

Fat Grafting: Basic Science, Techniques, and Patient Management

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Summary: In this review, a summary of the rich history of autologous fat grafting is provided, and a comprehensive summary of the science and theory behind autologous adipocyte transplantation, as well as the techniques commonly used is described. These include recipient site preparation, harvesting, processing, and engraftment. In addition, important considerations for preoperative and postoperative management are discussed to maximize graft retention. Special considerations in grafting to the breast, face, and buttocks are also summarized. (*Plast Reconstr Surg Glob Open* 2022;10:e3987; doi: [10.1097/GOX.0000000000003987](https://doi.org/10.1097/GOX.0000000000003987); Published online 18 March 2022.)

INTRODUCTION

Autologous fat grafting has become increasingly popular in recent years, with many new reconstructive applications for the breast and face, postradiation and burn injuries, and congenital anomalies, as well as the plethora of aesthetic applications in body contouring, breast augmentation, facial contouring, and more.^{1–12} Autologous grafting provides for inherent biocompatible properties, leading to a very successful treatment modality for general soft tissue augmentation and volume replacement, with little patient morbidity.^{13,14} A lack of immunogenicity, low cost, and easy accessibility make this the technique of choice in the face of many reconstructive and cosmetic challenges.^{15–18}

Widespread use has also led to the development of dozens of different techniques in both donor and recipient site preparation, fat harvesting, and postharvest processing.^{19–22} It is often difficult to decide the ideal donor site based on patient characteristics, recipient site volume requirements, and healing implications.^{23,24} Additionally, until recently there has been little evidence demonstrating the superiority of various harvesting and processing techniques, such as centrifugation, cotton gauze filtering, and sedimentation. In this review, the authors will summarize the rich history of autologous fat grafting and describe a comprehensive summary of the science and theory

behind autologous adipocyte transplantation, as well as the techniques commonly used. These include recipient site preparation, harvesting, processing, and engraftment.

HISTORY

The history of fat grafting is one of the most interesting and abundant within the field of plastic surgery. The first attempt at transferring autologous adipose tissue dates back all the way to 1889, in the first report by Meulen et al. In this study, omental fat was grafted between the liver and diaphragm to help treat a diaphragmatic hernia.²⁵ However, the more relevant transfer of adipose tissue was reported by Neuber et al in 1893 when he took fat from the forearm and used this to fill a volume and contour irregularity of the face caused by a scar, for which he obtained excellent aesthetic results.²⁶ Czerny et al in 1985 performed a similar transfer of autologous fat in the form of a lipoma from the back for breast reconstruction.^{27,28} Silex followed with fat transfer for cosmetic repair of periorbital scars, similar to the reconstructive use demonstrated by Neuber et al several years prior. From this time forward, hundreds of studies have been published that have continued to develop, modify, and refine the technique of autologous fat transfer to the modern techniques we have today.

In 1911, Brunning et al demonstrated the first use of a needle and syringe to transplant fat. He was the first to inject the autologous fat graft into the subcutaneous space to correct the aesthetic result of a rhinoplasty procedure.²⁹ However, he was first to note that these aesthetic results were short lived due to the reabsorption of the grafted fat over time. This injection technique was later modified by Miller et al, in which he used a metal cannula to transfer autologous fat, which was an early predecessor to those that we use today.³⁰

Lexer et al first presented a case of chronic cystic mastitis in 1931 that was completely reconstructed by autologous

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adipose tissue that was rotated as a local flap from the axilla, rather than injected as previously described.³¹

For several decades following the publication of these studies, fat grafting was mostly limited to injection fat grafting and transplantation, as previously noted. Major refinements did not occur again until 1975, when the Fischer father and son duo developed the modern technique of liposuction using metal cannulas.³² These cosmetic surgeons developed the blunt hollow cannula attached to a suction device to harvest the fat from multiple incision sites. Illouz et al popularized this technique in 1977 when he developed better suction equipment for use with the Fischer cannulas.³³ This was the beginning of the modern liposuction equipment that we use today.

In 1983, Benzaquen et al demonstrated the transfer of lipoaspirate that would soon develop as an offshoot of liposuction in the late 20th century.^{34,35} However, modern liposuction did not truly emerge until 1990, when Coleman et al first proposed a new method of harvesting fat tissue that minimized the trauma to adipocytes.^{7,36} This was later supplemented by the technique of preparing the harvest site with a tumescent solution as proposed by dermatologist Dr. Klein in 1993. The study detailing this technique proposed that this would further minimize adipocyte trauma and maximize harvesting of fat, while providing adequate hemostasis and local anesthesia.³⁷⁻³⁹

In this article, we propose several modern modifications and perioperative interventions that improve outcomes in our practices. These come from multiple iterative processes to improve fat take and engraftment.

PREOPERATIVE MANAGEMENT

The following considerations are exceedingly important in large volume fat grafting, for liposculpture, S-curve, Brazilian butt lift, or fat transfer to the breast.

Nutrition

It is recommended that patients' nutrition, oxygen tension, and overall health are maximized before autologous fat transfer. This ensures that the graft will receive adequate nutrition and oxygenation following engraftment. At the author's practice in Marina Del Rey, California, patients are started on two supplements before surgery: Juven (Abbott, Ill.) and HealFast (HealFast, N.Y.). Juven contains targeted nutrition for optimal wound healing, including beta-hydroxy and beta-methylbutyrate, arginine, glutamine, hydrolyzed collagen, zinc, vitamin C, vitamin E, and vitamin B12. These are clinically proven to be extremely important micronutrients for wound healing and allow for greater graft viability following surgery. The senior author starts patients on Juven supplements twice a day for 5 days prior surgery and continues the nutritional supplement for 3 weeks postoperatively. Patients are also started on HealFast for five days preoperatively, and for an additional three weeks postoperatively, which includes additional micronutrients and metal ions that are important for wound healing. These are bromelain, quercetin, magnesium selenium, folate, citrus flavonoids, and copper, in addition to high dose vitamin B complex.

