Lipofilling

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Although lipotransfer is not a new technique [1], it can be considered a technical revolution in plastic surgery which is widely performed all over the world for aesthetic surgery [2]. More recently, the lipofilling has been indicated in breast cancer patients to improve the results of breast reconstructions, and [3–6] current literature underlines the efficacy of the technique as well as the safety of the procedure in cancer patients. Applications of lipofilling have been performed to improve the shape of breast reconstruction with prosthesis or with autologous musculocutaneous flaps. Fat injection can also be used to reshape the bad results of the conservative treatment. Most of the defects observed after conservative treatment can be easily filled up with fat tissue instead of glandular or distant flaps. Different teams are now investigating the possibility of refilling the defect of the quadrantectomy immediately at the time of the quadrantectomy. Total breast reconstruction with pure fat refilling is also performed as demonstrated in several studies [7, 8].

39.1 Application of Lipofilling in Breast Cancer Surgery

Lipofilling is being indicated for soft tissue defect correction in many sites. It is not only for corrective surgery but also for cosmetic purpose. For breast cancer surgery, lipofilling procedure might be proposed in the following situations:

- Correction of defects and asymmetry following wide local excision (or breast conservative surgery), with or without radiotherapy
- Improvement of soft tissue coverage following implant-based breast reconstruction
- Volume replacement of implants in unsatisfactory onco-plastic breast reconstruction outcomes
- Augmentation of volume and refinement after autologous breast reconstruction
- Whole breast reconstruction with serial fat grafting
- Scar correction

39.2 Technique of Lipofilling

Lipofilling can be performed under general or local anesthesia. Generally, the aim of the technique is to decrease cell damage and to promote survival of the fat tissue and its composition. Success is heavily dependent on the technique used for harvesting, preparing, and grafting of the fat (Figs. 39.1, 39.2, 39.3, 39.4, 39.5, 39.6, 39.7, 39.8 and 39.9).

39.2.1 Identification of the Donor Site

The most common site is the abdominal fat because it is one of the most fat deposit area. Moreover, there is no need to change the patient's position in the operation room. The second site is the trochanteric region (saddle bags) and the inside of the thighs and knees. The harvesting areas are outlined with a skin marker. But every location showing an excess of fat tissue on the body can be used for fat liposuction.

39.2.2 Preparation of the Solution

The tumescent solution (so-called Klein's solution) is prepared to be injected into the donor site: 1 cc of epinephrine (1:500,000) diluted in 500 cc of 0.001% lactated Ringer's solution (LRS). The 50 cc of mepivacaine can be added in

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Fig. 39.1 Lipofilling technique: abdominal liposuction, centrifugation, purification of the fat, reinjection in the breast

