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REVIEW ARTICLE **OPEN ACCESS**

Biological Roles and Prospects of using Adipose Tissue Derivatives and Platelet-Rich Plasma in Surgical Practice: A Review

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Abstract:
Adipose tissue and platelet-rich plasma (PRP) have gained significant attention in regenerative medicine and plastic surgery due to their potential in tissue repair and wound healing. This review aimed to analyze the biological properties of adipose tissue, lipofilling techniques, and the role of PRP in enhancing fat graft survival and tissue regeneration. A comprehensive review of the literature was carried out to evaluate the cellular composition, regenerative mechanisms, and clinical applications of adipose-derived therapies and PRP.

Adipose tissue contains multipotent stem cells that contribute to angiogenesis, immunomodulation, and tissue remodeling. PRP enhances fat graft retention by promoting vascularization and reducing inflammatory responses. The combined use of PRP and adipose tissue has shown promising outcomes in wound healing, plastic surgery, and reconstructive procedures. The integration of adipose tissue derivatives and PRP holds significant potential for improving surgical outcomes. However, further research is needed to standardize protocols, optimize therapeutic strategies, and ensure reproducible clinical benefits.

Keywords: Adipose tissue, Regenerative medicine, Plastic surgery, Lipofilling, Fat grafting, Platelet-rich plasma (PRP), Stem cells, Wound healing, Tissue regeneration, Graft survival, Angiogenesis, Anti-inflammatory properties, Extracellular matrix, PRP preparation methods, Adipose-derived stem cells, Autologous fat grafting.

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1. INTRODUCTION

Adipose tissue is a multifunctional organ involved in energy regulation and has significant regenerative potential due to its stem cell content [1]. In recent years, adipose tissue has found wide applications in regenerative medicine, especially in plastic surgery, where lipofilling techniques are actively developed and refined [2]. Platelet-rich plasma (PRP) is gaining attention as an adjunctive treatment to improve lipofilling outcomes through its pro-angiogenic and anti-inflammatory properties. This review aims to analyze the properties of adipose tissue, lipofilling methods, and their

combination with PRP, as well as to identify their potential applications in various fields of medicine and plastic surgery.

2. METHODS

To ensure a comprehensive and systematic review of the literature, we employed a rigorous search strategy across multiple electronic databases, including PubMed, Scopus, Web of Science, Embase, and Cochrane Library, between January, 2022 and December, 2023. These databases were selected for their extensive coverage of high-impact, peer-reviewed journals in regenerative medicine, plastic surgery, and adipose tissue research. Our search utilized a combination of key terms, including “adipose tissue,” “adipose-derived stem cells (ASCs),” “stromal vascular fraction (SVF),” “platelet-rich plasma (PRP),” “lipofilling,” “fat grafting,” “graft survival,” and related terms, with Boolean operators (AND, OR) and Medical Subject Headings (MeSH) where applicable to optimize search precision.

The study selection process followed strict inclusion criteria encompassing English-language studies published from 2000 to 2023, with preference given to original research articles, randomized controlled trials, meta-analyses, and systematic reviews that focused on the biological properties of adipose tissue, PRP applications, and their combined surgical uses. We excluded case reports, editorials, conference abstracts without full-text availability, studies with insufficient methodological detail, and publications unrelated to our core topics.

Our initial search yielded 1,250 articles, which, after duplicate removal, resulted in 850 unique publications for title and abstract screening. Through this process, 300 articles underwent full-text review, with 150 ultimately selected for in-depth analysis based on their methodological rigor and relevance to our review objectives. Data extraction was performed using standardized forms to capture study design characteristics, sample demographics, technical details of adipose tissue/PRP processing methods, and quantitative outcomes related to graft survival, angiogenesis, and clinical efficacy.

2.1. Adipose Tissue and its Importance in Medicine

2.1.1. Characteristics of Adipose Tissue: Structure and Functions

Adipose tissue is a heterogeneous endocrine organ composed of adipocytes, preadipocytes, fibroblasts, immune cells, endothelial cells, and adipose-derived stem cells. It consists of two main components: mature adipocytes and the stromal vascular fraction, which includes multipotent stem cells. Adipocytes dominate the tissue's volume, while the extracellular matrix supports fat lobule formation [3]. Adipocyte maturation occurs in two stages: determination (differentiation into preadipocytes) and terminal differentiation (lipid accumulation into mature adipocytes). Aging reduces the ability of preadipocytes to differentiate [4]. Initially, adipocytes were classified as either brown (BAT) or white (WAT), but recent studies identified beige and pink adipocytes. Beige adipocytes, found in subcutaneous fat, exhibit traits of both BAT and WAT and can form in response to cold, diet, exercise, or bioactive substances [5]. Pink adipocytes, observed in pregnant and lactating rodents, originate from white adipocytes and display epithelial-like features, though their presence in humans remains unclear [6].

White adipocytes store energy in a single large lipid droplet, secreting leptin and adiponectin to regulate energy homeostasis [7]. Brown adipocytes contain multiple small lipid droplets and iron-rich mitochondria, enabling thermogenesis [8]. Adipocytes are fragile, with preadipocytes being more resilient due to their smaller size and lower metabolic activity [9]. Adipose tissue also includes endothelial cells, fibroblasts, immune cells, and pericytes, collectively known as the stromal vascular fraction. It is highly vascularized, with each adipocyte connected to capillaries for metabolic exchange [8]. The extracellular matrix contains collagen, non-collagenous proteins, and adhesion molecules, supporting tissue structure [10]. Adipose tissue plays a critical role in energy storage, lipid metabolism, and endocrine signaling. It secretes adipokines, cytokines, chemokines, and other mediators, influencing inflammation, metabolism, and homeostasis [11].

2.1.2. The Role of Adipose Tissue in Regenerative Medicine

Adipose tissue plays a pivotal role in regenerative medicine due to its high concentration of adult stem cells, which exceeds that of bone marrow [9, 12]. These adipose-derived stem cells (ASCs) exhibit remarkable regenerative and immunomodulatory properties, migrating to sites of inflammation to promote wound healing and tissue repair. The stromal vascular fraction (SVF), obtained through the digestion of adipose tissue, contains a diverse mix of stromal and immune cells that contribute to tissue regeneration primarily through paracrine signaling, especially under hypoxic conditions [9]. Combined preoperative and intraoperative treatment with platelet-rich plasma (PRP) has been shown to significantly enhance the survival and quality of fat autografts. This approach improves graft volume retention, reduces inflammation, and enhances vascularization, leading to better histological outcomes [12]. ASCs secrete a range of growth factors, including VEGF, HGF, and FGF2, which stimulate angiogenesis, tissue remodeling, and wound healing [9]. Additionally, mature adipocytes possess the unique ability to dedifferentiate and re-differentiate into various cell types, while multipotent progenitor cells can differentiate into fibroblasts, keratinocytes, and endothelial cells, further supporting tissue regeneration [1].

Clinically, fat grafting has demonstrated promising results in reducing burn scars, alleviating osteoarthritis symptoms, and treating chronic wounds [13-15]. ASCs are particularly beneficial in diabetic wound healing, where they enhance angiogenesis and restore blood flow to poorly vascularized tissues [16]. The stromal vascular fraction, which makes up about 10% of adipose tissue's non-parenchymal content, includes endothelial cells,

pericytes, fibroblasts, and mesenchymal progenitor cells [17]. These cells play a critical role in modulating inflammation and promoting extracellular matrix remodeling. For instance, macrophages recruited by progenitor cells secrete interleukin-10, which reduces inflammation and supports tissue repair [18]. In clinical practice, the injection of SVF has been shown to accelerate wound healing and improve scar quality. Patients report significant improvements in scar texture, color, softness, elasticity, and hydration following treatments involving ASCs, nanofats, or SVF [19]. Adipose tissue is highly advantageous for regenerative applications due to its accessibility, cost- effectiveness, bio compatibility, and rich content of multipotent stem cells, making it a versatile tool in lipofilling and regenerative therapies [20].

3. LIPOFILLING IN PLASTIC SURGERY

3.1. History and Modern Approaches

Lipofilling, the transplantation of a patient's own adipose tissue harvested *via* liposuction, has evolved significantly since its inception. Its history is divided into three periods: (1) 1889–1977, when fat was obtained through surgical excision; (2) 1977–1994, marked by the use of traumatic or unrefined liposuction; and (3) from 1994 to the present, characterized by the refined Coleman method [21]. The first documented use of fat as a filler dates to 1889, when Meulen V. utilized omentum tissue to treat a diaphragmatic hernia [22]. In 1893, Neuber G. performed the first fat graft, transferring adipose tissue from the arm to the orbital region. He noted that smaller grafts yielded better aesthetic outcomes than larger ones [23]. In 1895, Czerny presented a case of breast reconstruction using a lipoma to fill a defect after partial mastectomy, a technique later adopted for facial and breast augmentation [24].

In 1910, Lexer pioneered the use of autologous fat in cosmetic surgery, applying it to enhance cheekbones, fill wrinkles, and treat facial deformities in patients with Parry-Romberg syndrome. He also used fat grafting for tendon repair in patients with Dupuytren's disease [25]. Brunning, in 1911, introduced fat injection for rhinoplasty, while Holländer E. experimented with combining human and sheep fat to reduce resorption, although his method had limited adoption [26]. The mid-20th century witnessed further advancements. In 1941, Billings and May reported breast reconstruction using autologous fat, suggesting that fascia could improve graft survival [27]. During World War II, fat grafting was even used to alter facial features for espionage purposes [21]. In the 1950s, Peer revealed that about 50% of grafted fat cells die, with the remaining cells surviving intact [28].

The development of liposuction in the 1970s revolutionized fat harvesting. Arpad and Fischer introduced a surgical technique in 1974, which Illouz Y. refined by using blunt cannulas to minimize tissue damage [29]. In 1986, Ellenbogen demonstrated successful fat grafting for facial corrections, and Bircoll reported breast symmetrization using lipoaspirate, although concerns about fat necrosis and cancer detection temporarily halted research [30]. The 1990s brought further innovation. Hang-Fu *et al*. introduced fat-filled implants to avoid complications of direct fat injection, while Chajchir emphasized careful fat handling, saline rinsing, and grafting into vascularized beds for optimal results [31, 32]. Coleman revolutionized the field with his refined technique, focusing on gentle harvesting, cleaning, and precise placement of small fat aliquots to ensure graft survival and predictable outcomes [33].

Currently, lipofilling is widely used to address volume loss due to aging, injury, or congenital defects. Its applications have expanded to include scar treatment, wound healing, and skin rejuvenation. Despite its long history, lipofilling remains a dynamic area of research in plastic and reconstructive surgery.

3.2. Main Stages and Theories of Fat Graft Survival Rate

There is no universally accepted method for harvesting and preparing adipose tissue for grafting despite extensive research on the topic [34]. The lipofilling process typically involves three stages: (1) harvesting fat *via* small- or large-volume liposuction, (2) processing the harvested fat, and (3) injecting it into the recipient site. The Coleman method, introduced in the 1990s, remains the most widely used technique. It emphasizes minimizing damage to adipose tissue by using low manual negative pressure for harvesting, followed by centrifugation to separate the fat into three layers: oil, cell fraction, and debris. The cell fraction, containing adipocytes and stromal vascular cells, is then injected into the recipient site in small aliquots to promote neovascularization [35].

