Aesthetic Surgery Journal
2017, 1–11

DOI: 10.1093/asj/sjx029
www.aestheticsurgeryjournal.com

OXFORD
UNIVERSITY PRESS

Preliminary Report

Positive Margin Re-Excision Following Immediate Autologous Breast Reconstruction: Morbidity, Cosmetic Outcome, and Oncologic Significance

Oscar Ochoa, MD, MSc, FACS; Constantine Theoharis, MD; Steven Pisano, MD; Minas Chrysopoulo, MD; Peter Ledoux, MD; Gary Arishita, MD; and Chet Nastala, MD, FACS

Abstract

Background: Acquisition of negative resection margins is paramount in the surgical management of operable breast cancer. Management of positive margins following mastectomy and immediate breast reconstruction is presently poorly defined.

Objectives: The present study aims at defining morbidity and cosmetic sequela of re-excision procedures aimed at clearing involved mastectomy margins in the setting of immediate autologous breast reconstruction. Oncologic outcomes are recorded.

Methods: A retrospective study of patients that underwent skin-sparing mastectomy followed by immediate deep inferior epigastric perforator flap breast reconstruction was performed. Patients found to have positive mastectomy margins underwent margin re-excision during a separate procedure. Method of positive margin exposure and resection is described. Flap morbidity and cosmetic outcome following margin re-excision was compared between reconstructed breasts that underwent re-excision vs those reconstructed after prophylactic mastectomy (controls). Cancer recurrence was recorded during the follow-up period.

Results: Thirty-six (2.5%) out of 1443 patients were found to have positive mastectomy margins following immediate breast reconstruction between May 2007 and November 2012. Location of positive margins was evenly distributed in all breast regions. Although flap morbidity was similar, a trend ($P > 0.05$) toward higher seroma formation and fat necrosis was reported in breasts following re-excision vs controls. With a mean follow-up period of 28 months, cosmetic outcome between breasts that underwent re-excision vs controls were similar. Cancer recurrence was reported in 3 (8.3%) patients.

Conclusions: Re-excision of positive mastectomy margins following immediate autologous breast reconstruction requires a multidisciplinary approach and may be performed with minimal additional morbidity while preserving optimal cosmetic outcome.

Level of Evidence: 3

Editorial Decision date: January 31, 2017.

The principle objective of surgical management of operable breast cancer is complete excision of malignant lesions. However, involvement of specimen margins with invasive or in situ disease is occasionally detected on final pathologic evaluation. For example, following lumpectomy, the reported prevalence of positive margins is between 2.5%

Drs Ochoa, Pisano, Chrysopoulo, Ledoux, Arishita, and Nastala are plastic surgeons in private practice in San Antonio, TX. Dr Theoharis is a pathologist in private practice in San Antonio, TX.

Corresponding Author:
Dr Oscar Ochoa, 9635 Huebner Road, San Antonio, TX 78240, USA.
E-mail: dr.ochoa@prmaplasticsurgery.com

and 45%.[1-4] Surprisingly, the prevalence of positive margins following mastectomy, where complete glandular excision is performed, has also been reported between 2.5% and 14%.[5-9] A positive surgical margin is widely accepted as an independent risk factor for locoregional cancer recurrence among patients undergoing either breast conservation surgery[1,10] or mastectomy.[5,10] While re-excision of positive lumpectomy margins is a broadly accepted practice, management of positive margins following mastectomy remains an area of active research.[11,12]

While skin-sparing mastectomy may optimize cosmetic outcome in the setting of breast reconstruction, margin involvement with invasive or in situ disease may be increased.[13] In the setting of immediate breast reconstruction, management of positive mastectomy margins remains a subject of debate. When margin positivity is detected following mastectomy and immediate reconstruction, proposed management options include: close observation,[6,11,12] postmastectomy radiation, or margin re-excision. In order to eliminate the need for external beam radiation and associated complications in conjunction with immediate postmastectomy reconstruction,[14-18] positive margin re-excision is the most attractive option for the reconstructive surgeon. As such, operative morbidity, cosmetic sequela, and oncologic outcomes associated with positive margin re-excision following immediate autologous breast reconstruction requires further investigation. Not only is a detailed description of the preferred method of positive margin re-excision reviewed in the current study, but also efficacy of margin re-excision, procedural-associated morbidity, and influence on final cosmetic outcome is evaluated. Authors deny any conflict of interest or disclosures to report.

METHODS

A retrospective review was conducted after institutional review board approval (University of Texas Health Science Center San Antonio) among 1443 consecutive patients with breast cancer or ductal carcinoma in situ (DCIS) undergoing skin-sparing mastectomy and *immediate* deep inferior epigastric perforator (DIEP) flap reconstruction by 6 microsurgeons (Plastic Reconstructive & Microsurgical Associates Plastic Surgery) from May 2007 to November 2012. Patients with pathologic findings of residual cancer and/or DCIS by permanent section at the mastectomy margin (positive margin) were identified and comprised the study population. All the patients in the study population underwent skin sparing (nonnipple sparing) mastectomy by 15 unique general surgeons prior to reconstruction. Patient demographics, past medical history, body mass index (BMI), and neoadjuvant therapies were obtained from medical records. A positive margin was defined as invasive or in situ disease at an inked resection margin. Type of invasive or in situ disease, location of lesion(s) within the mastectomy specimen, tumor characteristics, pathologic prognostic factors, and axillary lymph node involvement were recorded from pathologic documents.

