Autogenous Fat Grafting to the Breast and Gluteal Regions: Safety Profile Including Risks and Complications

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Summary: Given the widespread utility and therapeutic potential of autogenous fat grafting, plastic surgeons should be familiar with its safety profile and associated adverse events. This article provides a critical review of the literature and delineates risk factors associated with various complications when grafting to the breast and gluteal regions. The majority of adverse events are related to fat necrosis and require minimal diagnostic or therapeutic intervention. Larger graft volumes, as in cosmetic augmentation, are associated with higher incidences of fatty necrosis. The oncologic safety of fat grafting is supported by multiple clinical studies with thousands of breast cancer patients, albeit predominantly retrospective in nature. Although less frequent, serious complications include fat emboli during gluteal augmentation. Identification of associated risk factors and implementation of proper surgical techniques may minimize the occurrence of life-threatening complications. (*Plast. Reconstr. Surg.* 143: 1625, 2019.)

Autogenous fat grafting is increasingly used by plastic surgeons to accomplish various reconstructive and aesthetic objectives.[1] Their relative abundance, ease of harvest, minimal donor-site morbidity, and low immunogenicity make adipose grafts an ideal substitute filler for soft tissues. Historically, fat transplantation was a frustrating enterprise plagued by inconsistent results; however, its systematization in the 1990s repopularized the nearly abandoned practice.[2] The main issues surrounding fat grafting today are focused less on variable resorption and fibrous replacement of the graft but rather on the safety profile. In particular, there is lingering concern regarding fat grafting to the breasts in the context of oncologic reconstruction, and growing concern regarding grafting to the gluteal regions.[3–5] Potential associations with locoregional recurrence and reports of life-threatening complications have heightened the awareness of both professional societies and the public. Given the widespread utility of fat grafting and its therapeutic potential, it would behoove plastic surgeons to familiarize themselves with its safety and associated adverse events. This article provides a critical review of the literature and delineates risk factors associated with various complications when grafting to the breast and gluteal regions.

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AUTOGENOUS FAT GRAFTING TO THE BREASTS

Locoregional Recurrence and Cancer Risk

Fat grafting to the breasts is generally a safe procedure, with the majority of complications classified as Clavien-Dindo I (i.e., no endoscopic, surgical, radiologic, or major pharmacologic intervention required).[3,6–8] In the setting of breast reconstruction in particular, the issue of locoregional tumor recurrence in association with fat grafting may be most concerning to many. However, despite in vitro and in vivo studies suggesting the oncologic potential of autogenous fat grafts,[9–19] an association has not been confirmed in clinical settings. The basic science evidence, however, is often based on models not reflective of fat

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grafting, but of isolated stem cells interacting with cancer cells. More accurate models of the interactions between fat graft and cancer cells are needed and do not suggest a higher rate of recurrence.[20] Rather, multiple retrospective case-control analyses and prospective case series have failed to show any elevation in recurrence risk.[21–33] These are well-organized investigations supported mostly by large study populations; however, they are limited by the inherent biases in their study design (e.g., retrospective, nonrandomized, nonblinded, and therefore susceptible to selection bias), inadequate follow-up (both timing and method of) to assess for tumor recurrence, and lack of clarity related to pertinent variables (e.g., management of positive margins after lumpectomy).

The most convincing studies include large comparative European and American cohorts that underwent either breast-conserving therapy or mastectomy with nearly 5-year follow-up periods. These studies did not reveal any significant increase in tumor recurrence after fat grafting.[21,28] In a subgroup analysis of in situ carcinoma, there was a significant association between tumor recurrence and fat transfer.[28] Although this finding was initially upheld in a subsequent comparative analysis,[30] longer term analysis showed that the control group recurrence rate caught up and the differences were no longer significant.[22,34] Aside from selection bias, other variables may have explained the originally observed risk and include the patient's age, modality of cancer treatment (often breast-conserving therapy in the setting of in situ disease), handling of margin status, and time to grafting.[33]

Breast conservation therapy is generally associated with a higher rate of local events. Nevertheless, a case-control study of 322 patients who received breast-conserving therapy and fat transfer (with equal number controls) with a 4.8-year follow-up revealed no increase in recurrence.[22] In prospective series of fat grafting after breast-conservation therapy, the local event rate per year is reported as either less than or equal to rates in the published literature.[23,27]

