



## Review

# Autologous fat grafting for postoperative breast reconstruction: A systemic review

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## ABSTRACT

Autologous fat grafting technology has become a new method for breast reconstruction after breast surgery due to its advantages of simple operation, low immunogenicity, fewer complications, high patient acceptance, and natural filling effect. However, the unpredictable fate of transplanted fat limits its widespread application. Currently, many studies have made certain progress in improving the survival rate of fat grafts. This article provides an overview of autologous fat grafting technology, including the mechanisms of fat graft survival, techniques for obtaining and transplanting adipose tissue, methods for enhancing graft survival, and complications associated with fat grafting.

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### 1. Introduction

The 2024 Cancer Statistics Report revealed that the estimated number of new cases of breast cancer was 310,720, ranking first among newly diagnosed cancers in women [1]. While surgical treatment remains the primary approach for breast cancer, it can result in postoperative breast tissue defects and contour abnormalities. Postmastectomy breast reconstruction can be used to achieve better cosmetic results, and more, help patients obtain physical integrity and psychological rehabilitation. The available techniques for breast reconstruction mainly include implants/expanders, autologous tissue flaps, and autologous fat. Among them, autologous fat grafting is noteworthy for its simplicity, natural appearance, high patient acceptance, and lower risk of complications. This makes it a promising option for breast tissue augmentation following breast-conserving surgery or lumpectomy. However, the unpredictable survival rate of fat grafts and the potential issues such as oil cysts, calcification, infection, and oncological safety restrict the widespread application of this technique. In recent years, more innovative strategies have emerged to improve the survival rate of fat grafts while reducing complications. This paper summarizes these research advancements in autologous fat grafting.

### 2. Methods

A thorough literature search was conducted to identify pertinent studies on fat grafting. PubMed database has been systematically searched for relevant animal and human research from inception to the year 2024. The medical subject headings (MeSH) terms and keywords searched included “breast reconstruction”, “fat grafting/engraftment/transplantation/transfer”, “fat transfer technique”, “fat graft enrichment”, “fat graft survival/retention”, “adipose-derived stem cell (ASC)”, “cell-assisted lipotransfer (CAL)”, “stromal vascular fraction (SVF)”, “platelet-rich plasma (PRP)”, “platelet-rich fibrin (PRF)”, “growth factor”, “oncological safety”, and “complications of fat injection”. The selection of relevant articles was based on an assessment of their titles and abstracts, as well as the reference lists of related articles (see Fig. 1).

### 3. Results

#### 3.1. Research background of autologous fat grafting

Over the past century, the practice of autologous fat grafting has continuously progressed and developed. The first traceable case of autologous fat grafting occurred in 1893 when Neuber, a German surgeon, successfully repaired a concave scar in the orbit using adipose tissue. Since then, researchers have been optimizing the grafting technique and refining the theoretical understanding of fat grafting, making it more clinically applicable. In the 1950s, Peer proposed the cell survival theory, suggesting that fat grafts can survive and maintain normal tissue structure under adequate blood perfusion [2]. Further studies indicated that adipocytes within a 2 mm range from the graft edge can receive sufficient nutrition through early neovascularization and survive, while larger volume of fat grafts are more prone to necrosis [3]. This suggests that increasing the contact area between the graft and the recipient site can reduce the rate of liponecrosis.

Subsequently, researchers observed that a majority of adipocytes die due to hypoxia and ischemia right after transplantation. The number of surviving adipocytes gradually decreases during the first six days and then starts to rebound from the seventh day onwards, revealing that the survival mechanism of adipose grafts involves not only adipocyte survival but also adipocyte regeneration [4,5]. The key cell for adipocyte regeneration is the adipose-derived stem cell (ASC). Zuk et al. [6] first isolated processed lipooaspirate cells (PLA) from adipose tissue and found that this fraction has the potential of multipotent differentiation, thus naming them adipose-derived stem cells (ASCs). With the in-depth study of ASCs, the graft replacement theory, proposed by Yoshimura, has gradually gained academic recognition. This theory suggests that adipocyte regeneration is the main mechanism for the survival of fat grafts. After transplantation, the adipose graft can be divided into three zones from the periphery to the center: the survival zone, the regeneration zone, and the necrosis zone. Except for the adipocytes in the survival zone (within 300 μm from the graft edge), all other adipocytes die within 24 h after transplantation and are phagocytosed by macrophages. Compared with adipocytes, ASCs