Table 1. Patient Demographics ($n = 36$)

Variable	Mean (range)
Age (years)	49 (35-69)
Body mass index (kg/m^2)	28 (19-40)
Follow-up (months)	27.7 (1.6-59.7)
Comorbidities	**No. (%)**
Hypertension	9 (25)
Cardiac disease	4 (11.1)
Hormone replacement treatment	4 (11.1)
Active tobacco use	4 (11.1)
Migraine headaches	3 (8.3)
Autoimmune disease	2 (5.6)
Pulmonary disease	1 (2.8)
Diabetes mellitus	1 (2.8)

Patients underwent re-excision of involved mastectomy margins during a separate procedure coordinated with the corresponding breast surgeon. Intraoperatively, the location of the involved margin was reviewed using the pathologic reports and verified directly by the pathologist of record. Exposure of the involved margin was obtained by incising the periphery of the DIEP flap skin island and elevating mastectomy skin flaps off the de-epithelialized DIEP flap dermal plane. Undermining of mastectomy flaps was advanced toward the location of the positive margin. After wide exposure of the area containing the positive margin was achieved, the mastectomy flap was thinned of any subcutaneous tissue deep to the dermis. In cases where positive margins were located on the deep surface of the mastectomy site, the pectoralis/serratus fascia and any residual overlying breast tissue was resected. For superficial or deep mastectomy site positive margins, a portion of the DIEP flap abutting the positive margin was also resected. Following positive margin resection, mastectomy flaps were redraped over the underlying DIEP flap with reinsetting of the skin island in its previous location. Excision of mastectomy flap skin was not required in any of the study cases.

Re-excision specimens were examined by permanent section and compared to the initial mastectomy pathologic report. Identification of residual disease *and* acquisition of negative margins following re-excision was defined in this study as a "cleared" margin. Alternatively, patients with no residual invasive or in situ disease within the re-excision specimen or persistent positive

Table 2. Breast Lesion Preoperative Diagnosis ($n = 36$)

Variable	No. (%)
DCIS	28 (77.8)
Invasive ductal CA	24 (66.7)
Invasive lobular CA	7 (19.4)
LCIS	5 (13.9)
Invasive medullary CA	2 (5.6)

CA, carcinoma; DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ.

Table 3. Preoperative Location of Breast Lesion ($n = 36$)

Variable	No. (%)
Multicentric	14 (38.9)
Quadrant	
Lower outer	7 (19.4)
Lower inner	5 (13.9)
Upper outer	5 (13.9)
Upper inner	3 (8.3)
Central	2 (5.6)

margins following re-excision were designated as "margin unclear." Locoregional recurrence and systemic failure between cohorts designated as "margin clear" vs "margin unclear" were compared. Postoperative adjuvant therapies were directed based on National Comprehensive Cancer Network (NCCN) criteria[19] including persistent positive margins.

From a prospectively kept database, DIEP flap morbidity pre- and postmargin re-excision was recorded and compared to the prophylactic contralateral reconstructed breast, if applicable. After planned nipple reconstruction and fat grafting, if necessary, long-term (mean follow up, 28 months) cosmetic sequela of margin re-excision was evaluated by a panel of 11 blinded board-certified plastic surgeons not involved in study patient care. Cosmetic outcome was scored for each individual reconstructed breast on a 1 to 5 Likert scale, with 1 representing unacceptable and 5 representing excellent cosmetic outcome. Relative effect of re-excision procedures was quantified by evaluating only patients that underwent bilateral reconstruction such that each patient served as her own control. The cosmetic outcome of the prophylactic contralateral reconstructed breast was compared to the corresponding breast that underwent margin re-excision.

Selection bias for entry in the study was eliminated by including all patients with positive mastectomy margins in the setting of immediate breast reconstruction during the study period. Potential biases in comparison of outcomes were minimized by designing 2 separate analyzes. First, the effects of re-excision procedures on DIEP flap morbidity and cosmetic outcome were analyzed by comparing the reconstructed breast that underwent re-excision with the contralateral breast that also underwent reconstruction without re-excision. By recording flap morbidity prospectively and using each individual patient as its own control, including blinded comparison of cosmetic outcome, minimized confounding patient variables and observer bias, respectively. Second, oncologic outcomes were compared between patients that were able to achieve a "clear" margin vs those designated as "margin unclear" as defined by the study.

The statistical significance of associations between categorical variables were assessed using Pearson's chi-square test or Fishers exact test, as appropriate. Group contrasts with regard to continuously distributed outcomes were carried out with the nonparametric Kruskal-Wallis test. The relation between the occurrence of paired flap complications (yes, no) and intervention (re-excision, control) was assessed with a generalized estimating equation model with a logit link adjusted for correlations introduced by bilateral reconstructions. Long-term cosmetic outcome was determined by calculating the difference between cosmetic scores (1-5) among breasts that underwent re-excision vs individual controls in order to correct for confounding patient variables. Cosmetic outcomes between breasts with re-excision and controls (with no re-excision) were compared using the Wilcoxon signed rank test. All statistical testing was two sided with a significance level of 5% and SAS Version 9.3 (SAS Institute, Cary, NC) was used throughout.

RESULTS

Following skin-sparing mastectomy and immediate DIEP reconstruction, positive mastectomy margins with invasive and/or in situ disease were identified in 36 (2.5%) out of 1443 patients. Mean patient age was 49 years (range, 35-69 years) and the average BMI was 28 kg/m^2 (range, 19-40 kg/m^2). Average follow up for the study population following planned nipple reconstruction and revision was greater than 2 years (mean, 28 months; range, 1.6-59.7 months) (Table 1). Hypertension was the most frequently reported (25%) medical comorbidity with active tobacco use reported in 4 (11%) patients (Table 1).

