Technical Article / *Teknik Yazı*

J Breast Health 2015; 11: 186-91
DOI: 10.5152/tjbh.2015.2572

Meme Koruyucu Cerrahide Rhomboid Flep Tekniği: Lumpektomi Defektini Kapatmak İçin Alternatif Metod

Rhomboid Flap Technique in Breast-conserving Surgery: An Alternative Method for the Reconstruction of Lumpectomy Defects

Ebru Menekşe[1], Sefa Özyazıcı[2], Faruk Karateke[2], Ümit Turan[2], Adnan Kuvvetli[2], Cihan Gökler[2], Mehmet Özdoğan[3], Safa Önel[2]

[1]Department of General Surgery, Ankara Numune Training and Research Hospital, Ankara, Turkey
[2]Department of General Surgery, Adana Numune Training and Research Hospital, Adana, Turkey
[3]Department of Surgery, Adana Medline Hospital, Adana, Turkey

ABSTRACT

Objective: We aimed to present our experience with rhomboid flap reconstruction, which is a simple technique, in breast cancer patients who underwent breast-conserving surgery.

Methods: We reviewed the medical records of 13 patients with breast cancer who underwent rhomboid flap reconstruction. The patients were evaluated for tumor size, safe surgical margin, and other clinical and pathological features.

Results: The mean age of the patients was 43.1 years (range: 28–69 years). The mean tumor diameter was 30.8 mm (range: 15–60 mm). The mean of the safe margin of resection was evaluated to be 17.8 mm (range: 5–30 mm). Re-excision was required for one patient in the same session.

Conclusion: Rhomboid flap reconstruction can facilitate the applicability of breast-conserving surgery in early breast cancer patients with large tumor-to-breast-size ratio or tumors close to the skin.

Keywords: Breast cancer, breast-conserving surgery, rhomboid flap

ÖZ

Amaç: Bu çalışmada meme koruyucu cerrahi yapılan meme kanseri hastalarında basit bir teknik olan rhomboid flep rekonstrüksiyonuna ait deneyimimizi sunmak amaçlanmıştır.

Yöntem ve Gereçler: Rhomboid flep rekonstrüksiyonu yapılmış 13 meme kanserli hastanın kayıtları incelendi. Hastalar tümör boyutu, sağlam cerrahi sınır, diğer klinik ve patolojik özelliklerine göre değerlendirildi.

Bulgular: Hastaların ortalama yaşı 43.1 idi (28-69). Ortalama tümör çapı 30.8 mm (15-60), ortalama sağlam cerrahi sınır ise 17.8 mm (5-30) idi. Reeksizyon 1 hastaya gerekti ve aynı seansta yapıldı.

Sonuç: Rhomboid flep rekonstrüksiyonu tümör meme oranı büyük veya cilde yakın tümöre sahip erken meme kanseri hastalarında meme koruyucu cerrahinin uygulanmasına yardımcı olabilir.

Anahtar sözcükler: Meme kanseri, meme koruyucu cerrahi, rhombid flep

Introduction

Breast-conserving surgery (BCS) and radiation therapy, in combination, have been accepted as the standard treatment in eligible patients with invasive breast cancer (1, 2). The oncologic goal in breast cancer surgery is to ensure adequate resection of a malignant tumor with safe margins (3). On the other hand, BCS aims to protect the shape of the postoperative breast. Unfortunately, optimum results cannot always be obtained in BCS because of both tumor- and treatment-related factors (4). Thus, the possibility of a deformed breast restricts the applicability of BCS. Various reconstructive methods have been applied to limit breast deformities after lumpectomy (5, 6). One of these methods is rhomboid flap (RF) reconstruction, with regard to which there are limited reports in literature (7).

The RF technique in BCS was first described in 1978 by Cooperman and Dinner (7), and it provides immediate reconstruction of partial defects of tissue and skin at the time of BCS, especially for outer quadrant tumors (7-10).

The aim of this study was to evaluate RF reconstruction, which could facilitate BCS in patients with a large tumor-to-breast size ratio and tumors close to the skin.

