Autologous Fat Grafting to the Breast and Adipose-derived Stem Cells

Description

Background

Autologous fat grafting to the breast

Autologous adipose tissue (fat) grafting for reconstructive purposes has been reported in the medical literature for at least 100 years. Fat tissue is typically available in abundance.

Harvesting of adipose tissue by liposuction is technically easy, minimally invasive, and associated with little patient discomfort and morbidity, and small amounts (100-200 mL) can be obtained under local anesthesia.

Adipose tissue is a highly vascularized tissue, and adipocytes are in direct contact with adjacent capillary vessels. In free fat grafting, graft survival requires the direct diffusion of nutrients from plasma in the surrounding bed and subsequent revascularization which typically occurs within 48 hours. Failure of revascularization results in grafted fat tissue necrosis. There is general unpredictability and a low rate of graft survival due to partial necrosis. Other complications include oil cyst formation, indurations in the subcutis or breast parenchyma, calcification, and severe breast deformity. (1)

Reports have been published on clinical experience in using fat grafting in various conditions. There are laboratory research publications that have reported on the biology of the adipose stem cell, physiology of graft survival and graft function post-transplantation. Concerns about complications of
fat grafting in the breast such as cyst formation, calcification and sclerosis and the possible adverse impact on the effectiveness of breast cancer screening with mammography initially led to restraint on its use in the breast. Adipose-derived stem cells

Stem cell biology, and the related field of regenerative medicine, involves multipotent stem cells that exist within a variety of tissues, including bone marrow and adipose tissue. Studies have shown that 1 gram of adipose tissue yields approximately $5 \times 10^3$ stem cells, which are up to 500 times greater than the number of mesenchymal stem cells in 1 gram of bone marrow. (1) Stem cells, because of their pluripotentiality and unlimited capacity for self-renewal, offer promise for tissue engineering and advances in reconstructive procedures. Adipose tissue in particular represents an abundant and easily accessible source of adipose-derived stem cells (ADSCs), which can differentiate along multiple mesodermal lineages. (1) ADSCs may allow for improved graft survival and generation of new fat tissue after transfer from another site.

**Regulatory Status**

Cytori Therapeutics, Inc. was awarded 510(k) marketing clearance in September 2006 from the U.S. Food and Drug Administration’s Center for Devices and Radiological Health (CDRH) for the Celution™ Cell Concentration System as a cell saver device. The system is cleared for the collection, concentration, washing and re-infusion of a patient’s own cells for applications that may include, but are not limited to, cardiovascular, plastic and reconstructive, orthopedic, vascular, and urological surgeries and procedures.

**Policy**

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

The use of autologous fat grafting and adipose-derived stem cells for reconstruction of the breast is considered **not medically necessary**.
Literature Review

The literature on the use of fat grafting to the breast, with or without adipose-derived stem cells, primarily consists of case series, case reports and review articles. Following is a summary of the key literature to date, detailing the largest case series using fat grafting to the breast and identified case series using fat grafting to the breast with the supportive use of adipose-derived stem cells.

In these reports, the indications for fat grafting included congenital breast defects, postlumpectomy or postmastectomy deformity or postradiation tissue damage.

The review articles summarize various applications of autologous fat grafting and the use of adipose-derived stem cells. (1, 2-4)

Autologous Fat Grafting in Breast Reconstruction – Clinical Reports.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Design</th>
<th>Description of Subjects</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Losken (5)</td>
<td>Retrospective case series review 1996-2010</td>
<td>107 patients with breast cancer and acquired breast deformity</td>
<td>Average volume of injection =40ml (range, 5-150ml). Average follow-up 8 months (range 1-2.5 years)</td>
<td>Complications (fat necrosis, scarring and pain) in 11% 83% of 17 patients with follow-up greater than 6 months responded to survey that treatment was associated with significant or moderate improvement.</td>
</tr>
<tr>
<td>Illouz (6)</td>
<td>Retrospective case series review 1983-2007</td>
<td>Post-mastectomy asymmetry (n=381) Congenital breast asymmetry (n=54) Aesthetic bilateral breast augmentation (n=385)</td>
<td>Mean graft volume per session =145 ml (range 25-180ml) Mean number of sessions=3 (range 1-5)</td>
<td>Complications: ecchymosis and hematoma=88, infection =5, striae =36. Ultrasound and mammography at 6</td>
</tr>
</tbody>
</table>
Autologous fat grafting and the use of adipose-derived stem cells

