (DIEA) perforator (DIEP) flap (1,2). The scan data can be 3D reconstructed to produce a “perforator map” that assists surgeons in selecting an appropriate perforator, donor site, and the flap. A plethora of studies have demonstrated a

high accuracy of CTA in detecting perforators, reporting a sensitivity and specificity close to 100% (3-12). In comparison to other perforator imaging modalities, such as Doppler ultrasound and magnetic resonance angiography (MRA), CTA has demonstrated superior visualization of the perforators and their subcutaneous course, respectively (7,10). While MRA may be evolving in this role, widespread outcome data is still lacking. The benefits of CTA have translated into improved clinical outcomes, such as increased flap survival, reduced donor site morbidity,

and reduced operating time (5,6,10,12-24). To this end, appropriate use of hardware and software is essential to obtain optimal perforator data from CTA.

Through various scanner hardware brands (i.e., Siemens, Toshiba, and Philips), varying number of multi-detector rows (i.e., 4-slice to 320-slice scanners) and differing contrast media and volumes, all scanners and techniques are able to achieve high quality and clinically useful images (1,2). In addition, we have published optimized CTA scanning techniques that enhance perforator visualizations, such as initiating contrast bolus trigger at the common femoral artery, moving the computed tomography table caudo-cranially, and disabling the Siemens Care Dose 4D feature (10).

High cost and limited accessibility of 3D imaging softwares that generate 3D reconstructions suitable for clinical use have been challenging for hospitals with relatively limited resources. Most of the currently available proprietary softwares, such as Siemens Syngo InSpace 4D (Siemens, Erlangen, Germany) (25) and VoNaviX (IVS Technology, Chemnitz, Germany) (26) are expensive. Some are not readily accessible outside the institution where it was originally developed, such as virSSPA (University Hospitals Virgen del Rocío, Sevilla, Spain) (15). Furthermore, many programs available cannot provide adequate images, with some not able to visualize perforators to a clinically useful degree. One particular program that we have found that can achieve optimal images is Siemens Syngo InSpace 4D (10). The program enables users to assign color to various contrast values using color look-up table (CLUT) function, providing superior contrast resolution to the 3D reconstructions. Again however, the cost and availability are significant limitations. Previously, we have demonstrated the application of a free 3D imaging program, Osirix (Pixmeo, Geneva, Switzerland).

Osirix is a free imaging processing software, specifically designed for medical imaging by a radiologist, and is readily downloaded online for use unreservedly (27). It is able to produce the same or better images than the currently available programs on a user-friendly interface. Furthermore, Osirix can be readily operated on a laptop computer, which enables viewing in the operating theatre or at home. Similar to Siemens Syngo InSpace, Osirix enables the user to create 3D volume-rendered reconstructions and assign colors using an appropriate CLUT function to optimize visualization of perforators and their course, as demonstrated in our previous case report (28).

In the current study, we investigate the accuracy of the freely available 3D imaging software, Osirix, by comparing

it to the proprietary program, Siemens Syngo InSpace 4D, and also comparing both softwares to the intraoperative findings.

Methods

The study design was a prospective case series. A total of 50 consecutive patients (i.e., 100 hemi-abdominal walls) underwent CTA prior to a DIEP flap breast reconstruction. All patients were aged between 30 and 60 years and spanned a wide range of body habitus. All imaging findings were recorded by a single operator and all intraoperative findings were recorded by the operating surgeon.

CTA technique

All scans were performed at a single institution (Future Medical Imaging Group, Melbourne, Australia) using a standardized protocol that has been modified and improved from the conventional CTA methodology in order to maximize the image quality and minimize radiation exposure (10,21). The computed tomography scanner used was a Siemens SOMATOM Sensation 64 multi-detector row computed tomography scanner (Siemens Medical Solutions, Erlangen, Germany) and the scan parameters are summarized in *Table 1*.

Patients were scanned in a position matching operative positioning: supine, with no clothing or straps to deform the abdominal contour. The scan range was limited to the tissue used intraoperatively and thus spanned from the pubic symphysis to 4 cm above the level of umbilicus. A bolus of 100 mL of intravenous omnipaque 350 was used for contrast, without oral contrast. We have previously described three major modifications introduced to the standard CTA protocol in order to enhance the arterial phase filling and the resolution of cutaneous vasculature (10). Briefly, the contrast bolus trigger to begin scanning was taken at the common femoral artery; the computed tomography table movement was reversed to scan caudo-cranially from the pubic symphysis to match the filling of DIEA; and the Siemens Care Dose 4D features was disabled, which maximized the abdominal wall signal-to-noise ratio.

Scan analysis

CTA scans were analyzed using both imaging softwares: Siemens Syngo InSpace 4D (Version 2006A; Siemens,

Table 1 Computed tomographic scan parameters

Parameters	
Scanner	Siemens SOMATOM Sensation 64
Scan type	Helical multi detector row CT angiography
Slice thickness	64 detector row x0.6 mm collimator width
Helical detector pitch	0.9
Gantry rotation speed	0.37 s
Tube potential	120 kV
Tube current	180 mA
Contrast	Omnipaque 350 100 mL IV injection 4 mL per second
Scanning range	Pubic symphysis to 4 cm above umbilicus
Scanning direction	Caudo-cranial
Bolus tracking	+100 HU from common femoral artery with minimal delay
Automatic dose modulation (Siemens Care Dose 4D)	Disabled
Imaging reconstruction	1 mm/0.7 mm overlapping axial images

CT, computed tomographic; HU, Hounsfield units.

Erlangen, Germany) and Osirix (Pixmeo, Geneva, Switzerland). The thin-slice (i.e., 1 mm or less) axial raw data were reformatted into 3D volume-rendered reconstructions and maximum intensity projections (MIPs) to identify the number and location of perforators, and the branching pattern of DIEA (29).

Perforator mapping

3D-reconstructed images of the abdominal wall perforators are generated using volume-rendering technique (VRT) and MIP techniques. VRT reconstructions required the use of the CLUT function found in both of the image processing softwares. Additionally in Osirix (Pixmeo, Geneva, Switzerland), we applied Gaussian blur to the final 3D reconstruction facilitating the removal of interference within the data (*Figures 1,2*). All infraumbilical perforators with diameter greater than 0.5 mm were identified and mapped on VRT reconstructions. Arrowheads were placed at the point of emergence of each perforator from the anterior rectus sheath. They were overlaid on to a 2D representation of each patient's abdominal wall with a grid of 4 mm squares applied to the image centered on the umbilicus as reference point. The transverse distances of each perforator from the midline were recorded to the closest 0.5 cm. The perforators were recorded as found in medial or lateral row. MIP reconstructions were used to illustrate intramuscular course of the perforators.

Intraoperative measurements

The perforator locations were compared with operative findings, where they were located on equivalent grids. Intraoperative grids were placed over the lower abdominal wall, with the umbilicus and midline as references, and the location of perforators was documented on it with sterile pens. A 0.5-cm margin of error was given for the location of each perforator. This was a conservative figure given as an estimate of the combined error associated with the calculation of concordance, and included the following factors: CTA error (e.g., patient movement, venous contamination), CTA reporting error (e.g., multiplanar reformatting error, reading error), intraoperative measurement error (e.g., limitation of measurement tool, reading error), and patient error (e.g., umbilical shift, abdominal pannus mobility). For the purpose of comparison, the operative findings were considered the standard.

All perforators were explored bilaterally, including the perforators not included in the flap. All perforators greater than 0.5 mm in diameter were included in the study and recorded in the manner described. As achieved during the CTA scan interpretation, the perforators identified intraoperatively comprised arterial perforators and not adjacent veins.

Statistical analysis

The perforator locations were recorded as exact values and the findings were compared between the two software

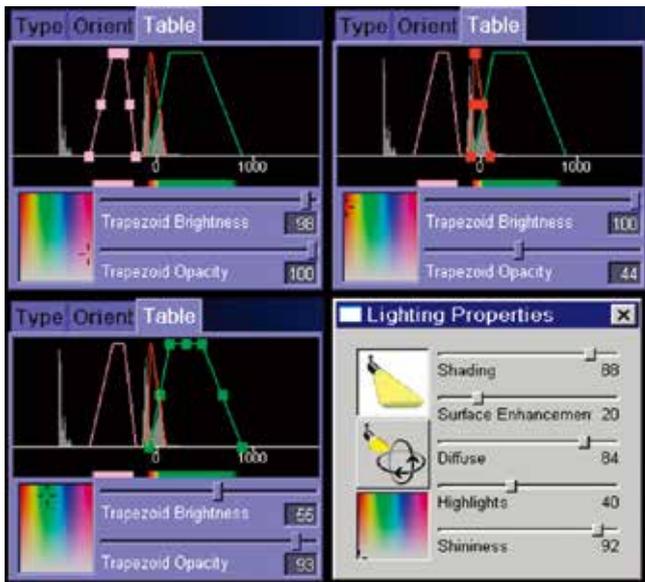


Figure 1 Color look-up table (CLUT) and ray cast lighting properties in Siemens Syngo InSpace 4D (Siemens, Erlangen, Germany). Reproduced with permission from Rozen *et al.* (25).

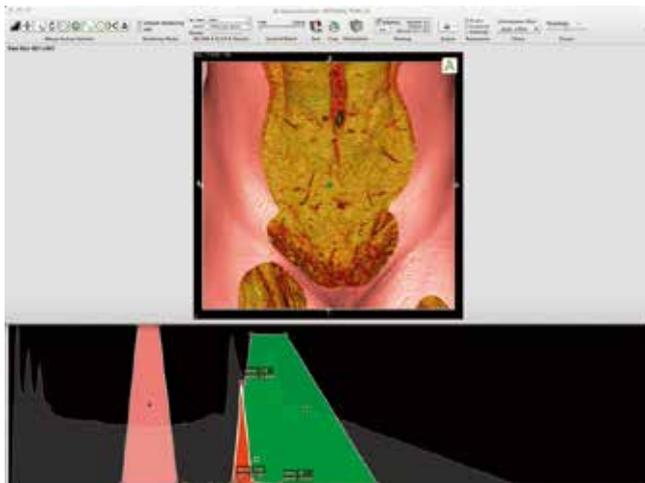


Figure 2 Color look-up table (CLUT) in Osirix (Pixmeo, Geneva, Switzerland), designed for perforator imaging. Reproduced with permission from Rozen *et al.* (28).

programs. In addition, the data from each program was compared to the operative findings. The comparative analysis was conducted using SPSS Statistics software package (IBM, Armonk, New York, USA) and the outcomes were analyzed using paired Student's *t*-test. A P value of <0.05 was accepted as statistically significant.

Results

A total of 50 CTA scans were performed in 50 consecutive cases (i.e., 100 hemi-abdominal walls) that identified 512 perforators of DIEA at an average of 5.12 perforators per hemi-abdomen. Concordance between Siemens Syngo InSpace 4D (version 2006A; Siemens, Erlangen, Germany) and Osirix (Pixmeo, Geneva, Switzerland) in accurately identifying perforator locations, and comparison between each of the software programs to intraoperative findings were evaluated.

Between Siemens Syngo InSpace 4D and Osirix, 510 out of 512 perforators (99.6%) had concordance. The two discordant perforators between the imaging programs were located in the lateral row and had only 0.5 cm of difference. Mean transverse distance from the midline using both software programs was 3.36 cm, with no statistical difference between them for measuring perforator location (*Table 2* and *Figure 3*).

Between each of the softwares and the operative findings, there was a mean difference of 0.7 mm per perforator using both programs (*Tables 3,4*). Although this difference was statistically significant ($P < 0.01$), this was not a clinically significant difference (i.e., less than 1 mm).

An analysis of perforators that had a difference between imaging and intraoperative findings was undertaken, with 40 perforators (7.8%) discordant between imaging and operative findings (*Table 5*). Of 18 perforators that had 0.5 cm difference with operative findings, 7 were located in medial row and 11 in lateral row. Of 12 perforators that had 1 cm difference, 5 were located in medial row and 7 in lateral row. Of 8 perforators that had 1.5 cm difference,

Table 2 Mean transverse distance of DIEA perforators from the midline as identified using the 3D imaging softwares: Siemens Syngo InSpace 4D (Siemens, Erlangen, Germany) and Osirix (Pixmeo, Geneva, Switzerland)

	Siemens Syngo InSpace 4D	Osirix	Difference	P value
Perforator location, lateral-to-midline (mean)	3.36 cm	3.36 cm	0 cm	1
DIEA, deep inferior epigastric artery.				

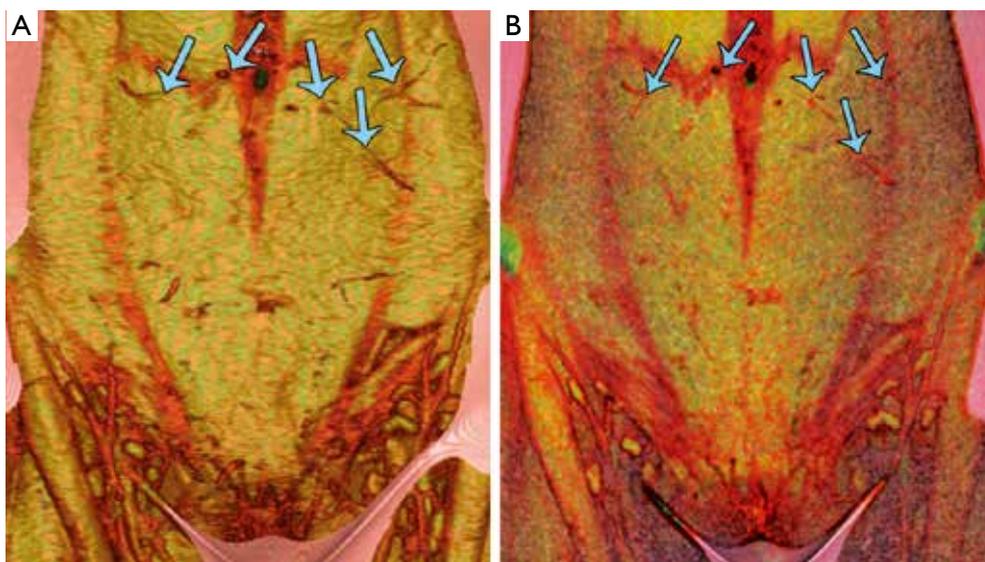


Figure 3 Preoperative computed tomography angiography (CTA), volume-rendered reconstruction of the abdominal wall vasculature with: (A) Osirix (Pixmeo, Geneva, Switzerland); and (B) Siemens Syngo InSpace 4D (Siemens, Erlangen, Germany). Both techniques clearly demonstrate several large periumbilical perforators (blue arrows), and highlight features of the abdominal wall soft-tissues. Reproduced with permission from Rozen *et al.* (28).

Table 3 Comparing the mean transverse distance of DIEA perforators from the midline calculated using Siemens Syngo InSpace 4D (Siemens, Erlangen, Germany) to the intraoperative measurements

	Siemens Syngo InSpace 4D	Operative findings	Difference	P value
Perforator location, lateral-to-midline (mean)	3.36 cm	3.43 cm	0.7 cm	<0.01

DIEA, deep inferior epigastric artery.

Table 4 Comparing the mean transverse distance of DIEA perforators from the midline calculated using Osirix (Pixmeo, Geneva, Switzerland) to the intraoperative measurements

	Osirix	Operative findings	Difference	P value
Perforator location, lateral-to-midline (mean)	3.36 cm	3.43 cm	0.7 cm	<0.01

DIEA, deep inferior epigastric artery.

Table 5 Analysis of discrepancy found in the perforator localization between imaging and operative findings and their distribution between medial and lateral rows

	Medial row	Lateral row	Total
Imaging: operative discrepancy 0.5 cm (number of perforators)	7	11	18
Imaging: operative discrepancy 1.0 cm (number of perforators)	5	7	12
Imaging: operative discrepancy 1.5 cm (number of perforators)	1	7	8
Imaging: operative discrepancy 2.0 cm (number of perforators)	0	2	2
Total	13	27	40

1 was located in medial row and 7 in lateral row. Of 2 perforators that had 2 cm difference, none were located in medial row and 2 in lateral row. Medial row perforators accounted for 13 out of 40 discordant results (32.5%) and lateral row 27 out of 40 (67.5%). Hence, imaging was more accurate when assessing medial row perforators (32.5% vs. 67.5%). Furthermore, when specifically assessing the larger discrepancies (>1 cm), medial row accounted for only 1 out of 10 (10%) and lateral row 9 out of 10 (90%).

Discussion

An improved understanding of the DIEA and its perforators from CTA has assisted reconstructive surgeons in the selection of the appropriate donor site, perforator, and hemi-abdominal wall of choice for reconstruction, which has translated to significant improvements in clinical outcomes (5,6,10,12-24). To achieve this, the use of appropriate hardware and software is vital. For CTA hardware, CT scanners from various brands using different multi-detector rows with varying IV contrast materials and volumes have demonstrated in the literature to deliver consistently sufficient scan data (1,3,5,10,12,15). In contrast, the high cost and limited accessibility of image processing software that can produce clinically useful 3D volume-rendered reconstructions have limited a wide application of CTA. To this effect, Osirix, a medical imaging program available for free online, have been useful. It is capable of producing the same or superior quality 3D reconstructions than the proprietary softwares and has added advantages of user-friendly interface and portability.

We have previously described the potential utility of Osirix for preoperatively planning a DIEP flap breast reconstruction in a case report (28). In the current case series, we demonstrate that Osirix is as accurate as the commonly used proprietary software, Siemens Syngo InSpace 4D, in identifying perforator number and location (99.6%). Furthermore, the measurements from both programs closely correlated to the operative findings (92.2%). The discordance between imaging and operative findings was most pronounced in assessing lateral row perforators (90% vs. 10%). For the purpose of the current study, we forewent comparing perforator diameters since these measurements can be made on standard axial slices of a CTA, regardless of the software program.

In addition to its accuracy in perforator localization, Osirix has the potential to yield superior quality 3D images than Siemens Syngo InSpace 4D due to its 16-bit CLUT

function and the capacity to apply Gaussian blur after the 3D reconstruction to reduce interference. Furthermore, Osirix exhibits an easy-to-navigate user interface that is readily accessible to clinicians without technological background and it is compatible on Mac operating system. As a result, surgeons can access the 3D reconstructed images on their portable computer in the operating theatre or at home.

Of note, although free for the basic version, there is a cost to the fully functional version that allows more images to be processed and your own presets to be used. Even this version offers a widely affordable option for most institutions compared to other options.

One of the limitations of the current study is our relatively small sample size. A larger randomized study with greater sample size will be required to further validate our findings. Moreover, a future study may consider comparing Osirix to a host of other proprietary softwares, such as VoNaviX, and their impact on clinical outcomes. For the purpose of this study, the comparative analysis was performed in cases of autologous breast reconstruction with DIEP flap. However, validating Osirix in assessing other free flap options for autologous breast reconstruction may be of value.

Conclusions

This comparative analysis demonstrates that the accuracy of Osirix, a freely available medical image processing software, is concordant with Siemens Syngo InSpace 4D, a commonly utilized proprietary software, in localizing perforators for autologous breast reconstruction with DIEP flaps. Measurements from both programs correlated equally to the intraoperative findings. Most of the discrepancies arose in the lateral row perforators.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Three routine free flaps per day in a single operating theatre: principles of a process mapping approach to improving surgical efficiency

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Background: Breast reconstruction is a multi-stage process, involving many individual procedures and many healthcare professionals which take the patient through from diagnosis of breast cancer to the completion of cancer treatment and ultimate breast reconstruction. With an experience of over 3,000 autologous breast reconstructions, we have refined both our surgical technique and overall approach to breast reconstruction to improve the efficiency in free flap based breast reconstruction surgery.

Methods: Through a process mapping approach similar to that employed by large-scale industry, we have broken down free flap based breast reconstruction into multiple smaller processes. By looking at various steps as a simple component of the whole, we have improved our theatre efficiency to maximize patient throughput and improve our outcomes for breast reconstruction patients.

Results: Since beginning free flap breast reconstruction surgery, we have improved overall efficiency by applying a process mapping approach. In our early experience, we undertook a single patient undergoing breast reconstruction with a free flap per theatre list, moving to two patients having breast reconstruction, and now carry out three free flap based reconstructions in a single theatre per day as a routine. Specific times are demonstrated, with no increased complication rate.

Conclusions: Through clearly defined processes, operative efficiency in autologous breast reconstruction can achieve three free flaps per day in a single theatre.

Keywords: Deep inferior epigastric artery; perforator flap; microsurgery; free flap; microsurgery

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Introduction

Microsurgical based breast reconstruction using autologous tissue has become the standard of care across Europe and the United States, although access to free tissue transfer expertise can be variable. In areas where free tissue transfer is available, the number of women being offered this type of reconstruction is increasing, matching increases in the

number of women being diagnosed with breast cancer who will require reconstruction. Furthermore, there has been a recent increase in the number of women requiring bilateral reconstructions, with a move towards bilateral risk reducing mastectomies. The reason for the increase in prophylactic mastectomies is only partially explained by the availability of BRCA-1 and -2 testing, but may also be due to an increased

awareness of the quality of breast reconstruction and recent coverage of well-known media personalities having bilateral mastectomies.

There are many popular options available for free flap autologous breast reconstructions, including transverse rectus abdominis myocutaneous (TRAM) flaps (1), transverse upper gracilis (TUG) flaps (2), and profunda femoris artery perforator (PAP) flaps (3), however the deep inferior epigastric artery perforator (DIEP) flap remains the commonest and most accessible perforator based flap used in autologous breast reconstruction (4). We have developed our breast reconstruction service and attempted to streamline the process, in the belief that microsurgical breast reconstruction should be viewed as a routine procedure rather than a complex procedure, which takes up an entire day's operating list as has been the case in the past. The current paper highlights our experience of breast reconstruction, and while it refers to DIEP flap based breast reconstruction, the principles can equally be applied to other types of free tissue transfer.

Methods and technique

A process mapping approach to free flap breast reconstruction is presented. The approach described has broken down the breast reconstruction procedure into several overlapping processes and describes the modifications taken to introduce efficiency savings at every step. Of note, this is "our" approach to process mapping, and while changes to the approach are inevitable between surgeons, the principles are presented for maximizing efficiency.

The first two processes do not specifically relate to operative timings, but if done efficiently, they contribute to reducing operative time.

Process 1—the initial consultations

The process mapping approach we adopt to streamline free flap based breast reconstruction begins from the time the patient is referred, having been given a diagnosis of breast cancer or has taken the decision for prophylactic mastectomy. Most often the patient will have been seen by her breast surgeon at a clinic distant to our hospital and is referred for plastic surgical opinion, at which stage we will first meet the patient at our next outpatient clinic. The time delay between referral and clinic appointment is usually a matter of days, and this first process in the patient's reconstructive journey can be optimized to streamline clinic

spaces available for these patients.

At this first point of patient contact, we discuss possible reconstructive options with the patient taking into account patient wishes, breast size, and available donor tissue and donor site morbidity. The aim by the end of the initial consultation is to formulate a reconstructive plan and offer appropriate informed consent. We aim for this initial consultation to be complete, so that the patient is ready to proceed with surgery and will not require further consultation until she is admitted for surgery. Given that there is a lot of information to be exchanged in this initial consultation and many women will have further questions that they may not have thought of during their consultation, a forum for further informal and formal discussions is essential, and we run weekly evening meetings to which all our pre-operative patients are invited. These are attended by specialist breast reconstruction nurses, past patients and medical staff intermittently. These consultations can also contribute directly to reducing operative time through proper documentation and consent, and can aid documentation as to examination findings for operative markings for surgery (and avoid perioperative changes to the operative plan).

Process 2—pre-operative assessment

All patients are seen pre-operatively by specialized nurses and anaesthetists familiar with free tissue transfer breast reconstruction to ensure they are fit for surgery, and nursing and anaesthetic plans are established early that may be specific to the patient. Pre-operative imaging with computed tomographic angiography (CTA) is performed, with a view to identifying the most suitable perforators and the most suitable hemi-abdomen for flap harvest. All aspects of the perforator course are assessed, with this "virtual surgery" able to preempt surgical dissection and reduce decision making intra-operatively (5-8). Upon admission to hospital, patients are also marked for surgery and perforator location confirmed using the hand-held Doppler probe.

Process 3—anaesthesia and turnaround time between patients

Time saving steps during the induction and maintenance of anaesthesia, while relevant, can only be employed if patient safety during anaesthesia can be maintained. For airway maintenance, we use a laryngeal mask as opposed to endotracheal intubation and use total intravenous



Figure 1 Intra-operative measurements with oesophageal Doppler monitor for haemodynamic monitoring in free perforator flap surgery.

anaesthesia rather than volatile gases for maintenance of anaesthesia. For our free flap procedures, we aim for the patient to be normotensive, normothermic and normovolaemic throughout the procedure.

Our experience with using the intra-operative oesophageal Doppler monitor for haemodynamic monitoring in free perforator flap surgery has been published previously (9), and in our experience, the placement of a central or arterial line can take up to 20 min which is compared to the 2 min taken for the siting of an oesophageal Doppler probe via the port on a laryngeal mask—a saving of 18 min. Further benefits of the oesophageal monitor are reduced fluid retention, reduced overall hospital stay and fewer post-operative complications, while offering all of the safety in haemodynamic monitoring offered by other more invasive means (see *Figure 1*).

Our theatre turnaround time between patient entering the anaesthetic bay to being fully anaesthetized in theatre and fully prepped and draped ready for surgery has been reduced to a mean of 17 min (range, 14–25 min).

Process 4—breast reconstruction surgery

We use a two-team approach with one team harvesting the flap whilst the other simultaneously carries out the mastectomy. The most common reconstructive option we employ is the DIEP flap, with the TUG flap, PAP and lumbar artery perforator (LAP) flaps, also used for autologous reconstruction on occasion. Regardless of operative position, we always undertake both flap harvest and mastectomy simultaneously. The reconstructive team

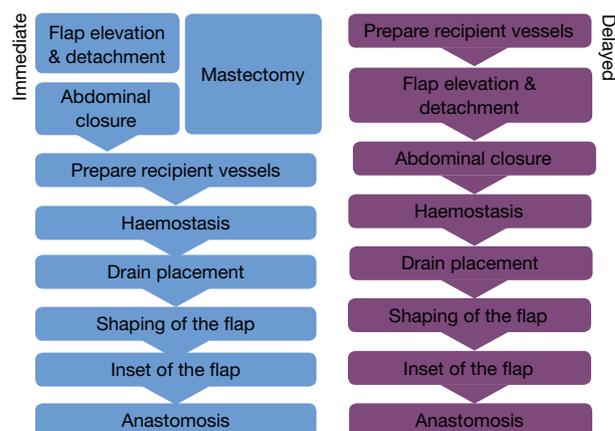


Figure 2 Sequence of steps involved in free flap breast reconstruction, for both delayed and immediate reconstructive settings.

harvesting the flap consists of a plastic surgeon with an assistant (typically a trainee plastic surgeon or scrub nurse). The specific steps involved for both immediate and delayed DIEP based reconstruction are set out in *Figure 2*. When performing three consecutive free flap reconstructions in a single theatre, each step becomes time critical, as a delay at any point has a knock-on effect in terms of timing for the subsequent patients.

Mastectomy

The timing of mastectomy is out of the control of the reconstructive surgeon but working with a regular breast surgeon can reduce potential variability. If the patient requires sentinel lymph node biopsy and subsequent axillary node dissection, this stage will be prolonged; however, the flap can be completely harvested and the donor-site closed whilst the breast surgeon completes their part (described in more detail below).

Perforator selection

Perforator selection at the suprafascial plane is anecdotally the step that causes most anxiety and is the largest delay in efficiency, particularly for the less experienced perforator flap surgeon. With an increased use of preoperative imaging, we plan our perforator selection completely preoperatively, and can then aim immediately for the perforator vessel which is of largest calibre and most central to the flap, with almost no intraoperative delay in decision making at this step (10). Perforator choice is

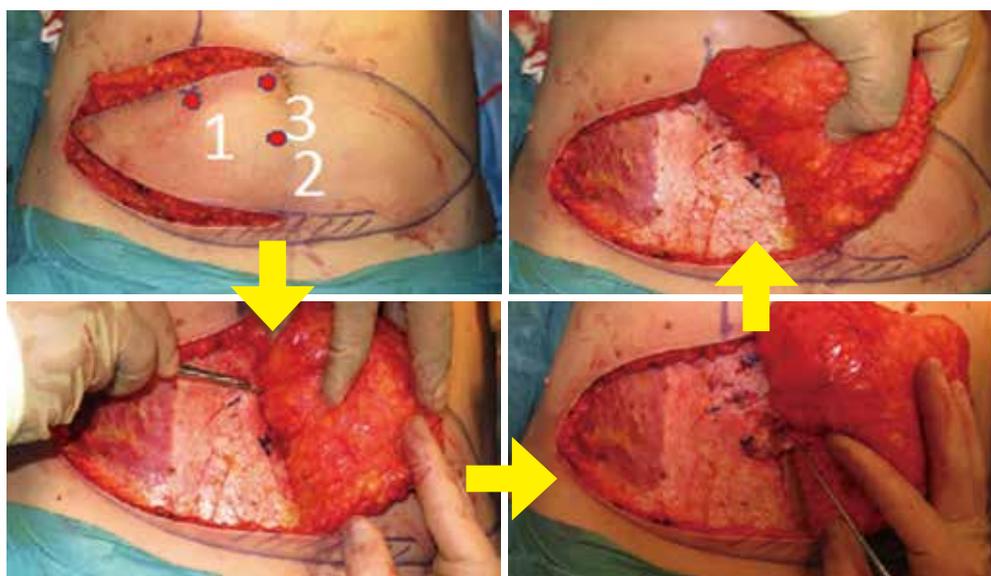


Figure 3 Photographic flow chart of operative sequence: three perforators identified preoperatively; upon dissection and perforator identification, the lateral perforator was of small calibre and on the edge of the flap; dissection was further progressed to the medial perforators of which the larger, more centrally located perforator (number 2) was selected.

optimally achieved with an objective imaging modality such as magnetic resonance angiography (MRA) or CTA, with our preference CTA due to cost, availability and resolution. While we do not rely on the hand held Doppler signal to identify the largest perforator (as we have found this to be reliable only for determining the location of the perforators but not the calibre) we do use it adjunctively for location confirmation.

When carrying out unilateral breast reconstruction we will harvest the contralateral hemi-DIEP flap and move rapidly towards the midline where we expect the larger perforators to be located, safe in the knowledge that we have the other hemi-DIEP flap if we do not find suitable perforators where we would expect them to be. A common pitfall is to preserve more lateral perforators which tethers the flap laterally, limits the rate and range of medial dissection of the flap and increases the risk of damage to the poorly visualised medial perforators. *Figure 3* highlights the sequence of perforator selection. If no single perforator is identified then we will on occasion take two smaller perforators and this choice is determined partly by the size of flap required which of course is dependent on breast size.

We do not expend time leaving the flap to perfuse on the perforator, nor dissect several perforators and place micro clamps on all but one perforator to check perfusion, if a

perforator is visibly and palpably pulsatile we are confident it will have adequate perfusion pressure to supply the flap. Further we will always discard the portion of flap most distal to the perforator to minimise potential perfusion problems and any future fat necrosis.

Perforator dissection

The time variability of this step depends both on anatomical variability and surgeon experience. The preoperative CTA is useful here to provide a picture of the intramuscular course of the perforator as a paramedian perforator with a short intramuscular course is faster to dissect than one with a long intramuscular course. If we are dissecting out two perforators this will also increase the time taken and may require division of part of the rectus muscle or if there is a wide section of muscle between the two perforators we may divide one of the perforators from the main deep inferior epigastric artery and reconnect the two perforators on the back table with the operating microscope which allows us to preserve more of the rectus muscle to minimise any potential post-operative abdominal wall weakness.

Once the perforator is dissected free from the rectus muscle, we continue the dissection towards the pelvis and divide the pedicle just caudal to the limit of the inferior



Figure 4 Demonstration of two surgical teams operating simultaneously, with the abdominal donor site closed by one team while the other completes the mastectomy.

abdominal incision as excessive pedicle length is often unnecessary, particularly when anastomosing to the internal mammary vessels.

Flap shaping

Once the flap is elevated, there are several concurrent manoeuvres that can save considerable time. Much time is used inefficiently by delaying donor site preparation, donor site closure, flap shaping and preparation, and deepithelialisation. These steps, if done early, can optimise patient heat-loss from exposed deep tissues, can prevent pedicle damage from overzealous retraction if done later and can facilitate concurrent operating at this early stage in flap transfer. We achieve this by temporarily inseting the flap in the mastectomy defect and establishing the required flap volume and shape, and determining the size of the required skin paddle and area for deepithelialisation.

Two surgical teams are thus optimally utilized, with the abdominal donor site closed by one team while the other completes the mastectomy (see *Figure 4*), and after donor closure, one team shapes the flap while the other prepares recipient vessels. In doing this, the flap undergoes



Figure 5 Further demonstrations of two surgical teams operating simultaneously, following donor closure, with one team shaping the flap while the other prepares recipient vessels. In doing this, the flap undergoes shaping and deepithelialisation early.

shaping and deepithelialisation (see *Figure 5*). At this point we will remove at least the Hartramp/Holm (1,11) zone 4 of the flap to minimise potential future fat necrosis and any more as necessary dependent on breast size. This part of the procedure can be carried out by an assistant whilst the recipient vessels are being prepared or by the primary surgeon if the mastectomy is still proceeding.

Recipient vessel preparation and anastomosis

Once the mastectomy is completed, an initial manoeuvre is to look for the second or third intercostal perforators, which is most often of sufficient calibre to allow a satisfactory anastomosis and obviates then need to dissect out the internal mammary vessels deep within the intercostals space and clearly avoids any rib resection. If the perforator has been damaged then our next choice is to explore the thoracodorsal axis which we access through a separate axillary incision. This is particularly useful after axillary dissection, as the entire subscapular axis is frequently exposed and requires minimal dissection. We then align the flap pedicle for anastomoses, with a hand sewing technique used for the artery and a micro-venous anastomotic coupler

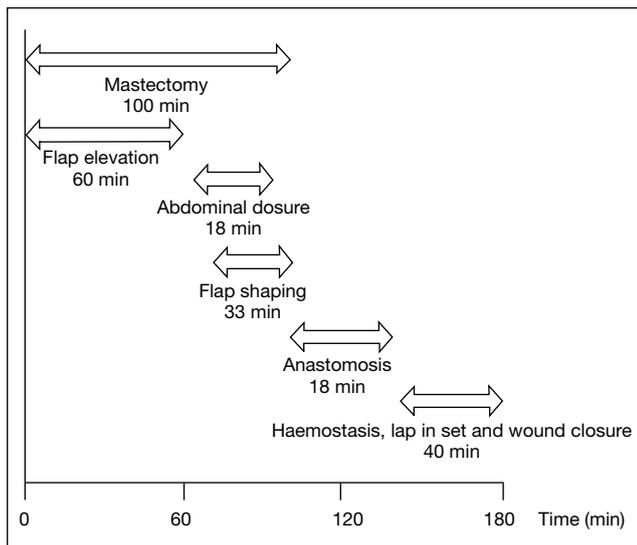


Figure 6 Chart showing the average timings of each process in DIEP flap based breast reconstructions, highlighting the processes that can overlap for time efficiency.

used for venous anastomosis. The efficacy and time saving benefits of which have been well documented (12,13).

Flap inset and abdominal closure

For abdominal closure we use an inlay Vicryl mesh (Ethicon, Wokingham, UK) placed under the rectus muscle and running two-layer non-absorbable sutures to the anterior rectus sheath. The upper abdominal flap is dissected to the costal margins centrally and closed with deep absorbable sutures then a single continuous barbed dermal suture (V-Loc, Covidien Mansfield, MA; or other) which is also time-saving in avoiding large numbers of deeper sutures. The flap is inset with several absorbable sutures to the chest wall superiorly and skin closed using several deep dermal absorbable sutures followed by a running barbed stitch.

Results

In a 12-month period, the senior author carried out 163 free flaps, both as primary operator and as an assistant to the primary operator. The multiple processes involved in DIEP flap based breast reconstruction are overlapping and varied depending on whether the breast reconstruction is immediate, delayed, unilateral or bilateral. *Figure 6* shows the steps and the mean timings involved in an immediate unilateral DIEP flap breast reconstruction.

Table 1 Times in cases of unilateral (monopedicle and bipedicle) reconstructions

Variables	Flap raise time	Ischaemic time	Anastomosis time
Mean times (min)	118.4	103.3	42.5
Range (min)	60-237	45-220	15-125
Standard deviation	39.2	32.6	16.4

Table 2 Times in cases of bilateral reconstructions

Variables	Flap raise time	Ischaemic time	Anastomosis time
Mean times (min)	173.0	228.2	71.4
Range (min)	86-270	120-450	25-120
Standard deviation	61.6	117.6	34.0

The mean operative time was 248 min, with the majority of cases completed such that 3 cases were completed within 12.5 h (between the hours of 08:30–21:00). The breakdown of times to facilitate these comprised anaesthetic time, flap harvest, micro-anastomotic times and flap inset and patient transfer. Anaesthetic times, comprising entry to the anaesthetic bay, line insertion and intubation and prepping and draping had a mean time of 17 min (range, 14–25 min). From the end of this “anaesthetic time”, flap raise time (comprising the time of knife to skin, until ischemic time begins) comprised a mean of 118 min (range, 60–237 min), ischaemic time (from the end of flap “flap raise time” until the end of anastomotic time—thus including the time for flap shaping and inset and vessel preparation) was 103 min (range, 45–220 min). The times for bilateral cases were somewhat longer, with combined flap raise time taking a mean of 173 min (range, 86–270 min) and ischaemic time a mean of 228 min (range, 120–450 min). The breakdown of ischaemic time to also include anastomotic time is presented in *Tables 1,2*. The additional 10 min over the combined means of each component equated to time for dressings and transfer out of theatre.

We have evolved the processes required so that there is as little unproductive time as possible and the sequence of events can be followed whether there is a single operator or whether there is an assistant involved. While the above times were recorded independently of simultaneous operating, the over-all times were routinely less than the combined totals of each component. Of note, in delayed reconstruction cases, if the operator is alone the sequence

is to first carry out the flap dissection then to prepare the recipient site and vessels and inset the flap; if there are two surgeons then the flap and recipient vessels can be prepared be simultaneously.

In our series of DIEP flaps for breast reconstruction over a 12-month period, 84% were raised on a single perforator which was felt to be large enough to supply the whole flap. The remaining 16% were raised on two perforators when we had concerns that a single perforator would not be adequate. Looking at recipient sites for the vascular anastomosis, we used the 2nd intercostal perforator in 32% of cases, 3rd intercostal perforator in 43%, internal mammary vessels in 14%, thoracodorsal pedicle 5% and serratus anterior pedicle in the remaining 6%.

The increased efficiency and decreased operating times associated with this series was not associated with an increased complication rate in any recorded outcome measures. There was an overall 98.5% flap survival rate. This was in the context of a 2.5% early return to theatre rate, due to a combination of pedicle compromise and haematoma, and a 4% readmission to hospital rate (associated with mastectomy flap necrosis and flap necrosis in the majority of cases). These figures were the same as in the preceding period.

Discussion

Perforator based flaps are now the gold standard for breast reconstruction, minimising donor morbidity and providing adequate volumes of autologous breast like tissue. The reliability of the DIEP flap has been well established with many centres across the world quoting flap survival rates between 95-99% (14,15). Despite this, there remains the perception that free tissue transfer for breast reconstruction is a high risk, time consuming procedure with aesthetic outcomes not too dissimilar to implant based reconstruction such that it is not worth the extra time and effort. In this paper we have tried to show that it is possible to provide a high volume free flap based breast reconstruction service through a process-led approach to maximise time efficiencies at every step.

Others have described manoeuvres to increase surgical efficiency so that two DIEP flaps can be carried out in one day across two theatres (10) which included the use of venous coupler device, Cook-Swartz implantable Doppler devices, CT angiography and team work. We have taken this one stage further and regularly carry out three free flap reconstructions in a single theatre by streamlining

the processes involved from the patient arriving in theatre, through their anaesthetic, their mastectomy and reconstruction to their recovery. Our regular theatre schedule is a 12-h day from 8.30 a.m. to 8.30 p.m. and we will routinely schedule two immediate unilateral reconstructions and a single unilateral delayed case in this time. As set out in *Figure 6*, our average time for an uncomplicated unilateral immediate reconstruction is 3 h so in a 12-h day, we have been able to operate on three patients with some flexibility in case one of the processes in the sequence takes longer than expected.

As patient awareness of breast reconstruction increases, as well as improvements in genetic testing and risk profiling for breast cancer, we are noticing an increase in the number of women referred for risk reducing mastectomies either at the same time as mastectomy for cancer or prophylactically. A combination of these factors has led to an increase in the number of bilateral breast reconstruction cases which clearly occupies more theatre time than a unilateral reconstruction. The trend towards a greater number of bilateral reconstructions is similar to recent data from the USA which found an increase from 3% in 1998 to 18% in 2007 (16), and this is likely to continue to increase. The ability to carry out more than one free flap breast reconstruction on a single operating list will become increasingly important if the demand for bilateral reconstructions continues to increase at the present rate.

Conclusions

The current paper demonstrates that it is possible to carry out three unilateral free flap breast reconstructions in one day in a single theatre. The safety of the patient remains of primary concern, followed by the importance of achieving sound oncological clearance and finally a pleasing aesthetic outcome with minimal donor site morbidity. In a healthcare environment increasingly sparse of resources however, health economics and operative efficiency are of increasing importance too. A process-mapped approach can contribute to operative efficiency.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest

to declare.

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Increasing options in autologous microsurgical breast reconstruction: four free flaps for ‘stacked’ bilateral breast reconstruction

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Abstract: For autologous breast reconstruction, there are cases where one free flap cannot provide the volume of tissue required, and the concept of ‘stacked’ bilateral deep inferior epigastric artery (DIEP) flaps was developed, in which hemi-abdominal flaps are raised on each deep inferior epigastric artery (DIEA), and both flaps transferred to the chest. In cases of bilateral breast reconstruction, stacked flaps may be required to achieve volume replacement, however options are not described. We demonstrate the use of stacked free flaps for bilateral breast reconstruction, using one DIEP flap stacked with one transverse upper gracilis (TUG) flap for each side. A 49-year-old woman, with BRCA1 mutation, presented for risk reduction mastectomies. Flap design was planned to achieve maximal projection and primary nipple reconstruction. This was able to be achieved by using the DIEP flap de-epithelialised and completely buried, with the flap orientated with the pedicle on its superficial surface, and the TUG flap lying superficially with its skin paddle used for nipple reconstruction and able to be monitored clinically. There were no flap or donor related complications and good aesthetic outcomes were achieved. This technique offers a further option in microsurgical breast reconstruction for patients in whom there is a paucity of abdominal tissue for reconstruction.

Keywords: Breast; abdominal; mastectomy; reconstruction; deep inferior epigastric perforator (DIEP) flap; transverse upper gracilis (TUG) flap

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Introduction

Autologous breast reconstruction is often considered a preference to alloplastic options, given that a more natural shape and feel can be achieved, as well as the creation of a breast with ptosis and volume. The deep inferior epigastric artery (DIEA) perforator flap is felt to be the most ideal option, with second tier options available that include the transverse upper gracilis (TUG), lumbar and latissimus dorsi flaps (1-5). There are cases, however, where even a deep inferior epigastric perforator (DIEP) flap cannot provide the volume of autologous tissue required for a unilateral breast reconstruction, and as a consequence, the concept of *simus dor* bilateral DIEP flaps was developed, in

which hemi-abdominal flaps are raised on each DIEA, and both flaps transferred to the chest recipient site.

While the terminology has been confusing, with terms used to mean various flap configurations, the terms ‘stacked’, ‘double-pedicled’ or ‘bipedicled’ have each been used to describe inclusion of the entire abdominal pannus on two pedicles, transferred to create a single breast reconstruction. Prior to the design of DIEP flaps being introduced into clinic practice, the abdominal wall was used in a bipedicled fashion in the way of bipedicled or stacked transverse rectus abdominis myocutaneous (TRAM) flaps (6). Bipedicled TRAM flaps were achieved through a pedicled TRAM flap (superior epigastric pedicle),

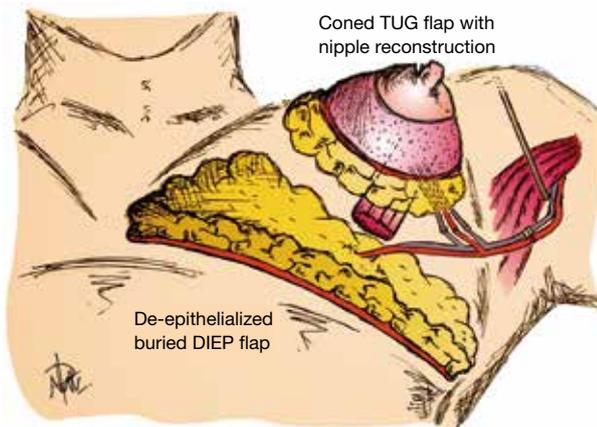


Figure 1 Schematic diagram of flap design, with the DIEP flap de-epithelialized and completely buried, with the flap orientated with the pedicle on its superficial surface, and the TUG flap lying superficially with its skin paddle used for nipple reconstruction and able to be monitored clinically. TUG, transverse upper gracilis; DIEP, deep inferior epigastric perforator.

supplemented with the use of a microsurgical anastomosis to the DIEA or vein, or with the use of both superior and inferior pedicles (6). Arnez *et al.* described the bipediced free TRAM flap, anastomosed onto both the thoracodorsal and serratus anterior branches, which was in particular described as useful for cases with midline abdominal scars that required larger volume reconstructions (7). Donor morbidity associated with sacrificing both rectus abdominis muscles was considered unacceptable, leading to diminishing use of both rectus muscles in the form of both TRAM flaps (8,9), however, microsurgical augmentation of a unilateral TRAM flap was widely described in a range of vascular configurations, with different pedicle arrangements, cross-over anastomoses and retro-grade vascular loops have all been described (10-16).

With the development of the DIEP flap (1-5), the use of 'stacked' or 'double-pediced' DIEP flaps was reintroduced by the current senior author of this paper (17). The stacked DIEP flap concept is of particular benefit for thinner patients and those with midline abdominal scars. The use of stacked DIEP flaps has been successfully reported now in a range of clinical series, and with a range of classifications for pedicle arrangements described (17-25). Where stacked DIEP flaps are not possible, the superficial inferior epigastric artery (SIEA) has been used as a secondary pedicle (19), and bilateral profunda artery perforator flaps stacked have been used (26).

In cases of bilateral breast reconstruction, stacked flaps may be required to achieve volume replacement; however options have not been described. Herein we demonstrate the utility of using stacked flaps for bilateral breast reconstruction, using one DIEP flap per side stacked with one TUG flap for the reconstruction of each breast.

Case presentation

A 49-year-old woman, with BRCA1 mutation, attended the multidisciplinary risk-reducing clinic, with a decision from the medical team and patient to undertake bilateral risk-reducing mastectomies, and immediate breast reconstruction. The patient had a strong preference for autologous reconstruction alone, and due to a paucity of abdominal tissue, a decision was made to use stacked flaps bilaterally: with a DIEP flap and TUG flap suitable for reconstruction of each side.

The patient was well, with no known comorbidities, a non-smoker and no medications.

Surgical technique

Flap design was planned in a manner to achieve maximal projection and primary nipple reconstruction. This was able to be achieved by using the DIEP flap de-epithelialized and completely buried, with the flap orientated with the pedicle on its superficial surface, and the TUG flap lying superficially with its skin paddle used for nipple reconstruction and able to be monitored clinically (see schematic in *Figure 1*).

A preoperative computed tomographic angiogram (CTA) of the abdominal wall vasculature was used to delineate the optimal perforators for DIEP flap harvest (see *Figure 2*). The CTA was able to also delineate the recipient pedicle for the TUG flap. This is highlighted in *Figure 3*, in which a type 1 DIEA was identified bilaterally, with the distal end of the DIEA thus selected as the recipient vessels for the TUG flap on each side.

Given the operative complexity, three concurrent surgical teams were operating, utilized in the following manner:

Stage 1—one team harvesting the first TUG flap, one team harvesting the first DIEP flap and one team performing the first mastectomy;

Stage 2—one team closing the first TUG flap donor site, one team on the side table performing an intra-flap anastomosis and flap shaping (each DIEP and TUG flap were anastomosed in series on a side table), and one team

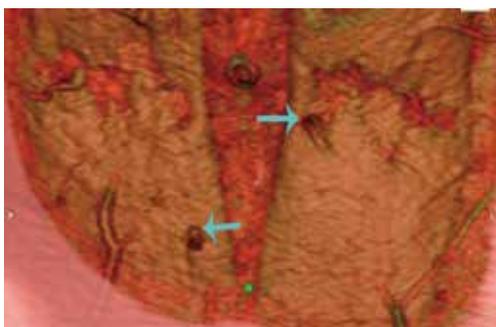


Figure 2 Preoperative computed tomographic angiogram (CTA), with three dimensional reconstruction demonstrating one dominant perforator per hemi-abdomen.



Figure 3 Preoperative computed tomographic angiogram (CTA), demonstrating the deep inferior epigastric artery (DIEA) and its branching pattern.

performing the second mastectomy;

Stage 3—one team raising the second TUG flap, one team raising the second DIEP flap, and one team performing the microsurgical anastomoses at the first chest wall recipient site;

Stage 4—one team closing the second TUG flap donor site, one team closing the abdominal donor site, and one team on the side table performing an intra-flap anastomosis and flap shaping of the second DIEP and TUG flaps;

Stage 5—one team completing donor site closure and dressings, one team completing inset and dressings of the first breast reconstruction, and one team performing microsurgical anastomoses and flap inset of the second



Figure 4 Early postoperative appearance of bilateral stacked breast reconstructions at 2 weeks postoperatively, demonstrating good flap volume and ptosis, and abdominal donor site.

breast reconstruction.

The case proceeded uneventfully, with a single perforator DIEP flap raised on each side (see CTA in *Figure 2*), and the thoracodorsal vessels used as recipient vessels bilaterally. For one side, the pedicle length necessitated a vein graft for reach, with a long saphenous vein tributary from the thigh donor site used (and thus no additional morbidity). The duration of the case was just under 8 hours, and the patient had an uneventful early perioperative and immediate postoperative course, discharged home on day 7 postoperatively (see *Figure 4*). Of note, the patient was given preoperative clexane for venous thrombo-prophylaxis, and this was continued for 1 week post-operatively with the concurrent use of graded compression stockings, until full mobilization was achieved. There were no flap-related complications, and the donor sites healed unremarkably (see *Figures 4-6*). The aesthetic result at 3 months postoperatively is shown in *Figure 7*.

There was, however, a significant complication that arose on day 14 postoperatively. The patient presented on the 14th postoperative day to the emergency department with a dense hemiplegia and aphasia consistent with a cerebrovascular stroke. Investigations were performed, including a carotid Doppler which demonstrated a right carotid free floating thrombus, and both CT and MRI which demonstrated a right-sided ischaemic stroke, mass effect with midline shift and decreased ventricular size. The patient underwent immediate transfer to a neurosurgical



Figure 5 Postoperative view of the transverse upper gracilis (TUG) donor site from the front.



Figure 6 Postoperative view of the transverse upper gracilis (TUG) donor site from the back.

centre, where she was taken to theatre for decompressive craniectomy. She responded well, with improvement in clinical and imaging findings, and discharge 7 days later. With ongoing neurologic rehab 2 months later, the patient has shown resolution of her aphasias/dysphasia, but an ongoing hemiplegia. The case was discussed within the neurosurgical and anaesthetic department meetings, and the cause for the stroke is unknown. No patient factors for the carotid thrombosis have been identified despite haematologic screening, no hyperextension of the neck during the anaesthetic was observed but may have contributed, and while a prolonged operation may be theoretically contributory, the 8 hours for this case was not clearly considered a factor.

Discussion

The use of stacked abdominal flaps has been a widely used



Figure 7 Postoperative appearance of bilateral stacked breast reconstructions at 3 months postoperatively.

and successful addition to the armamentarium of autologous breast reconstruction options in unilateral reconstruction cases. In bilateral cases, the options are much more limited. We present an option, in which stacked flaps are used for the reconstruction of each breast, with the TUG flap used to augment bilateral DIEP flaps. Our case demonstrates the relative efficiency of such an approach, and the aesthetic outcome able to be achieved in a patient with paucity of abdominal volume.

There are several key factors that are essential to achieve success in this approach. The first is the use of preoperative CTA. The preoperative CTA can highlight the optimal perforator for flap harvest, reducing harvest times and ensuring that the case is suitable, and optimized. The ability of CTA to achieve these ends with accuracy has been demonstrated in multiple previous studies (27-32), highlighting a high degree of specificity and sensitivity, and showing improvements in flap-related outcomes and operative times. In addition to CTA, the use of three surgical teams concurrently operating is essential for operative efficiency. In the five stages highlighted, there is never a team not contributing to the case, and we would advise this to ensure that such a case does not encroach upon excessive operative times.

While the aesthetic and reconstructive outcomes were all achieved, the devastating complication encountered is a reminder as to the risks of any surgery. The consent process is paramount, particularly in the case of risk-reduction surgery, and it is essential that each patient weigh-up the risks in electing to proceed in any breast reconstructive case. While no factors were implicated in the causality or even to be contributory to this outcome in our case, diligence in case selection and prophylactic measures for all

complications are essential.

Conclusions

We describe the use of stacked free flaps for bilateral breast reconstruction, using one DIEP flap per side stacked with a TUG flap from each side. The technique offers a further option in microsurgical breast reconstruction for patients in whom there is a paucity of abdominal tissue for reconstruction and in whom prosthetics are not considered an option.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Informed Consent: Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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The microvascular anastomotic coupler for venous anastomoses in free flap breast reconstruction improves outcomes

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Background: Venous couplers are ubiquitous around the world and are a useful tool for the reconstructive microsurgeon. A systematic review of coupler performance studies demonstrated a thrombosis rate range of 0% to 3%, whilst the average time of using the device is 5 minutes. There is sparse published data on cost analysis and the impact of operator experience on the anastomotic coupler device success. Improvements in outcomes other than time benefits have also not been shown. This study aims to address these deficiencies in the literature.

Methods: A retrospective clinical study was undertaken, aiming to compare equivalent groups of patients that had free flap surgery with venous micro-anastomoses with those that had sutured anastomoses. The cohort comprised all patients undergoing microsurgical breast reconstruction at the St Andrew's Centre for Plastic Surgery & Burns from January 2009 to December 2014.

Results: Between January 2010 to December 2014, 1,064 patients underwent 1,206 free flap breast reconstructions. The average age of patients was 50 years. Seventy percent of patients underwent mastectomy and immediate reconstruction during this period with the remaining 30% having a delayed reconstruction. The 1,206 free flaps comprised of 83 transverse myocutaneous gracilis (TMG) flaps, and 1,123 deep inferior epigastric artery perforator (DIEP) flaps. In total the coupler was used in 319 flaps, 26% of the cohort. There was a statistically significant clinical benefit in using the anastomotic coupler for venous anastomosis. Overall, the return to theatre rate was 12.69% whilst the overall flap loss rate was 0.75%. The overall coupler failure rate was significantly less at 1.4% whilst sutured vein failure rate was 3.57% (P=0.001).

Conclusions: The anastomotic coupler for venous anastomosis in free flap surgery is associated with reduced operating times, reduced take-backs to theatre and cost benefits. This is the first study to demonstrate clear clinical benefits to anastomotic couplers, and suggests that these may be the gold standard for venous microanastomosis. With increasing experience with their use and technological advances, these outcomes may continue to improve.

Keywords: Suture; vessel; rib; microsurgery; microvascular; free flap

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Introduction

Microvascular anastomotic techniques have evolved considerably since the first vessel anastomosis in 1902. Carrell sutured his anastomosis, and clinicians since then have proceeded to develop ways to build on this paradigm-changing achievement. Through new technology,

techniques and treatments, we continue with the aim of improving the quality of care offered through microsurgical reconstructive techniques. Traditionally, vessel anastomosis utilized hand-tied monofilament microsutures, under microscope magnification. There have been developments in suture materials over time, and more recently, the use

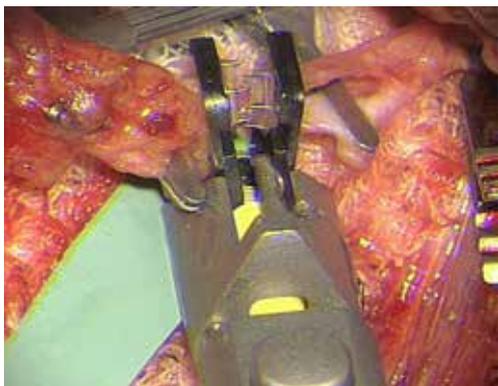


Figure 1 The coupling device is turned together to evert the vein wall edges ensuring intima to intima contact.

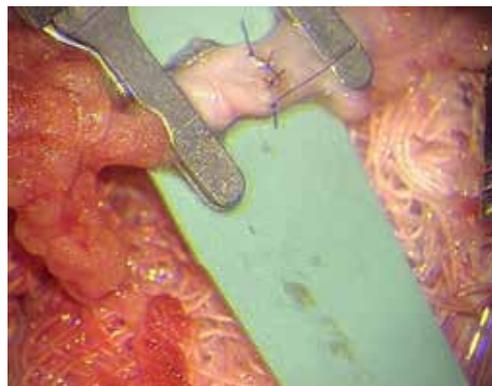


Figure 2 Arterial anastomosis performed in an end to end, interrupted sutured fashion.

of microclips or vascular staples have become increasingly used. More popularised still are the use of coupling devices, which use a ring and hooks for microvascular anastomosis. Venous couplers were first described in 1962 by Nakayama, who used an interlocking metal ring with 12 pins to achieve a patent venous anastomosis (1). A reliable device was developed in Sweden in the early 1980's known as the Unilink coupler and marketed by 3M (2). The technology has been since been refined further and is currently used across the world for microsurgical venous anastomosis as the microvascular anastomotic coupler system coupler system (Synovis Micro Companies Alliance, Birmingham, AL, USA). The venous coupler has been designed to provide intima to intima contact without intraluminal suture material which might act as a site for thrombus promotion.

A systematic review of coupler performance studies demonstrated a thrombosis rate range of 0% to 3%, whilst the average time of using the device is 5 minutes (3). There is sparse published data on cost analysis and the impact of operator experience on the anastomotic coupler device success. Improvements in outcomes other than time benefits have also not been shown. This study aims to address these deficiencies in the literature.

Methods

A retrospective clinical study was undertaken, aiming to compare equivalent groups of patients that had free flap surgery with venous micro-anastomoses with those that had sutured anastomoses. The cohort comprised all patients undergoing microsurgical breast reconstruction at the St Andrew's Centre for Plastic Surgery & Burns from January 2009 to December 2014. Specific data from all microsurgical

free tissue transfer operations were prospectively entered into a clinical database and collected. Key variables collected included patient demographics, operative time, coupler size, surgeon experience and complications. The surgeon level of experience was compared for consultant surgeon versus fellow/registrar; the recipient site was compared for the internal mammary versus the subscapular/thoracodorsal axis; and the number of flaps was compared as to whether a case required a unilateral reconstruction, bilateral reconstructions, a bipedicle flap (two anastomoses in the chest) or stacked flaps (two flaps in series with one anastomosis in the chest).

Venous anastomoses were undertaken with either a purely end to end, interrupted suturing technique, or the microvascular anastomotic coupling system (Synovis Micro Companies Alliance, Birmingham, AL, USA). Coupling technique comprised several key steps. Firstly, the use of a vessel sizer to determine the size of the coupler for any individual case, with the vessel end prepared and passed through the coupling ring. The vessel was fixed to the ring by everting the edges over sharp hooks. After each vessel end was prepared in this manner, the coupling device was turned to oppose the rings (*Figure 1*), and then detached from the ring to leave the completed anastomosis. All arterial anastomoses were performed in an end to end, interrupted sutured fashion (*Figure 2*).

There were two main outcome measures investigated: anastomotic time and clinical anastomotic failures. Anastomotic time was recorded prospectively, and comprised the time from the end of vessel preparation until removal of vessel clamps. Clinical outcomes assessed were anastomotic failure, returns to theatre and overall flap failure.

