

# Long-Term Outcomes following Fat Grafting in Prosthetic Breast Reconstruction: A Comparative Analysis

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**Background:** Autologous fat grafting has become a common technique for optimizing aesthetic outcomes following breast reconstruction. Its long-term oncologic implications, however, remain unclear. The authors evaluated long-term outcomes following tissue expander breast reconstruction with and without fat grafting.

**Methods:** A retrospective review was performed of consecutive patients undergoing mastectomy with immediate tissue expander reconstruction from April of 1998 to August of 2008. Demographic, operative, oncologic, and postoperative factors were recorded, including the use of fat grafting. Mean follow-up was  $42.1 \pm 28.8$  and  $43.6 \pm 27.2$  months for non-fat-grafting and fat-grafting patients, respectively ( $p = 0.63$ ), including  $24.8 \pm 5.9$  months after the first fat-grafting procedure. Fisher's exact test,  $t$  test, and regression analysis were used for statistics.

**Results:** A review of 886 patients ( $n = 1202$  breasts) revealed no significant differences in demographics, operative characteristics, tumor staging, or radiation therapy exposure between fat-grafting ( $n = 90$  breasts) and non-fat-grafting ( $n = 1112$  breasts) patients. Ninety-nine fat-grafting procedures were performed an average of 18.3 months after reconstruction, with one complication (fat necrosis). Grafting did not affect local tumor recurrence or survival when compared with non-fat-grafted breasts. Complication following reconstruction, including a poor cosmetic result, was an independent predictor of undergoing subsequent fat grafting ( $p < 0.0001$ ).

**Conclusions:** The analysis suggests that fat grafting after breast reconstruction does not adversely affect local tumor recurrence or survival on long-term follow-up. Autologous fat grafting can be used as an aesthetic adjunct to prosthetic reconstruction with minimal complications. These results also indicate the need for multi-institutional, prospective studies to definitively establish its oncologic safety. (*Plast. Reconstr. Surg.* 130: 984, 2012.)

**CLINICAL QUESTION/LEVEL OF EVIDENCE:** Therapeutic, III.

Autologous fat grafting has become an attractive, but controversial, procedure following breast reconstruction.<sup>1-11</sup> With increasing expectations for superior aesthetic outcomes, the injection of fat provides several advantages in the revision of a reconstructed breast. Grafting small, controlled amounts of fat allows for more precise

correction of volume defects and breast contour deformities, particularly following unilateral reconstruction in which achieving symmetry is critical to a successful result.<sup>12-15</sup> In addition, fat grafting replaces soft tissue with actual soft tissue (replacing "like with like"), providing a natural consistency and texture to the reconstructed breast.<sup>16</sup> Others have

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suggested that transferring autologous fat to areas damaged by premastectomy radiation may ultimately improve their healing.<sup>17-19</sup> Along with these aesthetic benefits, the inherent flexibility in the timing and number of procedures allows it to be individualized for each patient.

Despite its growing utility and appeal, the oncologic risks of injecting fat into a post-breast cancer field remain unclear.<sup>7,8,20-22</sup> Improved imaging techniques, and an increasing body of literature, have helped mitigate the concern over distinguishing necrotic and calcified fat grafts from early breast carcinoma radiologically.<sup>9-11</sup> Some *in vitro* studies, however, have indicated that adipocytes and their associated milieu may directly stimulate tumor growth and progression, particularly in the proximity of residual breast cancer cells.<sup>23-25</sup> Others have indicated that although adipose-derived stem cells within the graft may provide additional tissue healing benefits, they also pose the risk of malignant transformation.<sup>21</sup> From a clinical standpoint, the long-term oncologic impact of fat injections to the reconstructed breast remains unclear, with only a limited number of studies addressing this issue to date.<sup>6,15,20,22</sup> These potential concerns were underscored by a task force organized by the American Society of Plastic Surgeons in 2009 that concluded that there are “few data to provide evidence for the long-term safety and efficacy of fat grafting” and advocated continued clinical and basic science research.<sup>26</sup>