Materials and Methods

Thirteen female breast cancer patients who underwent RF after lumpectomy for BCS between 2008 and 2012 at the Surgery Department of Adana Numune Training and Research Hospital were retrospectively analyzed after obtaining approval for the study from the local

This study was presented at the 11. National Breast Diseases Congress, 2011, 5-9 October Antalya, Turkey.
Bu çalışma 11. Ulusal Meme Hastalıkları Kongresi'nde sunulmuştur, 5-9 Ekim 2011, Antalya, Türkiye.

Address for Correspondence / Yazışma Adresi:
Ebru Menekşe, e-mail / e-posta: drebrumenekse@gmail.com

Received / Geliş Tarihi: 04.03.2015
Accepted / Kabul Tarihi: 21.06.2015

ethics committee (ANEAH.EK.2013/38). Informed consent from all patients was preoperatively obtained. Four patients with large T2 tumors underwent excisional biopsy for diagnosis in another hospitals; the remaining patients were diagnosed at our hospital. Patient data collected from medical records include age, menopausal status, pathologic T and N stage, tumor size, tumor side, safe margin of resection, and re-excision.

Patient preparation and selection for BCS with RF reconstruction: Patients underwent physical examination and bilateral breast ultrasound and/or mammography. Preoperative definitive diagnoses of breast masses were confirmed by core needle biopsy in patients at the time of their first admission to our hospital. On the basis of patients' history, physical examination, and laboratory test results, some patients required abdominal and/or abdominopelvic computed tomography (CT) or magnetic resonance imaging, bone scintigraphy, and thoracic CT imaging. Patients without multifocal or multicentric lesions and lesions evaluated as stage 1 or 2 tumors were considered to be eligible and were selected for BCS.

Patients who underwent RF reconstruction had a preference to protect the breast, with appropriate staging for BCS; however, they had large-sized tumors, particularly in comparison with the breast size. Patients with T1 tumors required wide skin excision because of the close proximity of the tumor to the skin. These patients were offered RF as an option, in view of possible poor cosmetic results, which was performed in patients who consented to undergo BCS.

Design and surgical technique: Patients who were to undergo RF reconstruction after examination had incisions drawn preoperatively in the supine position in the examination room on the day of surgery. Tumor location was determined by palpation in patients with palpable tumors or by ultrasound in patients with non-palpable or excised tumors and was then marked. Then, 60° and 120° angle rhomboid flaps, at least 2 cm away from the tumor borders, were drawn on the skin surface. Tumors close to the lateral borders, breast tissue, and subcutaneous fat tissue located between the breast and median axillary borders were included in the rhomboid flap. From the AC line, an equal CE straight line was drawn. Flap borders were completed as an EF line, equal and parallel to BC, along the BC edge, and extended at a 60° angle from the E corner (7, 8) (Figure 1).

Intraoperatively, the marked rhomboid initially underwent full-thickness excision, including the pectoralis major fascia. The specimen was marked on four surfaces as lateral, superior, anterior, and medial and was sent for histopathologic examination. After obtaining safe margins of resection, the flap was prepared as examination during surgery. At this stage, sentinel samplings and axillary dissections were performed based on the proximity of the flap to the axilla, with close tumors such as lateral quadrant tumors excised from the same incision by dissecting them from the base of the donor area after flap removal, whereas farther tumors, such as upper and lower quadrant tumors, were excised by different axillary incisions (Figure 2). Suction drains were placed in the axillary and rhombus region. Subsequently, the flap was rotated such that the E corner was aligned on top of the D corner. The CE edge of the flap was sutured to the AD edge of the rhombus, and the EF edge of the flap was sutured to the DC edge of the rhombus with subcutaneous fixation (Figure 1). The RF technique was performed by a single surgeon who was experienced in this field.