Hyperbaric Oxygen

One of the most critical components of graft viability in the first 48 hours following transplantation is the availability of local oxygen.^{40,41} As such, one author has created a hyperbaric oxygen protocol to improve local wound oxygen tension both preoperatively, and postoperatively. Patients are advised to undergo one hyperbaric oxygen treatment session in the 5 days before surgery, at more than 2 atmospheres for 90 minutes. Following surgery, patients undergo hyperbaric oxygen treatment at 2.7 atmospheres for 90 minutes on postoperative day 1, and an additional two to three sessions at more than 2 atmospheres for 60 minutes during the following week. This process is discussed with patients preoperatively. It is required for all fat transfer patients in Marina Del Rey but is not required for the Beverly Hills practice.

HARVESTING

Many techniques have been proposed for the harvesting of adipose tissue from a donor site before transfer, including vacuum or syringe suction and surgical excision.^{19,22,42-45} Several studies have shown that the deep layer of the subcutaneous fat is the optimal site of harvest, as it contains the highest concentration of mature adipocytes and minimizes the collection of unwanted debris, erythrocytes, and dermal appendages.⁴⁶ Common donor sites include the abdomen, buttocks, and posterior thigh; however, studies^{23,24,42,47-50} have shown that there is no significant difference in harvest weight, volume retention, or cell viability across these various harvest sites (Table 1).

Harvest Site Preparation

Fat can be harvested using a dry technique or several variations of a wet or tumescent technique.⁵¹⁻⁵³ A dry technique is defined as no prior injectant used at the donor site, as first piloted by Fournier et al.^{54,55} This is often

Table 1. Studies Investigating the Effect of Harvest Site on Fat Graft Harvest Weight, Posttransplant Volume Retention, Cell Viability, and Concentration of Stem Cells

Author	Year	Model	Results
Hudson et al ⁵⁰	1990	Human	Posterior thigh and buttocks demonstrated greatest fat volume
Ullmann et al ⁵⁰	2005	Mice	Posterior thigh fat demonstrated the greatest structural integrity and was least likely to undergo necrosis, inflammation and fibrosis
Padoin et al ⁴⁸	2008	Human	Lower abdomen and posterior and inner thigh demonstrated higher concentration of mesenchymal stem cells
Lim et al ⁴⁷	2012	Mice	No statistical difference between abdominal fat and other donor sites with respect to posttransplant volume and symmetry
Li et al ²³	2013	Human	No statistical difference between donor sites with respect to graft weight or posttransplant volume
Small et al ²⁴	2014	Human	No statistical difference between donor sites with respect to posttransplant volume

performed under general anesthetic, as no local anesthetic solution is used to infiltrate the donor site. Wet techniques use a one-to-one ratio of injectant to the volume of fat being harvested. Super wet techniques use approximately a three to one ratio of injectant to volume of fat harvest; however, any ratio greater than that of one to one is often defined as super wet. Most often used, however, is the tumescent technique, which is a massive infiltration of the subcutaneous space to decrease bleeding, anesthetize the area, and maximize fat harvest while minimizing trauma as described by Klein et al.^{37–39,56} This technique can be used for the harvest of any volume of fat, and it is most often used in liposuction and larger volume grafting. Studies^{57–62} have shown that although there is a significant increase in cell viability with the use of a wet technique versus a dry technique, there is not significant difference when increasing the volume of tumescent solution used (Table 2).

Moore et al demonstrated that the use of lidocaine alone in tumescent solution was associated with a statistically significant decrease in adipocyte function at the recipient site.⁶¹ Studies to follow have shown no difference in graft weight or volume and graft histology. Even so, modern tumescent solutions usually include both lidocaine and another anesthetic such as bupivacaine. Interestingly, a study by Keck et al demonstrated that highest cell viability was seen with infiltration of bupivacaine alone, followed by mepivacaine and ropivacaine, lidocaine, and articaine.⁵⁹

Liposuction Technique

Automated negative pressure liposuction using commonly available machines such as the REVOLVE System (AbbVie, Ill.), Medela Aspirator (MFI Medical, Calif.), and HK Aspirator Pump (HK Surgical, Calif.) are much quicker than manual syringe aspiration and are often used for transfer of large amounts of fat, but may cause destruction of adipocytes, reduced survival of the fat graft at the donor site, and increased oil fraction of harvested fat. Cannula harvest using the Coleman technique published in the late 20th century, and refined in the earlier 21st century, is more often used for low volume grafting, and results in a much less traumatic harvesting process, with greater adipocyte viability and graft retention. Studies have shown that high negative pressure vacuum liposuction may cause disruption and trauma up to 90% of the adipocytes available in the harvested fat.