As the literature surrounding autologous fat grafting continues to grow, studies with appropriate controls and long-term follow-up are essential to establishing its safety and efficacy following breast reconstruction. With the sustained popularity of prosthetic-based reconstruction, understanding the impact of fat grafting in this population is of particular interest. Therefore, the goal of this comparative study was to understand the long-term, oncologic risks of revisional fat grafting in patients undergoing tissue expander breast reconstruction. In addition, through an analysis of preoperative patient factors and postoperative complications, we aimed to clarify the role of autologous fat grafting in different clinical situations.

## PATIENTS AND METHODS

This study was performed under the approval of the Northwestern University Institutional Review Board. Retrospective review of patients at Northwestern Memorial Hospital who underwent mastectomy with immediate tissue expander reconstruction from April of 1998 to August of 2008 was performed. For each patient, individual inpa-

tient and outpatient records for each procedure were thoroughly reviewed, including those associated with operative complications and procedures beyond second-stage permanent implant exchange. Relevant demographic information, preoperative characteristics, operative factors (including the use of autologous fat grafting by the reconstructive surgeon), postoperative pathology, and complications were recorded.

All patients included for analysis followed a protocol of first-stage prosthetic reconstruction, followed by outpatient expansion, postoperative radiotherapy if necessary, and finally, second-stage, permanent implant exchange. Patients who underwent immediate autologous tissue flap reconstruction or a combination of autologous tissue flap and tissue expander reconstruction (e.g., latissimus dorsi flap reconstruction) were excluded from this study. Patients were stratified into two groups based on whether or not they had undergone autologous fat grafting at some point during the breast reconstruction process. The earliest reconstruction that underwent subsequent fat grafting was in January of 2000. Patient groups were matched in time by only including reconstructions done after January of 2000. Mean follow-up time for non-fat-grafting and fat-grafting patients from the time of initial tissue expander insertion was  $42.1 \pm 28.8$  months (12 to 138 months) and  $43.6 \pm 27.2$  months (15 to 105 months), respectively ( $p = 0.63$ ). For fat-grafting patients, mean follow-up following the actual fat-grafting procedure was  $24.8 \pm 5.9$  months (10 to 82 months).

Harvest and grafting of fat was performed using syringe techniques described by Coleman and Saboeiro<sup>5</sup> and Coleman<sup>16</sup> with primary harvest sites, including the abdominal, hip, and lateral flank regions. Fat was separated and concentrated utilizing gravity and manual separation of fluid from fat on a Telfa (Tyco Healthcare Group, Mansfield, Mass.) dressing, without the use of any centrifugation. Volumes of fat grafted ranged from 20 to 200 cc per breast, with the majority of patients receiving 20 to 50 cc per breast. Fat was injected primarily in the superior portion of the reconstructed breast but in general was utilized for areas of visual depression to improve overall breast volume and contour. Injections were placed subcutaneously and intramuscularly, with a goal of even fat distribution in the space between the mastectomy flap and the expander or implant.

The primary outcome of interest was long-term safety of autologous fat grafting, in particular, breast cancer recurrence rates and survival. Secondary outcomes included timing of, and com-

plications associated with, autologous fat grafting. Complication rates following first-stage tissue expander placement, but before fat grafting, were also recorded. Complications were reported as an overall rate per breast, as well as categorized by end outcome, including nonoperative, operative except explantation, and explantation with or without conversion to autologous flap. Postoperative breast pain or tightness (if explicitly documented by the surgeon following at least one subjective patient complaint) and poor cosmesis (if explicitly documented following at least one subjective patient complaint or on assessment by the reconstructive surgeon) were also reported.

