




Simultaneous Fat Grafting During Tissue Expander-to-Implant Exchange: A Propensity Score-Matched Analysis

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Abstract

Background Implant-based breast reconstruction (IBBR) is the most common technique for breast reconstruction. The primary resource for correcting deformities, once patients have achieved an adequate volume with two-stage IBBR, is autologous fat grafting. We compared the surgical outcomes of simultaneous fat grafting during TE-to-implant exchange (SFG + TtIE) versus no fat grafting during TE-to-implant exchange (No-FGX).

Methods A retrospective review was performed of all consecutive patients undergoing two-stage implant-based breast reconstruction with TE from January 2011 to December 2020. Propensity score matching was implemented to optimize comparability. The control group did not receive fat grafting at the time of TE-to-implant exchange.

Results After propensity score matching, 196 reconstructions were evaluated, 98 in each group. Reconstructions in the SFG + TtIE received larger implants during exchange in comparison with the No-FGX group (539 ± 135.1 -cc versus 495.97 ± 148 -cc, $p=0.035$). The mean volume of fat lipoinjected during TE-to-implant exchange in the SFG + TtIE group was 88.79 ± 41 -ml. A higher

proportion of reconstructions in the SFG + TtIE group underwent additional fat grafting after exchange versus the No-FGX group (19% versus 9%, $p = 0.041$). After propensity score matching, only the rate of fat necrosis after exchange was significantly higher in the SFG + TtIE group (10% versus 2%, $p = 0.017$). The rate of breast cancer recurrence (3% versus 5%, $p = 1.00$) was comparable between the groups.

Conclusion SFG + TtIE is a safe procedure to improve the envelope of reconstructed breasts during two-stage IBBR. SFG + TtIE does not increase the rate of periprosthetic infection or wound-related complication versus no fat grafting during TE-to-implant exchange, but increases the rate of fat necrosis.

Level of Evidence III Therapeutic study. This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266

Keywords Breast implantation · Tissue expansion devices · Female · Postoperative complications · Treatment outcome

This article has not been presented in a national or international meeting.

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Introduction

Among all of the innovative techniques available to provide breast restoration after mastectomy, most patients elect to pursue implant-based breast reconstruction (IBBR) [1–3]. This can be accomplished with two-stage reconstruction with tissue expander (TE) followed by exchange for definitive implant or with direct-to-implant reconstruction in a single stage, the former being the most

popular in the U.S.A. [1–3]. By definition, a two-stage reconstruction requires an additional planned operation in which a permanent implant is placed after the expansion process has completed. During exchange, surgeons can not only modify the conus of the breast by inserting a larger or smaller sized implant but can also revise the breast footprint and envelope with a variety of procedures to optimize the esthetic outcomes of the reconstruction (e.g., capsulorrhaphy, dog ear excision, capsulectomy, advancement of capsular flaps, nipple reconstruction, etc.).

Fat grafting, also known as lipotransfer, is frequently performed as an adjunct to enhance the esthetic results and tissue quality of breast reconstruction [4]. In recent studies, fat grafting has shown the potential to reverse fibrosis secondary to postmastectomy radiation (PMRT) [5], and to improve sensation and pain when treating capsular contracture [6]. In the appropriate patients, simultaneous fat grafting during TE-to-implant exchange (SFG + TtIE) may be attempted in order to achieve optimal results more expeditiously, thereby avoiding revision procedures and their associated risks. SFG + TtIE incorporates a three-dimensional approach for the arrangement of the injected fat. In this setting, the mature capsule formed around the TE plays an important role as it defines the compliance and elasticity of the internal limit of the mastectomy flap [4].

Augmentation of the mastectomy flaps with autologous fat is usually achieved with various sessions of fat grafting after exchange with minimal complications [4]. However, when performed during TE-to-implant exchange, the amount of fat lipoinjected can increase the pressure within the mastectomy flap, compromising the perfusion to the periphery of the breast or incision site. Therefore, it is possible that SFG + TtIE may alter the ability of tissue to heal or increase the risk of infection after permanent implant placement. SFG + TtIE is not an uncommon procedure. Nonetheless, previous reports have not evaluated the impact and rate of complications associated with lipofilling of the mastectomy flap at the time of exchange. The aim of this study was to compare the rate of complications and the rate of additional fat grafting procedures between reconstructions that underwent SFG + TtIE and reconstructions that did not undergo fat grafting at the time of exchange (No-FGX).

Patients and Methods

Study Design

After approval by the institutional review board at a single large academic medical center, a retrospective review was performed of all consecutive patients undergoing two-stage IBBR with TE from January 2011 to December 2020.

Patients who did not undergo TE-to-implant exchange or abandoned IBBR during the first stage were excluded. Patients who underwent hybrid immediate reconstruction with autologous tissue during TE insertion or during TE-to-implant exchange were excluded (e.g., implant-enhanced latissimus dorsi flap). Patients undergoing direct-to-implant reconstruction and patients who had incomplete data were also excluded.

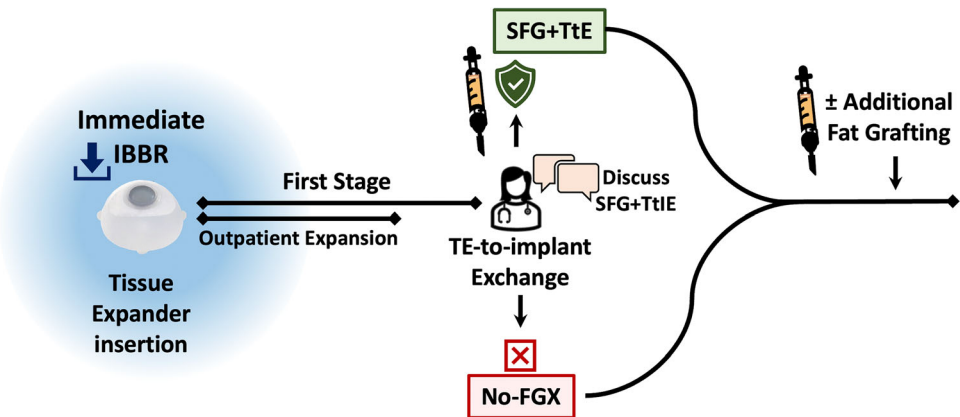
Patients were subsequently divided into two groups by the surgical method implemented during TE-to-implant exchange (Fig. 1): The intervention group comprised reconstructions that underwent SFG + TtIE, while the control group comprised reconstructions that did not undergo fat grafting during exchange (No-FGX). The decision to perform either technique was based on the surgeon's preference and after counseling with the patient. When an acellular dermal matrix (ADM) was used, the TE was either completely wrapped for a prepectoral device placement or partially wrapped along the inferior portion for submuscular reconstruction [7]. The surgical technique for a subpectoral or prepectoral approach has been previously reported [3, 7–9].

