80 Stem Cell-Enriched Fat Injection in Aesthetic, Reconstructive Breast Surgery

K. Tunc Tiryaki and M. Mustafa Aydınol

80.1 Background

Autologous fat grafting is a very popular technique in plastic surgery for volume augmentation and improvement of radiated or damaged tissues already. Plastic surgeons agree that fat grafting is a safe procedure with a low complication and high patient satisfaction rate, which can be used for a variety of aesthetic and reconstructive indications [1]. However, significant limitations to traditional fat transplantation remain, such as unpredictability and a variable rate of graft survival [2]. The lingering clinical confusion associated with the viability and predictability of fat grafting is related to the mechanism of fat survival in the recipient area. For large-volume fat transfers or transfers into a hostile recipient bed, the recipient area vascularity might be insufficient for the ischemic graft, leading to graft necrosis. This may be particularly true for injections into areas where the circulation and wound-healing capacity are impaired by previous fibrosis due to surgery, injections, radiotherapy, or any other acquired pathology [3].

Many steps to overcome these problems have been reported, including meticulous harvesting and injection techniques such as lipostructuring and lipolayering [4]. Still, in order to deal with these limitations, we need to deepen our understanding of the microenvironment and cellular dynamics of this graft-uptake process. Basic scientific research suggests that mature adipocytes, due to their high cytoplasmic oxygen consumption, are highly susceptible to hypoxia-induced apoptosis after grafting. Apoptosis of mature adipocytes, especially those located in the center of the lipoaspirate tissue fragment, leads to eventual loss of graft volume [5]. Mesenchymal progenitor cells are more likely to survive the physical stress and hypoxia and therefore play a vital role in adipose tissue regeneration through adipogenic and vascular differentiation as well as expression of angiogenic, antiapoptotic, and antioxidative factors [6]. There is also clinical data suggesting that the lipoaspirate tends to be deficient in these progenitor cells in comparison to intact fat tissue due to impartial harvesting and decantation during the processing.

Key Message

- Adipogenic and vascular differentiation as well as the expression of angiogenic, antiapoptotic, and antioxidative factors are important for fat graft survival.

Supplementary Information The online version of this chapter (https://doi.org/10.1007/978-3-030-77455-4_80) contains supplementary material, which is available to authorized users.

K. T. Tiryaki (✉)
Cadogan Clinic, London, UK

M. M. Aydınol
Teşvikiye Mahallesi Fulya, Nişantaşı Hospital, Şişli, Turkey

A. Kalaaji (ed.), *Plastic and Aesthetic Regenerative Surgery and Fat Grafting*,
https://doi.org/10.1007/978-3-030-77455-4_80

These observations and clinical limitations have led us to the enrichment of the fat graft, a technique we call stem cell-enriched tissue transfer (SET), or cell-assisted lipotransfer (CAL) as known in the literature [7]. This is a technique, in which lipoaspirated fat graft is enriched with autogenous stromal vascular fraction (SVF). Stromal vascular fraction contains a variety of cells such as pericytes, fibroblasts, and macrophages as well as a heterogeneous population of pluripotent adipose-derived stem cells (ADSC) and vascular progenitor cells as well as preadipocytes.

Although the exact mechanism of SVF cells is unknown, it is thought that these cells contribute to graft survival through proangiogenic, antiapoptotic, and proadipogenic effects. Indeed, SVF cells have been shown to promote adipose cell replication, incorporate into vessel walls, and decrease the local inflammatory response [8].

SVF is obtained during the surgery, in the same facility, from excess lipoaspirate using either a collagenase-based isolation technique or a three-step mechanical isolation technique to release the regenerative cells from the fibrous stroma [9]. By combining traditional fat grafting with SVF enrichment, it is possible up to a degree to overcome the problems associated with autologous fat transfer particularly into areas with an impaired environment for fat graft survival. In SET injections, autologous SVF is used to promote angiogenesis during the critical time of tissue engraftment, attempting to improve the survival rate of tissue and reduce postoperative volume loss as well as to reinforce the tissue quality, which is jeopardized by radiation therapy, physical or chemical trauma, and acquired or congenital diseases.

Experimental as well as clinical studies suggest a positive relationship between SET injections and improved operative outcomes [7]. Still, the acceptance of this technique around the world is limited due to the lack of long-term clinical data, issues related to cost, regulatory uncertainty, and safety of using a tissue dissociation enzyme mixture [10].

Key Message

- SVF has proangiogenic, antiapoptotic, and proadipogenic effects and is shown to improve fat graft survival.

80.2 Isolation Methods

Enzymatic digestion using collagenase is the gold standard to isolate adipose SVF. Even though there are slight variations in the different techniques, they follow the same basic steps. The lipoaspirate is washed using an aqueous salt solution, and a digesting reagent, usually collagenase, is added. An incubation period of 30–60 min is used in a heated shaker. The suspension is then centrifuged and four layers are obtained: the oily liquid, the adipose tissue, the aqueous layer, and the pellet. The pellet is kept and washed out from the active enzyme. Approximately 100,000–1,300,000 nucleated cells per gram of lipoaspirate can be obtained with more than 80% viability. Even though this method is giving remarkably high numbers of cells in the SVF, it also has disadvantages. It is expansive, raises legal and administrative concerns, and is time consuming (90–120 min). Many methods of mechanical isolation of SVF have surfaced as well, like shaking, vibrating, centrifuging, and washing the lipoaspirate manually and in automated device [11], which usually give much inferior cell counts. Considering the digestion, incubation, and centrifugation steps of enzymatic isolation methods, we are using a disposable kit for mechanical digestion, which consists also of three consecutive steps, mechanical mincing, buffer incubation, and centrifugation. This method enables us to harvest around 50% of regenerative cells from the same amount of fat in comparison to enzymatic digestion [9].

The choice of isolation method depends on the patients' needs. If the patient is having limited amount of fat, there is a need of higher number of cells in SVF like serious radiotherapy damage, or we need a significant amount of fat to be used as graft material, then it is preferable to use enzymatic digestion, since we can obtain higher cell numbers from a limited amount of fat. If we are not restricted by the amount of fat to be digested then mechanical digestion is our preferred method because it is less time consuming, is much more cost effective, and does not require a lab staff and environment.