Statistical analysis was performed using the *t* test and Fisher's exact test to determine significant differences in clinical characteristics, operative factors, pathological breast cancer stage, breast cancer recurrence, and survival between breasts with and without autologous fat grafting. Multiple linear regression analysis was performed to determine whether any patient characteristics or first-stage complications were associated with an increased likelihood of undergoing subsequent autologous fat grafting. Several independent variables were evaluated in these analyses, including age, body mass index, smoking status, radiation therapy before or after mastectomy and reconstruction, the use of acellular dermis, the individual mastectomy and reconstructive surgeon, and each complication subtype. Statistical significance was set at *p* less than 0.05. All analyses were performed using Prism, Version 4.0b (GraphPad Software, La Jolla, Calif.).

## RESULTS

Retrospective review revealed 886 consecutive patients (1202 breasts) eligible for analysis, which included the patients of 15 mastectomy surgeons and six reconstructive surgeons. On stratification, 69 patients (90 breasts; 7.5 percent) were found to have undergone autologous fat grafting at some point during reconstruction. Comparison of the two study groups revealed no significant differences in demographics or operative characteristics between fat-grafting and non-fat-grafting patients (Table 1). There were a total of 99 autologous fat-grafting procedures performed in 90 breasts, with the majority (*n* = 67; 67.7 percent) occurring as a separate revisionary procedure following second-stage permanent implant exchange (Fig. 1). The remaining procedures (*n* = 32; 32.3 percent) occurred during the second-stage procedure. The average time between initial reconstruction and the first fat-grafting procedure was

**Table 1. Demographic and Operative Factors of Breasts with and without Fat Grafting\***

Characteristic	No FG ( <i>n</i> = 1112 breasts; 817 patients)	FG ( <i>n</i> = 90 breasts; 69 patients)	<i>p</i>
Age, yr	48.0 ± 10.6	49.4 ± 8.8	0.22
BMI, kg/m <sup>2</sup>	25.3 ± 5.5	25.4 ± 5.2	0.87
Smoking	128 (11.5)	14 (15.6)	0.24
Prereconstruction XRT	73 (6.6)	2 (2.2)	0.11
NSM	38 (3.4)	3 (3.3)	1.00
Tumescent technique	422 (37.9)	29 (32.2)	0.31
Postreconstruction XRT	49 (24.6)	74 (18.8)	0.11

FG, fat grafting; BMI, body mass index; XRT, radiation therapy; NSM, nipple-sparing mastectomy.

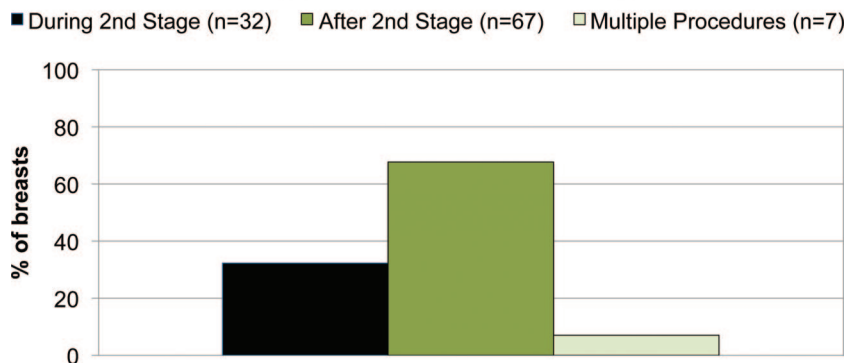
\*Data are reported as mean ± SD or number (percentage of breasts).

18.3 ± 10.5 months. Seven breasts underwent multiple fat-grafting procedures, including four breasts that had fat grafting done both during and after implant exchange. The maximum number of separate grafting procedures done for one breast was four. There was one postoperative complication (*n* = 1 of 99; 1.0 percent) associated with fat grafting, which was local fat necrosis at the site of injection. This was managed conservatively.