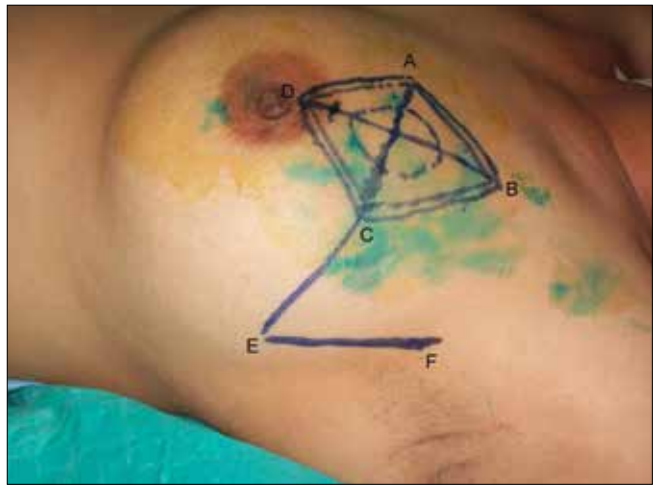

Figure 1. Preoperative ink mark to the rhombus, including tumor, and design of the rhomboid flap

Figure 2. Perioperative view: placement of rhomboid flap after tumor resection tumor and axillary dissection performed by another incision

Results

The mean age of patients was 43.1 years (range: 28–69 years). Table 1 shows the clinical characteristics of patients who underwent RF reconstruction. The mean tumor diameter was 30.8 mm (range: 15–60 mm). The mean safe margin of resection was evaluated to be 17.8 mm (range: 5–30 mm). All T1 tumors (n=4) were close to the skin and required skin resection for a safe anterior margin. However, there was no skin invasion of these tumors. The mean safe margin of resection was 16.7 mm (range: 7–20 mm). Four patients with T2 tumors of large size underwent surgery in another hospital. Re-excision for determining safe margin was necessary in these patients because some of them did not have a safe margin of resection or the surgical margins status could not be determined. Re-excision tissue was used to calculate the safe margin of resection in these patients. The mean safe margin of resection was 16.2 mm (range: 10–20 mm) in patients coming from other hospitals. The remaining five patients with early breast cancer had a large tumor-to-breast ratio, and their mean safe margin of resection was 18.5 mm (range: 5–30 mm). Only three patients with clinical lymph node-negative tumors underwent sentinel lymph node biopsy for axillary mapping because of the technical insufficiency of this facility in our hospital. Sentinel node biopsies were performed using isosulfan blue. Re-excision was required for one patient and was performed during the same session. The safe margin of resection of pre re-excision specimens was used. Pathological diagnoses were 12 cases of invasive

Table 1. Patient characteristics

Menstrual status	Patients n=13
Premenopausal (n, %)	10 (76.9)
Postmenopausal (n, %)	3 (23.1)
Side of the tumor	
Right (n, %)	6 (46.2)
Left (n, %)	7 (53.8)
Site of the tumor	
Upper outer (n, %)	8 (61.5)
Upper (n, %)	2 (15.4)
Lower outer (n, %)	1 (7.7)
Lower (n, %)	2 (15.4)
pTNM	
Stage I (n, %)	4 (30.8)
Stage II (n, %)	9 (69.2)
pT	
T1 (n, %)	4 (30.8)
T2 (n, %)	8 (61.5)
T3 (n, %)	1 (7.7)
pN	
N0 (n, %)	9 (69.2)
N1 (n, %)	4 (30.8)
Re-excision	
Not performed (n, %)	12 (92.3)
Performed in same surgery (n, %)	1 (7.7)
Performed in different surgery (n, %)	0 (0)

pTNM: Pathological tumor-node-metastasis staging
pT: Pathological primary tumor stage
pN: Pathological regional lymph nodes stage

ductal carcinomas and one case of apocrine carcinoma (92.3% and 7.7%, respectively).

Postoperative medial arm pain was observed in one patient, and seroma was noted in two patients, but there were no other surgical complications. All patients underwent postoperative radiation therapy. Eligible patients received chemotherapy and/or hormonal therapy. The average follow-up period was 33 months. Although the follow-up periods were not considered to be sufficiently long, no local recurrence was observed.

