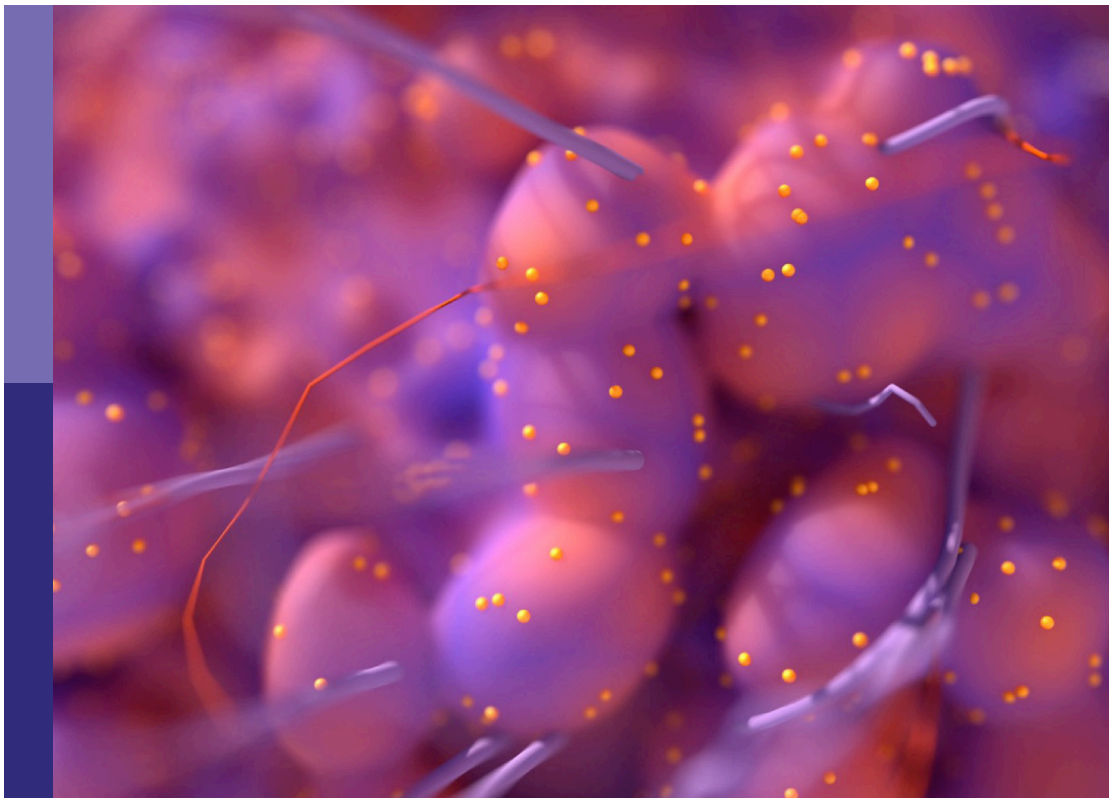
frontiers | Research Topics

Oncoplastic surgery for breast cancer

Edited by
René Aloisio Da Costa Vieira, Gil Facina, Daniel Tiezzi, Cicero Urban and Ruffo de Freitas Junior

Published in
Frontiers in Oncology



ISSN 1664-8714
ISBN 978-2-8325-4735-9
DOI 10.3389/978-2-8325-4735-9

About Frontiers

Frontiers is more than just an open access publisher of scholarly articles: it is a pioneering approach to the world of academia, radically improving the way scholarly research is managed. The grand vision of Frontiers is a world where all people have an equal opportunity to seek, share and generate knowledge. Frontiers provides immediate and permanent online open access to all its publications, but this alone is not enough to realize our grand goals.

Frontiers journal series

The Frontiers journal series is a multi-tier and interdisciplinary set of open-access, online journals, promising a paradigm shift from the current review, selection and dissemination processes in academic publishing. All Frontiers journals are driven by researchers for researchers; therefore, they constitute a service to the scholarly community. At the same time, the *Frontiers journal series* operates on a revolutionary invention, the tiered publishing system, initially addressing specific communities of scholars, and gradually climbing up to broader public understanding, thus serving the interests of the lay society, too.

Dedication to quality

Each Frontiers article is a landmark of the highest quality, thanks to genuinely collaborative interactions between authors and review editors, who include some of the world's best academicians. Research must be certified by peers before entering a stream of knowledge that may eventually reach the public - and shape society; therefore, Frontiers only applies the most rigorous and unbiased reviews. Frontiers revolutionizes research publishing by freely delivering the most outstanding research, evaluated with no bias from both the academic and social point of view. By applying the most advanced information technologies, Frontiers is catapulting scholarly publishing into a new generation.

What are Frontiers Research Topics?

Frontiers Research Topics are very popular trademarks of the *Frontiers journals series*: they are collections of at least ten articles, all centered on a particular subject. With their unique mix of varied contributions from Original Research to Review Articles, Frontiers Research Topics unify the most influential researchers, the latest key findings and historical advances in a hot research area.

Find out more on how to host your own Frontiers Research Topic or contribute to one as an author by contacting the Frontiers editorial office: frontiersin.org/about/contact

Oncoplastic surgery for breast cancer

Topic editors

René Aloisio Da Costa Vieira — Barretos Cancer Hospital, Brazil
Gil Facina — Federal University of São Paulo, Brazil
Daniel Tiezzi — University of São Paulo, Brazil
Cicero Urban — Hospital Nossa Senhora das Graças, Brazil
Ruffo de Freitas Junior — Federal University of Goiás, Brazil

Citation

Da Costa Vieira, R. A., Facina, G., Tiezzi, D., Urban, C., de Freitas Junior, R., eds. (2024). *Oncoplastic surgery for breast cancer*. Lausanne: Frontiers Media SA. doi: 10.3389/978-2-8325-4735-9

Table of contents

05 Editorial: Oncoplastic surgery for breast cancer
René Aloisio da Costa Vieira, Gil Facina, Daniel Guimarães Tiezzi, Cicero de Andrade Urban and Ruffo de Freitas Junior

08 Long-term oncological outcomes of oncoplastic breast-conserving surgery after a 10-year follow-up – a single center experience and systematic literature review
Jun Xian Hing, Byeong Ju Kang, Hee Jung Keum, Jeeyeon Lee, Jin Hyang Jung, Wan Wook Kim, Jung Dug Yang, Joon Seok Lee and Ho Yong Park

21 Does breast oncoplastic surgery improve quality of life?
René Aloisio da Costa Vieira, Antônio Bailão-Junior and Idam de Oliveira-Junior

30 Prospective study: Impact of breast magnetic resonance imaging on oncoplastic surgery and on indications of mastectomy in patients who were previously candidates to breast conserving surgery
Karina Furlan Anselmi, Cicero Urban, Maíra Teixeira Dória, Linei Augusta Brolini Delle Urban, Ana Paula Sebastião, Flávia Kuroda, Iris Rabinovich, Alessandra Amatuzzi Fornazari Cordeiro, Leonardo Paese Nissen, Eduardo Schunemann Jr., Cleverton Spautz, Julia Di Conti Pelanda, Rubens Silveira de Lima, Mario Rietjens and Marcelo de Paula Loureiro

38 Therapeutic mammoplasty: a "wise" oncoplastic choice—lessons from the largest single-center cohort from Asia
Chaitanyanand Koppiker, Sneha Joshi, Rupa Mishra, Devaki A. Kelkar, Pragnya Chigurupati, Anjali Joshi, Jisha John, Shweta Kadu, Amitkumar Bagdia, Deepti Thakkar, Chetan Deshmukh, Harikiran Allampati, Gautam Sharan, Upendra Dhar, Smeeta Nare, Sanket Nagarkar, Laleh Busheri, Beenu Varghese and Mugdha Pai

58 Dermoglandular advancement-rotation flap for conservative treatment of breast cancer – description of technique, objective and subjective assessments
Maria Carolina Soliani Bastos, Fábio Bagnoli, José Francisco Rinaldi, Thais Businaro Fernandes João and Vilmar Marques de Oliveira

66 Oncoplastic surgery for Paget's disease of the breast
Rafael José Fábio Pelorca, Idam de Oliveira-Junior and René Aloisio da Costa Vieira

75 How well are Brazilian mastologists (breast surgeons) trained in breast reconstruction and oncoplastic surgery? A study of the impact of a breast reconstruction and oncoplastic surgery improvement course
Thais Businaro Fernandes João, Vilmar Marques de Oliveira, Fábio Bagnoli, Maria Carolina Soliani Bastos, José Francisco Rinaldi, Fabrício Palermo Brenelli and Evandro Fallaci Mateus

85 Oncoplastic and reconstructive breast surgery
Primeera Wignarajah, Charles M. Malata and John R. Benson

104 Latissimus dorsi flap – the main force in breast reconstruction for breast tumor in Chinese population
Shuyue Zheng, Shuang Hao, Jiajian Chen, Yingying Zhang, Benlong Yang, Xiaoyan Huang, Guangyu Liu, Zhimin Shao and Jiong Wu

115 Factors associated with unsatisfactory cosmetic results in oncoplastic surgery
Idam de Oliveira-Junior, René Aloísio da Costa Vieira, Gabriele Biller, Almir José Sarri, Fabíola Cristina Brandini da Silva and Eliana Aguiar Petri Nahás

122 Impact of oncoplasty in increasing breast conservation rates Post neo-adjuvant chemotherapy
Chaitanyanand B. Koppiker, Devaki A. Kelkar, Madhura Kulkarni, Shweta Kadu, Mugdha Pai, Upendra Dhar, Chetan Deshmukh, Beenu Varghese, Vaishali Zamre, Nutan Jumle, Nutan Gangurde, Anjali Joshi, Rohini Unde, Rituja Banale, Namrata Namewar, Pooja Vaid, Laleh Busheri, George Thomas, Smeeta Nare, Jerome Pereira and Sunil Badve

138 Extreme oncoplasty: past, present and future
René Aloisio da Costa Vieira, Regis Resende Paulinelli and Idam de Oliveira-Junior

frontiers | Frontiers in Oncology

TYPE Editorial
PUBLISHED 27 March 2024
DOI 10.3389/fonc.2023.1348964

OPEN ACCESS

EDITED AND REVIEWED BY
Aali Jan Sheen,
Manchester Royal Infirmary, United Kingdom

*CORRESPONDENCE
RenéAloisio da Costa Vieira
reneacv@gmail.com

RECEIVED 03 December 2023
ACCEPTED 12 December 2023
PUBLISHED 27 March 2024

CITATION
da Costa Vieira RA, Facina G, Tiezzi DG, Urban C and Freitas-Junior R (2024) Editorial: Oncoplastic surgery for breast cancer. *Front. Oncol.* 13:1348964. doi: 10.3389/fonc.2023.1348964

Editorial: Oncoplastic surgery for breast cancer

René Aloisio da Costa Vieira[1,2]*, Gil Facina[3], Daniel Guimarães Tiezzi[4], Cicero de Andrade Urban[5] and Ruffo de Freitas Junior[6]

[1]Barretos Cancer Hospital, Barretos, Brazil, [2]Medical School of São Paulo State University, Botucatu, Brazil, [3]Federal University of São Paulo, São Paulo, Brazil, [4]Nossa Senhora das Graças Hospital, Curitiba, Brazil, [5]Hospital Nossa Senhora das Graças, Curitiba, Brazil, [6]Faculty of Medicine, Federal University of Goiás, Goiânia, Brazil

KEYWORDS

surgical flaps, breast conserving surgeries, breast neoplasms, breast reconstruction, oncoplastic surgery, extreme oncoplasty, oncoplastic reconstruction

Editorial on the Research Topic
Oncoplastic surgery for breast cancer

The surgical treatment of breast cancer has changed radically. We have moved from radical mastectomy to conservative treatment of the breast and axilla, as it was observed that less radical treatment did not change survival. Our concept of surgical margins has also changed, and we have begun to better understand tumour biology through molecular subtypes (1). We have begun to evaluate local recurrence, reduction of sequelae, cosmesis and quality of life.

In the 1990s, Audrestch proposed the term oncoplasty (2), and this concept has evolved. Regarding breast conservative treatment (BCT), non-oncological mammoplasty opened space for a set of techniques to be used in the treatment of breast cancer. The benefits of aesthetic techniques were assimilated, leading to improvements in breast cosmesis and quality of life. Such techniques were improved and adjusted according to the location of the tumor and the resection volume. Aiming at dissemination, standardization and medical education, classifications emerged. Initially, Urban C (2008) (3) proposed three levels of competence. Clough K.B. et all (2010) (4), proposed a classification based on the resected volume, and finally, the American Society of Breast Surgeons (ASBS, 2019) (5, 6) defined the term volume displacement for redistributing the resection volume. They also considered the term volume replacement, in the context of implant-based reconstruction or local/regional flap reconstruction (5).

Radical mastectomy, which was initially associated with delayed reconstruction with myocutaneous flaps, was modified with immediate breast reconstruction techniques that allow preservation of the skin and nipple with the addition of breast prostheses. Aiming to improve the results, we started using dermal matrices, subcutaneous prostheses and fat grafts. In some centres, robotic and video-assisted mastectomy are already performed. The term oncoplastic surgery has been associated with BCT, but some non-American authors associate it with breast reconstruction.

Although axillary surgery has decreased, the spectrum of breast surgeries has expanded, making it necessary to have knowledge and training in the range of surgical possibilities. Neoadjuvant chemotherapy allows the initial reduction of tumors, and resection of residual disease is increasing the rate of BCT (1). The concept of tumor size has shifted to a breast/volume ratio. Then, the concept of extreme oncoplasty emerged (2015) (7), allowing BCT for tumors larger than 5 cm, with multifocal and/or multicentric disease. Oncoplasty represents a new paradigm to be disseminated and assimilated by breast surgeons (8).

When evaluating publications related to breast oncoplasty in PubMed (oncoplastic surgery or oncoplasty), we began to observe an increasing annual publication rate, summing up to a total number of 1,415 references in 2022. These publications cover four main topics (9): (1) indication: type of patient and tumor; (2) type of surgery: technique, oncological safety, laterality, symmetrization, and local recurrence-free survival time; (3) cosmesis: type, patient acceptance, surgeon training, and symmetry; and (4) quality of life: general quality of life, breast quality and associated sequelae. No less important, we must consider three additional topics: (5) breast reconstruction; (6) special situations in mastology, where oncoplasty can be used; and (7) training in oncoplasty.

In 2022, given this growing demand, we had the opportunity to serve as the Guest Editorial Board on "*Oncoplastic Surgery for Breast Cancer*" (OSBC) topic. The main focus was to discuss oncoplasty through articles related to the seven main topics previously described. We made a list of the main authors who have been applying oncoplastic techniques and have been publishing it this field. A total of 330 researchers were invited to participate. To be part of this Research Topic, the author must have chosen a Research Topic in the OSBC context and accepted the conditions associated with open access publication. Over one year, 30 researchers considered sending articles, 18 manuscripts were fully submitted, and according to the standards of the journal and the reviewers, 12 articles were accepted within the estimated deadline. Fortunately, we have closed this special volume with the OSBC theme.

This special volume includes 3 reviews and 9 original articles encompassing the seven main themes in oncoplasty. The reviews discuss the multiple aspects associated with breast oncoplasty; the multiple indications, possibilities and results related to the extreme oncoplasty; and methodologies and results for assessing quality of life. In terms of patient selection, there is a publication discussing the impact of nuclear magnetic resonance imaging and another discussing the impact of neoadjuvant chemotherapy and potential therapeutic possibilities. From the point of view of surgical techniques, we have a review related to extreme oncoplasty. We also have original articles showing results associated with the use of dermoglandular advancement flaps and Wise Pattern Mammoplasty. Regarding the evaluation of long-term results, we have articles related to recurrence and conditions associated with unsatisfactory results in BCT. We also have a study related to the use of the latissimus dorsi in breast reconstruction. Under the theme of special conditions, we discuss the use of OSBC in Paget's disease of the breast. We have one article reporting a successful model of training in oncoplasty. We are happy to organize and assist the discussion of OSBC, allowing breast surgeons to broaden their horizons on such an important topic.

Our patients deserve qualified treatment. All breast surgeons must think about surgical possibilities associated with OSBC and be qualified. Breast oncoplasty is here to stay, and this publication is a gift from the journal, the editors, the reviewers and authors, to breast surgeons and mainly our patients, the reason for this entire publication.

Author contributions

RV: Conceptualization, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing. GF: Validation, Visualization, Writing – original draft, Writing – review & editing. DT: Validation, Visualization, Writing – review & editing. CU: Conceptualization, Validation, Visualization, Writing – review & editing. RF-J: Conceptualization, Validation, Visualization, Writing – review & editing.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

References

1. Curigliano G, Burstein HJ, Winer EP, Gnant M, Dubsky P, Loibl S, et al. De-escalating and escalating treatments for early-stage breast cancer: the St. Gallen International Expert Consensus Conference on the Primary Therapy of Early Breast Cancer 2017. *Ann Oncol* (2017) 28:1700–12. doi: 10.1093/annonc/mdx308

2. Audretsch WP, Rezai M, Kolotas C, Zamboglou N, Schnabel T, Bojar H, et al. Tumor-Specific immediate reconstruction in breast cancer patients. *Perspect Plast Surg* (1998) 11:71–100. doi: 10.1055/s-2008-1080243

3. de Andrade Urban C. New classification for oncoplastic procedures in surgical practice. *Breast* (2008) 17:321–2. doi: 10.1016/j.breast.2007.11.032

4. Clough KB, Kaufman GJ, Nos C, Buccimazza I, Sarfati IM. Improving breast cancer surgery: a classification and quadrant per quadrant atlas for oncoplastic surgery. *Ann Surg Oncol* (2010) 17:1375–91. doi: 10.1245/s10434-009-0792-y

5. Chatterjee A, Gass J, Patel K, Holmes D, Kopkash K, Peiris L, et al. A consensus definition and classification system of oncoplastic surgery developed by the american society of breast surgeons. *Ann Surg Oncol* (2019) 26:3436–44. doi: 10.1245/s10434-019-07345-4

6. Patel K, Bloom J, Nardello S, Cohen S, Reiland J, Chatterjee A. An oncoplastic surgery primer: common indications, techniques, and complications in level 1 and 2 volume displacement oncoplastic surgery. *Ann Surg Oncol* (2019) 26:3063–70. doi: 10.1245/s10434-019-07592-5

7. Silverstein MJ, Savalia N, Khan S, Ryan J. Extreme oncoplasty: breast conservation for patients who need mastectomy. *Breast J* (2015) 21:52–9. doi: 10.1111/tbj.12356

8. Weber WP, Morrow M, Boniface J, Pusic A, Montagna G, Kappos EA, et al. Knowledge gaps in oncoplastic breast surgery. *Lancet Oncol* (2020) 21:e375–e85. doi: 10.1016/S1470-2045(20)30084-X

9. Oliveira-Junior I, Haikel RL, Vieira RAC. Breast-conserving treatment in oncoplastic times: indications, cosmesis, and quality of life. *Mastology* (2021) 31: e20200040. doi: 10.29289/2594539420200040

frontiers | Frontiers in Oncology

TYPE Original Research
PUBLISHED 09 August 2022
DOI 10.3389/fonc.2022.944589

OPEN ACCESS

EDITED BY
René
Aloisio Da Costa Vieira,
Barretos Cancer Hospital, Brazil

REVIEWED BY
Idam Oliveira Junior,
Barretos Cancer Hospital, Brazil
Fábio Bagnoli,
Santa Casa of Sao Paulo, Brazil

*CORRESPONDENCE
Ho Yong Park
phy123@knu.ac.kr

†These authors have contributed equally to this work and share first authorship

SPECIALTY SECTION
This article was submitted to Surgical Oncology, a section of the journal Frontiers in Oncology

RECEIVED 15 May 2022
ACCEPTED 07 July 2022
PUBLISHED 09 August 2022

CITATION
Hing JX, Kang BJ, Keum HJ, Lee J, Jung JH, Kim WW, Yang JD, Lee JS and Park HY (2022) Long-term oncological outcomes of oncoplastic breast-conserving surgery after a 10-year follow-up – a single center experience and systematic literature review. *Front. Oncol.* 12:944589. doi: 10.3389/fonc.2022.944589

Long-term oncological outcomes of oncoplastic breast-conserving surgery after a 10-year follow-up – a single center experience and systematic literature review

Jun Xian Hing[1,2,3†], Byeong Ju Kang[1†], Hee Jung Keum[1], Jeeyeon Lee[1], Jin Hyang Jung[1], Wan Wook Kim[1], Jung Dug Yang[1,4], Joon Seok Lee[1,4] and Ho Yong Park[1*]

[1]Department of Surgery, School of Medicine, Kyungpook National University, Kyungpook National University Chilgok Hospital, Daegu, South Korea, [2]Division of Breast Surgery, Department of General Surgery, Changi General Hospital, Singapore, Singapore, [3]Singhealth Duke-NUS Breast Centre, Singapore Health Services Pte Ltd, Singapore, Singapore, [4]Department of Plastic and Reconstructive Surgery, School of Medicine, Kyungpook National University, Daegu, South Korea

Aim: While many studies reported the oncological outcomes of oncoplastic breast-conserving surgery (OBCS), there were inherent differences in the study population, surgeons' expertise, and classifications of techniques used. There were also limited studies with long term follow up oncological outcomes beyond 5 years. This current study aimed to compare long-term oncological outcomes of ipsilateral breast tumor recurrence (IBTR) disease-free survival (DFS) and overall survival (OS) following conventional and oncoplastic breast-conserving surgery using volume displacement and replacement techniques.

Methods: Between 2009 and 2013, 539 consecutive patients who underwent breast conservation surgery including 174 oncoplastic and 376 conventional procedures were analysed. A systematic review of studies with at least five years of median follow up were performed to compare long term oncological outcomes.

Results: At a median follow-up of 82.4 months, there were 23 (4.2%) locoregional recurrences, 17 (3.2%) metachronous contralateral breast cancer, 26 (4.8%) distant metastases, and 13 (2.4%) deaths. The hazard ratio of OBCS for IBTR, DFS and OS were 0.78 (95% confidence interval [CI] 0.21–2.94, p=0.78), 1.59 (95% CI, 0.88 to 2.87, p=0.12), and 2.1 (95% CI, 0.72 to 5.9, p=0.17) respectively. The 10-year IBTR-free, DFS and OS rate were 97.8%, 86.2%, and 95.7% respectively.

Conclusion: There remained a dearth in well-balanced comparative studies with sufficient long-term follow-up, and our study reported long-term

oncological outcomes for OBCS which were favourable of either VD or replacement techniques.

KEYWORDS

oncoplastic, breast-conserving surgery, oncological outcomes, volume displacement, volume replacement

Introduction

Historical data have shown that breast-conserving surgery followed by radiotherapy has equivalent oncological outcomes to those of mastectomy in early breast cancer (1, 2). As long-term survival after breast cancer treatment has become commonplace, more attention has been given to develop oncoplastic techniques to provide better patient and aesthetic satisfaction (3, 4). The primary role of oncoplastic breast-conserving surgery (OBCS) is to achieve oncological safety while minimizing the risk of unacceptable local deformity by allowing reconstruction of the defect and preventing the need for mastectomy (5, 6).

Following the inception of tumor-specific immediate breast reconstruction more than 20 years ago, Werner Audretsch coined the term oncoplastic surgery, and many international experts contributed to the burgeoning field of OBCS (5, 7–11). Despite the similarity in rationale behind various oncoplastic techniques, there remained differences across geographical locations in terms of surgeons' perspectives and practices in defining OBCS (12–14). Clough described a classification based on tumor volume, location, and glandular density, while Hoffmann and Wallweiner divided breast cancer surgery into two broad types with six tiers, each of increasing complexity (13, 14). A notable consensus definition came from the American Society of Breast Surgeons, which stated that OBCS incorporated oncologic partial mastectomy with ipsilateral defect repair using volume displacement (VD) and volume replacement (VR) techniques, with contralateral symmetry surgery as appropriate (11). For small-to-moderate breast volumes, however, there was also a difference in technical considerations compared with those for larger breast volumes, which require significantly more VR techniques (6, 15–17).

Korea had been an early adopter of oncoplastic surgery but long-term follow up data remained limited. As with any surgical procedures, long-term follow up was necessary to establish safety parameters of surgical techniques. Furthermore, locoregional recurrences after breast conservation surgery could occur later than mastectomy, perhaps due to the differences in biology or presentations that led to a decision for mastectomy (18). Having previously examined the short-term oncological safety and patient-reported outcomes of various OBCS techniques (17–20), this current study aimed to compare long-term oncological safety following conventional BCS (CBCS) and OBCS, focusing on overall survival (OS), ipsilateral breast tumor recurrence (IBTR) rates, and disease-free survival (DFS). We also report the rate of positive margins (PMR) detected in intraoperative frozen sections and eventual rate of conversion to mastectomy (CMR) following BCS during a 10-year follow-up period. A literature review was performed to discuss the available data on long-term oncological outcomes with at least five years median follow up duration reported to date and how our results compared with those of other centers.

Methods

We analyzed prospectively collected data from 539 consecutive breast cancer patients at Kyungpook National University Chilgok Hospital who underwent breast conservation surgery performed by four breast surgeons between January 2009 and December 2013. Treatment strategy was coordinated at multidisciplinary board discussions, which included breast surgeons, plastic surgeons, radiologists, pathologists, and medical and radiation oncologists. All breast conservation surgeries were performed by the breast surgeons, with oncoplastic techniques performed by either a breast or plastic surgeon.

A literature review was performed to summarise suitable studies for comparison of definitions and reported oncological outcomes (Tables 6, 7) (21–40). A search was conducted through the MEDLINE database using PubMed in March 2022. Our search terms included 'oncoplastic' [All Fields] AND ('breast' [MeSH Terms] OR 'breast' [All Fields]) AND ('surgery' [Subheading] OR 'surgery' [All Fields] OR 'surgical procedures, operative' [MeSH Terms]) AND ('oncological' [All Fields] OR 'outcomes' [All Fields]). A manual search of bibliographies of relevant articles was performed.

We included single center studies reporting on various oncoplastic breast conserving surgery to ensure consistency in the reported surgical procedures. Studies with cohort size less than 50 were deemed too small; similarly, a follow up period less than 60 months inadequate to capture late recurrences and death events and hence excluded. Case series or cohort studies reporting on particular

surgical techniques were also excluded as they were not generalisable to all oncoplastic breast conserving surgery. A PRISMA flowchart is available as supplementary material.

Definition of conventional and oncoplastic BCS techniques

CBCS involved a direct skin incision, including use of a parallelogram incision overlying the index tumor to allow direct parenchymal closure. Following excision of primary breast tumors with gross margins, a frozen section of the circumferential margins was processed. The defect was closed primarily without further mobilization. When tumor cells were detected on the frozen section, more extensive resection was performed until negative frozen section results were achieved or no further surgical margins were deemed necessary. A final paraffin block of the surgical margins was examined by pathologists for the presence of tumor cells, and the presence of no stained tumor cell was defined as a negative resection margin.

OBCS was performed as described previously in detail based on general principles of oncoplastic breast surgery in small-to-moderate-sized breasts (15–17).

The procedures were divided into VD and replacement techniques. VD techniques included dual-plane glandular flap mobilization-closure, purse string suture closure of central defect, roundblock mastopexy, tennis racket incision, batwing mastopexy, rotating flap, and reduction mammoplasty (Table 1) (15).

In cases of anticipated significant breast volume loss, VR techniques were individualized according to the excised breast volume and tumor location with planned use of either adipofascial flap, lateral thoracodorsal flap (LTD), intercostal artery perforators (ICAP), thoracodorsal artery perforator (TDAP), thoracoepigastric (TE), or latissimus dorsi (LD). LD myocutaneous flaps were preferred for excised specimen >150 g (16, 17).

Patient and tumor characteristics

Patient demographics, surgical details, clinicopathological characteristics, including clinical tumor size, specimen weight, tumor type, pathological tumor size, pathological tumor, nodal stage, receptor status, grade, presence of neoadjuvant and adjuvant therapy, metachronous contralateral breast cancer, locoregional and distant disease recurrences, and death were recorded (Table 2).

Follow-up

Patients were followed up after surgery using a standardized protocol. After completing adjuvant treatments, frequency of follow-up was biannually for the first 2 years and annually for 5 to 10 years. Locoregional recurrence or distant metastasis was evaluated with clinical examination, blood tests including tumor markers, mammography, breast ultrasonography, with or without magnetic resonance imaging, bone scans, and positron emission tomography/computed tomography.

Oncological outcomes

The oncological outcomes assessed include OS, DFS with disease events defined as local or regional recurrences, distant recurrences, and metachronous contralateral breast cancer.

Statistical analysis

Statistical analysis was performed in March 2022 using Stata software, v17.0 (StataCorp); a statistically significant difference was concluded when $p<0.05$. Categorical variables were analyzed using the chi-square or Fisher exact test. Continuous variables were analyzed using the Student's t-test. The Kaplan–Meier method was used to estimate survival function, and the log-rank test was used to compare survival functions. The univariate Cox proportional hazard regression model was also used to examine the correlation of clinically relevant covariates that were likely to affect oncological outcomes. These included patient age, tumor grade, hormonal profile, pathological tumor stage, nodal disease, and adjuvant therapy received. A multivariate analysis was performed with variables with significant p-values in the univariate model.

TABLE 1 Oncoplastic procedures divided into volume displacement and volume replacement techniques (N=174).

Volume displacement	N=98	Volume replacement	N=76
Tennis racket	32 (18.3%)	Latissimus dorsi myocutaneous flap	23 (13.2%)
Rotating flap	31(17.8%)	Intercostal artery perforator flap	20 (11.5%)
Reduction mammoplasty	14 (8.0%)	Lateral thoracodorsal flap	18 (10.3%)
Purse string suture closure	13 (7.5%)	Thoracodorsal artery perforator flap	11 (6.3%)
Batwing mastopexy	4 (2.3%)	Thoracoepigastric flap	2 (1.1%)
Glandular flap	4 (2.3%)	Adipofascial flap	2 (1.1%)

TABLE 2 Baseline characteristics of patients who underwent conventional and oncoplastic breast-conserving surgery (BCS).

	All, N=539	Conventional BCS, N=365	Oncoplastic BCS, N=174	p-value
Mean age (years, ± SD)	49.4 ± 9.0	50.7 ± 9.2	46.5 ± 7.5	<0.001
Mean body mass index (kg/m^2 ± SD)	23.6 ± 3.3	23.6 ± 3.5	23.5 ± 3.1	0.55
Mean specimen weight ± SD, g	68.1 ± 46.6	53.1 ± 26.8	96.3 ± 60.9	<0.001
Mean clinical tumor size (cm ± SD)	1.7 0.8	1.5 ± 0.7	2.1 ± 1.1	<0.001
Tumor location by quadrant (n, %)*				
Central	34	9 (6.0%)	26 (17.4%)	<0.001
Upper outer quadrant	140	87 (58.3%)	53 (35.6%)	
Upper inner quadrant	61	36 (24.2%)	25 (16.8%)	
Lower inner quadrant	16	5 (3.3%)	11 (7.4%)	
Lower outer quadrant	32	10 (6.7)	22 (14.8%)	
Multifocal	12	2 (1.3%)	10 (6.7%)	
Mean pathological tumor size (cm ± SD)	1.5 ± 0.7	1.3 ± 0.6	1.8 ± 0.8	<0.001
Axillary lymph node dissection	108 (20.5%)	66 (18.5%)	42 (24.6%)	0.10
Tumor type				
DCIS/pleomorphic LCIS	26 (4.8%)	19 (5.2%)	7 (4.0%)	0.81
Invasive ductal carcinoma	469 (87.0%)	318 (87.1%)	151 (86.8%)	
Invasive lobular carcinoma	17 (3.1%)	10 (2.7%)	7 (4.0%)	
Mixed/others	27 (5.0%)	18 (4.9%)	9 (5.2%)	
Pathological tumour staging				
0	23 (4.3%)	16 (4.3%)	7 (4.0%)	<0.001
1	401 (74.5%)	295 (80.1%)	106 (60.9%)	
2	113 (21.0%)	54 (14.8%)	59 (33.9%)	
3	1 (0.2%)	0	1 (0.5%)	
Pathological nodal staging				
0	430 (80.0%)	299 (81.9%)	131 (75.3%)	0.03
1	89 (16.5%)	55 (15.1%)	34 (19.5%)	
2	14 (2.6%)	6 (1.6%)	8 (4.6%)	
3	5 (0.9%)	5 (1.4%)	0	
Pathological TNM stage				
0	36 (6.1%)	23 (6.0%)	13 (7.5%)	0.002
1	325 (60.3%)	240 (65.7%)	85 (48.9%)	
2	158 (29.3%)	91 (25.2%)	67 (38.5%)	
3	20 (3.71%)	11 (3.0%)	9 (5.2%)	
Receptor profile				
HR+ Her2-	362 (67.2%)	249 (68.5%)	113 (64.9%)	0.89
HR+ Her2+	57 (10.6%)	38 (10.4%)	19 (10.9%)	
HR- Her2-	86 (16.0%)	57 (15.6%)	29 (16.7%)	
HR- Her2+	25 (4.6%)	15 (4.1%)	10 (5.7%)	
Grade				
1	114 (22.8%)	86 (23.5%)	28 (16.1%)	0.04
2	268 (53.5%)	184 (50.4%)	84 (48.3%)	
3	115 (23.0%)	67 (18.3%)	48 (27.6%)	
Positive frozen margin status	36 (6.8%)	32 (9.0%)	4 (2.3%)	0.04
Neoadjuvant therapy	19 (3.5%)	12(3.2%)	7 (4.0%)	0.67
Adjuvant chemotherapy	308 (57.1%)	196 (53.7%)	112(64.7%)	0.02
Adjuvant radiotherapy	467 (86.6%)	325 (89.0%)	142 (81.6%)	0.02
Adjuvant hormonal therapy	407 (75.5%)	282 (77.3%)	125 (71.8%)	0.17
Contralateral breast cancer	17 (3.2%)	10 (2.7%)	7 (4.0%)	0.42
Ipsilateral breast tumor recurrence	11 (2.0%)	8 (2.1%)	3 (1.7%)	0.78
Locoregional recurrence	23 (4.2%)	14 (3.8%)	9 (5.7%)	0.47
Distant recurrence	26 (4.8%)	16 (4.8%)	10(5.7%)	0.49
Death	13 (2.4%)	7 (1.9%)	6 (3.5%)	0.28

SD = standard deviation; DCIS = ductal carcinoma in situ; LCIS: lobular carcinoma in situ; HR = Hormone receptor (estrogen receptor and progesterone receptor); Her2 = human epidermal growth factor receptor 2.

*Available data from 149 consecutive conventional breast conserving surgery was compared with 147 oncoplastic breast conserving surgery between 2011 and 2013.

The study was approved by the Institutional Review Board of Kyungpook National University (2015-05-205) and conducted in compliance with the principles of the Declaration of Helsinki.

Results

Of the 539 patients who were analyzed, 365 (67.7%) patients underwent CBCS while 174 (32.3%) underwent OBCS. Of the 174 cases of OBCS, VR techniques were utilized in 98 (56.3%) cases, while VD techniques were utilized in 76 (43.7%) cases. Table 1 shows the breakdown of oncoplastic procedures in descending order. The most commonly employed techniques among the oncoplastic procedures were tennis racket incision (32), rotating flap (31), and LD myocutaneous flap (23). Five patients who defaulted further clinical visits or transferred care to other hospitals were considered lost to follow up.

Patient characteristics

Patients who underwent CBCS were older (50.7 vs. 46.5 years old), had smaller clinical tumor size (1.5 cm vs. 2.1cm), smaller specimen weight (53.1 g vs. 96.3 g), and smaller pathological tumor size (1.3 cm vs. 1.8 cm) compared to those who underwent OBCS. In terms of tumor characteristics, patients who underwent CBCS had earlier pathological T and N stage compared to those who underwent OBCS, while there was no statistically significant difference in histology subtype, grade, or hormone profile (Table 2) among the two groups.

Tumor location

OBCS was performed on a higher proportion of central (17.4%), lower outer quadrant (14.8%), lower inner quadrant (7.4%), and multifocal tumors (6.7%) than CBCS. The majority of all CBCS was performed on upper outer quadrant tumors (58.5%).

Intraoperatively detected involved margins on frozen section

The rate of intraoperatively detected involved margins on frozen section was higher in the CBCS than in the oncoplastic group, and further margins were excised intraoperatively. Three patients required completion mastectomy for close or involved final margins.

Disease recurrence, overall survival, and success of breast conservation surgery at 10 years

At a median follow-up of 82.4 months, (range, 1.4–156.7 months) there were 23 (4.2%) locoregional recurrences of which 11 had ipsilateral breast tumor recurrences, 17 (3.2%) metachronous contralateral breast cancer, 26 (4.8%) distant metastases, and 13 (2.4%) deaths. The hazard ratio of OBCS for IBTR, DFS and OS were 0.78 (95% confidence interval [CI] 0.21–2.94, p=0.78), 1.59 (95% CI, 0.88 to 2.87, p=0.12), and 2.1 (95% CI, 0.72 to 5.9, p=0.17) respectively. The 10-year IBTR-free, DFS and OS rate were 97.8%, 86.2%, and 95.7% respectively. Overall, five patients underwent mastectomy either from involved margins or disease recurrence, giving a successful BCS rate of 99.1%.

Statistical analysis of oncological outcomes

The use of oncoplastic surgery was not associated with a higher likelihood of IBTR or death in the Cox regression model analysis (Tables 3, 4, 5). Patients who underwent adjuvant chemotherapy had significantly lower IBTR rates, with a hazard ratio of 0.25 (95% CI, 0.07 to 0.98). Regarding OS, higher histological grade was significantly associated with higher risk of death, with a hazard ratio of 9.56 (95% CI, 2.41 to 37.86) (Tables 3 and 5). Univariate analysis was performed using the log-rank method stratified by tumor histological grade, pathological tumor staging, nodal disease, and hormone receptor profile. There was no difference in IBTR-free survival when performing OBCS after stratifying by high-grade tumors; larger tumors (T2/3); and node positive, hormone receptor-positive, or triple negative breast tumors (Figures 1, 2, 3).

Comparison of our current study with other similar studies reporting long-term oncological outcomes are summarized in Tables 6 and 7.

Discussion

Over the last two decades, oncoplastic breast surgery quickly gained widespread acceptance as a standard of care option that balanced oncological and aesthetic outcomes of oncological resection in breast cancer management (21–27). The main findings of this study were that there was an overall low rate of IBTR (2.2%) and death (4.3%) observed in this cohort of 539 patients after a median follow-up of 82.4 months. This study had one of the largest single center cohorts with a long follow-up period (Table 7). Like other studies, IBTR rates were estimated to be between 1.4% and 14.6%, and 10-year OS rates were approximately 90.2–100%. Stratified analysis did not reveal any associated difference in survival outcomes in larger tumors, higher grade disease, or disease with a nodal burden. The observed outcomes could be the result of other factors, such as younger age (mean age <50 year), earlier disease stage (majority stage 1 and 2), favorable histological subtype, and

TABLE 3 Univariate and multivariate Cox regression analysis with ipsilateral breast tumor recurrence-free survival as an endpoint.

	No. of cases, N=539	No. of IBTR, N=11	Univariate HR	p	Multivariate HR*	p
Type of BCS						
Oncoplastic	174	3	0.78 (0.21–2.94)	0.71	0.89 (0.23-3.39)	0.87
Conventional	365	8	Ref		Ref	
ALND						
Yes	108	5	2.91 (0.88–9.63)	0.09	–	–
No	420	6	Ref			
Missing	11					
Age	539	11	1.0 (0.96–1.08)	0.55	–	–
Histological subtype						
IDC	469	11	Ref	0.55	–	–
Others	70	0	0.67 (0.17–2.68)			
Grade						
Grade 1/2	386	9	Ref	0.74	–	–
Grade 3	115	2	0.77 (0.17–3.60)			
Missing	38					
Tumor stage						
T1	424	10	Ref	0.24	–	–
T2/3	115	1	0.34 (0.04–2.69)			
Nodal stage						
Node negative	430	7	Ref	0.27	–	–
Node positive	108	4	2.06 (0.60–7.08)			
Hormone receptor						
Positive	427	7	0.44 (0.21–1.51)	0.21	-	–
Negative	111	4	Ref			
Triple negative				0.50	-	
Yes	63	2	1.75 (0.37–8.10)			
No	476	9	Ref			
Adjuvant chemotherapy						
Yes	308	8	0.26 (0.07–0.96)	0.03	0.25 (0.07–0.98)	0.047
No	231	3	Ref		Ref	
Adjuvant radiotherapy						
Yes	467	9	0.71 (0.15–3.28)	0.67	–	–
No	72	2	Ref			
Adjuvant hormonal therapy						
Yes	407	7	0.52 (0.15–1.82)	0.32	–	–
No	132	4	Ref			

*Variables with p-values <0.05 in the univariate analysis were included in the multivariate analysis.

generally high uptake rates of adjuvant therapies such as chemotherapy, radiotherapy, and hormonal therapy, when indicated. The proportion of cases with neoadjuvant chemotherapy was lower than expected in current practice; this might be because of the trend of favoring upfront surgery 10 years ago. However, as this was a retrospective cohort analysis, the cumulative incidence of events could also be underestimated because of a loss to follow-up or selection bias.

We also observed a similar trend that oncoplastic techniques allowed higher resection volumes for larger tumors and reduced intraoperative positive margin rates. Large systematic reviews showed that oncoplastic surgery was more frequently performed in younger patients who required greater breast volume removal for larger tumors (23, 25, 27). While this may not translate to any survival benefit, there could be improvement in patients' satisfaction rates given the lower rate of reoperation and conversion to mastectomy (28).

Our literature review showed that there were several registry studies and meta-analyses published on oncological outcomes of oncoplastic breast surgery (21–42). However, we must caution that conclusions drawn from such meta-analyses or registries have inherent limitations. Many studies have difficulties pooling study subjects together due to the heterogeneity of the study population, surgeons' expertise, and techniques and classifications used (21–26, 42). Therefore, we analyzed the different definitions and breakdowns of oncoplastic techniques used across various studies (Table 5). We noted that majority of the studies were small observational studies on specific techniques, limiting their generalizability and had to be excluded from the meta-analysis. Most had a limited cohort

TABLE 4 Univariate and multivariate Cox regression analysis with disease-free survival[+] as an endpoint.

	No. of cases, N=539	No. of recurrences, N=47	Univariate HR	p	Multivariate HR*	p
Type of BCS						
Oncoplastic	174	19	1.59 (0.88–2.88)	0.13	1.95 (1.04–3.64)	0.04
Conventional	365	28	Ref		Ref	
ALND						
Yes	108	16	1.79 (0.97–3.31)	0.07	–	–
No	420	31	Ref			
Missing	11					
Age	539	47	1.02 (1.00–1.05)	0.05	1.05 (1.00–1.07)	0.03
Histological subtype						
IDC	469	43	Ref	0.48	–	–
Others	70	4	2.23 (0.31–16.2)			
Grade						
Grade 1/2	386	30	2.15 (1.17–3.94)	0.02	1.80 (0.91–3.55)	0.09
Grade 3	115	17				
Missing	38					
Tumor stage						
T1	423	35	1.21 (0.62–2.34)	0.57	–	–
T2/3	115	12				
Nodal stage						
Node negative	430	33	1.47 (0.78–2.76)	0.24	–	–
Node positive	108	14	Ref			
Hormone receptor						
Positive	427	31	0.49 (0.27–0.91)	0.03	0.70 (0.35–1.39)	0.31
Negative	111	16	Ref		-	-
Triple negative						
Yes	63	6	1.13 (0.48–2.68)	0.78		
No	476	41	Ref			
Adjuvant chemotherapy						
Yes	308	26	0.84 (0.47–1.51)	0.57	–	–
No	231	21	Ref			
Adjuvant radiotherapy						
Yes	467	37	0.62 (0.31–1.25)	0.20	–	–
No	72	10	Ref			
Adjuvant hormonal therapy						
Yes	407	31	0.57 (0.31–1.03)	0.07	–	–
No	132	16	Ref			

[+]Disease-free survival events were defined as any ipsilateral or contralateral breast recurrence (invasive or non-invasive) or regional or distant metastases.
*Variables with p-values <0.05 in the univariate analysis were included in a multivariate analysis.
HR = hazard ratio; Ref = Reference; BCS = breast conservation surgery; ALND = axillary lymph node dissection; IDC = invasive ductal carcinoma.

size or a barely sufficient follow-up duration to fully capture recurrence or death events. As it would be impossible to conduct any randomized control trial studying conventional and oncoplastic techniques because of ethical considerations, large cohort studies with long-term follow-up could be regarded as the highest level of evidence.

This study generated fresh data on long-term outcomes so as to compare with the reported standards over the last decade. First, the main strength of this study was the clear definition of procedures performed with balanced representations of both VD and replacement techniques. Second, consistency in surgical standards was maintained in the procedures performed by a dedicated oncoplastic team made up of both breast and plastic surgeons. Third, these 539 patients were followed up for more than a median of 80 months to allow for more valid capture of long-term outcomes.

Next, we examined the most commonly used definition of the Clough classification in the literature. The Clough classification of oncoplastic techniques primarily considers the excision volume ratio, requirement of skin excision for reshaping or mammoplasty, and tumor location. However, VR techniques were notably excluded because of their primary use in smaller breasts (13). Similarly, we found that many comparative studies with long-term outcomes reported a disproportionately low number of VD techniques, mainly level 2 oncoplastic mammoplasty with little or no representation of VR techniques. In our and many other East Asian populations, we adopted similar principles of deciding the type of oncoplastic

TABLE 5 Univariate and multivariate Cox regression analysis with overall survival as an endpoint.

	No. of cases,N=539	No. of deaths, N=13	Univariable HR	p	Multivariate HR*	p
Type of BCS						
Oncoplastic	174	6	1.78 (0.60–5.29)	0.31	1.82 (0.55–5.97)	0.33
Conventional	365	7	Ref			
Age	539		2.61 (0.87–7.82)	0.10	–	–
Histological subtype						
IDC	469	13	1.03 (0.98–1.09)	0.29	–	–
Others	70	0	Ref			
Grade						
Grade 1/2	386	3	Ref	0.0001	Ref	0.001
Grade 3	115	10	1.78 (2.96–39.2)		9.56 (2.41–37.86)	
Missing	38					
Tumor stage						
T1	423	10	Ref	0.98	–	–
T2/3	115	3	1.01 (0.28–3.68)			
Missing	1					
Nodal stage						
Node negative	430	9	Ref	0.62	–	–
Node positive	108	4	1.35 (0.41–4.42)			
Missing	1					
Hormone receptor						
Positive	427	7	0.31 (0.10–0.91)	0.04	0.80 (0.25–2.56)	0.70
Negative	111	6	Ref		Ref	-
Triple negative				0.24	-	
Yes	63	3	2.32 (0.63–8.43)			
No	476	10	Ref			
Adjuvant chemotherapy						
Yes	308	10	2.21 (0.61–8.06)	0.20	–	–
No	231	3	Ref			
Adjuvant radiotherapy						
Yes	467	11	0.92 (0.20-4.14)	0.91	–	–
No	72	2	Ref			
Adjuvant hormonal therapy						
Yes	407	7	0.36 (0.12–1.08)	0.08	–	–
No	132	6	Ref			

*Variables with p-values <0.05 in the univariate analysis were included in the multivariate analysis.
HR = hazard ratio; Ref = Reference; BCS = breast conservation surgery; ALND = axillary lymph node dissection; IDC = invasive ductal carcinoma.

TABLE 6 Retrospective studies showing single center studies with large cohort and long term follow up, comparing definitions of OBCS and breakdown of oncoplastic procedures by year of published study.

Study and center	Year	Cohort size	Classification of OBCS	Percentage of VR among OBCS
Our study, Kyungpook National University Chilgok Hospital, Korea	2022	539 -174 (OBCS) -365 (CBCS)	VD and VR	43.7
Oh, Seoul National University Hospital, Korea [28]	2021	742 -371 (OBCS) -371 (CBCS)	VD and VR	5.4
Kelemen, National Institute of Oncology, Hungary [29]	2019	756 -378 (OBCS) -378 (CBCS)	Clough bilevel	Excluded VR
Calabrese, Sapienza University Italy [36]	2018	1024 (All OBCS)	VD	Excluded VR

(Continued)

TABLE 6 Continued

Study and center	Year	Cohort size	Classification of OBCS	Percentage of VR among OBCS
Clough, Paris Breast Centre, France [30]	2017	350 (All OBCS)	Clough Bilevel	Excluded VR
Mansell, Victoria & Western Infirmary, UK [31]	2017	666 -108 (OBCS) -558 (CBCS)	Clough Bilevel	13.5
De Lorenzi, European Institute of Oncology, Italy 32	2016	1362 -454 (OBCS) -908 (CBCS)	Tumor location Includes VD, VR and implant	10.3
Chakravorty, Royal Marsden, UK [34]	2012	590 -150 (OBCS) -440 (CBCS)	By location and 3 standardized VD	Excluded VR
Fitoussi, Institut Curie Paris, France [35]	2010	540 (All OBCS)	Tumor location Aesthetic vs combination	Excluded VR

*No available data on breakdown
VD = volume displacement; VR = volume replacement; OBCS = oncoplastic breast-conserving surgery; CBCS = conventional breast-conserving surgery.

TABLE 7 Retrospective studies showing oncologic outcomes of oncoplastic breast conservation surgery according to surgeons, operation period, and follow-up interval to show directly reported results for local recurrence, disease-free survival, and overall survival.

Study	Surgeons	Operation period	Follow-up, months	IBTR rates (%)	Disease-free survival, %	Overall survival, %
Our study	Both breast and plastic surgeons	5 years (2009–2013)	82.5 (all) 82.9 (OBCS) 81.4 (CBCS)	2.2 (10 years, all) 1.8 (10 years OBCS) 2.4 (10 years CBCS)	86.2 (10 years, all) 79.7 (10 years, OBCS) 88.5 (10 years, CBCS)	95.7 (10 years, all) 92.6 (10 years, OBCS) 96.8 10 years, CBCS)
Oh [28]	Not specified	4 years (2011–2014)	84.4 (OBCS) 87.9 (CBCS)	3.1 (5 years, OBCS) 1.4 (5 years, CBCS)	92.9 (5 years, OBCS) 94.5 (5 years, CBCS)	–
Kelemen [29]	2 breast surgeons	7 years (2010–2017)	51 (OBCS) 52 (CBCS)	–	88.5 (5 years, OBCS) 78.2 (5 years, CBCS)	100 (5 years, OBCS) 97.3 (5 years CBCS)
Calabrese [36]	Breast and plastic surgeons	11 years (2000-2010)	74.2 (all)	4.7 (all)	95.0 (all)	98.4
Clough [30]	Not specified	13 years (2004–2016)	55 (all)	–	84.8	95.1 (5 years)
Mansell [31]	Either breast or plastic surgeons	4 years (2009–2012)	56.2 (all) 56.8 (OBCS) 57.2 (CBCS)	2 (5 years, OBCS) 3.4 (5 years, CBCS)	90.7 (5 years, OBCS) 93.2 (5 years, CBCS)	98.1 (5 years, OBCS) 95.1 (5 years, CBCS)
De Lorenzi [32]	Not specified	9 years (2000–2008)	86.4	6.7 (10 years, OBCS) 4.2 (10 years, CBCS)	69 (10 years, OBCS) 73.1 (10 years, CBCS)	91.4 (10 years, OBCS) 91.3 (10 years, CBCS)
Chakravorty [34]	2 oncoplastic surgeons	7 years (2003–2010)	28	4.3 (Projected 6 years, OBCS) 3.7 (Projected 6 years, CBCS)	–	–
Fitoussi [35]	Not specified	22 years (1986–2008)	49	6.8 (5 years, all)	87.9 (5 years, all)	92.9 (5 years, all)

OBCS = oncoplastic breast-conserving surgery; CBCS = conventional breast-conserving surgery.

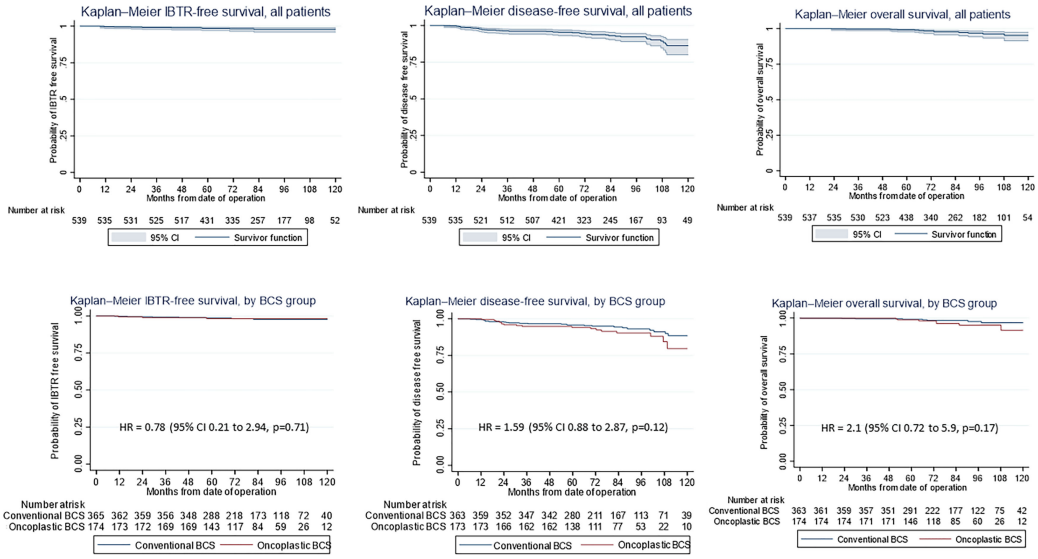


FIGURE 1
(First row) Kaplan–Meier estimates of (Left) ipsilateral breast tumor recurrence (IBTR)-free survival, (Middle) disease-free survival (DFS), and (Right) overall survival (OS) curves (shown with 95% confidence level) for all patients undergoing breast-conserving surgery (BCS) and (second row) by conventional (CBCS) versus oncoplastic breast-conserving surgery (OBCS) group.

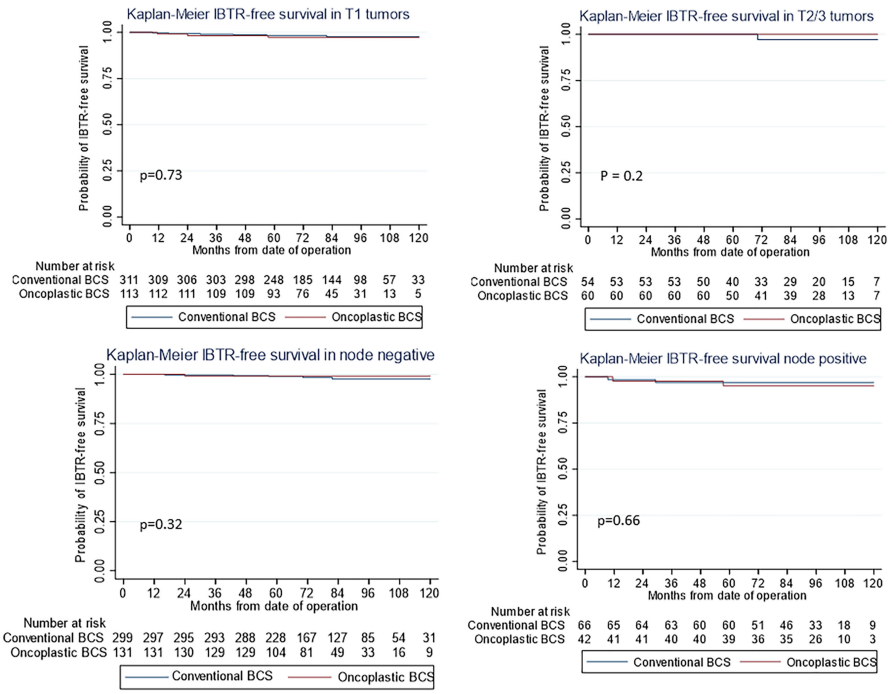


FIGURE 2
Kaplan–Meier estimates for ipsilateral breast tumor recurrence (IBTR)-free survival by (First Row) pathological tumor stage (first row) and (Second Row) nodal stage (second row) showing no difference between oncoplastic and conventional breast-conserving surgery (BCS).

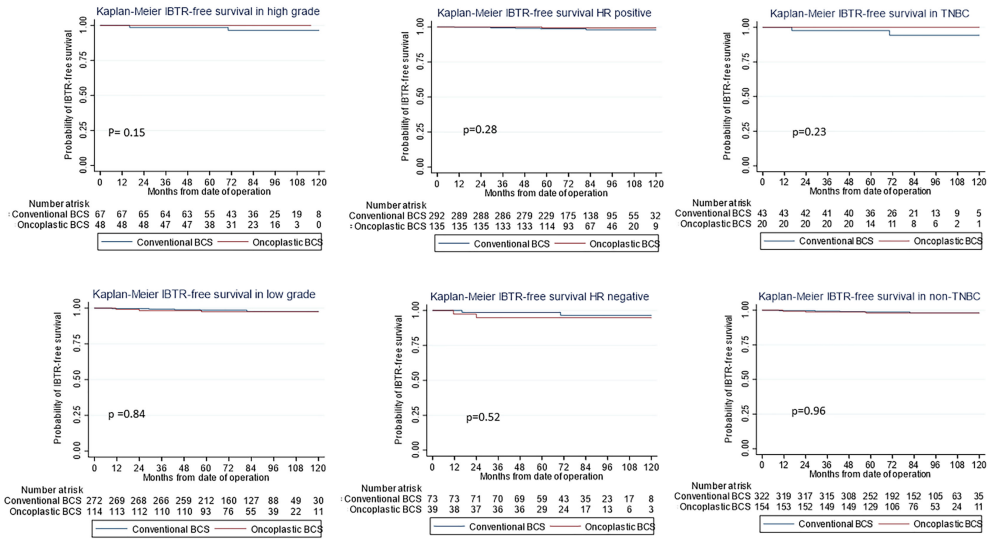


FIGURE 3
Kaplan–Meier estimates for ipsilateral breast tumor recurrence (IBTR)-free survival stratified by (Left) high-grade, (Middle) hormone-positive tumors, and (Right) triple negative breast cancer subtypes (first row) and others (second row) showing no difference between oncoplastic and conventional breast-conserving surgery (BCS).

procedures such as breast-to-tumor volume ratio, and tumor locations, but it was also proposed that an absolute value of tumor volume excised in itself could be an indication for VR techniques in small-to-moderate-sized breasts. These may be due to inherent differences in the patients' morphometric characteristics or influenced by different cultural beliefs and resource settings (15, 41). In a smaller native breast with less space for VD maneuvers, a different threshold for VR techniques may apply. Evidence also shows that patients are more accepting of VR options and have good functional outcomes regardless of the VR technique (17).

As a result, our percentage of VR performed among OBCS was the highest among the selected studies, with VR techniques accounting for 43% of all oncoplastic procedures. Most of the other studies either had less than 10% of procedures represented by VR, or did not specify the type of reconstruction techniques at all. Our cohort also showed that the LD myocutaneous flap was the most commonly used VR techniques followed by chest wall perforator flaps. This was concordant to our finding that the LD flap was the largest and the most commonly reported VR technique as a single cohort series in the literature (20, 25, 37–42). However, we did not report and compare the oncological results from these studies that only focused on singular technique such as LD flap or omental flap reconstruction because they would have limited generalizability to other oncoplastic techniques and patient selection (40, 41).

We maintained that both VD and VR techniques formed the fundamentals of oncoplastic techniques and would not need to be separately studied from each other. Hence, it remained vital to establish comparable oncological outcomes of various oncoplastic techniques to reassure patients that oncoplastic breast surgery would not compromise on oncological safety in the long run, and that both aesthetic outcomes and patient satisfaction were equally important performance indicators in the treatment of breast cancer.

Limitations

The main limitations of the study were largely in its retrospective nature, which could lead to underestimated incidence rates due to the nature of selection bias and loss to follow-up. The surgical teams involved a dedicated oncoplastic team including both breast and plastic surgeons; consequently, these findings may not be logistically reproducible in all centers. We acknowledged that there were many confounding factors that could affect oncological outcomes and tried to address these by adjusting for the variables in the statistical analysis. However, considering the limitations of cohort size and event rates, it would be prudent to avoid generating too many hypotheses regarding secondary analysis findings but rather appreciate the general theme of oncological safety established across various tumor characteristics and adjuvant therapies provided in our study population. We also noted there was a low percentage of patients treated with neoadjuvant chemotherapy in our cohort. Neoadjuvant chemotherapy has gained much traction in its role in increasing rates of breast conservation; therefore, future research should be directed to study its influence on long-term oncological outcomes (43).

Conclusion

Our review of existing literature on the oncological outcomes of OBCS highlighted the dearth in well-balanced comparative studies with sufficient long-term follow-up, and reported our center's own long-term oncological outcomes for OBCS to support the use of either VD or replacement techniques.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Kyungpook National University Chilgok Hospital. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

Acknowledgments

We would like to thank Editage (www.editage.co.kr) for English language editing.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fonc.2022.944589/full#supplementary-material

References

1. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* (2002) 347:1233–41. doi: 10.1056/NEJMoa022152

2. Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med* (2002) 347:1227–32. doi: 10.1056/NEJMoa020989

3. Keelan S, Flanagan M, Hill ADK. Evolving trends in surgical management of breast cancer: An analysis of 30 years of practice changing papers. *Front Oncol* (2021) 11:622621. doi: 10.3389/fonc.2021.622621

4. Kaufman CS. Increasing role of oncoplastic surgery for breast cancer. *Curr Oncol Rep* (2019) 21(12):111. doi: 10.1007/s11912-019-0860-9

5. Audretsch WP, Rezai M, Kolotas C. Tumor-specific immediate reconstruction in breast cancer patients. *Perspect Plast Surg* (1998) 11:71–100. doi: 10.1055/s-2008-1080243

6. Rainsbury RM. Surgery insight: oncoplastic breast-conserving reconstruction–indications, benefits, choices and outcomes. *Nat Clin Pract Oncol* (2007) 4:657–64. doi: 10.1038/ncponc0957

7. Clough KB, Kroll SS, Audretsch W. An approach to the repair of partial mastectomy defects. *Plast Reconstr Surg* (1999) 104:409–20. doi: 10.1097/00006534-199908000-00014

8. Petit JY, Rietjens M, Garusi C. Breast reconstructive techniques in cancer patients: which one, when to apply, which immediate and long-term risks? *Crit Rev Oncol Hematol* (2001) 38:231–9. doi: 10.1016/S1040-8428(00)00137-2

9. Silverstein MJ, Mai T, Savalia N, Vaince F, Guerra L. Oncoplastic breast conservation surgery: the new paradigm. *J Surg Oncol* (2014) 110:82–9. doi: 10.1002/jso.23641

10. Macmillan RD, James R, Gale KL, McCulley SJ. Therapeutic mammaplasty. *J Surg Oncol* (2014) 110:90–5. doi: 10.1002/jso.23659

11. Chatterjee A, Gass J, Patel K, Holmes D, Kopkash K, Peiris L, et al. A consensus definition and classification system of oncoplastic surgery developed by the american society of breast surgeons. *Ann Surg Oncol* (2019) 26:3436–44. doi: 10.1245/s10434-019-07345-4

12. Lebovic G. Oncoplastic surgery: a creative approach to breast cancer management. *Surg Oncol Clin N Am* (2010) 19:567–80. doi: 10.1016/j.soc.2010.04.003

13. Clough KB, Kaufman GJ, Nos C, Buccimazza I, Sarfati IM. Improving breast cancer surgery: a classification and quadrant per quadrant atlas for oncoplastic surgery. *Ann Surg Oncol* (2010) 17:1375–91. doi: 10.1245/s10434-009-0792-y

14. Hoffmann J, Wallwiener D. Classifying breast cancer surgery: a novel, complexity-based system for oncological, oncoplastic and reconstructive procedures, and proof of principle by analysis of 1225 operations in 1166 patients. *MC Cancer* (2009) 9:108. doi: 10.1186/1471-2407-9-108

15. Yang JD, Lee JW, Cho YK, Kim WW, Hwang SO, Jung JH, et al. Surgical techniques for personalized oncoplastic surgery in breast cancer patients with small- to moderate-sized breasts (part 1): volume displacement. *J Breast Cancer* (2012) 15:1–6. doi: 10.4048/jbc.2012.15.1.1

16. Yang JD, Lee JW, Cho YK, Kim WW, Hwang SO, Jung JH, et al. Surgical techniques for personalized oncoplastic surgery in breast cancer patients with small- to moderate-sized breasts (part 2): volume replacement. *J Breast Cancer* (2012) 15:7–14. doi: 10.4048/jbc.2012.15.1.7

17. Lee JW, Kim MC, Park HY, Yang JD. Oncoplastic volume replacement techniques according to the excised volume and tumor location in small- to moderate-sized breasts. *Gland Surg* (2014) 3:14–21. doi: 10.3978/j.issn.2227-684X.2014.02.02

18. Sabel MS, Hirsch A, Bellon JR. *Clinical manifestations and evaluation of locoregional recurrences of breast cancer* (2021). Available at: https://www.uptodate.com/contents/clinical-manifestations-and-evaluation-of-locoregional-recurrences-of-breast-cancer.

19. Lee J, Jung JH, Kim WW, Hwang SO, Chae YS, Lee SJ, et al. Five-year oncologic outcomes of volume displacement procedures after partial mastectomy for breast cancer. *Clin Breast Cancer* (2017) 17:70–5. doi: 10.1016/j.clbc.2016.06.018

20. Lee J, Jung JH, Kim WW, Hwang SO, Kang JG, Baek J, et al. Oncologic outcomes of volume replacement technique after partial mastectomy for breast cancer: A single center analysis. *Surg Oncol* (2015) 24:35–40. doi: 10.1016/j.suronc.2014.12.001

21. Kosasih S, Tayeh S, Mokbel K, Kasem A. Is oncoplastic breast conserving surgery oncologically safe? a meta-analysis of 18,103 patients. *Am J Surg* (2020) 220:385–92. doi: 10.1016/j.amjsurg.2019.12.019

22. Raufdeen F, Murphy J, Ahluwalia M, Coroneos CJ, Thoma A. Outcomes in volume replacement and volume displacement techniques in oncoplastic breast conserving surgery: A systematic review. *J Plast Reconstr Aesthet Surg* (2021) 74:2846–55. doi: 10.1016/j.bjps.2021.06.004

23. Haloua MH, Krekel NM, Winters HA, Rietveld DH, Meijer S, Bloemers FW, et al. A systematic review of oncoplastic breast-conserving surgery: current weaknesses and future prospects. *Ann Surg* (2013) 257:609–20. doi: 10.1097/SLA.0b013e3182888782

24. Chen JY, Huang YJ, Zhang LL, Yang CQ, Wang K. Comparison of oncoplastic breast-conserving surgery and breast-conserving surgery alone: A meta-analysis. *J Breast Cancer* (2018) 21:321–9. doi: 10.4048/jbc.2018.21.e36

25. Losken A, Dugal CS, Styblo TM, Carlson GW. A meta-analysis comparing breast conservation therapy alone to the oncoplastic technique. *Ann Plast Surg* (2014) 72:145–9. doi: 10.1097/SAP.0b013e3182605598

26. Rutherford CL, Barker S, Romics L. A systematic review of oncoplastic volume replacement breast surgery: oncological safety and cosmetic outcome. *Ann R Coll Surg Engl* (2022) 104:5–17. doi: 10.1308/rcsann.2021.0012

27. De La Cruz L, Blankenship SA, Chatterjee A, Geha R, Nocera N, Czerniecki BJ, et al. Outcomes after oncoplastic breast-conserving surgery in breast cancer patients: A systematic literature review. *Ann Surg Oncol* (2016) 23:3247–58. doi: 10.1245/s10434-016-5313-1

28. Gulcelik MA, Dogan L, Karaman N, Bahcecitapar M, Ozaslan C. Oncoplastic level II surgical techniques for breast cancer treatment: Long-term outcomes. *Breast Care (Basel)* (2022) 17:24–30. doi: 10.1159/000514468

29. Oh MY, Kim Y, Kim J, Cheun JH, Jung JG, Kim HK, et al. Comparison of long-term oncological outcomes in oncoplastic breast surgery and conventional breast-conserving surgery for breast cancer: A propensity score-matched analysis. *J Breast Cancer* (2021) 24:520–30. doi: 10.4048/jbc.2021.24.e52

30. Kelemen P, Pukancsik D, Újhelyi M, Sávolt Á, Kovács E, Ivády G, et al. Comparison of clinicopathologic, cosmetic and quality of life outcomes in 700 oncoplastic and conventional breast-conserving surgery cases: A single-centre retrospective study. *Eur J Surg Oncol* (2019) 45:118–24. doi: 10.1016/j.ejso.2018.09.006

31. Clough KB, van la Parra RFD, Thygesen HH, Levy E, Russ E, Halabi NM, et al. Long-term results after oncoplastic surgery for breast cancer: A 10-year follow-up. *Ann Surg* (2018) 268:165–71. doi: 10.1097/SLA.0000000000002255

32. Mansell J, Weiler-Mithoff E, Stallard S, Doughty JC, Mallon E, Romics L. Oncoplastic breast conservation surgery is oncologically safe when compared to wide local excision and mastectomy. *Breast* (2017) 32:179–85. doi: 10.1016/j.breast.2017.02.006

33. De Lorenzi F, Hubner G, Rotmensz N, Bagnardi V, Loschi P, Maisonneuve P, et al. Oncological results of oncoplastic breast-conserving surgery: Long term follow-up of a large series at a single institution: A matched-cohort analysis. *Eur J Surg Oncol* (2016) 42:71–7. doi: 10.1016/j.ejso.2015.08.160

34. Carter SA, Lyons GR, Kuerer HM, Bassett RLJr, Oates S, Thompson A, et al. Operative and oncologic outcomes in 9861 patients with operable breast cancer: Single-institution analysis of breast conservation with oncoplastic reconstruction. *Ann Surg Oncol* (2016) 23:3190–8. doi: 10.1245/s10434-016-5407-9

35. Chakravorty A, Shrestha AK, Sanmugalingam N, Rapisarda F, Roche N, Querci Della Rovere G, et al. How safe is oncoplastic breast conservation? comparative analysis with standard breast conserving surgery. *Eur J Surg Oncol* (2012) 38:395–8. doi: 10.1016/j.ejso.2012.02.186

36. Fitoussi AD, Berry MG, Fama F, Falcou MC, Curnier A, Couturaud B, et al. Oncoplastic breast surgery for cancer: analysis of 540 consecutive cases. *Plast Reconstr Surg* (2010) 125:454–62. doi: 10.1097/PRS.0b013e3181c82d3e

37. Calabrese C, Casella D, Di Taranto G, Marcasciano M, Kothari A, Sordi S, et al. Oncoplastic conservative surgery for breast cancer: long-term outcomes of our first ten years experience. *Eur Rev Med Pharmacol Sci* (2018) 22(21):7333–42. doi: 10.26355/eurrev_201811_16270

38. Teoh LY, Lai LL, Hanim Aa A, Teh MS, Jamaris S, Yahya A, et al. Oncological safety and postoperative complications in oncoplastic breast surgery among Asian women: A single institutional review. *Breast J* (2020) 26(11):2208–12. doi: 10.1111/tbj.14060

39. Rietjens M, Urban CA, Rey PC, Mazzarol G, Maisonneuve P, Garusi C, et al. Long-term oncological results of breast conservative treatment with oncoplastic surgery. *Breast* (2007) 16:387–95. doi: 10.1016/j.breast.2007.01.008

40. Rusby JE, Paramanathan N, Laws SAM, Rainsbury RM. Immediate latissimus dorsi miniflap volume replacement for partial mastectomy: use of intra-operative frozen sections to confirm negative margins. *Am J Surg* (2008) 196:512–18. doi: 10.1016/j.amjsurg.2008.06.026

41. Zaha H, Abe N, Sagawa N, Unesoko M. Oncoplastic surgery with omental flap reconstruction: a study of 200 cases. *Breast Cancer Res Treat* (2017) 162:267–74. doi: 10.1007/s10549-017-4124-9

42. André C, Holsti C, Svenner A, Oikonomou I, Appelgren M, Johansson A, et al. Recurrence and survival after standard versus oncoplastic breast-conserving surgery for breast cancer. *BJS Open* (2021) 5(1):zraa013. doi: 10.1093/bjsopen/zraa013

43. Youssef MMG, Namour A, Youssef OZ, Morsi A. Oncologic and cosmetic outcomes of oncoplastic breast surgery in locally advanced breast cancer after neoadjuvant chemotherapy, experience from a developing country. *Indian J Surg Oncol* (2018) 9:300–6. doi: 10.1007/s13193-017-0689-3

frontiers | Frontiers in Oncology

TYPE Review
PUBLISHED 12 January 2023
DOI 10.3389/fonc.2022.1099125

OPEN ACCESS

EDITED BY
Marco Invernizzi,
University of Eastern Piedmont, Italy

REVIEWED BY
Arianna Folli,
Università degli Studi del Piemonte Orientale, Italy
Vincenzo Vindigni,
University of Padua, Italy

*CORRESPONDENCE
René Aloisio da Costa Vieira
reneacv@gmail.com

SPECIALTY SECTION
This article was submitted to Surgical Oncology, a section of the journal Frontiers in Oncology

RECEIVED 15 November 2022
ACCEPTED 28 December 2022
PUBLISHED 12 January 2023

CITATION
Vieira RAC, Bailão-Junior A and de Oliveira-Junior I (2023) Does breast oncoplastic surgery improve quality of life? *Front. Oncol.* 12:1099125. doi: 10.3389/fonc.2022.1099125

Does breast oncoplastic surgery improve quality of life?

René Aloisio da Costa Vieira[1,2,3,4]*, Antônio Bailão-Junior[1,5] and Idam de Oliveira-Junior[1,2,5]

[1]Programa de Pós-Graduação em Tocoginecologia, Faculdade de Medicina de Botucatu, Botucatu/SP, Brazil, [2]Programa de Pós-Graduação em Oncologia, Hospital de Câncer de Barretos, Barretos/SP, Brazil, [3]Departamento de Cirurgia Oncológica, Divisão de Mastologia, Hospital de Câncer de Muriaé, Muriaé/MG, Brazil, [4]Active Member of European Organisation for Research and Treatment (EORTC) Quality of life Group, Brussels, Belgium, [5]Departamento de Mastologia e Reconstrução Mamária, Hospital de Câncer de Barretos, Barretos/SP, Brazil

Breast Oncoplastic Surgery (OS) has established itself as a safe procedure associated with the treatment of breast cancer, but the term is broad, encompassing procedures associated with breast-conserving surgeries (BCS), conservative mastectomies and fat grafting. Surgeons believe that OS is associated with an increase in quality of life (QOL), but the diversity of QOL questionnaires and therapeutic modalities makes it difficult to assess from the patient's perspective. To answer this question, we performed a search for systematic reviews on QOL associated with different COM procedures, and in their absence, we selected case-control studies, discussing the main results. We observed that: (1) Patients undergoing BCS or breast reconstruction have improved QoL compared to those undergoing mastectomy; (2) In patients undergoing BCS, OS has not yet shown an improvement in QOL, a fact possibly influenced by patient selection bias; (3) In patients undergoing mastectomy with reconstruction, the QoL results are superior when the reconstruction is performed with autologous flaps and when the areola is preserved; (4) Prepectoral implants improves QOL in relation to subpectoral implant-based breast reconstruction; (5) ADM do not improves QOL; (6) In patients undergoing prophylactic mastectomy, satisfaction is high with the indication, but the patient must be informed about the potential complications associated with the procedure; (7) Satisfaction is high after performing fat grafting. It is observed that, in general, OS increases QOL, and when evaluating the procedures, any preservation or repair, or the use of autologous tissues, increases QOL, justifying OS.

KEYWORDS

quality of life, systematic review, meta-analysis (MA), breast cancer, oncoplastic surgery, patient-reported outcome measures

Introduction

The World Health Organization (WHO) (1) defines quality of life (QOL) as "the individual's perception of their position in life, in the context of culture, value systems in which they live in relation to their goals, expectations, standards and concerns". In patients treated for breast cancer, many of the acute symptoms disappear. However, emotional deficits in social relationships and cognitive functions, associated with specific symptoms and concerns arising from cancer, impair QOL (2).

In the past, the only surgical treatment for breast cancer was mastectomy, with the possibility of late reconstruction with a myocutaneous flap (3). Subsequently, breast-conserving surgery (BCS) was established when combined with radiotherapy (4, 5). However, it is not always associated with good cosmetic results, as up to 30% of patients undergoing quadrantectomy require delayed repair due to unsatisfactory aesthetic results (6).

Thus, the concept of oncoplastic surgery (OS) is born, which is defined as the use of plastic surgery techniques to improve the aesthetic result of oncological surgery (7, 8). The surgery can be performed after mastectomy or BCS (9), with increasing indications in clinical practice. From an oncological point of view, greater ease of wide resection is observed, with the possibility of wider margins (10), a lower index of compromised margins (11) and a greater amount of resected tissue, without aesthetic damage (12).

Many patients who are not initially candidates for BCS (13) can undergo this procedure with the help of OS (14, 15), especially in the presence of tumours larger than 5 centimetres and with localized skin infiltration and multifocal and multicentric tumours, provided that it is possible to obtain neoplasia-free margins and that the residual breast volume allows an aesthetically satisfactory result. In this sense, the concept of extreme oncoplasty (EO) emerges (16).

Likewise, radical mastectomies have become more conservative, through skin preservation, with skin-sparing mastectomy (SSM) and nipple-sparing mastectomy (NSM) (17, 18). Immediate breast reconstruction, initially performed with myocutaneous flaps, was mostly replaced by the use of prostheses, and was considered a safe procedure, given the low cancer recurrence rates (19–22) and the high degree of patient satisfaction (23).

However, OS is generally used to describe a broad group of surgeries associated with BCS, including mastectomy with immediate reconstruction and late reconstruction surgeries (7, 8). Thus, when evaluating OS, we must consider the type of surgery, the conditions associated with its indication, the cosmetic quality and the QOL of the patient (24, 25). OS seems to be associated with the improvement of QOL (8). The articles usually assess specific situations and little studies evaluate all situations associated with OS and QOL (26–28). In this study, we sought to identify the main circumstances leading to OS, QOL questionnaires, systematic reviews and case–control studies.

Quality-of-life questionnaires

Several questionnaires can be found in the literature, but they need to be validated through a specific methodology (29, 30). The patient-reported outcome measures (PROMs) are organized in domains and questions. Domains correspond to the grouping of questions that evaluate the same subject. Grouping similar situations allows us to consider the subject and compare groups of patients in similar situations.

QOL associated with breast reconstruction were validated (26, 31, 32). To better understand and value the QOL questionnaires, we must understand how they are created (33, 34), the importance of the domains, the validation studies (35) and the steps associated with linguistic translation (36, 37).

The construction of a QOL questionnaire involves four main phases (34). The first phase is the question generation phase. Patients at different stages of the disease and health professionals are interviewed to determine the main questions to be asked. In the second phase, a list of questions is created, measurement scales are evaluated, health professionals are consulted, and an initial version of the questionnaire is drafted. A smaller group of patients evaluates questions for redundancy and low response rates, decreasing the number of questions, organizing the potential domains and drafts a potential questionnaire. In the third phase, the questionnaire is administered to a group of patients, and a validation test is performed. The acceptability, the structure of the questionnaire and the variability are evaluated, and changes are suggested. In the fourth phase, the module is completed, and validation tests are performed, aiming at a final review, regarding the number of questions and domains, and reaching a final version (33, 34).

There are several steps associated with the validation of a QOL questionnaire (38, 39). To validate a QOL questionnaire, in general, construct validity and reliability can be evaluated. Validity is the ability of a test to measure what it is proposed to measure. Factor analysis group questions organizing the domains. The internal consistency is assessed, which evaluates the degree of uniformity or coherence between the responses of the subjects to each of the domains that make up the instrument. In addition, the test-retest is performed, which evaluates the reliability at two different times, when no changes in the disease are observed. Construct validity evaluates the construction of the questionnaire through known, convergent or divergent (discriminant) groups and factor analysis. In the convergent validation of the scale, the correlations between the questionnaires and the conceptually related measures are evaluated, and they are expected to be substantially related to each other. For this purpose, domains of different QOL questionnaires are compared. This method allows the separation of the domains of the original questionnaire and tests whether the relationship of the original scale will be confirmed between other QOL and the variables observed in another language. Reliability evaluates whether the instrument is reliable and measures a construct over time between different individuals and situations. Confirmatory factor analysis is used to test the hypothetical scale structure and cross-cultural equivalence of the measurement properties.

A questionnaire is valid in the language in which it was created. To be used in another language, it must be translated, and the questions must have the same meaning in the translated language. There are different methods of translation and cultural adaptation (36, 37). Briefly, considering an example of translation into Portuguese/Brazil (36, 40), we have the following: translation from English to Portuguese/Brazil, by native Brazilians with English skills; synthesis of the translation by an expert committee; reverse translation into English; evaluating the versions by a committee of experts, comparing the versions and arriving at the initial version for

the Portuguese language; pretest with 10 patients, aiming to evaluate understanding, eliminate embarrassing items, respond to semantic questions, adapt the questions, and test them with a small number of patients, reaching the final Portuguese/Brazil version (40).

Quality-of-life questionnaires associated with breast cancer

There are several QOL questionnaires related to cancer. In the literature, we found questionnaires used to evaluate cancer in general, questionnaires associated with specific situations (such as anxiety and depression), specific questionnaires for breast cancer and questionnaires developed to evaluate surgical results. In addition, there were questionnaires used for other pathologies, which can be used in breast cancer given the sequelae associated with treatment. In the context of cancer, there are reviews on the subject (29, 32), and the most used in breast cancer studies are those presented in Table 1. Of these, the EORTC QLQ-BR45 (41) (update of EORTC QLQ-BR23) is in Phase 4 of validation.

Quality-of-life questionnaires associated with breast surgery

Despite the existence of general questionnaires for breast cancer, questionnaires were created to evaluate the relationship between the type of surgery and QOL (32).

For patients undergoing BCS, we have the BCTOS (*Breast Cancer Treatment Outcome Scale*) (35, 40) and the Breast-Q module for BCS (42). The BCTOS, when formulated, used another methodology for the construction of questionnaires, and for a long time it was the only questionnaire associated with BCS. The 22-item survey subjectively evaluates the aesthetic and functional outcomes after breast cancer treatment through questions about functional status, cosmetic status, specific breast pain and oedema (43). In patients undergoing BCS combined with radiotherapy, BCTOS was effective (44). It was observed, through the BCTOS, that the specific breast pain related to the treatment exceeds the importance of the cosmetic result in relation to QOL. Nevertheless, the appearance of the breast after conservation surgery is significantly associated with psychosocial outcomes, and women with large breast asymmetry are more likely to have a worse psychosocial state than those with minimal asymmetry (43). Regarding the Breast-Q, the initial questionnaire for plastic surgery was used, and recently a version of the BCS was created (42).

For patients who have undergone mastectomy and breast reconstruction, historically, the MBROS (32), followed by the Breast-Q reconstruction module (45) and EORTC QLQ BRECON23 (46) have been used. Using MBROS, delayed reconstruction increases emotional well-being and body image. Immediate and delayed breast reconstruction provide substantial psychosocial benefits for mastectomy patients, but the type of reconstruction did not impact in QOL (47). BRECON23 was published in 2018 and uses new methodology for QOL development. It is divided in scales are related to surgical side-effects, sexuality, satisfaction (breast cosmesis, nipple cosmesis, surgery), donor-site symptoms and single items (46). The number of publications using MBROS and BRECON are low.

New methodologies and validation studies were used for Breast-Q and BRECON questionnaires (31). The Breast-Q, initially developed for the evaluation of plastic and reconstructive breast surgery (48), is divided into six domains: satisfaction with the breasts, overall outcome, care processes, psychosocial, physical and sexual. In the first version, questionnaires related to augmentation mammoplasty, reduction mammoplasty and reconstruction were created (48). Currently, the Breast-Q is in its the second edition and is the most popular questionnaire for breast reconstruction (49, 50). Regarding the Breast-Q, the main domains related to cancer modules are summarized in Table 2.