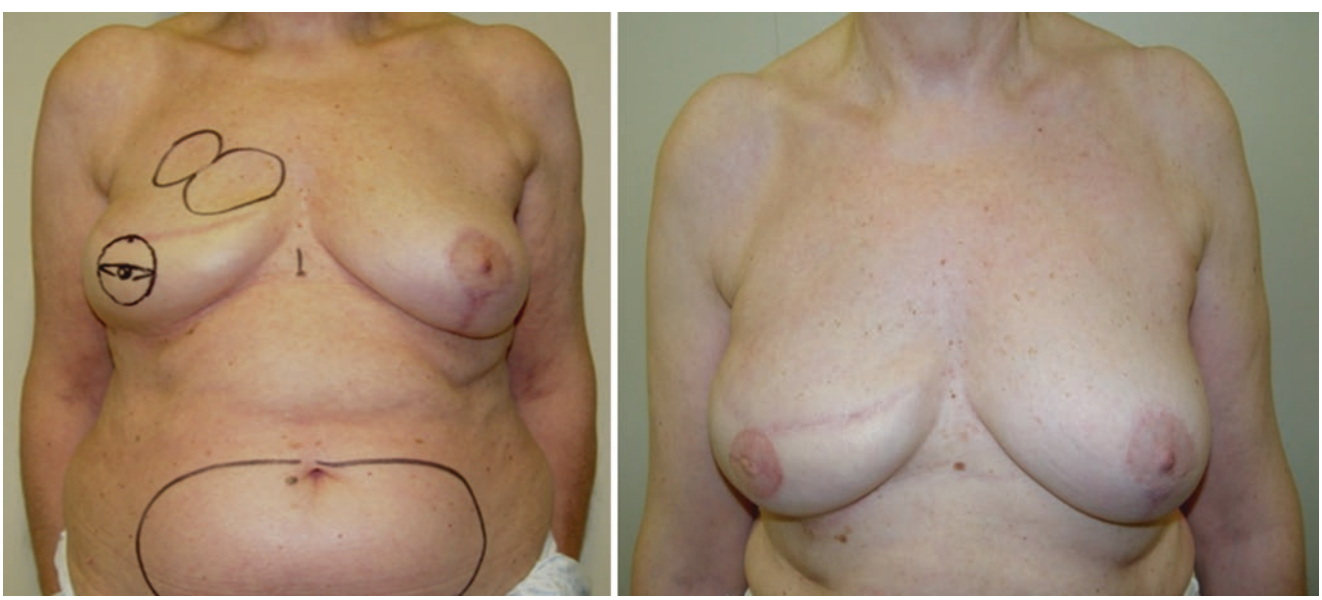

Fig. 39.2 Improvement of the *right* implant breast reconstruction with lipofilling

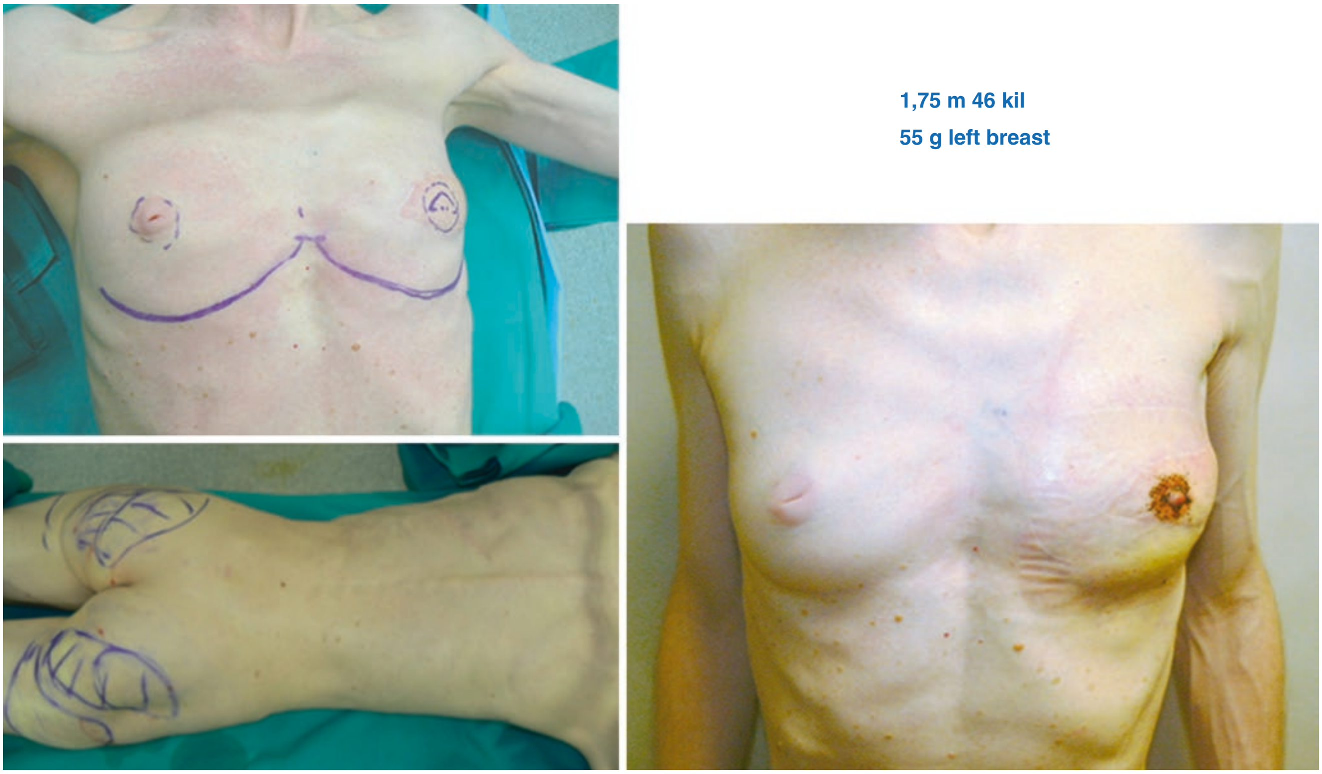

Fig. 39.3 Improvement of the *left* prosthetic breast reconstruction with lipofilling in a very thin patient