In using manual syringe aspiration, the Coleman technique is most common in practice.^{7,63–65} This traditional approach involves the use of cannulas of different length and caliber with 2-mm side ports that infiltrate the subcutaneous space and help disrupt the structural fat at the donor site into smaller, injectable subunits. The size of the port has no significant difference, but cannula bore size and length has been investigated^{44,45,52,53,66–72} and may affect the viability of the harvested fat (Table 3). Studies show that large bore cannulas reduce risk of cellular rupture due to more laminar flow of fat, while smaller bore cannulas may decrease risk of trauma to the recipient site. Coleman proposed the use of the 17-gauge blunt cannula as the most protective, which finds a balance between protection of harvested adipocytes and the recipient site. This was further demonstrated by Campbell et al,⁷³ who reported an inverse relationship between bore size and adipocyte trauma. It should also be noted that the speed of suction may result in sheer stress damage to harvested adipocytes and should remain constant throughout the harvesting process to minimize this risk.

The Coleman technique using the 17-gauge blunt cannula is described as using 3-mm donor site incisions, a 3-mm blunt edge at the apex of the cannula, and two 2-mm ports. This cannula is connected to a 10-mL Luer-Lok syringe and pushed through the harvest site. The syringe is fanned out in a crosshatch pattern to allow parcels of fat to dislocate and move into the cannula. The Luer-Lok syringe provides a negative pressure that allows for the fat to then travel through the cannula and fill the syringe.

Although optimal graft particle dimensions have yet to be determined, the consensus in practice is that fat harvested must be large enough to preserve adipocyte native architecture and their anatomic relationship in space with stromal components, but small enough to not limit diffusion of nutrients across the graft. Therefore, the most commonly used port size is 2-mm; however, this can vary depending on cannula size and volume of harvest and has not been shown to decrease graft viability.

To maximize graft viability and minimize sheer force and pressure-induced trauma, the Marina Del Rey author utilizes the closed system Wells Johnson Aspirator (Wells Johnson, Ariz.) with a three-pump aspirator (HERCULES) for consistent pressure modulation during liposuction. This system allows for the harvest of fat at a constant

Table 2. Studies Investigating the Effect of Harvest Site Preparation with Respect to Anesthetic Agent Used and Volume of Tumescence

Author	Year	Sample	Results
Moore et al ⁶¹	1995	20	Lidocaine and epinephrine had no significant effect on cellular adhesion, cell morphology, proliferation, and metabolism of adipocytes
Shoshani et al ⁶²	2005	20	Lidocaine and epinephrine demonstrated no significant difference in graft weight, volume, and histology
Keck et al ⁵⁸	2009	NR	Lidocaine and ropivacaine may reduce preadipocyte viability
Keck et al ⁵⁹	2010	15	All local anesthetics other than bupivacaine reduced cell viability, with greatest viability demonstrated with bupivacaine, followed by mepivacaine, ropivacaine, lidocaine, and articaine
Livaoğlu et al ⁶⁰	2012	24	No significant difference between saline, lidocaine, or prilocaine with respect to graft weight volume
Claire et al ⁶⁰	2013	18	Lidocaine negatively affected the viability of mesenchymal stem cells, with longer exposure resulting in less viability

NR, not reported.

Table 3. Studies Investigating the Effect of Cannula Size and Shape, and Aspiration Method on Fat Viability

Author	Year	Results
Huss and Kratz ⁶⁶	2002	Vacuum aspiration and centrifugation resulted in destruction of adipocytes
Pu et al ⁴⁴	2008	Vacuum aspiration lowered the metabolic function of harvested adipocytes
Ngyen et al ¹³⁷	1990	Vacuum aspiration decreased adipocyte integrity
He et al ¹³⁸	2001	Vacuum aspiration decreased adipocyte integrity
Hua et al ¹³⁹	2005	No significant difference between vacuum and syringe aspiration with respect to cell viability
Leong et al ⁶⁸	2005	No significant difference between vacuum and syringe aspiration with respect to cell viability and metabolic function
Kim et al ¹⁴⁰	2016	No significant difference between vacuum and syringe aspiration with respect to cell viability
Gonzalez et al ⁶⁹	2007	Low pressure suction reduced adipocyte damage and maintained cellular integrity, with the use of a 2-mm or 3-mm cannula
Shiffman et al ⁵³	2001	No significant difference between blunt and sharp end cannula with respect to cell viability
Ozsoy et al ⁷⁰	2006	Larger diameter cannulas directly correlated with increased adipocyte viability
Gonzalez et al ⁶⁹	2007	Smaller syringe resulted in lower negative pressure and increased cell viability and adipocyte proliferation
Erdim et al ⁷¹	2009	Greatest adipocyte viability was seen with the use of a 6mm cannula
Alharbi et al ⁷²	2013	No significant difference in graft weight with respect to 17- or 20-gauge Coleman cannula

negative pressure to reduce sheer force trauma to adipocytes and integrates postharvest processing and implantation in a fully closed system that reduces the risk of fat desiccation and loss of important stromal components.

The Beverly Hills practice utilizes a Medela (Medela Healthcare, Ill.) lipoaspiration tower with a sterile collection basin and a processing phase with injection through cannula and 60 cm³ syringes. This system takes advantage of filtration to reduce most of the liquid component from liposuction and syringe-based injection techniques developed over 15 years of practice.

PROCESSING

Fat graft survival depends primarily on the preservation of the largest proportion of intact mature adipocytes and mesenchymal stem cells in the stromal component. Thus, the overall goal of postharvest processing is to remove unwanted contaminants such as free oil from traumatic rupture of mature adipocytes, cellular debris, and other nonviable components such as erythrocytes or other hematogenous cells and inflammatory substrates to maximize the concentration of these substrates.^{22,43,53,74} Contaminants may lead to inflammatory reactions at the recipient site which could risk the survival of the graft.^{75,76} Studies have shown that erythrocytes and other heterogeneous components may further accelerate the degradation of grafted fat.⁷⁷ Minimizing their harvest using a tumescent technique, and further postharvest processing decreases this unwanted complication, and theoretically increases postgraft retention.

