Research Advances in Cell-Assisted Lipotransfer for Facial and Breast Surgery

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Mingtu Du[1], Haiyan Qin[1], Lianbo Zhang[1]

[1]Department of Plastic Surgery, China-Japan Union Hospital of Jilin University, 130033 Changchun, Jilin, China

Cell-assisted lipotransfer (CAL) is an advanced fat grafting technique in which adipose tissue is enriched with regenerative cellular components, most frequently stromal vascular fraction (SVF) or adipose-derived stem cells (ADSCs). This approach is intended to enhance the survival and structural stability of conventional fat grafts, thereby improving outcomes in soft-tissue augmentation and regeneration. By supporting early vascularization, reducing postoperative resorption, and enhancing long-term volume retention, CAL may also improve skin quality and local tissue remodeling. Nevertheless, key challenges remain, including the lack of standardized processing protocols, uncertainty about long-term safety, inadequate consensus on optimal cell dosing, and the need for clear regulatory guidelines. This review outlines the technical basis of CAL, presents the preparation and proposed mechanisms of its key bioactive components, including SVF, ADSCs, and platelet-rich plasma (PRP), and systematically examines recent clinical evidence for its application in facial rejuvenation and contour enhancement, as well as breast reconstruction and augmentation. Overall, the aim is to provide a foundation for developing standardized clinical protocols for CAL.

Keywords: cell-assisted lipotransfer; stromal vascular fraction; adipose-derived stem cells; facial rejuvenation; breast reconstruction; tissue engineering

Introduction

Autologous fat grafting is widely known as a fundamental technique for the reconstruction of soft tissue defects and for volume augmentation and aesthetic refinement in facial and breast regions, owing to the ready availability of donor tissue, excellent biocompatibility, and natural outcome [1]. However, conventional lipotransfer (CLT) is limited by a variable and substantially high rate of postoperative fat resorption [2]. This unpredictable volume loss usually requires repeated grafting sessions, thereby presenting a significant clinical challenge.

Advances in tissue engineering and regenerative medicine have led to the development of cell-assisted lipotransfer (CAL) [3]. Fundamentally, CAL is based on the principle of transforming fat graft from passive fillers into a biologically active, regenerative biomaterial enriched with viable cellular components [4]. This is achieved by supplementing harvested fat with adjunctive bioactive agents. These active components include stromal vascular fraction (SVF), a heterogeneous cell mixture typically obtained through enzymatic digestion (and processing such as centrifugation) of autologous adipose tissue, and *in vitro*-expanded adipose-derived stem cells (ADSCs) or platelet-rich plasma (PRP) [5]. The addition of these components is intended to enhance revascularization, suppress inflammatory and apoptotic pathways, and promote the survival and regenerative capacity of adipocytes and their precursor cells [6]. Collectively, these effects aim to improve graft retention, overall procedural efficiency, and long-term volume stability.

This article comprehensively outlines the underlying experimental evidence, clinical translation, and current applications of CAL in facial and breast surgery and presents key challenges and future perspectives for the field.

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Correspondence to: Lianbo Zhang, Department of Plastic Surgery, China-Japan Union Hospital of Jilin University, 130033 Changchun, Jilin, China (e-mail: lianbo@jlu.edu.cn).
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Core Techniques and Biological Rationale of CAL

Major Cellular/Bioactive Components

This manuscript focuses on three major bioactive agents, including stromal vascular fraction (SVF), adipose-derived stem cells (ADSCs), and platelet-rich plasma (PRP).

SVF is a heterogeneous cell population that can be rapidly isolated from adipose tissue, usually through enzymatic digestion (typically collagenase), followed by centrifugation [6]. Standard protocols centrifuge at about 800–1200 ×g for 5–10 minutes to isolate an SVF pellet, though optimal parameters remain inconsistent across studies, and alterations in processing can significantly affect cell yield and viability [7]. Similarly, collagenase digestion times vary widely (approximately from 30 to 90 minutes); longer ex-