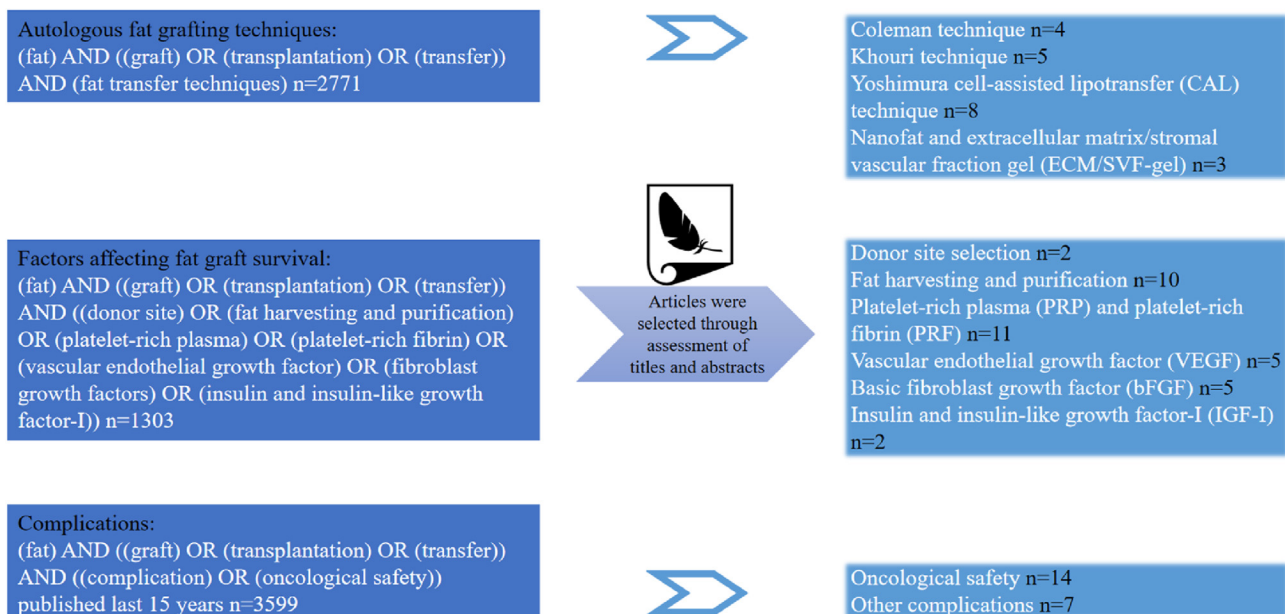


Fig. 1. The methodology of literature selection.

are more tolerant to hypoxia and ischemia. ASCs in the survival zone and regeneration zone can be activated by external signals such as hypoxia and adipocyte death. Then they proliferate and differentiate into adipocytes, which gradually replace the original necrotic adipose tissue. In the central necrosis zone, both adipocytes and ASCs die and are eventually replaced by fibrosis or oil cysts [7]. In addition, researchers have also demonstrated that ASCs, acting as “seeds,” may originate from both the donor and recipient by cross-transplanting normal mouse adipose tissue with green fluorescent protein (GFP)-expressing mouse adipose tissue [8].

In summary, the precise mechanism of fat graft survival after transplantation remains incompletely understood. Current understanding suggests that graft survival is dependent on the combined effects of neovascularization and adipose tissue regeneration. The absorption rate of fat grafts is influenced by various factors, ranging from 25 % to 80 % [9]. Further research into the mechanisms underlying fat graft survival is crucial for advancing autologous fat grafting techniques, improving graft survival rates, and enhancing clinical outcomes.

## 3.2. Autologous fat grafting techniques

### 3.2.1. Coleman technique

The most popular autologous fat grafting method is the Coleman technique. According to Coleman [10,11], different donor area has no bearing on the transplantation results. Therefore, Coleman typically selects the abdomen or inner thigh as the donor region because they are more practical and well-tolerated by patients. Local anesthesia is administered by injecting a tumescent fluid (0.5 % lidocaine and 1:200,000 epinephrine) in the same volume as the anticipated fat aspirate into the donor area. A 15 cm-long, 3 mm-diameter, blunt-tipped liposuction cannula is attached to a 10 ml syringe for liposuction. The harvested fat aspirate can be divided into three layers after centrifugation at 3000 rpm for 3 min. The upper layer (ruptured fat cells and oil) and the lower layer (water, blood, lidocaine, etc.) are discarded, while the middle layer (purified fat tissue) is used for transplantation. When injecting fat into the donor area, Coleman advocates using a 1 ml syringe connected to a 17-gauge blunt cannula and injecting fat into multiple tunnels. Further research has shown that purified fat from the Coleman procedure yields a higher number of fat cells with better cell function, resulting in superior transplantation outcomes compared to conventional liposuction [12,13]. The Coleman technique, which involves a minimally invasive approach to fat harvesting and injection, has standardized fat grafting techniques, improved the survival rate of fat graft, and demonstrated good repeatability, leading to its worldwide application.