For SFG + TtIE, we proceeded with fat harvest via suction lipectomy after tumescent infiltration. Fat was collected into injection syringes. Once the TE was explanted, capsulotomies, advancement of capsular flaps, and/or capsulorrhaphy sutures with PDS were performed as necessary. Sizers were opened and placed into the pocket. If the breast size was deemed appropriate with an optimal shape, contour, and good symmetry, fat was injected in the marked areas. Sizers were removed and the pockets were once again irrigated with antiseptic solution. The final implants were placed into the breast pockets afterward.

Study Variables

We recorded the following demographic and clinical variables of interest: the patient's age at the time of reconstruction; body mass index (BMI); race/ethnicity; history of hypertension and diabetes; smoking status; breast cancer diagnosis and staging, including tumor and node status; estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) status; follow-up; history of breast irradiation and chemotherapy; indication of mastectomy (therapeutic/prophylactic); type of mastectomy (nipple-sparing mastectomy, NSM; skin-sparing mastectomy, SSM); laterality of breast reconstruction (right/left); type of procedure (bilateral/unilateral); timing of TE placement (immediate/delayed); weight of mastectomy specimen; plane of implant placement (prepectoral/submuscular); use of ADM; time to reach TE-to-implant exchange; final TE volume; and time from last outpatient device expansion to definitive implant placement.

Fig. 1 Diagram of the surgical management for SFG + TtIE in comparison with No-FGX. (IBBR, implant-based breast reconstruction; SFG + TtIE, simultaneous fat grafting during TE-to-implant exchange; TE, tissue expander; No-FGX, TE-to-implant exchange without simultaneous fat grafting)



Intraoperative and postoperative outcomes of interest were documented as follows: size of the definitive implant; implant–TE volume difference (Δ); surface of the definitive implant (smooth/textured); capsule work during TE-to-implant exchange (capsulotomy/partial capsulectomy/ total capsulectomy); and volume of fat lipoinjected during TE-to-implant exchange and after definitive implant placement. Complications recorded include hematoma, seroma, fat necrosis, leakage, infection, infection-associated implant removal, implant malposition, implant malposition requiring capsulorrhaphy, wound complications (mastectomy flap necrosis or dehiscence), wound-related prosthesis removal, capsular contracture, capsular contracture requiring capsulotomy or capsulectomy, requirement of autologous tissue for reconstruction salvage, explantation of prosthesis for all causes, and failure of IBBR. Failure of IBBR was defined as abandonment of any reconstructive efforts with prosthetic devices. Explanted implants secondary to a complication were regarded as implant removal, even if the implant was replaced during delayed procedure or if it was immediately exchanged. Infection was considered when (i) the reconstruction exhibited local inflammatory signs and *per os* or intravenous antibiotics were prescribed or (ii) evidence of a positive culture.

Propensity Score Matching

To optimize comparability between the intervention and control group, we performed one-to-one propensity score matching using multivariate logistic regression with a nearest-neighbor caliper width of 0.02. The propensity score was defined as the probability of undergoing SFG + TtIE versus No-FGX (dependent variable). We incorporated the age, BMI, smoking status, history of diabetes or hypertension, type of mastectomy (NSM/SSM), plane of implant placement (prepectoral/subpectoral), use of ADM (yes/no), capsule work during TE-to-implant exchange, implant surface (smooth/textured), adjuvant

radiotherapy, and adjuvant chemotherapy in the propensity score model as independent variables.

Statistical Analysis

All breasts were treated as individual reconstructive cases; therefore, bilateral mastectomies in a single patient were regarded as two separate reconstructions. All statistical analyses were conducted with R statistical software, version 4.0.0 R Core Team [10]. The Fisher's exact test or the Chi-square test was used to evaluate categorical data. The Mann–Whitney test or independent t-test was used to examine continuous data. Continuous data were presented as mean \pm standard deviation. Univariate and multivariate logistic regression analyses were conducted to evaluate the effect of SFG + TtIE on fat necrosis adjusting for age, BMI, rate of fat grafting after TE-to-implant exchange (additional fat grafting after definitive implant placement), and follow-up.

Results

According to our inclusion criteria, 285 patients representing 474 reconstructions were initially included. One hundred and eighty-three reconstructions (38.6%) underwent SFG + TtIE, while 291 reconstructions (61.39%) were allocated in the control group (No-FGX). Before propensity score matching, the SFG + TtIE group had a lower proportion of reconstructions from patients with diabetes ($p = 0.041$), hypertension ($p = 0.002$), and patients receiving adjuvant chemotherapy ($p = 0.001$). The SFG + TtIE group had also a lower proportion of reconstructions for stage IIA, IIB, and IIIC breast cancer ($p = 0.037$); SSMs ($p < .001$); unilateral ($p = 0.028$), immediate ($p = 0.014$), subpectoral reconstructions ($p < .001$); and a reduced mean final TE volume ($p < .001$) (Table 1).

After propensity score matching, 98 reconstructions that underwent SFG + TtIE were eligible for inclusion in this study and were 1:1 matched to reconstructions that did not undergo simultaneous fat grafting during TE-to-implant exchange (No-FGX group) (Table 2). Groups were satisfactorily matched for the demographic, oncologic, and surgical variables. Overall, the mean age was 51.3 ± 10.9 years, and most patients had a BMI lower than 30 kg/m^2 . The proportion of patients with past medical history of hypertension (23%), diabetes (5%), and active smoking status (4%) were not significantly different between groups. Most cases were performed after SSMs (84%) and were immediate (94%), bilateral (81%) reconstructions using a subpectoral plane (64%). Overall, 15% of reconstruction required postmastectomy radiotherapy, and 19% required adjuvant chemotherapy. Outcomes of the first stage of IBBR including the complications reported during the expansion process were comparable between groups (Table 3).

