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Successful Immediate Staged Breast Reconstruction with Intermediary Autologous Lipotransfer in Irradiated Patients

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Background: As indications for radiotherapy in mastectomized patients grow, the need for greater reconstructive options is critical. Preliminary research suggests an ameliorating impact of lipotransfer on irradiated patients with expander-to-implant reconstruction. Herein, we present our technique using lipotransfer during the expansion stage to facilitate implant placement.

Methods: A retrospective review of postmastectomy patients with expander-to-implant reconstruction by one reconstructive surgeon was performed. All patients were treated with immediate expander and ADM placement at the time of mastectomy. Irradiated patients underwent a separate lipotransfer procedure after completion of radiotherapy but prior to prosthesis exchange. Our study compared postoperative outcomes between non-radiated patients and irradiated patients who underwent this intermediary lipotransfer. Clinical endpoints of interest included: overall complications, infection, delayed wound healing, dehiscence, capsular contracture, implant failure, and reoperation.

Results: One hundred and thirty-one breast reconstructions were performed; 18 (13.74%) were irradiated and 113 (86.26%) were not. Overall complication risk (infection, implant failure, or reoperation) was no higher in irradiated breasts treated with lipotransfer than non-irradiated breasts (p=0.387). Fifteen patients who had one radiated and one non-radiated breast were separately analyzed; no difference in complication by radiotherapy exposure (p=1) was found. Age, BMI, smoking status, and nipple-sparing versus skin-sparing mastectomy did not vary significantly between study groups (p=0.182, p=0.696, p=0.489, p=1 respectively).

Conclusions: Comparable postoperative outcomes were found between non-radiated breasts and radiated breasts treated with intermediary lipotransfer. The ameliorating effects of autologous lipotransfer on radiotoxicity may therefore offer irradiated patients the option of expander-to-implant reconstruction with acceptable risk and cosmesis. *(Plast Reconstr Surg Glob Open 2019;7:e2398; doi: 10.1097/GOX.0000000000002398; Published online 30 September 2019.)*

INTRODUCTION

With breast cancer rates continuing to rise,[1] more women are subject to mastectomy and subsequent reconstruction than ever before.[2] As such, identifying ways to optimize patients' reconstructive outcomes is paramount. Despite staged implant-based procedures being the predominant form of breast reconstruction,[3,4] these surgeries remain procedurally challenging when radiotherapy is part of the patient's oncologic treatment regimen.[5,6]

Wide variation exists in centers' use of radiotherapy for breast cancer, with some applying it to >70% of their patients.[1,7] Radiotherapy indications for breast cancer have increased,[8–12] as illustrated in the Early Breast Cancer

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Trialists' Collaborative Group meta-analysis, which found that postmastectomy radiation decreased the 10-year risk of breast cancer recurrence and the 20-year breast cancer mortality rate.[13,14]

In contrast to the benefits of radiation, higher surgical risks are associated with irradiated tissue.[15–17] Breast reconstructive outcomes are often poorer in irradiated patients as evidenced by increased risk of infection, capsular contracture, implant exposure, and reconstructive failure.[18–28] Radiation's deleterious impact on expander-to-implant breast reconstruction is especially pronounced[29] with reported complication rates as high as 68%.[30] Jagsi et al[31] evaluated 2,247 patients (622 with and 1,625 without radiation) prospectively amassed via the Mastectomy Reconstruction Outcomes Consortium study. The highest breast complication rate (38.9%) and reconstructive failure rate (18.7%) were seen in irradiated patients with implant-based reconstructions. Breast radiation is further associated with reduced quality-of-life parameters and diminished patient satisfaction.[31–33]

Based on these findings, irradiated patients are generally deemed poor candidates for prosthesis-based breast reconstruction.[5,19,21,34] Several recent studies, however, have challenged this notion by introducing strategies to improve outcomes in this patient population.[18,35–38] Some strategies include delaying the expander-to-implant exchange procedure for at least 6 months postradiotherapy completion,[39] using a counter incision at the IMF,[40] utilizing acellular dermal matrices (ADM),[39,41] and, most recently, introducing autologous fat to improve outcomes.[42–44]

Wide variability exists in the management of patients undergoing implant-based breast reconstruction who require radiotherapy.[45–47] Inconsistent findings are reported with respect to optimal timing of radiotherapy: be it after tissue expansion, during the process of capsule formation, or after implant placement.[24,48–54] When radiation is applied during tissue expansion, variation in methodology for addressing the expander fill is also observed.[22,55] Some data suggest poorer outcomes in irradiated tissue with expander deflation.[56] Other authors recommend expander deflation, arguing that partially/fully inflated expanders may interfere with beam geometry and, thus, hinder radiation delivery.[57,58] An emerging study compared the efficacy of radiation delivered to the chest wall, skin, and surrounding tissues with expanders at full expansion, 50% expansion, and full deflation.[59] The authors found that expanders in a fully inflated state offered the best delivery of radiation to targeted tissue with decreased toxicity.

