Mammographic Changes after Fat Transfer to the Breast Compared with Changes after Breast Reduction: A Blinded Study

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Background: One issue in the adoption of autologous fat transfer to the breast is concern over mammographic changes that may obscure cancer detection. The authors compared mammographic changes following fat grafting to the breast with changes seen after breast reduction.

Methods: Twenty-seven women who had normal preoperative mammograms were treated with fat grafting to the breast, including admixing of autologous adipose stem cells with the fat graft, for cosmetic augmentation. Repeated mammograms were performed 12 months after surgery. As a control group, postsurgical mammograms from 23 reduction mammaplasty patients were compared. Eight academic breast imaging radiologists reviewed each mammogram in a blinded fashion. Outcomes analysis accounting for individual radiologist's tendencies was performed using generalized estimating equations.

Results: The average volume of fat injected per patient was 526.5 cc. Fifty mammograms (27 lipotransfer, 23 breast reduction) were assessed. Differences in interpretation among individual radiologists were consistently observed ($p < 0.10$). Differences in abnormality rates were nonsignificant for oil cysts, benign calcifications, and calcifications warranting biopsy. Scarring ($p < 0.001$) and masses requiring biopsy ($p < 0.001$) were more common in the reduction cohort. Breast Imaging Reporting and Data System scores were higher after breast reduction ($p < 0.001$). Significant differences in the recommended follow-up time were also seen ($p < 0.01$).

Conclusions: Compared with reduction mammaplasty, a widely accepted procedure, fat grafting to the breast produces fewer radiographic abnormalities with a more favorable Breast Imaging Reporting and Data System score and less aggressive follow-up recommendations by breast radiologists. (*Plast. Reconstr. Surg.* 129: 1029, 2012.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, III.

Autologous fat transfer has been used for many years in clinical applications involving soft-tissue defects of the face, trunk, and extremities.[1–6] The first reports by Czerny for breast augmentation and Neuber for facial contour deformity heralded its clinical use over 100 years ago.[7,8] Illouz's introduction of a technique to remove fat cells from small port incisions via cannula provided surgeons with nearly limitless quantities of autologous fat.[9,10]

With autologous fat displaying many of the properties of an ideal filler, there has been a re-

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Received for publication July 6, 2011; accepted October 31, 2011.
Presented at the Northeastern Society of Plastic Surgeons Annual Meeting, in Washington, D.C., October of 2010; the Ohio Valley Society of Plastic Surgeons Annual Meeting, in White Sulfur Springs, West Virginia, June of 2011; and the American Society of Plastic Surgeons Annual Meeting, in Denver, Colorado, October of 2011. First prize winner of the 2010 D. Ralph Millard Investigator Award in the Plastic Surgery Foundation Essay Contest.

DOI: 10.1097/PRS.0b013e31824a2a8e

Disclosure: *The authors have no financial disclosures relating to the contents of this article.*

cent surge of popularity in fat grafting for volume replacement of soft-tissue defects. Given the issues that can accompany prosthetic breast implants, particular interest has developed in using fat transfer (also known as lipotransfer or lipomodeling) in breast augmentation. There have been numerous descriptions of the use of fat transplantation for reconstructive breast surgery and cosmetic breast augmentation utilizing fat obtained by liposuction.[11–21] Lipotransfer, however, has continued to be fraught with difficulties, including unpredictable rates of graft resorption. Many techniques have been introduced in an effort to improve graft viability.[22–24] Cell-assisted lipotransfer, a novel method of fat grafting, has been described by Yoshimura et al. as one potential solution to combat resorption by enriching the concentration of autologous adipose-derived stem/progenitor cells present within the graft material.[25]

Despite these technological advances, the greatest barrier to acceptance of autologous fat transfer for cosmetic breast enhancement has traditionally been safety concerns rather than graft survival problems. An ad hoc committee of the American Society of Plastic Surgeons in 1987 was unanimous in "deploring the use of autologous fat injection in breast augmentation," stating that "much of the injected fat will not survive, and the known physiologic response to necrosis of this tissue is scarring and calcification."[26] These changes were thought to obscure the early diagnosis of breast cancer by mammography and increase the number of breast biopsies for benign conditions. More recent consensus statement from the American Society of Plastic Surgeons Fat Grafting Task Force published in 2009 demonstrated a more accepting position: "Fat grafting may be considered for breast augmentation and correction of defects associated with medical conditions and previous breast surgeries; however, results are dependent on technique and surgeon expertise." The report went on to state that "fat grafting to the breast could potentially interfere with breast cancer detection; however, no evidence was found that strongly suggests this interference."[27]

Radiographic alterations on mammography are known to occur in all surgeries of the breast. We hypothesized that the mammographic changes seen after lipoaugmentation would be no more severe than those observed after the commonly performed and widely accepted reduction mammaplasty procedure.[28–31] The goals of this study were to assess whether mammographic changes following breast augmentation via cell-assisted lipotransfer are similar to those seen after reduction mammaplasty and whether lipoaugmentation leads to a comparatively greater number of suspicious findings, potentially resulting in increased biopsy rates.

