

<b>Medical Benefit</b>		<b>Effective Date:</b> 04/01/14	<b>Next Review Date:</b> 11/20
<b>Preauthorization</b>	Yes	<b>Review Dates:</b> 02/07, 02/08, 01/09, 01/10, 01/11, 01/12, 01/13, 01/14, 11/14, 11/15, 11/16, 11/17, 11/18, 11/19	

***Preauthorization is required.***

*The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.*

**DESCRIPTION**

Reconstructive breast surgery is defined as a surgical procedure that is designed to restore the normal appearance of the breast after surgery, accidental injury, or trauma. Breast reconstruction is distinguished from purely cosmetic procedures by the presence of a medical condition, e.g., breast cancer or trauma, which leads to the need for breast reconstruction.

Following a mastectomy, patients often experience pain and irradiated skin; as an adjunct to reconstructive breast surgery, surgeons will sometimes graft autologous fat to the breast. Adipose derived stem cells (ADSCs) have been proposed as a supplement to the fat graft in an attempt to improve graft survival; however, whether ADSCs play a role in tumorigenesis is still relatively unknown.

**SUMMARY OF EVIDENCE**

Breast reconstruction is intended for patients undergoing mastectomy for breast cancer, or who have an injury or trauma to the breasts. For the general population of women undergoing mastectomy, the evidence supports the conclusion that breast reconstruction improves psychosocial outcomes, such as anxiety, social functioning, and perception of body image. Thus, breast reconstruction may be considered medically necessary when reconstruction is needed as a result of breast cancer, injury, or trauma.

For individuals who have breast cancer who receive autologous fat grafting to the breast with ADSC enrichment of the graft, the evidence includes small single-arm studies, some of which are prospective. The relevant outcomes are symptoms, morbid events, functional outcomes, quality of life, resource utilization, and treatment-related morbidity. The observational studies were heterogeneous in the patient selection, methods in harvesting stem cells, number of procedures, and outcomes measured. Studies have mainly reported patient and investigator satisfaction and functional and cosmetic results. Limitations of the data include sample sizes, short-term follow-up, and uncertainty about the possible oncologic influence ADSC may have on the fat grafting procedure. In addition, no studies were identified which demonstrated incremental benefits of using ADSC enrichment with autologous fat grafting over autologous fat grafting alone. The evidence is insufficient to determine the effects of the technology on health outcomes.

**POLICY**

Reconstructive breast surgery may be considered **medically necessary** after a medically necessary partial (including but not limited to lumpectomy) or full mastectomy, or following accidental injury or trauma when there is functional impairment.

Explantation of a *silicone* gel-filled breast implant may be considered **medically necessary** in all cases for a documented implant rupture, infection, extrusion, Baker class IV contracture, or surgical treatment of breast cancer.

Explantation of a ruptured *saline*-filled breast implant may be considered **medically necessary** only in those patients who had originally undergone breast implantation for reconstructive purposes. Otherwise, indications for the explantation of a saline-filled implant are similar to those of a silicone-filled implant.

Explantation of a breast implant associated with a Baker class III contracture may be considered **medically necessary** only in those patients who had originally undergone breast implantation for reconstructive purposes.

Reconstructive breast surgery after explantation of an implant is considered **medically necessary** only in those patients who had originally undergone breast implantation for reconstructive purposes.

The following indications for explantation of implants are considered **not medically necessary**:

- Systemic symptoms, attributed to connective tissue diseases, autoimmune diseases, etc.;
- Patient anxiety;
- Baker class III contractures in patients with implants for cosmetic purposes;
- Rupture of a saline implant in patients with implants for cosmetic purposes;
- Pain not related to contractures or rupture.

The use of adipose-derived stem cells in autologous fat grafting to the breast is considered **investigational**.

**POLICY GUIDELINES**

Application of the above policy regarding explantation of implants requires documentation of the original indication for implantation and the type of implant, either saline- or silicone gel-filled, and the current symptoms, either local or systemic. The following chart should facilitate determination of the medical necessity of explantation. Yes indicates that the explantation would be considered medically necessary, given the symptoms, type of implant, and original indication for implantation.