Invasive ductal carcinoma and DCIS were the most frequent indications for skin-sparing mastectomy (67% and 78%, respectively) (Table 2). Lesions located in more than one quadrant (multicentric) were identified preoperatively

Table 4. Oncologic Characteristics of Breast Lesions

Variable	No. (%)
Tumor stage	
is	7 (21.2)
1mi	1 (3)
1 (A-C)	15 (45.5)
2	8 (24.2)
3	2 (6.1)
Nodal stage	
0	26 (72.2)
1mi	1 (2.8)
1a	7 (19.4)
2a	2 (5.6)
Oncologic stage	
0	6 (16.7)
1 (A-B)	14 (38.9)
2 (A-B)	13 (36.1)
3A	3 (8.3)
Receptor characteristics	
Estrogen receptor	29 (82.9)
Progesterone receptor	22 (62.9)
Her-2 receptor	7 (22.6)
Histologic characteristics of invasive cancer	
Tubule formation	
Unknown	7 (20)
1	1 (2.9)
2	0
3	27 (77.1)
Nuclear polymorphism	
Unknown	7 (20)
1	3 (8.6)
2	14 (40)
3	11 (31.4)
Mitotic count	
Unknown	7 (20)
1	15 (42.9)
2	7 (20)
3	6 (17.1)
Pathologic grade	
Unknown	7 (20)
1	5 (14.3)
2	12 (34.3)
3	11 (31.4)
Lymphovascular invasion	6 (20)
Histologic characteristics of DCIS	
Pathologic grade	
Unknown	4 (14.8)
1	3 (11.1)
2	7 (25.9)
3	13 (48.1)
Comedonecrosis	19 (70.4)

in 14 (39%) patients with the remainder located in the central breast area or in individual quadrants (Table 3).

Oncologic and histologic characteristics of resected lesions are presented in Table 4. Positive margins were most commonly identified on the mastectomy flaps of the upper and lower outer quadrants, in 8 patients (22%) and 7 patients (19%), respectively. Positive deep margins were seen infrequently and occurred in only 4 (11%) of patients (Table 5). The prevalence of positive margins was distributed evenly throughout all BMI groups. Mastectomy specimen margins contained DCIS in 20 patients (55%) within the study population, while invasive ductal carcinoma was present in 14 (39%) patients. Four patients had both invasive ductal carcinoma and DCIS present at the mastectomy margin (Table 6).

A total of 66 DIEP flaps were performed on the study population. Bilateral breast reconstruction was performed on 30 (83%) patients within the study population, while 6 (17%) patients had only the oncologically affected breast reconstructed. Following reconstruction, average number of days to re-excision of positive margins was 28 (range, 7-40 days) with 89% of patients undergoing only one re-excision procedure. After permanent section evaluation, 19 (53%) re-excision specimens did not contain any residual invasive or in situ disease within the re-excision specimen (Table 7). Residual invasive or in situ lesions were identified within 17 (47%) re-excision specimens (Table 7) with acquisition of negative margins (clear margin) in 13 patients (Table 8). Persistent positive margins were present in four patients due to extensive multicentric disease despite repeated attempts at re-excision. These 4 patients with persistent disease at the surgical margin as well as

Table 5. Location of Positive Margin

Variable	No. (%)
Multicentric	6 (16.7)
Quadrant	
Upper outer	8 (22.2)
Lower outer	7 (19.4)
Lower inner	6 (16.7)
Upper inner	3 (8.3)
Deep	4 (11.1)
Central	2 (5.6)

Table 6. Lesion(s) at Mastectomy Specimen Margin ($n = 36$)

Variable	No. (%)
DCIS, any	20 (55.6)
Invasive ductal CA, any	14 (38.9)
Invasive lobular CA	5 (13.9)
IDC/DCIS	4 (11.1)
Invasive medullary CA	1 (2.8)

CA, carcinoma; DCIS, ductal carcinoma in situ; IDC, invasive ductal carcinoma.

Table 7. Lesion(s) Identified in Re-Excision Specimen ($n = 36$)

Variable	No. (%)
Negative	19 (52.8)
DCIS	7 (19.4)
Invasive ductal CA	6 (16.7)
Invasive lobular CA	2 (5.6)
Mucinous CA/DCIS	1 (2.8)
ADH	1 (2.8)

ADH, atypical ductal hyperplasia; CA, carcinoma; DCIS, ductal carcinoma in situ.

Table 8. Lesion Found at Positive Margin

Characteristics	Margin clear no. (%)	Margin unclear no. (%)	*P*
Lesion			0.48
Invasive ductal CA, only ($n = 10$)	2 (20)	8 (80)	
Invasive lobular CA ($n = 5$)	2 (40)	3 (60)	
Invasive medullary ($n = 1$)	0	1 (100)	
DCIS, only ($n = 15$)	8 (53.3)	7 (46.7)	
IDC/DCIS ($n = 4$)	1 (25)	3 (75)	

CA, carcinoma; DCIS, ductal carcinoma in situ; IDC, invasive ductal carcinoma.