Sedimentation

Sedimentation is the least traumatic postharvest technique that maximizes the number of viable adipocytes.⁷⁵ This can be done by gravity separation or decantation and involves the process of allowing the lipoaspirate to settle into layers based on density over time. This is similar to the theory of centrifugation, in allowing the lipoaspirate to separate into major layers that include oil, fat, and aqueous components. The fat layer is later extracted for injection. However, by maximizing mesenchymal fat components, this method contains the least number of stromal components and stem cells. Furthermore, it does a poor job of separating inflammatory mediators such as erythrocytes,

and proinflammatory substrates found in the mesenchymal compartment that can be detrimental to graft survival and retention. Recent studies have shown that relative to centrifugation, there is a significant decline in graft viability. Commercial devices exist that provide a closed system for collection and gravity separation of lipoaspirate such as the Wells Johnson system. Sedimentation can be accelerated through the use of a vibrating tabletop stand, which helps reduce time to separation. These devices are easy to use and streamline the cleaning process, at the cost of including stromal components in the final graft. All close collection containers offer some degree of sedimentation during the lipoaspiration process.

Filtration

Filtration methods on the contrary eliminate most contaminants and inflammatory components and continue to maintain viable mature adipocytes as well as the adipose-derived mesenchymal stem cells of the fat stroma.⁷⁸ This is most commonly used in large-volume fat transfers in light of new automated filtration systems that provide a closed system for processing of harvested fat. This is integrated into systems such as the REVOLVE system or PUREGRAFT (Puregraft, Calif.), as previously discussed. Washing is also a common technique, and is often not mutually exclusive from filtration, during which washing is frequently performed in tandem with normal saline or lactated ringer's solution. The goal of washing in this setting is to eliminate contaminants and nonviable components. A study by Conde-Green et al demonstrated that washing preserved a greater number of stem cells when compared with centrifugation.⁸¹ As such, the REVOLVE systems integrate a washing approach in the filtration of harvested fat.

In the setting of smaller volume fat transfers, filtration can also be implemented in a traditional form with the use of a cotton gauze funnel, often made of Telfa gauze. This effectively concentrates the mesenchymal component while separating the tumescent solution that is absorbed into the gauze. In addition to passive filtration, the harvested fat can also be rolled back and forth within the gauze. This technique is easy to use and convenient for smaller volume fat grafts, however, is limited in its ability to remove free cellular components and unwanted debris and may cause desiccation of fat and reduced graft

viability. Even so, when compared with centrifugation, cotton-gauze filtration demonstrated no significant difference in graft viability.

Centrifugation

Centrifugation is the most widely used technique and also the most convenient for postharvest processing. Considered the gold standard by many, there is actually no significant difference^{19,45,49,75,79–86} between any of the harvesting techniques discussed herein (Table 4). However, in theory, centrifugation provides the most precise separation of graft components and allows a much more targeted approach to graft processing. Centrifugation separates components by density to create layers that can be easily divided and transferred (Fig. 1). As such, it obtains the highest possible concentration of adipocytes and mesenchymal stem cells when compared with other processing techniques. Even so, there has been no demonstrated difference in overall graft viability when compared with other techniques.

Coleman first introduced the centrifugation technique in his postharvest processing of lipoaspirate. The Coleman technique historically consists of loading 10-mL Luer-Lok syringes with lipoaspirate using blunt 17-gauge cannulas as described earlier, and then centrifuging the syringe at 3000 rpm for 3 minutes. The blood and tumescent aqueous solution fraction closest to the bottom of the syringe are drained. The oil in the top layer is then decanted and wicked with a cotton pad for several minutes until the only remaining fraction is the mesenchymal component. This has been refined over the past decade with many closed systems that now exist to maximize the efficiency of this process, especially for larger volume harvest.

RECIPIENT SITE

In more recent years, studies have begun to discuss the use of recipient site preparation techniques to maximize graft viability, although these have been mostly limited to animal studies.^{87,88} The most common techniques currently being investigated include volume expansion, implantation of alloplastic materials such as silicone,

administration of cell-proliferation factors such as VEGF or IL-8, iatrogenic ischemia, and micro-needling.^{89–91}

External volume expansion is a method in which an external expander is placed at the recipient site. In animal studies, it has shown to increase the proliferation rate of the graft and final cell count, as well as the total number of mature adipocytes.⁸⁹ Placement of alloplastic materials (such as silicone sheets) that provide an optimal graft bed did not result in any significant increases in graft viability or retention.

Cell proliferative factors were not shown to provide any significant increase in graft weight or viability following transplantation. There was also no significant increase in cell proliferation rates, adipogenesis, and stem cell concentration. Similarly, recipient site ischemia did increase tissue bed oxygen saturation and perfusion but did not result in greater graft viability.

Micro-needling is the practice of applying a device (Deeproller) with hundreds of microneedles to abrade the subcutaneous tissue in a crisscross pattern to maximize the recipient bed surface area before engraftment. A study by Sezgin et al demonstrated a higher level of vascularity and significantly less inflammation following graft placement; however, there was no significant improvement in cell proliferation or graft viability.⁹¹

Many of these experimental methodologies aim at maximizing oxygen tension and nutrition at the recipient site. As such, the senior author recommends preoperative nutrition and hyperbaric oxygen as a method of recipient site preparation that is noninvasive.