PATIENTS AND METHODS

Study Design and Subjects

A total of 27 Japanese women who had normal preoperative mammograms before aesthetic lipoaugmentation underwent mammograms 12 months after surgery at the University of Tokyo Medical Center. As a control group, 23 American patients of similar age who had normal digital presurgical mammograms and postsurgical mammograms performed 1 year after undergoing inferior or inferomedial pedicle breast reduction at the University of Pittsburgh Medical Center were compared. These patients were selected from the electronic medical records of plastic surgery and radiology through an honest broker, and selection was based on age, the availability of normal preoperative digital imaging, and 1-year follow-up digital mammograms. The protocol for this study was approved by the University Institutional Review Board under institutional review board number 09070131.

Eight University of Pittsburgh Mammography Quality Standards Act–certified academic breast imaging radiologists with expertise and experience in digital mammography reviewed each of the 50 postsurgical mammograms. Readers were blinded to all clinical information regarding the patient and were unaware of the nature of the surgical procedures being compared. Each radiologist assessed whether the patient showed radiographic evidence of oil cysts, benign calcifications typical of fat necrosis, scarring, calcifications warranting biopsy, or mass or architectural distortions requiring biopsy. In addition, each patient was scored according to the Breast Imaging Reporting and Data System and given a recommendation for follow-up in 1 year, 6 months, or immediate biopsy. The American College of Radiology version of the scale ranges from one to five, based on the category chosen by the reading radiologist: negative, benign finding, probably benign finding, suspicious abnormality, or highly suggestive of malignancy.[32]

All cases were loaded by an honest broker onto a U.S. Food and Drug Administration–approved mammography diagnostic workstation (Secureview Dx, Holgic Inc., Bedford, Mass.), and the cases were randomly displayed after deidentification of the in-house breast reduction studies. A hanging protocol was created so that simultaneous display of the mammograms before and following surgery was available as well as full resolution demonstration of all images. The workstation allowed demonstration of the images in any desired format and the radiologists were free to alter the display of images to best evaluate each case.

Surgical Technique

Lipoaugmentation of the breast was performed according to our previously described protocol.[25] In brief, with the patient under general anesthesia, adipose tissue was suctioned using a 2.5-mm cannula. Half of the aspirate was processed intraoperatively to isolate the stromal vascular fraction. The stromal vascular fraction was then recombined with the remaining half of the lipoaspirate to yield stromally enriched adipose tissue. Grafts were then injected diffusely in small aliquots to place fat into the subcutaneous tissue and pectoralis muscle. Breast reduction was performed using an inferior or inferomedial pedicle technique, designed within a Wise pattern marking.

Statistical Analysis

The primary outcome measures were the dichotomous presence of predetermined radiographic features (e.g., oil cysts) and the Breast Imaging Reporting and Data System score. The secondary outcome was the recommendation for follow-up or biopsy. All statistical analysis was performed using Stata/SE version 10.0 (StataCorp Inc., College Station, Texas). Assessments of overall differences in the primary outcomes by type of surgery were assessed using the Fisher's exact test for dichotomous radiographic abnormalities and the Mann-Whitney U test for the Breast Imaging Reporting and Data System score. In the secondary outcomes, the need for immediate biopsy (score 4 to 5 or radiologist recommendation) was analyzed using the Fisher's exact test, while the suggested course of action for the patient (biopsy, 6-month follow-up or 1-year follow-up) was analyzed with the Kruskal-Wallis test.

Analysis of the differences in primary and secondary outcomes accounting for both the correlation among multiple assessments performed on the same examinations and individual radiologist tendencies in assessment of the cases from the two groups was performed using a generalized estimating equation linked to a logistic function with an exchangeable correlation matrix. Examination of changes in the suggested follow-up period was assessed via a maximum-likelihood multinomial logit model. Variance between the two surgical cohorts was assessed via the Levene test, where appropriate. All statistical tests were two-sided, and significance was set to the level of $p \leq 0.05$.

RESULTS

A total of 50 mammograms (27 lipotransfer, 23 breast reduction) were assessed by eight radiologists, giving a total of 400 images read. Table 1 summarizes the demographic characteristics of patients undergoing lipoaugmentation and those undergoing breast reduction. The average total volume of fat injected per patient was 526.5 cc and ranged from 374 to 678 cc. Figures 1 and 2 show representative patients before and after lipoaugmentation.

Aggregate Mammogram Readings

The aggregate rates of radiologic findings are shown in Table 2, whereas Table 3 lists the distribution of Breast Imaging Reporting and Data System results. Scarring, benign calcifications, and masses warranting biopsy were all significantly less common in the lipotransfer patients. System scores were also significantly lower in the lipotransfer group by the Mann-Whitney test ($p < 0.001$). Table 4 shows the recommended next clinical step for all mammograms; again, biopsy and 6-month follow-up rates were higher in the breast reduction cohort ($p < 0.001$). Figure 3 shows rep-

Table 1. Patient Characteristics

	Lipoaugmentation Patients	Breast Reduction Patients
Patients, *n*	27	23
Age, yr (mean ± SD)	35.9 ± 9.9	50.0 ± 8.9
Right breast volume change, mean ± SD	267.2 ± 36.1 cc injected	943.7 ± 905.1 g removed
Left breast volume change, mean ± SD	260.0 ± 53.8 cc injected	820.0 ± 806.3 g removed

Fig. 1. (*Above*) Preoperative and (*below*) 1-year postoperative views of a 28-year-old woman who underwent cosmetic breast lipoaugmentation.

resentative findings of scar, fat necrosis, and oil cysts.