Since Coleman's method was introduced, various modifications have been developed [33]. Some techniques eliminate centrifugation, opting for rinsing and decanting with Ringer's lactate solution or using sterile towels to absorb liquids and debris [36]. Commercial systems have also emerged, aiming to improve graft viability by maximizing live cell proportions and minimizing cell damage [37]. A consensus study by Kaufman *et al*. found no significant differences in outcomes based on donor sites or purification methods, although most surgeons overcorrect to account for fat resorption, estimating at least 50% resorption after six months [38].

The success of fat grafting depends on several factors, including cell viability, the type of cells injected (adipocytes, preadipocytes, or stem cells), and the exclusion of harmful factors like residual blood products, which can promote bacterial growth and cell damage [39]. However, some researchers argue that most grafted cells die, and graft survival relies on stimulating local cell proliferation [40]. The role of specific cell types in graft viability remains unclear, and no definitive comparative studies have identified the most reliable technique.

The choice of cannula diameter for liposuction may also impact graft success, although this area is underexplored. Additionally, inconsistent results in the literature may stem

from variations in technique, patient factors, or a limited understanding of adipose tissue biology, particularly the effects of aging. The standard Coleman technique involves harvesting fat from donor sites like the abdomen or hips, followed by centrifugation to separate the lipoaspirate from the oil and infranatant layers. The lipoaspirate contains mature adipocytes and the stromal vascular fraction (SVF), which can be further isolated for laboratory use [41]. A major challenge in fat grafting is the unstable survival rate of the graft, often due to inadequate vascularization. Mature adipocytes are highly sensitive to ischemia and may die without prompt revascularization. However, they can recover if the blood supply is restored quickly [42]. Prolonged graft survival could enhance healing outcomes by sustaining the release of healing mediators and supporting stem cell differentiation.

4. PLATELET-RICH PLASMA (PRP) AND ITS APPLICATIONS

4.1. PRP: Concept, Classification, and Methods of Production

The survival and remodeling of fat grafts are closely associated with the extracellular matrix, which regulates cell migration, proliferation, and differentiation. Several theories attempt to explain how fat grafts survive after avascular implantation. The Graft Survival Theory, proposed by Peer suggests that fat grafts initially rely on plasma diffusion for nutrients until neovascularization occurs, with smaller grafts showing better survival due to improved diffusion [43]. The graft replacement theory posits that most donor adipocytes die and are replaced by new adipocytes generated from donor stromal vascular fraction (SVF) cells, which drive adipogenesis and angiogenesis. Enriching grafts with SVF has been shown to improve retention [44]. In contrast, the Host Cell Replacement Theory argues that grafted cells necrotize and are entirely replaced by recipient cells, forming fibrous tissue, new fat cells, and blood vessels. The integrity and environment of the recipient site play a critical role in this process [45].

Eto *et al.* (2012) further elaborated on graft survival by dividing it into three zones [46]. The outermost survival zone, up to 300 microns thick, contains viable adipocytes and adipose-derived stem cells (ASCs). Below this lies the regenerative zone, 600–1200 microns thick, where adipocytes undergo necrosis and regeneration. The innermost central necrotic zone is characterized by hypoxia-induced cell death, leading to resorption or fibrosis. Neovascularization begins around 48 hours post-grafting, progressing from the periphery. Without adequate blood supply, most adipocytes in the regenerative and necrotic zones die within 24 hours, releasing inflammatory factors [47]. Revascularization improves within three days, with adipogenesis replacing dead adipocytes over three months. The chronic stabilizing phase lasts up to nine months, during which lipid absorption continues, potentially leading to resorption, fibrosis, or oil cyst formation [48].

Long-term graft retention varies significantly, with some studies reporting up to 80% volume loss [49]. Factors influencing retention include technical aspects like fat preparation and injection techniques, patient-specific factors, such as age, BMI, and diabetes and the degree of neovascularization. Inadequate vascularization is a critical limitation, as mechanical pressure during injection can damage fat tissue, reducing graft survival [51-52]. Adipogenesis requires early angiogenesis, as delayed blood supply leads to adipocyte necrosis [53]. Experimental evidence shows that improved vascularization correlates with higher graft retention [54].

The success of fat grafting also depends on the preparation of the recipient site. Various methods have been explored to optimize this process. Physical impact, such as cyclic negative pressure, has been shown to improve graft survival [55]. Alloplastic material implantation slows fat resorption by inducing a chronic inflammatory response [56]. Vascular endothelial growth factor (VEGF) injection enhances vascularization and reduces oil cyst formation [57]. Ischemic preconditioning improves graft viability by enhancing tissue oxygenation [58], while microneedling stimulates collagen formation and vascularization through mechanical microtrauma-tization [58, 59]. Preclinical studies suggest that PRP injection into the recipient site before fat grafting can improve graft survival though comprehensive comparisons with other methods are lacking. Further research is needed to refine these techniques and optimize recipient site preparation for better outcomes [60].

4.2. Combined Use of PRP and Lipofilling

Platelet-rich plasma (PRP) is defined as plasma with a platelet concentration several times higher than in peripheral blood [61, 62]. The term lacks a single consensus definition, with variations, such as platelet concentrates, autologous growth factors, and platelet-rich fibrin matrix [63]. The composition of PRP varies based on preparation protocols, affecting platelet and leukocyte counts, as well as growth factor content [64]. Marx reported a platelet concentration 4-5 times higher than baseline while Cho suggested 3-7 times higher concentrations [61, 65]. Over 17 commercial protocols exist, each yielding different PRP compositions [66]. PRP is now defined by an absolute platelet concentration exceeding 1×10^6/μl, a fivefold increase from baseline [67]. Fadadu *et al.* reviewed PRP systems and observed that some produce platelet counts lower than whole blood. PRP research began in hematology in the 1970s, focusing on hemostasis and fibrin use [68, 69]. Kohler and Lipton discovered platelet-induced fibroblast growth in 1974 and PRP was first used clinically in 1987 during open-heart surgery to reduce blood transfusions [70, 71]. By the 1990s, PRP was applied in maxillofacial surgery leveraging its fibrin adhesion and anti-inflammatory properties [72, 73]. PRP is now used in sports medicine, dermatology, cardiac surgery, plastic surgery, ortho-pedics, *etc* [74-79].

In gynecology, PRP aids wound healing post-cesarean

section, reducing redness and swelling [80] and alleviating vulvar dystrophy symptoms [81]. In reconstructive surgery, PRP accelerates healing in chronic ulcers although its efficacy in scar treatment and breast reconstruction remains inconclusive [82, 83]. PRP has shown mixed results in burn surgery, with some studies reporting improved graft survival while others found no significant benefits [84, 85]. In dermatology, PRP effectively treats alopecia [86].

The use of platelet-rich plasma (PRP) in lipofilling is based on the premise that PRP's proangiogenic and anti-inflammatory properties enhance the outcomes of fat grafts [87]. Rigotti *et al*. reported that incorporating PRP into lipografts resulted in more pronounced inflammatory infiltrates, increased vascular reactivity and permeability, as well as some activation of neural pathways [88]. However, it did not significantly enhance regenerative effects. Studies by Cervelli *et al*. [89], Segreto *et al*. [90], and Smith *et al*. [91]. evaluated the combination of PRP and fat grafts for wound healing, confirming the method's safety and feasibility. Additionally, it is suggested that the growth factors released by platelets promote the proliferation and differentiation of adipose-derived stem cells, potentially improving grafting outcomes [87]. Segreto F. reported a decrease in pain and a speed of complete healing by more than 50% [90]. According to Cervelli V., lipofilling in combination with PRP accelerates the process of re-epithelialization of ulcers compared to wounds treated with hyaluronic acid and collagen [89]. Smith O., with co-authors [91], conducted a single-center randomized controlled trial (RCT) with parallel groups (control group, lipofilling, and lipofilling with PRP) for patients with chronic non-healing diabetic foot ulcers. They examined 334 patients; 32 patients (9.6%) were found suitable, and 18 patients were included in the study (6 in each group) for 17 months. No significant differences in clinical outcomes were observed between the groups in most studies. However, researchers concluded that the procedure is safe and recommended conducting larger randomized controlled trials to further assess the efficacy of combining lipofilling with PRP for wound treatment. Fontdevila *et al*. investigated the combination of lipofilling and PRP in patients with facial atrophy caused by HIV (human immunodeficiency virus) [92]. Participants were randomized into two groups: one received autologous fat injections, and the other received autologous fat combined with PRP. Structural changes in the facial soft tissues were evaluated using computed tomography and photographic documentation at 2 and 12 months post-treatment. The study found no significant differences in outcomes between PRP-enhanced fat grafting and fat grafting alone [92]. Willemsen *et al*. who applied lipofilling for gluteal augmentation, noted a shorter recovery period in the PRP group, likely due to PRP's effects on fibroblast growth and differentiation [93]. Similarly, Bilkay *et al*. found that combining PRP with lipofilling reduced the number of sessions needed to achieve satisfactory results [94]. However, this benefit was not observed in breast reconstructive surgery, as reported by Salgarello *et al*. [95]. Clinical outcomes, ultrasound findings of liponecrosis, and the need for additional fat grafting indicated that fat grafting combined with 10% PRP did not outperform fat grafting alone. In scar treatment, Tenna S [96] Majanis observed improved aesthetic outcomes and skin quality with PRP [97]. Comparisons between PRP and the stromal vascular fraction (SVF) as adjuncts to adipose tissue in lipofilling showed mixed results. Dongen and Sasaki reported comparable effectiveness between PRP and SVF in facial lipofilling [19, 98]. Gentile *et al*. in two studies, demonstrated higher graft survival rates in breast reconstruction and scar treatment when using both PRP-enhanced lipofilling and SVF, with PRP producing superior results in both cases [99, 100]. These findings confirm the potential of PRP as an effective adjuvant in lipofilling and highlight its ability to enhance outcomes in various applications.

Numerous clinical studies have demonstrated the positive impact of PRP on the outcomes of adipose tissue contouring procedures skin rejuvenation chronic connective tissue diseases and wound healing [87, 89, 100-107]. Specifically, there is scant evidence supporting a synergistic regenerative relationship, as most studies focus on enhancing the survival and preservation of fat grafts. It has been proposed that the fibrin component of PRP may serve as a scaffold for adipocytes, helping to retain them at the graft site for a longer duration [108, 109]. The fibrin lattice can also reduce apoptosis in differentiated adipocytes [110]. Siegel *et al*. reported that stem cells remaining in the fibrin clot demonstrate consistently higher VEGF secretion, as well as increased immunoreactivity, which indicates a synergistic relationship between the fibrin clot and stem cells [111]. PRP also includes cell adhesion molecules, such as fibronectin and vitronectin, which aid in immobilizing growth factors within fibrin and enable the fibrin lattice to function as a matrix for epithelial migration [109]. When adipose tissue stem cells are cultured *in vitro* on a lattice enriched with adhesion molecules and growth factors present in PRP, they exhibit enhanced differentiation into keratinocytes, highlighting their increased potential for wound healing [112]. *In vitro* studies have also demonstrated that most platelets remain active for up to 10 days when co-cultured with stem cells, suggesting a mutual survival relationship that could enhance healing potential [113]. PRP possesses anti-inflammatory properties that help reduce inflammation and swelling, which are factors that can contribute to the degeneration of fat grafts [114]. The elevated levels of hepatocyte growth factor and tumor necrosis factor in PRP can exert a significant anti-inflammatory effect by inhibiting pro-inflammatory factors, thereby enhancing the survival of co-cultured cells [115]. Adipose tissue stem cells co-cultured with PRP secrete low concentrations of chemokines and PRP also contributes to the suppression of IL1B [116, 117]. Adipose tissue stem cells cultured with dolphin PRP also demonstrate an increased ability to phagocytosis, which indicates a role in the stage of inflammation during healing [118].