The American Society of Plastic Surgeons considers adipose grafts to have uncertain oncogenic potential in the setting of breast reconstruction.[35] However, as highlighted by this review, there is a significant body of evidence based on large retrospective, comparative studies that argue against an association. The continued monitoring and accrual of prospective data may further support its oncologic safety. Nevertheless, traditional factors associated with local recurrence should be considered before adipose grafting. These characteristics include tumor size, nodal status, positive margins, histologic grade, and molecular (i.e., estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2) characteristics.[36–38] Although breast-conserving therapy has proven equal survival benefit in those undergoing a mastectomy, it is associated with an increased risk of local events.[39,40] Thus, breast-conserving therapy independently confers an elevated risk of recurrence along with other context-associated factors—such as younger age (younger than 35 years), premenopausal status, and peritumor vascular invasion—and should be considered by those who use fat grafting in this context. Irrespective of the modality of cancer treatment, proper adjuvant therapies should be pursued and completed before lipotransfer.

Similar to breast reconstruction, cosmetic augmentation with autogenous fat has not been associated with an increased likelihood of breast cancer beyond that of the average risk.[41] Practitioners are still cautioned when deciding to perform lipotransfer in healthy native tissue of patients with historical risk factors.

Fat Necrosis, Radiographic Abnormalities, and Other Complications

The most common complication following lipotransfer is directly related to graft loss and manifests as variable forms of fat necrosis. The location and degree of liquefied fat, fibrosis, and calcifications ultimately determine its clinical significance and radiologic appearance. Fatty necrosis often occurs when grafted adipocytes incur too great a stress during the harvest and/or transference processes, from direct damage related to tissue handling and/or inadequate diffusion of oxygen and nutrients before neovascularization. The Coleman technique is intended to optimize graft take by minimizing trauma and maximizing surface area–to-volume ratio with the recipient bed. Theoretically, techniques that adhere to these principles of fat grafting may allow for large-volume fat transfer with low risk of fat necrosis or other complications. However, proper handling and technique alone cannot overcome certain limitations, such as the compliance of the recipient bed. In large prospective series of cosmetic breast augmentation, the incidence of fat necrosis has been reported as high as 16 to 19 percent (based on imaging).[42,43] The wide range of fat necrosis reported in the literature may reflect a

difference in sensitivity of the methods used to detect such (i.e., magnetic resonance imaging versus ultrasound), the timing of such evaluations, and perhaps other variables. In reconstructive settings, usually in combination with implant or autologous flap transfer, the incidence of fat necrosis is reportedly lower.[44] The average volumes of autologous fat injected vary by at least 100 to 200 cc (with augmentation associated with larger volumes) and may contribute to the differential rates of fatty necrosis. Interestingly, oil cysts are more prevalent in reconstructive cases.[45] Perhaps adjuvant radiotherapy or chemotherapy modulates the immune response to fat necrosis and predisposes to cystic formation rather than fibrosis and calcification.

In 1987, autogenous grafting to the breast was condemned in part because of its perceived interference with breast cancer screening.[46] However, any surgical intervention to the breast is associated with a potential pathologic finding of fatty necrosis. These interventions include lumpectomy, reduction mammaplasty, and lipomodeling. Postprocedural radiographic abnormalities should be expected.[47] However, the majority of mammographic findings following lipotransfer can be classified as either Breast Imaging Reporting and Data System 1 or 2 (negative or benign findings, respectively).[48,49] On a meta-analysis of radiologic outcomes in 1979 patients who underwent breast reconstruction, nearly 12 percent of patients needed an interval mammogram, and over 2.5 percent needed a biopsy to diagnose the nature of a suspicious breast lump.[6] An alternative series of fat grafting to the breasts revealed a biopsy rate of 4.8 percent for radiographic and clinically suspicious lesions,[25] and all biopsy results were negative for malignancy. Infection, hematoma, seroma, induration, pneumothoraces, unsightly scars, and persistent pain are infrequently reported in the literature, likely reflecting their low incidence in clinical practice. The relevant risks and complications when fat grafting to the breasts are summarized in Table 1.

Table 1. Autogenous Fat Grafting to the Breasts*

	Reconstruction	Cosmetic Augmentation
Fat necrosis	4–4.6%	16–19%
Biopsy rate	2.5–4.8%	—
De novo cancer risk	No association	No association
Local recurrence/ distant metastases	No association	—

*Risks and complications with regard to cosmetic augmentation and breast reconstruction.

