Review of Autologous Fat Grafting in Postmastectomy Reconstruction Patients: Nonroutine Diagnostics and Oncologic Safety

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Background: Autologous fat grafting (FG) is increasingly used as an adjunctive reconstruction technique to augment volume, achieve symmetry, and improve contour deformities. This study aims to characterize the oncologic and surgical safety of FG in women undergoing autologous breast reconstruction (ABR) or implant-based reconstruction (IBR).

Methods: A retrospective chart review was performed for all patients undergoing FG at a multi-site single health system between 2015 to 2018. A total of 228 eligible breasts from 155 patients were identified using Current Procedural Terminology codes. Patients were divided by reconstructive technique. Bivariate analyses compared baseline characteristics and post-FG outcomes.

Results: Mean age for patients undergoing ABR (129 breasts) was 52.8 years compared to 48.6 years for those undergoing IBR (99 breasts; P = 0.002). A heavier volume of fat was grafted per ABR breast (143.8mL) than per IBR breast (102.2mL; P = 0.002). Forty-seven (20.6%) breasts required FG revision, more frequently in ABR breasts (31.0%) than IBR breasts (7.1%; P < 0.001). Following FG, 17.5% of patients experienced a palpable mass, and 18.9% of breasts underwent nonroutine diagnostics or procedures, with no difference between ABR and IBR groups. Most biopsies noted benign findings such as fat necrosis (2.2%) or a benign mass (0.9%), with recurrence only noted in two patients (0.9%). Mean follow-up was 20.4 months.

Conclusion: FG is a safe, surgically simple procedure more commonly performed in ABR breasts. FG use in ABR and IBR breasts is oncologically safe, with no impairment in breast surveillance and low rates of locoregional recurrence, but possibly increased incidence of nonroutine imaging and biopsies. (Plast Reconstr Surg Glob Open 2022;10:e4579; doi: 10.1097/GOX.0000000000004579; Published online 28 October 2022.)

INTRODUCTION

Autologous fat grafting (FG) is a technique used to treat volume and contour abnormalities of the breast following postmastectomy reconstruction. This surgical adjunct is increasingly performed, as evidence refuting concerns regarding impaired breast surveillance and affirming its short-term oncologic safety increases.1-5

Breast reconstruction techniques include autologous-based reconstruction (ABR) and implant-based reconstruction (IBR). ABR utilizes free tissue transfer harvested from donor sites, allowing for preservation of the natural breast contour. Alternatively, IBR uses a prosthetic device such as an implant or tissue expander. FG serves as a solution for deformities that may arise following reconstruction, such as “rippling” or “step-offs.” It is an important component of reconstructive surgery used in almost 30% of all breast reconstruction cases due to its minimal invasiveness, ability to camouflage irregularities of the shape and texture, and ability to approximate a more natural breast contour.6-9

Despite use of FG, there may be concern for an increased risk of oncologic recurrence with this technique.9 This concern arises from conflicting reports in previous literature regarding recurrence rates; while earlier reports indicated a risk of ductal carcinoma in

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situated associated with FG, more recent reports indicated no increase in locoregional or systemic recurrence rates of breast cancer (BC) or occurrence of a second BC. Long-term outcomes and reporting for larger cohorts are still necessary to establish oncologic safety with this procedure.

In this study, we evaluate the oncologic and operative safety of FG with ABR and IBR, as well as the incidence of unanticipated postmastectomy imaging and biopsies in reconstructive BC patients. Critical in this BC population, we sought to demonstrate that although the development of palpable masses at the site of grafting is common, they most often correlate with fat necrosis or benign tissue changes.

**PATIENTS AND METHODS**

**Study Design**

An IRB-approved (MHRI 2018-173), retrospective cohort study was developed from all women undergoing autologous FG at a multisite, single health system from 2015 to 2018. Eight academic, urban, and community hospitals distributed across the District of Columbia and Maryland regions encompass this healthcare system. Eligible patients were identified by Current Procedure Terminology codes for FG: 20926, 15771, 15772, 15769, 14774.

**Data Collection**

Patients included those who underwent mastectomy with immediate or delayed reconstruction and subsequent FG. Operative and postoperative clinic notes were evaluated using electronic medical records to gather information regarding radiation history, mastectomy and reconstructive techniques, and FG techniques and outcomes. Revision procedures were defined as repeat FG, skin excision, or capsulectomy/capsulorrhaphy.