Discussion and Conclusion

Cooperman and Dinner described RF as a technique that enables large resection of the breast with minimal deformity and minimal shift of the nipple–areola complex for partial mastectomy (7). Unintended consequences, such as deviation or distortion of the nipple–areola complex, loss of gland or skin, breast retraction, and breast asymmetry, may be seen after BCS (9-12). Large tumor size is a relative contraindication for BCS. However, patients with a large tumor size in comparison with the breast and tumors close to the skin generally lose an opportunity to undergo BCS because of poor outcome of cosmetic results against a safe margin of resection (11, 13). After BCS, RF and other reconstructive methods, such as implant application, rotation flap approach, autologous free dermal fat graft, intramammarian flap reconstruction, latissimus dorsi flap application, and pedicled local flap to the defective region, are currently used (7, 9, 11, 14-18). Reconstructions of lumpectomy defects include volume displacement and replacement techniques. In patients with large- or moderate-sized breasts, volume displacement techniques can be used after tumor resection and can help repair local skin defects. However, the volume replacement technique may be required in patients with smaller breasts and large skin defects (6, 19). Neoadjuvant chemotherapy for early-stage breast cancer should be suggested as an option today for eligible patients (20). The primary benefit of neoadjuvant chemotherapy for early-stage breast cancer is the downstaging of the tumor. Therefore, this approach may facilitate for BCS, but it has not been shown to improve the overall survival, except in patients younger than 50 years in large randomized controlled trials (21, 22). In our study, majority of women (77%) were younger than 50 years. We were unable to recommend neoadjuvant chemotherapy for three patients who underwent biopsy at a different hospital despite receiving appropriate treatment. The remaining patients were not eligible for neoadjuvant chemotherapy because of the status of the hormone receptor or the close proximity of tumors to the skin. However, potential disadvantages of neoadjuvant chemotherapy do exist. Tumor downstaging can be inadequate to perform BCS, chemotherapy-resistant tumors can progress, initial lymph node status cannot be determined, and patients with favorable tumor phenotypes could be over treated (23).

The safe margin of resection is important in patients with breast cancer and ductal carcinoma in situ who undergo BCS because it has an effect on local recurrence, with ductal carcinoma in situ being an important prognostic factor (24-27). However, there is no consensus about the safe margin of resection in breast cancer. Ideally, the lateral edge of macroscopic margins is at least 1 to 2 cm in the classic quadrantectomy technique defined by Veronesi (24, 28). However, safe margins of >1 mm are sufficient according to more conservative opinions. Even these more conservative opinions defend that the positive margin increases as the tumor size increases, particularly in tumors of >3 cm (28-30). The incidence of a positive postoperative tumor margin is lower in patients with a large defect undergoing immediate reconstruction (31). In our study, the safe margin of resection values of T2 tumor patients was greater than 1 cm in 87% patients. These results show that we could reach safer margins with the RF technique, even in patients with large tumors. In patients with T1 tumors who undergo RF reconstruction because of the close proximity of the tumor to the skin, concerns exist about the loss of skin and poor cosmetics, but not regarding the large size of the tumor or providing safe margins.

The purpose of BCS is to reach a tumor-free margin and, if required, to undertake re-excisions in the same session based on resected specimens intraoperatively examined (3). In breast cancer patients, by evaluating the intraoperative margin status, reconstruction could be initiated following the first re-excision at a positive close margin. However, if a second re-excision is required, the reconstruction option changes, and skin-sparing mastectomy and total reconstruction are generally performed (32). On the other hand, patients with local recurrence after BCS generally undergo mastectomy (24). Therefore, immediate reconstruction, performed after achieving the safe margin of in same session, is proposed for lumpectomy defects (6). In our study, a first re-excision