Quality of life and oncoplastic surgery

To evaluate QOL in OS setting, we performed a literature review in PubMed database. We choose the terms: Breast Neoplasms [Mesh] and ("Surgery, Plastic"[Mesh] or "oncoplastic surgery" or "oncoplasty" or "oncoplastic" or "Reconstructive Surgical Procedures"[Mesh] or "Mammaplasty"[Mesh] or "Mastectomy, Segmental"[Mesh]) and "Quality of Life"[Mesh]. The terms were evaluated (09/12/2022) without (n=926) or with filters (Meta-analysis, Review and Systematic Review; n=127). Based on title and

TABLE 1 Main questionnaires associated with breast cancer treatment.

Quality of Life	Type of evaluation
General	EORTC QLQ-30; FACT-G
Breast	FACT-B; EORTC QLQ-BR23; EORTC QLQ-BR45 (BR23 actualization)
Brest Surgery	Mastectomy: BREAST-Q/mastectomy module
	Breast-conserving Surgery: BCTOS; BREAST-Q/breast conserving surgery module
	Reconstruction: MBROS, EORTC BRECON23; BREAST-Q reconstruction module
Shoulder	FACT-B+4; SPADI; DASH; Quick-DASH
Special situation	Anxiety and depression (HADS)

EORTC, European Organisation for Research and Treatment; QLQ, quality of life questionnaire; FACT, Functional Assessment of cancer therapy; BCTOS, Breast Cancer Treatment Outcome Scale; BREAST-Q, Breast questionnaire; MBROS, Michigan Breast Reconstruction Outcomes Study; BRECON23, breast reconstructive; SPADI, Shoulder Pain and Disability Index; DASH, Disabilities of the Arm, Shoulder and Hand; HADS, Hospital Anxiety and Depression Scale

10.3389/fonc.2022.1099125

TABLE 2 Summary of domains and number of questions in BREAST-Q version 2.0 for breast cancer.

	BCS		Mastectomy		Reconstruction	
	Pre	Post	Pre	Post	Pre	Post
DOMAIN OF QUALITY OF LIFE						
Psychosocial well-being	10	10	10	10	10	10
Sexual well-being	6	6	6	6	6	6
Physical well being						
- Chest	10	9	10	11	10	11
- Abdomen	–	–	–	–	4	7
Adverse effects of radiation	–	6	–	6	–	6
SATISFACTION DOMAINS						
Satisfaction with Breast	4	11	4	4	4	15
Satisfaction with the Results						
- Nipple reconstruction	–	–	–	–	–	1
- Abdomen	–	–	–	–	1	3
- Implant	–	–	–	–	–	2
Satisfaction with care						
Satisfaction with Information						
- Surgeon	–	12	–	12	–	15
- Radiotherapist	–	11	–	–	–	–
Satisfaction experience						
- Surgeon	–	12	–	12	–	12
- Medical Team	–	7	–	7	–	7
- Office Staff	–	7	–	7	–	7
Satisfaction with Latissimus Dorsi						
Back	–	–	–	–	8	8
Back and shoulder	–	–	–	–	11	11
Sub-total	30	91	30	75	35	102
RECONSTRUCTION EXPECTATIONS						
Short form	–	–	–	–	5 questions	–
Long form	–	–	–	–	27 questions	–

BCS, Breast- conserving Surgery.

resume, 25 articles were selected. In the absence of review articles, case-control studies or observational studies were evaluated.

OS has become a generic term. With regard to BCS, the concept goes beyond reduction mastoplasty techniques, with different techniques aimed at the readjustment of breast tissue to contralateral symmetrisation. Char et al (26) performed a systematic review of QL in level 2 volume displacement or volume replacement OS, including NSM, SSM with autologous or IBBR. The studies used Breast-Q or other validated PROMs. Of the 702 initial articles, 43 were included, representing 14,994 patients, and the main questionnaire used was the Breast-Q (n = 11,176). Using Breast-Q, 1,400 patients who underwent BCS and OS, 2,970 who had reconstruction with autologous flap and 6,806 who received implants were selected. Superior results were observed in the BCS in relation to mastectomy with implant, in autologous reconstruction in relation to the implant, in nipple preservation in relation to the absence of nipple preservation, and in the use of the prepectoral implant in relation to the retro-pectoral (26).

Many studies have compared specific surgical situations of OS and its relationship with QOL. We then sought, through systematic reviews, to choose more representative studies that evaluated OS in different surgical situations related to the treatment of breast cancer. In the absence of systematic reviews case-control studies or case series were selected for discussion.

Conservative breast treatment and oncoplastic surgery

The relationship between BCS and OS involves several criteria, ranging from indication (tumour, patient, safety), type of surgery (technique, oncological safety, laterality, symmetrisation, follow-up time), and cosmetic quality, influencing QOL (24). QOL, in turn, is influenced by conditions associated with treatment, reflected in the sequelae, return to usual activities, whether in relation to work, family or sexuality.

A systematic review that evaluated the topic compared BCS associated or not with OS. Of the 688 initial articles, 6 were selected, which included 832 patients with controversial results; OS was not associated with QOL improvement in 5 studies, and an association with improvement was observed in only one study (51). The nature of the studies, usually retrospective, the patient selection bias, the time since the performance of the primary procedure and the absence of systematic use of symmetrisation in all patients negatively influenced the results of patients undergoing OS-BCS (25, 52).

With regard to BCS associated with EO (16), there is only one study in the literature (53), which analysed 204 patients, only 33 of whom had undergone EO. The results were superior when performing EO in the face of psychological well-being and satisfaction with the breast, outcome and nipple-areola complex (53).

Mastectomy and oncoplastic mastectomy

The history of breast reconstruction begins with late reconstructions using myocutaneous flaps (autologous) and changed over time to immediate reconstructions in which the flaps were replaced by breast prostheses. We proceeded to skin-preserving mastectomies, followed by nipple-preserving mastectomies and then prophylactic mastectomies. All of these surgeries have pros and cons. Over time, asymmetries and adverse effects became more pronounced, especially in the presence of radiotherapy. Recently, to refine the results, we resorted to fat grafting.

Breast loss, without shape replacement, implies a decrease in QOL. Meta-analysis evaluated the QOL of patients undergoing mastectomy without reconstruction compared to patients undergoing BCS (54). Initially, 892 articles were evaluated, and 6 including a total of 1,931 patients were selected. It was found that patients undergoing BCS have better body image and future prospects, with a decrease in the effects associated with local effects.

BCS or reconstruction is always better than mastectomy without reconstruction. The role of the presence of breast reconstruction in relation to mastectomy was evaluated. A review of 277 studies, 9 were identified and 1.734 analysed, observing that the absence of reconstruction was associate with increased risk of depression (55). A study conducted with 400 patients using Breast-Q evaluated four groups (control, BCS, mastectomy with and without reconstruction), observing better satisfaction with breast appearance and sexual wellbeing in patients undergoing reconstructive mastectomy, followed by BCS and mastectomy without reconstruction. When evaluating the BCS in relation to the control group, the results were similar in relation to breast satisfaction, but the sexual wellbeing was superior in the control group (56). Another study evaluated 618 patients divided into BCS, mastectomy, and mastectomy with reconstruction groups using the EORTC QLQ-C30 and QLQ-BR23 questionnaires. Similar results were observed for role functioning and social functioning in patients undergoing BCS and mastectomy with reconstruction. However, when evaluating body image, the results were higher in patients undergoing BCS, followed by patients undergoing mastectomy with reconstruction compared to patients undergoing mastectomy without reconstruction (57). A meta-analysis comparing BCS versus mastectomy evaluated 9 studies identify 2.301 patient, observing better QV associated to BCS in relation to body image, emotional function and social function (58).

A systematic review and meta-analysis evaluated the impact of breast reconstruction in relation to BCS. From 12,192 initial articles, there were 16 articles, with the analysis of 5,544 patients (1,458 mastectomies, 2,612 undergoing BCS and 1,474 undergoing mastectomy with reconstruction). The results showed great heterogeneity among the studies, with similar results in relation to BCS and mastectomy with reconstruction. In turn, the patients who underwent mastectomy without reconstruction exhibited poorer physical health and body image (27).

The role of the presence of breast reconstruction in relation to mastectomy was evaluated. From 277 studies, 9 were identified and 1.734 analysed, observing that the absence of reconstruction was associate with increased risk of depression (55).

Platt et al (59), performed a review of different conditions related to mastectomy with breast reconstruction and QV, reporting: (1) Immediate and delayed breast reconstruction increases satisfaction and quality of life; (2) Autologous reconstruction demonstrates superior PROMs over long-term when compared with implant-based breast reconstruction (IBBR); (3) NSM was associated with increased satisfaction than SSM.

Saldanha et al (28) performed a systematic review of breast reconstruction after mastectomy, selecting 83 nonrandomized studies, 8 randomized controlled trials and 69 single group studies. They observed that: (1) autologous reconstruction were associated with clinically better patient satisfaction with breast and sexual well-being than IBBR; (2) There is insufficient evidence about IBBR versus radiotherapy and QV; (3) Silicone and saline implants result in clinically similar patient satisfaction; (3) The evidence related to acellular dermal matrix (ADM) and QV is insufficient; (4) The type of Autologous reconstruction did not influence QV.

Also, in the comparison between the different breast reconstruction modalities (autologous tissue or implant), a meta-analysis performed on 219 initial studies yielded 9 studies suitable for analysis, encompassing 2,954 patients (2,129 with implants and 825 with autologous tissue). High overall satisfaction was observed among patients who had undergone breast reconstruction, and overall satisfaction and satisfaction with the breast was higher with the use of autologous tissue. On the other hand, psychosocial, psychic and sexual well-being was higher in patients with breast implants (60). Another meta-analysis evaluated the same item, selecting from 280 articles, 10 full-texts, including a total of 4,957 patients, of which 3,836 were evaluated using the Breast-Q questionnaire. It was found that satisfaction with the results, the breasts and sexual well-being was higher with the use of autologous tissue (61).

The use of prepectoral or subpectoral IBBR was evaluated. A meta-analysis evaluates 3.789 studies, 7 publications and 548 patients, observing that patients with prepectoral implants reported higher

Breast-Q scores and lower postoperative pain (62), suggesting the use of acellular dermal matrix (ADM). Although, the use of acellular dermal matrix (ADM) do not improve the QOL (63), and one or two-stage IBBR with ADM, also do not chance QOL (64).

Nipple-areolar preservation improves QOL, although the number of studies and casuistry are limited, positive results were observed (59). Char et al (26) performed a systematic review of QL including NSM and SSM with autologous or IBBR, observing superior results related do NSM. A non-randomized, cross-sectional study used evaluated the impact of areolar preservation with Breast-Q questionnaire. It evaluated 137 patients (83 SSM x 53 NSM), observing that body image and sexual functioning associated to SSM (65). Wei et al, prospective evaluate patients submitted to NSM (n=52) and patients submitted do SSM and areolar reconstruction (202). NSM patients reported higher scores in psychosocial and sexual well-being (66). Two studies performed matched comparison, all using Breast-Q. The first (n = 62), matched by reconstruction type and operative period, compared NSM (n = 32) and SSM (n = 32), observing better satisfaction of results and the breasts in NSM (67). The second, with smaller number of patients (n = 52; 26x26), matched by age, race and body index, observed a significant improvement only in sexual well-being, associated with NSM (68).

Prophylactic mastectomy has risen in popularity, a fact associated with the dissemination of genetic tests, facilitating the selection of patients. It is observed that the patients are satisfied with the indication, but have complaints related to the prosthesis (69, 70). The first systematic review found 1,082 studies and selected 22 studies with a total of 2,046 patients. Satisfaction with the indication, high psychosocial well-being and body image were observed, with social well-being and somatosensory function being the most affected items (69). The second review, based on 7,272 articles, selected 7 articles that included 730 women and used different questionnaires. Overall satisfaction and cosmetic results were high, but surgery was associated with complaints related to breast hardness, numbness and sex, suggesting the importance of informing patients about the complications associated with the procedure (70).

Contralateral prophylactic mastectomy for unilateral breast cancer was evaluated in a systematic review of 19 articles, representing 6.088 patients. High levels of satisfaction were observed with the decision for surgery, with high satisfaction with cosmesis and reconstruction (71).

Evaluating robotic mastectomy, one study (n=80), using Breast Q, evaluated the impact in QOL, observing that Breast-Q scores in satisfaction with breasts, psychosocial, physical and sexual well-being were significantly higher after robotic mastectomy in relation to conventional mastectomy (72).

To improve the cosmetic results, we have fat grafting. A systematic review evaluating the technique found 2,915 articles and selected 6 that reported on Breast-Q, representing 1,437 patients. Although fat grafting improves breast satisfaction, the difference was not significant (73).

Discussion

When evaluating studies that selected patients for OS, it is necessary to consider that most of them are retrospective, and even in prospective patients, there may be a selection bias. Commonly, patients subjected to OS have a large tumour size, are younger, undergo neoadjuvant chemotherapy, have higher education, or are potentially more demanding, not accepting major defects or mastectomy without reconstruction, a fact that may influence the results (24, 74).

Breast symmetry, the timing of the procedure and the individual who evaluates outcomes are also considerations. OS is not always synonymous with the performance of symmetrisation, which improves the cosmetic effects, and time is an important risk factor for the appearance of asymmetries. In patients undergoing BCS, the irradiated breast undergoes little volume change, even with the increase in weight, which is contrary to the contralateral breast, which may present a volume increase and accentuation of ptosis, without alteration of the consistency (24). In patients undergoing mastectomy with prostheses, capsular contracture, the emergence of rippling, elevation of the breast furrow height and, when associated with increased weight, increased asymmetry in the contralateral breast are observed. Such outcomes may influence QOL and breast satisfaction. Regarding the cosmetic result, it is observed that in general, patients are less demanding than health professionals, with disagreement between them regarding the quality of the results, which makes it difficult to compare cosmetic results and QOL (75).

For a long time, the number of QOL questionnaires directed at breast cancer were few and evaluated specific situations, and the breast shape and outcomes were poorly evaluated. For cosmetic breast evaluation we used the BCTOS (43) and MBROS (32). The Breast-Q initially used in plastic surgery has been improved, and new questionnaires specific to the different conditions associated with breast cancer have emerged, allowing better evaluation of the impact of OS in different situations (29, 48, 76). Recently, we started to have the Breast-Q associated with BCS (42), and all questionnaires associated with the Breast-Q are in their second edition (77). The EORTC questionnaires have also evolved in this direction, and the BRECON23 was recently created (46). Updated EORTC QLQ-BR45 (41) aspects associated with breast shape were included, allowing a better evaluation of this aspect as it relates to QOL, but these questionnaires are recent, and the number of publications is limited. The Breast-Q is a questionnaire that has the greatest number of associated publications (49).

Quality of life involves multiple aspects. In breast cancer, there are many sequelae resulted from the treatment (78), many of which are poorly contextualized, since evaluating objective measurements and QOL questionnaires (35). In this context, sequelae associated with shoulder mobility after reconstruction (79), alterations associated with the use of IBBR, or alterations associated with the use of myocutaneous flaps, mainly the rectus abdominis muscle, are observed. Although the degree of satisfaction is high associated with OS, the look under the functional part is little discussed, and me must take care evaluating sequelae and functional functioning. Also, the impact of rehabilitation (80) and exercise (81) in OS is under reported. Future reviews evaluating these conditions are necessary.

The limitation of this study was to group literature results and not evaluate the quality of the studies. Although this situation it was possible to report multiple conclusions. Many studies are needed to accumulate evidence, especially in different populations (39), as the systematic reviews note the presence of heterogeneity in the literature (27, 60–62), a fact possibly associated with the patient selection criteria,

techniques used, differences in time since OS, presence of symmetrization and nonuniformity in relation to the questionnaires. Despite these limitations, due to the aforementioned limitations, OS improves QOL. Based on articles presented, we can conclude the following from these studies: (1) Patients undergoing BCS or breast reconstruction have improved QOL compared to those undergoing mastectomy; (2) Patients undergoing BCS or OS have not yet shown improvement in QOL, a fact possibly influenced by patient selection bias; (3) Patients undergoing mastectomy with reconstruction demonstrate better QOL results when reconstruction is performed compared to BCS using autologous flaps and when preserving the nipple-areola complex; (4) Prepectoral implants improves QOL in relation to subpectoral IIBR; (5) ADM do not improves QOL; (6) Patients undergoing prophylactic mastectomy indicate high satisfaction, but patients should be informed about the potential complications associated with the procedure; (7) Satisfaction is high after fat grafting.

Oncoplasty has become a routine procedure. As the literature increases, more publication will occur and new meta-analysis will appear increasing the number of patients for evaluation. The impact of surgery (mastectomy versus mastectomy with fasciocutaneous or myocutaneos flaps for skin closure) in QOL for locally advanced breast cancer was never studied in case-control study, although we believe that this surgery improves QOL (82). Also, new techniques, new indications of EO and robotic surgery are becoming popular, making space for new studies related to QOL. While there is usually a selection bias in studies and the studies are heterogeneous, some results possibly will not change: the preservation of the breast or the nipple-areola complex and the use of autologous flaps are associated with better QOL results. OS already has a defined role in improving QOL.

Author contributions

RV and AB-J conceived the manuscript. RV, AB-J, IO-J wrote the manuscript. RV, IO-J supervised and edited the manuscript. RV and AB-J share the same authorship. All authors contributed to the article and approved the submitted version.

Funding

Fundação Pio XII, Hospital de Câncer de Barretos; Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

References

1. Heil J, Dahlkamp J, Golatta M, Rom J, Domschke C, Rauch G, et al. Aesthetics in breast conserving therapy: do objectively measured results match patients' evaluations? *Ann Surg Oncol* (2011) 18(1):134–8. doi: 10.1245/s10434-010-1252-4

2. Arndt V, Merx H, Stegmaier C, Ziegler H, Brenner H. Persistence of restrictions in quality of life from the first to the third year after diagnosis in women with breast cancer. *J Clin Oncol Off J Am Soc Clin Oncol* (2005) 23(22):4945–53. doi: 10.1200/JCO.2005.03.475

3. Kaya B, Serel S. Breast reconstruction. *Exp Oncol* (2013) 35(4):280–6.

4. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *New Engl J Med* (2002) 347(16):1233–41. doi: 10.1056/NEJMoa022152

5. Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *New Engl J Med* (2002) 347(16):1227–32. doi: 10.1056/NEJMoa020989

6. Clough KB, Cuminet J, Fitoussi A, Nos C, Mosseri V. Cosmetic sequelae after conservative treatment for breast cancer: classification and results of surgical correction. *Ann Plast surgery.* (1998) 41(5):471–81. doi: 10.1097/00000637-199811000-00004

7. Bertozzi N, Pesce M, Santi PL, Raposio E. Oncoplastic breast surgery: comprehensive review. *Eur Rev Med Pharmacol Sci* (2017) 21(11):2572–85.

8. Scomacao I, AlHilli Z, Schwarz G. The role of oncoplastic surgery for breast cancer. *Curr Treat Options Oncol* (2020) 21(12):94. doi: 10.1007/s11864-020-00793-1

9. Audretsch W, Andree C. Is mastectomy still justified – And if, in which patients?. *Onkologie* (2006) 29:243–5. doi: 10.1159/000093477

10. Losken A, Hart AM, Chatterjee A. Updated evidence on the oncoplastic approach to breast conservation therapy. *Plast Reconstr Surg* (2017) 140(5S Advances in Breast Reconstruction):14S–22S. doi: 10.1097/PRS.0000000000003951

11. Kaur N, Petit JY, Rietjens M, Maffini F, Luini A, Gatti G, et al. Comparative study of surgical margins in oncoplastic surgery and quadrantectomy in breast cancer. *Ann Surg Oncol* (2005) 12(7):539–45. doi: 10.1245/ASO.2005.12.046

12. Clough KB, Lewis JS, Couturaud B, Fitoussi A, Nos C, Falcou MC. Oncoplastic techniques allow extensive resections for breast-conserving therapy of breast carcinomas. *Ann Surg* (2003) 237(1):26–34. doi: 10.1097/00000658-200301000-00005

13. Carrara GF, Scapulatempo-Neto C, Abrahao-Machado LF, Brentani MM, Nunes JS, Folgueira MA, et al. Breast-conserving surgery in locally advanced breast cancer submitted to neoadjuvant chemotherapy. safety and effectiveness based on ipsilateral breast tumor recurrence and long-term follow-up]. *Clinics (Sao Paulo).* (2017) 72(3):134–42. doi: 10.6061/clinics/2017(03)02

14. Vieira RA, Carrara GF, Scapulatempo Neto C, Morini MA, Brentani MM, Folgueira MA. The role of oncoplastic breast conserving treatment for locally advanced breast tumors. a matching case-control study. *Ann Med Surg (Lond).* (2016) 10:61–8. doi: 10.1016/j.amsu.2016.08.001

15. Zucca Matthes AG, Uemura G, Kerr L, Matthes AC, Michelli RA, Folgueira MA, et al. Feasibility of oncoplastic techniques in the surgical management of locally advanced breast cancer. *Int J Surg* (2012) 10(9):500–5. doi: 10.1016/j.ijsu.2012.07.009

16. Silverstein MJ, Savalia N, Khan S, Ryan J. Extreme oncoplasty: breast conservation for patients who need mastectomy. *Breast J* (2015) 21(1):52–9. doi: 10.1111/tbj.12356

17. Foster RD, Esserman LJ, Anthony JP, Hwang ES, Do H. Skin-sparing mastectomy and immediate breast reconstruction: A prospective cohort study for the treatment of advanced stages of breast carcinoma. *Ann Surg Oncol* (2002) 9(5):462–6. doi: 10.1007/BF02557269

18. Patani N, Mokbel K. Oncological and aesthetic considerations of skin-sparing mastectomy. *Breast Cancer Res Treat* (2008) 111(3):391–403. doi: 10.1007/s10549-007-9801-7

19. Gieni M, Avram R, Dickson L, Farrokhyar F, Lovrics P, Faidi S, et al. Local breast cancer recurrence after mastectomy and immediate breast reconstruction for invasive cancer: a meta-analysis. *Breast* (2012) 21(3):230–6. doi: 10.1016/j.breast.2011.12.013

20. Yang X, Zhu C, Gu Y. The prognosis of breast cancer patients after mastectomy and immediate breast reconstruction: a meta-analysis. *PloS One* (2015) 10(5):e0125655. doi: 10.1371/journal.pone.0125655

21. Mota BS, Riera R, Ricci MD, Barrett J, de Castria TB, Atallah AN, et al. Nipple- and areola-sparing mastectomy for the treatment of breast cancer. *Cochrane Database Syst Rev* (2016) 11:CD008932. doi: 10.1002/14651858.CD008932.pub3

22. Lanitis S, Tekkis PP, Sgourakis G, Dimopoulos N, Al Mufti R, Hadjiminas DJ. Comparison of skin-sparing mastectomy versus non-skin-sparing mastectomy for breast cancer: a meta-analysis of observational studies. *Ann Surg* (2010) 251(4):632–9. doi: 10.1097/SLA.0b013e3181d35bf8

23. Galimberti V, Vicini E, Corso G, Morigi C, Fontana S, Sacchini V, et al. Nipple-sparing and skin-sparing mastectomy: Review of aims, oncological safety and contraindications. *Breast* (2017) 34 Suppl 1:S82–S4. doi: 10.1016/j.breast.2017.06.034

24. Oliveira-Junior I, Silva IA, Silva FCB, Silva JJ, Sarri AJ, Paiva CE, et al. Oncoplastic surgery in breast-conserving treatment: Patient profile and impact on quality of life. *Breast Care (Basel)* (2020) 15):1–11. doi: 10.1159/000507240

25. Oliveira-Junior I, Haikel RL, Vieira RAC. Breast-conserving treatment in oncoplastic times: indications, cosmesis, and quality of life. *Mastology* (2021) 31: e20200040. doi: 10.29289/2594539420200040

26. Char S, Bloom JA, Erlichman Z, Jonczyk MM, Chatterjee A. A comprehensive literature review of patient-reported outcome measures (PROMs) among common breast reconstruction options: What types of breast reconstruction score well? *Breast J* (2021) 27 (4):322–9. doi: 10.1111/tbj.14186

27. Zehra S, Doyle F, Barry M, Walsh S, Kell MR. Health-related quality of life following breast reconstruction compared to total mastectomy and breast-conserving surgery among breast cancer survivors: a systematic review and meta-analysis. *Breast Cancer.* (2020) 27(4):534–66. doi: 10.1007/s12282-020-01076-1

28. Saldanha IJ, Cao W, Broyles JM, Adam GP, Bhuma MR, Mehta S, et al. Breast reconstruction after mastectomy: A systematic review and meta-analysis. *AHRQ Comp Effectiveness Rev* (2021). doi: 10.23970/AHRQEPCCER245

29. Pusic AL, Chen CM, Cano S, Klassen A, McCarthy C, Collins ED, et al. Measuring quality of life in cosmetic and reconstructive breast surgery: a systematic review of patient-reported outcomes instruments. *Plast Reconstr Surg* (2007) 120(4):823–37. doi: 10.1097/01.prs.0000278162.82906.81

30. Oliveira IS, da Cunha Menezes Costa L, Fagundes FR, Cabral CM. Evaluation of cross-cultural adaptation and measurement properties of breast cancer-specific quality-of-life questionnaires: a systematic review. *Qual Life Res* (2015) 24(5):1179–95. doi: 10.1007/s11136-014-0840-3

31. Davies CF, Macefield R, Avery K, Blazeby JM, Potter S. Patient-reported outcome measures for post-mastectomy breast reconstruction: A systematic review of development and measurement properties. *Ann Surg Oncol* (2021) 28(1):386–404. doi: 10.1245/s10434-020-08736-8

32. Chen CM, Cano SJ, Klassen AF, King T, McCarthy C, Cordeiro PG, et al. Measuring quality of life in oncologic breast surgery: a systematic review of patient-reported outcome measures. *Breast J* (2010) 16(6):587–97. doi: 10.1111/j.1524-4741.2010.00983.x

33. Wheelwright S, Bjordal K, Bottomley A, Gilbert A, Martinelli F, Pe M, et al. *EORTC quality of life group guidelines for developing questionnaire modules Belgium: EORTC - European organization for research and treatment of cancer* (2021). Available at: https://www.eortc.org/app/uploads/sites/2/2022/07/Module-Guidelines-Version-5-FINAL.pdf.

34. Johnson C, Aeronson N, Blazeby JM, Bottomley A, Fayers P, Koller M, et al. *EORTC quality of life group. guidelines for developing questionnaire modules. 4th ed.* Brussels, Belgium: EORTC Quality of Life Group (2011).

35. Brandini da Silva FC, Jose da Silva J, Sarri AJ, Paiva CE, Aloisio da Costa Vieira R. Comprehensive validation study of quality-of-Life questionnaire using objective clinical measures: Breast cancer treatment outcome scale (BCTOS), Brazilian Portuguese version. *Clin Breast Cancer.* (2019) 19(1):e85–e100. doi: 10.1016/j.clbc.2018.10.004

36. Beaton DE, Bombardier C, Guillemin F, Ferlay MB. Guidelines for the process of cross-cultural adaptation of self-report measures. *Spine* (2000) 25(24):3186–91. doi: 10.1097/00007632-200012150-00014

37. Kulis D, Bottomley A, Velikova G, Greimel E, Koller M. *EORTC quality of life group translation procedure Brussels: EORTC - European organization for research and treatment of cancer* (2017). Available at: https://www.eortc.org/app/uploads/sites/2/2018/02/translation_manual_2017.pdf.

38. Fayers PM, Machin D. *Quality of life. 2nd ed.* England: Wiley (2007). 544 p.

39. Voineskos SH, Nelson JA, Klassen AF, Pusic AL. Measuring patient-reported outcomes: Key metrics in reconstructive surgery. *Annu Rev Med* (2018) 69:467–79. doi: 10.1146/annurev-med-060116-022831

40. Vieira R, Silva F, Silva MES, Silva JJD, Sarri AJ, Paiva CE. Translation and cultural adaptation of the breast cancer treatment outcome scale (BCTOS) into Brazilian Portuguese. *Rev Assoc Med Bras (1992).* (2018) 64(7):627–34. doi: 10.1590/1806-9282.64.07.627

41. Bjelic-Radisic V, Cardoso F, Cameron D, Brain E, Kuljanic K, da Costa RA, et al. An international update of the EORTC questionnaire for assessing quality of life in breast cancer patients: EORTC QLQ-BR45. *Ann Oncol* (2020) 31(2):283–8. doi: 10.1016/j.annonc.2019.10.027

42. O'Connell RL, DiMicco R, Khabra K, O'Flynn EA, deSouza N, Roche N, et al. Initial experience of the BREAST-q breast-conserving therapy module. *Breast Cancer Res Treat* (2016) 160(1):79–89. doi: 10.1007/s10549-016-3966-x

43. Stanton AL, Krishnan L, Collins CA. Form or function? part 1. subjective cosmetic and functional correlates of quality of life in women treated with breast-conserving surgical procedures and radiotherapy. *Cancer* (2001) 91(12):2273–81.

44. Krishnan L, Stanton AL, Collins CA, Liston VE, Jewell WR. Form or function? part 2. objective cosmetic and functional correlates of quality of life in women treated with breast-conserving surgical procedures and radiotherapy. *Cancer* (2001) 91 (12):2282–7.

45. Cordanto-Nopoulos FR, Sbalchiero JC, Silva CHD, Caiado-Neto BR, Derchain S. Tradução do questionário BREAST-q para a língua portuguesa e sua aplicação em mulheres com câncer de mama. *Rev Bras Cir Plast* (2013) 28(S1):79.

46. Winters ZE, Afzal M, Rutherford C, Holzner B, Rumpold G, da Costa Vieira RA, et al. International validation of the European organisation for research and treatment of cancer QLQ-BRECON23 quality-of-life questionnaire for women undergoing breast reconstruction. *Br J Surg* (2018) 105(3):209–22. doi: 10.1002/bjs.10656

47. Wilkins EG, Cederna PS, Lowery JC, Davis JA, Kim HM, Roth RS, et al. Prospective analysis of psychosocial outcomes in breast reconstruction: One-year postoperative results from the Michigan breast reconstruction outcome study. *Plast Reconstr Surg* (2000) 106(5):1014–25. doi: 10.1097/00006534-200010000-00010

48. Pusic AL, Klassen AF, Scott AM, Klok JA, Cordeiro PG, Cano SJ. Development of a new patient-reported outcome measure for breast surgery: the BREAST-q. *Plast Reconstr Surg* (2009) 124(2):345–53. doi: 10.1097/PRS.0b013e3181aee807

49. Cohen WA, Mundy LR, Ballard TN, Klassen A, Cano SJ, Browne J, et al. The BREAST-q in surgical research: A review of the literature 2009-2015. *J Plast Reconstr Aesthet Surg* (2016) 69(2):149–62. doi: 10.1016/j.bjps.2015.11.013

50. Seth I, Seth N, Bulloch G, Rozen WM, Hunter-Smith DJ. Systematic review of breast-q: A tool to evaluate post-mastectomy breast reconstruction. *Breast Cancer (Dove Med Press).* (2021) 13:711–24. doi: 10.2147/BCTT.S256393

51. Aristokleous I, Saddiq M. Quality of life after oncoplastic breast-conserving surgery: a systematic review. *ANZ J Surg* (2019) 89(6):639–46. doi: 10.1111/ans.15097

52. Ojala K, Meretoja TJ, Leidenius MH. Aesthetic and functional outcome after breast conserving surgery - comparison between conventional and oncoplastic resection. *Eur J Surg Oncol* (2017) 43(4):658–64. doi: 10.1016/j.ejso.2016.11.019

53. Acea Nebril B, Garcia Novoa A, Polidorio N, Cereijo Garea C, Bouzon Alejandro A, Mosquera Oses J. Extreme oncoplasty: The last opportunity for breast conservation-analysis of its impact on survival and quality of life. *Breast J* (2019) 25(3):535–6. doi: 10.1111/tbj.13267

54. Ng ET, Ang RZ, Tran BX, Ho CS, Zhang Z, Tan W, et al. Comparing quality of life in breast cancer patients who underwent mastectomy versus breast-conserving surgery: A meta-analysis. *Int J Environ Res Public Health* (2019) 16(24). doi: 10.3390/ijerph16244970

55. Padmalatha S, Tsai YT, Ku HC, Wu YL, Yu T, Fang SY, et al. Higher risk of depression after total mastectomy versus breast reconstruction among adult women with breast cancer: A systematic review and metaregression. *Clin Breast Cancer.* (2021) 21(5): e526–e38. doi: 10.1016/j.clbc.2021.01.003

56. Howes BH, Watson DI, Xu C, Fosh B, Canepa M, Dean NR. Quality of life following total mastectomy with and without reconstruction versus breast-conserving surgery for breast cancer: A case-controlled cohort study. *J Plast Reconstr Aesthet Surg* (2016) 69(9):1184–91. doi: 10.1016/j.bjps.2016.06.004

57. Kim MK, Kim T, Moon HG, Jin US, Kim K, Kim J, et al. Effect of cosmetic outcome on quality of life after breast cancer surgery. *Eur J Surg Oncol* (2015) 41(3):426–32. doi: 10.1016/j.ejso.2014.12.002

58. Li Y, Guo J, Sui Y, Chen B, Li D, Jiang J. Quality of life in patients with breast cancer following breast conservation surgery: A systematic review and meta-analysis. *J Healthc Eng.* (2022) 2022:3877984. doi: 10.1155/2022/3877984

59. Platt J, Zhong T. Patient-centered breast reconstruction based on health-related quality-of-Life evidence. *Clin Plast Surg* (2018) 45(1):137–43. doi: 10.1016/j.cps.2017.08.011

60. Toyserkani NM, Jorgensen MG, Tabatabaeifar S, Damsgaard T, Sorensen JA. Autologous versus implant-based breast reconstruction: A systematic review and meta-analysis of breast-q patient-reported outcomes. *J Plast Reconstr Aesthet Surg* (2020) 73 (2):278–85. doi: 10.1016/j.bjps.2019.09.040

61. Eltahir Y, Krabbe-Timmerman IS, Sadok N, Werker PMN, de Bock GH. Outcome of quality of life for women undergoing autologous versus alloplastic breast reconstruction following mastectomy: A systematic review and meta-analysis. *Plast Reconstr Surg* (2020) 145(5):1109–23. doi: 10.1097/PRS.0000000000006720

62. Ching AH, Lim K, Sze PW, Ooi A. Quality of life, pain of prepectoral and subpectoral implant-based breast reconstruction with a discussion on cost: A systematic review and meta-analysis. *J Plast Reconstr Aesthet Surg* (2022) 75(8):2550–60. doi: 10.1016/j.bjps.2022.02.019

63. Lohmander F, Lagergren J, Johansson H, Roy PG, Brandberg Y, Frisell J. Effect of immediate implant-based breast reconstruction after mastectomy with and without acellular dermal matrix among women with breast cancer: A randomized clinical trial. *JAMA Netw Open* (2021) 4(10):e2127806. doi: 10.1001/jamanetworkopen.2021.27806

64. Negenborn VL, Young-Afat DA, Dikmans REG, Smit JM, Winters HAH, Don Griot JPW, et al. Quality of life and patient satisfaction after one-stage implant-based breast reconstruction with an acellular dermal matrix versus two-stage breast reconstruction (BRIOS): primary outcome of a randomised, controlled trial. *Lancet Oncol* (2018) 19(9):1205–14. doi: 10.1016/S1470-2045(18)30378-4

65. Metcalfe KA, Cil TD, Semple JL, Li LD, Bagher S, Zhong T, et al. Long-term psychosocial functioning in women with bilateral prophylactic mastectomy: Does preservation of the nipple-areolar complex make a difference? *Ann Surg Oncol* (2015) 22(10):3324–30. doi: 10.1245/s10434-015-4761-3

66. Wei CH, Scott AM, Price AN, Miller HC, Klassen AF, Jhanwar SM, et al. Psychosocial and sexual well-being following nipple-sparing mastectomy and reconstruction. *Breast J* (2016) 22(1):10–7. doi: 10.1111/tbj.12542

67. Bailey CR, Ogbuagu O, Baltodano PA, Simjee UF, Manahan MA, Cooney DS, et al. Quality-of-Life outcomes improve with nipple-sparing mastectomy and breast

reconstruction. *Plast Reconstr Surg* (2017) 140(2):219–26. doi: 10.1097/PRS.0000000000003505

68. Yoon-Flannery K, DeStefano LM, de la Cruz LM, Fisher CS, Lin LY, Coffua LS, et al. Quality of life and sexual well-being after nipple sparing mastectomy: A matched comparison of patients using the breast q. *J Surg Oncol* (2018) 118(1):238–42. doi: 10.1002/jso.25107

69. Razdan SN, Patel V, Jewell S, McCarthy CM. Quality of life among patients after bilateral prophylactic mastectomy: a systematic review of patient-reported outcomes. *Qual Life Res* (2016) 25(6):1409–21. doi: 10.1007/s11136-015-1181-6

70. Aygin D, Cengiz H. Life quality of patients who underwent breast reconstruction after prophylactic mastectomy: systematic review. *Breast Cancer.* (2018) 25(5):497–505. doi: 10.1007/s12282-018-0862-8

71. Srethbhakdi A, Brennan ME, Hamid G, Flitcroft K. Contralateral prophylactic mastectomy for unilateral breast cancer in women at average risk: Systematic review of patient reported outcomes. *Psychooncology* (2020) 29(6):960–73. doi: 10.1002/pon.5379

72. Toesca A, Sangalli C, Maisonneuve P, Massari G, Girardi A, Baker JL, et al. A randomized trial of robotic mastectomy versus open surgery in women with breast cancer or BrCA mutation. *Ann Surg* (2022) 276(1):11–9. doi: 10.1097/SLA.0000000000004969

73. Schop SJ, Joosen MEM, Wolswijk T, Heuts EM, van der Hulst R, Piatkowski de Grzymala AA. Quality of life after autologous fat transfer additional to prosthetic breast reconstruction in women after breast surgery: A systematic review. *Eur J Surg Oncol* (2021) 47(4):772–7. doi: 10.1016/j.ejso.2020.10.021

74. Almeida NR, Brenelli FP, Dos Santos CC, Torresan RZ, Shinzato JY, Cardoso-Filho C, et al. Comparative study of surgical and oncological outcomes in oncoplastic versus non oncoplastic breast-conserving surgery for breast cancer treatment. *JPRAS Open* (2021) 29:184–94. doi: 10.1016/j.jpra.2021.05.010

75. de Oliveira-Junior I, Brandini da Silva FC, Nazima F, Ribeiro JCJr., Castellani L, Zucca-Matthes G, et al. Oncoplastic surgery: Does patient and medical specialty influences the evaluation of cosmetic results? *Clin Breast Cancer* (2021) 21(3):247–55.e3. doi: 10.1016/j.clbc.2020.09.012

76. Oliveira IGE. Breast-q - breast reconstruciton expectations module (Pre operative). In: *Tradução e adaptação cultural para o brasil*. São Paulo: Unidade Federal de São Paulo (2018).

77. Pusic AL, Klassen A, Cano S. *Qportfolio - setting the bar in patient reported outcome measurement* (2022). Available at: https://qportfolio.org/breast-q/breast-cancer/.

78. Vieira RAC, Silva FCB, Biller G, Silva JJ, Paiva CE, Sarri AJ. Instruments of quantitative and qualitative evaluation of breast cancer treatment sequels. *Rev Bras Mastol.* (2016) 26(3):126–32. doi: 10.5327/Z201600030008RBM

79. Vidt ME, Potochny J, Dodge D, Green M, Sturgeon K, Kass R, et al. The influence of mastectomy and reconstruction on residual upper limb function in breast cancer survivors. *Breast Cancer Res Treat* (2020) 182(3):531–41. doi: 10.1007/s10549-020-05717-z

80. Invernizzi M, de Sire A, Lippi L, Venetis K, Sajjadi E, Gimigliano F, et al. Impact of rehabilitation on breast cancer related fatigue: A pilot study. *Front Oncol* (2020) 10:556718. doi: 10.3389/fonc.2020.556718

81. Abbasi F, Pourjalali H, do Nascimento IJB, Zargarzadeh N, Mousavi SM, Eslami R, et al. The effects of exercise training on inflammatory biomarkers in patients with breast cancer: A systematic review and meta-analysis. *Cytokine* (2022) 149:155712. doi: 10.1016/j.cyto.2021.155712

82. Rini IS, Krisna MA, Kamayana J, Djarot KR, Gunardi AJ. Keystone perforator island flap for postmastectomy defect resurfacing in late-stage breast cancer patients. *Plast Reconstr Surg Glob Open* (2019) 7(11):e2457. doi: 10.1097/GOX.0000000000002457

frontiers | Frontiers in Oncology

TYPE Original Research
PUBLISHED 16 March 2023
DOI 10.3389/fonc.2023.1154680

OPEN ACCESS

EDITED BY
Damiano Caputo,
Campus Bio-Medico University, Italy

REVIEWED BY
Paolo Orsaria,
Campus Bio-Medico University, Italy
Antonella Grasso,
Campus Bio-Medico University Hospital, Italy

*CORRESPONDENCE
Karina Furlan Anselmi
karinafurlananselmi@gmail.com

†These authors have contributed equally to this work

SPECIALTY SECTION
This article was submitted to Surgical Oncology, a section of the journal Frontiers in Oncology

RECEIVED 31 January 2023
ACCEPTED 27 February 2023
PUBLISHED 16 March 2023

CITATION
Anselmi KF, Urban C, Dória MT, Urban LABD, Sebastião AP, Kuroda F, Rabinovich I, Cordeiro AAF, Nissen LP, Schunemann E Jr., Spautz C, Pelanda JDC, de Lima RS, Rietjens M and Loureiro MP (2023) Prospective study: Impact of breast magnetic resonance imaging on oncoplastic surgery and on indications of mastectomy in patients who were previously candidates to breast conserving surgery.
Front. Oncol. 13:1154680.
doi: 10.3389/fonc.2023.1154680

Prospective study: Impact of breast magnetic resonance imaging on oncoplastic surgery and on indications of mastectomy in patients who were previously candidates to breast conserving surgery

Karina Furlan Anselmi[1,2*†], Cicero Urban[1†], Maíra Teixeira Dória[1,3†], Linei Augusta Brolini Delle Urban[4†], Ana Paula Sebastião[5†], Flávia Kuroda[1†], Iris Rabinovich[1,3†], Alessandra Amatuzzi Fornazari Cordeiro[1†], Leonardo Paese Nissen[1†], Eduardo Schunemann Jr.[1,3†], Cleverton Spautz[1†], Julia Di Conti Pelanda[1†], Rubens Silveira de Lima[1†], Mario Rietjens[6†] and Marcelo de Paula Loureiro[2†]

[1]Breast Unit, Hospital Nossa Senhora das Graças, Curitiba, Brazil, [2]Post-Graduation Program in Biotechnology, Universidade Positivo, Curitiba, Brazil, [3]Department of Obstetrics and Gynecology, Universidade Federal do Paraná, Curitiba, Brazil, [4]Radiologist of DAPI Clinic, Curitiba, Brazil, [5]Department of Pathology, Universidade Federal do Paraná, Curitiba, Brazil, [6]Plastic and Reconstructive Surgery Department, European Institute of Oncology, Milan, Italy

Background: Routine use of magnetic resonance imaging (MRI) in the staging of patients with early breast cancer is still controversial. Oncoplastic surgery (OP) allows for wider resections without compromising the aesthetic results. This study aimed to assess the impact of preoperative MRI on surgical planning and on indications of mastectomy.

Methods: Prospective study including T1-T2 breast cancer patients treated between January 2019 and December 2020 in the Breast Unit of the Hospital Nossa Senhora das Graças in Curitiba, Brazil. All patients had indication for breast conserving surgery (BCS) with OP and did a breast MRI after conventional imaging.

Results: 131 patients were selected. Indication for BCS was based on clinical examination and conventional imaging (mammography and ultrasound) findings. After undergoing breast MRI, 110 patients (84.0%) underwent BCS with OP and 21 (16.0%) had their surgical procedure changed to mastectomy. Breast MRI revealed additional findings in 52 of 131 patients (38%). Of these additional findings, 47 (90.4%) were confirmed as invasive carcinoma. Of the 21 patients who underwent mastectomies, the mean tumor size was 2.9 cm (± 1,7cm), with

all having additional findings on breast MRI (100% of the mastectomies group vs 28.2% of the OP, p<0.01). Of the 110 patients submitted to OP, the mean tumor size was 1,6cm (± 0,8cm), with only 6 (5.4%) presenting positive margins at the final pathology assessment.

Conclusion: Preoperative breast MRI has an impact on the OP scenario, bringing additional information that may help surgical planning. It allowed selecting the group with additional tumor foci or greater extension to convert to mastectomy, with a consequent low reoperation rate of 5.4% in the BCS group. This is the first study to assess the impact of breast MRI in the preoperative planning of patients undergoing OP for the treatment of breast cancer.

KEYWORDS

breast magnetic resonance imaging, oncoplastic surgery, preoperative planning, breast conservative surgery, mastectomy

Introduction

Several prospective and randomized clinical trials have demonstrated equivalence of mastectomy and breast conserving surgery (BCS) in terms of survival and local disease control for the treatment of early breast cancer (1–6). However, up to 20% of patients submitted to BCS would undergo to a second procedure due to the involvement of the margins (7). Thus, accuracy in preoperative local staging is essential for choosing the best surgical treatment for the patient. Although clinical examination, mammography and ultrasound (US) represent the triad traditionally used in the preoperative planning, they fail to assess true tumor size in approximately one-third of patients eligible for BCS (8).

Breast magnetic resonance imaging (MRI) has a high sensitivity (95-100%) in the assessment of tumor extension, multifocality and multicentricity (9–13). However, the routine use of MRI in the staging of patients with early breast cancer is still controversial, as it increases the indications for broader resections and mastectomies (14, 15). Opponents of the routine use of MRI in preoperative staging argue that many of these additional lesions might not have clinical or biological relevance, or even be treated effectively by radiotherapy (16). Regarding the reduction of reoperation rates with the preoperative use of MRI, the literature is also controversial. Some studies failed to show this association (17–19), while others showed a reduction of up to a third of reoperations (20, 21).

Oncoplastic surgery (OP) associates the principles of breast plastic surgery with oncologic surgery and represents an important advance in BCS (22, 23). It allows for wider resections, which results in a lower risk of compromising surgical margins when compared to traditional BCS techniques and improves radiotherapy planning by creating smaller breasts (24–26). However, the accuracy of the imaging methods is also essential in the oncoplastic setting for adequate surgical planning (choosing which pedicles technique and better incision). Studies published to date have not evaluated the use of preoperative MRI in conjunction with OP.

Thus, this study aimed to assess the impact of preoperative MRI on surgical planning and changes in management in patients with early breast cancer and candidates for OP.

Materials and methods

Patients

One hundred and thirty-one patients with a diagnosis of T1-T2 breast cancer were enrolled in this prospective study between January 2019 and December 2020 in the Breast Unit of the Hospital Nossa Senhora das Graças in Curitiba, Brazil. All patients had indication for BCS with OP and performed breast MRI before the surgery for the surgical planning. We excluded patients diagnosed with locally advanced or metastatic breast cancer, those who opted for mastectomy despite having an indication for BCS, patients undergoing neoadjuvant chemotherapy, those submitted to breast MRI prior to diagnosis of breast cancer, patients with previous cancer treatment in the breast or other organs, and those with contraindications or limitations for breast MRI (allergy or claustrophobia).

Breast MRI

Breast MRIs were performed on a 1.5T MRI system (Avanto®, Siemens), in a prone position using Ominiscan® contrast (Gadolineo, HE Healthcare) with a dose of 0.2ml/kg and use of an infusion pump with 3ml/s. The imaging protocol included T2-weighted (axial plane) and STIR (sagittal plane) sequences, followed by a dynamic 3D T1-weighted sequence with fat saturation (axial) and immediate reconstruction with subtraction (on pre-contrast sequence and four sequences after contrast, with a time of 90 seconds/acquisition and a total time of 7 minutes). The dynamic

sequence was followed by a high-resolution 3D acquisition with fat saturation T1-weighted (sagittal) for reconstruction. Then, all exams were sent to a workstation (Carestrean Health) were the same radiologist, dedicated exclusively to breast imaging, evaluated the morphology and dynamic behavior of the lesions, classifying them according to the BI-RADS® system.

Nonspecific lesions, considered as BI-RADS 3 were not biopsied, following the standard recommendation for this type of lesion. Lesions classified as BI-RADS 4 on MRI were submitted to direct ultrasound (second-look) and percutaneous biopsy. If there was no translation of the lesion on US, they were submitted to percutaneous vacuum biopsy (Mamotomme®) guided by MRI or preoperatively marked with technetium and 4% activated charcoal and resected during oncoplastic surgery or mastectomy. Lesions classified as BI-RADS 5 on breast MRI were biopsied preoperatively.

Pathological analysis

A pathologist with dedication exclusively to breast pathology evaluated the tumor margins in two situations: first, during the intra-operative through imprint and frozen sections and, later, by definitive examination of the paraffin-embedded material. We considered as free-negative margins the tumor distance from the margin above 1mm; narrow when bellow 1mm; positive when carcinoma *in situ* or invasive were detected under the India-painted margin. Additional lesions detected on MRI were evaluated for size and whether it was invasive, *in situ* carcinoma, or a benign lesion.

Oncoplastic surgical techniques

OP used for conservative surgery were: inferior pedicle, superior pedicle, centralectomy or round-block. Patients undergoing mastectomy were evaluated in terms of tumor size, distance from the tumor to the skin and distance from the tumor to the nipple-areolar complex to decide which type of mastectomy they would be submitted (simple mastectomy, skin-sparing mastectomy or nipple-sparing mastectomy).

Statistical analysis

Patients were classified according to the following variables: age, menopausal status, family history of breast cancer, body mass index (BMI), breast size (small breasts if bra up to 42, medium if bra between 44 and 46 and large breast if bra 48 or more), type of surgical technique performed, tumor histology, presence of angiolymphatic invasion, margins status and axillary involvement. Family history was considered positive when a first degree relative or two second-degree relatives or male relative with breast cancer were present. The following variables were considered to evaluate the results and compare them with literature: change from BCS to mastectomy; change from unilateral to bilateral mastectomy; wilder resection in conservative surgery (if difference in tumor size between MRI and mammography or ultrasound were greater than 1cm); change in the surgical approach of the contralateral breast; rate of positive margins. We also evaluated the concordance between MRI, mammography, ultrasound and anatomopathological examination in relation to tumor size (variations of up to 5mm were concordant). The analysis of the primary outcome (post-MRI surgical indication) was performed using the Mann-Whitney U test (Wilcoxon Rank Sum Test). Secondary analyzes were designed according to the type of the variable in question: categorical dependent variables were evaluated with Chi-Square Test and Fisher's Exact Test; continuous variables were evaluated with Mann-Whitney U test (Wilcoxon Rank Sum Test). A p value <0.005 was considered significant. The software used was STATA 17.1.

Results

Between January 2019 and December 2020, we included 131 patients diagnosed with T1-T2 breast cancer and with indication to BCS based on clinical examination and imaging (mammography and ultrasound) findings. After undergoing breast MRI, 110 patients (84.0%) underwent BCS with oncoplastic techniques and 21 (16.0%) had their surgical procedure changed to mastectomy. Table 1 shows the clinical features of this cohort. The median age was 55.5 years. Most of the patients were postmenopausal (64.9%) and had no family history of breast cancer (74.8%). The mean tumor size on ultrasound, mammography, MRI and anatomopathological examination was, respectively, 1.5cm, 1.4cm, 2.2cm and 1.8cm.

Breast MRI revealed additional findings in 52 of 131 patients (38%) (Figure 1). The incremental information is shown in Table 2. Summarily, breast MRI revealed 29 multifocal lesions (22.1%), 8 multicentric (6.1%), 8 contralateral (6.1%) and 13 patients whose lesions were 1cm larger on MRI when compared with US and mammography (9.9%). Of the 8 patients with multicentric lesions, four also had lesions in the contralateral breast. One patient had multifocal lesions on breast MRI and a contralateral lesion, and another patient had multifocal lesions and a difference in tumor size greater than 1cm on MRI.

Of the 52 additional findings, 47 (90.4%) were confirmed as invasive carcinoma by pathological assessment: 22 of the 29 with multicentric lesions (75.9%); 7 of 8 with multifocal lesions (87.5%); 7 of 8 with contralateral lesions (87.5%) and 11 of 13 with altered tumor size (84.6%). Regarding the contralateral lesions evidenced by MRI, there were 7 cases of invasive carcinoma and 1 case of atypical hyperplasia. Half of the patients underwent mastectomy, and the other half underwent OP.

The surgical procedure was changed to mastectomy in 21 patients (16%): 11 (52.4%) due to multifocality, 7 (33.3%) because of multicentricity, 4 (19%) due to lesions in the contralateral breast and 3 (14.3%) because tumor size was greater than 1cm on MRI in relation to US and mammography. Only in two cases (9.5%), final pathologic analysis did not confirm additional disease seen on MRI. However, these two patients had small breasts and borderline indication for BCS. Table 3 shows clinical, imaging, and pathological features of patients submitted to OP or to

10.3389/fonc.2023.1154680

TABLE 1 Clinical and pathological features of study cohort.

Characteristic	No (%)
Median age, years	55.5 ± 10.5
Menopausa status	
Premenopausal	46 (35.1)
Postmenopausal	85 (64.9)
Family history	
Positive	33 (25.2)
Negative	98 (74.8)
Histological subtype	
Invasive ductal carcnome	122 (93.1)
Invasive lobular carcinoma	9 (6.9)
Angiolymphatic invasion	
Present	31 (23.7)
Absent	100 (76.3)
Estrogen receptor	
Positive	118 (90.1)
Negative	13 (9.9)
Progesterone receptor	
Positive	110 (84)
Negative	21 (16)
HER2-neu	
Positive	10 (7.6)
Negative	120 (91.6)
Unkown	1 (0.8)
Tumor size (cm)	
Ultrasound	1.5
Mammography	1.4
Breast MRI	2.2
Pathology	1.8

mastectomy. Patients who had their surgical procedure changed to mastectomy had larger tumors on MRI (3.7cm versus 2.0cm, p=0.03) and a higher percentage of family history of breast cancer (42.9% versus 21.8%, p=0.04). All patients submitted to mastectomy had additional findings on breast MRI, unlike most OP patients (100% vs 28.2%, p<0.01). The immunohistochemical subtype did not differ between the types of surgery.

Of the 110 patients submitted to OP, 6 (5.4%) presented positive margins at the final pathology assessment. Of these, two had multifocal tumors on breast MRI, one had a contralateral tumor, and one had a tumor size greater than 1cm on MRI when compared to US and mammography. The remaining two cases did not have additional findings on MRI. One patient submitted to mastectomy had positive margins on final pathology (4.8%). This patient had multifocal lesions on breast MRI and pathological tumor size of 6,0cm.

Discussion

In this study, preoperative breast MRI did provide relevant additional information for 38% of the patients candidates for BCS with oncoplastic techniques. These additional findings led to a change from BCS to mastectomy in 16% of the cases. The final pathological analysis confirmed invasive carcinoma in 90.5% of the additional findings that led to change in surgical management. This is the first study to assess the impact of breast MRI in the preoperative planning of patients undergoing OP for the treatment of breast cancer.

The studies published to date evaluating the role of preoperative breast MRI have heterogeneous designs and conflicting results, with no consensus on the real role of breast MRI in surgical planning. Regarding the rate of additional findings revealed by breast MRI, our results are in agreement with the POMB Trial, a prospective, randomized, multicenter study, which demonstrated a 38% rate of additional findings (20). The two published metanalysis on this topic separated the rates of multifocal/multicentric lesions from the rates of contralateral lesions (13, 15). The prevalence of additional foci in the same breast ranged from 6% to 34% across studies analyzed by Houssami et al. (median of 16%) and from 6 to 71% across the studies included in Plana et al. metanalysis (mean of 20%). In our study, considering only multifocal or multicentric lesions, the additional detection rate by MRI was 28.2%. Our rate of contralateral lesions (6.1%) was like that found by Plana's metanalysis (5.5%).

Despite being an important factor, few studies have evaluated the difference in tumor size found by MRI and its impact on changing the surgical management. In our study, 9.9% (13 of 131) of the cases had lesions that were 1cm larger on MRI when compared with US and mammography, a lower rate than that found in the POMB Trial (15%) (20). Several studies draw attention to the tendency of MRI to overestimate tumor size, with overestimation rates ranging from 28% to 33% (27–29). In our study, 11 of the 13 cases (84.6%) had their tumor size confirmed by pathological analysis, indicating a high accuracy of the breast MRI. Furthermore, although 13 patients had their tumor size altered by MRI, this led to a conversion to mastectomy in only 3 cases (2.3% of the total cohort). This may be because all patients underwent OP, which allows wider resections without compromising the aesthetic and functional results of the surgery.

A major concern and discussion in literature is regarding the increase in conversion to mastectomy when breast MRI is routinely used on surgical planning. Our results showed a rate of conversion of 16%, which was similar to that found in the POMB Trial (15%) (20) and slightly higher when compared to two other studies: BREAST-MRI (8.7%) and MIPA Trial (11.3%) (21, 30). Considering wide BCS and contralateral surgeries, in addition to conversion to mastectomy, the preoperative MRI was responsible for changing the surgical approach in 31.1% of patients in BREAST-MRI. MRI correctly modified the surgical procedure in 80% of the

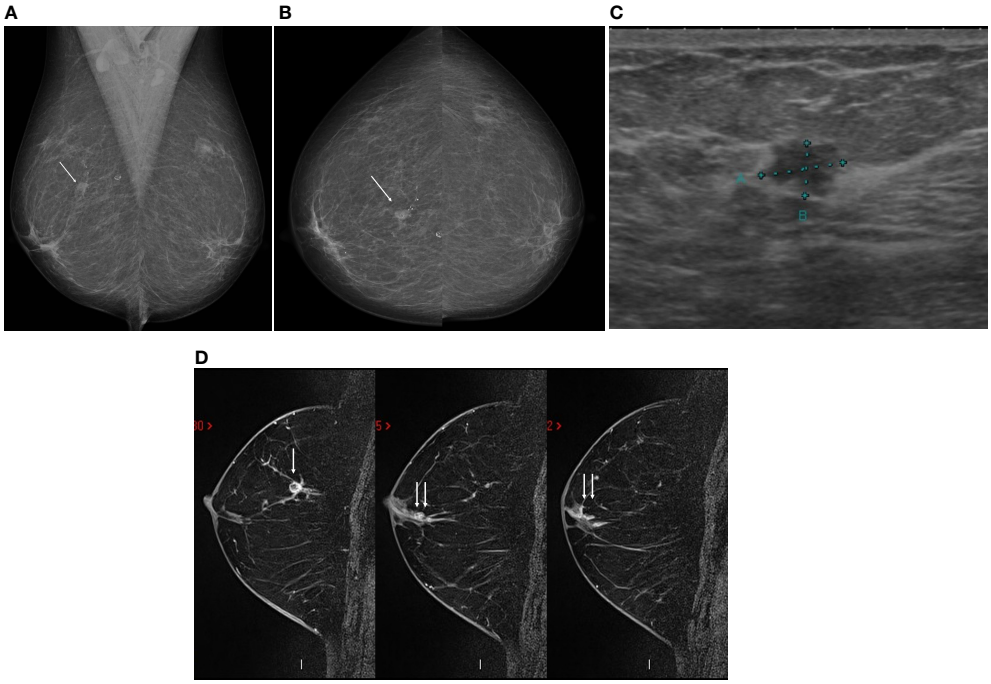


FIGURE 1
A 58-year-old asymptomatic patient underwent mammography in the mediolateral oblique **(A)** and cranio-caudal **(B)** views, which showed an irregular nodule, low density and indistinct margins in the middle third of the upper quadrants of the right breast (arrow). Ultrasound showed an irregular, hypoechoic nodule, with non-circumscribed margins, parallel to the skin, with no sound change in this topography **(C)**, with percutaneous biopsy demonstrating invasive ductal carcinoma, moderate grade, negative for estrogen and progesterone receptors (Luminal A). Magnetic resonance imaging for staging confirmed the nodule at the junction of the upper quadrants of the right breast (arrow), in addition to demonstrating non-nodular enhancement extending from the nodule to the papilla (double arrow), confirmed as ductal carcinoma *in situ* **(D)**.

cases in this trial. In our study, 90.5% of the additional findings that led to change in surgical management were confirmed by the pathological analysis. The evaluation of MRI images by the same radiologist, with years of experience in breast imaging, may be one of the explanations for the high accuracy of our results.

Interestingly, although our cohort was composed of patients undergoing oncoplastic surgery, this did not reduce the rate of conversion to mastectomy when compared to other studies in the literature. This may be explained by the fact that the decision to perform a mastectomy or BCS is multifactorial. It involves factors besides the imaging findings, such as the patient's desire, family history of breast cancer, and the relationship between tumor size and breast size.

In our study, patients had a lower reoperation rate due to positive margins (5.4%), when compared to the rates of BCS, whose values vary from 20% to 30% (7, 31, 32). This might be explained by two main factors: the use of OP and the role of MRI in preoperative planning. Several studies have already shown that OP significantly reduces the rates of positive margins and re-excisions, as it allows for larger resections with better aesthetic results (33–35). Our study was not comparative, as all patients underwent preoperative breast MRI. Therefore, we could not measure the impact of MRI in reducing reoperation rates in the scenario of OP. The trials published to date were performed with patients undergoing standard BCS and show conflicting results regarding the role of preoperative MRI in reducing reoperation rates. The POMB Trial, a randomized study, and the MIPA Trial, an observational study with 5896 patients, demonstrated a significant reduction in the reoperation rate in the group undergoing preoperative MRI (5% versus 15% and 8.5% versus 11.7%, respectively) (20, 21). Conversely, other studies have not demonstrated an impact of MRI on reoperation rates (18, 19, 30).

There are some limitations to the present study. First, the study was conducted in a single center, which limits the generalizability of the data. Second, this was a prospective observational study, with no control group. Therefore, the results found here and the real impact of preoperative MRI in the OP setting will require further studies to be confirmed. On the other hand, our study has several strengths, for example, the evaluation of all MRI images by a dedicated exclusively to breast imaging. Another strength is that this is the

TABLE 2 Breast MRI additional findigns in 131 patients.

Type of findings	n (%)
Multifocality	29 (22.1)
Muticentricity	8 (6.1)
Contralateral lesion	8 (6.1)
Altered tumor size	13 (9.9)

TABLE 3 Clinical, imaging and pathological features of patients submitted to OP or mastectomy.

Characteristic	OP (n=110)	Mastectomy (n=21)	*p*
Median age, y	56.1 ± 10.2	51.7 ± 11.7	0.07
Menopausa status			0.21
Premenopausal	36 (32.7%)	10 (47.6%)	
Postmenopausal	74 (67.3%)	11 (52.4%)	
Family history			0.04
Positive	24 (21.8%)	9 (42.9%)	
Negative	86 (78.2%)	12 (57.1%)	
Histological subtype			0.64
Invasive ductal carcinoma	103 (93.6%)	19 (90.5%)	
Invasive lobular carcinoma	7 (6.4%)	2 (9.5%)	
Tumor size (cm)			
Breast MRI	2.0 ± 1.1	3.7 ± 1.9	<0.01
Pathology	1.6 ± 0.8	2.9 ± 1.7	<0.01
Additional findings on MRI	31 (28.2%)	21 (100%)	<0.01
Multifocality	18 (16.4%)	11 (52.4%)	<0.01
Multicentricity	1 (0.9%)	7 (33.3%)	0.01
Contralateral lesion	4 (3.6%)	4 (19%)	0.02
Altered size	10 (9.1%)	3 (14.3%)	0.44
Positive margins	6 (5.4%)	1 (4.8%)	0.88
Immunohistochemical			
ER positive	101 (91.8%)	17 (80.9%)	0.18
PR positive	93 (84.5%)	17 (80.9%)	0.49
HER2 positive	8 (7.3%)	2 (9.5%)	0.63

OP, oncoplastic; y, years; MRI, magenetic resonance imaging; ER, estrogen receptor; PR, progesterone receptor.

first study to assess the impact of preoperative MRI in patients undergoing OP. After several studies have already proven that OP are not only oncologically safe, but also improves the aesthetic and functional results, these techniques have been increasingly used and are part of the day-to-day treatment of breast cancer.

In conclusion, our study demonstrated that preoperative breast MRI has a positive impact on the OP scenario, bringing additional information that may help the surgeon in the surgical planning. It allowed selecting the group with additional tumor foci or greater extension to convert to mastectomy, with a consequent low reoperation rate in the BCS group, which is important in the OP scenario.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Universidade Positivo. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

KA, CU, LU, MR and ML conceived of the original idea. KA, CU, MD, FK, IR, AC, LN, ES, CS and RD constitute the surgical team responsible for all the patients included. LU evaluated all the breast imaging exams. AS evaluated did the pathological analysis of all tumors included. JP and MD helped with the statistical analysis. MD and KA wrote the manuscript with support from CU and LU. RD, MR and ML supervised the project. All authors discussed the

results and contributed to the final manuscript. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

References

1. Blichert-Toft M, Rose C, Andersen JA, Overgaard M, Axelsson CK, Andersen KW, et al. Danish Randomized trial comparing breast conservation therapy with mastectomy: Six years of life-table analysis. *J Natl Cancer Inst Monogr* (1992) 11:19–25.

2. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* (2002) 347(16):1233–41. doi: 10.1056/NEJMoa022152

3. Jacobson JA, Danforth DN, Cowan KH, d'Angelo T, Steinberg SM, Pierce L, et al. Ten-year results of a comparison of conservation with mastectomy in the treatment of stage I and II breast cancer. *N Engl J Med* (1995) 332(14):907–11. doi: 10.1056/NEJM199504063321402

4. Poggi MM, Danforth DN, Sciuto LC, Smith SL, Steinberg SM, Liewehr DJ, et al. Eighteen-year results in the treatment of early breast carcinoma with mastectomy versus breast conservation therapy: The national cancer institute randomized trial. *Cancer* (2003) 98 (4):697–702. doi: 10.1002/cncr.11580

5. van Dongen JA, Voogd AC, Fentiman IS, Legrand C, Sylvester RJ, Tong D, et al. Long-term results of a randomized trial comparing breast conserving therapy with mastectomy: European organization for research and treatment of cancer 10801 trial. *J Natl Cancer Inst* (2000) 92(14):1143–50. doi: 10.1093/jnci/92.14.1143

6. Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, et al. Twenty-year follow-up of a randomized study comparing breast conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med* (2002) 347(16):1227–32. doi: 10.1056/NEJMoa020989

7. Jeevan R, Cromwell DA, Trivella M, Lawrence G, Kearins O, Pereira J, et al. Reoperation rates after breast conserving surgery for breast cancer among women in England: retrospective study of hospital episode statistics. *BJM* (2012) 345:e4505. doi: 10.1136/bmj.e4505

8. Faverly DR, Hendriks JH, Holland R. Breast carcinomas of limited extent: frequency, radiologic-pathologic characteristics, and surgical margin requirements. *Cancer* (2001) 91:647–59. doi: 10.1002/1097-0142(20010215)91:4<647::AID-CNCR1053>3.0.CO;2-Z

9. Warner E, Messersmith H, Causer P, Eisen A, Shumak R, Plewes D. Systematic review: using magnetic resonance imaging to screen women at high risk for breast cancer. *Ann Intern Med* (2008) 148(9):671–9. doi: 10.7326/0003-4819-148-9-200805060-00007

10. Sardanelli F, Giuseppetti GM, Panizza P, Bazzocchi M, Fausto A, Simonetti G, et al. Sensitivity of MRI versus mammography for detecting foci of multifocal, multicentric breast cancer in fatty and dense breasts using the whole-breast pathologic examination as a gold standard. *AJR Am J Roentgenol* (2004) 183 (4):1149–57. doi: 10.2214/ajr.183.4.1831149

11. Gurdal SO, Ozcinar B, Kayahan M, Igci A, Tunaci M, Ozmen V, et al. The incremental value of magnetic resonance imaging for breast surgery planning. *Surg Today* (2013) 43(1):55–61. doi: 10.1007/s00595-012-0137-5

12. Kuhl C, Weigel S, Schrading S, Arand B, Bieling H, König R, et al. Prospective multicenter cohort study to refine management recommendations for women at elevated familial risk of breast cancer: the EVA trial. *J Clin Oncol* (2010) 28(9):1450–7. doi: 10.1200/JCO.2009.23.0839

13. Houssami N, Ciatto S, Macaskill P, Lord SJ, Warren RM, Dixon JM, et al. Accuracy and surgical impact of magnetic resonance imaging in breast cancer staging: systematic review and meta-analysis in detection of multifocal and multicentric cancer. *J Clin Oncol* (2008) 26(19):3248–58. doi: 10.1200/JCO.2007.15.2108

14. Houssami N, Turner RM, Morrow M. Meta-analysis of pre-operative magnetic resonance imaging (MRI) and surgical treatment for breast cancer. *Breast Cancer Res Treat* (2017) 165(2):272–83. doi: 10.1007/s10549-017-4324-3

15. Plana MN, Carreira C, Muriel A, Chiva M, Abraira V, Emparanza JI, et al. Magnetic resonance imaging in the preoperative assessment of patients with primary breast cancer: systematic review of diagnostic accuracy and meta-analysis. *Eur Radiol* (2012) 22(1):26–38. doi: 10.1007/s00330-011-2238-8

16. Morrow M. Magnetic resonance imaging for screening, diagnosis and eligibility for breast-conserving surgery: promises and pitfalls. *Surg Oncol Clin N Am* (2010) 19 (3):475–92. doi: 10.1016/j.soc.2010.03.003

17. Bleicher RJ, Ciocca RM, Egleston BL, Sesa L, Evers K, Sigurdson ER, et al. Association of routine pretreatment magnetic resonance imaging with time to surgery, mastectomy rate, and margin status. *J Am Coll Surg* (2009) 209(2):180–7. doi: 10.1016/j.jamcollsurg.2009.04.010

18. Turnbull L, Brown S, Harvey I, Olivier C, Drew P, Napp V, et al. Comparative effectiveness of MRI in breast cancer (COMICE) trial: a randomized controlled trial. *Lancet* (2010) 375(9714):563–71. doi: 10.1016/S0140-6736(09)62070-5

19. Peters NHGM, van Esser S, van den Bosch MAAJ, Storm RK, Plaisier PW, van Dalen T, et al. Preoperative MRI and surgical management in patients with nonpalpable breast cancer: The MONET – randomized controlled trial. *Eur J Cancer* (2011) 47(6):879–86. doi: 10.1016/j.ejca.2010.11.035

20. Gonzalez V, Sandelin K, Karlsson A, Åberg W, Löfgren L, Iliescu G, et al. Preoperative MRI of the breast (POMB) influences primary treatment in breast cancer: a prospective, randomized, multicenter study. *World J Surg* (2014) 38(7):1685–93. doi: 10.1007/s00268-014-2605-0

21. Sardanelli F, Trimboli RA, Houssami N, Gilbert FJ, Helbich TH, Álvarez Benito M, et al. Magnetic resonance imaging before breast cancer surgery: results of an observational multicenter international prospective analysis (MIPA). *Eur Radiol* (2022) 32(3):1611–23. doi: 10.1007/s00330-021-08240-x

22. Urban C, Lima R, Schunemann E, Spautz C, Rabinovich I, Anselmi K. Oncoplastic principles in breast conserving surgery. *Breast* (2011) 20(Suppl 3):S92–5. doi: 10.1016/S0960-9776(11)70302-2

23. Urban CA, Anselmi K, Kuroda F, Schwartz JC. Oncoplasty as the standard of care in breast cancer surgery. *Eur Oncol Haematol* (2014) 10(1):43–7. doi: 10.17925/EOH.2014.10.1.43

24. Clough KB, Lewis JS, Couturaud B, Fitoussi A, Nos C, Falcou MC. Oncoplastic techniques allow extensive resections for breast conserving therapy of breast carcinomas. *Ann Surg* (2003) 237(1):26–34. doi: 10.1097/00000658-200301000-00005

25. Kaur N, Petit JY, Rietjens M, Maffini F, Luini A, Gatti G, et al. Comparative study of surgical margins of oncoplastic surgery and quadrantectomy in breast cancer. *Ann Surg Oncol* (2005) 12(7):539–45. doi: 10.1245/ASO.2005.12.046

26. Paulinelli RR, Oliveira VM, Bagnoli F, Chade MC, Alves KL, Freitas-Junior R. Oncoplastic mammaplasty with geometric compensation – a technique for breast conservation. *J Surg Oncol* (2014) 110(8):912–8. doi: 10.1002/jso.23751

27. Grimsby GM, Gray R, Dueck A, Barros N, Baracat CE, Filassi JR, et al. Is there concordance of invasive breast cancer pathologic tumor size with magnetic resonance imaging? *Am J Surg* (2009) 198(4):500–4. doi: 10.1016/j.amjsurg.2009.07.012

28. Guadalupe LP, Jesús J, Xiong Y, Rosa M. Tumor size and focality in breast carcinoma: Analysis of concordance between radiological imaging modalities and pathological examination at a cancer center. *Ann Diagn Pathol* (2020) 48:151601. doi: 10.1016/j.anndiagpath.2020.151601

29. Onesti JK, Mangus BE, Hlemer SD, Osland JS. Breast cancer tumor size: correlation between magnetic resonance imaging and pathology measurements. *Am J Surg* (2008) 196(6):844–48. doi: 10.1016/j.amjsurg.2008.07.028

30. Mota BS, Reis YN, Dória MT, Osland JS. Brazilian Randomized study: Impact of preoperative resonance in the evaluation for breast cancer conservative surgery (BREAST-MRI trial). *Ann Oncol* (2019) 30(Suppl 3):III39–40. doi: 10.1093/annonc/mdz098.002

31. van Leeuwen MT, Flaster MO, Vajdic CM, Crowe PJ, Lujic S, Klaes E, et al. Reoperation after breast-conserving surgery for cancer in Australia: statewide cohort study of linked hospital data. *BMJ Open* (2018) 8(4):e020858. doi: 10.1136/bmjopen-2017-020858

32. Mohamedahmed AYY, Zaman S, Srinivasan A, Peterknecht E, Saeed Mohammed S S. Do we need to routinely perform cavity shaving with breast-conserving surgery for breast cancer? a systematic review and meta-analysis. *Surg Oncol* (2021) 36:7–14. doi: 10.1016/j.suronc.2020.11.003

33. Benjamin MA, Sinnott C, Bawa S, Kaufman DI, Guarino K, Addona R. Re-excision rate after partial mastectomy in oncoplastic breast-conserving surgery. a single-institutional experience and review of the literature. *Ann Plast Surg* (2019) 82: S170–2. doi: 10.1097/SAP.0000000000001874

34. de la Cruz L, Blankenship AS, Chatterjee A, Geha R, Nocera N, Czerniecki BJ, et al. Outcomes after oncoplastic breast-conserving surgery in breast cancer: A systematic literature review. *Ann Surg Oncol* (2016) 23:3247–58. doi: 10.1245/s10434-016-5313-1

35. Crown A, Wechter DG, Grumley JW. Oncoplastic breast-conserving surgery reduces mastectomy and postoperative re-excision rates. *Ann Surg Oncol* (2015) 22:3363–68. doi: 10.1245/s10434-015-4738-2

frontiers | Frontiers in Oncology

TYPE Original Research
PUBLISHED 14 April 2023
DOI 10.3389/fonc.2023.1131951

OPEN ACCESS

EDITED BY
Cicero Urban,
Universidade Positivo, Brazil

REVIEWED BY
Ruth Exner,
Medical University of Vienna, Austria
Jiuzuo Huang,
Peking Union Medical College Hospital (CAMS), China

*CORRESPONDENCE
Chaitanyanand Koppiker
dr.koppiker@prashanticancercare.org

†These authors have contributed equally to this work

SPECIALTY SECTION
This article was submitted to Surgical Oncology, a section of the journal Frontiers in Oncology

RECEIVED 26 December 2022
ACCEPTED 06 March 2023
PUBLISHED 14 April 2023

CITATION
Koppiker C, Joshi S, Mishra R, Kelkar DA, Chigurupati P, Joshi A, John J, Kadu S, Bagdia A, Thakkar D, Deshmukh C, Allampati H, Sharan G, Dhar U, Nare S, Nagarkar S, Busheri L, Varghese B and Pai M (2023) Therapeutic mammoplasty: a "wise" oncoplastic choice—lessons from the largest single-center cohort from Asia. *Front. Oncol.* 13:1131951. doi: 10.3389/fonc.2023.1131951

Therapeutic mammoplasty: a "wise" oncoplastic choice—lessons from the largest single-center cohort from Asia

Chaitanyanand Koppiker[1,2,3,4]*, Sneha Joshi[2†], Rupa Mishra[2†], Devaki A. Kelkar[2†], Pragnya Chigurupati[3], Anjali Joshi[2], Jisha John[2], Shweta Kadu[2], Amitkumar Bagdia[3], Deepti Thakkar[3], Chetan Deshmukh[1], Harikiran Allampati[5], Gautam Sharan[6], Upendra Dhar[1,4], Smeeta Nare[1,2], Sanket Nagarkar[2], Laleh Busheri[1], Beenu Varghese[1] and Mugdha Pai[1,2]

[1]Orchids Breast Health Centre, Prashanti Cancer Care Mission, Pune, India, [2]Centre for Translational Cancer Research: A Joint Initiative of Indian Institute of Science Education and Research (IISER), Pune and Prashanti Cancer Care Mission (PCCM), Pune, India, [3]International School of Oncoplastic Surgery, Pune, India, [4]Jehangir Hospital, Pune, India, [5]Ruby Hall Clinic, Pune, India, [6]Department of Radiation Oncology, Inlaks and Budhrani Hospital, Pune, India

Introduction: The majority of breast cancer patients from India usually present with advanced disease, limiting the scope of breast conservation surgery. Therapeutic mammoplasty (TM), an oncoplastic technique that permits larger excisions, is quite promising in such a scenario and well suited to breast cancer in medium-to-large-sized breasts with ptosis and in some cases of large or multifocal/multicentric tumors. Here, we describe our TM cohort of 205 (194 malignant and 11 benign) patients from 2012 to 2019 treated at a single surgeon center in India, the largest Asian dataset for TM.

Methods: All patients underwent treatment after careful discussions by a multidisciplinary tumor board and patient counseling. We report the clinicopathological profiles and surgical, oncological, cosmetic, and patient-related outcomes with different TM procedures.

Results: The median age of breast cancer patients was 49 years; that of benign disease patients was 41 years. The breast cancer cohort underwent simple (n = 84), complex (n = 71), or extreme (n = 44) TM surgeries. All resection margins were analyzed through intra-operative frozen-section assessment with stringent rad-path analysis protocols. The margin positivity rate was found to be 1.4%. A majority of the cohort was observed to have pT1–pT2 tumors, and the median resection volume was 180 cc. Low post-operative complication rates and good-to-excellent cosmetic scores were observed. The median follow-up was 39 months. We observed 2.07% local and 5.7% distal recurrences, and disease-specific mortality was 3.1%. At median follow-up, the overall survival was observed to be 95.9%, and disease-free survival was found to be 92.2%. The patient-reported outcome measures (PROMs) showed good-to-excellent scores for all types of TMs across BREAST-Q domains.

Conclusion: We conclude that in India, a country where women present with large and locally advanced tumors, TM safely expands the indications for breast conservation surgery. Our results show oncological and cosmetic outcomes at acceptable levels. Most importantly, PROM scores suggest improved overall wellbeing and better satisfaction with the quality of life. For patients with macromastia, this technique not only focuses on cancer but also improves self-image and reduces associated physical discomfort often overlooked by women in the Indian setting. The popularization of this procedure will enable Indian patients with breast cancer to receive the benefits of breast conservation.

KEYWORDS

therapeutic mammaplasty (TM), largest cohort from Asia, quality of life, PROMS (patient reported outcome measures), oncoplasty, breast cancer

1 Introduction

Therapeutic mammoplasty (TM), an oncoplastic technique, combines oncological safety, breast reduction, and mastopexy techniques enabling breast conservation for select breast tumors in moderate-to-large breasts. In the last three decades, breast conservation therapy (BCT), which involves breast conservation surgery (BCS) followed by radiation therapy (RT), has gained acceptance as a standard of care for breast cancer (1, 2). Several large cohort studies have shown equivalent survival rates between BCT and mastectomy with long-term follow-up (3, 4). Recent studies have also suggested better disease-free and overall survival with improvement in quality of life (QoL) in patients undergoing BCT as compared with mastectomy (5–8).

However, in cases where large excisions of the breast tissue were required, unsatisfactory cosmetic outcomes, like BCT site defects, bird-beak deformity (9), or asymmetry in breasts or nipples post-BCT, have been observed (10), thus limiting the application of conventional BCT. In addition, BCT has limited applications in patients with multifocal or multicentric (MF/MC) disease and in cases of extensive microcalcifications. Though conventionally MF/MC cancers have been labeled as a contraindication for BCS, with modern extreme oncoplasty, they can be accommodated under the TM fold (11–15).

The concept of oncoplastic breast surgery (OBS) was first introduced in the 1990s by Prof. Audretsch when he described the technique of partial reconstruction of the breast using plastic surgical (15–17). OBS is now increasingly being accepted as the standard of care in the surgical management of breast cancer cases across the world due to benefits such as oncological safety with concurrent improvement in aesthetic results and QoL (5, 8, 18).

OBS procedures involving partial breast reconstruction are classified as volume replacement or displacement techniques (9, 19). TM is a commonly used volume displacement technique suitable for OBS in women with medium-to-extra-large breasts with ptosis. TM combines the advantages of an oncologically safe wide excision of the tumor with breast reduction, mastopexy, and contralateral symmetrization techniques (20–22). In addition, TM has been shown to achieve satisfactory outcomes by reducing breast size, thereby facilitating better delivery and distribution of RT regimens, achieving contralateral breast symmetry, and improving the QoL (23). TM is reported to have recurrence rates of between 0% and 9% and shows oncological outcomes comparable to those of BCS (24–26). Furthermore, TM offers an option for BCS in women who present with locally advanced breast cancer (LABC) (Stage IIB or greater) (27) or large operable breast cancer (LOBC) (>5 cm), MF/MC, or extensive microcalcifications wherein a mastectomy would be the surgical procedure of choice (20, 22). However, even though its use has been indicated for smaller ptotic breasts in selective cases, TM may not be effective due to the paucity of breast tissue (28). Recently, data from the national iBRA-2 and TeaM studies were combined to compare the safety and short-term outcomes of TM and mastectomy with or without immediate breast reconstruction (IBR). These data indicated that BCS was possible in 87% of TM cases without delay in adjuvant treatment, indicating that TM may allow high-risk patients who are not candidates for IBR to avoid mastectomy safely (22, 29). However, the need of the hour is large, randomized trials assessing the benefit of oncoplastic techniques with long-term follow-up.

Abbreviations: ACT, adjuvant chemotherapy; BCS, breast conservation surgery; BCT, breast conservation therapy; CQ, central quadrant; DCIS, ductal carcinoma *in situ*; DFS, disease-free survival; EO, extreme oncoplasty; FNAC, fine-needle aspiration cytology; IBR, immediate breast reconstruction; IDC, invasive ductal carcinoma; IMF, inframammary fold; LABC, locally advanced breast cancer; LIQ, lower inner quadrant; LOBC, large operable breast cancer; LOQ, lower outer quadrant; LQ, lower quadrant; MDT, multidisciplinary team; MF/MC, multifocal and/or multicentric; NAC, nipple–areolar complex; NACT, neoadjuvant chemotherapy; OBS, oncoplastic breast surgery; OS, overall survival; PET, positron emission tomography; PROMs, patient-reported outcome measures; QoL, quality of life; RT, radiation therapy; SIB, simultaneous integrated boost; SLNB, sentinel lymph node biopsy; TM, therapeutic mammoplasty; UIQ, upper inner quadrant; UOQ, upper outer quadrant; UQ, upper quadrant; USG, ultrasonography.