Since its first recorded debut in 1893,[60] lipotransfer procedures have evolved significantly via atraumatic techniques developed by Coleman et al[61–64] and the advent of fat transfer systems that permit rapid harvesting and processing of large fat volumes.[65,66] The benefits of fat grafting to treat a variety of conditions are well represented in the literature.[67–70] A substantial body of evidence also supports human adipose tissue as being a substantial source of stem cells.[71–75] Several investigations have suggested that adipose tissue promotes angiogenesis and healthy tissue formation via the mobilization of stem cells and the secretion of various growth factors.[64,76–78]

Lipotransfer has now extended into the treatment of radiation-induced tissue damage. The loss of regenerative cells is thought to be the main reason for the late effects of radiotherapy.[79] Fibrosis ensues as the irradiated skin develops a denser collagen content.[80,81] The application of human fat to irradiated murine tissue has demonstrated decreased dermal thickness, reduced collagen content, increased vascular density, and improved fat graft retention.[82,83]

Investigations have since emerged describing the ameliorating effect of fat grafting on irradiated human tissue. Autologous lipotransfer has been used to facilitate reconstructions involving radiated tissue within the orbit, head and neck, and lower extremity.[84–86] These studies suggest that lipotransfer can decrease radiotoxicity and prime soft tissues for reconstruction in the setting of radiation.

Lipotransfer to reconstructed breasts is a technique that has enjoyed increased popularity in recent years for creating a more natural-appearing breast.[87] It is most often performed as a revisionary procedure, after the permanent implant is in position, to address contour irregularities or asymmetries.[41] Although lipofilling is traditionally and frequently the final step in the reconstructive process, lipotransfer after radiation but before implant placement has only sporadically been reported[42,44] and not currently standard practice.

Our 3-stage approach was modeled on the best available evidence for mitigating radiotoxicity via lipotransfer.[42–44,79,88–90] The hallmarks of our algorithm included the use of ADM, maintenance of the expander in a fully inflated position during radiation, delay of the expander-to-implant procedure for 6+ months after radiotherapy completion, the use of a counter-incision at the IMF in cases of skin-sparing mastectomy (SSM), and performance of a separate surgery whereby autologous fat was transferred to the radiated breast before the final exchange. The goal of our study was to evaluate our 3-stage protocol in patients undergoing immediate breast reconstruction who desired implant-based techniques in the setting of postmastectomy radiation.

PATIENTS AND METHODS

Following Institutional Review Board approval, we performed a retrospective review of a prospectively maintained database of mastectomized patients with breast reconstruction. Eligibility criteria for inclusion into our study were consecutive female breast cancer patients who underwent SSM or nipple-sparing mastectomy and opted for immediate, postmastectomy, expander-to-implant breast reconstruction. Only patients with a minimum of 4 months of follow-up were included in the study. Included in our study were only patients who had reconstruction with tissue expander placement in a partial subpectoral plane with ADM utilized for soft tissue reinforcement of the lower pole. Surgeries were performed between August 28, 2014, and March 29, 2018, by one reconstructive surgeon at 4 community hospitals. Exclusion criteria were women with ADM and TE placement but who ultimately chose free tissue transfer.

Patients were separated by those requiring postmastectomy radiation and those who did not. Patients not requiring radiation underwent expansions beginning 2 weeks after their index surgery and were deemed ready for expander-to-implant exchange at least 4 months after their index surgery. Patients who required radiotherapy underwent expansions as per their nonradiated counterparts. Patients with unilateral mastectomy were radiated with their tissue expander fully inflated. Patients with bilateral mastectomy were also radiated with their expander fully inflated on the cancer side; however, their expander on the non-cancer side was deflated to assist with radiation delivery and to reduce intrathoracic toxicity.