Based on recorded postoperative pathology, patients from each study group were stratified based on breast cancer stage (Table 2). Complete pathology data were not available for one fat-grafting breast and six nongrafting breasts, which were excluded from this analysis. The majority of non-fat-grafting (*n* = 763; 69.0 percent) and fat-grafting (*n* = 67; 75.3 percent) breasts had evidence of carcinoma on pathology, of which 76.9 percent (*n* = 587) and 74.6 percent (*n* = 50) were invasive disease, respectively. Based on each individual breast cancer stage, there were no differences in cancer burden between non-fat-grafting and fat-grafting breasts. On long-term follow-up, breast cancer recurrence and overall survival were found to be similar between fat-grafting and non-fat-grafting patients (Table 2).

Having established the safety of autologous fat grafting within our study population, an analysis of those factors associated with an increased likelihood of undergoing fat grafting was performed. Regression analysis, adjusting for several demographic, operative, and complication variables, revealed that no preoperative or operative factors were independent predictors of patients undergoing subsequent fat grafting during the breast reconstruction process (Table 3). In particular, the individual mastectomy and reconstructive surgeon did not influence this likelihood. However,

**Timing of Revisional Fat Grafting**



**Fig. 1.** Timing of fat grafting during breast reconstruction. The majority of fat grafting procedures were performed following second-stage implant exchange. Only seven breasts underwent multiple fat-grafting procedures during the study period.

**Table 2. Oncologic Characteristics of Breasts with and without Fat Grafting\***

Characteristic	No FG (n = 1106 breasts; 812 patients)†	FG (n = 89 breasts; 68 patients)†	p
Pathology			
Negative/ prophylactic	343 (31.0)	22 (24.7)	0.23
Stage			
0 (in situ)	176 (15.9)	17 (19.1)	0.87
I	212 (19.2)	23 (25.8)	0.13
II	288 (26.0)	23 (25.8)	1.00
III	87 (7.9)	4 (4.4)	0.30
Local recurrence	17 (1.5)	0 (0.0)	0.63
Survival‡	776 (95.5)	68 (100.0)	0.10

FG, fat grafting.

\*Data reported as number (percentage of breasts).

†Pathology data were not available for all patients.

‡Data are reported as number (percentage of patients).

when looking at individual complication categories, patients were more likely to undergo fat grafting if they had a complication following tissue expander placement ( $p < 0.0001$ ), particularly an operative complication ( $p < 0.0001$ ), or poor cosmesis ( $p < 0.0001$ ) (Table 4).

**DISCUSSION**

The potential benefits of autologous fat grafting during breast reconstruction continue to be complicated by its unclear impact on long-term oncologic risk and survival.<sup>7,8,20–22</sup> Although it provides aesthetic precision and flexibility during revisional breast surgery,<sup>12–16</sup> these advantages must be weighed against the paucity of evidence that supports its routine use. Therefore, given its growing presence within reconstructive breast surgery, research aimed at solidifying our understanding of fat grafting remains critical. Our retrospective

**Table 3. Characteristics Associated with Fat Grafting**

Characteristic	OR	95% CI	p
Age >50 yr	0.89	0.57–1.37	0.87
BMI >30 kg/m <sup>2</sup>	1.00	0.59–1.69	0.66
Smoking	1.42	0.78–2.58	0.34
Prereconstruction XRT	0.32	0.07–1.34	0.11
Postreconstruction XRT	0.88	0.51–1.52	0.72
Acellular dermis	1.70	1.04–2.78	0.10

OR, odds ratio; CI, confidence interval; BMI, body mass index; XRT, radiation therapy.

review, the largest comparative study to date, suggested that fat grafting following prosthetic breast reconstruction imparts no increased risk of recurrent malignancy, relative to non-fat-grafted breasts, on long-term follow-up. We also confirmed that fat grafting allows for flexibility in timing while possessing a low-risk complication profile, allowing for multiple, safe procedures, particularly in those breasts with postoperative complications.

