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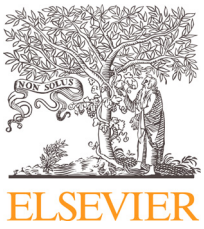

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Autologous fat grafting after breast conserving surgery: Breast imaging changes and patient-reported outcome

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KEYWORDS
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Summary *Background:* Autologous fat grafting (AFG) to the breast is known to cause radiologic breast imaging changes. However, these changes have primarily been investigated in breast augmentation settings, whereas the radiologic breast imaging changes after AFG in patients who underwent breast conserving surgery (BCS) have been only sparsely studied.
Methods: All women scheduled to receive AFG to reconstruct BCS defects at our institution between 2014 and 2015 were eligible to participate. Before and after AFG, participants underwent radiologic breast imaging and completed patient-reported outcome measures for body image, aesthetic breast appearance, scar quality, and fear of cancer recurrence. Moreover, an observer evaluated changes in the aesthetic breast appearance and scar quality.
Results: Of 49 eligible patients, 42 were included. Participants received 1–3 AFG procedures, with a mean total grafted volume of 135 ± 74 mL. Post-AFG breast imaging was performed 9 ± 5 (range 2–25) months after the final AFG procedure. Comparison of pre- and post-AFG radiologic breast images revealed that 21% had developed calcifications, 85% had developed oil cysts, and 3% had developed increased scarring. Five patients presented with breast imaging changes that required biopsy or additional radiologic evaluation. Significant improvements were observed in breast aesthetic appearance, body image, and scar quality. No major surgical complications occurred. Minor surgical complications were observed in 3% of the patients.
Conclusions: Using AFG to reconstruct BCS defects induces considerable radiologic breast imaging changes. Although the patients experience significant improvements in body image, breast aesthetic appearance, and scar quality, the long-term effect of breast imaging changes warrants further investigation.

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Introduction

Breast conserving surgery (BCS) followed by adjuvant radiation therapy is currently the standard treatment for T1 and T2 stage breast cancers.[1] The treatment provides an overall survival same as that provided by mastectomy, while being less mutilating for the patients.[2,3] However, even though women treated with BCS maintain a better body image than those treated with a mastectomy, 12–30% experience an unsatisfactory aesthetic outcome.[4-7] A poor aesthetic outcome after BCS may be improved by various reconstructive procedures including implants, autologous flaps, and local volume replacement with autologous fat grafting (AFG).[8] High patient-reported satisfaction and previous studies describing a scar-remodeling effect have contributed to plastic surgeons increasingly turning to AFG for this group of patients.[9-13] While AFG has been described as the ideal filler, not all the transplanted fat will survive.[14] The grafted fat that does not survive may cause the formation of oil cysts and calcifications at the recipient site.[15,16] Although substantial improvements in AFG technique during the past decade have made the outcome more predictable, recent studies still report the prevalence of oil cysts in 7–71% and calcifications in 16–45% of patients who had received AFG to the breast.[16-22] These radiologic complications lead to a concern as to whether AFG to the breast may obscure or delay the detection of breast malignancy (i.e., recurrence or a new cancer) in this group of patients. Predominantly, studies agree that the radiologic breast changes induced by AFG are discernable from cancer. However, previous studies have primarily focused on the radiologic changes observed in breast augmentation settings, and as such, in populations without prior surgery or radiation therapy to the breast. BCS patients continue to partake in radiologic surveillance for recurrences after the surgery, and an increasing proportion of BCS patients undergo AFG to correct their breast defects. Thus, it is essential to evaluate the radiologic impact of AFG to the breast in BCS patients. The primary aim of the present study was thus to investigate the breast imaging changes induced by AFG in a prospective cohort consisting exclusively of BCS patients. Secondarily, the study aimed to evaluate the patient-reported outcome and any scar remodeling effect observed after AFG.