Patients were seen midway through their radiation course and 1 week after radiotherapy completion. External beam radiation was uniformly used in our patient population (Fig. 1). At this latter visit, bilateral mastectomized patients began re-expansion of their tissue expander on the non-cancer side. A separate procedure of autologous lipotransfer was performed no sooner than 3 months following radiotherapy completion (Fig. 2). During this fat grafting procedure, expander volume (ranging from 0 to 90 ml) was removed to alleviate tension off the skin envelope and accommodate the transferred fat. We typically did not reinflate because the amount of transferred fat always exceeded the amount of fluid removed. After an additional 3 months, patients were deemed ready for expander-to-implant exchange. During the exchange procedure, a counter-incision within the inframammary-fold was made in SSM patients; nipple-sparing mastectomized patients underwent incision through their previous IMF scars. Three irradiated patients are shown in Figures 1–3. Our treatment protocol is diagramed in Figure 4.

Data were gathered from electronic medical records and a prospectively maintained patient database. Demographic data collected on all patients included age, body mass index (BMI), smoking status, diabetes mellitus, pre-/postmastectomy radiation, pre-/postmastectomy chemotherapy, expander fill volume, breast surgeon, and hospital in which the mastectomy and reconstruction took place. Reconstruction procedure data included dates of surgeries, number of fat grafting procedures, and number of revisions.

Our primary outcome of interest was the presence of any complication. Specific clinical endpoints examined were infection (major and minor), skin necrosis (major and minor), seroma, hematoma, device failure requiring explantation, number of postoperative nights in the hos-

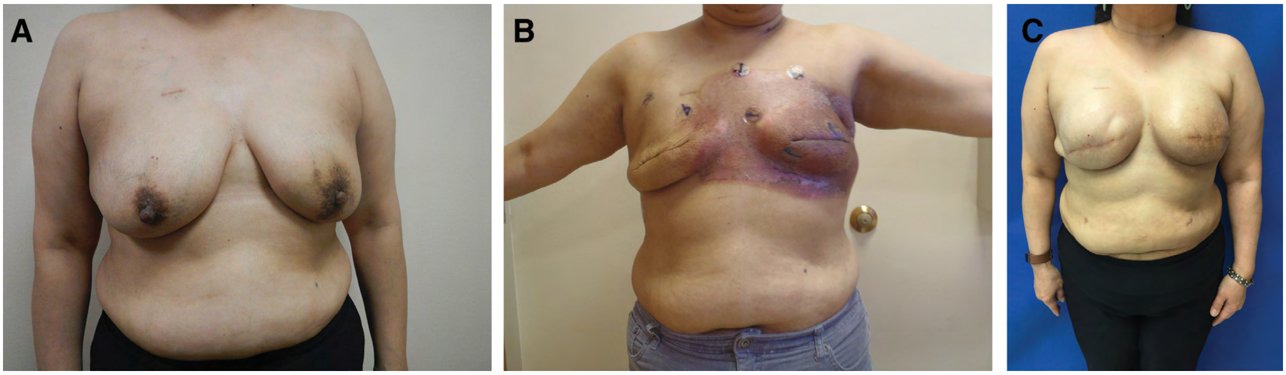

Fig. 1. Three cases of irradiated mastectomized patients who underwent autologous lipotransfer and staged breast reconstruction. A, Before bilateral mastectomy and 6 weeks after attempted lumpectomy with positive margins. B, Ten weeks status-post bilateral mastectomy with immediate TE placement and halfway through radiotherapy regime, with severe radiodermatitis. C, Twenty-two months following expander-to-implant exchange.