Statistical analysis was undertaken using SPSS (SPSS

Table 1 Clinical outcomes for sutured versus coupled veins

Variables	Sutured vein revision (%)	Coupled vein revision (%)	Pearson's χ^2	Overall return to theatre (%)
Reconstruction type				
Unilateral	4.20	1.70	0.039*	13.20
Bilateral	1.74	0	0.28	9.57
Unilateral bipedicle	2.94	0	0.46	1.40
Unilateral stacked	1.85	0	0.43	11.11
Total	3.57	1.44	0.01*	12.69
Grade of surgeon				
Consultant	3.60	0.57	0.034*	0.46
Fellow/Registrar	3.50	4.50	0.74	1.60
Total	3.57	1.44	0.01*	0.75
Anastomosis site				
Axilla	4.41	3.40	0.642	0.65
Chest	0.90	6.60	0.021*	1.30

*, $P \leq 0.05$.

Inc. IBM, Armonk, NY, USA). A P value of 0.05 was used to represent statistical significance.

Results

Between January 2010 to December 2014, 1,064 patients underwent 1,206 free flap breast reconstructions. The average age of patients was 50 years. Seventy percent of patients underwent mastectomy and immediate reconstruction during this period with the remaining 30% having a delayed reconstruction. The 1,206 free flaps comprised of 83 transverse myocutaneous upper gracilis (TUG) flaps, and 1,123 deep inferior epigastric artery perforator (DIEP) flaps. In total the coupler was used in 319 flaps, 26% of the cohort.

There was a statistically significant clinical benefit in using the anastomotic coupler for venous anastomosis (Table 1). Overall, the return to theatre rate was 12.69% whilst the overall flap loss rate was 0.75%. The overall coupler failure rate was significantly less at 1.4% whilst sutured vein failure rate was 3.57% ($P=0.001$). Of note, consultant surgeons had a lower coupler failure rate than more junior surgeons (fellows or registrars) at 0.57% versus 4.5%

There was also a statistically significant time benefit in using the anastomotic coupler (Table 2). The average time to undertake a sutured vein anastomosis was 21 minutes whilst using the coupler device it was significantly less at 9.3 minutes ($P=0.001$). Fellows or Registrars took significantly less time to use the coupler at 15 minutes versus

sutured vein at 35 minutes ($P=0.001$). When comparing different recipient sites, it took on average 4 more minutes to use a coupler in the axilla than a coupler in the internal mammary site, and 13 minutes more to suture at the internal mammary site as compared to using a coupler.

Discussion

Technology in free flap surgery has helped to transition what began as a high risk and significant undertaking in the early 1980's to routine options in many reconstructive settings. Venous problems are more commonly seen in free flap surgery, and means to counter such problems are eagerly sought. Venous complications requiring a return to theatre and re-anastomosis in sutured anastomosis was 3.57% in our study, and this is commensurate with existing published data on venous complications (4). This contrasts to the venous thrombosis rate achieved with the coupler device of 1.44%, found to be significantly lower than the sutured cohort ($P<0.01$). Sutured repairs have an inherently higher risk for thrombosis, and are technique dependant on success. Suture material within the lumen, incompletely everted vessel edges and poor suture placement leading to leaks can all contribute to anastomotic failure (5). Blood flow modelling using computational fluid dynamics that assesses flow through a coupler anastomosis versus sutured, show a reduction in the key precursors to thrombin formation, changes in flow velocity profile and decreased wall shear stress (6).

Table 2 Time for anastomosis

Variables	Patients	Flaps	Proportion (%)	Artery (mins)	Vein (mins)	Coupler (mins)	Student's <i>t</i> -test
Reconstruction type							
Unilateral	854	854	70.8	26	29	20	0.001**
Bilateral	115	230	19.1	20	20	7.5	0.034*
Unilateral bipedicle	68	68	5.6	20	19	5	0.001**
Unilateral stacked	27	54	4.5	18	15	5	0.003**
Total/Mean	1,064	1,206		21	20.75	9.3	0.001**
Grade of surgeon							
Consultant	–	–	–	–	30	20	0.001**
Fellow/Registrar	–	–	–	–	35	15	0.005**
Recipient site							
Axilla	–	–	–	–	20	31	0.0001**
Chest	–	–	–	–	16	29	0.0001**

*, $P \leq 0.05$; **, $P \leq 0.01$.

Anastomosis time was significantly quicker with the coupler device. The average anastomosis time of 9 minutes is higher than some other large series in the published literature (3,7), however this was a statistically significant difference to sutured anastomosis, as mirrored in those other publications. Time is an important factor when considering the potential length of a complicated procedure, with increase operative time in microsurgical breast reconstruction associated with lower haemoglobin levels and an increase risk of postoperative complications (8). The cost savings alone are a significant consideration.

Our unit began to routinely use the coupler system in late 2012, although the surgeons involved had all used the system in other hospitals. There was a significant difference in anastomosis times and failure rate in the coupler group when looking at surgeon seniority. Consultant surgeons took longer to use the coupler but had a significantly lower revision rate than fellows or registrars. Fellows and registrars took less time to use a coupler than sutured anastomosis but there was no significant difference in their anastomotic failure rates. This evidence points to a potential learning curve for the use of the coupler device, and that the time saving benefits must be tempered with the knowledge of potential increase in anastomosis revision rate in the hands of a more junior surgeon. This data reinforces the fact that with seniority and experience comes the insight and knowledge that microsurgery should never be rushed.

Within a resource-constrained healthcare system, time is a significant cost factor to consider. The average time

difference between sutured and coupler anastomosis was just over 11 minutes. Within our regional hospital system, the financial cost associated with running an operating theatre per hour has been calculated by the hospital as 14 GBP/min. Simplistically, this would indicate that couplers on average save £154. The current cost of the single use couplers excluding the initial investment in coupler set is £169.50. This would indicate that it could be perceived as a cost neutral device. This assumption holds if the time saving allows further use of the fixed costs associated with running a theatre. Given that in our unit the senior author has routinely undertaken three DIEP reconstructions in one theatre in a single day, time saved can be realised as a net cost saving. Furthermore, if you extrapolate the reduction in return to theatre rates which are strongly associated with significant cost increase (9), the net saving for coupler use will increase further. While not a formal cost analysis, this data does point to couplers not being a cost strain.

Coupler use has for the first time been demonstrated in a large cohort to be quicker not only in unilateral breast reconstruction but also in bilateral, bipediced and stacked breast reconstruction cases. Couplers demonstrated over 12 minutes time saving in bilateral reconstructions, 14 minutes in bipediced and 10 minutes in stacked flaps. There were no coupler failures in any of the bilateral, bipediced or stacked flaps. In these operations which add an extra layer of complexity and time as compared to unilateral reconstructions, the added benefit of time saved and potential reduced risk of thrombosis are significant factors which

may well influence a surgeon's decision to use couplers. The coupler is also recognised to reduce surgeon fatigue although this is difficult to quantify. In complex reconstructions the use of a coupler can dramatically reduce the complexity of required microsurgical demands. Multiple couplers can be used to extend vein grafts, in one case we have used five couplers in series to extend a vein graft.

Anastomosis site was a different variable we chose to explore. The use of a coupler was associated with a significant reduction in anastomosis time in both sites—the internal mammary system and the subscapular/thoracodorsal system. The time saving was greater using the coupler with the internal mammary artery and its perforators. It was also associated with a significant reduction in thrombosis rate at this site. When looking at the axilla there was a significant time saving but no difference in thrombosis rate. The coupler conveys time saving benefit irrespective of location of use, however in this cohort the thrombosis risk reduction benefit is only seen in its use on the anterior chest anastomosis location.

The benefits to microvascular coupler anastomosis can be seen however there are some documented drawbacks. There is a learning curve to correct use of the system which surgeons used to hand sewn anastomosis will need to adjust to. There is the theoretical deskilling of the ability to perform a robust hand sewn venous anastomosis, although until the advent of a reliable arterial coupler this skill will always be used (3). Cost issues have previously been cited as a disadvantage to the use of the coupler system however our data suggests that at worst it's a cost neutral device and at best it can save a substantial cost in the prevention of reoperation and flap failure.

Evolution in the coupler devices have continued over time, with a broader range of sizes available, improvements in the instrumentation for applying the vessels to the coupler device, and even couplers with in-built implantable Doppler probes for monitoring. With further technological advance, outcome measures may improve on current rates even further.

Conclusions

The anastomotic coupler for venous anastomosis in free flap surgery is associated with reduced operating times, reduced take-backs to theatre and cost benefits. This is the first study to demonstrate clear clinical benefits to anastomotic couplers, and suggests that these may be the gold standard for venous microanastomosis. With increasing experience with their use and technological advances, these outcomes may continue to improve.

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Footnote

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Nipple-areola complex reconstruction

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Abstract: Nipple areolar reconstruction (NAC) was introduced since 1940s and evolved as parallel with breast reconstruction since era of breast cancer treatment. It consists of nipple and areolar reconstruction. Ideal reconstruction of the NAC requires symmetry in position, size, shape, texture, and pigmentation and permanent projection. There are many innovative ways to create a nipple and each method has its unique characteristics that apply to certain breast types. NAC reconstruction techniques comprises of composite nipple grafts, local flap, flaps with autologous graft augmentation, flaps with alloplastic augmentation and flaps with allograft augmentation. Areolar reconstruction by using skin grafting and tattooing are the easiest and most common techniques. With the evolution of techniques and technology, perhaps the newer methods of NAC reconstruction can produce promising long-lasting aesthetically acceptable result with minimal morbidity.

Keywords: Nipple areolar reconstruction; composite nipple grafts; alloplastic; allograft; autologous graft; tattooing

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Background

Patients with loss of the nipple and areola from cancer excision, trauma, or congenital absence continue to experience psychological distress even long after breast mound reconstruction has taken place. Other conditions requiring nipple areolar complex (NAC) reconstruction include congenital or developmental pathology (athelia, amastia), posttraumatic or burn deformities, and complications from breast surgery such as reduction mammoplasty. In the cases of breast cancer, whole breast reconstruction following mastectomy can provide significant psychosocial benefits for women. Nipple reconstruction can be performed with all types of breast reconstructive procedures and at any time following completion. Nipple reconstruction represents the simplest from a technical perspective but is among the most important from an aesthetic perspective (1).

Studies have shown that recreation of the NAC has a high correlation with overall patient satisfaction and acceptance of body image (2). Thus, completion of the

breast reconstruction by creating a nipple-areola complex that matches the contralateral nipple in terms of size, shape, projection, and position adds significantly to the reconstructive result.

In this review, we concentrate only in general principles of NAC reconstruction and do not include any surgical techniques for NAC reconstruction. Readers can find relevant surgical techniques in various standard textbooks of plastic and reconstructive breast surgery.

History of the procedures

The history of nipple reconstruction parallels that of breast reconstruction with autologous tissue, from the development of the latissimus dorsi flap by Tanzini in 1906 to modern transverse rectus abdominis myocutaneous (TRAM) and microvascular-free TRAM breast reconstruction.

The evolution of NAC creation began when Adams initial description of the nipple-areola graft and labial graft in the 1940s (3,4). Following this, Millard proposed the nipple-

sharing concept, where the contralateral nipple tissue was used as a composite graft for the reconstructed nipple (5). Later, various other grafts from toe pulp, auricular cartilage, and mucous membranes were also attempted and proven somewhat successful in providing tissue with projection, but at the expense of a significant donor site morbidity (6,7). A paradigm shift occurred in NAC reconstruction with the descriptions of the quadropod flap, dermal fat flap, and T-flaps in the 1980s (8-10). These flaps, based on smaller local flaps, allowed for rearrangement into a nipple configuration. In the 1980s and 1990s, multiple different local flaps were being described using the concepts of local flap rearrangement with and without skin grafts including the skate flap, star flap, CV flap, Bell flap, and the S-flap. Lastly, the increasing use of synthetic materials and allografts in reconstructive surgery has allowed for new, innovative methods for projection augmentation and revisional NAC reconstruction.

Various techniques of nipple reconstruction ensued, allowing use of transferred tissue and scar to form a nipple prominence. Among them are Little's skate flap and its modifications, Anton and Hartrampf's star flap and Bostwick's C-V flap, Cronin's S-flap, Smith and Nelson's mushroom flap. Several studies looked at long-term projection of the various reconstructive techniques.

Various authors promoted their own techniques as being superior, but each has to decide which works best for himself. Becker was the first surgeon who introduced the tattooing technique for NAC reconstruction in 1986 (11). Spear popularized it in the years to follow (12). Currently, medical tattooing appliances are ubiquitous and of high quality and offer several tones and hues of pigment to match the color of the native areola. Some pigment fading over time is to be expected, and a few touch-up procedures may be required. Pigment fading was the most common long term complaint, voiced by up to 60%. A few required touch-ups and the majority were satisfied with their outcome.

Nipple reconstruction techniques have evolved significantly over the years. From simple tattooing to the more technologically advanced, although rarely available, tissue engineering, today's techniques are able to provide long-lasting, satisfactory reconstruction with minimal morbidity (13).

Relevant anatomy of NAC

Nipple-areola anatomy is remarkably variable in dimension,

texture, and color across ethnic groups and among individuals. Moreover, an appreciable difference often exists in the two nipple-areola complexes in the same patient. The presence of an elevated structure in the center of a pigmented area on the breast mound usually represents a nipple, yet wide variability exists as to what constitutes the normal dimensions of the complex.

The nipple areola complex is the primary landmark of the breast. As previously stated, it is located at the prominence of the breast mound. The nipple itself may project as much as ≥ 1 cm, with a diameter of approximately 4-7 mm. The areola consists of pigmented skin surrounding the nipple proper and is on average approximately 4.2-4.5 cm in diameter.

The central position of the nipple cylinder in the areola also has significant variability, ranging from one fourth to one half of the radius off-center. Nipple projection results from the primary location of the mammary ducts in the central portion of the nipple complex. This arrangement produces a semi-rigid structure with a significantly more fibrotic element than the soft and pliable surrounding areola. The contractile properties of the areola also contribute to the gradual change in nipple projection obtained with direct or neural stimuli.

General principles of NAC reconstruction planning

Ideal reconstruction of the NAC requires symmetry in position, size, shape, texture, and pigmentation and permanent projection. Generally, NAC reconstruction can be safely performed in an outpatient setting under local anaesthesia. The authors proposed the following suggestions general guidelines for the NAC reconstruction.

(I) NAC reconstruction is postponed till the final and stable setting of the reconstructed breast mound, optimally 3-4 months following breast reconstruction (14-17). Timing of NAC reconstruction is crucial to the final aesthetic result. Surgical decisions made too early may result in asymmetric placement of the nipple. Adjuvant therapies need to be taken into consideration as the tissue healing effects of radiation and chemotherapy may compromise final outcomes. The ideal timing for reconstruction is approximately 3-5 months after the last revisional reconstructive surgery. This allows for swelling and inflammation to subside, while allowing for settling of the reconstructed breast mound into its final position (18).

(II) In unilateral reconstruction, the contralateral NAC serves as a template.

Table 1 Various types of nipple reconstruction	
Examples of techniques	
Composite nipple graft	N/A
Local flap	Central based flaps Subdermal pedicle flap Double subdermal pedicle flap Pull-out/purse-string flap
Flaps with autologous graft augmentation	Cartilage graft Fat graft
Flaps with alloplastic augmentation	Silicone gel Hyaluronic acid Calcium hydroxylapatite (Radiesse™) Artificial bone substance (Cerattice™) Polytetrafluoroethylene (PTFE)
Flaps with allograft augmentation	AlloDerm™



Figure 1 Result of nipple reconstruction. Two weeks following composite nipple graft.

(III) In bilateral reconstruction, the surgeon must make use of standard values to create a nipple position, size, and areola size. A review of 600 breasts showed that the mean diameter of the areola is approximately 4 cm, with average nipple diameter being 1.3 cm and the average nipple projection is 0.9 cm (19). The average nipple-areola and areola-breast proportion is approximately 1.3 cm (20).

(IV) Loss of projection of the reconstructed nipple should always be anticipated due to contraction, and overcorrection of 25-50% of the desired result is advisory in NAC reconstruction with local flaps.

(V) The type of previous breast reconstruction is another important factor to consider in patient selection. Patients who undergo prosthetic-based breast reconstruction will

have a thin, expanded skin-subcutaneous tissue base, usually with a centrally placed mastectomy scar. On the other hand, in autologous reconstruction, patients will typically have a variable sized donor tissue skin paddle with an elliptical or circular shaped scar with a thick base. These factors are important in eventual NAC reconstruction as thin flaps can potentially decrease nipple projection and poorly located scars can prohibit the use of certain flap techniques due to interference with blood supply.

Classification of nipple reconstruction (according to techniques)

There are many innovative ways to create a NAC. Although many claim some methods are superior to others, each method has unique characteristics that apply to certain breast types (*Table 1*). In this section, multiple categories of reconstructive techniques will be explored, focusing on the desirable and undesirable aspects of each.

Composite nipple graft

Initiated by Adams in 1944 and described by Millard in 1972, contralateral nipple grafts have remained as a popular method for nipple reconstruction in patients with excess contralateral nipple projection (21,22). Patients with projection in excess of 5-6 mm are ideal candidates for composite nipple grafts (*Figure 1*). Many patients have reservations about this method of nipple reconstruction due to: (I) fear of contralateral surgery; (II) donor site morbidity; and (III) decreased contralateral nipple sensation.

Most patients decline to have surgery on the normal breast and NAC, and sharing is only used in selected cases such as hypertrophic contralateral nipple (Excellent option for patients with contralateral nipple >1 cm projection) or thin skin coverage in an alloplastic breast reconstruction (23). Banked nipple grafts for replantation is an alternative, however frequently lose pigmentation and produce variable aesthetic results (24), as cryopreservation causes severe damage to skin components of the nipple, which are seen when examined under electron microscopy (25).

Zenn *et al.* reviewed 57 patients who underwent composite nipple grafting. They found that only 47% of patients considered donor site sensation as “normal”, but found that 96% of patients were happy with the overall appearance, with 87% retaining erectile function in the donor nipple (26). In contrast, in the grafted nipple, the study found that 35% of patients had sensation in the

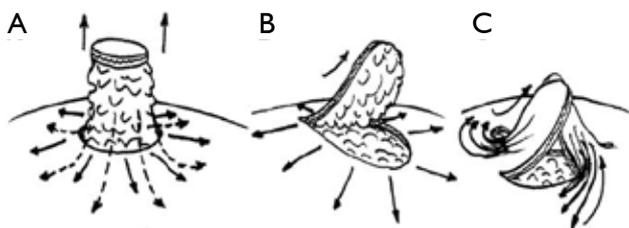


Figure 2 (A) Centrally based local flaps; (B) Subdermal pedicle local flaps: single pedicle; (C) Subdermal pedicle local flaps: double pedicle.

reconstructed nipple within an average of six months. Interestingly, 42% of patients reported to having erectile function in the reconstructed nipple within an average of three months. In addition, they found complete graft take in both patients that had previous irradiation.

Composite nipple graft was excellent option for patients with contralateral nipple >1 cm projection and early postoperative discoloration is normal and expected.

Local flaps

Local flaps for nipple reconstruction can be divided into three groups: centrally based flaps, subdermal pedicle and pull-out/purse-string flap techniques (Figure 2).

Of primary concern in nipple reconstruction is the creation of a long-lasting projection. This is influenced essentially by two factors: (I) retraction forces of surrounding and underlying tissues and (II) tissue contraction of the flap. The power of retraction forces significantly differ between centrally based and subdermal pedicle flaps. Centrally based flaps are subjected to the greatest retraction forces, which act on the entire base of the flap. In subdermal pedicle flaps these forces are significantly reduced, because the major part of the flap is freed from the underlying tissue and thus protected from retraction. Contraction, however, occurs to a variable degree in all local flaps, resulting in loss of flap volume and projection. Contracture of superficial scars adds to this effect. Flaps with complicated design are subjected to more scarring and contracture.

In addition, blood supply is an important determinant of flap shrinkage. Subdermal pedicle flaps are nourished through the rich subdermal plexus and thus have better blood supply compared to central core flaps, which depend on blood supply via the subcutaneous tissue. Scarring or irradiation can significantly compromise blood supply and, therefore, the final result of all flaps. Essential prerequisites

to achieve a stable flap size are a wide pedicle, simple flap design, and separation from retractile surrounding tissues.

Local flap techniques have evolved significantly over the past years. Evolution was directed towards improving blood supply, minimizing retraction forces by simplification of flap design and by rejection of centrally based flap techniques. Enhanced vascularization was achieved by widening of the subdermal pedicle base and development of double-pedicle flaps (Figure 2).

One example of subdermal pedicle base flap which is popular amongst the surgeon is Star Flap. This flap has the advantage of eliminating skin graft donor site morbidity by allowing for primary closure and possibly an improved cosmetic result. On the other hand, the main disadvantages of the star flap are the lack of projection (27). Kroll *et al.* followed 47 patients who underwent star flap nipple reconstruction. He found that mean projection achieved was 1.97 mm after a 2-year follow-up (28). Few *et al.* used a modified star-dermal fat flap technique on 93 nipple reconstructions. They designed a flap with a blunted central wing and two opposing lateral triangles, or wings. The flap lengths directly correlated to the gain in projection. They found that 1 cm in flap length gave 0.16 cm in projection. In addition, long-term projection loss was 59% using their modification (1).

Shestak *et al.* used the star flap in patients with <5 mm of contralateral nipple projection and no areola projection. He followed 28 patients for 12 months and analyzed the degree of loss of projection. Similar to the skate flap, he found that the greatest loss of projection occurred in the first three months and stabilized at six months. They found an average of 43% loss of projection at 12 months postoperatively (29).

Modifications of the “Star Flap” is also widely used. These flaps can all be assigned to the category of star and wrap flaps (Figure 3). Some surgeons incorporated more subcutaneous fat in the lateral arms of the flap for additional nipple bulk. Wong *et al.* tattooed the whole area of the future areola 2-3 weeks before nipple reconstruction (30). Eskenazi tattooed the ‘star flap’ only with subsequent dissection of the flap and followed by tattooing of the corrected area of the areola. The flap base was varied as dictated by the direction of local scars.

Pull-out/purse-string flap technique is the last techniques for nipple reconstruction using local flap described in the review. The designs described in the following section represent unique methods to create nipple and/or areolar projection using surrounding tissue mobilization and purse-string techniques. These flaps are best used when the breast



Figure 3 Result of nipple reconstruction with “Modified Star Flap” technique.

mound tissue is supple and able to be mobilized to enhance projection. The techniques include “Bell Flap”, “Double opposing peri-areolar/purse-string Flap” and “Top-hat Flap”.

Flaps with autologous graft augmentation

The concept of using autologous tissue for nipple augmentation is introduced in order to overcome the common problem of late flattening after reconstruction with local flap. The techniques include cartilage graft and fat graft.

Auricular cartilage was first advocated by Brent and Bostwick in 1977 as method to augment nipple reconstruction (31). This method was then modified by Tanabe *et al.* to be included within a dermal-fat flap to maintain projection (32). Some surgeons believe that the cartilaginous structure provides long lasting results with minimal loss of projection (33,34).

Costal cartilage grafts have been advocated by Guerra and colleagues in autologous breast reconstruction (35). They report successful use of the arrow flap in a large series of 454 patients in conjunction with a costal cartilage graft harvested and banked during the initial free flap reconstruction. Their group found a 4% cartilage graft loss attributed to local flap ischemia and infection. Despite these complications, long-term projection was maintained. Cheng *et al.* also described maintaining nipple projection in Asian females with the use of a modified top-hat flap in combination with costal cartilage banked at the initial flap inset (36). After long-term follow-up of 58 patients, they found an average of 26.1% projection loss after 45 months. In addition, they had a 12% complication rate, mostly related to partial flap loss, nipple malposition, and cartilage

exposure (37).

Fat grafting has become an increasingly popular method as a surgical adjunct for soft tissue augmentation in all aspects of plastic surgery. Therefore, the use in nipple reconstruction seems to be a logical step in fat grafting utility. Bernard outlines steps for the use of fat grafting in primary and secondary nipple reconstruction (38).

In primary reconstruction, the proposed neo-nipple location is marked but not incised. Donor fat is harvesting from the abdominal or other donor region using Coleman aspiration cannulas. After concentrating the fat, 1 cc syringes are prepared and instilled into the proposed nipple site. Only 1-2 cc are needed and this process may be repeated in interval settings. After sufficient time passes to allow for partial fat resorption, the original flap is elevated and sutured into place. This technique may be useful in patients who have had tissue expansion leading to thinned dermis and subdermal fat.

Flaps with alloplastic augmentation

Alloplastic grafts have been used for nipple reconstruction to provide stable projection. The main disadvantage to using nonautologous tissue is the risk of infection and extrusion. Fillers can bleed into surrounding tissue and may interfere with oncologic surveillance. Some of the currently used materials include hyaluronic acid and calcium hydroxylapatite (39-41).

Hallock advocated the use of a polyurethane-coated silicone gel implant for nipple creation as a salvage-type procedure. The study reported the use of silicone implants for two nipple reconstructions with no reported capsule contracture at one year (42). This type of implant is only reserved for special cases and is rarely used today.

Evans *et al.* used Radiesse™, injectable calcium hydroxylapatite embedded in a cellulose gel, to augment the reconstructed nipple. The gel scaffold allows for tissue ingrowth to aid in stability. The initial study included evaluation of six patients over an average of six months of follow-up. The average time from the original nipple reconstruction to the injection was 237 days. A majority of the group indicated major improvements to the appearance of the nipple and one patient reported a little decrease in projection. Overall, they found that all patients were satisfied with the use of Radiesse™ (39).

Hyaluronic acid is an attractive option for nipple projection augmentation. Panetti *et al.* used this to augment nipple reconstruction and performed injections at

2, 4, and 7 months after nipple creation. Reliable projection was maintained at 12 months, but they found that one patient had a false-positive result on PET scan (40).

Yanaga *et al.* evaluated 100 patients who underwent nipple reconstruction with bilobed dermal flaps and a skin graft with an artificial bone substance, Ceratite™, at the center to provide projection. This group found maintained long-term projection with an average of 80.5% nipple height symmetry to the contralateral side. In addition, there was a 5% exposure rate, which was related to dermal flap tension (43).

Wong *et al.* used polytetrafluoroethylene (PTFE) as a method to create nipple projection. This method was utilized in selected patients: either in secondary reconstruction or when there was a lack of donor tissue for a local flap. A total of 17 patients underwent placement of PTFE into a subcutaneous pocket at the desired nipple location. An amount of 3.5 mm PTFE are used to create the initial desired projection with 3.0 mm pieces used for added contour. In the series, all patients were reported to be satisfied or very satisfied with their results. One patient had implant extrusion secondary to infection, but was later replaced after the infection subsided. Overall, they found projection of 4-5 mm (44).

Flaps with allograft augmentation

Acellular dermal allografts represent a new and revolutionary product in the field of breast reconstruction. After gaining wide acceptance for the use in implant-based reconstruction, the use of acellular dermis has expanded to all aspects of revisional and secondary breast reconstruction, including nipple reconstruction. Long term projection will likely have mild moderate projection loss.

Allografts have many of the ideal properties of an implantable material, as they have a high rate of incorporation with limited resorption. Because of the ability to incorporate into surrounding tissues, infection is limited.

Nahabedian first used AlloDerm™, human-derived acellular dermis, for revisional nipple reconstruction in 2005. A small piece (1 cm × 2 cm) of AlloDerm™ is cut and folded upon itself and sutured in place with absorbable suture. The dimensions of the AlloDerm™ piece were 2 mm × 6 mm. This piece is then oriented vertically to serve as a strut within the pocket made by the wings of the flap. Among the five secondary nipple reconstructions using AlloDerm™, four of the nipple exhibited 4-5 mm of maintained projection at follow-up, ranging six months to one year. In addition, tertiary nipple reconstruction with AlloDerm occurred in three patients. A total of 4-5 mm of

projection was maintained in these patients as well at follow-up ranging from 6-8 months. AlloDerm™ was incorporated into the base of the reconstructed nipple using the C-V flap or elongated C-flap (45).

Garramone and Lam evaluated the long-term nipple projection after using AlloDerm™ in primary reconstruction. A total of 30 nipple reconstructions (16 implant-based breast mounds and 14 TRAM breast mounds) using a star dermal flap, were evaluated. In contrast to the previous technique, the AlloDerm™ piece was cut into a strip measuring 1.5 cm × 4.5 cm. This piece was then rolled upon itself and sutured together. This then was secured into the pocket formed by the flaps. Among the 16 patients who had TRAM flaps, the average initial projection was 1.2 cm, with the average 12-month projection being 0.7 cm. In the implant-based group, the average initial projection was 1.15 cm and the 12-month average projection was 0.5 cm. Maintained projection after 12 months was 56% for the TRAM group and 47% for the implant group. Overall, the average maintained projection was 51.2% after 12 months follow-up (46).

Recently developed, the Cook medical nipple reconstruction cylinder is another good option for acellular dermal augmentation. This cylindrically shaped product is shaped perfectly to fit into a subcutaneous pocket. This product eliminates the need to shape or roll acellular dermal products and eliminates any size discrepancies that would cause asymmetry.

Areola reconstruction

The major challenges of areola reconstruction are to recreate the pigmentation and texture typically associated with a native areola. The most commonly employed techniques involve using skin grafts, tattooing, and/or a combination of these two techniques. Also, the surgeon must choose an appropriate timing for the reconstruction. Skin grafting is preferentially performed in the immediate setting or at the time of nipple reconstruction. Tattooing usually occurs at 6-8 weeks after nipple reconstruction, but some have good results and advocate for simultaneous nipple creation and tattooing (47).

Skin grafting of the areola

Skin grafting of areola has the advantages of providing a textured, wrinkled surface and distinct pigment differences, both of which resemble a normal areola with Montgomery tubercles. Common donor sites for areola skin grafting include contralateral areola, inner thigh/groin region, revised/excess

breast skin, or other body areas, where revisional surgery is needed. In addition, to avoid a donor site, the planned areola can be elevated and raised as a skin graft and re-placed into its original position (48).

Tattooing

Tattooing is the other major adjunct to areola reconstruction. Either used by itself or in conjunction with skin grafting, tattooing can provide excellent areolar color match with limited morbidity. Initially introduced by Rees (49) and Spear *et al.* (50) in 1975. Tattooing uses intradermal pigments, typically mixtures of iron and titanium oxide chosen from a color plate. These pigments are then electrically deposited revised/excess breast skin, or other body areas, where revisional surgery is needed.

In addition, to avoid a donor into the upper and mid-papillary dermis. Sterile technique is mandatory as disease and viral transmission is possible. Pigment placement too superficially will result in pigment extrusion and sloughing, while deeper placement leads to macrophage processing and removal, both resulting in early pigment fading (51).

In unilateral cases, colors should be chosen that are slightly more pigmented than the contralateral areola. Spear and Arias found that 9.5% of areolas needed touch ups for pigment fading and that 60% of all areolas were described as being too light during the study interval (52). Thus, many patients will likely need touch-up tattooing after several months or years to achieve an aesthetically symmetric color match.

After tattooing is performed, the area will usually undergo sloughing and crusting for 3-5 days. The area should be kept moist with bacitracin or other type of petroleum jelly and dressings should be changed daily. After this period, slight de-pigmentation may occur and many patients will require touch-ups in the next few months.

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Footnote

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Bilateral breast reconstruction with bipedicle transverse rectus abdominis myocutaneous (TRAM) flap for simultaneous delayed and immediate breast reconstruction after therapeutic modified radical mastectomy and prophylactic nipple sparing mastectomy

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Abstract: Contralateral prophylactic mastectomy (CPM) rate is increasing worldwide recently due to better understanding of genetic and hereditary breast cancer. The evolution of mastectomy technique from modified radical mastectomy to nipple sparing mastectomy with immediate or delayed breast reconstruction is also a potential cause of increasing mastectomy rate. This case report presents a young woman who had breast cancer at very young age then she decided for CPM due to her sister and mother are also breast cancer victim. We report clinical course and immediate outcome of the oncologic and reconstructive surgery in this case.

Keywords: Breast reconstruction; transverse rectus abdominis myocutaneous flap (TRAM flap); modified radical mastectomy; prophylactic mastectomy; nipple sparing mastectomy

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Introduction

Breast cancer is the most commonly diagnosed cancer in women and the second leading cause of cancer mortality in women (1). It is estimated that between 5% and 10% of all incidents of breast cancer can be attributed to hereditary breast cancer susceptibility genes, including BRCA1 and BRCA2 (2). Women who inherit a BRCA1/2 mutation have a 40% to 65% lifetime risk of breast cancer (3).

BRCA testing is suggested to perform after the completion of primary surgery for breast cancer in the high-risk patient, for example, early-age-onset breast cancer, triple negative breast cancer, patient with breast cancer in first degree relative at the age of 50 (4). BRCA gene mutation testing has become widely available in clinical and research settings, many women are being tested and once their genetic testing found to have deleterious BRCA mutations, they will be counseled to undergo a second breast surgery including prophylactic mastectomy or bilateral salpingo-oophorectomy (SO) as the preventive and

management options for risk reduction.

Contralateral prophylactic mastectomy (CPM) is potentially indicated for risk reduction in patients at high risk for the contralateral breast cancer. After CPM is performed, breast reconstruction is the further options for patients. However, they have to choose between immediate reconstruction which has a better aesthetic outcome due to preservation of the three-dimensional breast skin envelope and the benefit in the psychological aspect. Whereas, delayed breast reconstruction is usually reserved for patients who will require post-mastectomy radiotherapy (PMRT) (5). Prostheses implant or autologous tissue for breast reconstruction is another topic that the surgeons must discuss with their patients.

We report a breast cancer patient who underwent immediate breast reconstruction and delayed breast reconstruction on the index breast.

Case report

A case of 29-year-old woman presented at breast cancer



Figure 1 Pre-operation.

clinic concerned about her risk of developing contralateral breast cancer. Ten years ago when she was 19 year-old, she had breast cancer diagnosed. She underwent left modified radical mastectomy followed by adjuvant chemotherapy and radiation therapy. The pathological report was invasive ductal carcinoma, stage IIB T3N0M0, triple negative subtype. At the age of 25, she had large multiple intramural myoma uteri and underwent transabdominal hysterectomy (TAH) with left salpingo-oophorectomy (SO).

She has family history of breast cancer in first degree relatives. Her mother and her sister were diagnosed of breast cancer at the age of 30 and 35 respectively. Her grandmother also died from breast cancer with unknown age of onset. Since her strong family history of breast cancer, she came to the breast cancer clinic and asked for prophylactic mastectomy for her right breast. She survives for ten years without any locoregional recurrence and distant metastasis evidence.

Right prophylactic nipple-sparing mastectomy with immediate breast reconstruction with ipsilateral pedicle transverse rectus abdominis myocutaneous (TRAM) flap was performed. Left delayed reconstruction with ipsilateral pedicle TRAM flap was done simultaneously. The entire operation lasted five hours and she had uneventful recovery during the admission. The pathological report of right breast showed benign breast parenchyma without evidence of malignancy. The last visit at the clinic three months post operation, there was no flap complication and the patient

was very satisfied with her cosmesis appearance.

Discussion

The rate of CPM is increasing worldwide. There are several reasons for patient and physician to opt for CPM, such as, better understanding of genetic and hereditary risk or immediate breast reconstruction. This woman is a good candidate for CPM, because she has strong family history of breast cancer. Her mother and her sister were diagnosed of breast cancer in the young age.

The individuals most likely to benefit from prophylactic mastectomy are BRCA gene carriers and those who have a strong family history of breast cancer. And this patient who has a personal history of breast cancer is also at higher risk for developing contralateral breast cancer (6).

Even though the BRCA mutation testing have not been done because of her financial problem, but from her strong family history of breast cancer, her risk of a second breast cancer is up to 35% much higher by 16 years after the diagnosis of index cancer (7). Moreover, her history of breast cancer will increase the cumulative risk of 17% at 20 years after the diagnosis of first breast cancer (8).

CPM is potentially indicated for risk reduction in patients at high risk for the contralateral breast cancer, patients in whom subsequent surveillance of the contralateral breast would be challenging because of the increased density or diffuse indeterminate microcalcifications, and for achieving symmetry in the contralateral breast or achieving balance in non-reconstructed patients (9). According to the report CPM can reduce 94% to 96% of breast cancer at a median follow-up of ten years in 745 women with a first breast cancer and family history of breast cancer (10).

Therefore, CPM is a reasonable choice for this patient. Considering her compliance to perform second surgery, we chose to perform the right nipple-sparing mastectomy with immediate breast reconstruction. Pedicle TRAM flap were raise bilaterally and transferred to both chest for right immediate breast reconstruction and left delayed breast reconstruction. This case is also a good candidate for other reconstruction techniques, for example, implant based reconstruction, bilateral extended latissimus dorsi flaps, latissimus dorsi flap with implant or bilateral microvascular free tissue transfer using autologous tissue (*Figures 1,2*).

Conclusions

The more advance knowledge and technology in diagnosis



Figure 2 Post-operation two months.

of hereditary breast along with evolution of breast cancer surgery has already altered the current breast cancer treatment. The rate of prophylactic mastectomy is increasing and therefore its benefit is proven among genetic and very high risk patient. The quality of life for post mastectomy patient as well as for mastectomy candidates are also improved and maintained due to breast reconstructive surgery. This case report shows a successfully treated young breast cancer patient who has CPM done ten years after primary oncologic surgery and also had simultaneous bilateral breast reconstruction. The oncologic and reconstructive benefit should always be discussed for individual patient to achieve maximal satisfaction and survival.

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Footnote

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Achieving ideal breast aesthetics with autologous reconstruction

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Abstract: Achieving ideal breast aesthetic has become a top priority for women considering breast reconstruction following mastectomy. The use of autologous tissue is generally regarded as providing the most natural results because donor tissues quality and consistency is similar to that of the native breast. There are several donor sites that are particularly useful for autologous reconstruction that include the abdomen, gluteal region, posterior thorax, and the thigh. Traditional and microsurgical techniques can be used. Shaping is a critical component and involves a basic understanding of the footprint, conus, and skin envelope. This manuscript will review many aspects of breast shaping in-order to achieve aesthetically pleasing results in a predictable manner.

Keywords: Breast reconstruction; autologous; flaps; microsurgery; pedicle flap; outcomes

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Introduction

Modern viewpoints of breast reconstruction following mastectomy have emphasized quality, outcome, and patient satisfaction as the ultimate endpoints. This is true for both prosthetic and autologous reconstruction. Traditional concepts of breast reconstruction had focused on creation of a mound that may or may not have resembled the natural breast contours. Modern concepts of breast reconstruction however focus on the creation of a breast that resembles if not improves upon the natural breast shape. Breast reconstruction has evolved from a purely reconstructive endeavor to one that places importance on artistry and aesthetics. This is especially true for autologous reconstruction because there is no template or prosthetic device to shape the breast mound. Autologous reconstruction requires a skill set that emphasizes shaping, configuring, and positioning the new breast based on patient expectations, body habitus, and surgeons' skill.

The evolution of autologous reconstruction has placed in increasing emphasis on reducing donor site morbidity and improving breast aesthetics. Autologous options have expanded and now include the traditional pedicle

flaps as well as the newer microvascular perforator flaps. Pedicle options such as transverse rectus abdominis musculocutaneous (TRAM) and the latissimus dorsi (LD) flaps continue to remain viable options and are capable of producing excellent aesthetic outcomes. Perforator flaps such as the deep inferior epigastric perforator (DIEP), superior gluteal artery perforator (SGAP), inferior gluteal artery perforator (IGAP), transverse upper gracilis (TUG), and the profunda artery perforator (PAP) flap are also equally capable of producing excellent aesthetic outcomes. This manuscript will focus on many of these autologous options and provide a template or framework based on the authors experience on achieving ideal breast aesthetics following in the setting of total breast reconstruction following mastectomy.

It is important to have an appreciation of ideal breast aesthetics when embarking on reconstruction. The position of the breast on the chest wall should serve as footprint for the breast to be reconstructed. The natural shape or cone of the breast should be appreciated in order to estimate the amount of skin that will be required to achieve ideal proportions. It is important to understand the relationship of the torso to the breast in order to reconstruct a breast

that will be appropriate for the patient's frame and body habitus. The ultimate goal is to create symmetry, proportion, and contour.

Traditional teaching for breast shaping occurs during residency or fellowship in plastic and reconstructive surgery. It is based on an apprenticeship or mentorship model where resident or fellow sees, does, and teaches. Initially the technical aspects of the operation are the most important and require mastery; however, with surgical maturation, the aesthetic aspects become as important and thus the artistic nature of breast reconstruction comes to fruition. The three-step principalization of breast reconstruction was described by Blondeel *et al.* and is an excellent foundation from which to start ones journey to achieving ideal breast aesthetics (1-4).

The concept is based on the breast footprint, the conus, and the skin envelope. The footprint is unique for each woman and defined and fixed for each breast. The borders of the footprint include the clavicle, lateral edge of the sternum, anterior axillary line, and the inframammary fold. It is important to appreciate that the footprint is stable and does not change with weight gain or loss. The footprint represents the foundation for the conus. The conus represents the 3-dimensional shape, volume, projection, and contour of the breast. This will vary with weight gain or loss. The conus is typically characterized with a lower pole prominence. In general, the ideal breast proportions based on the ratio of lower and upper pole is defined as 55% from the nipple to the IMF and 45% from the nipple to the upper edge of the breast. The final component is the skin envelope. In the setting of immediate reconstruction, the quality and quantity of skin is important. Skin quality is affected by previous surgery, radiation, scar, and vascularity.

Preoperative considerations

Preoperative factors are important considerations prior to autologous breast reconstruction (5). Patient co-morbidities must be assessed and managed. Conditions such as diabetes mellitus, hypertension, and cardiac disease must be optimized. Tobacco use is strictly discouraged. Preoperative or postoperative radiation is also noted and reviewed. Physical examination must include the breast, donor site, presence of scars, quality of tissue, as well as relevant measurements such as the base width and location of the nipple areolar complex. The footprint of the breast must be appreciated, as this will be the template for the new breast mound.

Timing of autologous reconstruction

Breast reconstruction with autologous tissue can be performed immediately following mastectomy, on a delayed basis following mastectomy, or following reconstruction using prosthetic devices. It can also occur prior to radiation therapy or after radiation therapy. There are several strategies that are useful for reconstructive surgeons in order to optimize aesthetic and surgical outcomes.

In cases of immediate breast reconstruction, the quality of the mastectomy will have a significant impact on the quality of the reconstruction. Most mastectomies are performed using either skin sparing techniques or nipple areolar sparing techniques. With both approaches, the vascularity of the remaining mastectomy skin flaps must be maintained. Incisional approaches for the mastectomy may be apical, inframammary, or lateral areolar. When there has been extensive undermining of the mastectomy flaps, the natural borders are reestablished by suturing the inframammary and lateral mammary folds back to the chest wall. If the vascularity of the mastectomy skin flaps is compromised, the edges are excised until normal bleeding is observed. With all of these approaches, autologous reconstruction can be performed with excellent aesthetic outcomes.

An important and sometimes overlooked aspect of achieving ideal breast aesthetics is to make the necessary adjustments to the skin envelope following mastectomy in the setting of immediate reconstruction. When the mastectomy skin is in excess, it should be debrided to fit the flap. In the setting of a skin sparing mastectomy, the circular excision pattern can be further excised and adjusted to fit the desired skin paddle of the flap with a purse string suture technique. An alternative option is to partially inset the flap medially and then excise the lateral mastectomy skin such that a laterally based "lollipop" pattern is created. With nipple sparing mastectomy it is important to ensure that enough donor tissue is present to fill the skin envelope.

In women considering delayed reconstruction, there are several factors that must be considered. In patients that have had radiation therapy prior to autologous reconstruction, adequate time must elapse in order to allow the tissues and vascularity to recover (6). This is typically 6-12 months. In those patients that will receive radiation therapy following reconstruction, consideration must be given to the type of reconstruction being performed. It is known that one of the long-term effects of radiation on breast tissue and fat is shrinkage and distortion. In order to eliminate these



Figure 1 The flap is positioned on the chest wall with the medial edge along the sternal border.

effects, many reconstructive surgeons have adopted the delayed-immediate approach as a means to avoid radiation damage to the flap (7). A subpectoral tissue expander is placed immediately following the mastectomy and becomes the conduit for the radiation beams. Following radiation, the device is removed and replaced by a flap. Most tissue expanders and implants are placed totally or partially behind the pectoralis major muscle. When these devices are removed, the pectoralis major muscle is always placed back on the chest wall such that the flap is positioned on top of the muscle. This will allow for optimal aesthetics. In addition, radiated tissue that has been extensively damaged or fibrotic is usually excised. In these cases, the inferior edge of the flap usually becomes the upper aspect of the inframammary fold.

Breast shaping with abdominal flaps

Abdominal flaps such as the TRAM, DIEP, and SIEA flaps remain the most commonly used flaps for autologous reconstruction (8,9). The reasons for this are that the abdominal donor site often provides ample tissue for a unilateral or bilateral reconstruction, is convenient for flap harvest, allows for reconstruction as a pedicle flap or free tissue transfer, has dimensions that can be tailored to the mastectomy specimen, can be used for immediate or delayed reconstruction, and has superior pliability that facilitates optimal breast shaping. The vascularity of abdominal flaps is based on the superior epigastric (pedicle TRAM), inferior epigastric (free TRAM, DIEP), and superficial epigastric (SIEA) systems. As with all flaps, perfusion must be assessed using conventional methods such as capillary refill, arterial bleeding from the distal edge, and surface temperature. Advanced technologies are also used to assess perfusion such

as fluorescent angiography and near infrared spectroscopy. The zones of perfusion are important and are subdivided into four zones. The perfusion is optimal when the skin and fat are in close proximity to the source vessel; thus zone 1 is the best perfused and zone 4 is least perfused.

Shaping the free abdominal flap

There are several shaping advantages using free flaps for breast reconstruction. The flap is not tethered to the donor site muscle that allows for optimal positioning on the chest wall. The recipient vessels are usually the internal mammary and also the thoracodorsal. The choice of vessel is surgeon dependent. The internal mammary vessels are usually exposed at the level of the 3rd or 4th costal rib segment and are the preferred recipient vessels for the majority of microsurgeons. The thoracodorsal vessels are exposed proximal or distal to the serratus branch. Because these vessels are laterally based, bilateral reconstructions may sometimes result in a slight medial/sternal volume deficiency. This is usually not a problem with unilateral cases because zone 3 can supplement the medial breast. With either recipient vessel couples to the flap vessel, there is usually ample length of the vascular pedicle such that the flap can be shaped and contoured without impediments.

With bilateral reconstruction, the abdominal donor tissue is bisected at the midline such that each flap contains a zone 1 and 2. With bilateral reconstruction, the weight of the mastectomy specimens is usually not important because that volume of flap is fixed. The medial edge of the flap is usually positioned along the sternal border and the lateral aspect of the flap is positioned on the lateral chest wall (*Figure 1*). Suturing of the flap to the chest wall is sometimes necessary with immediate reconstruction especially when the footprint of the old breast is larger than the footprint of the flap. These sutures can be placed superomedially, inferomedially, and laterally. With delayed reconstruction, the dimensions of the created subcutaneous pocket are made to match that of the flap. *Figures 2 and 3* illustrate a patient following bilateral skin sparing mastectomy and immediate reconstruction with bilateral DIEP flap.

With a unilateral reconstruction, it is important to achieve symmetry with the opposite breast. Assessment of patient expectations is critical because it is important to know if the opposite breast will be reduced, augmented, or left as is. The opposite breast is used as a template for the reconstruction. Typically with a unilateral reconstruction, zones 1-3 and sometimes zone 4 are utilized depending



Figure 2 Preoperative image of a patient with left breast cancer.



Figure 3 Postoperative image following immediate reconstruction with bilateral DIEP flaps. DIEP, deep inferior epigastric perforator.

on the amount of tissue required. Because there is usually more tissue with a unilateral flap (zones 1-3) compared to the bilateral flap (zones 1-2), there are more shaping options. The flap can be folded in a conical fashion or it can be folded laterally such that apical portion (zone 2) of the flap is tucked under zone 1 with zone 3 of the flap being positioned along the sternal border. With both maneuvers, the goal is to provide better projection. Suturing the flap laterally is always necessary and suturing the flap along the medial border is sometimes necessary. *Figures 4 and 5* illustrate a patient following delayed reconstruction with unilateral DIEP flap.



Figure 4 Preoperative image of a patient following 2-stage prosthetic reconstruction of the left breast.

Shaping the pedicled abdominal flap

Shaping of the pedicle TRAM flap is slightly different than that of the free flap. This is because the adipocutaneous component of the flap is attached to the rectus abdominis muscle. With a unilateral TRAM flap the flap is based on either the ipsilateral or contralateral rectus abdominis muscle. With a bilateral pedicle TRAM flap, the flaps are based on the ipsilateral rectus abdominis muscle. The advantage of a flap that is tethered to the abdomen and chest is that it is less likely to migrate when inset; therefore, extensive suturing to the chest wall is less likely. Like the free flaps, the pedicle flap can include zones 1-3; however, it is important to appreciate that the vascularity to the distal aspects of the flap may not be as robust compared to the free flaps based on the perfusion dynamics of the primary source vessels. In some patients with a thick adipose layer, the sub-Scarpa fat is sometimes excised to minimize the likelihood of fat necrosis. The orientation of the flap on the chest wall is typically with the cut edge of zone 2 or 3 being placed along the sternal border.

Flap inseting

When inseting the flap following a unilateral or bilateral reconstruction, it is recommended to sit the patient upright to approximately 45 degrees to assess the position, symmetry,



Figure 5 Postoperative image following removal of the left implant and reconstruction with a DIEP flap. DIEP, deep inferior epigastric perforator.



Figure 6 The technique of flap de-epithelization is illustrated.



Figure 7 The inferior edge of the flap is sutured to the lower edge of the mastectomy defect to recreate the inframammary fold in delayed reconstruction.

contour, and projection of the breast. In cases of a skin-sparing mastectomy, the skin territory to be exteriorized is delineated and the remainder of the flap is de-epithelized (*Figure 6*). When a nipple-sparing mastectomy has been performed, a doppler is used to identify an arteriovenous signal and delineated with a 2 cm circle. The remainder of the flap is de-epithelized and the skin paddle is exteriorized. With free flaps, the vascular pedicle must be inspected to ensure that it is not twisted or kinked. With pedicle flaps, the tunneling of the flap can sometimes compress the muscle and blood supply; therefore, it is imperative to reassess the perfusion of the flap to ensure that the perfusion is intact. With delayed reconstruction, the lower mastectomy skin is usually excised and the inferior edge of the autologous flap is used to recreate the inframammary fold (*Figure 7*). *Figures 8 and 9* illustrate a patient following delayed unilateral breast reconstruction with a muscle sparing free TRAM flap.

With both skin-sparing and nipple-sparing mastectomy, the flap can be monitored using traditional monitoring techniques that include hand held doppler, assessment of capillary perfusion, and skin turgor. Skin closure is always performed in a layered fashion using absorbable dermal and subcuticular sutures.

Breast shaping with latissimus dorsi (LD) flaps

The LD flaps can be used for immediate or delayed reconstruction as well as for unilateral or bilateral reconstruction (10-12). This flap has been considered by many plastic surgeons to be a workhorse flap in that it is useful in a variety of situations and can provide predictable outcomes. Although traditionally performed as a pedicle musculocutaneous flap, there are new variations based on the perforator concept that allow transfer of the adipocutaneous component of the flap on a single vascular pedicle without sacrificing the LD muscle. This is known as the thoracodorsal artery perforator flap or TDAP. Because of the limited quantity of fat harvested with this flap, it is commonly combined with an implant for volume and shape. These devices can be placed immediately at time of flap transfer or on a delayed basis as necessary.

Immediate reconstruction with the LD flap

As with all reconstructions, the volume and skin requirements of the new breast are assessed and juxtaposed



Figure 8 Preoperative photograph of a patient following right mastectomy.

in relation to the estimated flap volume. Because the LD flaps provides a limited quantity of skin and fat, the use of a prosthetic device is sometimes required. In making this decision, it is important to assess the footprint, conus, and skin envelope on the natural breast. In the case of a volume deficiency, a tissue expander or permanent implant can be considered. This will also help to augment the projection of the breast in order to better define the desired conus. Other methods to obtain additional volume using the LD flap include beveling the fat away from the skin paddle in order to increase the quantity of fat harvested from the back. This is known as an extended LD flap (11). In the case of a skin deficiency following mastectomy, the skin territory can be replaced using the back. This skin paddle is usually oriented horizontally or obliquely along the resting skin tension lines.

There are several decision points when considering use of the LD flap for breast reconstruction. The decision regarding denervation of the LD muscle is controversial. Some surgeons prefer to leave the thoracodorsal nerve intact to prevent muscle atrophy and to maintain greater volume. Others however, prefer to divide the nerve in order to prevent any animation that may occur with a contracting muscle. The LD muscle can be harvested in total or in part based on the volume requirements. In cases of total breast reconstruction, the entire muscle can be harvested; however,



Figure 9 Postoperative photograph following a delayed right free TRAM flap and contralateral mastectomy. TRAM, transverse rectus abdominis musculocutaneous.

in cases of partial breast reconstruction only a small segment of the muscle may be removed. The harvested LD flap is then passed through a high tunnel from the posterior thorax to the anterior chest wall corresponding to the desired footprint. Patient positioning is also an important consideration. With a unilateral reconstruction, the patient is placed in the lateral decubitus position such that the flap harvest and preparation of the recipient site can occur simultaneously. With a bilateral reconstruction, the flaps can be harvested simultaneously with the patient in the prone position (10). Insetting the flap requires that the patient be turned to the supine position.

Shaping the LD flap is sometimes achieved using the flap alone but more often than not requires the use of a prosthetic device. The device can be placed in the partial subpectoral or prepectoral space. When subpectoral, the edge of the LD can be sutured to the inferior edge of the pectoralis major muscle. This will provide for a larger pocket to accommodate a larger device. When prepectoral, the device is usually covered with the LD muscle itself. The devices can be either a tissue expander or a permanent implant depending on the reconstructive requirements. The advantages of a tissue expander are that the surrounding soft tissues can be expanded to provide a larger reconstruction. In addition, further shaping and contouring can be achieved at the second stage when the tissue expander is exchanged for a permanent implant. The disadvantage of a tissue expander is that in some cases, the thickness of the LD flap



Figure 10 Preoperative photograph following bilateral mastectomy and tissue expander reconstruction. The right breast was radiated and explanted due to infection.



Figure 12 Postoperative photograph following stage 2 (delayed tissue expander) and stage 3 (permanent implant).



Figure 11 Preoperative markings for stage 1 bilateral latissimus dorsi flap reconstruction. LD, latissimus dorsi.

can complicate localization of the expansion port. A remote access port rather than an integrated port is an alternative to mitigate this situation.

Delayed reconstruction with the LD flaps

Delayed reconstruction with the LD flap can be performed using the 1- or 2-stage techniques as described above. However, it is this author's preference to use a 3-stage technique. The first stage involves transfer of the LD muscle to recreate and establish the footprint of the breast, provide a small conus, and to increase the available skin envelope. The second stage involves placement of a tissue expander in the pre or subpectoral space to expand the conus and skin envelope. The third stage involves removal of the expander and placement of a permanent implant. The soft tissue envelope is contoured and shaped to recreate a more

natural breast mound. This 3-stage approach is generally recommended for women that have had either failure of an abdominal flap, premature removal of a prosthetic device due to infection or in women that have had previous radiation therapy. The staged approach allows for improvement of the recipient site by the transfer of vascularized muscle and fat. The use of devices can then be used to expand and contour the new breast mound. *Figures 10-12* illustrate a patient that had delayed bilateral LD musculocutaneous flaps utilizing the 3-stage approach.

Breast shaping with gluteal or thigh flaps

The final category of breast shaping will include the gluteal and thigh based flaps. These will be grouped together because these flaps are usually less voluminous than the abdominal counterparts and immediate shaping is not always possible. Because these flaps are remote from the breast, they can only be used as a free tissue transfer. Although effective, most surgeons consider these flaps to be a second choice in the event that the abdomen is not a suitable donor site either because it has been previously used, the patient is too thin, or prior operations/scars preclude its use.

Gluteal flaps

Gluteal flaps include the perforator (SGAP and the IGAP) as well as the musculocutaneous (gluteal) flaps (13-15). Both the upper and lower buttock regions can be used and provide similar quantities of skin and fat. These flaps tend to be thicker than most LD and abdominal flaps in women with BMI <30 and are usually not considered in women



Figure 13 Preoperative photograph following bilateral mastectomy and right chest wall radiation therapy.

with a BMI of >35 . These flaps tend to have a shorter vascular pedicle than the abdominal flaps and optimal positioning on the chest wall may be compromised. The dimensions of these flaps are usually based on the gluteal dimensions and typically range from 12 to 25 cm in length and 6 to 10 cm in width. Gluteal thickness in patients that are candidates for these flaps tends to range from 4 to 8 cm. For this reasons, many of these flaps cannot be coned or shaped and are therefore inset as it. Secondary contouring of these flaps is usually necessary. However, in some cases, extended or re-designed gluteal flaps can be harvested that will allow for coning or better shaping of these flaps (15). In cases of delayed reconstruction where a gluteal flaps is considered, pre-expansion of the breast skin to provide an increased skin envelope can improve aesthetic outcome (14). *Figures 13 and 14* illustrate a woman preoperatively and following staged bilateral SGAP flaps.

Thigh flaps

Flaps derived from the medial and posterior thigh are frequently considered when the abdomen is not a suitable donor site (16-18). Medial thigh flaps include the transverse musculocutaneous gracillis flap and posterior thigh flaps include the PAP flaps. The medial thigh flaps tend to be longer in width and shorter in height compared to abdominal and latissimus flaps and usually less bulky than gluteal flaps. Typical dimensions are 25-30 cm in length and 8-10 cm in height. Medial thigh flaps typically able to reconstruct a breast of mild to moderate volume (16,18). The dimensions of the flap can make inset challenging and ultimately necessitate a greater revision rate both for the ipsilateral and contralateral breast. The use of this



Figure 14 Postoperative photograph following staged bilateral SGAP flaps and delayed insertion of 100 cc saline implants at 3-year follow-up. SGAP, superior gluteal artery perforator.

flap is highly advocated for bilateral reconstructions when symmetry can be more easily achieved. Most medial thigh flaps will include a segment of the gracillis muscle whereas the posterior thigh flaps do not include any muscle.

Shaping the breast using medial thigh flaps has been described (17). The segment of gracillis muscle is usually placed along the area where the cartilaginous rib harvest has occurred to minimize visibility of this. Because of the added length of these flaps, they lend themselves nicely to coning by suturing the anterior and posterior edge of the flap together. The coned flap is positioned on the chest wall to ensure adequate coverage of the footprint and to generate adequate projection.

The posterior thigh also known as the PAP flap is rapidly becoming one of the more popular alternatives to the abdomen (19). Like the medial thigh flap it tends to be long and thin with dimensions that range from 20 to 30 cm by 6 to 10 cm. The vascular pedicle is 7-13 cm in length that permits for optimal placement of the flap on the chest wall as well as use of the internal mammary or thoracodorsal recipient vessels. The flap, by nature of its dimensions and elliptical design, can be easily shaped into a cone to provide optimal projection. These tissues are more pliable than the gluteal tissue and sometimes more pliable than the abdominal tissue that facilitates coning and achieving ideal aesthetics. Flap weight typically ranges from 250 to 600 grams and can be used unilaterally and bilaterally. The incidence of fat necrosis has been generally $<10\%$. Secondary recon contouring is usually not necessary.



Figure 15 Preoperative photograph of a woman following bilateral DIEP flap reconstruction. The breasts are too ptotic due to the redundant skin envelope. DIEP, deep inferior epigastric perforator.

Secondary revisions

Secondary revisions are often necessary following autologous reconstruction (20). This may be to restore volume, contour, and position. This may include both breasts in the setting of a bilateral reconstruction as well as the ipsilateral and contralateral breast in the setting of a unilateral reconstruction. Various techniques are available for the reconstructed breast that includes soft tissue recontouring, fat grafting, burying the flap, and implant placement. Achieving symmetry with a non-reconstructed breast can be achieved by augmentation, mastopexy, and reduction mammoplasty.