posure may increase cell yield, but excessive enzymatic stress can potentially impair cell function. These technical variations continue to complicate efforts toward SVF standardization. As the most frequently utilized cellular adjunct in CAL, SVF contains ADSCs, endothelial progenitor cells, hematopoietic cells, lymphocytes, and other stromal components [8]. A key advantage is that SVF can be used immediately, without *in vitro* expansion, which minimizes the risks of contamination and may preserve inherent intercellular synergies. After combining SVF with processed lipoaspirate and allowing brief contact, the SVF-enriched graft is ready for transplantation. Current evidence indicates that SVF enhances graft survival through complementary mechanisms: (1) secretion of pro-angiogenic mediators such as vascular endothelial growth factor (VEGF) and hepatocyte growth factor (HGF) [9]; (2) direct participation in neovascular formation through differentiation and vascular integration [10]; and (3) anti-apoptotic, anti-inflammatory, and immunomodulatory effects that are predominantly mediated through paracrine signaling [11].

ADSCs are the central functional component of SVF, combining multipotent differentiation potential with robust paracrine activity [12]. These cells are typically isolated by culturing freshly obtained SVF; sequential media changes eliminate non-adherent hematopoietic cells, yielding a purified population of adherent ADSCs [13]. These cells can then be expanded *in vitro* to achieve higher cell numbers before being combined with aspirated fat graft, producing an ADSC-enriched autologous transplant.

The precise mechanisms by which ADSCs enhance graft retention in CAL remain to be defined [14]. Current hypotheses include: (1) direct differentiation into functional adipocytes, thereby contributing to de novo adipose tissue formation; (2) stimulation of fibroblast proliferation and enhancement of adipogenic and endothelial lineage commitment; (3) secretion of cytokines and growth factors that support angiogenesis and graft retention; (4) production and remodeling of extracellular matrix components that facilitate structural integration; and (5) creation of a supportive, tissue-like microenvironment that functions as a biologically active scaffold for resident cells [15–17]. However, ADSC isolation and expansion are time-consuming and costly, and they fall under more stringent regulatory oversight as it qualifies as a cell-based therapeutic product [18].

Furthermore, PRP is an autologous blood-derived product enriched in platelets, obtained by centrifugation of whole blood to achieve supraphysiological platelet concentrations [19]. It contains a variety of growth factors, including platelet-derived growth factor (PDGF), transforming growth factor-β (TGF-β), and VEGF [20]. When used as an adjunct to, or alternative for, SVF/ADSC enrichment in CAL, PRP is proposed to recapitulate early wound healing [21]. By releasing platelet-stored bioactive factors, PRP primarily stimulates angiogenesis, enhances cellular proliferation, and improves the peri-graft microenvironment, thereby supporting survival and integration.

Main Technical Strategies

In 2006, Matsumoto *et al*. [22] were the first to introduce the application of ADSCs in fat grafting practice, demonstrating that enriching grafts with biologically active components such as ADSCs, SVF, PRP, or VEGF could substantially enhance survival outcomes. Subsequent clinical follow-up studies with observation periods of 12–19 months reported that CAL improved fat survival rates from approximately 24%–51.4% with CLT to 63%–90.4% [23,24]. Alongside these clinical findings, advances in tissue engineering and regenerative medicine have led to more refined adipose tissue processing approaches. Mechanical emulsification and optimized centrifugation strategies enable efficient removal of free oil droplets and damaged cellular debris, resulting in a concentrated preparation usually known as SVF-gel. This preparation contains a high-density, high-purity composite of SVF cell clusters and extracellular matrix. Compared with conventionally processed lipoaspirate, SVF-gel exhibits a significantly higher stem cell content, demonstrates enhanced post-injection volume retention, and has a finer, more homogeneous texture, rendering it particularly well-suited for precise grafting in anatomically delicate areas.

Research Advances in Facial Surgery Applications

Facial applications demand high precision, natural aesthetics, and skin quality enhancement, domains in which CAL demonstrates distinct advantages. Overall, CAL tends to deliver more reliable and consistent outcomes in facial procedures than in breast surgery, a difference likely due to smaller graft volumes and the presence of richly vascularized recipient tissues in the face.