Patients were divided into groups based on reconstructive technique: IBR or ABR. ABR was further subdivided into subpectoral and prepectoral groups for secondary analysis, while ABR was split by type of flap reconstruction. These included the deep inferior epigastric perforator (DIEP) flap, transverse rectus abdominal muscle (TRAM) flap, muscle-sparing (MS)-TRAM flap, latissimus dorsi (LD) flap, transverse upper gracilis (TUG) flap, and superior epigastric artery (SIEA) flap. TUG (n = 2) and SIEA (n = 1) flaps were excluded from stratified ABR analysis due to low numbers. Selection criteria for mastectomy and reconstructive technique was based on surgeon and patient preference, as well as intraoperative skin flap assessment as outlined in previous studies. Exclusion criteria included follow-up less than 1 month, recurrence or new breast malignancy between mastectomy and FG, and incomplete data regarding reconstructive technique.

Complications and radiologic surveillance data were gathered. Complications included incidence of infection, hematoma, seroma, dehiscence, or necrosis following FG of reconstructed breasts. Nonroutine imaging following FG was collected, defined as surveillance not included in typical postoperative radiologic recommendations. These included ultrasound, magnetic resonance imaging, and mammogram. Rates of unplanned biopsy and excision of tissue was measured. Qualitative evaluation of pathologic findings following biopsy was recorded.

**Fat Grafting Processing Techniques**

The following fat processing techniques were used in this study:

- **Centrifuge**
  - Centrifugation is one of the most commonly used techniques for fat processing. It is part of the Coleman technique, involving fat centrifugation in 10 cm³ syringes, for 3 minutes at 3000 rpm.

- **Telfa**
  - The Telfa technique is performed by rolling the harvested lipoaspirate over Telfa gauze, thereby allowing the aqueous portion of fat to be absorbed by the material.

- **Revolve**
  - The revolve technique separates tumescent fluid from lipoaspirate, washes, and vacuum-aspirates the processed content three times automatically.

- **HydraSolve**
  - The HydraSolve (HydraSolve, Andrew Technologies, Tustin, Calif.) technology uses a stream of warmed (37–55°C), low-pressure (300–1100 psi), and pulsed saline solution to liquefy targeted adipose tissue while preserving structures like the skin, blood vessels, nerves, and connective tissue.

- **PureGraft**
  - The PureGraft (Cytori Therapeutics, San Diego, Calif.) device is a closed membrane filtration system that washes and filters harvested fat. Its exact technology is yet to be publicly disclosed, but its functional mechanism mirrors that of dialysis units.

- **AquaVage**
  - The AquaVage (AquaVage, M.D. Resource, Livermore, Calif.) is a closed system device that harvests fat at low flow.
Once the fluid is separated from the fat, the fat is decanted into lock syringes that can be readily injected into the patient without further processing.

**Statistical Analysis**

Bivariate analysis comparing ABR and IBR baseline characteristics and FG characteristics and outcomes used either chi-squared, Fisher exact, or Student *t* test as appropriate. Statistical analysis was performed using STATA 17.0.

### RESULTS

#### Patient Demographics

A cohort of 155 patients underwent FG for 228 breasts. Mean age was 60.0 ± 10.3 years (Table 1). ABR patients were older (52.8 ± 10.0 years; *P* = 0.002). The majority of breasts underwent immediate reconstruction (n = 194, 85.1%). Most breasts underwent mastectomy for therapeutic concerns (n = 148, 64.9%). ABR breasts most commonly underwent skin-sparing mastectomy (n = 62, 48.1%), compared with IBR breasts undergoing nipple-sparing mastectomy (n = 38, 38.4%; *P* = 0.029). If a patient had a history of radiation, there was a trend toward undergoing ABR (n = 18, 14.0%) more than IBR (n = 6, 6.1%; *P* = 0.054). Adjuvant radiation did not affect reconstructive approach. ABR patients most commonly underwent reconstruction with LD (n = 55/129, 42.6%) or DIEP (n = 52/129, 40.3%) flaps. Most IBR patients underwent subpectoral (n = 67/99, 67.7%) compared with prepectoral reconstruction (n = 32, 32.3%).