80.2.1 Enzymatic Digestion

Once obtained, the lipoaspirate is digested using GMP-graded collagenase NB6 (Serva Electrophoresis, Heidelberg, Germany) at a concentration of 0.1 U/mL and a ratio of 1:1 (v/v). The lipoaspirate is then washed twice in a saline solution and centrifuged at 300 g, for 5 min. The mixture is placed in a shaker at 37 °C for 45 min under constant shaking, finally centrifuged at 300 g for 7 min, and drained through a 70 μm filter. After this, the pellet is resuspended in the desired amount of saline solution to be injected back to the patient.

80.2.2 Mechanical Digestion

After fat harvesting, ordinary pistons of 20 cc Luer-lock syringes are replaced with disposable disarmable pistons with concave gaskets. The lipoaspirate is transferred into syringes, connected to a closed unit, harnessing three different sets of blade grids on three different Luer-lock ports on a rotating canal. The lipoaspirate is placed in the first port and passed back and forth ten times through the first blade grid containing multiple 1000-μm holes. Changing the direction of the rotating canal and the flow to the second port, the lipoaspirate is passed through the second blade grid containing 750-μm holes and then through the 500-μm hole blade grid until full dissociation. A Ca-Mg balanced buffer solution is added to the lipoaspirate inside the syringes at a ratio of 1:3, incubated and shaken for 10 min. The pistons are then disattached and the syringes with the dissociated lipoaspirate are centrifuged at 2000 g for 10 min with the Luer-lock tips directed inward so that the SVF could be collected in concave gaskets (Fig. 80.1). Finally the pistons are reattached, the supernatant discarded, and the pellet in the gaskets resuspended. This procedure takes around 25 min in comparison to 90–120 min using enzyme digestion, with the downside of harvesting around 1/3 to half the number of cells in the SVF.

Whichever isolation technique may be used, at the final stage these cells are either mixed with the fat tissue to be grafted or injected into the damaged skin in order to be able to improve the skin quality. In every case the total number of viable cells is measured by LUNA cell counter (Table 80.1).

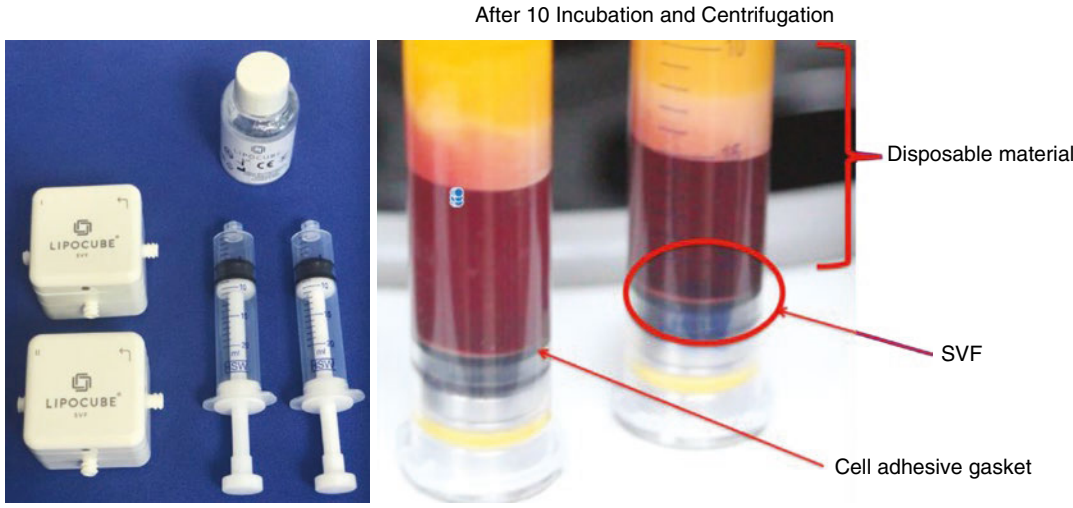

Fig. 80.1 Left: The disposable cubes harnessing three different sized sets of blades, disarmable pistons, concave gaskets, and buffer solution. Right: The SVF pellet concentrated on the gasket with the digested fat to be disposed

Table 80.1 Comparison of enzymatic and mechanical SVF isolation methods

	Isolation methods				Cell number/cc ($\times 10^5$)	Cell viability (%)	Flow cytometer results		
	1. Addition of the digestive agent	2. Incubation for digestion	3. Centrifugation for extraction of the pellet	4. Washing the reagent			CD73+/CD90+ ADSC cell content	CD45−/CD90+ ADSC cell content	CD73+/CD90+ Endothelial cell content
Enzymatic isolation	Collagenase	45 min at 37 °C	300 g for 5 min	Washing with PBS solution	33.86	82.86	85.31%	82.01%	20.40%
Mechanical isolation	Mincing/filtration with buffer solution	10 min at room temperature	2000 g for 10 min	No washing	13.45	85.82	83.63%	63.64%	6.74%

80.3 Fat Grafting Indications for Breast

Fat grafting to the breast and chest has numerous indications that can improve volume, shape, feel, projection, and silhouette of the region. Often, the main objective of breast surgeons is to create symmetrical, natural-looking breasts. Beyond just minimizing the need for prosthetic implants, grafts can also aid in aesthetic improvements to flap reconstructions, acquired or congenital chest and breast wall deformities, and aesthetic breast augmentation.

Aesthetic breast augmentation: Implantation of artificial breast prostheses is the most frequently performed surgical cosmetic procedure in the USA. Seeing that prosthetic implantation has long been the gold standard, autologous fat grafting offers several advantages including lack of scarring and complications associated with implanting foreign material in breasts, but with limited indications and success. Women who desire large, firm, or exceptionally round breasts, or who do not have enough fat to be harvested, are not appropriate candidates for autologous fat transfer.

Breast reconstruction: Autologous fat grafting can be used in several ways to reconstruct the breast after mastectomy or lumpectomy, as the main treatment modality in women with small breasts or women who have had a lumpectomy, or as an adjunct to implant or flap reconstruction by smoothing out contour abnormalities [12]. In addition, Rigotti et al. found fat to be particularly useful in women who had undergone radiation therapy after lumpectomy [13]. In our experience set injections are extremely useful in dealing with partial tissue defects, where rigorous rigottomies are followed by tunneled SET injections (Fig. 80.2).