Facial Rejuvenation

A meta-analysis including 722 patients demonstrated that fat graft survival rate with CAL was significantly higher than with the conventional grafting group (non-CAL group), with a standardized mean difference (SMD) of 2.81 (95% Confidence Interval (CI) 1.54–4.08, $p < 0.01$) [25]. Notably, overall complication rates were comparable between the CAL and CLT groups (Relative Risk (RR): 0.95, 95% CI 0.50–1.81), and the likelihood of requiring secondary surgery did not differ significantly (RR: 0.52, 95% CI 0.03–0.82). In a randomized study by Wufuer *et al*. [26], CAL was employed for facial volume augmentation. Twenty-three participants were enrolled for autologous fat transfer to the face and randomly assigned to the experimental (CAL) (n = 11) or control (CLT) (n = 12) group. The CLT group underwent standard CLT, whereas the CAL group received centrifuged fat (middle layer) supplemented with autologous SVF isolated using the PIOGEN-I sys-

tem. Mean injection volumes were 18.38 ± 1.65 mL (forehead), 10.32 ± 1.66 mL (temples), and 15.80 ± 2.00 mL (cheeks), with an average SVF concentration of 1.57 ± 0.33 × 10^6 cells/mL. No complications were reported in either group. Graft survival was quantified using MRI at 6 and 24 weeks postoperatively. MRI-based assessment revealed higher overall facial graft survival in the CAL group than the control group, 74.5% vs. 66.55% at 6 weeks; 71.27% vs. 61.98% at 24 weeks, confirming a significant improvement in retention with SVF supplementation ($p < 0.05$). Although the forehead generally showed lower retention than the temples and cheeks, CAL still resulted in significantly better forehead survival compared to CLT at both time points ($p < 0.05$). Conversely, temple and cheek retention was high in both groups, with no substantial intergroup difference, likely indicating comparatively favorable vascularity of these recipient sites.

Similarly, in a split-face comparative study, CLT and CAL were evaluated for temple augmentation in middle-aged women [24]. At 6 months follow-up, ultrasound biomicroscopy was used to assess the temple volume scale (TVS). Patient satisfaction and local sequelae, such as lumps, edema, and bruising, were comparable on both sides ($p = 1.000$). Although TVS decreased significantly in both groups (0.5 ± 0.5 vs. 1.1 ± 0.7, $p = 0.0001$), the CAL-treated side exhibited a considerably greater percentage increase in subcutaneous thickness/augmentation (70.92 ± 58.09% vs. 18.93 ± 19.33%, $p = 0.001$), indicating superior volume retention with CAL at 6 months. Furthermore, emerging evidence suggests that SVF concentration may be a crucial determinant of clinical effects. High SVF concentration (approximately 60–80%) appears to promote active adipose regeneration, making it particularly useful for correcting deeper facial depressions, whereas lower enrichment levels (about 20–40%) may predominantly support graft retention by enhancing survival and revascularization [27].

Facial Contour Remodeling

Autologous fat grafting is a primary treatment modality for type I and II facial hemiatrophy because donor tissue is readily available and the procedure is relatively minimally invasive [28]. In a comparative analysis, adipose tissue and ADSCs were harvested from 15 patients with facial hemiatrophy and 15 healthy controls and then transplanted into nude mice to evaluate adipocyte survival [29]. ADSCs obtained from affected individuals demonstrated reduced proliferation and migration, increased apoptosis, and alleviated tolerance to glucose-oxygen deprivation compared with ADSCs from healthy donors. The survival rate of fat grafts derived from patients was 27.44%, whereas ADSC-assisted grafting significantly increased retention to 40.66%, supporting the efficacy of CAL for managing facial hemiatrophy.

In another clinical study, Cao Z *et al*. [30] used centrifuged SVF-gel for facial augmentation in 13 patients with hemiatrophy. Long-term follow-up revealed satisfactory aesthetic contour and soft tissue consistency in the augmented regions. The study suggested that SVF-gel may outperform CLT for large-volume restoration and underscored that excess SVF-gel can be cryopreserved for subsequent sessions, potentially avoiding repeat liposuction for later treatments.