Patients and methods

The study was a single-site, prospective cohort study conducted at the Department of Plastic and Breast Surgery, Aarhus University Hospital, Aarhus, Denmark. Eligible patients were female, aged 18–75 years, and scheduled to undergo BCS defect reconstruction with AFG. Exclusion criteria were smoking, active cancer, and psychiatric illness preventing informed consent. Patients were recruited from January 2014 to November 2015. Included patients underwent radiologic breast examination with digital mammography and, if necessary, ultrasound before and after their AFG procedures. Additional pre-AFG breast imaging was not requested for patients who had undergone routine mammographic screening less than 6 months before their AFG procedure. For this group of patients, the mammographic screening breast images were used as their pre-AFG radiologic breast examination results. Furthermore, patient-reported outcome measures evaluating body image, aesthetic satisfaction, scar quality, and fear of cancer recurrence were completed the day before the first AFG procedure and at a follow-up visit at least 2 months after the final AFG procedure. The same observer (AAJ) conducted all follow-up visits. Data regarding the breast cancer treatment were retrieved from electronic patient charts.

Surgical procedure

AFG was performed by Coleman's technique in all cases.[11] After the infiltration of tumescent fluid, fat cells were harvested manually using a Khouris 2 mm cannula connected to a 10 mL Luer-Lock syringe. The lipoaspirate was centrifuged using a MediLite™ (Thermo Scientific, MA, USA) at 1800 RPM for 3 min. The top layer of residual oil and the bottom layer of tumescent fluid were removed. The purified lipoaspirate was subsequently transferred to 10 mL syringes and grafted to the recipient site using Coleman's type-2 cannula, after rigottomy was performed on any scar adhesions. Grafting was performed by multiple retrograde passes in the subcutaneous and subglandular planes. Donor sites were chosen on the basis of fat availability and the patient's preference, thereby balancing the estimated outcome of the harvest to the desired graft volume. The volume grafted per procedure was dependent on the interstitial pressure at the recipient site.

Radiologic evaluation of the breast

Digital mammographic images were recorded using a Siemens Inspiration system (Siemens AG, Munich, Germany) in craniocaudal, mediolateral oblique, and lateral projections. Ultrasound imaging was recorded using a Hitachi Ascendus scanner (Hitachi, Tokyo, Japan). One senior consultant breast radiologist (SR) evaluated all pre- and post-AFG breast images for the presence of calcifications, oil cysts, and scars. If present, the severity was scored as mild, moderate, or severe.

In accordance with the Danish National Guidelines set forth by the Danish Breast Cancer Cooperative Group,[23] each patient received a standardized breast imaging rating of 1–5. The five ratings are as follows: (1) normal breast imaging, (2) benign changes, (3) un-decided, atypical, indifferent findings, (4) findings suspicious of malignancy, and (5) findings highly suspicious of malignancy. Categories 3–5 warrant additional radiologic examination or biopsy. This five-tier classification system is not only used in European, and in particular northern European countries, including the UK, but also in Australia and New Zealand. The Breast imaging Reporting and Data System (BI-RADS) used in the United States is not applicable in some northern European countries, as it primarily recommends follow-up rather than biopsy verification.[24]

Hopwood's body image scale (HBIS)

Body image was evaluated using the HBIS, which is a validated breast cancer-specific 10-item scale.[25] Each item was

scored on a four-point Likert scale ranging from 0 (not at all) to 3 (very much) and summated into a total score ranging from 0 to 30, with lower scores indicating a better body image. The scale has shown good sensitivity to change in breast cancer populations.[25]

Patient and Observer Scar Assessment Scale (POSAS)

The quality of the scar was assessed using the POSAS. The instrument comprises two separate scales: one completed by the patient and the other completed by the observer.[26] Both scales consist of six items scored on 10-point numeric rating scales with 1 representing normal skin and 10 representing the worst possible scar. Patients rate whether the scar is painful or itching, and how different they perceive the color, stiffness, thickness, and irregularity of the scar from those of their normal skin. The observer scores the vascularity, pigmentation, thickness, relief, pliability, and surface area of the scar. The patient and the observer scales are summated into two separate scores ranging from 1 to 60, with lower scores indicating a better scar quality. The patients are unaware of the observer's evaluation of their scar.

Breast aesthetic evaluation

Breast aesthetic appearance was evaluated with a five-item study specific scale. The five items included satisfaction with the breast's appearance with bra, appearance without bra, size, shape, and softness. Each item is answered on a seven-point Likert scale, ranging from 1 (very dissatisfied) to 7 (very satisfied) and summated into a total score ranging from 5 to 35, with higher scores indicating greater satisfaction. Additionally, a single observer (AAJ) scored all participants using the same scale.