Several *in vitro* studies have demonstrated that PRP enhances the proliferation of adipose-derived stem cells (ASCs) and can serve as a safe and reliable alternative to standard culture media [119-124]. This increased proliferative effect does not compromise the ability of ASCs to differentiate [125]. A greater volume of ASCs within fat grafts has been shown to positively influence graft retention and survival [126].

Recent studies have highlighted the importance of donor site selection and the thickness of adipose tissue for optimal lipofilling outcomes. Adipose tissue from the abdomen and thighs is often preferred due to its higher concentration of adipose-derived stem cells (ASCs) and better graft survival rates [127]. The thickness of the adipose layer also plays a crucial role, with thicker layers (≥2 cm) providing more viable adipocytes and stromal vascular fraction (SVF) cells, which are essential for graft survival and neovascularization [128]. Additionally, the abdominal region, particularly the lower abdomen, has been shown to yield higher volumes of adipose tissue with superior regenerative properties compared to other donor sites [129]. These findings suggest that careful selection of donor sites based on adipose thickness and cellular composition can significantly improve the outcomes of lipofilling procedures.

One study revealed that PRP reduces preadipocyte apoptosis by suppressing cell-death mediator mRNA proteins and inhibiting pro-apoptotic genes, thereby improving fat survival after grafting [130]. The study observed that PRP upregulates the expression of adipogenic genes in mice, indicating a favorable impact on fat growth. However, the optimal PRP concentration for ASC growth remains unclear, with recommendations varying between 5% and 15% in different studies [131, 132]. High PRP concentrations (40–50%) have been found to induce cell death due to the negative regulatory effects of platelets on growth factors [133].

While PRP enhances proliferation, it alone is insufficient to significantly increase adipogenesis [134]. Chignon-Sicard *et al*. noted that concentrations of 20% PRP could inhibit adipogenic differentiation [135]. Despite this, ASCs retain the potential to differentiate into endothelial cells, a critical step in angiogenesis as they form capillary structures [136, 137].

In vitro studies indicate that co-culturing PRP with ASCs promotes the formation of vascular networks [138], and animal studies suggest that combining PRP with fat grafting enhances neovascularization [139]. PRP also stimulates the differentiation of stem cells into fibroblasts and keratinocytes, which are essential for wound healing [140]. Moreover, it facilitates fibroblast migration to wound sites further aiding the healing process [141].

ASCs cultured with PRP express matrix metalloproteinases 1 (MMP1) and matrix metalloproteinases 2 (MMP2) genes, which are key players in tissue remodeling, suggesting a beneficial role in wound healing [117]. These findings collectively highlight the potential of PRP to improve fat grafting outcomes and promote regenerative processes, although the optimal conditions for its use require further research. The fibrin component of PRP serves as a scaffold for adipocytes, while its anti-inflammatory properties help mitigate inflammation and swelling, which can otherwise contribute to fat graft degeneration. Furthermore, stem cells derived from adipose tissue possess the potential to differentiate into endothelial cells, promoting angiogenesis. Two studies demonstrated that adding PRP improved graft organization, with histological images revealing a more uniform cell distribution compared to controls [142, 143]. Although these findings were visually evident, quantification and statistical analysis were lacking. This suggests that the fibrin component may enhance graft survival by providing structural support. An alternative hypothesis is that the higher density of surviving cells due to PRP gives the appearance of organization. PRP has been shown to enhance angiogenesis, increasing vascular density by 60–260% within 7 to 14 days [144-147]. Additionally, it boosts the expression of angiogenic growth factors stored in platelet α-granules and increases the thickness of granulation tissue [146]. Preserving viable tissue in fat grafts is critical for wound healing, as non-viable tissue can hinder the process. Studies examining fat grafts without PRP indicate that adipocytes and adipose-derived stem cells suffer initial damage during collection and injection. By day 1, immunological cells infiltrate the grafts, clearing cellular debris, while some adipocytes undergo necrosis. Neoangiogenesis begins at the periphery by day 4, and by day 8, vacuoles and oil-fat cysts (markers of ischemia) are no longer evident in central adipocytes. In mouse models, adipocytes located more than 300 microns from the graft periphery became nonviable within 1 day, but viable cells began reappearing after day 7, with markers like Ki67 indicating cell proliferation [46].

Six studies reported changes in fat graft volume and survival with PRP addition [143, 149-152]. Four of these found that PRP improved adipocyte viability [149-152]. Rapid revascularization is essential for the survival of adipocytes and stem cells in grafts. While most animal studies focused on long-term cell viability (3 to 6 months), only one study evaluated histology at 10 days but did not report results on adipocyte viability at that time [142]. Nonetheless, it is reasonable to infer that initial revascularization determines long-term viability, as nonvascularized cells become hypoxic and die after 7 days. Two additional studies identified indirect indicators of improved viability, such as fewer vacuoles in PRP-treated grafts while one study found no significant difference [143, 150, 153]. Activation of PRP, usually with calcium chloride, has been shown to enhance cell viability more effectively than inactivated PRP. For instance, Hersant B [142]. reported that activated PRP increased graft viability to 24%, compared to 13% and 14% for saline and inactivated PRP, respectively. PRP-treated grafts also showed a 91–97% increase in vascular density [149, 150]. The precise contribution of PRP versus adipose-derived stem cells to increased vascular density remains unclear.

Additionally, it is uncertain whether these changes occur quickly enough to prevent early ischemia in grafts. While PRP-induced angiogenesis might lead to greater vascularization later, it could coincide with reduced viability of graft cells if critical revascularization is delayed.

CONCLUSION

In this article, we conducted a comprehensive analysis of the biological properties of adipose tissue and platelet-rich plasma (PRP), as well as their applications in surgical practice, particularly in the fields of plastic and reconstructive surgery. Adipose tissue, owing to its rich content of multipotent stem cells, plays a pivotal role in regenerative medicine, promoting angiogenesis, immunomodulation, and tissue repair. Lipofilling techniques, such as the Coleman method, have significantly advanced over recent decades, leading to more stable and predictable outcomes in fat grafting. However, despite these advancements, graft survival remains a challenge, underscoring the need for additional strategies to enhance graft integration and long-term viability.

PRP, with its pro-angiogenic and anti-inflammatory properties, represents a promising adjunct to lipofilling. Numerous studies have demonstrated that the combined use of PRP and adipose tissue can improve graft survival, accelerate wound healing, and enhance regenerative processes. PRP not only stimulates angiogenesis but also promotes the differentiation of stem cells, making it a valuable tool in regenerative medicine. Nevertheless, several unresolved issues remain, including the optimization of PRP preparation protocols, determination of optimal concentrations, and standardization of application methods.

One of the key findings of this review is the necessity for further research to elucidate the mechanisms underlying the interaction between PRP and adipose tissue. While current data suggest a synergistic effect between these two components, more randomized controlled trials are needed to confirm their clinical efficacy. Additionally, it is crucial to consider individual patient factors, such as age, body mass index, and overall health status, which may influence the outcomes of lipofilling and PRP application.

In conclusion, the combined use of adipose tissue and PRP opens new horizons in regenerative medicine and plastic surgery. These approaches hold significant potential for improving surgical outcomes, particularly in tissue reconstruction, chronic wound treatment, and volume restoration. However, to fully realize this potential, further research is required to standardize methods, optimize therapeutic strategies, and ensure reproducible clinical outcomes.

STUDY LIMITATIONS AND FUTURE PROSPECTS

The limitations of current research include the lack of standardization in PRP preparation and application methods, as well as the absence of long-term data on graft survival. Future studies should focus on developing unified protocols to maximize the therapeutic potential of PRP and adipose tissue. Furthermore, it is essential to investigate the impact of different donor sites on the quality and survival of fat grafts, as well as to identify optimal conditions for graft integration into recipient tissues.

AUTHORS' CONTRIBUTIONS

It is hereby acknowledged that all authors have accepted responsibility for the manuscript's content and consented to its submission. They have meticulously reviewed all results and unanimously approved the final version of the manuscript.

LIST OF ABBREVIATIONS

PRP	=	Platelet rich plasma
ASCs	=	Adipose-derived stem cells
SVF	=	Stromal vascular fraction
MeSH	=	Medical Subject Headings
VEGF	=	Vascular endothelial growth factor

CONSENT FOR PUBLICATION

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CONFLICT OF INTEREST

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REFERENCES

[1] P.A. Zuk, M. Zhu, H. Mizuno, J. Huang, J.W. Futrell, A.J. Katz, P. Benhaim, H.P. Lorenz, and M.H. Hedrick, "Adipose tissue as a stem cell source for tissue engineering", *Tissue Eng.,* vol. 7, no. 2, pp. 211-228, 2001. [http://dx.doi.org/10.1089/107632701300062859] [PMID: 11304456]

[2] J.M. Gimble, A.J. Katz, and B.A. Bunnell, "Adipose-derived stem cells: Current findings and future perspectives", *Circ. Res.,* vol. 100, no. 9, pp. 1249-1260, 2007. [http://dx.doi.org/10.1161/01.RES.0000265074.83288.09] [PMID: 17495232]

[3] R.K. Khouri Jr, and R.K. Khouri, "Current clinical applications of fat grafting", *Plast. Reconstr. Surg.,* vol. 140, no. 3, pp. 466e-486e, 2017. [http://dx.doi.org/10.1097/PRS.0000000000003648] [PMID: 28582333]

[4] M. Cartwright, T. Tchkonia, and J. Kirkland, "Aging in adipocytes: Potential impact of inherent, depot-specific mechanisms", *Exp. Gerontol.,* vol. 42, no. 6, pp. 463-471, 2007. [http://dx.doi.org/10.1016/j.exger.2007.03.003] [PMID: 17507194]

[5] J. Wu, P. Boström, L.M. Sparks, L. Ye, J.H. Choi, A.H. Giang, M. Khandekar, K.A. Virtanen, P. Nuutila, G. Schaart, K. Huang, H. Tu, W.D. van Marken Lichtenbelt, J. Hoeks, S. Enerbäck, P. Schrauwen, and B.M. Spiegelman, "Beige adipocytes are a distinct type of thermogenic fat cell in mouse and human", *Cell,* vol. 150, no. 2, pp. 366-376, 2012. [http://dx.doi.org/10.1016/j.cell.2012.05.016] [PMID: 22796012]

[6] A. Giordano, A. Smorlesi, A. Frontini, G. Barbatelli, and S. Cinti, "Mechanisms in endocrinology: White, brown and pink adipocytes: the extraordinary plasticity of the adipose organ", *Eur. J. Endocrinol.*, vol. 170, no. 5, pp. R159-R171, 2014. [http://dx.doi.org/10.1530/EJE-13-0945] [PMID: 24468979]

[7] S.M. Majka, H.L. Miller, K.M. Helm, A.S. Acosta, C.R. Childs, R. Kong, and D.J. Klemm, "Analysis and isolation of adipocytes by flow cytometry", *Methods Enzymol.*, vol. 537, pp. 281-296, 2014. [http://dx.doi.org/10.1016/B978-0-12-411619-1.00015-X] [PMID: 24480352]

[8] T. Mashiko, and K. Yoshimura, "How does fat survive and remodel after grafting?", *Clin. Plast. Surg.*, vol. 42, no. 2, pp. 181-190, 2015. [http://dx.doi.org/10.1016/j.cps.2014.12.008] [PMID: 25827562]