Intraoperative Outcomes of TE-to-Implant Exchange

After propensity score matching, the final TE volume achieved at the end of the first stage of reconstruction was comparable between groups ($426.3 \pm 139.6 \text{ cc}$ versus $459.8 \pm 149.2 \text{ cc}$, $p = 0.223$) (Table 3). Reconstructions in the SFG + TtIE group received larger implants during TE-to-implant exchange in comparison with the control group ($539 \pm 135.1 \text{ cc}$ versus $495.97 \pm 148 \text{ cc}$, $p = 0.035$), which was also supported by a higher mean implant–TE volume Δ in the SFG + TtIE group ($112.7 \pm 81.5 \text{ cc}$ versus $36.17 \pm 91.9 \text{ cc}$, $p < .001$). The total volume of fat injected during TE-to-implant exchange was $88.79 \pm 41.51 \text{ ml}$ in the SFG + TtIE group. The proportion of reconstructions that had different types of capsulectomies, partial capsulectomies, and total capsulectomies during TE-to-implant exchange ($p = 0.33$) and the proportion of reconstructions with smooth versus textured implants ($p = 0.579$) were not significantly different between groups after propensity score matching (Table 4).

Outcomes Following Exchange—Second Stage

After propensity score matching, a significantly higher proportion of reconstructions in the SFG + TtIE group underwent further fat grafting revisions following definitive implant placement when compared to the No-FGX group (19% versus 9%, $p = 0.041$). Nonetheless, the mean total volumes lipoinjected during revision procedures were not significantly different between groups ($135.21 \pm 90.5 \text{ ml}$ versus $89.3 \pm 35.2 \text{ ml}$, $p = 0.19$) (Table 4).

After propensity score matching, reconstructions from the SFG + TtIE group and the No-FGX group had comparable rates of postoperative hematoma (0% versus 0%), seroma (4% versus 1%, $p = 0.369$), implant infection (5% versus 4%, $p = 0.497$), capsular contracture (14% versus 6%, $p = 0.057$), implant malposition (7% versus 2%, $p = 0.08$), skin flap necrosis (1% versus 0%, $p = 1.00$), or dehiscence (4% versus 1%, $p = 0.174$) (Table 5).

The rate of fat necrosis following TE-to-implant exchange was significantly higher in the SFG + TtIE group versus the No-FGX group (10% versus 2%, $p = 0.017$). The rates of breast cancer recurrence (3% versus 5%, $p = 1.00$) and breast cancer mortality (0% versus 3%, $p = 0.496$) were comparable between the SFG + TtIE group and No-FGX group. Overall, 4% of the IBBRs failed in the SFG + TtIE group while 3% of the IBBRs failed in the No-FGX group ($p = 1.00$) at a mean follow-up of 38.03 ± 22.62 months. The average follow-up was not significantly different between groups (35.84 ± 15.41 months versus 40.22 ± 27.96 months, $p = 0.676$) (Table 5).

On univariate analysis, SFG + TtIE was individually associated with an increased likelihood of fat necrosis (OR 5.45, 95%CI 1.16 to 25.58, $p = 0.031$). When incorporating the age, BMI, the rate of revisions with fat grafting procedures performed after definitive implant placement, and the follow-up into a multivariate regression model, SFG + TtIE persisted as an independent predictor for fat necrosis after definitive implant placement [second stage] (OR 6.55, 95%CI 1.23 to 34.95, $p = 0.028$) (Table 6).

Discussion

Our matched cohort study for two-stage IBBR demonstrated comparable rates of complications following SFG + TtIE versus No-FGX, except for a significantly higher incidence of clinically notable fat necrosis after definitive implant placement in the SFG + TtIE group. To date, this is the largest study evaluating the surgical and clinical outcomes of simultaneous fat grafting during TE-to-implant exchange using a 1:1 propensity score-matching model which offers a consistent, accurate, and effective way to control possible confounder and effect modifiers for a homogenous pairwise comparison between groups. Furthermore, the comparable follow-up period between groups after propensity score matching also provides additional validity to our study results (35.84 ± 15.41 months versus 40.22 ± 27.96 months, $p = 0.676$).

Fat grafting as a single reconstructive modality offers an autologous, minimally morbid reconstructive approach; nonetheless, it usually requires several sessions to restore the shape and symmetry after mastectomy, even in small-

Table 1 Summary of baseline demographic and clinical characteristics before matching.

Variable	SFG + TtE	No-FGX	Total	<i>p</i> value
<i>Reconstructions (%)</i>	183 (38.6%)	291 (61.39%)	474 (100%)	
<i>Age (years)</i>	50.9 ± 11.5	51.2 ± 11	51.1 ± 11.2	0.876
<i>Body Mass Index</i>				0.107
<30 kg/m ² (%)	143 (78.1%)	208 (71.5%)	351 (74.1%)	
≥30 kg/m ² (%)	40 (21.9%)	83 (28.5%)	123 (25.9%)	
<i>Race/ethnicity</i>				0.172
White (%)	136 (74.3%)	243 (83.5%)	379 (80%)	
African-America/Black (%)	27 (14.8%)	26 (8.9%)	53 (11.2%)	
Hispanic/Latino (%)	8 (4.4%)	9 (3.1%)	17 (3.6%)	
Asian (%)	6 (3.3%)	8 (2.7%)	14 (3%)	
Unspecified (%)	6 (3.3%)	5 (1.7%)	11 (2.3%)	
<i>Smoke (%)</i>	5 (2.7%)	18 (6.2%)	23 (4.9%)	0.08
<i>Diabetes (%)</i>	6 (3.3%)	23 (7.9%)	29 (6.1%)	0.041†
<i>Hypertension (%)</i>	35 (19.1%)	93 (32%)	128 (27%)	0.002†
<i>Indication</i>				0.105
Therapeutic (%)	102 (55.7%)	184 (63.2%)	286 (60.3%)	
Prophylactic (%)	81 (44.3%)	107 (36.8%)	188 (39.7%)	
<i>Breast</i>				0.959
Right (%)	91 (49.7%)	144 (49.5%)	235 (49.6%)	
Left (%)	92 (50.3%)	147 (50.5%)	239 (50.4%)	
<i>Diagnosis</i>				0.359
No cancer (%)	81 (44.3%)	107 (36.8%)	188 (39.7%)	
IDC (%)	63 (34.4%)	127 (43.6%)	190 (40.1%)	
ILC (%)	13 (7.1%)	17 (5.8%)	30 (6.3%)	
DCIS (%)	23 (12.6%)	31 (10.7%)	54 (11.4%)	
LCIS (%)	0 (0.0%)	1 (0.3%)	1 (0.2%)	
Mixed (%)	0 (0.0%)	2 (0.7%)	2 (0.4%)	
Other (%)	3 (1.6%)	6 (2.1%)	9 (1.9%)	
<i>Stage</i>				0.037†
No tumor (%)	82 (44.8%)	108 (37.1%)	190 (40.1%)	
0 (%)	23 (12.6%)	34 (11.7%)	57 (12%)	
I (%)	52 (28.4%)	73 (25.1%)	125 (26.4%)	
IIA (%)	12 (6.6%)	41 (14.1%)	53 (11.2%)	
IIB (%)	5 (2.7%)	21 (7.2%)	26 (5.5%)	
IIIA (%)	7 (3.8%)	10 (3.4%)	17 (3.6%)	
IIIB (%)	2 (1.1%)	1 (0.3%)	3 (0.6%)	
IIIC (%)	0 (0.0%)	3 (1%)	3 (0.6%)	
<i>Tumor</i>				0.236
No tumor (%)	82 (44.8%)	108 (37.1%)	190 (40.1%)	
Tis (%)	24 (13.1%)	35 (12%)	59 (12.4%)	
T1 (%)	44 (24.0%)	74 (25.4%)	118 (24.9%)	
T2 (%)	22 (12.0%)	58 (19.9%)	80 (16.9%)	
T3 (%)	11 (6%)	15 (5.2%)	26 (5.5%)	
T4 (%)	0 (0%)	1 (0.3%)	1 (0.2%)	