Concerns about recurrence questionnaire (CARQ-3)

Fear of cancer recurrence was evaluated with the validated, breast cancer specific measure CARQ-3.[27] The measure consists of three items answered on a 11-point Likert scale, ranging from 0 "not at all" to 10 "a great deal". The three items are summated into a single score with higher scores indicating higher fear of cancer recurrence.

Statistical and ethical considerations

Pre- and post-AFG patient-reported outcome measures, as well as the observer's evaluation of the BCS scar and the breast aesthetic appearance, were analyzed by paired *t*-tests. Radiologic breast changes induced by AFG were investigated by deducting the radiologic breast imaging changes present pre-AFG from those present post-AFG. All participants gave written informed consent before entering the study. Approval of the study according to the Danish law of Research Ethics was given by the Central Denmark Regional board under the Danish National Committee on Biomedical Research Ethics (Req. Nr. 38/2013).

Results

Patients

A total of 49 patients fulfilled the inclusion criteria. Of these, 42 gave informed consent to participate. During the follow-up period, one patient developed distant bone metastasis and one patient was diagnosed with local recurrence of extramammary Paget's tumor. Two patients were lost to follow-up and did not participate in the follow-up visit but agreed to undergo post-AFG breast imaging. Furthermore, two patients had missing pre-operative breast imaging, and the patient diagnosed with distant metastasis did not undergo post-AFG breast imaging. Patient and tumor characteristics are described in Table 1.

AFG procedure

A total of 75 AFG procedures were performed, with an average of 1.8 (range 1–3) procedures per patient. The mean volume grafted per procedure was 75 $\pm$ 33 mL (range 30–180 mL), and the mean total volume grafted per patient was 135 $\pm$ 74 mL (range 30–334 mL). The fat was harvested from the lower abdomen ($n = 59$), inner thighs ($n = 6$), outer thighs ($n = 3$), flanks ($n = 5$), and the lateral breast region ($n = 2$). No major surgical complications were observed. Minor complications occurred after two of the procedures and consisted of minor hematomas at the recipient site in both cases. Additionally, 19 patients underwent symmetry enhancing surgery to the contralateral breast, consisting of mastopexy ($n = 13$), AFG ($n = 5$), and liposuction ($n = 1$).

Radiologic breast imaging changes

Post-AFG breast imaging was performed with a mean follow-up of 12 $\pm$ 5 months (range 4–27) after the first AFG procedure and 9 $\pm$ 5 (range 2–25) months after the final AFG procedure. Two patients had an additional AFG procedure after the follow-up breast imaging but before their clinical follow-up visit. Pre-AFG breast imaging was conducted 6 $\pm$ 6 months (range 0–26) before the first AFG procedure. Complete pre- and post-AFG breast imaging was available for 39 patients. Post-AFG breast imaging consisted of mammography and ultrasound in 37 cases and mammography only in two cases. Pre-AFG breast imaging consisted of mammography and ultrasound in 27 cases and mammography only in 13 cases. Comparison of pre- and post-AFG radiologic breast images revealed that 8 patients had developed additional calcifications, 33 patients had developed additional oil cysts, and 1 patient had developed more scars after the AFG procedure. Patients who developed additional oil cysts did not have a significantly longer follow-up than who had not (391 days 95% CI (338–444) vs. 380 days 95% CI (154–607), $p = 0.88$). However, patients who developed calcifications had a significantly longer follow-up than those who had not (491 days 95% CI (358–624) vs. 361 days, 95% CI (307–415) $p = 0.032$). No significant correlation was observed between the number of AFG procedures and the increase in oil cysts ($p = 0.11$) or calcifications ($p = 0.75$). Furthermore, no significant correlation was observed between the time

Table 1 Patient and tumor characteristics.