The reconstructed breast

Perhaps the most common method of revision is to recontour the soft tissue by direct excision of skin and fat as well as tissue rearrangement (20). This can be performed to reduce the volume, improve the shape, reposition the breast on the chest wall, and to better define the inframammary or lateral mammary folds. The use of autologous fat grafting to correct contour deformities and to improve skin quality has become another common method of revision that has achieved success. The placement of fat along the upper pole of the breast and chest wall is an ideal method to achieve natural contours. Fat grafting has also been used in radiated breasts where skin damage is present. The ability of fat and stem cells to regenerate, hydrate, and revascularize



Figure 16 Postoperative photograph following de-epithelialization and burying of the flaps at 2-year follow-up. Fat grafting was also performed in the upper pole of both breasts.

damaged skin has been described (21). For the autologous reconstruction that is too ptotic, the technique of burying the flap has demonstrated success. The skin territory is outlined with an elliptical extension and de-epithelialized. The mastectomy skin flaps are undermined superiorly and inferiorly and then re-approximated. *Figures 15* and *16* illustrate a patient that has had both flaps de-epithelialized and buried under the superior and inferior mastectomy skin flaps.

For the reconstructed breast that is deficient in volume, two methods of correction are commonly employed. The first is to fat graft the substance of the flap and the second is to place a small implant under the flap. The implant is usually saline and ranges in volume from 80 to 125 cc. In women with a history of chest wall radiation, the device is placed in the prepectoral position; whereas in women without a history of radiation therapy the device is placed in the subpectoral position. *Figures 17* and *18* illustrate a woman that had small implants placed beneath the flaps to augment volume.

The non-reconstructed breast

In unilateral reconstructions, the non-reconstructed breast is sometimes modified to achieve symmetry (22). Options include unilateral augmentation with an implant, mastopexy, and reduction mammoplasty. Implant selections is facilitated by volumetric analysis using 3-dimensional imaging. The technique is essentially that of a standard breast augmentation. When volumes are similar but the natural breast is ptotic, a mastopexy is often performed.

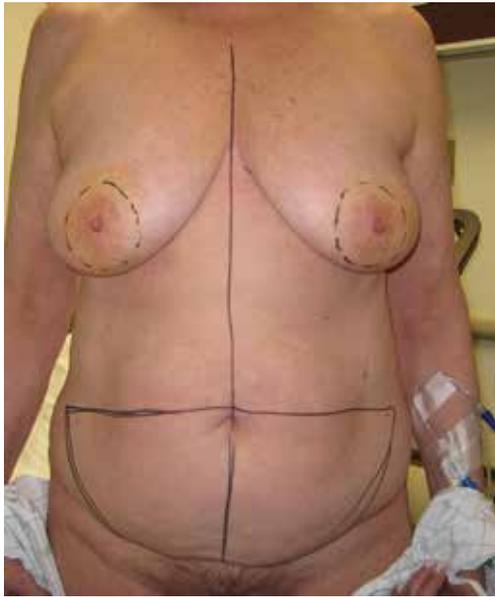


Figure 17 Preoperative image of a woman with right breast cancer scheduled for bilateral DIEP flap reconstruction. DIEP, deep inferior epigastric perforator.



Figure 18 Postoperative image following immediate reconstruction with bilateral DIEP flaps and delayed revision with 125 cc saline implants placed under the flaps at 2-year follow-up. DIEP, deep inferior epigastric perforator.

This is usually via a circumvertical approach; however, when extreme, inverted T techniques are performed. When the reconstructed breast is smaller than the natural breast, reduction mammoplasty is usually performed. This can be performed using a variety of techniques that include short scars when the difference is mild to moderate and inverted T scars when the difference is moderate to severe. *Figures 19 and 20* illustrate a woman following a symmetry procedure with a circumvertical reduction mammoplasty.



Figure 19 Preoperative photograph following right breast reconstruction with a free TRAM flap. There is a volume deficiency relative to the hypertrophic left breast. TRAM, transverse rectus abdominis musculocutaneous.



Figure 20 Postoperative photograph following left reduction mammoplasty using circumvertical approach at 1-year follow-up.

Conclusions

Achieving ideal breast aesthetics in the setting of autologous breast reconstruction requires artistic and technical expertise. Adherence to the basic tenants of the footprint, conus, and skin envelope as described by Blondeel *et al.* are essential. There are several autologous options that include pedicle flaps as well as free tissue transfers. Each flap has its unique characteristics that make it ideal or less ideal for a particular patient. Understanding the nuances of each flap is important when striving for ideal volume, contour and symmetry.

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Footnote

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Abdominal perforator vs. muscle sparing flaps for breast reconstruction

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Abstract: Abdominally based free flaps have become the mainstay for women that desire to use their own tissue as a means of breast reconstruction after mastectomy. As the techniques have evolved, significant effort has been invested in finding the best means of minimizing morbidity to the abdominal donor site while ensuring a viable reconstructed breast that is aesthetically pleasing. This manuscript reviews and compares the muscle sparing free transverse rectus abdominis myocutaneous (MsfTRAM), the deep inferior epigastric artery perforator (DIEP), and the superficial inferior epigastric artery (SIEA) flaps, regarding flap success rate, operative times, abdominal donor site morbidity and residual functionality, hospital lengths of stay and associated costs, impact of co-morbid conditions, and resilience after adjuvant radiation treatment.

Keywords: Muscle sparing free transverse rectus abdominis myocutaneous (MsfTRAM) flap; deep inferior epigastric artery perforator (DIEP) flap; superficial inferior epigastric artery (SIEA) flap; free flap breast reconstruction

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Over the last 40 years, breast reconstruction has been widely considered a significant component of the comprehensive treatment and management of breast cancer patients. This was heightened by the passage of the Women's Health and Cancer Rights Act (WHCRA) of 1998, that mandated insurance plans to provide breast cancer patients with coverage for reconstructive surgery and other benefits related to a mastectomy (1). With its initial description in 1979, the free transverse rectus abdominis myocutaneous (TRAM) flap became a pillar of autologous breast reconstruction (2). The concept of reconstructing the breast with reliable autologous tissue, that was soft, robust, and resulted in an aesthetically pleasing reconstruction lead to its widespread adoption. With the intent to reduce abdominal donor site morbidity, the original free TRAM flap has undergone numerous modifications resulting in the modern day muscle-sparing free TRAM (MsfTRAM), deep inferior epigastric perforator (DIEP), and superficial inferior epigastric artery (SIEA) flaps (3-13). Both the MsfTRAM and the DIEP flaps are based off of the same

axial blood supply and arguably yield the same amount of abdominal subcutaneous tissue and skin; however, the DIEP flap technique has received further notoriety as it spares the rectus abdominis muscle and anterior rectus fascia (6,14). In an effort to further reduce abdominal wall morbidity, the SIEA flap is based on a more superficially located blood supply obviating the need to violate the anterior rectus fascia or its underlying muscle all together (11-14).

Despite its presumed benefit of decreased donor site morbidity and pain, the DIEP flap technique has been slow to be collectively embraced due to initial concerns for increased flap loss, heightened rates of fat necrosis, more complex dissection, and skepticism over its reduction in donor site hernia or bulge. Although it is universally agreed upon that SIEA flaps limit donor site morbidity compared to MsfTRAM and DIEP flaps, it too has had detractors secondary to concerns about its reliability and heightened rates of fat necrosis. There have been numerous contributions to the literature comparing outcomes, complications, donor site functionality, and even cost differences between the

MsfTRAM, DIEP, and SIEA flap techniques. Most of these studies contain data from single institutions and admittedly none have been performed in a truly randomized fashion. Although all three reconstructive techniques have proven to be relatively reliable, safe, and yielding of good aesthetic results, we felt that it would be of value to review the most recently cited differences. Factors considered in this comparison of MsfTRAM, DIEP, and SIEA flaps include flap success rates, rates of fat necrosis, operative time, abdominal donor site morbidity and residual functionality, hospital lengths of stay and associated costs, impact of co-morbid conditions, and resilience after adjuvant radiation treatment.

Muscle sparing free transverse rectus abdominis myocutaneous (MsfTRAM)

Both MsfTRAM and DIEP flaps rely on the deep inferior epigastric vascular system as their axial blood supply. Both flaps require that the anterior rectus sheath and rectus abdominis muscle are incised; however, the MsfTRAM involves procurement of some of the muscle as a part of the flap while the DIEP flap contains no muscle. In 2002, Nahabedian *et al.* described a classification system for MsfTRAM flaps, employing the nomenclature MS-0 thru MS-3. They are described in the following manner: MS-0, the full width of the rectus abdominis muscle is procured with the overlying subcutaneous tissue and skin; MS-1, the lateral segment of the rectus abdominis muscle is preserved; MS-2, both medial and lateral segments of rectus abdominis muscle are spared; and MS3, the entire rectus abdominis muscle is preserved (DIEP flap) (15). The intended preservation of an increased amount of rectus abdominis muscle was twofold. It would ensure greater integrity of the abdominal wall as well as preserve the lateral intercostal nerve innervations that are theoretically as important, or even more vital, to the strength of the abdominal wall than the muscles themselves.

By procuring some of the rectus abdominis muscle with the overlying subcutaneous tissue and skin, the MsfTRAM flap has the benefit of preserving some of the small intramuscular perforators from the deep inferior epigastric artery and vein that would otherwise be lost (16). The clinical relevance of these small perforators continues to be debated, but remains one of the reasons that some surgeons prefer this technique over the DIEP flap.

Deep inferior epigastric perforator (DIEP)

The DIEP flap relies on 1-4 perforating vessels from

the deep inferior epigastric artery and vein, sparing procurement of the rectus abdominis muscle and anterior rectus fascia (14,17). Viable DIEPs are those said to have a visible artery, an accompanying visible vein, and a palpable pulse. The decision on how many of the perforators to procure with the flap is based on perforator size, location (medial or lateral row), and proximity to each other, all in an attempt to minimize the extent of intramuscular dissection. By minimizing the intramuscular dissection and basing the flap on medial row perforators only, disruption of the lateral intercostal innervations can be avoided leaving behind not only an intact rectus abdominis muscle but also one that has not been denervated.

The DIEP flap involves a more technically demanding dissection and there is an undeniable learning curve pertaining to perforator identification, preservation, and successful transfer of these flaps (18). The theoretical benefit of complete muscle preservation and reduced donor site morbidity is what has led many to endorse the DIEP flap over the MsfTRAM, however the lack of confidence in depending on one or two, small diameter perforators to perfuse a relatively large flap has posed the greatest barrier to its universal adoption (19,20).

Superficial inferior epigastric artery (SIEA)

First described as a viable autologous breast reconstructive option in 1991, the SIEA flap yields the advantage of leaving the abdominal fascia completely intact as its vascular supply travels superficial to the rectus abdominis fascia. The SIEA and vein originate from the common femoral vessels while the external iliac vessels supply the deep inferior epigastric artery and vein (11). Despite its diminished donor site advantage, the SIEA flap has not been universally adopted for several key reasons. The first is due to significant anatomic variability as several studies cite the SIEA being absent in upwards of 30% of patients (13,21,22). The second is that the SIEA consistently is smaller in diameter than the traditional recipient vessels for autologous free flap breast reconstruction (internal mammary and thoracodorsal) leading to the anastomoses being more technically demanding. Lastly, there have been significant concerns about the ability of the SIEA to adequately perfuse all four, historical zones of the abdominal wall skin and subcutaneous tissue (21). When used it has been documented that an SIEA >1.5 mm in diameter be used to improve the likelihood of flap viability (12,23).

Flap viability and fat necrosis

Comparing rates of total or partial flap loss and frequency of the occurrence of fat necrosis between MsfTRAM, DIEP, and SIEA flaps have been popular topics in the last 15 years. With full disclosure the authors of these published rates recognize that their data lack the scientific vigor of randomization and also that they are frequently reporting on a single institution, and many times a single surgeon's, experience. That being said, the most recently published rates of complete and partial flap loss for MsfTRAM flaps range from 0.3% to 3.6% and 2.2% to 7%, respectively (15,19,24-29). The most recently published rates of complete and partial flap loss for DIEP flaps are slightly higher than MsfTRAM flaps ranging from 0.5% to 6% and 2.5% to 8.7%, respectively (24,26,29-33). Undoubtedly contributing to the reluctance of the routine use of SIEA flaps, the published rates of SIEA total flap loss range from 1.9% to 12.6% (12,14,21-23,34,35). These heightened flap loss rates even in the most experienced of hands are 3-4 times higher than reported rates of MsfTRAM and DIEP flaps causing some to suggest that SIEA flaps may not be worth the risk despite its reduced donor site insult (21). The majority of recent studies comment that there is marginal difference in flap loss between MsfTRAM and DIEP flaps as both are safe and reliable; however, the DIEP flap also poses a slightly greater risk of fat necrosis over more muscle inclusive options (24).

Kroll *et al.* in 2000 was one of the first studies that specifically compared rates of fat necrosis between MsfTRAM and DIEP flap breast reconstruction. This single institution and single surgeon study reported that of their 310 reconstructed breasts, fat necrosis occurred in 12.9% of their MsfTRAM flaps compared to a significantly higher 29.0% in their DIEP flaps (25). More recently in a series of 130 flaps at another institution, they also cited a statistically significant ($P=0.001$) increased rate of fat necrosis in DIEP flaps compared to MsfTRAM flaps (33). In contrast, and highlighting institutional variability, several other recent single institution studies reported no statistically significant difference in rates of fat necrosis between their MsfTRAM and DIEP flaps (19,24,26). Fewer studies have assessed SIEA flaps rate of fat necrosis with limited reports ranging from 5.7% to 14% (35,36).

The variability of these findings suggests not only that these outcomes are surgeon or institutionally dependent, but also presume an inconsistency in how fat necrosis is defined. Kroll *et al.* was very specific in defining fat necrosis

as any palpable firmness greater than 1cm in diameter present 3 months after surgery and proven to not be a cancer recurrence (25), while other studies either gave a vague explanation or failed to define their definition of fat necrosis all together. Aware of the variability in reported rates of fat necrosis, Baumann *et al.* recently assessed how the number of perforators predicts fat necrosis in abdominally based free flap breast reconstruction. Their single institution, prospective study concluded that as the number of perforators supplying the flap diminishes, the amount of fat necrosis increases. The MsfTRAM flaps with ≥ 3 perforators had significantly less fat necrosis than the DIEP and SIEA flaps that rely on ≤ 2 perforators (36). Undeniably to more accurately answer this question with more scientific rigor, a multi-institutional, prospective study with strict guidelines defining fat necrosis would need to be employed.

Operative time

Historically there have been some reservations by surgeons to adopt the DIEP flap technique due to concerns of it being a more technically challenging and potentially time consuming procedure than the MsfTRAM. There have been no recent studies directly comparing operative times for MsfTRAM, DIEP, or SIEA flap techniques. With the early advent of MsfTRAM flaps, operative times for bilateral procedures were reported to take around 8.6 hours (37). One of the first reported large series of DIEP flaps revealed an average operative time of 9.2 hours for a bilateral procedure (38). One could reasonably speculate that without the need for an intramuscular dissection, SIEA flaps would yield shorter operative times. Once again there is a paucity of published data on this topic; however, one study contrarily found there to be no statistically significant difference between SIEA flap operative times compared to MsfTRAM and DIEP flaps ($P=0.67$) (12).

With refinements in techniques, and the availability of venous coupling devices, implantable dopplers, and efficient preoperative imaging modalities there has been a significant reduction in DIEP flap operative times (38,39). Recent studies report unilateral DIEP flaps being performed in less than 4.5 hours (39,40). A unifying theme throughout the literature is the undeniable learning curve involved with all three techniques. Acosta *et al.* reported over a 9-year experience that their unilateral DIEP operative times have reduced from an initial 7.3 hours to a current 4.1 hours, with a much lower complication rate (39).

Abdominal donor site morbidity

The much lauded benefit of the DIEP and SIEA flaps compared to the MsfTRAM flap is the presumed reduction in donor site morbidity. Ensuring a robust flap while minimizing the abdominal donor-site morbidity such as pain, weakness, bulges, and hernias has been the impetus for the evolution of these procedures. Abdominal wall discomfort, strength, and functionality after MsfTRAM, DIEP, and SIEA flap breast reconstruction is dependent on numerous factors inclusive of the amount of rectus abdominis muscle and fascia that remains after the flap has been raised, the prevailing blood supply to the rectus abdominis muscle, the integrity of the lateral intercostal innervations to the *in situ* rectus abdominis muscle, and the amount of scar tissue that develops as a result of the flap dissection and procurement (8,26,41).

The first to describe differences in donor site pain between MsfTRAM and DIEP flaps came from the British literature as they speculated that their DIEP flap patients had reduced amounts of pain secondary to the diminished amount of tension on their rectus abdominis fascia repair (9,32,42). These findings were confirmed and extrapolated upon by Kroll *et al.* when they correlated the amount of subjective pain patients reported to a more objective assessment of amount of narcotic used between MsfTRAM patients and DIEP patients. They found on average that patients with MsfTRAM flaps used on average over twice the amount of narcotic (1.65 mg/kg) than the patients with DIEP flap reconstruction (0.74 mg/kg), which was statistically significant ($P < 0.001$) (43). The literature further reveals that SIEA flap patients report nearly statistically significant less abdominal pain than both MsfTRAM and DIEP flap patients ($P = 0.06$) (44).

Contour abnormalities that can occur with abdominally based free flap breast reconstruction has been thoroughly assessed and described in the literature (3,8,10,15,19,24,26). These studies have all demonstrated that there is no statistically significant difference in contour between MsfTRAM (MS-2) DIEP, and SIEA flaps; however, several of the more recent studies confirm a heightened risk of bulge in the MsfTRAM flap reconstructions compared to DIEP and SIEA flaps (21,24,26,41,45). Interestingly, Egeberg *et al.* recently revealed that although there was a 20% greater risk of developing a physician identified bulge in the MsfTRAM cohort compared to the DIEP cohort, when bulge rates were self-reported via survey by patients there was no significant difference in bulge rates between

the two groups (45). This points to the clinical significance, if any, are of a post-operative bulge. Regardless, most authors encourage maximal preservation of the anterior rectus sheath, in conjunction with a strong suture closure, to minimize the development of any abdominal contour abnormalities.

No theoretical risk of hernia formation exists with SIEA flaps which have been corroborated in a few studies (13,21). However, comparison of hernia rates after MsfTRAM and DIEP flaps have been readily evaluated by many of the aforementioned studies (3,8,10,15,19,24,26). Although most reveal a slightly higher rate of abdominal wall hernias after unilateral MsfTRAM flaps than DIEP flaps, the difference does not meet the level of statistical significance ($P < 0.05$). For example, Nelson *et al.* reported a hernia rate of 2.6% in MsfTRAM flaps compared to 0% in their DIEP flaps ($P = 0.15$) (24). Nahabedian *et al.* reported an abdominal hernia rate of 1.5% in their unilateral DIEP flaps and a comparable 4.7% in their unilateral MsfTRAM flaps ($P = 0.36$) (26).

Notably this same study by Nahabedian *et al.*, as well as others, have revealed a statistically significantly greater risk of bulge and or hernia formation in the setting of bilateral MsfTRAM flaps (21%) compared to bilateral DIEP flaps (5%) (26,45). At this point it is universally accepted that bilateral MsfTRAM flaps pose a greater risk of hernia formation than bilateral DIEP flaps; however, there is growing evidence that when fascial preservation techniques are employed during MsfTRAM flaps, hernia or bulge formation are further reduced (41). The amount of muscle removed is proving less important as long as the vast majority of the fascial integrity remains intact.

The importance of a meticulous closure of the abdominal donor site to prevent the occurrence of hernia or bulge cannot be overstated. Wan *et al.* advocate that MsfTRAM flaps still very much have their utility as the hernia risk can be effectively addressed with mesh (46). They suggest that by reinforcing the abdominal wall defect with permanent mesh, hernia rates for bilateral MsfTRAM flaps can be reduced to that of bilateral DIEP flaps. They join several other studies that encourage the routine use of mesh in the donor site repair to reduce abdominal wall morbidity for both unilateral and bilateral MsfTRAM flaps (15,24,26,41,46). Further pointing to the significance of fascial preservation techniques, recent studies from the general and plastic surgery literature are advocating for primary fascial coaptation with mesh reinforcement as the most ideal repair of abdominal wall defects to prevent either hernia recurrence or occurrence, respectively (47,48).

Assessment of abdominal strength after abdominally based breast free flap reconstruction remains controversial. This is primarily due to the lack of consistency and consensus on how best it should be evaluated. Some surgeons believe that isolated testing of the rectus abdominis should be performed using isokinetic dynamometry, electromyography, or myosonography (9,26,49-51). Other physicians advocate for a more practical assessment such as sit-ups or surveying the patients to determine if they can carry out the activities of daily living that they subscribed to preoperatively (3,26,44,51-53).

Futter *et al.* compared patients that had undergone DIEP flaps, MsfTRAM flaps, and non-operated controls after assessment of their abdominal and back extensor strength on an isokinetic dynamometer (9). The DIEP flap and control groups displayed statistically significant better abdominal and back extensor strength than the MsfTRAM flap group. Additionally, patients from the MsfTRAM group reported greater rates of abdominally related functional difficulty and discomfort compared to the DIEP flap and control groups (9). Bottero *et al.* revealed through electromyography that the function of the rectus abdominis muscle after DIEP flap procurement was reduced only 30% after a follow-up of over a year (50). The authors advocate that their finding implies superiority of the DIEP flap over the MsfTRAM although they admittedly failed to compare MsfTRAM in the same fashion. Similarly without having a MsfTRAM flap comparison group, Kässmann *et al.* pre- and post-operatively examined DIEP flap patients using myosonography (49). Comparing unilateral DIEP flap patients operative side to their contralateral, non-operated side as a control, they reported almost identical rectus muscle function on both sides just 2 months postoperatively. The absolute muscle thickness at maximum contraction and the difference of muscle thickness between relaxation and contraction were also found to be almost identical on both sides (49).

Looking specifically at bilateral reconstruction and using a manual muscle function test, Selber *et al.* found muscle impairment to be consistent with theoretical predictions. The greatest amount of impairment was seen by patients with MsfTRAM/MsfTRAM, followed by MsfTRAM/DIEP, DIEP/DIEP, DIEP/SIEA, and finally SIEA/SIEA patients revealed the least functional impairment (53). Only the level of impairment of the bilateral MsfTRAM cohort relative to the functional preservation of the bilateral SIEA cohort reached the level of statistical significance ($P=0.04$) (53).

Patient surveys have been the most frequently employed model of assessing abdominal wall functionality after

abdominally based free flap breast reconstruction. Even the most recent of studies reveal mixed results. Some report that DIEP and SIEA flap patients perceive their core strength to be better or that they can more readily carry out prior activities, such as performing sit-ups, than patients that have undergone MsfTRAM flap reconstruction (8,9,26,44). Two studies reported no significant difference in patient perceived abdominal wall function after DIEP or MsfTRAM flap reconstruction (3,54). Fittingly, other recent studies have described that despite objective evidence of greater decline in abdominal function of MsfTRAM flap patients, this difference has not translated to significant detriments in the ability to carry out activities of daily living for MsfTRAM flap patients compared to their DIEP flap counterparts (53,55). The most recent meta-analysis on this topic agrees that the only way to legitimately answer the question of abdominal wall functionality comparing abdominally based free flaps will require a multicenter, longitudinal study, that employs consistent and valid measures (55). With that being said, there is a relatively universal consensus that both MsfTRAM, DIEP, and SIEA flaps yield far less donor site morbidity than its pedicle TRAM predecessor, particularly in the setting of bilateral reconstruction (51,56).

Hospital length of stay (LOS) and cost

Relative to the aforementioned topics, hospital LOS and cost comparisons between patients undergoing MsfTRAM, DIEP, and SIEA flaps have been less frequently assessed. Kroll *et al.* published that on average their DIEP flap patients remained in the hospital for a shorter duration (4.73 days) than their MsfTRAM patients (5.21 days) (43). Although this did reach statistical significance ($P=0.026$), it amounted to less than a full day (43). Kaplan *et al.* reported that on average, TRAM patients stayed in the hospital 4 days longer than perforator flap patients (57,58). Unfortunately, the study fails to disclose how many of the TRAM flaps were pedicled *vs.* free, and additionally non-abdominally based gluteal flaps were included in their perforator flap cohort which further confounds the results.

Several studies have included SIEA flaps in their assessment of hospital LOS. Vega *et al.* reported a significantly shorter hospital LOS in their DIEP and SIEA flap patients compared to their MsfTRAM patients (59). Chevray *et al.* also revealed a significantly shorter LOS for their SIEA flap patients (4.2 days) compared to their DIEP and MsfTRAM patients (5.1 days; $P=0.04$), but once again

this equated to less than 1 day (12). These studies conclude that the etiology of the LOS discrepancy is multifactorial but that donor site pain is likely a contributing factor. As surgeons become more facile with all three techniques and post-operative courses become more protocol driven, it is likely that even these small discrepancies in hospital LOS will further dissipate as is evident by one group's experience where no difference in LOS was identified between DIEP and MsfTRAM groups, 4.1 and 4.0 days, respectively ($P=0.10$) (24).

There are contradictory reports regarding the cost comparison of MsfTRAM, DIEP, and SIEA flaps. The aforementioned Kaplan *et al.* study originally published that the \$9,625 average cost for perforator flap breast reconstruction was far less expensive than the \$18,070 average TRAM reconstruction cost (57,58). Once again this study was confounded by the fact that there is no identification of how many of the TRAM flaps were pedicled *vs.* free, the perforator flap group included gluteal flaps; and although some cost adjustments were made, the perforator flaps were performed by one institution in Louisiana, while the TRAM flaps were performed by a separate institution in Texas.

Using a national database, Pien *et al.* recently published that DIEP flaps were associated with significantly higher charges and costs than pedicled TRAM and MsfTRAM flaps (60). The average cost of a DIEP flap was \$23,616 compared to \$15,538 and \$20,756 for pedicled TRAM and MsfTRAM flaps, respectively (60). The authors cited that the only potential cost determinant that significantly differed among the groups was that more of the DIEP patients were privately insured. There was no statistically significant difference in LOS between the groups.

The only cost-effectiveness data that specifically includes SIEA flaps comes from the Canadian literature. Although their initial data was promising regarding the cost effectiveness of SIEA flaps compared to DIEP flaps, there remains some caution due to the SIEA flaps high rate of re-exploration and conversion to a DIEP flap (61). Of note, the Canadians have also found that DIEP flaps are associated with a higher cost than MsfTRAM flaps (\$7,026 *vs.* \$6,058) (62).

Co-morbid conditions and post-operative radiation therapy

It is well described that regarding abdominally based free flap breast reconstruction, obesity [body mass index (BMI) ≥ 30] and smoking have higher rates of mastectomy skin flap

necrosis, flap complications, and abdominal wall donor-site complications than patients with a normal BMI or nonsmokers (63–66). There remains to be published studies that directly compare MsfTRAM, DIEP, and SIEA flaps in smokers or obese patients, but the historic teaching has been to include as many perforators as possible in the flaps of these two high risk groups (67). That philosophy would then favor MsfTRAM over DIEP or SIEA flaps. Without substantial evidence to the contrary, it is difficult to fault this approach; however, there is mounting evidence that DIEP and SIEA flaps are equally as safe and reliable in the obese and smokers as MsfTRAM flaps.

Garvey *et al.* found no difference in rates of flap loss or fat necrosis among obese, overweight, or normal weight patients that underwent DIEP flap reconstruction (68). Ochoa *et al.* found that although obesity predisposed DIEP flap patients to delayed wound healing of both the flap and the donor site, the overall flap complications were not significantly different in the obese compared to the normal weight patients (69). In a meta-analysis, Lee and Mun showed that compared to conventional free TRAM flaps, MsfTRAM, DIEP, and SIEA flaps showed a lower pooled incidence of flap loss, fat necrosis, and donor site hernias/bulges in obese patients (64). Most recently using a propensity score analysis, Zhong *et al.* compared MsfTRAM flaps to DIEP flaps in both obese patients and smokers and found no statistically significant difference in rates of flap loss or fat necrosis (70). This study did however find a greater risk of abdominal donor site complications in the MsfTRAM flaps compared to the DIEP flaps. So although it is still advised that all patients planning to have DIEP or SIEA flaps should stop smoking at least 4 weeks prior and after the operation as well as have a BMI of <30 to avoid a higher risk of complications, this is becoming less of a hard and fast rule.

Although it has been well documented that adjuvant radiation therapy after free flap breast reconstruction yields high rates of fat necrosis, fibrosis, contracture, and atrophy of the flap, there has been limited evidence favoring one form of free flap breast reconstruction over another (71–74). A more historical study suggested that MsfTRAM flaps should be employed rather than DIEP flaps to minimize the deleterious radiation side-effects (75). Their reasoning that MsfTRAM flaps have a more robust blood supply than DIEP flaps parallels the explanation for its preferential use in smokers and the obese. Some recent studies are bringing that philosophy into question. Garvey *et al.* followed free flap breast reconstruction patients over 5 years. They revealed that although both MsfTRAM and DIEP flaps had

Table 1 Comparisons of muscle sparing vs. abdominal perforator flaps for breast reconstruction

Variable	MsfTRAM flaps (Refs.)	DIEP flaps (Refs.)	SIEA flaps (Refs.)	Advantage
Total flap loss	0.3-3.6% (15,19,24-29)	0.5-6% (24,26,29-33)	1.9-12.6% (12,14,21-23,34,35)	MsfTRAM
Flap fat necrosis	4.6-12.9% (24,25,36)	5.9-29% (24,25,36)	5.7-14% (35,36)	MsfTRAM
Operative time (bilateral)	8.6-9.9 hours (37,57,58)	8.5-9.2 hours (37,57,58)	NP	Equivalent
Donor site pain*	211 (44)	195 (44)	165 (44)	SIEA
Donor site bulge/contour deformity (unilateral)	3-5% (24,26)	0-2% (24,26)	0% (21,23)	Equivalent
Donor site bulge/contour deformity (bilateral)	6-21% (24,26)	5-6% (24,26)	0% (21,23)	DIEP and SIEA
Donor site hernia (unilateral)	1.9-5% (21,24,26)	0-2% (24,26)	0% (21,23)	Equivalent
Donor site hernia (bilateral)	6-21% (24,26)	0-5% (24,26)	0% (21,23)	DIEP and SIEA
Residual abdominal functionality (unilateral) [†]	4.0 (52)	4.4 (52)	4.3 (52)	Equivalent
Residual abdominal functionality (bilateral) [†]	3.7 (53)	4.7 (53)	5.0 (53)	DIEP and SIEA
Hospital LOS	4.1-5.2 days (24,43)	4.0-4.7 days (24,43)	NP	Equivalent
Cost per flap (\$)	20,756 (60)	23,616 (60)	NP	Undetermined

*, according to weighted pain score: the lower the score, the lower the amount of pain reported; †, according to Upper Rectus Abdominis Manual Muscle Function Test: 0 (least function)-5 (best function). MsfTRAM, muscle sparing free transverse rectus abdominis myocutaneous; DIEP, deep inferior epigastric perforator; SIEA, superficial inferior epigastric artery; NP, not published in a comparative fashion; LOS, length of stay.

high rates of fat necrosis after adjuvant radiation therapy, MsfTRAM flaps fared no better than DIEP flaps and were not protective against radiation induced changes (74). Findings like these will likely warrant further investigation in a more prospective manner.

Conclusions

Abdominally based free flap breast reconstruction using MsfTRAM, DIEP, or SIEA flaps can be used safely and reliably with a relatively low risk of flap loss or major complications. Head to head comparisons of various factors pertaining to these flaps remains a challenge due to the paucity of randomized controlled studies; however, a very general summary using the currently available data is provided in *Table 1*. The existing data continues to reveal that DIEP flaps have a slightly increased rate of flap loss and fat necrosis than MsfTRAM, while SIEA flaps have 3-4 times the rate of immediate postoperative complications of DIEP and MsfTRAM flaps, respectively. There appears to be no significant difference in operative times among the three techniques and increased experience results in improved

expediency for the entire group. SIEA flaps continue to reveal the least amount of donor site morbidity, but must be balanced with the confirmed heightened risk of flap survival. Donor site morbidity comparisons between MsfTRAM and DIEP flaps remains debatable, although the objective measures give DIEP flaps the advantage. Hospital LOS appears to be comparable among all three flaps; however, early evidence reveals that DIEP flaps are the most expensive option. Despite further evidence that obesity poses a heightened risk of free flap complications and smoking yields greater mastectomy skin flap necrosis, DIEP flaps appear to be gaining credibility as a viable option in these high risk patients that were previously relegated to only pedicled or MsfTRAM flaps. The historical thinking that MsfTRAM flaps are more resilient to the deleterious effects of adjuvant radiation is being challenged as the amount of fat necrosis found in MsfTRAM flaps and perforator flaps appears to be comparable. Most current studies agree that ultimately, the choice of flap should be determined by the intra-operative anatomic findings, the patient's health status, the potential need for adjuvant therapy, and the surgeons' confidence in creating a viable breast flap at the least detriment to the donor site.

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Footnote

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Comparative analysis of fluorescent angiography, computed tomographic angiography and magnetic resonance angiography for planning autologous breast reconstruction

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Background: The high incidence of breast cancer and growing number of breast cancer patients undergoing mastectomy has led to breast reconstruction becoming an important part of holistic treatment for these patients. In planning autologous reconstructions, preoperative assessment of donor site microvascular anatomy with advanced imaging modalities has assisted in the appropriate selection of flap donor site, individual perforators, and lead to an overall improvement in flap outcomes. In this review, we compare the accuracy of fluorescent angiography, computed tomographic angiography (CTA), and magnetic resonance angiography (MRA) and their impact on clinical outcomes.

Methods: A review of the published English literature dating from 1950 to 2015 using databases, such as PubMed, Medline, Web of Science, and EMBASE was undertaken.

Results: Fluorescent angiography is technically limited by its inability to evaluate deep-lying perforators and hence, it has a minimal role in the preoperative setting. However, it may be useful intraoperatively in evaluating microvascular anastomotic patency and the mastectomy skin perfusion. CTA is currently widely considered the standard, due to its high accuracy and reliability. Multiple studies have demonstrated its ability to improve clinical outcomes, such as operative length and flap complications. However, concerns surrounding exposure to radiation and nephrotoxic contrast agents exist. MRA has been explored, however despite recent advances, the image quality of MRA is considered inferior to CTA.

Conclusions: Preoperative imaging is an essential component in planning autologous breast reconstruction. Fluorescent angiography presents minimal role as a preoperative imaging modality, but may be a useful intraoperative adjunct to assess the anastomosis and the mastectomy skin perfusion. Currently, CTA is the gold standard preoperatively. MRA has a role, particularly for women of younger age, iodine allergy, and renal impairment.

Keywords: Breast reconstruction; indocyanine green fluorescence angiography (ICGFA); computed tomographic angiography (CTA); magnetic resonance angiography (MRA)

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Introduction

Given the high prevalence and incidence of breast cancer in society (1,2) and a growing number of women with breast cancer opting for mastectomy over breast-conserving operations (3), breast reconstruction has become an

important part of breast cancer management. It can improve patients' psychosexual well-being and their overall psyche in response to breast cancer management (4-8). Autologous breast reconstruction (and in particular those with perforator-based free flaps) has demonstrated a natural-appearing,

aesthetically-pleasing, long-lasting restorative option, with low donor site morbidity (9,10). Recent advancements in operative techniques and imaging modalities have facilitated complex microvascular breast reconstructions to become safer, more reliable procedures (11-13).

Various autologous tissues have been utilized for breast reconstruction, such as omentum (14), latissimus dorsi (15-18), deep circumflex iliac artery (groin) flap (19,20), lateral thigh (tensor fascia latae) flap (21), gluteal musculocutaneous flap (22-25), gracilis flap (26), and triceps flap (27). In recent times, the anterior abdominal wall has become the most frequently used donor site due to the added aesthetic benefit at the donor site, akin to a concomitant abdominoplasty. Initially, transverse rectus abdominis muscle (TRAM) flaps were successful in providing adequate volume replacement for breast reconstructions (28,29). However, a high rate of donor site morbidity, such as rectus abdominis muscle weakness and ventral hernia, resulted in the development of muscle-sparing techniques, mainly the deep inferior epigastric artery perforator (DIEP) flaps (10,30). DIEP flaps are fasciocutaneous flaps based on musculocutaneous perforators derived from the deep inferior epigastric artery (DIEA) (31,32). They were able to provide sufficient tissue volume and a superior functional and aesthetic outcome at the donor site than the TRAM flaps (12,33). However, early studies reported a steep learning curve of the microsurgical technique leading to a longer dissection time, and an increased flap complications, such as fat necrosis and flap loss (34). To this effect, the use of preoperative imaging has been instrumental.

Preoperative assessment of the donor site microvasculature anatomy with advanced imaging modalities has assisted surgeons in the appropriate selection of the donor site, perforator, and flap leading to an overall improvement in the flap outcomes (35,36). According to the consensus reached at the Navarra meeting, a perforator should be selected on the basis of its caliber, central location within the flap, direct venous connection with the main superficial venous system, and it preferably demonstrates a broach subcutaneous branching pattern and has a shorter intramuscular (IM) course for ease of dissection (37). Hence, an ideal preoperative imaging technique should accurately demonstrate the individual variations in the location and caliber of the perforators, their IM course, and the branching pattern of the DIEA (38). Early investigators have relied on handheld Doppler probes and color duplex ultrasonography to detect perforators, characterize them in flow velocity and resistivity, and create a perforator map on the abdominal wall (39-41). Both ultrasound techniques are inexpensive, do not expose

patients to radiation or potentially nephrotoxic intravenous contrast agents, can detect perforators with diameter greater than 0.5 mm, identify any underlying vessel damage secondary to atherosclerosis or previous surgery (42-45). However, they are subject to significant inter-observer variability, and are associated with poor consistency with intraoperative findings, high false positive and negative rates (39,41,46,47). Hence, they are now superseded by modern imaging technologies with objective findings, such as fluorescent angiography, computed tomographic angiography (CTA), and magnetic resonance angiography (MRA).

In this review, we evaluate the accuracy of fluorescent angiography, CTA, and MRA, and compare their impact on the clinical outcomes of patients undergoing autologous breast reconstruction, mainly TRAM and DIEP flaps, since they have attracted the most number of clinical studies and have provided the highest level of evidence (48).

Methods

We reviewed the published English literature from 1950 to 2015 from well-known databases, such as PubMed, Medline, Web of Science, and EMBASE, using search terms, such as “autologous breast reconstruction”, “DIEP flap”, “fluorescent angiography”, “computed tomographic angiography”, and “magnetic resonance angiography”.

Results

Fluorescent angiography (FA)

FA utilizes intravenous dyes that fluoresce and emit infrared energy upon excitation by a light source, which produces real-time videos that facilitate evaluation of the anastomotic patency and the extent of soft tissue perfusion (49,50). Originally, the investigators employed fluorescein dye, which accumulates extracellularly in the soft tissue, fluoresces upon excitation by the ultraviolet (UV) light, and is renally excreted (51,52). However, the long time it takes to reach the maximum intensity (15 minutes), relatively frequent adverse effects, reports of allergic reaction, and the steep learning curve associated with using a Woods lamp for interpretation have resulted in the fluorescein dye being replaced by the indocyanine green (ICG) dye. ICG is an FDA-approved, biliary excreted, water-soluble dye that enables image capture within 2-3 minutes of intravenous administration (53). ICG is excited by laser and transmits infrared energy that is recorded by devices equipped with inbuilt software

Table 1 Comparison of basic characteristics of the perforator imaging technologies

Characteristics	ICGA	CTA	MRA
Availability	+	+++	+
Cost (USD)	795 (59)	400 (60)	600 (61,62)
Image acquisition	2-3 min (53)	<10 sec	20 min
Breath holding during scanning	NA	5 sec (63)	20 sec (64)
Reproducibility	+	+++	++
Operator dependence	Yes	No	No
Patient size dependence	Yes	No	No
Panoramic view	Yes	Yes	Yes
3D view	No	Yes	Yes

ICGA, indocyanine green angiography; CTA, computed tomographic angiography; MRA, magnetic resonance angiography; NA, not applicable; 3D, three-dimensional.

algorithms that generate quantitative data, such as LifeCell SPY system (LifeCell Corp, Branchburg, New Jersey, USA), IC-View (Pulsion Medical Systems AG, Munich, Germany), and FLARE imaging system (Beth Israel Deaconess Medical Center, Boston, MA, USA) (54-56). Furthermore, ICG has a short half-life (3-4 minutes) (57), which enables multiple consecutive measurements, in contrast to fluorescein, which is retained in the tissues (58). It strongly binds to the plasma proteins leading to rapid washout from the circulation and has a superior side effect profile with a low rate of anaphylaxis (1 in 42,000) (Table 1) (65,66).

Laser-assisted ICGFA (LA-ICGFA) has demonstrated utility by characterizing vascular flow dynamics and tissue perfusion in various disciplines (67-75). In reconstructive surgery, investigators have utilized LA-ICGFA intraoperatively to assess the patency of microvascular anastomosis in free flaps (76,77) and calculate the intrinsic transit time through the anastomosis (78) that correlate with postoperative flap compromise and accurately predict early re-exploration. One of the significant limitations of LA-ICGFA is that it can only provide information a few millimeters deep from the skin (55). This is adequate for evaluating thin areas, such as the extremities, head and neck, and the trunk (79). However, since majority of autologous breast reconstructions are based on the abdomen and a thick pannus is preferred for a DIEP flap, LA-ICGFA has a minimal role in the preoperative planning (55). In breast reconstruction, LA-ICGFA may be useful intraoperatively during flap harvest to assess the flap perfusion, confirm blood flow within the microvascular anastomosis, and detect acute changes in the flap circulation, such as arterial occlusion,

venous thrombosis, and pedicle torsion (80). Moreover, it can be used to evaluate the perfusion of mastectomy skin flaps and facilitate the reconstructive surgeon to debride areas that are likely to develop necrosis (59).

A number of studies in the literature have examined the accuracy of LA-ICGFA in estimating postoperative complications, such as mastectomy skin flap necrosis (81-83), partial flap necrosis (53) and microvascular thrombosis (Table 2) (84). Using fluorescein dye, Losken *et al.* reported a sensitivity and specificity of 75% and 71% respectively to detect mastectomy skin flap necrosis (81). Using ICG dye, Newman *et al.* retrospectively reviewed and derived that LA-ICGFA can detect postoperative skin necrosis with a sensitivity and specificity of 100% and 91% respectively (82). In a prospective study of 51 implant breast reconstructions in 32 patients, Phillips *et al.* compared the efficacy of fluorescein to the ICG dye and reported that both dyes have the same sensitivity of 90% in detecting skin necrosis but ICG had a slightly superior specificity (83). In a retrospective study of ten patients undergoing TRAM flaps, Yamaguchi *et al.* report that intraoperative LA-ICGFA can detect partial flap necrosis with a sensitivity of 75% (53). Moreover, Holm *et al.* have demonstrated that LA-ICGFA accurately detects microvascular thrombosis as the cause of free flap re-exploration with a sensitivity of 100% and specificity of 86% (84).

In the literature, there are only two studies where using LA-ICGFA is correlated with clinical outcomes (Table 3) (59,97). Komorowska-Timek *et al.* applied LA-ICGFA intraoperatively in 24 consecutive patients undergoing breast reconstruction and the areas of inadequate dye penetration

Table 2 Comparison of accuracy of the perforator imaging technologies

Perforator imaging technology	Author	Year	P/R	Patients	Technical parameters (dye/rows/Tesla)	Sensitivity (%)	Specificity (%)
FA	Yamaguchi (53)	2004	R	10	ICGD	75	
	Losken (81)	2008	P	42	FD	75	71
	Newman (82)	2010	R	12	ICGD	100	91
	Holm (84)	2010	P	20	ICGD	100	86
	Phillips (83)	2012	P	32	FD	90	30
	Phillips (83)	2012	P	32	ICGD	90	50
CTA	Alonso-Burgos (85)	2006	P	6	4	100	
	Rosson (86)	2007	P	17	64	100	
	Rozen (47)	2008	P	8	64	100	
	Rozen (61)	2009	P	6	64	100	
	Gacto-Sánchez (87)	2010	P	12	16	100	
	Scott (46)	2010	P	22	64	94.30	
	Masia (88)	2010	P	36	64	100	
	Pauchot (63)	2012	P	10	64	84.30	100
	Tong (89)	2012	R	69	128	79	92
	Cina (62)	2013	P	23	64	95.60	
	Pellegrin (90)	2013	R	41	64	97.60	
MRA	Rozen (61)	2009	P	6	1.5 & 3.0	50	100
	Chernyak (91)	2009	P	19	3	97	
	Greenspun (92)	2010	P	31	3	96	
	Newman (93)	2010	P	25	1.5	99	
	Alonso-Burgos (94)	2010	P	8	3	100	
	Masia (95)	2010	P	56	1.5	100	
	Pauchot (63)	2012	P	10	64	95.70	100
	Cina (62)	2103	P	23	64	91.30	
Versluis (96)	2013	P	23	1.5 EP	100		

FA, fluorescent angiography; CTA, computed tomographic angiography; MRA, magnetic resonance angiography; P, prospective study; R, retrospective study; ICGD, indocyanine green dye; FD, fluorescein dye; EP, equilibrium phase.

suggesting poor tissue perfusion were resected (97). The authors reported that a resultant total complication rate of 4%, which was lower than 15.1% recorded from their previous 148 patients and 206 breast reconstructions ($P < 0.01$) (97). Duggal *et al.* retrospectively reviewed the clinical outcomes in 184 patients undergoing breast reconstructions receiving intraoperative LA-ICGFA (59). The authors report that LA-ICGFA was associated with a significant reduction in mastectomy skin flap necrosis ($P = 0.01$) and re-operation rate ($P = 0.009$). There was also a trend demonstrated in the reduction of partial and complete flap loss rate ($P = 0.237$ and $P = 1.00$, respectively).

Computed tomographic angiography (CTA)

First reported by Masia *et al.* in 2006 (98), CTA is widely used for preoperative imaging and planning free tissue transfers by numerous institutions around the world and is currently considered the best of the three options due to its high accuracy and reliability (Table 1) (35,60,86,107-111). Ongoing advances in CTA, such as an increasing number of detector rows, ensure that the modality remains fast and produces high detail (48). For interpretation, the scan data can be three-dimensionally (3D) reconstructed digitally on either a free software, such as Osirix (Pixmeo, Geneva,

Table 3 Comparison of clinical outcomes from the perforator imaging technologies

Perforator imaging technology	Author	Year	Patients	Reduction in operative time (min)		Mastectomy skin necrosis (%)	Flap complications		Donor site morbidity		Incidental findings (%)
				Flap harvest	Total		Fat necrosis (%)	Partial flap loss (%)	Complete flap loss (%)	Abdominal bulge/herniation (%)	
ICGA	Komorowska-Timek (97)	2010	20	148		4 vs. 15.1 (P<0.01)					
	Duggal (59)	2014	71	59		13 vs. 23.4 (P=0.01)	14 vs. 22 (P=0.237)	1.4 vs. 3.4 (P=1)			
CTA	Masia (98)	2006	30	30	100						
	Rozen (47)	2008	8	NA			0	0			
	Rozen (35)	2008	40	48	9.8 (unilateral) (P=0.57), 76.5 (bilateral) (P=0.079)	7.5 vs. 16.7 (P=0.19)	0 vs. 10.4 (P=0.024)	0 vs. 0	0 vs. 14.6 (P=0.006)		
	Uppal (99)	2009	26	NA	76 (P<0.005)						
	Casey (100)	2009	68	145	89 (unilateral) (P<0.01), 142 (bilateral) (P<0.01)	10.9 vs. 13.4 (P>0.05)	2 vs. 3.8 (P>0.05)	1 vs. 9.1 (P<0.05)			
	Smit (101)	2009	70	68	90 (P=0.001)		0 vs. 4	0 vs. 1			
	Ghattaura (102)	2010	50	50	77 (unilateral) (P<0.001), 27 (bilateral) (P>0.05)		4 vs. 0	0 vs. 6			
	Masia (88)	2010	357	100	100 (P<0.05)		2 vs. 12	1 vs. 4			
	Minqiang (103)	2010	22	22	96 (P<0.05)		5 vs. 9	0 vs. 5			
	Gacto-Sanchez (87)	2010	35	35	98 (P<0.001)	127 (P<0.001)	Total complications: 0 vs. 14 (P<0.001)	2 vs. 15 (P=0.001)			
	Fansa (104)	2011	20	20	26 (P<0.028)						
	Tong (89)	2012	51	18	140 (unilateral) (P=0.017), 117 (bilateral) (P=0.05)		5 vs. 4 (P=1)	1 vs. 0 (P=1)			36
MRA	Malhotra (105)	2013	100	100	85 (P<0.05)		No difference				
	Pellegrin (90)	2013	41	NA							29.30
	Rozen (61)	2009	6	NA			No difference between MRA and CTA				
	Schaverin (106)	2011	126	NA	25 (unilateral) (P>0.05), 40 (bilateral) (P>0.05)		Reduction (P<0.05)				

ICGA, indocyanine green angiography; CTA, computed tomographic angiography; MRA, magnetic resonance angiography; vs., versus; NA, not available.

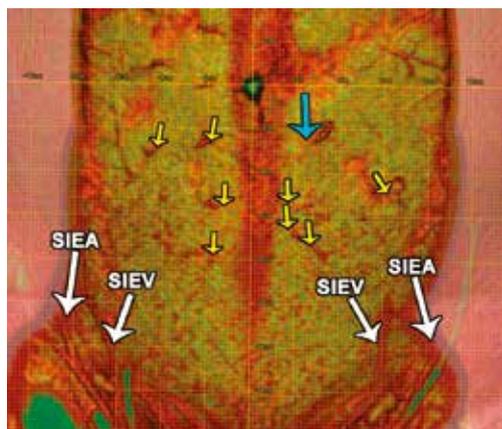


Figure 1 CTA with VRT reformat, demonstrating a large 1.5 mm perforator (blue arrow) and multiple smaller perforators (yellow arrows) at the point at which they pierce the anterior rectus sheath. A numbered grid is centered at the umbilicus for localization. The SIEA and SIEV on each side were demonstrated. Reproduced with permission from reference (112). CTA, computed tomographic angiogram; VRT, volume rendered technique; SIEA, superficial inferior epigastric artery; SIEV, superficial inferior epigastric vein.

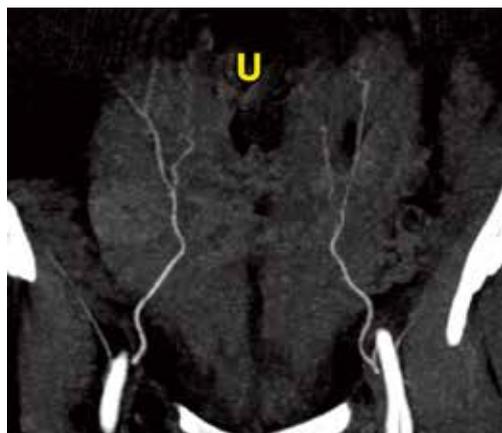


Figure 2 CTA with VRT reformat, demonstrating the branching pattern of the DIEAs. The left side is a type 2 (bifurcating) pattern and the right is a type 3 (trifurcating) pattern. U, umbilicus; CTA, computed tomographic angiogram; VRT, volume rendered technique; DIEAs, deep inferior epigastric arteries. Reproduced with permission from reference (112).

Switzerland), or a commercially available software, such as Siemens Inspace (Siemens, Berlin, Germany). Using 3D volume rendering technique in the software facilitates the creation of a perforator location map and illustrates the



Figure 3 Computed tomographic angiogram (CTA) with axial maximum intensity projection (MIP) reformat, demonstrating the subcutaneous course of perforators. Based on the subcutaneous distribution and branching pattern of the perforator selected (arrow), a preoperative estimate of well-vascularized flap volume can be achieved. CTA, computed tomographic angiogram; MIP, maximum intensity projection. Reproduced with permission from reference (112).

subcutaneous course of the perforators (see *Figure 1*); and secondly, the maximum intensity projection technique can help visualize the vascular pedicle in the coronal plane (see *Figure 2*) and in the axial plane, which can further depict its IM course (see *Figure 3*) (85,113).

The major advantages of CTA are its wide availability, affordability, non-invasive nature, high reproducibility and operator-independence. Furthermore, it has a fast scanning time of less than 5 minutes (36) and produces images in high spatial resolution and in multiplanar or 3D panoramic views that facilitates ease of interpretation. As a result, the location, caliber, and course of musculocutaneous perforators as small as 0.3 mm in diameter can be readily displayed (47). In contrast to ultrasonography, the image quality is less affected by the body habitus (47) and it can clearly demonstrate both DIEA and superficial inferior epigastric artery (SIEA), and their branching patterns. In addition, the CTA can be used to screen for comorbidities, such as metastatic diseases, and detect any underlying abdominal wall defects (48) or other incidentally discovered lesions, such as angiomyolipoma and adrenal mass, that may alter the surgical management (89,90).

A plethora of studies have been reported in the literature demonstrating high accuracy of CTA in detecting perforators suitable for perforator-based free flap reconstructions (*Table 2*). Most investigators report sensitivity and specificity close to 100% (46,47,61-63,85-90). Furthermore, CTA can also characterize the DIEA branches, IM course, and both superficial and deep venous systems supporting a flap with high sensitivity (100%, 97.1%, 91.3%, 94.4%, respectively) (62). In comparison to Doppler ultrasound, Rozen *et al.* demonstrated that CTA

produces superior visualization of the DIEA, its branching pattern, its perforators ($P=0.0078$), and additionally, the SIEA (47). Similarly, Scott *et al.* exhibit that CTA is significantly more sensitive than color Duplex ultrasound in detecting the top two perforators (94.3% *vs.* 66.3%, respectively) (46). Compared to the MRA, CTA has a superior fat-to-vessel contrast ($P=0.007$), but a poorer muscle-to-vessel contrast ($P=0.001$) (63). The former indicates that CTA is able to produce higher quality images of the subcutaneous course of a perforator; however, the latter signifies that MRA is technically superior at delineating the IM course of a perforator.

Enhanced understanding of the microvascular anatomy facilitated by CTA has assisted reconstructive surgeons in selecting an appropriate donor site, perforator, and flap, and numerous studies demonstrate that this has directly translated into an improvement in the clinical outcomes (*Table 3*). The studies have reported a significant reduction in the flap harvest time and the total operative time (35,87-89,98-106). This leads to reduced exposure to general anesthesia, reduced risk of infection, and reduced intraoperative bleeding (35). Furthermore, the use of CTA for preoperative planning is associated with a reduction in postoperative flap complications, such as fat necrosis, partial, and total flap loss, and donor site morbidity, such as abdominal bulge and herniation (35,47,87-89,100-103). Interestingly, one study by Malhotra *et al.* demonstrated no improvement in flap complications from preoperative CTA, even though there was a significant reduction in the operative time ($P<0.05$), intraoperative blood loss ($P<0.05$), and inpatient hospital stay ($P<0.05$) (105).

The main limitations associated with CTA stem from potential sensitivity to the iodinated intravenous contrast, contrast-induced nephrotoxicity in patients with renal impairment, and exposure to ionizing radiation. The latest CTA scanning protocols that assess a targeted area for identifying abdominal wall perforators (114) and the development of radiation dose reduction software and algorithms in the latest scanners (60,115) have decreased the average radiation exposure to 5 mSv per scan (62,98,107,111). This dose is equivalent of two abdominal X-rays, is significantly lower than a routine abdominal CT scan (63), and is theoretically associated with a 1-in-4,270 risk of fatal radiation-induced cancer (116). Moreover, perforators at the recipient site are not simultaneously imaged in order to minimize radiation. Most often, the patients have had a contrast-CT scan of the chest wall for their original breast cancer staging. Nonetheless, the

recipient vessels, most commonly the internal mammary perforators, can be adequately visualized using a handheld Doppler probe (114). Furthermore, thoracic imaging poses risk to the radiation-sensitive contralateral breast and thyroid.

Magnetic resonance angiography (MRA)

Recently, MRA with Gadolinium-based contrast has become popular in order to bypass the risk of radiation associated with CTA (*Table 1*) (61). Recent advances in the image acquisition technique, introduction of novel contrast agents, and increasing availability of MRI scanners with stronger field strength have significantly improved the accuracy and the quality of MRA images (117). Delayed equilibrium phase (EP) technique acquires images when both the artery and the vein are enhancing, compared to the conventional first-pass, or arterial-phase, technique (96). As a result, EP facilitates a longer image acquisition time leading to higher spatial and contrast resolution, produces diagnostic quality data despite minor motion artifacts, and has 100% sensitivity in detecting abdominal perforators (96). In addition, investigators have reported prone position to minimize respiratory-related motion artifacts (92,118,119). However, this method remains controversial since it alters the natural curved anatomy of the abdomen compromising the image quality of the perforators and since patients are indeed operated in supine position (62).

In contrast to the conventional gadolinium contrast agents, extracellular contrast agents, such as gadobenate dimeglumine, offer slightly higher relaxivity (120). However, it only has a short half-life of 100 seconds (120). Newer blood pool contrast agents, mainly gadofosveset trisodium (121), has demonstrated superior quality images secondary to a longer imaging window and a relatively large R1 (122). Gadofosveset trisodium has a long half-life of 28 minutes and reversibly binds to serum albumin with high fraction (90%) (123) leading to stronger contrast enhancement of the vessels (124,125). Stronger field strength 3.0 T scanners are increasingly becoming commonplace. They demonstrate superior spatial resolution and augment gadolinium-based contrast enhancements with reduced acquisition time and a decreased susceptibility to motion artifacts (126-129).

One of the significant benefits of MRA is that it eliminates exposure to ionizing radiation. Furthermore, gadolinium-based contrast agents have a safer risk profile, such as the rate of acute allergic reaction (0.07% *vs.* 3%), in comparison to radioactive contrasts (130,131). Thus, MRA

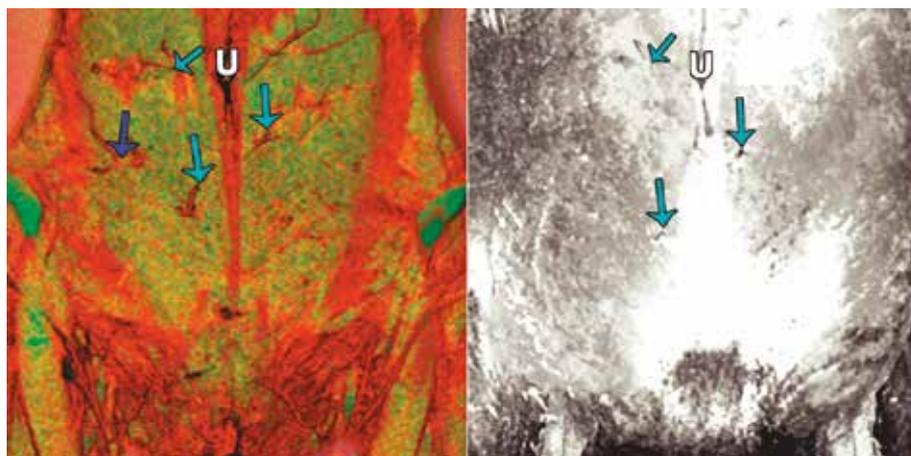


Figure 4 Volume-rendered, three dimensional reconstructions of the cutaneous perforators of the DIEA using CTA on the left, and MRA on the right. Three large (>1 mm) perforators were demonstrated with both modalities (light blue arrows), while one large perforator was demonstrated on CTA alone (dark blue arrow). DIEA, deep inferior epigastric artery; CTA, computed tomography angiography; MRA, magnetic resonance angiography. Reproduced with permission from reference (84).

may be advantageous in patients with younger age, iodine allergy, and impaired renal function. Moreover, muscle-to-vessel contrast ratio is superior in MRA, compared to CTA, leading to a clearer depiction of the perforator IM course (63). In autologous breast reconstructions, there are a growing number of reports demonstrating its accuracy in delineating perforators and its potential role in improving clinical outcomes.

Despite high specificity (100%), Rozen *et al.* reported in an earlier study that MRA has low sensitivity (50%) in detecting abdominal wall perforators for breast reconstruction, suggesting it as an inferior option to CTA for perforator mapping purposes (see *Figure 4*) (61). Advances in the imaging technique, contrast agents, and the application of higher field strength scanners have improved its accuracy in the last decade (*Table 3*) (36). As a result, more recent studies report a high sensitivity (91.3% to 100%) with MRA (62,63,91-96). Of note, the accuracy of IM course depiction is high with MRA (62,93-95). In contrast to CTA, there is a relative paucity in the literature describing MRA for a large clinical series describing its impact on clinical outcomes. Schaverien *et al.* report that in 126 patients, MRA reduced the rate of partial flap loss ($P<0.05$) and the total operative time in both unilateral and bilateral cases by 25 and 40 minutes, respectively (106). However, the latter did not reach statistical significance. In an early study, Rozen *et al.* demonstrated that using MRA reduced the incidence of flap complications to 0% in six

patients (61).