ENGRAFTMENT

Transplant and engraftment of the harvested fat is performed through a small skin incision that corresponds to the diameter of the cannula being used. As previously discussed, smaller gauge cannulas will minimize recipient site trauma; however, this must be weighed with the potential sheer force traumatic risk to the harvested fat. Potential recipient trauma includes bleeding and hematoma formation, which could result in poor graft oxygen diffusion and thus poor retention. As such, injection cannulas are much smaller gauge than harvesting cannulas, and only have

Table 4. Studies Investigating Different Methods of Postharvest Processing and Graft Treatment

Author	Year	Results
Butterwick et al ⁷⁹	2002	Centrifugation resulted in greater adipocyte longevity when compared with noncentrifuged tissues
Condé-Green et al ⁸⁰	2010	Washing resulted in greatest mesenchymal stem cell concentration in postprocessed lipoaspirate when compared with decanting and centrifugation
Botti et al ⁸²	2011	No significant difference between postharvest processing techniques
Ramon et al ⁸³	2005	No significant difference between postharvest processing techniques
Rose et al ⁸⁴	2006	Decantation resulted in highest cell concentration in lipoaspirate when compared with washing and centrifugation
Smith et al ⁴⁵	2006	No significant difference between postharvest processing techniques
Minn et al ⁸⁵	2010	No significant difference between postharvest processing techniques
Rohrich et al ⁴⁹	2004	No significant difference between postharvest processing techniques
Zhu et al ⁷⁵	2013	Washing or filtration method results in the least number of contaminating hematopoietic lineage cells, free oil, and demonstrated increased adipocyte function
Pfaff et al ⁸⁶	2014	Cotton gauze rolling resulted in a greater stromal vascular fraction retention when compared with centrifugation
Fisher et al ¹⁹	2013	Cotton gauze rolling removed oil and aqueous fraction most efficiently when compared with centrifugation and filtration

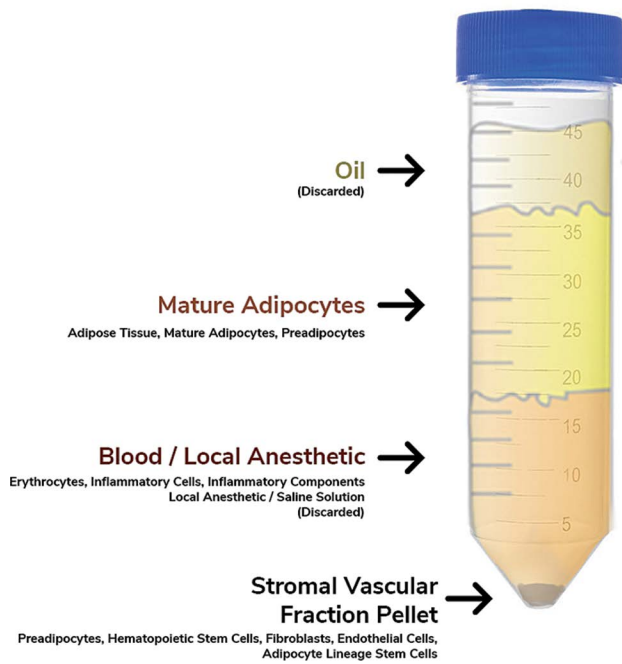


Fig. 1. Components of centrifuged fat graft.

one port at the distal end, in contrast to Coleman cannulas, which often have two ports. Different cannulas may be used for varying recipient site locations.^{70,71,92,93} Cannulas for the face are of much smaller caliber (1 mm) and vary in tip shape, diameter, and length.

Closed system aspirator and injection systems, as recommended by the senior author, allow for a continuous pressure of 11 mm Hg, which is similar to that of peripheral venous pressure.⁹⁴ This reduces the risk of local barotrauma and provides a consistent, laminar flow for infiltration of fat at the recipient site. Theoretically, this may also reduce the risk of fat embolism though this has never been proven or substantiated. Cannula selection is similar to that discussed above.

Once an engraftment cannula and system are selected, fat grafts are injected in small aliquots to maximize graft oxygenation and perfusion. The graft is fanned out in a crosshatch pattern and placed at varying depths to maximize surface area of distribution and to avoid excessive interstitial pressure at any one point at the recipient site. Multiple tunnels should be created upon injection, and fat should only be injected on withdrawal of the cannula from the tissue. This allows for the fat to fall into natural tissue planes. The senior author recommends overfilling by approximately 20% to accommodate for the tumescent solution that will be reabsorbed in the first few days postoperatively.

Graft survival is primarily through nutritive plasmatic imbibition in the first 48–72 hours.⁹⁵ This process maintains the graft, during which neovascularization of the graft occurs, which progresses at approximately 1 mm per day.^{96–98} The current literature describes that the graft contains three theoretical zones of cells, those at the outside in direct contact with the recipient site bed, an intermediate

regenerative zone, and a central necrotic zone that does not receive adequate oxygenation.²² Therefore, the diameter of any one graft placement should not exceed 2–3 mm at a maximum to avoid central necrosis of the fat deposit once the graft can no longer be maintained by imbibition alone. Closed system aspirators allow for a consistent deposition of fat in 1–2 mm aliquots to avoid overcrowding and necrosis of infiltrated fat.

The total volumes injected depend on the volume available at the recipient site. For example, a 250 g breast can accept up to this amount, and thus should not be grafted with more than 250 g of fat. This theoretically allows the graft to be perfectly distributed in 1:1 ratio, matching the donor site to recipient bed for delivery of oxygen nutrients and blood flow. There are, therefore, no general recommendations other than to allow the biometric parameters of the patient to dictate volume for transfer.