Variable	*N* (%) or mean ± SD
Age	53.6 ± 9.4 (range 33-75)
BMI	25.7 ± 3.7
Time from BCS to first AFG (years)	4.2 ± 3.9 (range 0.4-18.8)
Time from end of radiotherapy to first AFG (years)	3.5 ± 3.2 (range 0.2-15.0)
Cancer type	
IDC	32 (76%)
DCIS	6 (14%)
ILC	1 (2%)
Extramammary Paget's disease	1 (2%)
Microcalcifications	1 (2%)
Non-cancer	1 (2%)
Tumor grade	
0	1 (2%)
1	11 (26%)
2	12 (29%)
3	15 (36%)
Missing	2 (5%)
Tumor size	20.0 ± 10.0 mm
Her2	
Positive	9 (21%)
Negative	33 (79%)
ER status	
Positive	26 (62%)
Negative	16 (38%)
Axillary technique	
SN	15 (36%)
ALND	15 (36%)
SN + ALND	7 (17%)
No axillary procedure	4 (10%)
Missing	1 (2%)
Adjuvant therapy	
Radiotherapy received	39 (93%)
Chemotherapy received	27 (65%)

AFG - Autologous Fat Graft.
ALND - Axillary Lymph Node Dissection.
BCS - Breast Conserving Surgery.
DCIS - Ductal Carcinoma In Situ.
ER - Estrogen Receptor.
IDC - Invasive Ductal Carcinoma.
ILC - Invasive Lobular Carcinoma.
SN - Sentinel Node.

Table 2 Radiologic findings.

	Before AFG $n = 40$	After AFG $n = 39$	Increased after AFG
Oil cysts			33 (85%)
Not present	39 (98%)	5 (13%)	
Mild	1 (3%)	17 (44%)	
Moderate	-	12 (31%)	
Severe	-	5 (13%)	
Total	1 (3%)	34 (87%)	
Calcifications			8 (21%)
Not present	33 (83%)	25 (64%)	
Mild	5 (13%)	12 (31%)	
Moderate	1 (3%)	2 (5%)	
Severe	1 (3%)	-	
Total	7 (18%)	14 (36%)	
Scarring			1 (3%)
Not present	3 (8%)	2 (5%)	
Mild	36 (90%)	36 (92%)	
Moderate	1 (3%)	1 (3%)	
Severe	-		
Total	37 (93%)	37 (95%)	
Standardized imaging score			5 (13%)
1	1 (3%)	-	
2	39 (98%)	34 (87%)	
3	-	4 (10%)	
4	-	1 (3%)	
5	-	-	

AFG - Autologous Fat Grafting.

from end of radiotherapy to the first AFG procedure and the development of either oil cysts ($p = 0.57$) or calcifications ($p = 0.64$).

With regard to the standardized breast imaging score post-AFG, 34 patients were classified as belonging to Category 2, four patients to Category 3, and one patient to Category 4. All Category 3 scores were caused by cystic lesions. The Category 4 score was caused by a local recurrence of extramammary Paget's tumor. The abnormal breast images required biopsy verification in four patients and additional radiologic examination in one patient. Because of the developing palpable lumps at the recipient site, nine patients underwent an additional ultrasound examination of the breast during the month after the AFG procedure. Two of these patients underwent needle aspiration of oil cysts, without indication of malignancy. Detailed data on the breast imaging evaluation are presented in Table 2. Examples of radiologic breast imaging changes are displayed in Figure 1.

Patient-reported outcome measures and observer evaluation

Follow-up visits were conducted an average of 8 ± 5 (range 2-23) months after the final AFG procedure. A statistically significant decrease in the HBIS score, indicating an improved body image, was observed (pre-AFG 11.3 ± 6.5, post-AFG 5.5 ± 5.7, $p < 0.001$), with 80% of the patients reporting an improved body image. Satisfaction with breast appearance was significantly improved (pre-AFG 16.1 ± 6.8, post-AFG 26.0 ± 7.9, $p < 0.001$), with 85% of patients reporting an improvement. In line with the patient evaluation, the observer assessment of breast appearance was significantly improved after the AFG procedure (pre-AFG 22.4 ± 6.5, post-AFG 29.2 ± 4.6, $p < 0.001$). Neither the patient-reported change in body image ($p = 0.26$), aesthetic satisfaction ($p = 0.61$) nor the change in observer's evaluation of the breast appearance ($p = 0.12$) was dependent on