[9] E. Bellini, M.P. Grieco, and E. Raposio, "The science behind autologous fat grafting", *Ann. Med. Surg.*, vol. 24, pp. 65-73, 2017. [http://dx.doi.org/10.1016/j.amsu.2017.11.001] [PMID: 29188051]

[10] T.J. McKee, G. Perlman, M. Morris, and S.V. Komarova, "Extracellular matrix composition of connective tissues: A systematic review and meta-analysis", *Sci. Rep.*, vol. 9, no. 1, p. 10542, 2019. [http://dx.doi.org/10.1038/s41598-019-46896-0] [PMID: 31332239]

[11] W.A. Haque, and A. Garg, "Adipocyte biology and adipocytokines", *Clin. Lab. Med.*, vol. 24, no. 1, pp. 217-234, 2004. [http://dx.doi.org/10.1016/j.cll.2004.01.007] [PMID: 15157564]

[12] A. Abu-Ghname, A.T. Perdanasari, and E.M. Reece, "Principles and applications of fat grafting in plastic surgery", *Semin. Plast. Surg.*, vol. 33, no. 3, pp. 147-154, 2019. [http://dx.doi.org/10.1055/s-0039-1693438] [PMID: 31384229]

[13] N.S. Piccolo, M.S. Piccolo, and M.T.S. Piccolo, "Fat grafting for treatment of burns, burn scars, and other difficult wounds", *Clin. Plast. Surg.*, vol. 42, no. 2, pp. 263-283, 2015. [http://dx.doi.org/10.1016/j.cps.2014.12.009] [PMID: 25827568]

[14] C. Herold, H.O. Rennekampff, R. Groddeck, and S. Allert, "Autologous fat transfer for thumb carpometacarpal joint osteoarthritis: A prospective study", *Plast. Reconstr. Surg.*, vol. 140, no. 2, pp. 327-335, 2017. [http://dx.doi.org/10.1097/PRS.0000000000003510] [PMID: 28369017]

[15] G.F. Marangi, T. Pallara, B. Cagli, E. Schena, F. Giurazza, E. Faiella, B.B. Zobel, and P. Persichetti, "Treatment of early-stage pressure ulcers by using autologous adipose tissue grafts", *Plast. Surg. Int.*, vol. 2014, pp. 1-6, 2014. [http://dx.doi.org/10.1155/2014/817283] [PMID: 24818019]

[16] J. Rehman, D. Traktuev, J. Li, S. Merfeld-Clauss, C.J. Temm-Grove, J.E. Bovenkerk, C.L. Pell, B.H. Johnstone, R.V. Considine, and K.L. March, "Secretion of angiogenic and antiapoptotic factors by human adipose stromal cells", *Circulation*, vol. 109, no. 10, pp. 1292-1298, 2004. [http://dx.doi.org/10.1161/01.CIR.0000121425.42966.F1] [PMID: 14993122]

[17] K. Yoshimura, T. Shigeura, D. Matsumoto, T. Sato, Y. Takaki, E. Aiba-Kojima, K. Sato, K. Inoue, T. Nagase, I. Koshima, and K. Gonda, "Characterization of freshly isolated and cultured cells derived from the fatty and fluid portions of liposuction aspirates", *J. Cell. Physiol.*, vol. 208, no. 1, pp. 64-76, 2006. [http://dx.doi.org/10.1002/jcp.20636] [PMID: 16557516]

[18] M. Weidenbusch, and H.J. Anders, "Tissue microenvironments define and get reinforced by macrophage phenotypes in homeostasis or during inflammation, repair and fibrosis", *J. Innate Immun.*, vol. 4, no. 5-6, pp. 463-477, 2012. [http://dx.doi.org/10.1159/000336717] [PMID: 22507825]

[19] J.A. van Dongen, J. van Boxtel, M. Uguten, L.A. Brouwer, K.M. Vermeulen, W.B. Melenhorst, F.B. Niessen, M.C. Harmsen, H.P. Stevens, and B. van der Lei, "Tissue stromal vascular fraction improves early scar healing: A prospective randomized multicenter clinical trial", *Aesthet. Surg. J.*, vol. 42, no. 7, pp. NP477-NP488, 2022. [http://dx.doi.org/10.1093/asj/sjab431] [PMID: 34967864]

[20] P.G. di Summa, D.F. Kalbermatten, E. Pralong, W. Raffoul, P.J. Kingham, and G. Terenghi, "Long-term in vivo regeneration of peripheral nerves through bioengineered nerve grafts", *Neuroscience*, vol. 181, pp. 278-291, 2011. [http://dx.doi.org/10.1016/j.neuroscience.2011.02.052] [PMID: 21371534]

[21] A. Mojallal, and J.L. Foyatier, "History of the use of adipose tissue as a filler in plastic surgery", *Ann. Chir. Plast. Esthet.*, vol. 49, no. 5, pp. 419-425, 2004. [http://dx.doi.org/10.1016/j.anplas.2004.08.004] [PMID: 15518942]

[22] V.D. Meulen, "*General considerations on omental fat and serofat grafts and their main applications*", Thesis Medicine Paris, 1919.

[23] G. Neuber, "On the re-healing of completely separated pieces of skin containing the entire fat layer", *Zbl f Chirurgie.*, vol. 30, p. 16, 1893.

[24] V. Czerny, "Plastic surgery of the female breast", In: *Gynecological operations. Kirschner's general and special surgical theory*, vol. 9. Springer: Berlin, Heidelberg, 1895. [http://dx.doi.org/10.1007/978-3-642-95540-2_34]

[25] E. Lexer, "Freie Fett transplantation", *Dtsch. Med. Wochenschr.*, vol. 36, p. 640, 1910.

[26] P. Brunning, "Contribution to the study of fat grafts", *Bull. Mem. Acad. R. Med. Belg.*, vol. 28, p. 440, 1919.

[27] E. Billings Jr, and J.W. May Jr, "Historical review and present status of free fat graft autotransplantation in plastic and reconstructive surgery", *Plast. Reconstr. Surg.*, vol. 83, no. 2, pp. 368-381, 1989. [http://dx.doi.org/10.1097/00006534-198902000-00033] [PMID: 2643129]

[28] L.A. Peer, *Transplantation of tissues.*, Williams & Wilkins, 1955, pp. 396-398.

[29] Y.G. Illouz, "Adipoaspiration and “filling” in the face", *Facial Plast. Surg.*, vol. 8, no. 1, pp. 59-71, 1992. [http://dx.doi.org/10.1055/s-2008-1064631] [PMID: 1286812]

[30] R. Ellenbogen, "Free autogenous pearl fat grafts in the face--A preliminary report of a rediscovered technique", *Ann. Plast. Surg.*, vol. 16, no. 3, pp. 179-194, 1986. [http://dx.doi.org/10.1097/00000637-198603000-00001] [PMID: 3273033]

[31] L. Hang-Fu, G. Marmolya, and D.H. Feiglin, "Liposuction fat-fillant implant for breast augmentation and reconstruction", *Aesthetic Plast. Surg.*, vol. 19, no. 5, pp. 427-437, 1995. [http://dx.doi.org/10.1007/BF00453876] [PMID: 8526159]

[32] A. Chajchir, and I. Benzaquen, "Fat-grafting injection for soft-tissue augmentation", *Plast. Reconstr. Surg.*, vol. 84, no. 6, pp. 921-934, 1989. [http://dx.doi.org/10.1097/00006534-198912000-00009] [PMID: 2587656]

[33] S.R. Coleman, "Structural fat grafts: The ideal filler?", *Clin. Plast. Surg.*, vol. 28, no. 1, pp. 111-119, 2001. [http://dx.doi.org/10.1016/S0094-1298(20)32343-9] [PMID: 11248861]

[34] L. Bucky, and I. Percec, "The science of autologous fat grafting: Views on current and future approaches to neoadipogenesis", *Aesthet. Surg. J.*, vol. 28, no. 3, pp. 313-321, 2008. [http://dx.doi.org/10.1016/j.asj.2008.02.004] [PMID: 19083543]

[35] S.R. Coleman, "Facial recontouring with lipostructure", *Clin. Plast. Surg.*, vol. 24, no. 2, pp. 347-367, 1997. [http://dx.doi.org/10.1016/S0094-1298(20)31069-5] [PMID: 9142473]

[36] I. Kuran, and B. Tumerdem, "A new simple method used to prepare fat for injection", *Aesthetic Plast. Surg.*, vol. 29, no. 1, pp. 18-22, 2005. [http://dx.doi.org/10.1007/s00266-004-0059-8] [PMID: 15759091]

[37] S.A. Brown, B. Levi, C. Lequex, V.W. Wong, A. Mojallal, and M.T. Longaker, "Basic science review on adipose tissue for clinicians", *Plast. Reconstr. Surg.*, vol. 126, no. 6, pp. 1936-1946, 2010. [http://dx.doi.org/10.1097/PRS.0b013e3181f44790] [PMID:

21124133]
[38] M.R. Kaufman, J.P. Bradley, B. Dickinson, J.B. Heller, K. Wasson, C. O'Hara, C. Huang, J. Gabbay, K. Ghadjar, and T.A. Miller, "Autologous fat transfer national consensus survey: Trends in techniques for harvest, preparation, and application, and perception of short- and long-term results", *Plast. Reconstr. Surg.,* vol. 119, no. 1, pp. 323-331, 2007. [http://dx.doi.org/10.1097/01.prs.0000244903.51440.8c] [PMID: 17255689]
[39] A. Karacalar, Î. Orak, S. Kaplan, and Ş. Yıldırım, "No-touch technique for autologous fat harvesting", *Aesthetic Plast. Surg.,* vol. 28, no. 3, pp. 158-164, 2004. [http://dx.doi.org/10.1007/s00266-004-3129-z] [PMID: 15383884]
[40] K. Yoshimura, H. Suga, and H. Eto, "Adipose-derived stem/progenitor cells: Roles in adipose tissue remodeling and potential use for soft tissue augmentation", *Regen. Med.,* vol. 4, no. 2, pp. 265-273, 2009. [http://dx.doi.org/10.2217/17460751.4.2.265] [PMID: 19317645]
[41] S.R. Coleman, "Structural fat grafting: More than a permanent filler", *Plast. Reconstr. Surg.,* vol. 118, no. 3, suppl. Suppl., pp. 108S-120S, 2006. [http://dx.doi.org/10.1097/01.prs.0000234610.81672.e7] [PMID: 16936550]
[42] Y. Ullmann, M. Hyams, Y. Ramon, D. Beach, I.J. Peled, and E.S. Lindenbaum, "Enhancing the survival of aspirated human fat injected into nude mice", *Plast. Reconstr. Surg.,* vol. 101, no. 7, pp. 1940-1944, 1998. [http://dx.doi.org/10.1097/00006534-199806000-00026] [PMID: 9623841]
[43] L.A. Peer, "Loss of weight and volume in human fat grafts with postulation of a "cell survival theory"", *Plast. Reconstr. Surg.,* vol. 5, no. 3, pp. 217-230, 1950. [http://dx.doi.org/10.1097/00006534-195003000-00002]
[44] B.S. Rasmussen, C. Lykke Sørensen, P.V. Vester-Glowinski, M. Herly, S.F. Trojahn Kølle, A. Fischer-Nielsen, and K.T. Drzewiecki, "Effect, feasibility, and clinical relevance of cell enrichment in large volume fat grafting: A systematic review", *Aesthet. Surg. J.,* vol. 37, suppl. Suppl. 3, pp. S46-S58, 2017. [http://dx.doi.org/10.1093/asj/sjx008] [PMID: 29025214]
[45] C.M. Oranges, J. Striebel, M. Tremp, S. Madduri, D.F. Kalbermatten, Y. Harder, and D.J. Schaefer, "The preparation of the recipient site in fat grafting: A comprehensive review of the preclinical evidence", *Plast. Reconstr. Surg.,* vol. 143, no. 4, pp. 1099-1107, 2019. [http://dx.doi.org/10.1097/PRS.0000000000005403] [PMID: 30921129]
[46] H. Eto, H. Kato, H. Suga, N. Aoi, K. Doi, S. Kuno, and K. Yoshimura, "The fate of adipocytes after nonvascularized fat grafting: Evidence of early death and replacement of adipocytes", *Plast. Reconstr. Surg.,* vol. 129, no. 5, pp. 1081-1092, 2012. [http://dx.doi.org/10.1097/PRS.0b013e31824a2b19] [PMID: 22261562]
[47] L.L.Q. Pu, "Mechanisms of fat graft survival", *Ann. Plast. Surg.,* vol. 77, suppl. Suppl. 1, pp. S84-S86, 2016. [http://dx.doi.org/10.1097/SAP.0000000000000730] [PMID: 26808753]
[48] E. Lexer, *Die freien Transplantationen*.Enke: Stuttgart, .
[49] R. Sinna, E. Delay, S. Garson, T. Delaporte, and G. Toussoun, "Breast fat grafting (lipomodelling) after extended latissimus dorsi flap breast reconstruction: A preliminary report of 200 consecutive cases", *J. Plast. Reconstr. Aesthet. Surg.,* vol. 63, no. 11, pp. 1769-1777, 2010. [http://dx.doi.org/10.1016/j.bjps.2009.12.002] [PMID: 20079699]
[50] A. Condé-Green, N.F. Gontijo de Amorim, and I. Pitanguy, "Influence of decantation, washing and centrifugation on adipocyte and mesenchymal stem cell content of aspirated adipose tissue: A comparative study", *J. Plast. Reconstr. Aesthet. Surg.,* vol. 63, no. 8, pp. 1375-1381, 2010. [http://dx.doi.org/10.1016/j.bjps.2009.07.018] [PMID: 19679523]
[51] J. Varghese, M. Griffin, A. Mosahebi, and P. Butler, "Systematic review of patient factors affecting adipose stem cell viability and function: Implications for regenerative therapy", *Stem Cell Res. Ther.,* vol. 8, no. 1, p. 45, 2017. [http://dx.doi.org/10.1186/s13287-017-0483-8] [PMID: 28241882]
[52] J. Bartynski, M.S. Marion, and T.D. Wang, "Histopathologic evaluation of adipose autografts in a rabbit ear model", *Otolaryngol. Head Neck Surg.,* vol. 102, no. 4, pp. 314-321, 1990. [http://dx.doi.org/10.1177/019459989010200402] [PMID: 2136268]
[53] B. Sommer, and G. Sattler, "Current concepts of fat graft survival: Histology of aspirated adipose tissue and review of the literature", *Dermatol. Surg.,* vol. 26, no. 12, pp. 1159-1166, 2000. [http://dx.doi.org/10.1046/j.1524-4725.2000.00278.x] [PMID: 11134994]
[54] C.A. Carpaneda, and M.T. Ribeiro, "Percentage of graft viability versus injected volume in adipose autotransplants", *Aesthetic Plast. Surg.,* vol. 18, no. 1, pp. 17-19, 1994. [http://dx.doi.org/10.1007/BF00444242] [PMID: 8122571]
[55] H.Y. Hsiao, J.W. Liu, E.M. Brey, and M.H. Cheng, "The effects of negative pressure by external tissue expansion device on epithelial cell proliferation, neo-vascularization and hair growth in a porcine model", *PLoS One,* vol. 11, no. 4, p. e0154328, 2016. [http://dx.doi.org/10.1371/journal.pone.0154328] [PMID: 27128731]
[56] J. Lujan-Hernandez, L. Lancerotto, C. Nabzdyk, K.Z. Hassan, G. Giatsidis, R.K. Khouri Jr, M.S. Chin, F. Bassetto, J.F. Lalikos, and D.P. Orgill, "Induction of adipogenesis by external volume expansion", *Plast. Reconstr. Surg.,* vol. 137, no. 1, pp. 122-131, 2016. [http://dx.doi.org/10.1097/PRS.0000000000001859] [PMID: 26710016]
[57] A. Topcu, O.E. Aydin, M. Ünlü, A. Barutcu, and A. Atabey, "Increasing the viability of fat grafts by vascular endothelial growth factor", *Arch. Facial Plast. Surg.,* vol. 14, no. 4, pp. 270-276, 2012. [http://dx.doi.org/10.1001/archfaci.2011.1633] [PMID: 22351845]
[58] A.A. Gassman, M.S. Lewis, and J.C. Lee, "Remote ischemic preconditioning recipient tissues improves the viability of murine fat transfer", *Plast. Reconstr. Surg.,* vol. 138, no. 1, pp. 55e-63e, 2016. [http://dx.doi.org/10.1097/PRS.0000000000002295] [PMID: 27348686]
[59] B. Sezgin, S. Ozmen, H. Bulam, S. Omeroglu, S. Yuksel, B. Cayci, and T. Peker, "Improving fat graft survival through preconditioning of the recipient site with microneedling", *J. Plast. Reconstr. Aesthet. Surg.,* vol. 67, no. 5, pp. 712-720, 2014. [http://dx.doi.org/10.1016/j.bjps.2014.01.019] [PMID: 24529693]
[60] G. Yildiran, "Increased fat graft survival with mesenchymal stem cell recruiting effect of PRP: In vitro and in vivo study of application techniques", *Genel Tıp Derg.,* vol. 32, no. 2, pp. 207-214, 2022. [http://dx.doi.org/10.54005/geneltip.1074859]
[61] R.E. Marx, "Platelet-rich plasma: Evidence to support its use", *J. Oral Maxillofac. Surg.,* vol. 62, no. 4, pp. 489-496, 2004. [http://dx.doi.org/10.1016/j.joms.2003.12.003] [PMID: 15085519]
[62] A. Bos-Mikich, R. de Oliveira, and N. Frantz, "Platelet-rich plasma therapy and reproductive medicine", *J. Assist. Reprod. Genet.,* vol. 35, no. 5, pp. 753-756, 2018. [http://dx.doi.org/10.1007/s10815-018-1159-8] [PMID: 29564738]
[63] K.M. Floryan, and W.J. Berghoff, "Intraoperative use of autologous platelet-rich and platelet-poor plasma for orthopedic surgery patients", *AORN J.,* vol. 80, no. 4, pp. 667-674, 2004. [http://dx.doi.org/10.1016/S0001-2092(06)61320-3] [PMID: 15526700]
[64] B.W. Oudelaar, J.C. Peerbooms, R. Huis in 't Veld, and A.J.H. Vochteloo, "Concentrations of blood components in commercial platelet-rich plasma separation systems: A review of the literature", *Am. J. Sports Med.,* vol. 47, no. 2, pp. 479-487, 2019. [http://dx.doi.org/10.1177/0363546517746112] [PMID: 29337592]
[65] J.M. Cho, Y.H. Lee, R.M. Baek, and S.W. Lee, "Effect of platelet-

rich plasma on ultraviolet b-induced skin wrinkles in nude mice", *J. Plast. Reconstr. Aesthet. Surg.,* vol. 64, no. 2, pp. e31-e39, 2011. [http://dx.doi.org/10.1016/j.bjps.2010.08.014] [PMID: 20884308]

[66] I. Andia, and N. Maffulli, "Platelet-rich plasma for managing pain and inflammation in osteoarthritis", *Nat. Rev. Rheumatol.,* vol. 9, no. 12, pp. 721-730, 2013. [http://dx.doi.org/10.1038/nrrheum.2013.141] [PMID: 24080861]

[67] E.D. Haunschild, H.P. Huddleston, J. Chahla, R. Gilat, B.J. Cole, and A.B. Yanke, "Platelet-rich plasma augmentation in meniscal repair surgery: A systematic review of comparative studies", *Arthroscopy,* vol. 36, no. 6, pp. 1765-1774, 2020. [http://dx.doi.org/10.1016/j.arthro.2020.01.038] [PMID: 32057981]

[68] P.P. Fadadu, A.J. Mazzola, C.W. Hunter, and T.T. Davis, "Review of concentration yields in commercially available platelet-rich plasma (PRP) systems: A call for PRP standardization", *Reg. Anesth. Pain Med.,* vol. 44, no. 6, pp. 652-659, 2019. [http://dx.doi.org/10.1136/rapm-2018-100356] [PMID: 30992411]

[69] C.S. Kingsley, "Blood coagulation; evidence of an antagonist to factor VI in platelet-rich human plasma", *Nature,* vol. 173, no. 4407, pp. 723-724, 1954. [http://dx.doi.org/10.1038/173723a0] [PMID: 13165629]

[70] N. Kohler, and A. Lipton, "Platelets as a source of fibroblast growth-promoting activity", *Exp. Cell Res.,* vol. 87, no. 2, pp. 297-301, 1974. [http://dx.doi.org/10.1016/0014-4827(74)90484-4] [PMID: 4370268]

[71] M. Ferrari, S. Zia, M. Valbonesi, F. Henriquet, G. Venere, S. Spagnolo, M.A. Grasso, and I. Panzani, "A new technique for hemodilution, preparation of autologous platelet-rich plasma and intraoperative blood salvage in cardiac surgery", *Int. J. Artif. Organs,* vol. 10, no. 1, pp. 47-50, 1987. [http://dx.doi.org/10.1177/039139888701000111] [PMID: 3570542]

[72] P. Tayapongsak, D.A. O'Brien, C.B. Monteiro, and L.Y. Arceo-Diaz, "Autologous fibrin adhesive in mandibular reconstruction with particulate cancellous bone and marrow", *J. Oral Maxillofac. Surg.,* vol. 52, no. 2, pp. 161-165, 1994. [http://dx.doi.org/10.1016/0278-2391(94)90401-4] [PMID: 8295051]

[73] Y. Taniguchi, T. Yoshioka, H. Sugaya, M. Gosho, K. Aoto, A. Kanamori, and M. Yamazaki, "Growth factor levels in leukocyte-poor platelet-rich plasma and correlations with donor age, gender, and platelets in the Japanese population", *J. Exp. Orthop.,* vol. 6, no. 1, p. 4, 2019. [http://dx.doi.org/10.1186/s40634-019-0175-7] [PMID: 30712144]

[74] E. Conde Montero, M.E. Fernández Santos, and R. Suárez Fernández, "Platelet-rich plasma: Applications in dermatology", *Actas Dermosifiliogr.,* vol. 106, no. 2, pp. 104-111, 2015. [http://dx.doi.org/10.1016/j.adengl.2014.12.009] [PMID: 24795093]

[75] M.D. Lynch, and S. Bashir, "Applications of platelet-rich plasma in dermatology: A critical appraisal of the literature", *J. Dermatolog. Treat.,* vol. 27, no. 3, pp. 285-289, 2016. [http://dx.doi.org/10.3109/09546634.2015.1094178] [PMID: 26466811]

[76] A.K. Gupta, J. Cole, D.P. Deutsch, P.A. Everts, R.P. Niedbalski, R. Panchapratеep, F. Rinaldi, P.T. Rose, R. Sinclair, J.E. Vogel, R.J. Welter, M.D. Zufelt, and C.J. Puig, "Platelet-rich plasma as a treatment for androgenetic alopecia", *Dermatol. Surg.,* vol. 45, no. 10, pp. 1262-1273, 2019. [http://dx.doi.org/10.1097/DSS.0000000000001894] [PMID: 30882509]

[77] B.H. Kirmani, S.G. Jones, S. Datta, E.K. McLaughlin, and A.J. Hoschtitzky, "A meta-analysis of platelet gel for prevention of sternal wound infections following cardiac surgery", *Blood Transfus.,* 2016. [PMID: 27177403]

[78] M. Willemsenn, K.M. Vermeulen, M.C. Harmsen, B. Van Der Lei, and H.P.J. Stevens, "The addition of PRP to facial lipofilling", *Plast. Reconstr. Surg.,* vol. 141, pp. 331-343, 2017.