Individual Patient Analysis

Differences among the tendencies of individual radiologists were relevant ($p < 0.10$) for each type of finding. Figure 4 illustrates the ratings assigned by each radiologist to the two cohorts. When accounting for these differences and the readings by multiple radiologists of each image, the differences in abnormality rates were nonsignificant for oil cysts ($p = 0.15$), benign calcifications ($p = 0.1$), and calcifications warranting biopsy ($p = 0.1$). Scarring ($p < 0.001$) and masses requiring biopsy ($p < 0.001$) were significantly more common in the breast reduction patients.

Rates of immediate biopsy versus follow-up were nonsignificantly greater in the breast reduction group ($p = 0.12$). This difference was significant in analysis of recommended follow-up course (12 months versus 6 months versus biopsy), favoring the lipoaugmentation cohort ($p < 0.01$). The difference in Breast Imaging Reporting and Data System scores remained highly significant ($p < 0.001$).

DISCUSSION

Cosmetic breast augmentation with silicone or saline implants has become common in the

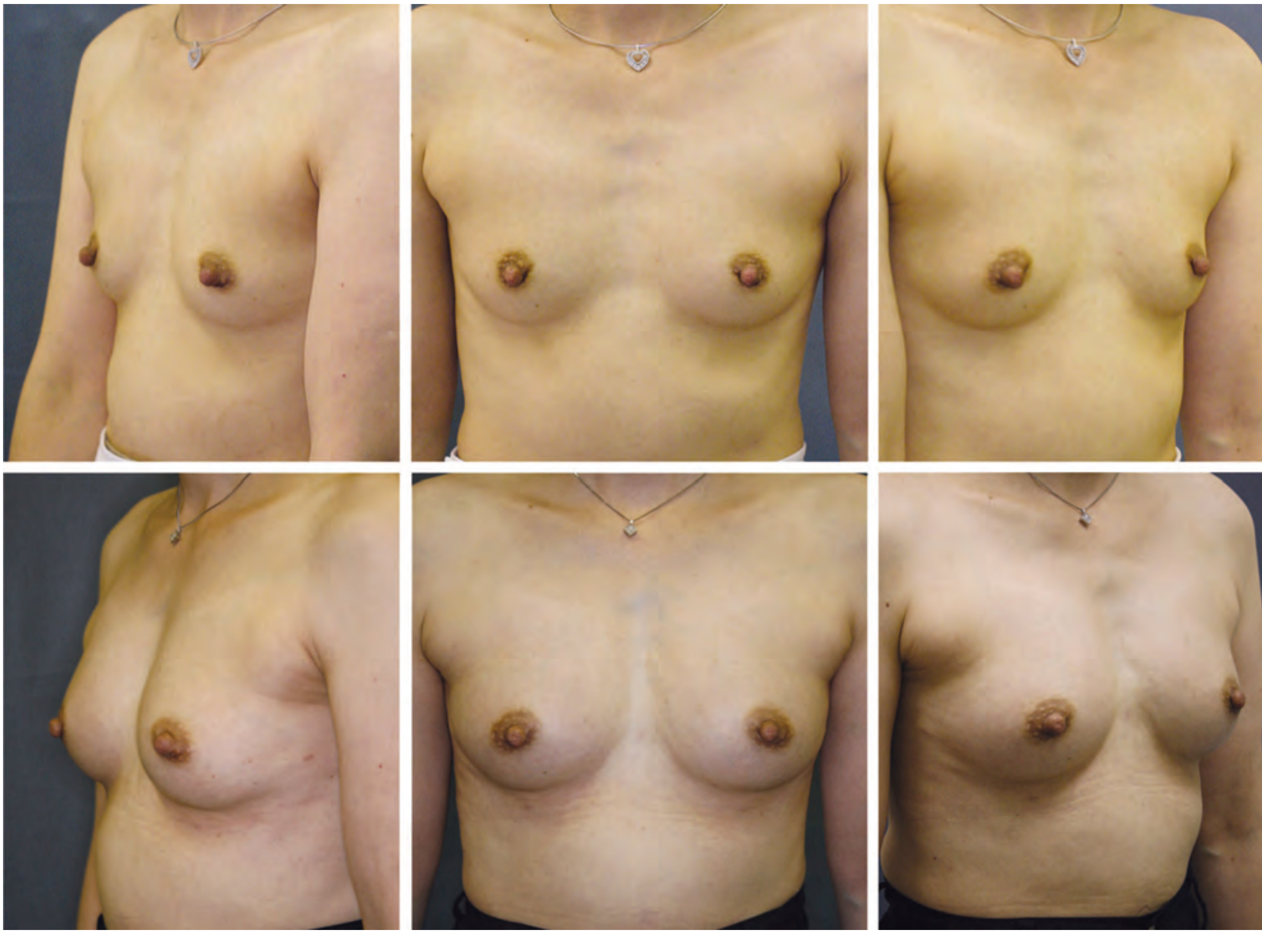

Fig. 2. (*Above*) Preoperative and (*below*) 1-year postoperative views of a 48-year-old woman who underwent cosmetic breast lipoaugmentation.