AUTOGENOUS FAT GRAFTING TO THE GLUTEAL REGION

Over the past decade, fat grafting to the gluteal region has seen a significant rise in popularity and demand among patients. Although the operation is performed more frequently, high-quality studies on the subject remain sparse. Many of the early reports on fat augmentation experimented with low volumes (30 to 210 ml) and do not document complication rates. Cardenas-Camarena et al. were one of the first groups to detail their complication rates with gluteal fat grafting, which ranged from minor complications (e.g., cellulitis, seroma, and tissue irregularities) to life-threatening fat embolism.[50] More recently, gluteal fat grafting has become the center of attention by plastic surgery task forces and experts because of reports of death by fat embolism during and following the procedure.[4,51,52] It should be emphasized that fat grafting to the gluteal region should be performed by experienced plastic surgeons who use risk-reduction techniques to minimize the chances for complications.

Historical and Preoperative Factors

Gluteal augmentation with fat grafting is a cosmetic procedure often sought after by women in their early thirties.[53,54] However, gluteal augmentation may be beneficial for patients who have undergone massive weight loss surgery or suffer from deformities of the buttocks. As with all surgical procedures, patient selection is critical in reducing the risk for complications in gluteal fat grafting. First, discussion with a patient about their risk factors—including but not limited to a history of hematologic disorders, use of anticoagulants, and a family history of deep venous thrombosis and pulmonary embolism—is pertinent.[55] Physical examination of the lower extremities for the presence of varicose veins, which increases the risk of venous injury, should be performed.[55] Finally, a complaint of sciatic nerve symptoms should be considered a contraindication for the procedure, as the pain may get worse, and patients with these symptoms tend to have worse varicose veins in the region of the sciatic nerve distribution.[56–58]

The most common fat harvesting sites for the procedure are the lower extremities, followed by the back, hip, flanks, and abdominal areas.[53] To date, studies have failed to show a significant difference in adipose cell viability and graft take in relation to fat harvesting site.[59,60] To obtain fat for gluteal augmentation, most surgeons use machine-assisted liposuction and often process

the lipoaspirate by means of decantation.[53] After processing, a 3- to -4 mm rigid cannula is most often used for lipoinjection into the gluteal region subcutaneously and/or intramuscularly.[53,55] Large meta-analysis of the literature shows that the mean injection volume per buttock is 402 ± 179.2 ml.[53]

Overall, reported complication rates range from 7 (6.7 percent major and 0.32 percent minor) to 10.5 percent, with 95.5 percent of these being classified as minor complications.[53,56,61] The most common minor complications include seroma formation (2.4 to 3.5 percent), infection, erythema, pain, sciatica, contour irregularities, and fat necrosis.[53,54,56,61,62] Major complications for gluteal augmentation include fat embolism (0.12 percent), anemia, hypovolemia, and septic shock, all of which can be devastating. In addition, this risk of adverse events has been associated with increasing body mass index.[63] Studies show that the average body mass index for those seeking the operation is approximately 23 kg/m^2, with the peak incidence of major complications occurring in those with body mass indexes of 25 to 30 kg/m^2.[53,63]

Venous Fat Embolism

Death because of fat embolism after gluteal augmentation has been a major area of concern and the subject of discussion among plastic surgeons. A survey conducted in 2015 by Cardenas-Camarena et al. of Mexican plastic surgeons uncovered 64 liposuction and 13 lipoinjection deaths caused by gluteal augmentation.[64] Among Colombian plastic surgeons, the same study found a total of nine cases of fat embolism.[64] In the United States, the Aesthetic Surgery Education and Research Foundation assembled a task force in 2017 to assess rates of fat embolism among board-certified plastic surgeons.[4] This study, which surveyed 692 surgeons across 198,857 gluteal fat grafting cases, found a total of 32 fatal (one of 6214 cases) and 103 nonfatal (one of 1931 cases) pulmonary fat embolisms, which were partially corroborated using public records.[4] However, it remains extremely difficult to accurately assess the rates of and practices involved with fat embolism because of the lack of a standardized database, lack of insurance claims relating to complications, and recall bias. It is likely that the overall numbers reported are actually quite different when taken into consideration with the low survey response rate and the fact that non–board-certified plastic surgeons are also performing the procedure. What is clear, however, is that death by gluteal lipoinjection is a problem that must be addressed through high-quality research that delineates safe methods that are subsequently dispersed in an effective manner to those interested in performing the procedure.