Table 9. Congruency of Lesion at Positive Margin with Findings at Re-Excision

Lesion at positive margin	Findings on re-excision no. (%)					
	IDC	Lobular CA	Mucinous CA	DCIS	ADH	Negative
Invasive ductal CA ($n = 10$)	2 (20)	0	0	1 (10)	0	7 (70)
Invasive lobular CA ($n = 5$)	0	2 (40)	0	0	0	3 (60)
Invasive medullary CA ($n = 1$)	0	0	0	0	0	1 (100)
IDC/DCIS ($n = 4$)	1 (25)	0	1 (25)	1 (10)	0	1 (25)
DCIS ($n = 16$)	3 (18.75)	0	0	5 (31.25)	1 (6.75)	7 (43.75)

CA, carcinoma; DCIS, ductal carcinoma in situ; IDC, invasive ductal carcinoma.

those patients that underwent re-excision with negative results were designated as "margin unclear" as per our study criteria (Table 8). Ability in obtaining "clear" margins after attempt(s) at re-excision was similar regardless of the type of lesion identified at the margin of the original mastectomy specimen (Table 8). Three patients with only DCIS identified at the original mastectomy specimen margin were found to have invasive ductal carcinoma within the re-excision specimen (Table 9). Following re-excision, 17 patients (47%) among the study population received adjuvant chemotherapy with 7 (19%) patients requiring postreconstruction radiation based on persistent positive margins, NCCN guidelines[19] for tumor, nodal stage, and lymphovascular invasion (Table 10).

DIEP flap complications were recorded and compared between those breasts that underwent a re-excision procedure and the contralateral breast that underwent prophylactic mastectomy and reconstruction without re-excision. The breasts (n = 36) of patients with re-excision did not differ significantly with the breasts (n = 30) of patients with no re-excision with regard to any of 7 types of flap complications (Table 11), although the re-excised breasts exhibited a numerically higher prevalence of delayed wound healing, clinically detected fat necrosis, and seroma.

Long-term (mean follow up, 28 months) cosmetic outcome was determined by evaluating patients that underwent bilateral reconstruction (30 out of 36 patients) and calculating the difference between cosmetic scores (1-5) among breasts that underwent re-excision vs corresponding controls in order to correct for confounding patient variables (Figures 1-2). Re-excised breasts (n = 30) did not differ significantly from non-re-excised control breasts (n = 30) with regard to the mean (SD) breast cosmetic outcome score (Table 12). With an average follow up of greater than 2 years (28 months; range, 1.6-59.7 months) following breast revision and nipple reconstruction among the study population, locoregional recurrence was diagnosed in 2 (5.7%) patients, while systemic failure was seen in only 1 (2.9%) patient. The breasts (n = 22) of patients whose margins were cleared were not significantly different from the breasts (n = 13) of patients whose margins were not cleared with regard to locoregional recurrence or systemic failure (Table 13).

Table 10. Adjuvant Therapies in the Study Population (n = 36)

Variable	No. (%)
Chemotherapy	
Preoperatively	4 (11.1)
Postoperatively	17 (47.2)
Radiotherapy	
Preoperatively	1 (2.8)
Postoperatively	7 (19.4)
Adjuvant endocrine therapy	25 (69.4)

DISCUSSION

Local control of operable breast cancer is dependent on obtaining a negative margin of resection during extirpative procedures. The near-complete removal of breast glandular parenchyma afforded by a mastectomy minimizes, but does not eliminate, the possibility of margin involvement. As previously reported, women with an advanced tumor burden and/or multicentric disease are at an increased risk of positive margins following mastectomy for breast carcinoma.[13,20] In the current study, positive margins following skin-sparing mastectomy were identified in 2.5% of cases, consistent with previous series.[5-9,13] As an independent risk factor for not only locoregional recurrence, but also systemic failure,[5,9-11,21,22] positive margins of resection following mastectomy must be addressed decisively. In cases in which immediate breast reconstructions have been performed, surgical eradication of positive margins may be performed, but lacks thorough description in the literature. As the first investigation of its kind, the current study details the surgical approach to and efficacy of positive margin eradication following immediate autologous breast reconstruction as well as its associated morbidity and long-term cosmetic sequelae.

Margin Re-Excision

In patients found to have positive mastectomy margins after immediate breast reconstruction, a multidisciplinary approach is encouraged in order to optimize appropriate treatment. In our practice, margin re-excision is pursued, even in patients with locally advanced disease that meet criteria for postmastectomy radiation by NCCN standards[19] in order to maximally decrease the risk of recurrence by

Table 11. Flap Complications Following Re-Excision of Positive Margins vs Controls

Variable	Total flaps (n = 66)	Re-excision (n = 36)	No Re-excision (n = 30)	P
Thrombosis	1 (1.5)	0	1 (3.3)	n/a
Acute hematoma	2 (3)	1 (2.8)	1 (3.3)	0.89
Infection	7 (10.6)	4 (11.1)	3 (10)	0.9
Delayed wound healing	3 (4.5)	2 (5.6)	1 (3.3)	0.34
Fat necrosis	11 (16.7)	8 (22.2)	3 (10)	0.16
Seroma	6 (9.1)	5 (13.9)	1 (3.3)	0.25
Flap loss	0	0	0	n/a

eradicating any gross residual disease. When margin re-excision is undertaken, collaboration between the corresponding plastic surgeon, breast surgeon, and pathologist familiar with the case is paramount. Reoperation must be pursued in a timely manner making identification of the plane between the mastectomy flaps and underlying autologous flap more readily visible and easy to separate. It is the opinion of the authors that re-excision procedures are best performed between 2 to 4 weeks following autologous reconstruction. Allowing sufficient time for the abdominal free flap to adequately adhere to the mastectomy skin envelope minimizes undesired undermining in areas of the breast remote from the exposure area required for margin re-excision potentially minimizing seroma formation. In our experience, thinning the involved mastectomy flap of additional subcutaneous tissue at the area of the previous positive margin did not result in areas of mastectomy flap necrosis. In the current study, mastectomy site positive margin location was similar between all mastectomy regions. In addition, BMI was not identified as a significant factor affecting the prevalence of positive mastectomy margins.