One of the major drawbacks of MRA is related to its relatively high cost and low availability since an average MRA scan costs USD 600, compared to USD 400 for a CTA (61). Furthermore, due to its poor spatial resolution, MRA is limited at detecting perforators smaller than 0.8 mm in diameter (61). However, the recent introduction of novel contrast agents (132) and higher field strength scanners (133) are expected to improve on this limitation. Moreover, due to an expanded examination window, MRA is more susceptible to motion artifacts and requires the patients to breath-hold for a long period of time (64). Despite its safer profile compared to ionizing contrast agents, gadolinium-based agents still presents with adverse effects, such as nephrogenic systemic fibrosis (134-137). Only 200 cases have been reported worldwide and this appears to be predisposed in patients with underlying impaired renal function. In addition, MRA is absolutely contraindicated in patients with severe obesity, implanted defibrillator or a pacemaker, implanted ferromagnetic device, and a cochlear implant. It is relatively contraindicated in patients with artificial heart valves and other types of implants. It is difficult to perform in patients with claustrophobia, severe anxiety, and confusion who are unable to lie still.

Discussion

Breast cancer is the most common cancer worldwide

and is associated with the most common cancer-related deaths in women worldwide (2,138). Since an increasingly number of women opt for mastectomy (3), postmastectomy breast reconstruction has become an essential component of the holistic treatment in patients with breast cancer to ensure their psychosexual wellbeing. To this end, breast reconstruction with autologous tissue has been demonstrated to provide the most functional and aesthetically pleasing outcome. Abdominal wall-based, rectus muscle-sparing DIEP flaps are considered the gold standard since they provide ample volume without causing significant donor site morbidity (10,30). However, DIEP flaps are associated with longer microsurgical dissection leading to longer operative times and an increase in the postoperative microvascular complications.

To this effect, preoperative planning with modern imaging technology has become a crucial component of fashioning a DIEP flap for breast reconstruction. Handheld Doppler probes and color Duplex ultrasound are the first modality to be adapted for use in the preoperative setting (45). Although widely available and affordable, Doppler ultrasound is not sensitive or specific enough to be reliable and used routinely (108). Furthermore, it is susceptible to inter-observer variability and is unable to illustrate SIEA anatomy (46). Fluorescent angiography has been studied to preoperatively delineate the caliber and the location of the perforators (139). However, since this technology is only able to provide information up to a few millimeters deep from the skin and thick abdominal pannus is preferred in DIEP flaps, it has become less frequently used preoperatively (55). Instead, investigators are now using LA-ICGFA to assess microvascular anastomotic patency intraoperatively and evaluate perfusion in mastectomy skin flap (55,77).

Since CTA was first reported for breast reconstruction by Masia *et al.* (98), it has become the preferred preoperative imaging modality due to its high accuracy and reliability (38,88,108). With a free software, 3D images of the perforator anatomy can be created, from which its caliber, location, subcutaneous branching pattern, the DIEA and the SIEA anatomy can be easily visualized (113,140). However due to concerns surrounding radiation exposure, high-risk contrast agents, and contrast-related nephrotoxicity, MRA has been investigated recently as an alternative (61,95). Despite early findings suggesting low sensitivity in detecting perforators (61), recent advances in the image acquisition technique, the introduction of higher quality contrast agents, and availability of stronger 3.0 T scanners have enhanced the quality of perforator imaging from MRA

(36,92,132). However, the image quality of CTA remains superior to the latest MRA technology. As a result, the latter has currently only preferred for a subset of patients in the younger age group, with iodine allergy and impaired renal function.

Conclusions

Preoperative imaging is an essential component of planning postmastectomy autologous breast reconstructions with DIEP flaps. Fluorescent angiography technology has been investigated as a preoperative imaging tool in the past. However, the investigators have demonstrated that it may instead be a useful intraoperative adjunct to evaluate the patency of microvascular anastomosis and the mastectomy skin perfusion. Currently, CTA is and remains the gold standard preoperative imaging modality due to its high accuracy, sensitivity, and specificity. In order to eliminate the radiation risk from CTA and the toxicity from radiosensitive contrast agents, MRA has been investigated in its role. Despite recent advancements, the image quality of MRA is still inferior to CTA and its widespread use is limited by high cost and lack of availability. Hence, MRA is best reserved for a subset of patients who are at a high risk from CTA, such as women with younger age, iodine allergy, and renal impairment.

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Footnote

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Conservative mastectomies and Immediate-DElayed AutoLogous (IDEAL) breast reconstruction: the DIEP flap

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Background: With the development of conservative mastectomies, there are an increasing number of women seeking immediate implant based and autologous breast reconstruction. Despite the oncologic safety of the procedures, the focus will be on the timing of reconstruction.

Methods: Our plastic surgery unit is focused primarily on autologous breast reconstruction and is part of an interdisciplinary breast center. We offer immediate breast reconstruction (IBR) with autologous tissue for patients with positive BRCA 1 and 2, ductal carcinoma in situ (DCIS), invasive cancer without margin problems to the skin, as well as to correct poor oncologic and aesthetic breast conserving therapy (BCT) outcomes. In the majority of cases we prefer an Immediate-DElayed AutoLogous (IDEAL) breast reconstruction concept with a two-stage procedure.

Results: Over the last 10 years we performed more than 1,600 breast reconstructions with free flaps, performing the deep inferior epigastric perforator (DIEP) flap as our first choice for autologous tissue. We recommend IDEAL breast reconstruction, however approximately 15% of our cases are immediate one stage conservative mastectomies and breast reconstruction with the DIEP flap.

Conclusions: For immediate reconstruction, the aesthetic outcome should not take precedence over oncologic considerations. Immediate one-stage, breast reconstruction with autologous tissue can be offered to the suitable patients which is most likely a healthy women with a small-to-medium sized non ptotic breast receiving a conservative mastectomy. In all other cases, we recommend an IDEAL breast reconstruction approach in order to achieve a final result that is both satisfyingly pleasing and oncologically safe.

Keywords: Mastectomy; deep inferior epigastric perforator flap (DIEP flap); immediate-delayed reconstruction; oncoplastic surgery

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Introduction

Breast cancer is the most common cancer affecting woman, appearing with a lifetime risk of up to 10%. As a method of treatment, one third of the patients diagnosed with breast cancer receive a mastectomy of various oncological extents resulting in a reconstructive challenge for the oncoplastic surgeon (1). Between 2005 and 2011 the mastectomy rate in the US increased up to 51% with an increasing number of patients receiving bilateral prophylactic mastectomy with immediate reconstruction (2). The term “conservative

mastectomies” was first used by Nava *et al.* in 2009. It outlined the need for preservation of mammary appearance, biomechanical balance, adequate volume restoration and symmetrical scarring in oncoplastic surgery (3,4). Moreover, the most common form of conservative techniques became the implant based breast reconstructions. Nava sees an increasing need of autologous breast reconstruction through increased indications for radiotherapy and therefore an unaccepted rate of capsular contractures and radiodermatitis in implant based reconstruction (3,5).

Breast reconstruction should always be attempted in a multidisciplinary approach. An optimal oncologic and surgical treatment takes the following into consideration:

- Breast conserving therapy (BCT);
- Mastectomy;
- Skin sparing mastectomy (SSM);
- Nipple sparing mastectomy (NSM).

Breast reconstruction following surgical treatment of breast cancer takes the choice of alloplastic or autologous reconstruction and the timing of reconstruction into consideration:

- Implant *vs.* autologous reconstruction;
- Immediate *vs.* delayed reconstruction.

Implant based breast reconstruction

Implant based breast reconstruction has many advantages, but to achieve the best results, the ideal indications must be met. When there is a lack of sufficient soft tissue coverage, the need of acellular dermal matrix (ADM) lead to substandard results. In addition, the possibility of pre- and post-reconstruction radiotherapy leads to a high rate of capsular contractures and with this, there is a high rate of secondary procedures involving capsular removal and implant changes (6,7).

Autologous breast reconstruction

Considering the high rate of complications in implant based breast reconstruction including capsular contracture and the need for implant removal, reconstruction with autologous tissue is preferable to implant based reconstructions, especially after radiation therapy (6,8-10). The downside of radiation therapy following autologous reconstruction is that it leads to inferior aesthetic results, such as fat necrosis and skin fibrosis.

Immediate vs. delayed reconstruction

The decision between immediate and delayed reconstruction is complex and needs to be approached in a multidisciplinary fashion. It is important to take the patient's choice into consideration, the need for postoperative radiotherapy, the extent of the disease, as well as other medical conditions, such as bleeding complications that may favor one method over the other.

Immediate breast reconstruction (IBR)—advantages

- Decreased risk of social or emotional difficulties;
- Better cosmetic results;

- Possibly fewer surgeries and lower surgery cost;
- No difference in rate of development of local cancer recurrence;
- No difference in the ability to detect local cancer recurrence.

Immediate breast reconstruction (IBR)—disadvantages

- Possible skin and nipple perfusion problems;
- Indications for radiation therapy unclear;
- Longer hospitalization and recovery times than mastectomy alone;
- More scarring than mastectomy alone;
- Surgery prolonged;
- Reimbursement is difficult.

Immediate-DElayed AutoLogous (IDEAL) breast reconstruction—advantages

- Best option to maintain the balance between optimal aesthetic outcomes and effective radiation delivery (11);
- Minimizing unpleasant aesthetic outcomes (contracture, distortions);
- Revision of the inframammary fold;
- Debridement of any nonviable mastectomy skin (if present) before the inseting of an autologous tissue flap (12).

IDEAL breast reconstruction—disadvantages

- More surgeries and hospitalizations;
- Possibly increased risk of social or emotional difficulties;
- Prolonged and elongated time of therapy;
- Higher costs.

Radiotherapy and immediate breast reconstruction (IBR)

The challenge in breast reconstruction remains to preoperatively predict the probability of the necessity of post mastectomy radiotherapy (PMRT). However, when immediate reconstructions are irradiated, the outcome might be compromised. The patient with an implant may develop capsular fibrosis. On the other hand, with a tissue flap there may be distortion and shrinkage of the tissue (5,7,13). In a meta-analysis overlooking 28 studies with autologous reconstruction published by Schaverien *et al.*, their conclusion found an increased risk of fat necrosis and a higher portion of revisional surgery after IBR and post mastectomy radiation therapy compared to delayed immediate reconstruction. They did however report satisfactory outcomes with adjuvant radiation therapy (14).

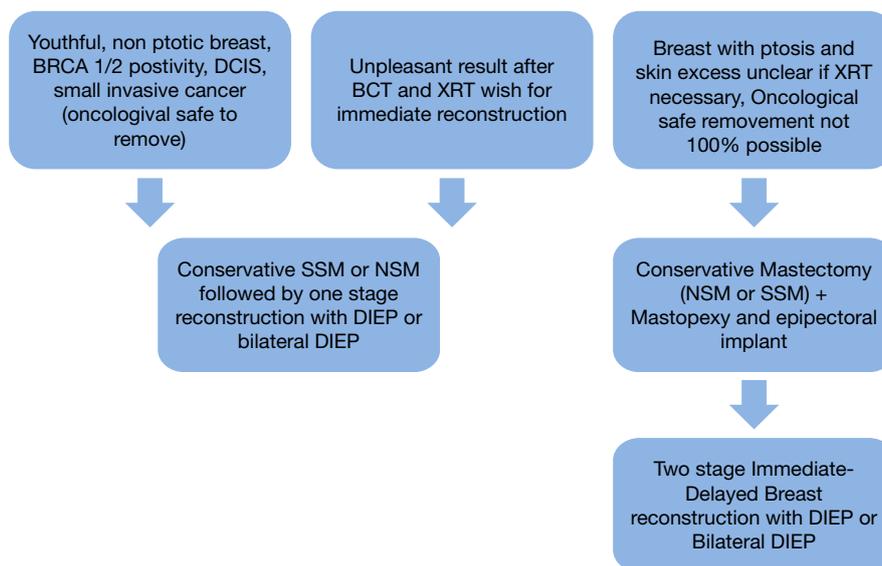


Figure 1 Timing and concept of breast reconstruction with the DIEP flap. DIEP, deep inferior epigastric perforator; DCIS, ductal carcinoma in situ; BCT, breast conserving therapy; XRT, radiation therapy; NSM, nipple sparing mastectomy; SSM, skin sparing mastectomy.

The ideal breast for primary autologous reconstruction

In a youthful, full and non ptotic breast, as often presented in patients with BRCA 1/2 mutations seeking prophylactic mastectomies, an immediate reconstruction after SSM can be performed using a uni- or bilateral deep inferior epigastric perforator (DIEP) flap. However, the one stage approach leads to a longer duration of the surgery and therefore increases the general intraoperative risks.

The average breast for primary autologous reconstruction

The patient presenting with a ptotic and large breast, which makes up the majority of our patients on the other hand, is more feasible for an IDEAL two-stage reconstruction approach. In a primary procedure, the tumor removal can be combined with a mastopexy of the skin; therefore the secondary autologous reconstruction has the ideal setting to achieve an aesthetic pleasing result (Figure 1).

Material and methods

Autologous breast reconstruction with the DIEP flap

The DIEP flap was first described by Koshima *et al.* in 1989 and since has evolved to the work horse of autologous breast reconstruction (15-21). Over the last two decades, multiple

free flap procedures have been performed, but after all, the DIEP flap procedure is the most feasible free flap for breast reconstruction. The benefits of the DIEP flap include all the benefits of the free transverse rectus abdominal myo-cutaneous (TRAM) flap without the donor site complications including abdominal hernias and weakness of the abdomen (16). Besides BCT and radiotherapy, the traditional concept of mastectomies, adjuvant therapy and delaying reconstruction is being supplemented by the increasing use of immediate reconstruction.

We have an interdisciplinary breast center that includes a department of senology for the oncologic treatment and a plastic surgery unit for the autologous breast reconstruction. Our plastic surgery unit specializes in breast reconstruction—over the last 10 years, we have performed over 1,600 free autologous breast reconstructions (8).

The crucial part of IBR with the DIEP flap is the right patient selection:

Indications:

- Young healthy women;
- Prophylactic mastectomy;
- No PMRT needed.

Contraindications:

- Classification of American Society of Anesthesiologists (ASA) >3;
- Previous abdominoplasty or abdominal surgery (when

perforators are destroyed);

- Severe haematological disorders.

Preoperatively, all patients receive a CT angiography to detect the perforator vessel nourishing the abdominal skin flap. The markings preoperatively are performed with the patient in the standing up position. Standard abdominoplasty markings are applied to the donor side area. The midline and inframammary fold are marked as well as the perforators as detected in the CT angiography. The DIEP flap is performed on a daily basis with a two-team approach. Two surgeons perform the flap harvesting while another surgeon is dissecting the recipient vessels for which we use the internal mammary artery and vein. The dissection of the flap and the recipient vessels is performed bloodless with bipolar micro-forceps. After dissection of the relevant perforators, temporary clamping of all the perforators, except the main perforators, will be done. The flap is now evaluated and depending on the number of perforators needed, the decision is made to choose a DIEP or a MS-2-TRAM flap. By using this protocol with standard CT angiography and intraoperative clamping of the perforators and flap evaluation, we were able to reduce the number of MS-2-TRAM flaps to around 10% of all autologous breast reconstructions with a constant flap loss rate below 1%.

The dissection is always performed with bipolar hemostasis. Perioperatively, the patients receive a shot of 2 g cefazolin over 24 hours. After detaching the flap, it is cooled during ischemia and the anastomosis to the internal mammary vessels is done with 9.0 Prolene. First the vein and then the artery is anastomosed. The patients receive single shot of 2.500 IE heparin. We use fibrin glue for stabilization of the anastomosis to prevent kinking and torsion of the pedicle. The flap is warmed again after the anastomosis is done and the flap is reperfused. If the blood supply of the skin of the mastectomy flap is questionable, we insert the flap without de-epithelization and wait 4-6 days until we finish the reconstruction. Postoperatively the patients are monitored hourly and the flap is controlled via Doppler detection on the intensive care unit. The patients receive aspirin 100 mg p.o. daily for 6 weeks and low molecular weight heparin (LMWH) subcutaneously until complete ambulation. The patients get out of bed the first postoperative day and will usually be discharged between day 7 and 10. The postoperative schedule involves appointments in the outpatients clinic 1, 3, 6, and 12 months after surgery as described in previous reports (8).

Immediate-DElayed AutoLogous (IDEAL) breast reconstruction concept

Regarding the timing of breast reconstruction, many different concepts have been published (12,22). Our protocol of patient selection according to cancer status and breast form as well as for the timing of breast reconstruction is shown in *Figure 1*. It has been developed in close cooperation with our Department of Senology as part of our breast center.

In patients with youthful, non ptotic breast, presenting positive BRCA 1/2, ductal carcinoma in situ (DCIS), or small invasive cancer, an IBR could be feasible, either with autologous or alloplastic reconstruction. However, the conservative mastectomy should be oncologically safe and no radiotherapy after immediate reconstruction is needed (*Figures 2-4*).

To exclude an advanced tumor stage, a complete diagnostic workup consisting of mammography, breast ultra sound and MRI is recommended in these cases. Sentinel biopsy should always be done before immediate reconstruction to rule out the need for PMRT. Before we consider a one stage reconstruction, the patients have a sentinel lymph node biopsy performed to detect lymph node status. If positive, we recommend axilla dissection and radiation therapy, therefore a one-stage procedure is not advisable.

This approach can also be used with any dissatisfying and unpleasing results after BCT, or previous reconstruction (implant or autologous) and postoperative radiation therapy that has altered the aesthetic outcome resulting in skin damage and capsular contracture. Still, in patients with breast ptosis, skin excess or with the uncertainty whether oncological safety can be guaranteed with the cancer removal where they must be followed with postoperative radiation therapy, we prefer our immediate-delayed-breast reconstruction concept. However, in patients with breast ptosis and skin excess, or with unclear oncologic breast tissue removal or postoperative radiation therapy that is indicated, we prefer our immediate-delayed-breast reconstruction concept. This concept consists of conservative mastectomy (NSM or SSM) combined with a mastopexy if needed and epieptoral implant or expander (in case of SSM) positioning. The radiation therapy is done before the implant reconstruction in a neo-adjuvant setting.

Patients that receive radiotherapy after DIEP flap reconstruction show poorer outcomes than patients who do not undergo radiation after surgery (23). Rogers *et al.* states that immediate reconstructed DIEP flaps, exposed to radiotherapy, experience significantly increased rates



Figure 2 A 45-year-old woman with invasive breast cancer on the right side. Preoperative view.



Figure 5 A 54-year-old woman with previous BCT and poor cosmetic outcome after radiation therapy and chemo therapy, immediate delayed concept. BCT, breast conserving therapy.



Figure 3 Result 3 months postoperatively after SSM + immediate bilateral breast reconstruction with a DIEP flap. SSM, skin sparing mastectomy; DIEP, deep inferior epigastric perforator.



Figure 6 Same patient 6 months postoperatively.



Figure 4 Result 3 years postoperatively after nipple reconstruction with star flaps and tattooing of the areolar complex.

of fat necrosis, fibrosis and contracture (23). The odds of the development of flap fat necrosis are almost three times higher when the flap was subjected to radiotherapy (24). Further, in the study of Motwani *et al.* it was concluded that IBR poses challenges for the treatment planning of post mastectomy radiation therapy because of suboptimal field coverage and organ protection (25). Thus, IBR is discouraged due to a potential risk of impaired tumor treatment and oncological surveillance (25). Patients who have their breast reconstructed before their radiotherapy are exposed to increased late complication rates (26) and unpredictable outcomes (23) due to which the timing of breast reconstruction has to be planned carefully.

After 3-6 months, the patients return for a secondary breast reconstruction with a DIEP flap. Also after BCT with poor outcomes an immediate delayed approach can be feasible (Figures 5,6).



Figure 7 Nipple sparing mastectomy with total breast tissue removal and preservation of blood supply to the skin.



Figure 8 Skin necrosis after immediate reconstruction due to poor skin perfusion after mastectomy.

The skin or NSM is routinely performed by the breast surgeon (*Figure 7*). In case of NSM the skin incision is placed in an inferolateral submammary area. Viable skin flaps are important for later reconstruction. When autologous reconstruction using the DIEP flap is planned, the implant is placed epieptorally. In a second stage the flap is also placed in an epieptoral plane to avoid animation problems (*Figure 8*).

Timing of secondary procedures

If symmetricalisation procedures are needed 6-12 months after the breast reconstruction, patients receive a mastopexy of the contralateral side and a nipple reconstruction. For the nipple reconstruction we prefer the Star flap (3,27,28). The Areolar complex is usually tattooed.

Discussion

The role of oncoplastic surgery constantly rises and

eventually leads to new concepts for a multidisciplinary treatment plan and team approach that consists not only of breast surgeons, but also oncologist and a plastic surgeon that discuss further treatment plans among each other (29). The possibility of conservative mastectomies provides the oncoplastic surgeon with an ideal basis for optimal skin saving, volume restoring and breast reshaping tissue transfer for results especially tailored to the patient's oncological and anatomical situation (3,21).

The most important aspects to keep in mind with any form of breast reconstruction is the oncological safety.

Motwani *et al.* concluded that IBR poses challenges for the treatment planning of post mastectomy radiation therapy because of suboptimal field coverage and organ protection (25). Thus, a multidisciplinary team has to discuss the option of immediate *vs.* immediate-delayed-breast reconstruction in regards to a potential risk of impaired tumor treatment and oncological surveillance (25). Secondly, after the oncological and patient safety, the patient quality of life and cosmetics plays another role in the well-being of the patient and influences their choice for additional reoperations. The decision of an IBR should be undertaken carefully and in close dialogue with an oncologist to be able to plan the time of breast reconstruction with the possibility to "immediately-delay" the surgery for a better oncological and complication-free result (29) and to avoid, at its best, radiotherapy to the reconstructed breast. It is without a doubt that IBR following conservative mastectomies for poor outcomes after BCT can lead to excellent results that are oncological safe (30) with a low complication rate (8). Nevertheless it has to be taken into account that these results can be achieved mainly when the immediately reconstructed breast is not radiated afterwards. Since the exposure to radiotherapy causes increased late complication rates (26) and unpredictable outcomes (23). The risk of developing a fat necrosis of the immediately reconstructed flap is almost three times higher when the flap was subjected to radiotherapy (24).

IBR may impose limitations on the treatment planning of PMRT but the challenge remains to preoperatively predict the probability of the necessity of PMRT. Since PMRT influences implant based and autologous reconstruction alike in a negative manner (31,32), the patient should always be offered a delayed primary reconstruction if the need of PMRT is unclear, in order to avoid the exposure of the patients to consecutive operations and unsatisfying aesthetic results. It is important to have a good doctor-patient communication to inform and prepare the patient for the following treatment possibilities and tailor the reconstruction

to the patient's needs, oncological state and anatomy.

In IBR after conservative mastectomies the perfusion of the breast envelope can sometimes be poor (*Figure 8*). Therefore, the concept of delayed de-epithelialization has been described and is a helpful tool in IBR, preventing poor outcomes with skin necrosis and extensive scarring and saves the patient of unnecessary re-operations and complications (33).

Last but not least, besides the oncological state of the patient, the shape of the breast is also an important factor in the timing of immediate versus delayed IBR (22). A youthful, non ptotic breast can be reconstructed in a single stage procedure while the average breast with ptosis and lax skin is preferred to be treated with the immediate delayed approach with mastopexy, epieptoral implant and finally autologous reconstruction using the DIEP flap in a second stage, thus called IDEAL breast reconstruction.

Conclusions

The ideal reconstruction is an individualized treatment plan. Immediate one stage breast reconstruction with a DIEP flap can be offered to the suitable patients which most likely is a healthy women with a small to medium size and non ptotic breast receiving prophylactic mastectomy. According to our selection criteria we offer patients immediate reconstruction with the DIEP flap. If risk of skin or nipple necrosis or tumor free margins cannot safely be achieved, and the patient would like autologous reconstruction, we prefer an IDEAL breast reconstruction approach. This approach consists of a conservative mastectomy followed by an immediate epieptoral implant placement, eventually combined with a skin reducing procedure. In a second stage 3-6 months later, the implant is removed and replaced by an autologous reconstruction favoring the DIEP flap. In no case should cosmetics take precedence over oncologic considerations.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Radiotherapy and breast reconstruction: oncology, cosmesis and complications

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Abstract: Breast reconstruction plays a highly important role in the management of patients with breast cancer, from a psycho-social and sexual stand-point. Given that immediate breast reconstruction does not impair the oncologic safety of breast cancer management, with no increase in local recurrence rates, and no delays in the initiation of adjuvant chemotherapy or radiotherapy, the need to balance cosmesis in reconstruction with the oncologic needs of breast cancer patients is no more evident than in the discussion of radiotherapy. Radiotherapy is essential adjuvant therapy in the treatment of breast cancer, with the use of adjuvant radiotherapy widely shown to reduce local recurrence after both partial and total mastectomy and shown to prolong both disease-free and overall survival in patients with nodal disease. In the setting of breast reconstruction, the effects of radiotherapy are potentially two-fold, with consideration required of the impact of breast reconstruction on the administration of and the initiation of radiotherapy, as well as the effects of radiotherapy on operative complications and cosmetic outcome following immediate breast reconstruction. The current editorial piece aims to analyze this balance, contrasting both autologous and implant-based reconstruction. The literature is still evolving as to the relative role of autologous *vs.* alloplastic reconstruction in the setting of radiotherapy, and the more recent introduction of acellular dermal matrix and other compounds further complicate the evidence. Fat grafting and evolving techniques in breast reconstruction will herald new discussions on this front.

Keywords: Implant; reconstructive surgery; radiation; adjuvant therapy; breast reconstruction

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The need to balance cosmesis in reconstruction with the oncologic needs of breast cancer patients is no more evident than in the discussion of radiotherapy (1). Radiotherapy is essential adjuvant therapy in the treatment of breast cancer, with the use of adjuvant radiotherapy widely shown to reduce local recurrence after both partial and total mastectomy and shown to prolong both disease-free and overall survival in patients with nodal disease (1-6). In the setting of breast reconstruction, the effects of radiotherapy are potentially two-fold, with consideration required of the impact of breast reconstruction on the administration of and the initiation of radiotherapy, as well as the effects of radiotherapy on operative complications and cosmetic outcome following

immediate breast reconstruction. The current editorial piece aims to analyze this balance, contrasting both autologous and implant-based reconstruction.

Oncologic issues

The impact of breast reconstruction on delaying the administration of radiotherapy has been explored in relatively few recent studies (7-11). This is surprising given the importance of the issue, with several significant studies demonstrating poorer oncologic outcomes with delays in radiotherapy (12-15). In fact, those studies which have addressed the issue have all been relatively low in numbers

and based at single institutions. Each of these studies showed no delay in the initiation of adjuvant radiotherapy in patients undergoing immediate breast reconstruction. Breast reconstruction may also impact the delivery of radiotherapy, by means of distorting the chest wall anatomy and thus altering the design of the radiotherapy fields. This is in the setting of radiation fields which include the chest wall, internal mammary lymph nodes, supraclavicular lymph nodes and the apex of the axilla. Distorting the anatomy with a reconstructive flap or implant may diminish the radiation administered to these regions, or more commonly, may dictate the need for a wider radiation field (16-18).

The mode of action of radiotherapy involves the use of ionizing radiation, delivered by external beam radiation, to the chest wall and/or the surrounding lymph nodes. It is the mechanism of this effect, via direct disruption of protein and DNA molecules and the formation of free radicals and electrons causing molecular damage, that dictates both positive and negative outcomes (15). While these effects are directly toxic to malignant cells, radiation also damages healthy tissue. Direct tissue cellular damage with chromosomal alteration, microvascular occlusion with ischemia and inhibition of fibroblast action, are all implicated as mechanisms in tissue damage (19-22), leading to progressive loss of endothelial cells in the walls of microvasculature and leading to characteristic blind ending capillaries and regional ischaemia. Structural changes to the skin include changes in epidermal and dermal keratinocytes and melanocytes, damage to skin appendages, skin thinning and fibrosis (19,21,22). These damaging tissue responses are associated with the increased incidence of operative complications, particularly those associated with healing.

Reconstructive outcomes

In the setting of implant reconstruction, adjuvant radiotherapy has been widely described as having an unacceptably high complication rate, particularly the complications of capsular contracture, and rupture of the implant envelope or fibrous capsule (23,24). This is particularly true for postoperative radiotherapy, but has been associated with preoperative radiotherapy as well. Where post-operative radiotherapy is predicted, such as those high-risk cancers that are large, multifocal or have lymph node involvement, implant reconstruction has been described widely as an ill-advised option. Many of the studies showing this were associated with older regimes and modes of administration of radiotherapy,

and more recent techniques, such as helical tomographic radiotherapy, may improve outcomes in the setting of breast reconstruction (25).

While the same conclusions for autologous reconstruction have certainly been less rigid, there has been no consensus in the literature. In fact, our experience suggests that there are indeed complications in autologous reconstruction from radiotherapy, and that the effects of radiotherapy on implants in the setting of skin-sparing mastectomies may be less than previously suggested. The differences between autologous and implant reconstruction in this setting may thus be more comparable than previously suggested (1,23,26-28). *Figures 1,2,3* highlight the effects of radiotherapy on autologous tissues alone, and highlight that these effects are not solely related to the alloplastic implant (*Figures 1,2,3*).

The effect of radiotherapy on operative outcome has been explored to a large extent, but not in any randomized control trials. For autologous reconstruction, there is conflicting data, with the timing of radiotherapy of importance. The complications that occur after autologous reconstruction in the previously irradiated chest are similar to those occurring in the setting of no radiation. However, given that the tissues have been afflicted with radiation damage, wound complications are more likely to be increased. Autologous reconstruction nevertheless, allows removal of some of the damaged tissue and the importation of donor healthy (non-irradiated) tissue.

The outcome of autologous reconstruction in the setting of previous (neoadjuvant) radiotherapy has been described in a large number of past studies (11,29-44), ranging from small, non-controlled studies, to large studies with over 100 cases that have been matched to a non-irradiated group. This diversity is echoed in their findings, with some of the larger studies demonstrating no significant difference in outcome and some showing significant increases in complication rates. The largest study was that of Williams *et al.* (1995), in which 118 patients with TRAM flap reconstruction after previous radiotherapy were compared to 572 patients without prior radiotherapy, with this study showing an increase in fat necrosis in patients with prior radiotherapy, but no increase in overall complications (35). Of the larger studies that assessed cosmetic outcome in the setting of previous radiotherapy, there were significantly poorer cosmetic scores (31,32). However, the overall incidence of these complications were not high, and as such autologous reconstruction is still considered safe after neoadjuvant radiotherapy. An additional consideration



Figure 1 Skin and flap contracture in a deep inferior epigastric artery (DIEA) perforator flap, in which postoperative radiotherapy was administered to the supero-medial pole of the breast. Marked skin changes, asymmetry, and nipple displacement are evident. Reproduced with permission from: Rozen WM, Ashton MW, Taylor GI. Defining the role for autologous breast reconstruction post-mastectomy: the social and oncological implications. Clin Breast Cancer 2008;8:134-42



Figure 2 Skin and scar retraction in the setting of adjuvant radiotherapy following partial mastectomy. Reproduced with permission from: Rozen WM, Ashton MW, Taylor GI. Defining the role for autologous breast reconstruction post-mastectomy: the social and oncological implications. Clin Breast Cancer 2008;8:134-42



Figure 3 Skin and nipple retraction in the setting of adjuvant radiotherapy following partial mastectomy. Reproduced with permission from: Rozen WM, Ashton MW, Taylor GI. Defining the role for autologous breast reconstruction post-mastectomy: the social and oncological implications. Clin Breast Cancer 2008;8:134-42

of preoperative radiotherapy is that it may reduce the incidence of loco-regional recurrence and increase disease-free survival, thus reducing the incidence of local recurrence following reconstruction (1,45,46).

The outcomes following autologous reconstruction with subsequent adjuvant radiotherapy has been similarly explored widely, with variable results (34,41,42,47-55). Although most studies described extremely low flap loss rates, the incidence of tissue complications was generally greater than comparative groups, particularly that of fat necrosis. Several studies documented fat necrosis rates of greater than 20% (34,41,47,48). The largest study however, by Huang *et al.* (2006), did not demonstrate high complication rates, with a 0 flap loss and 8.5% incidence of fat necrosis, a figure comparable to those without adjuvant radiotherapy (51). Despite this, if radiotherapy is expected, delaying the reconstruction is the preferred mode of management because all too often the authors have witnessed the effect of post-reconstruction radiotherapy on well matched autologous reconstruction, resulting in fibrosis, volume loss and displacement and elevation of the nipple and areolar complex (*Figure 1*).

With the more widespread use of skin-sparing

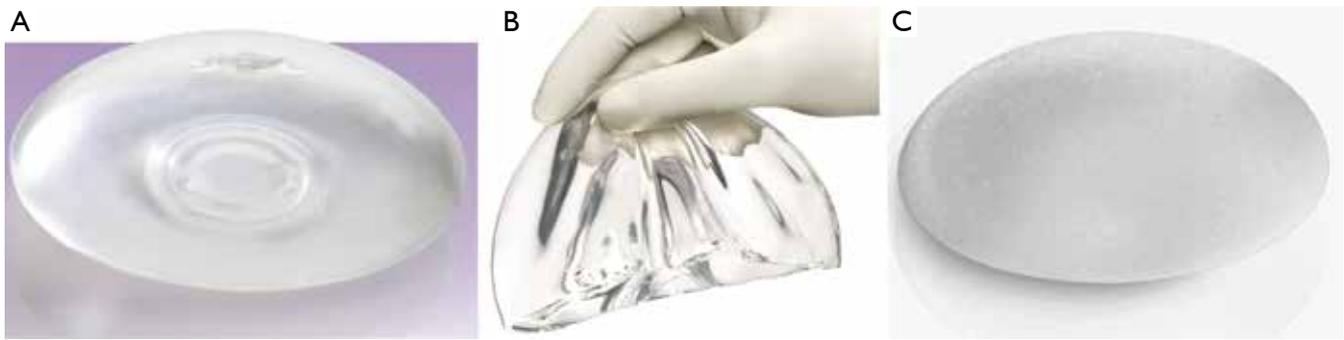


Figure 4 A. smooth saline implant; B. smooth, cohesive silicone gel implant; C. saline tissue expander. Images supplied by Mentor (California, USA). Reproduced with permission from: Rozen WM, Rajkomar A, Anavekar N and Ashton MW. Breast Reconstruction Post-Mastectomy: a History in Evolution. Clin Breast Cancer 2009;9:145-54

mastectomy (SSM) techniques, since the concept of preoperative plastic surgery planning together with SSM was first brought to the forefront by Toth *et al.* in 1991, an improvement in outcomes with implant reconstruction has developed (56,57). This involves the preservation of a native skin envelope with the removal of the breast, nipple-areolar complex, biopsy scars and skin overlying any superficial tumours, and the ideal SSM having a skin flap devoid of all breast tissue but having an adequate blood supply to prevent flap necrosis and delayed wound healing. It is believed that the preservation of the skin architecture and intact infra-mammary fold allows for immediate breast reconstruction, thereby reducing the number of reoperations and improving the cosmetic appearance of the breast, and diminish the need for tissue expansion and/or remodelling in the setting of radiotherapy. In many past studies, the expander/implant option was considered a poor option in post-mastectomy reconstruction, suggesting that tissue expansion was associated with a significantly higher complication rate (38,58-60). However, the field of implant-based reconstruction has undergone constant change, including the advent of dual chambers, anatomic and cohesive variations, texture modifications, and ever-evolving proprietary manipulation (*Figure 4*). As a result, implant-based reconstruction data are difficult to standardize between studies, or over any prolonged period of time. Similarly, size of implant, initial volume, final volume, and rapidity of expansion are tailored by individual surgeons to meet patient goals and expectations and can never be fully standardized. The development of skin-sparing and, more recently, nipple-sparing techniques also adds a distinct element to this variability.

We were recently involved in a study exploring the

outcome of breast implants following conservative mastectomy and SSM, examining the complication and reoperation rates in patients who underwent delayed versus immediate reconstruction, as well as patients who did and did not undergo radiation therapy (28). In several hundred patients, we found the overall complication rate of our implant-based reconstruction to be 15%, with a reoperation rate of 10%. This is lower than many of the previously described studies. Not only were we able to conclude that implant-based reconstruction can be associated with a low complication rate, even in the setting of radiotherapy, but that immediate reconstruction is also associated with a statistically significant lower reoperation rate. Previous studies have concluded that radiation therapy is associated with an unacceptably high rate of capsular contracture and rupture of the implant envelope or capsule (1,22,61), with a study by Spear and Onweyu in 2000 comprising 40 consecutive patients undergoing staged expander/implant placement and radiotherapy, showing a capsular contracture rate of 21% in the irradiated group *vs.* 0% in the control group (62). Our findings did not echo these. While we found irradiated breasts having a statistically higher reoperation rate, overall complication rates were similar to non-irradiated breasts, and we postulate that with improvements in the targeting of radiotherapy in order to limit damage to surrounding tissue, improved surgical techniques, or better quality of implants, past conclusions may be overstated to current thinking.

In comparing implant and autologous reconstruction, the literature is varied, with some authors finding no difference between autologous and implant reconstruction, both overall and in the setting of radiotherapy, with Rosen and colleagues finding that the complication rates were

similar between TRAM and tissue expander/implant reconstruction for breast reconstruction (63), and this has been echoed in other series (64-66). In light of these findings, the studies described above have varied in their conclusions. Several conclude that delayed reconstruction results in fewer complications and better outcomes, and others suggest that immediate reconstruction is safe and has no adverse consequences over delaying reconstruction. A further compromise, the 'delayed-immediate' reconstruction has also been postulated, in which a two-stage approach comprises a tissue-expander in the first stage, and autologous reconstruction ensuing if radiation is subsequently not required (67). The group at greatest risk for requiring adjuvant radiotherapy, those with locally advanced or multifocal disease, larger tumors and/or nodal metastases, certainly warrant greater consideration of a delayed reconstruction. However, this group is not always easily determined preoperatively, as although preoperative ultrasound can predict nodal status, there is a low sensitivity for small macro-metastases and/or micrometastases (68). Similarly, both axillary node frozen section and imprint cytology have significant false-negative rates making intraoperative prediction also difficult, and thus it is only post-operatively that a complete management plan can be formulated (69,70). As such, a significant number of those not expected to require adjuvant radiotherapy will ultimately be found to require it, warranting consideration of planning a delayed reconstruction from the outset.

A range of techniques have been introduced to 'protect' implants from the deleterious effects of radiotherapy. While the addition of overlying autologous tissues is an established technique, particularly with the use of local perforator flaps but also more distant regional or free flaps, more recent techniques have also been introduced. Acellular dermal matrix as an implant cover can reduce infection and capsular contracture rates even in the setting of radiotherapy (71), however the evidence for this is not yet well established, with more studies certainly needed (72).

Timing

Essential to the use of either implant or autologous reconstruction is the timing of both radiotherapy and reconstruction. In some settings, there is a preference to immediate radiotherapy, but where the oncology of the tumour permits delay to administration of radiotherapy, some principles can improve the reconstructive outcome. In implant reconstruction, there is a substantial benefit

to maximising tissue expansion prior to radiotherapy - by allowing an inserted tissue expander to reach full volume and preferably to swap to a definitive implant prior to radiotherapy, the deleterious effects of radiotherapy can be minimised, in terms of soft tissue contracture and tissue loss. This will clearly eliminate the need to expand irradiated tissues, an almost impossible feat.

Autologous tissue transfer is advantageous in the irradiated situation, as the transfer of any non-irradiated tissue (whether locoregional or free tissue transplantation) into an irradiated bed will 'revascularise' that tissue and reduce the deleterious effects of the radiotherapy in the region - fibrosis, contracture and wound breakdown. If autologous tissue alone is planned for reconstruction, use of a tissue expander to hold the soft tissue envelope out to stretch and reaching a desired volume, can maximise the amount of available regional tissue, and minimise the amount of tissue needing transfer. Irradiation while fully expanded, but prior to free tissue transfer, can maximise these benefits, while maintaining the importation of non-irradiated tissue in a transferred flap.

Modern techniques

A range of techniques have been introduced to 'protect' implants from the deleterious effects of radiotherapy. While the addition of overlying autologous tissues is an established technique, particularly with the use of local perforator flaps but also more distant regional or free flaps, more recent techniques have also been introduced. Acellular dermal matrix as an implant cover can reduce infection and capsular contracture rates even in the setting of radiotherapy (71), however the evidence for this is not yet well established, with more studies certainly needed (72).

Fat grafting is another evolving technique in breast reconstruction that will herald new discussions on this front. Fat grafting has been successfully used to augment the reconstructed breast in the setting of both autologous and implant reconstruction (73-77), as well as being successfully used in the setting of primary breast reconstruction by fat grafting alone (78). In the setting of radiotherapy, there is discussion in the literature that the importation of tissue that becomes well-vascularised through grafting, particularly adipose-derived stem cells, can 'revascularise' the irradiated bed and reduce radiotherapy-related complications (77,79). The use of fat grafting in the breast to achieve these ends has been described for both pre-radiotherapy and post-radiotherapy scenarios with benefit (76,80). Phulin *et al.*

(2009) used fat grafting in irradiated head and neck tissues, and found an improvement in the quality of skin radiation damage after fat injection (79). They postulated that clinical improvement could be induced by an increase in vascularization and a revitalization of interstitial tissues, through an enhancement of angiogenesis via the secretion of growth factor and extracellular matrices. The adipose tissue is a potent source of multipotent stem cells, such as mesenchymal stem cells, and their intrinsic ability to secrete growth factors, in particular, angiogenic and antiapoptotic factors has been widely described (77,79).

As such, the literature is still evolving as to the relative role of autologous *vs.* alloplastic reconstruction in the setting of radiotherapy, and the more recent introduction of acellular dermal matrix and other compounds further complicate the evidence. Fat grafting and evolving techniques in breast reconstruction will herald new discussions on this front. What is clear is that breast reconstruction plays a highly important role in the management of patients with breast cancer, from a psycho-social and sexual stand-point, and that immediate breast reconstruction does not impair the oncologic safety of breast cancer management, with no increase in local recurrence rates, and no delays in the initiation of adjuvant chemotherapy or radiotherapy. Both neoadjuvant and adjuvant radiotherapy can increase the incidence of post-operative complications, with greater effects in the setting of postoperative radiotherapy, and if adjuvant radiotherapy can be predicted, a delayed reconstruction should be considered. However, a comparison of implant reconstruction to autologous techniques is not clear-cut.

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Footnote

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Immediate breast reconstruction: does the pathology affect the reconstruction?

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Abstract: Immediate breast reconstruction is related to many factors like type of mastectomy, desire of the patient but pathology is not included which should be encountered in decision making in immediate breast reconstruction.

Keywords: Breast reconstruction; radiotherapy; pathology

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Although the screening mammogram succeeded in finding many cases of early breast cancer which can be managed early by conservative breast surgery with or without oncoplastic techniques, mastectomy remains an important option for breast cancer and with the revolution of skin sparing mastectomy (SSM) and nipple sparing mastectomy (NSM), immediate breast reconstruction is increasingly demanded by the patients and the surgeons (1).

Immediate breast reconstruction can be served in two ways either autologous flaps or implants based reconstruction and this depends on many factors as type of surgery (e.g., NSM, SSM, modified radical) and the medical history of the patient (Diabetic, Smoker) and the local circumstances after mastectomy (e.g., pectoral fascia) and laterality (unilateral or bilateral) and the patients preference (e.g., refused implants) and also the need of postoperative radiotherapy. Implant-based approaches are simpler to perform, avoiding the potential morbidities associated with the donor site, and can be offered to thin women who do not have adequate autologous tissue in potential donor sites. Also tissue expander can be placed between the chest wall musculature and serially inflated until an appropriate tissue envelope is created, at which time the expander is replaced with a permanent implant while autologous reconstructions are commonly performed using a transverse rectus abdominis myocutaneous (TRAM)

flap. Alternatively, a latissimus dorsi flap or a flap based on the deep inferior epigastric perforator (DIEP) artery or gluteal arteries can be used for the reconstruction. In general, immediate reconstructions are accompanied by a skin-sparing mastectomy, thus preserving sensate skin and a natural inframammary sulcus for the reconstruction (2-4).

Postoperative radiotherapy negatively impacts on the results of breast reconstruction. However, the rates of complications as well as the aesthetic outcomes vary depending on the timing of the radiation therapy in relation to the reconstruction as well as on the type of reconstruction employed. Postoperative radiotherapy can affect the implant, so the use of expanders is preferred in these situations. Postoperative radiotherapy increases the chance of capsular contracture for this reasons some surgeons prefer the use of autologous breast reconstruction as an immediate breast reconstruction which can sometimes be affected by the radiotherapy. Complications of infection of tissue expanders and implants in the setting of radiation can usually be salvaged by temporary removal of the implant followed by delayed reconstruction with an implant and a latissimus dorsi myocutaneous flap, which provides healthy, well-perfused tissue to cover the implant and replaces some of the radiation damaged skin (5,6).

Therefore the decision of reconstruction will depend on if the patient will receive radiotherapy or not. Radiotherapy can

be given in two ways as intraoperative radiotherapy (ELIOT) or postoperative radiotherapy either local or locoregional depending upon the lymph nodes (if more than 3 metastatic lymph nodes the patient will take locoregional radiotherapy). From previous we can conclude that radiotherapy is decided after the complete pathological analysis of the axilla if sentinel lymph node is positive, but if sentinel lymph node is negative, patients will not receive radiotherapy. So, metastasis to lymph nodes is not predictable except in the cases of pure in situ carcinoma as Ductal carcinoma insitu (DCIS) that is the only pathology which doesn't metastasize to lymph nodes only if it is mixed with invasive pattern. So during mastectomy for DCIS, it is better to do sentinel lymph node biopsy to exclude invasive pattern (7,8).

Inflammatory breast cancer is a distinct clinical entity within breast cancer that warrants urgent and aggressive treatment with neoadjuvant chemotherapy followed by multimodality locoregional therapy, it has a very bad prognosis and usually doesn't need immediate breast cancer and needs delayed breast reconstruction (9).

Another rare type of pathology is the breast phyllode which represent 1% of all breast cancer and may reach a very large size (up to 10 cm). At this type mastectomy with immediate breast reconstruction is valid as the patients don't receive radiotherapy except if the tumor is more than 5 cm or mixed with invasive carcinoma or there is lymph node metastasis (10).

So, we can conclude that pathology is important to decide the type of mastectomy, predict prognosis and not important for type of reconstruction except in the cases of pure DCIS or breast phyllode or invasive carcinoma with negative sentinel lymph node, the surgeon can do immediate breast reconstruction. On the contrary, inflammatory breast cancer is impossible.

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Footnote

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Minimizing incisional dehiscence following 2-stage prosthetic breast reconstruction in the setting of radiation therapy

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Abstract: Incisional dehiscence is a potential complication following prosthetic breast reconstruction. This is exacerbated in the setting of previous radiation therapy (RT) at the time of exchange of the tissue expander to a permanent implant. A technical modification is described that has successfully minimized this adverse event. Twenty-nine patients that had tissue expanders and RT underwent exchange of the device through a laterally based incision along the inframammary fold (IMF) rather than through the existing mastectomy scar. Adverse events were noted in 2 patients and included incisional dehiscence resulting from mechanical factors in one patient and a periprosthetic infection in the other. This modification has been demonstrated to be safe and effective in reducing the incidence of incisional dehiscence in previously radiated breasts.

Keywords: Breast reconstruction; breast cancer; radiation therapy (RT); incisional dehiscence

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Introduction

Minimizing morbidity in the setting prosthetic breast reconstruction associated with pre or post mastectomy radiation therapy (RT) remains an important area of clinical research. Studies have demonstrated that complications leading to prosthetic failure are increased in the setting of RT compared to the non-radiated breast and ranges from 40-45% (1,2). Some of these untoward events include capsular contracture, infection, device exposure, and cutaneous fibrosis. Etiology is multifactorial; however, damage to the subdermal vascular plexus, subcutaneous fat atrophy, cutaneous fibrosis, and skin tension are usually implicated.

A particular topic that has become increasingly appreciated is prosthetic exposure due to incisional dehiscence following the second stage of reconstruction in the setting of prior RT. Studies have demonstrated that the incidence of incisional dehiscence ranges from 10-15% in the setting of RT compared to 1-2% without RT (1,2). This observation has been noted when the incision to exchange the tissue expander for a permanent implant is made through the original mastectomy scar.

The purpose of this study is to describe a technical

modification that can minimize the incidence of incisional dehiscence during the second stage of prosthetic reconstruction in the setting of previous RT.

Methods/description of technique

At the time of exchange for the tissue expander to a permanent implant, the surgeon has two options to access the periprosthetic pocket. The first is to go through the original scar and the second is to create an incision at a new site (*Figure 1*). The modification utilized involves creating a new incision along the infero-lateral aspect of the inframammary fold (IMF).

Preoperatively, with the patient in the standing position, the IMF is delineated. The midline of the IMF is marked and is extended laterally for a distance that ranges from 4-6 centimeters depending on the volume of the device being removed as well as being inserted. Following the skin incision, the dissection extends through the subcutaneous tissue until the capsule is identified. The capsule is incised and the periprosthetic space is entered (*Figure 2*). The tissue expander is removed either intact or surgically deflated. Using a lighted



Figure 1 The two incisional options are delineated and include the previous mastectomy scar and the inferolateral inframammary fold.



Figure 2 The soft tissues following incision and extraction of the tissue expander is depicted.



Figure 3 A postoperative image of the inframammary scar is depicted.

retractor, headlamp, or overhead lighting, a capsulotomy or capsulectomy can be performed depending on the severity of capsule formation. The space is irrigated using an antibacterial solution, a closed suction drain is usually inserted, the skin

is prepped again with a povidone-iodine solution, and the permanent implant is inserted. The incision is closed in four layers that include the capsule, subcutaneous fat, dermis and epidermis. The epidermis can be approximated with an absorbable subcuticular suture or using a nonabsorbable interrupted vertical mattress suture. These sutures are usually removed 2-3 weeks following the operation.

Results

This technique has been used in 29 patients with tissue expanders that have had radiation either before skin sparing mastectomy (n=6) or after skin sparing mastectomy (n=23). No patients were noted to develop skin necrosis or delayed healing. Adverse events have occurred in 2 patients (6.9%). In the first patient, incisional dehiscence occurred in the setting of a previous IMF incision that was in the field of RT. There was no evidence of infection and this was felt to represent a mechanical problem related to the soft tissues. In this patient, the skin was debrided, the periprosthetic space was copiously irrigated with an antimicrobial solution, a closed suction drain was inserted, the device was exchanged for a smaller implant, and a layered closure was performed. In the second patient there was drainage noted from the incision due to a periprosthetic infection. In this patient the device was removed, the skin was debrided, the space was copiously irrigated with an antimicrobial solution, a closed suction drain was placed, and a layered closure was performed. Future implant reconstruction was not recommended and the patient underwent a successful reconstruction using autologous tissue. Long-term outcomes have been excellent 27/29 breasts (94%, *Figure 3*).

Discussion

In patients who have had a skin sparing mastectomy, tissue expander reconstruction, and RT, there are several noteworthy observations. In most cases, the incision is at the apex of the breast and has been directly targeted by the radiation. In some patients, an additional boost of electrons is delivered specifically to the incision site to enhance the tumoricidal effect. The effects on the targeted soft tissues typically include subcutaneous thinning or atrophy that is a consequence of RT as well as from the overlying pressure exerted by the expanding device.

Most plastic surgeons will typically exchange the tissue expander for a permanent implant following RT by re-excising the prior mastectomy scar. This is followed by a

“step-ladder” approach through the soft tissues such that the cutaneous and the capsular incision are off-set. In our previous study in whom incisional dehiscence occurred, the cutaneous structures were noticed to be very thin with a paucity of subcutaneous fat (1). The closure typically consisted of 2 layers of absorbable suture placed in the capsule/dermis followed by a subcuticular suture in the epidermis. Of those patients that experienced a dehiscence, it usually occurred 3-4 weeks postoperatively with a common theme that they were reaching for something when they felt the dehiscence.

There are clinical studies that confirm the fact that entering a breast implant pocket through a previously radiated incision will increase the likelihood of incisional dehiscence. In one study comparing non-radiated to radiated prosthetic reconstruction, Nahabedian demonstrated incisional dehiscence in 1/77 (1.3%) breasts that were not radiated compared to 3/23 (13%) that were radiated (1). All dehiscences occurred following the conversion of the tissue expander to the permanent implant. In another study, Nava demonstrated that device exposure due to incisional dehiscence was increased when RT was delivered prior to device exchange (7/50, 14%) compared to following device exchange (1/109, 0.9%) (2). There was good concordance between these two studies.

Based on these findings, it can be extrapolated that the exchange of a tissue expander for a permanent implant should ideally occur before RT. This has been the approach advocated by the Memorial Sloan Kettering (3). A caveat to this approach is that there must be enough time between the mastectomy and the radiation. Typically RT is commenced 3-4 weeks following mastectomy unless patients receive chemotherapy. This leaves little time to achieve optimal expansion. As a result, most surgeons tend to perform the exchange following RT.

Thus, in order to minimize the incidence of incisional dehiscence, the infero-lateral IMF counter-incision has been routinely performed in the setting of prosthetic reconstruction and RT. This approach has been used in 29 patients with only 1 true dehiscence noted that occurred in a patient that had a prior inframammary incision. This confirmed that re-entering a previously radiated scar is prone to incisional dehiscence based on mechanical factors. Obviously, infection can be another cause of incisional failure with or without radiation.

Initial concerns utilizing the IMF counter incision were that delayed healing may occur because of the bipedicle nature of the prior mastectomy incision and the new IMF

incision. This has not been the case as no patients have experienced delayed healing or tissue necrosis. This is most likely because of the vascular delay effect and the vascularity of the capsule. Reasons for the success of this approach, despite being within the radiated field, include a subcutaneous layer of normal or reasonable thickness and the ability to close the incision in 3-4 layers that includes the capsule, subcutaneous tissue, dermis, and epidermis. Another reason is that the IMF is not an area that typically receives a boost of electrons so the vascularity and tissue quality may be less compromised.

In summary, this series of patients illustrates that a infero-laterally based incision during the second stage of prosthetic reconstruction can reduce complications related to incisional dehiscence. Morbidities related to the incision can still occur but have been related to extenuating circumstances that include a previously radiated scar and infection. This approach is currently being performed by the author for nearly all patients that have had previous RT.

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Current perspectives on radiation therapy in autologous and prosthetic breast reconstruction

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Background: Postmastectomy radiation therapy (PMRT) has a well-established deleterious effect on both prosthetic and autologous breast reconstruction. The purpose of this study was to perform a literature review of the effects of PMRT on breast reconstruction and to determine predictive or protective factors for complications.

Methods: The MEDLINE and EMBASE databases were reviewed for articles published between January 2008 and January 2015 including the keywords “breast reconstruction” and “radiation therapy” to identify manuscripts focused on the effects of radiation on both prosthetic and autologous breast reconstruction. This subgroup of articles was reviewed in detail.

Results: Three hundred and twenty articles were identified and 43 papers underwent full text review. The 16 papers provided level III evidence; 10 manuscripts provided level I or II evidence. Seventeen case series provided level IV evidence and were included because they presented novel perspectives. The majority of studies focused on the injurious effects of radiation therapy and increased complications and concomitant lower patient satisfaction.

Conclusions: Prosthetic based breast reconstruction and immediate autologous reconstruction are associated with lower patient satisfaction in the setting of radiation therapy. Autologous reconstructions can improve patient satisfaction as well as lower revision surgery and long term complications when performed in a delayed fashion after PMRT.

Keywords: Radiation therapy; prosthetic; autologous breast reconstruction

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Introduction

Recent trends in the treatment of breast cancer include increased mastectomies both bilateral and prophylactic procedures, conservation of skin and nipple tissue, and expanded indications for the use of radiation therapy (1-4). Radiation therapy is an important adjunct in the treatment of breast cancer by eliminating subclinical disease in combination with surgical removal of gross tumor (5). This has led to a number of evolving therapeutic implications and operative considerations for reconstructive surgeons.

In general, autologous tissue tends to be superior to implant-based reconstructions in the setting of

postmastectomy radiation therapy (PMRT) (6). Autologous reconstructions that can be delayed until after PMRT avoid radiation-induced sequelae; however this approach is not always feasible. Prosthetic reconstruction of the irradiated breast is more challenging, results in lower patient satisfaction, and is heavily dependent upon timing of staged procedures. However, improved aesthetic outcomes are increasingly possible with the development of breast implant innovations, acellular dermal matrices (ADM), and fat grafting (7,8). In 2012, the senior author published two reviews in *Plastic and Reconstructive Surgery* on radiation therapy and prosthetic and autologous breast reconstruction (9,10). The purpose of this article is to update the previous

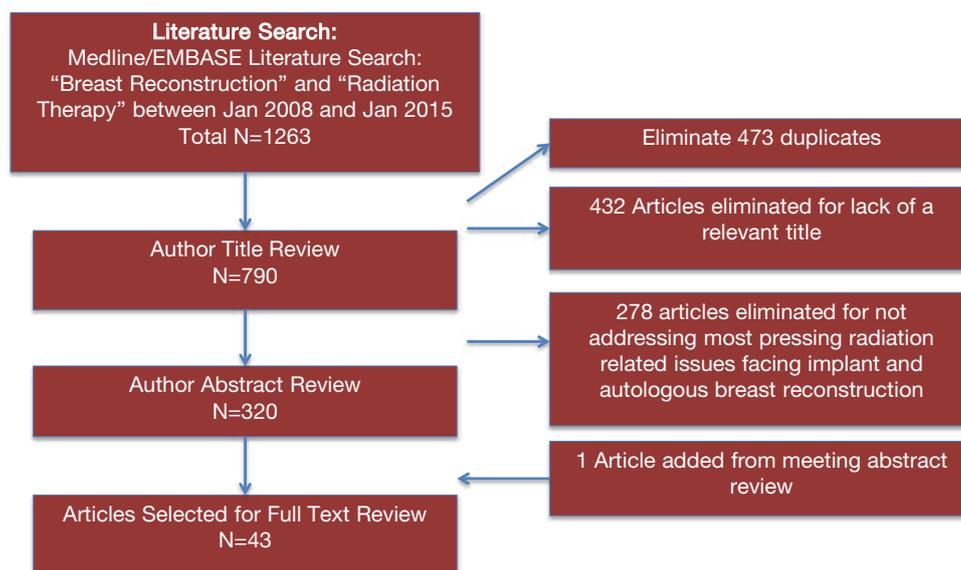


Figure 1 Citation attribution diagram.

literature reviews and revise recommendations for breast reconstruction in the setting of PMRT.

Overview of literature evaluation

A search and review of the MEDLINE and EMBASE databases was performed for articles published between January of 2008 and January of 2015 on breast reconstruction and radiation therapy (*Figure 1*). Relevant studies were assigned a level of evidence using the American Society of Plastic Surgeons (ASPS) Evidence Rating Scale for Therapy (11). Using the search terms, “radiation therapy” and “breast reconstruction” the query revealed 1,263 articles. A total of 473 articles were removed as duplicates and 432 were removed for lack of relevance. A title review was performed on the remaining 790 articles, and 278 were eliminated due to not directly addressing the search criteria. An abstract review was performed of the 320 remaining articles. Forty-three articles were selected for full text review, and bibliography review yielded an additional article from a meeting abstract (*Table 1*). This subgroup of articles was reviewed in detail. A total of 16 papers provided level III evidence; 10 manuscripts provided level I or II evidence. Seventeen case series provided level IV evidence and were included because they presented novel perspectives. The majority of studies focused on the injurious effects of radiation therapy and increased complications and concomitant lower patient satisfaction with reconstruction.