### 3.2.2. Khouri technique

For breast reconstruction using the Coleman technique, it takes approximately 2 h to transplant 100 cc of fat, and each additional 100 cc of fat increases the surgical time by about 45 min, making it more suitable for small-volume fat transfer [13]. Khouri et al. [3,14] proposed the BRAVA external tissue expander for pre-expansion of the breasts. External expansion of the breasts can improve tissue compliance, increase the space for fat graft, and promote vascular formation, providing an ideal environment for fat transplantation. During fat harvesting, Khouri developed the Lipografter device, which uses a 12-hole, size 12 cannula to aspirate fat at a constant low pressure (300 mmHg). The harvested fat is then centrifuged at a rate of 15g for 2–3 min and subsequently injected into the recipient area using the same closed system in a reverse operation. The injection is performed using a size 14 single-hole cannula at a uniform rate of 0.1 ml/cm until the interstitial fluid pressure reaches 9 mmHg, at which point the injection is stopped. Multiple

studies have confirmed that pre-expansion with BRAVA can accommodate large-volume fat grafting while improving graft survival rates [15,16]. However, BRAVA wearing takes a long time and patients may give up due to pain or skin complications, failing to achieve the desired breast reconstruction results.

### 3.2.3. Yoshimura cell-assisted lipotransfer (CAL) technique

Adipose-derived stem cells (ASCs) possess self-renewal and multi-directional differentiation capabilities, playing an important role in the survival and regeneration of transplanted fat. The aspirated adipose tissue, although retaining the basic structure of adipose tissue, contains fewer ASCs and more destruction of adipocytes and capillaries than normal adipose tissue. Therefore, Yoshimura et al. [17] suggested that the low content of ASCs may be the main cause of necrosis after fat transplantation, and supplementation of ASCs in the graft may improve the survival rate of transplanted fat. The Cell-assisted lipotransfer (CAL) technique, proposed by Yoshimura, divides the aspirated fat into two parts. One part is digested with collagenase and then centrifuged to obtain the precipitate, which is the stromal vascular fraction (SVF) containing ASCs. The SVF is mixed with the other part of the aspirated fat and finally transplanted together to the recipient area. ASCs account for 10%–40 % of the nucleated cells in the SVF, and their mechanisms of improving graft survival may include [1]: undergoing adipogenic differentiation and participating in adipose tissue regeneration [2]; differentiating into endothelial cells to promote neovascularization and increase blood perfusion, thus improving graft survival [3]; secretion of hepatocyte growth factor (HGF) and other cytokines in response to hypoxia and injury signals, promoting angiogenesis and cell regeneration [4]; survival as primitive ASCs [6,18,19]. There are also a variety of cells in SVF including endothelial cells, smooth muscle cells, fibroblasts, and macrophages, which can interact with each other to spontaneously assemble into functional microvessels in vivo, promoting angiogenesis [20–22]. Kølke et al. [9] reported a triple-blind, placebo-controlled trial and found that ASCs-enriched fat grafts had a volume retention rate of over 80 % at 4 months post-transplantation, which was significantly higher than the control group. In conclusion, the CAL technique increases the survival rate of grafts by enriching ASCs, enhances the reliability of autologous fat grafting technology, and has great prospects for future applications. However, further research is still required to validate ASCs' tumor safety, and some academics consider they might encourage the occurrence and growth of tumors.

### 3.2.4. Nanofat and extracellular matrix/stromal vascular fraction gel (ECM/SVF-gel)

Nanofat is a liquid emulsion formed by emulsifying and filtering the fat obtained through liposuction with a 27G fine aperture needle [23]. Nanofat does not contain viable adipocytes and its adipose tissue structure is completely destroyed, but it still contains ASCs capable of proliferation and differentiation. Yu et al. [24] performed co-transplantation of nanofat and aspirated fat and found that the co-transplanted group had better preservation of fat volume, histological structure, and capillary density compared to the control group, suggesting that nanofat can improve graft survival by promoting angiogenesis.