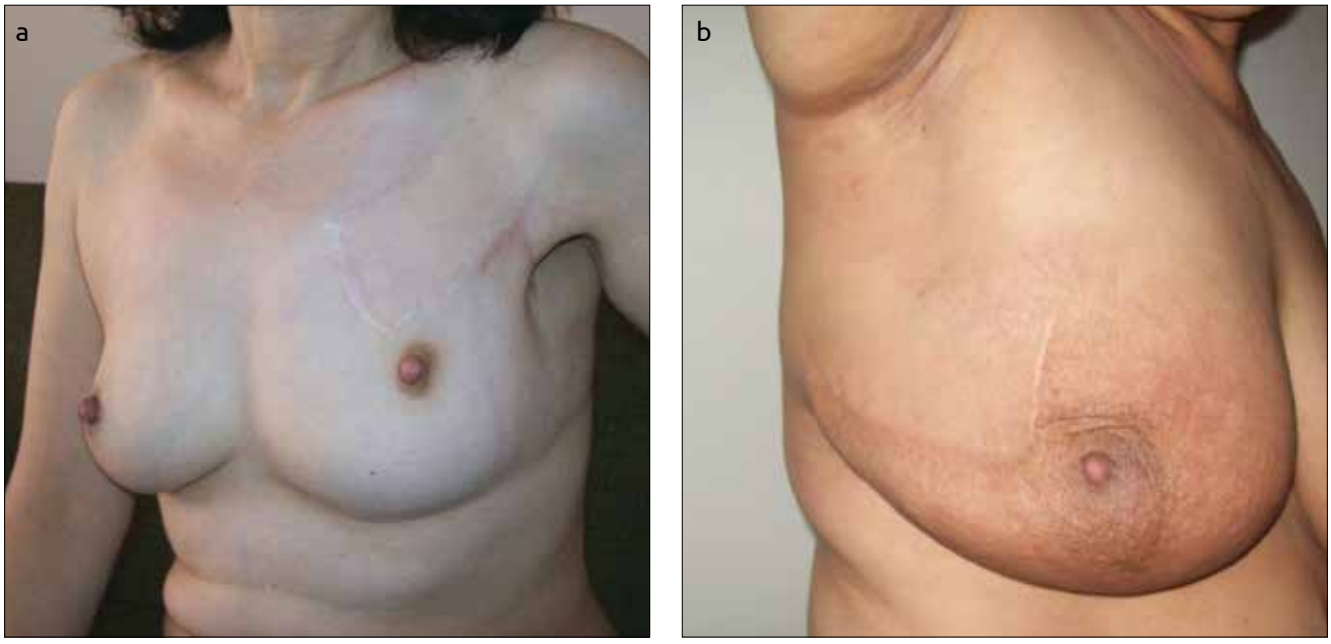

Figure 3. a, b. Two breast cancer patients with rhomboid flap reconstruction after 6 months

in the same session was required for only 1 of the 13 patients. None of the patients required a second re-excision, and there were no patients requiring re-operative reconstruction due to a positive margin. In our experience, RF transposition provides en bloc resection of the skin and gland tissue even in large tumors. Thus, the safe margin of resection is regular and adequate because large mass resection is performed with rhombus margins even in large tumors and tumors close to the skin. Therefore, RF transposition can facilitate immediate reconstruction in BCS.

The RF reconstruction technique has some other advantages. For example, compared with the intramammarian flap reconstruction technique, RF reconstruction provides enough dermal tissue, and compared with the latissimus dorsi flap RF reconstruction, it ensures a smaller donor tract scar and avoids sacrifice of muscle tissue. Compared with a local implant, it is low cost and feels more natural (6). In addition, and possibly most important, RF reconstruction is a simple technique to perform.

The upper and lower outer quadrant defects of the breast are favorable locations for applying RF reconstruction because ample loose donor tissues in this area allow closure without tension. On the other hand, the success of the flap will be the least in the inner quadrant defects of the breast because of the less stretched cutaneous and subcutaneous tissues. Gwynn and Williams used the RF technique to close the defect of partial mastectomy in seven patients. In their study, they emphasized that the breast tissue and skin healed successfully, with minimal deformity and cosmetic scar, after RF reconstruction (8). RF reconstruction was used for upper outer quadrant defects in breast cancer patients in their study (8). Because of its adequate cosmetic results, Tanaka et al. applied RF in distressed breast fields, involving two lower outer quadrant defects (9). We think that RF gives better cosmetic results in lower outer quadrant defects than upper outer quadrant defects because the scar tissue is hidden in the former (Figure 3). With regard to concerns of large and visible scarred tissues of the skin of the breast and donor area after RF reconstruction, da Silva Neto et al. (10) reported that the scar quality was fine in the long term, even after radiation therapy. Our cosmetic observations are similar to the findings of authors in other studies. The rate of our patients with outer quadrant tumor who underwent RF reconstruction was 69.2%, and none of the patients had an inner quadrant tumor. The disadvantage of RF reconstruction with respect to cosmetic observations is the presence of an incision scar on the cleavage line, particularly for large and upper quadrant tumors (Figure 3). However, according to our observations, patients who underwent the RF technique with BCS had better breast volume conservation than those who did not.

