Autogenous Fat Grafting and Breast Augmentation: A Review of the Literature

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Breast Surgery

Review Article

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Abstract

Since the 1980s, there has been an increased interest in autogenous fat grafting for breast augmentation. However, concerns over graft survival and interference with breast cancer screening have limited its application. Since its introduction, refinements in harvesting and grafting techniques have improved results. The available literature consists primarily of case reports and series. There are no controlled trials, and outcomes thus far have not been measured in a standardized way. The limited data relating to breast cancer screening did not note a significant interference. Concerns have been raised that the placement of mature adipocytes and adipocyte-derived stem cells into the hormonally-active environment of the breast may potentiate breast cancer, but there are no clinical trials that investigate this possibility and a consensus regarding the basic science is still developing. Large multicenter, controlled, prospective trials are necessary to further investigate the many issues relating to the application of autogenous fat grafting for augmentation of the breast.

Keywords

breast augmentation, autologous fat graft, autogenous fat graft, adipocyte-derived stem cells

Transplantation of autologous fat has been performed for over 100 years. Improvements in harvesting techniques and advantages such as availability and biocompatibility have led to its widespread application, especially in cosmetic facial surgery. Since the 1980s, there has also been an increased interest in autologous fat transfer for breast augmentation, but variability in long-term results and oncologic concerns have limited its application.

HISTORICAL PERSPECTIVE

Autogenous fat grafting was first utilized by Neuber in 1893 to fill facial depressions caused by tuberculosis.1 In 1895, Czerny transplanted a lipoma from the back to treat a mastectomy defect.2 By 1926, Miller had described deposition of fatty tissue through hollow metal cannulae with generally good results, although the technique never gained popularity.3 Enthusiasm for autologous fat transfers waned in popularity in the 1950s and 1960s after Peer showed a graft survival rate of only 50% at one year4 and after dermal adipose grafts and artificial materials gained in popularity.5 The 1980s saw a renewed interest in autogenous fat transfer and, in 1986, Ellenbogen6 published a preliminary report of a “rediscovered technique” of fat grafting to the face involving open placement of small fragments of adipose tissue that had been treated with an insulin solution to enhance viability.

Interest in autologous fat transfer further increased after the advent of liposuction provided a minimally invasive means of obtaining large amounts of adipose tissue in a semiliquid form. This byproduct demonstrated a large surface area-to-volume ratio, which was felt to have ideal characteristics for autotransplantation. In 1983, Illouz7 reported extraction of fat under suction and reinjection of the aspirate, but studies continued to document poor graft

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survival. Improvements in harvesting and injection techniques that emphasized minimal trauma to the adipose tissue and layering of small aliquots of aspirate have since limited resorption of injected fat.

Autogenous fat grafting has been historically employed primarily to correct facial defects, but interest in its applications for breast augmentation also increased with the advent of liposuction. In 1985 at the California Society of Plastic Surgeons meeting, Bircoll described autologous fat transplantation to the breast utilizing liposuction techniques. This proved controversial, and in 1987, the American Society of Plastic and Reconstructive Surgeons Ad-Hoc Committee on New Procedures issued a position paper condemning autologous fat transfer to the breast. The committee cited concerns over the development of scarring and microcalcifications that would lower the sensitivity of mammography. Despite this stance, there has been continued interest in this technique for breast augmentation, and several case series have been published.

RESULTS FROM PRIOR CASE SERIES

A careful search of the literature was conducted and relevant case series were selected, all of which included patients who underwent autogenous fat grafting for the purpose of cosmetic breast augmentation. In all, nine case series were found.

Illouz and Sterodimas published a series of 820 consecutive patients who underwent autologous fat transplantation to the breast from 1983 to 2007. These included patients with congenital asymmetries, patients undergoing breast reconstruction after tumor resection, and patients requesting breast augmentation. Of the total, 385 patients underwent bilateral breast augmentation over multiple sessions, spaced three months apart. Subcutaneous and intraparenchymal injections were utilized and retrograde injections were avoided. Thirty-six patients requested additional volume and had bilateral breast implants, but the majority of patients were satisfied with their results. The longevity of the augmentation was not measured, although a case was presented that demonstrated a durable aesthetic result 11 years after the procedure. Complications were not noted specifically for the subset of patients who underwent breast augmentation, but for the group as a whole, there were small areas of ecchymosis in 76 patients (9.3%), 36 patients with striae (4.4%), 12 hematomas (1.5%) that resolved without intervention, and five infections (0.6%) that resolved with antibiotics.