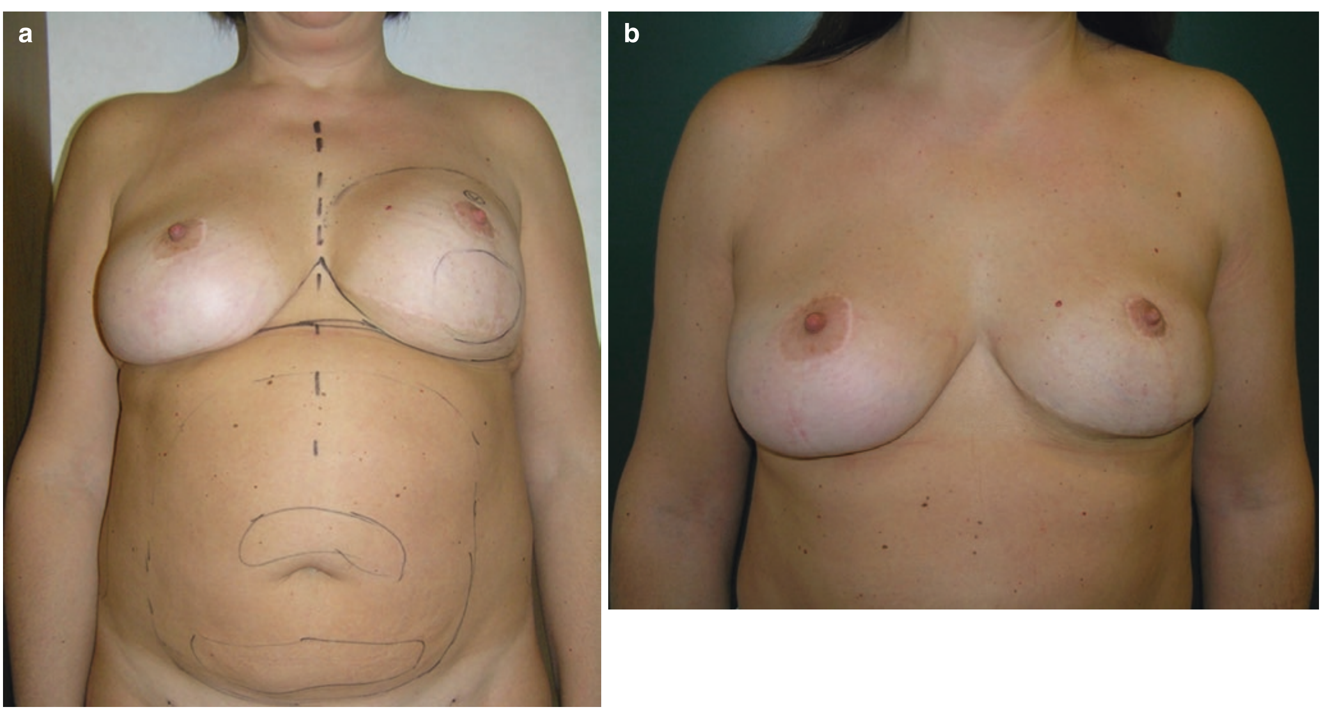

Fig. 39.4 Total *left* breast reconstruction with pure lipofilling

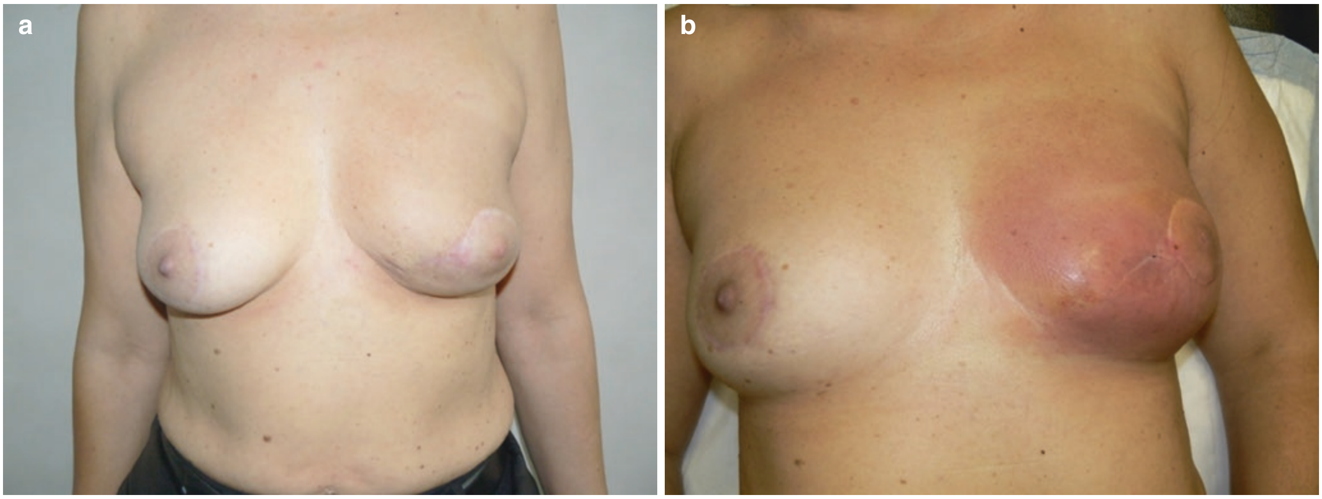

Fig. 39.5 Infection and result after drainage and antibiotherapy

Fig. 39.6 Improvement of the mastectomy scar after previous radiotherapy and before implant breast reconstruction

Fig. 39.7 Improvement of autologous latissimus breast reconstruction and improvement of the dorsal scar

Fig. 39.8 Improvement of BCT with lipofilling

Fig. 39.9 Reshaping of the *right* breast conservative treatment with lipofilling

the solution if the procedure is planned under local anesthesia. It is injected through a small-bore 4 mm blunt cannula that was attached to a 60-cc syringe. The estimate volume of solution is 1 cc for each 1 cm^3 of target fat harvest volume. The surgeon should wait at least 15 min before starting fat harvesting; the adrenaline is added to the solution in order to achieve well hemostasis and to decrease postoperative pain.

39.2.3 Fat Harvesting

The most well-known technique of fat harvesting has been described by Coleman [9]. The procedure starts through a small incision made in the abdomen by blade no.11 and gradually applies a blunt tip harvesting cannula (3 mm in diameter and 15 or 23 cm in length). Manually, the syringe is drawn to create to low negative pressure during fat harvesting. The cannula is attached to 10-cc Luer Lock syringes. However, various techniques of fat harvesting with different cannula or liposuction machine system have been reported with different outcome assessments.

An "experimental solution" study by Ozsoy et al. demonstrated a greater number of viable adipocytes when harvested with a 4-mm-diameter cannula compared with 2- or 3-mm cannulas. Erdim et al. also recommended the use of larger cannulas to increase cell viability. Their study showed more viability of fat cells when using 6-mm-diameter cannula than using 2 or 4 mm in diameter cannula.

Different vacuum pressures and some assisted techniques have been used in many clinical series. Rohrich et al. compared traditional liposuction, internal ultrasound-assisted liposuction, external ultrasound-assisted liposuction, and massage-assisted technique liposuction. There was no significant histologic or chemical effect of external ultrasound-assisted liposuction on harvested adipocytes. Pu et al.

compared the Coleman technique versus conventional liposuction technique and found significantly higher viable adipocyte level in the Coleman technique. Crawford et al. examined the hand aspirate at low-force centrifuge versus standard power-assisted liposuction and showed higher cell counts which were observed when using the low-force centrifuge [10–20].