#### Fat Grafting Techniques

Mean time from mastectomy to FG was 2.7 ± 0.6 months, with no difference in time to FG between ABR and IBR groups (Table 2). FG was most frequently performed as a revision procedure following reconstruction (n = 116/222, 52.3%), more frequently following ABR (n = 74/127, 58.3%) than IBR (n = 42/95, 44.2%; *P* = 0.025). In 47.8% (n = 106/222) of cases, FG occurred at the time of reconstruction (eg, tissue expander exchange, implant exchange, or ABR). When FG was performed with ABR, it was always as part of a LD and immediate fat transfer (LIFT) procedure. FG was more commonly used unilaterally in ABR patients than in IBR (59.3 versus 40.3%; *P* = 0.021) and bilaterally in IBR patients than ABR (59.7 versus 40.7%; *P* = 0.021). The abdomen served as the most common FG donor site (n = 92, 40.5%). The most common FG processing system used across all breasts was PureGraft (n = 91, 40.0%; *P* < 0.001). Tumescence was used for fat harvest in 95.9% of breasts (n = 208/217).

On average, fat was grafted to a greater number of locations in ABR breasts (1.7 ± 0.81) compared to IBR breasts (1.4 ± 0.67; *P* < 0.001). The superior breast was most commonly fat grafted (n = 122, 56.7%; *P* < 0.001); this was the most common site in IBR breasts (n = 75, 83.3%), compared with the LD in ABR breasts (n = 53, 42.4%). Across all breasts, an average 127.4 ± 7.4 mL of fat was grafted per breast; ABR breasts required a greater fat grafting volume (143.8 ± 10.6 mL) compared with IBR breasts (102.2 ± 8.5 mL; *P* < 0.001).

#### Outcomes following Reconstruction with Fat Grafting

FG outcomes following reconstruction were assessed in terms of postoperative revision procedures, complications, and length of follow-up (Table 3). Seventy-three (32.0%) reconstructed breasts underwent revisions, most commonly involving repeat FG (n = 47, 20.6%). ABR breasts experienced higher revision rates (n = 50, 38.8%) than IBR breasts (n = 18, 19.4%).
IBR breasts (n = 23, 23.2%; P = 0.013), with ABR breasts more often undergoing repeat FG (n = 40, 31.0%) than IBR breasts (n = 7, 7.1%; P < 0.001). IBR breasts underwent capsulectomy or capsulorrhaphy at a higher rate (n = 11, 11.1%) than ABR breasts with implants (n = 4, 3.1%; P = 0.016). The overall complication rate was 8.8% (n = 20), with ABR breasts experiencing a higher 30-day complication rate (n = 19, 14.7%) than IBR breasts (n = 1, 1.0%; P ≤ 0.001). There was no difference in occurrence of infection, hematoma, seroma, necrosis, or dehiscence between groups. Length of follow-up in ABR patients was significantly shorter than in IBR patients (16.3 ± 14.1 versus 25.8 ± 1.7 months; P < 0.001).

**Diagnostic Outcomes after Reconstruction**

Palpable lumps or nodules occurred in 17.5% (n = 40) of breasts following reconstruction with FG (Table 4), with 18.9% (n = 43) of all breasts undergoing nonroutine diagnostic workup, most frequently by ultrasound (n = 38, 16.7%). Ten breasts (4.4%) underwent biopsy, most
commonly with benign findings including fat necrosis ($n = 5, 2.2\%$) or a benign mass ($n = 2, 0.9\%$). Two breasts experienced recurrence ($0.9\%$) at mean 60.7-37.0 months since mastectomy. There were no differences in incidence of palpable mass, completion of nonroutine diagnostics, or biopsy findings between ABR and IBR breasts.

Among IBR breasts, 16.2\% ($n = 16$) experienced a palpable mass after FG, with 21.2\% ($n = 21$) undergoing nonroutine diagnostic workup. Three breasts (3.0\%) underwent biopsy and two (2.0\%) underwent excision. When stratified by pectoral plane, no differences were seen regarding these diagnostic outcomes.

Among ABR breasts, 24 (18.6\%) experienced a palpable mass after FG. This occurred in 11 (22.4\%) DIEPs, four (30.8\%) TRAMs, three (30.0\%) MS-TRAMs, and four (7.3\%) LDs ($P = 0.010$). Nonroutine diagnostics were performed in 22 (17.2\%) breasts. Excision occurred more frequently in MS-TRAMs ($n = 1, 16.7\%$) compared with other ABR techniques ($P = 0.022$).