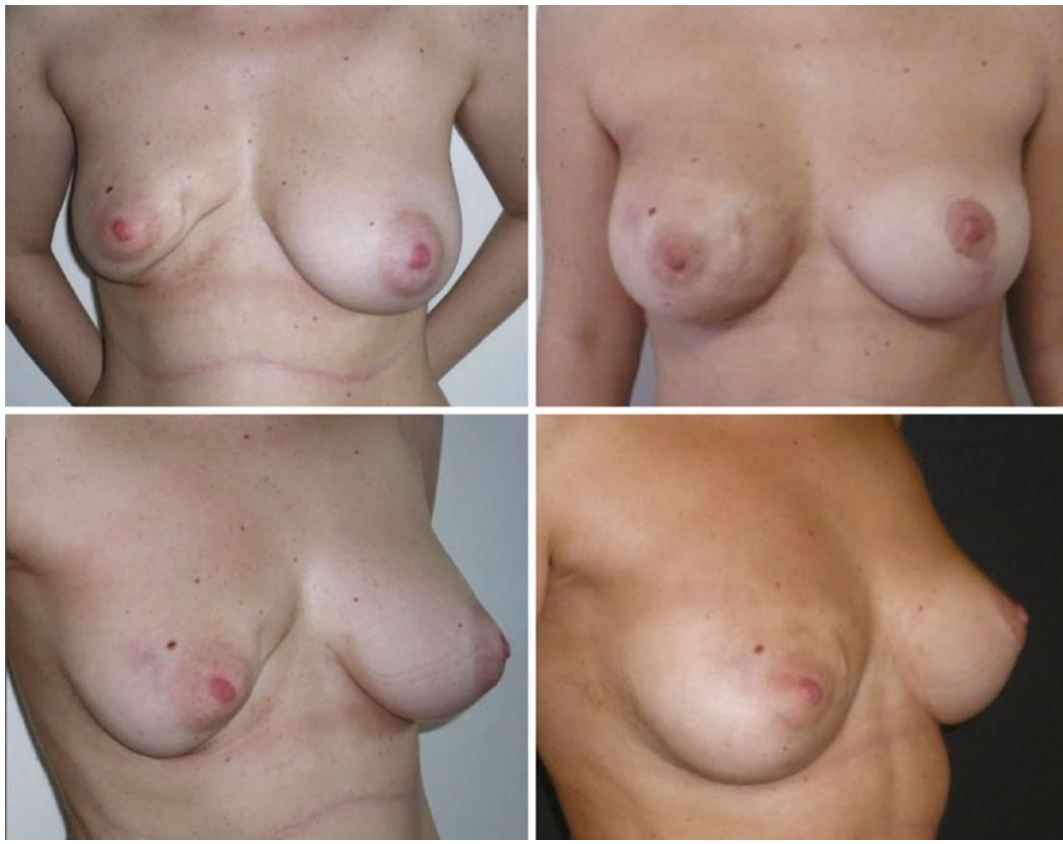

Fig. 80.2 Lumpectomy, radiotherapy, and chemotherapy. After the patient was declared clean by the single-session oncology of 280 cc SET transfer was performed to the right breast with simultaneous mastopexy to the left. Preoperative and 2-year postoperative results

Key Message

- Fat grafting can be used for breast augmentation, breast reconstruction, breast asymmetry, implant rescue, chest wall deformities, reinforcing and improving skin quality, and replacing implants.

Congenital Breast Asymmetry: Traditional treatment of congenital asymmetric breasts involves inserting a prosthetic implant into the hypoplastic breast. While results may be satisfactory initially, natural ptosis of the breasts over time may lead to asymmetric breasts years later. Autologous grafts on the other hand have the luxury of changing more naturally over time in the untreated and treated breast.

Implant Rescue: Artificial prostheses have a complication rate of 3–20% and occasionally result in implant replacement or removal. Yoshimura et al. described promising results when using ADRC-enriched fat grafts to reconstruct patients after prosthesis removal [14]. It is also our experience that patients who have their implants removed and get immediate fat grafting have extremely high levels of graft retention (Fig. 80.2).

Poland Syndrome, Pectus Excavatum, and similar deformities: Autologous fat grafts for patients suffering from chest wall deformities such as Poland syndrome show promising results. Limited scarring with the option of repeat procedures makes fat grafting a useful alternative to silicone prostheses. Autologous fat transfers may be used to supplement custom-made implants or used alone in reconstructing the affected area.

Radiated and Ischemic Breast Tissue: Most experts will discourage the use of prosthetic implants in irradiated breasts due to the high occurrence of complications and will instead recommend completely autologous reconstructive procedures. For these patients, ADSC-enriched fat grafting is an ideal reconstructive option for these women. Fat grafting necessitates very small, punctate wounds in the irradiated bed and therefore minimizes the risk of wound problems and the increased regenerative effect of ADSC enrichment usually gives much superior outcomes in these patients than traditional fat grafting alone. Reconstruction of irradiated breasts may require a second treatment so patient education during the initial consultation is important. In our experience, reinforcing the skin thickness and quality to reverse the radiotherapy damage is a very useful approach. In selected cases it is possible to reconstruct a total mastectomy defect with only SET injection and implant placement (Fig. 80.3).

Patients must be told of the achievable outcomes of breast grafting procedures. For example, fat grafting may not entirely replace prosthetic breast placement depending on the patient's available donor volume of fat and recipient-site anatomy. Also important is discussing a patient's family and/or personal cancer history. This is important in deciding which preoperative precautions should be taken as well as indicates what type of long-term follow-up is most appropriate.

Key Message

- Proper patient informing about achievable outcomes and detailed patient history for fat grafting procedure are mandatory.

Implant Removal: With recent developments about the implant-related lymphoma cases, more and more patients want to remove their implants and replace them with their own fat. Given the fact that they have enough fat tissue to be transplanted, this is a great indication for breast fat grafting. Our experience is that the graft uptake after immediate breast implant removal is much higher than primary cases. The technique is similar to primary breast fat injection, without any injections performed into the dead space of the implant capsule. As a rule of thumb, double amount of the volume of explanted devices is supposed to be injected (Fig. 80.4).