Scar Repair and Skin Regeneration

The regenerative potential of CAL has drawn considerable interest in treating acne scars and post-traumatic atrophic scars. Beyond simple volume replacement, stem cells within enriched grafts can modulate collagen metabolism and stimulate dermal remodeling through paracrine signaling, which may enhance scar texture, color uniformity, and elasticity while restoring volume in depressed regions. Currently, scar revision is commonly conducted using either vascularized tissue flaps or autologous fat grafting. Although flap reconstruction can be effective, it is generally more invasive and technically complex. Fat grafting offers a comparatively simpler and less invasive alternative that avoids additional donor-site scarring and is therefore often preferred in appropriate cases.

Emerging evidence indicates that ADSC-enriched CAL may provide additional benefits through immunomodulation and improved local tissue perfusion, potentially enhancing graft survival, downregulating TGF-β signaling, and suppressing fibroblast hyperplasia. In a prospective observational study of 60 patients with facial scars, Rao *et al*. [31] reported measurable improvements in scar quality and contour restoration following CAL. Similarly, in a prospective cohort of 25 subjects with facial atrophic scars, Gu *et al*. [32] reported significant reductions in scar assessment scores across multiple parameters, including color, stiffness, thickness, irregularity, and pigmentation after CAL treatment. These findings preliminarily support CAL as a safe and viable strategy for facial scar treatment, although the limited sample size warrants cautious interpretation.

Recently, the focus has increasingly shifted toward the use of highly processed adipose products such as SVF-gel and nano-fat, administered intradermally or into the superficial subcutaneous plane. This refined approach is aimed less at bulk augmentation and more at enhancing skin quality, reducing fine wrinkles, and softening neck lines, effectively repositioning fat grafting as a modality oriented toward cellular therapy. Consistent with this idea, Yin *et al*. [33] compared CAL (n = 25) with conventional lipotransfer (CLT, n = 25) for facial augmentation and reported, using VISIA complexion analysis at 6 months, that CAL exhibited greater improvement across multiple skin quality parameters, including spots, wrinkles, texture, pores, UV spots, brown spots, erythema-related red areas, and porphyrins.

Research Advances in Breast Surgery Applications

Breast surgery demands substantial large-volume restoration, smooth tissue integration and sustained long-term safety. Compared with implant-based strategies, autologous fat grafting yields a soft and natural texture, eliminates the risks such as implant rejection and capsular contracture, and avoids visible incision scars. In recent years, CAL has been widely adopted for both aesthetic breast augmentation and post-mastectomy breast reconstruction.

Breast Reconstruction

In patients with contour deformities following breast-conserving surgery, or in those undergoing reconstruction after total mastectomy, CAL may offer a dual benefit: it can restore breast volume and shape while leveraging regenerative effects to ameliorate radiation-related complications, such as chest-wall fibrosis, skin contracture, and associated pain [34,35]. Jeon *et al*. [36] conducted a prospective controlled study involving 20 patients with volume deficiency and asymmetry after initial breast reconstruction with rectus abdominis or latissimus dorsi flaps. Participants were divided into two groups: SVF-assisted fat grafting or CLT alone. Abdominal fat was harvested and centrifuged in both groups; in the SVF group, stromal vascular fraction was additionally isolated using collagenase type I and mixed with the processed fat before subcutaneous injection, whereas the CLT group received fat alone. Aside from one case of fat necrosis in each group, no other major complications occurred. Three-dimensional volumetric assessment conducted preoperatively and at 1, 6, and 12 months postoperatively demonstrated significantly higher graft retention with SVF enrichment: 73.8% at 6 months and 65.4% at 12 months compared to 62.2% and 48.4% in the CLT group, respectively ($p < 0.05$). Overall, these findings support SVF supplementation as an effective approach to enhance graft survival in post-reconstruction breast surgery.