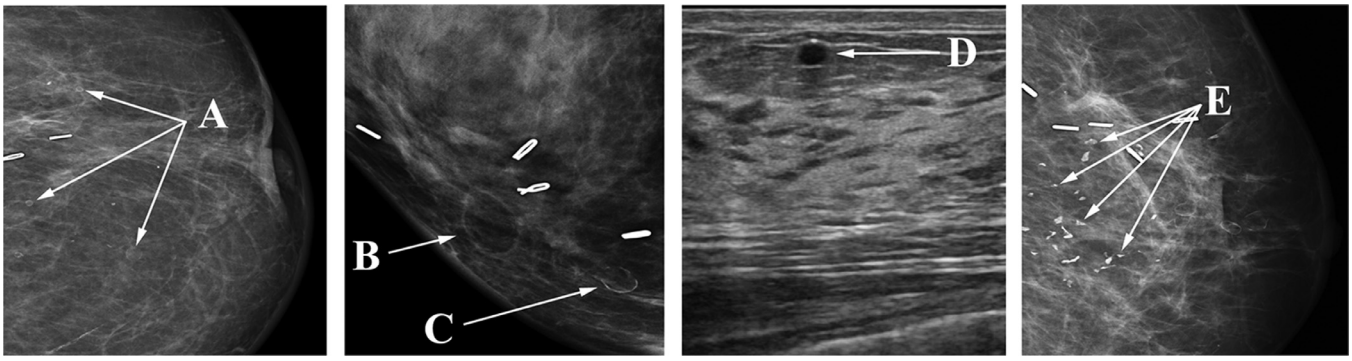

Figure 1 Radiologic appearance of oil cysts and calcifications after autologous fat grafting to reconstruct breast conserving surgery defects. (A) Small oil cysts with calcified rims; (B) oil cyst with thin fibrous rim without calcification; (C) oil cyst with rim calcification; (D) ultrasound image of oil cyst with beginning calcification in the top; (E) diffuse calcifications in the breast induced by autologous fat grafting.

Table 3 Summary of Patient and Observer Scar Assessment Scale (POSAS) scores.

	Before AFG $n = 43$	After AFG $n = 39$	p
Observer total score	22.2 ± 6.1	14.9 ± 3.9	<0.001
Vascularity	3.3 ± 1.6	2.4 ± 0.8	0.002
Pigmentation	3.8 ± 1.3	2.7 ± 0.7	<0.001
Thickness	3.3 ± 1.2	2.4 ± 1.0	<0.001
Relief	3.6 ± 1.3	2.4 ± 0.9	<0.001
Pliability	4.0 ± 1.7	2.4 ± 1.0	<0.001
Surface area	4.2 ± 1.6	2.6 ± 0.8	<0.001
Patient total score	29.4 ± 11.0	19.4 ± 9.7	<0.001
Painful scar	3.1 ± 2.4	1.6 ± 1.4	<0.001
Itching scar	2.2 ± 2.0	1.7 ± 1.1	0.09
Color	5.0 ± 2.9	3.4 ± 2.1	0.001
Stiffness	6.6 ± 2.8	4.8 ± 3.9	<0.001
Thickness	6.5 ± 2.8	4.1 ± 2.6	<0.001
Irregularity	6.1 ± 2.9	3.9 ± 2.5	<0.001

Data are presented as mean ± standard deviation.
AFG - Autologous Fat Grafting.

whether patients had received a contralateral procedure. Both the patient and observer POSAS scores were statistically significantly improved post-AFG ($p < 0.001$). Significant improvements were observed in all the POSAS observer subscales, except "itching," in all the POSAS patient subscales, Table 3. No significant change was observed in fear of cancer recurrence after the AFG procedure for the total cohort (pre-AFG 10.0 ± 8.8, post-AFG 8.2 ± 7.6 $p = 0.13$). A subgroup analysis was conducted to investigate whether the nine patients subjected to additional ultrasound examination due to developing palpable lumps had increased fear of cancer recurrence, finding no evidence for increased fear of cancer recurrence in this subpopulation ($p = 0.82$).