The majority of Indian breast cancer patients present with large tumors in advanced stages (30). This limits the scope of upfront BCS with or without OBS unless the patient has a favorable breast-to-tumor ratio. In such patients with large tumors but an unfavorable breast-to-tumor ratio, OBS with the TM procedure has been shown to effectively extend the boundaries of surgical excisions (31). However, the field of OBS is still nascent in India and is practiced only by a handful of breast surgeons in metropolitan cities.

With this background, we undertook the current study to investigate and analyze the outcomes of TM with a focus on oncological safety and efficacy. From our single-institutional TM cohort, we present data on 205 patients with breast disease who underwent 222 TM surgeries after analysis of the feasibility and safety of the procedure, careful counseling, and multidisciplinary team (MDT) discussion.

Based on the guidelines of the TeaM Study protocol, we report the clinicopathological profiles and oncological outcomes of our cohort and experiences related to various TM surgical techniques. In addition to being the largest single institutional study from Asia, a major asset of the study is the patient-reported outcome measures (PROMs) as well as cosmetic outcomes for a large portion of the cohort. This study also aims to provide recommendations and suggestions for breast oncosurgeons to easily adapt TM in their regular clinical practice for breast cancer management.

2 Methods

2.1 Patient selection

At our institution, detailed pre-op counseling is performed by the surgeon to discuss the various treatment and surgical options in a shared decision-making process. Patients presenting with breast disease who had moderate-to-extra-large breasts with ptosis were counseled for TM.

2.2 Clinical management

Triple assessment based on clinical examination, appropriate imaging, and image-guided core needle biopsy was routinely used to establish a diagnosis. Confirmed breast cancer cases underwent a breast surgery at a network hospital site. After clinical staging, patients were selected for neoadjuvant chemotherapy/neoadjuvant hormonal therapy (NACT/NAHT) and adjuvant treatment based on decisions made at MDT, in accordance with the unit's protocol and suggested global treatment guidelines.

2.3 Surgical procedures

In our practice, we classify TM techniques into four categories according to the indications described in Table 1 (9, 11, 19).

2.3.1 Pre-operative markings

In the pre-operative planning, appropriate markings are made on both breasts based on a Wise pattern or vertical scar incision. The nipple–areolar complex (NAC) is re-positioned between 19 and 23 cm from the sternal notch, which is often determined by placing the fingers at the inframammary fold (IMF) and projecting on the anterior surface of the breast into the meridian.

2.3.2 Tumor localization

Clinically palpable lesions are localized in the usual fashion intraoperatively. For impalpable lesions, tumor localization is performed pre-operatively by stereotactic guide-wire placement using mammography or high-resolution ultrasonography. For sono-localizable lesions, intra-op ultrasonography (USG) might be used. Post-NACT impalpable tumors may be localized with the help of marker clips placed pre/mid chemotherapy (Koppiker et al. unpublished observations).

TABLE 1 Classification of TM techniques.

Type	Description	References
Simple	For tumors within the reduction pattern (i.e., at 6 o'clock) The nipple is placed on the superior, supero-medial, and inferior pedicles, which are commonly used pedicles	(Savalia and Silverstein 2016) (28)
Complex	For tumors outside the pattern of reduction (i.e., between 12–3 o'clock position (left breast) and 12–9 o'clock (right breast) Dual pedicle technique is applied in which extended and/or secondary pedicles (inferior, infero-lateral, or infero-medial) act as fillers, which enhance vascularity as an added advantage* *Extended or secondary pedicles are the other parts of the breast that are generally excised, which are used to fill the defects. The latter are preferred, as they have better blood supply reaching the most distant areas of the pedicle as compared to extended ones	(Savalia and Silverstein 2016) (28)
Extreme	Include large multicentric, multifocal tumors, extensive DCIS, and poor response to NACT requiring large areas of resection (>5 cm), in which mastectomy would be the surgical procedure of choice	(Silverstein et al., 2015, Silverstein et al., 2016, Koppiker et al., 2019) (31–33)
Split reduction	For tumors that lie outside the reduction pattern wherein the skin needs to be resected due to involvement or close proximity with tumor The lower limb of the Wise pattern is shifted over the tumor site. Then, the outer limb of the Wise pattern is shifted upward to lie over the tumor so that there is no incision in the IMF on the outer side In contrast to those of the other techniques, the incisions on the IMF and the horizontal limb on the side of the skin excision are omitted to preserve the vascularity and restructure the breast	(Silverstein et al., 2015) (12)

TM, therapeutic mammoplasty; DCIS, ductal carcinoma in situ; NACT, neoadjuvant chemotherapy; IMF, inframammary fold.

2.3.3 Incision, tumor excision, and oncological clearance

The surgery begins by marking out the Wise pattern incision (Figure 1A). The Wise pattern is located to excise the localized tumor with wide margins. The area of the appropriate pedicle that will carry the nipple is marked and de-epithelized. The tumor is then excised with wide margins through one of the limbs of the Wise pattern. If required, further imaging of the specimen is performed using specimen mammography to ensure that the tumor is excised with wide margins. The shaved margins of the cavity are further excised and sent for frozen-section evaluation to ensure margin negativity and perform any cavity margin re-excision if needed. Once negative tumor margins of the excision cavity are achieved, the decision is made to use one of the appropriate pedicles.

2.3.4 NAC positioning

The NAC is marked out, and an incision is carefully made around the areola. The tumor and its quadrant are then widely excised through one of the limbs of a Wise pattern incision (based on the type of TM technique decided).

2.3.5 Marking out the tumor bed for targeting radiotherapy

The tumor bed is marked with Liga clips in the superior, inferior, medial, lateral, basal, and anterior margins. In our experience, the tumor margins remain contained within the initial tumor volume for targeted radiotherapy. The possibility of the tumor margin getting repositioned in some other quadrant is less likely (34, 35).

2.3.6 Choice of pedicles for various TM techniques

The appropriate pedicles are marked out and dissected according to the location of the tumor. According to quadrant diagrams (Figures 1B–E), if the tumor is at the 12 o'clock position in the upper outer quadrant (UOQ), an extended inferior pedicle is used. If a tumor is present in the outer quadrants (i.e., at the 2, 3, or 4 o'clock position of the left breast or the 8, 9, or 10 o'clock positions of the right breast), the dual pedicle technique is preferentially used. In this technique, the inferior pedicle fills up the gap, and the NAC is positioned on a superior, superomedial, or lateral pedicle. The main aim of the dual pedicle technique is to contour the defect with one pedicle and position the NAC on the other, thereby providing a dual vascular supply.

We also discuss representative cases from each type of surgery. Simple TM typically utilizes a single pedicle and is represented in Case 1. An extended inferior pedicle or a dual pedicle provides optimal outcomes in complex TM procedures (Cases 2 and 3). Extreme or split reduction TM is a suitable option for cases with large excisions that are otherwise indicated for mastectomy (Case Study 4).

2.3.7 Axillary management

Once these Wise pattern incisions are carried out through to the chest wall, the lateral dissection is taken into the axilla for axillary management through one of the limbs of the same incision (sentinel lymph node biopsy/axillary lymph node dissection (SLNB/ALND), as appropriate). No separate incision is taken on the axilla. Care is taken to dissect the lateral thoracic artery and to ensure that the lateral pillar is well-perfused by various perforators. Thereafter, the incisions are closed. Drains are not inserted in the axilla unless an axillary clearance has been performed.

2.4 Post-surgery protocols

2.4.1 Assessment of post-surgery complications

Post-surgery outcomes were assessed by breast oncoplastic surgeons and radiation oncologists. As per the Clavien–Dindo classification, post-surgery complications were classified as "major" when they required surgical intervention and "minor"

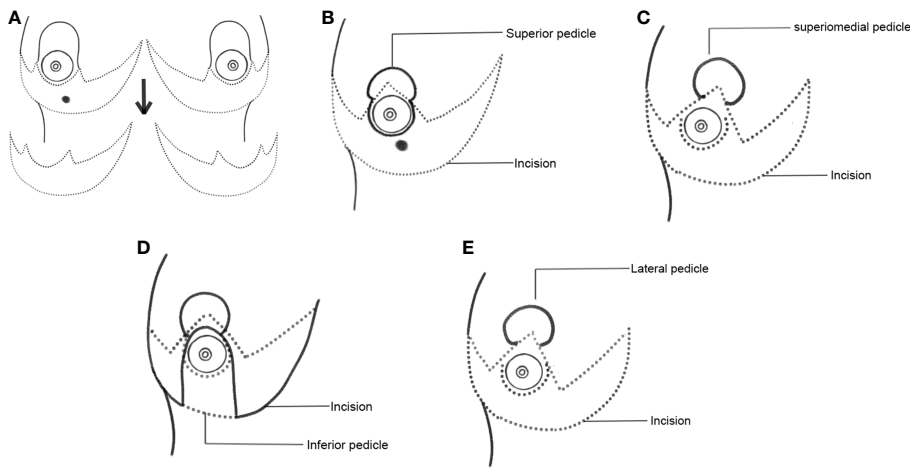


FIGURE 1
Schematic representation of Wise pattern incision and various choices of pedicles. **(A)** Wise pattern incision. **(B)** Superior pedicle. **(C)** Superior-medial pedicle. **(D)** Inferior pedicle. **(E)** Lateral pedicle.

when they were managed conservatively (36). We also noted the time between the completion of surgery and the start of adjuvant therapy to ascertain any delays in adjuvant therapy.

2.4.2 RT methodology

The RT dose planning was aimed at achieving a biologically effective dose (BED) of 40 Gy in 15 cycles (with an optional boost to the tumor bed, if indicated). The breast along with the supraclavicular region (if indicated) was irradiated by 6-MV photon beams using forward plan field-in-field intensity-modulated radiation therapy (F-P FiF IMRT) or volumetric modulated arc therapy (VMAT). Vac-Lok immobilization and CT-based contouring and planning were performed after target delineation after Eclipse™ treatment planning system (TPS) (Version 13.5.35) for F-P FiF IMRT plans and Monaco (Version 5.11) TPS for VMAT plans. Tangential fields with sub-fields were used for radiotherapy planning. Linac, Elekta Medical System™ (Crawley, UK) with 80-leaf multileaf collimator (MLCi) was used. RT plan was accepted if at least 95% of the prescribed dose covers 100% of the planning target volume (PTV). Hot spot in PTV was accepted up to 110% of the prescribed dose. Tumor bed boost, wherever indicated, was performed using either an electron portal or simultaneous integrated boost (SIB) technique with standard dose fractionation schedules.

2.4.3 Patient-reported outcome measures

PROMs were used to evaluate patient satisfaction and QoL after TM procedures. To assess PROMs, the standardized BREAST-Q questionnaire was utilized. Higher scores indicate greater patient satisfaction and functionality (37).

2.5 Data collection

2.5.1 Patient

Data collection was performed according to the recommendations of the TeaM study protocol. Data included demography, medical history, clinical findings, pathological reports (diagnostic biopsy and surgical histopathology including immunohistochemistry), details on neoadjuvant therapy, surgical intervention, pre- and post-operative images of patients, post-surgery complications, follow-up details, and PROMs. Clinical response (clinically complete response (cCR), clinically partial response (cPR), clinically stable disease (cSD), and clinically progressive disease (cPD)) and pathological complete response (pCR) to NACT of the primary tumor were calculated as per Response Evaluation Criteria in Solid Tumors (RECIST) criteria (V1.1) (38).

2.6 Survival analysis and statistics

Data were collected retrospectively from patient records. Follow-up information was taken as recorded in the patient file. The date of recurrence was taken from one of the biopsy pathologies, fine-needle aspiration cytology (FNAC), or PET reports. Overall survival was calculated as all-cause since in many cases it was difficult to ascertain if death was due to disease or other unrelated causes. The overall survival interval was taken as the time period between surgery and death. The exact date of death used in the analysis was in most cases taken as the closest approximation to the date of death as informed by relatives of the patient (especially for deaths that occurred in 2020–2021). Due to the COVID-19 pandemic, follow-up was very sparse starting from early 2020 until early 2022. This could be the cause for patients lost to follow-up since traveling was prohibited or much more challenging for a large part of this time period.

Median follow-up was calculated using the reverse Kaplan–Meir (KM) method of Schemper and Smith (39) in R. Survival analysis was performed in R Version 4.2 using the survivor and survminer packages (36, 40). Kaplan–Meir plots were plotted using ggpubr. Percent disease-free and percent overall survival were derived from the survival table when the time was the closest median follow-up.

3 Results

3.1 Overview of TM study cohort: characteristics of study cohort

The demographic distribution of study participants and their clinicopathological characteristics are summarized in Figure 2A and Tables 2–5. At our center, a total of 222 TM procedures were performed on 205 patients with moderate and large breasts with various grades of ptosis during 2012–2019. Among the 205 patients, 178 were unilateral breast cancer patients, 10 patients were identified with unilateral benign disease and 17 had bilateral breast disease. Among the 17 bilateral cases, eight were bilateral breast cancer cases, eight patients presented with one side benign and one side malignant, and one patient presented with bilateral benign disease. The median age at diagnosis of patients with breast cancer was 49 (29–75) years, while patients with benign breast disease had a median age of 41 (28–60) years at diagnosis. As observed in previous reports (40), a proportion of the breast cancer patients (i.e., 77/194, 40%) had comorbidities such as diabetes, making them poor candidates for a mastectomy with immediate reconstruction.

Among 194 breast cancer patients (quadrant-wise tumor location is represented in Figure 2B), 64.4% of tumors were observed in the upper quadrant. Of 222 TM procedures (breast cancer and benign cohort together), simple TM accounted for 92 (eight benign) surgeries, while 77 (six benign) complex and 49 (five benign) extreme surgeries were performed. Subtype distribution for the different surgeries among breast cancer patients is shown in Figure 2C. The median pathological tumor size was 25 mm (range 2–85 mm), and the median resection volume was 180 cc. Of our 194 breast cancer patients, 56 patients received NACT, 141 ACT, and 183 RT.

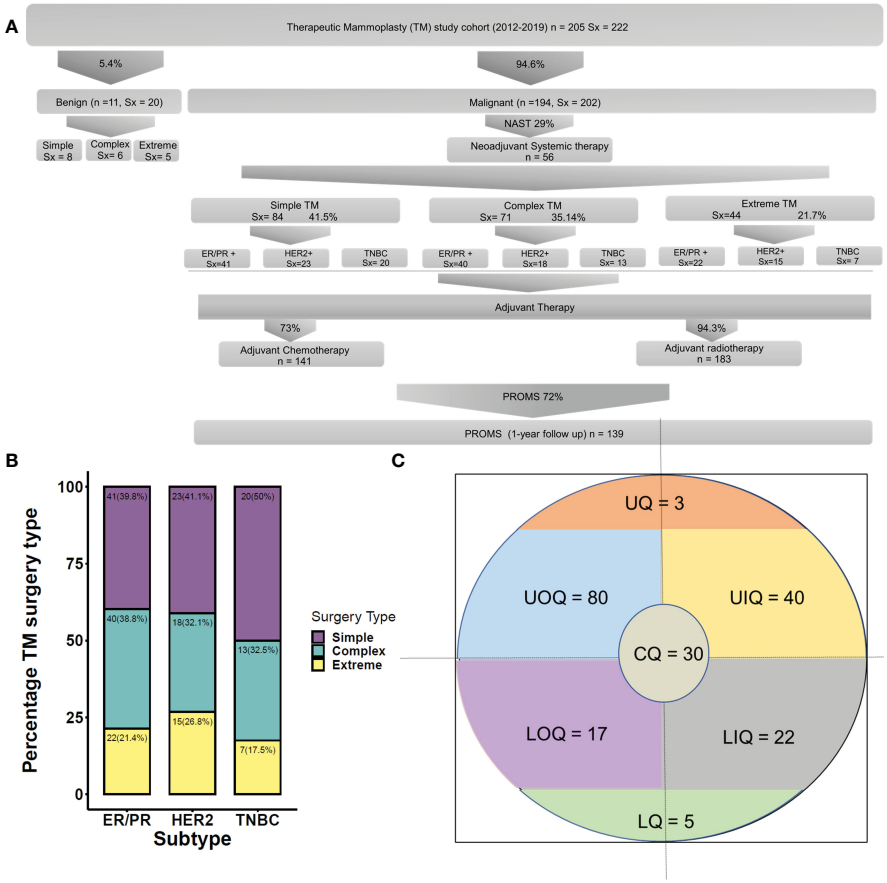


FIGURE 2
(A) Clinicopathological features of the cohort. **(B)** Quadrant-wise tumor location. CQ, central quadrant; LQ, lower quadrant; LIQ, lower inner quadrant; LOQ, lower outer quadrant; UIQ, upper inner quadrant; UOQ, upper outer quadrant; UQ, upper quadrant. **(C)** Molecular subtype-wise distribution of various TM techniques. TM, therapeutic mammoplasty.

3.2 Neoadjuvant chemotherapy (NACT/NAHT)

Among the 56 patients who received NACT, pCR was observed in 28.6% (16/56) patients. The distribution of response to NACT is given in Table 2. Our extreme oncoplasty cohort comprised 44 breast cancer patients of whom 18 received NACT and 4/18 showed pCR to NACT.

3.3 Surgical outcomes

3.3.1 Surgical margins and nodal clearance

The Wise pattern technique was used in 90.1% (181/202) of therapeutic procedures for breast cancer. Clear margins were achieved in all the cancer patients with only three of 194 (1.4%) cases having positive margins. Re-excision of margins was carried out in one patient, one patient underwent an immediate complete mastectomy, and one received an additional boost to the tumor bed. Sentinel node biopsy was performed in 121 (60.2%) and axillary lymph node dissection in 83 (41.3%) of the 202 malignant surgeries.

3.3.2 Post-operative complications

Post-operative complications were classified based on grades as per the Clavien–Dindo classification adapted for breast cancer (36). A total of 27/194 (14%) cases of complications were observed, similar to observations reported in earlier literature (2) (Figures 3A, B and Table 6). All complications were treated conservatively in the outpatient setting. In general, we observe immediately post-surgery a low rate of Grade I/II complications even with complex and extreme mammoplasty techniques.

3.4 Adjuvant radiotherapy

Of the 194 breast cancer patients included in our study cohort, 183 patients underwent RT as clinically indicated. Among those who did not receive RT, 11 patients did not comply with the RT treatment protocol. Among those who received RT, 46 did not have any adverse reactions to the RT, 113 developed Grade I–II reactions, while only five patients developed Grade III reactions. For 19 patients, post-RT complications were not reported in our data sources. The RT regimen for various types of TM procedures was thus considered effectively safe.

10.3389/fonc.2023.1131951

TABLE 2 Demographic distribution of breast cancer patients.

Feature	Class	N (194)
Age (years)	Median (range)	49 (29, 75)
	<40	45
	41–60	117
	>60	31
Comorbidities	Yes	77
	No	115
	NA	2
Size of breast	S	0
	M	75
	L	104
	XL	9
	NA	6
Ptosis	I	19
	II	69
	III	98
	No	3
	NA	5
Molecular subtype	ER/PR	99
	HER2	55
	TNBC	40
NACT response		N = 56
Clinical	cCR	6
Clinical	cPR	37
Clinical	cSD	3
Clinical	cPD	4
	NA	6
Pathological	pCR	16

ER, estrogen receptor; PR, progesterone receptor; TNBC, triple-negative breast cancer; NACT, neoadjuvant chemotherapy; cCR, clinically complete response; cPR, clinically partial response; cSD, clinically stable disease; cPD, clinically progressive disease; pCR, pathological complete response. NA, Not Available.

3.5 Survival outcomes

The median follow-up was 39 months. We observed four local (2.07%) and 11 distant recurrences (5.7%), with overall recurrence at 7%, over the complete follow-up available at the time of this report. Overall mortality was 3.6% (7/194), while disease-specific mortality was only 3.1% (6/194). At the median follow-up, the overall survival probability was found to be 95.9%, with all reported deaths occurring before the median follow-up. In addition, the disease-free survival probability at median follow-up was 92.2%. KM plots of overall survival and disease-free survival are shown in Figures 4A, B.

TABLE 3 Clinical features of surgeries for breast cancer.

Feature	Class	Surgeries (202)
Clinical tumor size (cT)	cT1	68
	cT2	111
	cT3	12
	NA	11
Tumor grade	I	12
	II	117
	III	56
	NA	17
Type of tumor (biopsy)	IDC	164
	IDC + DCIS	22
	ILC	3
	ILC + LCIS	3
	DCIS	8
	NA	2
Focality	Unifocal	165
	Multifocal/multicentric (MC/MF)	34
	NA	3
Quadrant	CQ	30
	LIQ	22
	LOQ	17
	LQ	5
	UIQ	40
	UOQ	80
	UQ	3
	NA	5
Pathological tumor stage	0	23
	IA	33
	IB	6
	IIA	77
	IIB	31
	IIIA	17
	IIIB	2
	IIIC	11
	IV	2

IDC, invasive ductal carcinoma; DCIS, ductal carcinoma in situ; ILC, invasive lobular carcinoma; LCIS, lobular carcinoma in situ; CQ, central quadrant; LIQ, lower inner quadrant; LOQ, lower outer quadrant; LQ, lower quadrant; UIQ, upper inner quadrant; UOQ, upper outer quadrant; UQ, upper quadrant. NA, Not Available.

TABLE 4 Demographic features of patients with benign breast disease.

Benign cases		
Feature	Class	N
Cases	Total	11
Age (years)	Median (range)	41 (28, 60)
	<40	4
	40–60	7
	>60	0
Comorbidities	Yes	1
	No	10
Size of breast	S	0
	M	3
	L	7
	XL	0
	NA	1
Ptosis	I	0
	II	2
	III	8
	No	0
	NA	1

NA, Not Available.

TABLE 5 Clinical features of surgeries for benign disease.

Benign surgeries		
Feature	Class	Surgeries (Sx = 20)
Type of tumor (biopsy)	Benign phyllodes	5
	Benign intraductal papilloma	3
	Fibroadenoma	9
	NA	3
Focality	Unifocal	15
	Multifocal/multicentric (MC/MF)	4
	NA	1
Quadrant	CQ	4
	IQ	1
	LIQ	0
	LOQ	0
	LQ	1
	UIQ	2
	UOQ	8
	UQ	1
	NA	3

CQ, central quadrant; IQ, inner quadrant; LIQ, lower inner quadrant; LOQ, lower outer quadrant; LQ, lower quadrant; UIQ, upper inner quadrant; UOQ, upper outer quadrant; UQ, upper quadrant; NA, Not Available.

3.6 Cosmetic score analysis

Out of 202 TM surgeries for 194 breast cancer patients, cosmetic scores were assessed by surgeons within 3–6 months post-surgery. Table 7 shows the cosmetic scores as reported by the surgeons. Satisfaction with breasts in the PROM analysis showed an average score of 78%.

3.7 Patient-reported outcome measures

PROM data were collected from the study participants after a minimum period of 12 months post-surgery using the BREAST-Q questionnaires. Out of 194 breast cancer patients, 139 (72.0%) responded to the questionnaire. High patient satisfaction scores were observed from our PROM data as seen in Figure 4C.

4 Discussion

The TeaM publication established a comprehensive protocol for extending indications of breast conservation through mammoplasty techniques for breast cancer patients who needed wider excisions. However, there were a few limitations to the report, as it was an analysis of short-term outcomes of the practice (41, 42). Here, we present the first comprehensive, globally largest single-institutional study of 222 TM surgeries in 205 patients from 2012 to 2019 with breast disease based on the recommendations of the TeaM protocol. The major strengths of our study include the largest cohort from a single surgeon unit from a middle-income country, assessment of oncological outcomes, and cosmetic outcomes along with patient-reported outcomes.

TM is a well-established oncoplastic technique that combines the advantages of an oncologically safe wide excision of tumors with breast reduction, mastopexy, and contralateral symmetrization techniques. It extends the indications of breast conservation by enabling wider excision margins, lower re-excision rates, and a reduction in the rate of mastectomies (25). TM has been shown to achieve satisfactory outcomes by reducing the breast size, thereby facilitating better delivery and distribution of RT regimens, achieving contralateral breast symmetry, and improving the QoL. The oncological safety and efficacy of TM have been confirmed in early breast cancer cases indicated by higher rates of overall survival (OS) and disease-free survival (DFS) with low recurrence, lower complication rates, and superior cosmeses (21, 25, 43). In the Indian context, wherein mastectomy is still the default approach to breast cancer management, it is essential to incorporate oncoplastic techniques like TM in the surgical management protocol and offers more options for breast conservation.

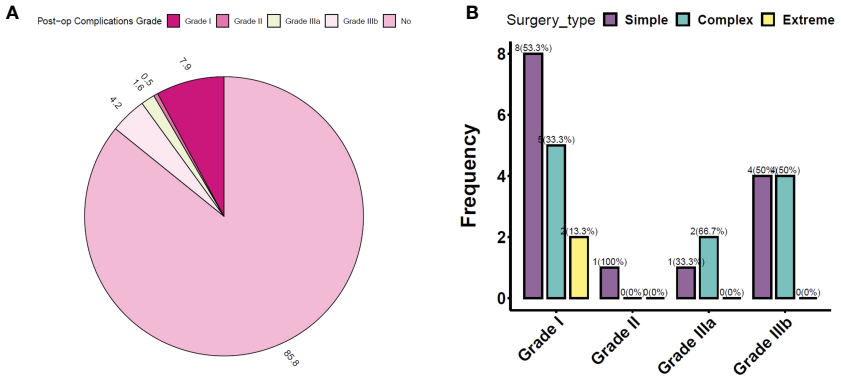


FIGURE 3
(A) Post-op complications observed in the study cohort (in percentage). **(B)** Distribution of post-op complications according to TM surgery type. TM, therapeutic mammoplasty.

4.1 Oncoplastic breast surgery and its relevance in Indian scenario

With many studies showing equivalent oncological outcomes for BCT compared to mastectomy, globally, BCT and oncoplasty have become a regular practice in the surgical management of breast cancer (41, 42). However, India brings about its own challenges, as the clinical, psychosocial, and economic profiles of breast cancer patients in India are significantly different than in Western countries. It is imperative that India rises above its current rigid mindset of mastectomy as the primary approach to breast cancer management. Another major contributor to this rigid mindset is the fact that India is a low- and middle-income country (LMIC), and for most of its population, any disease brings fear of an economic burden, aggravated by other factors like lack of education and low socio-economic status (44). Most Indian women not only are unaware of available healthcare options but also lack information regarding disease symptoms, screening modalities, self-breast examination, and/or routine mammographic screening due to societal circumstances and conservative social structure. This ultimately results in costly delays in diagnosis and treatment (45). Oncoplastic procedures are considered to be relatively expensive, and many women are not able to afford these procedures. As a result, total mastectomy is the standard of care, the rate of BCS is low, and mastectomy remains the most common option in many Tier II and III cities. BCT or OBS options are offered only by a few reputed tertiary cancer care centers in Tier I cities. The low rates of BCS are further augmented by the paucity of skilled oncoplastic surgeons in smaller centers in addition to a lack of awareness about OBS in the medical fraternity. Hence, it is essential that more surgeons are given an opportunity to train in oncoplastic techniques (45, 46).

Thus, the need for standard OBS procedures modified to fulfill the requirements of Indian breast cancer patients is even more pertinent. Taking into consideration multiple factors relevant to the Indian population, we have developed specific patient-related decision-making algorithms. These algorithms include extensive MDT discussions with a focus on the tumor location and breast size as well as patient counseling. We have developed a meticulous counseling protocol that concentrates on the psychology of the Indian woman. The counseling involves discussion of the associated pros and cons of available surgical options that enable patients to make an informed decision regarding their treatment.

Surgical management of breast cancer the world over has shifted focus from mere survival to post-breast cancer patient quality of life.

TABLE 6 Post-op complications in the cohort as per the Clavien–Dindo classification.

Characteristics	Complications, number (n = 194) No complications in n = 165, NA=2			
Grades	Total (27)	Simple TM (13)	Complex TM (11)	Extreme oncoplasty (2)
Grade I (seroma/hematoma not requiring drainage, minor skin necrosis, fat necrosis, delayed wound healing)	15	8	5	2
Grade II (wound infection)	1	1	0	0
Grade IIIa (seroma/hematoma were drained under USG guidance, lymphedema, nipple necrosis, skin necrosis undergoing debridement)	3	1	2	0
Grade IIIb (seroma/hematoma drained under general anesthesia—major skin necrosis, wound infection requiring debridement, bleeding)	8	4	4	0
Total	27	14	11	2

TM, therapeutic mammoplasty; USG, ultrasonography.

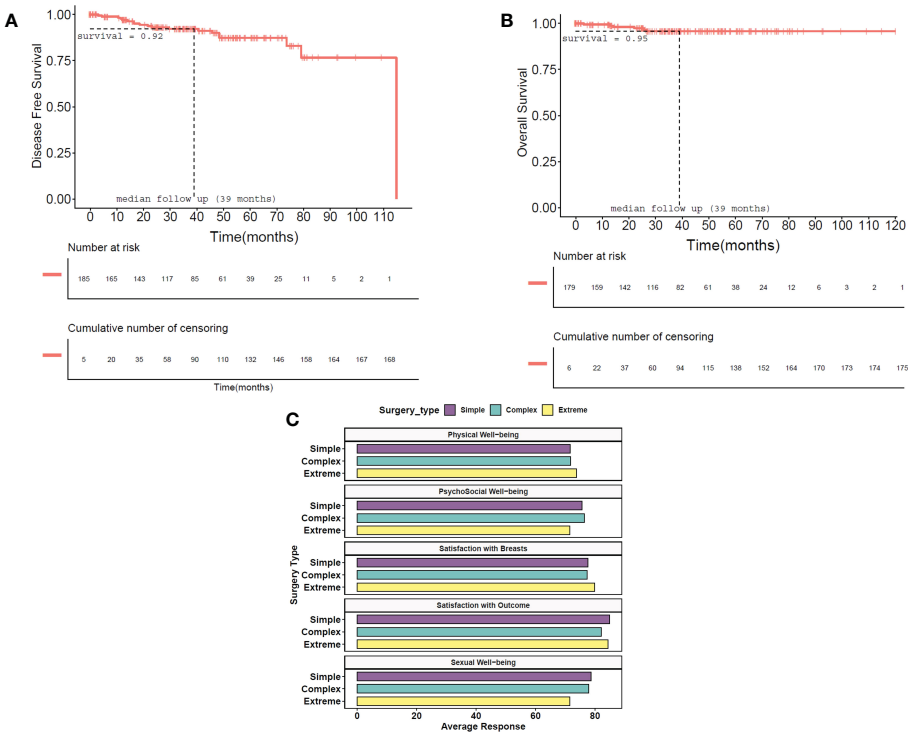


FIGURE 4
Survival Kaplan–Meir plots of disease-free and overall survival. **(A)** In disease-free survival, local and distant recurrences and metastasis are taken as events. Time is the time period in months between surgery and the known date of evidence of recurrence and is shown in months. The probability of a patient being disease-free at median follow-up (39 months) is 92.2%. **(B)** In overall survival, the approximate date of death due to any cause was taken as an event. Time is the time period in months between surgery and the approximate cause of death and is shown in months. The probability of survival at median follow-up (39 months) is 95.9%. Vertical bars indicate censored patients in both plots. **(C)** PROM scores according to TM surgery type represented graphically. Overall PROM scores are presented in the table. PROM, patient-reported outcome measure; TM, therapeutic mammoplasty.

Our oncoplastic practice believes that Indian breast cancer patients should also be given the opportunity to avail the benefits of breast conservation and when needed oncoplastic techniques. This will enable them to not only lead an oncologically safe life but also be cosmetically at-par. In pre-surgery counseling, our patients are made aware of the various options available to them and the advantages and disadvantages of each. Our patients are also counseled about the fact that it is necessary to think about life beyond the disease and consider the repercussions of mastectomy on their quality of life.

TABLE 7 Cosmetic scores for surgeries in breast cancer patients.

Category	Score	Classification	Number, (%)
1	0–3	Bad	0, (0)
2	4–5	Fair	6, (3.5%)
3	6–8	Good	117, (68.4%)
4	9–10	Excellent	48, (28.1%)
		Total	171
5	NA	Not available	23

NA, Not Available.

4.2 TM algorithm at our single surgeon center

Our study represents the first detailed report on surgical, oncological, and PROM outcomes after TM surgery in breast cancer patients from India as observed in a single breast oncoplasty unit.

MDT-based decisions and patient counseling identified TM as the most appropriate surgical approach for the 205 patients (194 malignant and 11 benign) in our cohort. Among these, 56 (29.01%) received NACT. In our post-NACT subset, 28.6% (16/56) had a pCR to NACT. For patients who had large residual tumors (>4 cm) post-NACT (6/56, 10.7%) an oncoplastic technique like TM, where large excisions can be achieved, facilitated breast conservation. Interestingly, in our NACT subset, a large majority of NACT non-responders were also able to undergo breast conservation through extreme oncoplastic procedures. In a parallel study from our center focused on post-NACT surgical protocols, TM was found to be an essential oncoplastic tool for successful breast conservation (Koppiker et al., manuscript in preparation).

TM gives superior cosmetic outcomes for ptotic breasts (Grades I–III) and moderate-to-large-sized breasts (47, 48). However, owing to financial and logistical challenges, Indian patients have reduced

acceptance of a second operative procedure (49). We hence perform a single-step TM procedure that involves simultaneous reconstruction of the NAC and contralateral reduction mammoplasty for bilateral symmetrization in which the nipple may undergo resection with a NAC graft. Most of the cases in our study cohort have been operated using the dual pedicle technique in which NAC was carried out on the superior pedicle and the inferior pedicle was used to fill the defect caused by the excision of the tumor. In patients with smaller breasts or with large excisions, we have frequently used the whole lower segments of the breast (i.e., infero-medial and infero-lateral pedicles), so the breast mound is advanced into the defect and NAC is reimplanted onto the pedicle. TM also improves self-image and reduces physical discomfort, especially for women with macromastia, which is often overlooked by women in the Indian setting. If the patient does not consent to opposite symmetrization, alternative OBS procedures to TM are recommended.

TM has a potential advantage in achieving lower rates of re-excision due to the scope of excising wider margins (50). However, re-excision in the case of TM could also be challenging due to glandular re-arrangement during mammoplasty. This should be considered carefully after discussing within the MDT and only if the operating surgeon is confident in identifying the tumor bed and orientation (51). The TeaM protocol showed a 21% margin positivity rate, while literature reports indicate rates of positive margins ranging from 0% to 36% (22, 52) with institutions reporting lower rates of margin positivity, after conducting intra-operative frozen-section analysis (53–55). Consistent with previous reports (32), with the inclusion of intra-operative frozen-section analysis, we were able to achieve lower margin positivity with 1.4% of cases having positive margins.

Consensus guidelines for optimal RT planning after oncoplastic procedures are unclear, and further methodical investigations are needed. Indeed, results are eagerly awaited from the MIAMI trial, which is the first randomized trial designed to address the clinical safety of TM associated with the excision of each cancer and the possibility of performing up to two tumor bed(s) boost(s) radiotherapy (56).

In our study, the mean duration from TM to the start of adjuvant treatment was 50 days without any delay. This observation is consistent with several studies that indicate OBS does not result in a delay in adjuvant treatment. Although the optimal duration between OBS and RT has not yet been established, in our practice, we prefer commencing RT within 6 months of treatment during which adjuvant chemotherapy is administered, wherever recommended. If no ACT is required, RT is started within 5–6 weeks post-op.

4.3 Therapeutic mammoplasty in extreme situations

In the recent past, several studies have now emerged where authors have reported acceptable oncological results with equivalent survival combined with much improved cosmetic results and QoL with OBS (48, 57, 58). This has finally culminated in the concept of extreme oncoplasty (EO) where large, multicentric, and multifocal tumors as well as extensive ductal carcinoma *in situ* (DCIS) have been effectively treated with BCS.

Prof. Melvin Silverstein first introduced the concept of extended resections using oncoplastic surgery and introduced the term *extreme oncoplasty* (11). Extreme oncoplasty patients are generally those with large tumors (>5 cm), MC/MF disease, locally advanced breast cancer, or recurrences in previously irradiated breasts.

In the Indian scenario, extreme oncoplasty holds special relevance. Several reports indicate that the majority of breast cancer patients in India are diagnosed at an advanced stage, with large-sized LABC or LOBC (59). For patients with large tumors and MC/MF disease, the surgical choice of EO looks very promising. The EO technique allows the resection of larger amounts of breast tissue with safer margins and acceptable aesthetic results, thereby increasing breast conservation rates (33, 60, 61).

Our cohort includes 48 (five benign) patients who underwent extreme oncoplasty of whom 30 (62.5%) underwent an upfront extreme procedure and 18 (37.5%) received NACT followed by extreme TM. Based on our experiences, we propose that EO surgery has excellent applications for OBS-based clinical management.

4.4 Post-surgery commentary: oncological and cosmetic outcomes

Many studies report complication rates between 15% and 30% for OBS (62, 63). Comparable to published literature from Western cohorts, we observed lower rates of complication (13%) with a majority being only minor complications. Similarly, recurrence rates in OBS have been reported to range from 0.5% to 12%, and we observed lower rates of recurrence with only 2% local recurrence and 7% overall recurrence in our cohort. In keeping with the literature, we report 3.6% overall mortality and only 3.1% disease-specific mortality (64, 65). Although TM is an established technique and is widely practiced as a standard of care in developed nations even in high-risk patients (40, 66), it is still finding its ground in developing countries. Our encouraging results with equivalent oncological outcomes suggest the adaptability of TM as an oncoplastic technique even in low-resource settings.

Cosmetic assessment by surgeons indicated that over 80% of cases exhibited good-to-excellent cosmetic outcomes. This cosmetic assessment is mirrored in patients' perspective as well, as we report high levels of satisfaction, with over 83% mean score of patient satisfaction with outcomes on BREAST-Q PROMs, which is expected (67), as the aim of TM is to provide an aesthetically pleasing breast along with oncological safety. In our study, a comparison of the PROMs among the types of TMs demonstrates almost equal scores, indicating that all types of TMs were well accepted. Our analysis also reveals a higher mean score of 77.05% for sexual wellbeing, which may be attributed to better body image and self-esteem arising from the satisfactory outcomes of the TM

procedure and contralateral reduction mammoplasty. This is in line with previous reports that have indicated that satisfaction with breasts was better in women who underwent OBS than in those who underwent a BCT alone (29).

4.5 Single institution, single surgeon practice—advantages

One of the many advantages of our institution is that it is a single surgeon practice and hence brings with it benefits such as improved level of patient engagement and involvement in shared decision-making, streamlined standard operating protocols, dedicated tumor board, reduced treatment delays, and a better understanding of the patient pathway. In fact, many benefits have been associated with the independent practice that contributes to more satisfied providers, successful practice management, and higher quality care for patients. Our encouraging results could thus be credited to a multitude of factors at our institution such as quality counseling, shared decision-making, surgical expertise, a dedicated medical and surgical team, and even nursing staff that has gained experience and expertise over years. This cohesive and proficient setup contributes to the lower complication rates, personalized hospital services, and comprehensive post-operative care provided at our center.

Protocols and surgical techniques established here along with PROMs would be a useful framework for replication by other breast units. As discussed, there is a paucity of trained oncoplastic surgeons and therefore an inherent need for a structured oncoplastic training program in the country. With this aim, to fill existing gaps in breast cancer surgical training in the niche field of oncoplastic breast surgery, a sister organization of our institution, the International School of Oncoplastic Surgery (ISOS), was founded in 2014, and a structured Masters in Oncoplastic Breast Surgery program in association with University of East Anglia (UEA), UK, was initiated. The program allows budding young surgeons to gain hands-on experience and training in oncoplastic techniques specific to the Indian scenario.

If the techniques and outcomes of OBS are popularized and the broad indications of TM are clearly defined, it is possible that more eligible breast cancer patients will receive the benefits of this procedure over the routine practice of mastectomy.

4.6 Surgeon's recommendations

- Careful marking placement so that the closures are not tight.
- The tumor excision should be maximum through one limb of the incision, and the axilla should be accessed through the same incision by identifying the lateral border of the pectoralis major and minor.
- The supero-lateral area and the lateral pillar should be carefully mobilized to prevent devascularization from the lower lateral segment.
- SLNB should be performed through the same incision using indocyanine green (ICG) or nuclear dye, and if the status is positive, axillary dissection should be carried out *via* the same incision.
- All the tumor margins should be analyzed on frozen sections and by a specimen mammogram. The breast restoration should be delayed until the results on frozen sections are negative. The contralateral reduction should be performed while frozen-section analysis is ongoing.
- The interruptive sutures should be used at the "T" junction instead of continuous sutures to minimize necrosis.

4.7 Post-surgery radiation therapy recommendations

In our opinion, in the majority of TM cases, margins around the tumor bed do not shift significantly due to the following reasons:

- During TM, adequate care is taken to check whether the tumor bed is well delineated with markings by Liga clips, as soon as the tumor is removed.
- In some cases, the margins may get advanced into the tumor cavity to form the bed of the tumor cavity (such as in an extended inferior pedicle). Herein, for dealing with the tumor in the superior quadrant, the lower margin (which is the highest point of the extended pedicle) shifts into the tumor cavity, where exactly the boost is required.
- In simple mammoplasty (or tumor in the lower quadrant or superior quadrant), in which the tumor is in a tissue segment within the specimen, it is likely that some of the margins may shift into the tumor cavity but not shift away from it.
- If the tumor is lying outside (i.e., in the outer quadrant or supero-medial quadrant) and if the excision is large, central mound advancement can be performed to fill up these cavities. In this situation, even if the infero-medial margin may shift, being a supero-medial margin, it will not go outside the tumor cavity.
- For the cavity on the outer side, if a dual pedicle technique is applied, even then inferior pedicle will be used only to fill in the gap.

5 Conclusion

Therapeutic mammoplasty is a promising and safe approach to manage breast cancer in medium-to-large breasts with ptosis even in the Indian context despite the scope and limitations. However, sociodemographic factors like its availability, feasibility, and resource constraints severely limit its uptake by providers and utilization by patients. Despite this, TM holds a potential promise of delivering the goal of good oncological outcomes with

aesthetically pleasing results without detrimentally affecting the course of adjuvant therapies.

Our study shows promising results for the adoption of TM in routine surgical practice in India. However, given the large variability in sociocultural, psychological, and economic ground realities of the general Indian population, similar TM-focused studies from Indian breast units as well as other parts of Asia are needed to corroborate the observations from our study.

We conclude that our TM technique(s) may be suited even for advanced-stage patients with moderate-to-large breasts with mild/severe ptosis. In general, our study observations are compliant with the guidelines of TeaM protocol except for a few non-compliances such as the lack of MRI, which has poor uptake in India due to cost barriers. At our center, we were able to mitigate this challenge by doing a detailed assessment using USG and 3D tomosynthesis. Additionally, we emphasize the need to include cosmetic and PROM outcomes to assess the efficacy of TM as a viable surgical option for breast disease patients from India.

6 Case discussion

6.1 Case I: Simple Therapeutic Mammoplasty

A patient aged <35 years (Grade II ptosis) presented with a lump in the left central quadrant. USG revealed a unifocal tumor that extended from the 11 o'clock position to the 12 o'clock position, taller than wider in shape, measuring 21 × 17 × 19 mm. Tru-Cut biopsy report revealed invasive ductal carcinoma (IDC) with triple-negative breast cancer (TNBC): estrogen receptor (ER) negative, progesterone receptor (PR) negative, and HER2 negative.

Pre-operative marking was performed using a Wise pattern incision with a plan of an inferior pedicle mammoplasty. The tumor was widely excised *via* the limbs of the marked incision with the volume of excision 8 × 7 × 2.5 cm (85 g). Margin negativity was confirmed radiologically using a specimen mammogram, and the shave margins analyzed on the frozen section were negative. The tumor bed was clipped with Liga clips. The sentinel node was dissected through the same incision and was node negative. An extended inferior pedicle was mobilized to fill the defect. Thereafter, the axilla was closed, and the inferior pedicle was fixed to the chest wall. The two pillars were brought together, and the nipple–areola was sutured. The left breast tissue was reshaped and reconstructed. Contralateral reduction mammoplasty was performed on the opposite breast (right side). The post-op histopathology revealed Grade III IDC with foci of DCIS of solid and comedo type with high nuclear grade and a lesion spanning 25 × 20 mm in the central quadrant. The patient received adjuvant chemotherapy (AC-4q + paclitaxel-12q) followed by adjuvant RT with a simultaneous electron boost to the tumor bed. The patient tolerated treatment well. Genetic testing had revealed BRCA2 pathogenic mutation in the patient, and she was thus advised and underwent a prophylactic salpingo-oophorectomy. Given the high-risk status of the patient, the PCCM team has ensured diligent follow-up with routine mammograms and check-ups for the patient. She is doing well and has not developed any abnormalities or recurrence at the latest follow-up 5 years post-diagnosis.

The case images for this patient are depicted in Figure 5, and the technique is demonstrated in Supplementary Video 1.

6.2 Case II: Complex Therapeutic Mammoplasty

A patient aged above 60 years, with Grade III ptosis, presented with a large diffuse lump in the right UOQ. Breast radiology revealed a hypoechoic lesion measuring 28.2 mm × 16.2 mm at 12.5 o'clock 2B position along with suspected right axillary lymphadenopathy. Tru-Cut biopsy suggested Grade II invasive lobular carcinoma (ILC), and immunohistochemistry (IHC) reports indicated ER/PR-positive, HER2-negative status.

The patient was marked for a Wise pattern incision followed by excision of the large area in the UOQ. The volume excised was 8.5 × 10.5 × 5.5 cm. Specimen mammography was performed to confirm the complete removal of the tumor. The tumor bed was clipped with Liga clips. The shave margins on the frozen-section evaluation were reported as negative. The marked area for the inferior pedicle including the medial and lateral wings was de-epithelialized. The tumor was excised *via* the marked incision, and the base was clipped. The skin over the lower, medial, lateral, and superomedial quadrants was mobilized in the mastectomy plane. An extended inferior pedicle was used to fill the defect in the UOQ. Further axillary dissections were performed through the same incision. Even though the tumor location was close to the nipple, the nipple core and margins of the NAC were negative for DCIS on frozen sections. Contrary to common practice, we marked the future nipple–areola complex after mobilization and restructuring to avoid any deviation of the nipple. The right breast was reshaped and closed in two layers. A contralateral symmetrization procedure was performed.

The post-op histopathology revealed Grade II IDC. The patient received adjuvant RT. The patient was counseled for adjuvant therapy and chose to have adjuvant endocrine therapy. The patient tolerated treatment well and is disease-free after 4 years post-diagnosis. The pre- and post-operative images for this patient are depicted in Figure 6, with the technique demonstrated in Supplementary Video 2.

6.3 Case III: Extreme Therapeutic Mammoplasty

A patient aged approximately 40 years with Grade II ptosis presented with a large diffuse lump in the right lower outer

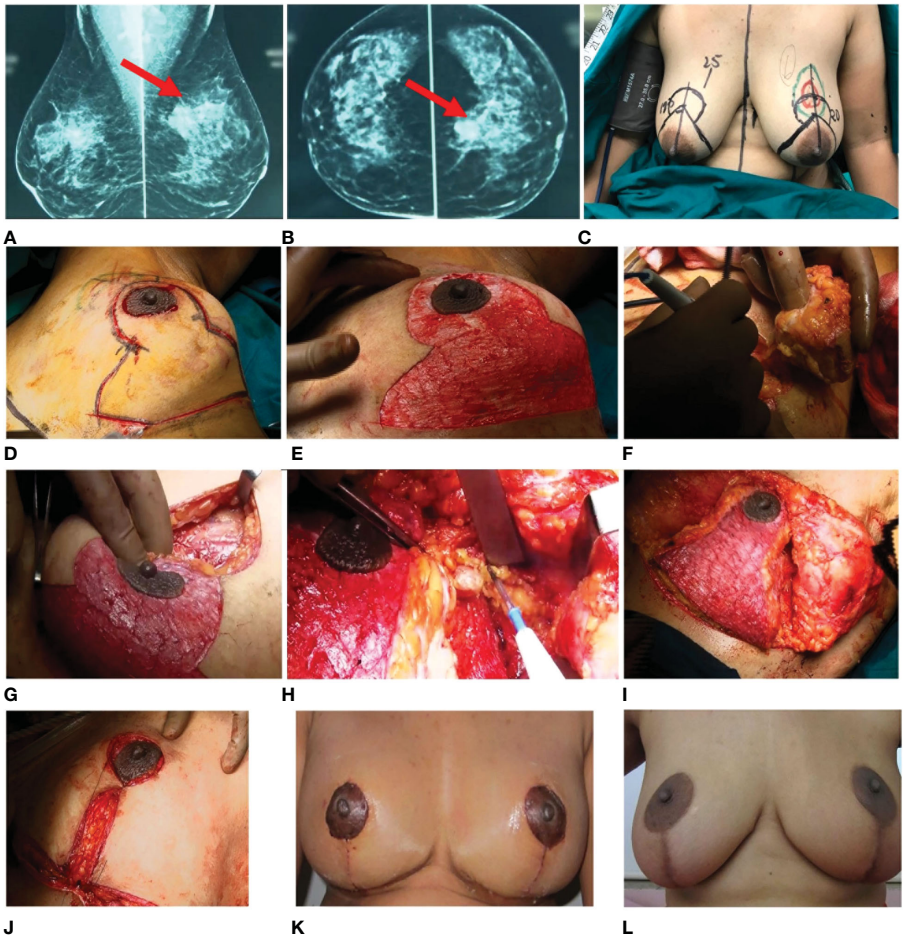


FIGURE 5
Simple TM. Pre-operative radiology images **(A, B)** show a partially circumscribed obscured iso- to hyperdense lesion seen in the upper central quadrant of the left breast. **(C)** Markings. **(D–J)** Intra-operative images. **(D)** Wise pattern incision marked. **(E)** De-epithelialized area. **(F)** Excision of the tumor. **(G)** Tumor bed. **(H)** Sentinel node biopsy. **(I, J)** Inferior pedicle is used to restructure the breast. **(K, L)** Post-operative images. **(K)** One-month follow-up. **(L)** Annual follow-up. TM, therapeutic mammoplasty.

quadrant (LOQ). Mammogram revealed an MF (multifocal) tumor occupying a large area of the outer quadrant at the 8 o'clock position measuring 17 × 12 mm with multiple enlarged axillary lymph nodes. USG-guided core biopsy suggested IDC Grade II and IHC revealed ER/PR-positive status. HER2-positive status was confirmed by fluorescence *in situ* hybridization (FISH). The patient underwent lumpectomy twice with axillary node dissection at an external surgery site. The histopathology report showed IDC Grade III + extensive DCIS with positive margins. Axillary lymph nodes 27/32 were positive.

Before she was referred to our clinic, she underwent external site surgery, with a wide local excision of Ca breast (right). The histopathology report revealed that margins were negative for the tumor except for the lateral margin, which was positive. The patient received adjuvant chemotherapy (paclitaxel + Herceptin 12 cycles followed by AC regimen for four cycles followed by completion of Herceptin regimen). The patient was advised for mastectomy at the external site.

After referral to our hospital, the ultrasound showed a large cavity with microcalcifications extending to the lower and mid-outer quadrants in the right breast and suspicious microcalcifications in the lower quadrant of the left breast. A stereotactic vacuum-assisted biopsy was performed on the left breast, and the histopathology report revealed no malignant disease. Clips were placed at the site of the biopsy. Thereafter, a right extreme TM was performed at our hospital. The patient was marked for a Wise pattern incision, and a wide excision of the outer quadrant was performed to excise the whole cavity along with calcifications with good and adequate margins. The specimen excised was 4 × 3 × 0.5 cm, 8 × 8 × 0.5 cm, 15 × 10 × 6 cm (900 cc). Intraoperative radiology was performed to ascertain the complete removal of microcalcifications. Shave margins were sent for frozen-section evaluation and were reported to be negative. The NAC was carried out on the supero-medial pedicle, and the inferior pedicle was used as a filler to restructure the breast. Since the woman had Grade II ptosis, the length of the inferior pedicle was adequate to reach the area of

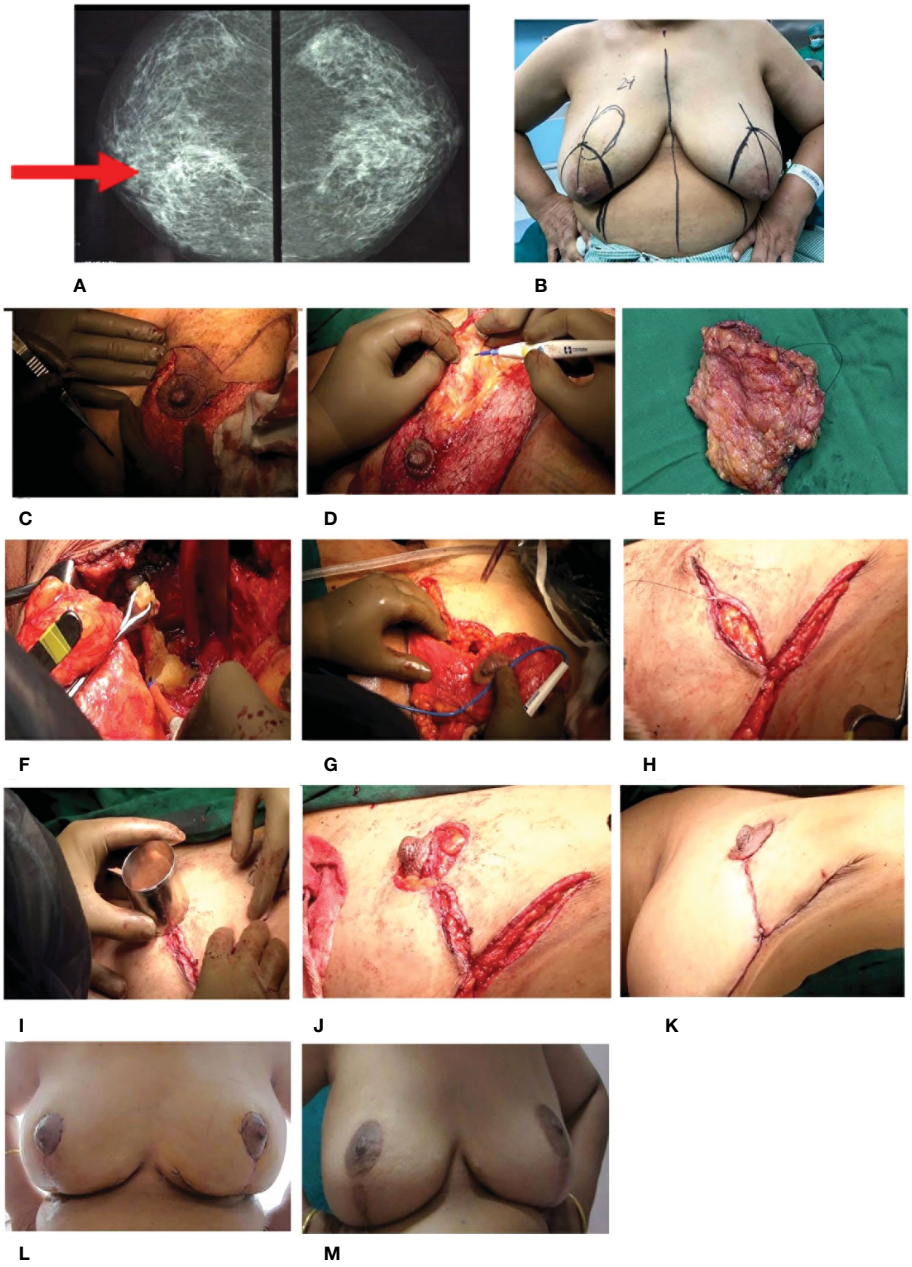


FIGURE 6
Complex TM. **(A)** Pre-operative radiology image: craniocaudal view of both breasts. Ill-defined radiodensity with spiculations and surrounding architectural distortion is seen in the deep central quadrant of the right breast. Pleomorphic amorphous microcalcification is also seen. **(B)** Markings for Wise pattern incision of the right with the tumor and contralateral breast for symmetrization. **(C–K)** Intra-operative images. **(C)** De-epithelialization of the inferior pedicle. **(D)** Excision of the tumor. **(E)** Excised tumor specimen. **(F)** Sentinel node biopsy. **(G)** Extended inferior pedicle to fill the defect. **(H)** Re-structuring of the breast. **(I)** Marking of the future nipple–areolar complex (NAC). **(J, K)** Re-structured breast with the final outcome. **(L, M)** Post-operative images. **(L)** One-month follow-up. **(M)** Annual follow-up. TM, therapeutic mammoplasty.

excision. The right breast was restructured and closed in two layers.

On the left, the remaining microcalcification was excised under wire guidance to reconfirm the diagnosis on the frozen section. As it was benign, a contralateral symmetrization procedure was performed.

The post-op histopathology report showed unclassified residual IDC with single axillary node positivity. The patient received adjuvant RT followed by an electron boost to the tumor bed. The patient was counseled for adjuvant hormone therapy. The patient tolerated the overall treatment well and is disease-free after 6 years post-oncoplastic surgery (Figure 7 and Supplementary Video 3).

6.4 Case IV: Split Reduction Mammoplasty

A patient >50 years with E-cup breasts (Grade III ptosis) presented with a large diffuse lump in the left UOQ measuring 23 × 36 × 34 mm on radiological evaluation. Tru-Cut biopsy suggested

10.3389/fonc.2023.1131951

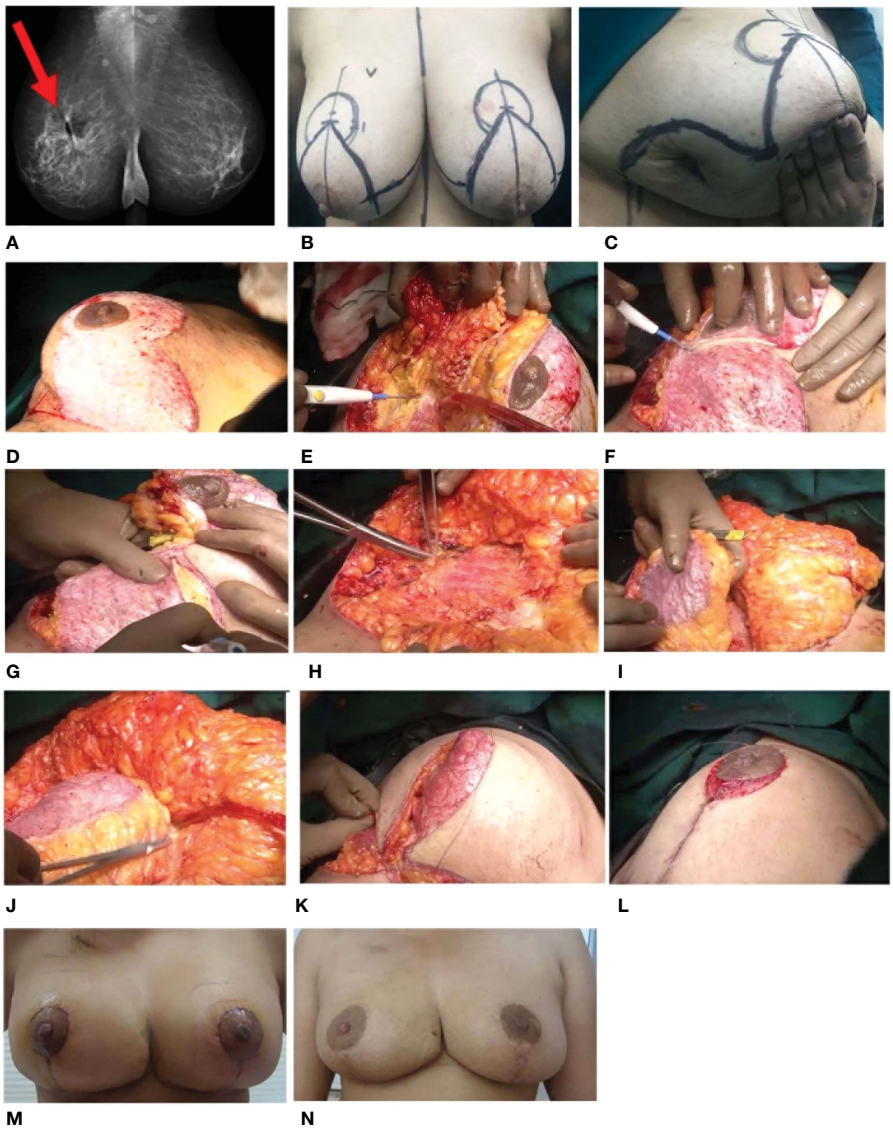


FIGURE 7
Extreme TM. **(A)** Pre-operative radiology imaging 2D mammogram—MLO view of both breasts. Ill-defined spiculated lesion is seen in the upper deep central quadrant of the right breast, and single enlarged right axillary node is seen. **(B)** Markings. **(C)** Previous lumpectomy scar. **(D–L)** Intra-operative images. **(D)** De-epithelialization of the infero-medial pedicle. **(E)** Excision of the tumor with skin. **(F)** Defining the pedicles. **(G)** Nipple–areolar complex (NAC) is on the superomedial pedicle, and inferior pedicle is defined to be used as a filler. **(H)** Clipping of the tumor bed. **(I)** Inferior pedicle used as a filler in the defect (arrow). **(J)** Inferior pedicle used as a filler and fixed. **(K)** Restructuring of the breast. **(L)** Re-structured breast. **(M, N)**. Post-operative images. **(M)** One-month follow-up. **(N)** Annual follow-up. TM, therapeutic mammoplasty; MLO, mediolateral oblique.

IDC Grade II, and IHC revealed ER/PR-positive and HER2-negative status.

The patient was marked for a Wise pattern incision. The inferior pedicle and the medial wing were de-epithelialized, but the lower lateral wing (LOQ) of the IMF incision was omitted. With the use of a separate incision, the whole UOQ was excised with the overlying skin. The dimensions of the specimen were 10 × 8 × 4 cm, 8 × 6 × 2.5 cm, and the weight was 320 cc. The shave margins were sent for frozen-section evaluation to confirm margin negativity. An axillary nodal clearance was performed following a sentinel node biopsy (2/3 nodes) *via* the same incision (2/14 nodes). The superomedial pedicle was dissected, and the de-epithelialized medial part of the lower pedicle was used as a filler. The lateral wing (LOQ) and tumor cavity were connected to create a continuum of the skin. The NAC was positioned on the superomedial pedicle, and the breast tissue was reshaped. After closure, an S-shaped incision was made, termed "split reduction".

The post-op histopathology revealed IDC Grade II. The patient received adjuvant RT followed by an electron boost to the tumor bed. The patient's hormonal therapy was continued. The patient tolerated treatment well and is disease-free after 4 years post-diagnosis. The pre- and post-operative images for this patient are depicted in Figure 8, and the technique demonstration is presented in Supplementary Video 4.

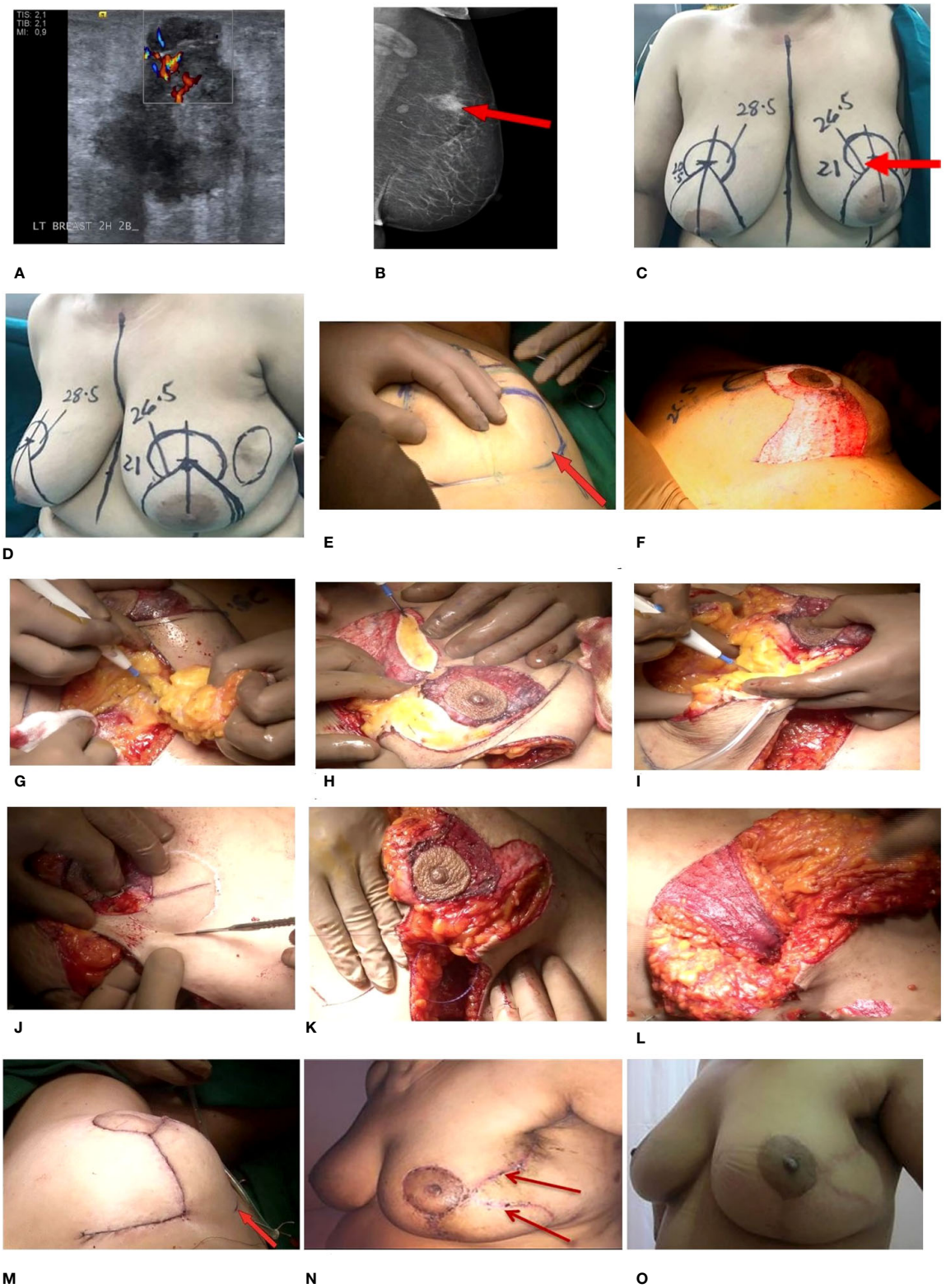


FIGURE 8
Split reduction TM. **(A, B)** Pre-operative radiology images. **(A)** 2D mammogram—MLO view of the left breast. Oval iso- to hyperdense lesion is seen in the upper quadrant of the left breast, which shows spiculations and a small enlarged left axillary node. **(B)** USG—a hypoechoic solid lesion, taller than wide is seen at the 2 o'clock 2B position of the left breast. **(C, D)** Markings also showing tumor in the UOQ with involved skin (arrow). **(E–M)** Intra-operative images. **(E)** No incision on lower outer part of IMF. **(F)** De-epithelialized inferior pedicle along with the medial wing. **(G)** Excision of the tumor along skin. **(H)** Dual pedicles being defined. **(I)** Delineating the superomedial pedicle. **(J)** Marking of the future NAC. **(K)** Connecting the tumor cavity and the lateral wing to create a continuum of skin. **(L)** Inferior pedicle being used as a filler. **(M)** Restructured breast, with the dermal incision in the lateral aspect taken inadvertently. Post-operative images at **(N)** 1-month follow-up and **(O)** 3-year follow-up. TM, therapeutic mammoplasty; MLO, mediolateral oblique; USG, ultrasonography; UOQ, upper outer quadrant; NAC, nipple–areolar complex.

Data availability statement

The datasets presented in this article are not readily available because the data collected is of clinicopathological profiles, surgical, oncological, cosmetic, and patient-related outcomes for cases treated at our centre. This data cannot be shared outside the institution unless ethical approval is given by our ethics committee for a specific project. Requests to access the datasets should be directed to CK email: dr.koppiker@prashanticancercare.org.

Ethics statement

The studies involving human participants were reviewed and approved by PCCM-CTCR Independent Ethics Committee EC/NEW/INST/2021/2443. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

CK: This author was involved in the conception and design, financial support, administrative support, manuscript writing, final approval of the manuscript and was generally accountable for all aspects of the work. SJ, RM, DAK: These authors have contributed equally and were involved in the collection and assembly of data, data analysis and interpretation, data visualization, manuscript writing, final approval of manuscript, accountable for all aspects of the work. PC: Data interpretation and manuscript writing. AJ, JJ: Collection of data. SK: Data representation and visualization AB, DT: Manuscript writing. GS, UD, CD, HA, BV: Data generation. SmN: Collection of data. SaN: Editorial help LB: Administrative support. MP: Data interpretation. All authors contributed to the article and approved the submitted version.

Funding

This study received funding from Bajaj Auto Ltd. (GC 0529 and GC 2528). The funder was not involved in the study design, collection, analysis, interpretation of data, the writing of this article, or the decision to submit it for publication. All authors declare no other competing interests.

Acknowledgments

We would like to thank all participants who consented to participate in this study. We would also like to thank Mr. Ankush Dewle for his editorial assistance. We acknowledge Bajaj Auto Ltd. for providing support to research activities at Prashanti Cancer Care Mission, Pune. We are grateful to the MAPI Research Trust for permission to use BREAST-Q (http://www.mapitrust.org) and the support from the management and staff of Ruby Hall Clinic, Pune, where all surgeries were performed. We would also like to sincerely thank the staff at PCCM for their continued support and efforts.

Conflict of interest

CK is Managing Trustee - PCCM, Principal investigator at CTCR, Founding Director ISOS, Director Oncosciences at Jehangir Hospital. SJ, RM, DAK, AJ, JJ, SK, SmN, SaN, and MP are employed by CTCR.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fonc.2023.1131951/full#supplementary-material

References

1. Fisher B, Redmond C, Poisson R, Margolese R, Wolmark N, Wickerham L, et al. Eight-year results of a randomized clinical trial comparing total mastectomy and lumpectomy with or without irradiation in the treatment of breast cancer. *N Engl J Med* (1989) 320(13):822–8. doi: 10.1056/NEJM198903303201302

2. Campbell EJ, Romics L. Oncological safety and cosmetic outcomes in oncoplastic breast conservation surgery, a review of the best level of evidence literature. *Breast Cancer (Dove Med Press)* (2017) 9:521–30. doi: 10.2147/BCTT.S113742

3. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* (2002) 347(16):1233–41. doi: 10.1056/NEJMoa022152

4. Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med* (2002) 347(16):1227–32. doi: 10.1056/NEJMoa020989

5. Ng ET, Ang RZ, Tran BX, Ho CS, Zhang Z, Tan W, et al. Comparing quality of life in breast cancer patients who underwent mastectomy versus breast-conserving surgery: A meta-analysis. *Int J Environ Res Public Health* (2019) 16(24):4970. doi: 10.3390/ijerph16244970

6. van Maaren MC, de Munck L, de Bock GH, Jobsen JJ, van Dalen T, Linn SC, et al. 10 year survival after breast-conserving surgery plus radiotherapy compared with mastectomy in early breast cancer in the Netherlands: a population-based study. *Lancet Oncol* (2016) 17(8):1158–70. doi: 10.1016/S1470-2045(16)30067-5

7. de Boniface J, Szulkin R, Johansson ALV. Survival after breast conservation vs mastectomy adjusted for comorbidity and socioeconomic status: A Swedish national 6-year follow-up of 48 986 women. *JAMA Surg* (2021) 156(7):628–37. doi: 10.1001/jamasurg.2021.1438

8. Engel J, Kerr J, Schlesinger-Raab A, Sauer H, Hölzel D. Quality of life following breast-conserving therapy or mastectomy: Results of a 5-year prospective study. *Breast J* (2004) 10(3):223–31. doi: 10.1111/j.1075-122X.2004.21323.x

9. Clough KB, Kaufman GJ, Nos C, Buccimazza I, Sarfati IM. Improving breast cancer surgery: A classification and quadrant per quadrant atlas for oncoplastic surgery. *Ann Surg Oncol* (2010) 17(5):1375–91. doi: 10.1245/s10434-009-0792-y

10. Thiessen FEF, Tjalma WAA, Tondu T. Breast reconstruction after breast conservation therapy for breast cancer. *Eur J Obstet Gynecol Reprod Biol* (2018) 230:233–8. doi: 10.1016/j.ejogrb.2018.03.049

11. Silverstein MJ. Oncoplastic breast surgery: From oblivion to mainstream. *Ann Surg Oncol* (2019) 26(11):3409–12. doi: 10.1245/s10434-019-07429-1

12. Silverstein MJ, Savalia NB, Khan S, Ryan J, Epstein M, DeLeon C, et al. Oncoplastic split reduction with intraoperative radiation therapy. *Ann Surg Oncol* (2015) 22(10):3405–6. doi: 10.1245/s10434-015-4671-4

13. Crown A, Laskin R, Rocha FG, Grumley J. Extreme oncoplasty: Expanding indications for breast conservation. *Am J Surg* (2019) 217(5):851–6. doi: 10.1016/j.amjsurg.2019.01.004

14. Acea Nebril B, García Novoa A, Polidorio N, Cereijo Garea C, Bouzón Alejandro A, Mosquera Oses J. Extreme oncoplasty: The last opportunity for breast conservation-analysis of its impact on survival and quality of life. *Breast J* (2019) 25(3):535–6. doi: 10.1111/tbj.13267

15. Savioli F, Seth S, Morrow E, Doughty J, Stallard S, Malyon A, et al. Extreme oncoplasty: Breast conservation in patients with Large, multifocal, and multicentric breast cancer. *Breast Cancer (Dove Med Press)* (2021) 13:353–9. doi: 10.2147/BCTT.S296242

16. Losken A, Hart AM, Broecker JS, Styblo TM, Carlson GW. Oncoplastic breast reduction technique and outcomes: An evolution over 20 years. *Plast Reconstr Surg* (2017) 139(4):824e–33e. doi: 10.1097/PRS.0000000000003226

17. Clough KB, Kroll SS, Audretsch W. An approach to the repair of partial mastectomy defects. *Plast Reconstr Surg* (1999) 104(2):409–20. doi: 10.1097/00006534-199908000-00014

18. Hoover S, Bloom E, Patel S. Review of breast conservation therapy: Then and now. *Yamamoto Y editor. ISRN Oncol* (2011) 2011:617593. doi: 10.5402/2011/617593

19. Chatterjee A, Gass J, Patel K, Holmes D, Kopkash K, Peiris L, et al. A consensus definition and classification system of oncoplastic surgery developed by the American society of breast surgeons. *Ann Surg Oncol* (2019) 26(11):3436–44. doi: 10.1245/s10434-019-07345-4

20. Winters ZE, Bernaudo L. Evaluating the current evidence to support therapeutic mammoplasty or breast-conserving surgery as an alternative to mastectomy in the treatment of multifocal and multicentric breast cancers. *Gland Surg* (2018) 7(6):525–35. doi: 10.21037/gs.2018.07.01

21. Iwuchukwu OC, Harvey JR, Dordea M, Critchley AC, Drew PJ. The role of oncoplastic therapeutic mammoplasty in breast cancer surgery–a review. *Surg Oncol* (2012) 21(2):133–41. doi: 10.1016/j.suronc.2011.01.002

22. O'Connell RL, Baker E, Trickey A, Rattay T, Whisker L, Macmillan RD, et al. Current practice and short-term outcomes of therapeutic mammaplasty in the international TeaM multicentre prospective cohort study. *Br J Surg* (2018) 105(13):1778–92. doi: 10.1002/bjs.10959

23. Mohsen, Sherief M MD Therapeutic reduction mammoplasty techniques in management of breast cancer in large-breasted females – a comparative study between inferior and superior pedicle reduction mammoplasty. *The Egyptian Journal of Surgery* 37(2):139–146. doi: 10.4103/ejs.ejs_89_17

24. McCulley SJ, Macmillan RD. Therapeutic mammaplasty–analysis of 50 consecutive cases. *Br J Plast Surg* (2005) 58(7):902–7. doi: 10.1016/j.bjps.2005.03.007

25. Macmillan RD, James R, Gale KL, McCulley SJ. Therapeutic mammaplasty. *J Surg Oncol* (2014) 110(1):90–5. doi: 10.1002/jso.23659

26. Coates AS, Winer EP, Goldhirsch A, Gelber RD, Gnant M, Piccart-Gebhart M, et al. Tailoring therapies–improving the management of early breast cancer: St gallen international expert consensus on the primary therapy of early breast cancer 2015. *Ann Oncol* (2015) 26(8):1533–46. doi: 10.1093/annonc/mdv221

27. Simos D, Clemons M, Ginsburg OM, Jacobs C. Definition and consequences of locally advanced breast cancer. *Curr Opin Support Palliat Care* (2014) 8(1):33–8. doi: 10.1097/SPC.0000000000000020

28. Savalia NB, Silverstein MJ. Oncoplastic breast reconstruction: Patient selection and surgical techniques. *J Surg Oncol* (2016) 113(8):875–82. doi: 10.1002/jso.24212

29. Dave R, O'Connell R, Rattay T, Tolkien Z, Barnes N, Skillman J, et al. The iBRA-2 (immediate breast reconstruction and adjuvant therapy audit) study: Protocol for a prospective national multicentre cohort study to evaluate the impact of immediate breast reconstruction on the delivery of adjuvant therapy. *BMJ Open* (2016) 6(10):e012678. doi: 10.1136/bmjopen-2016-012678

30. Doval DC, Radhakrishna S, Tripathi R, Kashinath RI, Talwar V, Batra U, et al. A multi-institutional real world data study from India of 3453 non-metastatic breast cancer patients undergoing upfront surgery. *Sci Rep* (2020) 10(1):5886. doi: 10.1038/s41598-020-62618-3

31. Silverstein MJ. Radical mastectomy to radical conservation (Extreme oncoplasty): A revolutionary change. *J Am Coll Surgeons.* (2016) 222(1):1–9. doi: 10.1016/j.jamcollsurg.2015.10.007

32. Silverstein MJ, Savalia N, Khan S, Ryan J. Extreme oncoplasty: breast conservation for patients who need mastectomy. *Breast J* (2015) 21(1):52–9. doi: 10.1111/tbj.12356

33. Koppiker CB, Noor AU, Dixit S, Busheri L, Sharan G, Dhar U, et al. Extreme oncoplastic surgery for Multifocal/Multicentric and locally advanced breast cancer. *Int J Breast Cancer* (2019) 2019:4262589. doi: 10.1155/2019/4262589

34. Gittleman MA. Single-step ultrasound localization of breast lesions and lumpectomy procedure. *Am J Surg* (2003) 186(4):386–90. doi: 10.1016/S0002-9610(03)00277-0

35. Nurko J, Mancino AT, Whitacre E, Edwards MJ. Surgical benefits conveyed by biopsy site marking system using ultrasound localization. *Am J Surg* (2005) 190(4):618–22. doi: 10.1016/j.amjsurg.2005.06.027

36. Panhofer P, Ferenc V, Schütz M, Gleiss A, Dubsky P, Jakesz R, et al. Standardization of morbidity assessment in breast cancer surgery using the clavien dindo classification. *Int J Surg* (2014) 12(4):334–9. doi: 10.1016/j.ijsu.2014.01.012

37. Pusic AL, Klassen AF, Scott AM, Klok JA, Cordeiro PG, Cano SJ. Development of a new patient-reported outcome measure for breast surgery: the BREAST-q. *Plast Reconstr Surg* (2009) 124(2):345–53. doi: 10.1097/PRS.0b013e3181aee807

38. Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R, et al. New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1). *Eur J Cancer* (2009) 45(2):228–47. doi: 10.1016/j.ejca.2008.10.026

39. Schemper M, Smith TL. A note on quantifying follow-up in studies of failure time. *Control Clin Trials* (1996) 17(4):343–6. doi: 10.1016/0197-2456(96)00075-X

40. Potter S, Trickey A, Rattay T, O'Connell RL, Dave R, Baker E, et al. Therapeutic mammaplasty is a safe and effective alternative to mastectomy with or without immediate breast reconstruction. *Br J Surg* (2020) 107(7):832–44. doi: 10.1002/bjs.11468

41. Joukainen S, Laaksonen E, Vanninen R, Kaarela O, Sudah M. Dual-layer rotation: A versatile therapeutic mammoplasty technique. *Ann Surg Oncol* (2022) 29(11):6716–27. doi: 10.1245/s10434-022-11977-4

42. Caruso F, Catanuto G, De Meo L, Ferrara M, Gallodoro A, Petrolito E, et al. Outcomes of bilateral mammoplasty for early stage breast cancer. *Eur J Surg Oncol* (2008) 34(10):1143–7. doi: 10.1016/j.ejso.2007.09.012

43. Gulcelik MA, Dogan L, Yuksel M, Camlibel M, Ozaslan C, Reis E. Comparison of outcomes of standard and oncoplastic breast-conserving surgery. *J Breast Cancer* (2013) 16(2):193–7. doi: 10.4048/jbc.2013.16.2.193

44. Rajpal S, Kumar A, Joe W. Economic burden of cancer in India: Evidence from cross-sectional nationally representative household survey, 2014. *PloS One* (2018) 13(2):e0193320. doi: 10.1371/journal.pone.0193320

45. Thakur KK, Bordoloi D, Kunnumakkara AB. Alarming burden of triple-negative breast cancer in India. *Clin Breast Cancer* (2018) 18(3):e393–9. doi: 10.1016/j.clbc.2017.07.013

46. Mishra V, Kelkar R, Agrawal A, Matcheswalla S. A survey on oncoplastic breast surgery awareness and practice patterns among indian surgeons: a cross-sectional study. *Int J Med Sci and Diagnosis Res* (2021) 5(2). doi: 10.32553/ijmsdr.v5i2.748

47. Goffman TE, Schneider H, Hay K, Elkins DE, Schnarrs RA, Carman C. Cosmesis with bilateral mammoreduction for conservative breast cancer treatment. *Breast J* (2005) 11(3):195–8. doi: 10.1111/j.1075-122X.2005.21610.x

48. Currie A, Chong K, Davies GL. Using therapeutic mammoplasty to extend the role of breast-conserving surgery in women with larger or ptotic breasts. *Ann R Coll Surg Engl* (2013) 95(3):192–5. doi: 10.1308/003588413X13511609958091

49. Koppiker CB, Chintamani & Dixit S. *Oncoplastic breast surgery in India: Thinking globally, acting locally*. SpringerLink. Available at: https://link.springer.com/article/10.1007/s12262-019-01890-8.

50. Singh KA, Losken A. Additional benefits of reduction mammaplasty: a systematic review of the literature. *Plast Reconstr Surg* (2012) 129(3):562–70. doi: 10.1097/PRS.0b013e31824129ee

51. Piper M, Peled AW, Sbitany H. Oncoplastic breast surgery: current strategies. *Gland Surg* (2015) 4(2):154–63. doi: 10.3978/j.issn.2227-684X.2015.03.01

52. McIntosh A, Freedman G, Eisenberg D, Anderson P. Recurrence rates and analysis of close or positive margins in patients treated without re-excision before radiation for breast cancer. *Am J Clin Oncol* (2007) 30(2):146–51. doi: 10.1097/01.coc.0000251357.45879.7f

53. Jorns JM, Visscher D, Sabel M, Breslin T, Healy P, Daignaut S, et al. Intraoperative frozen section analysis of margins in breast conserving surgery significantly decreases reoperative rates: one-year experience at an ambulatory surgical center. *Am J Clin Pathol* (2012) 138(5):657–69. doi: 10.1309/AJCP4IEMXCJ1GDTS

54. Garcia MT, Mota BS, Cardoso N, Martimbianco ALC, Ricci MD, Carvalho FM, et al. Accuracy of frozen section in intraoperative margin assessment for breast-conserving surgery: A systematic review and meta-analysis. *PloS One* (2021) 16(3):e0248768. doi: 10.1371/journal.pone.0248768

55. Boughey JC, Hieken TJ, Jakub JW, Degnim AC, Grant CS, Farley DR, et al. Impact of analysis of frozen-section margin on reoperation rates in women undergoing lumpectomy for breast cancer: evaluation of the national surgical quality improvement program data. *Surgery* (2014) 156(1):190–7. doi: 10.1016/j.surg.2014.03.025

56. *University college, london. can patients with multiple breast cancers in the same breast avoid mastectomy by having multiple lumpectomies to achieve equivalent rates of local breast cancer recurrence? a randomised controlled feasibility study*. clinicaltrials.gov (2021). Available at: https://clinicaltrials.gov/ct2/show/NCT03514654.