Yao et al. [25] concluded that the concentration of ASCs in nanofat is low and the contained fragmented adipocytes may cause inflammatory reactions after transplantation. Therefore, they further investigated and prepared an extracellular matrix/stromal vascular fraction gel (ECM/SVF-gel) based on nanofat. The ECM/SVF-gel removes the oily components and is rich in adipose stem cells and vascular endothelial cells, which have therapeutic effects on wound healing and tissue repair. Currently, nanofat and ECM/

SVF-gel are promising tissue engineering fillers mainly used for facial injection and skin rejuvenation, and their application in breast augmentation still requires further exploration.

### 3.3. Factors affecting fat graft survival

#### 3.3.1. Surgical techniques

Various factors, such as donor site selection, fat harvesting, fat purification, transplantation methods, recipient site conditions, and postoperative management, can influence the survival rate of transplanted fat. Currently, there is a lack of standardized clinical operating protocols, and higher-quality studies are strongly awaited.

**3.3.1.1. Donor site selection.** Common donor sites for fat grafting include the abdomen, thighs, buttocks, and other areas. It is currently unclear whether there are differences in the survival rates of fat grafts from different donor sites. Most studies found no significant differences in the quality, volume, and histological evaluation of fat from different donor areas after transplantation [26]. Some researchers have also taken a different attitude, suggesting that the lower abdomen and inner thigh adipose tissue have a higher concentration of adipocytes and are superior donor areas [27]. The ideal site for autologous adipose tissue harvesting has not been clearly established. Therefore, when selecting the donor site, physicians should communicate extensively with the patient and choose a site rich in fat, unlikely to cause deformities in the donor area, and more acceptable to the patient.

**3.3.1.2. Fat harvesting and purification.** The tumescent anesthesia and liposuction in negative pressure are commonly used to obtain adipose tissue. Tumescent anesthesia, first introduced by Klein, is a significant breakthrough in autologous fat grafting techniques. It involves local anesthesia by injecting tumescent fluid (a diluted solution of lidocaine and epinephrine) into the donor area. Most studies suggested that tumescent fluid does not affect the viability of ASCs and the transplantation outcomes [28]. Other studies found that short-time (<2 h) and low-concentration (<1.6 mg/mL) exposures had little effect on the viability of ASCs, while the cytotoxic effects of lidocaine increased with increasing dose and exposure time [29]. Although tumescent anesthesia may impair the differentiation capacity of ASCs, thus affecting the outcome of fat grafting, it is currently a more recommended method due to its advantages of precise liposuction and fewer complications compared to Illouz's 'wet technique' (injection of a low osmolarity solution containing hyaluronidase prior to liposuction) and Fournier's 'dry technique' (both requiring general anesthesia for liposuction).

Liposuction techniques include manual syringe liposuction, ultrasound-assisted liposuction (UAL), power-assisted liposuction (PAL), water jet-assisted liposuction (WAL), and laser-assisted liposuction (LAL). The most commonly used method is manual syringe liposuction, in which the selection of an appropriate-sized liposuction cannula and the application of appropriate negative pressure are crucial for maintaining the viability of adipocytes. Several studies have shown that a larger cannula size can better maintain the viability of adipocytes and increase the retention rate of transplanted fat. However, the optimal cannula size is still under exploration [30]. Additionally, the negative pressure during aspiration is a major factor causing cell damage. Researchers have demonstrated that pressure of  $-700$  mmHg can cause more than 10 % cell damage during vacuum collection. A lower negative pressure (e.g.,  $-250$  mmHg) can minimize the shear forces exerted on adipocytes, thereby maintaining cellular integrity [31].