Safety remains a major concern when using CAL for patients with a history of breast cancer. *In vitro* and preclinical studies have indicated that ADSCs can support tumor proliferation and metastasis through paracrine signaling, particularly when residual or subclinical disease is present [5]. However, emerging evidence suggests that when ADSCs are delivered as part of a fat graft (as in CAL), the surrounding adipose microenvironment may mitigate these effects by sequestering soluble mediators and limiting the effective local stem cell concentration [37]. To date, clinical studies have not shown a consistent increase in recurrence risk, although long-term follow-up remains limited. Strategies to enhance safety include thorough oncologic assessment before treatment, avoiding CAL in patients with active malignancy, and favoring minimally manipulated cellular products (such as freshly isolated SVF) over culture-expanded ADSCs to minimize *ex vivo* manipulation. Furthermore, postoperative calcifications and nodules resulting from fat grafting can mimic malignancy on breast imaging, potentially complicating early detection.

In contrast, Challapalli *et al*. [38] concluded that, based on currently available clinical evidence, CAL does not appear to increase breast cancer recurrence risk and may offer improved aesthetic outcomes with greater long-term volume retention. Consistent with this, a systematic review of seven studies indicated no significant increase in tumor recurrence among breast cancer patients undergoing CAL, including those who had received radiotherapy. In terms of aesthetic and functional outcomes, CAL demonstrates advantages such as higher long-term volume retention and improved contour. However, compared with non-irradiated patients, irradiated breast tissues undergoing CAL reconstruction often require larger graft volumes and are associated with relatively lower graft survival rates [39].

Breast Augmentation

For patients undergoing autologous fat grafting for breast augmentation, CAL has been proposed as a strategy to reduce the number of sessions required to achieve the targeted volume. Previous studies suggest that CAL may allow a modest increase in the volume of fat grafted per session, while making postoperative resorption more consistent and therefore easier to manage, ultimately supporting the development of soft, natural-appearing breast contours [40–42]. Additionally, complications such as cyst formation and fat liquefaction appear to be declining compared with traditional grafting methods. In a study by Yoshimura *et al*. [43], 40 patients were randomized to receive either CAL or CLT. The CAL group demonstrated significantly higher volume retention and greater patient satisfaction at 6 months ($p < 0.05$), suggesting that CAL is a particularly preferred approach for breast augmentation.

Conversely, several studies have reported that SVF-based CAL offers no statistically significant improvement in volume retention compared to CLT and does not consistently reduce the number of grafting sessions needed. For instance, a study compared CLT in 105 women (Group A) with SVF-based CAL in 101 women (Group B) [44]. Employing postoperative 3D laser scanning at 12 months, the mean retained breast volumes were 324.1 mL in Group A (67.9% survival) and 334.6 mL in Group B (68.7% survival), with no significant difference between groups ($p < 0.05$). These results do not support the routine use of CAL for breast augmentation, particularly because CAL often requires harvesting larger donor volumes and increases procedural costs, which are practical limitations in lean patients with limited adipose reserves.

Subgroup analyses from recent meta-analyses further suggest that CAL outcomes may vary across multiple context-specific variables, including graft volume, patient body mass index (BMI), surgical technique, and the specific cellular product used. For example, higher-BMI patients may show improved retention due to differences in adi-

pose quantity and quality, while SVF enrichment may offer more benefit in smaller-volume augmentations than in large-volume transfers. Technical factors, such as injection method (multi-tunnel vs. larger bolus deposits) and centrifugation or processing protocols, can influence graft survival and complication rates. Further insight was provided by a meta-analysis, which pooled 36 studies involving 1697 patients [8]. Their analysis showed that, in breast augmentation, the reoperation rate was 16.7% (90/539) in the CAL group, significantly higher than 7.33% (11/191) in the non-CAL group ($p = 0.0015$). Complications such as cysts, fat necrosis, calcification, and nodules were also more frequently reported in breast augmentation than in other recipient sites.

Conversely, for facial augmentation, CAL was associated with substantially higher fat survival (77% vs. 51% with non-CAL, $p < 0.0001$) without a significant increase in procedure frequency. Based on these findings, it has been concluded that CAL does not consistently reduce the need for repeat sessions in largevolume applications such as breast augmentation, likely because large graft volumes are more susceptible to central ischemia, necrosis, and subsequent resorption. Moreover, both Chiu [44] and Chen *et al*. [8] underscored that socioeconomic and preference-related factors could influence these outcomes. Patients opting for CAL (often the more expensive option) may be more likely to pursue secondary refinements, which can increase reoperation rates and complicate the interpretation of "surgical frequency" as a purely biological or technical outcome. A comparative assessment of CAL vs. CLT outcomes is summarized in Table 1 (Ref. [8,43,44]).