57. Rose M, Svensson H, Handler J, Hoyer U, Ringberg A, Manjer J. Patient-reported outcome after oncoplastic breast surgery compared with conventional breast-conserving surgery in breast cancer. *Breast Cancer Res Treat* (2020) 180(1):247–56. doi: 10.1007/s10549-020-05544-2

58. Bazzarelli A, Baker L, Petrcich W, Zhang J, Arnaout A. Patient satisfaction following level II oncoplastic breast surgery: A comparison with mastectomy utililizing the breast-q questionnaire will be published in surgical oncology. *Surg Oncol* (2020) 35:556–9. doi: 10.1016/j.suronc.2020.11.001

59. Bhattacharyya GS, Doval DC, Desai CJ, Chaturvedi H, Sharma S, Somashekhar SP. Overview of breast cancer and implications of overtreatment of early-stage breast cancer: An Indian perspective. *JCO Glob Oncol* (2020) 6:789–98. doi: 10.1200/GO.20.00033

60. Weber WP, Soysal SD, El-Tamer M, Sacchini V, Knauer M, Tausch C, et al. First international consensus conference on standardization of oncoplastic breast conserving surgery. *Breast Cancer Res Treat* (2017) 165(1):139–49. doi: 10.1007/s10549-017-4314-5

61. Franceschini G, Magno S, Fabbri C, Chiesa F, Di Leone A, Moschella F, et al. Conservative and radical oncoplastic approches in the surgical treatment of breast cancer. *Eur Rev Med Pharmacol Sci* (2008) 12(6):387–96.

62. Losken A, Dugal CS, Styblo TM, Carlson GW. A meta-analysis comparing breast conservation therapy alone to the oncoplastic technique. *Ann Plast Surg* (2014) 72(2):145–9. doi: 10.1097/SAP.0b013e3182605598

63. Kabir SA, Stallard S, Weiler-Mithoff E, Mansell J, Mallon E, Doughty JC, et al. Six-year follow-up of patients treated with oncoplastic reduction mammoplasty: A cohort study. *Int J Surg* (2016) 26:38–42. doi: 10.1016/j.ijsu.2016.01.001

64. De Lorenzi F, Hubner G, Rotmensz N, Bagnardi V, Loschi P, Maisonneuve P, et al. Oncological results of oncoplastic breast-conserving surgery: Long term follow-up of a large series at a single institution: A matched-cohort analysis. *Eur J Surg Oncol* (2016) 42(1):71–7. doi: 10.1016/j.ejso.2015.08.160

65. Clough KB, van la Parra RFD, Thygesen HH, Levy E, Russ E, Halabi NM, et al. Long-term results after oncoplastic surgery for breast cancer: A 10-year follow-up. *Ann Surg* (2018) 268(1):165–71. doi: 10.1097/SLA.0000000000002255

66. De La Cruz L, Blankenship SA, Chatterjee A, Geha R, Nocera N, Czerniecki BJ, et al. Outcomes after oncoplastic breast-conserving surgery in breast cancer patients: A systematic literature review. *Ann Surg Oncol* (2016) 23(10):3247–58. doi: 10.1245/s10434-016-5313-1

67. Shekhawat L, Busheri L, Dixit S, Patel C, Dhar U, Koppiker C. Patient-reported outcomes following breast reconstruction surgery and therapeutic mammoplasty: Prospective evaluation 1 year post-surgery with BREAST-q questionnaire. *Indian J Surg Oncol* (2015) 6(4):356–62. doi: 10.1007/s13193-015-0432-x

frontiers | Frontiers in Oncology

TYPE Original Research
PUBLISHED 03 May 2023
DOI 10.3389/fonc.2023.1137924

OPEN ACCESS

EDITED BY
René Aloisio Da Costa Vieira,
Barretos Cancer Hospital, Brazil

REVIEWED BY
Sherif Monib,
West Hertfordshire Hospitals NHS Trust, United Kingdom
Regis Resende Paulinelli,
Universidade Federal de Goiás, Brazil

*CORRESPONDENCE
Maria Carolina Soliani Bastos
carol.soliani@gmail.com

RECEIVED 05 January 2023
ACCEPTED 17 April 2023
PUBLISHED 03 May 2023

CITATION
Soliani Bastos MC, Bagnoli F, Rinaldi JF, João TBF and de Oliveira VM (2023) Dermoglandular advancement-rotation flap for conservative treatment of breast cancer – description of technique, objective and subjective assessments. *Front. Oncol.* 13:1137924. doi: 10.3389/fonc.2023.1137924

Dermoglandular advancement-rotation flap for conservative treatment of breast cancer – description of technique, objective and subjective assessments

Maria Carolina Soliani Bastos*, Fábio Bagnoli, José Francisco Rinaldi, Thais Businaro Fernandes João and Vilmar Marques de Oliveira

Gynecology and Obstetrics Department, School of Medical Sciences, Santa Casa de Misericórdia de São Paulo, Mastology Section, São Paulo, SP, Brazil

Objective: to describe and evaluate the dermoglandular advancement-rotation flap with no contralateral surgery as a technique for the conservative treatment of breast cancer when skin or a large proportion of gland requires resection.

Patients/Methods: 14 patients with breast tumors with a mean size of 4.2 cm and need for skin resection. The resection area is included within an isosceles triangle, with its apex located on the areola, which is the pivot for rotation of a dermoglandular flap released through a lateral extension along that triangle base. Symmetry before and after radiotherapy was objectively assessed by authors using the BCCT.core software, as well as subjectively by three experts and patients themselves using the Harvard scale.

Results: Experts considered the breast symmetry results to be excellent/good for 85.7% of patients in the early post-operative period and 78.6% in the late post-operative period. Excellent/good ratings provided by BCCT.core software amounted to 78.6% of cases in the early post-operative period and 92.9% in the late post-operative period. Symmetry was rated as excellent/good by 100% of patients.

Conclusion: Dermoglandular advancement-rotation flap technique with no contralateral surgery provides good symmetry when a large proportion of skin or gland requires resection on breast conservative cancer treatment.

KEYWORDS

breast-conservative surgery, breast neoplasms/surgery, breast reconstruction/methods, aesthetics, software, assessment of results/methods

Introduction

Breast-conservative surgery is the standard surgical treatment for most breast cancer cases. As demonstrated by solid and long-term follow-up studies, breast-conservative surgery associated with radiotherapy provides overall survival rates comparable to those of radical treatment, and even more recent studies suggest that breast-conservative surgeries may provide higher disease-free survival rates than radical mastectomies (1–9).

Various studies have reported breast asymmetries deriving from conservative surgery, especially when resections exceed 20% of breast volume. When located in the medial, inferior or central quadrants, resection volumes of more than 10% can already produce asymmetries (10–12). Numerous factors contribute to the risk of breast asymmetry, including younger age, high BMI, large tumors, unfavorable tumor location, compromise of skin, need for new surgeries, postoperative seroma and adjuvant radiotherapy (13, 14). An estimated 30% of all women undergoing locoregional treatment experience fair/poor esthetic results, which negatively impacts their psychosocial recovery and quality of life (10, 15).

It is necessary to resect the skin when it is compromised by the tumor or when the skin flap resulting from resection with appropriate margins would result very thin, and therefore, prone to necrosis. When necessary, resection of the skin overlying small tumors in breast-conserving surgeries can be performed using classical techniques, i.e. closing the resected area by approximation of the skin and glandular tissue. In medium to large tumor resections, however, this closure can lead to significant distortions of breast architecture and position of the nipple-areola complex and may require a contralateral mammoplasty as an attempt to achieve some breast symmetry. Resection and remodeling techniques focused on minimizing these distortions may allow for simpler and unilateral surgeries, which would help to save patients' biological resources – an advantage that is especially beneficial for patients in poor clinical condition. Furthermore, faster and more resolutive surgeries would preserve resources from health services, which may be already overwhelmed and incapable of providing proper care to all patients with breast cancer.

Burow's Triangle technique was first described in 1855 by Karl August von Burow as a procedure for facial reconstructions (16). This technique consists in releasing a full-thickness flap from adjacent tissues for large-size advancements. This principle can also be used for breast remodeling surgeries after quadrantectomies and involves the advancement-rotation of a full-thickness flap with its pivot centered on the nipple-areola complex. This approach uses adjacent breast tissue to close the resected area, minimizing the nipple's position distortion. However, an evaluation of the application of this method for breast cancer treatment seems to be unavailable in the literature.

Objective

The purpose of this study is to describe the surgical technique of dermoglandular advancement-rotation flap for breast remodeling as a breast-conserving treatment of breast cancers, avoiding the need for contralateral surgery, and to evaluate the breast symmetry results by means of objective and subjective assessments.

Patients and method

This study enrolled 14 patients diagnosed with invasive breast carcinoma who were treated at the Hospital da Santa Casa Misericórdia (São Paulo) between 2016 and 2020. The inclusion criteria for this study were: women older than 18, having breast cancer diagnoses that required the resection of skin that was compromised by the tumor or near it, and which underwent breast remodeling surgery using the dermoglandular advancement-rotation flap technique.

This study has been approved by the Research Ethics Committee of the Santa Casa de São Paulo and participating patients signed an informed consent.

Surgery

None of the selected patients had any contraindication to breast-conserving surgery. The axillary approach was performed using the same incision that was made for the breast surgery. Patients with clinically negative axillae underwent a biopsy of sentinel lymph node identified after the periareolar injection of 2 ml of blue dye. Axillary dissection was only performed in cases where the axilla was clinically positive or the patient had undergone neoadjuvant chemotherapy and had residual lesions under evaluation using the sentinel lymph node frozen section method.

Vacuum drains were used in all patients until flows amounted to less than 30 ml in 24 hours. No patients had any surgery-related complications, such as hematomas, surgical wound infections and dehiscence. No patients required reoperation.

Surgical site marking

In surgical site marking, the resection area is delimited with an isosceles triangle with its apex located on the papilla, which will serve as the pivot for rotation of the flap. The base of this triangle is extended laterally. Another isosceles triangle is subsequently marked at the end of this lateral extension. Smaller in size, the apex of this triangle is located on the opposite side of the first triangle. This second triangle demarcates the resection that will be used to correct the excess tissue that the flap advancement will produce. The minimal distance between both triangles must be equal to the base of the first triangle. Marking this second triangle is not mandatory, since sometimes it will also be possible to compensate the excess tissue after advancing the full-thickness flap with no further resection (Figure 1).

Description of surgical technique

After general anesthesia, the patient lies in the supine position with the arm adjacent to the side that will be operated open at 90

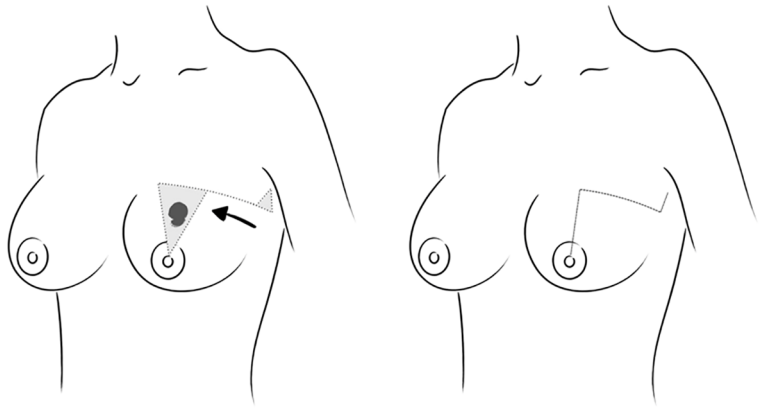


FIGURE 1
Pre-surgical marking and tissue movement to be performed using a dermoglandular advancement-rotation surgical technique and final appearance.

degrees, supported by an arm board. The full-thickness triangle, limited posteriorly by the pectoralis muscle and containing the tumor, is resected using a cold scalpel for the skin and an electric cautery for the gland. Resection is performed so as to provide free margins both macroscopically as well as for the frozen section. Following the previously described quadrantectomy, the extension of the triangle base is incised in full thickness, delimiting a dermoglandular flap that is released from the pectoralis muscle and subsequently advanced and reattached in order to close the resection. This repositioning causes a redundancy of the tissue that was not advanced. This can be corrected by resection of the second triangle or alternatively by distributing the excess tissue along the closure of the incision. Occasionally, it may be also necessary to further adjust the areola's position, a procedure that is carried out by demarcating the areola with an areola marker and de-epithelizing the adjacent skin to produce a round and properly positioned areola (Figure 2).

Assessment of results

All patients were assessed using photographs taken in the pre-operative, initial post-operative (6-15 days after surgery) and late post-operative (at least 30 days after the end of radiotherapy) stages. The aesthetic results particularly with regards to symmetry were assessed by two mastologists and a plastic surgeon, and rated by them using the Harvard scale in Excelent: when the operated breast is very similiar to the contralateral breast, Good: when the operated breast presents small differences compared to the contralateral breast, Fair: when the operated breast presentes a clear difference, but without serious distortion or Poor: when the operated breast presentes serious distortions when compared with contralateral breast (17). Patients were also requested to rate their results using the same scale. The objective tool chosen for symmetry evaluation was the Breast Cancer Conservative Treatment software Cosmetic results - BCCT.core (18–23).

Statistical analysis

Statistical analyses included central tendency and dispersion values of the study's quantitative variables, as well as absolute and relative frequencies of its categorical variables.

Ratings provided by the examiners and the software were grouped into the excellent/good or fair/poor categories for further agreement analyses to be carried out between the different operators and different scales.

This study analyzed the agreement between assessments provided by a panel of experts using the Harvard scale (in the early and late post-operative periods). Agreement between the ratings from experts and the BCCT.core software in both periods was also assessed. The tool used for this assessment was the Kappa coefficient of agreement and its respective 95% confidence intervals and included the subsequent categorization of the coefficients as per the criteria established by Landis & Koch.

The variation between subsequent assessments, i.e., the comparison between the early and late post-operative periods, was analyzed using the McNemar test, which enables the assessment of "before" and "after" situations in which each patient serves as his/her own matched control.

All statistical tests used an alpha error of 5%, in other words, the results were considered to be statistically significant when $p<0.05$.

Results

Analyzing the 14 patients, we found that their ages ranged from 42 to 67 years (mean = 58.9 years, standard deviation = 8.4 years). Tumor size ranged from 2 to 7 cm (mean=4.2 cm, standard deviation =1.6 cm). The mean follow-up time for patients was 21.7 months (standard deviation 9.8 months). All patients underwent radiotherapy with a fractionated 46Gy dose + 14Gy boost in 5 - 5.5 weeks. The patients' demographic and oncological characteristics can be seen in Tables 1–3.

10.3389/fonc.2023.1137924

FIGURE 2
Dermoglandular flap released and before tissue advancement and final surgical appearance after advancement- rotation of dermoglandular flap to correct a defect generated by segmental resection with adjustment of the shape of the nipple-areola complex.

In our sample, no patient required ree-excision, there were no post-surgical complications and the hospitalization time of all patients was less than 24 hours.

Experts considered the breast symmetry results to be excellent/good for 85.7% of patients in the early post-operative period and 78.6% in the late post-operative period. Excellent/good ratings provided by the BCCT.core software amounted to 78.6% of cases in the early post-operative period and 92.9% in the late post-operative period.

The study found no statistically significant differences between the early and late post-operative results, whether using the Harvard scale or the BCCT.core software.

Out of all the ratings provided by the experts and the software in both periods, the rate poor was used only once, by an expert, for a case in the late pos-operative treatment.

According to the criteria of Landis and Koch, agreement between experts was rated as fair for the early post-operative period and moderate for the late post-operative period. Agreement between the Harvard scale and the BCCT.core software yielded identical agreement results.

Half of the patients rated their final symmetry as good; the other half rated it as excellent.

Figure 3 presents the late post-operative image of the case shown in Figures 2, 4 presents typical cases treated with the advance-rotation flap technique.

Discussion

Oncoplastic surgery has been shown to be a safe and convenient option for patients requiring relatively large parenchyma or skin resections – or even for cases with challenging positions for resection closure (24, 25). The classical treatment for these patients would be a mastectomy or segmental resection, which

TABLE 1 Demographic and clinical characteristics of patients.

Variables	Category	N	%
Color/Breed	White	7	50
	Black	5	35,7
	Brown	2	14,3
Previous surgery	No	11	78,6
	Nodule excision	1	7,1
	Mastopexy	1	7,1
	Contralateral breast cancer	1	7,1
Systemic arterial hypertension	No	6	42,9
	Yes	8	57,1
Diabetes Mellitus	No	12	85,7
	Yes	2	14,3
Overweight/obesity	No	6	42,9
	Yes	8	57,1
Smoking	No	13	92,9
	Yes	1	7,1

TABLE 2 Tumor characteristics.

Variables	Category	N	%
Clinical Stage	IA	1	7,1
	IIA	4	28,6
	IIB	1	7,1
	IIIA	3	21,4
	IIIB	5	35,7
Skin involvement	No	9	64,3
	Yes	5	35,7
Localization	Upper outer quadrant	2	14,3
	Upper inner quadrant	7	50,1
	Union of upper quadrants	3	21,4
	Union of outer quadrants	1	7,1
	Union of inner quadrants	1	7,1
Tumor grade	I	1	7,1
	II	10	71,5
	III	3	21,4

would likely give rise to breast distortions and asymmetry. However, both options pose significant aesthetic consequences to patients.

For these patients, one option would be the oncoplastic surgical technique called mammoplasty with geometric compensation, which has been developed as an alternative to conventional conservative surgery, allowing for the resection of large tumors with skin resection in challenging locations such as the superior quadrants. This technique uses mammoplasty principles, therefore correcting breast ptosis and changing the shape and position of the nipple-areola complex. This would require contralateral surgery for symmetrization, which may be inconvenient in some situations (26, 27).

The proposed breast remodeling technique with dermoglandular advancement-rotation flap has made it possible to perform conservative surgery on relatively large tumors or even tumors requiring skin resection without the need for contralateral breast intervention. Unilateral surgery is faster and less morbid, an option that is especially beneficial for elderly women, patients with comorbidities, or even people who prefer to avoid bilateral surgery. None of the enrolled patients had any surgical complications.

In our sample, we observed a volumetric reduction of the operated breast in one pacient, associated with scar retraction after radiotherapy. In imaging tests performed, we observed areas of steatonecrosis that may explain what happened. Although this patient had undergone neoadjuvant systemic treatment, a 7 cm tumor was left for surgical approach. Due to the tumor size, a large dermoglandular advancement-rotation flap was necessary to correct the defect generated after removal of the tumor with free margins. Thus, this large area of breast tissue that was detached from the pectoralis major muscle associated with the action of radiotherapy evolved with areas of steatonecrosis and fibrosis, generating an unfavorable final aesthetic result.

Our study did not assess scar patterns as a specific item, rather it was incorporated as a parameter for the breast symmetry assessment. Even though the dermoglandular advancement-rotation flap technique proposed in this study requires an extensive incision, its tension-free closure considerably decreases the probabilities of complications such as dehiscence and pathological scarring. The study also indicated that the scar issue had no negative impact on the final ratings provided either by the patients or the experts.

The advantage of this technique that we describe is that it allows a unilateral approach in those cases in which the the conventional breast-conserving surgery would not be suitable because of tumors being large, in unfavorable locations or involving or near skin. This technique allowed a quick surgery and with lower morbidity, what is specially important for patients with comorbidities, elderly or even those who do not want bilateral surgery. It also provides the possibility of carrying out conservative surgery in cases where a mastectomy would be performed, and allowed a satisfactory result, both from an oncological and aesthetic point of view.

In the evaluations carried out using the Harvard scale by 3 specialists, we found that 12 (85.7%) cases were categorized as Excellent/Good in the initial postoperative period and 11 (78.6%) of them remained with this evaluation in the late postoperative period. In 1 case there was a worsening of symmetry when comparing the two moments, a fact that we relate to the complications of radiotherapy. Two cases evaluated in the initial postoperative period as Fair/Poor remained so in the late postoperative period. Thus, the final surgical outcome was found to be Excellent/Good in 78.6% of the cases and Fair/Poor in 21.4%.

10.3389/fonc.2023.1137924

TABLE 3 Adjuvant treatment and final results.

Variables	Category	N	%
Adjuvant Treatment			
Histology	Invasive breast carcinoma NST	12	85,7
	Invasive lobular carcinoma	1	7,1
	Invasive breast carcinoma NST + papillary	1	7,1
IHC	Luminal A	1	7,1
	Luminal B	8	57,2
	Triple negative	4	28,6
	Hybrid Luminal	1	7,1
Axillary surgery	Sentinel node biopsy	10	71,4
	Axillary dissection	4	28,6
Chemotherapy	No	1	7,1
	Neodiuvant	9	64,3
	Adjuvant	4	27,6
Endocrine Therapy	No	4	28,6
	Tamoxifen	3	21,4
	Aromatase inhibitor	7	50
Final Result			
Excelent/Good (Harvard Scale)	Early post-operative	12	85,7
	Late post-operative	11	78,6
Excelent/Good (BCCT.core)	Early post-operative	11	78,6
	Late post-operative	13	92,9

In the evaluation by the BCCT.core software, 11 (78.6%) cases were categorized as Excellent/Good in the initial postoperative period, 10 of these cases remained classified as such in the late postoperative period and there was a worsening of symmetry in 1 case, which was the same case mentioned above, in which the patient developed steatonecrosis. On the other hand, in the initial postoperative evaluation, 3 cases were categorized as Fair/Poor but all of them had an improvement in symmetry in the final postoperative evaluation, a fact that we can relate to the decrease in post-surgical edema and also due to the improvement in the quality of the photo taken correctly in a standardized fashion in the late postoperative period. The evaluation of the photo by the software can be hampered by poor positioning of the patient and poor image quality, impacting the result. Finally, evaluating the final surgical outcome using the BCCT.core software, we found 92.9% (13 cases) of Excellent/Good results and 7.1% (1 case) of Fair/Poor results.

The final outcome of the proposed technique amounted to an excellent/good rating of 78.6% according to the Harvard scale and 92.9% as per the BCCT.core software – figures that suggest that this technique can deliver satisfactory post-surgical symmetry results both according to subjective as well as objective criteria. These values are close to the ratings provided in the initial post-operative period, which demonstrates that satisfactory aesthetic results could already be seen in the initial post-operative period – an important aspect, especially at a time when patients are known to be emotionally vulnerable.

In our study, we identified that the percentage of cases evaluated as Excellent/Good by the Harvard scale applied by the specialists

FIGURE 3
Late post-operative image of the same case.

FIGURE 4
Preoperative, early post-operative and late post-operative images of typical cases treated using advancement-rotation flap technique.

was lower than the percentage of cases that are in this same category by the evaluation of the BCCT.core software. One of the facts that could explain this difference would be the evaluation of the scar incorporated into the evaluation of symmetry which, when performed by specialists, has a more rigorous judgment than the software which, as we know through other studies, has a deficit in the evaluation of the scar.[29]

Patients' self-assessments were also recorded and achieve excellent/good ratings in 100% of the cases. Some studies suggest that patients are likely to rate their own aesthetic results higher than the software or the expert panel (28). It is also known that patients' self-assessments provide important information not only with respect to the aesthetic results of the breast, but also its functional aspects. Thus, more recent studies that included surgical outcome assessments have indicated that patients' self-assessments should be carried out alongside expert panels and software assessments, since self-assessments reflect the patients' psychological adaptation to both the aesthetic as well as functional aspects of the breast (28, 29).

The contrasting results arising from the different assessment methods makes a case for their complementarity and the importance of using and reporting distinct subjective and objective tools to assess the aesthetic outcomes of breast surgery (29).

Conclusion

The dermoglandular advancement-rotation flap technique enables tumor resection with satisfactory margins and the correction of oncological defects in cases that are challenging due to location, size of the tumor or need for skin removal. Despite our small series, we found good results with oncological safety and it proved to be an effective technique to avoid mastectomy in selected cases.

Furthermore it provides good symmetry, as assessed both subjectively as well as objectively, and allows patients to undergo unilateral conservative surgery.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

MS contributed to the conception and design of the study, surgical procedures, use of software for symmetry assessment and statistical analysis, draft e wrote the manuscript. FB contributed to the conception and design of the study, surgical procedures, evaluations in postoperative appointments. JR contributed on surgical procedures, evaluations in postoperative appointments. TJ contributed on surgical procedures. VD contributed to the conception and design of the study, surgical procedures, evaluations in postoperative appointments. All authors contributed to the article and approved the submitted version.

Funding

This study is derived from the academic master's degree of author MS, for which she received a CAPES scholarship.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

References

1. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* (2002) 347(16):1233–41. doi: 10.1056/NEJMoa022152

2. Fisher B, Redmond C, Poisson R, Margolese R, Wolmark N, Wickerham L, et al. Eight-year results of a randomized clinical trial comparing total mastectomy and lumpectomy with or without irradiation in the treatment of breast cancer. *N Engl J Med* (1989) 320(13):822–8. doi: 10.1056/NEJM198903303201302

3. Fisher B, Bauer M, Margolese R, Poisson R, Pilch Y, Redmond C, et al. Five-year results of a randomized clinical trial comparing total mastectomy and segmental mastectomy with or without radiation in the treatment of breast cancer. *N Engl J Med* (1985) 312(11):665–73. doi: 10.1056/NEJM198503143121101

4. Veronesi U, Saccozzi R, Del Vecchio M, Banfi A, Clemente C, De Lena M, et al. Comparing radical mastectomy with quadrantectomy, axillary dissection, and radiotherapy in patients with small cancers of the breast. *N Engl J Med* (1981) 305 (1):6–11. doi: 10.1056/NEJM198107023050102

5. Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med* (2002) 347(16):1227–32. doi: 10.1056/NEJMoa020989

6. Hartmann-Johnsen OJ, Kåresen R, Schlichting E, Nygård JF. Survival is better after breast conserving therapy than mastectomy for early stage breast cancer: a registry-based follow-up study of Norwegian women primary operated between 1998 and 2008. *Ann Surg Oncol* (2015) 22(12):3836–45. doi: 10.1245/s10434-015-4441-3

7. Agarwal S, Pappas L, Neumayer L, Kokeny K, Agarwal J. Effect of breast conservation therapy vs mastectomy on disease-specific survival for early-stage breast cancer. *JAMA Surg* (2014) 149(3):267–74. doi: 10.1001/jamasurg.2013.3049

8. Litière S, Werutsky G, Fentiman IS, Rutgers E, Christiaens MR, Van Limbergen E, et al. Breast conserving therapy versus mastectomy for stage I-II breast cancer: 20 year follow-up of the EORTC 10801 phase 3 randomised trial. *Lancet Oncol* (2012) 13 (4):412–9. doi: 10.1016/S1470-2045(12)70042-6

9. van Dongen JA, Voogd AC, Fentiman IS, Legrand C, Sylvester RJ, Tong D, et al. Long-term results of a randomized trial comparing breast-conserving therapy with mastectomy: European organization for research and treatment of cancer 10801 trial. *J Natl Cancer Inst* (2000) 92(14):1143–50. doi: 10.1093/jnci/92.14.1143

10. Catsman CJLM, Beek MA, Voogd AC, Mulder PGH, Luiten EJT. The COSMAM TRIAL a prospective cohort study of quality of life and cosmetic outcome in patients undergoing breast conserving surgery. *BMC Cancer*. (2018) 18(1):456. doi: 10.1186/s12885-018-4368-8

11. Cochrane RA, Valasiadou P, Wilson AR, Al-Ghazal SK, Macmillan RD. Cosmesis and satisfaction after breast-conserving surgery correlates with the percentage of breast volume excised. *Br J Surg* (2003) 90(12):1505–9. doi: 10.1002/bjs.4344

12. Baildam A, Bishop H, Boland G, Dalglish M, Davies L, Fatah F, et al. Oncoplastic breast surgery-a guide to good practice. *Eur J Surg Oncol* (2007) 33 Suppl 1:S1–23. doi: 10.1016/j.ejso.2007.04.014

13. Waljee JF, Hu ES, Newman LA, Alderman AK. Predictors of breast asymmetry after breast-conserving operation for breast cancer. *J Am Coll Surg* (2008) 206(2):274–80. doi: 10.1016/j.jamcollsurg.2007.07.029

14. Vieira RADC, Biller G, Silva FCBD, Silva JJD, Oliveira MA, Bailão-Junior A. New criteria for breast symmetry evaluation after breast conserving surgery for cancer. *Rev Col Bras Cir*. (2021) 48:e20202698. doi: 10.1590/0100-6991e-20202698

15. Clough KB, Cuminet J, Fitoussi A, Nos C, Mosseri V. Cosmetic sequelae after conservative treatment for breast cancer: classification and results of surgical correction. *Ann Plast Surgery*. (1998) 41(5):471–81. doi: 10.1097/00000637-199811000-00004

16. Gormley DE. A brief analysis of the burow's wedge/tri angle principle. *J Dermatol Surg Oncol* (1985) 11(2):121–3. doi: 10.1111/j.1524-4725.1985.tb02978.x

17. Bayeh HA, Paulinelli RR, Soares LR, Prates AL, Morais PC, Albuquerque ICS, et al. The cosmetic outcome of breast reconstruction: reproducibility of different methods assessed by different professionals. *Mastology* (2019) 29(4):173–9. doi: 10.29289/25945394201920190001

18. Cardoso MJ, Cardoso J, Amaral N, Azevedo I, Barreau L, Bernardo M, et al. Turning subjective into objective: the BCCT.core software for evaluation of cosmetic results in breast cancer conservative treatment. *Breast* (2007) 16(5):456–61. doi: 10.1016/j.breast.2007.05.002

19. Cardoso MJ, Santos AC, Cardoso J, Barros H, Cardoso De Oliveira M. Choosing observers for evaluation of aesthetic results in breast cancer conservative treatment. *Int J Radiat Oncol Biol Phys* (2005) 61(3):879–81. doi: 10.1016/j.ijrobp.2004.06.257

20. Cardoso MJ, Cardoso JS, Vrieling C, Macmillan D, Rainsbury D, Heil J, et al. Recommendations for the aesthetic evaluation of breast cancer conservative treatment. *Breast Cancer Res Treat* (2012) 135(3):629–37. doi: 10.1007/s10549-012-1978-8

21. Cardoso MJ, Cardoso JS, Wild T, Krois W, Fitzal F. Comparing two objective methods for the aesthetic evaluation of breast cancer conservative treatment. *Breast Cancer Res Treat* (2009) 116(1):149–52. doi: 10.1007/s10549-008-0173-4

22. Cardoso JS, Cardoso MJ. Towards an intelligent medical system for the aesthetic evaluation of breast cancer conservative treatment. *Artif Intell Med* (2007) 40(2):115–26. doi: 10.1016/j.artmed.2007.02.007

23. Trakis S, Lord H, Graham P, Fernandez R. Reliability of the BCCT.core software in evaluation of breast cosmesis - a systematic review. *J Med Imaging Radiat Oncol* (2021) 65(6):817–25. doi: 10.1111/1754-9485.13190

24. Losken A, Hamdi M. Partial breast reconstruction: current perspectives. *Plast Reconstr Surg* (2009) 124(3):722–36. doi: 10.1097/PRS.0b013e3181b179d2

25. Baildam AD. Oncoplastic surgery for breast cancer. *Br J Surg* (2008) 95(1):4–5. doi: 10.1002/bjs.6098

26. Paulinelli RR, de Oliveira VM, Bagnoli F, Chade MC, Alves KL, Freitas-Junior R. Oncoplastic mammaplasty with geometric compensation-a technique for breast conservation. *J Surg Oncol* (2014) 110(8):912–8. doi: 10.1002/jso.23751

27. Paulinelli RR, de Oliveira VM, Bagnoli F, Letzkus JB, Chade MC, Picoli LB, et al. Oncoplastic mammaplasty with geometric compensation: evolution of the technique, outcomes and follow-up in a multicentre retrospective cohort. *J Surg Oncol* (2020) 121 (6):967–74. doi: 10.1002/jso.25860

28. Heil J, Dahlkamp J, Golatta M, Rom J, Domschke C, Rauch G, et al. Aesthetics in breast conserving therapy: do objectively measured results match patients' evaluations? *Ann Surg Oncol* (2011) 18(1):134–8. doi: 10.1245/s10434-010-1252-4

29. Haloua MH, Krekel NM, Jacobs GJ, Zonderhuis B, Bouman MB, Buncamper ME, et al. Cosmetic outcome assessment following breast-conserving therapy: a comparison between BCCT.core software and panel evaluation. *Int J Breast Cancer* (2014) 2014:716860. doi: 10.1155/2014/716860

frontiers | Frontiers in Oncology

TYPE Brief Research Report
PUBLISHED 17 May 2023
DOI 10.3389/fonc.2023.1151932

OPEN ACCESS

EDITED BY
Alba Di Leone,
Agostino Gemelli University Polyclinic (IRCCS), Italy

REVIEWED BY
Lorenzo Scardina,
Agostino Gemelli University Polyclinic (IRCCS), Italy
Elena Jane Mason,
Fatebenefratelli Hospital, Italy

*CORRESPONDENCE
Rafael José Fábio Pelorca
rafaelpelorca@hotmail.com

RECEIVED 27 January 2023
ACCEPTED 02 May 2023
PUBLISHED 17 May 2023

CITATION
Pelorca RJF, de Oliveira-Junior I and da Costa Vieira RA (2023) Oncoplastic surgery for Paget's disease of the breast. *Front. Oncol.* 13:1151932. doi: 10.3389/fonc.2023.1151932

Oncoplastic surgery for Paget's disease of the breast

Rafael José Fábio Pelorca[1]*, Idam de Oliveira-Junior[1,2,3] and René Aloisio da Costa Vieira[1,2,4]

[1]Programa de Pós-Graduação em Tocoginecologia, Faculdade de Medicina de Botucatu, Botucatu, SP, Brazil, [2]Programa de Pós-Graduação em Oncologia, Barretos Cancer Hospital, Barretos, SP, Brazil, [3]Departamento de Mastologia e Reconstrução Mamária, Barretos Cancer Hospital, Barretos, SP, Brazil, [4]Departamento de Cirurgia Oncológica, Divisão de Mastologia, Hospital de Câncer de Muriaé, Muriaé, MG, Brazil

Introduction: Paget's disease of the breast (PDB) is a rare nipple entity associated with multifocality. Due to its location, resection of the entire nipple-areolar complex is necessary. Historically central quadrantectomy and mastectomy have the surgical treatments of choice. The feasibility of oncoplastic breast surgery (OBS) for PDB is unknown.

Methods: This was a retrospective study performed in a Brazilian oncological hospital. We evaluated the factors related to the performance of OBS in PDB. In addition, the impact of OBS on local recurrence and survival was analysed. Comparisons were made between groups using the chi-square test, Mann–Whitney U test, and Kaplan–Meier method. To assess the impact factor of the variables on the performance of OBS, logistic regression was performed.

Results: Eighty-five patients were evaluated. OBS was performed in 69.4% (n=59), and of these, 16 (27.2%) were symmetrized with contralateral surgery. Mastectomy without reconstruction was performed in 28.3% of the patients. The primary procedure performed was mastectomy with reconstruction (n=38; 44.7%), and the preferential technique for immediate reconstruction was skin-sparing mastectomy with prosthesis; for late reconstruction, the preferred technique was using the latissimus dorsi. Breast conserving-surgery was performed in 27.0% (n=23), primarily using the plug-flap technique (OBS). Age was associated with the use of OBS; as patients aged 40-49 exhibited a higher rate of OBS (p = 0.002; odds ratio 3.22). OBS did not influence local recurrence (p=1.000), overall survival (p=0.185), or cancer-specific survival (p=0.418).

Conclusion: OBS improves options related to surgical treatment in PDB without affecting local recurrence or survival rates.

KEYWORDS

Paget's disease, mammary, breast neoplasms, breast reconstruction, plastic surgery, oncoplastic surgery

Introduction

The surgical treatment of breast cancer has changed radically in the last two decades, with improvements in mastectomy, breast-conserving surgery (BCS) and axillary preservation. The oncological safety of BCS has been extrapolated to larger tumours, provided a favourable breast/tumour ratio is maintained (1, 2). Likewise, indications for neoadjuvant chemotherapy have increased the rates of BCS (3), and when mastectomy is indicated, immediate reconstruction using implants or even myocutaneous flaps has become common practice (4).

In this context, oncoplastic breast surgery (OBS) has recently emerged (5), in which plastic surgery techniques are added to the therapeutic arsenal for the treatment of breast cancer. Thus, another dimension in the approach to the breast/tumour relationship has been created, expanding the indications for BCS (2), even for larger tumours, thus giving rise to the concept of extreme oncoplasty (1). In the case of mastectomies, immediate reconstruction with myocutaneous flaps was replaced by implants, which is associated with shorter surgical duration, lower complication rates and easier performance (6, 7). Thus, despite conceptual questioning, some authors have begun to consider OBS techniques both for BCS (2, 8) and breast reconstruction (6, 9, 10). As breast surgeons become qualified, the range of surgical options will expand, improving patient quality of life (11) with no increase in the risk of recurrence (12, 13).

Due to its central location, the surgical treatments for Paget's disease of the breast (PDB) have also been modified with OBS, which allows the use of different technical options (14). Patients initially were submitted to BCS with purse-string suturing or spindle incision, but now with OBS (14–16), patients are treated with local skin flaps using the plug-flap technique or with pedicle surgery or other techniques, which prepare the areolar region for future tattooing (16, 17). If the patient demonstrates indications for mastectomy, skin-sparing mastectomy with immediate reconstruction with a prosthesis (16) is one possibility and presents with good aesthetic results (4).

However, the spectrum of OBS techniques performed for PDB is unknown (18) given the rarity of this pathology and the need for a team trained in OBS. Few published studies have described OBS for PD (19, 20). Accordingly, we sought to evaluate this relationship in an oncology referral service where OBS is systematically performed.

Materials and methods

This retrospective study was approved by the institutional Research Ethics Committee under numbers 657293 and CAAE 31046314.5.0000.5437. Patients with PDB treated at a tertiary cancer hospital between 2000 and 2021 were evaluated.

The patients were selected based on the presence of Paget's disease in the surgical specimen of the breast according to the pathological database of the institution. The clinicopathological and surgical data of the patients, as well as data on local recurrence and survival, were obtained from the medical records and evaluated.

To evaluate tumour size, the total size of the tumour was considered, regardless of the associated *in situ* or invasive component. Likewise, in the molecular subtype analysis, the invasive component was evaluated, and in its absence, the ductal carcinoma *in situ* component was evaluated.

We sought to evaluate aspects related to surgery in PDB, particularly the use of oncoplasty techniques. We refer to oncoplastic breast surgery (OBS) for techniques used for breast-conserving surgeries (8) and techniques used for breast reconstruction after mastectomy (9, 10).

Patients were followed from the first to the last consultation at the hospital. If the patient did not return for more than twice the period stipulated in the consultation, the she was considered to have been lost to follow-up. Death was evaluated based on its cause. We considered death from cancer to be the presence of death related to breast cancer. Based on this definition, we examined overall survival (OS) and cancer-specific survival (CSS). The last date of patient evaluations was 29/09/2022.

In the statistical analysis, descriptive statistics were performed for categorical and continuous variables (Table 1). Continuous numbers were reported by means and standard deviation (± SD). We also sought to compare potential factors associated with the performance of OBS. The chi-square test was used to compare categorical variables; when there were fewer than five patients in a category, Fisher's test was performed. For continuous variables, a normality test was performed, and the Mann–Whitney U test was performed for non-normally distributed variables. For the variables associated with OBS, logistic regression was performed to evaluate the impact of each variable on the final result (Supplementary Table 1). The Kaplan–Meier method was used to analyse OS and CSS, and the log-rank method was used to evaluate the impact of OBS on survival. Differences were considered significant for p values <0.05. IBM SPSS® for Mac® was used for data collection, tabulation and all statistical analyses.

Results

During the study period, 85 women with PDB were evaluated. The mean age was 52.2± 13.3 years. Most patients were treated after 2010 (87.0%), and the majority were aged between 40-59 years (56.5%). A minority exclusively had PD (7.1%), and the other cases included DCIS (18.8%), invasive carcinoma (57.6%) and DCIS with invasive carcinoma (16.5%). From a clinical perspective, 58.8% had visible areolar disease, and 57.6% had a palpable tumour. PDB was unilateral in all patients, with a higher frequency on the right side (58.8%), despite the low presence of bilateral breast cancer (4.7%). The mean total size of the tumours was 4.1±3.3 cm. With respect to clinical stage, 27.1% had *in situ* disease, and one patient had metastatic disease at diagnosis (1.2%). With respect to the molecular subtype, HER2-overexpressed tumours represented50.6% of cases, followed by HER2-positive Luminal B tumours (22.9%).

In the evaluation of surgical treatment, 23 patients (27.0%) underwent BCS. Among those who underwent mastectomy (73.0%; n=62), 54.8% (n=34) underwent immediate reconstruction, typically with submuscular breast prostheses (n=31). Late reconstruction was performed in four patients (6.4%), three with latissimus dorsi and prosthesis (n=3), and one with sufficient skin,

10.3389/fonc.2023.1151932

TABLE 1 Characteristic of the groups related to Oncoplastic Breast Surgery for Paget disease.

Variable	Category	OBS absent	OBS present	Total	p
Age	mean + SD	58.0 ± 15.9	49.0 ± 11.7	52.2 ± 13.3	0.014
Total tumor size	mean + SD	2.2 ± 1.6	5.0 ± 4.0	4.1 ± 3.3	0.548
Follow up	mean + SD	66.5 ± 39.2	71.9 ± 45.3	71.2 ± 43.3	0.932
Age range	< 40	4	8	12 (14.1)	0.01
	40-49	3	25	28 (32.0)	
	50-59	7	13	20 (23.5)	
	60-69	6	11	17 (20.0)	
	> 70	6	2	8 (9.4)	
Treatment period	2000-2009	4	7	11 (12.9)	0.737
	2010-2013	10	18	28 (32.9)	
	2014-2017	4	11	16 (18.8)	
	2018-2021	7	23	30 (35/3)	
Paget	Clinic	15	35	50 (58.8)	0.475
	Pathologic	11	24	35 (41.2)	
Tumor	Palpable	17	32	49 (57.6)	0.475
	Non-palpable	9	27	36 (42.4)	
Laterality	Right	15	35	50 (58.8)	1.000
	Left	11	24	35 (41.2)	
Bilateral tumor	Absent	25	56	81 (95.3)	1.000
	Present	1	3	4 (4.7)	
Histology	PD alone	0	6	2 (2.4)	0.131
	PD+ in situ	6	10	20 (23.5)	
	PD+ invasive	18	31	49 (57.6)	
	PD+ *in situ* + invasive	2	12	14 (16.5)	
Clinical stage	0	5	18	23 (27.1)	0.05
	1	3	17	20 (23.5)	
	2	9	8	17 (20.0)	
	3	8	16	24 (28.2)	
	4	1	0	1 (1.2)	
Molecular	Luminal Her -	2	10	12 (14.5)	0.227
Subtype*	Luminal B Her +	9	10	19 (22.9)	
	Her +	11	31	42 (50.6)	
	Triple negative	4	6	10 (12.0)	
Local recurrence	Absent	25	55	81 (95.3)	1.000
	Present	1	3	4 (4.7)	
Death for cancer	Absent	22	55	76 (89.4)	0.276
	Present	4	5	9 (10.6)	
Death (overall)	Absent	19	51	70 (82.4)	0.215
	Present	7	8	15 (17.6)	

PD, Paget disease; *excluded missing information.

10.3389/fonc.2023.1151932

where pre-pectoral prosthesis was placed. Of the patients who underwent primary mastectomy without reconstruction, one required the use of the external oblique muscle for skin closure. Because external oblique muscle was used for skin closure, we not considered it as OBS. Overall, 27.0% (n=23) of the patients underwent BCS, and the majority underwent oncoplastic surgery (20 plug-flap, 1 pedicle). All patients had pathologically free margins. Thus, evaluating all surgeries performed (final results), OBS was performed in 69.4% (n=59) of the patients, and of these, 16 (27.2%) were symmetrized to the contralateral breast. The flowchart of the surgical techniques performed is presented in Figure 1, and the main types of surgery performed are presented in Figure 2.

In the evaluation of factors related to OBS (Table 1), an association was found with age and clinical stage at diagnosis. However, in the multivariate analysis, only age was associated with OBS (p = 0.035); the use of OBS was lowest in patients over 70 years of age (Supplementary Table 1) and highest in patients in the 40-49–years age group (p=0.002), with an odds ratio of 3.22 [CI 3.39-184.50].

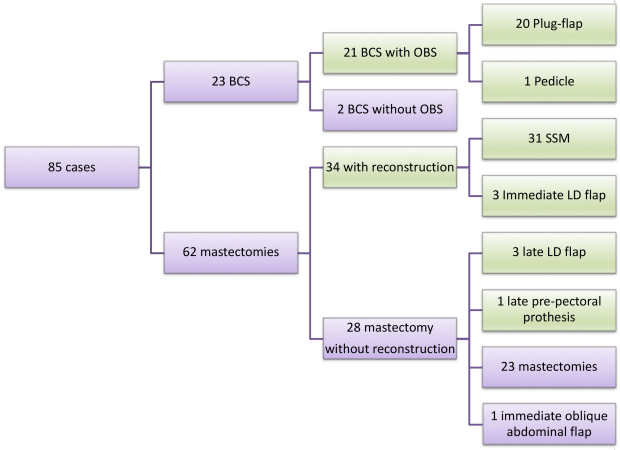


FIGURE 1
Surgery flowchart. OBS= oncoplastic breast surgery; BCS= breast conserving-surgery; LD= latissimus dorsi. Green = OBS; Purple for all group and non-OBS.

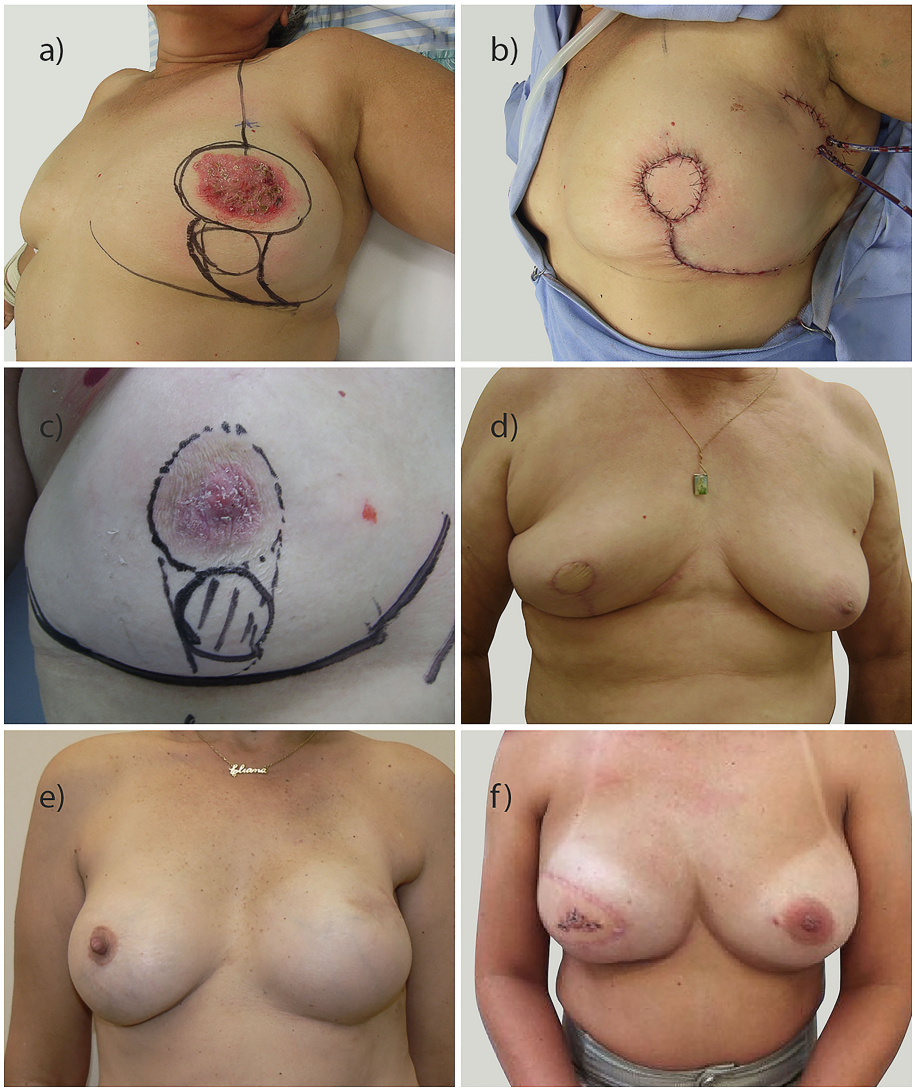


FIGURE 2
Examples of breast oncoplastic surgery performed. **(A–D)** conservative breast surgery with different plug-flap techniques; **(E)** reconstruction with prosthesis; **(F)** reconstruction with latissimus dorsi.

10.3389/fonc.2023.1151932

TABLE 2 Survival of patients with PDB in relation to the type of surgery.

Variable	Category	n	60 months	96 months	p (log rank)
Overall OS	–	85	89.1%	72.8%	–
OBS	Absent	30	89.3%	73.7%	0.558
	Present	55	88.3%	72.4%	
Initial OBS	BCS	2	100%	100%	0.675
	BCS + OBS	21	100%	68.6%	
	Mast.	28	88.4%	71.1%	
	Mast.+OBS	34	81.1%	76.1%	
BCS	BCS	2	100%	100%	0.400
	BCS + OBS	21	100%	68.6%	
Mastectomy	Mast.	28	88.4%	71.1%	0.523
	Mast.+OBS	34	81.1%	76.1%	
OBS	BCS	23	100%	74.1%	0.568
	Mast.	28	88.4%	71.1%	
	Mast.+OBS	34	81.1%	76.1%	
Overall CSS	–	85	92.3%	83.1%	–
OBS	Absent	30	100%	81.6%	0.785
	Present	55	91.3%	84.0%	
Initial OBS	BCS	2	100%	100%	0.709
	BCS + OBS	21	100%	90.0%	
	Mast.	28	92.9%	79.4%	
	Mast.+OBS	34	85.9%	80.5%	
BCS	BCS	2	100%	100%	0.400
	BCS + OBS	21	100%	90.0%	
Mastectomy	Mast.	28	92.9%	79.4%	0.523
	Mast.+OBS	34	85.9%	80.5%	
OBS	BCS	23	100%	74.1%	0.568
	Mast.	28	92.9%	79.4%	
	Mast.+OBS	34	85.9%	80.5%	

OS, Overall survival; CSS, cancer specific survival; OBS, oncoplastic breast surgery; Mast., mastectomy.

With regard to axillary surgical treatment, 41.2% underwent axillary lymphadenectomy. Adjuvant radiotherapy was performed for 60% (51) of patients, and fossa radiotherapy was performed for 3.5% (3) of patients. Due to the association with invasive disease, 57.6% (49 patients) underwent chemotherapy using various regimens.

For the patients undergoing chemotherapy, 16 were treated with a neoadjuvant regimen. Patients submitted to neoadjuvant chemotherapy had lower rate of OBS (17.1%- present versus 39.1%-absent). Trastuzumab was used in 30 patients (35.3%), primarily as an adjuvant therapy. Hormone therapy was used in 37 patients (43.5%), and tamoxifen (27.1%, n=23) was the primary hormonal medication.

In the mean follow-up period of 71.2± 43.3 months, all patients were followed. At the end of follow-up, 81.2% (n=69) of patients were alive without cancer, 1 (1.2%) developed lung metastasis, 10.6% (n=9) died secondary to disease progression, and 7.1% (n=6) died of non-cancer-related causes. Four patients experienced local recurrence, including patients treated with a variety of different surgical techniques (BCS-OBS, mastectomy without reconstruction, mastectomy with prosthesis, immediate mastectomy with latissimus dorsi reconstruction). The OS and CSS at 120 months were 69.6% and 83.1%, respectively.

OBS did not affect local recurrence or survival (Tables 1, 2). The presence or absence of OBS (Supplementary Figure 1) did not affect

OS (p=0.558) or CSS (p=0.785). Furthermore, the type of surgery performed did not affect OS or CSS (Table 2; Supplementary Figure 1).

Discussion

PDB is a rare entity, generally described in retrospective studies or large databases. Because most series include fewer than one hundred patients (19, 21–23), sample size is limitation; however, we reported 85 cases over 21 years.

Clinically, PDB is characterized by areolar changes such as eczema, desquamation, ulceration or bleeding (24) and a high rate of multifocality (25, 26). PDB has been described separately or in association with carcinoma in situ, invasive breast cancer or both (19, 26, 27), as seen in the current cohort. Because it is a clinical and/or pathological alteration, selected cases that show the clinical characteristics of PDB and subclinical diseases have been presented together in many review articles (28).

Due to the multifocal nature of PDB, simple central resection results in incomplete removal of the lesion in many cases (26). Thus, imaging evaluation is essential in the surgical planning for PDB (29, 30). Mammography typically reveals microcalcifications but can be negative in 50% of cases. The presence of nodulation is generally associated with invasive disease, which can be visualized on mammography and ultrasonography. Magnetic resonance imaging (MRI) of the breast, in turn, assists in the evaluation of new findings, and PDB is currently considered one of the indications for MRI (29, 30). However, its usefulness in radical surgical treatment, i.e., mastectomy, is unknown.

In recent years, with a better understanding of the disease, most patients with PDB and HER 2 expression (26), were submitted to targeted therapies. However, this association has not yet been thoroughly evaluated in the literature.

In previous studies, choices of surgical treatment have been limited to mastectomy or BCS through central quadrantectomy (19, 21, 22), which requires free surgical margins and radiotherapy (19, 30, 31). Depending on the multifocality and extension of the lesion, mastectomy is necessary (32–34). In general, the BCS rate is lower than that of mastectomy, ranging from 10% to 38% (18, 21–23, 27, 33), although one study reported a BCS rate of 60% (19). Past articles reported the feasibility of BCS without reference to the technique (21, 22, 30), although these studies were published when BCS was commonly performed with spindle incisions or purse-string sutures (24).

The surgical treatment of breast cancer has become more complex with the addition of oncoplastic surgery techniques (5), which require adequate treatment planning based on the tumor/breast volume ratio, the presence of ptosis and the tumor location (1, 5, 17, 35). In this regard, due to the preferential central location of PDB, central quadrant resection methodologies have become of great importance in preoperative planning (14, 17, 35, 36). Generally, the Grisotti technique, inferior pedicle reduction or inverted T resection is used (17, 37). The nipple-areola complex (NAC) is resected, and in its place, the tissue can be sutured or the NAC can be replaced by a circumferential island of skin that will be tattooed in the future (14, 37). Specific techniques (Supplementary Figure 2), including the Grisotti technique (17), mammoplasty, glandular remodeling (14, 36), and geometric compensation (38), allow the skin total circumference to be created and replace in the local of areola, or when it is difficult, the use of half-moon technique (superoinferior or mediolateral local flaps). Other repair possibilities include the use of locoregional skin flaps (15) and the latissimus dorsi myocutaneous flap for central filling (16, 20). Few articles have focused on the conservative oncoplastic treatment of PDB (15, 16, 24), and few studies have described approaches to reconstruct the central region (16, 17, 19, 36). Despite the limited number of cases in our study, the present work includes one of the largest series of PDB patients undergoing OBS, with the Grisotti plug-flap technique being preferred (n = 20) when using local flaps. In one case, mammoplasty was performed, and a circular area of skin was preserved to allow the tattooing of an areola.

The American Society of Breast Surgeons (8) defines the OBS term exclusively for techniques associated with breast-conserving surgery, but non-American publications (6, 7, 9, 10, 39) also use this term for breast reconstruction after mastectomy, and we opted to use OBS for both conditions. Patients with PDB who undergo mastectomy typically do not undergo reconstruction. There are only a few articles in the literature reporting on patients with PDB who undergo mastectomy also undergo reconstruction, which can be performed with a prosthesis, as in skin-sparing mastectomy or skin-reducing mastectomy (19, 40, 41), a myocutaneous flap, such as the latissimus dorsi (37), or local flaps (15). In one study of 115 patients, 46 mastectomies (40%) were performed, of which 17 (36.9% of the mastectomies) were skin sparing/skin reducing mastectomies (19). Our sample represents the largest series of PDB patients undergoing breast reconstruction, which was performed immediately in 54.1% (33/61) of the mastectomies, preferably with a prosthesis only, or, in some selected cases, the latissimus dorsi and a prosthesis. The decision to perform latissimus dorsi surgery was based on the desire to achieve a good long-term outcome and on selected patients who potentially would not need radiotherapy. Late reconstruction was performed in 4 of the patients who were initially mastectomized, and the preferred treatment was reconstruction with a latissimus dorsi flap and prosthesis. It should be noted that for one patient who underwent mastectomy, delayed reconstruction was possible with a direct prosthesis without the need for an expander due to excess skin associated with nonperformance of radiotherapy, which provided good local conditions.

OBS surgery represents the last paradigm for surgical treatment of breast cancer, and whether it is performed depends on the indication for surgery as well as several additional factors. The presence of a plastic surgeon or a breast surgeon with knowledge of oncoplastic techniques is fundamental. Breast surgeons are currently improving their techniques, and as time goes by, they have become more skilled in performing these techniques, which has led to the expansion of indications for OBS (42). Although the tumor board discusses case management, the surgery board discusses the surgical indications (43, 44). Our group is composed of six surgeons with experience in performing OBS. Since 2010, all cases have been discussed by the tumor board. The surgeon chooses the type of

surgery based on the tumor, patient condition, radiological exams and intraoperative frozen sections. Multiple factors are associated with OBS (45), but the surgeon is not a variable associated with OBS because all surgeons are trained in the approach. Few case series have reported on the use of OBS for PDB (19, 20). Our study includes the largest series of patients with PDB undergoing OBS. There was an apparent selection bias for OBS, as it was more likely to be performed in patients in the 40-49 age group, an age group that has previously been described in the literature as being likely to undergo BCS (45).

We opted to evaluate only conditions related to OBS and local recurrence to ensure the focus of this article is surgery. The local recurrence rate for PDB was low (4.7%), which has been observed in other studies (23, 46). The rate of local recurrence was different following different surgical techniques, but despite these results, OBS was not associated with an increased rate of local recurrence. Another study is underway to evaluate the conditions related to distant recurrence and factors related to survival in PDB.

We sought to present the total extent of the disease, which is the sum of the invasive disease and disease in situ, and the factors influencing surgical treatment. Thus, even with large tumors, OBS was performed in a considerable proportion of patients. In the presence of *in situ* disease, surgical treatment does not affect survival; however, whether patients with invasive disease experience worse (33) or similar survival outcomes after adjustment for different variables (47, 48) remains unknown. Similarly, the presence of a palpable lesion is associated with a worse prognosis (28). These factors are likely influenced by the conditions of the invasive disease. It is worth noting that the association of PDB with the Her2 molecular subtype (26) may be related to a worse prognosis for these patients, but paired case –control studies evaluating this association are needed. In this study, we sought to focus more on the conditions associated with surgery and OBS, which did not influence OS or CSS.

The primary limitation of this study is that it is a retrospective evaluation; however, it is difficult to perform prospective studies of rare diseases and evaluate nonadherence to OBS, as they are based on case selection and patient discussion. Because of the retrospective nature of the analysis, it was not possible to evaluate cosmesis and quality of life in our patients. OBS was shown in the present study to be feasible, and its performance was not associated with local recurrence, nor did it influence survival, thus justifying OBS for PDB.

As surgeons become more experienced in performing OBS, more patients with PDB will undergo OBS. We anticipate future publications on the topic, but we are the first to report a high rate of OBS for PDB.

Conclusion

OBS improves options related to surgical treatment for patients with PDB without affecting local recurrence or survival rates. To this end, it is necessary to select appropriate cases by means of clinical evaluation and imaging, and surgeons must be aware of the various OBS techniques.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Research Ethics Committee from Barretos Cancer Hospital under numbers 657293 and CAAE 31046314.5.0000.5437. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

RP and RV conceived and wrote the manuscript. RP and IdO evaluated the data. RV supervised the study and performed data analysis. All authors contributed to the article and approved the submitted version.

Funding

The “Hospital de Câncer de Barretos” provided funding for publication.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher’s note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fonc.2023.1151932/full#supplementary-material

SUPPLEMENTARY FIGURE 1
Actuarial survival associated with OBS. **(A, B)** Cancer-Specific Survival; **(C, D)** Overall Survival. OBS= oncoplastic breast surgery; Mast.=mastectomy; BCS= breast conserving-surgery.

SUPPLEMENTARY FIGURE 2
More solutions for breast central disease reconstruction in women with small/medium breasts. **(A)** Single half-moon skin flaps; **(B)** Half-moon flaps associated with reduction mammoplasty technique; **(C)** geometric compensation with areolar resection (Previously published with author authorization).

References

1. Silverstein MJ. Radical mastectomy to radical conservation (Extreme oncoplasty): a revolutionary change. *J Am Coll Surg* (2016) 222(1):1–9. doi: 10.1016/j.jamcollsurg.2015.10.007

2. Oliveira-Junior I, Haikel RL, Vieira RAC. Breast-conserving treatment in oncoplastic times: indications, cosmesis, and quality of life. *Mastol* (2021) 31(1): e20200040. doi: 10.29289/2594539420200040

3. Vieira RA, Carrara GF, Scapulatempo Neto C, Morini MA, Brentani MM, Folgueira MA. The role of oncoplastic breast conserving treatment for locally advanced breast tumors. a matching case-control study. *Ann Med Surg (Lond)* (2016) 10:61–8. doi: 10.1016/j.amsu.2016.08.001

4. Agrawal A, Sibbering DM, Courtney CA. Skin sparing mastectomy and immediate breast reconstruction: a review. *Eur J Surg Oncol* (2013) 39(4):320–8. doi: 10.1016/j.ejso.2012.12.015

5. Audretsch W, Andree C. Is mastectomy still justified–and if, in which patients? *Onkologie* (2006) 29(6):243–5. doi: 10.1159/000093477

6. Zucca-Matthes G, Manconi A, da Costa Viera RA, Michelli RA, Matthes Ado C. The evolution of mastectomies in the oncoplastic breast surgery era. *Gland Surg* (2013) 2(2):102–6. doi: 10.3978/j.issn.2227-684X.2013.05.03

7. Atiyeh B, Dibo S, Zgheib E, Abbas J. Skin sparing/skin reducing mastectomy (SSM/SRM) and the concept of oncoplastic breast surgery. *Int J Surg* (2014) 12 (10):1115–22. doi: 10.1016/j.ijsu.2014.08.401

8. Chatterjee A, Gass J, Patel K, Holmes D, Kopkash K, Peiris L, et al. A consensus definition and classification system of oncoplastic surgery developed by the American society of breast surgeons. *Ann Surg Oncol* (2019) 26(11):3436–44. doi: 10.1245/s10434-019-07345-4

9. Weber WP, Haug M, Kurzeder C, Bjelic-Radisic V, Koller R, Reitsamer R, et al. Oncoplastic breast consortium consensus conference on nipple-sparing mastectomy. *Breast Cancer Res Treat* (2018) 172(3):523–37. doi: 10.1007/s10549-018-4937-1

10. Weber WP, Shaw J, Pusic A, Wyld L, Morrow M, King T, et al. Oncoplastic breast consortium recommendations for mastectomy and whole breast reconstruction in the setting of post-mastectomy radiation therapy. *Breast* (2022) 63:123–39. doi: 10.1016/j.breast.2022.03.008

11. Char S, Bloom JA, Erlichman Z, Jonczyk MM, Chatterjee A. A comprehensive literature review of patient-reported outcome measures (PROMs) among common breast reconstruction options: what types of breast reconstruction score well? *Breast J* (2021) 27(4):322–9. doi: 10.1111/tbj.14186

12. Losken A, Hart AM, Chatterjee A. Updated evidence on the oncoplastic approach to breast conservation therapy. *Plast Reconstr Surg* (2017) 140(5S Advances in Breast Reconstruction):14S–22S. doi: 10.1097/PRS.0000000000003951

13. Galimberti V, Vicini E, Corso G, Morigi C, Fontana S, Sacchini V, et al. Nipple-sparing and skin-sparing mastectomy: review of aims, oncological safety and contraindications. *Breast* (2017) 34(Suppl 1):S82–4. doi: 10.1016/j.breast.2017.06.034

14. Vieira RAC, Zucca-Matthes G, Haikel RL. Central quadrantectomy. In: Zucca-Matthes G, editor. *Oncoplastic breast surgery: practical application, 1st ed.* Portland, Oregon: ESKA publishing (2016). p. 223.

15. Kijima Y, Yoshinaka H, Hirata M, Nakajo A, Arima H, Okumura H, et al. Oncoplastic breast surgery combining partial mastectomy with immediate breast reshaping using a keyhole-shaped skin glandular flap for paget's disease. *Surg Today* (2014) 44(9):1783–8. doi: 10.1007/s00595-013-0687-1

16. Moustafa A, Fakhr I. Outcome of different oncoplastic surgical (OPs) techniques for centrally located breast cancer (CLBC). *J Egypt Natl Canc Inst* (2014) 26(4):203–9. doi: 10.1016/j.jnci.2014.10.003

17. Canturk NZ, Simsek T, Ozkan Gurdal S. Oncoplastic breast-conserving surgery according to tumor location. *Eur J Breast Health* (2021) 17(3):220–33. doi: 10.4274/ejbh.galenos.2021.2021-1-2

18. Lin CW, Chiang MH, Tam KW. Treatment of mammary paget disease: a systematic review and meta-analysis of real-world data. *Int J Surg* (2022) 107:106964. doi: 10.1016/j.ijsu.2022.106964

19. Scardina L, Di Leone A, Magno S, Franco A, Biondi E, Sanchez AM, et al. Paget's disease of the breast: our 20 years' experience. *Front Oncol* (2022) 12:995442. doi: 10.3389/fonc.2022.995442

20. Kijima Y, Yoshinaka H, Shinden Y, Hirata M, Nakajo A, Arima H, et al. Oncoplastic breast surgery for centrally located breast cancer: a case series. *Gland Surg* (2014) 3(1):62–73. doi: 10.3978/j.issn.2227-684X.2013.11.01

21. Singh A, Sutton RJ, Baker CB, Sacks NP. Is mastectomy overtreatment for paget's disease of the nipple? *Breast* (1999) 8(4):191–4. doi: 10.1054/brst.1999.0025

22. Kawase K, Dimaio DJ, Tucker SL, Buchholz TA, Ross MI, Feig BW, et al. Paget's disease of the breast: there is a role for breast-conserving therapy. *Ann Surg Oncol* (2005) 12(5):391–7. doi: 10.1245/ASO.2005.05.026

23. Caliskan M, Gatti G, Sosnovskikh I, Rotmensz N, Botteri E, Musmeci S, et al. Paget's disease of the breast: the experience of the European institute of oncology and review of the literature. *Breast Cancer Res Treat* (2008) 112(3):513–21. doi: 10.1007/s10549-007-9880-5

24. Markarian S, Holmes DR. Mammary paget's disease: an update. *Cancers (Basel)* (2022) 14(10):2422–31. doi: 10.3390/cancers14102422

25. Sandoval-Leon AC, Drews-Elger K, Gomez-Fernandez CR, Yepes MM, Lippman ME. Paget's disease of the nipple. *Breast Cancer Res Treat* (2013) 141(1):1–12. doi: 10.1007/s10549-013-2661-4

26. Kothari AS, Beechey-Newman N, Hamed H, Fentiman IS, D'Arrigo C, Hanby AM, et al. Paget disease of the nipple: a multifocal manifestation of higher-risk disease. *Cancer* (2002) 95(1):1–7. doi: 10.1002/cncr.10638

27. Zheng S, Song QK, Zhao L, Huang R, Sun L, Li J, et al. Characteristics of mammary paget's disease in China: a national-wide multicenter retrospective study during 1999-2008. *Asian Pac J Cancer Prev* (2012) 13(5):1887–93. doi: 10.7314/APJCP.2012.13.5.1887

28. Piekarski J, Jeziorski A, Baklinska M, Szymczak W, Zadrozny M, Berner J. Patients with paget disease of nipple and with palpable mass in breast have unfavorable prognosis. *J Exp Clin Cancer Res* (2004) 23(1):33–7.

29. Lim HS, Jeong SJ, Lee JS, Park MH, Kim JW, Shin SS, et al. Paget disease of the breast: mammographic, US, and MR imaging findings with pathologic correlation. *Radiographics* (2011) 31(7):1973–87. doi: 10.1148/rg.317115070

30. Helme S, Harvey K, Agrawal A. Breast-conserving surgery in patients with paget's disease. *Br J Surg* (2015) 102(10):1167–74. doi: 10.1002/bjs.9863

31. Polgar C, Orosz Z, Kovacs T, Fodor J. Breast-conserving therapy for paget disease of the nipple: a prospective European organization for research and treatment of cancer study of 61 patients. *Cancer* (2002) 94(6):1904–5. doi: 10.1002/cncr.10405

32. Fu W, Mittel VK, Young SC. Paget disease of the breast: analysis of 41 patients. *Am J Clin Oncol* (2001) 24(4):397–400. doi: 10.1097/00000421-200108000-00019

33. Chen CY, Sun LM, Anderson BO. Paget disease of the breast: changing patterns of incidence, clinical presentation, and treatment in the U. *S Cancer* (2006) 107 (7):1448–58. doi: 10.1002/cncr.22137

34. Yasir M, Khan M, Lotfollahzadeh S. *Mammary paget disease*. Treasure Island (FL: StatPearls (2022).

35. Gainer SM, Lucci A. Oncoplastics: techniques for reconstruction of partial breast defects based on tumor location. *J Surg Oncol* (2011) 103(4):341–7. doi: 10.1002/jso.21672

36. Pasta V, D'Orazi V, Merola R, Frusone F, Amabile MI, De Luca A, et al. Oncoplastic central quadrantectomies. *Gland Surg* (2016) 5(4):422–6. doi: 10.21037/gs.2016.04.01

37. Farouk O, Attia E, Roshdy S, Khater A, Senbe A, Fathi A, et al. The outcome of oncoplastic techniques in defect reconstruction after resection of central breast tumors. *World J Surg Oncol* (2015) 13:285. doi: 10.1186/s12957-015-0688-1

38. Franca FC, de Oliveira-Junior I, Morgan AM, Haikel RL, da Costa Vieira RA. Breast-conserving surgery with the geometric compensation/split reduction technique. indications, oncologic safety and cosmesis. a cohort series and systematic review of the literature. *Surg Oncol* (2022) 44:101839. doi: 10.1016/j.suronc.2022.101839

39. Kolacinska A. How can we improve education of breast surgeons across Europe? *Chirurgia (Bucur)* (2017) 112(4):365–6. doi: 10.21614/chirurgia.112.4.365

40. Fushimi A, Kinoshita S, Kudo R, Takeyama H. Incidental discovery of follicular lymphoma by sentinel lymph node biopsy and skin-sparing mastectomy for paget's disease associated with invasive breast cancer. *J Surg Case Rep* (2019) 2019(1):rjz008. doi: 10.1093/jscr/rjz008

41. Pu Q, Zhao Q, Gao D. Local recurrence of mammary paget's disease after nipple-sparing mastectomy and implant breast reconstruction: a case report and literature review. *World J Surg Oncol* (2022) 20(1):285. doi: 10.1186/s12957-022-02746-4

42. Vieira RAC, Matthes AGZ, Michelli RAD, Ribeiro GFP, Mendonça MLH, Bailão-Junior A, et al. Oncoplastic surgery and breast surgeon training. *Rev Bras Mastol* (2010) 20(2):66–70.

43. Franceschini G, Mason EJ, Di Leone A, Scardina L, Masetti R. Multidisciplinary management of mammary paget's disease: recommendations to optimize oncological and aesthetic outcomes. *Ann Ital Chir* (2022) 93:481–2.

44. Hudson-Phillips S, Cox K, Patel P, Al Sarakbi W. Paget's disease of the breast: diagnosis and management. *Br J Hosp Med (Lond)* (2023) 84(1):1–8. doi: 10.12968/hmed.2022.0439

45. de Oliveira-Junior I, da Silva IA, da Silva FCB, da Silva JJ, Sarri AJ, Paiva CE, et al. Oncoplastic surgery in breast-conserving treatment: patient profile and impact on quality of life. *Breast Care (Basel)* (2021) 16(3):243–53. doi: 10.1159/000507240

46. Li YJ, Huang XE, Zhou XD. Local breast cancer recurrence after mastectomy and breast-conserving surgery for paget's disease: a meta-analysis. *Breast Care (Basel)* (2014) 9(6):431–4. doi: 10.1159/000368431

47. Yao Y, Sun L, Meng Y, Zhuang Y, Zhao L, Yu Q, et al. Breast-conserving surgery in patients with mammary paget's disease. *J Surg Res* (2019) 241:178–87. doi: 10.1016/j.jss.2019.03.025

48. Wu Q, Ding X, Li J, Sun S, Zhu S, Wu J, et al. Surgical treatment in paget's disease with invasive ductal carcinoma: an observational study based on SEER. *Sci Rep* (2017) 7:45510. doi: 10.1038/srep45510

frontiers | Frontiers in Oncology

TYPE Methods
PUBLISHED 23 May 2023
DOI 10.3389/fonc.2023.1139461

OPEN ACCESS

EDITED BY
René Aloisio Da Costa Vieira,
Barretos Cancer Hospital, Brazil

REVIEWED BY
Darley Ferreira,
Federal University of Pernambuco, Brazil
Hebatallah Gamal El Din Mohamed Mahmoud,
Cairo University, Egypt

*CORRESPONDENCE
Thais Businaro Fernandes João
thatabusi@gmail.com

RECEIVED 07 January 2023
ACCEPTED 24 April 2023
PUBLISHED 23 May 2023

CITATION
Businaro Fernandes João T, de Oliveira VM, Bagnoli F, Bastos MCS, Rinaldi JF, Brenelli FP and Mateus EF (2023) How well are Brazilian mastologists (breast surgeons) trained in breast reconstruction and oncoplastic surgery? A study of the impact of a breast reconstruction and oncoplastic surgery improvement course.
Front. Oncol. 13:1139461.
doi: 10.3389/fonc.2023.1139461

How well are Brazilian mastologists (breast surgeons) trained in breast reconstruction and oncoplastic surgery? A study of the impact of a breast reconstruction and oncoplastic surgery improvement course

Thais Businaro Fernandes João[1]*, Vilmar Marques de Oliveira[1], Fábio Bagnoli[1], Maria Carolina Soliani Bastos[1], José Francisco Rinaldi[1], Fabrício Palermo Brenelli[2,3] and Evandro Fallaci Mateus[1]

[1]Irmandade da Santa Casa de Misericórdia de São Paulo (ISCMSP); Faculty of Medical Sciences of Santa Casa de São Paulo (FCMSCSP), São Paulo, Brazil, [2]State University of Campinas (UNICAMP), Campinas, Brazil, [3]Beneficiência Portuguesa de São Paulo, São Paulo, Brazil

Introduction: The breasts are a female symbol, impacts self-image and self-esteem. Breast reconstructive and oncoplastic surgeries have an important role in minimizing injuries. In Brazil less than a third of public health system (SUS) users have access to immediate reconstructive surgery. The low rate of breast reconstructions has multiple causes and the deficiency in availability and surgeons' technical qualification play a role. In 2010, the Breast Reconstruction and Oncoplastic Surgery Improvement Course was created by professors of the Mastology Department of Santa Casa de São Paulo and State University of Campinas (UNICAMP). The objectives of this study were to evaluate the impact of the techniques learned on patients' management by the surgeons enrolled in the Course, as well as to characterize their profile.

Methods: All students enrolled in the Improvement Course between 2010 and 2018 were invited to answer an online questionnaire. Students who did not agree to answer the questionnaire or answered them incompletely were excluded.

Results: Total students included: 59. The mean age: 48.9 years, male (72%) with more than 5 years of Mastology practice (82.2%), from all regions of Brazil, 1.7% from the North, 33.9% from the Northeast, 44.1% from the Southeast, and 12% from the South. Most of the students considered they had little or no knowledge of breast reconstruction (74.6%) and 91,5% did not consider they had enough aptitude to perform breast reconstructions after finishing residency. After the Course, 96.6% considered themselves apt to perform such surgeries. Over 90% of the students considered the Course had impacted their practice and changed their surgical strategy view. Before the Course, 84.8% of the students stated that less than half of their patients who were operated on for breast cancer had breast reconstruction, compared to 30.5% after the Course.

Conclusion: The Breast Reconstruction and Oncoplastic Surgery Improvement Course studied here positively impacted the mastologists' management of patients. New training centers worldwide can help a lot of women with breast cancer.

KEYWORDS

breast cancer, breast reconstruction, oncoplastic surgery, medical training, breast surgeon, reconstruction course, reconstructive breast surgery

Introduction

Breasts are symbol of femininity. They impact on self-image, self-esteem, and the relationship between women with themselves and the world. For these reasons, breast conservative surgery (BCS) is preferred by patients (1, 2).. It is estimated that up to 30% of women who undergo BCS will have some residual deformity, many times difficult to correct (3).. Breast reconstruction began in 1895 with Vincent Czerny (4, 5). Since then, several surgical techniques have been developed and refined, such as myocutaneous flaps (3–15). Breast reconstructive and oncoplastic surgeries have an important role in minimizing injuries (13). Techniques that involve reconstruction of resection defects either by volume replacement or by volume displacement are adaptations of conventional methods of breast reconstruction or breast reduction and are applied to correct defects generated by oncological surgery (13).

In many countries, immediate reconstructive surgery is routinely offered to patients without contraindications (14). However, this is not a reality in Brazil. Less than a third of SUS´s (Sistema Único de Saúde - Brazil´s public health system) users have access to immediate reconstructive surgery (1, 16) even though they have the lawful right of having so (1). This low rate of breast reconstructions has multiple causes. Brazil´s population has important socioeconomic, ethnic and cultural diversity, and the deficiency in availability and surgeons' technical qualification (1, 16), which makes quality care a challenge (17). A greater number of surgeons trained to perform breast reconstructions and breast repairs tend to increase the percentages of these types of surgeries. One of the alternatives is through training courses after medical specialization (16).

Developing countries, such as Brazil, tend to diagnose breast cancer at more advanced stages, which also makes it harder to carry out breast-conserving surgery (17–19).

In 2010, the Breast Reconstruction and Oncoplastic Surgery Improvement Course was created by professors of the Mastology Department of Santa Casa of São Paulo and one professor of State University of Campinas (UNICAMP) whose scope is precisely to spread the knowledge of surgical techniques for breast reconstruction.

Objectives

The objectives of this study were to evaluate the impact of the surgical techniques taught in the Course and to characterize the profile of Brazilian mastologists (breast surgeons).

Methods

The study was approved by the Ethics and Research in Human Beings Committee of the Santa Casa de Misericórdia of São Paulo (ISCMSP).

Between 2010 and 2013, the course was held at the Department of Obstetrics and Gynecology at ISCMSP. It was divided into 5 modules. Each module consisted of 4 hours of theoretical classes: Module 1: anatomy of the breast applied in surgery, pedicles and it´s different types and locoregional flaps (epigastric thoracic, lateral thoracic, Burrow); module 2: mastectomies and reconstructions with implants, types of prostheses and expanders, anterior chest wall anatomy, skin-sparing and nipple-sparing mastectomy and use of acellular dermal matrix (ADM); module 3: posterior thoracic wall anatomy, abdominal wall anatomy, autologous latissimus dorsi reconstruction with different techniques (extended, with prosthesis and fat grafted), single and bipedicled TRAM, flap autonomization; module 4: capsular contracture management, nipple-areola reconstruction, fat grafting, asymmetry correction; module 5: post-operative care and management of complications, proper use of surgical materials (suture, drains, dressings), instructions of patients after surgery, management of dehiscence and necrosis, management of exposed/infected protheses. The practical training had 16 hours of surgeries. On each module 8 patients, on average, were operated, with the majority of bilateral surgeries. The students were divided into groups for the practical part. This was carried out in the operating room, where the student, with the instructor of the course, performed the preoperative marking on the patient and the surgery. For each breast there was one professor teaching and guiding one student according to what was discussed and planned in the theoretical class.

This workload was divided into 2 days once a month. The activities started with the theoretical part and then the practical.

10.3389/fonc.2023.1139461

Between 2014 and 2018, the course was held at Hospital Beneficência Portuguesa in São Paulo, with 10 modules, in the same format. The themes were repeated in order to reinforce/sediment knowledge (e.g. module 1 classes were repeated on module 6). In this other format more classes were added in module 9: nipple-sparing mastectomy in irradiated breasts, pre and subpectoral reconstruction and nanolipografting; and module 10: discussion of clinical cases brought by colleagues (students) and discussion of scientific articles.

There were eight classes, seven of which were composed by 10 students and one of 12 students. The Course had seven professors-instructors. All mastologists with long experience in breast reconstructive surgery and its different techniques. Four of them are Ph.D, two MS and one MD.

All students were physicians with active Regional Medicine Council (CRMs), mastologists and with Specialist Title in Mastology (TEMa) by the Brazilian Society of Mastology and the Brazilian Medical Association. They underwent curriculum analysis and had preference for enrollment, those who had links with teaching hospitals, to serve as replicators of the acquired knowledge.

All students who took the course between 2010 and 2018 were invited. Sample calculation for this study was not necessary. They were contacted by email and phone calls and invited to answer an online questionnaire that had 38 fields and an average response time of 10 minutes. Students filled out an informed consent form agreeing to participate in the study. Exclusion criteria: students who did not agree to answer the questionnaire or answered them incompletely.

Statistical analysis

Qualitative characteristics were described using absolute and relative frequencies, and the quantitative characteristics evaluated were described using mean and standard deviation (20). The performances of the procedures were described, and their frequencies compared, before and after the course, using McNemar test (20). For statistical purposes, in this study, surgeries were divided into complex and simple. The criterion used for this classification is the skill required by the surgeon to perform the procedure. In the group of complex surgeries, were allocated: skin sparing mastectomy with prosthesis, skin sparing mastectomy with expander, nipple sparing mastectomy with prosthesis, nipple sparing mastectomy with expander, TRAM and Latissimus dorsi flap. Simple surgeries were: sectorectomy with breast remodeling with superior/inferior/superior-medial/superior-lateral pedicle, round block, fat grafting, capsulotomy/capsulectomy and Nipple-Areola Complex Reconstruction.

Likelihood ratio tests were used to verify associations between certain characteristics of technical behavior and changes after the course was completed, based on the surgeons' profiles. Mann-Whitney or Kruskal-Wallis tests were used to compare the percentages of changes in the reconstructions. The IBM-SPSS for Windows version 22.0 software was used to perform the analyses. For data tabulation, the Microsoft Excel 2010 software was used. The tests were performed with a significant level of 5% ($p<0,05$).

Results

This study included 59 students.

Table 1 contains personal characteristics and information about the students' technical training. The mean age is, today, 48.9 years, most of

TABLE 1 Personal characteristics and information about the students' technical training.

Variant	Description (N=59)
Age, average± SO	48,9 ± 8,2
Gender	
Female	16 (27,1)
Male	43 (72,9)
Regions	
North	1 (1'7)
Northeast	20 (33,9)
Southeast	26(44,1)
South	12 (20,3)
Medical Residency / Specialization	
General Surgery	14 (23,7)
Gynecology and Obstetrics	41 (69,5)
Others	4 (6,8)
Current sector of work	
Private	16 (27,1)
Private and public	42 (71,2)
Others	1 (1'7)
Consider your knowledge about breast reconstruction after leaving medical residency as:	
None	15 (25,4)
Very Little	29 (49,2)
Reasonable	9 (15,3)
Enough	1 (1' 7)
Good	3 (5,1)
Very Good	2 (3, 4)
Did you finish the Medical Residency feeling capable of performing Breast Reconstruction surgeries?	
Yes	5 (8, 5)
No	54 (91,5)
End time of specialization*	
Up to 5 years	10 (17,9)
6 to 10 years	17 (30,4)
11 to 20 years	17 (30,4)
More than 20 anos	12 (21,4)

* not all responded.

them were male (72%), working in public and private settings simultaneously (71.2%) and with over 5 years of Mastology practice (82.2%). The Improvement Course enrolled students from all regions of Brazil, 1.7% from the North, 33.9% from the Northeast, 44.1% from the Southeast, and 12% from the South. Most of the students considered they had little or no knowledge of breast reconstruction (74.6%) and almost all of them did not consider they had enough aptitude to perform breast reconstructions after finishing residency (91.5%).