The cause of fat embolism during gluteal augmentation procedures is the inadvertent entry of fat into the deep gluteal veins. The mechanistic details underlying this event are not definitively known, and this represents one of several areas ripe for further research. Some postulate that venous fat embolism results from inadvertent cannulation of a vein with subsequent intraluminal injection of fat. Others theorize that it can result from the "passive" syphoning of perivascular fat into a torn or lacerated vein that is characterized by a greater subatmospheric pressure relative to the surrounding extravascular space (Fig. 1). Either, both, or additional explanations may be correct, and the rigorous delineation of mechanisms underlying venous fat embolism has direct implications for specific methodologic recommendations that may reduce the risk of this fatal event. Many assume that the risk of fat embolism during gluteal augmentation can be significantly reduced by establishing specific guidelines and techniques. However, this itself is only a hypothesis at present, and many knowledge gaps and controversies currently exist. At present, there is little if any consensus among experts about various aspects of this operation, including what is the best/safest positioning of the patient, which size and type of cannulas to use, whether bolus injection or intermittent injection during withdrawal is most effective, which entry sites and angulation of cannulas are ideal, what is the upper safe limit of fat volume that can be injected during a single procedure, and whether intramuscular injection is safe or not. A review of the literature will reveal differing theories and recommendations, often in direct conflict with one another.[4,51–53,55,63–69] Although all of these published (and unpublished) recommendations are grounded in critical thinking and sound logic, they are nonetheless speculative in nature. Currently, there is a lack of high-level scientific evidence to support any particular recommendation. However, this may change based on current anatomical research being undertaken by the Multi-Society Gluteal Fat Grafting Task Force and others interested in this topic. Just recently the Multi-Society Gluteal Fat Grafting Task Force advocated for subcutaneous injection *only*, given recent reports of additional deaths and the finding that every patient that has died from venous fat embolism during the procedure was found to

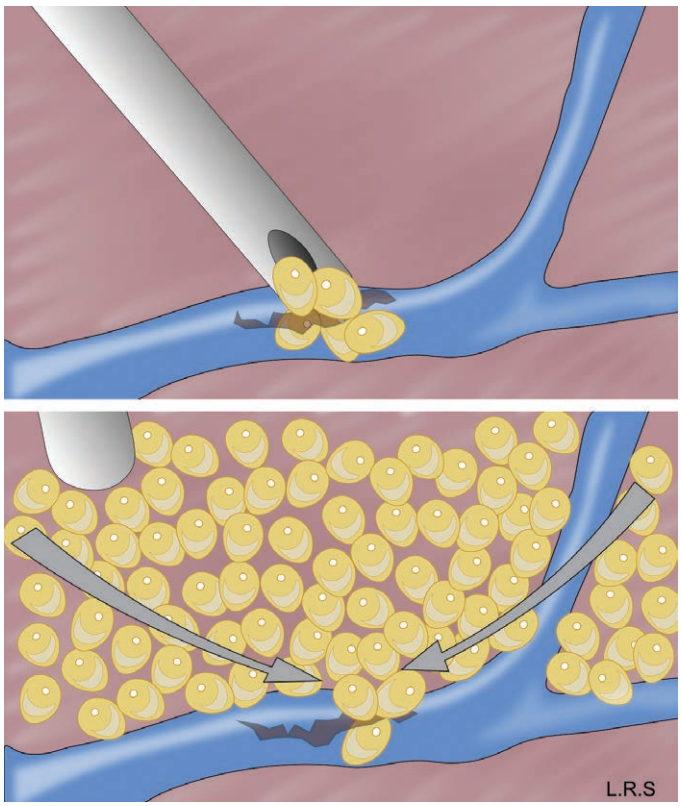

Fig. 1. Postulated mechanisms for venous fat embolism during gluteal augmentation. (*Above*) Inadvertent cannulation of gluteal vein with subsequent intraluminal injection. (*Below*) Passive siphoning of perivascular fat into a torn or lacerated vein.

have fat in the gluteal muscle, along with injury to the gluteal veins. In no cases of death has fat been found only in the subcutaneous space. As higher level evidence emerges pertaining to gluteal fat grafting, one recommendation remains unanimous among all practitioners: it is paramount that surgeons who choose to perform this operation have a detailed knowledge of the anatomy of the gluteal region and a full understanding of the risks involved in performing the procedure. At the time of this writing, the Multi-Society Task Force, composed of representatives from the American Society of Plastic Surgeons, the American Society for Aesthetic Plastic Surgery, the International Society of Aesthetic Plastic Surgery, the International Federation for Adipose Therapeutics and Science, and the International Society of Plastic Regenerative Surgeons, is conducting detailed anatomical studies to elucidate technical aspects that may improve safety.