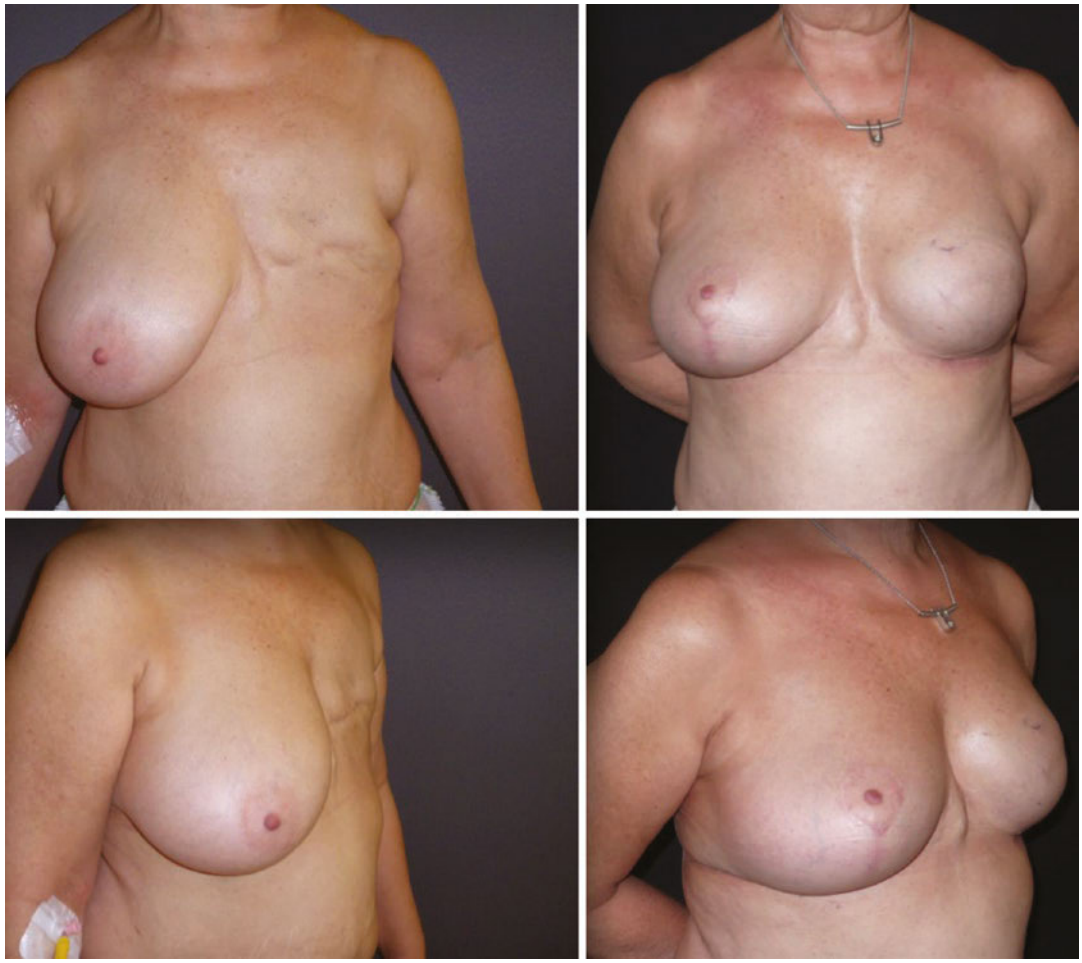

Fig. 80.3 Total mastectomy and radiotherapy. After declared to be free of disease, one session of 270 cc of SET for volume replacement and skin reinforcement was performed. Three months after the left-side injection, a 390 cc, CPG™ 323, gel breast implant was placed with simultaneous right reduction-mastopexy. Preoperative and 1-year postoperative results

80.4 Patient Consultation and Selection

Patients must understand the achievable outcomes of breast grafting procedures. Fat transplantation may not entirely replace prosthetic breast placement, depending on the patient's available donor volume of fat and recipient-site anatomy. Also important is discussing a patient's family and/or personal cancer history. Women who desire large and firm breast may not be appropriate candidates for autologous fat transfer as fat graft results in a more natural-looking appearance. Similarly, it cannot be overemphasized that fat grafts to the breast are not a viable option for women lacking significant sources of donor fat for liposuction, because the need for fat is much higher when compared to other indications for fat grafting procedures. The ideal patients for breast fat grafting are liposuction