In Table 2, 86.4% of the students reported having as motivation to start the course the need to expand their knowledge. Before the

TABLE 2 Description of characteristics and opinions about the Course.

Variant	Description (N=59)
What motivated you to start the course	
Need to expand knowledge	51 (86,4)
New and reievant subject	3 (5,1)
Incentive from a mastologist colleague	5 (8,5)
Did you feel able to perfonn reconstructions surgeries aner the course?	
Yes	57 (96,6)
No	2(3,4)
In which module have you already put Into practice what you learned? *	
1st	16 (28,6)
2nd	1 (1,8)
3rd	4(7,1)
4th	8 (14,3)
5th	8 (14,3)
6th	3(5,4)
7th	5 (8,9)
8th	2 (3,6)
9th	1 (1,8)
10th	8 (14,3)
Did you already perfonn any type of reconstruction before the course?	
Yes	26 (44,1)
No	33 (55,9)
Complexity of reconstructions before the course	
Did not perform	29 (49,2)
Simple	8 (13,6)
Complex	22 (37,3)
Who perfonned the reconstructions?	
The surgeon himself	6 (10,2)
Plastic surgeon	48 (81,4)
Mastologist surgeon who already perfOrmed reconstruction	5 (8,5)
If you didn't perfonn reconstruction before the course, why?	
Did not feel able to perform	48 (90,6)
There was no team to perfOrm	4(7,5)
I didn'think it was necessary	1 (1,9)
Complexity of reconstructions aner the course	
Simple	1 (1,7)
Complex	58 (98,3)
Quadrantectomy *I* Classic Sectorectomy	46 (78)
Did taking the course impact your daily clinical practice?	
Yes	
Changed the strategy surgical 1.1ew	54 (91,5)
I feel my patients are happier with the results.	32 (54,2)
The number of surgeries perfOrmed increased	21 (35,6)
Other impacts	3 (5,1)
Before taking the course, what Is the percentage of breast reconstructions performed In your service?	
0%	5 (8,5)
1-10%	24(40,7)
11-30"A.	13 (22)
31-50"A.	8 (13,6)
51-70"A.	1 (1,7)
n	5
Aner taking the course, which was the increase in the number of breast reconstructions in your service?	
!i%	1 (1,7)
1-10%	1 (1,7)
11-30"A.	3 (5,1)
31-50"A.	13 (22)
51-70"A.	15 (25,4)
71-90"A.	13 (22)
91-100%	13 (22)
Did taking the course encourage other mastologists colleagues to take the course as well?	
Yes	54 (91,5)
No	5 (8,5)
Do you keep improving/updating your knowledge in reconstruction?	
Yes	58 (98,3)
No	1 (1,7)

10.3389/fonc.2023.1139461

TABLE 2 Continued

Variant	Description (N=59)
Types of updates	
Taking other courses	23 (39)
Congresses *I* Symposiums *I* Conierences	54 (91,5)
Literature: Books and scientific articles	42 (71,2)
Other updates	7 (11,9)
How do you rate the course in general, average ± SO	91,5 ± 13,4
How do you rate the theoretical part, average ± SO	87,4 ± 17,9
How do you rate the practical part, average± so	90,5 ± 14,4

course, 44.1% already performed reconstructions in their surgeries, but 81.4% of them were performed by a plastic surgeon. Of these mastologists, 90.6% indicated that did not perform the reconstruction because believed they did not have the necessary technical skills.

After the Course, 96.6% considered themselves apt to perform such surgeries. After the 1st module, 28.6% put the acquired knowledge into practice. After half the course, this number reached 66.1%.

Over 90% of the students considered the Course had impacted their practice and changed their surgical strategy view. Before the Course, 84.8% of the students stated that less than half of their patients who were operated on for breast cancer had breast reconstruction, compared to 30.5% after the Course

Tables 3, 4 describe all the surgical techniques performed by the students, before and after completing the course. There was a statistically significant increase in the performance of all reconstruction techniques after completing the Course ($p < 0.05$). The muscle flap techniques (TRAM and latissimus dorsi) are the ones that students feel less confident/apt to perform.

TABLE 3 Description of the techniques used and the confidence in performing the techniques after the course.

Variant	Description (N =59)
Which types of reconstruction did you perform before the course?	
Sectorectomy with breast remodeling- superior pedicle	10 (16,9)
Sectorectomy with breast remodeling- superior- medial pedicle	7 (11,9)
Sectorectomy with breast remodeling- superior lateral pedicle	5 (8,5)
Sectorectomy with breast remodeling- inferior pedicle	4 (6,8)
Skin-sparing mastectomy with prosthesis/implant	12 (20,3)
Skin-sparing mastectomy with expander	9 (15,3)
Nipple-sparing mastectomy with prosthesis	8 (13,6)
Nipple-sparing mastectomy with expander	6 (10,2)
Round Block	19 (32,2)
TRAM	3 (5,1)
Latissimus Dorsi flap	6 (10,2)
Lipografting	2 (3,4)
Capsulectomy *I* Capsulotomy	6 (10,2)
Nipple-Areola Complex Reconstruction	3 (5,1)
After completing the course, which surgeries do you perform?	
Modified radical mastectomy without reconstruction	45 (76,3)
Sectorectomy with breast remodeling- superior pedicle	57 (96,6)
Sectorectomy with breast remodeling- superior- medial pedicle	56 (94,9)
Sectorectomy with breast remodeling- superior lateral pedicle	53 (89,8)
Sectorectomy with breast remodeling- inferior pedicle	56 (94,9)
Skin-sparing mastectomy with prosthesis/implant	56 (94,9)
Skin-sparing mastectomy with expander	53 (89,8)
Nipple-sparing mastectomy with prosthesis	58 (98, 3)
Nipple-sparing mastectomy with expander	52 (88,1)
Round Block	58 (98, 3)
TRAM	11 (18,6)
Latissimus Dorsi flap	33 (55, 9)
Lipografting	25 (42, 4)
Capsulectomy *I* Capsulotomy	50 (84, 7)
Nipple-Areola Complex Reconstruction	39 (66,1)
Which technique do you feel most confident and able to perform?	
Classic Quadrantectomy *I* Sectorectomy	31 (52, 5)
Modified radical mastectomy without reconstruction	32 (54,2)
Sectorectomy with breast remodeling- superior pedicle	48 (81, 4)
Sectorectomy with breast remodeling- superior- medial pedicle	41 (69, 5)
Sectorectomy with breast remodeling- superior lateral pedicle	36 (61)
Sectorectomy with breast remodeling- inferior pedicle	46 (78)
Skin-sparing mastectomy with prosthesis/implant	44 (74, 6)
Skin-sparing mastectomy with expander	39 (66,1)
Nipple-sparing mastectomy with prosthesis	43 (72, 9)
Nipple-sparing mastectomy with expander	37 (62, 7)
Round Block	41 (69,5)
TRAM	6 (10,2)
Latissimus Dorsi flap	23 (39)
Lipografting	15 (25, 4)
Capsulectomy *I* Capsulotomy	30 (50, 8)
Nipple-Areola Complex Reconstruction	30 (50, 8)

(Continued)

TABLE 3 Continued

TABLE 4 Description of techniques performed before and after the Course and results of comparative tests.

Types of reconstruction performed	Before	After	p
Sectorectomy with breast remodeling - superior pedicle	10 (16,9)	57 (96,6)	<0,001
Sectorectomy with breast remodeling - superior - medial pedicle	7 (11,9)	56 (94,9)	<0,001
Sectorectomy with breast remodeling - superior lateral pedicle	5 (8,5)	53 (89,8)	<0,001
Sectorectomy with breast remodeling - inferior pedicle	4 (6,8)	56 (94,9)	<0,001
Skin-sparing mastectomy with prosthesis/implant	12 (20,3)	56 (94,9)	<0,001
Skin-sparing mastectomy with expander	9 (15,3)	53 (89,8)	<0,001
Nipple-sparing mastectomy with prosthesis	8 (13,6)	58 (98,3)	<0,001
Nipple-sparing mastectomy with expander	6 (10,2)	52 (88,1)	<0,001
Round Block	19 (32,2)	58 (98,3)	<0,001
TRAM	3 (5,1)	11 (18,6)	0,008
Latissimus Dorsi flap	6 (10,2)	33 (55,9)	<0,001
Lipografting	2 (3,4)	25 (42,4)	<0,001
Capsulectomy/Capsulotomy	6 (10,2)	50 (84,7)	<0,001
Nipple-Areola Complex Reconstruction	3 (5,1)	39 (66,1)	<0,001
McNemar Test			

According to Table 5, male professionals performed more breast reconstruction surgery and with more complex techniques before the course ($p < 0.001$). Despite this, there was no statistically significant difference between the sexes regarding the gain in reconstructions in the services. ($p = 0.916$).

Finally, after analyzing the information in Tables 6-8, it is noted that the gains of students in relation to the complexity of

TABLE 5 Description of the complexities of the techniques performed before the Course and the change in the number of procedures in the service according to gender and results of statistical tests.

Variant	Gender		Total	p
	Female	Male		
Complexity before the course				<0,001#
Did not perform	14 (87,5)	15 (34,9)	29 (49,2)	
Simple	0 (0)	8 (18,6)	8 (13,6)	
Complex	2 (12,5)	20 (46,5)	22 (37,3)	
After the course, w hat is the increase in reconstruction rates in your service?				0,916*
0%	1 (6,3)	0 (0)	1 (1,7)	
1-10%	1 (6,3)	0 (0)	1 (1,7)	
11-30%	0 (0)	3 (7)	3 (5,1)	
31-50%	3 (18,8)	10 (23,3)	13 (22)	
51-70%	5 (31,3)	10 (23,3)	15 (25,4)	
71-90%	1 (6,3)	12 (27,9)	13 (22)	
91-100%	5 (31,3)	8 (18,6)	13 (22)	
Total	16 (100)	43 (100)	59 (100)	

#Likelihood ratio test; *Mann-Whitney Test.

TABLE 6 Description of the complexities of the techniques performed before the Course and the change in the number of procedures in the service according to the type of service and results of statistical tests.

Variant	Place of performance		Total	p
	Private	Private and Public		
Complexity before the course				0,981#
Did not perform	8 (50)	21 (50)	29 (50)	
Simple	2 (12,5)	6 (14,3)	8 (13,8)	
Complex	6 (37,5)	15 (35,7)	21 (36,2)	
After the course, w hat is the increase in reconstruction rates in your service?				0,101*
0%	1 (6,3)	0 (0)	1 (1,7)	
1-10%	0 (0)	1 (2,4)	1 (1,7)	
11-30%	0 (0)	3 (7,1)	3 (5,2)	
31-50%	3 (18,8)	10 (23,8)	13 (22,4)	
51-70%	2 (12,5)	13 (31)	15 (25,9)	
71-90%	4 (25)	9 (21,4)	13 (22,4)	
91-100%	6 (37,5)	6 (14,3)	12 (20,7)	
Total	16 (100)	42 (100)	58 (100)	

#Likelihood ratio test; *Mann-Whitney Test.

surgeries performed before and after the Course, having as parameters the places of performance (private or private and public service), the region of activity and the time of specialization were statistically similar (p> 0.05).

Discussion

Medicine is a dynamic science. However, it has a traditional and conservative bias, necessary for its own safety and validation as a

TABLE 7 Description of the complexities of the techniques performed before the Course and the change in the number of procedures in the service according to the region of trainning in Brazil and results of statistical tests.

Variant	Region				Total	p
	North	Northeast	Southeast	South		
Complexity before the course						0,629#
Did not perform	1 (100)	12 (60)	11 (42,3)	5 (41,7)	29 (49,2)	
Simple	0 (0)	2 (10)	3 (11,5)	3 (25)	8 (13,6)	
Complex	0 (0)	6 (30)	12 (46,2)	4 (33,3)	22 (37,3)	
After the course, what is the increase in reconstruction rates in your service?						0,938*
0%	0 (0)	0 (0)	1 (3,8)	0 (0)	1 (1,7)	
1-10%	0 (0)	1 (5)	0 (0)	0 (0)	1 (1,7)	
11-30%	0 (0)	1 (5)	1 (3,8)	1 (8,3)	3 (5,1)	
31-50%	0 (0)	4 (20)	4 (15,4)	5 (41,7)	13 (22)	
51-70%	1 (100)	6 (30)	8 (30,8)	0 (0)	15 (25,4)	
71-90%	0 (0)	4 (20)	6 (23,1)	3 (25)	13 (22)	
91-100%	0 (0)	4 (20)	6 (23,1)	3 (25)	13 (22)	
Total	1 (100)	20 (100)	26 (100)	12 (100)	59 (100)	

#Likelihood ratio test; *Mann-Whitney Test

TABLE 8 Description of the complexities of the techniques performed before the Course and the change in the number of procedures in the service according to graduation time and results of statistical tests.

Variável	Specialization time				Total	p
	Up to 5 years	6 to 10 years	11 to 20 years	> 20 years		
Complexity before the course						0,510#
Did not perform	3 (30)	10 (58,8)	9 (52,9)	6 (50)	28 (50)	
Simple	2 (20)	1 (5,9)	1 (5,9)	3 (25)	7 (12,5)	
Complex	5 (50)	6 (35,3)	After	3 (25)	21 (37,5)	
After the course, what is the increase in reconstruction rates in your service?						0,825*
O"k	0 (0)	0 (0)	1 (5,9)	0 (0)	1 (1,8)	
1-10%	1 (10)	0 (0)	0 (0)	0 (0)	1 (1,8)	
11-30%	0 (0)	0 (0)	1 (5,9)	1 (8,3)	2 (3,6)	
31-50%	2 (20)	4 (23,5)	4 (23,5)	3 (25)	13 (23,2)	
51-70%	3 (30)	4 (23,5)	6 (35,3)	2 (16,7)	15 (26,8)	
71-90%	1 (10)	6 (35,3)	1 (5,9)	4 (33,3)	12 (21,4)	
91-100%	3 (30)	3 (17,6)	4 (23,5)	2 (16,7)	12 (21,4)	
Total	10 (100)	17 (100)	17 (100)	12 (100)	56 (100)	

#Likeilhood rat1o test. *Mann-Whitney Test.

science. Breaking paradigms is always very challenging and adopting them, especially in practice, is not always an easy task. This was what Veronesi and Fisher observed when advocating breast conserving surgery (20–29).

Breast reconstruction can be immediate or delayed. The moment in which it is performed and the technique to be used are defined by some factors, among which are the desire and choice of the patient, stage of the disease, extension of the tumor, need or not for adjuvant therapies, comorbidities and surgical ability of the physician (30, 31). The immediate reconstruction is, in fact, an integral part of the treatment of breast cancer, even recommended by the NCCN (32), with aesthetic and psychological benefits (31), besides being less costly (32).

Although the safety, benefits and importance of oncoplasty and breast reconstruction in the treatment of breast cancer have already been well established (3, 33), it is still little performed in Brazil. The socioeconomic disparity between the regions of the country is also reflected in the screening rates, in numbers of early and advanced diagnoses, and, consequently, in different treatments for the disease (1, 17). Additionally, as we verified in the results of the analysis performed in this study, training in oncoplastic and breast reconstruction is poorly disseminated among mastologists. Most of the students, 91.5%, left the mastology residency without being able to perform such surgical techniques (Table 1). Of the few students who had reconstructions performed in their surgeries, almost all of them were performed by a plastic surgeon (Table 2).

It is certain that plastic surgery was pioneer when the subject is reconstruction and will always have its space (34). However, it is verified that there is a large number of women who do not have their breasts repaired and reconstructed, and one of the explanations is the lack of professionals able to perform such procedures. The training of a greater number of medical professionals, in fact, aims to provide an increasing number of women with the chance of having more satisfactory aesthetic results in the treatment of breast cancer, which, we cannot forget, is still very stigmatized.

Breast surgery is becoming more specialized, due to the emergence of proper courses, higher demand of patients in this direction and investment in the training of surgeons. Similar scenarios are found in other countries such as Australia, France, Germany, Italy, Portugal, Spain and United States (29)

In 2020, Brazil had 2,500 mastologists (0.6% of all medical specialists) and, in 2019, 306 physicians were pursuing medical residency in mastology (35). The number of residency programs with associated breast reconstruction teaching is uncertain. Observing the results of the present study, we can assume that this amount is low, since 91.5% of the students reported leaving the residency unable to perform reconstructions (Table 1).

The pioneering nature of this course, initiated by the group in 2010, and which already has seven other editions, has served as a reference, including with encouragement from the Brazilian Society of Mastology, for the implementation of others in various locations and regions of the country. The model of this course in monthly modules, with theoretical and practical content, is reproduced in other cities around the country and has proven to be very efficient (16, 29). The interest in learning about oncoplastic and breast reconstruction has been growing among mastologists, from the youngest to the most experienced.

The students participating in this study are approximately 50 years old on average today (Table 1). This shows that oldest medical residency programs in mastology, in fact, did not have this type of teaching. Exactly for this reason, mastologists linked to teaching hospitals were preferred to take the course. They became multipliers of knowledge, causing many medical residency programs throughout the country to offer the teaching of reconstruction.

In this study, we found that the students gained a lot of knowledge regarding oncoplastic and reconstruction techniques and began to perform these types of surgeries in their respective hospitals (Tables 5-8). The results obtained by this study indicate a higher concentration of students in the course coming from the Northeast and Southeast regions, 33.9% and 44.1%, respectively (Table 1). This, we believe, is a mere reflection of the distribution of mastologists across the country, which, of their total, by number obtained in 2020, 21.8% are from the Northeastern region and 51.4% from the Southeastern region (35).

In the course studied here, all students had the opportunity to learn the techniques listed in Table 3. Despite this, most reported less confidence in performing surgeries with muscle flaps (TRAM and Latissimus dorsi), as shown in the results presented in Table 3 as well. This result is expected, since these are more complex techniques that require a greater learning curve from the surgeon, in addition to the greater need for constancy in their performance.

In the daily practice of the mastologists, the so-called simpler techniques, such as sectorectomies with breast remodeling and its variations, are the most commonly used. In relation to these, it was noted that the gain in knowledge was quite expressive (Table 4), a fact that demonstrates in a more evident manner the optimal impact of the Course.

This Course was a pioneer and served as a model for others Brazilian Mastology Society courses Around the country: Brasília, Belo Horizonte, Goiânia (16) and Jaú.

During the Course the students didn´t had any kind of effective evaluation nor report of surgery done outside, we counted on the students recall and self-reportion. For future studies some bias like recall and self-report can be avoided with implementation of test and monthly report of surgery. This way we can objectively know the number of surgeries and complication each student have and evaluate his performance and knowledge.

Another point to improve is including classes about perforator flaps, free flaps and microsurgical flaps.

Conclusion

The Breast Reconstruction and Oncoplastic Surgery Improvement Course studied here positively impacted the mastologists' management of patients. New training centers worldwide can help a lot of women with breast cancer.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.

Author contributions

TB: main author. VO: professor and advisor. FB: professor and co-advisor. MS: co-author. JR: professor and co-author. FP: professor and co-author. EF: co-author. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

References

1. Freitas-Junior R, Ferreira-Filho DL, Soares LR, Paulinelli RR. Oncoplastic breast-conserving surgery in low- and middle-income countries: training surgeons and bridging the gap. *Curr Breast Cancer Rep* (2019) 11:136–142. doi: 10.1007/s12609-019-00317-3

2. Ng ET, Ang RZ, Tran BX, Ho CS, Zhang Z, Tan W, et al. Comparing quality of life in breast cancer patients who underwent mastectomy versus breast-conserving surgery: a meta-analysis. *Int J Environ Res Public Health* (2019) 16(24):4970. doi: 10.3390/ijerph16244970

3. Losken A, Dugal CS, Styblo TM, Carlson GW. A meta-analysis comparing breast conservation therapy alone to the oncoplastic technique. *Ann Plast Surg* (2014) 72 (2):145–9. doi: 10.1097/sap.0b013e3182605598

4. Goldwyn RM, Goldwyn RM. Vincenz czerny and the beginnings of breast reconstruction. *Plast Reconstructive Surg* (1978) 61(5):673–81. doi: 10.1097/00006534-197805000-00003

5. Homsy A, Rüegg E, Montandon D, Vlastos G, Modarressi A, Pittet B. Breast reconstruction. *Ann Plast Surg* (2018) 80(4):457–63. doi: 10.1097/sap.0000000000001312

6. Waljee JF, Hu ES, Ubel PA, Smith DM, Newman LA, Alderman AK. Effect of esthetic outcome after breast-conserving surgery on psychosocial functioning and quality of life. *J Clin Oncol* (2008) 26(20):3331–7. doi: 10.1200/jco.2007.13.1375

7. Bulstrode NW, Shrotria S. Prediction of cosmetic outcome following conservative breast surgery using breast volume measurements. *Breast.* (2001) 10(2):124–6. doi: 10.1054/brst.2000.0197

8. Freeman BS. Subcutaneous mastectomy for benign breast lesions with immediate or delayed prosthetic replacement. *Plast Reconstr Surg Transplant Bull* (1962) 30:676–82. doi: 10.1097/00006534-196212000-00008

9. Bostwick J3rd, Vasconez LO, Jurkiewicz MJ. Breast reconstruction after a radical mastectomy. *Plast Reconstr Surg* (1978) 61(5):682–93. doi: 10.1097/00006534-197805000-00004

10. Hartrampf CRJr. Hartrampf's breast reconstruction with living tissue. *Plast Reconstructive Surg* (1992) 89(1):151–2.

11. Snyderman RK, Guthrie RH. Reconstruction of the female breast following radical mastectomy. *Plast Reconstr Surg* (1971) 47(6):565–7. doi: 10.1097/00006534-197106000-00008

12. Toth BA, Lappert P. Modified skin incisions for mastectomy: the need for plastic surgical input in preoperative planning. *Plast Reconstr Surg* (1991) 87(6):1048–53.

13. Rainsbury RM. Surgery insight: oncoplastic breast-conserving reconstruction–indications, benefits, choices and outcomes. *Nat Clin Pract Oncol* (2007) 4(11):657–64. doi: 10.1038/ncponc0957

14. Bertozzi N, Pesce M, Santi PL, Raposio E. Oncoplastic breast surgery: comprehensive review. *Eur Rev Med Pharmacol Sci* (2017) 21(11):2572–85.

15. Maxwell GP. Iginio tansini and the origin of the latissimus dorsi musculocutaneous flap. *Plast Reconstr Surg* (1980) 65(5):686–92. doi: 10.1097/00006534-198005000-00027

16. Paulinelli RR, Ribeiro LFJ, Moura Filho JWC, Urban CA, Freitas-Junior R. Resultados do programa de educação continuada em oncoplastia e reconstrução mamária da sociedade brasileira de mastologia no hospital araújo Jorge em goiânia. *Rev Bras Mastologia.* (2016) 26(4):146–52. doi: 10.5327/Z201600040002RBM

17. Lee BL, Liedke PE, Barrios CH, Simon SD, Finkelstein DM, Goss PE. Breast cancer in Brazil: present status and future goals. *Lancet Oncol* (2012) 13(3):e95–e102. doi: 10.1016/s1470-2045(11)70323-0

18. Simon SD, Bines J, Werutsky G, Nunes JS, Pacheco FC, Segalla JG, et al. Characteristics and prognosis of stage I-III breast cancer subtypes in Brazil: the AMAZONA retrospective cohort study. *Breast* (2019) 44:113–119. doi: 10.1016/j.breast.2019.01.008

19. Simon S, Bines J, Barrios C, Nunes J, Gomes E, Pacheco F, et al Clinical characteristics and outcome of treatment of Brazilian women with breast cancer treated at public and private institutions – the AMAZONE project of the Brazilian breast cancer study group (GBECAM). *Cancer Res* (2009) 69(24 Suppl):3082. doi: 10.1158/0008-5472.SABCS-09-3082

20. Kirkwood BR, Sterne JAC. *Essential medical statistics. 2nd ed.* Massachusetts, USA: Blackwell Science (2006). p.502.

21. Veronesi U, Saccozzi R, Del Vecchio M, Banfi A, Clemente C, De Lena M, et al. Comparing radical mastectomy with quadrantectomy, axillary dissection, and radiotherapy in patients with small cancers of the breast. *N Engl J Med* (1981) 305 (1):6–11. doi: 10.1056/NEJM198107023050102

22. Veronesi U, Banfi A, del Vecchio M, Saccozzi R, Clemente C, Greco M, et al. Comparison of halsted mastectomy with quadrantectomy, axillary dissection, and radiotherapy in early breast cancer: long-term results. *Eur J Cancer Clin Oncol* (1986) 22(9):1085–9. doi: 10.1016/0277-5379(86)90011-8

23. Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *New Engl J Med* (2002) 347(16):1227–32. doi: 10.1056/nejmoa020989

24. Fisher B, Bauer M, Margolese R, Poisson R, Pilch Y, Redmond C, et al. Five-year results of a randomized clinical trial comparing total mastectomy and segmental mastectomy with or without radiation in the treatment of breast cancer. *N Engl J Med* (1985) 312(11):665–73. doi: 10.1056/NEJM198503143121101

25. Fisher B, Redmond C, Poisson R, Margolese R, Wolmark N, Wickerham L, et al. Eight-year results of a randomized clinical trial comparing total mastectomy and lumpectomy with or without irradiation in the treatment of breast cancer. *N Engl J Med* (1989) 320(13):822–8. doi: 10.1056/NEJM198903303201302.

26. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher N, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *New Engl J Med* (2002) 347(16):1233–41. doi: 10.1056/nejmoa022152

27. Fisher B, Jeong J-H, Anderson S, Bryant J, Fisher ER, Wolmark N. Twenty-Five-Year follow-up of a randomized trial comparing radical mastectomy, total mastectomy, and total mastectomy followed by irradiation. *New Engl J Med* (2002) 347(8):567–75. doi: 10.1056/nejmoa020128

28. Fisher B, Anderson S. Conservative surgery for the management of invasive and noninvasive carcinoma of the breast: NSABP trials. *World J Surg* (1994) 18(1):63–9. doi: 10.1007/bf00348193

29. Matthes AGZ, Viera RA, da C, Michelli RAD, Ribeiro GHFP, Bailão A, et al. The development of an oncoplastic training center – OTC. *Int J Surg* (2012) 10(5):265–9. doi: 10.1016/j.ijsu.2012.03.009

30. Chevray PM. Timing of breast reconstruction: immediate versus delayed. *Cancer J* (2008) 14(4):223–9. doi: 10.1097/ppo.0b013e3181824e37

31. Veronesi P, De Lorenzi F, Ballardini B, Magnoni F, Lissidini G, Caldarella P, et al. Immediate breast reconstruction after mastectomy. *Breast* (2011) 20:S104–7. doi: 10.1016/s0960-9776(11)70305-8

32. National Comprehensive Cancer Network. *Breast cancer (Version 8* (2021). Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf (Accessed 11/13/2021).

33. Kosasih S, Tayeh S, Mokbel K, Kasem A. Is oncoplastic breast conserving surgery oncologically safe? a meta-analysis of 18,103 patients. *Am J Surg* (2020) 220 (2):385–392. doi: 10.1016/j.amjsurg.2019.12.019

34. Urban CA. Oncoplastic in a pre-paradigm era: a Brazilian perspective in an American problem. *Plast Reconstructive Surg* (2010) 125(6):1839–41. doi: 10.1097/prs.0b013e3181cb61d5

35. Scheffer M, Cassenote A, Guerra A, Guilloux AGA, Brandão APD, Miotto BA, et al. *Demografia médica no brasil 2020*. São Paulo: SP: FMUSP, CFM (2020). 312 p.

frontiers | Frontiers in Oncology

TYPE Review
PUBLISHED 28 June 2023
DOI 10.3389/fonc.2023.1176915

OPEN ACCESS

EDITED BY
Cicero Urban,
Hospital Nossa Senhora das Graças, Brazil

REVIEWED BY
Lorenzo Scardina,
Agostino Gemelli University Polyclinic (IRCCS), Italy
René Aloisio Da Costa Vieira,
Barretos Cancer Hospital, Brazil

*CORRESPONDENCE
John R. Benson
John.benson7@nhs.net

RECEIVED 01 March 2023
ACCEPTED 15 May 2023
PUBLISHED 28 June 2023

CITATION
Wignarajah P, Malata CM and Benson JR (2023) Oncoplastic and reconstructive breast surgery.
Front. Oncol. 13:1176915.
doi: 10.3389/fonc.2023.1176915

Oncoplastic and reconstructive breast surgery

Primeera Wignarajah[1,2], Charles M. Malata[2,3,4] and John R. Benson[2,4]*

[1]Department of Breast Surgery, Royal Marsden Hospital NHS Trust, London, United Kingdom, [2]Department of Breast Surgery, Cambridge Breast Unit, Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom, [3]Department of Plastic and Reconstructive Surgery, Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom, [4]Anglia Ruskin University School of Medicine, Cambridge/Chelmsford, United Kingdom

This article provides an overview of the principles and techniques of oncoplastic and reconstructive breast surgery for patients with early-stage breast cancer. Oncoplastic breast surgery (OPBS) with partial breast reconstruction is a natural evolution in the application of breast conserving surgery and permits wide surgical resection of tumours that might otherwise mandate mastectomy and whole breast reconstruction. These reconstructive techniques must be optimally selected and integrated with ablative breast surgery together with non-surgical treatments such as radiotherapy and chemotherapy that may be variably sequenced with each other. A multidisciplinary approach with shared decision-making is essential to ensure optimal clinical and patient-reported outcomes that address oncological, aesthetic, functional and psychosocial domains. Future practice of OPBS must incorporate routine audit and comprehensive evaluation of outcomes.

KEYWORDS

breast reconstruction, oncoplastic breast surgery, breast implants, fat grafting, autologous free flap, nipple sparing mastectomy

Part 1

Introduction – Breast cancer epidemiology

Breast cancer remains the most common malignancy worldwide with recent lifetime estimates of 1 in 7 in the United Kingdom (UK) (1) where the annual number of cases has almost doubled in the past four decades. Globally, one-quarter of female cancers have breast as the primary site and the World Health Organisation (WHO) reported in 2020 that 2.3 million women worldwide were diagnosed with breast cancer and more than 600,000 women died from their disease (2). Within the UK, almost half of breast cancers are diagnosed within the screening age bracket and introduction of the screening programme led to a surge in incidence that was confined to women of initial screening age (3). Breast cancer is a disease

predominantly of post-menopausal women and rising rates during the final decade of the last century has been attributed to increased usage of hormone replacement therapy (HRT) amongst affluent women (4, 5). Use of exogenous hormones in women aged 45-69 years fell dramatically after 2002 and resulted in a transient reduction in breast cancer incidence amongst white American women but this decline has not been sustained despite limited contemporary usage of HRT (6, 7). Genetic factors are likely to be more important for breast cancer development in younger women with increasing recognition of lower penetrance genes that individually confer lower levels of risk but are collectively important. Breast cancers frequently display epigenetic phenomena that permit changes in gene expression without DNA sequence alterations and thereby acts as translators between the external environment and the genome.

Those countries that historically had moderate or low rates of breast cancer based on income levels are now experiencing rapid rate increases with an inexorable rise in the incidence of breast cancer in China and India and a doubling of rates in Japan over the past 50 years. The high incidence rates in Western industrial nations have been attributed to lifestyle factors that now have relevance to increasing rates amongst emerging economies. These include changes in reproductive behaviour, altered dietary habits with increased consumption of polyunsaturated fats and alcohol together with a more sedentary lifestyle and physical inactivity (8–10). These are potentially modifiable risk factors and breast cancer incidence could be significantly reduced by adoption of a healthier lifestyle with maintenance of optimum body weight, limited alcohol intake and regular exercise (11–13).

Mortality rates for breast cancer have fallen over the past 30 years despite a continued rise in incidence. This testifies to the success of interventional strategies such as screening and adjuvant systemic therapies that permit diagnosis of breast cancer prior to formation of micrometastatic disease or obliteration of established foci of disease at distant sites. Survival rates at 10 years for breast cancer in the UK are currently 80.4% compared with approximately 55% in the final quarter of the last century (1). Survivorship has become an important issue with an estimated 7.8 million patients around the world living with breast cancer diagnosed in the past 5 years (14). Survival rates will continue to improve with advances in translational research and development of tailored therapies (e.g antibody drug conjugates) that can effectively target micrometastatic disease with acceptable levels of serious side-effects – there is a balance between length and quality of life. Many women with breast cancer typically diagnosed when in their fifties are now surviving well into their eighties and any adverse effects of treatment (surgery, radiotherapy, chemotherapy, oestrogen deprivation) can have a lasting impact on the remaining period of the patient's life. With improved clinical outcomes for breast cancer treatments including both disease-free and overall survival, the focus has now shifted to quality-of-life issues. Although many studies have confirmed that aesthetic results of breast cancer surgery are a principal determinant of quality-of-life and patient satisfaction, functional and psychosocial outcomes are equally important and should be part of any shared decision-making process (15, 16).

Development of oncoplastic breast surgery

William Stewart Halsted (1852-1922) published the first formal description of an operation for breast cancer based on a series of patients treated at the Johns Hopkins Hospital in Baltimore, USA (17). He postulated that breast cancer is a loco-regional disease and metastatic dissemination occurs by centrifugal and contiguous spread of the primary tumour with progressive involvement of adjacent tissue and the lymphatic system of the breast. The operation of radical mastectomy aimed to remove *en bloc* the breast, pectoral musculature, and the axillary lymph nodes (up to level III). This operation was rapidly implemented as routine surgical practice for breast cancer patients in the first half of the twentieth century irrespective of clinical features (assuming the tumour was operable). A fundamental concept of this so-called *Halstedian paradigm* was that maximal efforts at local control would prolong survival; breast cancer was considered to originate as a localised disease, and it was surmised that cure rates could be improved by a more meticulous and comprehensive surgical approach. Local recurrence was considered to be the cause of distant metastases and the aim was to minimise rates of local relapse. Halsted observed that many patients developed local recurrence before they succumbed from distant metastatic disease. His operation of radical mastectomy reduced rates of local recurrence from 60% to 6% but had no impact on overall survival – so this mutilating operation did not provide patients with any additional years of life. There was a problem with the existing paradigm; hence an alternative hypothesis was proposed by the eminent surgeon Bernard Fisher (1918-2019) whose brother Edward ('Ed") was a pathologist. This paradigm was known as biological pre-determinism and contended that breast cancer is a local manifestation of a systemic disease with complex interactions between the host, the primary tumour and distant micrometastases (18). Breast cancer was considered capable of accessing the circulation at an early stage in carcinogenesis with cancer cells breaking away from the tumour bolus and entering the bloodstream *via* holes between the endothelial cells in the neovasculature. In addition, haematogenous dissemination was possible *via* lymphatico-venous communications in the regional (axillary) lymph nodes. It followed that surgery could only achieve local control of disease and some form of systemic treatment was necessary to improve overall survival (19). This paradigm of Fisher was supported by results of six randomised prospective trials that allocated breast cancer patients to either a breast conservation procedure (lumpectomy, wide local excision, quadrantectomy) or total mastectomy. The first of these trials was conducted by Umberto Veronesi (1925-2016) at the National Cancer Institute of Milan, Italy (20) and the largest trial (NSABP B-06) (21) by Bernard Fisher under the auspices of the National Surgical Adjuvant Breast and Bowel Project in Pittsburgh. Results of the Milan I trial appeared on the front cover of the New York Times in 1981 and provided level I evidence demonstrating survival equivalence for breast conservation therapy compared with radical or modified radical mastectomy (22). An update of the

NSABP B-06 trial with a 20 year follow up confirmed that post-operative irradiation improved local recurrence-free survival after breast conserving surgery (BCS) with similar distant disease-free and overall survival for modified radical mastectomy, wide local excision and radiotherapy or wide local excision alone (21). Hence permutations of breast surgery had no impact on breast cancer-specific mortality and BCS was deemed to be a safe surgical procedure for patients with tumours <5cm in size. This heralded the start of a trend for de-escalation of breast surgical procedures. Residual cancer cells are a determinant of local failure but not of distant metastatic disease with a finite rate of ipsilateral breast tumour recurrence (IBTR) when BCS is undertaken. Contemporary rates of IBTR are very low (<1% per annum) with combined multimodality treatments; systemic therapies reduce IBTR by approximately one-third and anti-HER2 directed treatments halve rates of in-breast recurrence. BCS represents a balance between oncological mandates and cosmetic outcomes with the aim of removing the tumour and a narrow margin of surrounding breast tissue such that negative margins are achieved. There is now international consensus that an adequate margin exists when tumour is not touching ink and wider margins do not reduce rates of local recurrence (23). Nonetheless, the Association of Breast Surgery (UK) have decreed that a negative margin requires tumour to be no closer than 1mm from the inked margin for both invasive and non-invasive breast cancer. A negative margin does not imply absence of any residual disease within the remaining breast tissue but indicates a residual tumour burden sufficiently low to be controlled with adjuvant treatments. Local surgery does not completely eliminate residual disease with local recurrence determined by a combination of surgery, tumour biology, radiation and systemic therapies (24).

A spectrum or intermediate paradigm is emerging which encompasses this variable capacity to form distant metastatic disease, with more indolent, slower growing tumours (luminal subtypes) behaving according to the *Halstedian paradigm* and more aggressive tumours (triple negative and HER2 positive cancers) disseminating early on – consistent with the *Fisherian paradigm* (25). Molecular profiling of tumours has revealed a dichotomy of gene expression patterns that permits assignment of tumours to one or other group based on predicted biological behaviour with appropriate intensities of loco-regional and systemic treatments.

The modified radical mastectomy removed breast and axillary tissue in continuity but preserved the pectoralis major muscle and much reduced the morbidity of the traditional radical operation. This operation was championed by David Patey of the Middlesex Hospital in London but was never widely adopted outside the UK (26). With the rapid development of breast reconstructive techniques over the past three decades, the modified radical mastectomy has evolved into skin-sparing and nipple-sparing forms of mastectomy that are now being applied to both prophylactic and therapeutic breast surgical procedures. Skin-sparing mastectomy (SSM) was introduced by Toth and Lappert in 1991 (27); initial concerns that greater skin preservation might lead to higher rates of local recurrence have not been justified. Several studies have now confirmed low rates of local recurrence (<5%) for skin-sparing procedures are not significantly higher than for conventional forms of mastectomy when patients are matched for stage of disease (28, 29). Nipple-sparing mastectomy (NSM) is the ultimate form of conservative mastectomy in which the entire breast envelope is preserved. Ongoing studies are attempting to define those breast cancer patients for whom NSM can be safely performed for the ipsilateral breast without adversely affecting oncological outcomes, especially recurrence within the territory of the nipple. It is particularly important that ductal tissue within the nipple is 'cored' out without compromising the vascular supply to the nipple-areola complex (30).

Axillary surgery is an integral component of breast cancer surgery and has undergone a revolutionary change with progressive de-escalation of nodal resection. The operations of both radical and modified radical mastectomy implied concomitant axillary lymph node dissection (ALND). However, with the advent of sentinel lymph node (SLN) biopsy, formal ALND is now much less commonly performed (as either a primary or a secondary procedure); a notable change has been omission of completion ALND in selected sentinel node positive cases with reliance on adjuvant non-surgical treatment modalities for eradication of low burden axillary disease in non-sentinel lymph nodes (31). The majority of patients nowadays undergo initial SLN biopsy, be this in the context of conventional mastectomy without reconstruction, SSM, NSM or BCS. Thus patients are more likely to undergo simple mastectomy combined with SLN biopsy rather than mastectomy and ALND – the modified radical mastectomy.

The development of oncoplastic surgery and partial breast reconstruction is a natural evolution in the application of BCS to management of breast cancer. Most patients who are considered eligible for BCS have a favourable tumour to breast size ratio and are suitable for conventional forms of wide local excision with local glandular readjustment but no formal remodelling of the breast. Even when re-excision of margins is required (in up to one-quarter of cases), an optimal cosmetic outcome should be attainable in the long term after irradiation of the breast. There is a 'grey area' where the limits of BCS are being approached and the patient may be better served with a skin/nipple-sparing mastectomy and immediate breast reconstruction at the outset. It becomes progressively more difficult to achieve a good cosmetic outcome as the proportion of breast tissue removed increases. When more than 10%-20% of breast tissue is removed, there is a risk of an unsatisfactory result, but relatively modest losses of 5%-10% of breast volume from tumours in cosmetically sensitive areas (medial and inferior quadrants) can adversely affect cosmesis (32). Oncoplastic breast surgery (OPBS) provides the opportunity for enhancing quality-of-life by improving cosmetic outcomes and psychological wellbeing after larger resections for unifocal and some multifocal breast cancers. OPBS can facilitate wide surgical clearance of a tumour and improve a patient's cosmetic outcome when larger volumes of resected tissue are required (33). Techniques for OPBS include volume replacement and volume displacement techniques (34). The former imports additional tissue in the form of a flap and attempts to compensate for loss of volume from surgical excision. By contrast, the latter rearranges the remaining breast tissue using methods of glandular advancement or rotation that serve to redistribute the parenchyma and minimise

the impact of wide local excision. Volume displacement techniques absorb volume loss over a wider area and do not incur donor site morbidity from harvesting of any local tissue flaps. Werner Audretsch from Dusseldorf in Germany is credited with pioneering many of these techniques for OPBS and incorporating techniques of aesthetic plastic surgery into routine breast surgery for partial breast reconstruction after extirpative procedures for breast cancer. Audretsch coined the term 'oncoplastic surgery' and worked closely with colleagues such as Krishna Clough in Paris and Richard (Dick) Rainsbury in UK to establish OPBS techniques and define indications for use of a variety of different techniques depending on the size of the tumour, location within the breast and whether uni- or multifocal (35, 36). The advent of oncoplastic techniques has very much defined the ethos of current approaches to breast surgery and acceptance that a good cosmetic result should be standard of care for all patients without compromise of oncological safety. A particular challenge is the integration of adjuvant treatments into management pathways for breast cancer patients with determination of optimum sequencing and timing of chemotherapy and radiotherapy. These techniques remain contentious, and Clough has referred to the oncoplastic 'frenzy' (37); careful selection of patients is crucial and partial breast reconstruction should not be attempted in patients who are not amenable to BCS from an oncological perspective and for whom mastectomy is warranted (38). These techniques of OPBS must be appropriately integrated with ablative breast surgery to avoid emergence of a 'breast cripple'. Cross-specialty training opportunities are fostering increasing numbers of oncoplastic breast surgeons and those without oncoplastic competencies should work co-operatively with plastic surgeons to provide a comprehensive service. Notwithstanding availability of surgical expertise, these OPBS techniques are relevant to a relatively small proportion of patients (10-15%) although indications for the use of oncoplastic techniques are increasing and breast surgeons are accruing more experience with these techniques for the benefit of patients (39). All 'breast surgeons' are in a sense 'oncoplastic' and whatever their precise breed must work co-operatively with plastic surgeons to ensure that a mix of surgical skills can be optimally applied to maximise oncological, aesthetic and patient reported outcomes.

The 'coming of age' of OPBS (40) has allowed many women to benefit from management planning by a multidisciplinary team offering a comprehensive breast cancer and reconstructive service. By restoring the size, shape and appearance of the breast, reconstruction improves a patient's gender identity and quality-of-life across multiple domains – psychological, social, sexual, emotional, and functional. The breast is a symbol of femininity and its characteristic curves have defined the female form throughout the ages. In addition, there is enhanced aesthetic satisfaction compared with mastectomy alone (41), and some patients with borderline conservable tumours may opt for mastectomy and whole breast reconstruction rather than BCS with partial breast reconstruction. Some women steadfastly want to keep their breast if at all possible, whilst others are adamant they want a mastectomy (often with a contralateral prophylactic mastectomy-so called 'big surgery') despite having a small tumour. It is therefore imperative that patients make fully informed decisions and are aware of reconstructive options early on in discussions of surgical management of their breast cancer. Breast surgical oncologists have a key role as gatekeepers in ensuring that patients have access to reconstructive surgeons and referrals to plastic surgery colleagues are made as soon as possible following diagnosis of breast cancer – including patients managed with primary chemotherapy. Interestingly, there is evidence that patients are significantly more likely to be referred for reconstruction if breast surgeons are female, have a high workload and are affliated with a designated cancer centre (42). Decisions made in terms of breast reconstruction are very much 'preference sensitive' and must be individualised and made jointly between a patient and her surgeon(s). They should take account not only of a patient's wishes, but also her personality, self-perception, hobbies, family, and socio-economic circumstances. There may be a selection bias with OPBS patients tending to be younger with higher levels of educational attainment and income that may influence their self-perception and attitudes towards body image. Outcomes of breast cancer surgery are better when clinical decision making integrates information giving, shared decision-making and patients' personal values. There is now greater appreciation of a patient's perspective and issues such as quality-of-life and patient choice. These complement traditional outcomes based on objective surgical criteria and are being formally measured with validated questionnaire-based instruments such as BREAST-Q that can measure more subjective outcomes related to psychological, emotional, and functional sequelae of reconstruction (43). Incorporation of patient reported outcome measures (PROMS) with more objective clinical parameters will inform future patient choice and lead to improvements in clinical care. Clinical decision making in the field of surgical oncology and OPBS has become increasingly complex in recent years and involves multidisciplinary team working and integration of a large number of variables requiring collective assessment before planning surgery. As previously mentioned, many treatment options are based on low levels of evidence that is of poor quality and often outdated and not necessarily related to contemporary practice. Artificial intelligence offers the potential opportunity to more accurately assess this complex array of variables and aid the clinical-decision making process; this can avoid personal judgement and bias and the adage 'my way and the wrong way'. Methodologies such as GRADE and Delphi interviews attempt to reconcile potentially conflicting viewpoints and assimilate opinion and experience from a large number of clinicians and place this in context with published data. The technique of text–mining can be employed to analyse decision drivers (44). Surgeons and other healthcare workers must be honest with patients when discussing cosmetic and other outcomes of breast reconstructive surgery. In particular, patients' expectations must be realistic and appreciate that the reconstructed breast is a facsimile of a normal breast. It is important to stress to the patient it is a 'breast mound' that is being created rather than a 'breast'. Whenever possible, patients should be offered a full repertoire of reconstructive options but the final surgical procedure undertaken will depend on several factors including surgeon experience and training, general health of the patient (including co-morbidities and smoking habits) and local healthcare resources.

A patient's expectations of the final cosmetic result will be determined by any relevant prior knowledge and influenced by

information derived from family, friends, other patients, the media and increasingly the internet. Any misperceptions must be corrected, and fully informed consent obtained before proceeding with any form of breast reconstruction. Levels of patient satisfaction are often more related to adequate information and a robust shared decision-making process than an aesthetically pleasing cosmetic result.

There must be alignment between the aims of the surgeon and the patient – the latter takes comfort and reassurance from a surgeon's knowledge and skills. Establishment of a good rapport will encourage shared decision-making and lead to optimal outcomes. Patients must be given sufficient time to assimilate all information and reach a decision that feels right for them; sometimes they will change their mind, and this must be accommodated. Surgeon preference should not dominate discussions and patients should be offered a full repertoire of reconstructive options and not compelled to accept a reconstructive option that is especially favoured by her surgeon (for whatever reason). Surveys have revealed that patients who chose reconstruction are motivated by body image rather than reasons relating to sexuality or femininity (45). By contrast the most common reason for patients declining breast reconstruction is to avoid additional surgery (45). Higher levels of patient satisfaction are associated with immediate breast reconstruction compared with mastectomy alone in terms of psychosocial, sexual and physical well-being (46, 47). Nonetheless, a desire to complete adjuvant cancer treatments prior to reconstructive surgery is a frequently cited reason for patients deliberately opting for a delayed breast reconstruction.

Increasingly breast units around the world are employing specialist breast care nurses as well as dedicated breast reconstruction nurses. These individuals exercise a valuable role in clarifying and processing information for patients. They can sometimes help frame relevant questions ahead of any consultation with the surgeon and this will facilitate shared decision-making. Introduction of separate oncoplastic multidisciplinary team meetings combines the expertise of breast surgeons, plastic surgeons, radiologists, and medical/radiation oncologists. It is important that these potentially problematic OPBS cases are discussed jointly between breast surgeons, plastic surgeons and oncologists to determine optimal management. Treatments are increasingly tailored to individual patients and based on tumor phenotype. Most triple negative and HER2 positive tumors >2cm will be managed with primary chemotherapy and in the latter case anti-HER2 therapy. Complete pathological response rates often exceed 50% and concentric shrinkage of tumors will facilitate subsequent surgery with breast conservation being an option instead of mastectomy (with or without whole breast reconstruction). Individual cases can be discussed in depth with access to clinical notes, radiological images and medical photography. Oncoplastic multidisciplinary team meetings are being widely adopted and used to aid in surgical decision making and providing options for patients. These meetings are also an excellent forum for trainees.

The range of OPBS options in the modern era is considerable and the potential choice of options available to a woman with a newly diagnosed breast cancer can be overwhelming. Extreme oncoplastic breast conserving surgery (EOBCS) refers to the use of oncoplastic breast conservation techniques in patients with multifocal, multicentric or locally advanced breast cancer (>5cm) which would be conventionally treated with mastectomy (+/- reconstruction). EOBCS has evolved with the improvements in systemic therapies, radiotherapy techniques and increased awareness of the psychological and quality-of-life benefits of breast conservation. In 2015 Silverstein et al. reported 66 cases of EOBCS in patients who were advised mastectomy and declined. There is a lack of long-term data on the impact on recurrence, overall survival and distant metastases in patients opting for EOBCS (48, 49). There is arguably no longer a primary decision of BCS versus mastectomy with or without reconstruction. Instead, two key questions are whether the patient is a candidate for conventional BCS and if not, can she be spared mastectomy with either pre-operative chemotherapy or an oncoplastic procedure? (50) Addressing these questions may involve complex surgeon-patient discussions with viewing of radiological images (preferably correlation with MRI) and anonymised before and after photographs of previous patients. These discussions will involve patient tailoring measurements and conceptualised diagrams. The possibility of retaining or improving shape whilst replacing or displacing breast tissue with OPBS may be an option. Alternatively, there will always be the option of removing all breast tissue with preservation of much of the skin envelope and whole breast reconstruction with prosthetic material, autologous tissue, or a combination thereof. The relative advantages and disadvantages of each option must be discussed with patients including surgeon-specific complication rates. It should be remembered that OPBS is not plastic surgery per se, but the use of plastic surgical techniques and principles to improve outcomes of cancer treatment. Patients should appreciate that surgery is only one aspect of their management pathway and other treatment modalities will affect the final cosmetic results.

Historically there has been a dearth of high quality research in OPBS with minimal level I evidence derived from randomised controlled trials – the latter are arguably more challenging to undertake in this field. This often relates to issues of patient and surgeon preference in terms of specific operative procedures that can undermine surgical equipoise and dissuade patients from accepting treatment options determined by a process of randomisation. A more pragmatic trial design for evaluation of clinical and patient reported outcomes is prospective observational studies whereby patients can chose a particular surgical option and different groups of patients will then be compared in terms of specific outcome measures. This type of design is subject to confounding from unmeasured bias but otherwise represents a way of encouraging trial participation and relatively rigorous evaluation of outcomes whilst allowing patients to chose their surgery (irrespective of how this might be influenced by their surgeon's personal procedural preference). Failure of trials to randomise OPBS patients provides valuable insights into how future clinical trials in this field should be designed (51).

Genetics, breast cancer and reconstruction

There has been a flurry of public interest in genetic testing and risk reduction strategies following revelations that the actress Angelina Jolie had chosen to undergo bilateral prophylactic

mastectomy due to carriage of a BRCA-1 gene mutation. In addition to increased demand for genetic testing amongst breast cancer patients, the number of contralateral prophylactic mastectomy (CPM) cases have increased three-fold since this story appeared in the New York Times in 2013 (52). Genetic counselling and testing for breast cancer predisposition has been formally implemented in many countries and the number of women seeking genetic testing continues to rise. In the UK, The National Institute for Health and Clinical Excellence (NICE) has recommended that women undergo genetic testing when the chance of finding a high-penetrance mutation is 10% (reduced from the previous mandate of 20%) (53). Most women over-estimate their risk and genetic testing allows accurate risk assessment that more confidently informs any proposed management decisions. Nonetheless, despite these advances in genetics, approximately 30% of familial breast cancer risk remains unaccounted for by mutations in currently known genes. Moreover, genetic changes do not necessarily have a causative association with a diseased state and phenotypic manifestations of cancer are variable. The clinical management of women with an asymptomatic mutation in BRCA1 and BRCA2 or carriage of a mutation in other high-risk genes such as TP53, PALB2 or pTEN is increasingly complex but often those with a pathogenic mutation in a high-risk gene will seek bilateral risk-reducing mastectomy (RRM) (with or without immediate breast reconstruction).The PALB2 gene encodes for a protein that interacts with the BRCA-2 gene product to repair damaged DNA and maintain fidelity of DNA replication. Mutations of the PALB2 gene are associated with a breast cancer risk of 35 - 40% by age 70 years that is slightly lower than for BRCA-2 mutations where the comparable risk is 40 – 60% (54). Increasing numbers of patients with PALB2 mutations are being referred from clinical genetics for consideration of bilateral RRM. Most patients with mutations in high/moderate risk genes are relatively young and seek immediate breast reconstruction – hence genetic testing has led to increased demand for reconstructive breast surgery. However, the risks associated with bilateral RRM must be carefully balanced against benefits in terms of reduced incidence (not mortality) of subsequent breast cancer (>90%) and psychological advantages with alleviation of uncertainty and concomitant anxiety. All patients undergoing prophylactic surgery (including CPM) must receive appropriate counselling and have a formal psychological assessment.

Genetic testing in the UK can take up to 12 weeks before results become available and management of younger women with primary chemotherapy (triple negative/HER2 positive breast cancer) provides a convenient surgical pause allowing genetic test results to be available when planning definitive surgical treatment. Some younger women without a documented pathogenic variant but a strong family history of breast/ovarian cancer may opt for risk-reducing surgery.

Part 2

The second part of this article will address the different types of techniques available for OPBS and criteria for selection of patients for appropriate options. The latter must ensure optimal oncological, and patient reported outcomes whilst minimising complications and delays in commencement of adjuvant treatments.

What are the aims of oncoplastic surgery in management of breast cancer patients?

The challenge of oncoplastic surgery is to reconcile oncological and aesthetic outcomes and maximise levels of patient satisfaction. There are broadly three primary aims that need to be addressed for each patient:

1) Optimal oncological outcome – performing an extirpative procedure that minimises the chance of recurrence by removing the tumour with a clear margin of normal surrounding breast tissue as part of either a partial or complete mastectomy.
2) Optimal cosmetic outcome – reconstituting the breast with either partial or whole breast reconstruction to provide optimal symmetry and shape in relation to the native breast.
3) Minimal delays in commencement of adjuvant treatments – prevention of post-operative complications such as infection, wound dehiscence, haematoma, seroma, or fat necrosis that interfere with delivery of adjuvant treatment such as radiotherapy and chemotherapy.

Reconstructive breast cancer surgery includes both mastectomy and whole breast reconstruction as well as partial breast reconstruction employing a variety of oncoplastic techniques that have been developed by breast surgeons and often drawn from plastic surgery principles. Oncoplastic breast surgery (OPBS) encompasses volume rearrangement, volume displacement and volume replacement techniques. *Volume rearrangement* involves the use of local tissues to optimize the shape after wide local excision. It incorporates careful incision planning, appropriate undermining of the breast skin, meticulous closure of the dead space and mobilization of the local tissues. *Volume replacement* imports additional tissue with a flap to compensate for loss of volume from surgical ablation. By contrast, *volume displacement* rearranges the remaining breast tissue using methods of glandular advancement/rotation/transposition that serve to redistribute parenchyma and minimize the cosmetic impact of tumour excision. This is also referred to as 'therapeutic mammoplasty'. In effect, the volume loss is absorbed over a wider area with concomitant re-shaping of the breast. Volume displacement surgery is less complex than autologous tissue transfer methods and avoids associated donor site morbidity. The reconstructed breast is notably of smaller volume and plastic surgery on the contralateral side is often required for symmetrization, which (more often than not) is an integral part of therapeutic mammoplasty. This applies especially to therapeutic mammoplasty where tumour excision is incorporated into standard/modified reduction procedure or breast lift. Volume displacement represents the simplest option for partial breast reconstruction and is usually preferred over techniques for volume

replacement that involve more extensive surgery with harvesting of a myocutaneous or subcutaneous perforator flap. Volume displacement techniques are preferably used in patients with medium to large breasts with a significant degree of ptosis that render these patients well suited to these techniques. By contrast, volume replacement techniques are indicated in small breasted women (48, 49, 55).

Partial breast reconstruction

Techniques for OPBS were formally classified by Krishna Clough in 2010 (35) and divide procedures into two categories based on the extent of breast tissue resection and degree of surgical complexity for reconstruction of the conserved breast:

Level 1 OPBS techniques - these involve resection of at least 20% of total breast volume that require relatively straightforward volume displacement techniques to achieve an acceptable cosmetic result with reshaping of the breast through advancement, rotation or transposition of existing parenchyma and skin with a resultant decrease in overall breast volume.

Level 2 OPBS techniques – these involve resection of between 20% and 50% of total breast volume with restoration using methods for either displacement or replacement of breast tissue that may be combined with skin reduction or transfer.

Level 1 OPBS

When up to 20% of breast volume is resected without any attempt to mobilize and re-model adjacent glandular tissue, then a significant defect in breast contour, shape and size may ensue. Resection of breast tissue in the upper outer or lower outer quadrants is less likely to result in a noticeable defect compared with resections in more cosmetically sensitive areas such as the upper inner quadrant. The cosmetic outcome after removal of a relatively small volume of tissue can be enhanced by simple mobilization of breast tissue adjacent to the surgical cavity. The extent of mobilization required will depend on the size of the defect and may involve undermining the whole breast plate. Extensive mobilization of breast tissue can sometimes threaten the blood supply to both the glandular tissue and skin. This can lead to post-operative necrosis and secondary infection with a poor aesthetic outcome and impaired quality-of-life (56). Therefore, mobilization and displacement of glandular tissue using advancement or rotational flaps to fill a defect presents an opportunity for improved cosmesis but can be technically challenging (57).

Level 2 OPBS

Volume displacement techniques – these can be employed to adjust for loss of larger breast volumes (20 – 50%) and usually involve some form of mammoplasty that includes a variety of techniques such as Wise pattern, batwing, Grisotti, Benelli, Round block and vertical mammoplasty (LeJour) pattern.

These various mammoplasty techniques involve resecting the tumour and a pre-determined volume of tissue and skin with rearrangement of the glandular tissue to re-form the breast. The re-fashioned breast is often smaller and less ptotic than the native breast and contralateral breast surgery is frequently indicated for symmetrization (especially for high percentage excision of breast volume) – Figure 1. Depending on tumour location and disease extent, it may be feasible to preserve the nipple-areola complex on a defined pedicle but otherwise this structure may need to be sacrificed (in which case a partial breast reconstruction can be performed using a Grisotti flap) – Figure 2. An inferior pedicle technique (Figure 3) preserves a pyramid of tissue in the inferior portion of the breast to maintain perfusion of the nipple. This can potentially compromise the oncological resection volume for a tumour in the inferior portion of the breast and therefore a superior pedicle is more appropriate. The superior pedicles can be superolateral or superomedial (Figure 4). The batwing and hemi-batwing mammoplasty are used for tumours in the superior breast that are relatively close to the nipple-areola complex and involve less mobilization of glandular tissue yet permit excision of tumours with an adequate margin and a good cosmetic result. A symmetrizing procedure on the contralateral breast can be undertaken simultaneously with the therapeutic procedure or at a later date following completion of adjuvant treatments such as chemotherapy and radiotherapy – and allowing time for radiotherapy changes to settle.

Volume replacement techniques – these have previously been reliant on use of the latissimus dorsi (LD) flap harvested as either a myocutaneous flap in the form of a standard LD flap or the mini-LD muscle flap, the latter popularized by Rainsbury (58). More recently replacement techniques have been increasingly based on local flaps such as chest wall perforator flaps. Chest wall perforator flaps have become popular in recent years as a method for partial breast reconstruction when larger volumes of tissue are resected in the inferior and lateral aspects of the breast (Figure 5). These highly specialized volume replacement techniques include the lateral intercostal artery perforator flap (LICAP), anterior intercostal artery perforator flap (AICAP), medial intercostal artery perforator flap (MICAP), lateral thoracic artery perforator (LTAP) flap as well as the thoracodorsal artery perforator which utilizes the same pedicle as the latissimus dorsi musculocutaneous or muscle flap (Figure 6) (59–62).

Although older forms of loco-regional flaps are associated with worse cosmetic results, these can be used on selected patients and permit breast conserving surgery to be undertaken based on random flaps (thoraco-epigastric, thoracolateral and bi-pedicled flaps).

Other methods for enhancing breast volume include lipo-modelling that has recently had a renaissance in the context of breast cancer surgery. This is especially useful as an adjunctive technique to 'plump up' mastectomy skin flap thickness around implants (Figure 7A) and restoring local volume defects following breast conservation (Figure 7B). Lipo-modelling (or fat grafting) involves harvesting fat from a donor site (lateral thigh, hip, lower

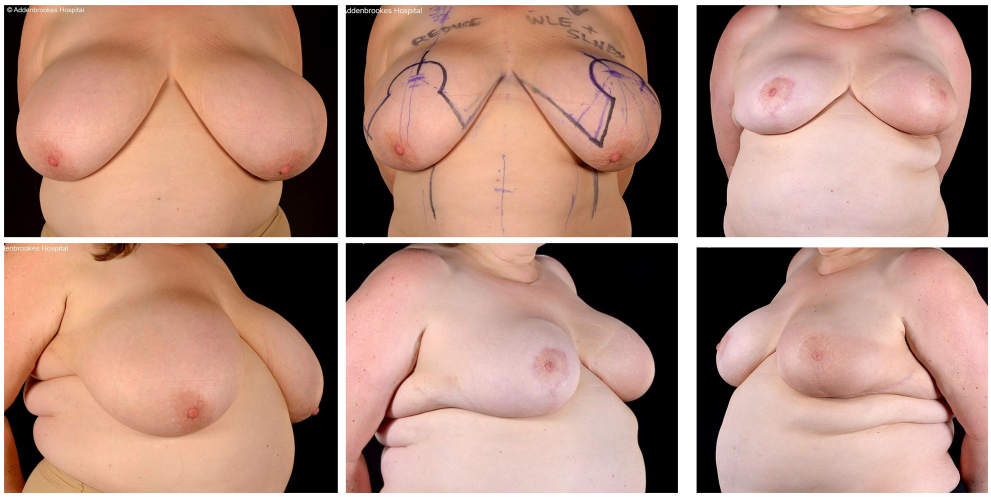


FIGURE 1
Left therapeutic mammaplasty in a patient with gigantomastia necessitating contralateral balancing breast reduction. Symmetrisation surgery is an integral part of therapeutic mammaplasty specifically and oncoplastic surgery in general.

back, buttocks or abdomen), filtering the fat and injecting it into the breast to improve volume, shape and symmetry. It can also be used to fill localized mastectomy flap defects after whole breast reconstruction. This is especially so after pre-pectoral (epi-pectoral) breast reconstruction when it is used to soften the sharp take off and pad the tissues around the implant. The benefits of fat grafting relate to its being bio-compatible and readily available coupled with its versatility and ability to integrate into host tissues and survive. Lipo-modelling can result in improved aesthetic outcomes but has some notable disadvantages, especially in terms of the donor site where there may be a defect, loose skin or cellulite-like appearance in the long term (63, 64). Moreover, short-term bruising and swelling can be associated with significant morbidity for patients. Only 40- 60% of the injected fat is likely to be retained at the recipient site with significant local absorption of grafted fat tissue (65, 66). There are also risks of fat necrosis and oil cyst formation and a requirement for multiple courses of lipo-modelling which often require general anaesthesia. Nonetheless, the advent of lipo-modelling has permitted correction of intractable aesthetic deformities and minor asymmetries that were previously difficult to ameliorate surgically. A notable usage is the improvement of the skin quality in radiotherapy-damaged skin either with lumpectomy or total breast reconstruction.

A wide range of OPBS techniques are now available and selection of the optimal method for any individual patient is dependent on breast size, degree of ptosis, tumour location

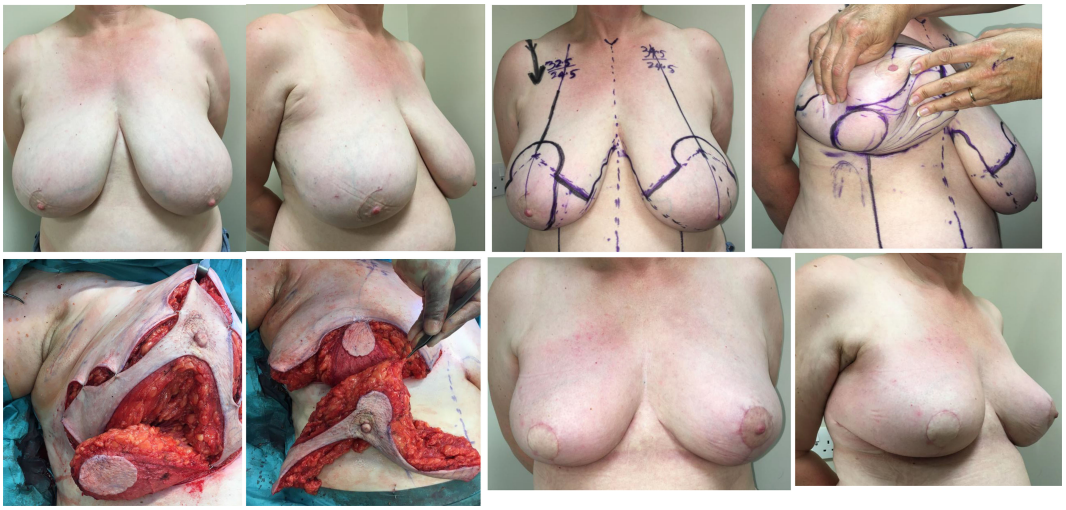


FIGURE 2
Right modified Grisotti flap based on the inferior pedicle, used for partial reconstruction to create a neo-areola after right therapeutic wise pattern mammoplasty with axillary clearance and left inferior pedicle based contralateral balancing reduction mammoplasty. Right therapeutic reduction weight 778g. Left breast reduction weight 842g.

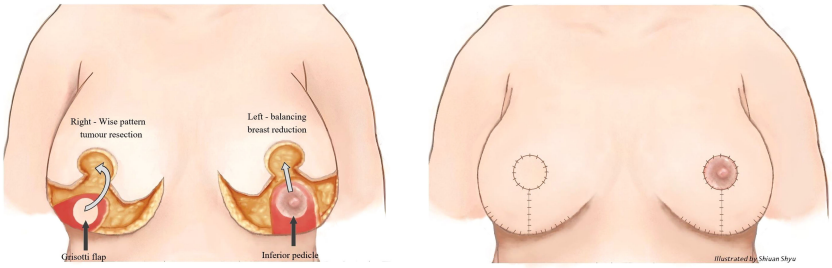


FIGURE 3
Right therapeutic wise pattern mammoplasty and contralateral symmetrising left breast wise pattern reduction mammoplasty using inferior pedicles. White arrows indicate the direction of flap rotation and final placement. Illustrated by Shiuan Shyu.

(quadrant), the surgeon's expertise and patient preference. In terms of patient satisfaction, it is important that expectations are realistic, and patients understand that their overall breast size many be smaller following oncoplastic breast surgery and scarring can be more extensive than anticipated for some level II OPBS techniques. The choice of OPBS technique will also be influenced by the surgeon's skills set.

Careful planning of skin incisions and appropriate orientation of the nipple-areola complex pedicle is essential when performing more complex volume displacement techniques that demand detailed knowledge of the blood supply of the breast and appreciation of plastic surgery principles. This applies particularly to transposition of glandular tissue when there has been extensive undermining from both chest wall and skin and secondary pedicles have been created during a classical Wise-pattern (therapeutic) mammoplasty to address complex/extensive defects and avoid a mastectomy (Figure 8). The nipple-areola complex must be preserved on a robust pedicle – be this superior or inferior or variations of these. These more complex cases of OPBS often demand a multidisciplinary approach involving collaboration between plastic and breast surgeons for optimal outcomes.

It is important to take account of treatment effects upon surgical outcomes for OPBS; any reduction in final breast volume and shape can be unpredictable following radiotherapy (Figure 9). The ultimate aesthetic result may fall short of patient and surgeon expectations even in the absence of any technical challenges during surgery or complications thereafter.

Whole breast reconstruction

In many parts of the world, reconstructive surgery is the exclusive remit of plastic surgeons, with breast surgeons undertaking the extirpative component of surgery only (namely skin/nipple-sparing mastectomy with axillary surgery). In the UK, breast surgeons are routinely trained in techniques of whole breast

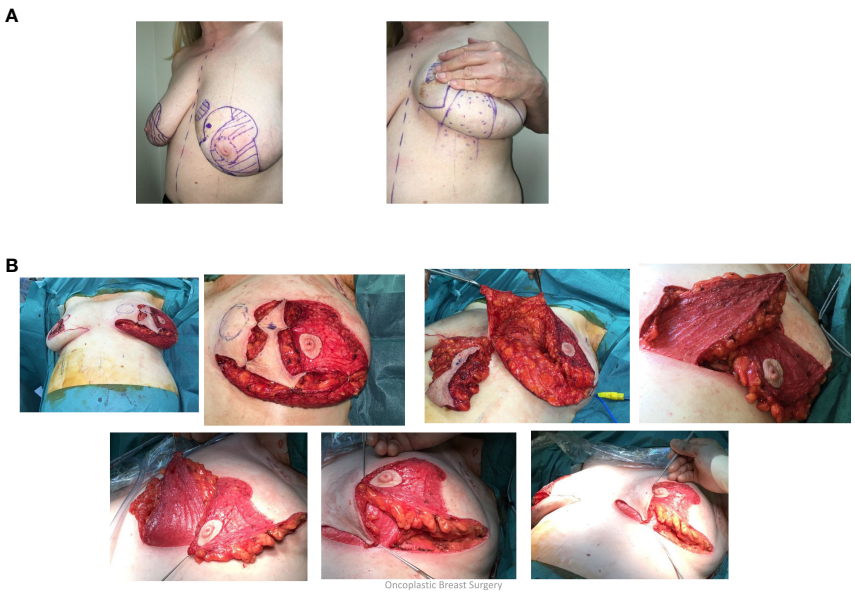
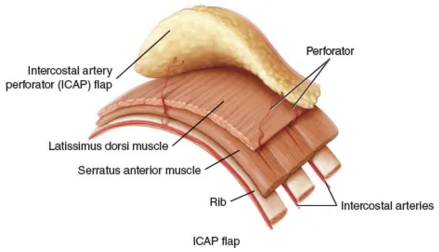
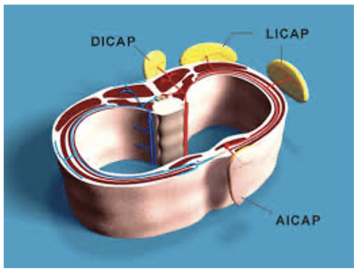


FIGURE 4
(A) Superolateral pedicle and secondary (de-epithelialised totally buried) inferior pedicle: Bilateral breast cancers – different locations, multifocal left breast cancer. **(B)** Intraoperative sequence.



Courtesy of Plastic Surgery Key



Reproduced by permission of Moustapha Hamdi & Elsevier

FIGURE 5
Schematic diagrams showing the intercostal artery perforator flaps: nomenclature and anatomy.

reconstruction that are implant-based with or without adjuvant material (matrix/mesh). NICE guidelines state that patients should be offered reconstruction unless existing co-morbidities pose a contraindication (67).

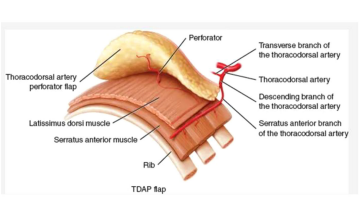
Breast reconstruction can be performed at the time of mastectomy (immediate breast reconstruction [IBR]) or at any time after mastectomy (delayed breast reconstruction [DBR]). In recent years, IBR has gained wider acceptance with improved cosmetic results and reassuring evidence that reconstruction does not mask detection of recurrent disease (68–72).

Furthermore, there are documented psychological benefits from IBR (73–76) and patients awake from anaesthesia with two breasts, albeit one being a facsimile of a breast (i.e a breast mound). By contrast, patients must endure being flat-chested on one or both sides for a period of time whilst awaiting DBR. Nowadays, patients most frequently request IBR and studies with PROMs have shown high levels of satisfaction for IBR (although some studies report higher scores for DBR as patients may compare the reconstructed breast with a flat chest rather than a native breast (77–79)).

For some patients, mastectomy is mandated for breast cancer treatment based on factors such as the tumour: breast ratio, multifocal/centric cancers, or perhaps failed attempts at breast conserving surgery. A decision for mastectomy may also relate to age, genetic predisposition, and availability of IBR. Not all patients seek IBR and this may be contraindicated for some patients based on cancer type (inflammatory cancers), co-morbidities, BMI and smoking history. When proceeding with IBR, one of the most important early decisions is whether the nipple-areola complex should be preserved, and this will be determined on grounds of oncological safety, aesthetic benefit, surgical feasibility, and patient wishes. If pre-operative imaging reveals no direct involvement of the nipple by tumour and there is sufficient distance to the nipple, then nipple preservation is usually feasible, and several studies have confirmed the safety of NSM in terms of local recurrence (80, 81). Nonetheless, some surgeons prefer to take nipple biopsies either pre-operatively with a needle or intra-operatively with frozen section examination of the specimen or intraoperative cores behind the nipple for paraffin sections.

Many breast units have strict selection criteria for IBR with smoking status and BMI being of paramount importance. A BMI in excess of 30 is associated with a 4-fold increase in major complications following IBR (82–84) but most breast units set a BMI threshold between 32 and 35 for IBR. It is essential that patients understand the relative risks and benefits associated with IBR, especially for autologous tissue reconstruction and show compliance with post-operative guidance/instruction.

Skin incisions for skin- and nipple sparing mastectomy should be discussed between surgeon and patient as these are associated with different rates of complications but a peri-areolar incision (+/- medial/lateral extensions) and infra-mammary fold (IMF) incision respectively are conventionally used and preferred by the majority of surgeons (Figure 10). The IMF incision is generally used for



Courtesy of Plastic Surgery Key

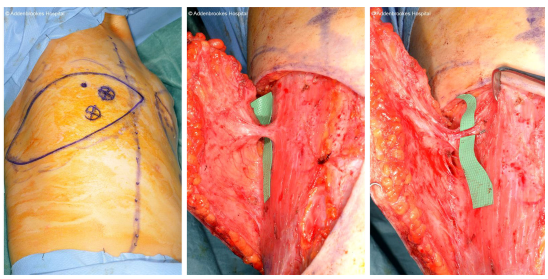


FIGURE 6
TDAP flap vascular anatomy and intraoperative harvest. Courtesy of Plastic Surgery Key. TDAP flap with key perforator 3cm posterior to the anterolateral border of the LD muscle. Intraoperative images show location of the perforator and the muscle split required to increase vascular pedicle length and increase its arc of rotation. No muscle is sacrificed. A small part of muscle can be sacrificed (type 1) vs type 2.

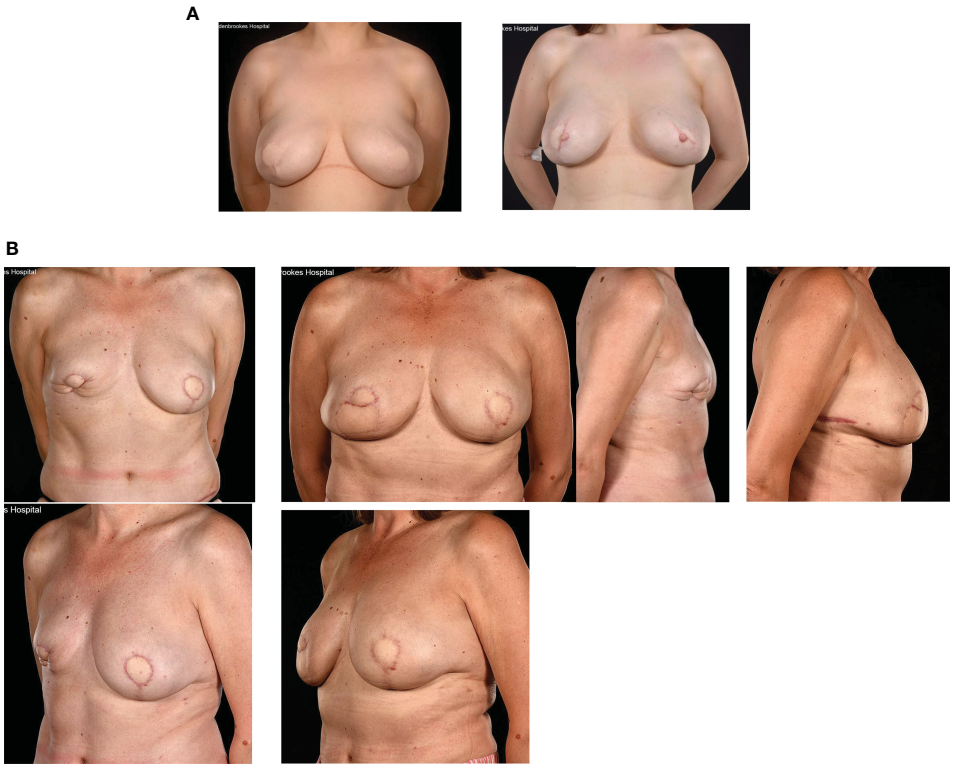


FIGURE 7
(A) Fat grafting of contour defects of bilateral LD + expandable implants for risk reducing surgery. **(B)** Fat necrosis of an immediate SIEA flap: treated by a TDAP flap and serial fat grafting from the abdomen and flanks.

smaller breasts with no pre-operative ptosis, but a radial incision can be employed for more central access to the breast parenchyma. For larger breasts it may be necessary to use special incisions for so-called skin-reducing mastectomies (Figure 11).

The technique for performing either skin- or nipple-sparing mastectomy should respect the oncological plane and ensure that dissection is confined to this plane between the anterior lamella of the superficial fascia and the subcutaneous tissue. It is crucial that subcutaneous blood vessels are preserved, and flaps are not too thin as this will compromise viability and lead to areas of flap necrosis. Adequate access is imperative to ensure that dissection continues to the extreme medial and superior limits of the breast; a separate axillary incision can be made if necessary to approach the ligament of Spence and axillary contents. Some patients require reduction of the breast skin envelope and this will usually be undertaken with a Wise pattern incision and occasionally an inferior dermal sling can be created to support the reconstruction (Figure 12).

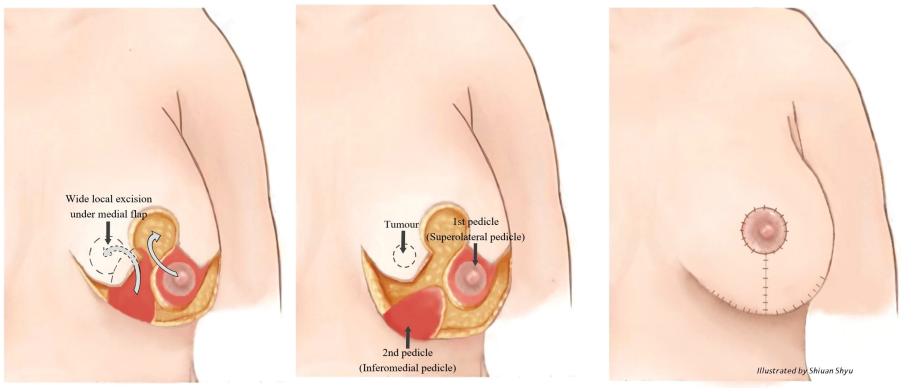


FIGURE 8
Superolateral pedicle and secondary (de-epithelialised totally buried) inferior pedicle. White arrows indicate the direction of flap rotation and final placement. Illustrated by Shiuan Shyu.

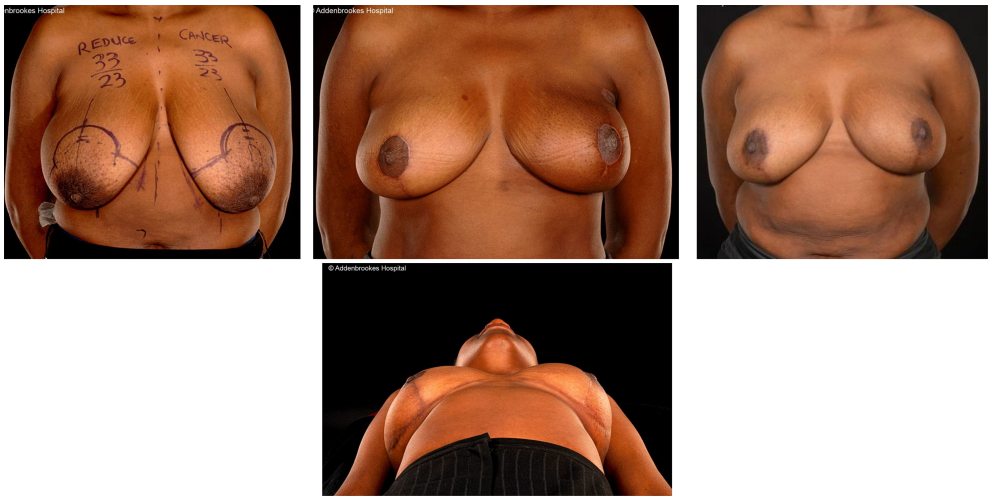


FIGURE 9
Effects of radiotherapy following inferior pedicle technique therapeutic mammaplasty in a 44 year old showing severe radiotherapy reaction and follow up 5 years later showing changes have largely settled.

Autologous tissue versus implant-based reconstruction

Breast reconstruction can be performed using either prosthetic material or autogenous tissue whether this be IBR or DBR. It is recommended that patients meet with their breast surgeon early on to discuss options for reconstruction and be fully informed about these, especially with regards to various types of autologous reconstruction; patients may underestimate the complexity and risks of reconstructive surgery involving tissue transfer techniques.

Autologous tissue reconstruction is most commonly undertaken using flaps harvested from the lower abdomen or the upper back. Abdominal flaps comprise the transverse rectus abdominis myocutaneous (TRAM) flap and deep inferior epigastric artery perforator flap (DIEP) and the superficial inferior epigastric flap (SIEA). The upper back flaps based on the thoracodorsal vessels are the standard latissimus dorsi (LD) flap and the totally autologous LD flap. Other potential flap donor sites for breast reconstruction include the thighs (TUG/TMG, PAP, ALT flaps) buttocks (IGAP, SGAP flaps) posterior trunk (LAP flap) and

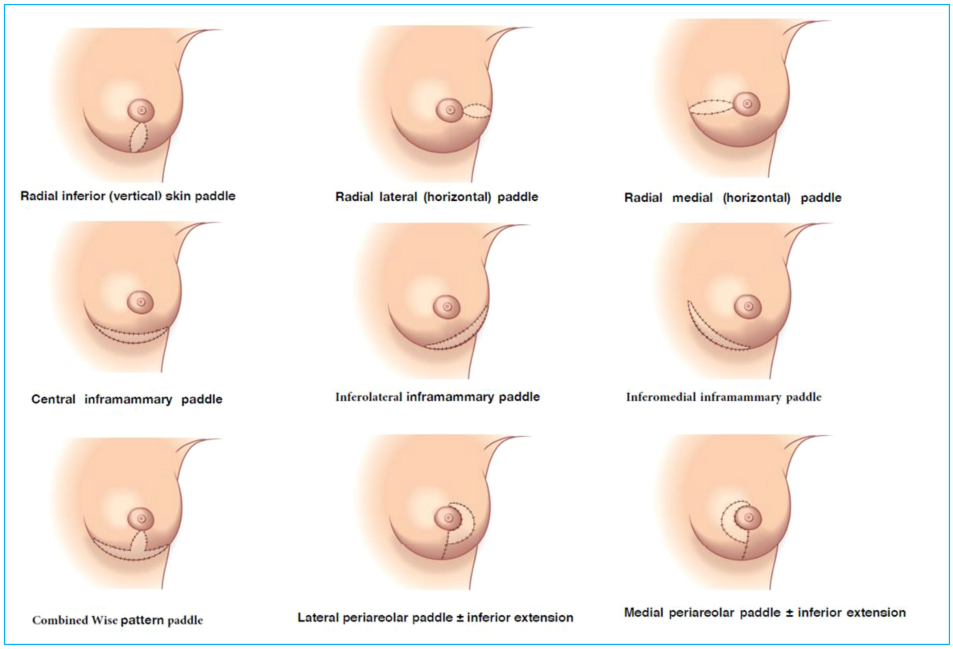


FIGURE 10
Access incisions for nipple-sparing mastectomies and flap reconstruction (85).