Impact of radiation on the reconstructed breast

Radiation increases the risk of complications, need for reoperations, and worsens aesthetic outcomes in breast reconstruction. In a retrospective review of 1,037 breast reconstruction patients, Barry and colleagues reported that tissue expander reconstructions had a major complication rate of 24.4% without radiation therapy and 45.4% with radiation therapy (23). The authors noted that only 70.1% implant-based reconstructions in the setting of PMRT were able to retain the implant and that 10.3% of the explantations would ultimately require an autologous reconstruction. Radiation was the greatest risk factor for major complications in tissue expander/implant reconstruction (level III evidence). However, among autologous reconstructions, multivariate analysis revealed no statistically significant difference in rates of major complications between patients receiving preoperative radiation therapy and those who did not ($P=0.84$). Another study utilizing the BREAST-Q reconstruction questionnaire investigated patient satisfaction in 482 patients undergoing implant breast reconstruction (24). A multivariate model demonstrated that prior radiation therapy ($P<0.001$) or PMRT ($P=0.002$) had a significantly negative effect on patient satisfaction (level I evidence). Sbitany and colleagues reviewed 903 immediate two stage breast reconstructions and found that any radiation delivery caused an increased rate of infection requiring antibiotics (21.6%, $P<0.001$) and an increased risk of expander/implant loss (18.75%, $P=0.03$) (14). Prior history of

Table 1 Articles selected for full text review based upon literature search with a summary of pertinent findings

Reference	Level of evidence	Number of patients undergoing reconstruction	Timing of reconstruction	Reconstructive technique	Results	Conclusions
Spear <i>et al.</i> (3)	IV	18	Immediate one and two stage	Prosthetic	Prosthetic reconstruction of NSM can be performed in the setting of RT but carries a 11.1% implant loss rate	NSM and radiation therapy results in high complications and revisionary surgery
Hirsch <i>et al.</i> (12)	III	876	Immediate one and two stage	Prosthetic	When compared to reconstruction without RT, radiation therapy is associated with higher overall complications rates of explanation (OR =3.45)	Timing of radiation is a critical factor in development of complications
Clemens <i>et al.</i> (13)	III	276	Immediate two-stage	Prosthetic	Use of ADM in irradiated breasts did not predispose to higher infection or overall complication rates	While radiation may slow mesh incorporation, ADMs may be used in the setting of radiation therapy
Sbitany <i>et al.</i> (14)	III	903	Immediate two-stage	Prosthetic	Radiation delivery caused an increased rate of infection requiring antibiotics (21.6%, P<0.001) and an increased risk of expander/implant loss (18.75%, P=0.03)	Both preoperative radiation and PMRT in immediate implant-based reconstruction results in higher complication risks
Garvey <i>et al.</i> (15)	III	625	Delayed-Immediate two stage	Autologous	Irradiated flaps (i.e., both DIEP and muscle-sparing free TRAM flaps) developed fat necrosis at a significantly higher rate (22.5%) than the nonirradiated flaps (9.2%, P=0.009)	TRAM flap does not result in a lower rate of fat necrosis than reconstruction with a DIEP flap
Cordeiro <i>et al.</i> (16)	III	2,133	Immediate two stage	Prosthetic	Predicted implant loss rates were 17.5% and 2.0% for irradiated and nonirradiated implants, respectively, at 12 years (P<0.01)	Through proper patient selection, most prosthetic patients achieved good to excellent aesthetic results
Burdge <i>et al.</i> (17)	III	527	Immediate one and two stage	Prosthetic	For prosthetic reconstruction, NSSM had higher rates of wound infection, tissue necrosis, and expander loss over SSM. Overall radiation induced complication rate in NSSM was 38.1% vs. 30.8% for SSM	Prosthetic reconstruction can be performed in NSSM in the setting of radiation but has a higher complication risk
Ho <i>et al.</i> (18)	III	751	Immediate two stage	Prosthetic	The 7-year PIRR free rate was 71%. The 7-year rate of implant replacement was 17.1% and removal was 13.3%	Prosthetic reconstruction followed by PMRT is associated with high rates of long term device replacement
Ho <i>et al.</i> (19)	III	604	Immediate two stage	Prosthetic	4.2 increased odds (P=0.001) of major complications in the irradiated group. Grade III/IV capsular contracture rate significantly higher in the irradiated group (21.7% vs. 10%; P<0.008)	Prosthetic reconstruction followed by PMRT is associated with high rates of short term and long term complications
Crisera <i>et al.</i> (20)	III	170	Immediate	Autologous	Skin sparing mastectomy with immediate free flap breast reconstruction followed by PMRT did not adversely affect local disease recurrence or overall survival rates for patients with advanced breast cancer	Immediate autologous reconstruction is oncologically safe
Mycatyn <i>et al.</i> (21)	III	86	Immediate two stage	Prosthetic	Chemotherapy with or without radiation adversely impacted type I collagen (P=0.02), cellular infiltration (P<0.01), extracellular matrix deposition (P<0.04), and neovascularization (P<0.01). Radiation exacerbated the adverse impact of chemotherapy.	ADM remodeling process may be adversely impacted in patients who require radiation therapy, which can influence neovascularization and cellular proliferation
Craig <i>et al.</i> (22)	III	1,376	Immediate two stage	Prosthetic	incidence of explantation was highest in the non-ADM with radiation therapy when compared to the ADM with radiation therapy group (20.4 % vs. 11.4%, P=0.0012)	ADM's, once incorporated, may play a protective role in preventing the need for re-operations and explanations in patients undergoing radiation therapy

ADM, acellular dermal matrices; TRAM, transverse rectus abdominis myocutaneous; PIRR, permanent implant removal or replacement; PMRT, postmastectomy radiation therapy.

radiation had a higher risk of wound breakdown ($P=0.012$) (level III evidence). The authors concluded that both preoperative radiation and PMRT in immediate implant-based reconstruction resulted in higher, albeit acceptable, complication risks.

Ho and colleagues reported their experience in immediate 2-stage tissue expander to implant reconstruction 604 patients, with 113 receiving PMRT (19). They noted a 4.2 increased odds ($P=0.001$) of major complications in the irradiated group. Grade III and IV capsular contracture rate was significantly higher in the irradiated group compared with matched controls (21.7% *vs.* 10%; $P<0.008$) (level III evidence). PMRT to tissue expanders is associated with high complications.

Radiation therapy and nipple sparing mastectomy

Spear and colleagues evaluated prosthetic reconstruction of nipple sparing mastectomies in the setting of radiation therapy. Of 18 patients, 72.2% had previous breast conserving therapy (BCT) with RT and 27.8% underwent PMRT. With an average follow-up of 3 years, patients were reported to have 33.3% first-stage complications and most common indications for revision were for correction of implant malposition (27.8%), capsular contracture (16.7%), and nipple malposition (22.4%). Capsular contracture occurred more commonly in patients who needed PMRT compared with those who had previously undergone breast-conservation therapy (40% *vs.* 7.8%). The authors found that a reconstruction was maintained or at least salvage in 88.9% patients, and only 11.1% of patients completely lost their implant.

The combination of nipple-sparing mastectomy, implant reconstruction, and radiation therapy results in an obviously high complication rate and high likelihood of revisionary surgery. While the authors concluded that nipple/areola complex preservation is safe in women undergoing radiation therapy, prosthetic complication rates of these challenging patients is similar to non-irradiated patients. Further studies are warranted to determine if autologous reconstruction is superior and/or confers any protective benefit to the reconstruction in comparison to prosthetic reconstruction (level IV evidence).

Burdge and colleagues found similar results in their review of 1,035 mastectomies (558 NSSM and 477 SSM) (17). For prosthetic reconstruction, NSSM had higher rates of wound infection, tissue necrosis, and expander when compared to patients with SSM. For both direct to implant immediate

reconstructions or two stage tissue expander to implant reconstructions, overall radiation induced complication rate was 38.1% in NSSM and 30.8% for SSM. The authors found that oncologic outcomes were similar for NSSM and SSM, and that prosthetic reconstruction can be performed in NSSM in the setting of radiation but has a higher complication risk.

Radiation therapy and delivered before reconstruction

While the effects of radiation are well-established, debate exists over whether previous radiation therapy in BCT may not be as detrimental to a reconstruction as PMRT. Patients treated with previous radiation therapy in BCT do not have the same complication profiles as patients receiving PMRT. Hirsch *et al.* reported on a series of 876 tissue expander to implant breast reconstructions to determine complication profiles by stage of reconstruction (12). The authors found that during final implant placement, any history of radiation had the strongest association with the development of complications leading to explantation and/or conversion to an autologous flap (OR =3.45). Risk factors associated with complications in either stage 1 or 2 were age greater than 50 years, active smoking, and a history of BCT with RT or PMRT (level III evidence).

Similarly, a study of 717 patients from the Danish Registry for Plastic Surgery evaluated the effect of radiation therapy timing on capsular contracture and reoperations in 1- or 2-stage prosthetic breast reconstruction (25). Radiation therapy was significantly associated with capsular contracture after both 1-stage [adjusted hazard ratio (HR) =3.3; 95% CI, 0.9-12.4] and 2-stage procedures (HR =7.2; 95% CI, 2.4-21.4), and risk of reoperation after both 1-stage (HR =1.4; 95% CI, 0.7-2.5) and 2-stage procedures (HR =1.6; 95% CI, 0.9-3.1). In the setting of radiation for 2 stage procedures, reconstruction failure was 13.2% (level II evidence). The data strongly suggests employing alternatives to prosthetic reconstruction in the setting of radiation therapy.

Hypofractionation is the delivery of radiation therapy in fewer albeit larger daily fractions. Hypofractionation was developed in an effort to improve local regional recurrence while maintaining acceptable cosmetic results and patient morbidity. Whitfield and colleagues reported on the reconstructive outcomes of using a 40 Gy in 15 fractions over 3 weeks protocol of radiation delivery (26). A total of 178 patients underwent implant-based breast reconstruction.

The actuarial rates of severe capsular contracture at 1, 2, 3, 4, 5, and 6 years of follow-up were 0%, 5%, 5%, 21%, 30%, and 30% whereas the nonirradiated group had no cases of severe capsular contracture ($P < 0.001$) (level III evidence). Khansa *et al.* investigated the effect of prior BCT on patient satisfaction in 802 breast reconstructions (27). Previous BCT with RT had higher rates of skin flap necrosis (12.4% *vs.* 6.8%, $P = 0.024$) but did not have higher rates of other complications or lower rates of satisfaction with aesthetic outcomes (Level III evidence). Definitive conclusions are difficult to draw given this cohort only had ten patients. A severe limitation of all studies evaluating the effect of previous BCT and RT is to treat these patients as a homogenous cohort. There is likely a reparative process that occurs so that after a sufficient amount of years, complication risk in BCT patients might very well fall to levels consistent with radiation-naïve patients, however without sufficient data addressing timing of BCT to subsequent mastectomy, this remains speculative.

Radiation therapy delivered after reconstruction

The effect of PMRT has a more significant impact on complications and failure of reconstruction than previous radiation with BCT. A study of the Danish Plastic Surgery Registry evaluated outcomes of direct to implant reconstruction at the time of mastectomy and found that patients who received PMRT had significantly increased revisions ($P = 0.047$) and lower aesthetic scores (level IV evidence) (28).

A prospective, multi-institutional study evaluated factors associated with reconstruction failure in 141 consecutive patients undergoing mastectomy and immediate 2-stage breast reconstruction and PMRT (29). After a median follow-up time of 37 months, 67.5% of patients had Baker I or II capsular contracture and 32.5% of patients had a Baker III or IV. Multiple regression analysis revealed T3 or T4 tumor, smoking, and positive axillary nodes were associated with reconstructive failure (level II evidence).

Jhaveri and colleagues reported long-term outcomes and aesthetic results in either two-stage prosthetic (69 patients) or autologous reconstructions (23 patients) (30). Major complication rate was 33.3% for prosthetic reconstruction *vs.* 0% for autologous reconstruction ($P = 0.001$). The rate of minor complications was 55% for prosthetic reconstruction *vs.* 8.7% for autologous reconstruction ($P < 0.001$). Acceptable cosmesis was only 51% of prosthetic patients compared to 82.6% of autologous patients ($P = 0.007$) (level II evidence). These results demonstrate that implant-based

reconstruction is associated with more major and minor long-term complications and worse cosmetic results than autologous reconstruction.

McKeown and colleagues reported on the effect of timing of radiation therapy on reconstruction with LD flaps and implants (31). A total of 13 patients who underwent immediate reconstruction followed by radiation therapy and were compared to 11 patients who underwent radiation therapy followed by delayed reconstruction. The authors noted a trend towards better long-term cosmetic outcome in patients undergoing delayed reconstruction, with volume and contour of the upper pole being most negatively affected by radiation (level II evidence).

Barry *et al.* performed a meta-analysis evaluating optimal sequencing of breast reconstruction and PMRT (32). A review of 1,105 patients from 11 studies demonstrated that the rate of adverse events was 4.2 times as high in patients undergoing PMRT as it is in patients not undergoing PMRT. When PMRT was delivered after immediate breast reconstruction, patients who had autologous tissue-based reconstruction had one-fifth the risk of adverse events of patients who had implant-based reconstruction. A similar pattern was seen when PMRT was delivered before delayed breast reconstruction (level III evidence). The results suggest that autologous reconstructions have superior outcomes to prosthetic reconstructions whether performed immediately or in a delayed fashion.

Evaluating post-radiation skin changes to predict complication rates

Parsa and colleagues hypothesized that an objective evaluation of post-radiation skin changes based upon a novel classification system could help guide surgeons as to which patients may be suitable candidates for a prosthetic reconstruction (33). In patients whose chest walls displayed moderate skin changes without induration after irradiation, aesthetic outcomes after reconstruction were similar on the irradiated and nonirradiated sides ($P > 0.50$). In contrast, in patients who developed induration or severe post-radiation skin changes, the rate of modified Baker IV capsular contracture was higher on the irradiated side, and the rate of poor aesthetic outcomes on the irradiated side was 75% in patients with severe skin changes and 100% in those with induration (level II evidence). While most reports suggest autologous reconstructions are preferable in the setting of radiation therapy, patients may be stratified as an acceptable prosthetic candidate based upon skin response to radiation therapy.

Consequence of a tissue expander, implant, or autologous flap on radiation delivery and oncologic outcomes

There is ongoing concern over the oncologic safety of radiation therapy and tissue expanders on the chest wall and whether a metallic port interferes with delivery particularly in patients where the internal mammary nodes require treatment. Kronowitz and colleagues reported that the presence of a tissue expander on the chest wall during radiation therapy does not impact recurrence-free survival (34). Locoregional recurrence risk was compared between 47 patients with advanced breast cancer with a tissue expander receiving PMRT and 47 disease-matched control patients who were treated with PMRT and no tissue expander. The 3-year recurrence-free survival rates were equal and there was no locoregional recurrence in the tissue expander cohort at a median follow-up time of 40 months. The 3-year recurrence-free survival rates were 92% for the tissue expander cohort compared to 86% for the control group ($P=0.87$) (level II evidence). Several important conclusions were emphasized by the authors. Full-height expanders should be avoided as they may theoretically interfere with radiation treatment of the clavicular nodal basins. If an expander requires deflation for PMRT, only partially deflate between one third and one half the expander volumes. Reinflation should be performed within 2 weeks post-radiation to preserve the skin envelope. For patients in whom the internal mammary nodes need to be treated with an implant on the chest wall, higher doses of radiation may have to be delivered to the heart and lungs, which may theoretically increase the risk of coronary artery disease and pulmonary fibrosis.

Radiated flaps clearly have worse aesthetic outcomes but some authors argued that an autologous flap interfere with radiation fields, especially the internal mammary lymph nodes (35,36). While routine treatment of internal mammary lymph nodes has not gained widespread support among radiation oncologists, the National Cancer Institute of Canada Clinical Trials Groups MA-20 study reported on a prospective randomized trial of patients with one to three positive lymph nodes treated with whole breast irradiation with or without regional nodal irradiation after segmental mastectomy (37). The study demonstrated that regional nodal irradiation resulted in a 30% relative improvement in disease-free survival, 41% lower rate of regional recurrence, and a 36% lower rate of distant recurrence. These findings are increasingly applied to mastectomy patients to receive

routine delivery of PMRT to the regional nodal basins, including the internal mammary chain. National trends among medical centers are still evolving and will have important implications for reconstructive surgeons.

Crisera and colleagues addressed the oncologic safety of performing immediate free flap reconstruction for advanced-stage breast cancer (stage IIB or greater) (20). The authors performed a retrospective cohort study of 170 patients with skin sparing mastectomy with immediate free flap breast reconstruction, and found that PMRT did not adversely affect local disease recurrence or overall survival rates. Radiation therapy was administered to 131 patients (28 preoperatively and 103 postoperatively) and local recurrences were noted in 15 patients (8.8%) after a median of 22.9 months (range, 3.0-59.2 months). A total of 13 patients experienced moderate to severe flap distortion/shrinkage, and an additional salvage flap was required in seven patients to correct deformities. It is important to note that the administration of postoperative chemotherapy was delayed in eight patients (4.7%) because of wound healing complications (level III evidence). Although performing immediate breast reconstruction with autologous tissue before PMRT has been shown to be oncologically safe, doing so subjects patients to higher rates of fat necrosis and diminished aesthetic outcomes.

Need for corrective surgery in irradiated reconstructed breasts

Ho and colleagues focused on the rates of permanent implant removal or replacement (PIRR) surgery following radiation therapy in a retrospective review of 751 patients receiving an immediate tissue expander placement (18). Of these, 151 patients went on to receive chemotherapy and exchange to a permanent implant, followed by PMRT. The 7-year PIRR free rate was 71%. The 7-year rate of implant replacement was 17.1% and removal was 13.3%. Most frequent reasons for implant removal included infection, implant extrusion, and malposition. Of note, two patients experienced local recurrence in the chest wall, both after 7 years and the 7-year distant metastasis-free survival rate was 81% and overall survival 93% (level III evidence). Prosthetic reconstruction followed by PMRT is associated with high rates of long-term device replacement and revision.

At the same institution, Cordeiro and colleagues reported a single surgeon experience of 2,133 prosthetic breast reconstructions with 319 receiving PMRT (16). Implant loss occurred in 9.1% of irradiated implants

compared to just 0.5% of nonirradiated implants ($P<0.01$). Capsular contracture grade IV was present in 6.9% of irradiated compared to just 0.5% of nonirradiated implants ($P<0.01$). Predicted implant loss rates were 17.5% and 2.0% for irradiated and nonirradiated implants, respectively, at 12 years ($P<0.01$) (level III evidence).

Traditionally, surgeons have delayed final reconstruction until after the administration of radiation therapy to avoid the damaging effects of ionizing radiation on the reconstruction. Garvey and colleagues evaluated whether certain types of autologous reconstructions could better withstand the effects of radiation therapy over others for development of fat necrosis and need for revision (15). The 625 flaps were analyzed, 6.4% irradiated *vs.* 93.6% non-irradiated. Overall complication rates were similar for both the irradiated and nonirradiated flaps. Irradiated flaps [i.e., both DIEP and muscle-sparing free transverse rectus abdominis myocutaneous (TRAM)] flaps developed fat necrosis at a significantly higher rate (22.5%) than the nonirradiated flaps (9.2%, $P=0.009$). There were no differences in fat necrosis rates between the DIEP and muscle-sparing free TRAM flaps in both the irradiated and nonirradiated groups. Surprisingly, there was no statistically significant difference in the need for reoperative surgery for fat necrosis between the irradiated and nonirradiated flaps (level III evidence).

Classen *et al.* assessed fibrosis and capsular contracture of breast reconstructions subjected to radiation therapy in 109 patients (38). The median radiation therapy dose was 50.4 Gy and 44 patients received a boost dose of 10 Gy. Eighty-two patients had implant-based reconstructions, 20 had autologous tissue-based reconstructions, and 7 had combined reconstructions. After a mean follow-up time of 34 months, the 3-year incidence of \geq grade III fibrosis was 20 percent for the implant-based reconstructions and 43% overall. The 3-year rate of surgical correction of the contralateral breast was 30%, and 39 patients (35.8%) required unplanned surgery on the reconstructed breast (level IV evidence).

Wong and colleagues evaluated revision surgery in 62 patients undergoing mastectomy, immediate reconstruction, followed by radiation therapy (39). Major corrective surgery was 40% (6/15 reconstructions) in the implant group and 9% (4/47) in the nonimplant group ($P=0.01$) (level III evidence). Patients who undergo mastectomy and immediate implant-based reconstruction followed by PMRT are at high risk for needing subsequent major corrective surgery.

Autologous fat grafting to salvage radiated reconstructions

Panettiere *et al.* evaluated whether fat grafting could salvage prosthetic reconstructions after irradiation (40). The study included 61 patients with twenty requiring multiple sessions of lipofilling, compared to 41 controls with no fat grafting. Fat grafted patients were significantly better aesthetic scores than those before fat grafting and were also significantly better than those for the untreated control breasts (level II evidence).

Serra-Renom and colleagues reported on outcomes of injecting autologous fat grafts during delayed expander placement after PMRT (41). In 65 patients, a tissue expander was inserted endoscopically under the pectoralis major muscle and underwent total immediate expansion. Next, a mean of 150 ± 25 cc of autologous fat was injected to superior quadrants between the skin and the pectoralis muscle. Exchange to a permanent implant was performed at three months with an additional injection of a mean of 150 ± 30 cc of fat to the lower quadrants. At 1 year follow-up, patients' mean satisfaction rating was 4 (Scale: 1—low to 5—high); and there were no cases of capsular contracture greater than Baker I (level II evidence). Fat grafting may have a role in thickening mastectomy skin flaps over an implant which may aid in improving radiation sequelae and fibrosis.

Losken and colleagues evaluated the need for autologous fat grafting to TRAM flaps versus irradiated TRAM breast reconstructions (42). While contour, shape, and increase volume could be achieved in either cohort group, irradiated TRAM flaps required a significantly increased incidence of repeated injections (36% *vs.* 18%, $P=0.002$) (level IV evidence). While fat grafting may be beneficial in salvaging an irradiated flap, patients frequently require multiple sessions to achieve similar non-radiated results.

Use of acellular dermal matrix (ADM) in the setting of radiation therapy

Over the past decade, ADM have gained in popularity for purported benefits of improved pocket control, faster expansion, lowered capsular contracture rates, and improved aesthetic results albeit at a significant monetary cost. We performed a meta-analysis to evaluate the clinical impact of radiation therapy on ADM-assisted breast reconstruction (13). In a review of 276 irradiated patients, ADMs in implant-based breast reconstruction in the setting of radiation therapy did not predispose to higher infection or overall complication rates or prevent bioprosthetic mesh

incorporation. However, the rate of mesh incorporation may be slowed (level III evidence). Use of ADM for implant-based breast reconstruction does not appear to increase or decrease the risk of complications beyond nonirradiated ADM patients, but it may provide aesthetic benefits in properly selected patients.

Myckatyn and colleagues corroborated that the ADM remodeling process may be adversely impacted in patients who require radiation therapy, which can influence neovascularization and cellular proliferation (21). In biopsy specimens collected from 86 women undergoing exchange of a tissue expander for a breast implant, the authors found that chemotherapy with or without radiation adversely impacted type I collagen ($P=0.02$), cellular infiltration ($P<0.01$), extracellular matrix deposition ($P<0.04$), and neovascularization ($P<0.01$). Radiation exacerbated the adverse impact of chemotherapy. Neoadjuvant chemotherapy also caused a reduction in type I ($P=0.01$) and III collagen ($P=0.05$), extracellular matrix deposition ($P=0.03$), and scaffold degradation ($P=0.02$) (level III evidence).

Craig and colleagues reported a retrospective review of 1,376 immediate tissue expander breast reconstructions in four cohorts: ADM without and without radiation therapy, and non-ADM with and without radiation therapy (22). Overall complication rate between ADM and non-ADM cohorts were 39% and 16.7% respectively ($P<0.001$). Incidence of seroma tended to be higher in the ADM cohort and highest within patients that did receive RT when compared to non-ADM (13.6% *vs.* 10.9%, $P>0.001$). However, incidence of explantation was highest in the non-ADM with radiation therapy when compared to the ADM with radiation therapy group (20.4% *vs.* 11.4%, $P=0.0012$) (level III evidence). While overall complication rates, infection, and seroma tend to be higher with the use of ADMs, if recognized and appropriately treated, the expander reconstruction is often salvaged. ADM's, once incorporated, may play a protective role in preventing the need for re-operations and explantations in patients undergoing radiation therapy.

Summary and clinical impact of the evidence

PMRT has a significant adverse impact on both short term and long term complication rates, aesthetic outcomes, and patient satisfaction with breast reconstruction. Most studies find a significant need for unplanned or major corrective surgery in irradiated breasts reconstructed with implants. However, with proper patient selection,

acceptable complication rates are possible and the majority of patients who undergo implant-based reconstruction and PMRT ultimately keep their implant-based reconstruction with only a minority of patients requires conversion to an autologous tissue flap.

In the setting of PMRT, implant-based reconstructions are associated with a higher incidence of major corrective surgery than autologous tissue-based reconstruction. However, superior aesthetic outcomes are achieved with delayed reconstruction after PMRT than with immediate reconstruction before PMRT because of lower rates of fat necrosis, as well as improved volume and contour in the upper pole of the reconstructed breast.

The presence of a tissue expander, permanent implant, or autologous flap on the chest wall did not impede radiation delivery or have a significant effect breast cancer recurrence. Autologous fat grafting and ADMs have gained in popularity and may play a protective or restorative role in radiated breast reconstruction, capsular contracture, and aesthetic outcomes.

In conclusion, advances in plastic surgical technique have helped to mitigate trends in the expansion of radiation therapy. With modern implants and focused radiotherapy regimens, expander and implant related complications can be diminished to acceptable ranges in select patients. However, autologous reconstruction performed in a delayed fashion after PMRT remains a workhorse in these challenging patients. Despite these hurdles, it is critical that patients are not dissuaded from receiving reconstructive surgery and denied its important quality of life benefit simply because of their need for radiation therapy.

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Footnote

Conflicts of Interest: Dr. Clemens has consulted for Allergan Medical (Irvine, CA). Dr. Kronowitz has participated on a Scientific Advisory Committee for Allergan Medical.

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Achieving ideal donor site aesthetics with autologous breast reconstruction

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Abstract: The appearance of the donor site following breast reconstruction with abdominal flaps has become an important topic for study. Given the variety of flaps that are derived from the abdomen, decisions are often based on how much muscle and fascia will be harvested. Comparisons between muscle sparing and non-muscle sparing techniques have been performed with outcomes related to function and contour. Closure techniques will vary and include primary fascial closure, mesh reinforcement and additional fascial plication all of which can produce natural and sometimes improved abdominal contours. Proper patient selection however is important. This manuscript will describe various techniques in order to achieve ideal abdominal contour following autologous reconstruction.

Keywords: Breast reconstruction; donor site; aesthetics

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Introduction

For many years, the emphasis with autologous breast reconstruction was focused on achieving ideal breast aesthetics. Although this remains of paramount importance, achieving ideal donor site aesthetics has become increasingly important and is now expected by patients. With the introduction of muscle sparing flaps, the ability to maintain the normal dynamics of the donor site are certainly enhanced; however, adverse events can still occur. These may include contour abnormalities, bulge, hernia, muscle weakness, delayed healing, complex scarring, and pain. Because the abdomen is the most commonly used donor site, the manuscript will focus on prevention and management of adverse events related to this donor site to achieve ideal aesthetics.

There are essentially five flaps that are derived from the abdomen that include the pedicle transverse rectus abdominis musculocutaneous (TRAM), free TRAM, muscle sparing free TRAM, deep inferior epigastric perforator (DIEP), and superficial inferior epigastric artery (SIEA) flaps. Each of these flaps has unique characteristics that

require special attention during harvest and closure to achieve ideal donor aesthetics. Reinforcement materials will sometimes be necessary; however, it should be remembered that maximal preservation of the natural abdominal anatomy should facilitate obtaining a desirable abdominal contour without the use of reinforcement materials.

The initial evaluation

As with all procedures, patient selection is critical (1). Some patients will be considered high risk for adverse events and less ideal abdominal aesthetics may result. These include patient that are actively using tobacco products, have poorly controlled diabetes mellitus, morbid obesity, and multiple prior operations. With overweight and obese patients, it is important to identify whether the fat is predominantly subcutaneous or intra-abdominal. Subcutaneous fat will lend itself nicely to having enough fat to adequately reconstruct the breast and usually result in improved abdominal aesthetics (*Figure 1*). Intraabdominal fat usually manifests as a convex anterior abdominal wall that is rarely ideally



Figure 1 Lateral view demonstrating a moderate pannus due to subcutaneous fat.



Figure 2 Lateral view demonstrating a convex abdominal wall due to intraabdominal fat.

contoured (*Figure 2*). It is important to inform patients with a convex abdominal wall that they will most likely remain so postoperatively unless they lose weight before or after surgery.

Patient related factors can affect the aesthetic outcome of the abdomen. Tobacco use and poorly controlled diabetes mellitus will lead to delayed healing, poor scarring, and distortions in abdominal contour. Patients with elevated HbA1C levels (>7) or who are actively using tobacco products are discouraged from proceeding with autologous breast reconstruction because of these risks. Once controlled, the autologous outcomes are generally improved, predictable, and reproducible. Prior abdominal operations can affect the outcome of surgery and impact both the breast and donor site (2-4). Paramedian abdominal incisions can injure vascular perforating vessels, lower transverse incisions can disrupt the superficial and deep inferior epigastric vessels, and multiple abdominal incisions can disrupt the anterior rectus sheath. The effects of these incisions may include an increase in contour abnormalities such as bulge or hernia as well as delayed healing due to compromised perfusion. Prior liposuction can disrupt the perforator system and result in delayed healing or abdominal fat necrosis.

Once patient selection criteria have been established,

achieving ideal abdominal aesthetics will be dependent on the type of flap selected, degree of fascial and muscle trauma, and operative technique. Preservation of the rectus abdominis muscle is classified based on subdivision into three vertical segments; medial, central, and lateral (3). Preservation of the entire muscle is classified as an MS-3 (DIEP) flap. Preservation of the medial and lateral segment is classified as an MS-2 (muscle sparing TRAM) flap. Preservation of the lateral or medial segment is classified as an MS-1 (muscle sparing TRAM) flap. Sacrifice of the entire width of the muscle is classified as an MS-0 (TRAM) flap. MS-1, MS-2, and MS-3 flaps preserve the continuity of the rectus abdominis muscle and therefore provide varying degrees of muscle function.

In general, the flaps that violate the integrity of the anterior abdominal least will provide the best outcomes (4). Theoretically, the SIEA flap should provide the best abdominal outcome because the anterior rectus sheath and rectus abdominis muscles are not incised. The DIEP flap requires a fasciotomy and myotomy to dissect out the deep inferior epigastric vessels (*Figure 3*). The free TRAM utilizes a short segment of the rectus abdominis muscle that can include the full or partial width of the muscle (*Figure 4*). The pedicle TRAM incorporates the full length of the muscle and either the entire or partial width of it.



Figure 3 Intraoperative photograph of an MS-3 bilateral DIEP flap. DIEP, deep inferior epigastric perforator.



Figure 4 Intraoperative photograph of an MS-1 bilateral free TRAM flap. TRAM, transverse rectus abdominis musculocutaneous.



Figure 5 Preoperative markings of an abdominal flap.

The abdominal markings

All abdominal flaps can be designed in a similar fashion in terms of the preoperative markings (*Figure 5*). The location and dimensions of the flaps are similar and subject to modification based on body habitus and location of scars.

Patient are marked standing. The anterior superior iliac spine (ASIS) are palpated and marked. The midline of the abdomen from the xiphoid to the pubic bone is delineated. The proposed upper and lower transverse incisions are delineated and communicated laterally at the ASIS. The final location of the lower transverse incision is determined intraoperatively when the patient is flexed about 30 degrees to ensure that the abdomen can be closed. Sometimes the proposed incision has to be elevated in order to ensure closure. This flap design incorporates the aesthetic units of the abdomen such that the final scar will be positioned as low as possible extending superolaterally towards the ASIS (5).

Operative strategies to achieve ideal abdominal contour

It is important to discuss with patients that performing an abdominal flap is different than a performing a cosmetic abdominoplasty except perhaps in the case of a SIEA flap where the abdominal fascia and muscle remain intact. With the MS—0-3 flaps, that anterior rectus sheath and muscle are violated therefore disrupting the normal anterior abdomen. More often than not, the disruption is beneficial but in some cases it is not and can be a source of consternation. The principles and techniques discussed in the ensuing paragraphs will assist in achieving ideal abdominal contours and characteristics, but it should be emphasized that it will be a different normal than previous.

Harvesting the flaps

Following the initial incisions, the dissection proceeds to the anterior rectus sheath. It should be remembered that the anterior rectus sheath is a vascularized lattice of collagen fibers that should be preserved as much as possible (*Figure 6*). The anterior rectus sheath is comprised of the aponeurosis of the external and internal oblique muscles. There is a loose areolar layer of tissue over the anterior sheath that contains a plexus of vessels that should be preserved to ensure vascularity and viability following the operation. It should be noted that sensory nerves usually pass through the fascia as neurovascular bundles en route to the skin. These nerves should be identified a cut. Clipping these sensory nerves should be avoided to prevent a painful neuroma (6). This has been noted in our practice and therefore use of clips is avoided when possible. Incising the anterior rectus sheath is not without consequence because it disrupts the normal lattice of fibers that is considered one of



Figure 6 Intraoperative photograph demonstrating the vascularity of the anterior rectus sheath.

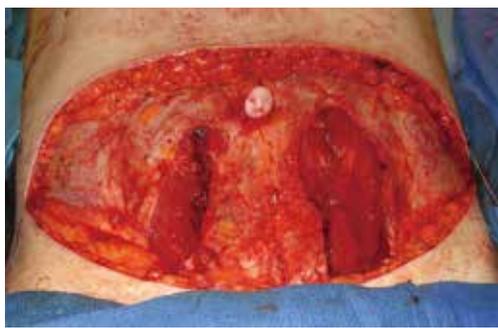


Figure 7 Intraoperative photograph demonstrating closure of the medial and lateral segments of the rectus abdominis muscle.



Figure 8 Fascial closure and plication following an MS-3 flap harvest.

the primary support systems of the anterior abdominal wall. Under normal circumstances, as intraabdominal pressure increases, the lattice will tighten to maintain contour. With sustained pressure over a long period of time, diastasis recti can develop. For this reason it is important to preserve as

much of the sheath as possible and to adequately close all layers of the anterior rectus sheath during the closing phase.

The other important aspect of maintaining the integrity of the anterior abdominal wall is to preserve the lateral innervation of the rectus abdominis muscle (7,8). The rectus muscle is segmentally innervated. The motor nerves typically enter the muscle along its posterior surface at the junction of the lateral and central thirds. When harvesting MS-1, MS-2, or MS-3 flaps, the lateral innervation should be preserved to ensure muscle contractility. Each of these flaps requires a myotomy or segmental excision of muscle. There are crossover motor nerve branches that will be encountered. Sometimes these nerves can be preserved and other times they require division. This should be done sharply without clips to permit axonal sprouting and medial segment neurotization.

Preservation of the rectus abdominis muscle and the anterior rectus sheath will usually improve functional outcomes related to the anterior abdominal wall (7,8). All variations of myotomy or myomectomy of the rectus abdominis will limit the contractility of the muscle because the contractile sarcomeres are replaced by scar. Loss of continuity of the muscle will result in a non-functional muscle; therefore MS-1, MS-2, and MS-3 flaps usually result in improved function as long as the nerves are preserved. Limiting the amount of anterior rectus sheath excision will minimize contour abnormalities of the abdomen (3,4).

Closing the abdomen

At time of closure, it is important to approximate the medial and lateral segments of muscle when an MS-2 or MS-3 flap has been performed (*Figure 7*). This will minimize the incidence of lateralization of the muscle as intraabdominal pressure increases. Closure of the anterior rectus sheath is perhaps the most important predictive aspect for outcome quality. When an MS-3 flap has been performed, a standard fascial approximation is typically performed using an absorbable or nonabsorbable monofilament suture placed in an interrupted figure-of-8 fashion. All lamellae of the anterior sheath are closed to ensure stability. A second row of sutures is typically placed in a running, continuous fashion for further reinforcement (*Figure 8*). When an MS-0, MS-1, or MS-2 flap has been performed, primary fascial closure is usually possible when there is enough laxity or redundancy of the fascia. In situations where it is not, the use of a mesh (biologic or synthetic) is typically necessary (9).



Figure 9 A biologic mesh is placed as an inlay graft.



Figure 10 A synthetic mesh is used for onlay reinforcement.



Figure 11 Preoperative image prior to abdominal flaps.



Figure 12 Postoperative image following bilateral breast reconstruction with DIEP flaps. DIEP, deep inferior epigastric perforator.

The purpose of the mesh is to prevent undue tension on the fascial closure that will have a higher likelihood of dehiscence or attenuation. The mesh can be placed as an inlay (*Figure 9*) when there is a fascial deficit and as an onlay (*Figure 10*) when the fascial closure needs additional reinforcement. The type of mesh used can vary from biologic composed of porcine dermis, synthetic of polypropylene, and resorbable collagen. In our experience, the use of a mesh has been necessary in 11.8% of patients (9). *Figures 11,12* demonstrate a pre and postoperative image of a woman following bilateral breast reconstruction with abdominal flaps.

Following fascial closure, plication of the remaining fascia is sometimes necessary to achieve ideal contour (*Figures 13-19*). With unilateral reconstructions, contralateral plication will serve to achieve uniformity of the anterior abdominal wall and to centralize the umbilicus. With bilateral reconstructions, the supraumbilical fascia is often plicated along the midline to prevent an upper abdominal bulge. These sutures are usually monofilament and placed in a figure-of-8 fashion. Infraumbilical midline sutures are also sometimes useful to achieve ideal contour.

Scarpas fascia in obese women that have abdominal flaps reconstruction is sometimes in excess along the



Figure 13 Preoperative image prior to mastectomy and bilateral free TRAM. TRAM, transverse rectus abdominis musculocutaneous.



Figure 16 Lateral view demonstrating severe distortion prior to fascial plication.

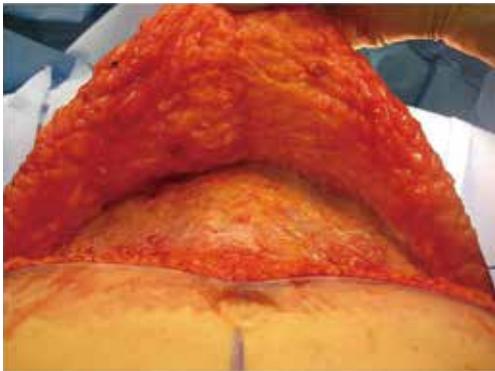


Figure 14 Intraoperative image demonstrating a rectus diastasis.

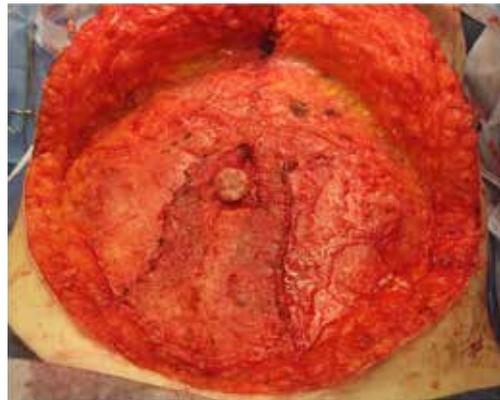


Figure 17 Anterior view following superior and lateral plication demonstrating improved contour.



Figure 15 Anterior view following bilateral fascial closure. There is significant distortion superiorly and laterally.



Figure 18 Lateral view demonstrating an improvement in abdominal contour.



Figure 19 Postoperative view demonstrating normal abdominal contour following bilateral free TRAM flaps. TRAM, transverse rectus abdominis musculocutaneous.

pubic area as well as the upper abdomen. This fat is often less vascularized than the fat above scarpas layer. For this reason, it is sometimes excised. The thickness of the upper and lower adipocutaneous layers of the abdominal wall should be similar to prevent any step-off deformity. The slight depression of the midline anterior abdominal wall can be recreated by excision a few millimeters of fat along the midline of the adipose layer. This maneuver will also tend to provide a more natural abdominal contour.

Skin closure is the final stage of abdominal closure and includes the umbilicus and the incisions. The inseting of the umbilicus is another important step to achieve ideal abdominal aesthetics. Various skin incision patterns are possible that include circular, oval, and “U” designs all of which are capable delivering good results. A technique that has demonstrated success for achieving a natural appearance is the 2-dermal flap umbilical transposition flap technique (10). With this technique, the umbilicus is invaginated to shorten the umbilical stalk and yield a very natural appearance. Skin closure is always performed in three layers that include scarpas fascia, the dermis, and epidermis. Closure of scarpas layer is important to prevent separation of the fat resulting in an involuted scar. Monofilament sutures are used for the dermis and subcuticular layers. Lateral dog-ears should be identified at time of closure and addressed. This will lead to lengthening of the abdominal incision but an improvement in abdominal contour. Two closed suction drains are always used to minimize the occurrence of a fluid collection.

Correcting postoperative abdominal abnormalities

There are several postoperative abnormalities that can be a significant source of patient dissatisfaction that include abdominal bulge, abdominal hernia, persistent pain, delayed healing and chronic fluid collection (11-13). Each of these typically requires operative intervention to correct. The first step is to address the patient concerns by performing a history and physical examination. Areas of abnormal contour, pain, induration, fluid collections and delayed healing are noted.

Abdominal bulge

An abdominal bulge is most often due to attenuation of the anterior rectus sheath and secondarily due to dehiscence of the fascial closure but it can be exacerbated by absence, weakness or denervation of the rectus abdominis muscle (4,12). It is important to differentiate between a bulge and hernia. A hernia will have a true fascial defect that can be palpated whereas a bulge will not. Imaging studies are usually not necessary with a bulge. The area of the bulge is delineated with the patient standing. During the operation, lower transverse incision is opened and the upper adipocutaneous layer elevated. The bulge is identified and plicated in two vertical layers using a nonabsorbable monofilament suture in a figure-of-8 fashion as well as a continuous suture. The use of a synthetic mesh is usually considered to further reinforce the anterior abdominal wall and typically extends from the costal margin to the pubic region. The sutures are usually absorbable monofilament and placed around the periphery of the mesh and centrally to anchor it to the anterior rectus sheath.

Upper abdominal bulge is sometimes seen with pedicle TRAM flap (3). These flaps can be rotated ipsilaterally or contralaterally to gain access to the breast pocket. As such an upper abdominal fullness may result and be bothersome to some patients. With time many of these bulges will spontaneously resolve as the rectus abdominis muscles atrophies because of denervation. However, when persistent surgical correction is considered, this may include liposuction of the affected area or direct surgical excision. Both maneuvers have demonstrated success.

Abdominal hernia

The repair of a true hernia differs from that of the bulge (7). The initial phase of the repair includes defining the fascial edges of the defect and then excision of the hernia sac.

An intra-abdominal approach to the repair is required. Mesh reinforcement is often necessary and can be used as an underlay or onlay fashion. Both synthetic and biologic meshes can be considered. Underlay and onlay mesh should span as much of the anterior abdominal wall as possible. Absorbable monofilament sutures are usually used to anchor the mesh to its surface. The fascial edges are re-approximated when possible using nonabsorbable monofilament sutures in an interrupted figure-of-8 fashion followed by a running continuous suture is placed along the linea alba. In complex situations associated with recurrence and loss of domain, the use of tissue expanders can be considered to repair a true hernia.

Pain

Chronic pain following abdominal flap reconstruction is usually due to a neuroma (6). The usual cause of this is a surgical clip that has been placed along a sensory branch of the intercostal neurovascular bundle as it traverses through the anterior rectus sheath to the adipocutaneous layer. Other etiologies may include entrapment of the ilioinguinal and iliohypogastric nerves. Conservative management is usually recommended for the first 6 months because most of these symptoms are self-limiting. However, when the pain is persistent and interferes with activities of daily living, surgical excision of the neuroma with burial of the nerve stump into the underlying muscle is recommended (6).

Fluid collections

Fluid collections following abdominal flap reconstruction can occur and may be due to premature drain removal, damage to the loose areolar layer of the anterior rectus sheath, and body habitus. Seromas are the most common but a hematoma is also possible. Fortunately many of these are small and self-limiting; however, when large and persistent, intervention is considered. This may include office procedures such as serial aspiration or by placing an indwelling catheter via interventional radiology. Operative evacuation may be considered when refractory to conventional maneuvers.

Conclusions

In summary, achieving ideal abdominal aesthetics following abdominal flap reconstruction is possible using various principles and concepts. Preoperative

assessment is important to determine who is at risk for abdominal morbidity. Intraoperatively, it is important to preserve the vascularity of the anterior rectus sheath and minimize its excision. Closure of the anterior sheath can be performed primarily or with the assistance of a surgical mesh. Fascial plication will serve to improve abdominal contours. Preservation of the rectus abdominis muscle and maintenance of its innervation will improve the integrity and function of the anterior abdominal wall. Closure of the incisions, contouring of the scarpas fat, and umbilical transposition are also relevant considerations to achieve ideal abdominal aesthetics.

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This research meets the ethical guidelines, including adherence to the legal requirements of the study country.

Footnote

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Does immediate reconstruction increase postmastectomy surgical site infection?

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Immediate reconstruction has become routine surgical practice in most breast cancer patients submitted to mastectomy. The opportunity to start - and sometimes to complete - breast reconstruction at the time of mastectomy represents a definite advance in the treatment of breast cancer.

Furthermore, a growing body of evidence suggests that the preservation of the whole skin envelope including the nipple-areola complex is often possible and oncologically safe both in high-risk individuals and in patients affected by early stage breast cancer (1,2). This is definitively one more reason to opt for immediate reconstruction and has certainly contributed to the steady increase of the number of reconstructive procedures involving breast implants and autologous tissue transfer performed over the last years (3).

In a recent paper published in the *Annals of Surgery*, Nguyen *et al.* looked for an association between immediate reconstruction and surgical site infection (SSI) rates in all mastectomies included in the American College of Surgeons' National Surgical Quality Improvement registry from 2005 to 2009 (4). The data presented are particularly interesting due to the large size and good quality of the database from which were derived and thus may help to shed some light on a debated issue.

The first consideration stems from the fact that Nguyen *et al.* (4) report a SSI rate of 2.5% in mastectomies without reconstruction, consistent with that provided for wounds classified as "clean" by the U.S. National Research Council group (5). In mastectomies followed by immediate reconstruction the SSI rate was significantly higher (3.5%, $P < 0.001$), and close to that of a "clean-contaminated" wound. Previous studies were inconsistent since they showed either no difference (6), or very large differences (7)

in the incidence of SSI when breast reconstruction was added to the oncological procedure.

But what does it cause the increase of SSI? Risk factors are the same for both mastectomy alone and mastectomy with reconstruction, and in particular they are: increased body mass index (BMI), preoperative alcohol use, standard American Society of Anesthesiologists classification of severity of illness (ASA), flap failure, and operative time. The first three factors are independent from the type of surgery performed, while the addition of breast reconstruction may clearly influence the last two. Operative time variably increases when reconstruction is performed, especially for procedures of autologous tissue transfer. As for any type of surgery, prolongation of operative time may favor infection by lowering immune defenses of the patients and increasing chances of microbial contamination.

Flap failure is likely the main factor responsible for the increase of SSI in patients who undergo breast reconstruction. Actually, flap necrosis is a very rare event after total mastectomy without reconstruction. Conversely, the transfer of autologous tissue is definitely linked to the risk of partial or total necrosis of the pedicled or microvascular flap, with possible subsequent bacterial infection. On the other hand, the pathogenesis of SSI after prosthetic reconstruction is less clear. A possible explanation may be that the tension of skin flaps caused by the underlying implant could facilitate the penetration of bacterial agents in the surgical site through microscopic ports of entry or even small diastases of the skin sutures.

With this regard, another consideration is needed. What is the role of infection in determining the final outcome of breast reconstruction? Surely, a distinction between

superficial and deep infection has to be made. Superficial infection usually causes only delayed healing and has a lower cosmetic impact on the final result. This is the case of small and medium-sized diastases without implant exposure, which can be solved by repeated dressings or outpatient surgery. Conversely, deep infections are a major problem, which can result in the complete loss of an autologous tissue flap or require implant removal.

A final comment is that a praise must be done to a system such as the American College of Surgeons' National Surgical Quality Improvement Registry which prospectively incorporates main data from all operations performed on the national territory. Only a systematic analysis of data like these can tell us if we have a problem with the surgery that we perform and if we should change our practice to solve it.

In conclusion, although we must carefully consider all factors that may increase SSI in patients undergoing mastectomy, the additional risk attributable to immediate breast reconstruction appears limited to 1%. We agree with Nguyen *et al.* (4) that, although statistically significant, such a small difference does not mandate any change of the current clinical practice that favors immediate reconstruction whenever suggested by the clinical conditions and personal preferences of the patient.

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The role of the physiotherapy in the plastic surgery patients after oncological breast surgery

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Introduction: Breast cancer is the disease which causes the greatest concern among women worldwide, with an estimated 1,152,161 new cases each year. The improvement of surgical techniques, neoadjuvant and adjuvant treatment enhance the survival time and recovery of these patients. As surgery is the first choice for the treatment of breast neoplasms reconstructive surgery has become an important procedure helping to reconstruct the mutilation after radical or conservative breast surgery. The objective of this article is to review the scientific literature and examine the available data regarding the role of physiotherapy in patients who undergo plastic reconstruction after oncological breast surgery, including suggestions on how physiotherapy could be applied in that population.

Materials and methods: Our review was obtained by searching the PubMed (National Library of Medicine, USA) and LILACS (Latin American and Caribbean Health Sciences) databases. Terms applied concerned physiotherapy and breast reconstructive surgery. The time of limit for our search was from 1995 until the present date.

Results: Fourteen articles were included in our review that matched our search criteria.

Conclusions: Physiotherapy is a field that still needs evidence based on daily routine and studies in the oncological physiotherapy field. Evaluation should be standardized and rehabilitation techniques used are empirical and should be researched in patients who undergo plastic reconstruction after breast surgery. The lack of post-surgery exercise protocols makes it difficult to analyse the patient's evolution and makes it a challenge to investigate the true role of physiotherapy in this population.

Keywords: Breast neoplasms; breast reconstruction; physiotherapy; rehabilitation

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Introduction

Breast cancer is the most insidious oncological disease in women all over the world, with an estimate of 1,152,161 new cases each year (1). The improvement of surgical techniques, neo adjuvant and adjuvant treatment enhance the survive time and recovery of these patients (2-6). As surgery has been the first choice for the treatment of breast neoplasm (3,5) reconstructive procedures became more request, helping to reconstruct the mutilation after a radical or conservatory breast treatment and enhance quality of live and physical function of these patients (7).

The most common modalities of reconstructive surgery are the use of expander and prosthesis based implants and the reconstruction using flaps tissues from other sites of the patient's body (8). Both techniques are not risk free and sequelae like implant capsular contracture (9), swelling, pain, upper limb restriction (8), scar tissues and biomechanical muscular changes are not uncommon and sometimes are over evaluated and over treated.

As part of the rehabilitation regime, physiotherapy can assist in patient's recovery after these reconstructive procedures, but the small number of specialized physiotherapy in the oncological field and lack of evidence

based techniques reduce the trust of the multidisciplinary team in physiotherapy professional.

The objective of this article is to review the scientific literature and examine the available data regarding the role of the physiotherapy in patients underwent plastic reconstruction after oncological breast surgery.

Search strategy and selection criteria

A literature search was carried in October 2013 to identify studies of where physiotherapy had an active role (in pre and post-surgery assessment and with rehabilitation protocols) after oncological breast reconstructive surgery. Our review was obtained by search the PubMed (National Library of Medicine, USA) and LILACS (Latin American and Caribbean Health Sciences) databases using the following search themes: “Physiotherapy and breast reconstructive surgery”, “physiotherapy and prosthesis breast reconstruction”, “physiotherapy and expander breast reconstruction”. For the flaps surgery the search themes were separate by the flaps donor site: “physiotherapy after dorsal flap breast reconstructive surgery”, “recovery After dorsal flap reconstructive surgery”, “rehabilitation after dorsal flap breast reconstruction”, “physiotherapy after abdominal flap breast reconstructive surgery”, “recovery after abdominal flap reconstructive surgery”, “rehabilitation after abdominal flap breast reconstruction”, “physiotherapy after DIEP flap breast reconstructive surgery”, “recovery after DIEP flap reconstructive surgery” and “rehabilitation after DIEP flap breast reconstruction”. In an attempt to minimize the omission of potentially relevant clinical studies, we also reviewed the reference lists of included studies and relevant reviews for additional eligible articles. The time of limit for our search was from 1995 until the present date. Only papers in English were cited. Publications and citations were selected with the remit of this review. The articles were selected according to each subheading purpose in the review.

Results

Fourteen articles were included in our review that matches our search criteria. The results are in *Figure 1*. Breast cancer surgery and reconstructive surgery can lead to post-surgical sequela and when surgery is concomitant, patients could be diagnosed with different kind of deficit of either axillary surgery or reconstructive surgery. These circumstances difficult the treatment and demand

specialized physiotherapy and a multi and inter disciplinary team to manage and follow these patients.

Implant based reconstructive surgery

The implant-based reconstruction is the most common type of reconstruction after oncological breast surgery in many countries and institutions (7). In our clinical practice we are aware that oncological patients underwent reconstruction with expander or prosthesis have more difficult to start the rehabilitation protocol used for patients after breast surgery or axillary surgery without reconstruction, as the reconstruction could lead to more pain and restriction in range of motion of the upper limb (8). We recommend our patients who underwent these procedures to start a rehabilitation protocol in the first postoperative day. Patients and surgeons should be informed that most of exercises protocols found in literature are indicated to patients underwent breast or axillary surgery without concern in reconstruction (10).

After surgery, collateral effects like prosthesis encapsulation, post-surgery scar tissues, and breast edema are not infrequent (8,9). The indication of upper limb exercise and correction of postural antalgic position are advised. The use of massage therapy techniques, neuromuscular taping and manual lymphatic drainage are usual in the clinical practice, but there is a lack of protocols and studies that prove the efficacy in patients underwent oncological plastic surgery reconstruction with implants.

Autologous based reconstructive surgery

In patients who underwent autologous based reconstructive surgery, the evaluation should be made at preoperative day and that practice should be standard, to compare end evaluate the impairment and patients' needs after surgery.

The post-operative evaluation should be executed in the range of 4 to 6 weeks. Postoperative condition of the patients and a correct communication between surgeon and physiotherapy should be taken in consideration prior to start any evaluation protocol. The use of the Kendall muscular evaluation (11) or manual muscle strength testing using the Medical Research Council (MRC) Scale (12) are broadly used by physiotherapist, but results tend to be subjective. We suggest the combination of digital dynamometers with the manual evaluation to give a more objective result (13). In literature the more used evaluation using an isokinetic machines (14-16), but they are expensive and most of

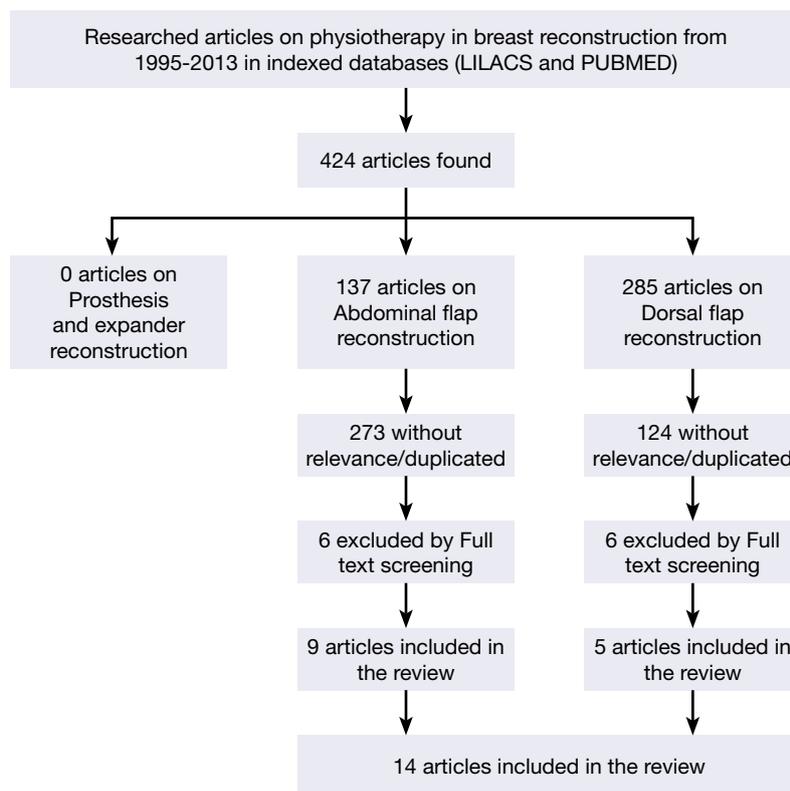


Figure 1 A flow chart of articles included in the review.

institutions and physiotherapy have no access to this machinery.

Several studies showed that patients underwent bi-pedicle transverse rectus abdominis myocutaneous (TRAM) flap had a decrease in strength during flexion movement six weeks after surgery. Kind *et al.* showed the modification in patients underwent unilateral pedicle TRAM flap finding a compensatory rotational strength pattern on the contra lateral side of surgery (14-17). These muscular changes tend to recovery between the three and six months after surgery (16,17). There are no studies that linked the abdominal strength changes with lower or upper back problems, even if it is well know that abdominal muscles is intrinsically related with the stabilization of the human body (18).

Patients underwent latissimus dorsi flap reconstruction had a reduction of rotator cuff and extension force 6 weeks after surgery, with a recovery in 3-6 months (19-23). Nevertheless that recovery did not reach the base lines find in pre-operative evaluation as demonstrated in the study of Forthomme *et al.* (22).

A small number of studies were found about deep inferior epigastric perforators (DIEP) procedure. All of

them showed little reduction of wall strength in the first weeks after surgery when compared with TRAM flaps reconstruction (15,24-26). Nevertheless, the indication of a correct posture after surgery should be given to all patients, as the pain and dyskinesia in the abdominal area could affect the correct imbalance in walk or execute daily activities in the first months. Patients who are more susceptible to venous congestion and fat necrosis (27) should be identified, so any rehabilitation procedure should be carefully discussed among the surgeon and patient.

The literature shows a small probability of embolic events or respiratory complications after TRAM and DIEP surgeries (28). Respiratory physiotherapy should be a concern in the first postoperative day as patients underwent breast reconstruction with abdominal flap tends to be long time in the operation room, bed immobilization and pain in abdominal area. The use of respiratory exercises can help prevent atelectasis and mucus mobilization and early ambulation deep venous thrombosis. Patients should be inform on how assume a correct posture, mobilization from bed to stand position, to walk, and seat (29,30). It's important to correct any kind of antalgic position after surgery that

could evoke muscular contractions and more pain.

As part of the assessment, a validated questionnaire (10,31) could be used to assess the results of the physiotherapy, quality of life and any emotional distress. The physiotherapy must collaborate with the multidisciplinary team, as the collateral effects of reconstructive surgery could be more than only mechanical or physical (32).

During our review, there were no studies regarding exercises or postural education protocols aimed to patients who underwent TRAM, DIEP or latissimus dorsi procedures. The suggestion of postural global reeducation (33,34), Pilates (35-37), CORE exercise (38) and upper limb exercise (10) could be part of the rehabilitation protocol but these techniques need to be studied and researched in patients who underwent reconstructive surgery after breast cancer surgery.

Conclusions

Physiotherapy is a field that still needs evidence based in the daily routine and studies in the breast oncological physiotherapy field are warranted. Evaluation should be standardized. Rehabilitation techniques used are empirical and should be researched in patients who underwent plastic reconstruction after breast surgery. The lack of post-surgery exercise protocols difficult the analyses of patient's evolution and making challenging to prove the real role of the physiotherapy in this population.

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Footnote

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Metabolic syndrome and outcome after breast reconstruction

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Abstract: Metabolic syndrome with its core components including obesity, insulin resistance, dyslipidemia and hypertension; is has been proven as a multiplex risk factor for cardiovascular disease. It is also recently shown by meta-analysis for its association with increased risk of common cancers including breast cancer. Multiple studies have shown metabolic syndrome prone to have poor perioperative outcome and complications for multiple type of surgery including vascular and flap surgery due to compromising microvascular circulation in this group of patient. However, lack of data on consequences of metabolic syndrome on breast cancer surgery as well as in breast reconstructive surgery indicate the need of further study in this area for the improvement of outcome of breast cancer and reconstructive surgery.

Keywords: Metabolic syndrome; breast cancer; obesity; breast reconstruction

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Breast cancer is now the most common cancer among women with an estimated 1.38 million new cancer cases diagnosed in 2008 (23% of all cancers) (1), and only in the United States 211,731 women were diagnosed with breast cancer in 2009. Incidence rates vary between different regions, but there are higher in developed regions. Although, breast cancer stills the most frequent cause of cancer death in women in both developing and developed regions, mortality from breast cancer has been declining in developed countries over the last two decades due to the advancement in treatment and diagnostic procedures. However, today more favorable result of breast cancer maybe not only to cure and save lives, but also to save or rebuild their breasts to maintain the body image and self-esteem. As a result, breast conservation surgery can be another choice to response with patient physical and emotional need to recreate the shape of the breast following a breast cancer surgery.