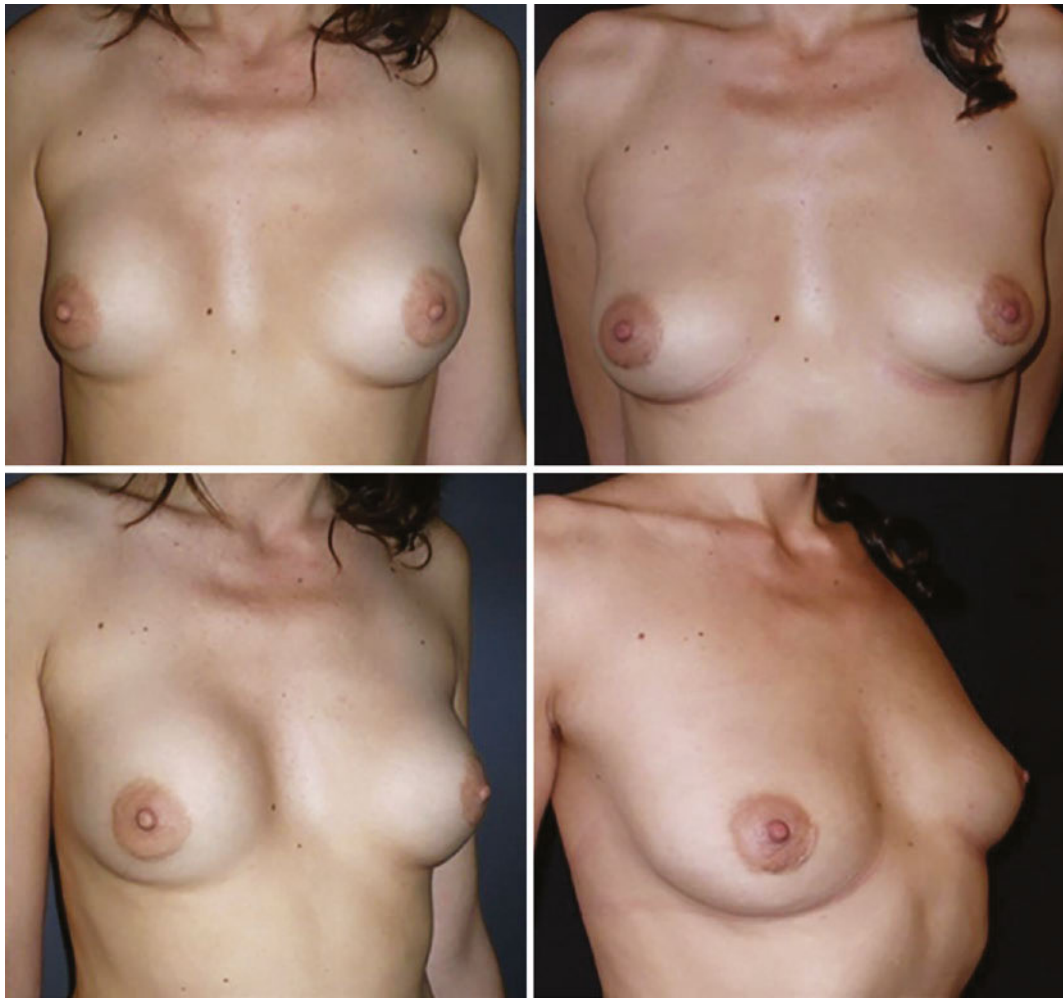

Fig. 80.4 Removal of 195 cc implants and 310 cc SET injection to each breast. Single session, PO 1 year

patients, who do not desire very big volume changes on their breasts.

Limitations of the technique:

1. High breast cancer risk
2. Continuous breast cancer relapse risk
3. Patients who desire large and firm breasts
4. Patients with limited autologous fat resources

Key Message

- The ideal patients for breast fat grafting are liposuction patients, who do not desire very big volume changes on their breasts.

80.5 Surgical Technique

80.5.1 Preferred Donor Site

There is no good evidence to clearly define the best donor site for fat grafts. Rohrich et al. found that common harvest areas (abdomen, flank, thigh, medial knee) produce statistically equivalent numbers of viable cells [15]. Von Heimburg et al. found the viability of preadipocytes from the abdomen, breast, and buttock to all be greater than 94% [16]. The abdominal region has been reported as the most common harvest location due to

patient preference and ease of supine position for graft harvest and delivery [4], but our experience proved contrary. Since the abdomen is the most flask skin area of the body, the donor-harvest sequelae are much more common, particularly in inexperienced hands. In our clinical setup, in the first operation we harvest the fat from the lateral and medial thigh as well as love handles with the patient face-down and under general anesthesia. If need arises for a secondary touch-up, we use the abdominal area for harvesting due to its ease, without turning the patient per-operatively, usually under only sedative anesthesia.

80.5.2 Preoperative Hydroexpansion

If the patient's skin envelope is very tight, or there is not enough recipient tissue volume, we ask the patients to come to the office 1 week and 3 days before the surgery. In the office setup, the breasts are injected with tumescent solution under local anesthesia in order to release the skin tightness. The amount of tumescence injection is decided upon the planned graft injection volume. Usually a 1:1 ratio of fluid is injected and the patient is sent home with expanded breasts (Fig. 80.5).

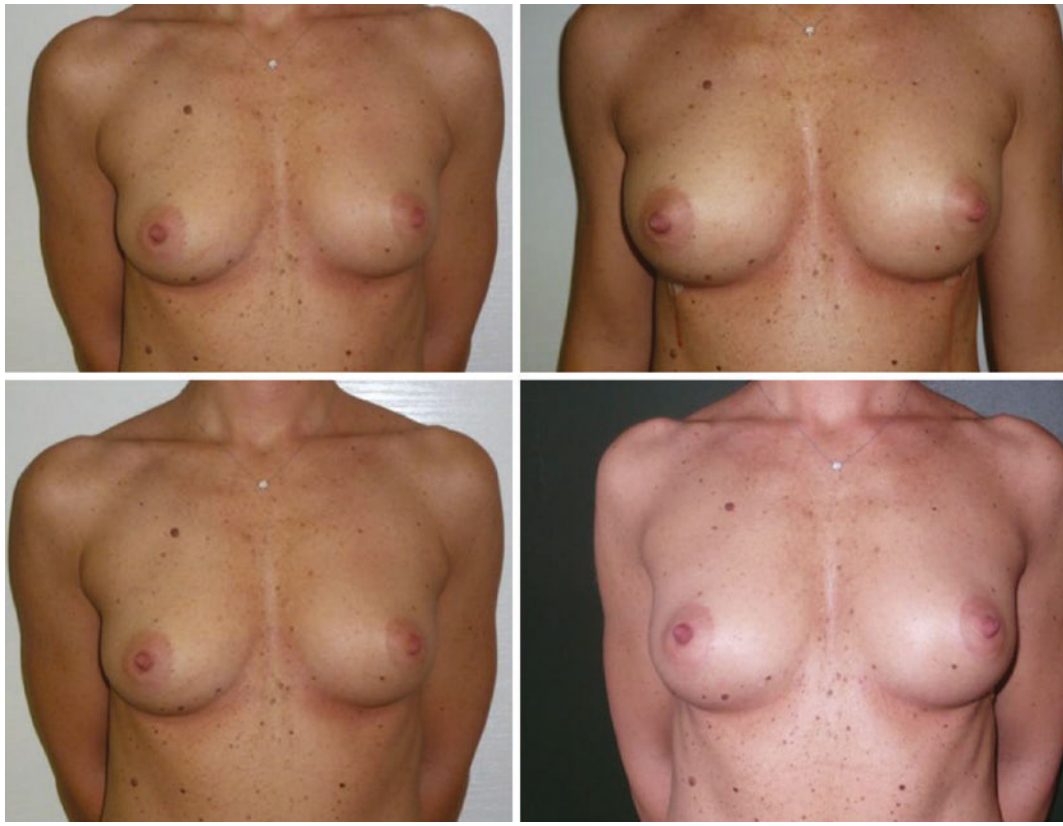

Fig. 80.5 Preoperative hydroexpansion. In tight-skinned patients, we ask the patients to come to the office 3 and 7 days before surgery to be infiltrated with tumescence solution under local anesthesia in the amount of planned fat injection. On the upper right picture, the patient is after tumescence injection, on lower right 1 year after 350 cc of traditional fat grafting

Key Message

- Preoperative hydroexpansion with tumescent solution is a technique that can be used to reduce skin tightness to improve the outcome of the procedure and increase fat graft survival.