Although literature discussing the aesthetic benefits of autologous fat grafting continues to grow, few studies have focused on its oncologic risks in the reconstructed, postmastectomy patient. Work by de Blacam et al.,<sup>12</sup> Kanchwala et al.,<sup>13</sup> and Losken et al.<sup>14</sup> has looked at series of patients who underwent postreconstruction fat grafting ( $n = 49, 110,$  and  $107$  patients, respectively), finding that fat grafting had low complication rates and improved contour deformities. Unfortunately, despite their encouraging results, none of these studies reported on their associated oncologic outcomes. Meanwhile, Delay et al.<sup>6</sup> reported a large series of patients who underwent fat injection ( $n = 734$  following breast reconstruction), with highly satisfactory results and no increased risk of cancer recurrence on long-term follow-up. Similarly, a multicenter review by Petit



**Table 4. Complications Associated with Fat Grafting**

Complication	No FG ( <i>n</i> = 1112 breasts; 817 patients)	FG ( <i>n</i> = 90 breasts; 69 patients)	OR	95% CI	<i>p</i>
Total complications	203 (18.3)	33 (36.7)	2.90	1.84–4.58	<0.0001
Pain/tightness	42 (3.8)	4 (4.4)	1.03	0.40–2.64	0.81
Poor cosmesis	17 (1.5)	3 (3.3)	6.86	4.37–10.77	<0.0001
Nonoperative	105 (9.4)	8 (8.9)	1.17	0.54–2.50	0.70
Operative	136 (12.2)	26 (28.9)	2.92	1.79–4.76	<0.0001
Explantation	98 (8.8)	3 (3.3)	0.36	0.11–1.15	0.07

FG, fat grafting; OR, odds ratio; CI, confidence interval.

et al.<sup>20</sup> looked at fat-grafting procedures in 513 patients, reporting a low rate of oncologic events. Rigotti et al.<sup>22</sup> also conducted an oncologic review of their fat injection patients (*n* = 137 patients) in which they compared patient follow-up before and after fat grafting, concluding that recurrence rates were not affected. All of these studies, however, acknowledged the need for an appropriate, independent control group with matched cancer status, which would have enhanced the value of their findings. Furthermore, although review articles, such as those by Fraser et al.,<sup>7</sup> Chan et al.,<sup>8</sup> and Saint-Cyr et al.,<sup>27</sup> have effectively outlined the available biological and clinical evidence surrounding fat grafting, they also underscore the lack of prospective series currently available in the literature. Studies that improve upon all of these limitations are necessary to solidify the reputation of fat grafting as a safe and effective technique for revising the reconstructed breast.

Using a large, comparable patient population with long-term follow-up, we have demonstrated that autologous fat grafting does not increase the rate of local breast cancer recurrence, or decrease survival, following mastectomy with prosthetic breast reconstruction. Unlike many previous studies in the literature, we have reported outcomes following approximately 3.5 years of patient follow-up, including 2 years following the initial fat-grafting procedure. The net volume of fat uptake over time may be important to this relationship, as numerous studies have demonstrated significant volume loss after only a short time postoperatively.<sup>28,29</sup> With a decreasing number of adipocytes, its potential tumor-promoting effects may be mitigated by the death and reabsorption of many of the initially injected cells, decreasing the potential risk for oncologic transformation. It is difficult, however, to definitively conclude that our results contradict the potential tumor-promoting effects outlined by previous *in vitro* research.<sup>24</sup> Instead, they delineate a time frame within which the risk of malignant transformation due to injected fat may be low. Continued surveillance of our patient population would be

needed to comment on any lasting effects of these adipocytes and their secreted factors. Nevertheless, the low risk seen in our study, combined with improved radiographic imaging,<sup>9,10</sup> provides additional support for the safe use of autologous fat following breast reconstruction, assuming the appropriate oncologic follow-up.