The fat obtained from aspiration cannot be directly transplanted. It requires purification to remove inactive cells, fragmented oil droplets, local anesthetics, blood, etc. Purification of fat serves two purposes: it avoids unnecessary inflammatory reactions that may occur at the recipient site, and it maximizes the proportion of intact adipocytes and ASCs in the fat graft, thereby increasing the graft's survival rate. Purification techniques for fat include sedimentation, filtration, gauze or cotton pad adsorption, centrifugation, etc. Currently, there is no consensus on the optimal purification method. Many studies have concluded that no significant differences were found between the different treatment methods in terms of adipocyte viability and graft volume [32,33]. Among them, centrifugation is the most widely used due to its convenience and ability to achieve more precise stratification of the aspirate. Centrifugation separates the aspirate into four distinct layers: the top layer is made up of ruptured fat cells and oil, the second layer is the purified fat suitable for grafting, the third layer consists of water, blood, and local anesthetics, and the bottom layer contains stromal vascular fraction (SVF) with ASCs [34]. The classic Coleman method of centrifugation at 3000 rpm for 3 min has shown good transplantation results. However, an increasing number of studies have found that higher centrifugation speeds can cause cell damage. Ferraro et al. [35] showed that centrifugation at speeds greater than 500 rpm disrupts the structural integrity of adipose tissue, increases cell necrosis and apoptosis, and reduces the differentiation capacity of stem cells. They concluded that centrifugation at 1300 rpm for 5 min compared to the Coleman method, reduces the number of damaged cells while preserving the phenotype and differentiation capacity of stem cells. Hoareau et al. [36] recommended centrifugation at 400g for 1 min, as higher centrifugal forces result in excessive adipocyte death, while lower forces may not effectively remove inflammatory substances, leading to local inflammation after transplantation. This is consistent with the findings of Palumbo et al. [37], who compared different centrifugation conditions and found that centrifugation at 400g for 3 min yields highly active ASCs and adipocytes. Currently, most studies are limited to in vitro and animal experiments, and the conclusions of different researchers vary. Therefore, the most appropriate methods for fat harvesting and purification remain to be explored.

#### 3.3.2. Effect of different additives

**3.3.2.1. Platelet-rich plasma (PRP) and platelet-rich fibrin (PRF).** Platelet-rich plasma (PRP) is autologous plasma with a platelet concentration higher than baseline, typically obtained through secondary centrifugation of whole blood [38]. It is now a promising adjuvant therapy for the treatment of diabetic foot ulcers, musculoskeletal disorders, and osteoarthritis [39,40]. Activation of platelets in PRP can be achieved by adding thrombin, calcium chloride, and other substances. Then platelet alpha granules and dense bodies release platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF- $\beta$ ), vascular endothelial growth factor (VEGF), epithelial growth factor (EGF), and other growth factors, collectively promoting wound healing [41]. In autologous fat grafting, the graft initially survives on nutrients diffused from plasma. Subsequently, the dynamic changes in adipocyte death and regeneration determine the fate of the graft. Several studies suggest that the addition of PRP to autologous fat grafts can improve graft survival. Researchers speculated that the possible mechanisms include: direct nutrient supply from the plasma component of PRP, release of various growth factors by PRP to promote angiogenesis, ASCs proliferation and differentiation, and inhibition of apoptosis [41–44]. Gentile et al. demonstrated that the addition of PRP to fat grafts improved soft tissue defects in the breast. One year after transplantation, the maintenance rate of

breast volume was 69 % in the PRP group compared to only 39 % in the control group, and the results were statistically significant [45]. However, some scholars hold different opinions. A retrospective study found that adding 10 % PRP to fat grafts did not outperform standalone Coleman fat grafting [46]. The PRP concentration and activation methods used in different studies varied, and there is no unified standard for the preparation of PRP, which may contribute to the conflicting research results. Currently, the appropriate ratio of PRP to fat is still being explored. Besides, the use of PRP in combination with fat grafting for breast reconstruction would require the extraction of large amounts of blood and is therefore not recommended for clinical use.

Platelet-rich fibrin (PRF), also known as the second-generation PRP, was first described by Choukroun. After collecting the blood sample, it is immediately centrifuged at a speed of 3000 rpm (approximately 400g) for 10 min. The middle layer in the test tube, which contains fibrin clots with serum and platelets, is the PRF. Similar to PRP, PRF contains a large amount of growth factors, which may improve the survival rate of fat grafts by promoting angiogenesis and adipogenesis, while inhibiting cell apoptosis [47]. Considering that a high proportion of PRF also requires a large amount of blood, Yu et al. [48] suggested that a mixing ratio of 1:10 between PRF and fat ensures a higher graft retention rate while being more suitable for clinical application. Compared to PRP, the preparation process of PRF does not require the addition of anti-coagulants or thrombin, making it more convenient to handle and reducing the risk of immune rejection and allergic reactions. Furthermore, multiple growth factors in PRF are trapped within the fibrin mesh, allowing for slow and sustained release, and providing a more stable and long-lasting effect.