Table 2. Rates of Radiologic Findings across All Readings

	Breast Reduction (n = 184)	Lipoaugmentation (n = 216)	p
Oil cysts	58 (31.5%)	55 (25.5%)	0.18
Scarring	158 (85.6%)	38 (17.6%)	<0.001
Calcifications, benign/fat necrosis	50 (27.2%)	37 (17.1%)	0.02
Calcifications warranting biopsy	3 (1.6%)	10 (4.6%)	0.16
Mass or distortion warranting biopsy	25 (13.6%)	6 (2.8%)	<0.001

Table 3. Breast Imaging Reporting and Data System Scores across Readings

	1	2	3	4	5
Breast reduction	9 (4.9%)	130 (70.7%)	19 (10.3%)	26 (14.1%)	0 (0.0%)
Lipoaugmentation	78 (36.1%)	114 (52.8%)	10 (4.6%)	14 (6.5%)	0 (0.0%)

United States. It is estimated that more than 1 percent of the adult American female population (between 1 and 2 million) has undergone the procedure.[33] Prosthetic augmentation, however, is not without problems. Complications, including capsular contracture, implant leak or rupture, and

Table 4. Radiologist Follow-Up Recommendations

	12-Month Follow-Up	6-Month Follow-Up	Biopsy
Breast reduction	76 (41.3%)	80 (43.5%)	28 (15.2%)
Lipoaugmentation	191 (88.4%)	11 (5.1%)	14 (6.5%)

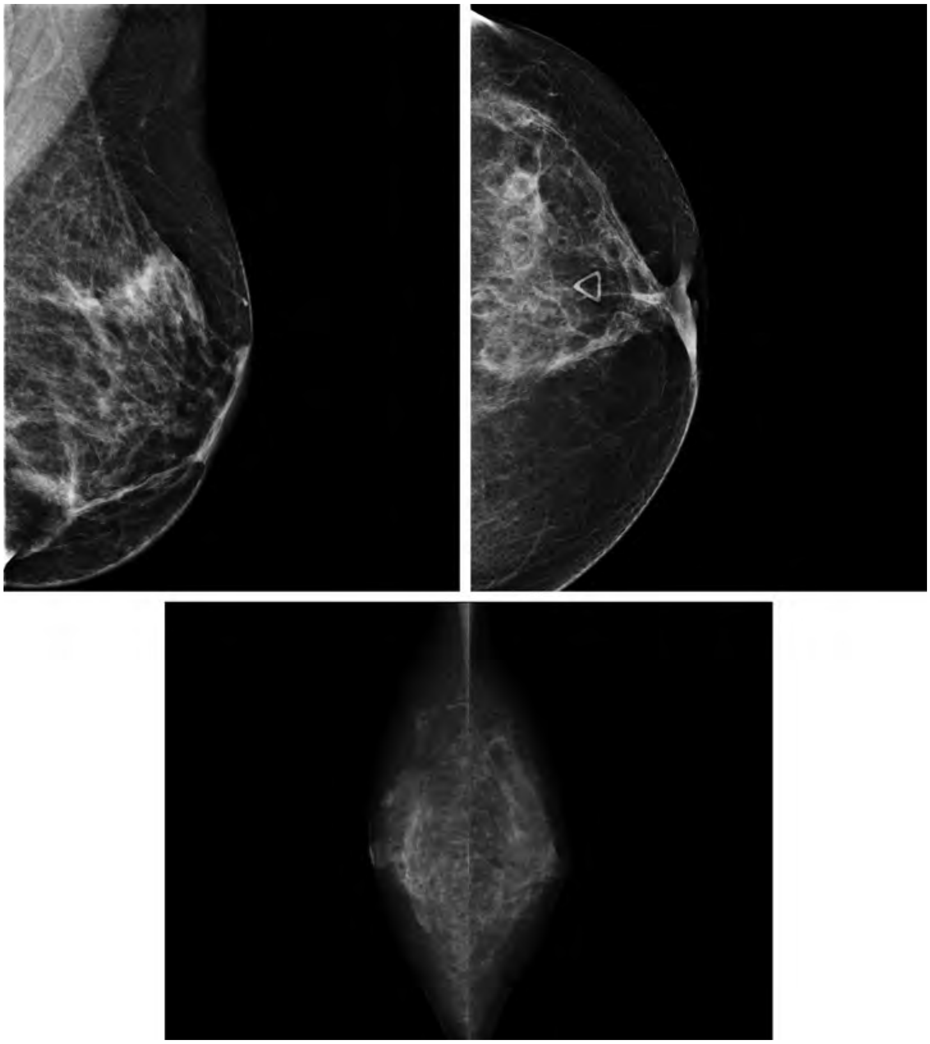

Fig. 3. (*Above, left*) A scar observed on mammography after reduction mammaplasty. (*Above, right*) Oil cysts from fat necrosis observed on mammography following reduction mammaplasty. (*Below*) Oil cyst seen on mammography following breast lipoaugmentation.

the possibility of interference with breast cancer surveillance, pose challenges, leading surgeons to continue the search for the ideal breast augmentation material.