Zocchi and Zuliani reported that they initially employed the Fournier technique of en bloc intraparenchymal injection but were disappointed by the high rate of complications and “almost complete reabsorption of the graft fat.” In order to address these problems, a technique was developed that involved preexpansion of the breast with a BRAVA negative pressure device, minimal trauma to the tissue, and application of a vibration table rather than centrifuge to separate the layers of the aspirated tissue. This was applied to a series of 181 patients who underwent autologous fat injection into the retroglandular space, prefascial space, and superficial subcutaneous plane of the upper pole of the breast. Intraparenchymal injection was avoided. Fat graft survival ranged from 40% to 70% (average, 55%) at one year. All complications and side effects were minimal, with the most common being edema and bruising.

In a paper on the complications of breast augmentation with autogenous fat grafting, Mu and coauthors reported a series of 140 patients who underwent breast augmentation with autologous fat mixed with vascular endothelial growth factor (VEGF). The fat was injected diffusely in multiple layers into the subpectoral, pectoral, retromammary, and subcutaneous planes. In a follow-up period of six months to two years, sclerotic nodules occurred in only one patient. There were no other outcomes reported, as this study was primarily concerned with complications.

In 1992, a report on 20 breast augmentation patients was published by Fulton. Fat was collected from the ipsilateral thigh and flank under a variety of negative pressures (25-in Hg maximum) and washed three times in lactated Ringers. No centrifuge was utilized. The fat was then injected into the prepectoral fascial plane in 1- to 3-cc aliquots. Special emphasis was placed on upper quadrant injection. Patients were seen at one, three, and six months after surgery for volumetric measurements and yearly thereafter for mammography and long-term volumetric measurement. Average initial injection was 289.5 cc and average retention was 71%. In some cases, there was an increase in the size of the breast over time, possibly secondary to weight gain.

Fulton published a second series of 65 patients in 2003. The transferred adipose tissue was “incubated” in plateletrich plasma (PRP) obtained by centrifuging the patients’ blood. This method was believed to increase the retained volume of the transplant by enmeshing the fat cells and coating them in fibrin and platelet-derived growth factors. The adipose tissue was injected in the subpectoral plane, the pectoralis muscle, and the retroglandular space. The average breast augmentation was equivalent to an implant of approximately 200 to 250 cc, and the average retained breast volume was 73%. Two patients developed striae and there were no hematomas or fat emboli. Fulton noted that the best results were seen in mature multiparous women with atrophic but not ptotic breasts who have areas of disharmonious obesity and would be content with a one-cup size increase in breast volume. The most disappointing results were noted in women who were thin with ptotic breasts and had no areas of disharmonious obesity.

In an effort to address the problems of unpredictability and low rates of graft survival due to partial necrosis, Yoshimura and coauthors developed a technique known as cell-assisted lipotransfer (CAL), which produces autogenous fat rich in autologous adipose-derived stem cells (ASC). A series of 40 patients underwent autologous fat transfer for breast augmentation. Final breast volume was augmented by 100 to 200 mL after a mean injection of 270 mL of fat. Volume did not change significantly after two months and all patients were satisfied with their result. When compared with patients who had breast augmentation by conventional autogenous lipoinjection, it was noted that there was an increase of
breast circumference from 2 to 3 cm with the conventional technique, compared to 4 to 8 cm with CAL. This was not a controlled trial and appears to be a historical comparison. The data regarding the results with the traditional technique were not presented in this study. It is postulated that ASC prevented postoperative atrophy of the transplanted fat. The only complications noted were cyst formation or microcalcifications in four patients.

