

Oncologic Safety and Surveillance of Autologous Fat Grafting following Breast Conservation Therapy

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Background: Autologous fat grafting is a useful adjunct following breast reconstruction. The impact of autologous fat grafting on oncologic safety and surveillance remains questionable, particularly following breast conservation therapy.

Methods: The authors performed a retrospective review of patients who underwent delayed fat grafting following breast conservation therapy between 2006 and 2016. A control group of conservatively managed patients without grafting was matched for cancer stage, age, body mass index, and follow-up. Outcomes included locoregional recurrence and oncologic surveillance.

Results: Seventy-two patients were identified per cohort. There were no differences in median age (50 years versus 51 years; $p = 0.87$), body mass index (28.2 kg/m^2 versus 27.2 kg/m^2 ; $p = 0.38$), or length of follow-up (61.9 months versus 66.8 months; $p = 0.144$) between controls and grafted patients, respectively. Overall, four patients in each cohort experienced recurrence (5.6 percent; $p = 1.00$) with similar cumulative incidence estimates observed (log-rank test, $p = 0.534$). There were no significant differences in palpable mass (9.7 percent versus 19.4 percent; $p = 0.1$), fat necrosis (34.7 percent versus 33.3 percent; $p = 0.86$), calcifications (37.5 percent versus 34.7 percent; $p = 0.73$), or indication for breast biopsy (15.3 percent versus 22.2 percent; $p = 0.23$) between breast conservation and breast conservation therapy plus autologous fat grafting cohorts, respectively.

Conclusions: Overall, the authors found no difference in recurrence rates after breast conservation with or without delayed fat grafting. Furthermore, there were no differences in the rates of fat necrosis, palpable mass, and abnormal radiographic findings. This study represents the longest follow-up to date in in a large matched study of autologous fat grafting with breast conservation therapy demonstrating oncologic safety and no interference with follow-up surveillance. (*Plast. Reconstr. Surg.* 146: 215, 2020.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, III.

Breast cancer remains the most common malignancy in women, with surgical treatment at the foundation of multidisciplinary care. Breast conservation therapy including lumpectomy or partial mastectomy followed by

irradiation offers survival rates similar to those for mastectomy in patients with early-stage cancers.¹⁻³ Although the oncologic outcomes of

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these treatments may be comparable, the resulting breast aesthetics and options for reconstruction may be very different. In fact, partial breast reconstruction with breast conservation therapy may present a greater challenge than reconstruction after mastectomy, particularly in the setting of radiation therapy. Whereas patient satisfaction after breast conservation therapy is generally good, authors have reported significant asymmetry in more than one-third of patients surveyed in addition to adverse changes over time.⁴⁻⁸

Autologous fat grafting is commonly used to correct contour irregularities, volume defects, and asymmetry in breast reconstruction. Adipose grafts add soft-tissue volume and adipose tissue stroma, which is rich in progenitor cells and cytokines, making an adipose graft a potentially abundant resource in regenerative medicine.⁹ Furthermore, there is evidence supporting beneficial effects of autologous fat grafting in irradiated tissue, improving scar quality, and reducing chest wall pain.¹⁰⁻¹² Although the utility of autologous fat grafting has been known for decades, its safety, particularly in breast reconstruction, continues to be questioned. The 2009 Task Force statement from the American Society of Plastic Surgeons highlighted theoretical concerns about autologous fat grafting such as stimulation of cancer growth, increased cancer recurrence, and fat necrosis and calcifications that may interfere with mammography and subsequent cancer detection.¹³ In the decade following the American Society of Plastic Surgeons consensus statement, few studies have examined outcomes of autologous fat grafting in breast cancer patients after mastectomy,¹⁴⁻²¹ finding that the risk of recurrence and metastatic disease did not increase with lipotransfer.

Breast surgery, including breast reduction and autologous fat grafting, is known to alter the tissue architecture and often leads to calcifications or scarring within the parenchyma.²² However, whether these changes interfere with long-term cancer surveillance is unclear. The most common reported mammographic findings after cosmetic autologous fat grafting were oil cysts (25 percent), calcifications consistent with fat necrosis (17.6 to 25.0 percent), and architectural distortion (2.8 to 12.0 percent).^{22,23}

Given the findings described above, the present retrospective study was performed to compare oncologic outcomes in breast cancer patients who underwent delayed autologous fat grafting after breast conservation therapy (lumpectomy with irradiation) with those in a control cohort of breast conservation therapy patients who did not undergo reconstruction with autologous fat

grafting. The authors hypothesized that the rate of locoregional recurrence would not differ in the two cohorts. Our secondary objectives were to characterize and compare postoperative complications and radiographic surveillance findings after breast conservation therapy with and without autologous fat grafting.