Fat transfer has been gaining attention for breast augmentation. A variant of the technique, cell-assisted lipotransfer, involves the use of autologous adipose-derived stem/progenitor cells in combination with lipoinjection. The stromal vascular fraction is intraoperatively isolated from half of the aspirated fat and recombined with the other half, thereby converting relatively adipose-derived stem/progenitor cell–poor aspirated fat to adipose-derived stem/progenitor cell–rich fat.[26] Adipose-derived stem/progenitor cells have been hypothesized to support adipocytes by a variety of mechanisms, including secretion of growth factors, differentiation into endothelial cells to promote angiogenesis, direct differentiation into adipocytes, and participation in adipose remodeling.[34–38] Liposuction has been shown to deplete the quantity of adipose-derived stem/progenitor cells present when compared with whole fat.[35] Enrichment of these cells, therefore, has the potential to enhance fat graft survival and decrease unwanted complications, such as volume loss and cyst formation. Randomized comparison of human adipose tissue grafted into mice demonstrated that using the cell-assisted lipotransfer technique increased graft survival by 35 percent and led to greater angiogenesis within the transferred fat.[35] Controlled human studies supporting the beneficial effects of enriching the fat graft with adipose-derived stem/progenitor cells

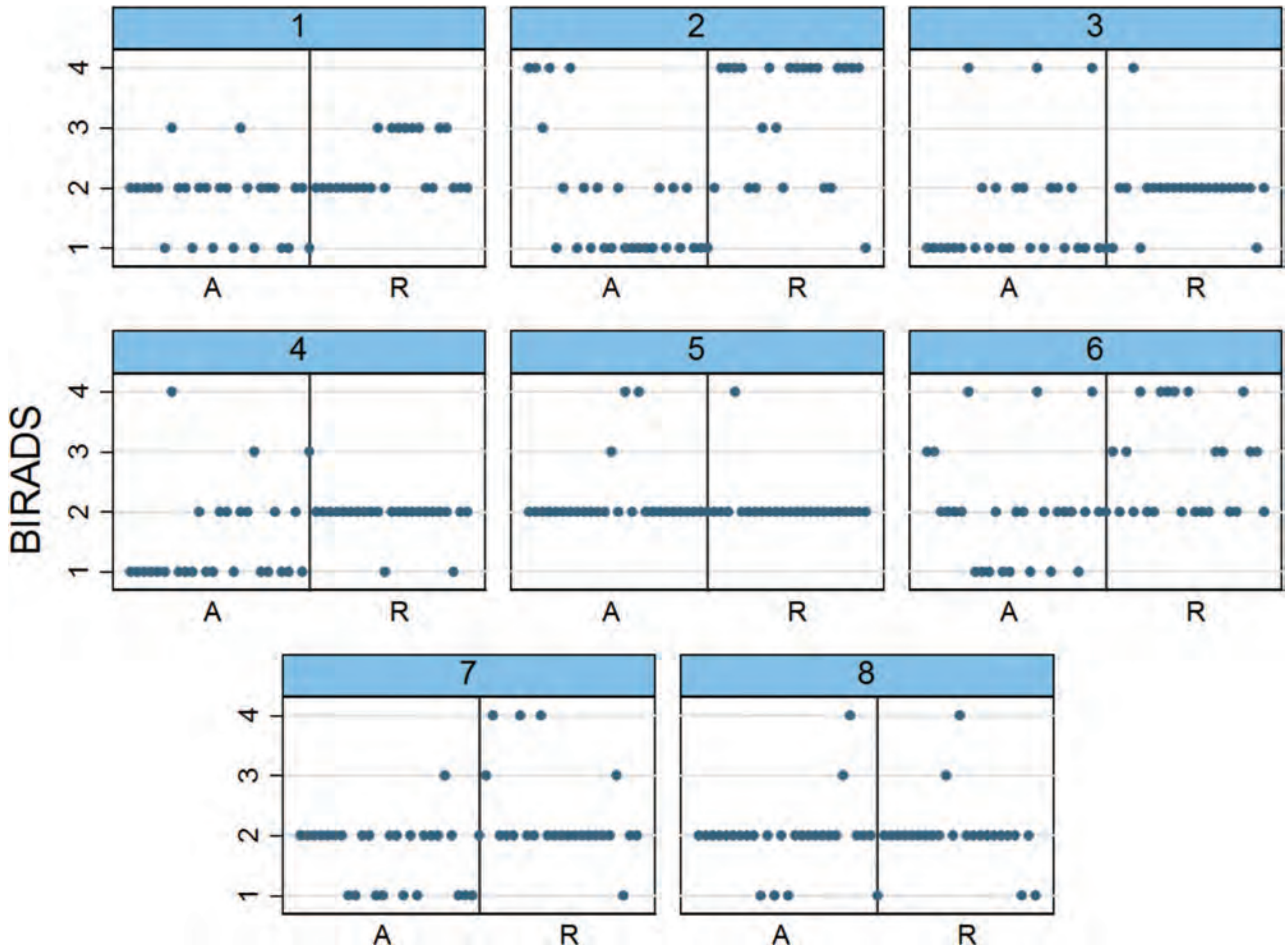

Fig. 4. Breast Imaging Reporting and Data System scores from the eight radiologist readers for each augmentation (*A*) and reduction (*R*) patient in sequence from one to fifty. Although each radiologist had a different threshold for scoring, there was a consistent tendency to assign lower (i.e., better) scores to patients undergoing lipoaugmentation when compared with breast reduction.

are not available at this time. This patient population, however, presents an opportunity to evaluate mammographic changes after fat grafting to the breast with a higher concentration of bioactive stromal cells present.