Following re-excision, residual invasive or in situ disease was identified in 17 (47%) patients. However, similar to previous findings,[20] approximately half (53%) of re-excision specimens contained no residual invasive or in situ disease (Table 7). The oncologic significance of this phenomenon is difficult to determine as these negative re-excisions may represent either a false positive postmastectomy pathologic report or miscalculation of the location of the positive margin at time of re-excision.

In an attempt to elucidate this issue further in a retrospective manner, the current study performed a subset analysis where patients were classified as "margin clear" only if residual disease was identified and novel negative margins were obtained following re-excision. In patients where residual invasive or in situ disease was identified at the re-excision specimen but persistent positive margins were present, repeat attempts at re-excision was performed. Patients were classified as "margin unclear" if persistent positive margins were present or no residual disease was identified within the re-excision specimen (negative re-excision). Negative re-excision patients did not undergo further attempts at margin clearance based on multidisciplinary tumor board recommendations but were classified as "margin unclear" in this subset analysis since the true margin status was not definitively known. Patients were considered for adjuvant external beam radiation based on persistent positive margins, NCCN tumor, nodal stage, and lymphovascular invasion criteria.[19] With an average follow up of 28 months, patients that were classified as "margin clear" experienced a similar incidence of locoregional recurrence and systemic failure vs patients classified as "margin unclear" (Table 13).

A significant limitation of the current study is the lack of lengthy follow up (28 months) making oncologic outcomes difficult to interpret definitively. Previous studies, however, evaluating the effect of margin status on recurrence among mastectomy patients report recurrence to be concentrated within 2 to 3 years following mastectomy. Freedman et al[11] analyzed the incidence of recurrence following mastectomy with close or positive margins. With 5- and 8-year cumulative incidence of chest wall recurrence of 9% and 18%, respectively, all recurrences (5 patients) occurred within 26 months following surgery.[11] Separately, Truong et al[6] reported an all-site recurrence rate of 19.5% with a median time to recurrence of 2.6 years among patients with positive mastectomy margins not receiving adjuvant radiation. Similarly, Hastings et al[23] reported a median time to recurrence among early stage breast cancer patients (without adjuvant radiation therapy) of 2.5 years. In the setting of immediate breast reconstruction, as in our study, Vaughan et al[8] reported cases of recurrence to be concentrated within 2.5 years of surgery. In that study, the majority (73%; 8/11) of recurrences were identified within 30 months of surgery with nearly half (45% (5/11) of patients) detected in within 12 months. Based on the early incidence of recurrence reported in these previous studies, 28-month follow up would likely be sufficient to detect a noticeable difference in our subset analysis. Moreover, the reported decreased prevalence of recurrence (8%) following positive margin re-excision in our study compared to those previously reported that did not undergo re-excision or

Table 12. Cosmetic Outcomes Following Re-Excision

Variable	Control breasts (n = 30)	Re-excised breasts (n = 30)	P
Likert score, mean (SD) [range]	3.74 (0.33) [2–5]	3.65 (0.67) [2–5]	0.96

Table 13. Oncologic Outcome and Length of Follow-Up

Variable	Margin cleared (n = 22)	Margin not cleared (n = 13)	Total (n = 36)	P
Locoregional recurrence, No. (%)	1 (4.5)	1 (7.7)	2 (5.7)	1
Systemic failure, No. (%)	1 (4.5)	0	1 (2.9)	1
Follow-up days, mean (SD)	886 (429)	752 (578)	836 (486)	0.232