Delay et al published a series of 880 autogenous fat transfers to the breast over a 10-year period. The majority of these patients underwent breast reconstruction (n = 734), whereas only 30 had aesthetic breast surgery. Standardized techniques of harvest were utilized and the injected volume was 140 cc for every 100 cc of desired final volume. Volume loss was noted to be between 30% and 40% and remained stable after that time, provided that the patient maintained a constant weight. There was a high degree of patient and surgeon satisfaction. Complications included an infection rate of 0.7% and a 3% rate of clinical fat necrosis. The rate of fat necrosis was higher in the authors’ early experience (15%) but decreased once oversaturation of the recipient sites was avoided.

Zheng et al reported a series of 66 patients who underwent autogenous fat grafting to the breast for cosmetic enhancement. Of these, 24 were for micromastia and the results for this subset were reported. The results were measured by three independent plastic surgeons and breast contour was judged to be significantly improved in 33%, improved in 58%, and not improved in 8%. Thirty-three percent of patients were very satisfied, 63% were satisfied, and 4% were unsatisfied. There was no measurement of graft retention. The only complications noted were the development of liponecrotic cysts in 16.7% of the total of patients.

Coleman and Saboeiro described autogenous fat grafting of the breast in 17 patients, 10 of which were breast augmentations. The description of the technique emphasized small incisions, blunt cannulae, injection of small aliquots of fat, and limited intraparenchymal injections. There was no quantization of long-term maintenance of volume; however, a photograph of a breast augmentation patient demonstrated excellent durability of the aesthetic result seven years after the procedure. By four to six months, the volume of the breast appeared to stabilize and did not significantly reduce over the ensuing years. No complications were specifically noted for the breast augmentation group.

In summary, the current literature consists primarily of case series that differ in their techniques, follow-up, and outcome measures (Table 1). Some included breast augmentation as part of a larger series without subset analysis. No prospective, blinded or unblinded, or controlled trials were noted.

**COSMESIS**

Several cosmetic themes emerged in the reviewed series. The technique was felt to produce a moderate increase in volume. There was less projection compared to an implant, but a more natural contour to the breast was produced. Other benefits included an unnoticeable scar and improved skin texture with decreased appearance of stretch marks.

Special attention to injection of the upper pole of the breast was advocated and at least one series recommended manual reshaping to reproduce the shape of an anatomic implant. The postoperative result was seen to be sensitive to fluctuations in weight and avoidance of postoperative weight loss was recommended to preserve the fullness of the breasts. One series measured cosmetic results by a panel of three independent plastic surgeons and found a close correlation with patient satisfaction (Table 2). The least cosmetic improvement was found in ptotic breasts.

**DETECTION OF BREAST CANCER**

One of the main concerns with autogenous fat grafting of the breast is the development of fat necrosis leading to liponecrotic cysts and microcalcifications that could possibly interfere with breast cancer screening. These abnormal radiographic findings have been well documented. Several case series were found that address these issues. It should be noted that these studies deal with autogenous fat grafting to the breast in general and are not specific to breast augmentation.

Pierrefeu-Lagrange et al reported a series of 30 patients who had autogenous fat grafting of the breast after reconstruction with a latissimus dorsi flap. Microcalcifications were noted in only four patients and were obviously benign.

In Illouz and Sterodimas’s series, 670 patients underwent mammography six months and one year after autogenous fat grafting. There were no BI-RADS Grade 4 or 5 lesions, which would suggest that the radiologists did not confuse the postoperative findings with suspicious lesions.

Carvajal and Patiño presented a series of 20 patients who obtained bilateral screening mammograms an average of 34.5 months after autogenous fat grafting. Mammographic findings of fat necrosis included radiolucent oil cysts, microcalcifications, coarse microcalcifications, focal masses, and spiculated areas of increased opacity. Only three patients had BI-RADS Grade 3 lesions (microcalcifications), and these were reclassified as BI-RADS Grade 2 at six-month follow-up. It was concluded that knowledge of the expected mammographic findings after autogenous fat grafting would prevent unnecessary biopsy but that this procedure should be avoided in patients with a family history of breast cancer.