Considering breast reconstructive surgery, several types of procedures are available using implant, tissue flap, or a combination of both. According to operation using flap techniques, healthy blood vessels are needed for the tissue's blood supply, so flap procedures are not usually offered to

women risk with vascular problems.

On the other hand, from researches many risk factors for breast cancer have been well documented and several studies have shown the association of the metabolic syndrome and its individual components with breast cancer (2-5). More recent studies have shown it to be an independent risk factor for breast cancer. It has also been associated with poorer prognosis, increased incidence, a more aggressive tumor phenotype (6-9). The contribution of various modifiable risk factors, excluding reproductive factors, to the overall breast cancer burden has been calculated by Danaei *et al.* (10). They conclude that 21% of all breast cancer deaths worldwide are attributable to alcohol use, overweight and obesity, and physical inactivity. This proportion was higher in high-income countries (27%), and the most important contributor was overweight and obesity.

Metabolic syndrome is identified as a multiplex risk factor for cardiovascular disease and metabolic syndrome is also known for its association with increased risk of common cancers; for some cancers, the risk differs between sexes, ethnics group, and definitions of metabolic syndrome. Overall From the meta-analysis and the systematic review presence of metabolic syndrome was associated with breast

postmenopausal, endometrial, pancreatic, rectal, and colorectal cancers in women, and it was associated with liver, colorectal, and bladder cancer in men (11). The evidence indicates the increasing prevalence of metabolic syndrome. The clustering of risk factors that constitute the metabolic syndrome is found to be common in most countries of the world. In the Americas, in Europe, and in India, at least one-fourth of the adults carry the syndrome (12). Considering criteria diagnosis, a number of expert groups have developed clinical criteria for the metabolic syndrome. The most widely accepted of these have been produced by the WHO, the European Group for the Study of Insulin Resistance (EGIR), and NCEP ATP III (13). But all groups agree on the core components of the metabolic syndrome including obesity, insulin resistance, dyslipidaemia and hypertension. However, they apply the criteria differently to identify such a cluster. The risk for ASCVD accompanying the metabolic syndrome is approximately doubled compared with an absence of the syndrome (14). It also associated with a very risk for type 2 diabetes or with diabetes itself, the likelihood of developing diabetes is increased approximately 5-fold. In addition, the metabolic syndrome is often associated with other medical conditions, notably, fatty liver, cholesterol gallstones, obstructive sleep apnea, gout, depression, musculoskeletal disease, and polycystic ovarian syndrome. For the reason, metabolic syndrome undoubtedly affects a surgical result.

There are many researchers studied about effects of metabolic syndrome on surgery outcomes.

Metabolic syndrome has previously been found as a risk factor for poor outcomes for vascular surgery. For instance, metabolic syndrome associated with an increase in mortality and morbidity both early and late after coronary artery bypass grafting (15). Patients with metabolic syndrome have lower survival and cumulative patency rates of hemodialysis access patency (16), metabolic syndrome patients required more complex interventions, more systemic complications and major adverse limb events, and associated with poorer symptomatic and functional outcomes compared with control in superficial femoral artery interventions (17). From many researches, metabolic syndrome also affects the outcome of organ transplantation surgery. It is a risk factor for allograft failure after kidney transplant (18-21), and presence of metabolic syndrome developed a higher risk of cardiac allograft vasculopathy (CAV) in the heart transplant patients. Patients with more criteria of metabolic syndrome had a higher development of CAV (21). There is also a strong correlation between truncal obesity, which is a component of MS and skin graft failure (22). The MS is

associated with faster bioprosthetic valve degeneration in patient underwent aortic valve replacement (23).

Moreover in other types of surgery metabolic syndrome also associated with the adverse outcomes. For examples, metabolic syndrome is an independent risk factor for the development of major complications, nonroutine discharge, and increased hospital cost among total joint arthroplasty recipients (24). Colorectal patients with metabolic syndrome had a higher rate of postoperative complication and a longer length of hospital stay than patients without metabolic syndrome (25). Metabolic syndrome is associated with increase perioperative mortality in hepatectomy (26).

In addition, there is a relationship between metabolic syndrome and post-operative surgical wound infection in coronary artery bypass graft patients (27-29).

As a result from the available evidence base medicine and literatures, the author set a hypothesis that metabolic syndrome may effect result of breast cancer surgery and breast reconstructive surgery. However, there is no available research study about this association. As a result, Further researches are needed to answer this question, and for the improvement of outcome in breast cancer and reconstructive surgery.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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A multiple logistic regression analysis of complications following microsurgical breast reconstruction

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Background: Although we practice in an era of high flap success rates following microsurgical breast reconstruction, complications can still occur. Several studies have evaluated the impact of risk factors on microvascular outcomes in the setting of a particular type of patient or with a particular type of flap. However, few studies that have evaluated a consecutive series of high-risk patients will all types of microvascular breast reconstruction. Our goal was to gain a better understanding of the relationship between risk factors and complications in order to provide useful information for patients and surgeons considering free flap breast reconstruction in high-risk patients.

Methods: We performed a retrospective review of all patients who underwent microsurgical breast reconstruction by the senior author (M.Y.N) from July 2005 July 2010. Patient records were analyzed for risk factors (age, BMI, smoking history, medical history, adjunct therapies, timing of reconstruction, type of reconstruction), and complications (hematoma, seroma, infection, wound dehiscence, pulmonary embolism (PE), deep venous thrombosis (DVT), pneumonia, fat necrosis, leech use, partial flap loss, total flap loss). Statistical methods were employed to determine statistically significant relationships.

Results: A total of 352 patients underwent 490 microvascular breast reconstructions during the study period. Active smoking was found to be a statistically significant risk factor for seroma [P<0.0001; odds ratio (OR) =36; 95% confidence interval (CI), 5.9-193.9], infection (P=0.0081; OR =4.3; 95% CI, 1.3-14.1), and pneumonia (P<0.0001; OR =17.1; 95% CI, 3.3-89.9). Unilateral reconstruction was found to be a statistically significant factor for fat necrosis (P=0.0083; OR =4; 95% CI, 1.4-11.4). Additionally, BMI was found to be a statistically significant risk factor for infection (P<0.00001).

Conclusions: This study corroborates findings from previous studies. Tobacco use was demonstrated to be a significant risk factor for infection, seroma, and pneumonia. Obesity was demonstrated to be a significant risk factor for infection. Unilateral reconstruction was demonstrated to pose additional risk for fat necrosis compared to bilateral reconstruction. Patients who choose to have microsurgical breast reconstruction should be informed of the complication profile associated with certain risk factors.

Keywords: Breast reconstruction; microsurgery; complications; radiation therapy; tobacco

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Introduction

High-risk patients are considered to be some of the most challenging to reconstructive surgeons. These patients are defined as those with co-morbidities such as obesity, tobacco use, and poorly controlled diabetes mellitus as well as prior reconstructive failures and previous radiation therapy. In these high risk patients, complications are often increased and because of that, reconstructive algorithms may require modification. Traditional methods of reconstruction may not provide predictable outcomes and therefore alternative options should be considered.

Breast reconstruction following mastectomy ranks among the most common of all reconstructive procedures performed. With changing demographics and cancer treatment algorithms such as radiation therapy, breast reconstruction has become more challenging. Obesity has become an epidemic problem in the USA and with it comes a multitude of other problems such as diabetes mellitus and hypertension. Tobacco use remains a social botheration and poses additional challenges to the reconstructive surgeon. The indications for radiation therapy continue to increase and the number of women who are plagued by the vascular and soft tissue effects of radiation therapy is not trivial.

Microvascular breast reconstruction has been a significant advancement in overcoming many of the limitations of traditional breast reconstruction especially in the high-risk patient. Although we practice in an era of high flap success rates following microsurgical breast reconstruction, complications can still occur. Several studies have evaluated the impact of risk factors on microvascular outcomes in the setting of a particular type of patient or with a particular type of flap. However, few studies that have evaluated a consecutive series of high-risk patients will all types of microvascular breast reconstruction. With that in mind, it was the intent of this study to gain a better understanding of the relationship between risk factors and complications in order to provide useful information for patients and surgeons considering free flap breast reconstruction in high-risk patients.

Methods

A retrospective review of all patients who underwent microsurgical breast reconstruction by the senior author (M.Y.N) from July 2005-July 2010 was performed. Patient records were analyzed for risk factors (age, BMI, smoking history, medical history, adjunct therapies, timing of

reconstruction, type of reconstruction), and complications (hematoma, seroma, infection, wound dehiscence, pulmonary embolism (PE), deep venous thrombosis (DVT), pneumonia, fat necrosis, leech use, partial flap loss, total flap loss). The specific risk factors studied are listed in *Table 1*.

Statistical analysis

The LOGISTIC Procedure of the SAS System (SAS 9.2, Cary, North Carolina) was used to relate the complications (dependent variables) and risk factors (independent variables). We used the STEPWISE option of the LOGISTIC procedure to select the explanatory variables with significant effects. The FREQ procedure of the SAS System was used to generate contingency tables and exact P values if a cell within a contingency table was smaller than 5.

Results

A total of 352 patients underwent 490 microvascular breast reconstructions during the study period. Average patient age was 49.6 years (range, 27-74 years) and average BMI was 27.7 (range, 19.0-47.0). Risk factors and reconstruction data are shown in *Table 1*. Of 490 reconstructions, 380 were performed in non-smokers, while 25 were performed in active smokers and 85 in former smokers. Twenty four reconstructions were performed in patients with diabetes mellitus, 86 in patients with hypertension, and five in patients with coronary artery disease. Ten reconstructions were performed in patients with connective tissue diseases and 3 in patients on chronic steroids. American Society of Anesthesiologist score (ASA) class distribution included 309 reconstructions that were class 1, 174 that were class 2, and 7 that were class 3. One hundred eighty two reconstructions were performed after chemotherapy and 37 reconstructions were performed prior to chemotherapy. One hundred fifty one reconstructions were performed in the setting of prior irradiation and nine reconstructions were radiated post-operatively. Two hundred forty nine reconstructions were performed in the immediate setting and 241 were performed in a delayed fashion. There were 214 unilateral reconstructions and 138 bilateral reconstructions, 244 left-sided reconstructions and 246 right-sided reconstructions. Distribution of flap type was: 6 MS-0 free TRAM flaps, 42 MS-1 free TRAM flaps, 102 MS-2 free TRAM flaps, 321 deep inferior epigastric perforator flap (DIEP) flaps (223 single perforator, 86 two-perforator, 12 three-plus perforator), and 19 superior gluteal artery perforator flap (SGAP) flaps.

Table 1 Risk factors & reconstruction data

Factors	Data
Smoking	
Non	380
Active	25
Former	85
Diabetes	24
Hypertension	86
CAD	5
Connective tissue disease	10
Steroid use	3
Breast cancer	363
ASA class	
1	309
2	174
3	7
4	0
Chemotherapy	
Pre-reconstruction	182
Post-reconstruction	37
Radiation	
Pre-reconstruction	151
Post-reconstruction	9
Timing of reconstruction	
Immediate	249
Delayed	241
Unilateral reconstructions	214
Bilateral reconstructions	138
Side of reconstruction	
Left	244
Right	246
Flap type	
Free TRAM	6
MS1 TRAM	42
MS2 TRAM	102
1 perforator DIEP	223
2 perforator DIEP	86
3+ perforator DIEP	12
SGAP	19

CAD, coronary artery disease; ASA, American Society of Anesthesiologist score; DIEP, deep inferior epigastric perforator flap; SGAP, superior gluteal artery perforator flap.

Table 2 Complications data

Complication	No. of occurrences	%
Hematoma	32	6.5
Seroma	7	1.4
Infection	21	4.3
Wound dehiscence	13	2.7
PE	3	0.6
DVT	0	0.0
Pneumonia	6	1.2
Fat necrosis	20	4.1
Leech use	12	2.4
Partial flap loss	4	0.8
Total flap loss	22	4.5

PE, pulmonary embolism; DVT, deep venous thrombosis.

Complications data is listed in *Table 2*. Complication rates were as follows: hematoma, 6.5%; seroma, 1.4%; infection, 4.3%; wound dehiscence, 2.7%; PE, 0.6%; DVT (without PE), 0%; pneumonia, 1.2%; fat necrosis, 4.1%; leech use, 2.4%; partial flap loss, 0.8%; total flap loss, 4.5%. Donor site complications were not examined in this study. All complications reported were related to the breast/chest.

The findings of our statistical analysis are shown in *Table 3*. Active smoking was found to be a statistically significant risk factor for seroma [P<0.0001; odds ratio (OR) =36; 95% confidence interval (CI), 5.9-193.9], infection (P=0.0081; OR =4.3; 95% CI, 1.3-14.1), and pneumonia (P<0.0001; OR =17.1; 95% CI, 3.3-89.9). Unilateral reconstruction was found to be a statistically significant factor for fat necrosis (P=0.0083; OR =4; 95% CI, 1.4-11.4). Additionally, BMI was found to be a statistically significant risk factor for infection (P<0.00001). As BMI is a continuous variable with a range of values, OR could not be calculated, however, a positive coefficient of 0.1617 indicates that as BMI increases, the chance of infection increases. No other risk factors or reconstructive parameters analyzed were found to have statistically significant associations with any of the complications reviewed.

Discussion

Despite advancements in microsurgical technique, post-operative complications remain an issue in high-risk patient populations (*Figures 1-3*). In an effort to better understand

Table 3 Statistically significant associations

Risk factor	Complication	P value	Odds ratio	95% confidence interval
Smoking (active)	Seroma	<0.0001	36	5.9-193.9
	Infection	0.0081	4.3	1.3-14.1
	Pneumonia	<0.0001	17.1	3.3-89.9
Unilateral reconstruction	Fat necrosis	0.0083	4	1.4-11.4

Additionally, BMI was found to be a statistically significant risk factor for infection ($P < 0.00001$). As BMI is a continuous variable with a range of values, odds ratios could not be calculated, however, a positive coefficient of 0.1617 indicates that as BMI increases, the chance of infection increases.

**Figure 1** Delayed healing in a morbidly obese patient.**Figure 3** Venous congestion of flap in a patient with active tobacco use.**Figure 2** Mastectomy flap necrosis in a patient with previous radiation.

how certain risk factors impact reconstructive outcomes, microsurgeons have studied these relationships. Our goal was to add to the data on this subject by analyzing the risk factors and complications based on the experience of a single surgeon at a single institution.

Similar to other studies, this study demonstrated that tobacco use and obesity were significant risk factors for postoperative complications. Specifically, active tobacco use was found to increase the risk of flap seroma, infection,

and pneumonia. Other groups have identified the impact of smoking on complications in free flap breast reconstruction as well. In a study of 936 free TRAMs in 718 patients, Chang *et al.* found that smokers had significantly higher rates of abdominal flap necrosis, hernia, and mastectomy flap necrosis compared to former and non-smokers (1). Booi *et al.* found a statistically significant increase in free TRAM flap complications in smokers compared to non-smokers ($P < 0.000$), and using Laser Doppler flow measurements found that in patients with high flap weights (> 800 g), smoking leads to decreased microcirculatory flow, particularly in zone 4 (2). Padubidri *et al.* identified a 20% rate of fat necrosis in smokers undergoing free TRAM breast reconstruction compared to 10% in non-smokers, however, this was not statistically significant (3). In a study of 569 free TRAMs in 500 patients, Selber *et al.* found smoking to be a significant risk factor for fat necrosis, wound infection, mastectomy flap necrosis, and abdominal flap necrosis (4). Seidenstuecker *et al.* identified smoking as a significant risk factor for donor site complications ($P = 0.007$) (5). Looking at 10-year experience of 758

microvascular breast reconstructions led by Allen, an overall complication rate of 30.2% was noted, with higher incidences of breast complications in smokers ($P=0.0043$), particularly fat necrosis ($P=0.0226$) (6).

As with smoking, the relationship between obesity and complications has also been well described. We found that as BMI increased, the risk of infection increased. Chang *et al.* found obese and overweight patients undergoing free TRAM reconstructions had significantly higher total flap loss, flap hematoma, flap seroma, mastectomy skin flap necrosis, donor-site infection, donor-site seroma, and hernia compared with non-obese patients (7). In a study of 612 abdominal flap reconstructions, Jandali *et al.* found that the morbidly obese (BMI >40) had significantly higher rate of total flap loss ($P=0.02$), total major postoperative complications ($P=0.05$), and delayed wound healing of the abdominal incision ($P=0.006$). Additionally, they identified a linear trend between increasing BMI and increased wound healing complications (8). Selber *et al.* discovered that obese patients were more likely to have higher rates of mastectomy flap necrosis ($P=0.01$) and hematoma ($P=0.01$) (4). In a retrospective review of 1,195 microvascular breast reconstructions in 952 patients, Mehrara *et al.* found that obesity was a major predictor of complications with obese patients having a statistically significant increased risk of arterial thrombosis ($P=0.06$; OR =1.7), partial flap loss ($P=0.03$; OR =2.6), and donor-site complications ($P=0.01$; OR =3). They also found an association between obesity and fat necrosis (9).

Multiple studies have examined causes for fat necrosis in free flap breast reconstruction. Noted risk factors described, in addition to smoking and obesity, are flap type (10,11), number of perforators (6), and neoadjuvant chemotherapy (9). In our study, unilateral reconstructions were found to be a significant risk factor for the occurrence of fat necrosis compared to bilateral reconstructions. While this association has not been previously described in the literature, it makes good sense. The goal of unilateral reconstruction is to achieve symmetry with the contralateral breast. Sometimes this may require a contralateral reduction mammoplasty but more often than not, a larger flap is used to minimize the need for contralateral surgery. The inclusion of zone 3 of an abdominal flap in unilateral reconstructions, and perhaps even part of zone 4, can push the limits of flap perfusion compared to a hemi-abdominal flap in bilateral reconstructions that by definition include only zones 1 and 2. Careful intra-operative assessment of flap perfusion in unilateral reconstructions can minimize future fat necrosis.

Laser-assisted indocyanine green imaging (fluorescent angiography) may be a useful adjunct in assessing flap perfusion, allowing poorly vascularized territories of the flap to be discarded intra-operatively, preventing the inclusion of poorly perfused tissue from evolving into fat necrosis or partial flap loss.

Conclusions

Tobacco use and obesity are well-described risk factors for complications following microvascular breast reconstructions. This study corroborates these findings from previous studies. Tobacco use was demonstrated to be a significant risk factor for infection, seroma, and pneumonia. Obesity was demonstrated to be a significant risk factor for infection. Unilateral reconstruction was demonstrated to pose additional risk for fat necrosis compared to bilateral reconstructions. Patients who choose to have microsurgical breast reconstruction should be informed of the complication profiles associated with certain risk factors. A better understanding of the relationships between these risk factors and complications will allow for better patient counseling, which can provide useful information during the consent process.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Lymphatic mapping and lymphedema surgery in the breast cancer patient

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Abstract: Upper limb lymphedema can be an unfortunate sequela following the oncologic treatment of breast cancer. The surgical treatment of lymphedema has had a recent renewed clinical interest paralleling innovative descriptions of surgical techniques and imaging modalities. In addition, an improved understanding of the physiology and pathophysiology of lymphedema has allowed improved translation to the clinical condition. Various surgical options exist to decrease the symptom-burden of upper limb lymphedema, including vascularized lymph node (VLN) transfer, lymphovenous bypass (LVB), liposuction, lymphatic grafting, and excisional procedures. Modern imaging techniques help to improve the consistency and accuracy of these surgical treatment options. A multi-modal treatment plan utilizing non-operative and surgical therapies has the potential to improve various factors related to overall patient quality of life. This review details all of the current operative treatment strategies and modern imaging modalities used in the treatment of lymphedema.

Keywords: Lymphatic mapping; lymphedema; lymphatic surgery; microsurgery; lymphovenous bypass (LVB); vascularized lymph node (VLN) transfer; liposuction; lymphatic grafting

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Introduction

Lymphedema is a condition characterized by persistent edema related to lymphatic injury or disease. Over time, chronic lymphedema leads to fat deposition and subsequent fibrosis of the surrounding tissues (1). Lymphedema is classified into primary and secondary types. Primary lymphedema is of congenital (genetic, developmental abnormalities) or idiopathic origin. Secondary lymphedema occurs following injury to lymphatic structures, often following infection surgery, and radiation (2,3). Worldwide *Wuchereria bancrofti*, a parasitic infection, is the leading cause of lymphedema. It is estimated that between 140 and 250 million people are affected by this condition around the world. However, in western and industrialized societies,

breast cancer treatment involving lymphadenectomy and/or radiation to the regional lymphatic system is the major source of clinical lymphedema (4,5). Lymphedema has been reported to occur within days and up to 30 years after breast cancer treatment (6). In addition, 80% of patients experience onset of symptoms within 3 years of surgery as the remainder of patients have a 1% incidence of lymphedema each year (7).

The incidence of breast cancer-related lymphedema (BCRL) varies from 6-49% following axillary lymph node dissection and between 2-7% in patients after sentinel lymph node biopsy (1,3,5,8-11). Although many patients will experience mild symptoms in the early stages of disease, chronic lymphedema is a progressive disease that significantly decreases patients' quality of life, with known

consequences related to a woman's physical, psychological, and emotional well-being (12). Mainstay treatment algorithms focus on non-surgical modalities of treatment, including comprehensive physiotherapy involving multilayer compression wrapping, manual drainage techniques, and various exercises. Modern lymphedema care is slowly incorporating surgical interventions into multimodal treatment plans in treating patients with BCRL (12).

Pathophysiology of lymphedema

The lymphatic system has multiple functions including transport of lipids, regulation of body fluid homeostasis, and immune cell trafficking (2,4,8). The lymphatic structural components act in concert to achieve a unidirectional egress of lymph in the normally functioning lymphangion (functional unit of the lymphatic system). The pathophysiologic process begins when there is an accumulation of interstitial fluid at the lymphatic capillary level resulting in a net fluid efflux. Venous capillaries reabsorb 90% of the fluid in the interstitium, while the remaining fluid is transported to the blood by the lymphatics as lymph (2). This occurs at the level of lymphatic capillaries through a semi-permeable endothelial membrane facilitating physiologic uptake of fluid and macromolecules. As fluid moves toward lymphatic pre-collectors (containing valves) and collecting ducts, phenotypic changes occur within the ultrastructure of the lymph vessels with a resultant increasing smooth muscle cells (SMC) (13). The extracellular structural environment prevents valve incompetence and lymph stasis or reflux. This is also in part due to a synchronized pump mechanism that has been described to propel lymph from lymphangion to lymphangion. Under normal conditions, the same volume of efferent lymph is transported from the interstitium as the volume of afferent lymph transported back to the blood stream through the major lymphatic drainage pathways and through the nodal circulation. Any lymphatic dysfunction resulting in reduction of lymph transport capacity causes an imbalance of intraluminal volume resulting in increases in intraluminal pressure. Persistent lymphatic hypertension leads to histological changes such as SMC hypertrophy, extracellular remodeling, reduction in valve competence, bi-directional luminal flow, and pathologic lymphatic ectasia (14). Early impairment of lymphodynamics can have downstream effects that perpetuate lymphatic dysfunction and ultimately overwhelm the lymphatic system resulting in regurgitant lymphatic fluid into the subdermal lymphatics

(dermal backflow) and the interstitial compartment. These processes result in progressive fluid accumulation and extremity swelling.

Because the aforementioned pathophysiology of the lymphatic system is time dependent, the clinical manifestation of lymphedema are similarly time dependent. Typically early lymphedema is amenable to compression physiotherapy, but with time the chronic fluid compartments will lead to fat deposition. As disease progresses, skin fibrosis and hyperkeratosis will develop. This is commonly associated with an immunologic impairment often manifesting as recurrent cellulitis or dermatolymphangioadenitis (DLA) attacks. Additionally, immune cells such as CD4⁺, Th2 cells are also implicated in promoting a pro-fibrotic environment through cytokine release (15-17). The ability to reduce infection, restore lymphatic flow, reduced extremity circumference, improve patient quality of life, and slow the progression of fibrosis are all associated with the goals of novel surgical techniques, which is why a thorough understanding of the pathophysiology aids the surgeon in interpreting lymphatic mapping and patient symptoms to select ideal candidates for surgery.

Lymphatic imaging and mapping

Lymphoscintigraphy

Lymphoscintigraphy or isotopic lymphoscintigraphy, is an objective and reliable non-invasive imaging modality used to diagnose extremity lymphedema, characterize its severity, and assess post-therapeutic results (18). This imaging modality involves an intradermal injection of radiolabeled colloid in the distal aspect of the edematous limb and subsequent imaging of the lymphatic vasculature (2,19,20). The study provides information regarding both lymphatic anatomy as well as lymphatic function (21). Typical abnormalities seen in patients with lymphedema include absent or delayed radiotracer transport, cutaneous flare, dermal infiltration or backflow, and poorly visualized lymphatic collectors and lymph nodes (22) (*Figure 1*).

According to previous studies (23,24), baseline lymphoscintigraphy can be useful to predict long term response to complex decongestive therapy (CDT) in patients with early stage unilateral limb lymphedema. Both qualitative and quantitative lymphoscintigraphy can be used to assess the severity of disease. Qualitative lymphangiographic scoring typically involves the visual

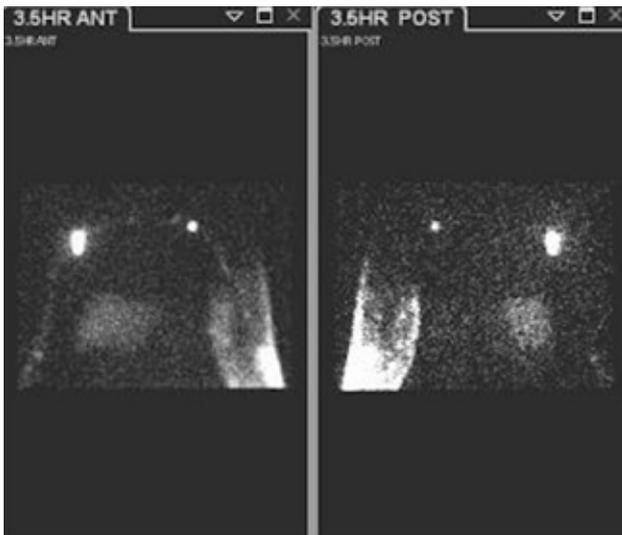


Figure 1 A 59-year-old female with a history of left mastectomy and axillary nodal dissection 8 years prior to the lymphoscintigraphic evaluation shown. Dermal backflow on the left side can be appreciated at 3.5 h after injection in the forearm, while right side lymphatic transport is normal. A lymphatic vessel draining into an axillary node can be seen indicating delayed clearance and partial obstruction.

interpretation of lymphoscintigraphy and the presence of lymphatic trunks, caliber of trunks, visualization of lymph nodes, collateralization of lymphatics, dermal back flow, and subjective delay in uptake of radiotracer. Quantitative lymphoscintigraphy may vary in methodology amongst groups. However, quantification typically focuses on lymphatic tracer uptake through time of initial and delayed uptake at the injection site, clearance time from the injection site, clearance times from anatomic limb, detectable radioactive residual radiolabelled colloid, and various other calculations. Qualitative lymphoscintigraphy alone can provide a reliable diagnosis (25), but it has been shown to have lower diagnostic value than a combination of quantitative and qualitative lymphoscintigraphy (19). Several recent studies have used quantitative lymphoscintigraphy to assess the severity of lymphatic insufficiency in BCRL, as well as the outcomes following treatment in patients with lower-limb lymphedema (26,27).

Currently, lymphoscintigraphy is considered the gold-standard imaging modality for the diagnosis of patients with lymphedema and for evaluation of lymphatic disorders in the swollen extremity (28,29). Lymphoscintigraphy can detect delayed tracer transport even in mild lymphedema

without morphological abnormalities and is useful to evaluate the functional lymph flow in patients following physiologic surgery for lymphedema.

Magnetic resonance angiography and lymphangiography (MRL) and computed tomography (CT)

MRL has been used as an aid in the clinical diagnosis of lymphatic disorders since 1990 (30,31). MRL has a number of potential advantages compared with lymphoscintigraphy, including higher spatial resolution enabling depiction of lymphatic channels, higher temporal resolution, production of three-dimensional (3D) images, higher signal-to-noise ratio, fewer artifacts, assessing the thickness of the underlying tissues and the absence of exposure to ionizing radiation (32). In recent years, a number of different contrast agents have also been developed and tested in MR lymphangiography for imaging of the lymphatic system (33-35). A common agent used is the extracellular, water soluble paramagnetic Gd-BOPTA (Gadolinium dimeglumine) (36). The advantages of using MRL are the capability to map the morphologic architecture of the affected lymphatic system while simultaneously analyzing the lymphatic vessels and nodes in a dynamic fashion (36-38). This technique has been shown to be safe and feasible and with minimal complications (37). Most of these agents are injected into the dermis for the staging of malignant lymph nodes or to show lymphatic drainage patterns.

CT imaging is a valuable imaging modality for many disease entities including lymphedema. In the setting of lymphedema, CT imaging has been used to aid in the diagnosis of unilateral extremity swelling, as other common sources of swelling, including deep venous thrombosis (DVT), lipedema, lymphedema, cellulitis, hematomas, and Baker's cyst rupture, can be detected with this imaging modality. In addition, CT scans are useful for assessing skin thickening, subcutaneous swelling, and calculating limb volume measurements. However, as an imaging modality used to evaluate lymphedema, it is not considered a first-line choice due to concerns for radiation exposure and less diagnostic and prognostic precision (39).

Ultrasonography (US)

U/S is a non-invasive, low cost, non-radiating technique that is routinely used to assess edema and thickness of limbs. With a high-resolution ultrasonographic imaging,

there are some reports that support its use in differentiating lymphedema from lipedema (40). Conventional U/S creates images based on differences in reflection and diffraction of ultra-high frequency sound waves. To be useful for lymphatic imaging, contrast enhancers (microbubbles) consisting of gaseous cores enclosed in lipid or polymer shells are injected, allowing visualization of lymph nodes as the microbubbles are disrupted by the applied acoustic waves. Lymph nodes are able to be targeted using this method because microbubbles are phagocytosed by macrophages and subsequently transported to reside in selected lymph nodes (41-43). Furthermore, U/S can be crucial in the pre-operative planning of vascularized lymph node (VLN) transfer. Duplex US has been found to be valuable for understanding the exact location and number of lymph nodes present in a given donor site, the size and caliber of the vascular pedicle, the flap thickness of the flap, and the associated structural anatomy (44).

Near-infrared (NIR) fluorescence imaging, indocyanine green (ICG)

Fluorescence imaging is an optical technique in which incident photons excite molecules in tissue, which then emit light (usually at a longer wavelength) as the electrons return to the ground state (41). ICG is a tracer that is injected in the dermis and visualized with the NIR technology. When injected intravenously, ICG does not contain any active metabolites, which facilitates rapid processing and excretion into bile without secondary effects (45). High-performance optics and NIR detectors are able to visualize relatively high resolution images up to several centimeters into soft tissues (46). This technique evaluates the lymphatic channels in real time. In addition to detecting lymph flow abnormalities, this technique has been shown to be safe (nontoxic/nonionizing). Also, the tracer has a short half-life which allows for repetitive application, making it a convenient, minimally invasive, and suitable method for preoperative, intraoperative, and postoperative lymphatic channel evaluation (47,48). In addition, it is easy to use, has a high-noise-signal ratio, separating the target from the background, very sensitive even with small concentrations of the ICG, it is a low cost, user-friendly technology (45). The use of ICG imaging technology has rapidly expanded and although procedural protocols may differ slightly, this novel technology now permeates into multiple surgical specialties. Intravenous administration serves as a useful tool in cerebral angiography, coronary

angiography, assessment of peripheral artery disease and vascular graft patency, perfusion prior to transplantation of solid organs, evaluation of sentinel lymph node biopsy and lymphadenectomy during oncologic resections, aids in flap monitoring, and is used to delineate biliary and hepatic anatomy during general surgery procedures. Specifically related to its application in lymphedema, ICG injection into the dermis is able to delineate the morphologically of the lymphatic system and provide a real-time functional analysis of the lymphatic channels and nodes. As a result, ICG lymphography is the most clinically implemented imaging tool used to evaluate severity of disease and monitor surgical outcomes in primary and secondary lymphedema (49-51). In addition, ICG lymphography has been able to demonstrate the efficacy of manual lymphatic drainage therapy in increasing lymph flow and to detect early signs of lymphatic dysfunction in breast cancer survivors (41,52,53).

Clinical lymphedema

Lymphedema is a chronic condition of the lymphatic system in which there is interstitial accumulation of protein-rich fluid and subsequent inflammation, adipose tissue hypertrophy, and fibrosis (2). In addition to inflammation, slowed lymphatic flow has also been shown to incite lipogenesis and fat deposition and later leading to increased fibrocyte activation and connective tissue overgrowth. Affected patients develop progressively firmer subcutaneous tissue as fibrosis ensues, in addition to hypertrophy of adipose tissue. These pathologic changes manifest initially as swelling of the affected limb or region, described as soft and pitting, but later progress to a more firm and fibrotic state. As this condition gets worse, it can cause physical, emotional, and social distress to any patient (1,4,54,55).

Lymphedema is diagnosed by history, physical examination, and physiologic measures. In more advanced stages, the clinical presentation is very evident. However, if a patient presents in an early stage, this scenario can be more challenging since there are many causes of limb swelling. Physical examination features classically unique to lymphedema include peau d' orange changes of the skin, indicating cutaneous and subcutaneous fibrosis (56), and a positive Stemmer sign (the inability to grasp the skin of the dorsum of the second digit). Documentation and diagnosis of lymphedema has classically been made through circumferential measurements or volumetric documentation comparing the patient's affected and unaffected limb (>2 cm limb difference or a volume differential of greater

than 200 cc). Crucial to the diagnosis is a thorough understanding of a patient's previous treatment history, including surgery and radiation therapy. Non-invasive methods that can be used during a patient's clinical examination include bioelectric impedance analysis (57,58), tonometry (59), and perometry (60). Bioimpedance technologies are commonly used in body composition analysis and allow for a more direct measure of differences in edema volume, versus simple measure of differences in limb volume that do not take specific tissue compartment changes into account (61,62).

The differential diagnosis of lymphedema is broad and includes systemic causes of edema, such as cardiac failure, renal failure, malignancy, and protein losing conditions, and local etiologies, including lipedema, deep vein thrombosis, chronic venous insufficiency, myxedema, cyclical, and idiopathic edema.

There are several classification scales for lymphedema. However, the most commonly accepted is based on the International Society of Lymphology (ISL) (63).

- (I) Stage 0: a subclinical state where swelling is not evident despite impaired lymph transport. This stage may exist for months or years before edema becomes evident.
- (II) Stage I: this represents early onset of the condition where there is accumulation of tissue fluid that subsides with limb elevation. The edema may be pitting at this stage.
- (III) Stage II (early): limb elevation alone rarely reduces swelling and pitting manifest.
- (IV) Stage II (late): there may or may not be pitting as tissue fibrosis is more evident
- (V) Stage III: the tissue is hard (fibrotic) and pitting is absent. Skin changes such as thickening are seen.

Severity:

- (I) Mild: <20% excess limb volume;
- (II) Moderate: 20–40% excess limb volume;
- (III) Severe: >40% excess limb volume.

Surgical treatment of lymphedema

Although the gold standard for treatment of lymphedema is considered physiotherapy, termed complete decongestive therapy (CDT), surgical therapy has gained momentum in recent years. The burden of massive fibrosis may hamper the benefits of microsurgical procedures, which is why excisional surgery may be of use in cases dominated by excess subcutaneous tissue and skin. In addition, liposuction

techniques have been described as a valuable method to remove subcutaneous tissues with the potential for sustained limb volume reduction. Overall, the surgical treatment for lymphedema may be divided into two groups: excision procedures and physiologic procedures. Recent and future clinical experiences have devised combination and staged procedures using multiple modalities to achieve a desirable outcome.

Excisional surgery

First described in 1912, the Charles procedure is a debulking surgery used to remove skin and subcutaneous tissue, leaving the deep fascia intact. Split-thickness skin grafts are used to cover raw areas, and many times, grafted skin can be obtained from the excised areas (64). This procedure is reserved for patients with late stage lymphedema historically termed 'elephantiasis'. Indications for performing an extensive surgery as the Charles procedure are focused on functional disability and recurrent infections or cellulitis events.

Shortly thereafter, Sistrunk described another method for debulking lymphedematous tissue in 1918, known as the modified Kondoleon procedure or Thompson procedure (65,66). The procedure involves a lateral elliptical, partial excision of skin, subcutaneous structures, and the deep fascia along the lower extremity. The exposed muscle is then covered by local flaps. This procedure was reserved for end stage lymphedema marked by hyperkeratosis. Conceptually, Sistrunk described the potential to reconnect the superficial lymphatics with deep lymphatics to restore lymphatic function, but he emphasized the success of the surgery was dependent on the excision of diseased portions of the superficial system (67). In the upper limb, a medial ellipse of skin and subcutaneous tissue may be excised along the length of the extremity or where excess tissue exists (*Figure 2A,B*). Careful dissection around superficial venous structures and adjacent lymphatics can help to preserve remaining lymphatic drainage. The outcomes of such procedures have been poorly studied and indications for such excisional procedures are limited in upper limb lymphedema.

Another option for removal of subcutaneous tissue includes the use of liposuction for the treatment of lymphedema. In clinical stages dominated by fatty infiltration and fibrosis, liposuction allows for selective removal of these tissues with preservation of the overlying skin. When excessive fibrosis exists, liposuction may be

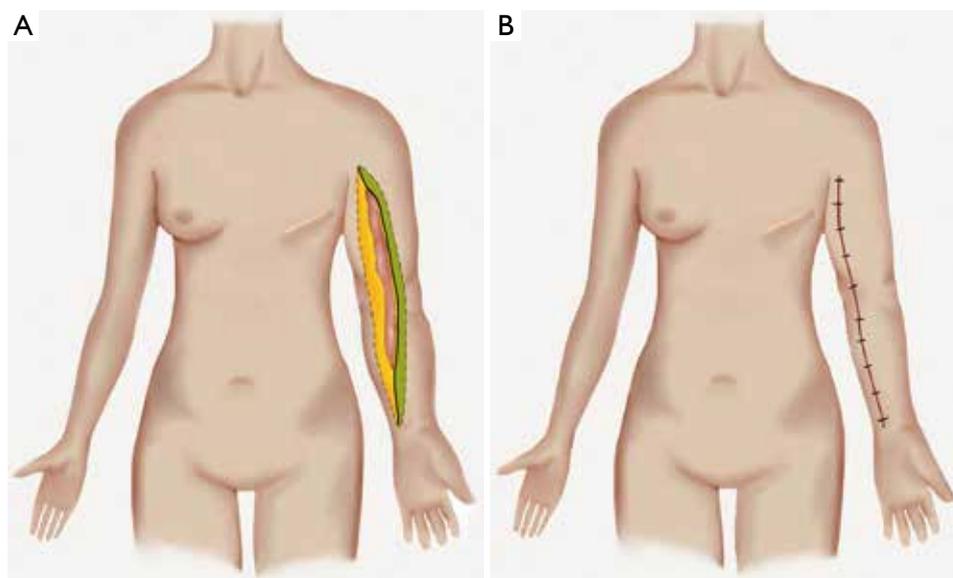


Figure 2 (A) The medial elliptical excision pattern is shown; (B) undermining of the lateral flap (in green) will allow for appropriate closure of the wound following excision.

technically challenging due to the resistance to suctioning from the fibrotic tissue. This volume reducing technique may be used in conjunction with CDT to maintain specific limb volumes. Short-term outcomes have shown a reduction of 61-101% with long-term outcomes after 4- and 15-year showing persistent reduction in limb circumference along with improvements in patient quality of life metrics (68-72). The major limitation to long-term success following liposuction techniques is strict adherence to lifelong CDT and compression therapy. Despite encouraging results, liposuction techniques do not reverse or slow the pathophysiologic process of the lymphatic system. As surgeons become familiarized with both excisional and physiologic procedures (described below), combination or staged procedures are likely to increase in frequency around the world with improved and sustainable results.

Physiologic surgery

Physiologic surgery describes a constellation of sophisticated microsurgical procedures to treat lymphedema using common microsurgical techniques. Although numerous techniques have been historically described, only few techniques are currently being used and these include lymphaticovenous anastomosis (LVA), VLN transfers, and lymphatic grafting. Advances in microsurgical technique

within the last 20 years have largely propelled the field to boast safe and efficacious outcomes following these procedures.

Lymphovenous bypass (LVB)

LVB surgery was described in the 1960s to provide a physiologic shunt for accumulated intraluminal lymphatic fluid to drain to the venous system via a microsurgical anastomosis (73). Early experience promoted the use of this technique in the treatment of lymphedema, but later studies found only temporary relief of symptoms (74,75). Since that early experience, advances in technology and surgical technique have allowed surgeons to change their approach to LVB surgery. Imaging techniques, particularly lymphodynamic evaluation with ICG, have allowed clinicians to assess lymphatic vessel patency and function. Better visualization prior to surgery has allowed for more reliable planning, technical execution, and likely improved long-term patency.

Current techniques for LVB utilize either subdermal lymphatics or the deeper epifascial system. The use of subdermal lymphatics, termed LVA, has been championed by Koshima using supermicrosurgical techniques (0.3-0.8 mm) to create a physiologic shunt (76-78). This procedure takes advantage of the highly compliant subdermal lymphatic

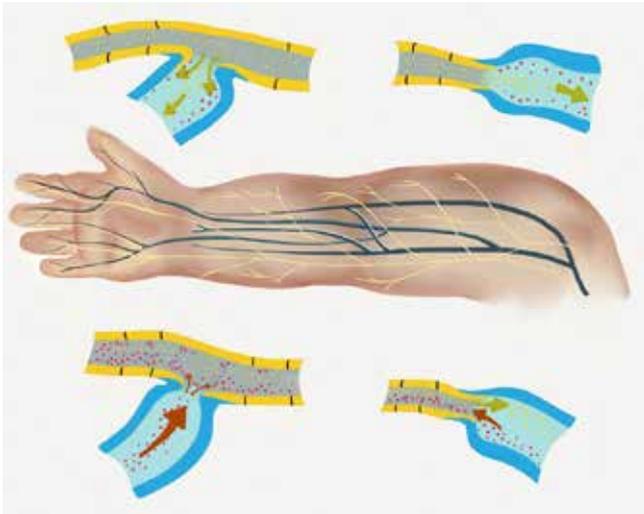


Figure 3 Lymphovenous bypass configurations are shown. End-end and side-end techniques are utilized and dependent on the flow-directionality of both the lymphatic and venous systems.

system, which is responsible for a majority of regurgitant lymphatic fluid seen in dermal backflow. In addition, subdermal and subcutaneous venules are used as recipient veins and have little/no backflow, which will create a favorable gradient following LVB. Reported outcomes using this technique have been favorable for populations with earlier staged disease (79,80).

LVB techniques utilizing deeper lymphatic collectors and pre-collectors are of larger caliber without the need for specialized instrumentation. In these cases, particular attention must be paid to the directionality of flow in these larger lymphatic vessels. ICG dynamic lymphography may be used to show shadows of larger/deeper lymphatics to help guide the surgeon to identify these structures. Flow directionality may help to stratify surgical technique to end-to-end or side-to-end techniques for LVB (*Figure 3*). In addition to considerations for the lymphatic vessel, flow characteristics of the chosen vein or venule must be identified to prevent venous blood regurgitation into the lymphatic system, creating an unfavorable gradient.

VLN transfer

VLN transfers have greatly increased in popularity recently. This method of reconstruction uses common microsurgical techniques to transfer lymph nodes to either the axilla or distally in the arm/forearm to restore lymphatic flow. This physiologic reconstructive technique relies on both the



Figure 4 Regional anatomy of the groin is shown. Superior and lateral chain lymph nodes can be appreciated. These nodes are nourished by the superficial circumflex vessels and/or the superficial inferior epigastric vessels and are located between the inguinal ligament and the groin crease.

intrinsic nodal blood circulation, and lymphangiogenesis/lymphatic sprouting to provide a method to drain excess lymphatic fluid into the venous circulation.

Selection of the VLN transfer donor site, upper limb recipient site, and selecting an optimal patient that may benefit from VLN transfer requires multiple considerations. Multiple donor sites include the groin, submental, and supraclavicular regions, where selective lymph nodes from these regions may be incorporated into a free flap and harvested as a VLN flap.

The groin VLN flap has been critically examined as recent reports of donor site morbidity have been published related to groin VLN flap harvest (81,82). Multiple lymph node chains exist in the groin region and selective harvest of draining nodes from the lower abdomen minimize the risk of inducing lower limb lymphedema (*Figure 4*). Reverse lymphatic mapping has been recently described as a method to visualize and identify both lower limb draining nodes and lower abdominal lymph nodal drainage patterns to avoid less surgically induced lymphedema complications (83). Lymph nodes in the superficial transverse chain may be harvested based off of either the superficial circumflex iliac artery (SCIA) and superficial circumflex iliac vein (SCIV) or the superficial inferior epigastric artery (SIEA) and superficial inferior epigastric vein (SIEV). In a recent imaging evaluation, Dayan *et al.* found that the epicenter of these

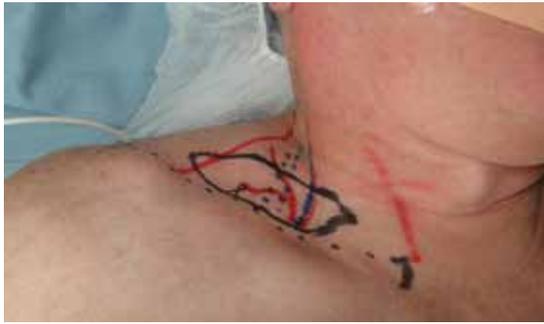


Figure 5 The right supraclavicular VLN flap is shown marked. The transverse cervical vessels serve as the main pedicle as the supraclavicular vessel emerges from this main vessel. Standardized markings utilizing common landmarks will ensure a consistency in flap elevation.

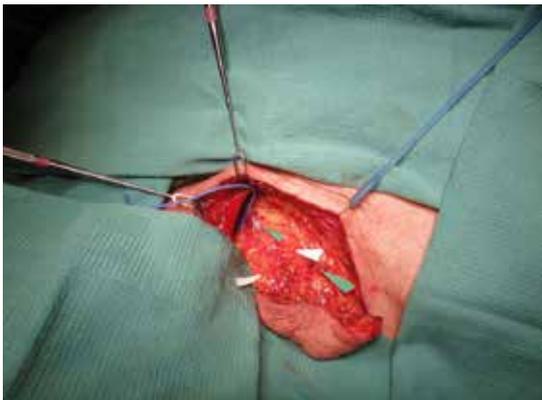


Figure 6 Green arrows indicate available venous drainage options. Lymph nodes are identified by white arrows and can be palpated within the deep portion of the flap.

lymph nodes was located one-third the distance lateral from the pubic tubercle to the anterior-superior iliac spine and 3.1 cm below this line (inguinal ligament). The superficial nodes were typically located within the bifurcation of the SCIV and SIEV (67%), while a lesser incidence medial to the SIEV (19%) and inferior to the SCIV (14%) (83).

The submental VLN flap has been described as an alternative lymph node flap. Level 1a and 1b lymph nodes are harvested based on the submental artery and vein. This perfusing artery emanates from the facial artery approximately 1 cm below the angle of the mandible and travels anteriorly toward the mandibular symphysis. This flap has the advantage of providing a high quantity of lymph nodes (approximately 4 nodes per side) at a remote site from the extremities, which minimizes any risk of developing

iatrogenic lymphedema. In addition, the flap size is small, allowing for a smaller recipient site (44,84).

The supraclavicular VLN flap has also been described as another option for VLNs. Harvest of level V lymph nodes in the posterior triangle of the neck is possible based off of the supraclavicular vessels (*Figures 5,6*). The transverse cervical artery and vein in addition to the external jugular vein are commonly harvested with this flap. The right neck is the preferred site for harvest given the left-side location of the main thoracic duct. Avoiding injury to these large lymphatic channels is of paramount importance as to avoid iatrogenic lymphedema (85,86).

The choice of recipient site has become a recent topic of debate. Anatomic and distal placement of VLN transfers has been advocated as the preferred choice by authors worldwide. Advocates for anatomic placement in the axilla cite that replacement of functioning nodes into the previous site of axillary node removal will better restore lymphatic flow through lymphatic regeneration, lymphangiogenesis, and axillary scar release (87,88). On the other hand, advocates for distal transfers at the level of the wrist or elbow cite the mechanism of action related to the nodal blood circulation and intrinsic lymphovenous connections creating a local lymphovenous shunt powered by the arterial and venous anastomosis. Long-term mechanism of action related to distal VLN transfers have proven the existence of local lymphatic fluid decompression through these connections (49). Likely, a combination of these two theories provides relief from the symptoms of lymphedema.

Lymphatic grafting

One of the earliest methods of physiologic lymphedema surgery related to the process of providing lymphatic vessels to either bridge an area of obstruction or bypass the region. Sir Harold Gillies provided early descriptions of his famous “waltzing” flap containing lymphatic wicks to bridge either pelvic lymphatic obstruction in lower limb lymphedema or axillary obstruction in upper limb lymphedema (89). Further evaluation of this concept led Baumeister and Siuda to describe and popularize a method of lymphatic grafting to re-establish lymphatic flow in an affected limb (*Figure 7*). In an early evaluation of 37 patients with BCRL, the authors found a majority of patients had volumetric limb measurement improvements up through 3 years of follow-up evaluation. In addition, functional studies indicated significantly improved lymphatic transport indices and decreased episodes of cellulitis (90). Recently, free lymphatic

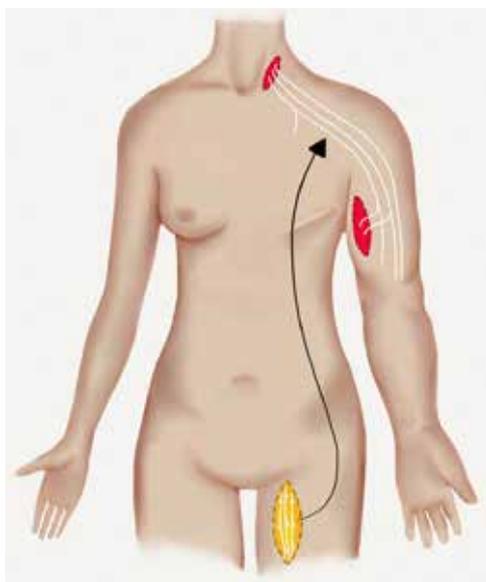


Figure 7 Lymphatic grafts are harvested from the medial aspect of the thigh. Two to three are harvested and are used to bypass an axillary obstruction in upper limb lymphedema.

grafts have been used with reported successful outcomes. In order to improve upper limb lymphedema, Felmerer *et al.* used free lymphatic grafts in 7 patients isolated from the ventromedial thigh. Two or three lymphatic collectors can be identified superficial to the deep fascia and were harvested at lengths of up to 30 cm. These free grafts were anastomosed to ascending lymphatics of the upper limb to a central drainage location in the neck. MRL was used to identify functioning lymphatic structures to aid in surgical identification and dissection. Favorable outcomes were reported with most patients (6 of 7 patients) eliminating the dependence on compression and/or lymphatic drainage physiotherapy (91).

Outcomes of lymphedema treatment

With increasing and growing options related to the surgical treatment of lymphedema, improved understanding of outcomes assessment is necessary in order to critically evaluate an optimal treatment modality. Currently, objective and subjective outcomes parameters are used to determine efficacy of treatment. The most common objective outcomes used include circumference limb measurements, volumetric limb measurements, and rate of treated cellulitis episodes. Information related to these outcomes are

routinely measured and compared given specific treatment algorithms. In addition to these objective outcomes, subjective outcomes assessment has become increasingly important. Variations in limb measurements exist given the dynamic nature of swelling in lymphedema patients. Global patient quality of life and functional assessment may represent an ideal outcomes assessment method, which would allow more accurate tracking of longitudinal outcomes. Validated questionnaires exist for evaluating symptoms related to lymphedema. Condition-specific questionnaires, such as the LYMQOL (92) and the ULL-27 (93), provide a comprehensive assessment of multiple domains that contribute to overall quality of life. A recent study prospectively evaluating patients who underwent VLN transfer for upper limb lymphedema, found that all QoL domains as measured by the LYMQOL validated questionnaire, improved as soon as 1-6 months following VLN transfer, which closely mirrored improvements in limb circumference improvements (94). Ongoing studies related to this aspect of lymphedema care will help to gain an understanding of the utility of these surgical procedures.

Conclusions

Comprehensive lymphedema care encompasses a full spectrum of evaluation and work-up, imaging interpretation, and non-surgical and surgical interventions. A management team focused on optimizing care of this subset of patients will maximize both limb circumference reduction and improvements in quality of life. Novel surgical therapies offer unique solutions and can be implemented individually or in combination with other therapeutic modalities. As the understanding of these surgical therapies improves, surgical decision-making will become increasingly enhanced to optimize objective and subjective outcomes.

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Footnote

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Breast reconstruction following conservative mastectomies: predictors of complications and outcomes

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Abstract: Breast reconstruction can be performed using a variety of techniques, most commonly categorized into an alloplastic approach or an autologous tissue method. Both strategies have certain risk factors that influence reconstructive outcomes and complication rates. In alloplastic breast reconstruction, surgical outcomes and complication rates are negatively impacted by radiation, smoking, increased body mass index (BMI), hypertension, and prior breast conserving therapy. Surgical factors such as the type of implant material, undergoing immediate breast reconstruction, and the use of fat grafting can improve patient satisfaction and aesthetic outcomes. In autologous breast reconstruction, radiation, increased BMI, certain previous abdominal surgery, smoking, and delayed reconstruction are associated with higher complication rates. Though a pedicled transverse rectus abdominis myocutaneous (TRAM) flap is the most common type of flap used for autologous breast reconstruction, pedicled TRAMs are more likely to be associated with fat necrosis than a free TRAM or deep inferior epigastric perforator (DIEP) flap. Fat grafting can also be used to improve aesthetic outcomes in autologous reconstruction. This article focuses on factors, both patient and surgical, that are predictors of complications and outcomes in breast reconstruction.

Keywords: Breast reconstruction; complications; outcomes; tissue expander/implant; autologous reconstruction

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Introduction

Breast reconstruction following mastectomy can be performed using alloplastic techniques, most commonly tissue expansion followed by implant placement, or autologous techniques in which numerous flap options exist. The goal of breast reconstruction surgery, whether autologous or alloplastic, is to create a breast mound that appears as natural as possible under clothing, and ideally without clothing as well (1). To achieve this goal, certain patient factors and surgical factors that can influence outcomes and complication rates must be taken into consideration.

Patient factors affecting complication rates and outcomes in breast reconstruction that are typically investigated

include radiation, chemotherapy, smoking, obesity, age, and medical comorbidities (1-3). Surgical factors common to both alloplastic and autologous reconstruction, such as the timing of the reconstruction and the use of fat grafting, have an effect on outcomes and complications (4-6).

In alloplastic reconstructions, patients are exposed to less surgical risk, fewer scars, less donor site morbidity and fewer irreversible consequences. However, surgical factors like implant type, number of surgical stages, and use of an acellular dermal matrix (ADM) can influence outcomes (7-10). Typical complications and their frequencies in four large series of alloplastic based reconstruction are displayed in *Table 1*.

The optimal method of breast reconstruction differs from patient to patient, however reconstruction with autologous tissue can provide a long lasting, natural

feeling breast mound (11). An obvious surgical factor that influences outcomes in autologous reconstruction is the type of autologous flap used. Complication rates in seven large series of autologous reconstruction patients are presented in *Tables 2 and 3*.

This article will describe patient factors and surgical factors that are predictors of outcomes and complications in alloplastic and autologous breast reconstruction.

Tissue expander/implant based reconstruction

Patient factors influencing complications and outcomes

Radiation

Radiation adversely impacts expander/implant based breast reconstruction. Regardless of the timing of administration of radiation therapy, expander placement in a radio-treated field, radiation to temporary expanders postmastectomy, or radiation postmastectomy to implant, patients are at an increased risk of complications and reconstructive failure (2,22). Capsular contracture (23,24), infection (25) and wound-related complications are more common (1), with a wide spectrum of reported complication rates, ranging from 5% to 48% (26). Both aesthetic satisfaction and general satisfaction rates appear to be similar in expander/implant based reconstruction patients with and without radiotherapy (23,27). However, a long-term multicenter analysis demonstrated that patients receiving radiation had significantly lower satisfaction with the surgical outcome, as well as their psychosocial, sexual, and physical well-being (28). The increased complication rate does not exclude a patient requiring radiotherapy from an expander/implant based reconstruction, but the potential for the requirement of an autologous/prosthetic combination, in the form of a latissimus dorsi flap with implant, or a completely autologous reconstructive approach, should be discussed with the patient (1,2).

Chemotherapy

Both neoadjuvant and adjuvant chemotherapy regimens have been investigated in the setting of postoperative complications after mastectomy and breast reconstruction. It appears that neither neoadjuvant (2,13,29,30) nor adjuvant (12,13,30) chemotherapy increase the rate of complications or implant failure in patients undergoing postmastectomy expander/implants breast reconstruction, including in patients who undergo tissue expansion concomitantly. Bevacizumab in particular has been shown to

affect surgical wound healing (31). To date, it has not been shown to increase complications in breast reconstruction, though evidence is limited (32). It is suggested to wait 6-8 weeks after completing bevacizumab therapy before performing surgery to minimize risks of complications (31).

Smoking

Smoking is universally considered to be a risk factor for surgical complications. For patients undergoing expander/implant based breast reconstruction, smoking is an independent risk factor for the development of perioperative complications and is associated with an increased risk of reconstructive failure (2,13,33). The rates of mastectomy skin flap necrosis and infectious complications are significantly higher in smokers compared to non-smokers (33). Complication rates as high as 37.9% in smokers have been reported (33), a 2-3 fold increase compared to non-smokers (13,33). Smokers are also five times more likely to experience reconstructive failure (13). The rate of complications in ex-smokers, defined as patients who have stopped smoking between 1 and 12 months preoperatively, can also be higher than non-smokers (33). The significant association between cigarette smoking and complications in the setting of tissue expander/implant reconstruction necessitates advising patients on smoking cessation and informing them of the increased risks.

Obesity/body mass index (BMI)

Obesity is defined as a BMI of 30 or greater. Obesity is an independent risk factor for the development of perioperative complications in patients undergoing expander/implant based reconstruction (13,14). Patients who are obese have nearly twice the risk of developing a perioperative complication (13). The risk of reconstructive failure is seven times greater in obese patients when compared to non-obese patients. Overweight patients, defined as a BMI of 25 or greater, are also at an increased risk of postoperative complications and reconstructive failure, though their risk is notably smaller (2,4,9).