PATIENTS AND METHODS

A prospectively maintained database of consecutive breast cancer patients who underwent autologous fat grafting following breast conservation therapy (breast conservation therapy plus autologous fat grafting) performed at our cancer center from January of 2006 to December of 2016 was reviewed retrospectively. The protocol was approved by our institutional review board. To ensure that treatment and follow-up were consistent in these patients, the following inclusion criteria were used and were all performed at our institution: breast conservation surgery, pathologic review, postlumpectomy external beam radiation therapy, annual follow-up including mammograms, the autologous fat grafting operation, and subsequent follow-up including post-autologous fat grafting mammograms. Patients who had care initiated elsewhere and were seen for fat grafting only; with a history of *BRCA* mutations; who did not undergo imaging for oncologic surveillance; who received partial breast irradiation, brachytherapy, or a variant of irradiation on a study protocol; who declined recommended chemotherapy, radiation therapy, or hormonal therapy; or who underwent other types of reconstruction after lumpectomy, such as pedicled flaps and implants, were excluded. Of note, an oncoplastic reconstruction performed at the time of breast conservation therapy, such as a mastopexy, breast reduction, or local tissue rearrangement, was not an exclusion criterion, provided that the patient underwent follow-up mammography before autologous fat grafting. A control cohort of patients who received breast conservation therapy during the same period and met the inclusion criteria but did not undergo autologous fat grafting or other reconstruction procedures following treatment were also identified.

Patient, treatment, reconstruction, and outcome data on the breast conservation therapy and breast conservation therapy plus autologous fat grafting groups were analyzed and compared directly. The operative reports were reviewed to verify tumor type and location, concurrent oncoplastic surgery, presence of clear margins, time

from oncologic surgery to autologous fat grafting, volume of fat injected into the defect, and method of graft preparation. For the patients who underwent autologous fat grafting, mammographic reports before and after autologous fat grafting were reviewed. All patients underwent routine, institutionally guided oncologic surveillance, which included follow-up visits with the multidisciplinary team (medical oncology, radiation oncology, and plastic surgery) in addition to mammography and sonography. Locoregional recurrence and metastatic disease were recorded throughout the study period. Follow-up notes were reviewed for the following findings: palpable mass on physical examination, contour irregularity, additional grafting procedures, overall complications, and evidence of recurrent or distant disease. Mammographic reports were reviewed for any aberrant findings following either breast conservation therapy or autologous fat grafting. Findings of “postsurgical changes consistent with baseline imaging” and “post-lumpectomy scar consistent with baseline imaging” described on subsequent mammograms were not included in the “abnormal mammogram” surveillance. Specifically, we looked for distinct descriptions of new calcifications (benign or suspicious), evidence of fat necrosis, cysts, or locoregional recurrence, and indications for biopsy according to either physical examination or mammography.

Demographic and clinical characteristics were summarized using means, standard deviations, medians, and ranges for continuous data. Frequencies and percentages were used to summarize categorical data, and comparisons between study cohorts were conducted using a chi-square test or the Fisher’s exact test when appropriate. An independent samples *t* test or the Wilcoxon rank sum test was used to compare continuous variables. Time to local recurrence was defined as the time from the date of surgery to the date of local recurrence. Patients who remained alive and recurrence-free were censored at the date of their last follow-up or the date of diagnosis of distant metastasis, whichever occurred first. For time-to-event analysis, cumulative incidence curves were derived using 1 – Kaplan-Meier estimates. Values of $p < 0.05$ were considered statistically significant, and all analyses were conducted using the Stata software program (release 15; StataCorp, College Station, Texas).

RESULTS

Patient Characteristics

The authors retrospectively identified 72 breast cancer patients who underwent unilateral

breast conservation therapy followed by delayed autologous fat grafting to the affected breast who met inclusion criteria. We compared data on this cohort with data on 72 patients in a matched comparison cohort who underwent breast conservation therapy without autologous fat grafting and had similar ages, body mass index, clinical stages, and follow-up lengths. **Table 1** summarizes the sociodemographic characteristics of the study participants. The median ages were similar in the breast conservation therapy and breast conservation therapy plus autologous fat grafting cohorts [50 years (range, 22 to 76 years) versus 51 years (range, 28 to 68 years); $p = 0.869$], as were the median body mass indexes [28.2 kg/m² (range, 19.3 to 48.8 kg/m²) versus 27.2 kg/m² (range, 18.5 to 39.4 kg/m²); $p = 0.375$]. The median follow-up length in the breast conservation therapy group was 61.9 months (range, 14.5 to 182.6 months), whereas that in the breast conservation therapy plus autologous fat grafting group was 66.8 months (range, 14.3 to 320.4 months; $p = 0.144$). The median time from diagnosis to autologous fat grafting was 39.2 months (range, 6.5 to 250.5 months).