39.2.4 Fat Processing

The most frequently used methods for fat processing are centrifugation, washing, and decantation. The purified fat can be separated from cell debris by centrifugation, as described in the widely used protocol by Coleman. After centrifugation, the lipoaspirated specimen can be separated into four layers: (I) the oily fraction, leaked out of disrupted adipocytes; (II) the watery fraction consisting of blood, lidocaine, and saline, injected before the liposuction; (III) a cell pellet on the bottom; and (IV) the purified fat between the oily and the watery fractions. For washing technique, the fat is washed using normal saline or 5% glucose solution in order to wash out the blood and the oil part and cellular debris from the aspirated fat. The least popular technique is decantation, which uses the gravity effect to precipitate the cellular component from the oily and water component.

39.2.5 Fat Transfer (Injection)

At EIO, we are using modified Coleman technique by injecting the processed fat via 2-mm-diameter cannula attached to 1 mL to 3 or 10 mL disposable syringe. The fat is transferred directly to the breast, trying to avoid intraparenchymal injection and avoid creating the bolus injection. The entry site of the cannula can be made by sharp blade or a sharp 17-gauge needle to minimize the scar. It is mandatory to overcorrect the defects because 40–60% of the transferred fat is expected to be resorbed. Experimental studies have found that up to 90% of transplanted adipose tissue could be lost, while clinically reported figures range between 40% and 60%, and most of the volume loss occurs within the first 4–6 months following surgery. Despite, several novel techniques proclaimed that they produced more effective outcomes. Nonetheless, surgeon should calculate the quantity of fat preparation and injection before the procedure. The limitation of volume inject can be due to the recipient tissue quality such as in irradiation tissue or thick scar. If the target volume cannot be achieved by a single lipofilling procedure, then the patient should be informed for the possibility of repeated lipofilling. In general the overcorrection reaches an excess of around 40% of the amount of fat required to correct the defect.

39.2.6 Lipofilling in Reconstruction of Irradiated Breast

External radiation is required in breast conservative treatment and after total mastectomy in case of positive nodes. Salgarello et al. retrospectively studied 16 patients who underwent lipofilling to the chest wall after irradiation and then followed by prosthesis introduction and found high success rate of prosthetic-based procedure with no complication or oncological recurrence [21]. Sarfati et al. performed lipofilling prior to implant introduction after irradiation in 28 patients. They reported high success rate with only one prosthesis exchange due to prosthesis exposure after lipofilling [22]. Rigotti also demonstrated the efficacy of lipotransfer to improve the radiodystrophic sequelae [23].

39.3 Complication

39.3.1 Recipient Site Complications [23, 24]

- Fat necrosis, oil cyst formation, and calcifications can occur due to injection of large volumes into a single area or injecting fat into poorly vascularized areas resulting in failure of “graft take” with palpable mass formation resulting from fat necrosis which may be difficult to distinguish clinically from local recurrence in breast cancer patients and lead to a need for additional imaging and needle biopsy (3–15%). Moreover, post-lipofilling calcification can be found in mammogram (0.7–4.9%).
- Infection (0.6–1.1%).
- Under-correction or overcorrection of deformity.
- Damage to underlying structures, e.g., breast implants and pneumothorax.
- Intravascular injection with fat embolism.

39.3.2 Donor Site Complication

Complications appear to be minimal and related to liposuction technique. The possible complications include bruising, swelling, hematoma formation, paresthesia or donor site pain, infection, hypertrophic scarring, contour irregularities, and damage to underlying structure such as intraperitoneal or intramuscular penetration of the cannula.