DISCUSSION

Before the emergence of structural fat grafting, the clinical unpredictability of adipose transplantation had plagued surgeons for nearly a century.[70] En bloc resection and transference of fatty tissue would invariably lead to cystic formation, as highlighted by Lyndon A. Peer's work in the 1950s. The advent of liposuction by Illouz and Fournier improved harvesting; however, the encouraging results by Sydney Coleman in the 1990s helped to codify the techniques that are often used in today's practice. The Coleman technique forms the basis of modern autogenous fat grafting,[71] and given its prevalence, patient historical factors, characteristics of the recipient bed, and the amount of fat injection largely influence risk and complications.

Autogenous fat grafting to the breasts is overall a safe procedure, with the majority of complications related to fat necrosis requiring minimal therapeutic or radiographic intervention. The oncologic safety of fat grafting is supported by multiple large, retrospective analyses. Although clinical studies argue against the tumorigenic potential of adipose grafts, further investigations with improved study designs may be required to convincingly assess for any associative, locoregional

tumor recurrence. The decreased fraction of adipose-derived stem cells in standard grafts (as opposed to those used in experimental studies) may account for the lack of any association.[72]

Furthermore, there are no studies available that guide the timing of lipotransfer in oncologic reconstruction. Most included studies allowed for at least 6 months to 1 year between breast cancer surgery and grafting. Generally, the risk of recurrence decreases as time from oncologic surgery increases; however, traditional factors of locoregional recurrence or distant metastases (i.e., positive margins or nodal status) will likely delay any grafting procedures because of the necessity for adjunctive cancer therapies. Also, early grafting is cautioned in the context of breast-conserving therapy because of the increased local event rate and potential for confounding foci of fatty necrosis. Other risk factors for recurrence after breast-conserving therapy, including younger age, premenopausal status, and tumor vascular invasion, should also be considered. In all patients considering cosmetic breast augmentation, with implants and/or autologous fat, a thorough and relevant history should be solicited for factors that may increase the likelihood of breast cancer above the average risk.

The amount of fat injected into a given recipient site is also associated with greater risk of fat necrosis, operative time, and other related complications. As such, the greater volumes of adipose graft needed to achieve augmentation as opposed to contouring may account for the differential rates of complications in the setting of reconstruction and cosmesis. Of note, the reported rates of fat necrosis following grafting to the breasts were based on imaging; thus, clinically detectable rates of fat necrosis may be less than indicated.

Gluteal augmentation by fat grafting is a cosmetic procedure with growing popularity. Unfortunately, the risk of complications following the procedure is 20 times higher than for other procedures performed at ambulatory surgery facilities.[73] In the future, research is needed to address and clarify pertinent anatomy, patient selection and positioning, injection cannula size and shape, continuous injection versus injection during cannula withdrawal only, safe zones/layers for injection, and more. There is also a need for new techniques and technologies such as those that enable the real-time visualization of a cannula tip in relation to tissue planes and structures. Table 2 lists summary statements regarding autogenous fat grafting to the breast and gluteal regions.

Table 2. Summary Statements Regarding Autogenous Fat Grafting to the Breast and Gluteal Regions

Breasts
Overall a safe procedure, with the majority of complications requiring little to no intervention
The most common complication is fatty necrosis, which may be observed or imaged to clarify its nature
The oncologic safety of fat grafting is supported by many large, retrospective analyses
Gluteal
Although gaining popularity, the risk of complications is much higher than for other ambulatory procedures
Fat embolus is an area of major concern and is currently being investigated by the Multi-Society Task Force
The Multi-Society Task Force advocates for subcutaneous injection only
Surgeons who choose to perform this operation should have detailed knowledge of the anatomy of the gluteal region and a full understanding of the risks involved in performing the procedure
Further research is needed to address and clarify pertinent anatomy, patient selection and positioning, cannula size and shape, continuous injection vs. injection during cannula withdrawal, and safe zones/layers for injection

LIMITATIONS

Regarding published work on the topic of autogenous fat grafting to the breasts and gluteal regions, levels of evidence are generally low. The majority of published studies regarding the breasts were retrospectively or prospectively designed as case series. Aside from the technical deviations from the Coleman technique (harvesting, processing, and reinjection), there is yet considerable heterogeneity among included articles regarding indications, population characteristics, classification and reporting of complications, use of adjunctive therapies (e.g., external volume expansion device, platelet-rich plasma, cell-assisted lipotransfer), and follow-up periods. Even fewer and less rigorous studies are available regarding fat grafting to the gluteal regions, with the focus primarily on expert opinion and recommendations for risk-reduction techniques. Despite seeking the highest level of evidence for synthesis, this review is limited by the quality of available literature.

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