The protection of flap vitality is very important in terms of cosmetic appearance for repairing defects. Therefore, the surgeon should be aware of appropriate peduncle flap preparation. Moreover, choosing and using a blue dye are also important for a healthy flap in patients who have planned to undergo sentinel lymph node dissection. The intradermal injection of methylene blue dye, different from isosulfan blue, can cause inflammatory cutaneous adverse effects such as skin erythema, ulcers, and necrosis (33,34). Therefore, isosulfan blue, instead of methylene blue, can be used for sentinel mapping in breast cancer patients scheduled for RF reconstruction. We used isosulfan blue in three patients for sentinel mapping, and we did not encounter any inflammation or perfusion disturbance of the donor tissue. If methylene blue is used for sentinel mapping, an intraparenchymal preparation (5 ml) of a 1% blue dye injection will be much safer to avoid undesirable complications of the flap (33, 34).

In conclusion, the RF reconstruction technique, which is an easy technique, can facilitate BCS in patients with relatively large tumors and tumors close to the skin. However, different studies comparing the cosmetic results of primary closure and other breast reconstruction techniques with RF are required to assess the applicability of RF transposition in BCS.

Ethics Committee Approval: Ethics committee approval was received for this study.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - E.M., S.Ö., M.Ö., Ü.T.; Design - E.M., Ü.T., M.Ö.; Supervision - S.Ö., M.Ö.; Funding - S.Ö.; Materials - S.Ö., FK.; Data Collection and/or Processing - A.K., C.G.; Analysis and/or Interpretation - S.Ö., ZY., F.K., A.K.; Literature Review - E.M., S.Ö, ZY., C.G.; Writer - E.M.; Critical Review - E.M., S.Ö., ZY., F.K., Ü.T., A.K., C.G., M.Ö., S.Ö.; Other - E.M.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

Etik Komite Onayı: Bu çalışma için etik komite onayı alınmıştır.

Hasta Onamı: Yazılı hasta onamı bu çalışmaya katılan hastalardan alınmıştır.

Hakem değerlendirmesi: Dış bağımsız.

Yazar Katkıları: Fikir - E.M., S.Ö., M.Ö., Ü.T.; Tasarım - E.M., Ü.T., M.Ö.; Denetleme - S.Ö., M.Ö.; Kaynaklar - S.Ö.; Malzemeler - S.Ö., F.K.; Veri toplanması ve/veya işlemesi - A.K., C.G.; Analiz ve/veya yorum - S.Ö., ZY., F.K., A.K.; Literatür taraması - E.M., S.Ö., Z.Y., C.G.; Yazıyı yazan - E.M.; Eleştirel İnceleme - E.M., S.Ö., Z.Y., F.K., Ü.T., A.K., C.G., M.Ö., S.Ö.; Diğer - E.M.