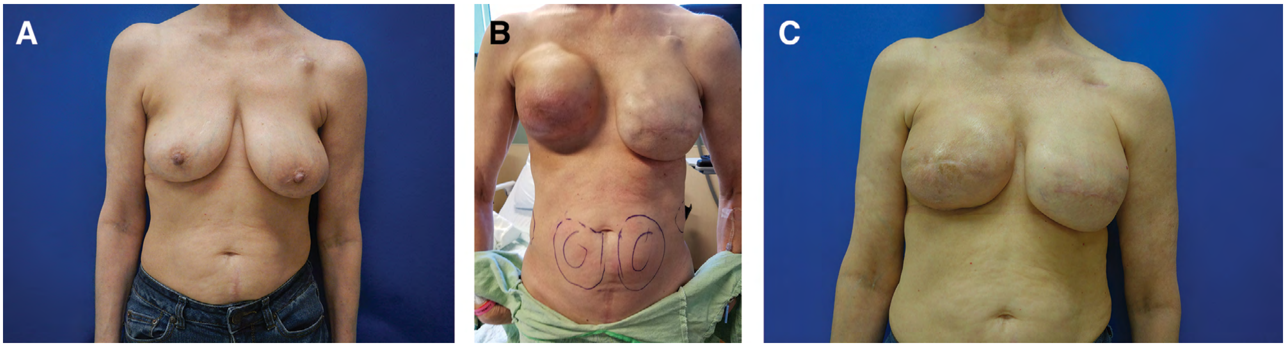

Fig. 2. Three cases of irradiated mastectomized patients who underwent autologous lipotransfer and staged breast reconstruction. A, Newly diagnosed right breast cancer before bilateral mastectomy. B, Five months after bilateral mastectomy with immediate TE placement and 3 months after radiotherapy completion, photograph taken on the day of lipotransfer surgery with markings for fat harvest from abdomen. C, Seven months following lipotransfer to right breast and 4 months post expander-to-implant exchange.

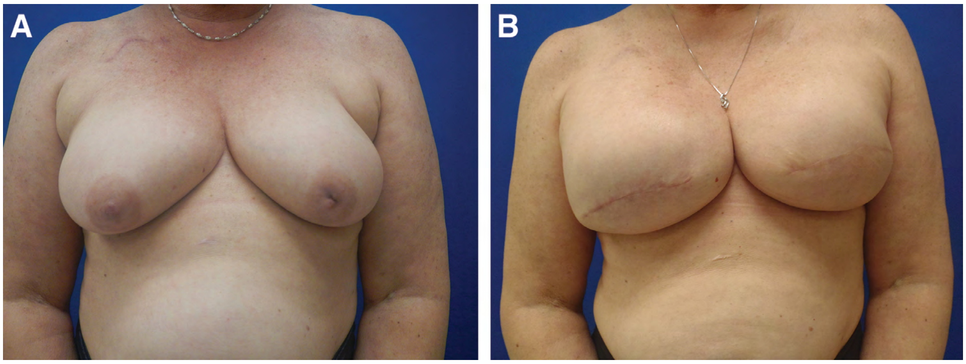

Fig. 3. A case of an irradiated mastectomized patient who underwent autologous lipotransfer and staged breast reconstruction. A, Newly diagnosed left breast cancer before bilateral mastectomy. B, Six months after completion of expander-to-implant reconstruction, near-normal skin coloration and character noted. Patient previously underwent radiation of left breast, followed 3 months later by lipotransfer to irradiated side, and expander-to-implant exchange performed after 3 additional months.