39.4 Oncological Safety [4, 24–35]

Experimental studies have shown that adipocytes can stimulate breast cancer cells. Adipokines are factors that can stimulate breast cancerous cells through endocrine, paracrine, and autocrine pathways; theoretically, the “tumor stroma interaction" can potentially induce cancer reappearance by fueling dormant tumor cancer cells in the tumor bed. There is increasing evidence that obesity, an excess accumulation of adipose tissue occurring in mammalians when caloric intake exceeds energy expenditure, is associated with an increased frequency and morbidity of several types of neoplastic diseases, including postmenopausal disruption of the energy homeostasis results in obesity, inflammation, and alterations of adipokine signaling that may foster initiation and progression of cancer. Other recent studies, some of which are based on endogenous WAT expressing a transgenic reporter, showed a significant level of adipose cell contribution to tumor composition. However, WAT contains several distinct populations of progenitors, and these data were obtained using crude or mixed cell populations. We therefore decided to purify by sorting the two quantitatively most relevant populations of WAT progenitors (endothelial cells and adipose stromal cells, ASC) and to investigate in vitro and in vivo their role in several orthotopic models of local and metastatic breast cancer. Compared with bone marrow-derived CD34+ cells mobilized in blood by granulocyte colony-stimulating factor (G-CSF), purified human WAT-derived CD34+ cells were found to express similar levels of stemness-related genes and significantly increased levels of angiogenesis-related genes and of FAP-α, a crucial suppressor of antitumor immunity. In vitro, WAT-CD34+ cells generated mature endothelial cells and endothelial tubes. In vivo, the co-injection of human WAT-CD34+ cells contributed to tumor vascularization orthotopic and significantly increased tumor growth and metastases in models of human breast cancer in nonobese diabetic severe combined immunodeficient (NOD/SCID) interleukin-2 receptor γ (IL-2Rγ)-null (NSG) mice.

The oncological safety should be considered as a priority problem for lipofilling. Many studies are showing the safety of lipofilling such as the multicentric study (Milan-Paris-Lyon) performed by Petit et al. dealing with 646 lipofilling procedures performed on 513 patients. The average interval between oncologic surgical interventions and lipofilling was 39.7 months. Average follow-up after lipofilling was 19.2 months. They observed a low complication rate; the overall oncologic event rate was 5.6 percent (3.6 percent per year). The overall locoregional event rate was 2.4 percent. Petit et al. reported a retrospective matched cohort study on 321 consecutive patients operated for primary breast cancer who subsequently underwent lipofilling for reconstructive purpose. The median follow-up of 56 months from primary surgery and 26 months from the lipofilling had shown no significant local recurrence when compared to 642 patients as a control group. However, there is a trend of higher risk of local event in subgroup of ductal carcinoma in situ. In 2010, Rietjens et al. reported a series of lipofilling procedures in breast cancer treatment and reconstruction. They followed 158 patients and found that postoperative complication rates are very low (3.6 percent) and that there is little alteration in post-lipofilling mammographic finding (5.9%). Seth et al. made a retrospective comparative study on 886 patients (1202 breasts) from 1998 to 2008 and revealed no significant differences in demographics, operative characteristics, tumor staging, or radiation therapy exposure between fat grafting (n = 90 breasts) and nonfat grafting (n = 1112 breasts) patients. Ninety-nine fat-grafting procedures were performed an average of 18.3 months after reconstruction, with only one complication (fat necrosis); they concluded that fat grafting did not affect local tumor recurrence or survival when compared with nonfat-grafted breasts. In 2007, the French Society of Plastic Surgery (SOFCPRE) announced that that they would not support the use of lipofilling for treating defects resulting from breast-conserving treatment (BCT) as a result of the lack of evidence on its oncological safety. A phase III multicenter randomized, controlled trial is currently taking place in France with the goal of investigating this issue. Also the American Society of Plastic Surgeons had set up a task force in 2009 (ASPS Fat Graft Task Force) to assess the indications, the safety, and the efficacy of autologous fat grafting on 283 patients; it showed the risk of malignancy with lipofilling could not be identified due to lack of standardized techniques and randomized controlled trials. Even though lipofilling seems to be a safe procedure in breast cancer patients, longer follow-up and further experiences from large multicentric oncological series are urgently required to confirm these findings [38–41].

Conclusions

Lipofilling in breast cancer surgery can be performed as a day surgery procedure, and it has acceptable efficacy in correction of deformities without compromising oncological outcomes. Although an apparent increase of local recurrences was observed at the IEO in the intraepithelial breast cancer patients, two recent match-control studies showed the cancer safety of lipofilling [36, 37]. More studies are needed to confirm that the risk of stimulation of local recurrences observed in the experimental setting is not observed in breast cancer patients. Moreover, application of experimental and fundamental researches on tissue engineering and stem cells can carry more hopes to augment the role of lipofilling in the future.

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