Fat necrosis is a well-described and typically minor consequence of many common surgeries of the breast. Radiographic and clinical changes secondary to fat necrosis may, however, mimic breast cancer, requiring biopsy to exclude malignancy. Similar to our findings, a study by Danikas et al. in 2001 demonstrated a 25.6 percent incidence of calcifications and oil cysts in 19.4 percent of patients after breast reduction surgery, likely caused by local fat necrosis.[30] A recent population-level analysis of 4473 Australian patients who had undergone breast reduction out of 244,147 women screened found no difference in the rate of recall for reduction patients (46.1 per 1000 screening episodes versus 50.7 per 1000 for patients who had not undergone surgery).[39]

Although this is the first study to directly compare mammographic changes from lipoaugmentation with another procedure, some authors have included patient mammogram data in their case series. Zocchi and Zuliani[40] reported a 3.9 percent rate of microcalcifications after fat injection, whereas Delay et al. found a 20 percent incidence of oil cysts.[41] Gosset et al. observed microcalcifications in 19 percent of mammograms, though up to 47 percent of magnetic resonance imaging scans found cystic masses.[42] Utilizing a negative pressure breast expansion device, Del Vecchio and Bucky found no new cysts or masses on magnetic resonance in 12 patients 6 months after lipoaugmentation.[43]

In an analysis of 20 patients, Carvajal noted microcalcifications in 45 percent, with oil cysts in 20 percent and no focal masses.[44] Three patients (15 percent) were classified as Breast Imaging Reporting and Data System 3, while the remainder were in the Breast Imaging Reporting and Data

System 2 category. In a large series in which a subgroup of 230 patients had complete long-term follow-up (average, 11.3 years), Illouz and Sterodimas[15] noted no long-term issues with cancer surveillance or tumorigenesis. At 1 year after lipoaugmentation, 17.5 percent of patients were classified as Breast Imaging Reporting and Data System score 3, 31 percent as score 2, and 47 percent as score 1.

Wang et al. performed fat grafting for breast augmentation in 48 women over 10 years. They found that eight (16.7 percent) demonstrated microcalcifications.[45] Concluding that mammography "cannot differentiate between benign and malignant microcalcifications," they performed biopsies and found these to represent fat necrosis in all eight cases. Based on their high rate of reoperation, they stated that "[lipoaugmentation] should continue to be prohibited." Similarly, Veber recently reviewed 31 postoperative mammograms and found microcalcifications in 16 percent and macrocalcifications in 9 percent.[46] In this series, however, no biopsies were performed, with the authors citing the ability of fellowship-trained breast radiologists to distinguish between benign and suspicious changes. Establishment of strong collaborations with colleagues in radiology will therefore be an essential component in the broader adoption of breast lipoaugmentation.

In all facets of our analysis, we found no evidence to suggest that lipoaugmentation by the cell-assisted lipotransfer technique presents greater problems for breast cancer screening than reduction mammaplasty, which has been safely performed for many years with no evidence of significant impairment of screening efficacy.[39] In particular, significantly lower rates of scarring and calcifications indicative of fat necrosis, as well as more favorable Breast Imaging Reporting and Data System scores, were seen in the lipoaugmentation cohort. Although the difference in immediate biopsy rates did not reach significance on multivariate analysis, the lipoaugmentation cohort did have significantly longer times until their next recommended surveillance. A weakness of this study is that the patient populations are intrinsically different. The breast reduction patients tended to be older, due to the fact that most younger women having breast reduction are at an age below the threshold for screening mammography in the United States. All patients had normal preoperative mammograms, however. In addition, the breast augmentation patient tends to be leaner whereas the breast reduction patient, often limited in mobility from symptoms of macromastia, tends to have a higher body mass index. These two independent variables are nearly impossible to eliminate between the two cohorts but are unlikely to be the cause of the significantly different mammographic changes after reduction as compared with lipoaugmentation.

Longer follow-up is necessary to confirm that the radiographic findings of lipoaugmentation remain comparable to those of breast reduction over time, though previous studies with serial mammography have noted that the majority of changes occur within the first 6 months after fat grafting and typically remain stable thereafter.[15] In addition, we could not address the actual incidence of cancer in this cohort. Large, prospective studies with long-term follow-up are needed to ensure that baseline cancer rates remain comparable to the general population. The main focus of this study was to compare mammographic findings between patients treated with lipoaugmentation to the breast versus reduction mammaplasty.

A strength of this study is the use of blinded, multiple radiology readers. Differences between individual radiologists were highly significant for all radiographic findings and highlights differing degrees of concern regarding postsurgical changes. Prior studies analyzing mammograms after breast surgery have typically relied on a single examiner. As Figure 4 demonstrates, if only one reader had participated, these study data may have been skewed. Given the significant variation seen between even experienced radiologists, multiple readers and statistical methods to examine and control for these differences are necessary.