Current Challenges and Future Perspectives

Challenges

Despite its increasing adoption in plastic and reconstructive surgery, CAL remains under close assessment because crucial aspects of human stem cell behavior *in vivo* are still poorly elucidated. From a safety perspective, CAL carries the same baseline risks as conventional fat grafting, including partial resorption, fat embolism, infection, hematoma, and, in facial procedures, rare but devastating vision complications. Specific to its cellular component, the enzymatic digestion with collagenase required for SVF isolation introduces concerns regarding cytotoxicity. Furthermore, the theoretical tumorigenic potential of ADSCs cannot be conclusively excluded, making long-term clinical surveillance essential.

Supporting this caution, *in vitro* co-culture analysis has demonstrated that ADSCs can increase gene expression, proliferation, migration, and angiogenic activity in dermatofibrosarcoma protuberans (DFSP) cells, an effect that appeared to be mediated by paracrine signaling within the ADSC-related microenvironment [45]. In contrast, evidence from a mouse tumor model revealed tumor promotion and metastasis only when ADSCs were administered alone, whereas no such outcomes were observed when cells were delivered within a fat graft, either through CAL or CLT [37]. The study hypothesized that adipocytes within the graft may act as a biological barrier, sequestering soluble ADSC-derived factors and reducing the effective ADSC concentration at the tumor niche. This altered microenvironment could shift signaling toward adipogenic rather than angiogenic pathways, consistent with the lower vascular density observed in tumors from the CAL group. While the model supports the relative safety of fat-based delivery (both CLT and CAL), the long-term oncological safety profile of CAL in clinical settings requires further validation through extended follow-up studies.

Regarding efficacy, evidence supporting CAL for facial applications is increasingly consistent. Hence, CAL enhances graft survival and potentially reduces the need for repeat procedures in facial rejuvenation and contouring. A meta-analysis by Shen *et al*. [46] involving 15 studies and 755 patients revealed significantly higher fat survival rates and greater patient satisfaction with CAL than with CLT for facial rejuvenation and contouring. However, efficacy in large-volume settings, particularly breast augmentation, remains a subject of debate, with outcomes being less consistent across clinical studies.

Future Directions and Translational Barriers

Research continues to focus on improving fat graft survival, and several emerging biologic adjuncts are being explored. One innovative approach involves AdE4+ endothelial cells, which are generated by transducing endothelial cells with the human adenovirus 5 *Early region 4 open reading frame 1* (*E4ORF1*) gene. These cells can sustain proliferative and pro-angiogenic capacity over time without becoming immortalized. In a nude mouse model, Dong *et al*. [47] reported that enriching fat graft with these endothelial preparations improved graft survival. This result suggests that AdE4+ endothelial cells could serve as a promising "off-the-shelf" pro-vascularization adjuvant to enhance graft volume retention, tissue quality, and procedural safety. However, their clinical translation into clinical practice remains challenging due to the need for scalable manufacturing, safety concerns regarding genetic modification, complex regulatory approval pathways for genetically modified products, and uncertain cost-effectiveness compared with autologous strategies.

Another widely investigated adjunct is PRP, an autologous concentrate containing supraphysiological platelet levels. Upon activation, PRP releases a mixture of growth factors, such as PDGF, VEGF, TGF-β, and Epidermal Growth Factor (EGF), along with adhesion-related proteins like fibrinogen and fibronectin [5]. While PRP is widely used in chronic wound healing and aesthetic indications, robust, high-quality clinical evidence specifically supporting its efficacy in fat grafting remains limited [48]. Existing studies are inconsistent in outcomes, underscoring the need for

Table 1. Comparative outcomes of CAL vs. CLT in breast augmentation across selected studies.