Breast size

Some genetic factors that contribute to breast size are shared with those that influence BMI. Though the extent to which they are related is not clear, they are covariates (34). In patients undergoing expander/implant based reconstruction, large preoperative breast size, a cup size of D or larger, may be associated with an increased risk of complication and an increased risk of reconstructive failure (25). However, the

Table 1 Complication rates in tissue expander/implant reconstruction

Publication	Total patients	Total expanders	Unilateral		Total complications, N (%)	Failed expansion, N (%)	Expander deflation, N (%)	Mastectomy skin flap necrosis, N (%)		Hematoma, Seroma, Infection, N (%)	
			Bilateral	Bilateral				Mastectomy skin flap necrosis, N (%)	Mastectomy skin flap necrosis, N (%)	Hematoma, Seroma, Infection, N (%)	Hematoma, Seroma, Infection, N (%)
Spear <i>et al.</i> 1998 (11)	142	171	113	29	-	12 (7.0)	3 (1.8)	14 (8.1)	2 (1.0)	-	8 (4.7)
Cordeiro <i>et al.</i> 2006 (12)	1,221	1,522	920	301	(5.8)	2 (0.1)	2 (0.1)	45 (2.0)	10 (0.4)	5 (0.2)	58 (2.5)
McCarthy <i>et al.</i> 2008 (13)	884	1,170	597	287	206 (17.6)	2 (0.2)	-	102 (8.7)	-	-	57 (4.9)
Colwell <i>et al.</i> 2014 (14)	274	471	-	-	60 (12.7)	-	-	25 (5.2)	8 (1.7)	8 (1.7)	16 (3.3)

Table 2 Complication rates in autologous reconstruction

Publication	Total patients	Total flaps	Unilateral		Total complications, N (%)	Total flap loss, N (%)	Partial flap loss, N (%)	Arterial occlusion, N (%)		Venous occlusion, N (%)		Fat necrosis, N (%)
			Bilateral	Bilateral				Arterial occlusion, N (%)	Arterial occlusion, N (%)	Venous occlusion, N (%)	Venous occlusion, N (%)	
Blondeel <i>et al.</i> 1999 (15)	87	100	74	13	-	2 (2.0)	7 (7.0)	2 (2.0)	4 (4.0)	-	6 (6.0)	
Chang <i>et al.</i> 2000 (16)	718	936	-	-	328 (45.7)*	8 (0.9)	13 (1.4)	-	-	-	55 (5.9)	
Gill <i>et al.</i> 2004 (17)	609	758	460	149	229 (30.2)*	4 (0.5)	19 (2.5)	4 (0.5)	29 (3.8)	29 (3.8)	98 (12.9)	
Mehrara <i>et al.</i> 2006 (18)	952	1,195	695	250	266 (27.9)*	6 (0.5)	26 (2.3)	9 (0.8)	15 (1.3)	15 (1.3)	134 (11.2)	
Selber <i>et al.</i> 2006 (19)	500	569	431	69	119 (20.9)*	2 (0.3)	9 (1.6)	1 (0.2)	-	-	19 (3.3)	
Damen <i>et al.</i> 2013 (20)	285	406	164	121	120 (42.1)*	2 (0.5)	10 (3.5)	2 (0.5)	7 (1.7)	7 (1.7)	14 (3.4)	
Fischer <i>et al.</i> 2013 (21)	849	1,303	395	454	542 (63.9)*	18 (2.1)	7 (0.8)	-	-	-	49 (5.8)	

* , percentage reported using number of patients as denominator; ♦ , percentage reported using number of flaps as denominator.

Table 3 Complication rates in autologous reconstruction

Publication	Total patients	Total flaps	Mastectomy skin flap necrosis, N (%)		Hematoma, Seroma, Infection, N (%)	Donor site* complication, N (%)	Abdominal wall* laxity/hernia, N (%)	Delayed donor* site healing, N (%)
			Mastectomy skin flap necrosis, N (%)	Mastectomy skin flap necrosis, N (%)				
Blondeel <i>et al.</i> 1999 (15)	87	100	1 (1.0)	2 (2.0)	1 (1.0)	3 (3.0)	1 (1.0)	2 (2.0)
Chang <i>et al.</i> 2000 (16)	718	936	96 (10.3)	16 (1.7)	38 (4.1)	17 (1.8)	41 (5.7)	11 (1.5)
Gill <i>et al.</i> 2004 (17)	609	758	-	14 (1.8)	35 (4.6)	21 (2.8)	5 (0.7)	-
Mehrara <i>et al.</i> 2006 (18)	952	1,195	-	19 (1.6)	-	110 (9.2)	29 (3.0)	-
Selber <i>et al.</i> 2006 (19)	500	569	17 (3.0)	3 (0.5)	7 (1.2)	20 (3.5)	11 (1.9)	19 (3.3)
Damen <i>et al.</i> 2013 (20)	285	406	15 (3.7)	19 (4.7)	-	7 (2.5)	10 (3.5)	13 (4.6)
Fischer <i>et al.</i> 2013 (21)	849	1,303	-	-	45 (3.9)	64 (7.5)	29 (3.4)	154 (18.2)

* , percentage reported using number of patients as denominator.

effect of breast size has not been isolated from BMI and therefore it is not yet established whether large breast size on its own contributes to complications in these patients (2).

Age

Expander/implant reconstruction rates have been increasing in the elderly (28). Age is another factor that is universally associated with poorer outcomes following surgical procedures. Limited data exists on the relationship between age and outcomes in expander/implant based breast reconstruction. Age might be an independent risk factor for complications, though it does not appear to be a significant predictor of reconstructive failure (13). Patients older than 65 may have an increased risk of perioperative complications when compared to younger patients (13).

Medical comorbidities

Hypertension

In a review of 1,170 consecutive expander/implant reconstructions (884 patients) hypertension was found to be an independent risk factor for perioperative complications (13). In this series, a patient was classified as having hypertension if they required medical therapy. The risk was quantified as being two times greater than in a patient without hypertension. The odds of premature removal of a tissue expander and/or explantation of a permanent implant were four times higher in the hypertensive patient (13).

Diabetes mellitus

No significant associations between implant infection and diabetes have been found (13,35). Diabetes has not been shown to be an independent risk factor for the development of postoperative complications or for reconstructive failure (2,13,22). However, it is still advised that breast cancer patients attempt glycemic control in the perioperative period (2).

Prior breast conserving therapy (lumpectomy/irradiation combination)

Expander/implant based reconstruction may be an option in carefully selected patients with cancer recurrence following lumpectomy with irradiation. Patients who have undergone breast conserving therapy are at higher risk of early complications, of higher capsular contracture grade, and slightly inferior aesthetic results (36). Patients with severe breast deformity, multiple scars on the irradiated breast, or with tight/poor soft tissue might be appropriate candidates for the use of a latissimus dorsi flap to cover the prosthesis or for autologous reconstruction (36,37).

Mastectomy type: nipple sparing, skin sparing, skin reducing

The proportion of patients undergoing nipple sparing mastectomies (NSM) is increasing due to its perceived aesthetic benefits (38). The oncologic safety of NSMs is the greatest concern associated with this procedure, as nipple areola complex (NAC) involvement is related to tumor size, distance from the NAC, multicentricity, nuclear grade and lymph node status (38). A percentage of patients undergoing this procedure will have occult disease in the NAC [reported at 9.1% in one series of 66 patients (38)]. Wound healing problems within the NAC and either partial or complete NAC loss are unique complications to this procedure. Patients with larger breasts are at greater risk of nipple necrosis (39). The overall rate of complications in NSMs appears to be similar to that in skin-sparing mastectomies (SSM) (39). NAC preservation is associated with favorable results in aesthetic outcome, nipple sensitivity, and patient satisfaction (40).

SSMs are the conventional approach where the skin ellipse surrounding the NAC is extended (41). SSM is the most common type of mastectomy surgery performed for breast cancer treatment and does not have any unique complications.

Skin reducing mastectomies (SRMs) are performed using a Wise Pattern incision when skin envelope reduction is required (41). The vertical scar approach is an alternative to the Wise pattern technique (41). SRMs are often used for large breasts which in turn are at an increased risk of complications and reconstructive failure (25).

Surgical factors influencing complications and outcomes

Implant texture, shape, and material

Saline and silicone gel implants are available as the final implant material for expander/implant based postmastectomy reconstruction. All implant models have a bladder, or outside shell, made of solid silicone. The shell can be either textured or smooth. Modern expanders are textured to help prevent migration and early capsular contracture. Both saline and silicone implants can be either round, or anatomically shaped (like a teardrop). Patient satisfaction and aesthetic outcome does not appear to be affected by the shape (round or anatomic) of the implant used in the reconstruction (42,43).

Silicone gel implants are traditionally thought to provide a softer, more natural feeling breast when compared to saline implants (3). Decreased visible wrinkling has been

thought to be a benefit of silicone implants, however this advantage is not always apparent (44). Patients receiving silicone implants have greater satisfaction with their breasts than those with saline implants (7,8). Silicone is no longer believed to be linked to immunologic (45) or other systemic diseases (3), however degradation of the silicone bladder over time will cause an implant to rupture (1). Thus, due to the possibility of silicone leakage into local tissues, some patients may choose saline implants for peace of mind.

Timing of reconstruction

Alloplastic reconstruction can be performed concomitantly with the mastectomy (immediate), or weeks, months or years later (delayed). While the timing of reconstruction can depend on many factors, immediate reconstruction is generally preferable as the mastectomy skin flaps are pliable and the native inframammary fold is present (1). The greatest benefit of immediate reconstruction could be the potential for fewer operations.

The impact of the timing of alloplastic breast reconstruction on outcomes is not clear. In a prospective, multicenter study, Alderman *et al.* found complications (both total and major) to be associated with immediate reconstructions (4). They suggested that the higher complication rate in the immediate setting might be due to any additional complications from the mastectomy procedure. In comparison, a review of a prospectively maintained database, from a single center examining only expander/implant reconstruction, did not find the timing of reconstruction to be a significant predictor of reconstructive failure (13). Satisfaction with immediate reconstruction has been reported to be greater than delayed reconstruction (5).

Single-stage breast reconstruction

Single-stage breast reconstruction is appropriate in a patient with small, non-ptotic breasts, and good quality skin and muscle (3). An implant is placed at the time of mastectomy and an ADM is used for support and implant coverage. This is also known as direct-to-implant reconstruction. The disadvantage of a direct-to-implant reconstruction is that aesthetic outcomes might not be as good as tissue expander/implant reconstructions, and often a revision procedure is required (3). Increasing breast cup size is associated with a need for early revision surgery (46). When direct-to-implant reconstruction is used in the right patient, both complication rates and revision rates appear to be comparable to two-staged tissue expander/implant based reconstruction (10). The role for this procedure in

patients who will require post-mastectomy radiation is still unclear (46).

Use of an acellular dermal matrix

Traditional submuscular placement of a tissue expander requires the elevation of, and coverage with, the pectoralis major and serratus anterior (and sometimes the rectus abdominis). The use of an ADM has been increasing (47), whereby the pectoralis muscle is used to cover the prosthesis anteromedially, and the ADM is used for coverage laterally. This technique allows placement of tissue expanders with greater intraoperative fill volumes, and therefore fewer expansions are required before exchange for the permanent implant (47). In addition, it might have the potential to reduce the rate of encapsulation (48,49).

The use of ADM avoids elevation of the serratus anterior, which was once thought to decrease post-operative pain. However, a multicenter, blinded, randomized controlled trial did not demonstrate any reduction in postoperative pain when using ADM (50). In addition, an increased risk in complications has been demonstrated when using ADM, in particular, seroma (9,47,51), infection (51,52), and reconstructive failure (9,51) rates.

Use of an autologous flap

Tissue expansion/implant based reconstruction requires enough of a healthy skin envelope for a tension-free closure. The native skin and/or muscle envelope may not be adequate to undergo expansion if there are multiple scars, previous radiation injury, or if there was a large skin resection during mastectomy. In these cases, the use of an autologous flap (most commonly the latissimus dorsi myocutaneous flap) can provide coverage of the expander, and eventually implant. Patients requiring a salvage mastectomy after failed lumpectomy/irradiation can benefit from a latissimus dorsi/implant reconstruction (53).

Use of an autologous flap in previously irradiated breasts appears to reduce the incidence of implant related complications (54). The addition of an autologous flap to the implant based procedure increases the length and complexity of the operation, and adds a donor site with potential morbidity (3). In previously irradiated patients, complication rates and reconstructive failure rates in latissimus dorsi flap plus implant reconstruction are not statistically significant when compared to purely abdominal based autologous reconstruction (55). The most common complication when using a latissimus dorsi flap is a dorsal seroma (56).

Use of fat grafting

Fat grafting is an important tool to manage contour deformities in breast reconstruction. It can smooth out a “step-off” between the chest wall and implant, and help camouflage implant rippling. Fat grafting might help to achieve greater satisfaction, improve surrounding skin quality, and decrease implant exposure in patients who undergo implant based reconstruction after radiation (57,58). However, multiple procedures are often necessary, and potential complications include infection, fat necrosis, and oil cysts. Concerns have also been related to the theoretical interference with breast cancer detection (59), though the American Society of Plastic Surgeons task force did not find evidence to support this (60).

Volume of implant-based breast reconstruction practice

High volume implant-based breast reconstruction teams (surgical oncologist and plastic surgeon) tend to have lower complication rates when compared to low volume teams (where high volume teams had performed greater than 300 procedures together) (61). Low volume teams (fewer than 150 procedures performed together) were shown to have higher rates of infection (61). However other studies have failed to show this relationship between complications and surgical team volume (62).

Autologous reconstruction

Patient factors influencing complications and outcomes

Radiation

Radiation appears to negatively affect certain outcomes in autologous breast reconstruction. Radiation contributes to poor cosmesis (63,64), though does not appear to increase major complication rates (63,65). Flaps experience a higher rate of fat necrosis when irradiated. When irradiated muscle-sparing free transverse rectus abdominis myocutaneous (TRAM) flaps were compared to irradiated deep inferior epigastric perforator (DIEP) flaps, rates of fat necrosis were similar (66).

Challenges exist when radiotherapy is required after reconstruction (67). The autologous breast mound can compromise the design and delivery of radiotherapy (68), however increased tumor recurrence and worse clinical outcomes have not been demonstrated (1). Nevertheless, it has been suggested that the technique of delayed-immediate reconstruction (explained below under “Timing of Reconstruction”) can be used to balance aesthetic outcomes

with the ability to provide optimal radiotherapy (67).

Chemotherapy

Neoadjuvant chemotherapy does not seem to be a predictor of flap loss, microvascular complications (18), or reoperation rate (69). Similarly, fascial healing at the donor site does not appear to be adversely affected (18). However, it has been associated with an increase in overall complications (70), early complications, in the form of wound healing difficulties, and late complications, such as fat necrosis (18). The timing of chemotherapy does not seem to have a significant effect on surgical outcomes (30).

Smoking

The effect of smoking on wound healing and blood supply is known to be harmful. In autologous breast reconstruction, studies have confirmed the deleterious relationship between smoking and post-operative complications (17,19), however the specific complications demonstrated have been variable. Smoking has been associated with an increased risk of wound infection (19), mastectomy flap necrosis (19,71,72), abdominal flap necrosis (19,71,72), abdominal hernia (71), and fat necrosis (19). On the other hand, some studies have not demonstrated an association between smoking and complications (4,18). Regardless, many reconstructive surgeons insist their patients quit smoking before proceeding with an autologous reconstruction.

Obesity/BMI

Patients with a higher BMI are prone to complications (9). Risks increase with the patient's BMI, and obese patients have a greater risk of overall complications when compared to normal weight and overweight patients (73). This increased risk has partly been attributed to intraoperative technical difficulty, as obesity is associated with longer operative times in abdominally based autologous reconstruction (74). Increased health care resource consumption and greater hospital costs also appear to be consequences of the increased perioperative risk in these patients (74).

Overall, minor, early, and late complications are shown to be greater in the obese patient, with a 1.5- to 2-fold increase in flap complications (16) and a 3-fold increase in donor site complications (18). While the majority of overweight and even obese patients can complete autologous breast reconstruction successfully, they should be appropriately counselled that both the risk of failure, and complication rates are higher than normal weight

patients (16,18). On the other hand, a retrospective analysis comparing implant reconstruction versus abdominal-based free flap reconstruction concluded that obese patients, particularly morbidly obese patients, experience lower failure rate with autologous reconstruction rather than implant reconstruction (75).

Age

In general, increasing age is associated with poorer outcomes following surgical procedures. Limited data exists on the relationship between age and outcomes in autologous breast reconstruction. Older patients are more likely to stay in hospital longer than younger patients (76) after autologous breast reconstruction. Rates of post-operative complications, including flap thrombosis (77), do not appear to be significantly different in elderly patients (76). Autologous breast reconstruction can be performed safely in the elderly (76), and age by itself should probably not be viewed as a risk factor for complications. However, older patients are more likely to have other medical comorbidities, and therefore this should be taken into account.

Other medical comorbidities

Hypertension

Hypertension is a risk factor for complications in the setting of autologous breast reconstruction. Hypertension is associated with both minor and major surgical complications (21), and with both breast and abdominal (donor) complications (17). It is also an independent predictor of unplanned readmission after autologous reconstruction, with the risk of readmission quantified as being at least 2 times greater than in a patient without hypertension (78).

Diabetes mellitus

The predisposition of diabetics to infection (79) and microvascular and macrovascular disease (79) are valid reasons to expect an increased rate of complications in these patients. Diabetes has been correlated with both minor surgical complications and post-operative medical complications (21). However, in other studies, diabetes mellitus has demonstrated trends toward association with complications but no statistically significant associations (17,18). Nevertheless, it is sensible for a breast reconstruction patient to attempt glycemic control in the perioperative period.

Mastectomy type: nipple sparing, skin sparing, skin reducing

A high quality autologous reconstruction can be obtained using either a NSM or SSM technique (80). With the preservation of the original skin envelope, inframammary

fold, and the NAC in a NSM, the flap can be used to recreate the volume and shape of the original breast. SSM and immediate autologous reconstruction is an oncologically safe procedure (81). For patients undergoing NSMs, aesthetic results are significantly better when compared to SSM (82). However, in NSMs, anastomosis of the pedicle to the internal mammary artery can be difficult due to limited exposure (83), and traction during the operation can increase the chance of partial or complete nipple areola necrosis. While cancer recurrence in the NAC remains a concern, autologous reconstruction after NSM is a reasonable option in the appropriate patient (84).

Prior abdominal surgery

When planning to use an abdominal flap for autologous reconstruction, the finding of an abdominal scar on physical exam could potentially alter the approach to breast reconstruction due to concerns of flap loss and/or donor site complication. Prior abdominal surgery in patients undergoing TRAM based breast reconstruction is associated with minor, major, and overall complication rates (18). Most of the major complications involve partial flap loss (18). Donor site complication rates, including hernia/laxity and wound healing, are also found to be greater. Careful patient selection is especially important in these patients, as smokers with a subcostal scar have been found to have a greater than 6-fold increase in donor site complications (85).

Surgical factors influencing complications and outcomes

Free flap choice

The pedicled TRAM is most common method for autologous breast reconstruction in the United States (1,86,87). Common free tissue transfer options for reconstruction use tissue from the abdomen in the form of either a TRAM, DIEP, or superficial inferior epigastric artery (SIEA) flap. Autologous reconstruction can also be performed using tissue from the thigh or buttock in the form of transverse upper gracilis (TUG), superior gluteal artery perforator (SGAP), inferior gluteal artery perforator (IGAP), or profunda artery perforator (PAP) flaps. The distinct advantage of an autologous reconstruction is the ability to replace “like with like”, and provide the patient with a lifelong, natural feeling breast.

When comparing outcomes of pedicled TRAM reconstructions to free flap reconstructions, the incidence of complications (overall, flap-related and nonflap-related) was greater in free flaps in a review of over 2,000 flaps (88).

However, after regression modelling these differences did not appear to be significant. The pedicled TRAM tends to be associated with more fat necrosis than free abdominal flaps (89,90) and with an increased risk of partial and total flap loss in obese patients (91). To decrease these types of complications, especially in “high risk” patients, a vascular delay procedure can be used, where the inferior vascular pedicle is ligated 2 to 3 weeks before reconstruction (92).

The criticism of the free TRAM flap has been related to morbidity from sacrificing the rectus muscle at the donor site (93,94). Patients reconstructed with a free TRAM flap have decreased abdominal strength and have twice the risk of an abdominal bulge or hernia compared to DIEP reconstructions (95). The DIEP flap is thought to offer patients decreased donor site morbidity. Although many studies are able to demonstrate the advantage of the DIEP with respect to the donor site objectively, changes in the ability to perform activities of daily living do not appear to be significantly different from TRAM patients (96). In a systematic review of studies comparing DIEP and free TRAM flaps, DIEP flaps were found to have a higher rate of flap-related complications, and a 2-fold increase in the risk of fat necrosis and flap loss compared to free TRAM flaps (95). Therefore the reconstructive advantage of the DIEP flap has remained uncertain, in general seems to be less reliable than the free TRAM flap, and has gained only cautious acceptance among many reconstructive surgeons (95).

The major benefit of the SIEA flap is the ability to harvest abdominal tissue without violating the abdominal wall fascia, therefore leaving both the fascia and rectus muscle intact and minimizing donor site morbidity (97). On the other hand, the flap has a smaller pedicle length and diameter (98), and flap size is limited to only half of the abdominal skin island for reconstruction (1). When compared to free TRAM and DIEP flaps, use of the SIEA flap has also been found to be a risk factor for flap thrombosis (77), and is associated with an increased risk of fat necrosis (1). The significantly higher rate of thrombotic complications associated with the SIEA flap limits the indications for this type of reconstruction.

Autologous reconstruction using tissue from the thigh or buttock (TUG, SGAP, IGAP, PAP) is less common, typically only indicated in patients who require a small to medium size breast reconstruction, have either abdominal scarring or limited abdominal tissue, and excess tissue in the thigh/buttock region. The literature describing outcomes and complications using autologous thigh/buttock flaps is in its infancy compared to abdominal based flaps.

Timing of reconstruction

Similar to alloplastic reconstruction, autologous reconstruction can be performed either immediately or in a delayed fashion with respect to the mastectomy. Immediate reconstruction potentially exposes the patient to fewer operations, can save resource costs (99,100), and gives the patient the best chance at a good aesthetic result (101). In delayed reconstruction, mastectomy skin flaps are often scarred and less compliant (1), and a higher rate of free flap thrombosis has been found to occur (77). However similar rates of both major and minor complications have been reported between patients undergoing either immediate or delayed reconstruction with a TRAM free-flap (102).

The requirement of post-mastectomy radiotherapy has been considered to be a relative contraindication to immediate reconstruction (103). An alternative strategy, known as “delayed-immediate” autologous reconstruction, has been used (104). This is a two stage approach in which a filled tissue expander is placed after mastectomy. If radiotherapy is not required, definitive autologous reconstruction is performed. If radiotherapy is required, the expander is deflated, radiotherapy is administered, the expander is re-inflated, and autologous reconstruction performed (104). When compared to “delayed” reconstruction, “delayed-immediate” has been shown to have similar flap-related complication rates, decreased rates of revision surgery (105), and a better aesthetic outcome (106).

Fat grafting

Fat grafting can be used to address step-off deformities (between the chest wall and the flap), intrinsic deformities (e.g., from fat necrosis) and extrinsic deformities (e.g., from radiation or scar contracture) (6). Fat grafting can also be used to help augment size in a volume-deficient reconstruction, therefore allowing certain patients with barely enough soft tissue for a microvascular free flap to undergo autologous reconstruction (107). In a review of mostly autologous reconstructed patients, aesthetic outcomes were significantly improved with fat grafting, though half of the patients required more than one procedure, and complications occurred in approximately 6% of procedures (6).

Volume of autologous breast reconstruction practice

High volume autologous breast reconstruction centers tend to have lower complication rates when compared to low and medium volume centers (where high volume was “greater

than 44 procedures per year”) (108). Both surgery-specific and systemic complications were inversely related to volume of reconstruction at the center (108). When examining microsurgical cases, low-volume centers had a 2-fold increase in surgery-specific complications when compared to high-volume centers (108).

Summary

Alloplastic breast reconstruction outcomes can be negatively affected by certain patient factors. Pre- or post-mastectomy radiotherapy, smoking, increased BMI, hypertension, and prior breast conserving therapy are all associated with an increase in complications and/or inferior outcomes. Silicone gel implants provide a softer, more natural feeling breast and these patients appear to have greater satisfaction than those with saline implants. Patient satisfaction and aesthetic outcomes are not different between reconstructions that use either round or anatomically shaped implants. Immediate reconstruction, and the use of fat grafting techniques are likely to improve aesthetic outcomes.

Autologous breast reconstruction outcomes are affected in a deleterious manner by radiation, increased BMI, certain previous abdominal surgery, delayed reconstruction, smoking, hypertension, and most likely diabetes. When these risk factors are present, a free microvascular reconstructive technique is preferred over a pedicled flap for patients undergoing autologous reconstruction. Reduced donor site morbidity can be seen in DIEP flap reconstruction, compared to TRAM flap, but is more obvious in bilateral reconstructions. The use of the SIEA flap in breast reconstruction is limited due to the higher rate of vessel thrombosis. Other types of free flaps, TUG, SGAP, IGAP and PAP flaps, tend to be options when abdominal tissue is not available. Fat grafting can be used to improve aesthetic outcomes, and high volume centers are associated with fewer complications, especially in free flap reconstruction.

Offering patients an opportunity for breast reconstruction is an important component of the treatment for breast cancer. There are many options for both alloplastic and autologous reconstruction. Ultimately, patient and surgical risk factors should be considered in concert with the patient’s wishes when deciding upon a reconstructive strategy.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Stem cell and tissue engineering in breast reconstruction

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Abstract: Breast cancer worldwide is the most common cancer in women with incidence rate varying from geographic areas. Guidelines for management of breast cancer have been largely established and widely used. Mastectomy is one of the surgical procedures used treating breast cancer. Optionally, after mastectomy, appropriately selected patients could undergo breast reconstruction to create their breast contour. Many techniques have been used for breast reconstructive surgery, mainly implant-based and autologous tissue reconstruction. Even with highly-experienced surgeon and good-quality breast and autologous substitute tissue, still there could be unfilled defect after mastectomy with reconstruction. Stem cell, in particular, adipose-derived stem cell residing within fat tissue, could be used to fill the imperfection providing optimal breast shape and natural feeling of fat tissue. However, whether surgical reconstruction alone or in combination with stem cell and tissue engineering approach be used, the ultimate outcomes are patient safety first and satisfaction second.

Keywords: Stem cell; adipose-derived stem cell; tissue engineering; breast reconstruction

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Introduction

Breast cancer is the most common form of female cancers, accounting for approximately 30 percent of all cancerous case in women. There were 1.4 million new cases of breast cancer amongst women worldwide, an increase of 4% over ten years (1,2). With advanced technological development in screening, detection, and treatment of breast cancer, survival rate has been continuously increasing with a current 5-year survival rate at nearly 90% in the United States (3). Approximately 40 percent of patients will undergo mastectomy as part of the surgical treatment for their breast cancer (4,5). By increased improvement in early detection and survival, mastectomy is considered more to have a negative impact on body image together with sexual function with longer life. Breast reconstruction following mastectomy for breast cancer is currently an optional treatment which helps women to recover from the physical and psychological emotion of breast cancer management. A systematic review presented that international breast reconstruction rates ranged widely from 4.9% to

81.2% among different countries (6). Rates of breast reconstruction in the United States and United Kingdom are estimated around 25% which is gradually mounting (7). Breast reconstruction may be performed as a simultaneous or delayed procedure, using breast implants, autologous tissue or a combination of the two. Cell-based approach and tissue engineering also play an advantageous role in breast reconstruction, particularly in the context of increased breast circumference and improved natural sensation of the outcomes of breast reconstruction. Conventional fat grafting or cell-assisted lipotransfer method mainly depends on adipose-derived stem cells resulting in superior and durable outcomes. Tissue engineering in breast reconstruction is not limited solely to cell-based techniques. To use acellular dermal matrix enables surgeon to modify the breast pocket in desired position for the placement of expander or permanent implant leading to optimal breast contour and patient satisfaction. In this review, stem cells principles and tissue engineering will be discussed. Furthermore, the potential benefits of these cells and tissue-constructed material will be presented. The use of stem

cell and tissue engineering approach in practical breast reconstruction will be explored and elaborated.

Stem cell principles

Cells are the basic structural and functional units in biology. In mammalian development, it begins with the formation of unicellular zygote, which arises from the fertilization process between a sperm and an egg from the paternal and maternal origins respectively. A total of 10^{14} cells have been estimated to reside in the human body, and which can be categorized into approximately 230 specialized cell types according to their functional phenotypes (8). Stem cells are cells which possess an ability to maintain self-renewal or differentiate to any specialized cells. The stemness of every cell type arises from the inner cell mass (ICM) cells of the blastocyst in an embryonic stage (9,10). Later on, these ICM cells give rise to all of different stem cell types or differentiated mature cells, forming tissues and organs. Characteristically, the particular stem cells have a restricted capacity to turn into only specific mature cells which phenotypically characterize the tissue where they reside. For instance, hematopoietic stem cells and epidermal stem cells differentiate into blood cells and skin cells, respectively.

The initial concept of stem cell biology originated from the study back in 1961. James Till and Ernest McCulloch published serendipitous findings proving the existence of stem cells in hematopoietic tissues (11). Subsequent evidence of stem cells in the hematopoietic system has also been demonstrated in peripheral blood and bone marrow (12,13). In addition, clinical experiments also proved the promise of bone marrow transplantation for the treatment of cancer and non-cancer hematopoietic diseases (14,15). Taken all together, these findings in hematopoietic stem cells have led to an opening of the stem cell biology paradigm.

In the basic principle of stem cell, stem cell fates and states are of importance and considered as a core of stem cell biology. Understanding cell-fate decisions in stem cell population is important for translating stem cell biology towards clinical medicine. While much still remain to be understood, the four cell-fate options for stem cell have been described (16), including self-renewal, differentiation and lineage-specification, programmed cell death or apoptosis, and quiescence. Self-renewal is division with maintenance of the undifferentiated state whereas quiescence is the undifferentiated state with no division.

Furthermore, stem cells also undergo changes resulting

in loss of stem cell state, either differentiation or death (apoptosis). These cell-fate decisions are regulated by both cell-intrinsic mechanisms and cell-extrinsic signals from the niche, the microenvironment that stem cells populate. In addition, the developmental potency of stem cell can be classified into four categories according to differentiated progeny states, including totipotency, pluripotency, multipotency, and unipotency.

Resources of stem cells

Resources of stem cells come from many sources in humans. They are categorized as adult stem cells, umbilical cord blood stem cells, embryonic germ cells, and embryonic stem cells. Besides, recently, reprogrammed stem cells and partially reprogrammed cells have also been created and identified. Briefly, adult stem cells or somatic stem cells populate, proliferate and generate differentiated offspring in a tissue or organ (17). Adult stem cell population in human body has been identified in, for instance, bone marrow, intestine, brain, epidermis, hair follicles and adipose tissue. They are able to divide and differentiate into mature cells when needed in a particular tissue.

Human embryonic stem (ES) cells

In the past decades, one key scientific discovery was the derivation of mouse and human embryonic stem cells. Evidence has shown that these ES cells could be manipulated to generate various cell types from all three germ layers *in vitro* and *in vivo*. Since the discovery of mouse ES cells in 1981 by two independent research groups (9,10), great attention from scientists has been focused towards insights into the biology of stem cell development. The consequent intellectual skeleton of human ES cell biology was originated and enabled from the comprehension and conception of mouse ES cells. In 1998, James Thomson and colleagues published the first derivation of human ES cells from human blastocysts (18). The established human ES cell lines expressed cell surface markers which characterized undifferentiated cells, including stage-specific embryonic antigen (SSEA)-3, SSEA-4, TRA-1-60, TRA-1-81, and alkaline phosphatase. In sum, these ES cell lines should hold gigantic promise in studying human developmental biology, drug discovery, transplantation, and regenerative medicine. The derivation of pluripotent human ES cells has opened new exciting paradigm for stem cell biology; however, there were still concerns about potential risks,

such as uncontrolled or misdirected growth, and ethical controversy associated with the source of human ES cells.

Following the characterization of first human ES cell lines in 1998, standard protocols have been steadily developed towards clinical-grade applications, including maintenance of these cells under animal-derived-free and defined culture components (19,20). Moreover, essential protocols for induced differentiation processes of human ES cells into various differentiated cell lineages such as neurons, keratinocytes, and cardiomyocytes have been largely optimized (21-23). In addition, by integrating with an engineering approach, several of these envisioned applications of ES cells would require production of high number of stem cells and their derivatives in a scalable process, effective automated bioprocessing systems are required to achieve a large-scale production and to reduce the amount of associated labor energy and time (24,25). Preclinical studies in animals have proved that derivatives of differentiated human ES cells could provide functional replacements in diseased tissues, typically marked by loss of cells, such as for Parkinson's disease, macular degeneration and cardiac insufficiency following infarction (26-28), and clinical trials have been approved for cellular therapy in humans for macular degenerative disease (29). Despite the promise of ES cells in regenerative medicine, there are essentially two major risks of immunogenicity and tumorigenicity which are potentially associated with clinical uses of ES cells. Besides these biological concerns, controversy about ethical issues of using human ES cells has been broadly debated (30).

Induced pluripotent stem cells

In 2006, Yamanaka astonished the world by demonstrating that transcription factor-induced cell reprogramming was achievable in somatic cells (31). The enforced expression of four key transcription factors, Oct4, Sox2, Klf4, and c-Myc, could reprogram mouse fibroblasts to pluripotent states. These reprogrammed pluripotent cells expressed similar characteristics to ES cells and obtain comparable developmental potential as ES cells. "Induced Pluripotent Stem Cells or iPSCs" was first used to describe these reprogrammed cells. Subsequently, a year later, first human reprogrammed pluripotent stem cells were successfully generated from human fibroblasts by two research groups (32,33). Yamanaka's team successfully transformed human fibroblasts into iPSCs using the same four pivotal genes, *OCT4*, *SOX2*, *KLF4*, and *c-MYC*, with a retroviral-

mediated transfection system whereas another team, led by Thomson, used different combination of genes, *OCT4*, *SOX2*, *NANOG*, and *LIN28*, with lentiviral system for cell reprogramming. The observation from these two independent results indicated that Oct4 and Sox2 were core transcription factors in common and might not be dispensable for human iPSC reprogramming. This phenomenal generation of iPSC has created the possibility that human iPSCs might provide the same therapeutic potential as human ES cells without ethical dilemma of using human embryos. Since this first establishment of human iPSCs, enormous scientific discoveries and techniques have been described to facilitate both mechanistic insights and translational studies of iPSCs for clinical settings.

Over the past seven years, various reports on generating iPSCs with a reduction in genetic manipulation and genome-integrating viruses with more efficiency have been described (34-36). In addition, microRNAs recently have been effectively applied for iPSC production without any required exogenous transcription factors (37,38). Differentiation protocols for iPSCs into specific lineages have been established (39-41). Moreover, because these iPSCs can be derived from patient's own cells, they give researchers the ability to model human diseases and to promise a new framework in drug development in an unprecedented manner (42-44). The proof-of-concept in which iPSC technology can be used for the generation of disease-corrected and patient-specific cells with potential value for cell therapy applications has also been demonstrated (45,46). Patient-own iPSCs pose a reduced risk of immunological rejection and result in an avoidance of ethical dilemmas. Several concerns of iPSCs need to be addressed before patient-specific iPSCs can advance into the clinic. For instance, a single reprogramming experiment usually generates multiple iPSC cell lines which are not always identical or even not fully reprogrammed iPSCs (47). Each individual iPSC cell line needs to be fully characterized with reliable standard protocol to identify bona fide iPSCs and to ensure pluripotency capacity and safety. Another risk of iPSCs when applying iPSC treatment to human subject is tumorigenicity. This problem also exists in human ES cell transplantation. Furthermore, genetic and epigenetic instability of iPSCs (48-50) must be considered. Thus, the justification of safety for the use of pluripotent stem cell or reprogrammed pluripotent stem cell is of utmost importance in clinical settings.

Adipose-derived stem cells (ADSCs)

Adipose-derived stem cells are characterized as one type of somatic stem cells which reside in adipose tissue. Although absolute characteristics of these cells still remain questionable, they indeed contain multipotent property (51). ADSCs could be applied in regenerative medicine in various conditions. They can differentiate into adipocytes, osteoblasts, chondrocytes, myocytes and neurons under specific ingredients and conditions (52). Adipose tissue represents an abundant and accessible source of ADSCs which are one of the most promising stem cell types. ADSCs are not only easy to recover but also stable to large-scale expand. The large volume of adipose tissue obtained from a liposuction procedure in combination with the relatively high frequency of ADSC results in substantial stem cell sources. There were also attempts to derive adipocyte from inducing differentiation from ES cells and iPSCs (53,54). However, the protocols to obtain the induced cells have not provided a homogenous population of adipocytes. Together with the large resource and easy access of adipose tissue, the differentiation of ES cells and iPSCs into adipocytes or adipose stem cells seems unnecessary. Methods for the isolation and expansion of ADSCs have been established and well-described (55). Regarding their multipotent property, concern remains regarding the potential risk of tumorigenicity in ADSCs. Until now, there has been no report, statistically significant, presenting neoplastic occurrence when using ADSCs.

Tissue engineering

Tissue and organ contain complex characteristics. It is obvious that in order to understand tissue and organ level performance, complex cellular and intracellular control mechanisms must be profoundly comprehended. With innovative tools in genetic, molecular, cellular, and printing technology, the relevance of designed structure and function combined with bioartificial fabrication is possible (56,57). The purpose is to construct the biological substitutes that can resemble tissues for diagnostics and can replace diseased or damaged tissues. A great portion of this successful approach has been demonstrated in constructed skin and cartilage components (58,59). *In vivo*, stem cells reside in a complex microenvironment characterized by their local geometry, by specific types of surrounding cells and ECM components. Their cell-cell and cell-ECM interactions are vital for stem cell intra- and inter-cellular signaling

mechanisms. Growth factors are a particular group of proteins that play major signaling ingredients to activate proliferation and differentiation pathways. Novel material used in tissue engineering scaffolds has been introduced such as recombinant proteins and synthetic polypeptides (60). In addition, scaffold-free production techniques have been developed for potential use in regenerative medicine, solely based on cell-based and cell-aggregated engineered tissues. The recent developed scaffolds are smart in several ways; however, *in vivo* environment creates dynamic changes and, thus, temporal control over the process is still hardly to be monitored and maintained.

Clinical use of stem cell and tissue engineering in breast reconstruction

ADSCs have been widely used in breast reconstruction, commonly named as lipofilling or lipotransfer or fat-grafting method. This conventional technique has been shown beneficial in both implant-based and autologous breast reconstruction (61), mainly on cosmetically breast contour and emotionally natural sensation of reconstructive breast. One of paramount concerns for fat-grafting is potential associated risk of ADSCs with tumor seed activation and neoplastic formation. Theoretically, ADSCs could potentiate cancer risk or recurrence from endocrine, paracrine, and autocrine effects, stimulating angiogenesis and cell proliferation. Nevertheless, thus far, no clinical evidence supports a higher risk of tumor recurrence and cancer formation in lipotransfer patients (62). Even with higher relative proportion of ADSCs in cell-assisted lipotransfer (CAL) method (63), rates of local tumor recurrence and metastatic cancer remain unchanged. On the contrary, CAL might result in more durable outcomes and less cancer recurrence than conventional fat transfer (63). More prospective clinical data should be monitored and warranted to determine whether lipofilling is dangerous and potentially increases cancerous recurrence in patients. More importantly, performing autologous fat grafting can lead to major complications such as severe breast infection requiring emergent corrective operation. Therefore, should only well-trained surgeons perform this procedure. One interesting unpublished data showed that more fat necrosis and breast complication occurred in old-age group patients. One possible theory could be a reduction of ADSCs in fat tissues. This assumption still requires justification whether it is, in fact, true.

Acellular dermal matrix (ADM) is a tissue scaffold

providing additional tissue support and minimizing rippling and wrinkling of breast contour (64). In two-stage expander and implant reconstruction, ADM provides similar safety but less need for manipulation of the prosthetic comparing to conventional technique. In future, many developing advanced materials together with superior scaffold fabrication technique will offer more suitable and easy-to-use substitutes with improved patient outcomes.

Stem cell and tissue engineering approach is a promising field in breast reconstructive surgery. To understand the basic biology of stem cell is an important step in cell-based and tissue-constructed therapy for patients with breast reconstruction. Further challenges are how we can reduce the complications, avoid tumor recurrence, and increase patient satisfaction with state-of-the-art stem cell and tissue engineering paradigm for breast reconstructive surgery.

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Footnote

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Fat grafting and breast reconstruction: tips for ensuring predictability

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Abstract: Autologous fat grafting is widely used in breast surgery to refine and optimize aesthetic outcomes. Despite its widespread use, obtaining predictable, reliable, and consistent outcomes remains a significant challenge and is influenced by the technique used for procurement, processing, and placement of the fat. At present, there is no published consensus on the optimal technique. The purpose of this article is to review current techniques at each stage of fat grafting and provide tips on best practices based on the published literature as well as our extensive clinical experience.

Keywords: Autologous fat grafting; breast reconstruction; fat harvesting; processing; injection; lipofilling

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Introduction

Autologous fat grafting is widely used in breast surgery to refine and optimize aesthetic outcomes, both in breast reconstruction as well as in breast aesthetic surgery. In breast reconstructive surgery, it is primarily used as an adjunct to standard breast reconstruction procedures (1) although the feasibility of using fat alone as a primary method of reconstruction has also been recently demonstrated (2). As an adjunct to reconstruction, fat grafting has been successfully used for a variety of indications including the correction of volume, shape, and contour deformities (3-9); treatment of irradiated breast tissue; and priming of the irradiated field for breast reconstruction (10-12). There is some evidence that fat grafting may also help in mitigating postmastectomy pain syndrome (13) and in the treatment of capsular contracture (10).

Fat is an appealing filler material for it is biocompatible, is abundantly available, can be easily harvested and processed, and can be injected in controlled amounts. Despite the appeal of fat and widespread adoption of fat grafting in plastic and reconstructive surgery, challenges/concerns remain with this procedure. In particular, obtaining predictable, reliable, and consistent outcomes remains a significant challenge and is due to the high

variability in graft volume retention. As much as 40-60% of the volume of fat injected could be lost (4,14-16) due to necrosis or resorption (17). The unpredictable outcome is largely attributed to the technique of fat grafting that encompasses three stages: procurement, processing, and placement of the fat.

At present, there is no published consensus on the optimal technique for fat grafting. The purpose of this article is to review current techniques at each stage of fat grafting and provide tips on best practices based on the published literature as well as our extensive clinical experience.

Procurement

Donor site

Fat can be harvested from a number of sites, including the abdomen; medial, lateral, or anterior thighs; trochanteric region; flank; lower back, and knees. Whether there is an optimal donor site for fat grafting remains to be established but evidence suggests that some sites may be preferable to others.

In an *in vitro* study, Padoin *et al.* showed that fat from the lower abdomen and medial thighs consist of a higher concentration of adipose-derived stem cells compared with

fat from the upper abdomen, trochanteric region, knee, and flank (18). As adipose-derived stem cells are believed to play a vital role in graft survival through adipogenesis and angiogenesis (19-22), these data suggest that the lower abdomen and medial thighs may be preferred over other donor sites.

Other studies, however, have reported no influence of the donor site on fat viability (23-26). In a study by Rohrich *et al.*, fat removed from the abdomen, thigh, flank, or knee were immediately evaluated without treatment for adipocyte viability as well as after centrifugation as a method of processing. No statistically significant difference in fat viability was seen among the donor sites in both untreated and treated samples in this *in vitro* study (23). In an *in vivo* study, Ullmann *et al.* harvested fat from the abdomen, lateral thigh, and breast of a single patient and grafted it into nude mice. They found no significant difference in fat graft take across the different harvest sites (24). In another *in vivo* study, Li *et al.* harvested fat from the flank, upper abdomen, lower abdomen, inner thigh, and lateral thigh of six young female patients. Again no significant differences were found on fat graft take in nude mice (25). In a clinical study, Small *et al.* harvested fat from the abdomen and thighs of 73 patients that was used in fat grafting to their reconstructed breasts; 46 patients (66 breasts) received fat from the abdomen and 27 patients (43 breasts) received fat from the thighs. Fat volume retention evaluated at various time points (16, 49, and 140 days) after grafting using 3-dimensional scanning showed no significant difference between fat harvested from the abdomen and the thighs (26). These studies, however, did not take into consideration patient characteristics that might influence graft survival.

Geissler *et al.* suggested that patients' age might influence adipocyte survival and that age should be taken into consideration when selecting a donor site (27). They found that in younger patients (≤ 45 years) adipocyte viability was greater in the lower abdomen than in the flank. In older patients (≥ 46 years), there was no difference in viability of adipocytes from the lower abdomen and the flank; but, compared with younger patients, viability of fat from the flank region was greater in older patients. There was no difference in inner thigh fat viability between the two age groups. The body mass index (BMI) of the patients [normal (BMI < 25) or overweight (BMI ≥ 25)] did not appear to influence viability of fat from any particular donor site.

Collectively, these data suggest that the lower abdomen and medial thighs may be preferred over other donor sites both from the standpoint of adipose-derived stem cells and

the age of patients. However, oftentimes, availability of fat may dictate the site chosen, especially in thin patients. Also, some patients may have a preference for a specific donor site.

Infiltration

Prior to fat aspiration, the donor site is typically infused with tumescent solution, usually consisting of a local anesthetic (lidocaine, ropivacaine, prilocaine, or bupivacaine) for pain relief and epinephrine for hemostasis in Lactated Ringer's solution or normal saline.

Several studies have examined the effect of the local anesthetic or epinephrine on fat viability. In an *in vitro* study, cell attachment in culture, cell morphology, proliferation, or adipocyte metabolic activity appeared to be unaffected by the use of lidocaine and epinephrine (28). Moreover, various doses of epinephrine (1:100,000, 1:200,000, and 1:400,000) did not impact fat cell viability (29). When the procured fat was implanted in nude mice, local anesthesia solution consisting of lidocaine and epinephrine administered to the fat donor site was found not to alter the take of fat grafts or had any influence on adipocyte viability (30). However, there is some evidence that local anesthetics may modulate the viability of isolated preadipocytes (lidocaine, ropivacaine, and prilocaine, but not bupivacaine) as well as their differentiation into mature adipocytes in *in vitro* studies (31,32). But, the preadipocytes in these studies were directly exposed to high concentrations of anesthetics (2%) compared with *in vivo* conditions where the relative concentration of anesthetic would be lower due to dilution effects.

In summary, there is no strong evidence to suggest that the use of local anesthetics or epinephrine adversely affects fat graft survival.

Mechanism of liposuction

Fat can be harvested using a number of techniques, including conventional liposuction (syringe with vacuum suction), power-assisted liposuction (specialized cannula with mechanized movement), hand-held syringe liposuction (syringe with manual suction, Coleman technique), internal ultrasound-assisted liposuction (specialized cannula that transmits ultrasound vibrations within the body), and external ultrasound-assisted liposuction (ultrasonic energy applied from outside the body, through the skin). In addition, there are also fat harvesting devices such as the Viafill system (Lipose Corp., Maitland, Fla.; manual syringe liposuction) and LipiVage system (Genesis Biosystems,

Lewisville, Texas; syringe aspiration at low vacuum pressure). The influence of liposuction techniques on fat viability and retention has been evaluated in a number of studies, most of which have compared conventional liposuction with suction- or power-assisted liposuction.

Leong *et al.* compared syringe liposuction to pump-assisted liposuction and found no differences in cell viability, cell metabolic activity, or adipogenic responses of cultured mesenchymal precursor cells processed from pump and syringe lipoaspirates (33). In contrast, Pu *et al.* demonstrated that syringe liposuction (Coleman technique) yields a greater number of viable adipocytes and sustains a more optimal level of cellular function within fat grafts than conventional liposuction, although normal histologic structure was maintained in fat grafts obtained by both methods (34). Similarly, the newer harvesting devices, LipiVage (Genesis Biosystems) and Viafill (Lipose Corp.), also fared better than conventional liposuction. Liposuction using the LipiVage (Genesis Biosystems) or Viafill (Lipose Corp.) systems was associated with higher yields of viable adipocytes, demonstrating the importance of low pressure suction for fat viability (35,36). Gonzalez *et al.* have proposed the use of fine needle aspiration (comprising a 2-mm blunt needle with a 10-cc syringe adapted to a fine-needle aspiration apparatus) as an alternate method of liposuction which exerts a significantly lower pressure than hand-held syringe liposuction (using a 3-mm liposuction cannula with a 60-cc syringe). Fine needle aspiration yielded better fat viability (37).

Two studies evaluated the impact of ultrasound-assisted liposuction on adipose viability. In one study, Rohrich *et al.* showed that external ultrasound had no significant impact on adipocyte cellular integrity while internal ultrasound resulted in thermal liquefaction of mature adipocytes (38). Similarly, Shiffman and Mirrafati also showed that external ultrasound does not destroy fat cells, although it produces smaller bundles of fat (39). A more recent study that used a third generation internal ultrasound device (VASER; Sound Surgical Technologies, Louisville, CO) found no difference in fat graft retention between the ultrasound device and suction-assisted liposuction in a xenograft model (40).

In addition to the method of liposuction, other variables such as cannula size and suction pressure employed during liposuction could also have an impact on adipocyte viability. Irrespective of the method of liposuction, a blunt-tip harvesting cannula is utilized to withdraw the lipoaspirate from the donor site. Two studies have established that the use of large bore size cannulas yields a greater number of viable

adipocytes in the lipoaspirate. In one study, a 4-mm cannula was shown to be better than 2-3 mm cannulas (41) and in another study, a 6-mm cannula was shown to be better than 4- and 2-mm cannulas (42). Shiffman and Mirrafati tested the effect of various suction pressures on adipocyte viability and noted adipocyte damage of greater than 10% with the use of -700 mmHg vacuum (39). This finding was corroborated by Cheriyan *et al.* who demonstrated that a low harvest pressure (-250 mmHg) resulted in an adipocyte count that was 47% higher than a high harvest pressure (-760 mmHg) (43).

Based on these studies, it appears that currently available liposuction methods are all relatively adipocyte friendly harvesting techniques. When using suction-assisted liposuction, the use of low suction pressure is preferable. Although there is no clear evidence for the superiority of any one type of harvesting technique, a survey of members of the American Society of Plastic Surgeons revealed that hand-held manual suction appears to be the preferred technique (1). With respect to harvesting cannulas, larger sizes (≥ 4 mm) may be preferable as they appear to increase viable adipocyte yield.

Processing

Prior to fat grafting, the harvested fat is typically processed in some manner to eliminate tumescent fluid, blood, cell fragments, and free oil (from disrupted adipocytes) (17). By eliminating these contaminants, processing aims to retain viable adipocytes in a concentrated form, which is believed to enhance graft take (44,45). The most commonly performed fat processing methods are filtration, centrifugation, or sedimentation (decantation) (1). The filtration technique uses a platform for concentrating fat cells and separating them from fluids, oil, and debris. As a platform, various materials such as filters with defined pore size, cotton gauze, metal sieve, mesh, and operating room cloth have been used for the purpose of filtering lipoaspirate. In the centrifugation technique, the syringe containing the lipoaspirate is placed in a centrifuge and spun at a specified speed and time. In the sedimentation technique, the syringe containing the lipoaspirate is allowed to sit for decantation to occur under the action of gravity. In a variation of this technique the lipoaspirate is washed with 1-3 times the volume with normal saline or Lactated Ringer's solution and then left to decant under gravity. In all three cases, centrifugation, sedimentation, and washing, the lipoaspirate is separated into three layers: an upper oil layer, a middle purified and concentrated fat layer, and a lower

aqueous layer consisting of blood, infiltration or washing liquids. In addition, in the centrifugation technique, a pellet is seen at the bottom of the centrifuge.

Attempts to determine the optimal method of fat processing has thus far been inconclusive because of conflicting results as summarized below.

Centrifugation vs. sedimentation

In a prospective, randomized, double-blind clinical study, Butterwick grafted fat processed by centrifugation in one hand and non-centrifuged fat (sedimentation) in the contralateral hand in 14 patients (46). At 3 and 5 months postoperatively, hands that received centrifuged fat displayed improved aesthetic outcome measured subjectively and objectively (vein prominence and depth of metacarpal space). In direct contrast to this study, Khater *et al.* demonstrated in a series of 51 patients lipofilling with non-centrifuged fat (sedimentation) that was serum washed resulted in improved clinical outcome at 1-year postoperatively compared with lipofilling with centrifuged fat (3,400 rpm for 3 min) (47). *In vitro* examination revealed the presence of a greater amount of preadipocytes in the cultured non-centrifuged adipose tissue and more distinctly expressed cell proliferation. Likewise, Condé-Green *et al.* showed that cell count per high-powered field of intact nucleated adipocytes was significantly greater in decanted lipoaspirates, whereas centrifuged samples showed a greater majority of altered adipocytes (48). However, mesenchymal stem cell concentration was significantly higher in washed lipoaspirates compared to decanted and centrifuged samples but the pellet collected at the bottom of the centrifuged samples had the highest concentration. The authors concluded that washing may be the best processing technique for adipose tissue graft take and recommended that if centrifugation is used, the pellet containing mesenchymal stem cells should be added to the concentrated adipose phase to augment graft take.

Centrifugation vs. filtration

In a clinical study, using subjective and objective evaluations, clinical outcome was deemed comparable between centrifuged fat (3,000 rpm for 3 min) and filtered, washed fat (49). In this prospective, double-blind study in 25 patients undergoing facial fat transplantation, half the face was injected with filtered and washed fat while the other half injected with centrifuged fat. At an average

follow-up period of 12 months, the implanted hemifacial regions demonstrated comparable results.

In a nude mouse model, Ramon *et al.* demonstrated that human fat processed by operating room cloth concentration was comparable to that processed by centrifugation (50). After 16 weeks postimplantation, no significant differences in weight and volume of explanted fat graft were noted between the two processing methods. Histologic analysis of the fat grafts revealed significantly less fibrosis within the graft processed by operating room cloth, suggesting that the quality of the fat graft was better than that processed via centrifugation. Similar to this study, Minn *et al.* reported no significant differences in fat graft survival rates in nude mice between grafts prepared by centrifugation, metal sieve concentration, and cotton gauze concentration (51). Two recent studies have further corroborated the comparable outcome of centrifugation and filtering as processing methods. Salinas *et al.* reported that lipoaspirate processed by centrifugation at 1,200 \times g or using mesh/gauze concentration yields an equivalent amount of concentrated fat, about 90% concentrated fat (45). In addition, the number of adipose-derived stem cells in 1 g of concentrated fat was equivalent. The explanted fat grafts from the two methods also exhibited equivalent weights after 4 or 6 weeks implantation in nude mice. Fisher *et al.* demonstrated in the nude mice model that filtration (using an 800- μ m pore size filter) and centrifugation both effectively removed fluid fractions and resulted in comparable graft retention (40). When they compared these two methods with cotton gauze rolling, the latter method resulted in greater fat graft retention. The authors suggested that cotton gauze rolling may be best suited for grafting cosmetically sensitive areas of the body in which optimal retention is critical and lower total graft volumes are needed while filtration and centrifugation would be preferable when larger volumes are required.

Optimal centrifugation conditions

The Coleman technique is the most widely used centrifugation protocol in which the lipoaspirate is centrifuged at \sim 1,200 \times g (3,000 rpm) for 3 min (52). Some studies that evaluated optimal centrifugation conditions have also suggested a centrifugal force of \sim 1,200 \times g (3,000 rpm) to be optimal in concordance with Coleman's protocol. Kurita *et al.* compared 6 centrifugation speeds (0, 400, 700, 1,200, 3,000, or 4,200 \times g for 3 min) to evaluate the effects of centrifugation on lipoaspirates and graft take in nude

mice (53). They reported that centrifugation at more than 3,000 $\times g$ significantly damaged adipose-derived stem cells and recommended 1,200 $\times g$ as an optimized centrifugal force for obtaining good short- and long-term results in adipose transplantation. In an *in vitro* study, Kim *et al.* compared the number of viable fat cells after fat samples were centrifuged for 1, 3, and 5 min at 1,500, 3,000, and 5,000 rpm, respectively, with uncentrifuged fat (29). Cell survival rates were significantly lower when centrifuged at 1,500 and 3,000 rpm for more than 5 min and when centrifuged at 5,000 rpm for more than 1 min. The authors recommended centrifugation at 3,000 rpm for 3 min as being optimal.

Other studies have contended that even lower centrifugal forces than the Coleman protocol may be more adipocyte friendly. Hoareau *et al.* subjected adipose tissue to soft (100 $\times g/1$ min and 400 $\times g/1$ min) and strong (900 $\times g/3$ min and 1,800 $\times g/10$ min) centrifugal forces and evaluated graft viability in immunodeficient mice (54). Strong centrifugation resulted in 3-fold more adipocyte death than soft centrifugation. The authors suggested that soft centrifugation (400 $\times g/1$ min) seems to be the most appropriate protocol for the reinjection of adipose tissue.

While other studies have found that centrifugation irrespective of the centrifugal force is deleterious to adipocytes. Xie *et al.* subjected lipoaspirates to four different centrifugal forces (1,000, 2,000, 3,000, 4,000 rpm) and evaluated fat cell viability via an *in vitro* glucose transport test (55). Compared with no centrifugation, centrifuged samples demonstrated a significant and linear reduction in fat cell viability with increasing centrifugal force. Histological analyses revealed significantly distorted and fractured adipocytes when the centrifugal force reached 4,000 rpm (1,145 $\times g$).

Yet other studies suggest that centrifugal force has no effect on adipocyte viability. Using eight different centrifugal forces (up to 20,000 $\times g$) Pulsfort *et al.* showed no significant alterations in the viability of centrifuged adipocytes (56). Further, cultivation of isolated adipocyte after centrifugation revealed no apoptotic changes. However, lipoaspirates centrifuged with higher accelerations seemed to be better cleansed of oil and cell debris than samples treated with lower centrifugal forces. Lee *et al.* centrifuged lipoaspirates at various speeds (50 $\times g$, 200 $\times g$, 1,200 $\times g$, 5,000 $\times g$, 10,000 $\times g$, and 23,000 $\times g$) for 3 min and injected aliquots of purified fat into nude mice to evaluate graft weight and histology at 4 weeks post implantation (57). A statistically significant linear increase in graft take was seen as the speed

was increased up to 10,000 $\times g$ but there was no histological difference between the grafts. In a subsequent study by the same group, the increase in graft take with increasing centrifugation speeds was associated with increasing concentration of the adipocyte fraction as the speed was increased to 5,000 $\times g$ (45). Beyond 5,000 $\times g$ the adipocyte fraction did not change significantly, suggesting that 5,000 $\times g$ results in nearly 100 percent concentrated fat. Adding back tumescent solution (surgical or fresh) or cell pellet to the concentrated fat before grafting resulted in reduced graft retention while adding back oil did not affect graft take.

Newer processing techniques

Fat processing using the conventional methods (centrifugation, filtering, and sedimentation) can be cumbersome and time consuming to perform in the operating room, particularly if processing large volumes of fat. In order to simplify fat processing, commercial fat processing systems are now available that simultaneously wash and filter lipoaspirates in a closed system (e.g., Puregraft™, Cytori Therapeutics, Inc., San Diego, CA and REVOLVE™, LifeCell Corp., Branchburg, NJ). These systems have also been shown to result in greater fat retention than conventional methods. Zhu *et al.* demonstrated that grafts prepared by the Puregraft™ (Cytori Therapeutics) system exhibited significantly reduced blood cell and free lipid content with significantly greater adipose tissue viability than grafts prepared by sedimentation or Coleman centrifugation (58). Ansoerge *et al.* showed that the REVOLVE™ (LifeCell Corp.) system yielded significantly less blood cell debris, a higher percentage of adipose tissue, and a lower percentage of free oil compared with sedimentation or Coleman centrifugation (59). In nude mice, fat tissue retention from REVOLVE™ (LifeCell Corp.) samples was significantly higher than that from decanted samples and similar to that from centrifuged samples.

Based on the published literature, any one method of fat processing doesn't appear to be superior. A survey of American Society of Plastic Surgeons indicates that filtering, sedimentation, and centrifugation are all equally popular (1).

Our current protocol for fat processing is via the REVOLVE™ (LifeCell Corp.) system; prior to which, we used the Coleman centrifugation technique. With the REVOLVE™ (LifeCell Corp.) system, the lipoaspirate can be channeled directly into the system (*Figure 1*), which is convenient as this eliminates lipoaspirate handling in



Figure 1 REVOLVE™ (LifeCell Corp.) fat grafting system.

Table 1 Comparative analyses of fat processing using the REVOLVE™ (LifeCell Corp.) system and centrifugation

Endpoint	REVOLVE system [mean ± SD (range)]	Centrifuge method [mean ± SD (range)]	P value
Volume of fat harvested, mL	507.8±106.4 [200-700]	137.4±45.6 [70-350]	<0.0001
Volume of fat injected, mL	179.0±44.1 [80-260]	82.4±32.0 [40-200]	<0.0001
Operative time*, min	30.0±5.9 [20-45]	84.9±13.1 [60-124]	<0.0001

*, from harvest to completion of grafting; P value was calculated using unpaired *t*-test. SD, standard deviation.

syringes. In addition, according to the manufacturer, the system can process up to 800 mL of lipoaspirate in less than 15 min which may translate to a reduction in operating room time. To evaluate this claim, we performed a retrospective review of our patients who underwent autologous fat grafting to the breast over a 2-year period (60). The volume of fat harvested, volume of fat injected after processing, time taken to complete fat grafting (from harvest to injection), and complications within 60 days of grafting were compared between the two processing methods. There were a total of 118 patients in the centrifugation and 103 patients in the REVOLVE™ (LifeCell Corp.) group. We found that the mean volume of fat harvested and injected were significantly higher in the REVOLVE™ (LifeCell Corp.) group and the time to complete fat grafting was significantly shorter, 30 vs. 85 min (Table 1). There were no complications in either group. These results suggest that the convenience of using a streamlined system for fat harvesting and processing allows for a larger volume of fat to be harvested and injected

than would normally be the case using a conventional method. The all in one system also eliminates unnecessary fat handling time which could translate to reduced operative time.