In summary, although there are reports in the literature on the role of PRP and PRF in promoting fat transplantation results, further exploration is needed to understand their specific mechanisms.

**3.3.2.2. Vascular endothelial growth factor (VEGF).** Vascular endothelial growth factor (VEGF) is a secreted mitogen for endothelial cells. There is ample evidence to demonstrate that VEGF is involved in physiological and pathological angiogenesis. The typical signaling pathway of VEGF involves the binding of VEGF-A to VEGFR1/R2, which regulates various kinase activities, guiding processes such as cell proliferation and migration [49]. Therefore, it is reasonable to believe that VEGF can promote post-transplant vascularization and improve graft survival. Yu et al. [50] transfected ASCs with modRNA encoding VEGF and found that modVEGF-engineered ASCs exhibited a stronger capacity for proliferation and angiogenesis, resulting in higher graft preservation rates, while significantly reducing ischemia-induced fibrosis, apoptosis, and necrosis. In addition, ASCs were able to secrete VEGF under external stimuli such as hypoxia and oxidative stress. The secreted VEGF promotes the proliferation, differentiation, and migration of ASCs through autocrine effects, and it also binds to the VEGF receptor to exert paracrine effects, promoting angiogenesis and anti-apoptosis functions [51]. It has been reported that incorporating VEGF into fat grafts using multiple biomaterial approaches can increase graft survival [52,53].

**3.3.2.3. Basic fibroblast growth factor (bFGF).** Fibroblast growth factors (FGFs) are heparin-binding growth factors that can interact with various endothelial cell surface receptors to promote angiogenesis [54]. Among the FGF family, FGF2, also known as basic fibroblast growth factor (bFGF), has been extensively studied and shown to play a role in tissue repair and wound healing [55]. Lu et al. [56] suggested that bFGF may promote adipogenic differentiation of ASCs through the PI2K/Akt signaling pathway. Interestingly, Kawaguchi et al. [57] found that injection of matrix gel with

bFGF alone induced significant adipogenesis. This may be due to the extensive distribution of precursor adipocytes in connective tissue, where endogenous precursor adipocytes actively migrate into stromal gel and differentiate into adipocytes after bFGF-induced angiogenesis. Several animal experiments have also shown that ASCs combined with bFGF can improve the vascularization of fat grafts and increase graft survival rates [58].

**3.3.2.4. Insulin and insulin-like growth factor-I (IGF-I).** Insulin and Insulin-like Growth Factor-I (IGF-I) regulate cell proliferation and differentiation and can mediate the differentiation of precursor adipocytes into mature adipocytes through the IGF-I receptor (IGF-IR) [59]. Yuksel et al. [60] evaluated the long-term local delivery of insulin and insulin-like growth factor-I (IGF-I) and its impact on fat graft. They found a significant increase in the volume of the surviving grafts, but no significant difference compared to the group with added bFGF and other growth factors. Further research is still needed to explore the effects of IGF-I on autologous fat transplantation.

### 3.4. Complications

#### 3.4.1. Oncological safety

Recent studies have indicated that adipocytes and ASCs are involved in the progression of breast cancer, raising concerns about their application in post-mastectomy breast reconstruction. While ASCs play a crucial role in enhancing fat graft survival, a number of studies have revealed that ASCs may also have pro-tumorigenic properties. Paino et al. [61] co-cultured MCF-7 breast cancer cells with human adipose-derived stem cells (hASCs) and found increased proliferation in the co-culture group. Animal experiments showed that injecting MCF-7 cells and hASCs together into nude mice subcutaneously resulted in larger tumor size, faster growth, and increased tumor vascularization compared to MCF-7 cells alone. Research by Orbay et al. [62] also demonstrated a significant increase in the migration rate of breast cancer cells when co-cultured with ASCs. Kamat et al. [63] found that ASCs had different effects on tumor progression and metastasis in different types of breast cancer cells, but phenotypic switching was observed in both MDA-MB-231 and MCF-7 breast cancer cell lines, leading to a more aggressive and proliferative phenotype. This may be due to the fact that some cytokines secreted by ASCs that promote tissue regeneration and angiogenesis facilitate not only the survival of adipose grafts but also the growth and metastasis of tumor cells. Wang et al. [64] suggested that hASCs promote angiogenesis and proliferation of estrogen receptor alpha-positive (ER $\alpha$ +) tumor cells by secreting pro-angiogenic factors CXCL1 and CXCL8, thus exerting a pro-carcinogenic effect. Reggiani et al. [65] found that GM-CSF and MMP9 were upregulated in white adipose tissue progenitor cells co-cultured with breast cancer cells, and inhibiting GM-CSF and MMP9 could reduce tumor growth and metastasis. Fajka-Boja et al. [66] proposed that ASCs may promote tumor cell proliferation by upregulating IGF-I secretion. In addition to the above research, there are no human trials to support the oncological safety of ASCs due to ethical concerns, and additional compelling evidence is required to substantiate its safety. The oncological safety of traditional fat grafting has also been questioned, but animal experiments and clinical studies suggest that the transplantation of fat tissue alone does not increase the risk of breast cancer recurrence in patients. Tsuji et al. [67] designed two animal experimental schemes to evaluate whether fat grafting supports the growth of tumor cells and to simulate fat grafting in a tumor microenvironment. The results indicated that fat grafting did not induce breast cancer cell growth and might even have inhibitory effects. Petit et al. [68,69] found that the risk of local or distant