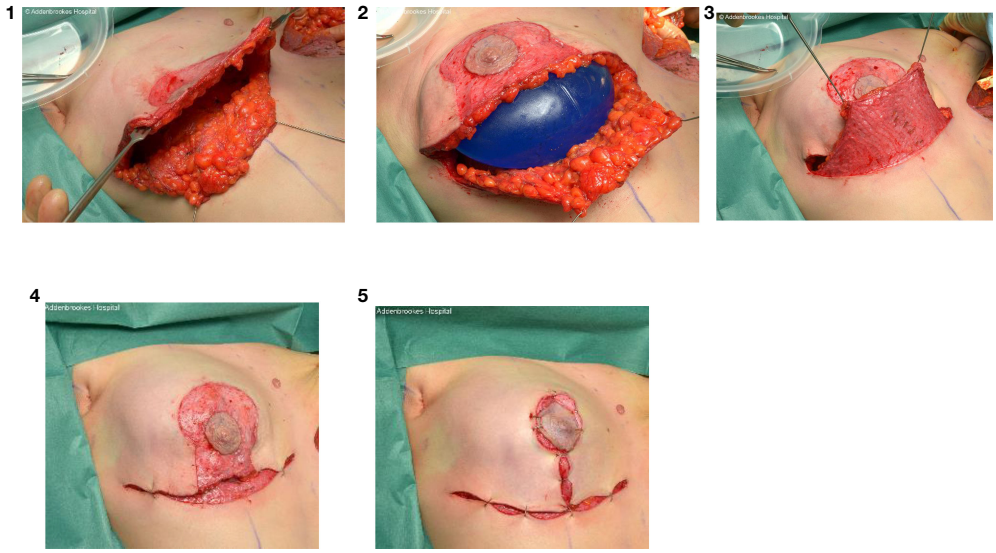


FIGURE 11
Intraoperative sequence of skin-reducing mastectomy with nipple-preservation, pre-pectoral implant and dermal sling reconstruction.

iliac region (Ruben's peri-iliac flap). Interestingly the use of the LD flap in conjunction with an implant (implant-assisted LD flap) for breast reconstruction has dramatically fallen in recent years with the advent of acellular dermal matrices that provide alternative coverage and support for an implant (86, 87). Similarly, a totally autologous LD flap (usually only possible in 15% of patients undergoing LD flaps) is now less frequently performed with emergence of pre-pectoral approaches to implant-based breast reconstruction that minimize animation and reduce post-operative pain. There has also been a reduction in the percentage of complex lower abdominal flaps for breast reconstruction.

The lower abdominal pannus provides generous tissue bulk for reconstruction purposes and therefore supplementation with an implant is unnecessary. These abdominal flap-based reconstructions have pedicle and free-flap variants and are more technically challenging with a greater risk of complications than implant only methods and may entail a microvascular anastomosis. Training in these autologous flap techniques is often protracted and involves specific microsurgical training (e.g. one year fellowship) and therefore these procedures are performed exclusively by plastic surgeons. The free-TRAM flap necessitates harvesting a variable amount of the ipsilateral rectus abdominis muscle (Nahabedian types 1-4) with consequent associated morbidity. The DIEP flap involves dissection and isolation of vascular perforators that pass from the inferior epigastric artery through to the rectus muscle fibres to supply the overlying skin and fat. The muscle therefore remains intact without compromise of abdominal wall integrity but retaining a large infra-umbilical pannus of skin and subcutaneous tissue with which to reconstruct the breast. The evolution of the free-TRAM into the DIEP flap has helped reduce donor site morbidity but there remains a finite risk of complete flap failure. This is generally between 3% and 5% and surgeon-specific rates should be made available to patients who may then chose not to embark on these higher risk reconstructive procedures. Rates of flap failure as low as 3% are achievable in units with high volume throughput and dedicated plastic surgeons with a predominant interest in breast reconstruction. Pre-operative CT angiography has helped predict the chance of success with a DIEP flap reconstruction by identifying candidate perforators and conversely indicating those patients who are technically unsuitable for this procedure. The biggest advantage of CT angiography in breast reconstruction has been to speed up the surgery (88) as it provides an intraoperative roadmap for perforator selection, location and dissection.

Implant-based procedures are the most commonly performed type of reconstruction worldwide and constitute about 70% of breast reconstructions in the UK (and a progressively increasing proportion of cases in the United States). This represents a simpler reconstructive option and has a more acceptable risk profile for many patients than autogenous forms of breast reconstruction. A particular advantage of implant-based IBR is a more rapid return to work and daily activities including familial and other commitments. Most women prefer to retain the same breast size but bilateral mastectomy and implant reconstruction provides the option for either downsizing or upsizing. This can also be possible with abdominal flap reconstruction depending on the relative sizes of the breasts and lower abdomen (Figure 13).

Implant-based reconstruction is technically easier and faster to perform but can be associated with an overall complication rate of 25%. A recent national audit was completed in the UK revealing a mean implant loss rate of 9% (89).

Key issues with implant-based reconstruction relate to type of implant (fixed volume or temporary expander or expandable implant), anatomical site (sub-pectoral or pre-pectoral), shape (anatomical or round) and implant size and to a lesser extent projection. More recently whether to use a smooth or textured surface prostheses has become important in the light of the causative association of implant surface texturing with ALCL.

Round implants provide uniform projection all around and especially in the upper pole. Rotation of such implants has minimal

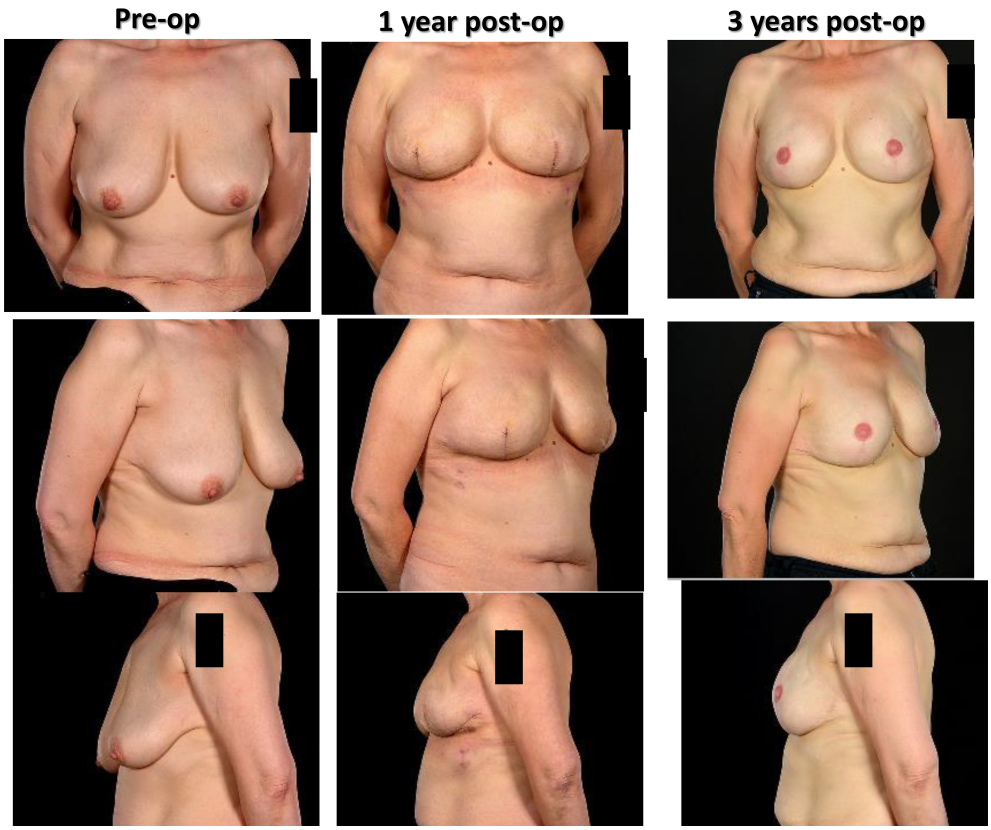


FIGURE 12
Skin reducing mastectomy, expandable implant and dermal sling reconstruction.

consequence in terms of cosmetic appearance. By contrast, anatomical/bi-dimensional implants are tear drop in shape and more closely mimic the natural anatomical shape of the breast. Their *in situ* rotation can have serious consequences for the cosmetic appearance by producing weird breast shapes. Fortunately, anatomical implants only come with textured surfaces which reduce malrotation, malposition and flicking over.

Fixed volume implants are exactly as their name implies and have an immutable size and volume compared with expander implants whose volume is adjustable *via* a port that is tunnelled subcutaneously. This can be minimally filled initially to relieve any pressure effects on the mastectomy flaps and wound during healing and can then be slowly expanded. Expanders can be temporary or permanent and ports can be removed separately if required (under local anaesthesia).

Fixed volume implants and tissue expanders can be placed in a sub-muscular location with complete muscle coverage (beneath a pocket formed from the pectoralis major and serratus anterior muscles). Today prostheses are generally placed in the subpectoral position with partial coverage in a dual plane setting with a combination of pectoralis major muscle and a piece of ADM that is sutured between the lateral border of pectoralis major and the chest wall (IMF) to complete the implant pocket. Increasingly, the implant is placed in a pre-pectoral (epipectoral) location without disruption of the pectoralis major muscle. In consequence there is no muscle animation, less post-operative pain and possibly evidence of less capsular contracture (90). A potential disadvantage of pre-pectoral implants is rippling which is more apparent in patients with a lower BMI and hence thinner flaps. The latter can be subsequently lipo-filled to improve overall contour of the flaps (increasingly oncoplastic surgeons are considering pre-pectoral reconstruction as a multiple stage procedure factoring in 2-3 rounds of postoperative fat grafting). Emerging data including a meta-analysis (90, 91) suggests there is no difference in patient reported outcome measures (Breast Q scores) between pre-pectoral and sub-pectoral implant reconstruction but significant differences in rates of capsular contracture, animation deformity and prosthesis failure favouring pre-pectoral placement of implants (92–94). In addition to issues such as pain and animation, dissection of a sub-pectoral pocket with elevation of the pectoralis major muscle in a dual plane approach with ADM can cause significant upper limb morbidity with associated arm weakness.

The current generation (5^{th}) of implants are composed of material that is unlikely to cause an issue with longevity and necessitate routine replacement. Capsular contracture is an individual response of the host and exacerbated by exposure to irradiation which may require further surgery with capsulotomy and implant exchange. Breast implant associated anaplastic large cell lymphoma (BIA-ALCL) and breast implant-related illness are well publicized conditions which remain poorly understand but explanation of associated risks are part of the standard consent process. The risk of BIA-ALCL is commonly quoted as 1 in 28,000 but figures vary widely. This rare form of lymphoma arises in an

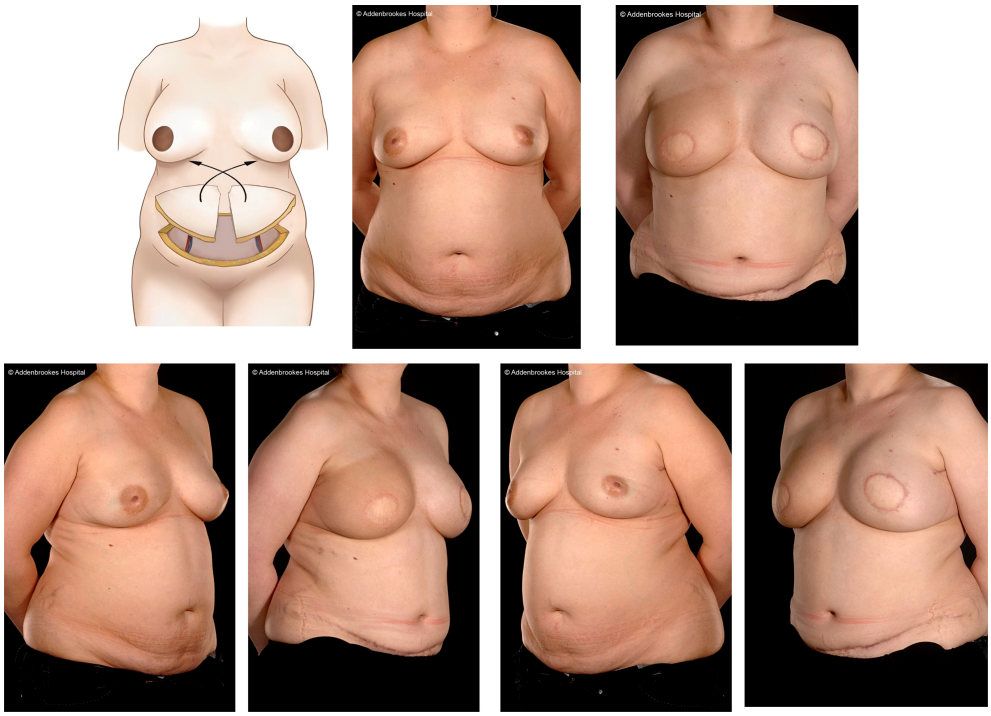


FIGURE 13
Bilateral DIEP flap immediate breast reconstruction following right therapeutic and left prophylactic skin sparing mastectomies. Illustration by Shiuan Shyu.

effusion or scar capsule and patients are warned that any sudden breast swelling occurring more than 8-10 years from original surgery should be investigated to exclude BIA-ALCL. Fluid aspirated from around the implant can be tested for CD30 and the disease-specific marker ALK (anaplastic lymphoma kinase), reflecting a translocation in the tyrosine kinase receptor gene. Treatment in most cases is local and involves excision of the capsule and removal of the implant with later stages sometimes requiring systemic treatment with chemotherapy that is more effective for ALK positive cases (95).

Radiotherapy has a major impact on aesthetic outcomes following irradiation of skin and remaining breast parenchyma after OPBS and in the context of post-mastectomy radiotherapy (PMRT) with whole breast implant-based reconstruction. Although all cases of breast conservation will require radiotherapy, often a final decision on PMRT is made post-operatively when results of definitive histopathology are available. Nonetheless, PMRT may be anticipated, and this will be factored into the decision-making process in terms of surgical approach. Reports to-date suggest that ADM offers some protection from radiotherapy effects (96) and pre-pectoral reconstruction is not associated with significantly higher rates of capsular contracture following PMRT (94).

Complications of oncoplastic surgery

The Dindo classification of surgical complications introduced in 2004 is widely employed in breast surgery and permits objective comparison of outcomes between different studies.

Complications relating to breast surgery patients are generally of mild to moderate severity and lie somewhere between grade 1 and grade 3b, grade 1 being a deviation from normal surgical course without the need for any type of intervention; grade 2 being a complication that requires pharmacological intervention or blood transfusion; grade 3a requiring surgical or radiological intervention without general anaesthetic (97). Nonetheless, these levels of complication can cause significant harm to a patient's physical and mental well-being as well as trust in their surgeon. Neoadjuvant chemotherapy (NACT) patients often require some form of oncoplastic or reconstructive surgery and are more susceptible to surgical complications. The latter may lead to delays in radiotherapy (breast, chest wall, regional nodes) or systemic adjuvant treatments that are increasingly being used in patients with residual disease following NACT (e.g. capecitabine or CDK4/6 inhibitors). Major complications and problems with wound healing can impact significantly on long term breast cancer outcomes in terms of overall and disease-free survival and efforts should be made to minimize the incidence of any adverse surgical events. This includes appropriate selection of patients for more complex procedures, judicious use of surgical adjuvant materials and administration of antibiotics and thromboembolic prophylaxis.

Neoadjuvant chemotherapy approaches increase rates of breast conservation from down-sizing of tumors with rates of mastectomy reduced by 25% - 50% after induction chemotherapy (98, 99) Studies have shown a benefit to patients in terms of physical morbidity and psychological well-being from breast conservation surgery (BCS) compared with mastectomy which is also a more cost-effective treatment with significantly fewer surgical complications.

Moreover, there are several other potential advantages for patients with larger lesions undergoing primary chemotherapy. They include *in vivo* determination of tumor sensitivity, eradication of micrometastatic disease with improved overall survival and downstaging of axillary nodes to de-escalate definitive surgery and minimize upper limb morbidity. Some patients have dramatic clinical response to standard pre-operative chemotherapy regimens and for patients with HER2 positive disease and triple negative cancers, complete pathological response rates can be as high as 70%. Those patients with a complete pathological response (pCR) in both the breast and axilla have improved longer term survival (100) but recent improvements in pCR have failed to translate into higher rates of breast conserving surgery (101). Furthermore, there is an increasing body of evidence that BCS and radiotherapy produces better overall survival outcomes compared with mastectomy (102). Nonetheless, a meta-analysis of clinical trials comparing neoadjuvant to adjuvant chemotherapy reported an increase in local recurrence for the breast conserving surgery group (99). The increase in local recurrence was greatest in the trials that included "no surgery" after NACT. When these 2 trials were excluded then there was only a 3.2% absolute increase in local recurrence in the NACT group at 10 years (RR 1.28, 95% CI: 1.06-1.55). During these trials there was no marking of the tumour site, so in patients with a complete imaging response who had residual disease, the surgeon performed an excision without guidance and is likely to have missed this residual disease in a significant number. It is for this reason that marking the tumour site is now standard practice and there is no reason to resect the original tumour footprint when there is radiological evidence of concentric shrinkage or no residual tumour is apparent. Techniques of OPBS may permit breast conserving surgery in large breasted patients with a 'honeycomb' pattern of shrinkage; there are many advantages of achieving, determining, and utilizing treatment response prior to surgical intervention and patients should be encouraged to undergo breast conserving surgery after neoadjuvant chemotherapy when indicated (103).

Shared decision making

The clinical decision-making process for oncoplastic and reconstructive surgery is broadly based on a range of patient-related factors (including patient preference), surgeon-related factors (including preference and skills set) and healthcare resources (including availability of theatre/capacity).

Patients should be encouraged to engage in a shared decision-making process and will derive information from discussion with surgeons and breast care nurses often supplemented with online resources. They must be given sufficient time to absorb and process information before reaching a final decision on surgical management. Some studies have reported that only one-third of patients recalled being adequately informed about surgical options upon being questioned 3 months following surgery (104, 105). These have emphasized the importance of a balanced information giving process such that patients can make an informed decision regarding breast reconstruction without feeling overwhelmed. More than one-third (35%) of patients in one study who declined reconstruction stated that they considered the amount of information provided on surgical options was insufficient. In the study of Alderman et al, patients who were well informed of reconstructive options were four times more likely to undergo mastectomy (with IBR) than oncoplastic breast conserving surgery. Patients' personal preference may be influenced by family, financial and social pressures depending on her particular circumstances and socio-economic background. Patients may have already formed a clear decision on what type of surgery they want but remain receptive to additional information; there is evidence that levels of patient satisfaction post-operatively are partly determined by the degree to which a surgeon influences a patient's decision. Surgeons should strive to understand why patients chose a particular option and understand that most patients are motivated by body image issues such as "seeking to maintain a balanced appearance" (45).

More objective patient-related factors that influence suitability for an oncoplastic or reconstructive procedure include tumour: breast ratio, breast size and shape (degree of ptosis), body habitus, BMI, co-morbidities, anticipated adjuvant treatments, smoking habits, anatomical factors determining available tissue volume for breast reconstruction/replacement and previous radiotherapy.

Patient factors and co-morbidities that influence healing, recovery, and tolerance of surgical/adjuvant treatments (chemotherapy and radiotherapy) include factors such as: smoking, diabetes, high BMI, vasculopathy, connective tissue diseases. Other factors to consider are patient expectations and understanding of their disease and treatment together with the need for any psychological evaluation and support.

Breast cancer treatment involves a variety of modalities with possible side effects, which can be difficult for patients to understand and accept. One patient compared her journey through chemotherapy, surgery, and radiotherapy to being "poisoned, slashed, and burnt." She revealed that she was unprepared for the whirlwind experience and its considerable impact. From a holistic perspective, breast cancer treatment affects patients' families, relationships, work, sexuality, confidence, independence, and mortality perception. With deadlines looming, patients must overcome obstacles and make decisions, even though they recognize that their choices may affect their survival. It is not unreasonable for patients to question the consequences of failure.

As we have all seen once patients cross that initial phase of treatment and suddenly their chemotherapy and radiotherapy has finished, they are left with the one visible reminder of their journey; the breast. It can be a conflicting entity, a symbol of their sexuality, motherhood, cancer, and mortality. Many studies have confirmed that better aesthetic outcomes improve quality-of-life. The aforementioned catalogue of oncoplastic and reconstructive procedures provide breast cancer patients with a variety of options that can maintain or improve overall well-being and quality-of-life.

Future directions of oncoplastic and reconstructive breast cancer surgery includes the sharing of information on a national and international level to identify trends and learn from good practice. BCCT.core software can help breast surgeons evaluate

cosmetic outcomes of OPBS more objectively and 3D imaging for reconstruction can help with the consent and planning process (106). As we continue to perfect aesthetic outcomes the next frontier in OPBS may be sensation preservation (107).

Other patient-related factors that impact wound healing, post-operative recovery and how well patients tolerate adjuvant treatments include diabetes (types I and II), vasculopathy and connective tissue disorders. These latter conditions can affect viability of mastectomy flaps and transposed glandular tissue of the breast and some connective tissue diseases are a relative contraindication to radiotherapy.

Concluding comments

The diagnostic and treatment pathway for breast cancer patients is a difficult journey psychologically and it is important to gauge patients' understanding of their disease and in particular expectations from breast reconstructive surgery. Patients should not undergo simultaneous contralateral prophylactic mastectomy without formal psychological assessment. There is a relatively restricted timeline once a tissue diagnosis of breast cancer has been made and this may prove challenging and overwhelming for some patients who need more time to adjust to the diagnosis and accept a management plan that is likely to involve multi-modality treatment. Patients must cope with the mutilating effects of surgery and adverse side-effects of radiotherapy and systemic treatments (that usually include hair loss – a major concern and frequent source of alarm for many younger patients). A breast cancer diagnosis has wider implications for a patient's family and relationships be this work-related or more intimate. Apart from negatively affecting body image, self-confidence and sense of femininity, breast cancer is a potentially life-threatening disease and can abruptly remind a patient of their own mortality. Survivorship has come to the forefront in recent years with more attention to quality-of-life and minimising the sequelae of breast cancer treatments – especially surgery and radiotherapy. Patients should have not only an acceptable cosmetic result, but also optimal functional outcomes without chronic symptoms of niggling discomfort or more overt pain symptoms. Nonetheless, the majority of women are successfully treated and will live for many years following breast cancer treatment.

Author contributions

PW and JRB wrote the article. JRB edited article. CMM edited second part of the article, contributed photography and diagrams. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

References

1. *Facts and figures | breast cancer UK*. Available at: https://www.breastcanceruk.org.uk/about-breast-cancer/facts-figures-and-qas/facts-and-figures/.

2. *Breast cancer*. Available at: https://www.who.int/news-room/fact-sheets/detail/breast-cancer.

3. *Breast cancer statistics and facts | breast cancer now*. Available at: https://breastcancernow.org/about-us/media/facts-statistics.

4. Group on Hormonal Factors in Breast Cancer C. Type and timing of menopausal hormone therapy and breast cancer risk: individual participant meta-analysis of the worldwide epidemiological evidence. *Lancet* (2019) 394(10204):1159–68. doi: 10.1016/S0140-6736(19)31709-X

5. Beral V, Peto R, Pirie K, Reeves G. Menopausal hormone therapy and 20-year breast cancer mortality. *Lancet* (2019) 394(10204):1139. doi: 10.1016/S0140-6736(19)32033-1

6. Ravdin PM, Cronin KA, Howlader N, Berg CD, Chlebowski RT, Feuer EJ, et al. The decrease in breast-cancer incidence in 2003 in the united states. *N Engl J Med* (2007) 356(16):1670–4. doi: 10.1056/NEJMsr070105

7. Banks E, Canfell K. Recent declines in breast cancer incidence: mounting evidence that reduced use of menopausal hormones is largely responsible. *Breast Cancer Res* (2010) 12(1):1–3. doi: 10.1186/bcr2463

8. Mcdonald JA, Goyal A, Terry MB. Alcohol Intake and Breast Cancer Risk: Weighing the Overall Evidence. *Curr Breast Cancer Rep*. (2013) 5(3):10.1007/s12609-013-0114-z. doi: 10.1007/s12609-013-0114-z

9. Seitz HK, Pelucchi C, Bagnardi V, Vecchia C. *REVIEW epidemiology and pathophysiology of alcohol and breast cancer*. Available at: https://academic.oup.com/alcalc/article/47/3/204/145832.

10. Smith-Warner SA, Spiegelman D, Yaun SS, van den Brandt PA, Folsom AR, Goldbohm RA, et al. Alcohol and breast cancer in women: a pooled analysis of cohort studies. *JAMA* (1998) 279(7):535–40. doi: 10.1001/jama.279.7.535

11. Williams LA, Olshan AF, Tse CK, Bell ME, Troester MA. Alcohol intake and invasive breast cancer risk by molecular subtype and race in the Carolina breast cancer study. *Cancer Causes Control* (2016) 27(2):259–69. doi: 10.1007/s10552-015-0703-4

12. Klintman M, Rosendahl AH, Randeris B, Eriksson M, Czene K, Hall P, et al. Postmenopausal overweight and breast cancer risk; results from the KARMA cohort. *Breast Cancer Res Treat* (2022) 196(1):185–96. doi: 10.1007/s10549-022-06664-7

13. Neuhouser ML, Aragaki AK, Prentice RL, Manson JAE, Chlebowski R, Carty CL, et al. Overweight, obesity, and postmenopausal invasive breast cancer risk: a secondary analysis of the women's health initiative randomized clinical trials. *JAMA Oncol* (2015) 1(5):611–21. doi: 10.1001/jamaoncol.2015.1546

14. *Exercise recommended to improve lives of women with breast cancer | WCRF international*. Available at: https://www.wcrf.org/latest/news-and-updates/exercise-recommended-to-improve-lives-of-women-with-breast-cancer/.

15. Zwakman M, Tan A, Boersma C, Klinkenbijl JHG, Noorda EM, de Jong TR, et al. Long-term quality of life and aesthetic outcomes after breast conserving surgery in patients with breast cancer. *Eur J Surg Oncol* (2022) 48(8):1692–8. doi: 10.1016/j.ejso.2022.02.011

16. Stolpner I, Heil J, Riedel F, Wallwiener M, Schäfgen B, Feißt M, et al. Long-term patient satisfaction and quality of life after breast-conserving therapy: a prospective study using the BREAST-q. *Ann Surg Oncol* (2021) 28(13):8742–51. doi: 10.1245/s10434-021-10377-4

17. Halsted W. The results of operations for the cure of cancer of the breast performed at the johns Hopkins hospital from June, 1889, to January, 1894. *Ann Surg* (1894) 20(5):497–555. doi: 10.1097/00000658-189407000-00075

18. Fisher B, Anderson S, Fisher ER, Redmond C, Wickerham DL, Wolmark N, et al. Significance of ipsilateral breast tumour recurrence after lumpectomy. *Lancet* (1991) 338(8763):327–31. doi: 10.1016/0140-6736(91)90475-5

19. Halsted CP, Benson JR, Jatoi I. A historical account of breast cancer surgery: beware of local recurrence but be not radical. *Future Oncol* (2014) 10(9):1649–57. doi: 10.2217/fon.14.98

20. Veronesi U, Banfi A, Saccozzi R, Salvadori B, Zucali R, Uslenghi C, et al. CONSERVATIVE TREATMENT OF BREAST CANCER a trial in progress at the cancer institute of m i l a n. *Cancer* (1977) 39:2822–6. doi: 10.1002/1097-0142(197706)39:6<2822::AID-CNCR2820390670>3.0.CO;2-#

21. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* (2002) 347(16):1233–41. doi: 10.1056/NEJMoa022152

22. Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med* (2002) 347(16):1227–32. doi: 10.1056/NEJMoa020989

23. Moran MS, Schnitt SJ, Giuliano AE, Harris JR, Khan SA, Horton J, et al. Society of surgical oncology-American society for radiation oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in stages I and II invasive breast cancer. *Int J Radiat Oncol Biol Phys* (2014) 88(3):553–64. doi: 10.1016/j.ijrobp.2013.11.012

24. Morrow M, Harris JR, Schnitt SJ. Surgical margins in lumpectomy for breast cancer {[/amp]]mdash; bigger is not better. *New Engl J Med* (2012) 367(1):79–82. doi: 10.1056/NEJMsb1202521

25. Della Rovere GQ, Benson JR. Ipsilateral local recurrence of breast cancer: determinant or indicator of poor prognosis? *Lancet Oncol* (2002) 3(3):183–7. doi: 10.1016/S1470-2045(02)00683-6

26. Patey DH, Dyson WH. The prognosis of carcinoma of the breast in relation to the type of operation performed. *Br J Cancer* (1948) 2(1):7. doi: 10.1038/bjc.1948.2

27. Toth BA, Lappert P. Modified skin incisions for mastectomy: the need for plastic surgical input in preoperative planning. *Plast Reconstr Surg* (1991) 87(6):1048–53.

28. Joo JH, Ki Y, Kim W, Nam J, Kim D, Park J, et al. Pattern of local recurrence after mastectomy and reconstruction in breast cancer patients: a systematic review. *Gland Surg* (2021) 10(6):2037046–2032046. doi: 10.21037/gs-21-15

29. Vaughan A, Dietz JR, Aft R, Gillanders WE, Eberlein TJ, Freer P, et al. Patterns of local breast cancer recurrence after skin-sparing mastectomy and immediate breast reconstruction. *Am J Surg* (2007) 194(4):438–43. doi: 10.1016/j.amjsurg.2007.06.011

30. Rusby JE, Smith BL, Gui GPH. Nipple-sparing mastectomy. *Br J Surg* (2010) 97(3):305–16. doi: 10.1002/bjs.6970

31. Jatoi I, Benson JR. Surgical management of the axilla in early breast cancer. *Curr Probl Surg* (2018) 55(2):47–65. doi: 10.1067/j.cpsurg.2018.01.003

32. Cochrane RA, Valasiadou P, Wilson ARM, Al-Ghazal SK, Macmillan RD. Cosmesis and satisfaction after breast-conserving surgery correlates with the percentage of breast volume excised. *Br J Surg* (2003) 90(12):1505–9. doi: 10.1002/bjs.4344

33. Losken A, Dugal CS, Styblo TM, Carlson GW. A meta-analysis comparing breast conservation therapy alone to the oncoplastic technique. *Ann Plast Surg* (2014) 72(2):145–9. doi: 10.1097/SAP.0b013e3182605598

34. Benson JR, Absar MS. Volume replacement and displacement techniques in oncoplastic surgery. *Adv Breast Cancer* (2008) 5(1):3–10.

35. Clough KB, Kaufman GJ, Nos C, Buccimazza I, Sarfati IM. Improving breast cancer surgery: a classification and quadrant per quadrant atlas for oncoplastic surgery. *Ann Surg Oncol* (2010) 17(5):1375–91. doi: 10.1245/s10434-009-0792-y

36. Clough KB, Benyahi D, Nos C, Charles C, Sarfati I. Oncoplastic surgery: pushing the limits of breast-conserving surgery. *Breast J* (2015) 21(2):140–6. doi: 10.1111/tbj.12372

37. Clough KB, Meredith I. The oncoplastic frenzy: beware the swing of the pendulum. *Ann Surg Oncol* (2019) 26(12):3792–3. doi: 10.1245/s10434-019-07755-4

38. Rocco N, Catanuto G, Cinquini M, Audretsch W, Benson J, Criscitiello C, et al. Should oncoplastic breast conserving surgery be used for the treatment of early stage breast cancer? using the GRADE approach for development of clinical recommendations. *Breast* (2021) 57:25–35. doi: 10.1016/j.breast.2021.02.013

39. de Oliveira-Junior I, de Araujo da Silva I, Cristina Brandini da Silva F, José da Silva J, José Sarri Carlos Eduardo Paiva A, Aloisio da Costa Vieira a-c R, et al. Oncoplastic surgery in breast-conserving treatment: patient profile and impact on quality of life keywords breast cancer · conserving surgery · conserving treatment · oncoplastic surgery · quality of life · cosmetic techniques. *Res Article Breast Care* (2021) 16:243–53. doi: 10.1159/000507240

40. Benson JR, Down SK. Coming of age of oncoplastic breast surgery. *Br J Surg* (2017) 104(10):1269–71. doi: 10.1002/bjs.10579

41. Jagsi R, Li Y, Morrow M, Janz N, Alderman A, Graff J, et al. Patient-reported quality of life and satisfaction with cosmetic outcomes after breast conservation and mastectomy with and without reconstruction: results of a survey of breast cancer survivors. *Ann Surg* (2015) 261(6):1198–206. doi: 10.1097/SLA.0000000000000908

42. Alderman AK, Hawley ST, Waljee J, Morrow M, Katz SJ. Correlates of referral practices of general surgeons to plastic surgeons for mastectomy reconstruction. *Cancer* (2007) 109(9):1715–20. doi: 10.1002/cncr.22598

43. Pusic AL, Klassen AF, Scott AM, Klok JA, Cordeiro PG, Cano SJ. Development of a new patient-reported outcome measure for breast surgery: the BREAST-q. *Plast Reconstr Surg* (2009) 124(2):345–53. doi: 10.1097/PRS.0b013e3181aee807

44. Catanuto G, Rocco N, Maglia A, Barry P, Karakatsanis A, Sgroi G, et al. Text mining and word embedding for classification of decision making variables in breast cancer surgery. *Eur J Surg Oncol* (2022) 48(7):1503–9. doi: 10.1016/j.ejso.2022.03.002

45. Duggal CS, Metcalfe D, Sackeyfio R, Carlson GW, Losken A. Patient motivations for choosing postmastectomy breast reconstruction. *Ann Plast Surg* (2013) 70(5):574–80. doi: 10.1097/SAP.0b013e3182851052

46. Eltahir Y, Werners LLCH, Dreise MM, Van Emmichoven IAZ, Jansen L, Werker PMN, et al. Quality-of-life outcomes between mastectomy alone and breast reconstruction: comparison of patient-reported BREAST-q and other health-related quality-of-life measures. *Plast Reconstr Surg* (2013) 132(2):201e–209e. doi: 10.1097/PRS.0b013e31829586a7

47. Atisha DM, Rushing CN, Samsa GP, Locklear TD, Cox CE, Shelley Hwang E, et al. A national snapshot of satisfaction with breast cancer procedures. *Ann Surg Oncol* (2015) 22(2):361–9. doi: 10.1245/s10434-014-4246-9

48. Silverstein MJ. Radical mastectomy to radical conservation (Extreme oncoplasty): a revolutionary change. *J Am Coll Surg* (2016) 222(1):1–9. doi: 10.1016/j.jamcollsurg.2015.10.007

49. Silverstein MJ, Savalia N, Khan S, Ryan J. Extreme oncoplasty: breast conservation for patients who need mastectomy. *Breast J* (2015) 21(1):52. doi: 10.1111/tbj.12356

50. Kronowitz S, Benson J, Nava M. (Eds.). *Oncoplastic and Reconstructive Management of the Breast, Third* Edition (3rd ed.). CRC Press. (2020). Available at: doi: 10.1201/9781003005476

51. Ingram J, Beasant L, Benson J, Brunt AM, Maxwell A, Harvey JR, et al. The challenge of equipoise: qualitative interviews exploring the views of health professionals and women with multiple ipsilateral breast cancer on recruitment to a surgical randomised controlled feasibility trial. *Pilot Feasibility Stud* (2022) 8(1):46. doi: 10.1186/s40814-022-01007-1

52. Basu NN, Hodson J, Chatterjee S, Gandhi A, Wisely J, Harvey J, et al. The Angelina jolie effect: contralateral risk-reducing mastectomy trends in patients at increased risk of breast cancer. *Sci Rep* (2021) 11(1):e13686. doi: 10.1038/s41598-021-82654-x

53. NICE. *Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer*. London: National Institute for Health and Care Excellence (NICE) (2019). Available at: https://www.ncbi.nlm.nih.gov/books/NBK552606/.

54. Evans MK, Longo DL. PALB2 mutations and breast-cancer risk. *N Engl J Med* (2014) 371(6):566. doi: 10.1056/NEJMe1405784

55. Franca FC, de Oliveira-Junior I, Morgan AM, Haikel RL, da Costa Vieira RA. Breast-conserving surgery with the geometric compensation/split reduction technique. indications, oncologic safety and cosmesis. a cohort series and systematic review of the literature. *Surg Oncol* (2022) 44:101839. doi: 10.1016/j.suronc.2022.101839

56. Blok YL, Verduijn PS, Corion LUM, Visser JM, van der Pol CC, van der Hage JA, et al. An analysis of complication rates and the influence on patient satisfaction and cosmetic outcomes following oncoplastic breast surgery. *J Plastic Reconstructive Aesthetic Surg* (2022) 75(11):4152–9. doi: 10.1016/j.bjps.2022.06.088

57. Massey EJD, Gouveia PF, Nos C, Poulet B, Sarfati I, Clough KB. A new level 1 oncoplastic technique for breast conserving surgery: rotation glandular flap. *Breast* (2013) 22(2):186–9. doi: 10.1016/j.breast.2013.01.012

58. Rainsbury RM. Breast-sparing reconstruction with latissimus dorsi miniflaps. *Eur J Surg Oncol* (2002) 28(8):891–5. doi: 10.1053/ejso.2002.1350

59. Hamdi M, Van Landuyt K, Monstrey S, Blondeel P. Pedicled perforator flaps in breast reconstruction: a new concept. *Br J Plast Surg* (2004) 57(6):531–9. doi: 10.1016/j.bjps.2004.04.015

60. Hamdi M, Van Landuyt K, de Frene B, Roche N, Blondeel P, Monstrey S. The versatility of the inter-costal artery perforator (ICAP) flaps. *J Plast Reconstr Aesthet Surg* (2006) 59(6):644–52. doi: 10.1016/j.bjps.2006.01.006

61. Hamdi M, Spano A, Landuyt KV, D'Herde K, Blondeel P, Monstrey S. The lateral intercostal artery perforators: anatomical study and clinical application in breast surgery. *Plast Reconstr Surg* (2008) 121(2):389–96. doi: 10.1097/01.prs.0000298317.65296.cf

62. McCulley SJ, Schaverien MV, Tan VKM, Macmillan RD. Lateral thoracic artery perforator (LTAP) flap in partial breast reconstruction. *J Plast Reconstr Aesthet Surg* (2015) 68(5):686–91. doi: 10.1016/j.bjps.2015.01.008

63. Ørholt M, Larsen A, Hemmingsen MN, Mirian C, Zocchi ML, Vester-Glowinski PV, et al. Complications after breast augmentation with fat grafting: a systematic review. *Plast Reconstr Surg* (2020) 145(3):530E–7E. doi: 10.1097/PRS.0000000000006569

64. Skillman J, McManus P, Bhaskar P, Hamilton S, Roy PG, O'Donoghue JM. UK Guidelines for lipomodelling of the breast on behalf of plastic, reconstructive and aesthetic surgery and association of breast surgery expert advisory group. *J Plast Reconstr Aesthet Surg* (2022) 75(2):511–8. doi: 10.1016/j.bjps.2021.09.033

65. Sowa Y, Inafuku N, Tsuge I, Yamanaka H, Morimoto N. Patient-reported outcomes after autologous fat grafting in prosthetic breast reconstruction: prospective cohort study using a multivariate analysis. *Ann Plast Surg* (2023) 90(2):123–7. doi: 10.1097/SAP.0000000000003383

66. Groen JW, Negenborn VL, Twisk JWR, Ket JCF, Mullender MG, Smit JM. Autologous fat grafting in cosmetic breast augmentation: a systematic review on radiological safety, complications, volume retention, and Patient/Surgeon satisfaction. *Aesthet Surg J* (2016) 36(9):993–1007. doi: 10.1093/asj/sjw105

67. NICE Guideline [NG101]. Early and locally advanced breast cancer: diagnosis and management. (2018).

68. Siotos C, Naska A, Bello RJ, Uzosike A, Orfanos P, Euhus DM, et al. Survival and disease recurrence rates among breast cancer patients following mastectomy with or without breast reconstruction. *Plast Reconstr Surg* (2019) 144(2):169–E177E. doi: 10.1097/PRS.0000000000005798

69. Bargon CA, Young-Afat DA, Ikinci M, Braakenburg A, Rakhorst HA, Mureau MAM, et al. Breast cancer recurrence after immediate and delayed postmastectomy breast reconstruction-a systematic review and meta-analysis. *Cancer* (2022) 128 (19):3449–69. doi: 10.1002/cncr.34393

70. Nedumpara T, Jonker L, Williams MR. Impact of immediate breast reconstruction on breast cancer recurrence and survival. *Breast* (2011) 20(5):437–43. doi: 10.1016/j.breast.2011.04.006

71. Costeira B, da Silva FB, Oom R, Costa C, Moniz JV, Abecasis N, et al. Locoregional recurrence in skin-sparing and nipple-sparing mastectomies. *J Surg Oncol* (2022) 125(3):352–60. doi: 10.1002/jso.26725

72. Langstein HN, Cheng MH, Singletary SE, Robb GL, Hoy E, Smith TL, et al. Breast cancer recurrence after immediate reconstruction: patterns and significance. *Plast Reconstr Surg* (2003) 111(2):712–20. doi: 10.1097/01.PRS.0000041441.42563.95

73. Gil-Olarte P, Gil-Olarte MA, Gómez-Molinero R, Guil R. Psychosocial and sexual well-being in breast cancer survivors undergoing immediate breast reconstruction: the mediating role of breast satisfaction. *Eur J Cancer Care (Engl)* (2022) 31(6):e13686. doi: 10.1111/ecc.13686

74. Fernández-Delgado J, López-Pedraza MJ, Blasco JA, Andradas-Aragones E, Sánchez-Méndez JI, Sordo-Miralles G, et al. Satisfaction with and psychological impact of immediate and deferred breast reconstruction. *Ann Oncol* (2008) 19(8):1430–4. doi: 10.1093/annonc/mdn153

75. Al-Ghazal SK, Sully L, Fallowfield L, Blamey RW. The psychological impact of immediate rather than delayed breast reconstruction. *Eur J Surg Oncol* (2000) 26(1):17–9. doi: 10.1053/ejso.1999.0733

76. Heimes AS, Stewen K, Hasenburg A. Psychosocial aspects of immediate versus delayed breast reconstruction. *Breast Care (Basel)* (2017) 12(6):374–7. doi: 10.1159/000485234

77. Pusic AL, Matros E, Fine N, Buchel E, Gordillo GM, Hamill JB, et al. Patient-reported outcomes 1 year after immediate breast reconstruction: results of the mastectomy reconstruction outcomes consortium study. *J Clin Oncol* (2017) 35 (22):2499–506. doi: 10.1200/JCO.2016.69.9561

78. Cordova LZ, Hunter-Smith DJ, Rozen WM. Patient reported outcome measures (PROMs) following mastectomy with breast reconstruction or without reconstruction: a systematic review. *Gland Surg* (2019) 8(4):441–51. doi: 10.21037/gs.2019.07.02

79. Santosa KB, Qi J, Kim HM, Hamill JB, Wilkins EG, Pusic AL. Long-term patient-reported outcomes in postmastectomy breast reconstruction. *JAMA Surg* (2018) 153(10):891–9. doi: 10.1001/jamasurg.2018.1677

80. De La Cruz L, Moody AM, Tappy EE, Blankenship SA, Hecht EM. Overall survival, disease-free survival, local recurrence, and nipple-areolar recurrence in the setting of nipple-sparing mastectomy: a meta-analysis and systematic review. *Ann Surg Oncol* (2015) 22(10):3241–9. doi: 10.1245/s10434-015-4739-1

81. Smith BL, Tang R, Rai U, Plichta JK, Colwell AS, Gadd MA, et al. Oncologic safety of nipple-sparing mastectomy in women with breast cancer. *J Am Coll Surg* (2017) 225(3):361–5. doi: 10.1016/j.jamcollsurg.2017.06.013

82. Fischer JP, Nelson JA, Kovach SJ, Serletti JM, Wu LC, Kanchwala S. Impact of obesity on outcomes in breast reconstruction: analysis of 15,937 patients from the ACS-NSQIP datasets. *J Am Coll Surg* (2013) 217(4):656–64. doi: 10.1016/j.jamcollsurg.2013.03.031

83. Panayi AC, Agha RA, Sieber BA, Orgill DP. Impact of obesity on outcomes in breast reconstruction: a systematic review and meta-analysis. *J Reconstr Microsurg* (2018) 34(5):363–75. doi: 10.1055/s-0038-1627449

84. Srinivasa DR, Clemens MW, Qi J, Hamill JB, Kim HM, Pusic AL, et al. Obesity and breast reconstruction: complications and patient-reported outcomes in a multicenter, prospective study. *Plast Reconstr Surg* (2020) 145(3):481E–90E. doi: 10.1097/PRS.0000000000006543

85. Samaras S, Malata C. An algorithm for selecting Buoy skin paddle design for flap monitoring in total autologous breast reconstruction after nipple-sparing mastectomy. *Cureus* (2023) 15(1):e33443. doi: 10.7759/cureus.33443

86. Kankam HKN, Hourston GJM, Fopp LJ, Benson JR, Benyon SL, Irwin MS, et al. Trends in post-mastectomy breast reconstruction types at a breast cancer tertiary referral centre before and after introduction of acellular dermal matrices. *J Plast Reconstr Aesthet Surg* (2018) 71(1):21–7. doi: 10.1016/j.bjps.2017.08.016

87. Leff DR, Bottle A, Mayer E, Patten DK, Rao C, Aylin P, et al. Trends in immediate postmastectomy breast reconstruction in the united kingdom. *Plast Reconstr Surg Glob Open* (2015) 3(9):e507. doi: 10.1097/GOX.0000000000000484

88. Ngaage LM, Oni G, Di Pace B, Hamed RR, Fopp L, Koo BC, et al. The effect of CT angiography and venous couplers on surgery duration in microvascular breast reconstruction: a single operator's experience. *Gland Surg* (2018) 7(5):44048–448. doi: 10.21037/gs.2018.07.11

89. Potter S, Conroy EJ, Cutress RI, Williamson PR, Whisker L, Thrush S, et al. Short-term safety outcomes of mastectomy and immediate implant-based breast reconstruction with and without mesh (iBRA): a multicentre, prospective cohort study. *Lancet Oncol* (2019) 20(2):254–66. doi: 10.1016/S1470-2045(18)30781-2

90. Ostapenko E, Nixdorf L, Devyatko Y, Exner R, Wimmer K, Fitzal F. Prepectoral versus subpectoral implant-based breast reconstruction: a systemic review and meta-analysis. *Ann Surg Oncol* (2023) 30(1):126–36. doi: 10.1245/s10434-022-12567-0

91. NK L, S P, J D, KS G, RT W, CJ S, et al. A comparison of BREAST-q scores between prepectoral and subpectoral direct-to-Implant breast reconstruction. *Plast Reconstr Surg* (2021) 148(5):708E–14E. doi: 10.1097/PRS.0000000000008410

92. Highton L, Johnson R, Kirwan C, Murphy J. Prepectoral implant-based breast reconstruction. *Plast Reconstr Surg Glob Open* (2017) 5(9):e1488. doi: 10.1097/GOX.0000000000001488

93. Elswick SM, Harless CA, Bishop SN, Schleck CD, Mandrekar J, Reusche RD, et al. Prepectoral implant-based breast reconstruction with postmastectomy radiation therapy. *Plast Reconstr Surg* (2018) 142(1):1–12. doi: 10.1097/PRS.0000000000004453

94. Sobti N, Weitzman RE, Nealon KP, Jimenez RB, Gfrerer L, Mattos D, et al. Evaluation of capsular contracture following immediate prepectoral versus subpectoral direct-to-implant breast reconstruction. *Sci Rep* (2020) 10(1):1–11. doi: 10.1038/s41598-020-58094-4

95. Turton P, El-Sharkawi D, Lyburn I, Sharma B, Mahalingam P, Turner SD, et al. UK Guidelines on the diagnosis and treatment of breast implant-associated anaplastic Large cell lymphoma on behalf of the medicines and healthcare products regulatory agency plastic, reconstructive and aesthetic surgery expert advisory group. *Br J Haematol* (2021) 192(3):444–58. doi: 10.1111/bjh.17194

96. Craig ES, Clemens MW, Koshy JC, Wren J, Hong Z, Butler CE, et al. Outcomes of acellular dermal matrix for immediate tissue expander reconstruction with radiotherapy: a retrospective cohort study. *Aesthet Surg J* (2019) 39(3):279–88. doi: 10.1093/asj/sjy127

97. Dindo D, Demartines N, Clavien PA, Clavien PA. Classification of surgical complications a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* (2004) 240(2):205–13. doi: 10.1097/01.sla.0000133083.54934.ae

98. Killelea BK, Yang VQ, Mougalian S, Horowitz NR, Pusztai L, Chagpar AB, et al. Neoadjuvant chemotherapy for breast cancer increases the rate of breast conservation: results from the national cancer database. *J Am Coll Surg* (2015) 220(6):1063–9. doi: 10.1016/j.jamcollsurg.2015.02.011

99. Asselain B, Barlow W, Bartlett J, Bergh J, Bergsten-NordstrÃ E, Bliss J, et al. Articles long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: meta-analysis of individual patient data from ten randomised trials. *Lancet Oncol* (2018) 19:27–39. doi: 10.1016/S1470-2045(17)30777-5

100. Fisher B, Brown A, Mamounas E, Wieand S, Robidoux A, Margolese RG, et al. Effect of preoperative chemotherapy on local-regional disease in women with operable breast cancer: findings from national surgical adjuvant breast and bowel project b-18. *J Clin Oncol* (1997) 15(7):2483–93. doi: 10.1200/JCO.1997.15.7.2483

101. Karakatsanis A, Tasoulis MK, Wärnberg F, Nilsson G, MacNeill F. Meta-analysis of neoadjuvant therapy and its impact in facilitating breast conservation in operable breast cancer. *Br J Surg* (2018) 105(5):469–81. doi: 10.1002/bjs.10807

102. Johns N, Dixon JM. Should patients with early breast cancer still be offered the choice of breast conserving surgery or mastectomy? *Eur J Surg Oncol* (2016) 42 (11):1636–41. doi: 10.1016/j.ejso.2016.08.016

103. Re: Rethinking neoadjuvant chemotherapy for breast cancer, John Benson, Dorin Dumitru, Ismail Jatoi. *BMJ* (2018) 360:j5913.

104. Jeevan R. Reconstructive utilisation and outcomes following mastectomy surgery in women with breast cancer treated in England. *Ann R Coll Surg Engl* (2020) 102(2):110–4. doi: 10.1308/rcsann.2019.0101

105. Alderman AK, Hawley ST, Waljee J, Mujahid M, Morrow M, Katz SJ. Understanding the impact of breast reconstruction on the surgical decision-making process for breast cancer. *Cancer* (2008) 112(3):489–94. doi: 10.1002/cncr.23214

106. O'Connell RL, Stevens RJG, Harris PA, Rusby JE. Review of three-dimensional (3D) surface imaging for oncoplastic, reconstructive and aesthetic breast surgery. *Breast* (2015) 24(4):331–42. doi: 10.1016/j.breast.2015.03.011

107. Peled AW, Peled ZM. Nerve preservation and allografting for sensory innervation following immediate implant breast reconstruction. *Plast Reconstr Surg Glob Open* (2019) 7(7):e2332. doi: 10.1097/GOX.0000000000002332

frontiers | Frontiers in Oncology

TYPE Original Research
PUBLISHED 20 July 2023
DOI 10.3389/fonc.2023.1159073

OPEN ACCESS

EDITED BY
Cicero Urban,
Hospital Nossa Senhora das Graças, Brazil

REVIEWED BY
Wenbin Zhou,
Nanjing Medical University, China
Cleverton Cesar Spautz,
Oncoclinica/Breast Center Disease, Brazil

*CORRESPONDENCE
Jiong Wu
wujiong1122@vip.sina.com

†These authors have contributed equally to this work and share first authorship

RECEIVED 09 February 2023
ACCEPTED 06 July 2023
PUBLISHED 20 July 2023

CITATION
Zheng S, Hao S, Chen J, Zhang Y, Yang B, Huang X, Liu G, Shao Z and Wu J (2023) Latissimus dorsi flap – the main force in breast reconstruction for breast tumor in Chinese population.
Front. Oncol. 13:1159073.
doi: 10.3389/fonc.2023.1159073

Latissimus dorsi flap – the main force in breast reconstruction for breast tumor in Chinese population

Shuyue Zheng[1,2,3†], Shuang Hao[1,3†], Jiajian Chen[1,3], Yingying Zhang[1,3], Benlong Yang[1,3], Xiaoyan Huang[1,3], Guangyu Liu[1,3], Zhimin Shao[1,3] and Jiong Wu[1,3*]

[1]Department of Breast Surgery, Fudan University Shanghai Cancer Center, Shanghai, China, [2]Department of General Surgery, Zhongshan Hospital, Fudan University, Shanghai, China, [3]Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China

Background: The latissimus dorsi flap (LDF) is the most commonly used autologous flap for breast reconstruction (BR) in China. We conducted this study to explore the current status of BR using LDF with/without implants.

Methods: This study was a single-center retrospective study that included breast tumor patients who underwent LDF breast reconstruction at Fudan University Shanghai Cancer Center (FUSCC) between 2000 and 2021.

Results: We analyzed 4918 patients who underwent postmastectomy BR, including 1730 patients (35.2%) with autologous flaps. LDF was used for BR in 1093 (22.2%) patients, and an abdominal flap was used in 637 (13.0%) patients. The proportion of LDFs used in autologous BR patients decreased each year and dropped to approximately 65.0% after 2013 due to the increased use of abdominal flaps. Among these patients, 609 underwent extended LDF (ELDF) BR, 455 underwent LDF BR with implants, and 30 received a LDF as a salvage flap due to previous flap or implant failure. Patients who underwent ELDF reconstruction were older and had a higher BMI than those who received a LDF with implants. There was no significant difference in the mean postoperative hospital stay, neoadjuvant chemotherapy rates, or adjuvant radiotherapy rates between the two groups. Major complications requiring surgical intervention occurred in 25 patients (2.29%). There was no significant difference in the incidence of major complications between the two groups (P=0.542).

Conclusions: LDF breast reconstruction is a well-developed and safe procedure. The duration of postoperative hospitalization nor the incidence of major complications was affected by implant use.

KEYWORDS

breast tumor, latissimus dorsi flaps, implants, breast reconstruction, complications

Introduction

Owing to increasing public awareness and the development of screening programs, more patients with breast cancer can be diagnosed at much earlier stages, and the survival rate of these patients has greatly increased (1, 2). Patients have become increasingly concerned about changes in body shape and complain about diminished femininity and self-confidence after mastectomy. Thus, breast reconstruction has become an important part of breast cancer management and can improve patient satisfaction without affecting multidisciplinary adjuvant treatment (3).

Implant-only breast reconstruction remains the most performed type of immediate breast reconstruction, but autologous techniques involving donor sites account for approximately 20% (4). The common donor sites for autologous breast reconstruction are the latissimus dorsi flap (LDF) and the abdominal flap. Kamali et al. conducted a retrospective study using the Nationwide Inpatient Sample database (2008 to 2012), which showed a trend of a significant increase in the use of the LDF both nationally ($P < 0.001$) and regionally ($P < 0.001$) (4). Asian women have relatively smaller breasts than European and American women, so the latissimus dorsi flap (LDF) is the most used autologous flap for breast reconstruction in Chinese patients with breast tumors. In 2017, a nationwide cross-sectional survey of 110 hospitals conducted in China showed that among patients with autologous flap reconstruction, 69.8% (1562 cases in 2238 cases) underwent LDF reconstruction, including 625 extended latissimus dorsi flaps (ELDFs) and 927 LDFs with implants (5). Compared to abdominal flaps, latissimus dorsi flaps are beneficial in that they have reliable vessel distribution, favorable proximity to defects and simple dissection, so effective application requires a relatively shorter learning curve for surgeons and a shorter operating time.

Although several researchers have reported successful clinical outcomes after autologous flap breast reconstruction to date, there is a lack of large-scale studies in which researchers focus on the development of LDF breast reconstruction over time in China (6). We conducted this study to explore the status of breast reconstruction using LDF with or without implants (IMP) and the potential factors influencing the choice of reconstruction procedure.

Methods

Patients with breast tumors who underwent breast reconstruction after mastectomy at Fudan University Shanghai Cancer Center (FUSCC) between 2000 and 2021 were included in the retrospective study. Patients who underwent breast reconstruction using LDF with/without implants were analyzed. This study was approved by the Ethics Committee of FUSCC (Shanghai, China; ID: 1612167-18) and conducted in accordance with the Declaration of Helsinki. Informed consent was not needed for the retrospective study.

Female patients aged 18 to 85 years with breast tumors who underwent postmastectomy breast reconstruction were analyzed in this study. Patients who underwent prophylactic mastectomy, breast-conserving surgery, partial reconstruction, poor cardiopulmonary function or with contraindications to surgery were excluded. We obtained data on basic clinicopathological information, the timing and type of reconstruction, the duration of postoperative hospitalization and the incidence of major complications requiring surgical intervention. The clinical and pathological stages of patients included in the analysis were classified according to the AJCC version 8. The pathological diagnoses were confirmed independently by two expert pathologists. Only patients with invasive carcinoma were classified by pathological tumor stage (pT), pathological nodal stage (pN), estrogen receptor (ER) status, progesterone receptor (PR) status, pathologic HER2 status and Ki67 status. Pathologic HER2 status was defined according to the ASCO/CAP 2007 guidelines (7). For ER and PR, ≥1% of cells with strongly stained tumor nuclei were considered positive, and <1% were considered negative (8). For a more accurate analysis of postoperative complications, only those requiring reoperation were included.

For patients planned for immediate breast reconstruction, standard skin sparing mastectomy (SSM) or nipple sparing mastectomy (NSM) was performed. Autologous breast reconstruction included latissimus dorsi flaps with or without implants and abdominal flap breast reconstruction, including pedicle transverse rectus abdominis myocutaneous (pTRAM) flaps, and free tissue transfers using abdominal flaps, including free TRAM, muscle-sparing free TRAM, and deep inferior epigastric perforator flap (DIEP). Implant-only based breast reconstruction included tissue-expander prosthetic placement and prosthetic placement alone.

Continuous variables are expressed as the mean values or median values, and categorical variables are expressed as frequencies. The consecutive variables were analyzed by t test. Categorical variables were analyzed by using Chi-square and Kruskal–Wallis tests. Multivariate logistical regression analysis was performed to determine factors associated with the selection of LDF breast reconstruction with or without implants. Statistical analyses were performed using SPSS version 26. All P values reported were two-sided and were calculated at a significance level of 0.05.

Results

Trends in breast reconstruction technology from 2000 to 2021

From 2000 to 2021, a total of 4918 patients with breast tumors underwent postmastectomy breast reconstruction at FUSCC. The proportion of reconstruction in total breast tumor surgery has increased year by year, reaching 13.7% in the past 2 years. Advances in breast reconstructive techniques have broadened the postmastectomy reconstruction choices for female patients. Significant progress has been made in both implant- and autologous-based breast reconstruction in the past 22 years (Figures 1A, B). During the past 22 years, the proportion of autologous-based breast reconstructions performed in patients

who underwent postmastectomy breast reconstruction gradually decreased to a relatively stable proportion of approximately 24.7% after 2016 due to IBBR being increasingly performed, and the proportion of LDF breast reconstructions decreased to approximately 15.4% (Figure 1C). The proportion of LDFs used in autologous breast reconstruction patients also decreased each year and dropped to a relatively stable proportion of approximately 65.0% after 2013 due to the increased use of abdominal flaps (Figures 2A, B). Of all reconstruction cases, 35.2% were autologous reconstruction, and LDF was the most popular option for use in autologous reconstruction (Figure 2C).

Current status of LDF breast reconstruction

In a total of 1093 (63.2% of autologous reconstruction patients) patients, a LDF was used for breast reconstruction, and in 637 (36.8%) patients, abdominal flaps were used for autologous breast reconstructions. Among patients who underwent LDF breast reconstruction, most (1043/1093, 95.42%) underwent immediate breast reconstruction, only 29 (2.65%) underwent delayed reconstruction and 21 (1.92%) underwent immediate-delayed reconstruction. In patients who underwent immediate-

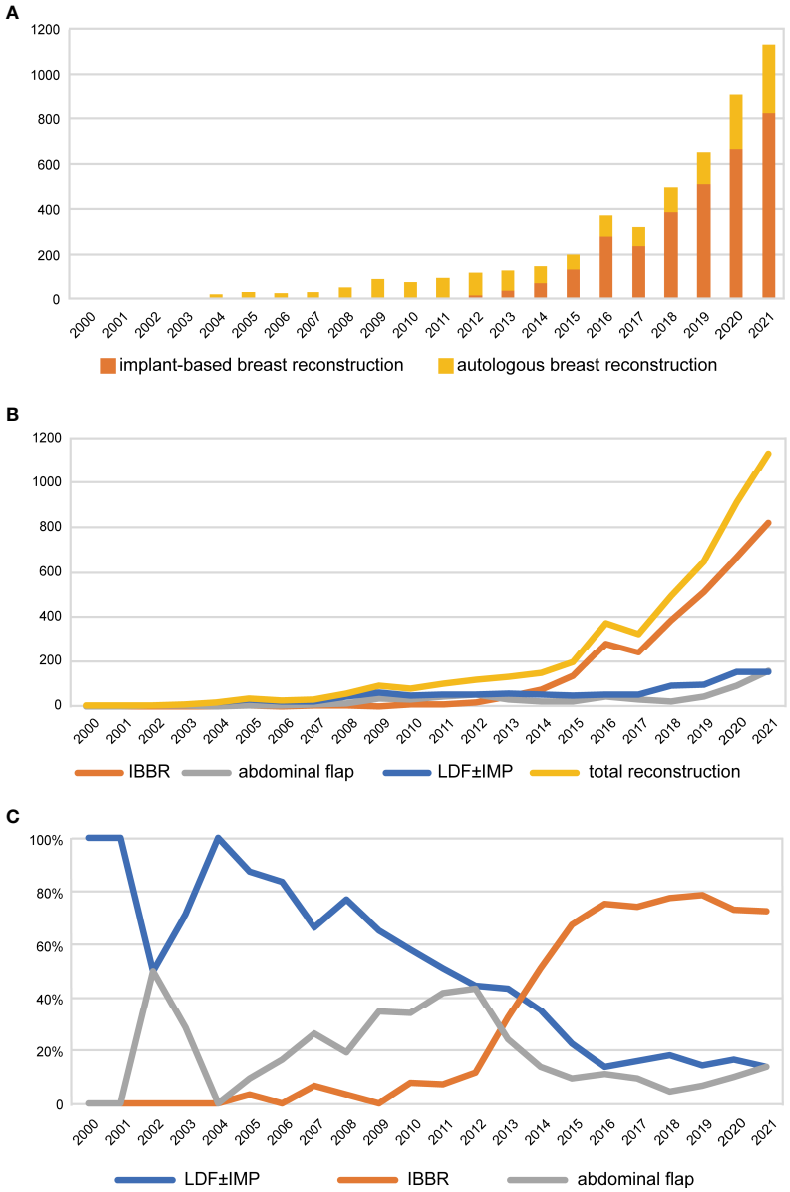


FIGURE 1
Trends of breast reconstruction from 2000 to 2021. **(A)** Trends of the proportion of IBBR and autologous breast reconstruction over years. **(B)** Trends of different types of breast reconstruction over years. **(C)** Trends of the proportion of different types in all breast reconstruction over years. LDF, latissimus dorsi flap; IMP, implants; IBBR, implant-based breast reconstruction.

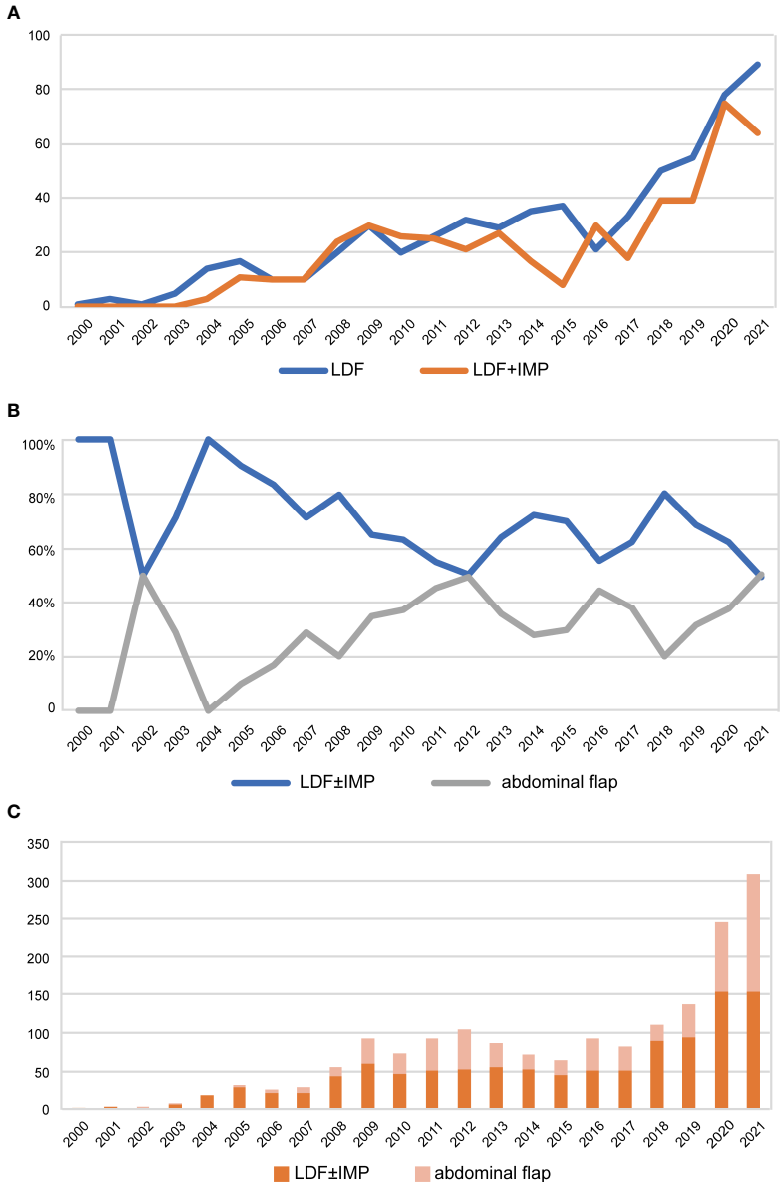


FIGURE 2
Trends of autologous breast reconstruction from 2000 to 2021. **(A)** Trends of LDF and LDF+implant breast reconstruction over years. **(B)** Trends of the proportion of LDF ± implant and abdominal flap in autologous breast reconstruction over years. **(C)** Histogram of the proportion of LDF ± implant and abdominal flap to autologous reconstruction over years. LDF, latissimus dorsi flap; IMP, implants.

delayed reconstruction, an expander was implanted immediately after mastectomy. After inflating the expander with saline over a period of time or adjuvant radiotherapy, the expander was then replaced by a LDF with or without a permanent implant. A total of 615 patients underwent extended LDF breast reconstruction, and 478 (43.6%) patients underwent LDF combined with implant breast reconstruction, including 34 patients who underwent two-stage expander-to-implant LDF flap breast reconstruction. Thirty patients received a LDF as a salvage flap in cases of previous flap or implant failure and chest wall defects. Among these patients, 27 received a LDF due to unsatisfactory outcomes of expander reconstruction or failed implant reconstruction, including 11 patients who underwent ELDF reconstruction and 16 patients who underwent LDF with implant reconstruction. One patient received a LDF to repair a poorly healed breast incision, and two patients underwent LDF reconstruction due to failed abdominal flap reconstruction, including one TRAM and one DIEP.

The mean age of the patients at the time of breast reconstruction surgery was 38.14 years (range 19 to 77). The mean BMI of the LDF reconstruction patients was 22.30 kg/cm2. The mean duration of postoperative hospitalization was 9.41 days. In terms of pathological type, 925 (84.63%) patients had invasive carcinoma, 135 (12.35%) had carcinoma in situ, 21 (1.92%) patients had phyllodes tumors and 11 (1.90%) patients had other malignancies. There were 264 (24.15%) patients treated with neoadjuvant chemotherapy and 356 (32.57%) treated with adjuvant radiotherapy.

Major complications requiring surgical intervention occurred in 25 patients (2.29%). The incidence of major complications over the

years is shown in Figure 3, and the list is shown in Table 1. Fourteen patients underwent surgical debridement or scar revision due to wound infection or poor healing, 8 patients underwent implant or flap removal due to serious infection or vascular crisis, and one patient underwent breast reconstruction revision operations concurrently with nipple reconstruction. The reconstructed breast and implant were removed in 1 patient due to the recurrence of breast cancer. One patient requested replacement of a smaller prosthesis 10 years after reconstruction because she perceived that the reconstructed breast was too large.

Potential influencing factors of LDF combined with or without implants

The clinicopathological information of patients who underwent postmastectomy LDF breast reconstruction with or without implants is summarized in Table 2. Compared with the LDF combined with implants group, the patients in the LDF without implants breast reconstruction group were older (39.46 vs. 36.44, P <0.0001) and had a higher mean BMI (22.16 ± 2.91 kg/cm^2 vs. 21.60 ± 2.65 kg/cm^2, P=0.001). In terms of reconstruction timing, 97.4% of ELDF breast reconstructions were immediate, only 2.3% of ELDF reconstructions were delayed, and 0.3% were immediate-delayed. For patients treated with a LDF combined with implants, 19 (4.0%) were immediate-delayed, and 15 (3.1%) were delayed. The patients with phyllodes tumors and other malignant tumors tended to undergo extended latissimus dorsi flap reconstruction (P=0.021). There were no significant differences in the duration of postoperative hospitalization (P=0.540), the rate of neoadjuvant chemotherapy (P=0.569), or the rate of adjuvant radiotherapy (P=0.852) between patients treated with ELDF breast reconstruction and those treated with a LDF combined with implants. There was also no significant difference in the incidence of major complications requiring surgical intervention between the patients who underwent extended LDF and those who underwent LDF combined with implant reconstruction, P=0.542.

Among the patients diagnosed with invasive carcinoma, there was no significant difference in pT, pN, ER, PR, HER2, Ki67, or the rate of neoadjuvant chemotherapy and adjuvant radiotherapy between the patients who underwent extended LDF and those who underwent LDF combined with implant breast reconstruction (Table 3). To further explore the potential factors influencing the choice of reconstruction procedure, we performed univariate logistical regression analysis and constructed forest plots. The results showed that age and BMI were important factors influencing whether LDF combined with implant breast reconstruction was chosen (Figure 4). Multivariate logistic regression analysis was performed using the factors that showed significance in the univariate logistic regression analysis, and the results suggested that age (OR (95% CI): 0.957 (0.942-0.973), P<0.0001) and BMI (OR (95% CI): 0.948 (0.907-0.991), P=0.019) were independent factors influencing the choice of LDF or LDF combined with implant breast reconstruction.

Discussion

Breast reconstruction retains the shape of the breast and significantly improves the quality of life and increases the confidence of patients after mastectomy (9, 10) In this study, we analyzed the trends of breast reconstruction performed in China from 2000 to 2021 and found a steady increase over time in implant-based, LDF and abdominal flap breast reconstruction, which was consistent with the trends observed in America (4, 11, 12). The scale of autologous breast reconstruction is affected by IBBR, and it has reached a relatively stable state. According to a nationwide cross-sectional survey of 110 hospitals in China, the proportion of breast reconstruction procedures performed after mastectomy was 10.7%, with 70% being implant-based reconstruction, 17% being autologous tissue reconstruction, and 13% being a combination (13). Consistent with changes in MD Anderson's reconstruction methods over the past ten years, the number of free flaps for breast reconstruction has steadily increased as the use of prostheses has increased, which is an international trend (14). In Europe, Petit et al. showed that autologous breast reconstruction was used in approximately 20% of all reconstructions (15). This finding suggested that the advantages of autologous reconstruction has continued to be affirmed. In autologous reconstruction, the patient's own tissue is used, thus ensuring a breast that appears and feels more natural, is permanent, better withstands the aging process and better tolerates radiation.

The proportion of LDFs used in autologous breast reconstruction patients also decreased each year and decreased to a relatively stable proportion of approximately 65.0% after 2013. The proportion of breast reconstruction using abdominal flaps has increased over time, and the trend is expected to surpass LDF thus becoming the most used autologous flap. However, the latissimus

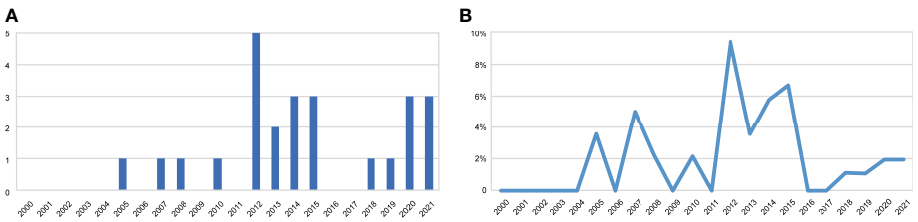


FIGURE 3
The trend of major complications requiring surgical intervention over the years. **(A)** The incidence of major complications. **(B)** The cases of major complications.

10.3389/fonc.2023.1159073

TABLE 1 Cases with complications requiring surgical intervention.

Type of reconstruction		Complications	Solution	Time after surgery
LDF+implant	1	Postoperative hemorrhage	Debridement and hemostasis	1 day
	2	Reconstructed latissimus dorsi flap venous crisis	Debridement, hemostasis and remove the implant	5 days
	3	Implant infection	Remove implant	8 days
	4	Prosthesis exposure	Remove the prosthesis	4 months
	5	Insufficient expansion volume	Remove the expander	1 year
	6	Breast cancer recurrence	Remove the reconstructed breast and prosthesis	2 years
	7	Reconstructed breast pain	Remove implant	6 years
	8	Perceived prosthesis too large	Replace a smaller prosthesis	10 years
	9	Implant infection	Remove implant	2 years
LDF	1	Postoperative hemorrhage	Debridement and hemostasis	2 days
	2	Back incision dehiscence	Debridement and suturing	1month
	3	Back incision dehiscence	Debridement and suturing	7 months
	4	Back incision poor healing	Suturing	12 days
	5	Poor incision healing	Debridement and suturing	4 months
	6	Incision not healing	Debridement and suturing	2 months
	7	Reconstructed breast fat liquefaction	Debridement	2 months
	8	Seroma in back	Debridement	6 months
	9	Breast incision scarring	Scar excision	4 months
	10	Back incision scarring	Scar excision	6 months
	11	LDF necrosis	Remove the reconstructed breast	2 months
	12	Vascular crisis	Remove the graft flap	1 day
	13	Back incision dehiscence	Debridement and suturing	7 months
	14	Reconstructed breast deformity	Revision	1 year
	15	Postoperative hemorrhage	Debridement and hemostasis	1 day
	16	Sinus tract formation of back incision	Flap repair	4 months

dorsi flap is still the most used autologous flap for breast reconstruction in China. This was in contrast to the situation in the United States, where abdominal flaps were most commonly used in autologous reconstruction (16). In Europe, LDF and TRAM flaps are the most frequently used for breast reconstruction (17). Compared with the data from MROC, patients undergoing LDF reconstruction in the study were younger than those in America (37 vs. 53.5 years old). The mean age of patients who underwent reconstruction using a LDF was younger than that of those receiving a DIEP, which is in contrast to the results of MROC (16). The proportion of delayed reconstruction and radiotherapy was lower than that in American patients (16). The LDF has a small amount of tissue and can be combined with the implant to reconstruct a satisfactory breast shape. For American patients with larger or more ptotic breasts desiring reconstruction, a single LDF may be insufficient in providing enough tissue volume, while DIEP might be more sufficient in providing adequate tissue volume (5, 18). Compared with breast reconstruction using an abdominal flap, LDF with/without implants breast reconstruction is advantageous in that the operation is simple and safe, produces a concealed back scar, and can fill subclavian defects and form breast axillary folds, which is especially suitable for patients who have not given birth and wish to have children (9). The comparative study performed by Lee et al. showed that the risk of complications of LDF breast reconstruction was similar to that of abdominal-based autologous breast reconstruction, despite having a shorter operative time than abdominal-based autologous breast reconstruction (19). In addition, the learning curve of surgeons for latissimus dorsi reconstruction is relatively short, which is more conducive to its adoption in local hospitals. The extensive use of prostheses has jointly improved the popularity of LDF in China.

LDF is a solid and reliable donor site for autologous breast reconstruction, and it has wide applicability in breast reconstruction. A LDF is used more often for immediate breast reconstruction and less often for delayed reconstruction. This may be related to the relatively small tissue volume of the LDF, which is insufficient for

10.3389/fonc.2023.1159073

TABLE 2 The clinicopathological information of patients underwent LDF with or without implants breast reconstruction.

Characteristics	ELDF	LDF+implant	*P*-value
	N(%)	N(%)	
Postoperative hospital stay, Mean ± SD	9.50 ± 5.90	9.29 ± 5.37	0.540
Age, Mean ± SD	39.46 ± 8.56	36.44 ± 7.52	<0.0001
Age			0.002
<35	201(32.7%)	200(41.8%)	
35-64	406(66.0%)	277(57.9%)	
>64	8(1.3%)	1(0.2%)	
BMI Mean ± SD	22.16 ± 2.91	21.60 ± 2.65	0.001
BMI			
<18.5	43(7.0%)	46(9.6%)	0.213
18.5-28	546(88.8%)	418(87.4%)	
>28	22(3.6%)	10(2.1%)	
Unknown	4(0.7%)	4(0.8%)	
Neoadjuvant therapy			0.569
No	462(75.1%)	367(76.8%)	
Yes	153(24.9%)	111(23.2%)	
Pathological types			0.021
Invasive carcinoma	515(83.7%)	410(85.8%)	
Carcinoma in situ	73(11.9%)	62(13.0%)	
Phyllodes tumors	19(3.1%)	3(0.6%)	
Other tumors	8(1.3%)	3(0.6%)	
Timing of reconstruction			<0.0001
Immediately	599(97.4%)	444(92.9%)	
Delay	142(2.3%)	15(3.1%)	
Immediate to delay	2(0.3%)	19(4.0%)	
Radiotherapy			0.852
Yes	199(32.4%)	157(32.8%)	
No	341(55.4%)	268(56.1%)	
Unknown	75(12.2%)	53(11.1%)	
Complications			0.542
No	599(97.4%)	469(98.1%)	
Yes	16(2.6%)	9(1.9%)	

delayed reconstruction. The LDF can be easily transposed to the anterior chest for primary breast reconstruction and coverage of chest wall defects, for salvage of previous flap failure, such as abdominal flap necrosis or partial necrosis, and for salvage of implant reconstruction failure, exposed expander/implant or as part of a combined approach (20, 21). It can be used for oncoplastic surgery, especially in volume replacement technology.

There are two main technical modalities of LDF breast reconstruction, including ELDF and LDF with implant reconstruction. In our study, we found that age and BMI were independent factors influencing the reconstruction options, and older patients or those with a higher BMI tended to receive an ELDF. There was no significant difference in choosing radiotherapy or neoadjuvant chemotherapy. Considering that patients with more metastatic lymph nodes are more likely to receive subsequent radiotherapy, surgeons tend to choose extended LDF breast reconstruction rather than LDF combined with implants. A prospective study performed by Cowen et al. showed that T3 or

10.3389/fonc.2023.1159073

TABLE 3 The clinicopathological information of patients diagnosed with invasive carcinoma.

Characteristics	ELDF	LDF+implant	*P*-value
	N(%)	N(%)	
Postoperative hospital stay Mean ± SD	9.22 ± 5.70	9.09 ± 5.35	0.722
Age, Mean ± SD	39.40 ± 8.50	36.32 ± 7.66	<0.0001
Age			0.002
<35	173(33.6%)	181(44.1%)	
35-64	336(65.2%)	228(55.6%)	
>64	6(1.2%)	1(0.2%)	
BMI Mean ± SD	22.31 ± 2.99	21.72 ± 2.61	0.002
BMI			
<18.5	37(7.2%)	37(9.0%)	0.156
18.5-28	453(88.0%)	361(88.0%)	
>28	22(4.3%)	8(2.0%)	
Unknown	3(0.6%)	4(1.0%)	
Neoadjuvant therapy			0.461
No	366(71.1%)	301(73.4%)	
Yes	149(28.9%)	109(26.6%)	
pT			0.239
0	44(8.5%)	32(7.8%)	
1	216(41.9%)	203(49.5%)	
2	179(34.8%)	121(29.5%)	
3	46(8.9%)	31(7.6%)	
Unknown	30(5.8%)	23(5.6%)	
pN			0.485
0	278(54.0%)	232(56.6%)	
1	142(27.6%)	105(23.6%)	
2	60(11.7%)	54(13.2%)	
3	29(5.6%)	14(3.4%)	
Unknown	6(1.2%)	5(1.2%)	
ER			0.857
–	144(28.0%)	111(27.1%)	
+	352(68.3%)	286(69.8%)	
Unknown	19(3.7%)	13(3.2%)	
PR			0.750
–	190(36.9%)	161(39.3%)	
+	307(59.6%)	236(57.6%)	
Unknown	18(3.5%)	13(3.2%)	
Her2			0.510
–	323(62.8%)	250(61.0%)	
+	158(30.7%)	125(30.5%)	

(Continued)

TABLE 3 Continued

Characteristics	ELDF	LDF+implant	*P*-value
	N(%)	N(%)	
Unknown	33(6.4%)	35(8.5%)	
Ki-67			0.386
<20%	158(30.7%)	136(33.2%)	
≥20%	272(52.8%)	198(48.3%)	
Unknown	85(16.5%)	76(18.5%)	
Radiotherapy			0.924
Yes	275(53.4%)	217(52.9%)	
No	184(35.7%)	150(36.6%)	
Unknown	56(10.9%)	43(10.5%)	
Major complications			0.304
Yes	16(3.1%)	8(2.0%)	
No	499(96.9%)	402(98.0%)	

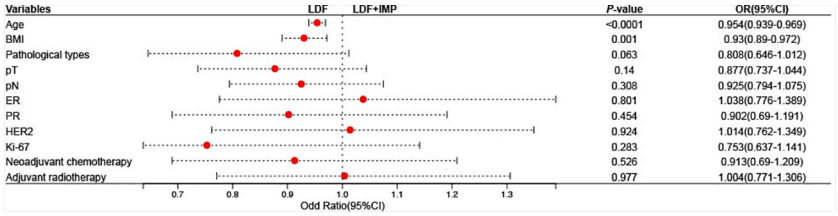


FIGURE 4
Forest plots for the potential influencing factors of the type of reconstruction.

T4 tumors (P = 0.0005), smoking habit (P = 0.001), and pN+ axillary status (P = 0.004) were significant factors associated with IBBR failure after radiotherapy (22). In this study, LDF reconstruction with implants did not increase the duration of hospitalization or decrease the rate of adjuvant radiotherapy. Leuzzi S et al. showed that there was no significant difference in the hospitalization duration of patients receiving a LD flap with an implant or lipofilling, which is consistent with this study. However, they found that the surgical complication rate was higher in patients undergoing LDF combined with implant reconstruction (14.2% vs. 18.8%), which was not observed in this study (major complications of LDF vs. LDF+implant: 2.6% vs. 1.9%, *P*=0.542).