A secondary outcome of our study was to understand which patients within our breast reconstruction population tended to undergo autologous fat grafting. There are two significant, or interesting, findings to discuss with regard to this analysis. First, patients who experienced a complication during the reconstructive process, particularly those requiring further surgery or having a poor cosmetic result, were more likely to undergo fat grafting independently of other patient and operative variables. These findings reinforce its role as a useful adjunct to traditional breast reconstruction. However, given our subjective definition of poor cosmesis, this association may also underscore the increasing demand among patients for improved aesthetic outcomes. Patients with a complaint of a poor appearance after first-stage tissue expander placement, despite still awaiting their implant exchange, may put their aesthetic result as a higher priority than other patients. As a result, given the opportunity to improve upon their final result, they may be more likely to inquire about additional revisional surgery, of which fat grafting may be the easiest to perform and repeat if necessary. The association with operative complications may, however, also be explained by the desire of reconstructive surgeons to take advantage of each trip to the operating room. With fat grafting being a relatively quick and simple adjunct procedure that allows for a stepwise improvement in outcomes, surgeons may take advantage of the opportunity to simultaneously remedy the complication and improve patient aesthetic outcomes under one anesthetic exposure.

Another interesting finding was that variables, such as smoking and radiation exposure, which

are well known risk factors for postoperative complications,<sup>30</sup> were not significant predictors of subsequent fat grafting. This finding appears to stand in contrast to our finding of an independent association between overall complication rates and subsequent fat grafting. Many of the patient factors we examined, however, have been associated with more significant complications, such as delayed or poor wound healing and capsular contracture. These complications, unlike a seroma or local infection, may eventually result in tissue expander explantation and/or conversion to autologous flap. Therefore, as one might expect, in situations in which complications have compromised the integrity of the reconstruction, fat grafting may not have an immediate role. The greater priority for these patients may initially be salvaging their reconstruction rather than performing minor revisional surgery to improve cosmesis, thus potentially explaining our findings. It is important to note that some have suggested that fat grafting before or alongside delayed implant reconstruction in previously irradiated breasts may be beneficial in avoiding the aforementioned complications.<sup>17-19</sup> These findings do not apply to our results, as no patients in our review underwent this type of fat-grafting protocol.

Given its retrospective design, our study is limited in the conclusions that can be drawn. In particular, the disparity in size between our study cohorts must be acknowledged, which may be explained by the slow increase in popularity of fat grafting over the time of our study period. However, with no significant differences in demographic, operative, or pathologic variables, and comparable long-term follow-up, we believe our study presents a valid comparison between fat-grafted and nongrafted patients that has not been previously performed. Our study also does not report on aesthetic outcomes; however, with a large amount of literature surrounding this aspect of fat grafting,<sup>12-15</sup> we chose to address the lack of large, comparative studies addressing the oncologic safety of this technique. It is important, however, to recognize that breast cancer locoregional recurrence rates of 1 to 12.9 percent following mastectomy have been reported from studies with greater than 5-year follow-up.<sup>31</sup> The true additional risk of fat grafting to this baseline is unknown but is presumably not high, given the lack of increased recurrence seen in our cohort of 90 patients. If the recurrence risk attributable to fat grafting is low, our study may not be appropriately powered to discern its true impact on breast cancer recurrence. This lack of statistical power is

likely to affect future studies similar to ours, as much larger breast reconstruction populations with and without fat grafting would be needed. In addition, the large number of patients, the time, and the resources necessary to perform an appropriately powered, randomized prospective trial are seemingly prohibitive. Therefore, with continued controversy over the ultimate impact of autologous fat grafting on local cancer recurrence, we believe this study is only the foundation for future research that needs to be performed. We advocate that investigators continue to report their own institutional series to supplement the literature, allowing for the pooling of patient data from multiple authors' experiences, rather than relying on the findings of one study.

## CONCLUSIONS

Autologous fat grafting remains an attractive, and flexible, tool for optimizing aesthetic outcomes during breast reconstruction, with an associated low risk of complications. Although its definitive impact on local breast cancer recurrence remains unclear, our large retrospective review demonstrates no measurable increase in recurrence rates secondary to fat grafting on long-term follow-up. Continued research in a prospective manner, however, is needed to establish fat grafting as a safe and routine technique for revisional breast surgery. We encourage reconstructive breast surgeons to continue to utilize fat grafting with careful oncologic follow-up and to report their experience in the scientific literature when possible.

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