GRAFT RETENTION

Stem Cells

In the last decade, several studies have demonstrated that human adipose tissue contains the largest percentage of adult stem cells of any tissue in the body.^{95,99,100} These adipose-derived stem cells have the ability to undergo multilineage differentiation and are extremely versatile in animal models, with the ability to differentiate into not just fat, but also bone, cartilage, muscle, nerve, and vascular tissues. These cells are part of the stromal vascular fraction of adipose tissue, which also includes many other adipose associated stromal cells such as preadipocytes, hematopoietic cells, fibroblasts, endothelial cells, and other adipocyte lineage cells. The stromal vascular fraction, however, is difficult to isolate in postharvest processing and is not yet approved by the Food and Drug Administration for transplantation. Even so, the goal of many postharvest techniques is to maximize the stromal vascular fraction available for engraftment.

The regenerative features of the stromal vascular fraction are secondary to its paracrine secretory effects on local adipocytes.^{101–103} These cells secrete many important factors that promote neovascularization, increased local oxygen tension, but also lead to local inflammation. Paracrine signals include vascular endothelial growth factor, hepatocyte growth factor, fibroblast growth factor, and various inflammatory cytokines and interleukins such as IL-1, IL-8, and IL-13.^{101,104} These are secreted in response to local hypoxia, which can lead to postoperative inflammation and distortion of the local anatomy. This can be minimized by the practice of pre and postoperative hyperbaric oxygen treatment to increase the availability of oxygen at the recipient site, thus reducing postoperative inflammation.

Survival

The primary problem in autologous fat transfer is that of graft survival and volume retention postoperatively. Over the past decades, many studies have been published demonstrating a retention of only 25%–50% of implanted

volume, whereas others have shown retention of up to 80%–90%.^{105–110} The theory of adipocyte survival was first introduced by Peer et al, who argued that the final volume of the graft was dependent on the number of surviving adipocytes present at the immediate time of engraftment.^{111,112} This theory encourages the practice of minimizing adipocyte trauma throughout the grafting process.

Later studies found that mature adipocytes are extremely fragile cells and have a very low resistance to trauma as previously described, but also to hypoxic insults and desiccation.^{113,114} Preadipocytes, on the other hand, are much more resistant to ischemia and trauma and are likely the greatest surviving graft fraction following processing and implantation.¹¹⁵ Progenitor cells in general are much more resistant to severe circumstances in their inherent ability to differentiate into various different cell types in unpredictable environments. As such, it is important that postgraft processing maximizes the viability and transfer of preadipocytes in addition to mature cells.

This variability is often due to the technique used across donor site preparation, harvesting, processing, and implantation, although very little high-quality evidence exists to advocate for one over the other, as previously discussed. However, it is known that adipocyte necrosis and subsequent loss of volume is likely due to graft trauma during transplantation, and recipient site viability following engraftment.

Postoperative Management

The senior author has demonstrated in practice that graft volume retention of up to 90%+ can be achieved when minimizing trauma and maximizing recipient site nutrition and oxygenation. As discussed earlier, pre and postoperative management includes nutritional supplementation and hyperbaric oxygen use. In addition, patients are advised to avoid any compression garments to the site of the graft for 4 weeks postoperatively. Patients with fat graft to the breast are advised to wear supportive bras that lift the breast but do not compress. Similarly, patients with fat graft to the gluteal region are advised not to sit directly on the grafted site for 4 weeks. Patients are

also instructed to undergo lymphatic massage and compression stockings in the lower extremities to improve lymphatic flow and prevent distortion of local anatomy due to lymphatic obstruction.

SPECIAL CONSIDERATIONS

Breast

One of the most common sites of fat graft is the breast, where fat is injected in the subcutaneous space and prepectoral plane, and into the breast tissue itself (Fig. 2). Although there has been no evidence to show increased incidence of cancer, it remains unclear how much of the fat is absorbed after grafting, and if a potential risk exists of local “dormant” tumor cells being stimulated to induce a local recurrence.^{116–122} There are also no long-term data.

The senior author recommends discussing with patients the risk of reabsorption following excessive replacement of implant volume. Patients with a 200-g breast would only be able to support a 200-g graft initially. If a 600-g implant is removed, discussing a staged procedure would lead to much better outcomes as the breast would be able to support a 400-gram additional volume following the first procedure (Fig. 3).

Face

Facial fat grafting is often performed as an augmentation to facelift procedures. Fat is placed between the loose areolar tissue space and retaining ligaments, it can be utilized to enhance results through a lift and fill, or fill then lift technique.¹²³ The authors of this article typically perform the lift then fill technique (Figs. 4, 5). Other authors have popularized nanofat and microfat injections for volume and as a filler substitute.^{124,125} Key locations are the temples, cheeks, prejowl sulcus, and nasolabial fold.

An area of key interest is the buccal fat pad, a particularly novel fat source with favorable embryologic and histology properties that make it an ideal donor for facial fat grafting.^{126,127} This fat is unique in its high concentration of adipose-derived stem cells and low levels of fibrous



Fig. 2. Primary breast augmentation of bilateral breasts (A) before and (B) 6-months postoperative.