Discussion

In the present study, the radiologic breast imaging changes and patient-reported outcome for 42 patients who had received AFG to reconstruct BCS defects were investigated. With a mean follow-up of 7 months after the final AFG procedure, five patients (14%) presented with breast imaging changes that necessitated additional examination, of which four cases required a biopsy. The rate of abnormal breast imaging in the present study is comparable to the 11–20% reported in previous studies investigating AFG to the breast.[16,20,28,29] The leading cause of radiologic abnormalities in the present study was oil cysts. In this study, a prevalence of 86% was found, which is considerably higher than the 7–71% prevalence reported in the literature.[16,18–21] However, until the capsule around the oil cyst thickens and becomes visible on mammography as a rounded radiolucent area with a slender fibrotic or calcified rim, mammography by itself may be inadequate for detecting oil cysts.[20,21] Studies employing mammography without ultrasound are thus likely to underestimate the prevalence. This is exemplified in the wide prevalence range reported in the literature, where studies with a high oil cyst prevalence used ultrasound,[21] whereas studies with a low prevalence predominantly relied on mammography.[16,19,20] While oil cysts are discernable from cancer recurrence, they may cause considerable anxiety for the patients, especially if manifesting as palpable lumps, which have been described as the most frequent complication to AFG.[30]

Calcifications were present in 43% of patients post-AFG. Whereas oil cysts were almost exclusively developed after

the AFG procedure, only 23% had developed new calcifications after the procedure. The prevalence in the present study is thus in accordance with the prevalence of 16–45% reported in the literature.[16,19-22,31] As the presence of clustered or ductal calcifications is among the earliest signs of breast cancer, calcifications caused by AFG have been suspected of interfering with breast cancer detection. However, in others and our experience, post-AFG calcifications are discernable from cancer recurrence, as they are more evenly spread throughout the breast tissue and are not located in the mammary ducts.[18,19,21] In the present study, patients who developed calcifications had a significantly longer follow-up ($p = 0.032$). However, no correlation was observed between the follow-up time and the development of oil cysts. Furthermore, no correlation was found between the time from end of radiotherapy to AFG and the development of calcifications or oil cysts. While the delineation of these correlations was not the primary aim of the present study, we believe they are important questions to raise in future studies.

As the present population consisted solely of BCS patients, scars were present in 95% of patients' radiologic breast images before AFG. Additional scars post-AFG were observed in only 3% of patients and did not instigate difficulties in radiologic evaluation. Although no statistical evidence of increased fear of recurrence was found in the CARQ-3 scores, our clinical experience indicates an increased anxiety in patients who developed palpable lumps. To mitigate this anxiety, it is essential to inform patients about the risk of developing palpable lumps at the recipient site. Furthermore, our results further underline the necessity of a close collaboration with the breast radiologist who perform the evaluations, as to ensure up-to-date knowledge of the breast imaging changes AFG may induce.

As the primary purpose of AFG in BCS defect reconstruction is to restore the contour and appearance of the breast, patient-reported outcome measures constitute a key aspect in evaluating the outcome of the procedure. With statistically significant improvements in both patient and observer breast aesthetic evaluation and in the patient-reported body image, the outcome was good. Furthermore, both patients and the observer noted a significant improvement in the scar quality post-AFG. This observation is in line with results from previous studies investigating the effect of AFG on burns, radiation, and surgical scars.[10,13,32-34] The scar quality-enhancing effect observed after AFG is often attributed to the adipose-derived stem cells (ASCs); however, the process remains to be fully understood. The scar remodeling properties of AFG render the procedure especially beneficial for BCS patients, as they have predominantly received adjuvant radiation therapy.[4,9] As other types of reconstructive procedures in irradiated breast are susceptible to surgical complications, the low surgical complication rate favors the use of AFG in BCS defect reconstruction.[29,30,35]

Despite the increased use of AFG, its oncological safety to the breast remains debated.[12] Petit et al.[36] reported a high risk of local recurrence in patients with intraepithelial neoplasia who received AFG. However, recent studies found no increased risk of loco-regional recurrences.[17,29,37,38] In the present study, one patient developed local recurrence in the follow-up period, caused by extramammary Paget's tumor, which is known to have a high recurrence rate. The loco-regional recurrence rate observed in our study is thus below the expected recurrence rate for BCS populations.[2] However, our small study sample prohibits conclusions on oncological safety to be drawn.