Advantages of the LDF used for breast reconstruction include minimal donor site morbidity, relatively quick recovery, and reasonably good aesthetic outcome. A previous study showed that only 2.29% of patients experienced major complications, suggesting that LDF combined with or without implant breast reconstruction was reliable and safe. Berthet G et al. suggested that immediate breast reconstruction using LDF appeared to have excellent tolerance to subsequent radiotherapy, and adjuvant radiotherapy had no impact on patient aesthetic satisfaction (23). Even combined with prosthetic reconstruction, the latissimus dorsi muscle can provide better prosthesis coverage compared with the mesh, which greatly reduces the rate of postoperative infection and prosthesis exposure. Patients who underwent LDF with lipofilling had a higher BREAST-Q score (6). Santosa KB et al. performed a prospective, multicenter trial to determine the outcomes of patients undergoing IBBR or autologous breast reconstruction using Breast-Q. The study showed that patients who underwent autologous reconstruction were more satisfied with their body (*P*<0.001) and had better psychosocial well-being (*P*=0.002) and sexual well-being (*P*<0.001) at 2 years postoperatively (24). Several studies have shown that patients with LDF flaps or rectus abdominis flap breast reconstruction have similar satisfaction scores (25, 26).

In this cohort study with a large number of patients, we comprehensively and reliably described the current development status of latissimus dorsi breast reconstruction in China. However, there were still several limitations. First, the inherent bias caused by a single-center retrospective study is inevitable. Second, seroma is an important complication after a latissimus dorsi (LD) flap procedure, but due to the limitation of retrospective studies, we failed to obtain the incidence of seroma in these patients. Aesthetics outcomes are indeed one of the important evaluation criteria for breast reconstruction surgery, but the aesthetics evaluation is

relatively subjective. The lack of patient-reported outcomes made it impossible to analyze the development status of latissimus dorsi reconstruction with or without implants from the patients' perspective. We will perform relevant studies on the patient-reported outcomes of patients with breast reconstruction in the future and compare the aesthetics outcomes of patients who received ELDF with those who received LDF with implants.

Conclusion

The latissimus dorsi flap with or without implant breast reconstruction is a well-developed and safe reconstruction procedure performed in our center. Whether combined with implant reconstruction, the duration of postoperative hospitalization nor the incidence of major complications was affected.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethics Committee Review Board of the Fudan University Shanghai Cancer Center (Shanghai, China; ID: 1612167-18). Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

SZ: Conceptualization, investigation, writing–original draft and writing–review, and editing. SH: Help analysis data and draft–review. SZ and SH contribute equally to this article and were considered co-first authors. JC, BY, XH, GL, YZ: Help to collect the data. JW: Supervise the planning and design of the study; data collection; statistical analysis and data interpretation; have full access to all the data in the study and be responsible for the integrity of the data and the accuracy of the data analysis; and manuscript review, revision, and reporting. All authors contributed to the article and submitted and approved the submitted section.

Funding

This work was supported by the National Key R&D Program of China (2017YFC1311004).

Acknowledgments

Thank SH for helpful study design, data collection, and draft–review, JC, BY, XH for data collection, JW for supervising the planning and design of the study, manuscript review and revision.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

References

1. Fitzmaurice C, Allen C, Barber RM, Barregard L, Bhutta ZA, Brenner H, et al. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 32 cancer groups, 1990 to 2015: A systematic analysis for the global burden of disease study. *JAMA Oncol* (2017) 3 (4):524–48. doi: 10.1001/jamaoncol.2016.5688

2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin* (2020) 70 (1):7–30. doi: 10.3322/caac.21590

3. Jia-Jian C, Nai-Si H, Jing-Yan X, Ben-Long Y, Guang-Yu L, Gen-Hong D, et al. Current status of breast reconstruction in southern china: a 15 year, single institutional experience of 20,551 breast cancer patients. *Med (Baltimore)* (2015) 94(34):e1399. doi: 10.1097/MD.0000000000001399

4. Kamali P, Paul MA, Ibrahim AMS, Koolen PGL, Wu W, Schermerhorn ML, et al. National and regional differences in 32,248 postmastectomy autologous breast reconstruction using the updated national inpatient survey. *Ann Plast Surg* (2017) 78 (6):717–22. doi: 10.1097/SAP.0000000000000963

5. Wang J, Xiu B, Guo R, Zhang Q, Su Y, Li L, et al. Autologous tissue reconstruction after mastectomy-A cross-sectional survey of 110 hospitals in China. *Eur J Surg Oncol* (2020) 46(12):2202–7. doi: 10.1016/j.ejso.2020.07.008

6. Leuzzi S, Stivala A, Shaff JB, Maroccia A, Rausky J, Revol M, et al. Latissimus dorsi breast reconstruction with or without implants: A comparison between outcome and patient satisfaction. *J Plast Reconstr Aesthet Surg* (2019) 72(3):381–93. doi: 10.1016/j.bjps.2018.10.003

7. Wolff AC, Hammond ME, Schwartz JN, Hagerty KL, Allred DC, Cote RJ, et al. American Society of Clinical Oncology/College of American Pathologists guideline recommendations for human epidermal growth factor receptor 2 testing in breast cancer. *J Clin Oncol* (2007) 25(1):118–45. doi: 10.1200/JCO.2006.09.2775

8. Hammond ME, Hayes DF, Dowsett M, Allred DC, Hagerty KL, Badve S, et al. American Society of Clinical Oncology/College Of American Pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer. *J Clin Oncol* (2010) 28(16):2784–95. doi: 10.1200/JCO.2009.25.6529

9. Liu Q, Li W, Wu X, Xu L, Hu P, Cao Y. Immediate breast reconstruction using latissimus dorsi muscular flap: A retrospective study of Chinese patients with breast cancer. *Med (Baltimore)* (2021) 100(24):e26175. doi: 10.1097/MD.0000000000026175

10. Ter Louw RP, Nahabedian MY. Prepectoral breast reconstruction. *Plast Reconstr Surg* (2017) 140(5S):51s–9s. doi: 10.1097/PRS.0000000000003942

11. Pien I, Caccavale S, Cheung MC, Butala P, Hughes DB, Ligh C, et al. Evolving trends in autologous breast reconstruction: is the deep inferior epigastric artery perforator flap taking over? *Ann Plast Surg* (2016) 76(5):489–93. doi: 10.1097/SAP.0000000000000339

12. Wilkins EG, Alderman AK. Breast reconstruction practices in north america: current trends and future priorities. *Semin Plast Surg* (2004) 18(2):149–55. doi: 10.1055/s-2004-829049

13. Yang B, Ren G, Song E, Pan D, Zhang J, Wang Y, et al. Current status and factors influencing surgical options for breast cancer in china: a nationwide cross-sectional survey of 110 hospitals. *Oncologist* (2020) 25(10):e1473–80. doi: 10.1634/theoncologist.2020-0001

14. Yu P. Breast reconstruction at the MD Anderson Cancer Center. *Gland Surg* (2016) 5(4):416–21. doi: 10.21037/gs.2016.05.03

15. Petit JY, Gentilini O, Rotmensz N, Rey P, Rietjens M, Garusi C, et al. Oncological results of immediate breast reconstruction: long term follow-up of a large series at a single institution. *Breast Cancer Res Treat* (2008) 112(3):545–9. doi: 10.1007/s10549-008-9891-x

16. Wilkins EG, Hamill JB, Kim HM, Kim JY, Greco RJ, Qi J, et al. Complications in postmastectomy breast reconstruction: one-year outcomes of the mastectomy reconstruction outcomes consortium (mroc) study. *Ann Surg* (2018) 267(1):164–70. doi: 10.1097/SLA.0000000000002033

17. Petit JY, Rietjens M, Lohsiriwat V, Rey P, Garusi C, De Lorenzi F, et al. Update on breast reconstruction techniques and indications. *World J Surg* (2012) 36(7):1486–97. doi: 10.1007/s00268-012-1486-3

18. Thiruchelvam PT, McNeill F, Jallali N, Harris P, Hogben K. Post-mastectomy breast reconstruction. *Bmj* (2013) 347:f5903. doi: 10.1136/bmj.f5903

19. Lee HC, Lee J, Park SH, Yoon ES. The hybrid latissimus dorsi flap in immediate breast reconstruction: a comparative study with the abdominal-based flap. *Ann Plast Surg* (2021) 86(4):394–9. doi: 10.1097/SAP.0000000000002565

20. Serletti JM, Fosnot J, Nelson JA, Disa JJ, Bucky LP. Breast reconstruction after breast cancer. *Plast Reconstr Surg* (2011) 127(6):124e–35e. doi: 10.1097/PRS.0b013e318213a2e6

21. Hultman CS, Bostwick J 3rd. Breast reconstruction following mastectomy: review of indications, methods, and outcomes. *Breast Dis* (2001) 12:113–30. doi: 10.3233/BD-2001-12112

22. Cowen D, Gross E, Rouannet P, Teissier E, Ellis S, Resbeut M, et al. Immediate post-mastectomy breast reconstruction followed by radiotherapy: risk factors for complications. *Breast Cancer Res Treat* (2010) 121(3):627–34. doi: 10.1007/s10549-010-0791-5

23. Berthet G, Faure C, Dammacco MA, Vermesch C, Delay E, Ho Quoc C, et al. Tolerance of latissimus dorsi in immediate breast reconstruction without implant to radiotherapy. *J Plast Reconstr Aesthet Surg* (2018) 71(1):15–20. doi: 10.1016/j.bjps.2017.08.010

24. Santosa KB, Qi J, Kim HM, Hamill JB, Wilkins EG, Pusic AL. Long-term patient-reported outcomes in postmastectomy breast reconstruction. *JAMA Surg* (2018) 153(10):891–9. doi: 10.1001/jamasurg.2018.1677

25. Augustinho LBZ, Sabino Neto M, Veiga DF, Abla LEF, Juliano Y, Ferreira LM. Patient satisfaction with breast reconstructionusing musculocutaneous flap from latissimus dorsiversus from rectus abdominis: a cross-sectional study. *Sao Paulo Med J* (2018) 136(6):551–6. doi: 10.1590/1516-3180.2018.032916112018

26. Benditte-Klepetko HC, Lutgendorff F, Kästenbauer T, Deutinger M, van der Horst CM. Analysis of patient satisfaction and donor-site morbidity after different types of breast reconstruction. *Scand J Surg* (2014) 103(4):249–55. doi: 10.1177/1457496913512829

frontiers | Frontiers in Oncology

TYPE Original Research
PUBLISHED 24 July 2023
DOI 10.3389/fonc.2023.1071127

OPEN ACCESS

EDITED BY
Sung Gwe Ahn,
Yonsei University Health System, Republic of Korea

REVIEWED BY
Janghee Lee,
Hallym University Dongtan Sacred Heart Hospital, Republic of Korea
Regis Resende Paulinelli,
Universidade Federal de Goiás, Brazil

*CORRESPONDENCE
Idam de Oliveira-Junior
idamjr88@gmail.com

†These authors have contributed equally to this work

‡These authors have contributed equally to this work and share senior authorship

RECEIVED 15 October 2022
ACCEPTED 10 July 2023
PUBLISHED 24 July 2023

CITATION
de Oliveira-Junior I, da Costa Vieira RA, Biller G, Sarri AJ, da Silva FCB and Nahás EAP (2023) Factors associated with unsatisfactory cosmetic results in oncoplastic surgery. *Front. Oncol.* 13:1071127. doi: 10.3389/fonc.2023.1071127

Factors associated with unsatisfactory cosmetic results in oncoplastic surgery

Idam de Oliveira-Junior [1,2,3*†], René Aloísio da Costa Vieira [1,2‡], Gabriele Biller [2,4†], Almir José Sarri [3†], Fabíola Cristina Brandini da Silva [2,3†] and Eliana Aguiar Petri Nahás [1‡]

[1]Postgraduate Program of Tocogynecology, Botucatu Medical School, Sao Paulo State University, UNESP, Sao Paulo, Brazil, [2]Postgraduate Program of Oncology, Barretos Cancer Hospital, Sao Paulo, Brazil, [3]Nucleous of Mastology, Barretos Cancer Hospital, Sao Paulo, Brazil, [4]Faculty of Health Sciences of Barretos Dr. Paulo Prata (FACISB) School of Medicine, Sao Paulo, Brazil

Introduction: Oncoplastic surgery (OS) has expanded the indications for breast-conserving surgery associated with an adequate aesthetic result. However, few studies have described the factors associated with unsatisfactory cosmetic outcomes from this surgical modality.

Materials and methods: This is a cross-sectional prospective study that included patients undergoing breast-conserving surgery (BCS) with or without OS. The patients self-evaluated the cosmetic results of the breasts posttreatment and had them photographed. The photos were analyzed by BCCT.core. Individual and treatment factors (local and systemic) for all patients were evaluated. These factors were dichotomized according to the use of OS and to the cosmetic result (satisfactory and unsatisfactory). Categorical variables were tested for association with surgical outcome using the chi-square test while numerical variables using the Mann–Whitney U test. Variables with p <0,2 were selected for multivariate analysis.

Results: Of the 300 patients evaluated, 72 (24,0%) underwent OS. According to the patient self-evaluations, an unsatisfactory cosmetic result from OS was significantly associated with younger age at diagnosis, higher body mass index (BMI) at the time of evaluation, larger tumor size and greater weight of the surgical specimen. According to the BCCT.core, only the laterality of the tumor (left) was significantly associated with an unsatisfactory cosmetic result. In logistic regression, considering OS as a control variable, the risk of an unsatisfactory outcome according to patient self-evaluation was related to the tumor ≥ T2 odds ratio (OR) 1,85 (1,027-3,34) and age at diagnosis < 40 [OR 5,0 (1,84-13,95)]. However, according to the software, the variables were associated with an increased risk of an unsatisfactory outcome were the time interval between surgery and evaluation [OR 1,27 (1,16-1,39)], the presence of lymphedema [OR 2,97 (1,36-6,46)], surgical wound infection [OR 3,6 (1,22-11,16)], tumor location on the left side [OR 3,06 (1,69-5,53)], overweight [OR 2,93 (1,48-5,8)] and obesity [OR 2,52 (1,2-5,31)].

Conclusion: There is no standard methodology for breast cosmesis evaluation, which influences the factors associated with unsatisfactory results. Younger patients and those with increased BMI, left breast cancer and extensive resections tend to present with unsatisfactory cosmetic results when OS is performed.

KEYWORDS

breast cancer, conservative surgery, breast-conserving surgery, oncoplastic surgery, cosmesis

Introduction

The outcome of the surgical treatment of breast cancer extends beyond purely oncological issues (1–3). The unsatisfactory cosmetic results of breast conservative surgery motivated the development of oncoplastic surgery (OS), which, by incorporating concepts and techniques of plastic surgery in the treatment of breast cancer, has allowed an increase in the number of breast conservation indications as well as better cosmetic results (4–6). However, OS is highly technically variable, which involves from small parenchyma remodeling to complex resections, making it difficult to judge the results and limiting oncological and cosmetic comparisons (2, 7, 8).

Cosmetic analysis after conservative breast treatment can be performed through subjective methods, which take into account the self-evaluation of the patient or the analysis of the health professionals involved in the treatment, and objective methods, which consider the measurement of asymmetry between the treated *versus* untreated breast. The lack of standards in the evaluation of these results and the low agreement between them directly influence the reproducibility and validity of the methods (9–13). In this sense, the BCCT.core (*Breast Cancer Conservative Treatment Cosmetic Results*) software, which employs algorithms for calculating breast symmetry and yields highly correlated results calibrated by specialists, was established to contend with these problems (14, 15).

Unsurprisingly, breast conserving-surgery (BCS) typically results in varying degrees of breast asymmetry, which can negatively affect the quality of life of women (16). The main factors associated with unsatisfactory cosmetic results after BCS classical surgery (CS) include high body mass index (BMI) and tumor size, advanced age, tumor location (medial, central or lower quadrants), reexcision, small breast volume, heterogeneity of the radiation dose and resection of the breast parenchyma greater than 100 cm^3 (17–19). However, few studies have investigated the factors that can influence the outcomes of OS. Therefore, it necessary to investigate these factors to better understand them, to optimize the information delivered to the patient, and prevent their onset. Such a study would also assist in monitoring the cosmetic results over time and their relationship with the patient profile, surgical technique and adjuvant therapies.

Materials and methods

This was a prospective cross-sectional study approved by the Research Ethics Committee under number 782/2014 with support from FAPESP (2014/08197-0) that randomly included patients followed up at the Mastology and Breast Reconstruction outpatient clinic of the Barretos Cancer Hospital who underwent BCS (CS or OS) for the treatment of breast cancer.

Patients who had completed radiotherapy at least one year prior, without metastatic disease and/or locoregional recurrence and who signed the informed consent form were included in the study. Patients with bilateral breast cancer, male patients and those with cognitive limitations for cosmetic self-assessment were excluded.

The patients were photographed in a standardized manner (1 meter distance with a point marked on the sternal furcula and another 20 cm below, at the sternal level, for distance calibration) and self-assessed the cosmetic result of the breast (excellent, good, reasonable, or poor). The photographs were analyzed prospectively, cross-sectionally and blindly using BCCT.core software, which provides results on a 4-point scale (1-excellent, 2-good, 3-fair, 4-poor). For patients with no areola, a central point on the breast was marked when possible. This methodology was previously published (12, 13).

In the cosmetic evaluation, classifications of excellent and good, both by the patient and by BCCT.core, were considered satisfactory. Conversely, evaluations classified as reasonable/fair and poor were categorized as unsatisfactory cosmetic results.

Next, breast cosmesis categorized as satisfactory and unsatisfactory were evaluated by the patient and the BCCT.core software and correlated with the patient's personal and oncological history, obtained retrospectively from the medical records.

Statistical analysis

The data were initially analyzed for all patients undergoing conservative breast treatment (classic and with oncoplasty). Subsequently, they were dichotomized according to the use of breast oncoplasty and according to the cosmetic result

(satisfactory and unsatisfactory). For the categorical variables, the frequencies (absolute and relative) are reported. Numerical variables are reported as the mean, median and standard deviation.

The associations between surgical outcome and categorical variables were performed using the chi-square test; those for continuous variables were calculated with the Mann–Whitney test.

The variables with a descriptive p level<0,20 in the analysis of all cases and OS group were selected for multivariate analysis. An adjusted logistic regression model was derived to calculate the odds ratio (OR) and its respective 95% confidence interval (95% CI) for an unsatisfactory cosmetic result. Because it is important for analysis, oncoplastic surgery (present vs. absent) was considered as a control variable in all cases. The analyses were performed using IBM-SPSS software version 27.0, and a 5% significance level was adopted.

Results

A total of 300 patients were evaluated, as described in a previous study, for validation of the BCTOS questionnaire (12). Of these, 298 had their photographs evaluated by BCCT.core, and 297 performed a breast self-assessment. A total of 228 (76,0%) patients underwent CS, and 72 (24,0%) underwent OS; of these, 37 (51,4%) underwent contralateral symmetrization surgery. The mean follow-up time from the first medical evaluation to participation in the study was 7,4 years (1,2-20,6; standard deviation 4,3). Among patients who underwent OS, 73,6% self-assessed a satisfactory cosmetic result, and 26,4% considered the outcome unsatisfactory; according to the software analysis, 29,2% and 70,8% of the outcomes were satisfactory and unsatisfactory, respectively.

In the patient self-evaluations, across all patients (Supplementary Tables 1, 2), factors such as younger age at diagnosis and at the time of evaluation (gross and by age group), larger tumors (either categorically according to the T stage in the TNM classification or numerically), the use of radiation therapy boost and a longer time interval between surgery and evaluation and between the end of radiotherapy and evaluation were significantly associated with unsatisfactory cosmetic results.

Among patients who underwent classical conservative treatment (quadrantectomy), according to their self-assessment, factors such as younger age at diagnosis (categorical or numerical), variability in radiotherapy dose, the use of boost and a longer time interval between surgery and evaluation and between the end of radiotherapy and evaluation were significantly associated with unsatisfactory cosmetic results. However, among those treated with OS, an unsatisfactory result was significantly associated with younger age at diagnosis, higher BMI at the time of assessment (categorical or numerical), larger tumor size and greater weight of the surgical specimen. In the logistic regression for overall unsatisfactory cosmetic outcome (Table 1), in the patient selfevaluation, a significantly increased risk was observed for tumors ≥ T2 odds ration (OR) 1,86 (1,035–3,35)] and age <40 years [OR = 5,1 (1,86–14,01)]. When using OS variable as a control (Table 1), tumor ≥ T2 [OR =1,85 (1,027–3,34)] and age <40 years [OR = 5,1 (1,86-14,01)]. When using OS variable as a control (Table 1), tumor ≥ T2 odds ratio (OR) 1,85 (1,027-3,34) and age at diagnosis < 40 years [OR 5,0 (1,84-13,95)] was associated with increased risk of an unsatisfactory outcome. In the OS group (Table 2), only tumor size was associated with an increased risk of an unsatisfactory result [≥ T2 OR = 7,205 (1,403 – 37,017)].

In the analysis of the BCCT.core software (Supplementary Tables 3, 4) across all patients, a higher BMI (numerical and categorical) at diagnosis and at the time of evaluation, tumors with a higher T stage (TNM), a tumor of the left side, axillary lymphadenectomy, chemotherapy, radiotherapy dose of 28 x 180 cGy, presence of lymphedema (evaluated based on the water displacement methodology, considered present when the difference between the upper limbs had a value greater than or equal to 200 milliliters (12)), greater weight of the surgical specimen, greater distance from the surgical margins and longer time interval between surgery and evaluation and between the end of radiotherapy and evaluation were significantly associated with unsatisfactory cosmetic results. Conversely, among patients undergoing CS, higher BMI at diagnosis (categorical and numerical) and at the time of evaluation, lower patient educational level, tumor on the left side, axillary lymphadenectomy and chemotherapy, radiotherapy dose of 28 x 180 cGy, higher weight of the specimen and distance from the surgical margins and a longer time interval between surgery and evaluation and between the end of radiotherapy and evaluation were significantly associated with unsatisfactory cosmetic results. However, among those treated with OS, only tumors on the left side were related to an unsatisfactory cosmetic result. In the logistic regression analysis for unsatisfactory cosmetic outcomes across all patients (Table 1), there was an increased risk for the weight of the surgical specimen [OR = 1,004 (1,001-1,008)], the time interval between surgery and evaluation [OR = 1,26 (1,15-1,38)], the presence of lymphedema [OR = 2,54 (1,17-5,53)], the occurrence of surgical wound infection [OR 3,06 (1,04-8,99)], tumor on the left side [OR 2,96 (1,64-5,34)] and overweight at diagnosis [OR = 2,57 (1,3-5,0)]. Using OS as a control variable in the logistic regression (Table 1), an increased risk of unsatisfactory results was observed in the time interval between surgery and evaluation [OR 1,27 (1,16-1,39)], the presence of lymphedema [OR 2,97 (1,36-6,46)], surgical wound infection [OR 3,6 (1,22-11,16)], tumor location on the left side [OR 3,06 (1,69-5,53)], overweight [OR 2,93 (1,48-5,8)] and obesity [OR 2,52 (1,2-5,31)]. In the logistic regression in the OS group (Table 2), only the laterality of the tumor influenced the unsatisfactory result [left side OR 4,21 (1,43-15,27)].

Discussion

OS includes oncological treatment *versus* adequacy of the residual breast volume, whether or not associated with symmetrization of the contralateral breast. In addition to expertise, in choosing the technique, the surgeon must consider the characteristics of both the tumor and the breast and understand the expectations and frustrations of the patient, remaining cognizant to the fact that there is no single formula to solve the difficulties imposed by the tumor and that OS is not a guarantee of good cosmetic results (2, 20).

10.3389/fonc.2023.1071127

TABLE 1 Logistic regression for unsatisfactory cosmetic results in all cases according to different criteria for evaluation.

Type of evaluation	Category	Variable	OR	p variable	p group
Patient's evaluation	**TNM stage - T**	Tis and T1	reference		0,038
		≥ T2	1,86 (1,035 – 3,35)		
	Age at diagnosis (years)	≥ 60	reference		0,003
		50 – 59	1,84 (0,762 – 4,45)	0,175	
		40 – 49	1,2 (0,49 – 3,04)	0,667	
		< 40	5,1 (1,86 – 14,01)	0,002	
Patient's evaluation	**Oncoplastic surgery**	Absent	reference		0,817
OS control variable		Present	1,09 (0,52 – 2,25)		
	TNM stage - T	Tis and T1	reference		0,04
		≥ T2	1,85 (1,027 – 3,34)		
	Age at diagnosis (years)	≥ 60	reference		0,003
		50 – 59	1,83 (0,76 – 4,44)	0,177	
		40 – 49	1,2 (0,48 – 3,03)	0,679	
		< 40	5,0 (1,84 – 13,95)	0,002	
BCCT.core software	**Weight of the surgical specimen (g)**	Continuous	1,004 (1,001 – 1,008)		0,01
	Time between surgery and evaluation (years)	Continuous	1,26 (1,15 – 1,38)		<0,001
	Lymphedema	Absent	reference		0,018
		Present	2,54 (1,17 – 5,53)		
	Surgical wound infection	Absent	reference		0,04
		Present	3,06 (1,04 – 8,99)		
	Tumor side	Right	reference		<0,001
		Left	2,96 (1,64 – 5,34)		
	BMI at diagnosis (kg/m^2)	<25	reference		0,02
		25 – 29,9	2,57 (1,3 – 5,0)	0,006	
		≥ 30	1,85 (0,86 – 4,01)	0,115	
BCCT.core software	**Oncoplastic surgery**	Absent	reference		0,065
OS control variable		Present	2,13 (0,95 – 4,76)		
	Time between surgery and evaluation (years)	Continuous	1,27 (1,16 – 1,39)		<0,001
	Distance from the surgical margin	Continuous	1,68 (0,97 – 2,92)		0,062
	Lymphedema	Absent	reference		0,006
		Present	2,97 (1,36 – 6,46)		
	Surgical wound infection	Absent	reference		0,02
		Present	3,6 (1,22 – 11,16)		
	Tumor side	Right	reference		<0,001
		Left	3,06 (1,69 – 5,53)		
	BMI at diagnosis (kg/m^2)	<25	reference		0,005
		25 – 29,9	2,93 (1,48 – 5,8)	0,002	
		≥ 30	2,52 (1,2 – 5,31)	0,01	

OS – oncoplastic surgery/BMI – body mass index.

TABLE 2 Logistic regression for unsatisfactory cosmetic results in OS group according to different criteria for evaluation.

Type of evaluation	Category	Variable	OR	p group
Patient's Assessment	TNM stage - T	Tis and T1	reference	0,018
		≥ T2	7,205 (1,403 – 37,017)	
BCCT.core Software	Tumor side	Right	reference	0,01
		Left	4,21 (1,43 – 15,27)	

Our study, which included only patients undergoing BCS, sought to evaluate the factors associated with an unsatisfactory cosmetic outcome in OS, both according to the patient and through a previously consolidated and reproducible objective methodology *via* BCCT.core. The correlation among cosmetic evaluations of breast surgery is low among different methodologies (16, 21), as are the factors that influence unsatisfactory results. In the patient self-assessment, younger women with higher BMI at the time of evaluation, with larger tumors and heavier surgical specimen tended to present with unsatisfactory breast results. However, according to the software, only the laterality of the tumor influenced these results. We observed a non-significant increase in the unsatisfactory result in the logistic regression using OS as a control variable. However, this fact may be related to the presence of larger tumors, younger patients (potentially questioning) and the small number of contralateral symmetrization in the oncoplastic surgery group.

Understanding these factors allows sharing of the decision-making process with the patient and guidance of training programs for breast surgeons. Indeed, the aesthetic result of breast surgery is closely related to the woman's body self-image, sexual function and quality of life. In addition, because breast cancer survival has been a reality and patients end up experiencing greater treatment morbidity over the years, the aesthetic outcome of the breast has become one of the pillars of cancer treatment, with a priority of patient satisfaction. Thus, the results reported by the patients are a current issue that deserves to be discussed and addressed, as in the present study (21, 22).

In judging the cosmetic result of the breasts after conservative treatment, it is necessary to take into account considerations, often not found in the literature, that influence the factors related to unsatisfactory outcomes. The first corresponds to the time in which the evaluation is performed. Over the years, the woman presents with body changes, sequelae of systemic therapy, and the chronic and progressive effect of radiotherapy, which accentuates the asymmetry in breast size and shape and causes the deceleration of natural breast ptosis and asymmetry in the position of the areolo-papillary complex and skin color (22, 23). Second, we emphasize that the analysis of cosmetic results requires a gold standard and that current methods can show wide variability. Likewise, the literature is heterogeneous with regard to the predisposing factors for unsatisfactory breast cosmesis, primarily due to differences in the studies with regard to the design, size and different instruments of cosmetic evaluation and even with the different classifications of OS, making comparisons difficult (24). In addition, the cosmetic concept in cancer is relatively recent and, from the patient's perspective, involves several psychosocial factors, posttreatment body acceptance, educational level, socioeconomic level and factors related to her own experience with the disease and treatment process, with the corresponding complications and sequelae.

A recent study, in which the surgeon involved in the treatment evaluated the cosmetic outcome of BCS-OS subjectively, analyzed 755 patients subjected to OS, with a mean follow-up of 74,3 months, and found 89 cosmetic sequelae. Most of these occurred during the first 3 years of follow-up; however, for major deformities classified as type III, the mean time of onset was longer. In the multivariate evaluation, postoperative complications and level II oncoplasty techniques (in which there is resection of more than 20% of the breast parenchyma, requiring remodeling and contralateral symmetrization in most cases) increased the risk of cosmetic sequelae in 4,6 and 2,6 times, respectively (22). Another study, evaluating 103 patients, found that increased BMI and breast size were associated with unsatisfactory results. A similar result was found in our study, but due to its retrospective nature, breast size was not evaluated (25).

We found different variables that negatively influenced the cosmetic outcome of classical BCS-CS and BCS-OS, both from the patient's perspective and according to the software analysis. The time of the analysis may influence our results, as patients dissatisfied with their breasts during follow-up likely seek surgical approaches to improve the cosmetic result. In addition, when performing the OS, the surgeon has already preselected the best candidate for the procedure, typically a younger and more educated patient, which can be inferred as greater questioning of the final result of their breast reconstruction procedures. Moreover, OS is more likely to be performed for larger tumors, which requires greater resection and heavier surgical specimens to avoid mastectomy (26). These three conditions represent a bias selection associated with retrospective studies. Our analyzed population is composed of Brazilian patients assisted by the public health system, which have their particularities, requiring further studies in private patients, other centers and in other countries.

Future studies are necessary to assess the unsatisfactory results, which may help surgeons in patient selection and surgical technique. In practice it is not easy because we usually try to perform the BCS and we have many modalities associated with OS (4–7). For this condition the creation of a nomogram may anticipated unsatisfactory results, adding information for the surgeon, in order to understand whether, for the best late aesthetic result, a new surgery should be performed on the breast treated for cancer or on the contralateral one (symmetrization).

Among the limitations of the study are its retrospective and cross-sectional nature and the limited number of patients undergoing OS, which justifies the need for further longitudinal studies. In contrast, its strengths include the use of an objective, standardized and reproducible methodology (BCCT.core) associated with patient self-assessment in long-term follow-up.

Conclusion

The different methods for evaluating cosmetic results after surgical treatment of breast cancer directly influence the identification of factors related to unsatisfactory results. Younger patients with extensive resections (large tumor size and heavy surgical specimen) and increased BMI tend to self-report evaluate the cosmetic result from OS as unsatisfactory. Understanding these results helps in sharing the decision-making process with the patient and in the training programs for breast surgeons.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material. Further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by Research Ethics Committee - Barretos Cancer Hospital. The patients/participants provided their written informed consent to participate in this study.

Author contributions

Conceptualization and Methodology: IO-J, FS, RV, AS, EN. Funding acquisition: RV. Project administration and Supervision: EN, RV. Data curation - Patient Evaluation: FS. Data curation - BCCT.core: GB. Formal analysis: IO-J, RV, EN. Writing: IO-J, RV. Writing review & Editing: All authors. All authors contributed to the article and approved the submitted version.

Funding

Fundação de Amparo à Pesquisa do Estado de São Paulo - FAPESP 2014/08197-0.

Acknowledgments

We acknowledge Statistician Marco Antônio de Oliveira (Barretos Cancer Hospital) provided orientation regarding the methodology to be used and the evaluation of the results.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fonc.2023.1071127/full#supplementary-material

References

1. De Lorenzi F, Hubner G, Rotmensz N, Bagnardi V, Loschi P, Maisonneuve P, et al. Oncological results of oncoplastic breast-conserving surgery: Long term follow-up of a large series at a single institution: A matched-cohort analysis. *Eur J Surg Oncol* (2016) 42(1):71–7. doi: 10.1016/j.ejso.2015.08.160

2. Vieira RA, Carrara GF, Scapulatempo Neto C, Morini MA, Brentani MM, Folgueira MA. The role of oncoplastic breast conserving treatment for locally advanced breast tumors. *A matching case-control study Ann Med Surg (Lond)* (2016) 10:61–8. doi: 10.1016/j.amsu.2016.08.001

3. Franca FC, de Oliveira-Junior I, Morgan AM, Haikel RL, da Costa Vieira RA. Breast-conserving surgery with the geometric compensation/split reduction technique. Indications, oncologic safety and cosmesis. A cohort series and systematic review of the literature. *Surg Oncol* (2022) 44:101839. doi: 10.1016/j.suronc.2022.101839

4. Clough KB, Ihrai T, Oden S, Kaufman G, Massey E, Nos C. Oncoplastic surgery for breast cancer based on tumour location and a quadrant-per-quadrant atlas. *Br J Surg* (2012) 99(10):1389–95. doi: 10.1002/bjs.8877

5. Canturk NZ, Simsek T, Ozkan Gurdal S. Oncoplastic breast-conserving surgery according to tumor location. *Eur J Breast Health* (2021) 17(3):220–33. doi: 10.4274/ejbh.galenos.2021.2021-1-2

6. Gainer SM, Lucci A. Oncoplastics: techniques for reconstruction of partial breast defects based on tumor location. *J Surg Oncol* (2011) 103(4):341–7. doi: 10.1002/jso.21672

7. Paulinelli RR, de Oliveira VM, Bagnoli F, Chade MC, Alves KL, Freitas-Junior R. Oncoplastic mammaplasty with geometric compensation–a technique for breast conservation. *J Surg Oncol* (2014) 110(8):912–8. doi: 10.1002/jso.23751

8. Resende Paulinelli R, de Oliveira VM, Bagnoli F, Letzkus Berrios J, Cezar Chade M, Bragatto Picoli L, et al. Oncoplastic mammaplasty with geometric compensation: Evolution of the technique, outcomes and follow-up in a multicentre retrospective cohort. *J Surg Oncol* (2020) 121(6):967–74. doi: 10.1002/jso.25860

9. Cardoso MJ, Cardoso J, Santos AC, Barros H, Cardoso de Oliveira M. Interobserver agreement and consensus over the Esthetic evaluation of conservative

treatment for breast cancer. *Breast* (2006) 15(1):52–7. doi: 10.1016/j.breast.2005.04.013

10. Cardoso MJ, Cardoso JS, Vrieling C, Macmillan D, Rainsbury D, Heil J, et al. Recommendations for the Aesthetic evaluation of breast cancer conservative treatment. *Breast Cancer Res Treat* (2012) 135(3):629–37. doi: 10.1007/s10549-012-1978-8

11. Chen CM, Cano SJ, Klassen AF, King T, McCarthy C, Cordeiro PG, et al. Measuring quality of life in oncologic breast surgery: a systematic review of patient-reported outcome measures. *Breast J* (2010) 16(6):587–97. doi: 10.1111/j.1524-4741.2010.00983.x

12. Brandini da Silva FC, Jose da Silva J, Sarri AJ, Paiva CE, Aloisio da Costa Vieira R. Comprehensive validation study of quality-of-life questionnaire using objective clinical measures: breast cancer treatment outcome scale (BCTOS), Brazilian Portuguese version. *Clin Breast Cancer* (2019) 19(1):e85–100. doi: 10.1016/j.clbc.2018.10.004

13. Vieira R, Biller G, Silva F, Silva JJD, Oliveira MA, Bailao-Junior A. New criteria for breast symmetry evaluation after breast conserving surgery for cancer. *Rev Col Bras Cir* (2021) 48:e20202698. doi: 10.1590/0100-6991e-20202698

14. Cardoso MJ, Cardoso J, Amaral N, Azevedo I, Barreau L, Bernardo M, et al. Turning subjective into objective: the BCCT.core software for evaluation of cosmetic results in breast cancer conservative treatment. *Breast* (2007) 16(5):456–61. doi: 10.1016/j.breast.2007.05.002

15. Cardoso MJ, Cardoso JS, Oliveira HP, Gouveia P. The breast cancer conservative treatment. Cosmetic results - BCCT.core - Software for objective assessment of esthetic outcome in breast cancer conservative treatment: A narrative review. *Comput Methods Programs Biomed* (2016) 126:154–9. doi: 10.1016/j.cmpb.2015.11.010

16. Santos G, Urban C, Edelweiss MI, Zucca-Matthes G, de Oliveira VM, Arana GH, et al. Long-term comparison of aesthetical outcomes after oncoplastic surgery and lumpectomy in breast cancer patients. *Ann Surg Oncol* (2015) 22(8):2500–8. doi: 10.1245/s10434-014-4301-6

17. Waljee JF, Hu ES, Newman LA, Alderman AK. Predictors of breast asymmetry after breast-conserving operation for breast cancer. *J Am Coll Surg* (2008) 206(2):274–80. doi: 10.1016/j.jamcollsurg.2007.07.029

18. Savalia NB, Silverstein MJ. Oncoplastic breast reconstruction: Patient selection and surgical techniques. *J Surg Oncol* (2016) 113(8):875–82. doi: 10.1002/jso.24212

19. Hennigs A, Hartmann B, Rauch G, Golatta M, Tabatabai P, Domschke C, et al. Long-term objective esthetic outcome after breast-conserving therapy. *Breast Cancer Res Treat* (2015) 153(2):345–51. doi: 10.1007/s10549-015-3540-y

20. Zucca-Matthes G, Vieira RA. The value of patients' expectation on breast oncoplastic surgery. *Breast J* (2014) 20(6):676–8. doi: 10.1111/tbj.12344

21. de Oliveira-Junior I, Brandini da Silva FC, Nazima F, Ribeiro JCJr., Castellani L, Zucca-Matthes G, et al. Oncoplastic surgery: does patient and medical specialty influences the evaluation of cosmetic results? *Clin Breast Cancer* (2020) 21(3):247–55.E3. doi: 10.1016/j.clbc.2020.09.012

22. Acea-Nebril B, García-Novoa A, Cereijo-Garea C. Cosmetic sequelae after oncoplastic breast surgery: long-term results of a prospective study. *Breast J* (2021) 27(1):35–43. doi: 10.1111/tbj.14142

23. Agrawal A. Oncoplastic breast surgery and radiotherapy-Adverse aesthetic outcomes, proposed classification of aesthetic components, and causality attribution. *Breast J* (2019) 25(2):207–18. doi: 10.1111/tbj.13193

24. Hennigs A, Biehl H, Rauch G, Golatta M, Tabatabai P, Domschke C, et al. Change of patient-reported aesthetic outcome over time and identification of factors characterizing poor aesthetic outcome after breast-conserving therapy: long-term results of a prospective cohort study. *Ann Surg Oncol* (2016) 23(5):1744–51. doi: 10.1245/s10434-015-4943-z

25. Olfatbakhsh A, Mehrdad N, Ebrahimi M, Alavi N, Hashemi E, Kaviani A, et al. Evaluation of factors impacting cosmetic outcome of breast conservative surgery–a study in Iran. *Asian Pac J Cancer Prev* (2015) 16(6):2203–7. doi: 10.7314/APJCP.2015.16.6.2203

26. de Oliveira-Junior I, da Silva IA, da Silva FCB, da Silva JJ, Sarri AJ, Paiva CE, et al. Oncoplastic surgery in breast-conserving treatment: patient profile and impact on quality of life. *Breast Care (Basel Switzerland)* (2021) 16(3):243–53. doi: 10.1159/000507240

frontiers | Frontiers in Oncology

TYPE Original Research
PUBLISHED 07 September 2023
DOI 10.3389/fonc.2023.1176609

OPEN ACCESS

EDITED BY
Cicero Urban,
Hospital Nossa Senhora das Graças, Brazil

REVIEWED BY
Cleverton Cesar Spautz,
Oncoclinica/Breast Center Disease, Brazil
René Aloisio Da Costa Vieira,
Barretos Cancer Hospital, Brazil

*CORRESPONDENCE
Chaitanyanand B. Koppiker
dr.koppiker@prashanticancercare.org

RECEIVED 28 February 2023
ACCEPTED 19 July 2023
PUBLISHED 07 September 2023

CITATION
Koppiker CB, Kelkar DA, Kulkarni M, Kadu S, Pai M, Dhar U, Deshmukh C, Varghese B, Zamre V, Jumle N, Gangurde N, Joshi A, Unde R, Banale R, Namewar N, Vaid P, Busheri L, Thomas G, Nare S, Pereira J and Badve S (2023) Impact of oncoplasty in increasing breast conservation rates Post neo-adjuvant chemotherapy.
Front. Oncol. 13:1176609.
doi: 10.3389/fonc.2023.1176609

Impact of oncoplasty in increasing breast conservation rates Post neo-adjuvant chemotherapy

Chaitanyanand B. Koppiker[1,2,3,4,5*], Devaki A. Kelkar[1,2], Madhura Kulkarni[1,2], Shweta Kadu[1,2], Mugdha Pai[1,2], Upendra Dhar[3,5], Chetan Deshmukh[3,5], Beenu Varghese[3,5], Vaishali Zamre[4], Nutan Jumle[3], Nutan Gangurde[1,2], Anjali Joshi[1,2], Rohini Unde[1,2], Rituja Banale[1,2], Namrata Namewar[1,2], Pooja Vaid[2,6], Laleh Busheri[1], George Thomas[5], Smeeta Nare[1,2], Jerome Pereira[7] and Sunil Badve[8]

[1]Prashanti Cancer Care Mission, Pune, India, [2]Center for Translational Cancer Research, a Joint venture between Prashanti Cancer Care Mission and Indian Institute of Science Education and Research (IISER), Pune, India, [3]Department of Onco-Sciences, Jehangir Hospital, Pune, India, [4]International School of Oncoplasty, Pune, India, [5]Orchids Breast Health Centre, A Prashanti Cancer Care Mission (PCCM) Initiative, Pune, India, [6]Ashoka University – Department of Biology, Ashoka University, Haryana, India, [7]Norwich Medical School, University of East Anglia, Norwich, United Kingdom, [8]Department of Pharmacology and Chemical Biology, Emory University, Atlanta, GA, United States

Introduction: The essential goal of neoadjuvant chemotherapy (NACT) is to downstage the primary tumor making it amenable for breast conservation surgery (BCS). However, since the safety of this surgery is paramount, post-NACT breast conservation rates remain low. As per the recommendation of the 2018 Early Breast Cancer Trialists' Collaborative Group (EBCTCG) overview of long-term post-NACT follow-up, we have devised a protocol for imaging, localization, rad-path analysis, and documentation of radiotherapy techniques to ensure the safety of post-NACT breast conservation.

Methods: This is a retrospective cohort of 180 breast cancer patients who received NACT and were operated on by a single surgical oncologist from 2015 to 2020. After selection based on published guidelines, patients were treated with neoadjuvant systemic (chemo or hormone) therapy. In cases where primary tumors responded and reduced to 1–2 cm in size mid-NACT, the residual tumors were localized by clips under ultrasound guidance and calcification was wire localized. All patients were treated using appropriate surgical and oncoplastic techniques where indicated. Negative margins were ensured by intra-operative rad-path analysis. Adjuvant chemotherapy and radiotherapy were given as per protocol.

Results: In 81 cases that required mastectomy at presentation, we were able to achieve a 72.8% post-NACT BCS rate with the help of oncoplasty. Overall, 142 of 180 (80%) patients were treated with breast conserving surgery of which 80% (121 of 142) were oncoplasty. Margins were assessed on intra-operative frozen and re-excised in the same setting. No positive margins were reported in final

histopath of 142 breast conservation procedures. Post-operative complication rates after breast conservation in the first year were at 17% (24 of 142 including two major complications). Patient reported outcomes were satisfactory with increased satisfaction for breast conservation compared with immediate breast reconstruction.

Discussion: Employing oncoplastic breast surgery (OBS) techniques following stringent protocols for accurate localization of the residual tumor, intra-operative rad-path analysis, and adjuvant treatments, we show successful breast conservation in 72.8% of our mastectomy-qualified patients after downstaging by NACT. We also report satisfactory outcomes for post-NACT surgery, patient-reported satisfaction, and survival.

KEYWORDS

neoadjuvant chemotherapy, breast cancer, breast conservation for large tumors, mastectomy, oncoplastic breast conservation, frozen section analysis, tumor localization

Introduction

Breast cancer is the most diagnosed cancer and the leading cause of cancer-related death in India and globally(1, 2). Population-based screening in Western Europe and the USA has enabled early diagnosis, making early intervention possible. With the acceptance of conventional breast conservation surgery (BCS) as a safe technique (3), it has become possible to reduce or completely avoid mastectomy in breast cancer patients, leading to better quality of life (4–6). BCS is now becoming the gold standard of surgical treatment for early breast cancer (7–9). Locally advanced breast cancers (LABCs) and large operable breast cancers (LOBC) are treated with neoadjuvant therapy (NACT) with the aim to downstage these advanced cancers loco-regionally. Downstaging helps to avoid mastectomy in favor of BCS where oncologically and esthetically feasible (9–11).

Conventional BCS is limited to selected patients where it has been shown to be oncologically safe and demonstrable esthetically superior outcomes (12). A hurdle in expanding BCS to patients outside, this limited set is the extent to which post-NACT excision volumes can safely be minimized (13). The Early Breast Cancer Trialists' Collaborative Group (EBCTCG) overview of long-term adjuvant and neoadjuvant therapy outcomes (14) showed increased loco-regional recurrence rates for post-NACT BCS as compared with mastectomy in long-term follow-up. This overview created more doubts about the safety of post-NACT BCS even though the authors accepted that there were several flaws in the studies included in the overview (discussed later). A combination of these factors has resulted in the slow uptake of post-NACT BCS despite adequate data that show post-NACT BCS to be safe (15). The conversion rates for mastectomy to BCS post-NACT downstaging have therefore remained low (~40%) (14, 16, 17).

Oncoplastic techniques have been demonstrated to expand the indications for breast conservation in a variety of situations (12–22). Multiple studies in recent years have shown oncoplastic breast conservation surgeries (OBS) to be as safe as BCS with superior esthetic outcomes (20, 23). Silverstein first reported on breast conservation performed in a series of cases where mastectomy was the only recommended surgical option and termed the procedure "Extreme Oncoplasty" (18). Subsequently such procedures have been shown to be a safe and viable option in selected cases with good patient reported outcomes (15, 19, 22). In a comparison of post-NACT BCS and oncoplastic volume displacement surgery, patients treated with either surgery had similar survival outcomes (24).

Here, we present an audit of our cohort of 180 breast cancer patients who were treated with post-NACT surgery, assessing breast conservation rates, oncological outcomes, and 1 year patient reported outcomes measures (PROMs). We present a series of precautions and procedures that we carried out to ensure safe breast conservation to address the lacunae/issues raised by the EBCTCG overview. At our center, we routinely perform OBS whenever needed and possible for all breast tumors, including LABC and LOBC downstaged with NACT. In recent times, the scope of patients for whom guidelines recommend neoadjuvant therapy has been broadened (25). In this scenario, evidence for the safety of post-NACT breast conservation and approaches to expand the scope of breast conservation are urgently required. Currently, although there are reports of post-NACT oncoplastic breast conservation (19, 22, 24, 26–28), most of these reports focus on a single approach for oncoplastic breast conservation. As with breast conservation, each surgical approach is appropriate only for a specific set of patients. The current study utilizes an arsenal of oncoplastic techniques and a series of precautions in a variety of scenarios to safely increase post-NACT breast conservation. In our experience, oncoplastic breast conservation has proven to be an oncologically safe procedure with good cosmetic and patient reported outcomes (19, 22). This comprehensive report on post-NACT oncoplastic breast conservation demonstrates how such techniques can be carefully leveraged to increase post-NACT breast conservation rates.

Methods

Patient selection

This is a single institutional study involving retrospective analysis of prospectively collected data. The following pathological criteria were used for patient selection for neoadjuvant systemic treatment: (1) LABC (not including node positive T1 and T2 LABC cases), (2) LOBC, (3) luminal HER2-positive and HER-positive (non-luminal) tumors greater than 2 cm; (4) Triple Negative Breast Cancer (TNBC) greater than 3 cm, (5) luminal HER2 negative large T2/T3 tumors, and (6) any patient with clinically or histologically proven positive axillary nodes. Patients with demonstratable metastatic disease were excluded. All patients underwent definitive breast surgery post-NACT in the period between January 2015 and December 2020. Patients were deemed qualified for upfront mastectomy based on the following criteria: (1) LABC; (2) LOBC; that is, Stage IIB and above (T3N0 but not T2N1) as described by Simos et al. (29); (3) small breast volume to tumor ratio; and (4) multicentric/multifocal tumors. Having upfront qualification for mastectomy enabled us to compute conversion rates to BCS/OBS post-NACT. The plan of management (NACT and proposed surgical plan) was discussed with the patient, and written informed consent was obtained for each step/procedure, for each patient.

Data collection

Data included demography, medical history, clinical findings, pathological reports (diagnostic biopsy and surgical histopathology including immunohistochemistry), details of NACT, surgical intervention, pre- and post-operative images of patients, post-surgery complications, follow-up details, and PROMs.

Clinical management

Triple assessment based on clinical examination, imaging and image-guided core needle biopsy was routinely used to establish a diagnosis. Systemic staging was assessed based on Positron Emission Tomography (PET) imaging. Patients were selected for neoadjuvant treatment based on decisions made by the multidisciplinary team (MDT). After clinical staging, NACT was administered based on NCCN guidelines.

Tumor response

After every other cycle of chemotherapy and at the completion of NACT, the patient was monitored clinically and radiologically. Clinical response of the primary tumor to therapy was calculated according to the RECIST Ver 1.1 criteria (30). The pathological response was determined by comparing the pre-therapy clinical stage with the stage at final histopath.

Tumor localization

For all cases, the residual tumor was pre-operatively localized by ultrasound (USG) imaging. In cases where the tumor responded to NACT, the residual tumor was clipped mid-NACT at ~1cm size by USG guided insertion of liga clips. At least four clips were used to facilitate identification by intra-operative USG (Figure 1). We believe that accurate delineation of the center is difficult in a 4- to 5-cm tumor and therefore needs to be done after response to therapy and reduction in tumor volume. Mid-NACT localization after good NACT response mitigated the requirement of another localization procedure such as wire guidance before the definitive surgery. Pre-operative localization by mammography-guided wire bracketing was done only where there was extensive residual calcification post-NACT. Intra-operative USG was used to target the clipped center, and a wide excision of the clip-bearing area was carried out. Intra-operative specimen mammography and USG were used to confirm that all wire-bracketed calcifications and/or clipped specimen were excised with negative margins. Figure 1 also shows specimen mammogram from clipped residual tumors that were T0 and T1 on final pathology.

In this report, paraffin slides of margin tissue were accessed from the pathology laboratory to verify the negative margin outcome. Slides of tissue assessed at frozen were quality checked for tissue integrity on Mantra (PerkinElmer). Frozen and pathology slides were imaged on an OS-15 (OptraSCAN, San Jose, CA, USA) bright field digital scanner. These digital images were blinded and shared from our server with the second pathologist (SB) to assess concordance in margin assessment.

Surgical techniques

In every case, wide local excision of the residual tumor was identified by palpation as well as USG of the residual tumor and the marker clips used for localization. Post-excision margin adequacy was assessed on the table by USG or by specimen mammography. In addition, all specimens were sent for frozen section margin assessment to the pathologist. Any close margin (1–2 mm) seen on specimen mammogram or reported on frozen section (including focally positive margins) was revised in the same sitting before restoration of the breast form. Margin guidelines based on the consensus on margin safety by the American Society of Clinical Oncology, Society of Surgical Oncology, and American Society for Radiation Oncology Consensus Guideline (31) were followed.

The surgical plan was determined based on assessment at diagnosis, post-therapy clinical-radiological assessment of residual disease, residual tumor location, and extent of calcification, breast size, and ptosis. Patients were counseled for safety and esthetic outcomes. Final decisions were based on patient choice. Volume displacement and volume replacement techniques were employed in all cases where conventional breast conservation was deemed unsuitable. In cases where breast conservation was not feasible mastectomy with immediate whole breast reconstruction was performed. Very few patients did not undergo reconstruction. The surgical procedures used are described here.

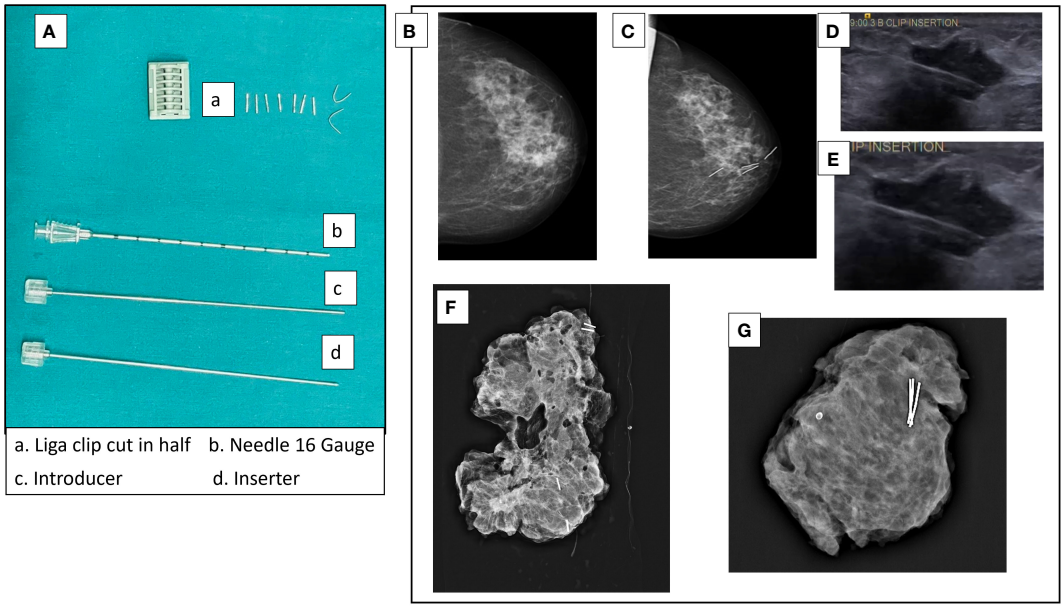


FIGURE 1
Tumor localization by liga clips mid-NACT. **(A)** Liga clips and needles used for USG-guided clip insertion. The liga clip is cut in half and deposited in the tumor mass under USG guidance with the 16-gauge needle. **(B)** Mammogram of pre-NACT lesion HER2-positive non-luminal 3 × 1.8 cm in size in upper and inner quadrant of left breast. **(C)** Mammogram of the residual lesion after two cycles of AC with clips inserted. **(D, E)** USG images of clip insertion into a tumor. **(F)** Specimen mammogram of a clipped specimen with ypT1 residual IDC + DCIS. The residual tumor was clipped at 16.5 mm on USG. The specimen is from a simple therapeutic mammoplasty procedure (volume displacement, Level 2). **(G)** Specimen mammogram of a clipped specimen with complete response (ypT0). Clipping was done when the residual tumor was 18 mm on USG. The specimen is from a complex therapeutic mammoplasty procedure (volume displacement, Level 2).

Conventional breast conservation surgery

BCS with primary breast closure was performed in patients with small residual tumors with adequately sized breasts or tumors in favorable locations.

Oncoplastic breast conservation

Oncoplastic surgeries have been classified based on the recent recommendations of the American Society of Breast Surgeons (32) and as expanded on by Silverstein (20). As defined in these recommendations, oncoplastic surgery refers purely to oncoplastic breast conservation surgery. Oncoplastic techniques performed were simple: Level 1, complex; Level 2, volume displacement and more complex; and Level 3, volume replacement and by perforator flap in most cases. Mini-Latissimus dorsi (LD) flaps were only used in surgeries performed prior to 2019 before perforator flaps were incorporated in routine practice.

Mastectomy with reconstruction

In certain situations, a complete mastectomy was performed. Seventy percent cases of mastectomy were followed by immediate breast reconstruction by implant or LD flaps. Dermal sling was employed for larger ptotic breasts, which has been shown to be a safe procedure (33). For cases with small breasts, an Advanced–Lower Dermal Sling (A-LDS) was used in place of an acellular dermal matrix (34).

Post-surgical oncological management decisions regarding chemoradiation protocols were undertaken by a multidisciplinary clinical team in accordance with guidelines.

Surgical outcomes

Surgical outcome data were recorded as minor or major based on the presence or absence of surgical complications such as seroma, delayed wound healing, fat necrosis, lymphedema, and infection and the interventions required to treat them. Major complications were those that required surgical intervention, whereas minor complications could be treated by therapy in the clinic.

Oncological outcomes

Margin status was assessed by histopathology of frozen sections intra-operatively and paraffin section post-operatively. Patients were carefully monitored for local and distant recurrences, quarterly for the first 2 years post-surgery and then every 6 months. Suspicious symptoms or signs were assessed by appropriate imaging and histological confirmation wherever feasible.

Patient reported outcomes measures

Patients were evaluated for patient reported outcome measures (PROMs) using the BREAST-Q questionnaire (35) at 1-year post-surgery follow-up. BREAST-Q questionnaire was offered to all patients at the completion of 1-year post-surgery follow-up, and data are presented for all patients who responded.

Statistical methods

Data were analyzed using Fishers Exact Count Statistic (when less than five cases), chi-square test, Wilcoxon Rank Test, and Student's t-test using the stat and BSDA (36) package in R Ver 4.0 (37). Median follow-up was calculated using the reverse KM method of Schemper and Smith (38) using the Prodlim (39) and Hmisc (40) packages in R Ver 4.0. All graphs were plotted using ggpubR (41) in R Ver 4.0. Survival parameters were calculated using the survival (42) package in R. Kaplan–Meier plots were plotted using the survminer (43) package.

Results

Patient cohort

One hundred eighty breast cancer patients treated with neoadjuvant therapy and operated between January 2015 and December 2020 were included in the study. Table 1 describes the demographic and clinical features of the patients included in the cohort. The median age of the patients was 50 years (range: 23–75). Most cases (41%, 74 of 180) were luminal HER2 negative, followed by TNBC (31%, 57 of 180) and HER2 + 27% (49 of 180). HER2-positive cases comprise 21 luminal HER2-positive cases and 28 HER2-positive non-luminal cases.

A majority of cases (86%) were diagnosed at biopsy as IDC (155 of 180), and the rest were IDC with DCIS (9 of 180, 5%) and ILC (7 of 180, 4%). Most tumors were T2 at presentation (63%, 113 of 180), and 85% of patients were node positive (153 of 180). Most of these cases were N2 on imaging (56%, 86 of 153). A significant number of cases were clinically stage IIIA at presentation (38%, 69 of 180). The three cases that were treated with neoadjuvant therapy post an excisional biopsy performed at other centers. Excision biopsy is performed on lumpectomy specimens. These are the results of surgical procedures performed for diagnosis, immediately after a suspicious imaging report or clinical examination, without any initial biopsy. This is a common practice in many centers. Such patients often come to our center for reconstructive surgery to regain breast shape, remove scars, and so forth. This is a common practice in many centers. Such patients often come to our center for reconstructive surgery to regain breast shape, remove scars, and so forth. Since margin positivity is often not assessed after such procedures, patients are always assessed for residual tumor by imaging or a histopathological review of specimen tissue when

TABLE 1 Demographic and clinical features of cohort.

Features	Class	N(%)
Total patients		180
Age	Average ± SD years	51.5 ± 11.3
	Median (Range)	50 (23,75)
	< 40 years	27 (15%)
	40-60 years	112 (62.2%)
	> 60 years	41 (22.8%)
*Clinical stage**	IIA	25 (13.9%)
	IIB	43 (23.9%)
	IIIA	71 (39.4%)
	IIIB	35 (19.4%)
	IIIC	3 (1.7%)
	Not available	3 (1.7%)
*Clinical tumor size**	T1	19 (10.6%)
	T2	113 (62.8%)
	T3	20 (11.1%)
	T4	24 (13.3%)
	Not available	4 (2.2%)
*Clinical node status***	Positive	154 (85.6%)
	Negative	23 (12.8%)
	Not available	3 (1.6%)
Subtype	Luminal HER2 negative	75 (41.7%)
	HER2-positive non-luminal	28 (15.6%)
	Luminal HER2 positive	21 (11.6%)
	TNBC	56 (31.1%)
Tumor type	IDC (post-excision biopsy)*†	3 (1.7%)
	IDC	156 (86.7%)
	IDC + DCIS	9 (5.0%)
	IDC + ILC	2 (1.1%)
	ILC	7 (3.9%)
	Other	3 (1.6%)
Tumor grade	I	3 (1.7%)
	II	111 (61.7%)
	III	53 (29.4%)
	Not available	13 (7.2%)

Demographic distribution of NACT cohort.
*Clinical tumor size was assigned based on pre-NACT radiological and clinical assessment of tumor.
**Node status was assigned based on ultrasound observations and biopsy/FNAC data where available. These were used to assign a clinical stage.
*†Three cases that presented post an excision biopsy have been included. All had IDC with positive margins on biopsy histopathology, and two cases had a palpable node on presentation at our clinic. These cases were treated with neoadjuvant therapy prior to definitive surgery.

available. The three cases included here came to us post such a procedure from other centers with reported positive margins. Two of these cases also had positive nodes that had not been treated. The cases included in this cohort were young age (< 40 years) and offered NACT prior to surgery.

Neo-adjuvant treatment

Among patients with luminal HER2-negative tumors, 49% (36 of 74) received hormonal therapy and 51% (38 of 76) were given Anthracycline- or Anthracycline- and Paclitaxel-based chemotherapy. Patients on hormone therapy were significantly older (mean age: 61 + 9.6, (range: 41–75 years) than the chemotherapy group (mean age: 48 + 10.3, (range: 29–67 years), p = 6.39e–07), and all except 1 were post-menopausal. Seventy-seven percent (38 of 49) of HER2-positive (luminal and non-luminal) patients received trastuzumab, a very high rate in an Indian setting for the use of HER2-directed therapy due to the prohibitive cost involved (44). Fifty-eight percent of TNBC patients (33 of 56) received AC followed by a Taxane, and the rest were treated with protocols such as AC alone, Fluorouracil, Epirubicin, Cyclophosphamide (FEC) with Taxane and Taxane with platinum drug as per guidelines. These variations in drug regimen are unavoidable confounders in our data and are a result of the socio-economic realities that patients face during treatment. In some cases where the delay in surgery and/or increased costs due to neoadjuvant therapy proved unacceptable, the preferred regiment of AC + taxane was cut down to four cycles of AC alone.

Response to treatment and surgery

OBS dominated as the choice of surgery in our cohort (Figure 2). Seventeen of 20 patients who had complete clinical response underwent OBS, while 53 of 73 patients with partial response were treated with OBS. Patients with progressive disease had the highest percent of mastectomy with immediate breast reconstruction (31%) or without reconstruction (9%).

The clinical response to treatment was determined by RECIST criteria Ver 1.1. (30). The pattern of response based on molecular subtype is similar to the reported data (45). Complete response (pathological) was high in TNBC and HER2-positive non-luminal (pCR in 48 and 60%, respectively), and low in luminal HER2-positive and luminal HER2-negative (pCR in 29 and 10% cases, respectively). The clinical and pathological response is shown in Figure 3.

Mastectomy to BCS conversion rates

Patients were classified as qualified for upfront BCS (99 of 180) or upfront mastectomy (81 of 180). The basis for qualification for mastectomy is summarized in Table 2. Definitive surgery was performed at the end of the prescribed NACT period, based on the clinical response of the tumor to NACT (Figure 2).

Out of 81 cases that initially qualified for mastectomy, 59 showed a good response to NACT and hence were converted to BCS/OBS with the conversion rate from mastectomy to BCS/OBS of 72.8%. The rest underwent mastectomy with reconstruction (15) or mastectomy alone (7) (see Table 3 and Supplementary Table S1). These patients received mastectomy despite being pre-therapy candidates for breast conservation. Two of these patients had progressed on treatment, and two patients had a complete response but missed mid-NACT USG examination for clip placement and therefore had to be treated with mastectomy. For the rest of the cases, the surgery choice was based on patient preference. In some of these cases, after inadequate response to therapy and with worrisome biology, the patients were not convinced of the safety of breast conservation and were therefore treated with a mastectomy.

Post-NACT oncoplastic—breast-conserving surgery

Overall, 142 (80%) breast-conserving surgeries were performed in the cohort. A substantial proportion (79%) of the breast conservative operations is oncoplastic procedures (OBS) (121 of 142). The types of OBS carried out in the cohort and for the subset that qualified for upfront mastectomy are shown in Table 4. The frequency and type of oncoplastic surgeries in the mastectomy qualified cohort (81 of 180) and those amenable to upfront BCS (99 of 180) are not significantly different. The complexity of oncoplastic surgeries varied from volume displacement techniques (Level 1 techniques) such as rotational mammoplasty to more complex skilled procedures for extreme oncoplasty such as therapeutic mammoplasty and perforator flaps. Volume replacement procedures (46 of 142) following partial mastectomy utilized perforator flaps in most cases (83%, 38 of 46) and for the rest mini-LD (17%, 7 of 46) was performed, if such procedures could achieve superior outcomes. Mini-LD partial reconstructions were mostly done before 2019 when we had yet to adopt perforator flap as a routine technique in our practice. Examples of imaging findings and oncoplastic procedures are illustrated in Figure 4.

Patients who were selected for volume displacement Level 2 surgeries were also counseled for contralateral symmetrization. Only patients who consented for symmetrization were treated with this oncoplastic technique (40 cases). In addition, three cases of perforator flap volume replacement and 11 cases of immediate breast reconstruction received simultaneous symmetrization.

The tissue volume after resection was significantly smaller in BCS (82 ± 53 cc) as compared with average resection volume in OBS procedures (235 ± 280 cc, p = 0.0012) (Figure 5A). To ensure the oncological safety of breast conservation, larger volumes of excisions were required in some cases; hence, we had to adopt OBS techniques. The volume and the location of the excision required dictated the complexity of the OBS technique required (Figure 5A).

Adjuvant treatment

A total of 40% patients (72 of 180) received adjuvant chemotherapy. A majority of HER2-positive (luminal and non-

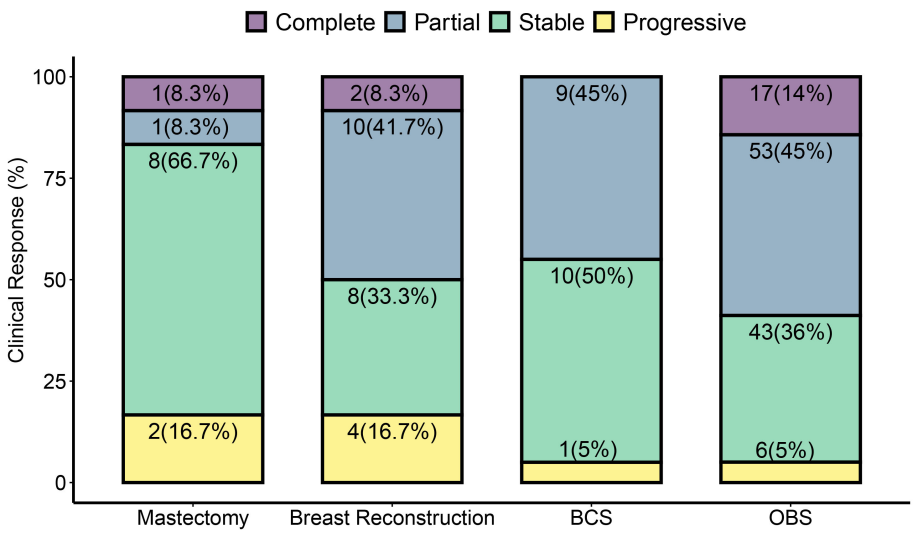


FIGURE 2
Surgery types and clinical tumor response to NACT. Post-NACT surgery type is dependent on the clinical response observed. Clinical response was determined to be complete, partial, stable, or progressive by pre-operative imaging according to RECIST criteria. A greater than 30% increase was taken as progressive disease and greater than 20% decrease as a partial response. Tumors that did not sufficiently decrease to be classified as a partial response or increase enough for progressive response were classified as stable. Cases that did not show any residual breast tumor on imaging were classified as complete response. Surgery types are classified as described in methods. Each bar represents the percent of each surgery type performed for the given clinical response type. In some cases, pre-surgical imaging was unavailable—one in mastectomy, one in breast reconstruction, two cases of OBS, and one case of BCS, and these cases are therefore omitted from this figure. Each subsection is labeled with the total number of surgeries shown in the figure. Numbers in parenthesis are % values for the response type in each surgery type.

luminal) patients received adjuvant trastuzumab (57%), while only 45% (25 of 56) TNBC patients and 49% (36 of 74) luminal HER2-negative patients received adjuvant chemo- or hormonal therapy. Most patients received adjuvant radiotherapy (RT) (92%—167 of 180). Of the patients who did not receive RT, seven were lost to follow up, and six patients refused RT. Of these six patients, none had recurred at the time of last follow-up (average follow-up for these patients = 39 months).

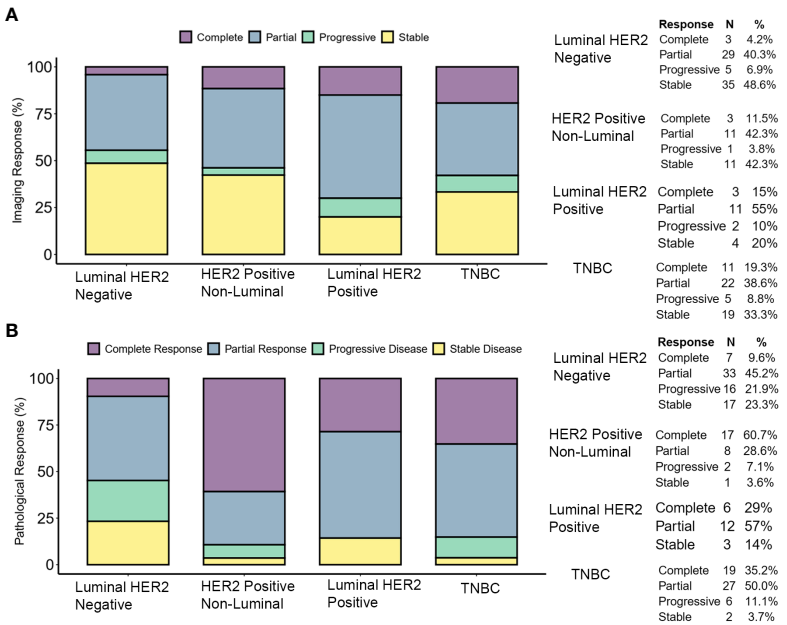


FIGURE 3
Tumor response to therapy. **(A)** Clinical response determined by pre-operative imaging. The response was determined by comparing the longest dimension of the tumor as reported by pre-operative (i.e., post-therapy) imaging versus the longest dimension reported by the same methods at the time of diagnosis. **(B)** Pathological response was determined by comparing the pre-therapy clinical stage (cTcN) to the post-therapy pathological stage (ypTypN). Complete responses shown here are ypT0ypN0 (pCR).

TABLE 2 Upfront mastectomy qualification (n = 81).

Reason for qualification	N	%
≥ 3-cm tumor in small-sized breast	**16**	**20%**
≥ 4-cm tumor in moderate-sized breast	**13**	**16%**
LABC	**23**	**28%**
LOBC	**20**	**25%**
Multicentric/multifocal	**9**	**11%**

Basis for classification of upfront mastectomy qualification.**(A)** Cases were labeled as qualified for upfront mastectomy based on *#tumor size and spread (LABC/LOBC), †‡Smaller tumors with high tumor to breast ratio and multicentric, multifocal tumors. One case with a small invasive tumor but extensive DCIS component has been included. LABC and LOBC were assigned as described by (27).

Post-surgical complications

The frequency and type of post-surgical complications observed in the NACT cohort in the first year post-surgery are shown in Table 5. Minor complications including seroma, fat necrosis, and insignificant delayed wound healing in OBS surgeries were observed in 19% of cases (23 of 121) and in 16% of immediate breast reconstruction surgeries (4 of 25). Two patients had major complications due to delayed wound healing post and OBS surgery, leading to flap necrosis and completion mastectomy in one case and abdominal flap graft in the other. Delayed wound healing in one case of breast reconstruction led to loss of implant (more than 1 year post-surgery). All other complications were minor and were treated with either no intervention or conservatively without needing to go back to the theater.

Oncological outcomes

Surgical margins

We assessed margin positivity rates and the minimum tumor margin size in BCS and OBS surgeries. Due to the extreme care during the surgical procedure with stringent radiological and pathological analysis and revision of margins in the same setting (see Methods), none of our patients needed a second surgery. To independently verify intra-operative frozen assessment of negative margins, pathology margin slides were imaged, blinded, and shared with an independent US-board certified pathologist (SB) for assessment of margin involvement. One hundred sixty-two slides (68 specimen margins, 46 revised margins, 43 frozen specimen margins, and five frozen-revised margins) from 23 patients were re-examined. All the examined margins were found to be negative. In patients with scattered tumor in excised tissue, much wider than 2-mm margins were taken to ensure not to miss any scattered residual disease. The average margin in breast conservation surgeries was 12.2 ± 13.4 mm, with larger average margins for OBS compared with BCS (12.8 ± 14.3 mm compared with 8.5 ± 5.3 mm). Figure 5B shows the spread in tumor margins for breast conservative surgeries (OBS and BCS) in the cohort. There were no cases of a positive margin on final pathology. In 15 cases (10.5%), margins were found to be involved or close intra-operatively (≤ 2 mm) on frozen and were revised in the same surgery. The revised re-excision margins were free of tumor on frozen and final pathology.

Survival outcomes

The median follow-up for this cohort is 38 months (minimum 6.1 months and maximum 86 months, i.e., 7.2 years). Sixteen cases (9%) have less than 1-year follow-up. At median follow-up (38 months), the entire cohort had an overall survival (OS) rate of 90.5%, distant disease–free survival of 84%, and loco-regional recurrence free survival at 93% (Figure 6 upper panel and Table 6). The 142 breast conservation–treated cases had an OS rate of 91.3%, distant disease free at 86.0%, and LRR-free survival of 93.5%. (Figure 6 lower panel). These are acceptable rates for post-NACT–treated cohorts. The Kaplan–Meier plot for surgery stratified disease free and OS is shown in Figure 6. Surgery-type specific local and distant recurrences that occurred during median follow-up time are shown in Table 7. Further details for each breast conservation type are shown in Supplementary Table S2. Cox proportional hazards showed no significant difference at median follow-up (38 months) between breast conservation (conventional BCS and OBS) and mastectomy (mastectomy with or without immediate breast reconstruction) for both distant and local disease free and OS (data not shown). This pattern was seen even in the comparison of the outcomes for the mastectomy qualified versus unqualified cohort (Figure 7). Subtype-stratified distant and local disease free and OS was significantly worse for TNBC subtype. Multivariate cox proportional hazards showed that only TNBC subtype and pathological node status are significantly associated with disease free outcomes in this dataset (data not shown).

TABLE 3 Surgery types in the entire (n = 180) and mastectomy qualified (n = 81) cohort.

Surgery	Entire cohort (n = 180)		Mastectomy qualified (n = 81)	
Mastectomy	13	7.2%	7	8.6%
Breast reconstruction	25	13.9%	15	18.5%
BCS	21	11.7%	7	8.6%
OBS	121	67.2%	52	64.2%

Surgery types performed in the mastectomy qualified and entire cohorts. The mastectomy qualified cases are the cases identified in Table 2. Breast conservation (conventional and oncoplastic) accounts for 78.9% cases in the entire cohort and 72.8% in the mastectomy qualified subset. 72.8% is the rate of conversion from mastectomy to breast conservation.

TABLE 4 Oncoplastic breast conservation techniques used.

Oncoplastic surgery type and subtype	NAT cohort	Upfront mastectomy
	N (%)	N (%)
Volume displacement: Level 1 - Round block technique	14 (11.6%)	4 (7.7%)
Volume displacement: Level 1 - Lateral mammoplasty	10 (8.3%)	2 (3.8%)
Volume displacement: Level 1 - Simple oncoplastic closure	6 (5.0%)	1 (1.9%)
Volume displacement: Level 1 - Rotational mammoplasty	2 (1.7%)	2 (3.8%)
Volume displacement: Level 1 - Wise pattern incision	2 (1.7%)	2 (3.8%)
Volume displacement: Level 1 - Grisotti flap	1 (0.8%)	-
Volume displacement: Level 1 - Medial mammoplasty	1 (0.8%)	1 (1.9%)
Volume displacement Level 1	**36 (29.8%)**	**12 (23.1%)**
Volume displacement: Level 2 - Therapeutic mammoplasty: Simple	17 (14%)	7 (13.5%)
Volume displacement: Level 2 - Therapeutic mammoplasty: Extreme	8 (6.6%)	6 (11.5%)
Volume displacement: Level 2 - Therapeutic mammoplasty: Complex	13 (9.1%)	2 (3.8%)
Volume displacement: Level 2 - Therapeutic mammoplasty: Type unavailable	2(1.7%)	2 (3.8%)
Volume displacement: Level 2	**40 (33.1%)**	**17 (32.7%)**
Volume replacement: mini-LD flap	**7 (5.8%)**	**4 (7.7%)**
Volume replacement: Perforator flap	**38 (31.4%)**	**19 (36.5%)**
Total cases	**121 (100%)**	**52 (100%)**

Distribution of oncoplastic breast conservation techniques used in post-NAST surgery. Level 1 surgeries were of a wide variety with reduced excision volumes (Figure 4). Volume replacement surgeries by perforator flaps were mostly LICAP (n = 26/40) and included TDAP, LTAP, MICAP, Epigastric thoracic flap, and two cases of LICAP with an LTAP flap. Text in bold is a summation of the previous data and scores corresponds to how the levels of oncoplastic surgery are related to surgery.
*Two cases of therapeutic mammoplasty have not been classified as simple, complex or extreme, and have therefore not been included in the details.

PROMs

The PROM scores from the BREAST-Q questionnaire (35) (Questions 1–5) are shown in Table 8. The data represent 1-year PROM scores collected for 18 of 25 patients who had a mastectomy with immediate breast reconstruction, and 72 of 121 patients who underwent OBS (22 volume displacement Level 1, 25 volume displacement Level 2, and 25 volume replacement—perforator flaps). All parameters are satisfactory in all three surgery types, that is, breast reconstruction, BCS, and OBS (values range from 67% to 88%). The variation among surgery types for scores of Question 1 (satisfaction with breasts) was significantly different in ANOVA analysis. OBS showed significantly better satisfaction scores compared with reconstruction, for Question 1 (Table 8) ($P < 0.001$) by Mann–Whitney Test.

Discussion

Breast conservation gives the best surgical outcome for breast cancer in appropriately selected patients (15). Recently, BCS has been shown to be associated with better survival outcomes in early breast cancer compared with mastectomy (46, 47) in data from the Dutch national registry (T1-T2, N0-N2), and the Danish National Registry cohort (pT1-3/pN1-3), (47) even after adjusting for confounding factors such as age, tumor size, and treatment. Conventionally, mastectomy is considered the safe surgical option for LABC/LOBC disease regardless of the response to NACT (15). Encouraged by the establishment of BCT as a safe treatment, breast conservation in LABC patients with good response to NACT has been shown to be as safe as mastectomy, with comparable LRR, disease-free survival (DFS), and OS rates (23, 48). Meta-analyses show that the rate of conversion from mastectomy to BCT post-NACT using conventional BCT techniques is around 40% globally (14, 16, 17). In the EBCTCG overview of 2018, the average conversion rate of planned mastectomy to breast conservation was 33% in the post-NACT setting. In India, this rate is still lower at 11–23% (49), with few isolated cases of higher conversion rates of up to 46.5% (50). Breast conservation gives the best surgical outcome for breast cancer in appropriately selected patients (15). Given this fact, there is a need for better utilization of this technique in the post-NACT setting.

The long-term EBCTCG overview of neoadjuvant compared with adjuvant therapy (14) did not show any specific survival benefit for NACT. Instead, NACT-treated cases had a higher rate of local recurrence. This difference was substantially reduced when cases not treated with surgery were removed from the dataset. The remaining increase in local recurrence was attributed to the increase in post-NACT BCS. The authors discuss that this increase could be a result of flaws in the included studies such as the inconsistency of imaging protocols, tumor localization, and rad-path analysis. In addition to these flaws, the assumption that post-NACT excision

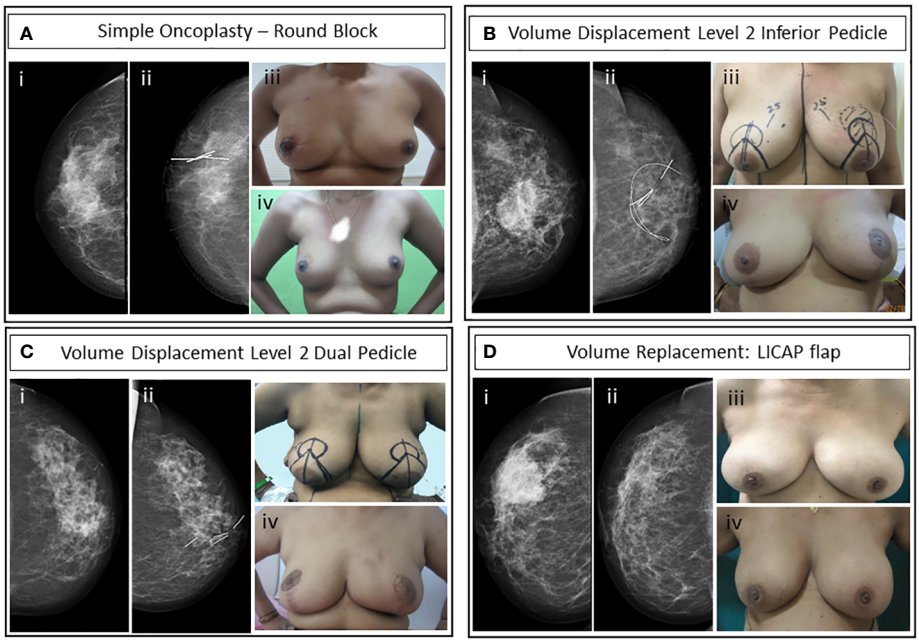


FIGURE 4
Case studies of representative OBS techniques. **(A)** Simple oncoplasty—round block incision surgery of post-NACT HER2-positive non-luminal grade II invasive breast carcinoma **(i)** pre-NACT mammogram, **(ii)** post-NACT CC view of right breast with liga-clip localization, **(iii)** immediate post-operative, and (iv) 3-year post-operative upright patient image. **(B)** Volume displacement Level 2: Inferior pedicle therapeutic mammoplasty with contralateral symmetrization reduction mammoplasty. Luminal HER2-positive grade II IDC after one cycle of NACT with paclitaxel intolerance. Bracketing wires were placed for residual microcalcifications localization. **(i)** Pre-NACT mammogram, **(ii)** post-NACT mammogram left CC view with wire localized area of residual microcalcifications and clip localized residual tumor, **(iii)** patient with pre-operative markings and wire localized tumor for left therapeutic mammoplasty and right reduction mammoplasty, and (iv) 8-month post-operative and post-RT upright patient image. **(C)** Volume displacement Level 2: Dual pedicle therapeutic mammoplasty with NAC graft and contralateral symmetrization reduction mammoplasty. Post-NACT HER2-positive non-luminal grade II IDC. **(i)** Pre-NACT mammogram CC view, **(ii)** post-NACT mammogram left CC view shows a residual lesion with marker clips, **(iii)** upright patient with pre-operative markings, and (iv) upright patient's image 15-month post-operative. **(D)** Volume replacement: Partial breast reconstruction with LICAP flap of post-NACT grade II TNBC IDC. **(i)** Pre-NACT mammogram CC view, **(ii)** post-NACT mammogram CC view of the lesion, **(iii)** pre-operative upright patient image, and (iv) 7-month postoperative image.

volumes decrease as residual tumor decrease in size (13) has led to high-positive margin and re-excision rates for post-NACT BCS (51). Conventional BCS requires small excision volumes and favors specific breast quadrants for acceptable cosmetic outcomes (12). Even post-NACT, conventional BCS, is appropriate and safe only in selected patients with a large breast to tumor volume ratio for tumors in the appropriate quadrants (14, 52, 53). In addition, even after good NACT response, large tumors may respond with a honeycomb-like residual tumor (13, 54, 55) and with residual calcifications or fibrosis, which mimic residual tumor on visual examination. Such cases would require increased excision volumes, making conventional BCS an inappropriate surgical choice.