Oncologic Characteristics

All patients underwent unilateral breast assessments. Their oncologic characteristics are outlined in **Table 2**. Tumor stage was used to match the cohorts, with the most common stages being I (49 percent) and II (38 percent). The majority of the cancers were estrogen receptor–positive (76 percent), progesterone receptor–positive (63 percent), and Her2/neu-negative (92 percent). Approximately 20 percent of the overall study group had abnormality consistent with triple-negative breast cancer (i.e., estrogen receptor–negative, progesterone receptor–negative, and Her2/neu-negative). There were no statistically significant differences in the proportion of patients receiving neoadjuvant chemotherapy, adjuvant chemotherapy, and hormone therapy (**Table 3**). All patients received radiation therapy to the affected breast as part of breast conservation therapy before autologous fat grafting.

Surgical Characteristics

The patients’ surgical characteristics are outlined in **Tables 4** and **5**. Overall, the tumor location was heterogeneous, with the majority occurring at the upper outer quadrant (47 percent) and central breast (26 percent). The predominant histology was invasive ductal carcinoma (71 percent). The mean tumor size was 1.9 ± 1.3 cm. The majority of

T4,T5

Table 1. Summary of Patient Characteristics*

Characteristic	BCT (%)	BCT plus AFG (%)	<i>p</i>	Total (%)
No. of patients	72	72		
Age at diagnosis, yr			0.869†	
Median	50	51		50.5
Range	22–76	28–68		22–76
BMI, kg/m ²			0.375†	
Median	28.2	27.2		27.6
Range	19.3–48.8	18.5–39.4		18.5–48.8
Race			0.043‡	
Caucasian	49 (69.0)	51 (70.8)		100 (69.9)
African American	12 (16.9)	6 (8.3)		18 (12.6)
Spanish Hispanic	7 (9.9)	15 (20.8)		22 (15.4)
Asian Pacific Islander	3 (4.2)	0 (0)		3 (2.1)
Time from diagnosis to oncologic surgery, mo			0.272§	
Median	1.7	1.4		1.6
Range	0–9.1	0–9.6		0–9.6
Last follow-up, mo			0.144§	
Median	61.9	66.8		64.5
Range	4.5–182.6	14.3–320.4		4.5–320.4

BCT, breast conservation therapy; AFG, autologous fat grafting; BMI, body mass index.

*Proportions may not equal 100 percent because of round-off error.

†Independent samples *t* test.

‡Fisher's exact test.

§Wilcoxon rank sum test.

Table 2. Summary of Tumor Characteristics

Characteristic	BCT (%)	BCT plus AFG (%)	<i>p</i>	Total (%)
No. of patients	72	72		
Histology			0.362*	
Invasive ductal carcinoma	53 (73.6)	49 (68.1)		102 (70.8)
Invasive lobular carcinoma	4 (5.6)	2 (2.8)		6 (4.2)
DCIS	4 (5.6)	10 (13.9)		14 (9.7)
Unknown	0 (0.0)	0 (0.0)		0 (0.0)
Invasive mixed ductal-lobular	11 (15.3)	11 (15.3)		22 (15.3)
Stage			0.872*	
0	4 (5.6)	5 (6.9)		9 (6.2)
I	38 (52.8)	33 (45.8)		71 (49.3)
II	26 (36.1)	28 (38.9)		54 (37.5)
III	4 (5.6)	5 (6.9)		9 (6.2)
IV	0 (0.0)	0 (0.0)		0 (0.0)
ER-positive			0.331†	
No	15 (20.8)	20 (27.8)		35 (24.3)
Yes	57 (79.2)	52 (72.2)		109 (75.7)
PR-positive			0.168†	
No	23 (31.9)	31 (43.1)		54 (37.5)
Yes	49 (68.1)	41 (56.9)		90 (62.5)
HER2-positive			1.000†	
No	66 (91.7)	66 (91.7)		132 (91.7)
Yes	6 (8.3)	6 (8.3)		12 (8.3)
TNBC			0.218†	
No	60 (83.3)	54 (75.0)		114 (79.2)
Yes	12 (16.7)	18 (25.0)		30 (20.8)

BCT, breast conservation therapy; AFG, autologous fat grafting; DCIS, ductal carcinoma in situ; ER, estrogen receptor; PR, progesterone receptor; HER2, Her2/neu gene amplification; TNBC, triple-negative breast cancer (i.e., ER-negative, PR-negative, and HER2-negative).

*Fisher's exact test.