## Indication/Type of Implant

Indication for Explantation	Reconstruction/silicone	Reconstruction/saline	Cosmetic/silicone	Cosmetic/saline
<b>Systemic Illness</b>				
Connective tissue disease	no	no	no	no
Autoimmune disease	no	no	no	no
Rheumatic conditions	no	no	no	no
Neurologic symptoms	no	no	no	no
Fibromyalgia	no	no	no	no
Chronic fatigue syndrome	no	no	no	no
Patient Anxiety	no	no	no	no
<b>Absolute Medical Indications</b>				
Rupture*	yes	yes	yes	no
Baker class IV contracture	yes	yes	yes	yes

Indication for Explantation	Reconstruction/silicone	Reconstruction/saline	Cosmetic/silicone	Cosmetic/saline
Recurrent infection	yes	yes	yes	yes
Extruded implant	yes	yes	yes	yes
Surgery for breast cancer	yes	yes	yes	yes
<b>Other Indications</b>				
Baker class III contractures	yes	yes	no	no
Pain**	no	no	no	no
<b>Post-Explantation Procedures</b>				
Reimplantation of implants	yes	yes	no	no
Autologous reconstruction	yes	yes	no	no

\*Rupture of implants requires documentation with an imaging study, such as mammography, magnetic resonance imaging, or ultrasonography. Lack of imaging confirmation of rupture in association with persistent local symptoms requires case by case consideration.

\*\*Pain as an isolated symptom is an inadequate indication for explantation. The pain should be related to the Baker classification or a diagnosis of rupture.

Reconstructive breast surgery may consist of any of the following procedures:

- Immediate or delayed insertion of breast prosthesis with or without associated tissue expansion;
- Autologous reconstruction using autologous tissue, e.g., latissimus dorsi flap, transverse rectus abdominis myocutaneous flap, or free flap;
- Revision of reconstructed breast;
- Nipple/areola reconstruction and nipple tattooing when the breast reconstruction is considered eligible for coverage;
- Mastopexy or reduction mammoplasty on the contralateral breast to achieve symmetry.

Medically necessary mastectomies are most typically done as treatment for cancer. Reconstruction may be performed by an implant-based approach or through the use of autologous muscle tissue. After reconstructive breast surgery on one side, insertion of an implant on the contralateral, normal side is rarely necessary to achieve symmetry.

The Cosmetic vs. Reconstructive Services Protocol may also be applicable for other than post medically necessary mastectomy reasons for breast reconstruction.

## BACKGROUND

The most common indication for reconstructive breast surgery is a prior mastectomy. Cosmetic breast surgery is defined as surgery designed to alter or enhance the appearance of a breast that has not undergone surgery, accidental injury, or trauma. Reduction mammoplasty is a common example of cosmetic breast surgery, but surgery to alter the appearance of a congenital abnormality of the breasts, such as tubular breasts, would also be considered cosmetic in nature.

There is a broadening array of surgical approaches to breast reconstruction. The most common is insertion of a breast implant, either a silicone gel-filled or saline-filled prosthesis. The implant is either inserted immediately at the time of mastectomy or sometime afterward in conjunction with the previous use of a tissue expander.

The breast may also be reconstructed using autologous tissues, such as a free flap, a latissimus dorsi flap, or more commonly using a transverse rectus abdominis flap (TRAM procedure). Nipple areola reconstruction or nipple tattooing may also be considered reconstructive breast surgery. Since the purpose of reconstructive breast surgery is to restore the normal appearance of the breast, these procedures may be performed on the

contralateral, normal breast to achieve symmetry, such as mastopexy and reduction mammoplasty. These procedures fall into the category of reconstructive breast surgery only when performed in conjunction with a contralateral mastectomy with associated reconstruction. Except for medically necessary reduction mammoplasty, these procedures are considered cosmetic in other circumstances.

This protocol describes different types of reconstructive breast surgery and reviews the evidence on efficacy for the different approaches. It also establishes criteria for the explantation of breast implants based on whether the original implant was cosmetic or reconstructive in nature, and whether the implant is silicone gel-filled or saline-filled.