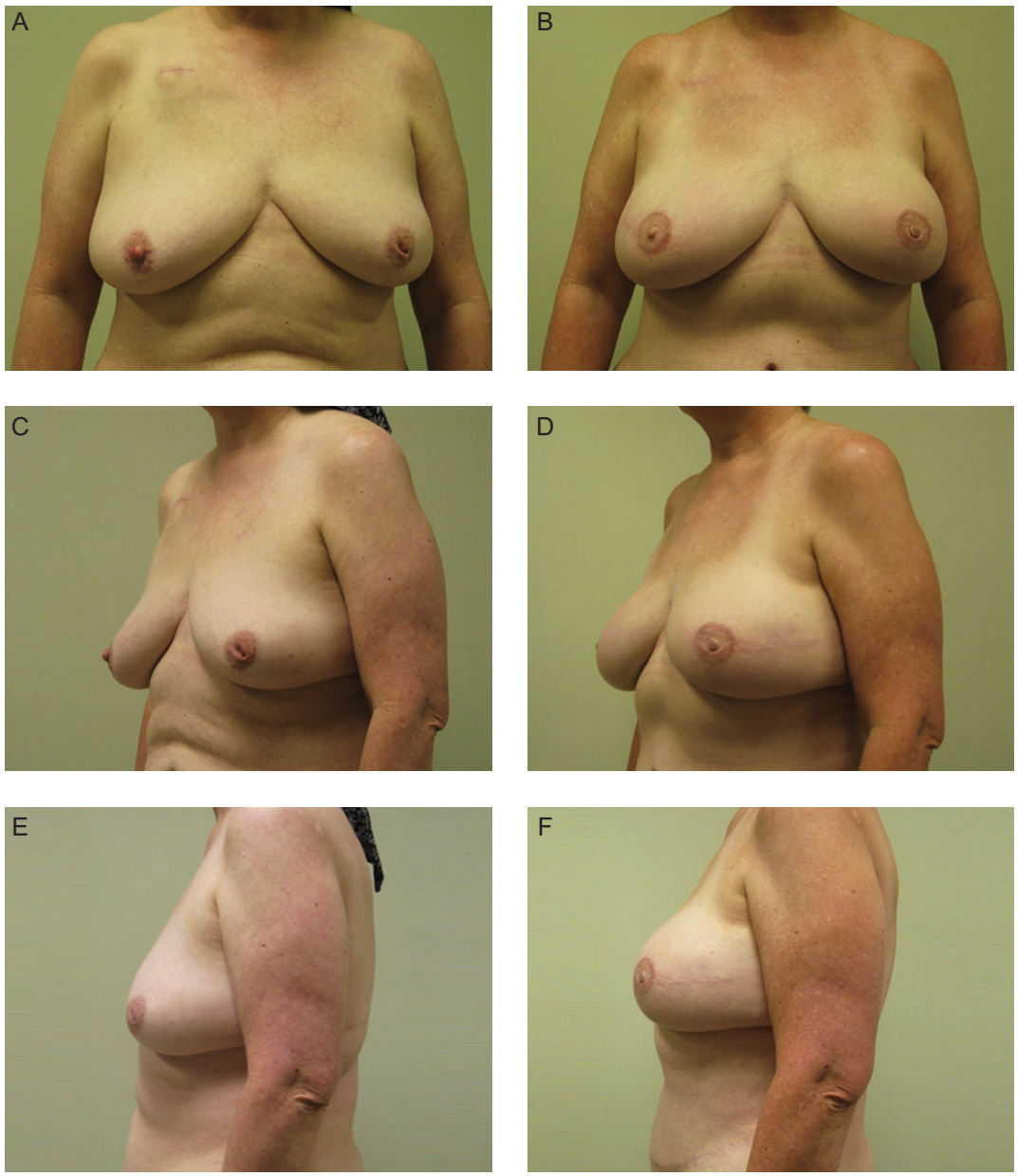

Figure 1. (A, C, E) Preoperative appearance of a 59-year-old woman with left breast cancer. (B, D, F) Postoperative appearance at 33 months following bilateral skin-sparing mastectomies and immediate bilateral reconstruction with deep inferior epigastric perforator (DIEP) flaps and re-excision of left breast positive margins.

radiation[6,11] implies clinically significant benefit of re-excision in such a high-risk population.

When comparing lesions found on re-excision with those of the original mastectomy report (Table 9), 3 patients that had only DCIS at the mastectomy margin were found to have invasive ductal carcinoma at re-excision. This significant finding suggests margin re-excision for DCIS is clearly warranted and may be the etiology behind the invasive nature of local recurrences following mastectomy for DCIS previously reported.[9,12,24-26]

Flap Morbidity

DIEP flap morbidity has previously been reported thoroughly in the literature.[27] However, in the current study, in order to most accurately determine the effects of the re-excision procedure on flap site complications, comparison was made between the breasts that underwent re-excision vs the contralateral breasts that did not undergo re-excision correcting for any unforeseen confounding factors (Table 11). The authors believe this is a more