80.5.3 Donor-Site Preparation

Donor sites are marked preoperatively. Additionally, photographic documentation and/or three-dimensional imaging should be obtained for postoperative comparison. Standard sterile technique is observed during the harvest and conventional prophylactic perioperative antibiotics are typically sufficient. Additionally, it is critical to remember that all grafts contain some amount of fluid, which is introduced into the graft during the harvest process. This fluid will be absorbed postoperatively, and one must account for this loss of volume.

80.5.4 Wetting Solution, Infiltration

The composition and quantity of wetting solution injected at the donor site depend on the volume of fat to be harvested, donor site, as well as physician preference. Most surgeons use a standard tumescent solution of 0.5% lidocaine and 1:100,000 epinephrine in 1 L of lactated Ringer's or 0.9% saline solution. The ratio of solution to epinephrine can vary from 1:80,000 to 1:200,000 and sodium bicarbonate is used if done under sedation or local anesthesia. The ratio of tumescent fluid injected to volume of tissue harvested depends on the site and the volume to be harvested, with large volume cases approaching 1:1. It is demonstrated that the safe dose of lidocaine increases to between 35 mg/kg and 50 mg/kg when used in tumescent fluid (Klein, 1990). Tumescent fluid should be injected evenly throughout the subcutaneous fat in the area to be liposuctioned. It is advisable to resist the temptation to progress through the case and wait the full 10 min.

80.5.5 Cannula Selection

Instruments should be chosen to minimize trauma to the donor adipocytes and thus enhance the probability of graft survival. In contrast to sharp tips, blunt tips allow for penetration of tissue while minimizing cell destruction and trauma to the fibrous septa, neurovascular bundles, and dermis. "Multiple opening" cannulae allow for a more resourceful fat collection with each pass. Overall, fat to be grafted should be harvested with 3–4 mm cannula with parcels small enough to pass through a 2 mm injection cannula, whereas 3 mm, sharp, multi-hole cannula seems to be better to harvest fat to be digested, due to the initial damage to the cell niche. It has been shown that fat harvested by sharp cannula contains higher numbers of regenerative cells per ml of lipoaspirate [17].

80.5.6 Harvesting

Traditional mechanical liposuction uses machine-generated negative pressure to remove the fat as the surgeon pushes the cannula through the adipose tissue. Studies show that mechanical liposuction and manual aspiration yield grafts with similar metabolic activity and ability to generate new adipocytes [18]. There are also "assisted liposuction" devices like ultrasound-assisted liposuction (UAL), power-assisted liposuction (PAL), laser lipolysis systems, and liquid flow-assisted liposuction claiming better cell viability and yields. However, given the lack of consensus, we feel that using a particular machine or syringe for harvesting should be based on availability, accessibility, and amount needed. Under any circumstance, care is taken to keep the sterile environment for the graft.

80.5.7 Graft Processing

First, the amount of lipoaspirate to manage the volume defect is harvested, and then liposuction is continued for harvesting fat for SVF digestion,

which will be discharged after the digestion and isolation. The fat to be grafted is processed to separate healthy adipocytes and ADRCs from unnecessary debris while minimizing damage to the cells [19]. The choice of "cleaning" the fat depends on the amount of graft to be transferred and what kind of structural support is needed. If strong support is needed like in facial deep fat injections, centrifugation is preferable since it gives a drier and denser fat. For breast injections however, wet fat with a significant amount of water serves as a spacer against the skin envelope tension. Therefore in our practice we use centrifugation for 1 min with 1000 rpm for facial injections, but use decantation only for breast grafting.

Key Message

- Wet fat can be used as a spacer against skin tension and therefore can increase graft survival. If strong support is needed centrifugation is used to make fat denser and drier.

80.5.8 Adding the SVF to the Graft

The isolated SVF can be added to the graft in vitro, where some of the graft is spared to be mixed with the SVF solution and injected at the end of the surgery. This is our approach while doing breast injections. It does not prolong the operative time since we give the firstly harvested fat to be digested. Until we finish full harvesting and start injecting the breast, the SVF isolation is usually over, so we mix it with our graft to have a homogenous enriched graft. If we are doing facial fat injections, it is another possibility to finish the procedure and inject the SVF later into the fat-grafted areas as well as intradermally, in the recovery room (Fig. 80.6).

80.5.9 Lipo-Delivery

Fat should be injected under light pressure while withdrawing the cannula. Although one must overcorrect for the relative amount of fluid in the graft, it is more important not to overfill the area such that the overlying skin is taut. This pressure may cause ischemia to the recipient bed [3]. Current delivery techniques are based on the belief that to optimize fat graft survival, close proximity to a blood supply is imperative. Grafts placed within 2 mm of an arterial blood supply have minimal necrosis and should be expected to survive [4]. Therefore, delivery techniques that maximize the graft surface area-to-vascularized tissue ratio are preferred. Grafts are most rou-