† χ^2 test.

patients had negative margins at the index operation (82 percent). There was a small number of patients with positive or close margins, and reexcision rates were similar between the two cohorts (12.5 percent for breast conservation therapy versus 16 percent for breast conservation therapy plus

autologous fat grafting; $p = 0.479$). No patient had positive margins on pathologic evaluation at the time of radiation therapy. The majority of patients underwent sentinel lymph node biopsy at the time of partial mastectomy (86.8 percent), whereas only 29.6 percent underwent axillary lymph node

Table 3. Summary of Adjuvant Treatment Characteristics

Characteristic	BCT (%)	BCT plus AFG (%)	P	Total (%)
No. of patients	72	72		
Neoadjuvant chemotherapy			0.560*	
No	56 (77.8)	53 (73.6)		109 (75.7)
Yes	16 (22.2)	19 (26.4)		35 (24.3)
Adjuvant chemotherapy			0.731*	
No	46 (63.9)	44 (61.1)		90 (62.5)
Yes	26 (36.1)	28 (38.9)		54 (37.5)
Adjuvant radiation therapy			—	
No	0 (0.0)	0 (0.0)		0 (0.0)
Yes	72 (100)	72 (100)		144 (100)
Adjuvant hormonal therapy			0.717*	
No	21 (29.2)	23 (31.9)		44 (30.6)
Yes	51 (70.8)	49 (68.1)		100 (69.4)

BCT, breast conservation therapy; AFG, autologous fat grafting.

* χ^2 test.

Table 4. Summary of Oncologic Surgical Characteristics

Characteristic	BCT (%)	BCT plus AFG (%)	P	Total (%)
No. of patients	72	72		144
Side of breast tumor			0.067§	
Left	31 (43.1)	42 (58.3)		73 (50.7)
Right	41 (56.9)	30 (41.7)		71 (49.3)
Tumor location*			0.597¶	
UOQ	38 (52.8)	29 (40.3)		67 (46.5)
UIQ	7 (9.7)	7 (9.7)		14 (9.7)
LOQ	4 (5.6)	2 (2.8)		6 (4.2)
LIQ	3 (4.2)	5 (6.9)		8 (5.6)
Multifocal	4 (5.6)	4 (5.6)		8 (5.6)
Central	15 (20.8)	22 (30.6)		37 (25.7)
Unknown	1 (1.4)	3 (4.2)		4 (2.8)
Margin at index operation			0.290§	
Negative	59 (81.9)	59 (81.9)		118 (81.9)
Close†	9 (12.5)	5 (6.9)		14 (9.7)
Positive	4 (5.6)	8 (11.1)		12 (8.3)
Reexcision			0.479§	
No	63 (87.5)	60 (83.3)		123 (85.4)
Yes	9 (12.5)	12 (16.7)		21 (14.6)
Sentinel lymph node biopsy performed			0.218§	
No	12 (16.7)	7 (9.7)		19 (13.2)
Yes	60 (83.3)	65 (90.3)		125 (86.8)
Results of sentinel lymph node biopsy‡			0.002§	
Negative	50 (83.3)	38 (58.5)		88 (70.4)
Positive	10 (16.7)	27 (41.5)		37 (29.6)
Axillary lymph node dissection performed			0.067§	
No	56 (77.8)	46 (63.9)		102 (70.8)
Yes	16 (22.2)	26 (36.1)		42 (29.2)
Results of axillary lymph node dissection‡			0.303§	
Negative	10 (62.5)	12 (46.2)		22 (52.4)
Positive	6 (37.5)	14 (53.8)		20 (47.6)
Oncoplastic reconstruction			0.077§	
No	43 (59.7)	53 (73.6)		96 (66.7)
Yes	29 (40.3)	19 (26.4)		48 (33.3)

BCT, breast conservation therapy; AFG, autologous fat grafting; UOQ, upper outer quadrant; UIQ, upper inner quadrant; LOQ, lower outer quadrant; LIQ, lower inner quadrant.

*Percentages may not total exactly 100% because of round-off error.

†Close margins meaning tumor present <2 mm from specimen edge.

‡Of patients who had a sentinel lymph node biopsy or axillary lymph node dissection.

§ χ^2 test.