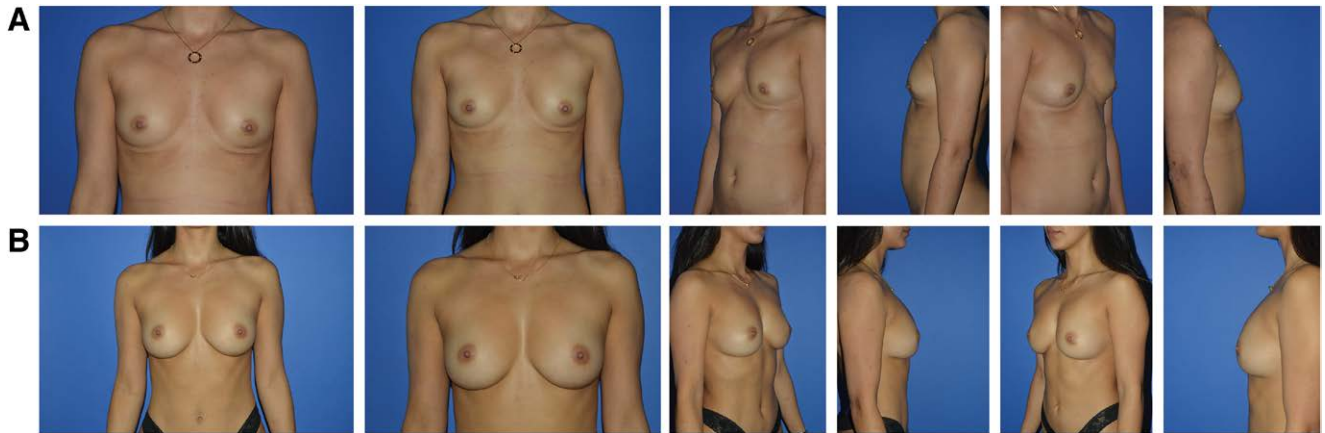


Fig. 3. Fat grafting to the breast after implant removal performed in a single-stage procedure (A) before and (B) 6-months postoperative.

tissues and associated inflammatory factors.¹²⁸ In addition, the fat exists in a glide plane, and is therefore not reticular, globular in nature, and ideal for transplantation.¹²⁹ This is advantageous for facial fat grafting during facelift but can also be derived in non-facelift grafting. It can be harvested without lidocaine or tumescent solution; so the entirety of extracted fat is viable for injection.

Brazilian Butt Lift

Fat grafting to the buttock is often performed as an adjunct to body contouring (Fig. 6). The risk of fat embolism exists due to the presence of the large gluteal vessels. To reduce the risk, it is recommended to never inject into the muscle, use a cannula that is 5 mm or larger, and inject at an acute angle to the skin.³ Safe subcutaneous