Table 1 continued

Variable	SFG + TtIE	No-FGX	Total	<i>p</i> value
<i>Node</i>				0.501
N0 (%)	163 (89.1%)	255 (87.6%)	418 (88.2%)	
N1 (%)	17 (9.3%)	30 (10.3%)	47 (9.9%)	
N2 (%)	3 (1.6%)	3 (1%)	6 (1.3%)	
N3 (%)	0 (0.0%)	3 (1.0%)	3 (0.6%)	
<i>ER positive (%)</i>	82 (44.8%)	146 (50.2%)	228 (48.1%)	0.255
<i>PR positive (%)</i>	72 (39.3%)	126 (43.3%)	198 (41.8%)	0.395
<i>HER2 positive (%)</i>	14 (7.7%)	24 (8.2%)	38 (8%)	0.816
<i>Neoadjuvant radiotherapy (%)</i>	1 (0.5%)	6 (2.1%)	7 (1.5%)	0.183
<i>Neoadjuvant chemotherapy (%)</i>	32 (17.5%)	47 (16.2%)	79 (16.7%)	0.704
<i>Mastectomy</i>				<.001†
SSM (%)	135 (73.8%)	268 (92.1%)	403 (85%)	
NSM (%)	48 (26.2%)	23 (7.9%)	71 (15%)	
<i>Reconstruction</i>				0.028†
Unilateral (%)	27 (14.8%)	67 (23%)	94 (19.8%)	
Bilateral (%)	156 (85.2%)	224 (77%)	380 (80.2%)	
<i>Timing</i>				0.014†
Immediate (%)	169 (92.3%)	283 (97.3%)	452 (95.4%)	
Delayed (%)	14 (7.7%)	8 (2.7%)	22 (4.6%)	
<i>Plane</i>				< .001†
Prepectoral (%)	86 (47%)	42 (14.4%)	128 (27%)	
Subpectoral (%)	97 (53.0%)	249 (85.6%)	346 (73%)	
ADM (%)	165 (90.2%)	252 (86.6%)	417 (88%)	0.245
<i>Adjuvant radiotherapy (%)</i>	27 (14.8%)	51 (17.5%)	78 (16.5%)	0.428
<i>Adjuvant chemotherapy (%)</i>	30 (16.4%)	86 (29.6%)	116 (24.5%)	0.001†

ADM acellular dermal matrix, DCIS ductal carcinoma in situ, IDC invasive ductal carcinoma, LCIS lobular carcinoma in situ, ILC invasive lobular carcinoma, ER estrogen receptor, PR progesterone receptor, HER2 human epidermal growth factor receptor 2, NSM nipple-sparing mastectomy, SSM skin-sparing mastectomy, No-FGX no autologous fat grafting during exchange, SFG + TtIE simultaneous fat grafting during TE-to-implant exchange.

volume breasts [4]. One of its major drawback is the unpredictable resorption rate [4]. On the other hand, when combined with alloplastic alternatives, it recreates natural esthetic outcomes and optimizes the implant's interface with the mastectomy flaps and surrounding soft tissue [4]. Although previous reports have noted the implementation of serial sessions of autologous fat grafting during the expansion process and then during TE-to-implant exchange to optimize the outcomes of reconstruction [4], the most common practice to correct any contour deformity or to improve the mastectomy flaps is fat transfer after exchange or fat grafting simultaneously performed at the time of exchange (Fig. 2). Remarkably, although SFG + TtIE is an ingenious strategy to optimize the breast envelope and contour during definitive implant placement without increasing the risk of periprosthetic infection or wound-related complications, it may not provide definitive results (Fig. 3). In fact, our study demonstrated that after TE-to-

implant exchange 6% of reconstructions required surgical interventions to address implant malposition, while 19% still required additional fat grafting procedures in the SFG + TtIE group.

We found that a higher rate of clinically relevant fat necrosis was reported in the SFG + TtIE group when compared with the No-FGX group even though similar fat grafting volumes were lipoinjected after exchange (135.21 ± 90.5 versus 89.3 ± 35.2 , $p = 0.191$). In this setting, it is important to highlight that SFG + TtIE, individually (OR 5.45, $p = 0.031$) and during multivariate analysis (OR 6.55, $p = 0.028$), was an independent predictor significantly associated with increased odds of fat necrosis after definitive implant placement. Previous studies have also identified a higher incidence of palpable masses (38% versus 18.3%; $p = 0.003$) and requirement of postmastectomy imaging (47.3% versus 29%; $p = 0.01$) with fat grafting for breast reconstruction versus no fat

Table 2 Summary of baseline demographic and clinical characteristics after matching