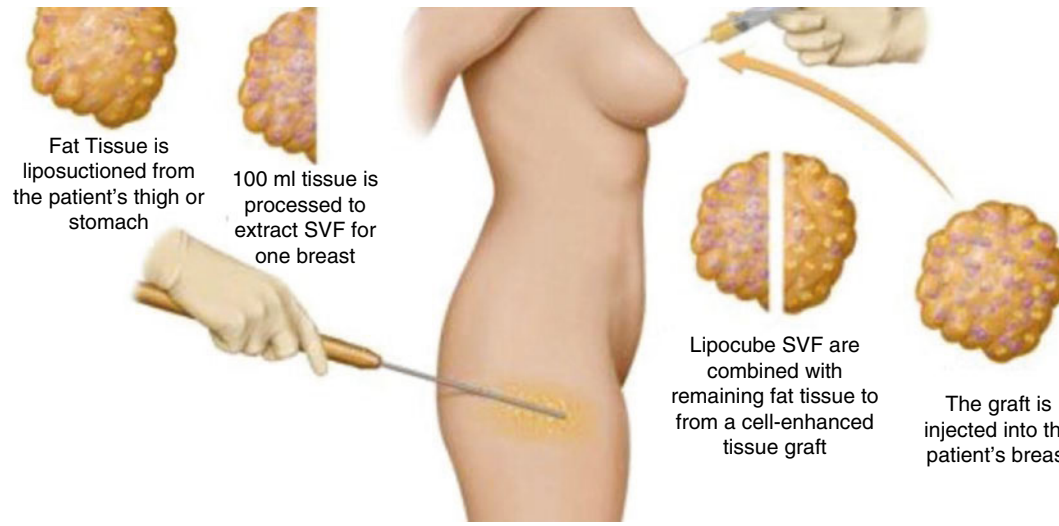

Fig. 80.6 The first 100–200 cc of fat is digested while the liposuction is continued. The isolated SVF is usually added to the graft in vitro and the mix is injected together

tinely administered into the subcutaneous space. For breast injections, graft should be injected in the retromammary space or subcutaneous space but not in the mammary gland itself. The literature reports satisfactory clinical experience with injection into the muscle. In our practice, usually three ports of entry are used, one at the mid-inframammary fold, one lateral to the breast tissue, and one at the medial edge of the areola. The amount of fat to be injected is divided into three portions and 1/3 is injected to the upper pole, 1/3 to the lower pole, and 1/3 to the retroglandular space (Fig. 80.7).

Key Message

- During fat injection to breast, graft should not be injected to mammary gland itself. There is also satisfactory clinical experience with injection into the muscle.

80.5.10 Handling Scarred Recipient Beds

It is often difficult but particularly necessary to layer fat effectively into highly scarred regions. In order to be able to treat iatrogenic or radiotherapy-induced fibrotic bands rigottomies are necessary, which are done in a sponge-release fashion but not incisional releases, which create dead space without vascular support [13].

80.5.11 Postoperative Care

Fine, rapidly absorbed sutures are preferred to close the incisions with dry dressings applied as needed. Edema and bruising are common and are expected to resolve in up to 1 month. Note that due to swelling alone, 30–40% of the initial apparent graft volume will most likely be lost in the first few weeks after surgery [20].

80.5.12 Radiologic Follow-Up

Benign oil cysts, micro-calcifications, and fat necrosis may occur subsequent to any breast surgery and can be readily distinguishable from malignant lesions. Patients should commit to close postoperative radiology follow-up for 1–3 years following fat grafting to the breast.

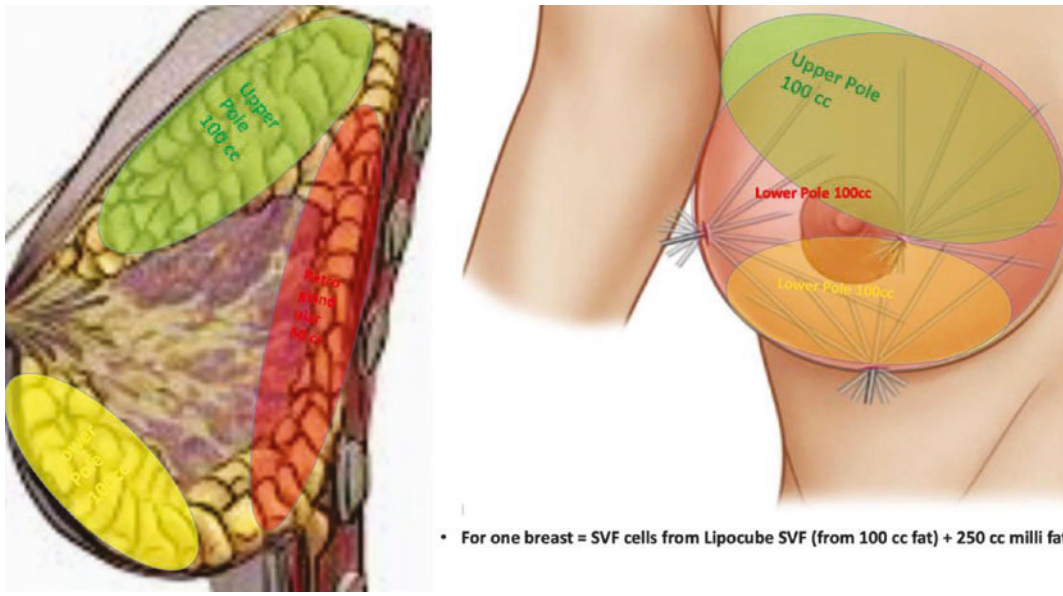

Fig. 80.7 Usually three ports of entry are used, one at the mid-inframammary fold, one lateral to the breast tissue, and one at the medial edge of the areola. The amount of fat to be injected is divided into three portions and 1/3 is injected to the upper pole, 1/3 to the lower pole, and 1/3 to the retroglandular space

80.6 Complications

80.6.1 General Complications

The majority of fat grafting operations are performed without complication with usual risks of pain, infection, bruising, bleeding, edema, numbness, contour irregularity, skin necrosis, hematoma, perforation of an abdominal organ, fat emboli, or even death. Respecting current guidelines, which limit the volume of fat harvested, would guard the surgeon against catastrophic incidences.

The majority of fat graft complications result from the volume or manner in which the graft is placed by the physician. Grafting complications have been shown to markedly decrease with physician experience like graft loss, focal fat necrosis, chronic inflammation, infection in graft bed, lipid cysts, and calcifications [1].

80.6.2 Fat Grafting and Breast Cancer

Patients should undergo a breast imaging workup prior to grafting to confirm that no breast cancer is present. Doing so will help mitigate the impact that any coincidental concurrence of grafting and cancer would have on the physician and patient. Physicians should inform patients that should they develop breast cancer, grafting would not hinder any conventional cancer treatment options. Long-term follow-up in several breast lipo-graft and CAL patients shows no increased recurrence or new development of cancer [1]. Furthermore, fat grafting does not hinder early cancer diagnosis when rigorous pre- and postoperative surveillance is performed. Mammography remains the most accurate tool for monitoring breasts after grafting procedures. While some may be concerned that necrosis or calcifications hinder screening, experienced radiologists generally have no problems distinguishing between calcifications caused by surgery.