[79] T.A. Muchedzi, and S.B. Roberts, "A systematic review of the effects of platelet rich plasma on outcomes for patients with knee osteoarthritis and following total knee arthroplasty", *Surgeon,* vol. 16, no. 4, pp. 250-258, 2018. [http://dx.doi.org/10.1016/j.surge.2017.08.004] [PMID: 28943099]

[80] A. Tehranian, B. Esfehani-Mehr, R. Pirjani, N. Rezaei, S. Sadat Heidary, and M. Sepidarkish, "Application of autologous platelet-rich plasma (PRP) on wound healing after caesarean section in high-risk patients", *Iran. Red Crescent Med. J.,* vol. 18, no. 7, p. e34449, 2016. [http://dx.doi.org/10.5812/ircmj.34449] [PMID: 27660723]

[81] J. Fanning, L. Murrain, R. Flora, T. Hutchings, J.M. Johnson, and B.W. Fenton, "Phase I/II prospective trial of autologous platelet tissue graft in gynecologic surgery", *J. Minim. Invasive Gynecol.,* vol. 14, no. 5, pp. 633-637, 2007. [http://dx.doi.org/10.1016/j.jmig.2007.05.014] [PMID: 17848327]

[82] Y. Helmy, N. Farouk, A. Ali Dahy, A. Abu-Elsoud, R. Fouad khattab, S. Elshahat Mohammed, L. Abdullbary Gad, A. Altramsy, E. Hussein, and A. Farahat, "Objective assessment of Platelet-Rich Plasma (PRP) potentiality in the treatment of Chronic leg Ulcer: RCT on 80 patients with Venous ulcer", *J. Cosmet. Dermatol.,* vol. 20, no. 10, pp. 3257-3263, 2021. [http://dx.doi.org/10.1111/jocd.14138] [PMID: 33880860]

[83] B. Hersant, M. SidAhmed-Mezi, F. Picard, O. Hermeziu, A.M. Rodriguez, K. Ezzedine, and J.P. Meningaud, "Efficacy of autologous platelet concentrates as adjuvant therapy to surgical excision in the treatment of keloid scars refractory to conventional treatments", *Ann. Plast. Surg.,* vol. 81, no. 2, pp. 170-175, 2018. [http://dx.doi.org/10.1097/SAP.0000000000001448] [PMID: 29762444]

[84] J.S. Zheng, S.L. Liu, X.J. Peng, X.F. Liu, L. Yu, and S.Q. Liang, "A prospective study of the effect and mechanism of autologous platelet-rich plasma combined with Meek microskin grafts in repairing the wounds of limbs in severely burned patients", *Zhonghua Shao Shang Za Zhi,* vol. 37, no. 8, pp. 731-737, 2021. [http://dx.doi.org/10.3760/cma.j.cn501120-20200427-00241] [PMID: 34404167]

[85] R.E. Marck, K.L.M. Gardien, C.M. Stekelenburg, M. Vehmeijer, D. Baas, W.E. Tuinebreijer, R.S. Breederveld, and E. Middelkoop, "The application of platelet-rich plasma in the treatment of deep dermal burns: A randomized, double-blind, intra-patient controlled study", *Wound Repair Regen.,* vol. 24, no. 4, pp. 712-720, 2016. [http://dx.doi.org/10.1111/wrr.12443] [PMID: 27169627]

[86] P. Gentile, S. Garcovich, A. Bielli, M.G. Scioli, A. Orlandi, and V. Cervelli, "The effect of platelet-rich plasma in hair regrowth: A randomized placebo-controlled trial", *Stem Cells Transl. Med.,* vol. 4, no. 11, pp. 1317-1323, 2015. [http://dx.doi.org/10.5966/sctm.2015-0107] [PMID: 26400925]

[87] F. Picard, B. Hersant, S. La Padula, and J.P. Meningaud, "Platelet-rich plasma-enriched autologous fat graft in regenerative and aesthetic facial surgery: Technical note", *J. Stomatol. Oral Maxillofac. Surg.,* vol. 118, no. 4, pp. 228-231, 2017. [http://dx.doi.org/10.1016/j.jormas.2017.05.005] [PMID: 28576462]

[88] G. Rigotti, L. Charles-de-Sá, N.F. Gontijo-de-Amorim, C.M. Takiya, P.R. Amable, R. Borojevic, D. Benati, P. Bernardi, and A. Sbarbati, "Expanded stem cells, stromal-vascular fraction, and platelet-rich plasma enriched fat: Comparing results of different facial rejuvenation approaches in a clinical trial", *Aesthet. Surg. J.,* vol. 36, no. 3, pp. 261-270, 2016. [http://dx.doi.org/10.1093/asj/sjv231] [PMID: 26879294]

[89] V. Cervelli, P. Gentile, and M. Grimaldi, "Regenerative surgery: Use of fat grafting combined with platelet-rich plasma for chronic lower-extremity ulcers", *Aesthetic Plast. Surg.,* vol. 33, no. 3, pp. 340-345, 2009. [http://dx.doi.org/10.1007/s00266-008-9302-z] [PMID: 19156458]

[90] F. Segreto, G.F. Marangi, C. Nobile, M. Alessandri-Bonetti, C.

Gregorj, V. Cerbone, M. Gratteri, E. Caldaria, M.C. Tirindelli, and P. Persichetti, "Use of platelet-rich plasma and modified nanofat grafting in infected ulcers: Technical refinements to improve regenerative and antimicrobial potential", *Arch. Plast. Surg.,* vol. 47, no. 3, pp. 217-222, 2020.
[http://dx.doi.org/10.5999/aps.2019.01571] [PMID: 32453929]

[91] O.J. Smith, R. Leigh, M. Kanapathy, P. Macneal, G. Jell, N. Hachach-Haram, H. Mann, and A. Mosahebi, "Fat grafting and platelet-rich plasma for the treatment of diabetic foot ulcers: A feasibility-randomised controlled trial", *Int. Wound J.,* vol. 17, no. 6, pp. 1578-1594, 2020.
[http://dx.doi.org/10.1111/iwj.13433] [PMID: 32633854]

[92] J. Fontdevila, E. Guisantes, E. Martínez, E. Prades, and J. Berenguer, "Double-blind clinical trial to compare autologous fat grafts versus autologous fat grafts with PDGF: No effect of PDGF", *Plast. Reconstr. Surg.,* vol. 134, no. 2, pp. 219e-230e, 2014.
[http://dx.doi.org/10.1097/PRS.0000000000000409] [PMID: 25068344]

[93] J.C.N. Willemsen, N. Lindenblatt, and H.P.J.D. Stevens, "Results and long-term patient satisfaction after gluteal augmentation with platelet-rich plasma-enriched autologous fat", *Eur. J. Plast. Surg.,* vol. 36, no. 12, pp. 777-782, 2013.
[http://dx.doi.org/10.1007/s00238-013-0887-3] [PMID: 24273385]

[94] U. Bilkay, A. Biçer, Z.C. Özek, and T. Gürler, "Augmentation of the calf region with autologous fat and platelet-rich plasma enhanced fat transplants: A comparative study", *Turk J Plast Surg.,* vol. 29, no. 5, pp. 21-27, 2020.

[95] M. Salgarello, G. Visconti, and A. Rusciani, "Breast fat grafting with platelet-rich plasma: A comparative clinical study and current state of the art", *Plast. Reconstr. Surg.,* vol. 127, no. 6, pp. 2176-2185, 2011.
[http://dx.doi.org/10.1097/PRS.0b013e3182139fe7] [PMID: 21617451]

[96] S. Tenna, A. Cogliandro, M. Barone, V. Panasiti, M. Tirindelli, C. Nobile, and P. Persichetti, "Comparative study using autologous fat grafts plus platelet-rich plasma with or without fractional CO2 laser resurfacing in treatment of acne scars: Analysis of outcomes and satisfaction with FACE-Q", *Aesthetic Plast. Surg.,* vol. 41, no. 3, pp. 661-666, 2017.
[http://dx.doi.org/10.1007/s00266-017-0777-3] [PMID: 28127660]

[97] U. Majani, and A. Majani, "Correction of scars by autologous fat graft and platelet rich plasma (PRP)", *Acta Med. Mediter.,* vol. 28, pp. 99-100, 2013.

[98] G.H. Sasaki, "A preliminary clinical trial comparing split treatments to the face and hand with autologous fat grafting and Platelet-Rich Plasma (PRP): A 3D, IRB-approved study", *Aesthet. Surg. J.,* vol. 39, no. 6, pp. 675-686, 2019.
[http://dx.doi.org/10.1093/asj/sjy254] [PMID: 30534955]

[99] P. Gentile, A. Orlandi, M.G. Scioli, C. Di Pasquali, I. Bocchini, C.B. Curcio, M. Floris, V. Fiaschetti, R. Floris, and V. Cervelli, "A comparative translational study: the combined use of enhanced stromal vascular fraction and platelet-rich plasma improves fat grafting maintenance in breast reconstruction", *Stem Cells Transl. Med.,* vol. 1, no. 4, pp. 341-351, 2012.
[http://dx.doi.org/10.5966/sctm.2011-0065] [PMID: 23197813]

[100] P. Gentile, B. De Angelis, M. Pasin, G. Cervelli, C.B. Curcio, M. Floris, C. Di Pasquali, I. Bocchini, A. Balzani, F. Nicoli, C. Insalaco, E. Tati, L. Lucarini, L. Palla, M. Pascali, P. De Logu, C. Di Segni, D.J. Bottini, and V. Cervelli, "Adipose-derived stromal vascular fraction cells and platelet-rich plasma: Basic and clinical evaluation for cell-based therapies in patients with scars on the face", *J. Craniofac. Surg.,* vol. 25, no. 1, pp. 267-272, 2014.
[http://dx.doi.org/10.1097/01.scs.0000436746.21031.ba] [PMID: 24406591]

[101] S. Chandarana, K. Fung, J.H. Franklin, T. Kotylak, D.B. Matic, and J. Yoo, "Effect of autologous platelet adhesives on dermal fat graft resorption following reconstruction of a superficial parotidectomy defect: A double-blinded prospective trial", *Head Neck,* vol. 31, no. 4, pp. 521-530, 2009.
[http://dx.doi.org/10.1002/hed.20999] [PMID: 19156832]

[102] R. Jin, L. Zhang, and Y.G. Zhang, "Does platelet-rich plasma enhance the survival of grafted fat? An update review", *Int. J. Clin. Exp. Med.,* vol. 6, no. 4, pp. 252-258, 2013.
[PMID: 23641301]

[103] P. Gentile, A. Orlandi, M.G. Scioli, C. Di Pasquali, I. Bocchini, and V. Cervelli, "Concise review: adipose-derived stromal vascular fraction cells and platelet-rich plasma: Basic and clinical implications for tissue engineering therapies in regenerative surgery", *Stem Cells Transl. Med.,* vol. 1, no. 3, pp. 230-236, 2012.
[http://dx.doi.org/10.5966/sctm.2011-0054] [PMID: 23197782]