CONCLUSIONS

Fat grafting to the breast represents an area of plastic surgery that has been the subject of substantially increased interest in the past several years. Technological advances, including technique refinements and the use of adipose-derived stem/progenitor cells enhanced grafts, have the potential to improve results. Lipoaugmentation of the breast has been controversial, however, due to concerns regarding its interference with mammography and cancer surveillance. We have demonstrated that when compared with a widely accepted surgical procedure of the breast, reduction mammaplasty, lipoaugmentation with autologous stem cell enrichment produces lower rates of radiographic abnormalities and a more favorable Breast Imaging Reporting and Data System score.

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ACKNOWLEDGMENTS

The authors thank the radiologists who participated in this study: Cathy S. Cohen, M.D.; Ronald L. Perrin, M.D.; Jules H. Sumkin, M.D.; Luisa P. Wallace, M.D.; Christiane M. Hakim, M.D.; Maria L. Anello, M.D.; Ratan Shah, M.D.; and Amy E. Kelly, M.D.

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Plastic Surgery Level of Evidence Rating Scale—Diagnostic Studies

Level of Evidence	Qualifying Studies
I	Highest-quality, multicentered or single-centered, cohort study validating a diagnostic test (with “gold” standard as reference) in a series of consecutive patients; or a systematic review of these studies
II	Exploratory cohort study developing diagnostic criteria (with “gold” standard as reference) in a series of consecutive patient; or a systematic review of these studies
III	Diagnostic study in nonconsecutive patients (without consistently applied “gold” standard as reference); or a systematic review of these studies
IV	Case-control study; or any of the above diagnostic studies in the absence of a universally accepted “gold” standard
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Discussion: Mammographic Changes after Fat Transfer to the Breast Compared with Changes after Breast Reduction: A Blinded Study

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The authors report a study that attempts to answer the question "Are the mammographic changes following autologous fat transfer to the breast more clinically concerning than those following Wise-pattern, inferior pedicle breast reduction?"[1] The article's prime strength is its study design: 27 lipotransfer patients were compared with 23 breast reduction patients. Mammograms were performed before surgery and then 1 year following surgery, and breast imaging-trained radiologists, who were blinded to treatment, read the mammograms. The authors appropriately conclude that autologous fat transfer to the breast produces fewer radiographic abnormalities 1 year following surgery than does breast reduction. Specifically, scarring seen on mammography and masses that warranted biopsy were more common following breast reduction, and Breast Imaging Reporting and Data System scores were higher following breast reduction. The radiographic abnormalities found following breast reductions in this study match those from previous studies.[2–4]

Lipoaugmentation of the breast is an appealing concept for the patient and surgeon alike—soft, supple tissue, autologous, and presumptively safe.[5–8] Yet nowhere is the practice of fat grafting more controversial, and has more potential for liability, than in cosmetic breast surgery.[9] Breast lipoaugmentation has a number of discrete concerns. Most important, some of the fat injected into the breast may calcify and could interfere with future cancer surveillance.[10,11] Second, grafted lipoaspirate is purported to contain stem cells and proangiogenic proteins, which raises the fear of cancer causation or potentiation.[1,12,13] Third, lipoaugmentation—like any other surgical procedure—has the potential for complications, such as cysts and infection.[6,14–16] Fourth, serious consideration needs to be given to the efficacy of this labor-intensive procedure and the resultant cost. Finally, breast lipoaugmentation can create significant liability for the plastic surgeon, even if the harm claimed occurs decades following surgery.

This study aims to address one concern of autologous fat grafting to the breast—the implications for mammographic changes, or essentially possible interference with future cancer screening and early detection. Although grafted fat might result in mammographic changes that would complicate future breast cancer screening, this study suggests that its radiographic distortions are no worse than those following another common breast surgery, namely reduction mammaplasty.

There are a number of interesting issues raised by this article. First, what is the ideal control or comparison group? Are patients who have had breast reduction surgery the best control? Second, although multiple radiologic abnormalities are evaluated in this study, the major concern with lipoaugmentation is the development of suspicious calcifications,[10,11,14] and more attention could have been focused on that specific question and the almost three-fold higher incidence of this finding in lipoaugmentation patients. Third, the findings of the article raise significant questions as to where the fat is actually injected—that is, around versus into the breast parenchyma. Fourth, the study employs radiologists who are specifically trained in breast imaging, which might not reflect the skill sets of radiologists found at most diagnostic imaging centers across the United States today. In addition, even among this highly trained group of radiologists, intergrader variation was high. Finally, this study uses a lipoaugmentation tech-

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Received for publication December 11, 2011; accepted December 27, 2011.

DOI: 10.1097/PRS.0b013e31824a29ef

Disclosure: *Dr. Spear is a paid consultant to Allergan, Inc. (Irvine, Calif.) and LifeCell Corp. (Branchburg, N.J.). Dr. Al-Attar has no disclosures.*

nique (creating stromally enriched adipose tissue) that is presumed to concentrate stem cells; this protocol is not a widely used method, and it is not relevant to the main objective of the study.