recurrence did not increase in invasive breast cancer patients after fat grafting, but patients with ductal intraepithelial neoplasia (DIN) or lobular intraepithelial neoplasia (LIN) had a higher risk of developing local events (including local recurrence, regional recurrence, and local recurrence with distant metastasis). Semprini et al. [70] suggested that Petit's data may be related to the multifocality of ductal carcinoma in situ, where some undetected tiny lesions lead to tumor recurrence, highlighting the need for more precise imaging and pathological examinations. Generally, the majority of researchers believe that autologous fat grafting is safe. Krastev et al. [71], through a 5-year follow-up, found no statistically significant difference in local recurrence and distant metastasis rates between patients who underwent autologous fat grafting and the control group. Several clinical studies have also indicated that autologous fat grafting does not increase the risk of postoperative local recurrence and distant metastasis in breast cancer patients undergoing breast-conserving surgery or modified radical mastectomy [72–74].

### 3.4.2. Others

Common complications after traditional autologous fat grafting are mostly related to fat necrosis. The dead adipocytes release oil droplets, a small amount of which can be absorbed, and those that are not completely absorbed are phagocytosed by M1 macrophages and later surrounded by M2 macrophages to form fibrous cyst walls, eventually leading to the formation of oil cysts and calcifications [5,75]. Oil cysts and calcifications can cause palpable nodules and changes in breast imaging, which some experts believe can not only cause anxiety in patients but also interfere with breast cancer screening. Veber et al. [76] compared X-ray images of breasts before and after traditional fat grafting and found no statistically significant differences in the results using either the American College of Radiology classification or the personalized rating system. Most experts indicate that the radiological findings after traditional fat grafting are similar to images after any other type of breast surgery and have some features such as “eggshell-like” calcifications, which can differentiate them from breast tumors and have no impact on radiological follow-up [77]. Other relatively rare complications after traditional autologous fat grafting include infection, hematoma, abnormal breast secretions, pneumothorax, tissue necrosis caused by fat embolism, blindness, and cerebral infarction [78–80].

## 4. Summary and outlook

Autologous fat grafting technology has broad prospects in clinical applications, particularly in breast reconstruction after breast surgery. Although it offers clear benefits, challenges remain, such as variable graft survival rate and the lack of standardized techniques. Ongoing research is expected to improve fat grafting outcomes, further standardize the procedure, and expand its clinical application.

This paper discusses novel strategies in this field. First, we talked about the mechanism of fat graft survival after transplantation and recognized the important role of ASCs. Second, based on the Coleman technique, recent advances in autologous fat grafting techniques focus on the different additives, especially ASCs, to promote fat graft survival and achieve a certain degree of success. However, more robust evidence of the safety and efficacy of the additives is required. Last but not least, the absence of standard concentrations and procedures for applying ASCs in fat grafting leads to varied outcomes, which makes it challenging to draw comparisons between the results of different studies. Our research group is also investigating the optimal concentration of ASCs in the

hope of contributing to a standardized procedure and clinical application of ASCs-enriched fat grafting.

In conclusion, evidence-based practice and ongoing research are crucial for optimizing fat grafting techniques and improving patient outcomes. Despite the present challenges, the prospects offered by nascent technologies will contribute to a promising future for autologous fat grafting.

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## Declaration of competing interest

We have no conflicts of interest to disclose.

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