¶Fisher's exact test.

dissection. More patients in the breast conservation therapy plus autologous fat grafting group than in the breast conservation therapy group had positive sentinel lymph nodes (41.5 percent versus

16.7 percent; $p = 0.002$). In addition, there was a trend of more patients in the breast conservation therapy plus autologous fat grafting group than in the breast conservation therapy group having

Table 5. Summary of Autologous Fat Grafting Surgery

Characteristic	Value (%)
Time to AFG, mo	
Median	39.2
Range	6.5–250.5
No. of AFG sessions	
Median (range)	1 (1–3)
1	5 (79.2%)
2	11 (15.3%)
3	4 (5.6%)
Total volume grafted, ml	
Mean ± SD	102.8 ± 94
Median	80
Range	12–490
Processing technique	
Centrifugation	44 (61.0)
PureGraft	20 (27.8)
Revolve	7 (9.7)
Telfa gauze	1 (1.4)

BCT, breast conservation therapy; AFG, autologous fat grafting.

positive findings in the axillary lymph node dissection, although the difference was not significant (54 percent versus 38 percent; $p = 0.303$). The percentages of patients in the breast conservation therapy and the breast conservation therapy plus autologous fat grafting cohorts who underwent concurrent oncoplastic reconstruction at the time of partial mastectomy were similar (40 percent versus 26 percent; $p = 0.077$).

The median time from oncologic surgery to autologous fat grafting was 38.4 months. The median volume of fat injected into the affected breast was 80 ml (range, 12 to 490 ml). The median number of autologous fat grafting sessions was one (range, one to three), and 21 percent of the patients had more than one autologous fat grafting session. Given the time frame of the study period, the majority of the grafts were prepared using a centrifugation technique (61 percent) similar to that described by Coleman.²⁴ As device-based systems such as PureGraft (Cytori Therapeutics, San Diego, Calif.) and subsequently REVOLVE (LifeCell Corp., Branchburg, N.J.) were introduced, these were also used to process fat for grafting (28 percent and 10 percent, respectively). In one case, the surgeon prepared a low volume of fat using Telfa gauze (Covidien, Minneapolis, Minn.).

Outcomes

Overall, there were four patients in each cohort who were found to have locoregional recurrence (5.56 percent; $p = 1.00$) (Table 6). Similarly, the incidence of metastatic disease did not differ in the two groups (2.8 percent for breast conservation therapy versus 4.1 percent for breast conservation therapy plus autologous

fat grafting; $p = 1$). The cumulative incidence curves for recurrence were similar (Fig. 1), with no statistically significant difference between the study cohorts ($p = 0.534$, log-rank test). All patients in the study had available radiographic imaging data, including 1 year after oncologic surgery and yearly thereafter. Approximately half of the patients in both groups had abnormal mammograms following breast conservation therapy (46 percent for breast conservation therapy versus 50 percent for breast conservation therapy plus autologous fat grafting; $p = 0.617$). Table 6 also shows the oncologic surveillance findings, which were most commonly benign calcifications (36 percent) followed by fat necrosis (34 percent). Overall, the biopsy rate was 19 percent (15.3 percent in the breast conservation therapy cohort and 22.2 percent in the breast conservation therapy plus autologous fat grafting cohort; $p = 0.286$). Those who underwent autologous fat grafting more commonly had palpable masses on examination (19 percent versus 10 percent); however, this difference was not statistically significant ($p = 0.098$). The proportion of patients with visible contour irregularities documented in the last follow-up assessment in the study period was higher in the breast conservation therapy than in the breast conservation therapy plus autologous fat grafting cohort (44 percent versus 29 percent; $p = 0.057$).

Details of the four locoregional recurrences in the breast conservation therapy plus autologous fat grafting cohort are outlined in Table 7. There were two recurrences within the same quadrant of the lumpectomy and subsequent fat graft, and one occurred deep to the defect in the pectoralis major muscle where no graft was delivered. The fourth recurrence was in a postoperative scar 5 months after a concurrent mastopexy and fat-grafting procedure. This patient reported persistent firmness adjacent to the mastopexy scar. Biopsy revealed recurrent intraductal carcinoma. Each patient had only one autologous fat grafting procedure at a range of 12 to 83 months after oncologic surgery. The times from autologous fat grafting to diagnosis of recurrence ranged from 5 to 149 months. Three of the four patients had node-negative disease.

DISCUSSION

Autologous fat grafting is a minimally invasive form of tissue transfer used to address deformities

Table 6. Summary of Surveillance Findings

Characteristic	BCT (%)	BCT plus AFG (%)	<i>p</i>	Total (%)
No. of patients	72	72		
Palpable mass			0.098*	
No	65 (90.3)	58 (80.6)		123 (85.4)
Yes	7 (9.7)	14 (19.4)		21 (14.6)
Visible contour irregularity			0.057*	
No	40 (55.6)	51 (70.8)		91 (63.2)
Yes	32 (44.4)	21 (29.2)		53 (36.8)
Abnormal mammogram			0.617*	
No	39 (54.2)	36 (50.0)		75 (52.1)
Yes	33 (45.8)	36 (50.0)		69 (47.9)
Fat necrosis			0.860*	
No	47 (65.3)	48 (66.7)		95 (66.0)
Yes	25 (34.7)	24 (33.3)		49 (34.0)
Cyst			0.731*	
No	68 (94.4)	67 (93.1)		135 (93.8)
Yes	4 (5.6)	5 (6.9)		9 (6.2)
Calcifications			0.729*	
No	45 (62.5)	47 (65.3)		92 (63.9)
Yes	27 (37.5)	25 (34.7)		52 (36.1)
Biopsy performed			0.286*	
No	61 (84.7)	56 (77.8)		117 (81.2)
Yes	11 (15.3)	16 (22.2)		27 (18.8)
Local recurrence			1.000*	
No	68 (94.4)	68 (94.4)		136 (94.4)
Yes	4 (5.6)	4 (5.6)		8 (5.6)
Metastasis			1.000†	
No	70 (97.2)	69 (95.8)		139 (96.5)
Yes	2 (2.8)	3 (4.2)		5 (3.5)