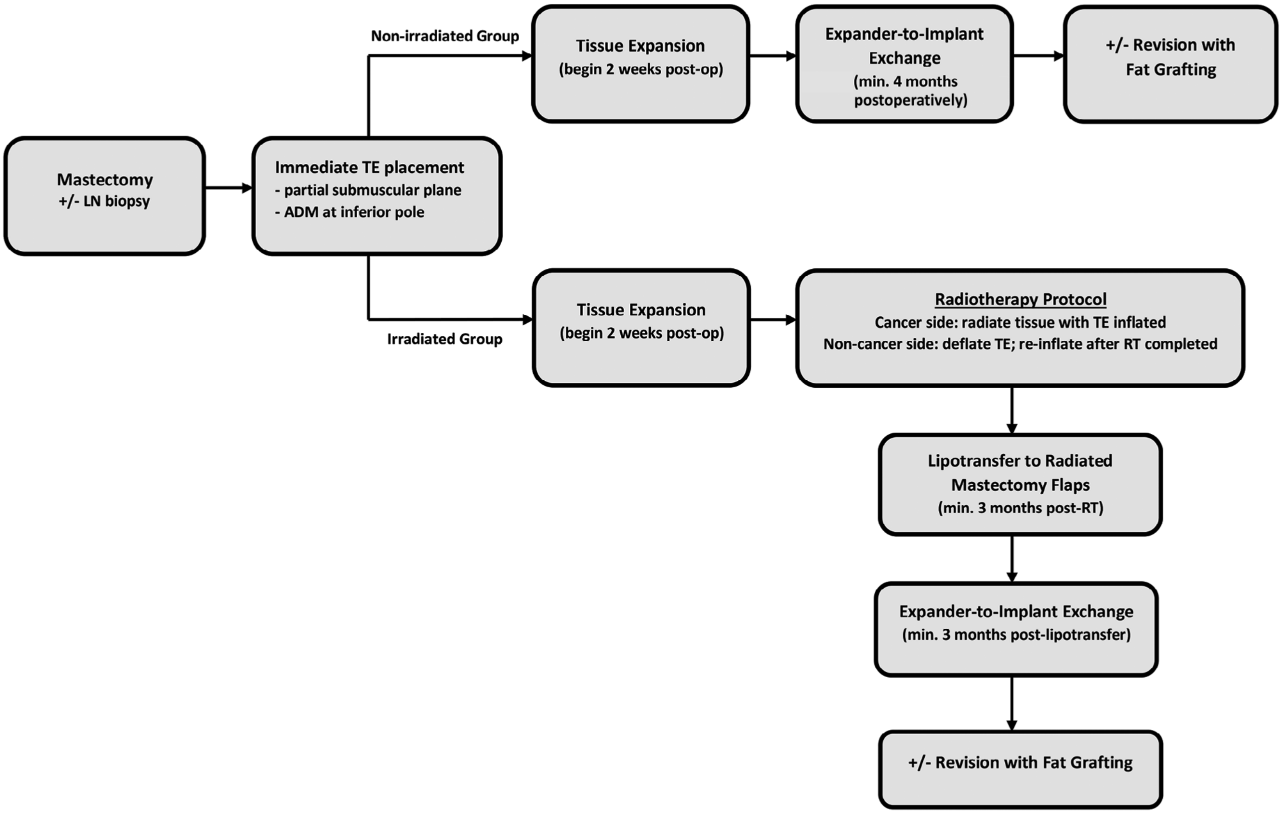

Fig. 4. Treatment protocol.

pital, need to increase antibiotics, readmission to the hospital, and reoperation.

For patients with infections, minor infections were defined as patients who presented with erythematous areas treatable with oral antibiotics on an outpatient basis. Major infections were defined as those requiring intravenous antibiotics and/or admission to the hospital, including patients who failed reconstruction due to infection. Mastectomized patients who suffered from skin necrosis during the expansion stage were further broken down into subgroups of minor and major skin necrosis. Minor skin necrosis was defined as being treatable on an outpatient basis with resolution occurring via local wound care alone. Major skin necrosis was defined as any amount of skin necrosis requiring surgical excision and secondary closure and those severe enough to prompt treatment with hyperbaric oxygen therapy. Obesity was defined as a BMI >30. Smoking was defined as any tobacco use within 1 year of surgery.

Statistical Analysis

The data were analyzed by breast, assuming each breast was independent. Irradiated and nonirradiated breasts were compared using Fisher's exact test for the categorical comparisons of nipple-sparing mastectomy versus SSM, smoking status, and any complication (defined as the presence of any of the following: infection, dehiscence, reoperation, implant failure, or capsular contracture). Unpaired *t* tests were used to compare the study groups by age and BMI. An additional analysis was performed using only the patients with 1 irradiated and 1 nonirradiated breast, using the same methods as the full sample.

RESULTS

One hundred thirty-one breast reconstructions were performed: 18 (13.74%) were irradiated and 113 (86.26%) were not. Age (t = 1.375; P = 0.182), BMI (t = 0.396; P = 0.696), smoking status (P = 0.489), and nipple-sparing mastectomy versus SSM (P = 1) did not vary significantly between study groups (Table 1). The dose of radiation administered to our patients ranged from 4,600 to 5,040 cGy. Two patients received 4,600 cGy, followed by 5,040 cGy. Eleven patients received 5,040 cGy. The remainder of patients received 5,000 cGy. Ten patients received a boost dose of 1,000 cGy. One patient received a boost dose of 800 cGy.

The average follow-up time for the radiated group was 6.29 months. The average follow-up time for the nonradiated group was 9.74 months. The amount of fat transferred ranged from 45 to 153 ml. Overall complication risk (infection, implant failure, or reoperation) was no higher in irradiated breasts treated with lipotransfer than nonirradiated breasts (P = 0.387). Table 2 reports all complication rates by breast radiation for the full sample. Fifteen patients acting as internal controls due to having 1 radiated and 1 nonradiated breast were separately analyzed. No difference in complication by radiotherapy exposure (P = 1) was found (Table 3).