In 2011, Kamakura and Ito reported on the use of autologous adipose-derived stem cell (ADSC) enriched fat grafting for breast augmentation in a prospective, nonrandomized open-label study of 20 Japanese women. (8) After the adipose tissue was harvested by liposuction, it was processed in the Celution 800 System® to wash and isolate the adipose-derived regenerative cells and produce a fat graft enriched with the regenerative cells. The average number of cells per gram of harvested adipose tissue was $3.4 \times 10^5$, and mean cell viability as measured with an automated cell counting system before graft delivery was 85%. Clinical outcomes measured included improvement in circumferential breast measurement from baseline state. There was improvement in circumferential breast measurement in all patients, and breast measurements were stable by 3 months after grafting. At 9 months, the mean breast measurement had increased 3.3 cm from preoperative measurements. Through 9 months, overall patient satisfaction was 75% and physician satisfaction 69%. The procedure was well-tolerated without any serious adverse events. Postoperative cyst formation was seen in 2 patients.
In 2008, Yoshimura and colleagues reported on the development of a novel strategy known as cell-assisted lipotransfer (CAL), in which autologous ADSCs are used in combination with lipoinjection. (9) From 2003-2007, the group performed CAL in 70 patients: in the breast in 60 patients (including 8 who had breast reconstruction after mastectomy). They reported outcomes for 40 patients with healthy thoraxes and breasts who underwent CAL for purely cosmetic breast augmentation; patients undergoing breast reconstruction for an inborn anomaly or after mastectomy were not included. Nineteen of the 40 patients had been followed for more than 6 months, with a maximum follow-up of 42 months. The authors observed that the transplanted adipose tissue was gradually absorbed during the first 2 postoperative months, and the breast volume showed a minimal change thereafter. Final breast volume showed augmentation by 100 to 200 mL after a mean fat amount of 270 mL was injected. The difference in breast circumference (defined as the chest circumference at the nipple minus the chest circumference at the inframammary fold) had increased in all cases by 4 to 8 cm at 6 months. Cyst formation or microcalcification was detected in 4 patients. The authors concluded that their preliminary results suggest that CAL is effective and safe for soft tissue augmentation and superior to conventional lipoinjection but that additional study is necessary to further evaluate the efficacy of this technique.

National Cancer Institute’s Clinical Trial Database
No randomized, controlled trials were identified.

Practice Guidelines and Position Statements
The American Society of Plastic Surgeons (ASPS) Task Force Report on Current Applications and Safety of Autologous Fat Grafts concluded that there was a less than expected beneficial outcome to fat grafting. The Task Force stated: “Based on a review of the current literature and a lack of strong data, the task force cannot make specific recommendations for the clinical use of fat grafts. Although fat grafts may be considered for use in the breast and other sites, the specific techniques of graft harvesting, preparation, and injection are not standardized. The results, therefore, may vary depending on the surgeon’s technique and experience with the procedure. Although there are few data to provide
evidence for long-term safety and efficacy of fat grafting, the reported complications suggest that there are associated risks. Regarding fat grafting to the breast, there are no reports suggesting an increased risk of malignancy associated with fat grafting. There is a potential risk of fat grafts interfering with breast physical examination or breast cancer detection; however, the limited data available suggest that fat grafts may not interfere with radiologic imaging in detecting breast cancer. (10)

In addition, the ASPS published “Fat Transfer/Fat Graft and Fat Injection Guiding Principles” (11). The guiding principles intended to apply only to fat grafting in the breast provide a succinct overview of the key points made in the evidence review.

In 2011, ASPS and the American Society for Aesthetic Plastic Surgery (ASAPS) issued a joint position statement on stem cells and fat grafting. This statement addressed the limitations of the evidence for stem cell use for this purpose as well as the potential marketing claims for superiority of stem cells that may result in misinformation being provided to patients. (12)

**Summary**

The mechanisms of injected fat survival as well as the way to control adipose-derived stem cell differentiation and the ultimate disposition of the stem cells in the body unknown. The impact of fat grafting and the use of adipose-derived stem cells on net health outcome in reconstruction of the breast are unknown and therefore, are considered to be *not medically necessary*.

**Medicare National Policy**

There is no national coverage determination.

**References**


Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>September 2012</td>
<td>New Policy</td>
<td></td>
</tr>
</tbody>
</table>

Keywords

Adipose-derived Stem Cells, Breast Reconstruction
Autologous Fat Grafting, Breast
Breast Reconstruction with Adipose-derived Stem Cells

This policy was approved by the FEP Pharmacy and Therapeutics Committee on September 13, 2012 and is effective October 1, 2012.

Signature on File

James A. Ferrendelli, M.D.