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

References

1. Fisher B, Anderson S, Redmond CK, Wolmark N, Wickerham DL, Cronin WM. Reanalysis and results after 12 years of follow-up in a randomized clinical trial comparing total mastectomy with lumpectomy with or without irradiation in the treatment of breast cancer. N Engl J Med 1995; 333:1456-1461. (PMID: 7477145) [CrossRef]
2. Veronesi U, Salvadori B, Luini A, Banfi A, Zucali R, Del Vecchio M, Galimberti V, Mezzanotte G, Sacchini V, Tana S, Marubini E. Conservation treatment of early breast canver: long-term results of 1232 cases treated with quadrantectomy, axillary dissection, and radiotherapy. Ann Surg 1990; 211: 250-259. (PMID: 2106841)
3. Canavese G, Ciccarelli G, Garretti L, Ponti A, Bussone R, Giani R, Ala A, Berardengo E. Role and efficacy of intraoperative evaluation of resection adequacy in conservative breast surgery. ISRN Oncol 2011; 2011:247385. (PMID: 22084726)
4. Vrieling C, Collette L, Fourquet A, Hoogenraad WJ, Horiot JH, Jager JJ, Pierart M, Poortmans PM, Struikmans H, Maat B, Van Limbergen E, Bartelink H. The influence of patient, tumor and treatment factors on the cosmetic results after breast-conserving therapy in the EORTC 'boost vs. no boost' trial. EORTC Radiotherapy and Breast Cancer Cooperative Groups. Radiother Oncol 2000; 55:219-232. (PMID: 10869738) [CrossRef]
5. Kijima Y, Yoshinaka H, Owaki T, Aikou T. Early experience of immediate reconstruction using autologous free dermal fat graft after breast conservational surgery. J Plast Reconstr Aesthet Surg 2007; 60:495-502. (PMID: 17399658) [CrossRef]
6. Ballard TN, Momoh AO. Advances in breast reconstruction of mastectomy and lumpectomy defects. Surg Oncol Clin N Am 2014; 23:525-548. (PMID: 24882349) [CrossRef]
7. Cooperman AM, Dinner M. The rhomboid flap and partial mastectomy. Surg Clin North Am 1978; 58:869-873. (PMID: 684564)
8. Gwynn BR, Williams CR. Use of the Limberg flap to close breast wounds after partial mastectomy. Ann R Coll Surg Engl 1985; 67:245-246. (PMID: 4037638)
9. Tanaka S, Nohara T, Nakatani S, Iwamoto M, Sumiyoshi K, Kimura K, Takahashi Y, Sato N, Tanigawa N. Esthetic result of rhomboid flap repair after breast-conserving surgery for lower quadrant breast cancer lesion with skin invasion: report of two cases. Surg Today 2011; 41:832-836. (PMID: 21626332) [CrossRef]
10. da Silva Neto MP, Adão O, Scandiuzzi D, Chaem LH. The rhomboid flap for immediate breast reconstruction after quadrantectomy and axillary dissection. Plast Reconstr Surg 2007; 119:1134-1136. (PMID: 17312548) [CrossRef]
11. Kijima Y, Yoshinaka H, Hirata M, Umekita Y, Sohda M, Koriyama C, Mizoguchi T, Arima H, Nakajo A, Ishigami S, Ueno S, Natsugoe S. Clinical and pathologic evaluation of implanted free dermal fat grafts after breast cancer surgery: a retrospective analysis. Surgery 2012; 151:444-455. (PMID: 21911237) [CrossRef]
12. Ozmen T, Polat AV, Polat AK, Bonaventura M, Johnson R, Soran A. Factors affecting cosmesis after breast conserving surgery without oncoplastic techniques in an experienced comprehensive breast center. Surgeon 2015; 13:139-144. (PMID: 24529831) [CrossRef]
13. Winchester DP, Trabanino L, Lopez MJ. The evolution of surgery for breast cancer. Surg Oncol Clin N Am 2005; 14:479-498. (PMID: 15978425) [CrossRef]
14. Almasad JK, Salah B. Breast reconstruction by local flaps after conserving surgery for breast cancer: an added asset to oncoplastic techniques. Breast J 2008; 14:340-344. (PMID: 18537916) [CrossRef]
15. Dean NR, Yip JM, Birrell S. Rotation flap approach mastectomy. ANZ J Surg 2013; 83:139-145. (PMID: 23171002) [CrossRef]
16. Rageth CJ, Tausch C. Intramammarian flap reconstruction (IFR) technique in breast conserving surgery. Breast 2009; 18:387-392. (PMID: 19913416) [CrossRef]
17. Hernanz F, Regaño S, Redondo-Figuero C, Orallo V, Erasun F, Gómez-Fleitas M. Oncoplastic breast-conserving surgery: analysis of quadrantectomy and immediate reconstruction with latissimus dorsi flap. World J Surg 2007; 31:1934-1940. (PMID: 17674094) [CrossRef]
18. Claro F Jr, Figueiredo JC, Zampar AG, Pinto-Neto AM. Applicability and safety of autologous fat for reconstruction of the breast. Br J Surg 2012; 99:768-780. (PMID: 22488516) [CrossRef]
19. Emiroğlu M, Sert İ, İnal A. The Role of Oncoplastic Breast Surgery in Breast Cancer Treatment. J Breast Health 2015; 11:1-9. [CrossRef]
20. Kummel S, Holtschmidt J, Loibl S. Surgical treatment of primary breast cancer in the neoadjuvant setting. Br J Surg 2014; 101:912-924. (PMID: 24838656) [CrossRef]
21. Teshome M, Hunt KK. Neoadjuvant therapy in the treatment of breast cancer. Surg Oncol Clin N Am 2014; 23:505-523. (PMID: 24882348) [CrossRef]
22. Rastogi P, Anderson SJ, Bear HD, Geyer CE, Kahlenberg MS, Robidoux A, Margolese RG, Hoehn JL, Vogel VG, Dakhil SR, Tamkus D, King KM, Pajon ER, Wright MJ, Robert J, Paik S, Mamounas EP, Wolmark N. Preoperative chemotherapy: updates of National Surgical Adjuvant Breast and Bowel Project Protocols B-18 and B-27. J Clin Oncol 2008; 26:778-785. (PMID: 18258986) [CrossRef]
23. Mieog JS, van de Velde CJ. Neoadjuvant chemotherapy for early breast cancer. Expert Opin Pharmacother 2009; 10:1423-1434. (PMID: 19505212) [CrossRef]
24. Luini A, Rososchansky J, Gatti G, Zurrida S, Caldarella P, Viale G, Rosali dos Santos G, Frasson A. The surgical margin status after breast-conserving surgery: discussion of an open issue. Breast Cancer Res Treat 2009; 113:397-402. (PMID: 18386174) [CrossRef]
25. Tartter PI, Kaplan J, Bleiweiss I, Gajdos C, Kong A, Ahmed S, Zapetti D. Lumpectomy margins, reexcision, and local recurrence of breast cancer. Am J Surg 2000; 179:81-85. (PMID: 10773138) [CrossRef]
26. Mirza NQ, Vlastos G, Meric F, Buchholz TA, Esnaola N, Singletary SE, Kuerer HM, Newman LA, Ames FC, Ross MI, Feig BW, Pollock RE, McNeese M, Strom E, Hunt KK. Predictors of locoregional recurrence among patients with early-stage breast cancer treated with breast-conserving therapy. Ann Surg Oncol 2002; 9:256-265. (PMID: 11923132) [CrossRef]
27. Horiguchi J, Iino Y, Takei H, Maemura M, Yokoe T, Niibe H, Yamakawa M, Nakajima T, Oyama T, Morishita Y. Surgical margin and breast recurrence after breast-conserving therapy. Oncol Reports 1999; 6:135-138. (PMID: 9864416) [CrossRef]