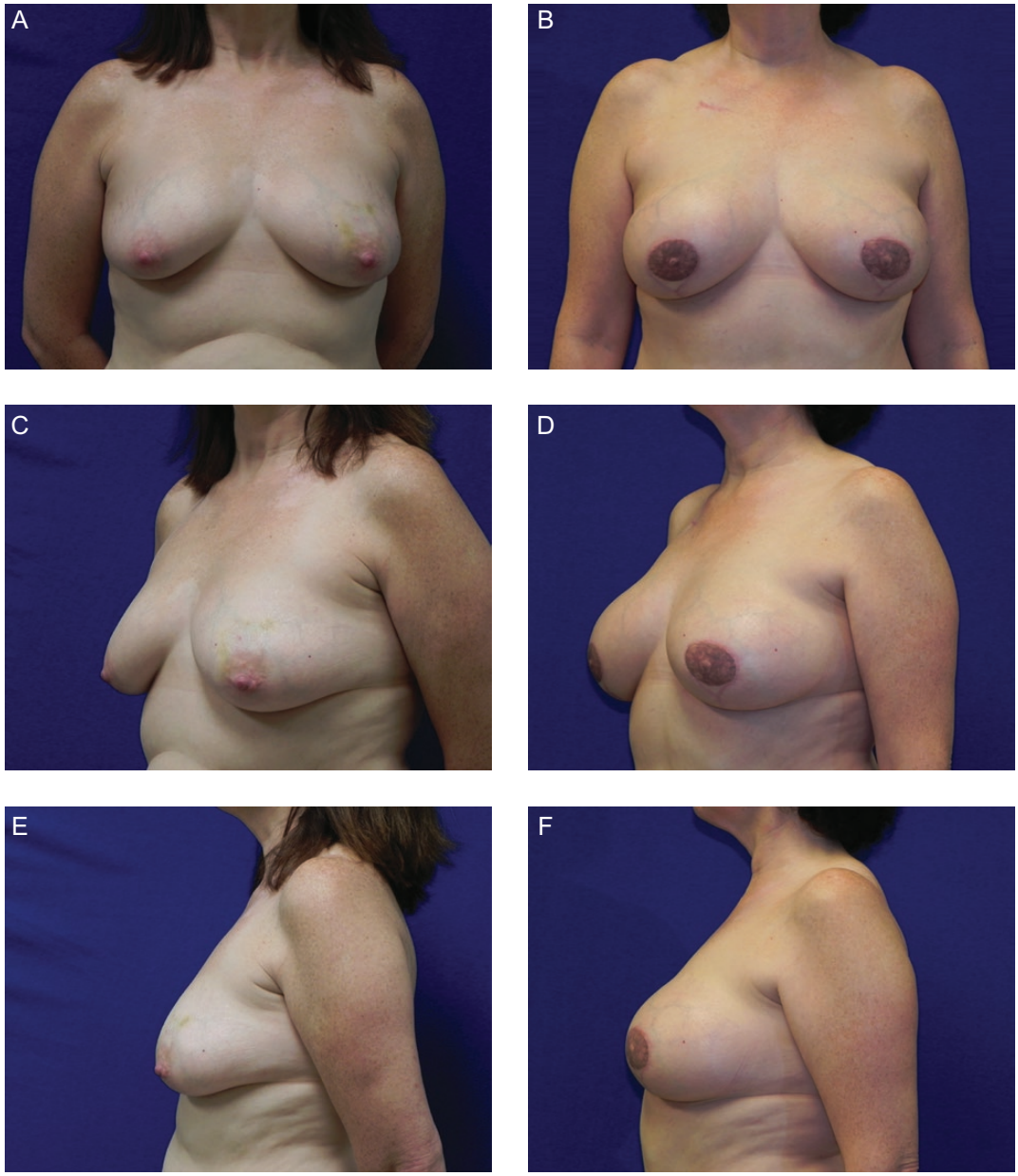

Figure 2. (A, C, E) Preoperative appearance of a 48-year-old woman with left breast cancer. (B, D, F) Postoperative appearance at 16 months following bilateral skin-sparing mastectomies and immediate bilateral reconstruction with deep inferior epigastric perforator (DIEP) flaps and re-excision of left breast positive margin.

accurate analysis than evaluating flap morbidity within a single breast pre- and post-re-excision as this will give results difficult to isolate as a consequence of the original reconstruction vs secondary to the re-excision procedure. The prevalence of individual complications did not significantly differ between both groups of breasts although certain trends were identified. Clinically detected fat necrosis was reported twice as often in breasts following margin re-excision (22% vs 10%). The etiology of this finding is difficult to determine due to the retrospective nature of the current study. Certainly, a bias toward more extensive physical examination on the breast that underwent positive margin re-excision during postoperative surveillance may lead to higher rates of fat necrosis detection. In addition, some areas of flap firmness may be at least partially attributed to thermally injured areas within the DIEP flap caused during mastectomy skin flap reelevation as these were concentrated in areas of previous undermining. Similarly, due to the wide exposure required for margin re-excision, seroma formation was higher in

breasts following re-excision compared to controls (14% vs 3.3%). It is now our standard practice to utilize aerosolized fibrin sealants and/or reinsertion of surgical drains during re-excision procedures. Nonetheless, the current series demonstrates an acceptable safety profile of margin re-excision evidenced by similar overall site-specific morbidity compared to the contralateral breast that did not undergo re-excision. Undoubtedly, the possible marginal increase in morbidity attributed to margin re-excision is superior vs the alternative which involves external beam radiation[15-18] in patients with early stage breast cancer and/or DCIS. Margin re-excision was able to eliminate the need for external beam radiation in a vast majority (81%) of patients in the current study with the exception of higher stage cancer patients that would require external beam radiation regardless based on NCCN criteria.

Cosmetic Outcome

The cosmetic benefits of skin-sparing mastectomy and immediate autologous reconstruction are undeniable. Through re-excision of positive margins, the cosmetic advantage of immediate reconstruction may be maintained (Figures 1-2). However, thinning of mastectomy skin flaps during margin re-excision could lead to contour irregularities detracting from the ultimate cosmetic outcome. In our series, this was not observed following margin re-excision with liberal utilization of fat grafting at the time of breast revision and nipple reconstruction. The long-term cosmetic sequela following margin re-excision was analyzed by comparing the oncologically affected breast with the contralateral breast reconstruction. Evaluating all bilateral reconstruction patients (n = 30), including 7 patients that required postreconstruction external beam radiation, blinded evaluators did not perceive significant differences between reconstructed breasts that underwent margin re-excision compared to those that did not (Table 12). This underscores the minimal, if any, detrimental long-term cosmetic effects of re-excision procedures, which facilitates patient counseling and reassurance.

CONCLUSION

Identification of positive postmastectomy margins in the setting of immediate breast reconstruction represents a therapeutic dilemma for both the oncologic and reconstructive surgeon. In order to minimize the necessity of postmastectomy radiation, margin re-excision is recommended with close collaboration with breast surgeons and pathologists. The findings of this study suggest margin re-excision may be performed safely with acceptable flap site morbidity while optimizing cosmetic outcomes.

Disclosures

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

Funding

The authors received no financial support for the research, authorship, and publication of this article.