Some limitations to the present study must be acknowledged. Primarily, the cohort is based on a relatively small single-center population, which may limit the generalizability. Furthermore, the follow-up time does not allow conclusions to be drawn on long-term radiologic changes. However, as BCS-treated patients undergo annual surveillance, the follow-up time in the present study likely corresponds to the radiologic breast imaging changes one may expect to see at the first post-AFG follow-up screening. The prospective design strengthens the study, especially as BCS patients present radiologic breast imaging changes before AFG that must be considered.

In conclusion, the present study indicates that using AFG to reconstruct BCS defects significantly improves body image, breast aesthetics, and scar quality. However, the procedure induces significant breast radiologic changes, even within a relatively short follow-up period. Further studies are needed to ensure that the induced breast imaging changes do not interfere with the mammographic surveillance protocols of BCS patients, which causes unnecessary additional examinations or masking a local cancer recurrence.

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Conflict of interest

None.

References

1. Darby S, McGale P, et al., Early Breast Cancer Trialists' Collaborative Group (EBCTCG) Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. *Lancet* 2011;**378**:1707–1716.
2. Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med* 2002;**347**:1227–32.
3. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* 2002;**347**:1233–41.
4. Lyngholm CD, Christiansen PM, Damsgaard TE, Overgaard J. Long-term follow-up of late morbidity, cosmetic outcome and body image after breast conserving therapy: a study from the