BCT, breast conservation therapy; AFG, autologous fat grafting.

* χ^2 test.

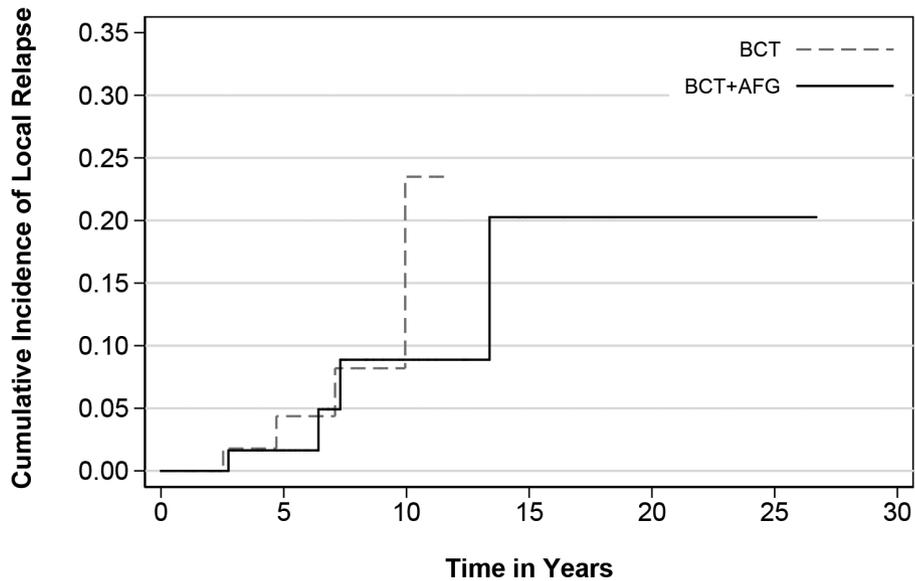
†Fisher's exact test.

and asymmetry following breast conservation therapy and to potentially mitigate the effects of radiation therapy on the breast. Over 30,000 grafting procedures for noncosmetic breast reconstruction were performed in the United States in 2017 according to American Society of Plastic Surgeons member statistics.²⁵ Although this trend will likely increase, several questions remain regarding optimal graft techniques, improving graft viability and retention, and oncologic safety.²⁶ In the present study, we sought to answer the question of oncologic safety in well-defined matched cohorts of patients who underwent breast conservation therapy with and without autologous fat grafting at a single cancer center. We found no difference in locoregional recurrence rate between the two groups, with a mean of 6 years of follow-up and no evidence of interference with cancer surveillance as a result of autologous fat grafting.

Early reported series looking at all indications for autologous fat grafting in the breast (cosmetic or reconstructive) demonstrated that the incidence of breast cancer did not increase.²⁷ Although these studies included breast conservation therapy among the list of indications for autologous fat grafting, they had little oncologic data for drawing meaningful conclusions in this

subgroup. More recent studies examined the oncologic safety of autologous fat grafting in breast cancer patients, particularly following mastectomy and breast reconstruction. Kronowitz et al.²⁰ reported on a matched series at our institution of 719 breasts treated with lipofilling after breast reconstruction compared with 670 control breasts without autologous fat grafting and found no significant differences in locoregional recurrence or systemic disease rates. Within the lipotransfer group were 305 noncancer prophylactic mastectomies, including in patients with known *BRCA* mutations, and no primary breast cancers identified after delayed fat grafting.