#### FAT GRAFTING TO THE BREAST

Autologous fat grafting to the breast has been proposed for indications that include breast augmentation following oncologic surgery. Grafting would be performed as an adjunct to reconstruction after mastectomy or lumpectomy, and it would be of benefit in the following areas: for contouring purposes, improving breast shape and volume; and for alleviating post mastectomy pain syndrome (neuropathic pain) and irradiated skin (thereby reducing complication and failure rates of implant reconstruction). Variability in long-term results and oncologic concerns have limited application of autologous fat grafting in the breast.

This protocol does not address the use of autologous fat tissue in aesthetic breast augmentation (i.e., cosmesis).

#### 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. A single gram of adipose tissue yields approximately 5000 stem cells; this is 100 to 500 times the number of mesenchymal stem cells found in an equivalent amount of bone marrow.<sup>1</sup> Stem cells, because of their pluripotentiality and unlimited capacity for self-renewal, offer promise for tissue engineering and advances in reconstructive procedures. In particular, adipose tissue represents an abundant and easily accessible source of ADSCs, which can differentiate along multiple mesodermal lineages. ADSCs may allow for improved graft survival and generation of new fat tissue after transfer from another site.<sup>1,2</sup>

The potentially therapeutic properties of ADSC have led to novel techniques of fat grafting in conjunction with ADSC therapy for breast fat grafting. Differentiation of ADSC into adipocytes may provide a reservoir for adipose tissue turnover. Differentiation of ADSC into endothelial cells, with the release of angiogenic growth factors by ADSC, may decrease the rate of graft resorption by increasing blood supply to the grafted fat tissue. Further, ADSC may serve to accelerate wound healing and protect the graft from ischemic reperfusion injury.<sup>1</sup> Current methods for isolating ADSCs can involve various processes, which may include centrifugation and enzymatic techniques that rely on collagenase digestion-which, in turn, is followed by centrifugal separation to isolate the stem cells from primary adipocytes. Isolated ADSCs can be expanded in a monolayer on standard tissue culture plastic surfaces with a basal medium containing 10% fetal bovine serum.<sup>3</sup> Newly developed culture conditions provide an environment in which the study of ADSCs can be done without the interference of animal serum and may also allow rapid expansion of autologous ADSCs in culture for use in human clinical trials. A standard expansion method has not yet been established.

To address the problems of unpredictability and low rates of fat graft survival, Yoshimura et al (2008) developed a technique known as cell-assisted lipotransfer, which produces autogenous fat rich in ADSCs.<sup>4</sup> In cell-assisted lipotransfer, half of the lipoaspirate is centrifuged to obtain a fraction of concentrated ADSCs; meanwhile, the other half is washed, enzymatically digested, filtered, and spun down to an ADSC-rich pellet. The latter is then mixed with the former, converting a relatively ADSC-poor aspirated fat to ADSC-rich fat.

A point-of-care system is available for concentrating ADSC from mature fat. The Celution System is designed to transfer a patient's adipose tissue from one part of the body to another in the same surgical procedure.

## REGULATORY STATUS

In September 2006, Celution™ Cell Concentration System (Cytori Therapeutics; San Diego, CA) was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process as a cell saver device. The system is cleared for the collection, concentration, washing, and reinfusion of a patient's cells for applications that may include, but are not limited to, cardiovascular, plastic and reconstructive, orthopedic, vascular, and urologic surgeries and procedures. In 2007, Cytori Therapeutics received the FDA 510(k) clearance to market the Autologous Fat Transfer system, which transfers a patient's own adipose tissue from one part of the patient's body to another. FDA product code: CAC.

In 2017, the Revolve Envi 600 Advanced Adipose System (LifeCell Corporation, Branchburg, NJ) was cleared for marketing by the FDA through the 510(k) process. The system harvests, filters, and transfers autologous adipose tissue for fat grafting. Uses include reconstructive surgery. FDA product code: MUU.

## RELATED PROTOCOLS

Bio-Engineered Skin and Soft Tissue Substitutes

Cosmetic vs. Reconstructive Surgery or Services

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Services that are the subject of a clinical trial do not meet our Technology Assessment and Medically Necessary Services Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment and Medically Necessary Services Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

## REFERENCES

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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