80.7 Conclusion

Because of two revolutions in the last decade, namely, the recognition of fat tissue as the most important source of stem cells in the human body and the relatively simple techniques of isolating these stem cells from fat, plastic surgeons are emerging as the specific group capable to use body's own regenerative power. It is getting more and more clear that enriching fat graft with autologous adipose-derived stem cells is a promising strategy to improve the predictability, consistency, and efficacy of fat grafting results.

From the safety perspective, our 10-year experience supports the notion that SET does not increase the risk for development of cancer or accelerate the growth of an existing undetected neoplasm. This remark does of course not nullify the theoretical risks associated with the SVF cell yield injection theorized from in vitro studies of adipose-derived stem cell (ASC) trophic factors and their effects in co-cultures with breast cancer cells. However, as per today, there seems no basis for a causal relationship between fat grafting with or without SVF enrichment and breast cancer. According to us, the real limiting factors are twofold: first, the amount of available autologous fat, and second, patients' unrealistic expectations.

Finally, the fact that we can also mechanically isolate 30–50% of stromal vascular cells of that isolated with enzymatic digestion makes the usage of SVF enrichment a much more approachable and viable alternative to traditional fat grafting.

Key Message

- SET does not increase the risk for cancer development nor accelerate the growth of an existing neoplasm. Amount of available autologous fat and unrealistic patient expectations are two major limiting factors.

References

1. Delay E, Garson S, Tousson G, Sinna R. Fat injection to the breast: technique, results, and indications based on 880 procedures over 10 years. Aesthet Surg J. 2009;29(5):360–76.

2. Toledo LS, Mauad R. Fat injection: a 20-year revision. Clin Plast Surg. 2006;33(1):47–53, vi.
3. Nguyen A, Pasyk KA, Bouvier TN, Hassett CA, Argenta LC. Comparative study of survival of autologous adipose tissue taken and transplanted by different techniques. Plast Reconstr Surg. 1990;85(3):378–86; discussion 87-9.
4. Coleman SR. Facial recontouring with lipostructure. Clin Plast Surg. 1997;24(2):347–67.
5. Kato H, Mineda K, Eto H, Doi K, Kuno S, Kinoshita K, et al. Degeneration, regeneration, and cicatrization after fat grafting: dynamic total tissue remodeling during the first 3 months. Plast Reconstr Surg. 2014;133(3):303e–13e.
6. Naderi N, Wilde C, Haque T, Francis W, Seifalian AM, Thornton CA, et al. Adipogenic differentiation of adipose-derived stem cells in 3-dimensional spheroid cultures (microtissue): implications for the reconstructive surgeon. J Plast Reconstr Aesthet Surg. 2014;67(12):1726–34.
7. Tiryaki T, Findikli N, Tiryaki D. Staged stem cell-enriched tissue (SET) injections for soft tissue augmentation in hostile recipient areas: a preliminary report. Aesthet Plast Surg. 2011;35(6):965–71.
8. Rehman J, Traktuev D, Li J, Merfeld-Clauss S, Temm-Grove CJ, Bovenkerk JE, et al. Secretion of angiogenic and antiapoptotic factors by human adipose stromal cells. Circulation. 2004;109(10):1292–8.
9. Tiryaki T. In vitro investigation of the effect of stromal vascular fraction isolated by mechanical and enzymatic methods on wound healing. J Ist Faculty Med. 2020;83(3):241–6.
10. McCarthy RC, Breite AG, Dwulet FE. Biochemical analysis of crude collagenase products used in adipose derived stromal cell isolation procedures and development of a purified tissue dissociation enzyme mixture. International Federation for Adipose Therapeutics and Science (IFATS).
11. Aronowitz JA, Lockhart RA, Hakakian CS. Mechanical versus enzymatic isolation of stromal vascular fraction cells from adipose tissue. Springerplus. 2015;4:713.
12. Spear SL, Boehmler JH, Bogue DP, Mafi AA. Options in reconstructing the irradiated breast. Plast Reconstr Surg. 2008;122(2):379–88.
13. Rigotti G, Marchi A, Stringhini P, Baroni G, Galie M, Molino AM, et al. Determining the oncological risk of autologous lipoaspirate grafting for post-mastectomy breast reconstruction. Aesthet Plast Surg. 2010;34(4):475–80.
14. Yoshimura K, Sato K, Aoi N, Kurita M, Hirohi T, Harii K. Cell-assisted lipotransfer for cosmetic breast augmentation: supportive use of adipose-derived stem/stromal cells. Aesthet Plast Surg. 2008;32(1):48–55; discussion 6-7.
15. Rohrich RJ, Sorokin ES, Brown SA. In search of improved fat transfer viability: a quantitative analysis of the role of centrifugation and harvest site. Plast Reconstr Surg. 2004;113(1):391–5. discussion 6-7
16. von Heimburg D, Hemmrich K, Haydarlioglu S, Staiger H, Pallua N. Comparison of viable cell yield from excised versus aspirated adipose tissue. Cells Tissues Organs. 2004;178(2):87–92.
17. Tonnard P, Verpaele A, Peeters G, Hamdi M, Cornelissen M, Declercq H. Nanofat grafting: basic research and clinical applications. Plast Reconstr Surg. 2013;132(4):1017–26.
18. Leong DT, Hutmacher DW, Chew FT, Lim TC. Viability and adipogenic potential of human adipose tissue processed cell population obtained from pump-assisted and syringe-assisted liposuction. J Dermatol Sci. 2005;37(3):169–76.
19. Conde-Green A, Kotamarti VS, Sherman LS, Keith JD, Lee ES, Granick MS, et al. Shift toward mechanical isolation of adipose-derived stromal vascular fraction: review of upcoming techniques. Plast Reconstr Surg Glob Open. 2016;4(9):e1017.
20. Aronowitz JA, Ellenhorn JD. Adipose stromal vascular fraction isolation: a head-to-head comparison of four commercial cell separation systems. Plast Reconstr Surg. 2013;132(6):932e–9e.