Danish breast cancer cooperative group (DBCG). *Acta Oncol* 2013;**52**:259–69.
5. Clough KB, Cuminet J, Fitoussi A, Nos C, Mosseri V. Cosmetic sequelae after conservative treatment for breast cancer: classification and results of surgical correction. *Ann Plast Surg* 1998;**41**:471–81.
6. Moyer A. Psychosocial outcomes of breast-conserving surgery versus mastectomy: a meta-analytic review. *Health Psychol* 1997;**16**:284–98.
7. Kim MK, Kim T, Moon HG, et al. Effect of cosmetic outcome on quality of life after breast cancer surgery. *Eur J Surg Oncol* 2015;**41**:426–32.
8. Losken A, Pinell-White X, Hodges M, Egro FM. Evaluating outcomes after correction of the breast conservation therapy deformity. *Ann Plast Surg* 2015;**74**(Suppl 4):S209–13.
9. Rigotti G, Marchi A, Galie M, et al. Clinical treatment of radiotherapy tissue damage by lipoaspirate transplant: a healing process mediated by adipose-derived adult stem cells. *Plast Reconstr Surg* 2007;**119**:1409–22 discussion 1423-4.
10. Klinger M, Caviggioli F, Klinger FM, et al. Autologous fat graft in scar treatment. *J Craniofac Surg* 2013;**24**:1610–15.
11. Coleman SR. Structural fat grafting: more than a permanent filler. *Plast Reconstr Surg* 2006;**118**:108S–120S.
12. Kling RE, Mehrara BJ, Pusic AL, et al. Trends in autologous fat grafting to the breast: a national survey of the American society of plastic surgeons. *Plast Reconstr Surg* 2013;**132**:35–46.
13. Juhl AA, Karlsson P, Damsgaard TE. Fat grafting for alleviating persistent pain after breast cancer treatment: a randomized controlled trial. *Journal of Plastic, Reconstructive & Aesthetic Surgery* 2016;**69**:1192–202.
14. Coleman SR. Structural fat grafts: the ideal filler? *Clin Plast Surg* 2001;**28**:111–19.
15. Hivernaud V, Lefourn B, Guicheux J, et al. Autologous fat grafting in the breast: critical points and technique improvements. *Aesthetic Plast Surg* 2015;**39**:547–61.
16. Rubin JP, Coon D, Zuley M, et al. Mammographic changes after fat transfer to the breast compared with changes after breast reduction: a blinded study. *Plast Reconstr Surg* 2012;**129**:1029–1038.
17. Silva-Vergara C, Fontdevila J, Descarrega J, Burdio F, Yoon TS, Grande L. Oncological outcomes of lipofilling breast reconstruction: 195 consecutive cases and literature review. *J Plast Reconstr Aesthet Surg* 2016;**69**:475–81.
18. Delay E, Garson S, Tousson G, Sinna R. Fat injection to the breast: technique, results, and indications based on 880 procedures over 10 years. *Aesthet Surg J* 2009;**29**:360–76.
19. Veber M, Tourasse C, Toussoun G, Moutran M, Mojallal A, Delay E. Radiographic findings after breast augmentation by autologous fat transfer. *Plast Reconstr Surg* 2011;**127**:1289–99.
20. Carvajal J, Patino JH. Mammographic findings after breast augmentation with autologous fat injection. *Aesthet Surg J* 2008;**28**:153–62.
21. Fiaschetti V, Pistolese CA, Fornari M, et al. Magnetic resonance imaging and ultrasound evaluation after breast autologous fat grafting combined with platelet-rich plasma. *Plast Reconstr Surg* 2013;**132**:498e–509e.
22. Wang CF, Zhou Z, Yan YJ, Zhao DM, Chen F, Qiao Q. Clinical analyses of clustered microcalcifications after autologous fat injection for breast augmentation. *Plast Reconstr Surg* 2011;**127**:1669–73.
23. The Danish Breast Cancer Group. Available at: www.dbcg.com. [Accessibility verified March 15 2018].
24. Maxwell AJ, Ridley NT, Rubin G. The royal college of radiologists breast group breast imaging classification. *Clin Radiol* 2009;**64**:624–7.
25. Hopwood P, Fletcher I, Lee A, Al Ghazal S. A body image scale for use with cancer patients. *Eur J Cancer* 2001;**37**:189–97.
26. van de Kar AL, Corion LU, Smeulders MJ, Draaijers LJ, van der Horst CM, van Zuijlen PP. Reliable and feasible evaluation of linear scars by the patient and observer scar assessment scale. *Plast Reconstr Surg* 2005;**116**:514–22.
27. Thewes B, Zachariae R, Christensen S, Nielsen T, Butow P. The concerns about recurrence questionnaire: validation of a brief measure of fear of cancer recurrence amongst Danish and Australian breast cancer survivors. *J Cancer Surv* 2015;**9**:68–79.
28. Illouz YG, Sterodimas A. Autologous fat transplantation to the breast: a personal technique with 25 years of experience. *Aesthetic Plast Surg* 2009;**33**:706–15.
29. Brenelli F, Rietjens M, De Lorenzi F, et al. Oncological safety of autologous fat grafting after breast conservative treatment: a prospective evaluation. *Breast J* 2014;**20**:159–65.
30. Claro F Jr, Figueiredo JC, Zampar AG, Pinto-Neto AM. Applicability and safety of autologous fat for reconstruction of the breast. *Br J Surg* 2012;**99**:768–80.
31. Gosset J, Guerin N, Toussoun G, Delaporte T, Delay E. Radiological evaluation after lipomodelling for correction of breast conservative treatment sequelae. *Ann Chir Plast Esthet* 2008;**53**:178–89.
32. Maione L, Memeo A, Pedretti L, et al. Autologous fat graft as treatment of post short stature surgical correction scars. *Injury* 2014;**45**:S126–32.
33. Bruno A, Delli Santi G, Fasciani L, Cempanari M, Palombo M, Palombo P. Burn scar lipofilling: immunohistochemical and clinical outcomes. *J Craniofac Surg* 2013;**24**:1806–14.
34. Pallua N, Baroncini A, Alharbi Z, Stromps J. Improvement of facial scar appearance and microcirculation by autologous lipofilling. *Journal of Plastic, Reconstructive & Aesthetic Surgery* 2014;**67**:1033–7.
35. Hamdi M, Wolfli J, Van Landuyt K. Partial mastectomy reconstruction. *Clin Plast Surg* 2007;**34**:51–62.
36. Petit JY, Rietjens M, Botteri E, et al. Evaluation of fat grafting safety in patients with intraepithelial neoplasia: a matched-cohort study. *Ann Oncol* 2013;**24**:1479–84.
37. Gale KL, Rakha EA, Ball G, Tan VK, McCulley SJ, Macmillan RD. A case-controlled study of the oncologic safety of fat grafting. *Plast Reconstr Surg* 2015;**135**:1263–75.
38. Kronowitz SJ, Mandujano CC, Liu J, et al. Lipofilling of the breast does not increase the risk of recurrence of breast cancer: a matched controlled study. *Plast Reconstr Surg* 2016;**137**:385–93.