Unlike with mastectomy, after breast conservation therapy, the remaining breast tissue may be at increased risk for recurrence when exposed to adipose-derived progenitor cells or cytokines within a processed tissue graft.²⁸ Thus, autologous fat grafting in the setting of breast conservation therapy warrants dedicated evaluation. The literature contains no randomized, prospective comparisons at this time. Brenelli and colleagues reported on 59 patients who underwent delayed autologous fat grafting after breast conservation therapy and a minimum of 6 months of follow-up.²⁹ During the study period, the authors found



Number at risk

BCT:	72	36	5	0	0	0	0
BCT+AFG:	72	42	15	4	1	1	0

Fig. 1. Cumulative incidence of local recurrence in the breast conservation therapy (BCT) and breast conservation therapy plus autologous fat grafting (BCT+AFG) cohorts. The follow-up time is shown in years. The cumulative incidence curves remained similar up to year 10. The cumulative incidence rates for local recurrence were 1.8, 4.4, 4.4, and 23.5 percent in the breast conservation therapy group and 1.6, 1.6, 4.9, and 8.8 percent in the breast conservation therapy plus autologous fat grafting group at 3, 5, 7, and 10 years, respectively. The differences in the rates between the two study cohorts were not significant ($p = 0.534$, log-rank test).

a locoregional recurrence rate of 4 percent and an abnormal postoperative imaging rate of 20 percent. However, not all of the patients underwent imaging, and they did not include a control group. Juhl and colleagues³⁰ reported on 42 patients who underwent delayed autologous fat grafting after breast conservation therapy with an average of 12 months of follow-up and found better body image scores after than before autologous fat grafting. They also observed high rates of cysts (85 percent) and calcifications (21 percent) on follow-up imaging.

In a prospective observational study, patients with benign or small breast cancers (<T2) underwent resection and immediate autologous fat grafting.³¹ In this series of 37 patients, two had positive margins requiring additional excision, and no patients had local recurrences at 1-year follow-up. In a similar prospective nonrandomized study, Biazus and colleagues reported on their experience with breast conservation therapy and immediate autologous fat grafting initially in 20 patients with an average of 1-year follow-up³² and subsequently in 65 patients with an average of 40.8 months of follow-up.³³ A total of 10 patients had cancer recurrence or systemic disease, with

an annual locoregional recurrence rate of 0.44 percent.

Given the absence of randomized controlled trials, matched case-control studies provide the best available level of evidence; however, the literature contains only a few of them that can be highlighted. Gale and colleagues reported on autologous fat grafting in breast reconstruction, including 35 patients who received breast conservation therapy, matched 2:1 with control patients, with a mean follow-up duration of almost 3 years.³⁴ Locoregional recurrence rates were similar in the autologous fat grafting and control groups. Also, Mestak et al.³⁵ compared 32 patients treated with autologous fat grafting after breast conservation therapy with 45 patients who did not undergo autologous fat grafting, with a mean follow-up time of 27 months. Again, the locoregional recurrence and distant metastasis rates in the autologous fat grafting and control groups were similar.

Researchers at the European Institute of Oncology reported on several variations of their experience with autologous fat grafting to the breast, with all but one study demonstrating no increased risk of recurrence or metastatic disease following autologous fat grafting.^{15,16,36,37} In a series

Table 7. Summary of Cases of Recurrence after Autologous Fat Grafting

Patient	Age at Diagnosis (yr)	Histology of Primary Cancer	Treatment	AFG	Time			Histology of Recurrence
					A–B (mo)*	B–C (mo)†	A–C (mo)‡	
1	43	Mixed IDC/ILC, stage III, ER ⁺ /PR ⁺ /HER2 ⁻ node-positive	Neoadjuvant chemotherapy, tamoxifen	60 ml for contour	12	14	26	Mixed IDC/ILC, ER ⁺ /PR ⁻ /HER2 ⁻ , same quadrant
2	56	IDC, stage IIB, ER ⁺ /PR ⁺ /HER2 ⁺ node-negative	Adjuvant chemotherapy, anastrozole	36 ml for contour	64	54	118	IDC, pectoralis muscle§ ER ⁺ /PR ⁺ /HER2 ⁺
3	37	IDC, stage IA, ER ⁻ /PR ⁻ /HER2 ⁻ Node-negative	Neoadjuvant plus adjuvant chemotherapy	24 ml for contour	14	149	163	IDC, same quadrant ER ⁻ /PR ⁻ /HER2 ⁻
4	39	IDC, stage IIA, ER ⁺ /PR ⁺ /HER2 ⁻ node-negative	Neoadjuvant chemotherapy, tamoxifen	70 ml for contour, mastopexy	83	5	89	IDC, along cutaneous scar¶ ER ⁺ /PR ⁺ /HER2 ⁺

AFG, autologous fat grafting; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; ER, estrogen receptor; PR, progesterone receptor; HER2, Her2/neu gene amplification.

*Time (in months) between initial cancer operation and delayed AFG.

†Time (in months) between AFG and diagnosis of recurrent disease.

‡Time (in months) between original cancer operation and diagnosis of recurrence.

§Distant from original defect, as there was no grafting reported to the pectoralis muscle.