Variable	SFG + TiIE	No-FGX	Total	<i>p</i> value
<i>Reconstructions (%)</i>	98 (50%)	98 (50%)	196 (100%)	
<i>Age (years)</i>	51.2 ± 10.8	51.4 ± 11	51.3 ± 10.9	0.886
<i>Body Mass Index</i>				1.00
< 30 kg/m ² (%)	76 (78%)	76 (78%)	152 (78%)	
≥ 30 kg/m ² (%)	22 (22%)	22 (22%)	44 (22%)	
<i>Race/ethnicity</i>				0.344
White (%)	73 (74%)	81 (83%)	154 (79%)	
African America/Black (%)	14 (14%)	6 (6%)	20 (10%)	
Hispanic/Latino (%)	3 (3%)	5 (5%)	8 (4%)	
Asian (%)	5 (5%)	4 (4%)	9 (5%)	
Unspecified (%)	3 (3%)	2 (2%)	5 (3%)	
<i>Smoke (%)</i>	3 (3%)	4 (4%)	7 (4%)	1.00
<i>Diabetes (%)</i>	5 (5%)	4 (4%)	9 (5%)	0.733
<i>Hypertension (%)</i>	24 (24%)	22 (22%)	46 (23%)	0.736
<i>Indication</i>				1.00
Therapeutic (%)	58 (59%)	58 (59%)	116 (59%)	
Prophylactic (%)	40 (41%)	40 (41%)	80 (41%)	
<i>Breast</i>				0.755
Right (%)	48 (49%)	50 (51%)	98 (50%)	
Left (%)	50 (51%)	48 (49%)	98 (50%)	
<i>Diagnosis</i>				0.472
No Cancer (%)	40 (41%)	40 (41%)	80 (41%)	
IDC (%)	36 (37%)	41 (42%)	77 (39%)	
ILC (%)	6 (6%)	4 (4%)	10 (5%)	
DCIS (%)	14 (14%)	8 (8%)	22 (11%)	
LCIS (%)	0 (0%)	0 (0%)	0 (0%)	
Mixed (%)	0 (0%)	2 (2%)	2 (1%)	
Other (%)	2 (2%)	3 (3%)	5 (3%)	
<i>Stage</i>				0.837
No Tumor (%)	41 (42%)	40 (41%)	81 (41%)	
0 (%)	14 (14%)	9 (9%)	23 (12%)	
I (%)	24 (24%)	27 (28%)	51 (26%)	
IIA (%)	9 (9%)	11 (11%)	20 (10%)	
IIB (%)	4 (4%)	7 (7%)	11 (6%)	
IIIA (%)	4 (4%)	3 (3%)	7 (4%)	
IIIB (%)	2 (2%)	1 (1%)	3 (2%)	
IIIC (%)	0 (0%)	0 (0%)	0 (0%)	
<i>Tumor</i>				0.337
No tumor (%)	41 (42%)	40 (41%)	81 (41%)	
Tis (%)	15 (15%)	10 (10%)	25 (13%)	
T1 (%)	25 (26%)	25 (26%)	50 (26%)	
T2 (%)	13 (13%)	21 (21%)	34 (17%)	
T3 (%)	4 (4%)	1 (1%)	5 (3%)	
T4 (%)	0 (0%)	1 (1%)	1 (1%)	
<i>Node</i>				0.710
N0 (%)	84 (86%)	85 (87%)	169 (86%)	

Table 2 continued

Variable	SFG + TiIE	No-FGX	Total	<i>p</i> value
N1 (%)	12 (12%)	11 (11%)	23 (12%)	
N2 (%)	2 (2%)	1 (1%)	3 (2%)	
N3 (%)	0 (0%)	1 (1%)	1 (1%)	
<i>ER</i> positive (%)	45 (46%)	44 (45%)	89 (45%)	0.886
<i>PR</i> positive (%)	40 (41%)	38 (39%)	78 (40%)	0.770
<i>HER2</i> positive (%)	9 (9%)	5 (5%)	14 (7%)	0.267
Neoadjuvant radiotherapy (%)	0 (0%)	1 (1%)	1 (1%)	1.00
Neoadjuvant chemotherapy (%)	17 (17%)	20 (20%)	37 (19%)	0.584
Mastectomy				0.845
SSM (%)	83 (85%)	82 (84%)	165 (84%)	
NSM (%)	15 (15%)	16 (16%)	31 (16%)	
Reconstruction				0.201
Unilateral (%)	15 (15%)	22 (22%)	37 (19%)	
Bilateral (%)	83 (85%)	76 (78%)	159 (81%)	
Timing				0.233
Immediate (%)	90 (92%)	94 (96%)	184 (94%)	
Delayed (%)	8 (8%)	4 (4%)	12 (6%)	
Plane				0.551
Prepectoral (%)	37 (38%)	33 (34%)	70 (36%)	
Subpectoral (%)	61 (62%)	65 (66%)	126 (64%)	
ADM (%)	88 (90%)	88 (90%)	176 (90%)	1.00
Adjuvant radiotherapy (%)	17 (17%)	13 (13%)	30 (15%)	0.427
Adjuvant chemotherapy (%)	19 (19%)	18 (18%)	37 (19%)	0.855

ADM acellular dermal matrix, DCIS ductal carcinoma in situ, IDC invasive ductal carcinoma, LCIS lobular carcinoma in situ, ILC invasive lobular carcinoma, ER estrogen receptor, PR progesterone receptor, HER2 human epidermal growth factor receptor 2, NSM nipple-sparing mastectomy, SSM skin-sparing mastectomy, No-FGX, no autologous fat grafting during exchange, SFG + TiIE simultaneous fat grafting during TE-to-implant exchange.

grafting [11]. However, this did not translate into a significantly higher rate of biopsies performed for the histological characterization of fat necrosis or to rule out breast cancer recurrence (11.8% versus 7.5%; $p = 0.32$) [11].

Implant-based reconstruction of irradiated breast is associated with high postoperative capsular contracture rates [5, 12]. It is hypothesized that adipose-derived stem cells in lipofilling may play a major role in the therapeutic effect of autologous fat grafting against radiation-induced tissue changes [12]. Enhancement of periprosthetic tissue with fat grafting has shown promising results in reversing radiation-induced fibrosis via several mechanisms. These include decreasing collagen content (59% reduction), decreasing capsular density scores ($p = 0.001$), and decreasing fiber alignment scores ($p < .001$) of implant capsules [13]. Nonetheless, in accordance with previous reports [12], no protective effect on the development of capsular contracture for two-stage IBBR was observed in our study. In this setting, further prospective, randomized

studies are required to improve the assessment of the effect of autologous fat to reduce or prophylactically prevent capsular contracture in IBBR, especially taking into consideration that the proportion of adipose-derived stem cells in lipofilling may play a major role on the therapeutic effect of autologous fat grafting against radiation-induced tissue changes [12].

Interestingly, before propensity score matching a higher recurrence rate and mortality was reported in the No-FGX group when compared with the SFG + TiIE. The occurrence of this phenomenon was attributed to a significantly extended long-term follow-up, as well as a higher proportion of stage IIA, IIB, and IIIC breast cancers in the No-FGX when compared with the SFG + TiIE in the pre-matched analysis (Supplementary Material 1). After propensity score matching, the rates of breast cancer recurrence and mortality were comparable between groups.