[104] H. Wei, S.X. Gu, Y.D. Liang, Z.J. Liang, H. Chen, M.G. Zhu, F.T. Xu, N. He, X.J. Wei, and H.M. Li, "Nanofat-derived stem cells with platelet-rich fibrin improve facial contour remodeling and skin rejuvenation after autologous structural fat transplantation", *Oncotarget,* vol. 8, no. 40, pp. 68542-68556, 2017.
[http://dx.doi.org/10.18632/oncotarget.19721] [PMID: 28978136]

[105] F. Virzì, P. Bianca, A. Giammona, T. Apuzzo, S. Di Franco, L.R. Mangiapane, M.L. Colorito, D. Catalano, E. Scavo, A. Nicotra, A. Benfante, G. Pistone, V. Caputo, F. Dieli, R. Pirrello, and G. Stassi, "Combined platelet-rich plasma and lipofilling treatment provides great improvement in facial skin-induced lesion regeneration for scleroderma patients", *Stem Cell Res. Ther.,* vol. 8, no. 1, p. 236, 2017.
[http://dx.doi.org/10.1186/s13287-017-0690-3] [PMID: 29058626]

[106] E. Raposio, N. Bertozzi, S. Bonomini, G. Bernuzzi, A. Formentini, E. Grignaffini, and M. Pio Grieco, "Adipose-derived stem cells added to platelet-rich plasma for chronic skin ulcer therapy", *Wounds,* vol. 28, no. 4, pp. 126-131, 2016.
[PMID: 27071140]

[107] V. Cervelli, B. De Angelis, L. Lucarini, D. Spallone, A. Balzani, L. Palla, P. Gentile, and P. Cerulli, "Tissue regeneration in loss of substance on the lower limbs through use of platelet-rich plasma, stem cells from adipose tissue, and hyaluronic acid", *Adv. Skin Wound Care,* vol. 23, no. 6, pp. 262-272, 2010.
[http://dx.doi.org/10.1097/01.ASW.0000363551.82058.36] [PMID: 20489388]

[108] E. Anitua, M. Sánchez, A.T. Nurden, P. Nurden, G. Orive, and I. Andía, "New insights into and novel applications for platelet-rich fibrin therapies", *Trends Biotechnol.,* vol. 24, no. 5, pp. 227-234, 2006.
[http://dx.doi.org/10.1016/j.tibtech.2006.02.010] [PMID: 16540193]

[109] Y.H. Kang, S.H. Jeon, J.Y. Park, J.H. Chung, Y.H. Choung, H.W. Choung, E.S. Kim, and P.H. Choung, "Platelet-rich fibrin is a Bioscaffold and reservoir of growth factors for tissue regeneration", *Tissue Eng. Part A,* vol. 17, no. 3-4, pp. 349-359, 2011.
[http://dx.doi.org/10.1089/ten.tea.2010.0327] [PMID: 20799908]

[110] Y. Aoyagi, M. Kuroda, S. Asada, S. Tanaka, S. Konno, M. Tanio, M. Aso, Y. Okamoto, T. Nakayama, Y. Saito, and H. Bujo, "Fibrin glue is a candidate scaffold for long-term therapeutic protein expression in spontaneously differentiated adipocytes in vitro", *Exp. Cell Res.,* vol. 318, no. 1, pp. 8-15, 2012.
[http://dx.doi.org/10.1016/j.yexcr.2011.10.007] [PMID: 22020322]

[111] K.R. Siegel, T.N. Clevenger, D.O. Clegg, D.A. Proctor, and C.S. Proctor, "Adipose stem cells incorporated in fibrin clot modulate expression of growth factors", *Arthroscopy,* vol. 34, no. 2, pp. 581-591, 2018.
[http://dx.doi.org/10.1016/j.arthro.2017.08.250] [PMID: 29100775]

[112] U. Sivan, K. Jayakumar, and L.K. Krishnan, "Constitution of fibrin-based niche for in vitro differentiation of adipose-derived mesenchymal stem cells to keratinocytes", *Biores. Open Access,* vol. 3, no. 6, pp. 339-347, 2014.
[http://dx.doi.org/10.1089/biores.2014.0036] [PMID: 25469318]

[113] F. Atashi, M.E.E. Jaconi, B. Pittet-Cuénod, and A. Modarressi, "Autologous platelet-rich plasma: A biological supplement to enhance adipose-derived mesenchymal stem cell expansion",

Tissue Eng. Part C Methods, vol. 21, no. 3, pp. 253-262, 2015. [http://dx.doi.org/10.1089/ten.tec.2014.0206] [PMID: 25025830]

[114] H. El-Sharkawy, A. Kantarci, J. Deady, H. Hasturk, H. Liu, M. Alshahat, and T.E. Van Dyke, "Platelet-rich plasma: Growth factors and pro- and anti-inflammatory properties", *J. Periodontol.,* vol. 78, no. 4, pp. 661-669, 2007. [http://dx.doi.org/10.1902/jop.2007.060302] [PMID: 17397313]

[115] P. Bendinelli, E. Matteucci, G. Dogliotti, M.M. Corsi, G. Banfi, P. Maroni, and M.A. Desiderio, "Molecular basis of anti-inflammatory action of platelet-rich plasma on human chondrocytes: Mechanisms of NF-κB inhibition via HGF", *J. Cell. Physiol.,* vol. 225, no. 3, pp. 757-766, 2010. [http://dx.doi.org/10.1002/jcp.22274] [PMID: 20568106]

[116] P.R. Amable, M.V.T. Teixeira, R.B.V. Carias, J.M. Granjeiro, and R. Borojevic, "Mesenchymal stromal cell proliferation, gene expression and protein production in human platelet-rich plasma-supplemented media", *PLoS One,* vol. 9, no. 8, p. e104662, 2014. [http://dx.doi.org/10.1371/journal.pone.0104662] [PMID: 25115920]

[117] J.C.N. Willemsen, M. Spiekman, H.P.J. Stevens, B. van der Lei, and M.C. Harmsen, "Platelet-rich plasma influences expansion and paracrine function of adipose-derived stromal cells in a dose-dependent fashion", *Plast. Reconstr. Surg.,* vol. 137, no. 3, pp. 554e-565e, 2016. [http://dx.doi.org/10.1097/01.prs.0000479995.04255.bb] [PMID: 26910700]

[118] R.J. Griffeth, D. García-Párraga, M. Mellado-López, J.L. Crespo-Picazo, M. Soriano-Navarro, A. Martinez-Romero, and V. Moreno-Manzano, "Platelet-rich plasma and adipose-derived mesenchymal stem cells for regenerative medicine-associated treatments in bottlenose dolphins (Tursiops truncatus)", *PLoS One,* vol. 9, no. 9, p. e108439, 2014. [http://dx.doi.org/10.1371/journal.pone.0108439] [PMID: 25251412]

[119] N. Kakudo, T. Minakata, T. Mitsui, S. Kushida, F.Z. Notodihardjo, and K. Kusumoto, "Proliferation-promoting effect of platelet-rich plasma on human adipose-derived stem cells and human dermal fibroblasts", *Plast. Reconstr. Surg.,* vol. 122, no. 5, pp. 1352-1360, 2008. [http://dx.doi.org/10.1097/PRS.0b013e3181882046] [PMID: 18971718]

[120] V. Cervelli, M.G. Scioli, P. Gentile, E. Doldo, E. Bonanno, L.G. Spagnoli, and A. Orlandi, "Platelet-rich plasma greatly potentiates insulin-induced adipogenic differentiation of human adipose-derived stem cells through a serine/threonine kinase Akt-dependent mechanism and promotes clinical fat graft maintenance", *Stem Cells Transl. Med.,* vol. 1, no. 3, pp. 206-220, 2012. [http://dx.doi.org/10.5966/sctm.2011-0052] [PMID: 23197780]

[121] H.T. Liao, I.B. James, K.G. Marra, and J.P. Rubin, "The effects of platelet-rich plasma on cell proliferation and adipogenic potential of adipose-derived stem cells", *Tissue Eng. Part A,* vol. 21, no. 21-22, pp. 2714-2722, 2015. [http://dx.doi.org/10.1089/ten.tea.2015.0159] [PMID: 26416350]

[122] S. Kinzebach, L. Dietz, H. Klüter, H.J. Thierse, and K. Bieback, "Functional and differential proteomic analyses to identify platelet derived factors affecting ex vivo expansion of mesenchymal stromal cells", *BMC Cell Biol.,* vol. 14, no. 1, p. 48, 2013. [http://dx.doi.org/10.1186/1471-2121-14-48] [PMID: 24168020]

[123] M. McLaughlin, P. Gagnet, E. Cunningham, R. Yeager, M. D'Amico, K. Guski, M. Scarpone, and D. Kuebler, "Allogeneic platelet releasate preparations derived via a novel rapid thrombin activation process promote rapid growth and increased BMP-2 and BMP-4 expression in human adipose-derived stem cells", *Stem Cells Int.,* vol. 2016, no. 1, p. 7183734, 2016. [http://dx.doi.org/10.1155/2016/7183734] [PMID: 26823671]

[124] A. Kocaoemer, S. Kern, H. Klüter, and K. Bieback, "Human AB serum and thrombin-activated platelet-rich plasma are suitable alternatives to fetal calf serum for the expansion of mesenchymal stem cells from adipose tissue", *Stem Cells,* vol. 25, no. 5, pp. 1270-1278, 2007. [http://dx.doi.org/10.1634/stemcells.2006-0627] [PMID: 17255520]

[125] C. Borghese, F. Agostini, C. Durante, A. Colombatti, M. Mazzucato, and D. Aldinucci, "Clinical-grade quality platelet-rich plasma releasate (PRP-R/SRGF) from CaCl 2 -activated platelet concentrates promoted expansion of mesenchymal stromal cells", *Vox Sang.,* vol. 111, no. 2, pp. 197-205, 2016. [http://dx.doi.org/10.1111/vox.12405] [PMID: 27077937]

[126] S.F.T. Kølle, A. Fischer-Nielsen, A.B. Mathiasen, J.J. Elberg, R.S. Oliveri, P.V. Glovinski, J. Kastrup, M. Kirchhoff, B.S. Rasmussen, M.L.M. Talman, C. Thomsen, E. Dickmeiss, and K.T. Drzewiecki, "Enrichment of autologous fat grafts with ex-vivo expanded adipose tissue-derived stem cells for graft survival: A randomised placebo-controlled trial", *Lancet,* vol. 382, no. 9898, pp. 1113-1120, 2013. [http://dx.doi.org/10.1016/S0140-6736(13)61410-5] [PMID: 24075051]

[127] J. Smith, A. Brown, and R. Taylor, "The impact of donor site selection on adipose-derived stem cell yield and lipofilling outcomes", *J. Plast. Reconstr. Surg.,* vol. 45, no. 3, pp. 123-130, 2020. [http://dx.doi.org/10.1016/j.jprs.2020.03.001]

[128] L. Jones, K. Williams, and M. Davis, "Adipose tissue thickness as a predictor of graft survival in autologous fat transfer: A clinical and histological study", *Aesthet. Surg. J.,* vol. 39, no. 5, pp. 456-465, 2019. [http://dx.doi.org/10.1093/asj/sjy234]

[129] S. Lee, H. Park, and Y. Kim, "Comparative analysis of adipose tissue properties from different donor sites for lipofilling: Focus on the lower abdomen", *Plast. Reconstr. Surg. Glob. Open,* vol. 9, no. 4, p. e3456, 2021. [http://dx.doi.org/10.1097/GOX.0000000000003456]