REFERENCES

1. Singletary SE. Surgical margins in patients with early-stage breast cancer treated with breast conservation therapy. *Am J Surg*. 2002;184(5):383-393.
2. Munhoz AM, Montag E, Arruda E, et al. Immediate reconstruction following breast-conserving surgery: management of the positive surgical margins and influence on secondary reconstruction. *Breast*. 2009;18(1):47-54.
3. Aziz D, Rawlinson E, Narod SA, et al. The role of reexcision for positive margins in optimizing local disease control after breast-conserving surgery for cancer. *Breast J*. 2006;12(4):331-337.
4. 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):145-149.
5. Rowell NP. Are mastectomy resection margins of clinical relevance? A systematic review. *Breast*. 2010;19(1):14-22.
6. Truong PT, Olivotto IA, Speers CH, Wai ES, Berthelet E, Kader HA. A positive margin is not always an indication for radiotherapy after mastectomy in early breast cancer. *Int J Radiat Oncol Biol Phys*. 2004;58(3):797-804.
7. Yu J, Al Mushawah F, Taylor ME, et al. Compromised margins following mastectomy for stage I-III invasive breast cancer. *J Surg Res*. 2012;177(1):102-108.
8. Vaughan A, Dietz JR, Aft R, et al. Scientific Presentation Award. Patterns of local breast cancer recurrence after skin-sparing mastectomy and immediate breast reconstruction. *Am J Surg*. 2007;194(4):438-443.
9. Childs SK, Chen YH, Duggan MM, et al. Surgical margins and the risk of local-regional recurrence after mastectomy without radiation therapy. *Int J Radiat Oncol Biol Phys*. 2012;84(5):1133-1138.
10. Behm EC, Beckmann KR, Dahlstrom JE, et al. Surgical margins and risk of locoregional recurrence in invasive breast cancer: an analysis of 10-year data from the Breast Cancer Treatment Quality Assurance Project. *Breast*. 2013;22(5):839-844.
11. Freedman GM, Fowble BL, Hanlon AL, et al. A close or positive margin after mastectomy is not an indication for chest wall irradiation except in women aged fifty or younger. *Int J Radiat Oncol Biol Phys*. 1998;41(3):599-605.
12. Chan LW, Rabban J, Hwang ES, et al. Is radiation indicated in patients with ductal carcinoma in situ and close or positive mastectomy margins? *Int J Radiat Oncol Biol Phys*. 2011;80(1):25-30.

13. Sheikh F, Rebecca A, Pockaj B, et al. Inadequate margins of excision when undergoing mastectomy for breast cancer: which patients are at risk? *Ann Surg Oncol*. 2011;18(4):952-956.
14. Tran NV, Chang DW, Gupta A, Kroll SS, Robb GL. Comparison of immediate and delayed free TRAM flap breast reconstruction in patients receiving postmastectomy radiation therapy. *Plast Reconstr Surg*. 2001;108(1):78-82.
15. Rogers NE, Allen RJ. Radiation effects on breast reconstruction with the deep inferior epigastric perforator flap. *Plast Reconstr Surg*. 2002;109(6):1919-1924; discussion 1925.
16. Chang EI, Liu TS, Festekjian JH, et al. Effects of radiation therapy for breast cancer based on type of free flap reconstruction. *Plast Reconstr Surg*. 2013;131;1e-8e.
17. Albino FP, Koltz PF, Ling MN, Langstein HN. Irradiated autologous breast reconstructions: effects of patient factors and treatment variables. *Plast Reconstr Surg*. 2010;126(1):12-16.
18. Garvey PB, Clemens MW, Hoy AE, et al. Muscle-sparing TRAM flap does not protect breast reconstruction from postmastectomy radiation damage compared with the DIEP flap. *Plast Reconstr Surg*. 2014;133(2):223-233.
19. National Comprehensive Cancer Network. *NCCN Guidelines for Treatment of Breast Cancer*. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp#site. Accessed September 29, 2016.
20. Cao D, Tsangaris TN, Kouprina N, et al. The superficial margin of the skin-sparing mastectomy for breast carcinoma: factors predicting involvement and efficacy of additional margin sampling. *Ann Surg Oncol*. 2008;15(5):1330-1340.
21. Jagsi R, Raad RA, Goldberg S, et al. Locoregional recurrence rates and prognostic factors for failure in node-negative patients treated with mastectomy: implications for postmastectomy radiation. *Int J Radiat Oncol Biol Phys*. 2005;62(4):1035-1039.
22. Katz A, Strom EA, Buchholz TA, Theriault R, Singletary SE, McNeese MD. The influence of pathologic tumor characteristics on locoregional recurrence rates following mastectomy. *Int J Radiat Oncol Biol Phys*. 2001;50(3):735-742.
23. Hastings J, Iganej S, Huang C, Huang R, Slezak J. Risk factors for locoregional recurrence after mastectomy in stage T1 N0 breast cancer. *Am J Clin Oncol*. 2014;37(5):486-491.
24. Kim JH, Tavassoli F, Haffty BG. Chest wall relapse after mastectomy for ductal carcinoma in situ: a report of 10 cases with a review of the literature. *Cancer J*. 2006;12(2):92-101.
25. Montgomery R, Fowble B, Goldstein L, et al. Local recurrence after mastectomy for ductal carcinoma in situ. *Breast J*. 1998;4:430-436.
26. Silverstein MJ, Lagios MD, Martino S, et al. Outcome after invasive local recurrence in patients with ductal carcinoma in situ of the breast. *J Clin Oncol*. 1998;16(4):1367-1373.
27. Ochoa O, Chrysopoulo M, Nastala C, Ledoux P, Pisano S. Abdominal wall stability and flap complications after deep inferior epigastric perforator flap breast reconstruction: does body mass index make a difference? Analysis of 418 patients and 639 flaps. *Plast Reconstr Surg*. 2012;130(1):21e-33e.