DISCUSSION

We observed promising outcomes of expander-to-implant reconstruction with lipotransfer performed as a separate, intermediary procedure. Our protocol resulted in complication rates equivalent to those seen in patients not requiring radiation. In patients who did experience complications, we believe that additional examination

Table 1. Patient Demographics and Risk Factors

	Total No. Patients (n = 131)	Nonirradiated (n = 113; 86.26%)	Irradiated* (n = 18; 13.74%)	*P*
Categorical variables, n (%)				
SSM	114 (87.02)	98 (86.73)	16 (88.89)	1†
NSM	17 (12.98)	15 (13.27)	2 (11.11)	1†
Smoking	21 (16.03)	17 (15.04)	4 (22.22)	0.489†
Continuous variables, mean (SD)				
Age	—	48.85 (10.35)	52.22 (9.51)	0.182‡
BMI	—	27.18 (7.27)	27.84 (6.47)	0.696‡

*External beam radiation; doses ranged from 4,600 to 5,040 cGy.
†Categorical *P* values were derived using Fisher's exact test.
‡Continuous *P* values were derived using unpaired *t* tests.
SSM, skin sparing mastectomy; NSM, nipple sparing mastectomy; BMI, body mass index.

Table 2. Patient Outcomes

	Total No. Patients (n = 131)	Nonirradiated (n = 113; 86.26%)	Irradiated (n = 18; 13.74%)	*P**
Categorical variables, n (%)				
Complications (any)	13 (9.92)	10 (8.84)	3 (16.67)	0.387
Infection	2 (1.53)	2 (1.77)	0 (0)	1
Dehiscence	5 (3.82)	3 (2.65)	2 (11.11)	0.139
Reoperation	11 (8.39)	8 (7.08)	3 (16.67)	0.177
Implant failure	4 (3.05)	3 (2.65)	1 (5.56)	0.451
Capsular contracture	4 (3.05)	3 (2.65)	1 (5.56)	0.451

*Categorical *P* values were derived using Fisher's exact test.

Table 3. Patient Outcomes of Internal Controls

	Total No. Patients (n = 30)	Nonirradiated (n = 15; 50%)	Irradiated (n = 15; 50%)	*P**
Categorical variables, n (%)				
Complications (any)	5 (16.67)	2 (13.33)	3 (20)	1
Infection	0 (0)	0 (0)	0 (0)	—
Dehiscence	3 (10)	1 (6.67)	2 (13.33)	—
Reoperation	5 (16.67)	2 (13.33)	3 (20)	—
Implant Failure	1 (3.33)	0 (0)	1 (6.67)	—
Capsular Contracture	2 (6.67)	1 (6.67)	1 (6.67)	—

*Categorical *P* values were derived using Fisher's exact test.

of their cases is warranted. Our one case of implant failure occurred 7 months after the exchange procedure in a patient with tobacco use. This patient had a persistent open wound along her mastectomy incision (not along the counter-incision at the IMF). Owing to this chronic wound, her procedures were performed sooner than that typified by our protocol in an attempt to salvage the reconstruction. Her wound was present before radiotherapy with tenuous healing recurring almost immediately after intermediary lipotransfer. Despite conservative management with dressing changes, her wound progressed, so the decision was made to complete her exchange procedure at approximately 1.5 months postlipotransfer. During the exchange surgery, we also performed a wound excision and reclosure. The wound ultimately recurred with subsequent infection, implant exposure and removal 8 months later. The patient received a latissimus dorsi flap with expander-to-implant exchange. Of note, her nonradiated side suffered a very similar complication 8 months after her exchange procedure; this side was salvageable with implant exchange, wound excision, and reclosure. This particular case prompted modification of our patient selection criteria; going forward, we excluded from our protocol any patients with wound healing complications. In salvage situations, we believe that the chance of success is compromised and heavy consideration for autologous options should be given.

Our patient population also demonstrated one additional case of reoperation following the exchange procedure. This patient had undergone NSM, so a counter-incision was not able to be performed as the mastectomy was performed via an IMF incision during the index surgery. She was the first patient to complete our 3-stage reconstruction, and, during the expander-to-implant surgery, additional lipotransfer was performed. This appeared to strain the skin envelope when the implant was placed. At her reoperation, the implant was exchanged for a slightly smaller device and the patient went on to heal completely. Since this case, we discontinued concomitant fat grafting at the time of exchange, instead proceeding with implant placement followed by revision fat grafting at a later date (if necessary). After instituting this change to our protocol, we no longer encountered incisional dehiscence issues.