Study (Year)	Design	Group (n)	Graft volume (mL)	Volume retention (%)	Complication rate (%)	Reoperation rate (%)	Patient satisfaction (Scale)
Yoshimura *et al.* (2020) [43]	RCT	CAL (30)	250 ± 45	78.2 ± 8.1	6.7	10.0	8.5/10
		CLT (30)	245 ± 50	65.3 ± 9.4	10.0	16.7	7.2/10
Chiu (2019) [44]	Cohort	CAL (101)	320 ± 60	68.7 ± 7.2	12.9	15.8	7.8/10
		CLT (105)	310 ± 55	67.9 ± 6.8	11.4	14.3	7.6/10
Chen *et al.* (2021) [8]	Meta-analysis	CAL (539)	Varied	69–75	18–24	16.7	N/A
		CLT (191)	Varied	65–70	12–18	7.33	N/A

CAL, cell-assisted lipotransfer; CLT, conventional lipotransfer; RCT, randomized controlled trial; N/A, not applicable.

well-designed mechanistic investigations and sufficiently powered clinical trials to clarify where PRP truly adds value. Key practical barriers include the lack of standardization in PRP preparation (centrifugation protocols, activator use), considerable inter-individual variability in growth factor composition, and no clear consensus about optimal dosing, timing, or delivery approach when used in CAL [49,50].

More recently, ADSC-derived exosomes have emerged as a focus of significant interest [51–53]. Exosomes are nanoscale, lipid bilayer extracellular vesicles that carry a diverse range of bioactive molecules, including DNA fragments, various RNA species, proteins, and metabolites. By delivering these molecules to recipient cells, they enable intercellular communication and can regulate processes central to graft integration and repair, such as angiogenesis, cell proliferation, immunomodulation, and tissue regeneration [54]. Compared with their parent ADSCs, exosomes may offer potential advantages, including lower immunogenicity and enhanced biodistribution due to their small size, making them a promising "cell-free" therapeutic platform [55,56]. However, translational is still limited by major challenges: large-scale production and purification, standardization of exosome content and potency, stability during storage and transport, regulatory classification (as a biologic, drug, or advanced therapy), and the need for efficacy in controlled clinical trials.

Another unresolved but clinically significant concern in CAL optimization is identifying the optimal ADSC dose. There is no accepted standard; however, evidence suggests that greater cellular enrichment may be linked to better outcomes. Rasmussen et al. reported that ADSC concentrations exceeding 5×10^6 cells/mL may correlate with improved clinical outcomes and higher graft survival [57].

Moving forward, the field must also address broader translation barriers. Priorities include developing standardized, Good Manufacturing Practice (GMP)-compliant workflows for SVF/ADSC isolation and characterization; performing comprehensive cost-benefit analyses to justify the additional complexity and expense of CAL; establishing clear regulatory guidelines for minimally manipulated versus culture-expanded products; and conducting multicenter randomized trials with long-term follow-up to generate level I evidence for both facial and breast indications.

Conclusions

The CAL combines regenerative components such as SVF and ADSCs to improve the predictability, long-term stability, and tissue-repair quality of traditional fat grafting in both facial and breast surgery. As such, it represents a pivotal advancement in regenerative plastic surgery. In facial applications, CAL elevates the procedure from mere volume restoration to a form of regenerative rejuvenation. In breast surgery, CAL serves as a potent adjunct for complex reconstruction and may offer a safer alternative for aesthetic augmentation.

Despite these promising advances, several challenges remain. Protocols for cell harvesting, processing, and cell enrichment are not yet standardized, the underlying physiological mechanisms are still being elucidated, and long-term safety, particularly in oncologic contexts, requires robust evidence. Additionally, clinical efficacy varies across indications, especially in large-volume applications.

As mechanistic research progresses, processing techniques improve, and high-quality clinical data become available, CAL has the potential to provide more effective, safer, and increasingly personalized options for soft-tissue repair and aesthetic refinement. Achieving this will depend on comprehensive investigation, well-designed multicenter trials with extended follow-up, and a clear, stringent regulatory framework to guide reasonable clinical translation and application.

Availability of Data and Materials

The data that support this study are available from the corresponding author upon request.

Author Contributions

MTD, HYQ and LBZ analyzed the data. MTD drafted the initial manuscript. All authors contributed to the critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

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