Placement

The placement of the processed concentrated fat into a recipient site is one of the most challenging aspects of fat grafting. The general principle is to position small parcels of fat between layers of host tissue so as to encourage uniform survival, stability, and integration into the surrounding tissues (52). This could be particularly challenging in a postmastectomy reconstructed breast where host subcutaneous tissue has been voided. Thus, in this case, fat parcels are positioned between the overlying breast skin and the pectoralis major muscle. It is also generally understood that injecting a single bolus of a large volume of fat is to be avoided as this leads to fat necrosis and a poor outcome because of a lack of sufficient contact with vascularized host tissue.

Although there is no standardized fat placement technique, the Coleman technique is the most widely used (52). In this technique, fat is injected using a blunt Coleman infiltration cannula attached to a 1 mL syringe while withdrawing the cannula. Other syringe sizes (3 and 10 mL) as well as various cannula tip shapes, diameters, lengths, and curves may be used depending on the volume of fat to be placed and the recipient site. The use of wider-diameter cannulas (2.5 mm) may however be preferred as they have been shown to potentially improve fat graft survival and reduce fat graft resorption compared with small-diameter cannulas (1.6 or 2 mm) (41). Instead of cannulas, needles may also be used for fat injection. Evidence suggests that the size of the needles does not appear to affect cell viability, at least when using 14, 16, and 20 gauge needles (42). But for any given needle size, it appears that fat viability is influenced by the shear stress, which is a function of flow rate. Fat injected at a slow rate (low shear stress) results in better fat graft retention than fat injected at a fast rate (high shear stress) (57).

The volume of fat injected appears to be another important variable that may influence graft viability and retention. Choi *et al.* applied 3-dimensional imaging technology to assess volumetric fat graft survival following autologous fat transfer to the breast (61). They reported that patients receiving higher volumes (average of 151 cc) of injected fat had slower volume loss and greater total volume retention than those receiving smaller volumes (average of 51 cc). Moreover, the time from fat injection also impacted retention rates; the longer the time from fat

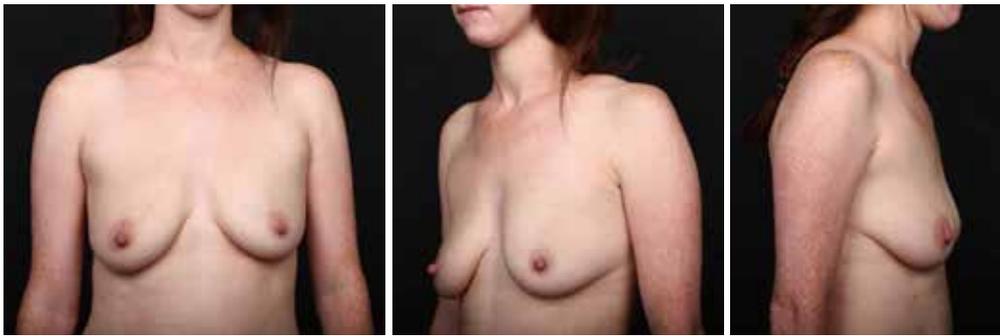


Figure 2 Preoperative views of a 31-year-old BRCA positive female who elected prophylactic mastectomy with immediate reconstruction.

injection, the lower the fat retention. In further evaluating the impact of graft volume, Del Vecchio *et al.* identified the graft-to-capacity ratio (defined as the volume of grafted fat in relation to the volume of the recipient site) as another important variable to consider (62). In 30 patients undergoing large-volume fat transplantation to the breast, the authors calculated the average graft-to-capacity ratio using pre-operative quantitative volumetric analysis (using 3-dimensional breast imaging), volume of fat injected, and post-operative quantitative volumetric breast imaging at 12 months. Patients whose graft-to-capacity ratio exceeded 1 standard deviation (SD) of the calculated average had a lower percentage of volume maintenance at 12 months. Conversely, those who had a graft-to-capacity ratio that was 1 SD lower than the average demonstrated a higher percentage of volume maintenance. Thus, an understanding of the biology and volumetric capacity of the recipient site may lead to more consistent outcomes following fat grafting.

In reconstructed breasts, prior irradiation is also an important variable that could impact graft retention. In an experimental study, human fat grafts injected into irradiated mice were shown to reduce radiation-induced fibrosis but fat graft retention was significantly lower than in nonirradiated tissue (63). In contrast to this study, two clinical studies have shown that prior irradiation to the breasts had no impact on fat retention (26,61).

In summary, current data suggests that fat should be ideally injected with low shear stress taking into consideration the volume or graft-to-capacity to optimize graft retention.

Authors' tips

We have been using fat grafting for over 7 years to correct

volume, shape, and contour deformities at the second stage of implant-based reconstructions in irradiated as well as nonirradiated breasts (*Figure 2*). As delineated in the review of the literature above, the outcome of fat grafting is highly dependent on the technique. Over the years we have refined our technique and established some principles:

- (I) Handling of fat tissue. When handling fat tissue, surgeons need to be cognizant that fat tissue is living tissue. Delicate handling during harvesting, processing, and injection is of utmost importance to preserve its integrity. Exposure to inappropriate external forces, including mechanical, chemical, or barometric, should be avoided to minimize the risk of cellular damage and necrosis which could adversely affect graft viability and retention. In addition, the harvested fat should be maintained as close as possible to body temperature to maximize its survival;
- (II) Preoperative planning. As with any surgical procedure, preoperative planning is important. A thorough patient evaluation should be performed that includes an assessment of the patient's body habitus, prior breast surgeries, and any medical history that might complicate surgery. The amount of fat that would be required to address a particular breast deficit and the potential site of procurement should also be assessed and determined prior to the surgical procedure. In assessing for a suitable donor site, clinical judgment is needed to select a site that is likely to have a good outcome keeping in mind that sometimes donor site irregularities, as a secondary complication of fat grafting, may be more difficult to treat. In addition, one has to be mindful that a total autologous reconstruction may be needed

depending on the patient's cancer stage and breast reconstruction outcome, especially if the patient is considering it, and therefore the abdomen, at least the lower portion and peri-umbilical area should be preserved;

- (III) Sterile technique. General principles of sterile technique should be observed at all stages of the procedure. Preoperative preparation using antimicrobial scrubs and prep solutions should be adhered to;
- (IV) Tumescence solution. In general, about 1 mL of tumescence solution is injected for every 1 mL of lipoaspirate to be extracted. At least 7 min is needed for the vasoconstrictive effects to set in before fat extraction can be performed. Our standard tumescence solution is 20 cc of 1% lidocaine and 1 ampule of epinephrine in 1 L of Lactated Ringer's solution;
- (V) Fat aspiration. We typically use a 3-4 mm cannula size, depending on the location of the donor site, with low-suction vacuum. Suction-assisted lipectomy is preferred as it allows for more control in setting the pressure and gentle movements are utilized to harvest the fat;
- (VI) Processed fat. At times, the processed fat is kept for a period of time prior to injection as the surgeon is busy performing another procedure. However, this can be detrimental to graft survival given that the fat has now lost the core body temperature that was harvested from. The goal is to harvest, process, and inject immediately;
- (VII) Fat injection. We advocate use of low-pressure when injecting the processed fat into the recipient site. However, increased pressure may sometimes be needed, for example, when injecting into scarred planes of tissues; but, it is important to be aware of the amount of pressure that is being exerted to inject the fat. High pressures on a plunger have a negative effect on fat survival;
- (VIII) The efficacious combination of procurement, processing, and placement should always be considered during fat grafting.

Future of fat grafting

Given the versatility of fat tissue as well its biocompatibility, fat grafting will continue to be an important component of breast reconstruction. Although currently fat grafting

is utilized almost exclusively as an adjunctive procedure in breast reconstruction (1), the stage is being set for its use as the primary means of reconstruction (2). However, fat grafting alone to reconstruct a breast cannot be feasible in all patients because of fat availability which is a major limitation. But, as surgeons become more comfortable with fat grafting and with technology evolving to simplify the process, we could see fat grafting playing a more prominent role in breast reconstruction; for example, in partial substitution of the implant for fat (i.e., changing the ratio of implant volume to fat by using a smaller implant and substituting with a larger volume of fat). Again, fat availability would pose a limitation. Fat may also be combined with biologic scaffolds to create what we call "bioengineered breasts" (Figures 3,4). In this construct, an acellular matrix is used at the lower pole with a tissue expander in the first stage of reconstruction followed by submuscular placement of a second acellular matrix at the upper pole plus fat grafting along with an implant in the second stage. The combination of acellular matrix and autologous fat provides the soft tissue volume to address tissue deficiency. The acellular matrix placed submuscularly serves as a scaffold to support tissue regeneration, generating a layer of soft tissue at the upper pole while autologous fat grafting provides the extra padding to smooth out deficiencies in the breast shape/contour as well as mask deformities. This powerful combination of constructs will better allow us to achieve the ultimate goal of breast reconstruction—to recreate a breast that looks and feels like the natural breast.

Conclusions

Although it is well acknowledged that the clinical outcome of fat grafting is dependent on the technique, a review of the published literature does not provide clear guidance as to the optimal technique at each of the stages of fat grafting. Nonetheless, the use of lower abdomen and medial thigh as donor sites, use of low suction pressure for liposuction, use of large bore-sized harvesting cannulas, use of low centrifugation forces (if using centrifugation for processing), use of low shear stress during injection, placement of small parcels of fat, and optimizing the volume of fat injected to the capacity of the recipient site were noted to be associated with improved fat retention. Surgeons should be cognizant that the injected fat tissue has to survive at times in a hostile recipient site. Thus, every effort needs to be made to enhance graft take and all the factors mentioned

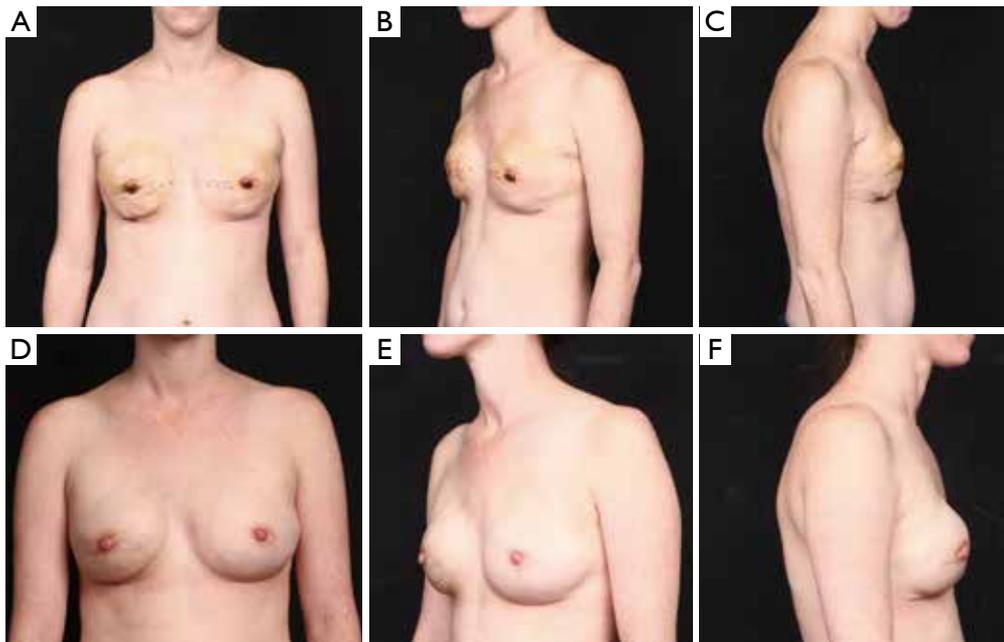


Figure 3 Patient in *Figure 2* after bilateral nipple sparing mastectomy and immediate breast reconstruction with 133 MV 400 cc expanders, AlloDerm RTU, and Botox for muscle relaxation. (A-C) Post-operative day 10 following surgery; (D-F) 2 months after surgery.

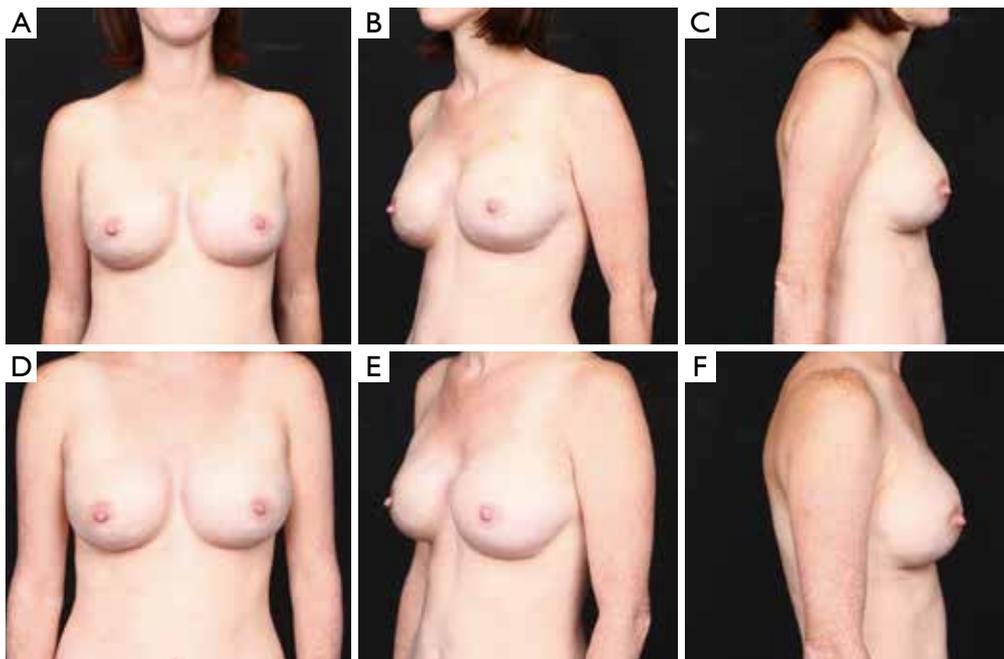


Figure 4 Patient in *Figure 2* following bilateral breast reconstruction with silicone implants (410 MV 550 cc) and fat grafting. Fat was processed using the REVOLVE (LifeCell Corp.) system. (A-C) 2 weeks after surgery; (D-F) 10 months after surgery.

above should be taken into consideration. In addition, one must not forget that maintaining the fat as close to core body temperature as possible and immediate grating following harvest also enhances graft take. Clearly, rigorous, controlled studies are needed to determine optimal grafting conditions; but, for now surgeons may have to rely on optimizing their technique of choice.

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Footnote

Conflicts of Interest: Allen Gabriel, MD and G. Patrick Maxwell, MD are consultants for LifeCell Corporation, Branchburg, NJ. The other author has no conflicts of interest to declare.

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Current status of breast reconstruction in China: an experience of 951 breast reconstructions from a single institute

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Background: Since mastectomy remained the primary strategy for treating breast cancer in China, post-mastectomy reconstruction is of great importance in the Chinese population. The current study aimed to assess the current status of breast reconstruction in China.

Methods: We reviewed all patients who received breast reconstruction from August 2000 to July 2015 in the Department of Breast Surgery in our institute. Patients' baseline characteristics, reconstruction strategy, final pathology and loco-regional recurrence (LRR) information were collected.

Results: A total of 951 breast reconstructions were conducted during the past 15 years, among which 247 (27.0%) were abdominal flap reconstruction; 471 (51.5%) were latissimus dorsi myocutaneous ± implant; and 233 (25.5%) were prosthesis-based reconstruction. The majority of cases (78.1%) were invasive breast cancer and up to 894 cases (94.0%) were immediate reconstruction. Prosthesis-based reconstruction rapidly increased in recent years, and was associated with bilateral reconstruction, contralateral augmentation and higher complications. 18 patients (2.0%) developed local-regional recurrence at the median follow-up time of 26.6 months (range, 3.7–62.0 months). A total of 66 nipple-areolar complex-sparing mastectomies (NSMs) (6.9%) were performed, none of which developed recurrence.

Conclusions: Breast reconstruction cases increased over the 15 years with the change of paradigm. Most strikingly, prosthesis-based reconstruction rapidly gained its prevalence and became the most common strategy. NSM was only performed for highly selected patients. Patients with breast reconstruction were able to achieve satisfactory loco-regional control in our cohort.

Keywords: Breast reconstruction; breast cancer; China; current status

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Introduction

With the improvement of systemic treatment, the surgical management of breast cancer experienced substantial revolution over the years. Although breast-conserving therapy (BCT) has become the primary surgical treatment

for breast cancer worldwide, and approximately 60–70% of stage 0–II patients in the United States undergo BCT (1), a multi-center retrospective study in China indicated that modified radical mastectomy remained the primary strategy for treating breast cancer (2).

Thus, post-mastectomy reconstruction is of great

importance in the Chinese population. In recent years, attentions have been focused on this field, which would significantly improve aesthetic outcome for breast cancer patients on the basis of not affecting the oncological results. Multiple mastectomy techniques, such as skin-sparing mastectomy (SSM) and nipple-areolar complex-sparing mastectomy (NSM), combined with immediate breast reconstruction, were adopted for patients with reconstruction demand. Also, various techniques were performed for reconstruction, including pedicle transverse rectus abdominis myocutaneous (TRAM) flap reconstruction, free-TRAM flap reconstruction, latissimus dorsi myocutaneous flap (LDMF) reconstruction and prosthesis-based reconstruction.

The current study aimed to assess the current status of breast reconstruction in China, by reviewing 951 breast reconstruction cases over the past 15 years in Fudan University Shanghai Cancer Center (FUSCC). We also described the paradigm change and local-regional control of these patients.

Materials and methods

Patients

We reviewed all patients who received breast reconstruction from August 2000 to July 2015 in the Department of Breast Surgery FUSCC. The following inclusion criteria were applied: (I) female patients who received reconstruction after mastectomy; (II) therapeutic and prophylactic cases; (III) unilateral and bilateral patients with breast reconstruction; (IV) immediate and delayed reconstruction. However, patients with breast-conserving surgery and partial reconstruction were excluded. Patients' baseline characteristics, reconstruction strategy, final pathology and loco-regional recurrence (LRR) information were collected. The 7th edition of the AJCC TNM was utilized to stage the patients. The protocol for the present study was approved by the Ethics Committee of FUSCC.

Reconstruction methods

The surgical management of the patients was grouped as follows: LDMF flap reconstruction (including extended LDMF flap reconstruction and LDMF + implant reconstruction), abdominal flap reconstruction (pedicle-TRAM and free-TRAM reconstruction), and prosthesis-based reconstruction (direct to implant reconstruction and

two-stage reconstruction). In the two-stage prosthesis-based reconstruction, patients were implanted with a soft-tissue expander immediately after mastectomy. After inflating the expander with saline over a period of time, the expander is then replaced with a permanent implant. Nipple reconstruction, return to operation room (OR) complications, contralateral breast aesthetic surgeries, and ipsilateral breast modification were also included into analysis.

Follow-up

The follow-up data on the breast cancer patients were acquired from the Department of Clinical Statistics of FUSCC. LRR was defined as any progression in the ipsilateral breast, skin, muscles of the chest wall and/or axillary/supraclavicular lymph nodes (LNs). Survival was calculated from the date of surgery to the date of clinical relapse. Patients whose last follow-up was ≤ 3 months after surgery were regarded as lost to follow-up and were excluded from analysis.

Results

Baseline characteristics of patients

From August 2000 to July 2015, a total of 951 breast reconstructions were conducted in our institute. Among these cases, 885 patients had unilateral breast reconstruction; 31 patients had bilateral breast reconstruction; one patient had bilateral reconstruction while received a third reconstruction after flap loss of her right breast. The median age of patients to have breast reconstruction was 39 years old (range, 19–77 years old). In 31 bilateral reconstruction patients, 23 suffered from bilateral breast cancer, and 8 had unilateral breast cancer and contralateral prophylactic mastectomy.

The clinical pathological characteristics of patients' primary breast disease were demonstrated in *Table 1*. The majority of cases (78.1%) were invasive breast cancer and breast cancer *in situ* (17.1%). The median size for invasive breast cancer was 2.2 cm (IQR: 1.5–3.0 cm), for breast cancer *in situ* was 2.0 cm (IQR: 1.2–2.5 cm) and for other breast tumor was 4.5 cm (IQR: 2.5–5.6 cm), respectively. Of all patients, 26 had previous breast-conserving surgery and developed ipsilateral breast recurrence. They subsequently had mastectomy and breast reconstruction; 39 cases received neo-adjuvant chemotherapy prior to surgery

and reconstruction, seven of which achieved pathological complete remission (pCR).

Current status and trend of breast reconstruction in FUSCC

In 915 cases, 247 (27.0%) were abdominal flap reconstruction; 471 (51.5%) were LDMF ± implant reconstruction; and 233 (25.5%) were prosthesis-based reconstruction, among which 188 were expander-implant reconstruction and 45 were direct-to-implant reconstruction. In terms of timing, 894 cases (94.0%) were immediate reconstruction; 51 cases (5.4%) were delayed reconstruction; and six cases were delayed-immediate reconstruction.

The trend of breast reconstruction by year was illustrated in Table 2 and Figure 1. There was a significant

change in breast reconstruction strategy over the years. Notably, although the total breast reconstruction cases increased steadily, the percentile of reconstruction strategies varied. LDMF ± implant (Figure 2) had remained most common method until 2014, while prosthesis-based reconstruction rose rapidly from eight cases in 2012 to 106 cases in 2015, increased more than 10-fold during this short period (Figure 3). Pedicle-TRAM reconstruction was gradually replaced by free-TRAM reconstruction since 2011 (Figure 4). Nevertheless, free abdominal flap reconstruction decreased gently in recent years.

Among all reconstructions, 20 cases failed to complete reconstruction, including total flap loss in three cases of free TRAM reconstruction, 16 cases of expander or implant loss in prosthesis-based reconstruction, and one case in LDMF + implant reconstruction due to implant exposure. Most interestingly, 13 out of 16 (81.2%) cases in the prosthesis-based group lost their expander/implant without specific complications, except for patients regretting their decision to receive reconstruction. Two patients lost their expander/

Table 1 Baseline clinical-pathological characteristics of patients' primary breast disease according to final pathology

Pathology	N (%)
Invasive breast cancer	743 (78.1)
Stage 0-I [†]	277 (37.3)
Stage II	275 (37.0)
Stage III	79 (10.6)
<i>In situ</i> breast cancer	163 (17.1)
Ductal carcinoma <i>in situ</i>	156 (95.7)
Lobular carcinoma <i>in situ</i>	7 (4.3)
Phyllodes tumor	28 (2.9)
Other malignant breast tumor	7 (0.7)
Prophylactic mastectomy	8 (0.8)
Unknown	3 (0.3)

[†], seven patients received neo-adjuvant achieved pathological complete remission and staged 0.

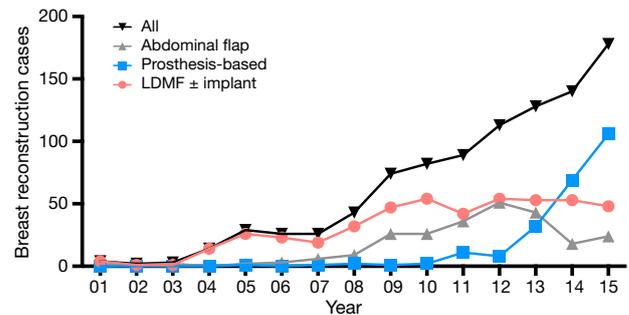


Figure 1 Trend of breast reconstruction in FUSCC. FUSCC, Fudan University Shanghai Cancer Center.

Table 2 Breast reconstruction trends in different surgical groups

Year [†]	2000–2001	2001–2002	2002–2003	2003–2004	2004–2005	2005–2006	2006–2007	2007–2008	2008–2009	2009–2010	2010–2011	2011–2012	2012–2013	2013–2014	2014–2015	Total
LDMF ± implant, N (%)	4 (100.0)	1 (50.0)	1 (33.3)	14 (100.0)	26 (89.7)	23 (88.5)	19 (73.1)	32 (74.4)	47 (63.5)	54 (65.9)	42 (47.2)	54 (47.8)	53 (41.4)	53 (37.9)	48 (27.0)	471 (49.5)
Prosthesis-based, N (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.4)	0 (0.0)	1 (3.8)	2 (4.7)	1 (1.4)	2 (2.4)	11 (12.4)	8 (7.1)	32 (25.0)	69 (49.3)	106 (59.6)	233 (24.5)
Pedicle-TRAM, N (%)	0 (0.0)	1 (50.0)	2 (66.7)	0 (0.0)	2 (6.9)	3 (11.5)	2 (7.7)	7 (16.3)	23 (31.1)	23 (28.0)	7 (7.9)	7 (6.2)	10 (7.8)	4 (2.9)	0 (0.0)	91 (9.6)
Free-TRAM, N (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (15.4)	2 (4.7)	3 (4.1)	3 (3.7)	29 (32.6)	44 (38.9)	33 (25.8)	14 (10.0)	24 (13.5)	156 (16.4)
Total	4	2	3	14	29	26	26	43	74	82	89	113	128	140	178	951

[†], time interval was calculated from August of the prior year to July of the next year.



Figure 2 LDMF flap breast reconstruction. (A,B) Pre-operative pictures; (C,D) postoperative pictures with reconstructed breast and donor site scar. LDMF, latissimus dorsi myocutaneous flap.

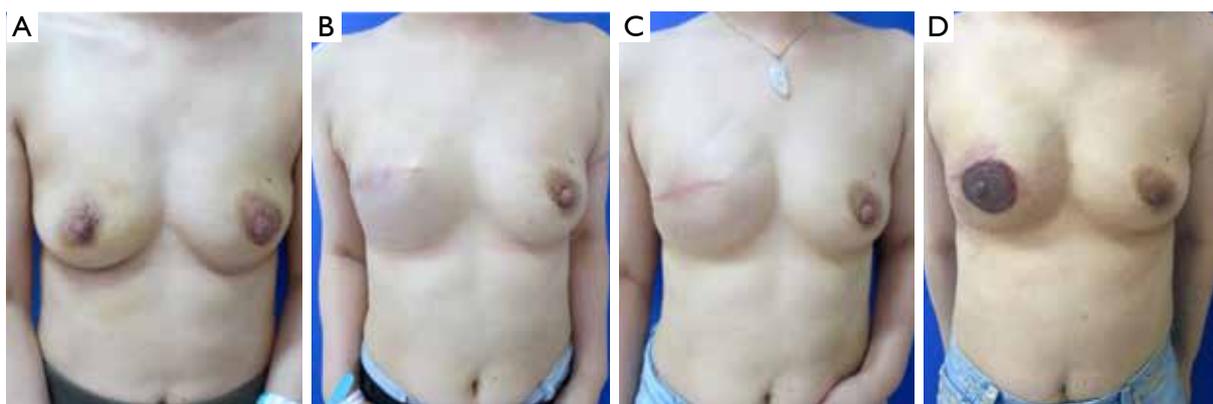


Figure 3 Expander-implant two stage breast reconstructions. (A) Pre-operative pictures; (B) after skin-sparing mastectomy and immediate expander reconstruction, the patient's expander was injected with saline bi-weekly with satisfied appearance; (C) the patient's expander was replaced by permanent implant; (D) the patient received nipple reconstruction and tattoo of nipple-areolar complex (NAC).

implant because of post-operative infection; and one patient required her implant removal due to discomfort. Moreover, three patients (two unilateral cases and one bilateral case) failed to turn up in our institute for permanent implant placement after expander reconstruction for more than 2 years, indicating they probably did not complete the two-stage reconstructive surgery.

Thirty-eight cases (4.0%) developed post-operative complications that required re-operation. In prosthesis-based reconstruction, 15 cases returned to operation room with varied reasons, such as infection, expander rupture and expander/implant exposure. Prosthesis-based reconstruction also had more contralateral breast surgery than other reconstructive surgeries, the majority of which were contralateral breast reconstruction (15.9%) and contralateral

breast augmentation (9.9%). In the meantime, abdominal flap group had the most contralateral breast reduction/mastopexy cases (4.9%) (Figure 5). Abdominal flap reconstruction also had the most percentiles of ipsilateral breast modification (5.7%) and nipple reconstruction (24.7%) among three reconstruction surgeries (Table 3).

NSM in breast reconstruction

For reconstructive patients, we routinely performed SSM. A total of 66 NSMs (6.9%) were performed in 61 patients, 11 of which in LDM ± implant group and 55 in prosthesis-based group. The breast diseases for these cases were as follows: 34 (61.8%) were invasive breast cancer; 14 (25.4%) were *in situ* breast cancer; 12 (21.8%) were phyllodes



Figure 4 Muscle-sparing free TRAM flap reconstruction. (A,B) Pre-operative pictures; (C,D) 3 months after skin-sparing mastectomy and immediate reconstructive surgery; (E,F) 1 year after initial breast reconstruction followed by second-stage nipple reconstruction and tattoo of nipple-areolar complex (NAC).

tumor; five for prophylactic mastectomy; and one for other malignant breast tumor. One case received intra-operative single-dose nipple-areola complex (NAC) radiotherapy; in another case, the patient required to resect the NAC because of concerns of NAC recurrence. None of the patients developed NAC, other loco-regional or distant recurrence in our cohort.

Loco-regional control of breast cancer patients with reconstruction

A total of 887 cases were more than three months. The median follow-up time was 28.2 months (range, 3.0–159.1 months). Eighteen patients (2.0%) developed local-regional recurrence at the median follow-up time of 26.6 months (range, 3.7–62.0 months). Eight patients developed distant metastasis prior to or at the same time of local-regional recurrence. Two patients developed local-regional recurrence prior to distant metastasis and seven patients developed

local-regional recurrence only (*Table 4*). In terms of the site of local-regional recurrence, 9 out of 18 patients developed breast/chest wall recurrence, four patients had supra-clavicle LN recurrence, two had axillary LN recurrence, two had internal mammary LN recurrence and one patient was not documented the specific site of recurrence. None of these patients died in our cohort.

Discussion

The current study revealed a significant trend of increase in breast reconstruction cases in FUSCC. However, compared with the great amount of mastectomies performed in China, breast reconstruction stays at a rather stable low rate of 3.5–4.5% over the past 15 years (3,4). Several reasons were thought to contribute to the low rate of reconstruction in China. Firstly, traditional Chinese women have low demand for their body image, and many of them are unaware of the possibility of breast reconstruction, especially for the older

generations, which explained why the median age for breast reconstruction was 39 years old while the median age for breast surgery was around 50 in our institute (5). Secondly, the heavy workload hampered the generalized application of reconstruction techniques. As reported by previous studies, there was a 4-fold increase of breast surgeries between 2006

and 2014 while the number of breast surgeons increased from 13 to 15 in FUSCC (3). Next, the dramatic increase of prophylactic mastectomy in Western countries increased reconstruction rate (6,7), while in China, this has little impact since such procedures are rarely performed. Lastly, limited patient education resulted that some patients were not aware of the option of breast reconstruction.

Significant shift in breast reconstruction paradigm was observed in our cohort. Prosthesis-based reconstruction displayed a more than ten-fold increase from 2012 to 2015, which echo with the worldwide transformation. In US, prosthesis-based reconstruction rates increased on average 11% per year from 8.52% in 1998 to 25.8% in 2008, surpassing autologous reconstruction to be the leading reconstructive method (8). The use of prosthesis can achieve aesthetical symmetrical appearance in bilateral reconstruction patients, especially in slim women whose autologous tissue may not be abundant enough for reconstruction. In our cohort, up to 15.9% patients had bilateral reconstruction in the prosthesis-based reconstruction group, much higher than other modalities; and another 9.9% patients had contralateral breast augmentation. In sum, up to 25% patients had bilateral implants placed. Notably, despite the advantages of short operation time and in-hospital time, prosthesis-based reconstruction had the highest fail-to-complete-reconstruction rate and return-to-operation room rate. Most surprisingly, the majority of patients had their implant/expander removed because that they regretted their decision to have prosthesis-based reconstruction. Further investigations are awaited to explore the reason behind this phenomenon.

For autologous reconstruction, on the other hand, our data suggested that pedicle-TRAM reconstruction

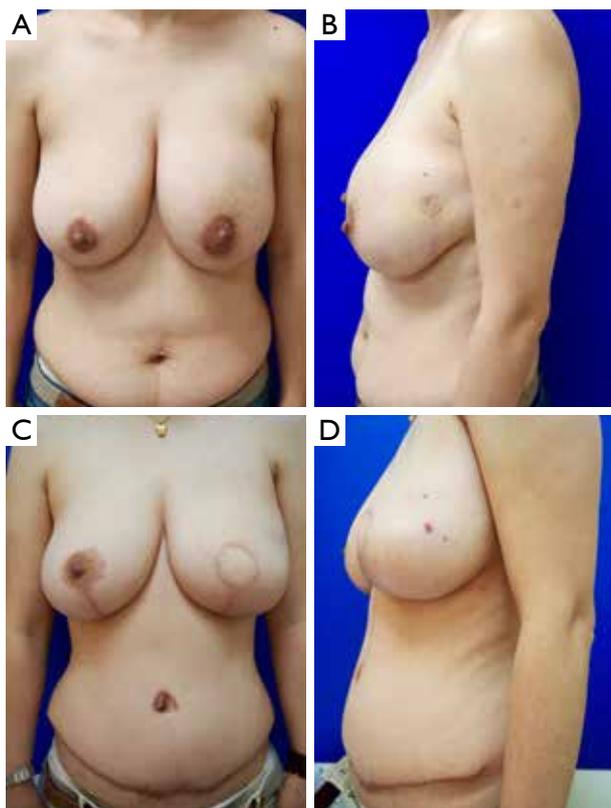


Figure 5 Free abdominal flap reconstruction with immediate contralateral breast reduction. (A,B) Pre-operative pictures; (C,D) postoperative pictures.

Table 3 Comparisons of other surgical conditions besides reconstruction in different surgical groups

Surgical conditions	Total, N=951 (%)	Abdominal flap, N=247 (%)	LDM ± implant, N=471 (%)	Prosthesis-based, N=233 (%)
Fail to complete surgery	20 (2.1)	3 (1.2)	1 (0.2)	16 (6.9)
Return to OR complications	38 (4.0)	13 (5.3)	10 (2.1)	15 (6.4)
Contralateral breast surgery [†]	108 (11.4)	21 (8.5)	18 (3.8)	69 (29.6)
Reconstruction	53 (5.6)	7 (2.8)	9 (1.9)	37 (15.9)
Reduction/mastopexy	44 (4.6)	12 (4.9)	9 (1.9)	9 (3.9)
Augmentation	11 (1.2)	2 (0.8)	0 (0.0)	23 (9.9)
Ipsilateral breast modification	19 (2.0)	14 (5.7)	2 (0.4)	3 (1.3)
Nipple reconstruction	102 (10.7)	61 (24.7)	34 (7.2)	7 (3.0)

[†], biopsy and breast-conserving surgery and mastectomy of the contralateral breast were excluded. OR, operation room.

Table 4 Characteristics of breast reconstruction patients who developed LRR prior to distant metastasis or LRR only

No.	Age	Reconstruction	Pathology	Stage	LRR time (mo)	LRR site	Status (mo)
1	30	LDMF	IDC	IIB	37.5	Chest	DRFS 117.1
2	54	LDMF + implant	IDC	pCR	37.6	Chest	Bone m at 56.6
3	50	Pedicled TRAM	IDC	IIB	24.2	Chest	DRFS 84.9
4	42	Free TRAM	IDC	IIA	6.9	Supra-clavicle LN	DRFS 18.3
5	40	LDMF	IDC	IIB	50.6	Axillary LN	DRFS 68.5
6	34	Free TRAM	DCIS + micro invasion	IIA	19.6	Chest	DRFS 36.2
7	36	LDMF + implant	DCIS + micro invasion	IA	36.2	Chest	DRFS 49.1
8	44	Free TRAM	IDC	IIA	8.0	Internal mammary LN	Lung m at 29.2
9	35	LDMF + implant	DCIS + micro invasion	IIA	28.9	Chest	DRFS 34.7
10	27	Prosthesis-based	IDC	IIA	12.5	IMLN	DRFS 26.6

LRR, loco-regional recurrence; LDMF, latissimus dorsi myocutaneous flap; IDC, invasive ductal carcinoma; pCR, pathological complete remission; m, metastasis; DRFS, distant recurrence-free survival; TRAM, transverse rectus abdominis myocutaneous; DCIS, ductal carcinoma *in situ*; LN, lymph node; met, metastasis; mo, months.

was gradually replaced by free-TRAM reconstruction since 2011. Compared with pedicle-TRAM, free-TRAM has significantly lower rate of the complication including abdominal bulge, abdominal strength weaken and hernia, with improved blood supply (9,10). Despite all the advantages, the application of free-TRAM was largely restricted by professional microsurgery skills and techniques as well as a much longer learning curve (11). As a typical cancer center in mainland China, there is no Department of Plastics and Reconstructive Surgery in FUCSS and all free-TRAM cases were performed by one single surgeon, which explained why LDMF reconstruction remained the most common method of autologous reconstruction. Furthermore, patients with abdominal flap reconstruction were more likely to have ipsilateral breast modification surgeries and nipple reconstruction than other reconstruction modalities, which implied these patients might have a higher demand for breast symmetry and self-image.

Although SSM is routinely performed for patients who received breast reconstruction in our institute, the use of NSM is still limited. In our cohort, there are 6.9% NSMs performed, all of which are highly selected cases—no suspected cancer infiltration to NAC measured by imaging techniques, phyllodes tumor and prophylactic mastectomy. NSM, with preservation of the NAC, is reported to improve patients' satisfaction, body image, and psychological adjustment (12,13). However, the indication of NSM is still under debate. Multiple studies have demonstrated that tumor size, tumor location, LN metastasis, lymphovascular

invasion, histologic type, immunological characteristics like HER2 should be taken into consideration when propose NSM to breast cancer patients (14-16). In terms of LRR of NSM, none of our cases developed loco-regional or distant recurrence because of relative short follow-up time and highly selective cases. According to previous studies, Orzalesi *et al.* reported loco-regional, NAC, systemic recurrence accounting for 2.9%, 0.7% and 1.0% respectively, with 0.7% death record among a 6-year study in Italy (17). NAC recurrence cases could be treated with NAC removal and had good prognoses, which suggested that NSM might be a safe procedure after selecting proper patients (18).

Despite NSM, same concerns was raised for all patients with breast reconstruction, that residual mammary tissue might be present and that breast reconstruction could negatively affected adjuvant chemotherapy and radiotherapy, especially in loco-regional control. Some study demonstrated that immediate breast reconstruction was associated with delay of adjuvant chemotherapy for women under the age of 60 (19); while another debated that immediate breast reconstruction did not delay adjuvant chemotherapy, compared with patients with no reconstruction (41 *vs.* 42 days, $P=0.61$) (20). As for post-mastectomy radiotherapy, Liljegren *et al.* found that the delivery of radiation was compromised in more than half of the patients underwent prosthesis-based immediate breast reconstruction, however the time from mastectomy to the start of radiotherapy was similar in reconstruction group versus non-reconstruction group (21). Kronowitz suggested

that immediate breast reconstruction did not pose negative impact on recurrence free survival in patients who received post-mastectomy radiotherapy in neither autologous tissue-based reconstruction nor implant-based reconstruction (22,23). In the current study, at a median follow-up time of 28.2 months, only 2.0% patients developed LRR, suggesting a satisfactory loco-regional control. Nevertheless, the interaction between breast reconstruction and adjuvant therapy was beyond the scope of our study.

Conclusions

The current study described a 15-year study of 951 breast reconstruction cases in FUSCC. The reconstruction cases increased over the years with the change of paradigm. Most strikingly, prosthesis-based reconstruction rapidly gained its prevalence and became the most common strategy in last year. Prosthesis-based reconstruction was associated with bilateral reconstruction, contralateral augmentation and higher complications. SSM was routinely performed for all reconstruction patients while NSM was only performed for highly selected patients. Patients with breast reconstruction were able to achieve satisfactory loco-regional control in our cohort.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Breast reconstruction at the MD Anderson Cancer Center

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Abstract: The introduction of the transverse rectus abdominis myocutaneous flap in the 1970s marks the beginning of modern breast reconstruction although implants were available even earlier mainly for breast augmentation. Mastectomy techniques have evolved from the early Halsted radical mastectomy to the modern skin sparing mastectomy. The latter made possible using implants for breast reconstruction. Although prosthetic reconstruction provides a simpler procedure with quick recovery, autologous reconstruction offers more natural and long-lasting results especially in the setting of radiotherapy. Both forms have been extensively used at the MD Anderson Cancer Center (MDACC) while microsurgical breast reconstruction has been the hallmark of the MDACC experience. One of the most challenging areas of breast reconstruction is how to achieve good results without compromising adjuvant therapy when post-mastectomy radiotherapy is required. Managing upper extremity lymphedema following breast cancer treatment is another difficult issue which has gained great attention in recent years. This article highlights the important work in various aspects of breast reconstruction that has been done at the MDACC.

Keywords: Breast reconstruction; deep inferior epigastric perforator flap (DIEP flap); post-mastectomy radiotherapy; delayed-immediate breast reconstruction; lymphedema

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Introduction

Breast reconstruction at the University of Texas, MD Anderson Cancer Center (MDACC) started in the early 1980s. The Department of Plastic Surgery was established in 1988, initially with only two plastic surgeons. Dr. Stephen S. Kroll was a notable pioneer in breast reconstruction. The department has grown tremendously since then (*Figure 1*).

MD Anderson's Nellie B. Connally Breast Center is one of the largest breast cancer centers in the United States, treating 40,000 patients a year. The number of breast reconstruction cases has increased significantly over the years (*Figure 2*). All types of breast reconstructions are performed including autologous tissue and prosthetic reconstructions, delayed and immediate reconstructions, pedicled flaps and free tissue transfers. The number of free flaps for breast reconstruction had a steady increase until recently when the use of prosthesis has increased (*Figure 3*). This is a nationwide trend due to a number of

factors such as patient choices (early return to work etc.) and decreased reimbursement for free flap reconstructions. The type of pedicled flaps has also changed significantly (*Figure 4*). Initially the pedicled transverse rectus abdominis musculocutaneous (TRAM) flap was popular for pedicled flap reconstruction. This was largely replaced by free TRAM or DIEP flaps. The pedicled latissimus dorsi myocutaneous flap became popular in combination with a prosthesis. The latissimus dorsi flap alone, however, is usually inadequate to create a sizable breast.

Over the years, the faculty of Plastic Surgery at MDACC has contributed hundreds of high quality publications on breast reconstruction and addressed numerous issues surrounding breast reconstruction. Their experience and research helped shaping up breast reconstruction in the 1980s and 1990s. New advances in breast reconstruction and radiation as well as the surgical management of lymphedema also made significant contributions in this field.

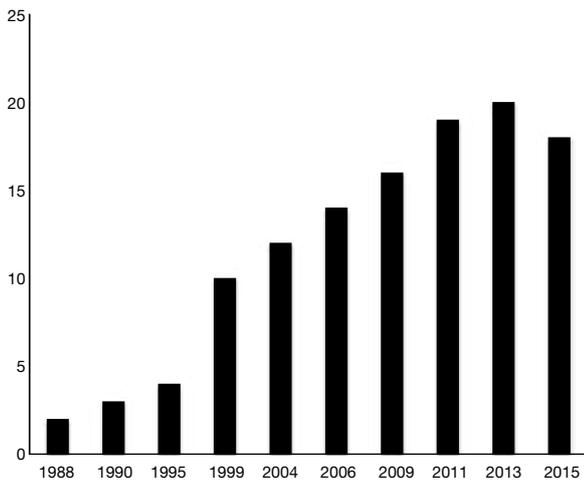


Figure 1 Number of faculties in the Department of Plastic Surgery at the MD Anderson Cancer Center (MDACC).

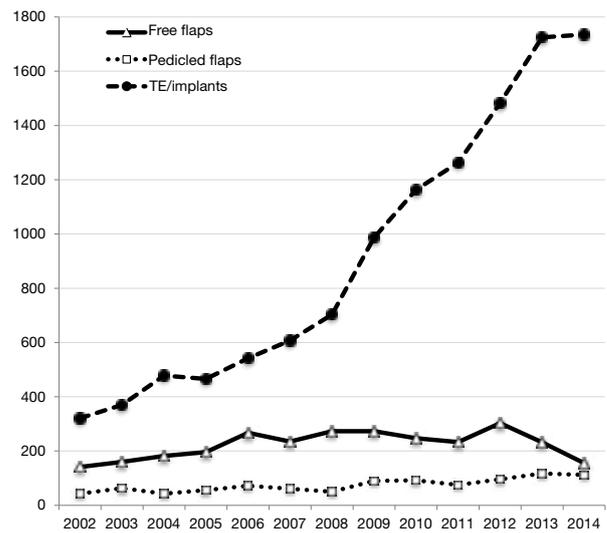


Figure 3 Types of breast reconstruction.

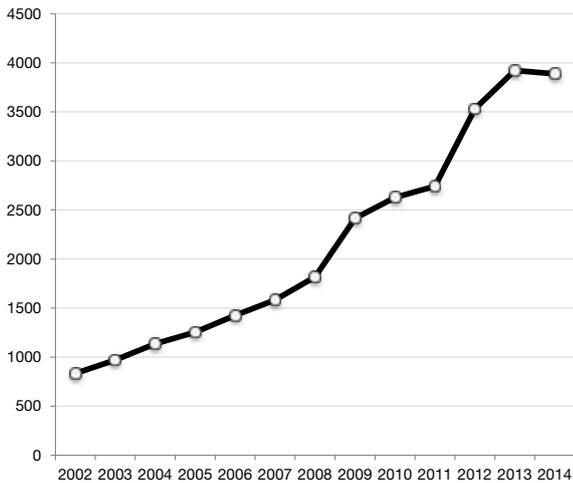


Figure 2 Total number of breast reconstructive cases.

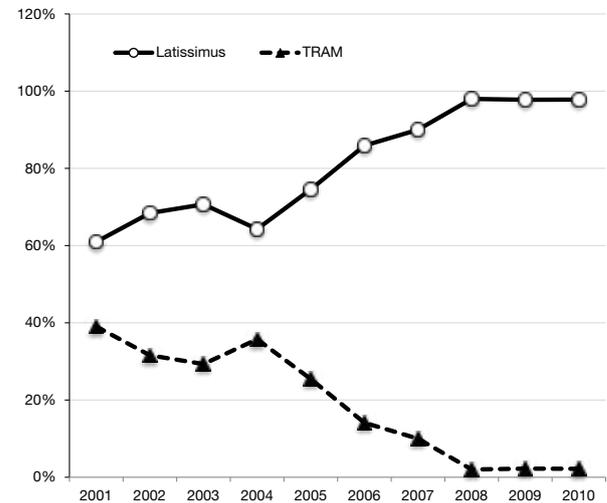


Figure 4 Types of pedicled flaps for breast reconstruction.

Delayed vs. immediate reconstruction

In the early years, breast reconstruction was usually performed in a delayed fashion. The reasons were the limited awareness and resource availability for breast reconstruction and the concerns for oncologic safety. Further experience and studies showed that immediate reconstruction was oncologically safe (1,2). In addition, immediate reconstruction clearly yields superior cosmetic results and psychosocial benefits, and gradually gained popularity in the 1990s. With skin sparing mastectomy, the breast envelop is well preserved. Immediate reconstruction, therefore, can yield near normal appearance of the reconstructed

breast. The relative contraindication for immediate breast reconstruction is the need for postmastectomy radiotherapy.

Evolution of mastectomy techniques

Mastectomy techniques have evolved from a Halsted “tissue-eradicating” to a modern “tissue-sparing” philosophy, from radical mastectomy, modified radical mastectomy, to skin-sparing mastectomy and nipple-sparing mastectomy (NSM). Numerous studies from MDACC and others have confirmed the oncologic safety of the

conservative approaches (1,3-5). Skin- and nipple-sparing mastectomies preserve the breast envelop, reduce scar formation, and significantly improve the aesthetic outcomes of breast reconstruction. Skin-sparing mastectomy is the current standard mastectomy procedure. However, removing the nipple-areola complex still causes significant dissatisfaction and psychosocial impact in patients. This led clinicians to explore the technical and oncologic feasibility of nipple-sparing mastectomy (NSM). For oncologic safety, it is generally accepted that the indications for NSM include: (I) tumor size <3 cm; (II) tumor located >2 cm from the nipple; (III) there is no skin involvement of tumor; (IV) negative axillary nodes on clinical examination; and (V) negative margins beneath nipple. Relative contraindications for NSM include smoking history, diabetes, hypertension, larger breast size, significant ptosis, and history of radiotherapy. All these are significant risk factors for nipple areola complex necrosis. The benefit of NSM is only evident when immediate breast reconstruction is performed. If immediate reconstruction is not performed, the breast skin envelop contracts once healed to the chest wall. Re-elevation of the skin envelop and nipple-areola complex can never obtain adequate volume and the nipple will end up in the upper portion of the breast. During delayed reconstruction, the nipple-areola complex and most of the breast skin will need to be removed and replaced with autologous tissue, thus defeating the purpose of NSM.

Autologous vs. prosthetic reconstruction

Autologous and prosthetic reconstruction each has its own advantages and disadvantages. The main advantages of autologous reconstruction are that it is the patient's own tissue, looks and feels more natural, ages gracefully, tolerates radiation better, and it is permanent. The main disadvantage is the complexity, lengthy surgery, and long recovery. Prosthetic reconstruction is quite the opposite. It is quick and simple, fast recovery, but looks and feels less natural, may develop capsular contracture and rupture that require replacement, does not tolerate radiation, and it is not permanent. The average life of a breast implant is 10 years. For these reasons, plastic surgeons at MD Anderson have long been advocates for autologous reconstruction. In recent years, however, driven by patients, economics, and national trends, implant based reconstruction has also become popular at our institution (*Figure 3*). Kroll *et al.* found that although the initial cost for TRAM flap reconstruction was higher, the cost advantage of implant-

based reconstruction disappeared over time due to complications and the need for subsequent surgeries (6).

Implants for breast reconstruction were first developed by Cronin and Gerow in 1962—the Dow Corning Corporation. These silicone gel implants underwent several refinements and the 3rd and 4th generation silicone implants in the 1980s had elastomer-coated shells to decrease leakage and offered textured surface and anatomic models. However, during the 1990s, thousands of women claimed sickness from their breast implants. The medical complaints included neurological and rheumatological health problems. Silicone implants were banned in the US in 1990. The Dow Corning Corporation went bankrupt in 1995 when it faced 19,000 breast implant sickness lawsuits. After 10 years of research and investigation, the Institute of Medicine published the Safety of Silicone Breast Implants study in 1999 which reported no evidence that saline filled and silicone-gel filled breast implant devices caused systemic health problems and that their use posed no new health or safety risks. On November 17, 2006, the US Food and Drug Administration lifted its restrictions against using silicone-gel breast implants for breast reconstruction and for augmentation mammoplasty. Long before the Institute of Medicine study, the MD Anderson plastic surgery group published a report in 1993 in which they prospectively studied patients who underwent breast reconstruction between 1986 and 1992 and found that the incidence of autoimmune disease in mastectomy patients receiving silicone gel implants was not different from those who had reconstruction with autologous tissue (7). They also found, in a cadaveric study, that silicon levels at distant tissue were no different between those with silicone gel implants and those without; and that there was no correlation between intact or ruptured implants and symptoms of collagen-vascular disease (8).

Free vs. pedicled TRAM flaps

Since the introduction of TRAM flap, pedicled TRAM flap dominated breast reconstruction in the early days. Although it does not require microsurgical techniques, frequent fat necrosis and partial flap loss with the pedicled TRAM flap were encountered in obese patients, smokers, diabetic patients as well as those with hypertension. Pedicled TRAM flap is based on the superior epigastric vessels whereas the main blood supply to the TRAM flap is based on the deep inferior epigastric vessels which are the vascular pedicle of the free TRAM flap. Schusterman *et al.*, in 1992, found that

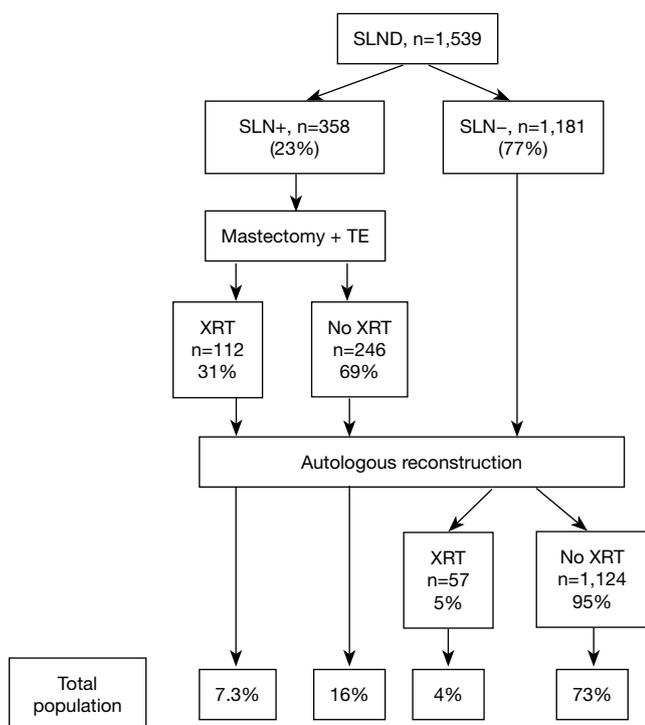


Figure 5 Sentinel node dissection before mastectomy.

the free TRAM flap resulted in much lower complications than the pedicled TRAM flap (9-11). Harvesting the rectus abdominis muscle inevitably causes abdominal weakness (12). In order to reduce the abdominal morbidity, Dr. Stephen Kroll and others pioneered the deep inferior epigastric perforator (DIEP) flap for breast reconstruction (13-15). With advances in perforator anatomy, various muscle-sparing TRAM flaps were then created. The superficial inferior epigastric artery (SIEA) flap has also been used for breast reconstruction but Dr. Pierre Chevray found that the SIEA was present or large enough in only 30–40% of the patients (16).

Breast reconstruction and radiation

Breast reconstruction in patients requiring postoperative radiotherapy can be a difficult clinical dilemma (17-25). Current indications for postoperative radiotherapy at MDACC include: (I) T3 or T4 tumor; (II) N2 fixed axillary lymph nodes or positive internal mammary nodes; (III) N3 nodal disease (infraclavicular, supraclavicular, internal mammary and axillar nodes); (IV) extranodal extension; (V) presence of 4 or more positive lymph nodes. However, there

have been reports showing that postoperative radiotherapy may be beneficial in 1–3 positive lymph nodes or in T1, T2 tumors. This is still controversial. Postoperative radiotherapy can have significant effect on the reconstructed breast, including high incidences of fat necrosis, volume loss, and contracture. The effect on implant-based reconstruction is even worse, often leading to implant failure requiring removal and autologous reconstruction. Therefore, immediate breast reconstructions are not recommended at MDACC when postoperative radiotherapy is planned. There are occasions, however, patients may have clinically negative nodal status preoperatively and undergo breast reconstruction while permanent histology reveals positive lymph nodes that require postoperative radiotherapy. In a recent unpublished review of autologous breast reconstructions at MDACC, among 1,539 cases of sentinel lymph node dissections (SLND), 23% (n=358) were positive and underwent mastectomy with tissue expander. Among them, 31% (n=112) required postoperative radiotherapy and 69% did not. In the 77% (n=1,181) negative SLN who underwent autologous reconstruction, 57 patients required postoperative radiotherapy based on permanent pathologic findings (Figure 5). For this patient population in which postoperative radiotherapy is uncertain at the time of surgery, the concept of “delayed-immediate reconstruction” was introduced by Dr. Steve Kronowitz in 2004 to address this issue (17,22,23). In brief, a tissue expander is placed at the time of mastectomy with maximum possible initial saline fill. If postmastectomy radiotherapy is indicated based on permanent sections, the tissue expander is deflated to allow effective radiation delivery. The tissue expander is re-inflated after radiation therapy followed by definitive breast reconstruction with autologous tissue flaps with or without implants (Figure 6).

Recipient vessel selections have also undergone significant changes. The thoracodorsal vessels have been gradually replaced by the internal mammary vessels as recipient vessels for free flap breast reconstruction (26-28). The internal mammary vessels are closer to the defect, have sufficient calibers and flow, and easier for positioning during anastomosis. They are also less affected by radiation. In patients with narrow rib spaces, the 3rd costal cartilage is often removed for adequate exposure during recipient vessel dissection. With wide rib spaces, the internal mammary vessels can be safely dissected out without removing the rib cartilage. Some patients have large internal mammary perforators that can be used as recipient vessels without exposing the main internal mammary vessels.

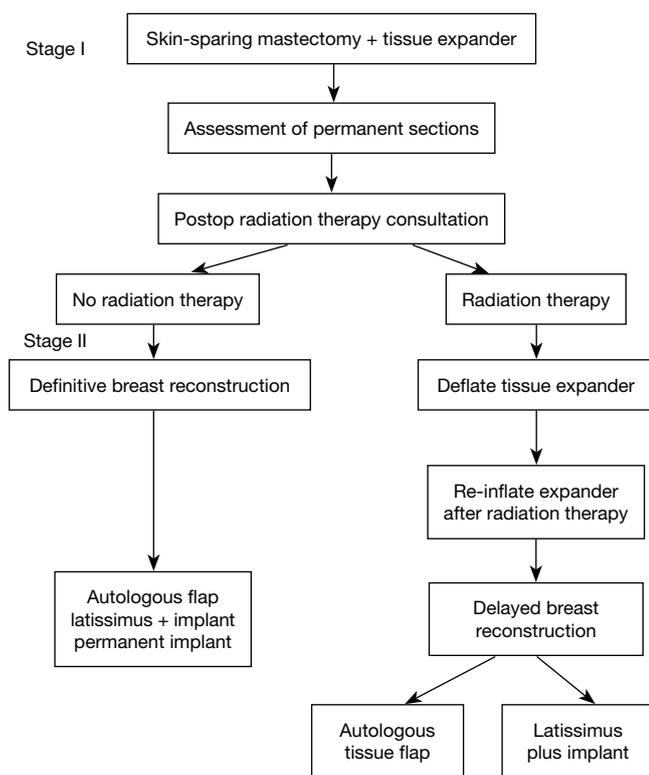


Figure 6 Delayed-immediate breast reconstruction.

Management of upper extremity lymphedema after treatment for breast cancer

One side effect of breast cancer treatment with mastectomy, axillary lymph node dissection, and radiation therapy is the development of upper extremity lymphedema. It is estimated that the incidence of breast-cancer related lymphedema is 8–30% in all breast cancer survivors. Koshima first reported the use of “super microsurgery” with lymph-venous bypass to treat lymphedema in 2000. Dr. David Chang first introduced this technique to MDACC and the United States in 2005 and published his experience in 2010 (29). Since then, management of lymphedema has become a hot topic throughout the world from anatomy, physiology, imaging, to clinical management (30–36). However, it is generally accepted that the effectiveness of lymphovenous bypass surgery is 50% at best and long-term results are still unclear. Lymphovenous bypass is less effective for long-standing lymphedema patients. For these patients, lymph node transfer may be a better alternative.

In summary, as the nation’s premier cancer center, MDACC has extensive experience in breast reconstruction

and its related issues, and has made significant contributions in the development and advancement of breast reconstruction and breast-cancer related lymphedema treatment.

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None.

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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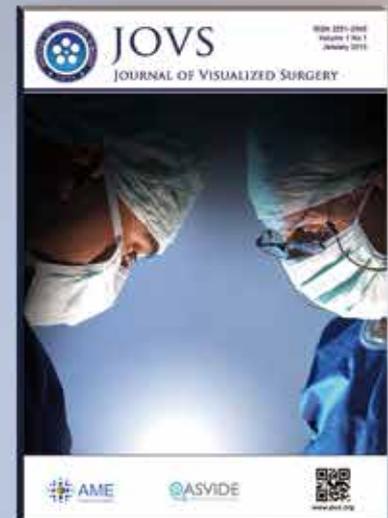
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