Although infrequently encountered, complications of autologous fat grafting do arise.[91] Graft longevity is variable and resorption fluctuates with a patient's weight, which may necessitate additional procedures with attendant clinical risk. Although fat retention is seemingly better at higher injected volumes,[92] this must be balanced with excessive lipofilling causing increased fat necrosis and mastectomy flap tension. Fat necrosis can present as palpable masses leading to unwarranted patient concern, clinical workup, and interference with diagnostic imaging.[93]

Further investigations of the biomolecular impact of fat grafting upon irradiated breast tissue would be useful. A predominance of inflammatory cells and fibroblast-like cells have been observed in breast capsules contracted postradiotherapy.[94,95] Yet, some studies have shown that adipose-derived stem cells can also promote dermal fibroblast proliferation.[96,97] Given the array of these histologic findings, it remains elusive how fat grafts improve both fibrosis and capsular contracture. Additional research is needed to elucidate the mechanisms underlying the effects of autologous lipotransfer.

Ours is not the first study to examine the role of autologous lipotransfer in salvaging implant-based reconstruction for patients who have undergone mastectomy followed by radiation. Some studies have shown the beneficial effect of lipotransfer on previously irradiated tissue in reviving damaged skin envelopes after completed reconstruction or before the expander was even attempted.[79,88–90] Our technique differs in that our aim was to prevent radiotoxicity symptoms and clinical complications at the time of prosthesis exchange while still proceeding with immediate mastectomy reconstruction. This strategy is similar to that by Ribuffo et al[43] who reported a 0% complication rate for 16 mastectomized patients who underwent lipotransfer during their tissue expansion stage.[44] A strength of their study was their control group of 16 mastectomized, irradiated patients without lipofilling. Five control cases developed ulceration leading to implant extrusion (31.25%) and 2 cases exhibited Baker 4 capsular contracture (12.5%). Their study differs from ours in that the authors only analyzed patients who underwent modified radical mastectomies, they did not utilize ADM in their protocol, and patients underwent 1–2 fat grafting procedures 6 weeks after the completion of radiotherapy.

Expanding this concept further, Serra-Renom et al[42] described their protocol of serial fat grafting during expander-to-implant reconstruction of 65 mastectomized, irradiated patients. The authors contend that introducing lipoaspirate at each stage of surgical intervention allowed them to create a new plane of subcutaneous tissue. No complications from fat grafting were reported in their 1-year follow-up period. This investigation was weakened by the absence of a control group who did not undergo radiation and lack of analyses demonstrating a statistically significant reduction in complications using their described protocol. Importantly, the studied patient population had no signs of radiodermatitis or radionecrosis, so the efficacy of their algorithmic approach for patients with radiation-induced damage remains unknown.

Limitations of our study include (1) lack of a control group consisting of irradiated patients who underwent expander-to-implant breast reconstruction without lipofilling; (2) small sample size; (3) consistency of skin flaps (even among internal controls as skin flaps were not formally assessed); (4) additional surgery necessitated by our 3-stage algorithm; and (5) our retrospective study design which precludes random, independent assignment.

Notwithstanding, the ameliorating influence of lipotransfer in irradiated tissue is an exciting prospect, particularly for implant-based reconstructions, as it affords irradiated mastectomized patients' increased reconstruction choices. This is useful as flap-based reconstructions are not always feasible and radiotherapy is not always predictable. Finally, expanding indications for radiotherapy will necessitate more efficacious treatment of irradiated tissue.

CONCLUSIONS

Radiation-induced tissue damage poses a challenge for the reconstructive surgeon, especially in the setting of postmastectomy prosthesis-based procedures. There is increasing evidence that fat grafting has beneficial effects on radiated tissue. Our investigation demonstrated encouraging results when autologous lipotransfer was used in facilitating staged expander-to-implant breast reconstructions in irradiated mastectomized patients. Although limited in terms of samples size, we believe this work to be important as it contributes to a growing body of literature that will potentially advance our ability to salvage breast tissue and foster a wider range of reconstructive options for irradiated postmastectomy patients.

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