Fat grafting does not induce neoplastic disease. The effect of progenitor adipose cells on small breast cancer

Table 3 Summary of clinical and surgical outcomes during the first stage of reconstruction after matching

Variable of the first stage	SFG + TtIE	No-FGX	Total	<i>p</i> value
<i>Reconstructions (%)</i>	98 (50%)	98 (50%)	196 (100%)	
<i>TE seroma (%)</i>	16 (16%)	22 (22%)	38 (19%)	0.278
<i>TE hematoma (%)</i>	7 (7%)	4 (4%)	11 (6%)	0.352
<i>TE periprosthetic infection (%)</i>	10 (10%)	13 (13%)	23 (12%)	0.506
<i>Infection-related TE removal (%)</i>	4 (4%)	3 (3%)	7 (4%)	1.00
<i>Wound-related complications (%)</i>	22 (22%)	16 (16%)	38 (19%)	0.279
<i>Skin flap necrosis (%)</i>	11 (11%)	10 (10%)	21 (11%)	0.817
<i>Wound dehiscence (%)</i>	11 (11%)	7 (7%)	18 (9%)	0.323
<i>E/D & C (%)</i>	12 (12%)	13 (13%)	25 (13%)	0.83
<i>Early capsular contracture (%)</i>	1 (1%)	2 (2%)	3 (2%)	1.00
<i>TE leak (%)</i>	1 (1%)	2 (2%)	3 (2%)	1.00
<i>Final TE volume (ml)</i>	426.3 ± 139.6	459.8 ± 149.2	443.1 ± 145.1	0.223
<i>Time For TtIE (days)</i>	207.5 ± 163.1	195.9 ± 189.2	201.7 ± 176.3	0.639
<i>Time form last expansion to exchange (days)</i>	151 ± 163.1	131.8 ± 180.1	141.4 ± 171.6	0.379

E/D & C excision/debridement and closure of wound, *No-FGX* no autologous fat grafting during exchange, *SFG + TtIE* simultaneous fat grafting during TE-to-implant exchange, *TE* tissue expander, *TtIEI* TE-to-implant exchange

Table 4 Summary of surgical outcomes of the second stage of reconstruction after matching

Variable of the second stage	SFG + TtIE	No-FGX	Total	<i>p</i> value
<i>Reconstructions (%)</i>	98 (50%)	98 (50%)	196 (100%)	
<i>Implant volume (ml)</i>	539 ± 135.1	495.97 ± 148	517.5 ± 142.96	0.035†
<i>Implant–TE volume Δ (ml)</i>	112.7 ± 81.5	36.17 ± 91.9	74.44 ± 94.7	< .001†
<i>Implant surface</i>				0.579
<i>Smooth (%)</i>	90 (92%)	92 (94%)	182 (93%)	
<i>Textured (%)</i>	8 (8%)	6 (6%)	14 (7%)	
<i>Capsule work during exchange</i>				0.330
<i>None (%)</i>	14 (14%)	13 (13%)	27 (14%)	
<i>Capsulotomy (%)</i>	72 (73%)	66 (67%)	138 (70%)	
<i>Partial Capsulectomy (%)</i>	11 (11%)	19 (19%)	30 (15%)	
<i>Total Capsulectomy (%)</i>	1 (1%)	0 (0%)	1 (1%)	
<i>Volume of Fat for SFG + TtIE (ml)</i>	88.79 ± 41.51	NA		
<i>Fat grafting after exchange[§]</i>				
<i>Reconstructions (%)[§]</i>	19 (19%)	9 (9%)	28 (14%)	0.041†
<i>Amount of Fat Grafted (ml)[§]</i>	135.21 ± 90.5	89.3 ± 35.2	122.85 ± 81.4	0.191

NA not applicable, *No-FGX* no autologous fat grafting during exchange, *SFG + TtIE* simultaneous fat grafting during TE-to-implant exchange; *TE* tissue expander

[§]Fat grafting procedures performed solely after definitive implant placement (TE-to-implant exchange).

foci remains of concern when fat lipotransfer is performed after the ablative treatment has been accomplished, especially in locally advanced tumors [14, 15]. Certainly, although this current report has a limited long-term follow-up, previous studies have shown comparable 5-year overall locoregional recurrence-free survival rates (95.1% [95%CI 89.6–100%] versus 96.2% [95%CI 92.1–100%]) and 5-year overall survival rates (94.6% [95%CI 88.7–100%]

versus 95% [95%CI 89.6–100%]) between patients receiving fat grafting versus no fat grafting after breast reconstruction [11]. Still, prospective studies with an extensive follow-up are required [11].

Table 5 Summary of the complications of the second stage of reconstruction and oncologic after matching

Variable of the second stage	SFG + TtE	No-FGX	Total	<i>p</i> value
<i>Reconstructions (%)</i>	98 (50%)	98 (50%)	196 (100%)	
<i>Hematoma (%)</i>	0 (0%)	0 (0%)	0 (0%)	
<i>Seroma (%)</i>	4 (4%)	1 (1%)	5 (3%)	0.369
<i>Epidermolysis of Flaps (%)</i>	2 (2%)	0 (0%)	2 (1%)	0.497
<i>Implant Infection (%)</i>	5 (5%)	4 (4%)	9 (5%)	0.733
<i>Infection-related Implant Removal (%)</i>	1 (1%)	2 (2%)	3 (2%)	1.00
<i>Capsular contracture (%)</i>	14 (14%)	6 (6%)	20 (10%)	0.057
<i>Capsulotomy/capsulectomy (%)</i>	5 (5%)	1 (1%)	6 (3%)	0.097
<i>Contracture-related implant removal (%)</i>	2 (2%)	0 (0%)	2 (1%)	0.497
<i>Fat necrosis (%)</i>	10 (10%)	2 (2%)	12 (6%)	0.017†
<i>Implant malposition (%)</i>	7 (7%)	2 (2%)	9 (5%)	0.08
<i>Capsulorrhaphy (%)</i>	6 (6%)	1 (1%)	7 (4%)	0.054
<i>Implant rupture (%)</i>	0 (0%)	1 (1%)	1 (1%)	0.316
<i>Wound complications (%)</i>	5 (5%)	1 (1%)	6 (3%)	0.097
<i>Skin Flap Necrosis (%)</i>	1 (1%)	0 (0%)	1 (1%)	1.00
<i>Dehiscence (%)</i>	4 (4%)	1 (1%)	5 (3%)	0.174
<i>E/D + C (%)</i>	3 (3%)	1 (1%)	4 (2%)	0.621
<i>Wound-related implant removal (%)</i>	2 (2%)	0 (0%)	2 (1%)	0.497
<i>Implant-enhanced LD Flap (%)</i>	1 (1%)	0 (0%)	1 (1%)	1.00
<i>Latissimus Dorsi (%)</i>	0 (0%)	0 (0%)	0 (0%)	–
<i>Request for implant removal (%)</i>	4 (4%)	3 (3%)	7 (4%)	1.00
<i>Failure of reconstruction (%)</i>	4 (4%)	3 (3%)	4%	1.00
<i>Breast cancer recurrence (%)¶</i>	2 (3%)	3 (5%)	5 (4%)	1.00
<i>Breast cancer mortality (%)¶</i>	0 (0%)	2 (3%)	2 (2%)	0.496
<i>Follow-up (months)</i>	35.84 ± 15.41	40.22 ± 27.96	38.03 ± 22.62	0.676

E/D + C excision/debridement and closure, *No-FGX* no autologous fat grafting during exchange, *SFG-TtE* simultaneous fat grafting during TE-to-implant exchange.