In cases where the fat graft processing system used was known, the rate of palpable lumps stratified by type of system was studied. This rate was significantly higher in patients who underwent fat grafting by AquaVage ($n = 4, 66.7\%$) compared with other processing systems ($P = 0.039$; Table 5).

### DISCUSSION

To our knowledge, this is the first and largest study comparing oncologic safety outcomes following FG for postmastectomy autologous-based versus implant-based reconstruction in BC patients. We found that FG use in either ABR or IBR is oncologically safe, with low locoregional recurrence rates (0.9\%). Rates of palpable masses following reconstruction with FG were comparable between reconstructive techniques (18.6\% ABR versus 16.2\% IBR), as well as rates of nonroutine diagnostics within each group (17.2\% ABR versus 21.2\% IBR). Stratification of reconstructive techniques within ABR and IBR groups, such as flap type or pectoral plane also found no differences in outcomes. We provide evidence of oncologically safe reconstruction with FG no matter which reconstructive technique a patient chooses to undergo.

Despite increasing use of FG in recent years, with nearly 30\% of all breast reconstructions cases utilizing FG in 2016, it was not previously accepted as a safe and effective reconstructive option in postmastectomy women. FG was labeled “experimental” by the 1987 American Society of Plastic Surgeons committee report, which strongly advised against its use due to its potentially adverse impacts on breast imaging and BC screening. A more recent position statement in 2012 outlined evidence indicating that FG in postmastectomy reconstruction yielded aesthetic improvements and improved patient satisfaction while maintaining low complication rates. Despite this conditional support, the report acknowledged the limited evidence available and need for additional studies assessing oncologic safety and efficacy of FG. The current study serves to provide evidence supporting FG as a safe adjunctive reconstruction option for BC patients.

### Benefits and Complications of Fat Grafting following Reconstruction

With mastectomy serving as a common option in BC treatment and prophylaxis, many patients choose postmastectomy breast reconstruction to lessen adverse impacts of...
mastectomy on psychosocial functioning and quality of life.\textsuperscript{23} Unfortunately, the desired aesthetic outcome is not always achieved following reconstruction.

In recent years, popularization of prepectoral implant placement resulted in their wide acceptance as an alternative to submuscular implants, given the reduction in pain and muscle impairment and the new development of acellular dermal matrices.\textsuperscript{24,25} However, the decreased availability of overlying soft tissue for prepectoral implants presents unique challenges of “rippling” and “step-offs”, especially in thin women.\textsuperscript{26,27} FG application to the upper pole and to the plane between the acellular dermal matrices and overlying skin flap can enhance overall breast volume and mask deformities (Fig. 1).\textsuperscript{25,28-30} Following FG at the time of implant exchange for subpectoral IBR, FG targets the upper poles of the breast, upper edge of the implant, and midline plane to reduce implant visibility, rippling, and achieve a natural-appearing anatomic upper pole slope.\textsuperscript{31} In the current study, adjunctive FG following IBR was applied to the superior pole in 83\% of cases, as well as the superior lateral (1\%) and superior medial (4.4\%) poles. The addition of FG to traditional IBR increases patient satisfaction regarding aesthetic outcomes compared with those who do not undergo the procedure.\textsuperscript{22,32}

Similar to IBR breasts, FG in ABR improves volume in thin patients and eases transition contours between tissue flaps and the native chest wall (Fig. 2).\textsuperscript{31,32} Adjuvantive FG use also expands the population able to undergo ABR, allowing patients with a thin body habitus or medium- to large-sized breasts to undergo ABR despite having inadequate donor-site volume.\textsuperscript{30} ABR augmentation with large-volume fat grafts additionally yielded high levels of patient and surgeon satisfaction without prolongation of treatment periods or additional take-backs when compared to ABR without FG.\textsuperscript{33} Our study found FG was used more often to revise contour deformities following primary ABR reconstruction than IBR, and that ABR breasts utilized a greater volume of fat grafted.

FG is complicated by the unpredictable nature of fat resorption, with a 40 to 60\% volume loss within the first 6 months following FG requiring 15 to 24\% of patients to undergo additional grafting procedures.\textsuperscript{23,35-38} In 31.0\% of our ABR breasts, patients opted for repeat FG procedures, a significantly higher rate than for IBR breasts (7.1\%). Cohen et al previously reported an overall FG complication rate of 9.4\%, comparable to the 8.8\% experienced in our overall cohort.\textsuperscript{39} A study utilizing the National Surgery Quality Improvement Program Participant Use Files to compare outcomes following breast reconstruction reported a complication rate of 4.5\% in IBR patients and 9.1\% in ABR patients.\textsuperscript{40} Rates of IBR complications were comparable to rates seen in our study, despite patients undergoing additional FG. We report higher rates of complications in ABR patients with FG (14.7\%), possibly due to the greater volume of FG and revision procedures required in these patients.