Oncoplastic techniques have previously been shown to drastically increase the scope of breast conservation and reduce the rate of mastectomy with better margin positivity and re-excision rates (28, 56–58). Silverstein et al.(18, 59) first reported on extreme oncoplasty where patients who would be advised mastectomy in the conventional and contemporary practice were offered breast conservation with the use of oncoplastic techniques. We, in 2019, reported a series of patients with large tumors, multifocal and limited multicentric disease, post-NACT large residual tumor/calcifications, and certain extreme conditions who underwent extreme oncoplastic breast surgery (OBS) with excellent cosmesis and oncological outcomes. There are a few reports of the effective use of oncoplastic surgical techniques in post-NACT cohorts (24, 26, 28) with better outcomes with the technique. Losken and group compared simple BCS with volume displacement oncoplastic surgery in a series of late-stage (> T2 or N1) cases. Even though the group treated with oncoplastic techniques had significantly larger tumors and higher T stage, recurrence, metastasis, and survival rates were not significantly different between BCS and OBS (24).

Here, we report post-NACT outcomes for a series of 180 patients. All cases were operated by a single surgical oncologist after extensive patient counseling and with the aim of providing the best result to the patient in terms of oncological safety, long-term outcomes, cosmetic outcome, and patient satisfaction. Mastectomy has been shown to have an adverse effect on quality of life end points for most patients (5). In our practice, we aim to offer the advantage of breast conservation where oncologically safe to every patient. In India, due to a complex interplay of social norms and economic status of women, a second surgery is not an option for most patients. Hence, negative margins on the first surgery are essential. To achieve this, every tumor is widely excised and margins < 2 mm are revised. In certain situations where there is a large residual scar or lesion or scattered tumor in the excised specimen on

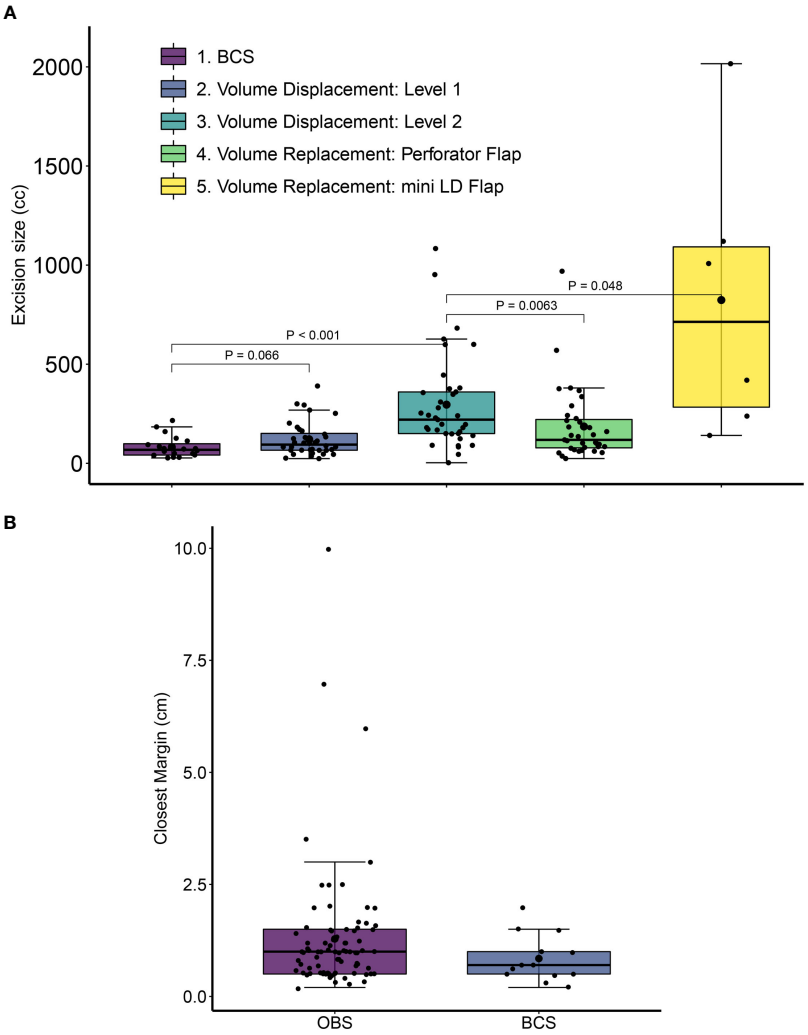


FIGURE 5
Excision volumes and closest margin distance for post-NACT breast conservative surgery. **(A)** Excision volumes were calculated from the sum of the specimen volume and the volume of the cut margins. Error bars represent standard deviation values. *P*-values are from Wilcoxon Rank Sum tests with 95% confidence intervals. Error bars represent standard deviation values. **(B)** The distance of the closest margin from residual tumor at final pathology is shown for conventional breast conservative (BCS) and oncoplastic breast conservative surgeries (OBS) in the cohort. All distances are in cm. For OBS margins the closest margin is calculated after considering revised margin dimensions. Margin data were available for 13 BCS and 83 OBS cases.

TABLE 5 Early surgical complications observed in NACT cohort (at 1-year post-surgery).

Complication type	Surgery type			
	Mastectomy	Breast reconstruction	BCS	OBS
Delayed wound healing	–	1	–	7 + 2*
Haematoma	-	-	-	1
Seroma	–	2	1	6
Lymphedema	1	-	-	-
Fat necrosis	–	1	–	6
Hematoma	-	-	-	1
Capsular contracture	–	–	–	–
Complication rate %(n)	7.7% (1/13)	16% (4/25)	4.8% (1/21)	19% (23/121)

Surgical complications: Post-operative surgical complications in the NACT cohort at 1-year post-surgery. Complications are described as major or minor depending on the intervention required. The rate of complications in oncoplastic breast conservation versus breast reconstruction was not significantly different. *Major complications.

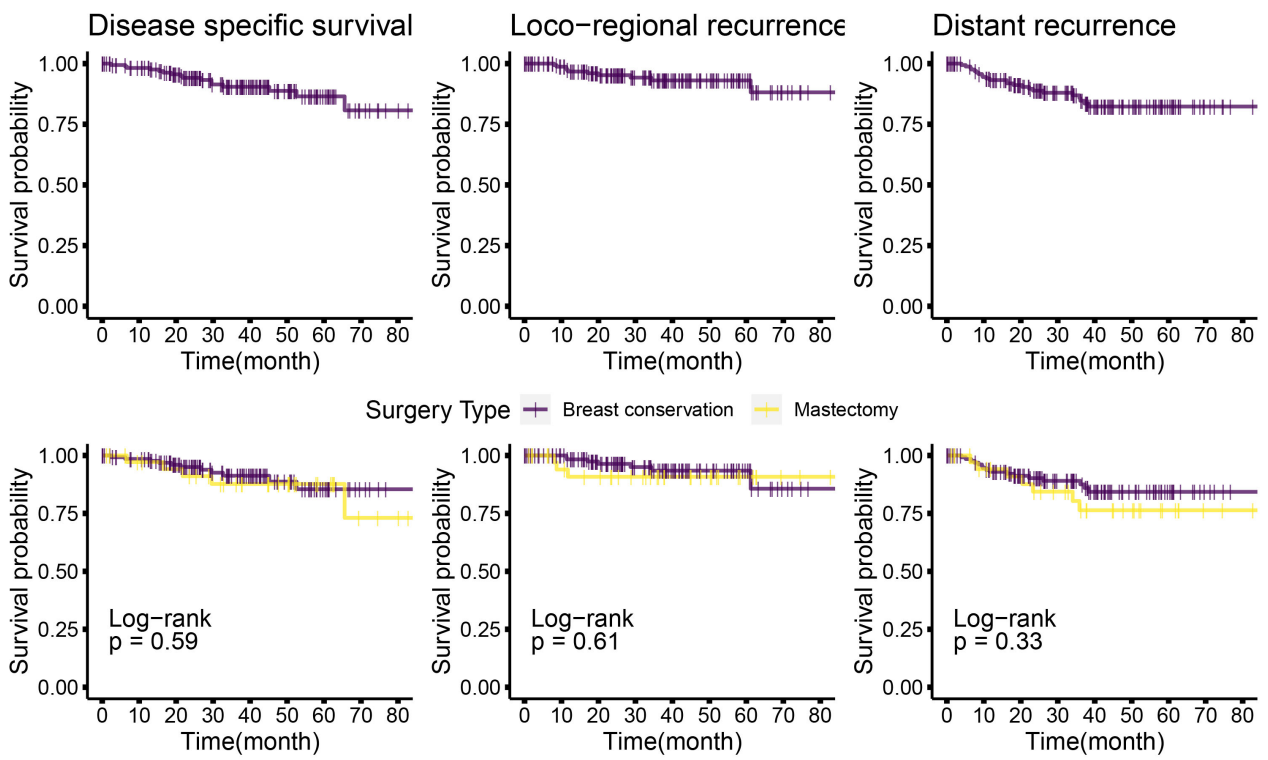


FIGURE 6
Kaplan–Meier plots of disease-specific, distant disease–free, and locoregional disease–free survival for the entire cohort, and mastectomy or breast conservation treated subsets. Top panel: Kaplan–Meier plots for the entire cohort for different survival types; bottom panel: Kaplan–Meier plots for the mastectomy and BCS-treated subsets. Log rank *P*-values are shown; survival types: The left most plots show the disease specific survival; central panel shows the plots for locoregional disease–free survival and the right most are for distant disease–free survival. Disease-free interval is calculated from the time of surgery to the first recurrence (local or distant) observed. OS time is calculated from the time of surgery to the most accurately available date of death where the death is known to relate to cancer. In cases where date of death was not available, the date of last follow-up has been used. Distant disease–free survival is plotted for the time from surgery to a distant recurrence or detection of systemic metastasis. Distant recurrence may be the first recorded recurrence or subsequent or concomitant to a local recurrence. Similarly, loco-regional recurrences shows data for the first recorded recurrence or concomitant with a distant recurrence.

frozen, much larger margins were taken (average margin 1.2 cm, Figure 5B). This may come at the expense of surgical simplicity, thus requiring complex oncoplastic techniques to achieve acceptable esthetic outcomes.

The flaws brought out by the EBCTCG overview about the inconsistency of the protocol of imaging, tumor localization, and rad-path analysis were mitigated by adherence to a strict protocol as discussed. In case of tumors that responded well to NACT, the tumor center was localized mid-NACT at ~1–2 cm by USG-guided insertion of at least four liga clips (see Figure 1) as discussed in methodology. The four clips used here were used to aid the identification of the residual tumor by intra-operative USG. The clips are inserted under USG guidance in the center of the residual tumor and not at the edges of the residual tumor. Accurate location of the center of the residual tumor by intra-operative USG also allows us to avoid additional procedures for wire localization. By placing the radio-opaque clips mid-NACT after a good response, as opposed to pre-NACT, we ensure that procedures such as wire localization of the clips are not routinely required (60). Only in cases where there is extensive calcification post-NACT, wire localization was done pre-operatively

TABLE 6 Survival outcomes at 3 years (median follow-up) post-surgery local, distant recurrence, and survival percentages.

Follow up status	Mastectomy N = 13	Breast reconstruction N = 25	BCS N = 21	OBS N = 121
At median follow-up (3-year post-surgery)				
Local recurrence	3 (23%)	0	0	7 (6%)
Distant recurrence	1 (8%)	6 (24.0%)	5 (24%)	10 (8%)
Death due to Cancer	2 (15%)	2 (8.0%)	1 (5%)	8 (7%)
Death due to unrelated cause	-	-	1 (5%)	-

Survival outcomes: Crude survival and recurrence rates at median follow-up (3 years) post-surgery. Outcomes are shown according to surgical treatment received. Numbers represent the number of events for each survival type that occurred before median time point. Percentages are calculated from the total number of surgeries of the given type performed.

TABLE 7 Kaplan–Meier survival estimates*.

Time (months)	NACT cohort	Mastectomy	Breast conservation	Log rank p
				Disease-specific survival
38	0.904(80)	0.877 (22)	0.913 (59)	0.59
				Distant disease–free survival
38	0.835(70)	0.763 (17)	0.860 (54)	0.33
				Locoregional recurrence–free survival
38	0.931(70)	0.908(17)	0.935(54)	0.61

Kaplan–Meier estimate of disease (local and distant)-free and overall survival. Survival probabilities for the entire cohort and stratified by surgery type (mastectomy and breast conservation) are shown with log-rank p-values (at 95% confidence interval) for the comparison between mastectomy and breast conservation outcomes. Survival is analyzed for overall survival, distant disease–free survival, and locoregional recurrence–free survival. Data are taken from the actuarial tables used to plot Figure 6.

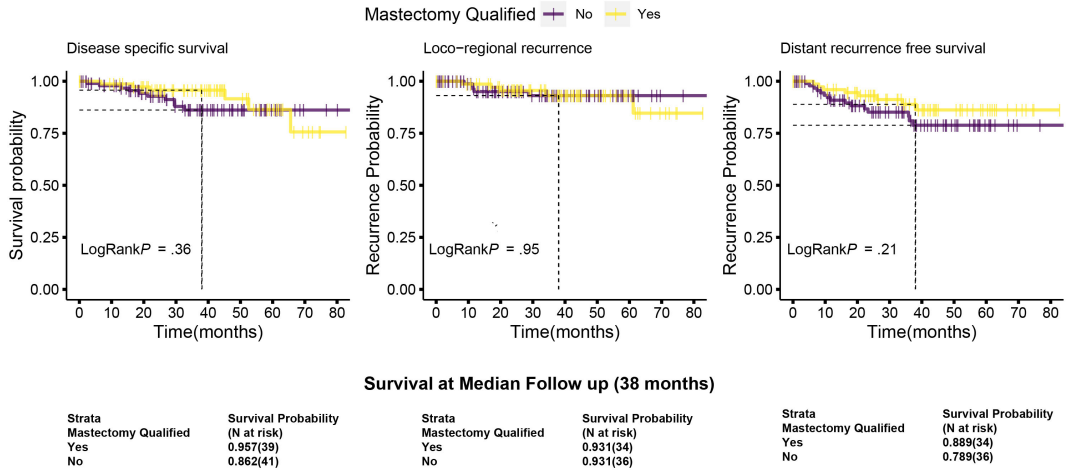


FIGURE 7
Kaplan–Meier plots of disease-specific, distant disease–free and locoregional disease–free survival for the mastectomy qualified and unqualified subsets. Survival types: The left most plots show the disease-specific survival; central panel shows the locoregional disease free survival and the right most are for distant disease free survival. Dotted lines indicate the survival probabilities at median follow-up stratified by mastectomy qualification and log-rank *p*-values (at 95% confidence interval) for each survival type. Survival is calculated as described in Figure 6. Survival probabilities at median follow-up are given in the table below with number at risk. Data are taken from the actuarial tables used to plot the survival curve.

to identify the area of calcifications (Figure 4B). At times, this was in addition to prior mid-NACT clip localization of residual tumor. Other authors have used clip insertion before us; however, the purpose was to identify the tumor footprint (61). We follow the current recommendations of excision of post-NACT residual tumor rather than pre-NACT tumor footprint. This addressed the problem reported by the EBCTCG overview concerning improper localization. Two cases with a complete response missed mid-NACT follow-up and had to be treated with mastectomy since the tumor bed could not be accurately identified. Residual calcifications were targeted with

TABLE 8 Patient-reported outcome measures at 1-year follow-up.

Breast-Q question	Breast† reconstruction	BCS†	OBS†	**p
1.Satisfaction with breasts	68 ± 16 (16)	80 ± 19 (7)	81 ± 14 (72)	0.0046
2.Satisfaction with outcome	88 ± 16.6 (16)	73 ± 14.7 (7)	84 ± 9.5 (72)	0.0188
3.PsychoSocial well-being	83 ± 20 (16)	86 ± 20 (7)	87 ± 17 (72)	0.66 (N.S)
4.Sexual well-being	52 ± 37 (5)	76 ± 22 (5)	80 ± 25 (34)	0.11(N.S)
5.Physical well-being	72 ± 17 (16)	68 ± 6 (7)	73 ± 13 (72)	0.63 (N.S)
Response rate	**16/25 (67%)**	**7/21 (64%)**	**72/121 (80%)**	

Patient-reported outcomes measure. Mean scores for patient response to selected Breast-Q questions. The number of patients who responded varied by question and is given in parenthesis. The total rate of response for each surgery type is given as response rate (bold) at the bottom of the table.

bracketing and excised completely with immediate radiological confirmation. We employed intra-operative assessment of margins on frozen sections to ensure clear margins. The use of frozen sections to ensure clear margins has been reported and encouraged earlier by an Italian group of oncologists (62). This helped in ensuring zero margin positivity rates and reduced the repeat surgery rates to zero. Margin negativity was confirmed by blinded assessment by a second independent US-board certified pathologist of 100 randomly selected margin slides.

A recent meta-analysis on outcomes of post-NACT BCS (51), reported 2–33.6% positive margins with 0–12.4% re-excision rates. In contrast, in our cohort, even though 80% (142 of 180) surgeries are breast conserving, we report 0 positive margins with 0 re-excisions. In the subset that qualified for mastectomy at presentation, 73% cases (59/81) could be converted to breast conservation post-NACT. This conversion rate is mostly achieved by OBS, since 88% of breast conservation surgeries are oncoplastic surgeries (52/59). Previously, 6% positive margins were reported in a series of 47 post-NACT oncoplastic surgeries (24). Similar rates in our setting would put a strain on our system where socio-economic issues make second surgeries extremely difficult to perform. The use of frozen section removed this concern in our dataset, since we report 0 positive margins on final pathology. Stringent and extensive imaging and rad-path analysis with accurate delineation of the tumor bed were followed by well-planned radiation techniques. All these measures have resulted in excellent tumor control in the median follow-up of three years with an overall survival rate of 91.3%, distant disease free at 86% and LRR free survival 93.5% for breast conservation treated cases. These compare very well with 5 year rates reported by Chen et al. for 401 post-NACT BCT-treated patients with 63-month median follow-up (87, 89, and 91%, respectively) (48) despite the fact that conventional BCT makes up only 15% of the breast conservation surgeries (21 of 142) in our dataset. Importantly, disease-free interval is dependent on only disease characteristics such as TNBC subtype and pathological node positivity (data not shown). The type of surgical procedure used (breast conservation or mastectomy) does not affect the disease-free or survival outcomes. These results also hold true for the mastectomy qualified cohort.

The relatively short median follow-up of 38 months (~3 years) may have biased some of the oncological outcome presented here. This cohort covers 6 years of retrospective data from 2015 to 2020. The first 3 years (2015–2018) have a median follow-up of 50 months and account for 60% of the cases. Cases from 2019/2020 have shorter follow-up of 29–20 months. However, many of the patients in this cohort are in active follow-up and the outcomes of this cohort will be subsequently updated. In addition, in the time covered by this retrospective cohort, the practice was to offer the PROM questionnaire only once at the time of the 1 year follow-up. We are therefore unable to present long-term patient outcomes.

With a range of oncoplastic techniques, we were able to achieve a rate of 80% breast conservation in our cohort despite having 61% (110/180) LABC cases. Oncoplasty conferred the ability to excise a variety of volumes as was required in each case with adequate margins to make the surgery oncologically safe. These included cases where the residual tumor was large or the excised specimen sent for the frozen section showed scattered tumor foci. The esthetic outcomes were deemed acceptable based on the satisfactory PROM scores. Carefully carried out breast oncoplasty has the potential to increase breast conservation rates and patient satisfaction in the post-NACT setting. The incorporation of oncoplastic techniques helps treat larger tumors, achieves better cosmetic outcomes, and maintains comparable survival rates as that of mastectomy.

Our experience shows that meticulous protocol for imaging and targeting the tumor with mid-cycle clipping, intra-operative evaluation of margins, stringent RAD-PATH analysis, and application of appropriate oncoplastic and RT techniques confers a major benefit in terms of surgical, oncological, and patient-reported outcomes. Using these protocols, we were successful in avoiding re-excisions by a second surgery and providing breast conservation in our socio-economic conditions. In fact, avoiding second surgeries should be an aim even in the developed world as it would help save on resources. The inclusion of oncoplastic surgery in the armamentarium of surgical techniques will improve breast care for patients presenting with larger tumors and more advanced disease, which is found to a larger extent in developing countries.

Data availability statement

The datasets presented in this article are not readily available because The dataset is composed of clinical data with follow up of individual patients treated by us and is therefore not shareable with others outside our institutions. Requests to access the datasets should be directed to dr.koppiker@prashanticancercare.org.

Ethics statement

The studies involving human participants were reviewed and approved by PCCM-CTCR Independent Ethics Committee. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

CK was involved in the conception and design, financial support, administrative support, manuscript writing, and final approval of the manuscript and was generally accountable for all aspects of the work; DK was involved in the collection, analysis, visualization and interpretation of data, manuscript writing, final approval of the manuscript; MK was involved in the collection, analysis and visualization and interpretation of data, manuscript writing; SK was involved in the collection, analysis and visualization of data; MP was involved in the collection and analysis of data; UD, CD, BV, NJ: Assembly of data; VZ in data interpretation and manuscript writing; NG, AJ in data collection and analysis; RU, RB, NN in data collection; PV in data analysis; LB Administrative support; GT and SN data assembly and collection; JP in data

interpretation; SB in data analysis and interpretation. All authors contributed to the article and approved the submitted version.

Funding

MK is supported by DBT-Ramalingamswamy Re-entry Fellowship. Research at Prashanti Cancer Care Mission - CTCR is supported by a research CSR grant from Bajaj Auto Ltd (GC2528). This study received funding from a Research CSR grant from Bajaj Auto Ltd GC2528. The funder was not involved in the study design, collection, analysis, interpretation of data, the writing of this article or the decision to submit it for publication.

Acknowledgments

The authors would like to acknowledge the efforts of Rateeka Johri, Shaheen Shaikh, and Ruhi Reddy for data collection in the early stages of this project. We would like to particularly thank Aeijazul Noor, and Santosh Dixit for their efforts in taking this work forward in the early stages. We are very grateful to the late Dr. Pooja Deshpande for her work to put this project together. We thank Sneha Joshi and Rupa Mishra for their insightful comments on this manuscript. Our work would not be possible without the efforts of the entire staff at Orchids Breast Health Centre. We would particularly like to thank Ruth Navgire for helping to arrange Figure 1 and to Dnyaneshwari Muknak for her help in cataloguing PROM questionnaires. MK is supported by a DBT-Ramalingamswamy Re-entry Fellowship. Research at Prashanti Cancer Care Mission - CTCR is supported by a research CSR grant from Bajaj Auto Ltd (GC2528).

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fonc.2023.1176609/full#supplementary-material

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* (2018) 68(6):394–424. doi: 10.3322/caac.21492

2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* (2021) 71(3):209–49. doi: 10.3322/caac.21660

3. Hofvind S, Holen Å, Aas T, Roman M, Sebuødegård S, Akslen LA. Women treated with breast conserving surgery do better than those with mastectomy independent of detection mode, prognostic and predictive tumor characteristics. *Eur J Surg Oncol* (2015) 41(10):1417–22. doi: 10.1016/j.ejso.2015.07.002

4. Kim MK, Kim T, Moon HG, Jin US, Kim K, Kim J, et al. Effect of cosmetic outcome on quality of life after breast cancer surgery. *Eur J Surg Oncol* (2015) 41 (3):426–32. doi: 10.1016/j.ejso.2014.12.002

5. Acea Nebril B, García Novoa A, Polidorio N, Cereijo Garea C, Bouzón Alejandro A, Mosquera Oses J. Extreme oncoplasty: The last opportunity for breast conservation-analysis of its impact on survival and quality of life. *Breast J* (2019) 25(3):535–6. doi: 10.1111/tbj.13267

6. Curran D, van Dongen JP, Aaronson NK, Kiebert G, Fentiman IS, Mignolet F, et al. Quality of life of early-stage breast cancer patients treated with radical mastectomy or breast-conserving procedures: results of EORTC trial 10801. *Eur J Cancer* (1998) 34 (3):307–14. doi: 10.1016/S0959-8049(97)00312-2

7. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* (2002) 347(16):1233–41. doi: 10.1056/NEJMoa022152

8. Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med* (2002) 347(16):1227–32. doi: 10.1056/NEJMoa020989

9. Mieog JSD, van der Hage JA, Van De Velde CJH. Neoadjuvant chemotherapy for operable breast cancer. *Br J Surg* (2007) 94(10):1189–200. doi: 10.1002/bjs.5894

10. Kaufmann M, Hortobagyi GN, Goldhirsch A, Scholl S, Makris A, Valagussa P, et al. Recommendations from an international expert panel on the use of neoadjuvant (primary) systemic treatment of operable breast cancer: An update. *J Clin Oncol* (2006) 24(12):1940–9. doi: 10.1200/JCO.2005.02.6187

11. American Cancer Society. *NCCN guidelines (breast cancer)*. National Comprehensive Cancer Network, PA, USA, Vol. NA. (2019). pp. 1–215.

12. Clough KB, Kaufman GJ, Nos C, Buccimazza I, Sarfati IM. Improving breast cancer surgery: a classification and quadrant per quadrant atlas for oncoplastic surgery. *Ann Surg Oncol* (2010) 17(5):1375–91. doi: 10.1245/s10434-009-0792-y

13. Boughey JC, Peintinger F, Meric-Bernstam F, Perry AC, Hunt KK, Babiera GV, et al. Impact of preoperative versus postoperative chemotherapy on the extent and number of surgical procedures in patients treated in randomized clinical trials for breast cancer. *Ann Surg* (2006) 244(3):464–9. doi: 10.1097/01.sla.0000234897.38950.5c

14. Asselain B, Barlow W, Bartlett J, Bergh J, Bergsten-Nordström E, Bliss J, et al. Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: meta-analysis of individual patient data from ten randomised trials. *Lancet Oncol* (2018) 19(1):27–39. doi: 10.1016/S1470-2045(17)30777-5

15. Murugappan K, Saboo A, Kuo L, Ung O. Paradigm shift in the local treatment of breast cancer: mastectomy to breast conservation surgery. *Gland Surg* (2018) 7(6):506–19. doi: 10.21037/gs.2018.09.01

16. Petruolo O, Sevilimedu V, Montagna G, Le T, Morrow M, Barrio AV. 'How often does modern neoadjuvant chemotherapy downstage patients to breast-conserving surgery?' In: *Annals of surgical oncology*. U.K.:Springer Nature (2020). doi: 10.1245/s10434-020-08593-5

17. Straver ME, Rutgers EJT, Rodenhuis S, Linn SC, Loo CE, Wesseling J, et al. The relevance of breast cancer subtypes in the outcome of neoadjuvant chemotherapy. *Ann Surg Oncol* (2010) 17(9):2411–8. doi: 10.1245/s10434-010-1008-1

18. Silverstein MJ, Savalia N, Khan S, Ryan J. Extreme oncoplasty: Breast conservation for patients who need mastectomy. *Breast J* (2015) 21(1):52–9. doi: 10.1111/tbj.12356

19. Koppiker CB, Noor AU, Dixit S, Busheri L, Sharan G, Dhar U, et al. Extreme oncoplastic surgery for Multifocal/Multicentric and locally advanced breast cancer. *Int J Breast Cancer* (2019) 2019:4262589. doi: 10.1155/2019/4262589

20. Silverstein MJ. Oncoplastic breast surgery: From oblivion to mainstream. *Ann Surg Oncol* (2019) 26(11):3409–12. doi: 10.1245/s10434-019-07429-1

21. Silverstein MJ, Mai T, Savalia N, Vaince F, Guerra L. Oncoplastic breast conservation surgery: The new paradigm: Oncoplastic breast conservation surgery. *J Surg Oncol* (2014) 110(1):82–9. doi: 10.1002/jso.23641

22. Koppiker C, Joshi S, Mishra R, Kelkar DA, Chigurupati P, Joshi A, et al. Therapeutic mammoplasty: a "wise" oncoplastic choice—lessons from the largest single-center cohort from Asia. *Front Oncol* (2023) 13:1131951. doi: 10.3389/fonc.2023.1131951

23. Sun Y, Liao M, He L, Zhu C. Comparison of breast-conserving surgery with mastectomy in locally advanced breast cancer after good response to neoadjuvant chemotherapy: A PRISMA-compliant systematic review and meta-analysis. *Med (Baltimore)* (2017) 96(43):e8367. doi: 10.1097/MD.0000000000008367

24. Broecker JS, Hart AM, Styblo TM, Losken A. Neoadjuvant therapy combined with oncoplastic reduction for high-stage breast cancer patients. *Ann Plast Surg* (2017) 78(6):S258–62. doi: 10.1097/SAP.0000000000001062

25. Gradishar WJ, Moran MS, Abraham J, Abramson V, Aft R, Agnese D, et al. NCCN guidelines® insights: Breast cancer, version 4.2023. *J Natl Compr Cancer Netw JNCCN* (2023) 21(6):594–608.

26. Emiroglu M, Sert I, Karaali C, Aksoy SO, Ugurlu L, Aydın C. The effectiveness of simultaneous oncoplastic breast surgery in patients with locally advanced breast cancer. *Breast Cancer* (2016) 23(3):463–70. doi: 10.1007/s12282-015-0585-z

27. Vieira RA da C, Carrara GFA, Scapulatempo Neto C, Morini MA, Brentani MM, Folgueira MAAK. The role of oncoplastic breast conserving treatment for locally advanced breast tumors. a matching case-control study. *Ann Med Surg* (2016) 10:61–8. doi: 10.1016/j.amsu.2016.08.001

28. Bogusevicius A, Cepuliene D, Sepetauskiene E. The integrated evaluation of the results of oncoplastic surgery for locally advanced breast cancer. *Breast J* (2014) 20 (1):53–60. doi: 10.1111/tbj.12222

29. Simos D, Clemons M, Ginsburg OM, Jacobs C. Definition and consequences of locally advanced breast cancer. *Curr Opin Support Palliat Care* (2014) 8(1):33–8. doi: 10.1097/SPC.0000000000000020

30. Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer Oxf Engl 1990* (2009) 45(2):228–47. doi: 10.1016/j.ejca.2008.10.026

31. Pilewskie M, Morrow M. Margins in breast cancer: How much is enough? *Cancer* (2018) 124(7):1335–41. doi: 10.1002/cncr.31221

32. Chatterjee A, Gass J, Patel K, Holmes D, Kopkash K, Peiris L, et al. A consensus definition and classification system of oncoplastic surgery developed by the american society of breast surgeons. *Ann Surg Oncol* (2019) 26(11):3436–44. doi: 10.1245/s10434-019-07345-4

33. Koppiker CB, Noor AU, Dixit S, Mahajan R, Sharan G, Dhar U, et al. Implant-based breast reconstruction with autologous lower dermal sling and radiation therapy outcomes. *Indian J Surg* (2019) 81(6):543–51. doi: 10.1007/s12262-018-1856-7

34. Koppiker CB, Noor AU, Dixit S, Busheri L, Sharan G, Dhar U, et al. Advanced autologous lower dermal sling technique for immediate breast reconstruction surgery in small and non-ptotic breasts. *Indian J Surg Oncol* (2022) 13(3):564–73. doi: 10.1007/s13193-022-01524-8

35. Pusic AL, Klassen AF, Scott AM, Klok JA, Cordeiro PG, Cano SJ. Development of a new patient-reported outcome measure for breast surgery: the BREAST-q. *Plast Reconstr Surg* (2009) 124(2):345–53. doi: 10.1097/PRS.0b013e3181aee807

36. Arnholt AT, Evans B. *BSDA: Basic statistics and data analysis [Internet]* (2021). Available at: https://cran.rproject.org/package=BSDA.

37. Core Team R. *R: A language and environment for statistical computing [Internet]*. Vienna, Austria: R Foundation for Statistical Computing (2020). Available at: https://www.r-project.org/.

38. Schemper M, Smith TL. A note on quantifying follow-up in studies of failure time. *Control Clin Trials* (1996) 17(4):343–6. doi: 10.1016/0197-2456(96)00075-X

39. Thomas G. *Prodlim: Product-limit estimation for censored event history analysis [Internet]* (2019). Available at: https://cran.r-project.org/package=prodlim.

40. Harrell FE Jr. *Hmisc: Harrell miscellaneous [Internet]* (2021). Available at: https://cran.r-project.org/package=Hmisc.

41. Kassambara A. *Ggpubr: 'ggplot2' based publication ready plots r package version 0.4.0. [Internet]* (2020). Available at: https://cran.r-project.org/package=ggpubr.

42. Therneau T, Crowson C, Atkinson E. *Multi-state models and competing risks (vignette survival package)*, Vol. (0). (2016). pp. 1–27.

43. Kassambara A, Kosinski M, Przemyslaw B. *Survminer: Drawing survival curves using 'ggplot2'. r package version 0.4.7. [Internet]* (2020). Available at: https://cran.r-project.org/package=survminer.

44. Gupta N, Verma RK, Gupta S, Prinja S. Cost effectiveness of trastuzumab for management of breast cancer in india. *J Glob Oncol* (2020) 6:205–16. doi: 10.1200/JGO.19.00293

45. Matuschek C, Jazmati D, Bölke E, Tamaskovics B, Corradini S, Budach W, et al. Post-neoadjuvant treatment strategies in breast cancer. *Cancers* (2022) 14(5):1246. doi: 10.3390/cancers14051246

46. van Maaren MC, de Munck L, de Bock GH, Jobsen JJ, van Dalen T, Linn SC, et al. 10 year survival after breast-conserving surgery plus radiotherapy compared with mastectomy in early breast cancer in the netherlands: a population-based study. *Lancet Oncol* (2016) 17(8):1158–70. doi: 10.1016/S1470-2045(16)30067-5

47. Christiansen P, Carstensen SL, Ejlertsen B, Kroman N, Offersen B, Bodilsen A, et al. Breast conserving surgery versus mastectomy: overall and relative survival–a population based study by the danish breast cancer cooperative group (DBCG). *Acta Oncol* (2018) 57(1):19–25. doi: 10.1080/0284186X.2017.1403042

48. Chen AM, Meric-Bernstam F, Hunt KK, Thames HD, Oswald MJ, Outlaw ED, et al. Breast conservation after neoadjuvant chemotherapy: The M.D. anderson cancer center experience. *J Clin Oncol* (2004) 22(12):2303–12.

49. Raina V, Bhutani M, Bedi R, Sharma A, Deo S, Shukla N, et al. Clinical features and prognostic factors of early breast cancer at a major cancer center in north india. *Indian J Cancer* (2005) 42:40–5. doi: 10.4103/0019-509X.15099

50. Ali SH, Somashekhar SP, Kumar AN. Rate of breast-conserving surgery vs mastectomy in breast cancer: a tertiary care centre experience from South India. *Indian J Surg Oncol* (2019) 10(1):72–6. doi: 10.1007/s13193-018-0818-7

51. Volders JH, Negenborn VL, Spronk PE, Krekel NMA, Schoonmade LJ, Meijer S, et al. Breast-conserving surgery following neoadjuvant therapy-a systematic review on surgical outcomes. *Breast Cancer Res Treat* (2018) 168(1):1–12. doi: 10.1007/s10549-017-4598-5

52. Buchholz TA, Mittendorf EA, Hunt KK. Surgical considerations after neoadjuvant chemotherapy: Breast conservation therapy. *J Natl Cancer Inst - Monogr* (2015) 2015(51):11–4. doi: 10.1093/jncimonographs/lgv020

53. Golshan M, Loibl S, Wong SM, Houber JB, O'Shaughnessy J, Rugo HS, et al. Breast conservation after neoadjuvant chemotherapy for triple-negative breast cancer: Surgical results from the BrighTNess randomized clinical trial. *JAMA Surg* (2020) 155 (3):e195410. doi: 10.1001/jamasurg.2019.5410

54. Wang S, Zhang Y, Yang X, Fan L, Qi X, Chen Q, et al. Shrink pattern of breast cancer after neoadjuvant chemotherapy and its correlation with clinical pathological factors. *World J Surg Oncol* (2013) 11:2–710.1186/1477–7819-11-166. doi: 10.1186/1477-7819-11-166

55. Vaidya JS, Massarut S, Vaidya HJ, Alexander EC, Richards T, Caris JA, et al. Rethinking neoadjuvant chemotherapy for breast cancer. *BMJ Online* (2018) 360 (January):11–6. doi: 10.1136/bmj.j5913

56. Crown A, Laskin R, Rocha FG, Grumley J. Extreme oncoplasty: Expanding indications for breast conservation. *Am J Surg* (2019) 217(5):851–6. doi: 10.1016/j.amjsurg.2019.01.004

57. Clough KB, Lewis JS, Couturaud B, Fitoussi A, Nos C, Falcou MC. Oncoplastic techniques allow extensive resections for breast-conserving therapy of breast carcinomas. *Ann Surg* (2003) 237(1):26–34. doi: 10.1097/00000658-200301000-00005

58. Zucca Matthes AG, Uemura G, Kerr L, Matthes ÂCS, Michelli RAD, Folgueira MAAK, et al. Feasibility of oncoplastic techniques in the surgical management of locally advanced breast cancer. *Int J Surg Lond Engl* (2012) 10(9):500–5. doi: 10.1016/j.ijsu.2012.07.009

59. Silverstein MJ. Radical mastectomy to radical conservation (Extreme oncoplasty): A revolutionary change. *J Am Coll Surg* (2016) 222(1):1–9. doi: 10.1016/j.jamcollsurg.2015.10.007

60. Minella C, Villasco A, D'alonzo M, Cellini L, Accomasso F, Actis S, et al. Surgery after neoadjuvant chemotherapy: A clip-based technique to improve surgical outcomes, a single-center experience. *Cancers [Internet]* (2022) 14(9). doi: 10.3390/cancers14092229

61. Manfrin E, Remo A, Falsirollo F, Pollini GP, Parisi A, Nottegar A, et al. Intra-operative frozen section technique for breast cancer: end of an era. *Pathologica* (2011) 103:325–30.

62. Manfrin E, Remo A, Falsirollo F, Pollini GP, Parisi A, Nottegar A, et al. Extreme oncoplasty: The last opportunity for breast conservation-Analysis of its impact on survival and quality of life. *Breast J* (2019) 25(3):535–6. doi: 10.1111/tbj.13267

frontiers | Frontiers in Oncology

TYPE Systematic Review
PUBLISHED 30 January 2024
DOI 10.3389/fonc.2023.1215284

OPEN ACCESS

EDITED BY
Mangesh A. Thorat,
Guy's and St Thomas' NHS Foundation Trust, United Kingdom

REVIEWED BY
Nidhi Garg,
Guy's and St Thomas' NHS Foundation Trust, United Kingdom
Marco Materazzo,
Policlinico Tor Vergata, Italy

*CORRESPONDENCE
René Aloisio da Costa Vieira
reneacv@gmail.com

RECEIVED 01 May 2023
ACCEPTED 08 November 2023
PUBLISHED 30 January 2024

CITATION
Vieira RAdC, Paulinelli RR and de Oliveira-Junior I (2024) Extreme oncoplasty: past, present and future. *Front. Oncol.* 13:1215284. doi: 10.3389/fonc.2023.1215284

Extreme oncoplasty: past, present and future

René Aloisio da Costa Vieira[1,2,3,4]*, Regis Resende Paulinelli[1,5] and Idam de Oliveira-Junior[1,2,5]

[1]Postgraduate Program in Tocogynecology, Botucatu School of Medicine, Botucatu, SP, Brazil, [2]Postgraduate Program in Oncology, Barretos Cancer Hospital, Barretos, SP, Brazil, [3]Department of Surgical Oncology, Division of Breast Surgical Oncology, Muriaé Cancer Hospital, Muriaé, MG, Brazil, [4]Department of Gynecology and Obstetrics, University of Goiás, Goiania, GO, Brazil, [5]Department of Mastology and Breast Reconstruction, Barretos Cancer Hospital, Barretos, SP, Brazil

Breast surgery has evolved from mastectomy to breast-conserving surgery (BCS). Breast oncoplastic surgery later emerged with the inclusion and development of techniques used in plastic surgery for breast neoplasms. Recently, a new paradigm has been considered for mastectomy candidates with large multifocal and multicentric tumours, designated extreme oncoplasty (EO), which has allowed new techniques to be applied to tumours that would have been ineligible for BCS before. There are few publications and no uniform descriptions grouping all the technical possibilities and new indications together. We performed this a review with the objective of evaluating the indications and surgeries performed in the EO context, representing a new perspective for BCS. We observed new indications as extensive microcalcifications, locally advanced breast carcinoma with partial response to chemotherapy, small to moderate-sized non-ptotic central tumours and extreme ptosis. Small breasts are able for EO since the presence of ptosis. New surgeries are reported as disguised geometric compensation, perforators flaps, local/regional flaps, latissimus dorsi miniflap and partial breast amputation. It is important to decrease barriers to oncoplastic surgery if we want to increase the use of EO and BCS rates.

KEYWORDS

breast neoplasms, oncoplastic surgery, extreme oncoplasty, breast conserving therapy, surgical procedures, surgical flaps

Introduction

Oncoplastic surgery (OS) allows for higher levels of care in breast-conserving surgery (BCS). BCS was initially advised for the treatment of tumours up to 3–5 cm with a favourable breast/tumour ratio, being deemed safe and having an acceptable recurrence rate (1, 2). OS associated with BCS evolved from breast remodelling (3, 4), causing a loss of 20–50% of the breast parenchyma, to the mammoplasty and mastopexy techniques, which was classified as a type II procedure for the above tumours (5, 6). OS was later used for tumours up to 5 cm or multicentric/multifocal tumours, in which case it was designated extreme oncoplasty (EO) (7).

EO is a group of new BCS techniques for patients who are initial candidates for mastectomy. This new paradigm for BCS includes diverse techniques. Recently, a systematic review article described geometric compensation (GC)/split reduction based on Wise pattern (WP) mammoplasty, but it only reviewed one technique that fell under EO (8), noting the improvement of the initial indications. We aimed to review the EO concepts in more detail to summarize the state of the art and propose future directions.

Materials and methods

A review was conducted to evaluate the indications and surgeries performed in the context of EO. We used the PICO system for article evaluation: Problem = breast neoplasm; Intervention =EO; Comparison = all; Outcome = indication and type of surgery. We also considered OS and reconstructive surgical procedures to find associated surgeries related to EO.

Based on the concept of EO with resection for tumours larger than 5 cm or multicentric/multifocal tumours, and referring to previous publications, we based our search strategy on the following search terms: extreme oncoplasty, geometric compensation, regional flaps and mammaplasty. A review was performed by screening two databases (PubMed and LILACS). To evaluate articles in PubMed, we used the following terms: (((“breast neoplasms”[Mesh]) AND (“surgery, plastic”[Mesh] OR “plastic surgery procedures”[Mesh] OR “mammaplasty”[Mesh] OR “mastectomy, segmental”[Mesh])) AND (“oncoplastic surgery” OR “oncoplasty” OR “oncoplastic” OR “extreme oncoplasty” OR “extreme oncoplastic” OR “regional flaps” OR “geometric compensation”)). The terms used in LILACS were “neoplasias da mama” and “ procedimentos cirúrgicos reconstrutivos”; “neoplasias da mama” and “ cirurgia oncoplastica ou oncoplastia.” The deadline for article publication was 12/31/2022. There was no language restriction. Two authors (RACV, I-OJr) performed the revision and jointly evaluated the full articles selected. Each article selected was evaluated based on the type of study, its main endpoints (Table 1; Supplementary Table 1) and indications related to EO (Table 2). Based on main endpoints we group variables to be considered in future studies (Supplementary Table 2). The quality of the studies was evaluated using the MINORS instrument (24) (Supplementary Table 3) and NOS (Newcastle-Ottawa Scale) instrument (25) (Supplementary Table 4).

Results

Initially, 806 articles were identified from the PubMed database and 2 articles from LILACS. All articles identified and selected were in English. The titles and abstracts were evaluated, and 140 articles

TABLE 1 Main studies reporting Extreme Oncoplasty*.

Author (ref)	Year	Number of patients	Type of study	Endpoint
Silverstein (7)	2014		Viability	Options
Paulinelli (9)	2014	17	Descriptive; CG	Clinic results, cosmesis
Silverstein (10)	2015	–	Conceptual; Case-control	Conceptual EO
Silvestein (11)	2016	–	Descriptive	Evolution of EO
Acea Nebril (12)	2017	33 EO 171 control	Case-control	PS, quality of life
Crown (13)	2019	111	Casuistry	PS, techniques, complications
Koppiker (14)	2019	39	Casuistry	PS, techniques, complications, quality of life
Pearce (15)	2020	90	Case-control	PS, techniques, complications recurrence; Subgroup analysis
Paulinelli (16)	2020	73	Descriptive; CG	PS, techniques, complications, follow-up, cosmesis
Savioli (17)	2021	50	Casuistry	PS, techniques, complications
Alder (18)	2021	–	Conceptual	Inclusion of miniflap
Nigram (19)	2021	4	Case series	Inclusion of perforating vessels
Joukainen (20)	2021	98	Casuistry	Imaging
Cakmak (21)	2021	–	Conceptual	Evolution of EO
Paulinelli (22)	2021	29	Disguised CG	Clinic results, cosmesis
De Lorenzi (23)	2022	100	Case-control	Recurrence and survival
Franca (8)	2022	34 + 243 (review)	Casuistry and literature review	Clinic results, cosmesis, literature review

CG, Geometric compensation; EO, extreme oncoplasty; PS, patient selection.
* Summary of the main endpoints of case-control or observational studies is reported in the Supplementary Table 1.

TABLE 2 Extreme oncoplasty: Indications and surgeries.

	Indication	Type of Surgery
Classical	Tumour > 5cm	Wyse Pattern
	Multicentric and multifocal tumours	Geometric compensation
	Initial candidates for mastectomy	
	Breast/tumour unfavourable ratio	Modified mammoplasty
New indications	Breast/tumour unfavourable ratio	Modified mammoplasty
	Extensive CDIS or microcalcifications	–
	New or recurrence in irradiated breasts	–
	Locally advanced breast carcinoma with partial response to chemotherapy	–
	Inappropriate scare	–
	Medium and low breast with ptosis	Geometric compensation
New situations	Small to moderate-sized non-ptotic with centrally located breast cancer	Perforators flaps
	Small to moderate sized-breast	Regional volume replacement
	Random	Local/regional flaps
	Pedicle flap	Pedicle flap
	–	Latissimus dorsi miniflap
	Extreme ptosis	Partial breast amputation

were selected for reading. After content evaluation, 46 articles were selected for this study. For EO specifically, 23 original articles and four comments were evaluated. Supplementary Figure 1 shows the PRISMA flowchart.

Silverstein suggested the term "EO" and the articles selected here (7, 10, 11). Paulinelli considered the term "GC using WP resection" (9, 16), and similar articles were selected based on modified techniques (22), case descriptions (26–28), and one institutional casuistic with systematic reviews (8). We found articles related to preoperative care (15, 20, 29–31), traditional indications (13, 17), multicentric/multifocal tumours (14, 23), increased indications (8, 13, 19, 21), casuistic (14, 17), and case reports (27, 32, 33). Quality of life (12, 14) was also evaluated. In addition, four replies were found (29–31, 34).

Evaluating the quality of the studies MINORS (Supplementary Table 3) score range of 12 to 19 points, and NOS (Newcastle-Ottawa Scale) evaluation (Supplementary Table 4) range of 3 to 7 stars. Most studies are retrospective. The best methodological study was a matched case-control study comparing EO with mastectomy (23). Four case–control studies, evaluated level II oncoplastic procedures (10, 12, 23), the indications and surgeries were different and one study performed matched evaluation (23) and one compare volume replacement with latissimus dorsi flaps (15). Of the case-control studies, the comparisons patients who underwent OE or not (10, 12, 23). Two studies present a retrospective component and prospective collection of information such as cosmesis assessment photos (8) and quality of life questionnaires (14). Two studies are prospective, showing the geometric compensation technique and its variation (9, 22). In most studies, follow-up time was short, limiting the assessment of local recurrence. Follow-up is stated in a generic way, without description related to patients' loss of follow-up, being considered positive in studies with cosmesis and with quality outcomes.

EO was associated with higher tumour size, higher specimen weight, narrower margins, and possible conversion to mastectomy, without increasing the recurrence rate. Of the seven observational studies (8, 9, 13, 14, 16, 17, 22), four used the geometric compensation technique or its modification (8, 9, 16, 22). The main endpoint was related to indications, postoperative complications and cosmesis. Table 1 summarizes the main published results related to EO. Supplementary Table 1 shows the main results related to the studies.

Retrospective cohort studies maintained the indications for EO (13, 14, 17), showing that it is a safe procedure for large tumours (> 5 cm), multicentric tumours, and multifocal tumours with acceptable complication rates (7.7% to 28%) (8, 9, 13, 14, 17) and low recurrence rates at a follow-up of > 5 years (6% to 9%) (12, 17). Some studies mentioned breast sized/tumour size ratio or resection size to breast size ratio (35, 36), which can be used for small- and medium-sized breasts, using regional tissue transfer with local/regional flaps (18, 35–37). We also observed new options, such as regional flaps (38–47), partial breast amputation (48–51), and flap guides for central tumours (52). It is important to accept and include these new indications in the spectrum of EO. With this in mind, Table 2 summarizes all possible indications, and Figures 1 and 2 show the indication flowchart.

The re-excision rate of EO is acceptable (0–12.5%) (7, 8, 12, 14, 15, 17). It was high (37.8%) in a study in which 73.9% of patients had multifocal/multicentric disease (13). The rate of conversion to mastectomy ranges from 0% to 13.5% (8, 13, 14, 34). One study reported 21% and 3% of mastectomy when EO was associated with traditional mammoplasty or latissimus dorsi, respectively (34).

The studies reported different follow-up, which were generally short and approximately 12 (14, 22), 24 (9, 10), and 36 months (8, 13, 16). Four studies had a follow-up higher than 60 months (12, 15, 17, 23).The recurrences were described as locoregional or local recurrences. Although limited follow up, local recurrence reported is lower than 3.5% (14/413 patients). The rate of breast symmetrisation is variable (48–100%) (10, 13, 17), and although it is not part of EO, it allows us to evaluate symmetry and cosmesis. All studies have shown that EO is a safe procedure (7, 12) with acceptable cosmetic results (8, 9, 16).

OS is associated with high satisfaction with the breasts (78%–83.5%) (8, 9, 12, 16, 22) and seems to improve the quality of life (12, 14, 22). Three studies evaluated quality of life using the Breast-Q questionnaire. One, a case series (n=39), reported high (>75%) satisfaction with the breast, outcomes, psychosocial well-being, and sexual well-being (14). The second study reported high scores

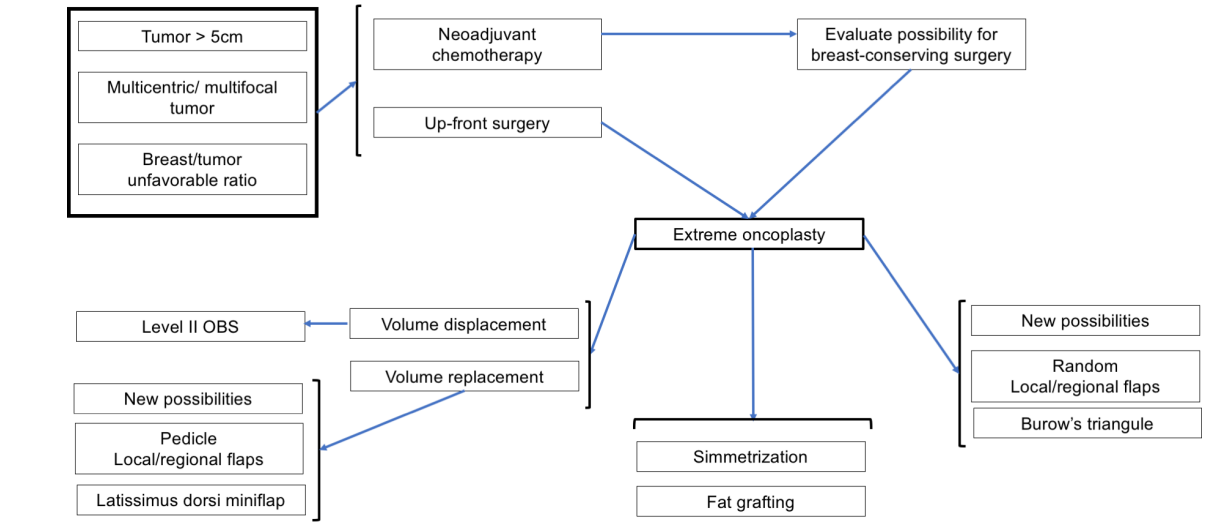


FIGURE 1
Indications flow associated with Extreme Oncoplasty and associated surgeries. NCT, neoadjuvant chemotherapy.

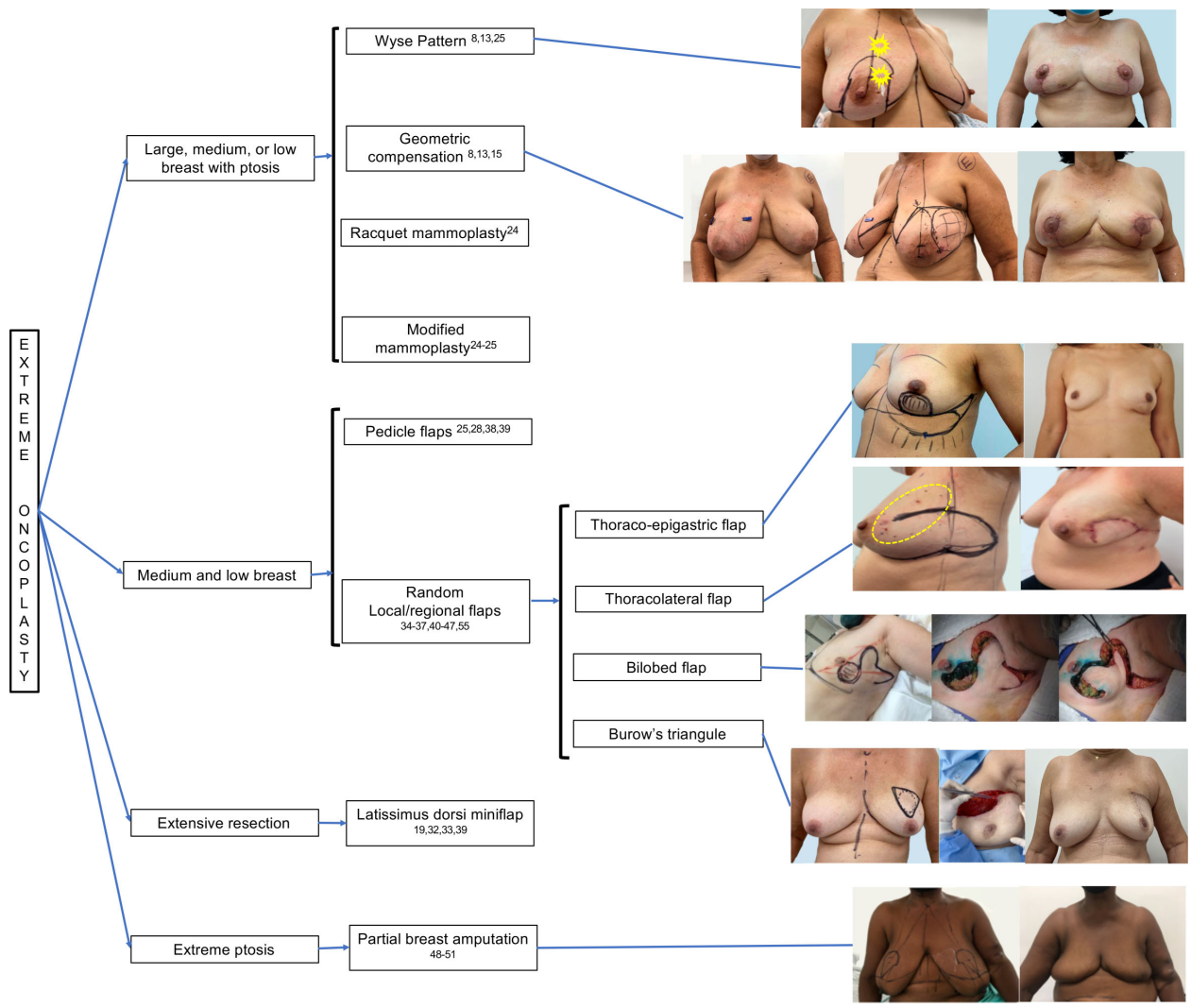


FIGURE 2
Indications for Extreme Oncoplasty based on breast characteristics.

associated with satisfaction with outcome and satisfaction with breasts (22). The third was a case–control study, which evaluated BCS (n=171) versus OE (n=33) and observed superior scores for OE in the outcome, satisfaction with the nipple complex, and psychological well-being (12).

Discussion

In 2014, Silverstein et al. (7) presented a new paradigm for OS, putting forth the concept of EO (10). Sixty-six potential candidates for a mastectomy with an unfavourable breast/tumour ratio due to the presence of tumours larger than 5 cm and/or multicentric/multifocal tumours (10) were subjected to standard WP reduction or split reduction procedures and immediate contralateral surgery to achieve symmetry (10). In the same year (2014), another publication showed, through mammaplasty techniques, the achievement of BCS in 17 cases of advanced tumours using the modified WP, called GC (9). This technique emphasizes breast preservation in situations when a breast-versus-tumour relationship is unfavourable for BCS. The skin is resected over the tumour, but using a modification of the standard WP and constituting an EO, which shows satisfactory cosmetic results (9, 28). The procedure is also performed for unicentric tumours < 5 cm with resection of the skin over the tumour, valuing other indications for EO (9), which was also evidenced in a larger series that used split reduction (16). A recent case series with systematic review refined the indications, considering the breast-size ratio, and it showed results associated with small and medium breasts (8). Since the objective of this study was to evaluate the indications, techniques and main results associated with EO, we opted to separately discuss all aspects related to EO, performing an integrative review.

EO is not for beginners (31). For OS, it is necessary to plan, perform clinical and imaging evaluations, and have surgical training (30, 34). Clinical evaluation, preoperative radiological evaluation, intraoperative frozen section margins, intraoperative specimen radiography, and clipped cavity margins are helpful for patient selection and operative evaluation (29, 31). Only one publication has considered the importance of breast nuclear magnetic resonance for surgical planning in the presence of multifocal/multicentric lesions (20).

The EO definition is extended to candidates for mastectomy who underwent BCS (14, 30), including patients with extensive ductal in situ, previously irradiated breast, locally advanced breast carcinoma with limited or partial imaging response to neoadjuvant chemotherapy, past excision biopsy with inappropriate scarring (14), extensive microcalcifications, and an unfavourable tumour/breast volume ratio (8, 21).

With the wide knowledge and dissemination of EO, it is necessary to review potential techniques and group them to facilitate decision-making regarding the indications, surgical possibilities, technical training, and associated complications (8, 18). GC (9) is a technical modification of the initially described procedure (22). An exceptional example of such a literature review was recently published that evaluated patients undergoing GC and WP and examined 243 patients previously described to have undergone this procedure (8). In that review (8), 36 patients were included. The indication for GC was extended to single tumours of smaller size and medium-to-small breasts, provided that they presented with ptosis and that EO was possible in tumours with an unfavourable breast/tumour ratio, valuing the indication for EO in tumours smaller than 5 cm.

When evaluation studies about EO, we have to review the level of oncoplastic surgery. Urban (53) considered three levels of Oncoplasty and EO would be considered for Level II procedures. Clough et al. (3) considered two levels and EO would be considered for Level II: extensive resections, requiring mammoplasty techniques, representing 20-50% of the breast/volume ratio. In 2019, the American Society of Breast Surgeons (6) began to use the term volume displacement and volume replacement. Volume displacement techniques are Level I (< 20%) and Level II techniques (20-50%), and volume replacement (>50%) are local/regional flap reconstruction, miocutaneous flaps and implants. Among the procedures performed for EO, most used WP reduction mastoplasty (8, 9, 17), followed by mastopexy and racquet mammoplasty (13), which is associated with Level II OS procedures associated with volume displacement (6). We have to add volume replacement techniques to arsenal of options related to EO (Figures 1, 2). After reviewing the concept of extensive resection associated with BCS, we found that other techniques could be included, such as pedicled flaps (17) and flaps with lateral thoracic perforators (19). One study compared traditional EO with latissimus dorsi (LD) miniflap (15), with lower complications and higher revision related to LD but no impact on local recurrence.

The EO concept extends the original technique to the use of locoregional flaps (37) and other techniques where extensive resections would lead to loss of cosmetic results (54), while OS allows safe resection with acceptable results. New possibilities for EO are random flaps (55), pedicled flaps (38), latissimus dorsi miniflaps (12, 39), and partial breast amputation (48–51). The techniques are associated with volume replacement (37) for small-to-moderate-sized breasts. For example, of random flaps, we have thoraco-epigastric flap, thoracic-lateral flap, bilobed flap and Burow's triangle (55), but they can be used in lower resections. Older techniques used before the emergence of OS should not be forgotten. They are usually performed in a nonstandard way for patients in whom preservation of the breast is desired and cosmesis is not the primary endpoint. These techniques are locoregional flaps (37, 38, 40–47, 52, 55) and nonpedicled flaps, such as thoracoepigastric, thoracic-lateral, and bilobed flaps (55). It is necessary to accept and group these new techniques, allowing other reviews in the future.

Articles have shown images of voluminous breasts (7–10, 16, 19, 32) and medium-sized breasts (7, 8) subjected to EO. Hence, we must use techniques such as mammoplasty WP, GC (8, 9, 16, 22), and other mammoplasty techniques (13, 17). Some techniques are associated with volume replacement for small- to moderate-sized breasts (37). The presence of a small-to-moderate-sized nonptotic breast presenting centrally located breast cancer was initially considered a limitation, but perforator flaps are useful in this condition (19).

All patients who are candidates for EO should be aware of the possibility of conversion to mastectomy (8), and skin-preserving mastectomy may eventually be an option. This requires prior reservation of a breast prosthesis if BCS with OS is not safe during surgery based on the tumour margins of breast cosmesis.

Symmetrisation has an unknown impact on quality of life (56) since patients evaluate their cosmesis better than health professionals (57). Another option that can be used after extensive resection associated with BCS is immediate autologous fat grafting (58), which can improve patient selection for EO.

We try to evaluate the quality of the studies, but there was no randomized study and RoB 2.0 assess risk of bias was not performed, and for observational studies we used MINORS (Supplementary Table 3) and NOS scores (Supplementary Table 4). The major problem observed was too little description of the control group and short follow up in some studies. Although scores are low these studies are important to show the importance of EO. As it is an innovation, the follow up is low and we need more time to evaluate local recurrence. There is a lack of a paired matched case-control study, and new studies need to be performed, comparing EO, oncoplastic surgery and simple breast-conserving surgery. Locorregional recurrence would not be an endpoint but local recurrence. The future authors must take care reporting adequate follow up, loss of patient and local disease-free recurrence.

EO arose due to the need for breast preservation in cases that were difficult to resolve. This fact makes it impossible to carry out prospective randomized studies. It is unethical to perform a mastectomy when breast-conserving treatment can be performed. It limits the quality of the studies (Supplementary Table 3). Therefore, we must improve the literature (59), seeking to report the main metrics reported in previous studies (Supplementary Table 2), aiming to standardize information. Future studies determine the complexity of performing different procedures, reporting the experience of training centres in oncoplasty, and evaluating the learning curve, mastectomy conversion rate, complications, re-excision rate, local recurrence, patient satisfaction, and cosmetic results of different techniques. Also, it is necessary to perform matched case-control studies, with a long follow-up period.

EO implies developing clinical training to select cases, technical knowledge to evaluate different oncoplastic solutions, a fact that denotes a long learning curve. It is important to decrease barriers to OS (60) if we want to increase the use of EO. When performing OS, it is important to report the indications, type of surgeries (61, 62), postoperative endpoints and long term results (Supplementary Table 2). The EO qualifies the service and should be one of the parameters to be used in the quality assessment of breast centres.

Reflections and discussions of published articles (29, 30, 34) are important, but systematic reviews (8) are essential. Since the definition of EO (7, 11), the literature has evolved in indications, and this review considers the new technical possibilities (Table 2). Future systematic reviews evaluating the different techniques will facilitate a better understanding of the multiple technical availabilities and results, helping surgical oncologists choose the right procedure for BCS from the multiple techniques of EO.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material. Further inquiries can be directed to the corresponding author.

Author contributions

RV: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Supervision, Visualization, Writing – original draft, Writing – review & editing. IdO-J: Formal analysis, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing. RP: Methodology, Visualization, Writing – original draft, Writing – review & editing.

Funding

The author(s) declare financial support was receive fot the publication of this article. The “Barretos Cancer Hospital” provided funding for publication.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher’s note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fonc.2023.1215284/full#supplementary-material

References

1. Carrara GF, Scapulatempo-Neto C, Abrahao-MaChado LF, Brentani MM, Nunes JS, Folgueira MA, et al. Breast-conserving surgery in locally advanced breast cancer submitted to neoadjuvant chemotherapy. Safety and effectiveness based on ipsilateral breast tumor recurrence and long-term follow-up. *Clinics (Sao Paulo)* (2017) 72 (3):134–42. doi: 10.6061/clinics/2017(03)02

2. Santos G, Urban C, Edelweiss MI, Zucca-Matthes G, de Oliveira VM, Arana GH, et al. Long-term comparison of aesthetical outcomes after oncoplastic surgery and lumpectomy in breast cancer patients. *Ann Surg Oncol* (2015) 22(8):2500–8. doi: 10.1245/s10434-014-4301-6

3. Clough KB, Ihrai T, Oden S, Kaufman G, Massey E, Nos C. Oncoplastic surgery for breast cancer based on tumour location and a quadrant-per-quadrant atlas. *Br J Surg* (2012) 99(10):1389–95. doi: 10.1002/bjs.8877

4. Gainer SM, Lucci A. Oncoplastics: techniques for reconstruction of partial breast defects based on tumor location. *J Surg Oncol* (2011) 103(4):341–7. doi: 10.1002/jso.21672

5. Clough KB, Kaufman GJ, Nos C, Buccimazza I, Sarfati IM. Improving breast cancer surgery: a classification and quadrant per quadrant atlas for oncoplastic surgery. *Ann Surg Oncol* (2010) 17(5):1375–91. doi: 10.1245/s10434-009-0792-y

6. Chatterjee A, Gass J, Patel K, Holmes D, Kopkash K, Peiris L, et al. A consensus definition and classification system of oncoplastic surgery developed by the american society of breast surgeons. *Ann Surg Oncol* (2019) 26(11):3436–44. doi: 10.1245/s10434-019-07345-4

7. Silverstein MJ, Mai T, Savalia N, Vaince F, Guerra L. Oncoplastic breast conservation surgery: the new paradigm. *J Surg Oncol* (2014) 110(1):82–9. doi: 10.1002/jso.23641

8. Franca FC, de Oliveira-Junior I, Morgan AM, Haikel RL, da Costa Vieira RA. Breast-conserving surgery with the geometric compensation/split reduction technique. Indications, oncologic safety and cosmesis. A cohort series and systematic review of the literature. *Surg Oncol* (2022) 44:101839. doi: 10.1016/j.suronc.2022.101839

9. Paulinelli RR, de Oliveira VM, Bagnoli F, Chade MC, Alves KL, Freitas-Junior R. Oncoplastic mammaplasty with geometric compensation–a technique for breast conservation. *J Surg Oncol* (2014) 110(8):912–8. doi: 10.1002/jso.23751

10. Silverstein MJ, Savalia N, Khan S, Ryan J. Extreme oncoplasty: breast conservation for patients who need mastectomy. *Breast J* (2015) 21(1):52–9. doi: 10.1111/tbj.12356

11. Silverstein MJ. Radical mastectomy to radical conservation (Extreme oncoplasty): A revolutionary change. *J Am Coll Surg* (2016) 222(1):1–9. doi: 10.1016/j.jamcollsurg.2015.10.007

12. Acea Nebril B, Garcia Novoa A, Polidorio N, Cereijo Garea C, Bouzon Alejandro A, Mosquera Oses J. Extreme oncoplasty: The last opportunity for breast conservation-Analysis of its impact on survival and quality of life. *Breast J* (2019) 25(3):535–6. doi: 10.1111/tbj.13267

13. Crown A, Laskin R, Rocha FG, Grumley J. Extreme oncoplasty: Expanding indications for breast conservation. *Am J Surg* (2019) 217(5):851–6. doi: 10.1016/j.amjsurg.2019.01.004

14. Koppiker CB, Noor AU, Dixit S, Busheri L, Sharan G, Dhar U, et al. Extreme oncoplastic surgery for multifocal/multicentric and locally advanced breast cancer. *Int J Breast Cancer* (2019) 2019:4262589. doi: 10.1155/2019/4262589

15. Pearce BCS, Fiddes RN, Paramanathan N, Chand N, Laws SAM, Rainsbury RM. Extreme oncoplastic conservation is a safe new alternative to mastectomy. *Eur J Surg Oncol* (2020) 46(1):71–6. doi: 10.1016/j.ejso.2019.09.004

16. Paulinelli RR, de Oliveira VM, Bagnoli F, Letzkus Berrios J, Cezar Chade M, Bragatto Picoli L, et al. Oncoplastic mammaplasty with geometric compensation: Evolution of the technique, outcomes and follow-up in a multicentre retrospective cohort. *J Surg Oncol* (2020) 121(6):967–74. doi: 10.1002/jso.25860

17. Savioli F, Seth S, Morrow E, Doughty J, Stallard S, Malyon A, et al. Extreme oncoplasty: breast conservation in patients with large, multifocal, and multicentric breast cancer. *Breast Cancer (Dove Med Press)* (2021) 13:353–9. doi: 10.2147/BCTT.S296242

18. Alder L, Zaidi M, Zeidan B, Mazari F. Advanced breast conservation and partial breast reconstruction - a review of current available options for oncoplastic breast surgery. *Ann R Coll Surg Engl* (2022) 104(5):319–23. doi: 10.1308/rcsann.2021.0169

19. Nigam S, Eichholz A, Bhattacharyya M, Parulekar V, Roy PG. Extreme oncoplasty for centrally located breast cancer in small non-ptotic breasts: extending the indications of chest wall perforator flaps with areolar reconstruction. *Ecancermedicalscience* (2021) 15:1311. doi: 10.3332/ecancer.2021.1311

20. Joukainen S, Okuma H, Kaarela O, Laaksonen E, Karja V, Vanninen R, et al. Can supine breast magnetic resonance imaging help hit the target in extreme oncoplastic surgery? *Eur J Surg Oncol* (2021) 47(11):2788–96. doi: 10.1016/j.ejso.2021.07.027

21. Cakmak GK. Innovative standards in oncoplastic breast conserving surgery: from radical mastectomy to extreme oncoplasty. *Breast Care (Basel)* (2021) 16(6):559–73. doi: 10.1159/000518992

22. Paulinelli RR, Ribeiro LFJ, Santos TD, Caires EMS, Pontes MGM, Faria BM, et al. Oncoplastic Mammoplasty with disguised geometric compensation. *Surg Oncol* (2021) 39:101660. doi: 10.1016/j.suronc.2021.101660

23. De Lorenzi F, Borelli F, Pagan E, Bagnardi V, Peradze N, Jereczek-Fossa BA, et al. Oncoplastic breast-conserving surgery for synchronous multicentric and multifocal tumors: is it oncologically safe? A retrospective matched-cohort analysis. *Ann Surg Oncol* (2022) 29(1):427–36. doi: 10.1245/s10434-021-10800-w

24. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (minors): development and validation of a new instrument. *ANZ J Surg* (2003) 73(9):712–6. doi: 10.1046/j.1445-2197.2003.02748.x

25. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. *The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses: The Ottawa Hospital Research Institute* (2009). Available at: https://www.ohri.ca/programs/clinical_epidemiology/oxford.htm.

26. Marongiu F, Bertozzi N, Sibilio A, Gasperoni M, Curcio A. "Bifidus pedicle", the use of bilobed superomedial pedicle for breast reshaping following upper outer quadrantectomy: A new oncoplastic breast surgery technique. *Aesthetic Plast Surg* (2021) 45(3):866–74. doi: 10.1007/s00266-020-01982-x

27. Mele S, Falco G, Borgonovo G, Castagnetti F, Cenini E, Coiro S, et al. Bifurcate inferior pedicle mammoplasty in large ptotic breast for tumor located at the upper outer quadrant with skin involvement-a novel technique allowing good cosmetic outcome: case report. *Gland Surg* (2020) 9(5):1590–5. doi: 10.21037/gs-20-349

28. Paulinelli RR, Marinho ER. Double independent pedicle oncoplastic mammaplasty: a technique for breast preservation. *Rev Bras Mastol* (2012) 22(1):25–32.

29. Franceschini G, Di Leone A, Masetti R. Comment on "Extreme oncoplastic surgery for multifocal/multicentric and locally advanced breast cancer". *Int J Breast Cancer* (2019) 2019:4693794. doi: 10.1155/2019/4693794

30. Franceschini G, Masetti R. Extreme oncoplastic breast conserving surgery: Is surgical dexterity all that is need? *Am J Surg* (2020) 219(1):211–2. doi: 10.1016/j.amjsurg.2019.04.008

31. Franceschini G, Masetti R. Evidence-based surgery to realize a successful extreme oncoplastic breast conservation. *Eur J Surg Oncol* (2020) 46(5):924–5. doi: 10.1016/j.ejso.2020.02.003

32. Bordoni D, Cadenelli P, Falco G, Rocco N, Manna P, Tessone A, et al. Extreme oncoplastic breast surgery: A case report. *Int J Surg Case Rep* (2016) 28:182–7. doi: 10.1016/j.ijscr.2016.09.037

33. Giacaman N, Abu Al-Halawa D, Tos SM, Ibdah MG, Sharaf K. Extreme Oncoplastic Breast Surgery: A case series of three patients from a lower-middle income country. *Ann Med Surg (Lond)* (2022) 84:104899. doi: 10.1016/j.amsu.2022.104899

34. Pearce BCS, Fiddes RN, Paramanathan N, Chand N, Laws SAM, Rainsbury RM. Reply to: Evidence-based surgery to realize a successful extreme oncoplastic breast conservation. *Eur J Surg Oncol* (2020) 46(5):926–7. doi: 10.1016/j.ejso.2020.02.004

35. Losken A, Chatterjee A. Improving results in oncoplastic surgery. *Plast Reconstr Surg* (2021) 147(1):123e–34e. doi: 10.1097/PRS.0000000000007478

36. Salibian AA, Olson B, Shauly O, Patel KM. Oncoplastic breast reconstruction: Principles, current techniques, and future directions. *J Surg Oncol* (2022) 126(3):450–9. doi: 10.1002/jso.26897

37. Yang JD, Lee JW, Cho YK, Kim WW, Hwang SO, Jung JH, et al. Surgical techniques for personalized oncoplastic surgery in breast cancer patients with small- to moderate-sized breasts (part 2): volume replacement. *J Breast Cancer* (2012) 15(1):7–14. doi: 10.4048/jbc.2012.15.1.7

38. Schaverien MV, Kuerer HM, Caudle AS, Smith BD, Hwang RF, Robb GL. Outcomes of volume replacement oncoplastic breast-conserving surgery using chest wall perforator flaps: comparison with volume displacement oncoplastic surgery and total breast reconstruction. *Plast Reconstr Surg* (2020) 146(1):14–27. doi: 10.1097/PRS.0000000000006911

39. Abdelrahman EM, Nawar AM, Balbaa MA, Shoulah AA, Shora AA, Kharoub MS. Oncoplastic volume replacement for breast cancer: latissimus dorsi flap versus thoracodorsal artery perforator flap. *Plast Reconstr Surg Glob Open* (2019) 7(10):e2476. doi: 10.1097/GOX.0000000000002476

40. Lee J, Bae Y, Audretsch W. Combination of two local flaps for large defects after breast conserving surgery. *Breast* (2012) 21(2):194–8. doi: 10.1016/j.breast.2011.09.011

41. Schoeller T, Bauer T, Haug M, Otto A, Wechselberger G, Piza-Katzer H. A new contralateral split-breast flap for breast reconstruction and its salvage after complication: an alternative for select patients. *Ann Plast Surg* (2001) 47(4):442–5. doi: 10.1097/00000637-200110000-00015

42. Kijima Y, Yoshinaka H, Hirata M, Nakajo A, Arima H, Okumura H, et al. Oncoplastic breast surgery combining partial mastectomy with immediate breast reshaping using a keyhole-shaped skin glandular flap for Paget's disease. *Surg Today* (2014) 44(9):1783–8. doi: 10.1007/s00595-013-0687-1

43. Joshi S, Jaiswal D, Chougle Q, Wadasadawala T, Badwe RA. Transposition flap for the oncoplastic reconstruction of outer quadrant breast defects. *J Plast Reconstr Aesthet Surg* (2021) 74(9):2176–83. doi: 10.1016/j.bjps.2020.12.037

44. Hirata M, Toda H, Higo N, Shinden Y, Ohtsuka T, Kijima Y. Modification of oncoplastic breast surgery with immediate volume replacement using a thoracodorsal adipofascial flap. *Breast Cancer* (2022) 29(3):531–40. doi: 10.1007/s12282-022-01331-7

45. Kijima Y, Hirata M, Higo N, Toda H, Shinden Y. Oncoplastic breast surgery combining partial mastectomy with resection of double equilateral triangular skin flaps. *Surg Today* (2022) 52(3):514–8. doi: 10.1007/s00595-021-02355-w

46. Hong S, Wang S, Liu J, Qiang Z, Zheng X, Chen G. Usefulness of lateral thoracic adipofascial flaps after breast-conserving surgery in small-to moderate-sized breasts. *Clin Breast Cancer* (2019) 19(5):370–6. doi: 10.1016/j.clbc.2019.04.009

47. Kollias V, Kollias J. Safety and efficacy of anterior intercostal artery perforator flaps in oncoplastic breast reconstruction. *ANZ J Surg* (2022) 92(5):1184–9. doi: 10.1111/ans.17496

48. Kijima Y, Yoshinaka H, Hirata M, Mizoguchi T, Ishigami S, Arima H, et al. Oncoplastic surgery combining partial mastectomy with breast reconstruction using a free nipple-areola graft for ductal carcinoma in *situ* in a ptotic breast: report of a case. *Surg Today* (2011) 41(3):390–5. doi: 10.1007/s00595-010-4294-0

49. Kijima Y, Yoshinaka H, Hirata M, Shinden Y, Nakajo A, Arima H, et al. Therapeutic mammoplasty combining partial mastectomy with nipple-areola grafting for patients with early breast cancer: a case series. *Surg Today* (2016) 46(10):1187–95. doi: 10.1007/s00595-015-1294-0

50. Manie TM, Youssef M, Taha SN, Rabea A, Farahat AM. Batwing mammoplasty: a safe oncoplastic technique for breast conservation in breast cancer patients with gigantomastia. *Ann R Coll Surg Engl* (2020) 102(2):115–9. doi: 10.1308/rcsann.2019.0129

51. Mattioli WM, Penazzi-Júnior SA, de Melo DSF. Use of the back-folded dermaglandular inferior pedicle in mammary amputation: improving results. *Rev Bras Cir Plast* (2017) 32(3):340–5. doi: 10.5935/2177-1235.2017RBCP0057

52. Carstensen L, Bigaard J. Management of central breast tumours with immediate reconstruction of the nipple-areola complex; a suggested guide. *Breast* (2015) 24(1):38–45. doi: 10.1016/j.breast.2014.11.002

53. Urban C, Gazoto-Junior O, Pires DM, Garcia GN, Paulinelli RR, Amoroso V, et al. Trends and attitues toward oncoplastics training in Mastology in Brazil. *Mastology* (2017) 27(3):182–6. doi: 10.5327/Z2594539420170000221

54. Winters ZE, Bernaudo L. Evaluating the current evidence to support therapeutic mammoplasty or breast-conserving surgery as an alternative to mastectomy in the treatment of multifocal and multicentric breast cancers. *Gland Surg* (2018) 7(6):525–35. doi: 10.21037/gs.2018.07.01

55. Paulinelli RR, Luz MV, Faria BM, Ribeiro FJR. Oncoplastia e cirurgia conservadora: Retalhos locorregionais. In: Boff RA, Brenelli FP, Almeida NR, editors. *Compêndio de mastologia abordagem multidisciplinar*, *2nd ed.* São Paulo: Lemar & Goi (2022). p. 1061–70.

56. de Oliveira-Junior I, da Silva IA, da Silva FCB, da Silva JJ, Sarri AJ, Paiva CE, et al. Oncoplastic surgery in breast-conserving treatment: patient profile and impact on quality of life. *Breast Care (Basel)* (2021) 16(3):243–53. doi: 10.1159/000507240

57. de Oliveira-Junior I, Brandini da Silva FC, Nazima F, Ribeiro JCJr., Castellani L, Zucca-Matthes G, et al. Oncoplastic surgery: does patient and medical specialty influences the evaluation of cosmetic results? *Clin Breast Cancer* (2021) 21(3):247–55 e3. doi: 10.1016/j.clbc.2020.09.012

58. Biazus JV, Stumpf CC, Melo MP, Zucatto AE, Cericatto R, Cavalheiro JA, et al. Breast-conserving surgery with immediate autologous fat grafting reconstruction: oncologic outcomes. *Aesthetic Plast Surg* (2018) 42(5):1195–201. doi: 10.1007/s00266-018-1155-5

59. de Oliveira-Junior I, Haikel RL, Vieira RAC. Breast-conserving treatment in oncoplastic times: indications, cosmesis, and quality of life. *Mastology* (2021) 31: e20200040. doi: 10.29289/2594539420200040

60. Chatterjee A, Gass J, Burke MB, Kopkash K, El-Tamer MB, Holmes DR, et al. Results from the American society of breast surgeons oncoplastic surgery committee 2017 survey: current practice and future directions. *Ann Surg Oncol* (2018) 25 (10):2790–4. doi: 10.1245/s10434-018-6586-3

61. Emiroglu M, Sert I, Karaali C, Aksoy SO, Ugurlu L, Aydin C. The effectiveness of simultaneous oncoplastic breast surgery in patients with locally advanced breast cancer. *Breast Cancer* (2016) 23(3):463–70. doi: 10.1007/s12282-015-0585-z

62. Araujo Pereira Lisboa FC, Paulinelli RR, Campos Veras LP, Jube Ribeiro LF, Padua Oliveira LF, Sousa Rahal RM, et al. Aesthetic results were more satisfactory after oncoplastic surgery than after total breast reconstruction according to patients and surgeons. *Breast* (2023) 71:47–53. doi: 10.1016/j.breast.2023.07.006

Frontiers in Oncology

Advances knowledge of carcinogenesis and tumor progression for better treatment and management

The third most-cited oncology journal, which highlights research in carcinogenesis and tumor progression, bridging the gap between basic research and applications to imrpove diagnosis, therapeutics and management strategies.

Discover the latest Research Topics

See more →

Frontiers

Avenue du Tribunal-Fédéral 34
1005 Lausanne, Switzerland
frontiersin.org

Contact us

+41 (0)21 510 17 00
frontiersin.org/about/contact