¶Only reconstructions performed after oncologic mastectomy (does not include risk-reducing or prophylactic mastectomies)

Table 6 Predictors for fat necrosis after TE-to-implant exchange

Predictor fat necrosis after exchange	Odds ratio	95% Lower	CI Upper	<i>p</i> value
<i>Univariate analysis</i>				
SFG + TtE	5.45	1.16	25.58	0.031†
<i>Multivariate analysis</i>				
SFG + TtE	6.55	1.23	34.95	0.028†
Age (years)	1.02	0.96	1.08	0.455
BMI (kg/m ²)	1.11	0.98	1.27	0.109
Fat grafting after TE-to-implant exchange	2.6	0.61	11.03	0.195
Follow-up	1.03	1	1.06	0.069

BMI body mass index, *SFG + TtE* simultaneous fat grafting during TE-to-implant exchange, *TE* tissue expander.

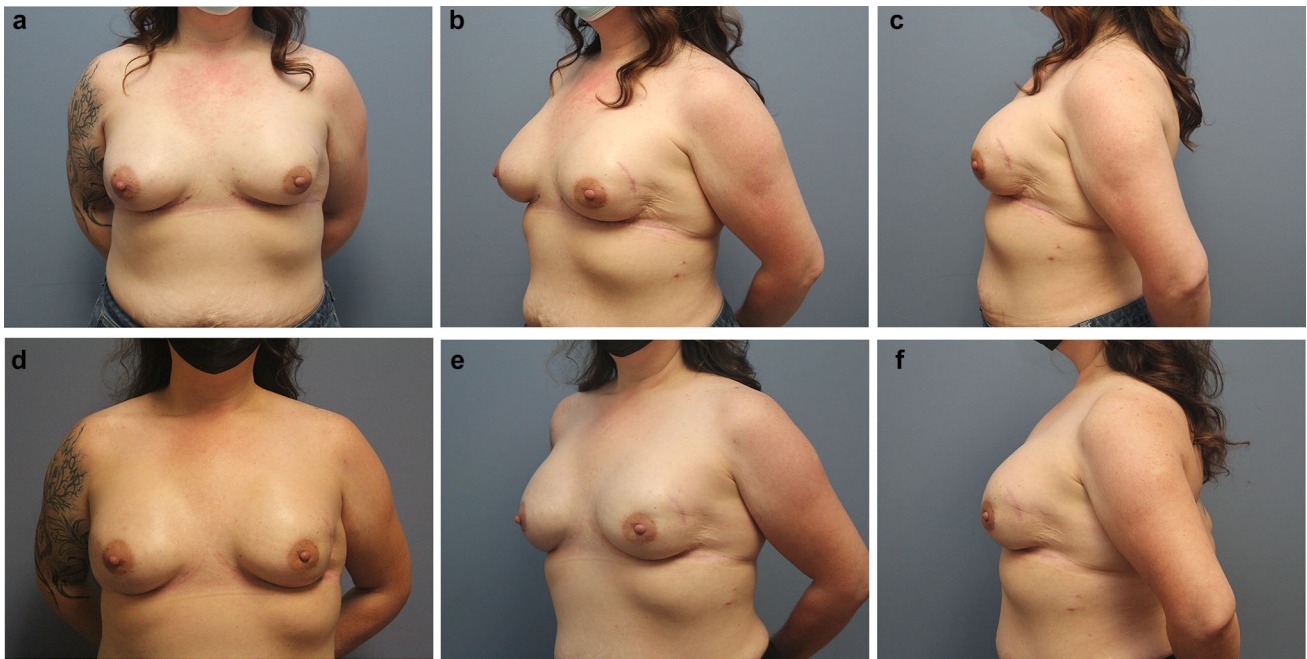


Fig. 2 A 45-year-old patient who underwent bilateral prepectoral two-stage IBBR. TEs were filled with 440cc of air at the end of the expansion process before TE-to-implant exchange (**a** frontal, **b** left

oblique, **c** left lateral). Postoperative photographs 17 months following SFG + TtIE (right, 65 cc; left, 80 cc) with 450cc definitive implants (**d** frontal, **e** left oblique, **f** left lateral).