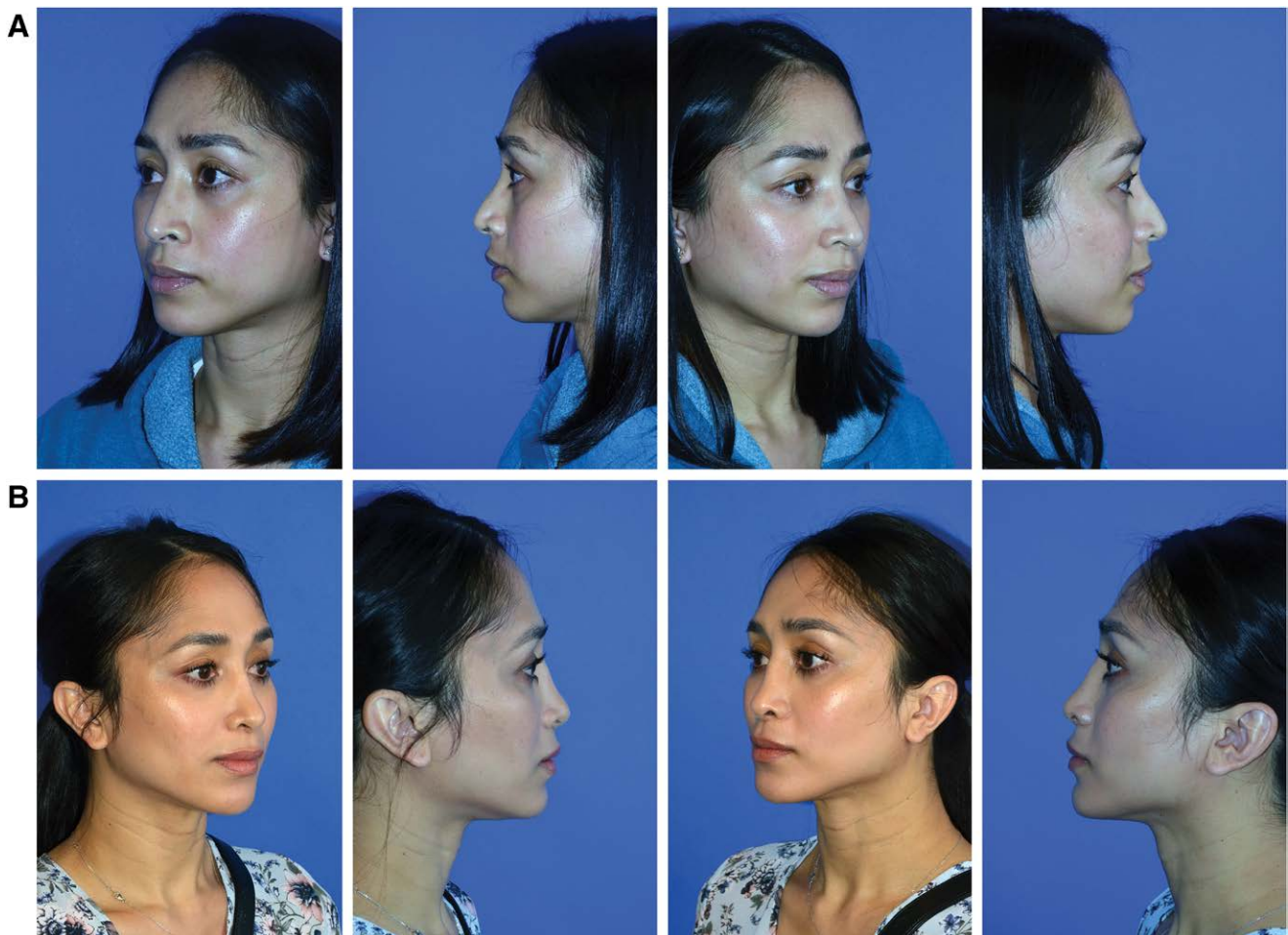


Fig. 4. Fat grafting to the face (A) before and (B) 6-months postoperatively.

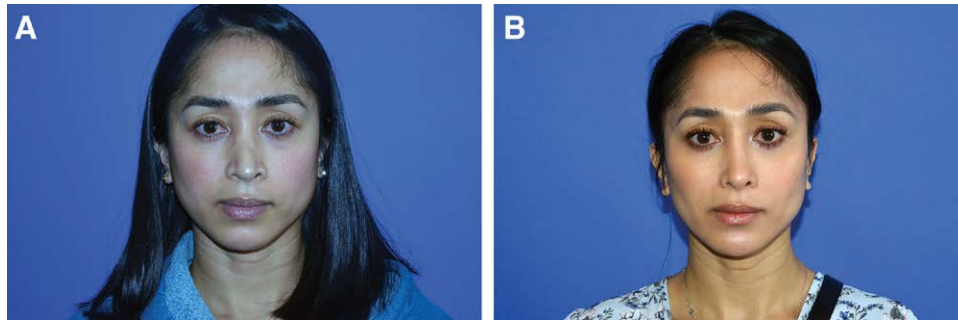


Fig. 5. Fat grafting to the face shown preoperative (A) and 7-months postoperative (B).

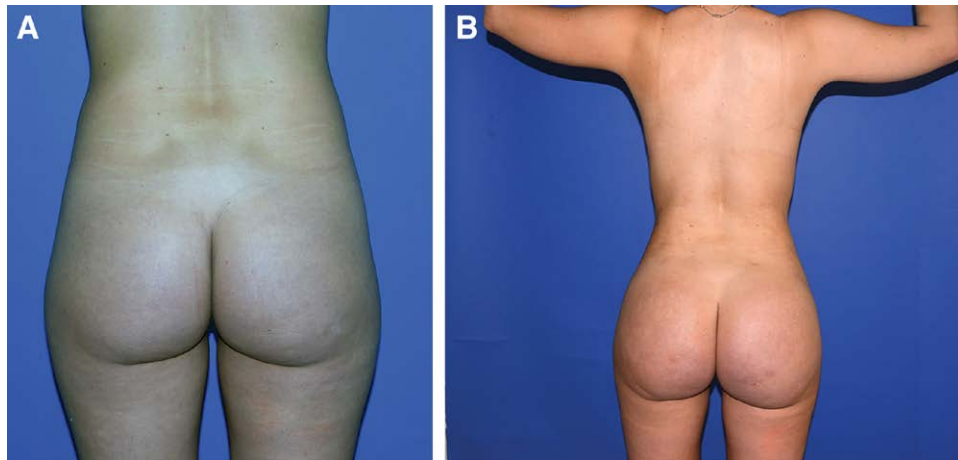


Fig. 6. Fat grafting to the buttock shown before (A) and 7-months postoperative (B).

injection is key as is anatomic knowledge of the safety zones.¹³⁰ Many articles have been written surrounding this procedure and safety, and this is not the main focus of this article. In addition, sex is not a determinant of fat survival in this population—wherein Brazilian butt lift and S-curve male patients have excellent survival, as do facial fat grafting and chest fat grafting patients. No data support any difference in man versus woman.

Injectable Fillers

Injectable fillers are not an adequate alternative to autologous fat grafting, and patients should be advised of the common complications.^{131–134} These most commonly include swelling, infection, and pain, and in a review of litigation surrounding filler, in litigated cases almost 40% of patients had to be treated with antibiotics to reduce swelling and inflammation at the site of injection.¹³⁵

Additional complications for hyaluronic-acid-based fillers such as Teoxane RHA, Restylane, Belotero, and Juvederm included nodule formation, intra-arterial injection with subsequent sequelae, and local site tissue necrosis. Blindness was also a complication that was reported significantly more often with the use of Radiesse injections, whereas nodule formation was more often reported with Sculptra injections.¹³⁵ In the review of publicly available court records in litigation of

physicians, inadequate informed consent was the most often citing factor.¹³⁵

CONCLUSIONS

A tremendous amount of data exist in the world of autologous fat grafting. Many decisions must be made with respect to how to prepare the donor site, which technique to use for harvest, the method of postharvest processing, and finally cannula choice and recipient site preparation in the process of engraftment. The purpose of this review is to present the available data to provide a concise resource for this broad decision-making process. There is still much to be learned in the attempt to maximize graft viability and retention so as to provide patients with reliable and lasting results. The future of fat grafting should focus on homing in on techniques and perioperative management, which improve the quality of the results. We believe that improving the technique is key for safety, but long-lasting and durable results also depend on postoperative care.

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PATIENT CONSENT

Patients provided written consent for the use of their images.

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