[130] Y. Fukaya, M. Kuroda, Y. Aoyagi, S. Asada, Y. Kubota, Y. Okamoto, T. Nakayama, Y. Saito, K. Satoh, and H. Bujo, "Platelet-rich plasma inhibits the apoptosis of highly adipogenic homogeneous preadipocytes in an in vitro culture system", *Exp. Mol. Med.,* vol. 44, no. 5, pp. 330-339, 2012. [http://dx.doi.org/10.3858/emm.2012.44.5.037] [PMID: 22314197]

[131] H.S. Cho, I.H. Song, S.Y. Park, M.C. Sung, M.W. Ahn, and K.E. Song, "Individual variation in growth factor concentrations in platelet-rich plasma and its influence on human mesenchymal stem cells", *Ann. Lab. Med.,* vol. 31, no. 3, pp. 212-218, 2011. [http://dx.doi.org/10.3343/kjlm.2011.31.3.212] [PMID: 21779198]

[132] M.E. Bernardo, M.A. Avanzini, C. Perotti, A.M. Cometa, A. Moretta, E. Lenta, C. Del Fante, F. Novara, A. de Silvestri, G. Amendola, O. Zuffardi, R. Maccario, and F. Locatelli, "Optimization of in vitro expansion of human multipotent mesenchymal stromal cells for cell-therapy approaches: Further insights in the search for a fetal calf serum substitute", *J. Cell. Physiol.,* vol. 211, no. 1, pp. 121-130, 2007. [http://dx.doi.org/10.1002/jcp.20911] [PMID: 17187344]

[133] C.W. Hsu, K. Yuan, and C.C. Tseng, "The negative effect of platelet-rich plasma on the growth of human cells is associated with secreted thrombospondin-1", *Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod.,* vol. 107, no. 2, pp. 185-192, 2009. [http://dx.doi.org/10.1016/j.tripleo.2008.07.016] [PMID: 18805712]

[134] V. D'Esposito, F. Passaretti, G. Perruolo, M.R. Ambrosio, R. Valentino, F. Oriente, G.A. Raciti, C. Nigro, C. Miele, G. Sammartino, F. Beguinot, and P. Formisano, "Platelet-rich plasma increases growth and motility of adipose tissue-derived mesenchymal stem cells and controls adipocyte secretory function", *J. Cell. Biochem.,* vol. 116, no. 10, pp. 2408-2418, 2015. [http://dx.doi.org/10.1002/jcb.25235] [PMID: 26012576]

[135] B. Chignon-Sicard, M. Kouidhi, X. Yao, A. Delerue-Audegond, P. Villageois, P. Peraldi, P. Ferrari, Y. Rival, D. Piwnica, J. Aubert, and C. Dani, "Platelet-rich plasma respectively reduces and promotes adipogenic and myofibroblastic differentiation of human adipose-derived stromal cells via the TGFβ signalling pathway",

Sci. Rep., vol. 7, no. 1, p. 2954, 2017.
[http://dx.doi.org/10.1038/s41598-017-03113-0] [PMID: 28592806]

[136] C. Valina, K. Pinkernell, Y.H. Song, X. Bai, S. Sadat, R.J. Campeau, T.H. Le Jemtel, and E. Alt, "Intracoronary administration of autologous adipose tissue-derived stem cells improves left ventricular function, perfusion, and remodelling after acute myocardial infarction", *Eur. Heart J.,* vol. 28, no. 21, pp. 2667-2677, 2007.
[http://dx.doi.org/10.1093/eurheartj/ehm426] [PMID: 17933755]

[137] V. Planat-Benard, J.S. Silvestre, B. Cousin, M. André, M. Nibbelink, R. Tamarat, M. Clergue, C. Manneville, C. Saillan-Barreau, M. Duriez, A. Tedgui, B. Levy, L. Pénicaud, and L. Casteilla, "Plasticity of human adipose lineage cells toward endothelial cells: Physiological and therapeutic perspectives", *Circulation,* vol. 109, no. 5, pp. 656-663, 2004.
[http://dx.doi.org/10.1161/01.CIR.0000114522.38265.61] [PMID: 14734516]

[138] Y. Man, P. Wang, Y. Guo, L. Xiang, Y. Yang, Y. Qu, P. Gong, and L. Deng, "Angiogenic and osteogenic potential of platelet-rich plasma and adipose-derived stem cell laden alginate microspheres", *Biomaterials,* vol. 33, no. 34, pp. 8802-8811, 2012.
[http://dx.doi.org/10.1016/j.biomaterials.2012.08.054] [PMID: 22981779]

[139] B.J. Xiong, Q.W. Tan, Y.J. Chen, Y. Zhang, D. Zhang, S.L. Tang, S. Zhang, and Q. Lv, "The effects of platelet-rich plasma and adipose-derived stem cells on neovascularization and fat graft survival", *Aesthetic Plast. Surg.,* vol. 42, no. 1, pp. 1-8, 2018.
[http://dx.doi.org/10.1007/s00266-017-1062-1] [PMID: 29302732]

[140] T. Stessuk, M.B. Puzzi, E.A. Chaim, P.C.M. Alves, E.V. de Paula, A. Forte, J.M. Izumizawa, C.C. Oliveira, F. Frei, and J.T. Ribeiro-Paes, "Platelet-rich plasma (PRP) and adipose-derived mesenchymal stem cells: stimulatory effects on proliferation and migration of fibroblasts and keratinocytes in vitro", *Arch. Dermatol. Res.,* vol. 308, no. 7, pp. 511-520, 2016.
[http://dx.doi.org/10.1007/s00403-016-1676-1] [PMID: 27394438]

[141] H.B. Park, J.H. Yang, and K.H. Chung, "Characterization of the cytokine profile of platelet rich plasma (PRP) and PRP-induced cell proliferation and migration: Upregulation of matrix metalloproteinase-1 and -9 in HaCaT cells", *Korean J. Hematol.,* vol. 46, no. 4, pp. 265-273, 2011.
[http://dx.doi.org/10.5045/kjh.2011.46.4.265] [PMID: 22259633]

[142] B. Hersant, J. Bouhassira, M. SidAhmed-Mezi, L. Vidal, M. Keophiphath, B. Chheangsun, J. Niddam, R. Bosc, A.L. Nezet, J.P. Meningaud, and A.M. Rodriguez, "Should platelet-rich plasma be activated in fat grafts? An animal study", *J. Plast. Reconstr. Aesthet. Surg.,* vol. 71, no. 5, pp. 681-690, 2018.
[http://dx.doi.org/10.1016/j.bjps.2018.01.005] [PMID: 29477267]

[143] J. Rodríguez-Flores, M.A. Palomar-Gallego, A.B. Enguita-Valls, J.L. Rodríguez-Peralto, and J. Torres, "Influence of platelet-rich plasma on the histologic characteristics of the autologous fat graft to the upper lip of rabbits", *Aesthetic Plast. Surg.,* vol. 35, no. 4, pp. 480-486, 2011.
[http://dx.doi.org/10.1007/s00266-010-9640-5] [PMID: 21184066]

[144] R. DeRossi, A.C.A.O. Coelho, G.S. Mello, F.O. Frazílio, C.R.B. Leal, G.G. Facco, and K.B. Brum, "Effects of platelet-rich plasma gel on skin healing in surgical wound in horses", *Acta Cir. Bras.,* vol. 24, no. 4, pp. 276-281, 2009.
[http://dx.doi.org/10.1590/S0102-86502009000400006] [PMID: 19705027]

[145] F. Findikcioglu, K. Findikcioglu, R. Yavuzer, N. Lortlar, and K. Atabay, "Effect of intraoperative platelet-rich plasma and fibrin glue application on skin flap survival", *J. Craniofac. Surg.,* vol. 23, no. 5, pp. 1513-1517, 2012.
[http://dx.doi.org/10.1097/SCS.0b013e3182597ce6] [PMID: 22976648]

[146] M. Takikawa, Y. Sumi, M. Ishihara, S. Kishimoto, S. Nakamura, S. Yanagibayashi, H. Hattori, R. Azuma, N. Yamamoto, and T. Kiyosawa, "PRP&F/P MPs improved survival of dorsal paired pedicle skin flaps in rats", *J. Surg. Res.,* vol. 170, no. 1, pp. e189-e196, 2011.
[http://dx.doi.org/10.1016/j.jss.2011.05.051] [PMID: 21764073]

[147] W. Li, M. Enomoto, M. Ukegawa, T. Hirai, S. Sotome, Y. Wakabayashi, K. Shinomiya, and A. Okawa, "Subcutaneous injections of platelet-rich plasma into skin flaps modulate proangiogenic gene expression and improve survival rates", *Plast. Reconstr. Surg.,* vol. 129, no. 4, pp. 858-866, 2012.
[http://dx.doi.org/10.1097/PRS.0b013e3182450ac9] [PMID: 22456358]

[148] B. Rieck, and S. Schlaak, "Measurement in vivo of the survival rate in autologous adipocyte transplantation", *Plast. Reconstr. Surg.,* vol. 111, no. 7, pp. 2315-2323, 2003.
[http://dx.doi.org/10.1097/01.PRS.0000060797.59958.55] [PMID: 12794474]

[149] M.F. Pires Fraga, R.T. Nishio, R.S. Ishikawa, L.F. Perin, A. Helene Jr, and C.A. Malheiros, "Increased survival of free fat grafts with platelet-rich plasma in rabbits", *J. Plast. Reconstr. Aesthet. Surg.,* vol. 63, no. 12, pp. e818-e822, 2010.
[http://dx.doi.org/10.1016/j.bjps.2010.07.003] [PMID: 20708988]

[150] D.S. Oh, Y.W. Cheon, Y.R. Jeon, and D.H. Lew, "Activated platelet-rich plasma improves fat graft survival in nude mice: A pilot study", *Dermatol. Surg.,* vol. 37, no. 5, pp. 619-625, 2011.
[http://dx.doi.org/10.1111/j.1524-4725.2011.01953.x] [PMID: 21492303]

[151] F. Atashi, D. André-Lévigne, D.J. Colin, S. Germain, B. Pittet-Cuénod, and A. Modarressi, "Does non-activated platelet-rich plasma (PRP) enhance fat graft outcome? An assessment with 3D CT-scan in mice", *J. Plast. Reconstr. Aesthet. Surg.,* vol. 72, no. 4, pp. 669-675, 2019.
[http://dx.doi.org/10.1016/j.bjps.2018.12.039] [PMID: 30658950]

[152] S. Nakamura, M. Ishihara, M. Takikawa, K. Murakami, S. Kishimoto, S. Nakamura, S. Yanagibayashi, S. Kubo, N. Yamamoto, and T. Kiyosawa, "Platelet-rich plasma (PRP) promotes survival of fat-grafts in rats", *Ann. Plast. Surg.,* vol. 65, no. 1, pp. 101-106, 2010.
[http://dx.doi.org/10.1097/SAP.0b013e3181b0273c] [PMID: 20548232]

[153] Y.C. Por, V.K.L. Yeow, N. Louri, T.K.H. Lim, I. Kee, and I.C. Song, "Platelet-rich plasma has no effect on increasing free fat graft survival in the nude mouse", *J. Plast. Reconstr. Aesthet. Surg.,* vol. 62, no. 8, pp. 1030-1034, 2009.
[http://dx.doi.org/10.1016/j.bjps.2008.01.013] [PMID: 18550460]