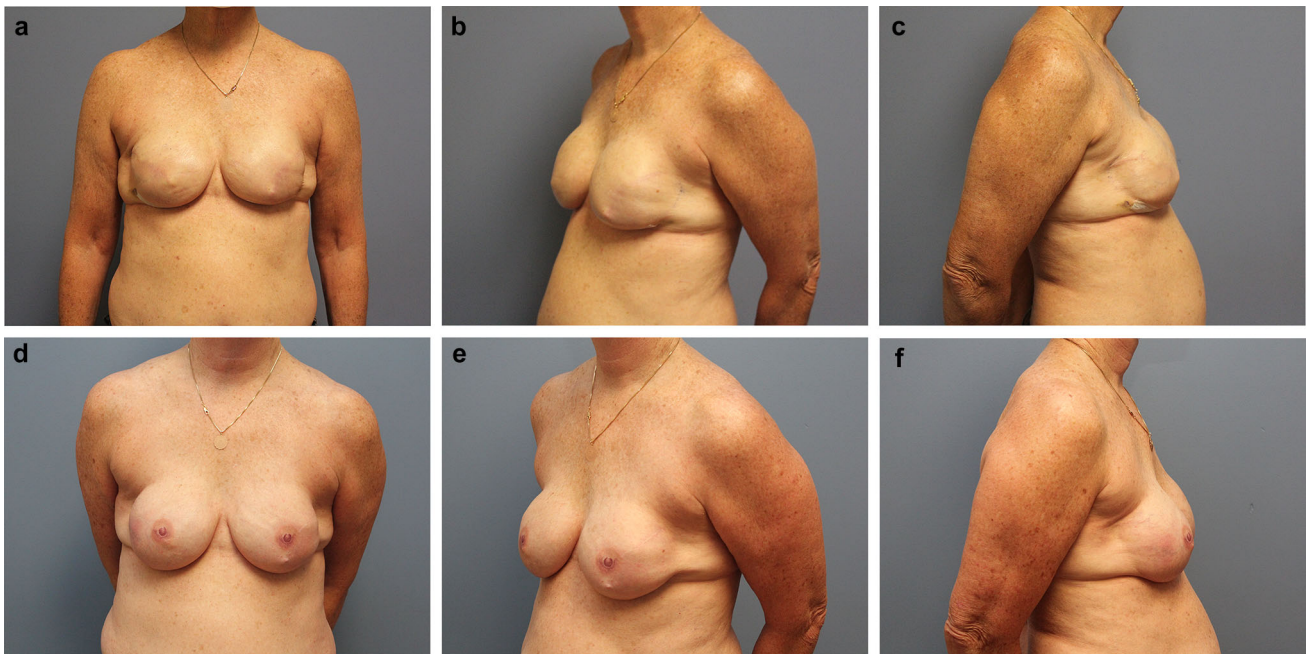


Fig. 3 A 66-year-old patient who underwent bilateral prepectoral two-stage IBBR. TEs were filled with 200cc at the end of the expansion process before TE-to-implant exchange (**a** frontal, **b** left oblique, **c** right lateral). Postoperative photographs 8 months after TE-

to-implant exchange, without simultaneous fat grafting (No-FGX), and 335cc and 295cc definitive implants in the right and left breast, respectively (**d** frontal, **e** left oblique, **f** right lateral).

Limitations

This study has a retrospective design for chart review and database synthesis. Due to the strict selection criteria and

limited sample size, there is a latent probability for type II error. The impact of fat grafting during TE exchange, or as a revision procedure after definitive implant placement, was not evaluated with patient-reported outcomes

measurements (PROMs). Volume retention and quality of the fat grafts were not assessed using histologic analysis or imaging. As patients were not randomized or blindly allocated into the intervention or control groups, there is a latent risk of selection or performance bias; however, this was minimized after propensity score matching. There are other factors that may have an impact on the incidence of complications in reconstructions performed with SFG + TtIE that we did not examine such as dose of postmastectomy radiotherapy, chemotherapeutic regimen, and inadvertent breast microtraumas causing fat necrosis.

Conclusion

SFG + TtIE is an alternative to improve the conus and envelope of reconstructed breasts during two-stage IBBR. SFG + TtIE does not increase the rate of periprosthetic infection or wound-related complication when compared with no fat grafting during TE-to-implant exchange. Additionally, it does not increase the rate of breast cancer recurrence at an average 3-year follow-up. Although SFG + TtIE is oncologically safe, a higher rate of clinically noticeable fat necrosis is expected, even if further fat grafting procedures are not performed after exchange.

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Declarations

Conflict of interests None of the authors received any compensation or financial support for this study. None of the authors have commercial associations to disclose related to this study.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

References

- Albornoz CR, Bach PB, Mehrara BJ et al (2013) A paradigm shift in U.S. Breast reconstruction: increasing implant rates. *Plast Reconstr Surg* 131:15–23
- Weissler JM, Banuelos J, Jacobson SR et al (2020) Intravenous tranexamic acid in implant-based breast reconstruction safely reduces hematoma without thromboembolic events. *Plast Reconstr Surg* 146:238–245
- Manrique OJ, Kapoor T, Banuelos J et al (2020) Single-stage direct-to-implant breast reconstruction: a comparison between subpectoral versus prepectoral implant placement. *Ann Plast Surg* 84:361–365
- Stillaert FB, Lannau B, Van Landuyt K, Blondeel PN (2020) The prepectoral, hybrid breast reconstruction: the synergy of lipofilling and breast implants. *Plast Reconstr Surg Glob Open* 8:e2966
- Rigotti G, Marchi A, Galìè M et al (2007) Clinical treatment of radiotherapy tissue damage by lipoaspirate transplant: a healing process mediated by adipose-derived adult stem cells. *Plast Reconstr Surg* 119:1409–1422
- Papadopoulos S, Vidovic G, Neid M, Abdallah A (2018) Using fat grafting to treat breast implant capsular contracture. *Plast Reconstr Surg Glob Open* 6:e1969–e1969
- Sbitany H, Sandeen SN, Amalfi AN, Davenport MS, Langstein HN (2009) Acellular dermis-assisted prosthetic breast reconstruction versus complete submuscular coverage: a head-to-head comparison of outcomes. *Plast Reconstr Surg* 124:1735–1740
- Manrique OJ, Charafeddine A, Abu-Ghname A et al (2019) Two-staged implant-based breast reconstruction: a long-term outcome study in a young population. *Medicina (Kaunas)* 55:481
- Manrique OJ, Banuelos J, Abu-Ghname A et al (2019) Surgical outcomes of prepectoral versus subpectoral implant-based breast reconstruction in young women. *Plast Reconstr Surg Glob Open* 7:1–5
- R Core Development Team. R Core Team (2021) R: a language and environment for statistical computing. (Version 4.0) [Computer Software]. Retrieved from <https://cran.r-project.org/>. 2021. Available: https://cran.r-project.org
- Cason RW, Shammas RL, Broadwater G et al (2020) The influence of fat grafting on breast imaging after postmastectomy reconstruction: a matched cohort analysis. *Plast Reconstr Surg* 146:1227–1236
- Martin S, Cai L, Beniwal A, Tevlin R, Lee G, Nazerali RS (2021) Autologous fat grafting and the occurrence of radiation-induced capsular contracture. *Ann Plast Surg* 86:S414–S417
- Komorowska-Timek E, Jaźwiec A, Adams NS, Fahrenkopf MP, Davis AT (2021) Peri-prosthetic fat grafting decreases collagen content, density, and fiber alignment of implant capsules. *Plast Reconstr Surg Glob Open* 9:e3687
- Kolasinski J, Pyka P (2022) Fat grafting following internal tissue expansion: an option for breast reconstruction after total mastectomy. *Plast Reconstr Surg Glob Open* 10:e4088
- Bertolini F, Petit J-Y, Kolonin MG (2015) Stem cells from adipose tissue and breast cancer: hype, risks and hope. *Br J Cancer* 112:419–423

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