Of the 17 patients in the Coleman and Saboeiro series, 15 underwent follow-up mammography. Of those, seven (47%) developed abnormal mammograms. Two (13%) had breast cancer that was correctly identified, and the remainder, five (33%), had benign-appearing calcifications, sometimes in association with nodules (one of which was aspirated and proved to be fat necrosis).
In Delay et al’s series,\textsuperscript{24} long-term radiographic follow-up was performed. The majority of images were normal, with some oily cysts and fat necrosis noted. These changes were believed to be easily distinguishable from suspicious lesions. Most of the abnormal findings were oily cysts, which were present in 15% of cases. It was noted that the most complex radiographic findings were seen in autogenous fat grafting after breast conservation therapy.

Although there are no prospective, controlled trials, the majority of the literature seems to indicate that the radiologic changes resulting from autogenous fat grafting are distinguishable from suspicious lesions.

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of patients\textsuperscript{a}</th>
<th>Preparation</th>
<th>Injection site</th>
<th>Volume retention</th>
<th>Patient satisfaction</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illouz and Sterodimas\textsuperscript{19}</td>
<td>385</td>
<td>Fat allowed to decant from syringe by gravity; no centrifuge</td>
<td>Subcutaneous and intraparenchymal</td>
<td>No data</td>
<td>No data</td>
<td>Striae 4.4%  Hematomas 1.5%  Infections 0.6%</td>
</tr>
<tr>
<td>Zocchi and Zuliani\textsuperscript{5}</td>
<td>181</td>
<td>Vibration table and washing in saline; negative pressure preexpansion of breast</td>
<td>Retroglandular, prefascial, subcutaneous</td>
<td>55% at one year (40% - 70%)</td>
<td>Excellent 23%  Good 72%  Fair 6%  Insufficient 3%</td>
<td>Edema 100%  Bruising 78%  Dysesthesia 5.8%  Liponecrosis 1.2%  Microcyst 1.8%  Microcalcifications 3.9%</td>
</tr>
<tr>
<td>Mu et al\textsuperscript{20}</td>
<td>140</td>
<td>VEGF mixed with fat at 1 µg/mL</td>
<td>Subpectoral, pectoral, retromammary</td>
<td>No data</td>
<td>No data</td>
<td>Sclerotic nodules in one patient (0.7%)</td>
</tr>
<tr>
<td>Fulton 1992\textsuperscript{21}</td>
<td>20</td>
<td>Fat washed in LR; no centrifuge</td>
<td>Prepectoral fascial plane</td>
<td>71%</td>
<td>No data</td>
<td>Minor bruising</td>
</tr>
<tr>
<td>Fulton 2003\textsuperscript{22}</td>
<td>65</td>
<td>Platelet-rich plasma added; no centrifuge</td>
<td>Subpectoral, pectoralis, retroglandular</td>
<td>73%</td>
<td>No data</td>
<td>Striae in two patients (3.1%)</td>
</tr>
<tr>
<td>Yoshimura et al\textsuperscript{23}</td>
<td>40</td>
<td>Enriched with ASC; centrifuge used in some patients</td>
<td>“Fatty layers” around mammary gland and in the pectoralis muscle</td>
<td>No data</td>
<td>No data</td>
<td>Cyst formation or microcalcifications in four patients (10%)</td>
</tr>
<tr>
<td>Delay et al\textsuperscript{24}</td>
<td>30</td>
<td>Centrifuge at 3200 rpm for 3 minutes</td>
<td>No data</td>
<td>60%-70%</td>
<td>Results considered good or very good in majority of cases</td>
<td>Infection 0.7%  Fat necrosis 3%  Pneumothorax 0.1%</td>
</tr>
<tr>
<td>Zheng et al\textsuperscript{25}</td>
<td>24</td>
<td>Washed with saline and centrifuged at 600 rpm (26 g) for 2 minutes</td>
<td>Subcutaneous and subglandular</td>
<td>No data</td>
<td>80.3% very satisfied or satisfied 19.7% unsatisfied</td>
<td>Liponecrotic cysts 16.7%</td>
</tr>
<tr>
<td>Coleman and Saboeiro\textsuperscript{26}</td>
<td>10</td>
<td>Centrifuge</td>
<td>Majority into pectoralis, less to pre- and retropectoral spaces; intraparenchymal injection limited</td>
<td>No data</td>
<td>“All patients pleased”</td>
<td>No data</td>
</tr>
</tbody>
</table>