¶Recurrence found adjacent to concurrent mastopexy scar.

of 59 patients with intraepithelial neoplasia who underwent autologous fat grafting matched 2:1 with controls, Petit et al.³⁶ found that the 5-year rate of local event incidence was 18 percent in the autologous fat grafting group but 3 percent in the control group. However, in a more recent study of 322 matched cases, including overlapping cases from the intraepithelial neoplasia cohort, Petit et al. reported no statistical differences in locoregional recurrence and referred to an “additional unpublished analysis” of the earlier series, which did not demonstrate a statistical difference in event rates.³⁷ In the present study, less than 10 percent of cases were stage 0 breast cancer. However, we found no locoregional recurrences in the ductal carcinoma in situ subset in either cohort.

Our study is the first to compare radiographic surveillance following breast conservation therapy in patients with and without delayed autologous fat grafting. There were a considerable number of mammographic changes observed following the combination of lumpectomy and radiation therapy regardless of whether delayed autologous fat grafting was performed. Overall, these changes were mostly benign calcifications and fat necrosis, which was consistent with other studies of breast surgery,^{22,23} and these changes were equally prevalent after autologous fat grafting. Grafted adipose tissue appears lucent on follow-up mammograms but may lead to development of calcifications consistent with fat necrosis, prompting biopsy or follow-up visits at shorter intervals than routine surveillance. In the breast conservation therapy

plus autologous fat grafting cohort, mammographic detection occurred in one case of locoregional recurrence, whereas it was detected on sonography in the other three. Furthermore, only one patient had a palpable mass that appeared suspicious on imaging. We also found similar biopsy rates in the breast conservation therapy and breast conservation therapy plus autologous fat grafting cohorts (approximately 20 percent). Overall, we found that autologous fat grafting did not interfere with the ability to detect locoregional recurrence by means of follow-up imaging, particularly in the setting of postsurgical and post-radiation therapy changes after breast conservation therapy.

Also in our study, the incidence of postoperative palpable mass was higher than that reported previously,²¹ although this is not routinely reported in the literature. Even though the difference in palpable mass between the two groups was not statistically significant, it is important to recognize the potential for palpable abnormalities for several reasons, including patient counseling, surveillance, and grafting technique. Patients who undergo breast conservation therapy should continue oncologic surveillance, including breast self-examinations, and should be made aware of the possibility of palpable mass development as a result of either breast conservation or subsequent autologous fat grafting. All palpable examination findings were followed with mammography and ultrasound. If this imaging demonstrated benign findings, a 3- to 6-month follow-up interval was arranged. If either mammography or ultrasound

was suspicious for malignancy, biopsy was performed. Only one palpable mass per cohort was a local recurrence. The majority of palpable lesions in our study were benign fat necrosis or cysts and anecdotally resolved by means of massage and time. Still, a palpable mass in a patient with a history of breast cancer may be distressing and should be included in the informed consent process for autologous fat grafting.

Although the primary limitations of this retrospective study were similar to those of others referenced here, namely, smaller sample size and short follow time, our mean follow-up duration was longer than 6 years, and this was the largest study of autologous fat grafting and breast conservation therapy to include oncologic surveillance. Our study demonstrated the absence of a significant difference in locoregional recurrence rate between the breast conservation therapy and breast conservation therapy plus autologous fat grafting cohorts. To show a difference in risk of locoregional recurrence of just 5 percent between the cohorts using Fisher's exact test, more than 950 patients per study group would be needed to achieve 80 percent power. Our sample size was limited by very specific inclusion criteria, particularly focusing on oncologic treatment and follow-up, which is actually a strength of our study design. As we have shown, architectural changes, including cysts, fibroses, and calcifications, occur as a result of breast cancer changes independently of autologous fat grafting. Because early-stage breast cancers are commonly treated with breast conservation therapy (i.e., lumpectomy and irradiation), autologous fat grafting is a less invasive means of addressing volume loss, contour irregularities, and radiation fibrosis than are autologous flaps and has a lower risk profile following irradiation than does a breast implant. Our study provides evidence further refuting the concern that fat grafting in the native breast can interfere with surveillance or detection of recurrence following early breast cancer treatment.

CONCLUSIONS

Autologous fat grafting remains a promising tool in breast reconstruction. This study demonstrates that the risk of breast cancer recurrence is not increased in patients who undergo breast conservation therapy followed by delayed autologous fat grafting. Furthermore, the rates of postoperative abnormal examination and mammographic findings were the same in the breast conservation therapy with autologous fat grafting group as in

the matched breast conservation therapy control group. This is the first reported study of oncologic follow-up in breast cancer patients undergoing breast conservation therapy plus autologous fat grafting compared with breast conservation therapy alone that specifically shows no interference by autologous fat grafting on surveillance imaging.

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