28. Kurniawan ED, Wong MH, Windle I, Rose A, Mou A, Buchanan M, Collins JP, Miller JA, Gruen RL, Mann GB. Predictors of surgical margin status in breast-conserving surgery within a breast screening program. Ann Surg Oncol 2008; 15:2542-2549. (PMID: 18618180) [CrossRef]
29. Singletary SE. Surgical margins in patients with early-stage breast cancer treated with breast conservation therapy. Am J Surg 2002; 184:383-393. (PMID: 12433599) [CrossRef]
30. Keskek M, Kothari M, Ardehali B, Betambeau N, Nasiri N, Gui GP. Factors predisposing to cavity margin positivity following conservation surgery for breast cancer. Eur J Surg Oncol 2004; 30:1058-1064. (PMID: 15522551) [CrossRef]
31. Sacchini V, Luini A, Tana S, Lozza L, Galimberti V, Merson M, Agresti R, Veronesi P, Greco M. Quantitative and qualitative cosmetic evaluation after conservative treatment for breast cancer. Eur J Cancer 1991; 27:1395-1400. (PMID: 1835855) [CrossRef]
32. Munhoz AM, Montag E, Arruda E, Aldrighi CM, Filassi JR, Piato JR, Prado LC, Aldrighi JM, Gemperli R, Ferreira MC. Immediate reconstruction following breast-conserving surgery: management of the positive surgical margins and influence on secondary reconstruction. Breast 2009; 18:47-54. (PMID: 19110425) [CrossRef]
33. Sumer F, Gozeneli O, Piskin T, Unal B. Skin necrosis of the breast due to methylene blue injection. J Breast Health 2012; 8:150-151.
34. Bleicher RJ, Kloth DD, Robinson D, Axelrod P. Inflammatory cutaneous adverse effects of methylene blue dye injection for lymphatic mapping/sentinel lymphadenectomy. J Surg Oncol 2009; 99:356-360. (PMID: 19189298) [CrossRef]