ASC, autologous adipocyte-derived stem cells; LR, lactated Ringer’s solution; VEGF, vascular endothelial growth factor.
\textsuperscript{a}The number of patients in each case series who underwent cosmetic breast augmentation. The remainder of the data in the table is for the total number of patients in the series as there were insufficient data for subset analysis. Zocchi and Zuliani’s 181 patients also included some patients who had revisional surgery and combined reductive mastoplasty.
**Table 2. Summary of Patient Satisfaction and Surgeon Evaluation of Aesthetic Results for Zheng et al[^25]**

<table>
<thead>
<tr>
<th>Evaluation by plastic surgeons[^4]</th>
<th>% Patient satisfaction</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significantly improved</td>
<td>33</td>
<td>Very satisfied</td>
</tr>
<tr>
<td>Improved</td>
<td>58</td>
<td>Satisfied</td>
</tr>
<tr>
<td>Not improved</td>
<td>8</td>
<td>Unsatisfied</td>
</tr>
</tbody>
</table>

[^4]: Panel of three independent plastic surgeons.

### TUMORIGENESIS

Another set of concerns relates to possible tumorigenesis or promotion of existing subclinical breast cancer by autologous fat transfer. In a commentary by Mojallal et al.,[^32] it was noted that some in vitro and animal models suggested that mature adipocytes and ASC favored an increase in tumor growth.[^33][^35]

It has been shown that cytokines derived from mature adipocytes influence breast cancer cell lines by inducing several transcriptional programs that are involved in tumorigenesis in vitro. An in vivo effect was also noted by demonstrating that coinjection of a mature adipocyte cell line with breast cancer cells potentiated tumor growth in a murine model.[^33] Similarly, mature adipocytes (but not preadipocytes) were noted to promote the growth of several estrogen receptor (ER)–positive breast cancer cell lines in a collagen matrix.[^33] Local estrogen production by adipocyte-derived aromatase was one of many mechanisms suggested for this effect.

Considerable attention has been given to the potential role of ASC in the promotion of breast cancer. In vitro and murine in vivo experiments have demonstrated that ASC will home to breast cancer tumor sites and promote growth.[^36] These cells are stimulated to secrete stromal cell–derived factor-1 by the breast cancer cells, which then acts in a paracrine fashion to stimulate tumor growth. Human ASC have also been noted to increase tumor cell viability in mice and decrease apoptotic cell death.[^34] The invasiveness of breast cancer cells has been shown to be potentiated by human ASC production of CCL5 in vitro.[^37]

In contrast, intravenous injection of human adipocyte-derived mesenchymal stem cells (i.e., ASC) has been shown to inhibit tumor growth and lung metastases in a mouse model with human breast cancer cells.[^38] E-cadherin is known to correlate closely with invasiveness of breast cancer and preadipocytes have been shown to decrease expression of E-cadherin in breast cancer cells.[^33]

One of the reviewed series, from Mu et al.,[^20] reported on transplanted autogenous fat mixed with VEGF. VEGF is a glycoprotein that binds to a transmembrane receptor with an intracellular tyrosine kinase domain.[^39] It is known to play a central role in the promotion of metastases and in tumor angiogenesis, which is critical to the growth of a tumor beyond 1 to 2 mm³ in size.[^40] Increased expression of VEGF has been shown to correlate with decreased survival in both node-positive[^41] and node-negative breast cancer[^42] and predicts poor response to adjuvant systemic therapy in advanced disease.[^43] A humanized murine monoclonal anti-VEGF antibody (bevacizumab) has been developed to exploit this knowledge of tumor biology. Bevacizumab has been shown to have efficacy in combination with cytotoxic chemotherapy for metastatic breast cancer.[^39] Given the knowledge that VEGF is critical for the promotion of breast cancer, there is some concern regarding its injection into the breast. No studies were found that addressed this issue.