Oncologic Safety of Fat Grafting

Oncologic safety following reconstructive procedures is paramount. Previous studies demonstrated the involvement of adipocytes and preadipocytes in tumor-stromal interaction, suggesting their role in oncogenesis; however, no in vivo studies support this association. For women with BC undergoing mastectomy, the 20-year locoregional recurrence rate ranges from 1 to 2.3\%.\textsuperscript{41-46} Prior studies reported no significant association between FG and disease recurrence in women treated for BC.\textsuperscript{45,47} At mean follow-up of 20.4 months, we report rates of locoregional recurrence comparable to prior studies in patients who underwent FG (0.9\%), with no significant difference between ABR and IBR techniques. Our results support the oncologic safety profile of adjuvant FG use with any reconstructive technique.

Postmastectomy Nonroutine Diagnostics

With the increasingly pervasive use of FG, there is a potential for unintended consequences such as increased incidence of palpable fat-related changes. Complications have been reduced following refinements in technique; however fat necrosis still occurs at rates of 5 to 22.1\%.\textsuperscript{47-52} In BC patients, a new palpable mass in the reconstructed breast can be a source of significant concern for both the patient and multidisciplinary BC team, reflexively leading
to nonsurveillance imaging and possible additional invasive procedures. Currently, there is still no consensus regarding the use of routine or diagnostic breast imaging in reconstructed patients. Shammas et al reported the limited effects of surveillance imaging of palpable masses on locoregional-recurrence-free survival in reconstructed patients, emphasizing the importance of a multidisciplinary approach in defining the likelihood of benign findings such as inherent complications of reconstructive techniques. This approach may reduce the incidence of unnecessary imaging and biopsy postmastectomy.

Previous studies reported postmastectomy diagnostic imaging rates of 22 to 31.7% in patients reconstructed with additional FG, and rates of biopsy ranging from 4.8 to 7.8%. Overall, 17.5% of our FG patients experienced palpable masses. Patients who underwent AquaVage experienced the highest rate of palpable lumps (66.7%), while more commonly used systems like PureGraft and Revolve had the lowest rates (14.3% and 17.6%, respectively). Pinell-White et al reported that FG patients underwent 22% more imaging studies than non-FG counterparts and twice as many breast biopsies. We report a lower rate of patients who underwent postmastectomy nonroutine diagnostics (18.9%), which most frequently involved ultrasound. In cases of suspicious findings on imaging, invasive diagnostics such as biopsy or excision were performed in 6.1% of patients, comparable to prior reports. Most findings were benign, such as normal postoperative changes or fat necrosis. Given that most diagnostics resulted in benign findings, we further highlight the need for multidisciplinary communication between oncology and surgery teams before ordering nonroutine diagnostics.

Inherent study limitations include the retrospective nature of our study design, which depended on the quality of data reported within patients' medical records. Data were included from a single institution, limiting the generalizability and comprehensiveness of the findings, as well as the sample size. Additionally, the short follow-up period may reflect the lower rate of recurrence observed. Patients in this cohort could have possibly sought care for postoperative complications in other hospitals not included in this analysis. A weakness of this study is the lack of inclusion of cancer stage data in the setting of discussions surrounding cancer recurrence. The operative notes were written by different surgeons and were not standardized to include the same details. The choice of FG processing technique was based on surgeon preference and resource availability, preventing the ability to effectively account for the variations in techniques used in each case of FG. Future prospective cohort studies, ideally with multi-institutional collaboration, are needed to assess the long-term safety and efficacy of this technique.

**CONCLUSIONS**

This study demonstrates FG following ABR or IBR as a safe adjunctive technique for postmastectomy reconstruction. We highlight the surgical and oncologic safety provided by this technique and emphasize the need for a multidisciplinary approach in evaluating palpable masses that may arise following reconstruction. This can help
in reducing unnecessary nonroutine diagnostic imaging and procedures, further improving quality of care for BC patients.

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