The main technical concern of this article is in the selection of breast reduction patients as the control group for comparison with the lipoaugmentation patients. Granted, selecting an appropriate control group is difficult. Many disparities, however, exist that make these two procedures poor comparisons. Although it would be difficult to identify two analogous populations for this study, younger Japanese patients undergoing lipoaugmentation are going to have vastly different mammograms than Midwestern U.S. patients having significant breast reductions. Their breast density and therefore mammograms are qualitatively dissimilar, and using one group as the control for the other group reduces the relevance of the study. Furthermore, breast reduction is generally a reconstructive procedure with functional goals; lipoaugmentation in this study is cosmetic. The risks that would be acceptable to a patient undergoing a reconstructive procedure (i.e., mammographic abnormalities) are not necessarily seen as comparable when the indication is cosmetic. Selecting a different and cosmetic control group would probably have been more clinically relevant. In clinical practice, a patient who would approach a surgeon for breast augmentation would hypothetically have the options of implant-based augmentation or lipoaugmentation. Therefore, the more ideal control group would be a matched cohort (matched for age and breast size) that had implant-based breast augmentation. When comparing mammograms 1 year postoperatively, the study would then provide information so that a surgeon could inform a prospective patient of what her radiographic abnormalities would be following her other enlargement option. Breast reduction and its potential radiographic sequelae are not directly part of that clinical conversation.

The authors compare radiologic abnormalities following breast reduction and lipoaugmentation, and find that the global rate of radiographic abnormalities is greater in the former group. The truly concerning mammographic change following lipoaugmentation, however, is calcification warranting biopsy.[10,11,14] The concern is that the lipoaugmented breast would develop calcifications suggesting or warranting biopsy and, with each new lesion (and each successive negative biopsy), there might be a sometimes erroneous temptation to attribute the next calcification to transplanted fat.[9,14] Although the global rate of mammographic abnormalities was higher in patients in the breast reduction cohort, the incidence of calcifications warranting biopsy was almost three times greater in lipoaugmentation patients (4.6 versus 1.6 percent; see Table 2). Although this three-fold difference did not reach significance ($p = 0.16$), the study was not powered to detect this difference, and the incidence of this finding—not just of global radiologic abnormalities—is an important outcome measure for analysis in the study.

In breast lipoaugmentation, where is the fat injected? A number of surgeons who perform breast lipoaugmentation suggest that transplanted fat is meant to reside external to the breast parenchyma—in the subcutaneous and submammary spaces (and possibly in the pectoralis major muscle).[1,6] In fact, this is the technique purportedly performed in this study. The large number of mammographic abnormalities detected, however, argues against the notion that this well-intentioned localization actually consistently occurs. Indeed, according to this study, mammographic abnormalities were found in at least a quarter, and in possibly up to two-thirds, of lipoaugmented breasts after 1 year.

It is apparent from this study that even well-trained radiologists will differ in their interpretation of mammographic lesions, at least in the lipoaugmented breast. The intergrader variation of the radiologists in this study is surprising, given that they are all academic radiologists with Mammography Quality Standards Act certification—a level of expertise probably not reflective of skills available at all diagnostic imaging centers today. Furthermore, some authors claim that highly trained radiologists might be able to distinguish between calcifications after lipotransfer and those associated with malignancy[17]; however, this skill set is also not necessarily available at all breast imaging centers. Although the variation between radiologists might be more a problem of mammographic interpretation in general, this article raises the prospect that mammographic lesions in lipoaugmented breasts may increase the level of clinical confusion.

Lipoaugmentation in this study is performed using a protocol previously described by the authors that aims to enhance the biologic activity of grafted fat.[18] Specifically, the lipoaspirate is processed to enhance the stromal vascular fraction of the grafted fat, presumably increasing the concentration of stem cells and the angiogenic potential of the grafted tissue. This processing technique is not widely performed for breast lipoaugmentation today, and its use in this study detracts from the primary focus of the manuscript. Furthermore, if this processing technique does successfully increase the concentration of stem cells and enhance the angiogenic potential of the grafted fat, the added benefit of graft survival might be offset by heightened concern for oncologic effects.

A final but critical point must be noted: that the risks associated with autologous fat grafting in the reconstructed (postmastectomy) breast are qualitatively different from those associated with fat grafting in the native breast for cosmetic purposes. In the former, the breast tissue has been largely removed, the surgery is reconstructive (with appropriately higher acceptance of potential complications), future clinical breast examinations by a physician are scheduled regularly and indefinitely, and the grafted fat is placed in a subcutaneous plane where it is always palpable. In fat grafting for cosmetic breast augmentation, fat is injected above and below (and sometimes into) the breast parenchyma, complications and adverse effects are poorly tolerated as in all cosmetic procedures, and the rate of compliance for annual breast examinations by a physician is lower in this generally younger population.

In summary, the controversy surrounding cosmetic breast lipoinfiltration or lipoaugmentation involves multiple nuanced concerns. This article does an excellent job of addressing one component of these concerns, namely the extent of mammographic changes following breast lipoinfiltration and comparing that to the well-accepted radiographic changes following breast reduction. For that specific concern, this article very effectively resolves the question and appropriately concludes that mammographic changes are more extensive following breast reduction compared with lipoinfiltration. As discussants, however, we felt obliged to evaluate these findings in the greater context of the many various concerns associated with cosmetic breast lipoinfiltration to encourage an ongoing thoughtful and sophisticated review of this exciting and important topic. We applaud the authors on the high quality and rigor of their study and encourage others to similarly continue to investigate other aspects of this subject in a systematic, scientific, and thorough fashion.

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