In all, no controlled human studies were found that specifically addressed the issue of promotion of breast cancer by autogenous fat grafting; however, one case series followed patients who had autogenous fat grafting after tumor resection and did not note an increased incidence of recurrence.[^24]

### DISCUSSION

Although there is one registered prospective, noncontrolled trial in progress (BRAVA, clinicaltrials.gov ID: NCT00466765), the literature regarding the outcomes associated with autogenous fat grafting of the breast for augmentation consists primarily of case reports and series. The noted series emphasized refinements in technique, which included the application of blunt cannulas, low negative pressures for aspiration, and minimal trauma to the adipocytes. Methods of adipocyte isolation from the aspirate varied, with most employing different centrifuge protocols and one employing a vibrating table.[^5] Various additives to the adipocyte fraction included[^22] autologous adipocyte stem cells,[^23] and VEGF.[^20] One study utilized preoperative tissue expansion with a negative pressure device.[^5] Diffuse injection of the tissue in small aliquots with a high surface area to volume ratio was recommended. Avoidance of large injections in any one area was felt to maximize the chance of graft survival and avoid large liponecrotic cysts.

Refinements in harvest and transplantation techniques continue. In 2009, Khouri and DelVecchio[^44] described their technique, which utilized preexpansion of the breast with the BRAVA negative pressure device. The fat was harvested with a 12-gauge blunt cannula with multiple side ports and manual aspiration to avoid high negative pressures. Desiccation was avoided through a closed system. To process the adipose tissue, a low-G-force manual centrifuge was employed. Fibrous bands to the breast were released with an 18-gauge needle and the fat was placed into 3-mL syringes. A “mapping” technique utilizing a 16-gauge blunt needle was employed for injection. The prepectoral and subcutaneous planes were utilized, and parenchymal injection was strictly avoided. Postoperatively, the BRAVA device was utilized for five to seven days. This was believed to promote neovascularization, immobilize the graft, and protect the breast from pressure and trauma.

Another recent refinement in harvest technique not included in the above series is the LipiVage system, which is an automated, closed system utilizing low negative pressures.
Table 3. Potential Study Characteristics for Future Investigation of Autogenous Fat Grafting for Breast Augmentation

<table>
<thead>
<tr>
<th>Study Characteristic</th>
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<tbody>
<tr>
<td>Multicenter, controlled, randomized</td>
</tr>
<tr>
<td>Standardized measurement of outcomes</td>
</tr>
<tr>
<td>Measurement of volume retention</td>
</tr>
<tr>
<td>Measurement of patient satisfaction</td>
</tr>
<tr>
<td>Objective evaluation of cosmesis by independent plastic surgeons</td>
</tr>
<tr>
<td>Measurement of the incidence of abnormal mammograms and subsequent biopsies</td>
</tr>
<tr>
<td>Measurement of the incidence of breast cancer</td>
</tr>
</tbody>
</table>

CONCLUSIONS

The interest in autogenous fat grafting to the breast has increased since the 1980s. Since that time, refinements in harvesting and grafting techniques have improved graft survival. The literature on this topic consists primarily of case reports and series. There were no prospective or controlled trials and the outcome measures varied. In many studies, graft retention and patient satisfaction were not measured. Proper patient selection, informed consent, and proper communication of realistic expectations regarding breast size are critical when applying this technique in a clinical practice. Initial concerns over interference with breast cancer screening do not appear to be valid, but given the quality of the data, the technique should not be utilized in patients with a family history of breast cancer, and BI-RADS Grade 3 lesions should be considered for additional evaluation with magnetic resonance imaging. No clinical trials have considered whether autogenous fat grafting promotes breast cancer and thus far there is no consensus regarding the basic science underlying these concerns. Large multicenter, prospective, controlled trials are necessary to further investigate these issues.
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