Fat, Stem Cells, and Platelet-Rich Plasma

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KEYWORDS

• Autologous fat • Adipose-derived stem cells • Coleman technique • Facial augmentation • Facial rejuvenation • Fat • Fat grafting • Lipoaspirate • Regenerative medicine • Stem cells • Stromal vascular fraction • Structural fat grafting • Platelet-rich plasma • PRP

KEY POINTS

- Advances in technique led to the development of Coleman fat grafting, which has been well studied and standardized, and is a reliable technique for minimally invasive facial rejuvenation.
- However, over the past 10 years, advances in regenerative medicine have opened the door to new strategies designed to enhance graft retention and regenerative potency.
- Adipose-derived stem cells (ASCs) and platelet-rich plasma (PRP) are among the most promising current options, but research in the field is still in its infancy.
- Even with the promise that stem cell–based therapies might hold for the future of the field, the benefits and risks have not yet been adequately studied for widespread adoption beyond clinical trials.
- More importantly, physicians, researchers, and national societies/organizations need to work to inform the public about which practices are evidence based and to encourage support of additional research.

BACKGROUND

The ideal filler for aesthetic surgery is inexpensive and easy to obtain, natural in appearance and texture, immunologically compatible, and long lasting without risk of infection. By most metrics, autologous fat grafts meet these criteria perfectly. Since the first reported case more than 120 years ago, fat grafting has had a waxing and waning role in plastic surgery practice, with resorption being a primary clinical problem. Advances in harvesting and injection technique have made facial aesthetic applications more reliable and very effective.[1–3] Accordingly, facial fat grafting, alone or in combination with open procedures, is widely practiced. Although facial fat grafting is a commonly accepted surgical procedure, there has been a wave of activity in stem cell and platelet-rich plasma (PRP) therapies in aesthetic practice. This article addresses technical considerations in the use of autologous fat transfer for facial rejuvenation, and also explores the current evidence for stem cell and PRP therapies in aesthetic practice.

HISTORY OF FAT GRAFTING

Neuber[4,5] was the first to describe autologous fat transfer in 1893 when he transferred fat from the arm to a depressed facial scar. Even then, he reported that the primary limitation of the technique was the inability to transplant anything "[larger than an almond]" because of resorption. Two years later, Czerny[6] published the first description of fat transfer to the breast, using a large lipoma from the lower back to fill a lumpectomy defect. In 1909, Hollander described a

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technique involving fat injection through a cannula to correct contour deformities. The problem of fat reabsorption was well known, so he combined his patients' fat with a special preparation of male ram fat in attempt to thicken and preserve the graft. Although patients experienced a painful rash when they rejected the xenograft, he reported generally favorable long-term aesthetic results.[7,8]

The first reports of applying fat transfer specifically to aesthetic surgery also came in 1909 when Lexer[9] described the use of fat to solve several facial aesthetic challenges. Numerous surgeons followed suit, reporting the use of fat for a wide variety of facial defects.[10] In 1926, Miller[11] published a detailed review of his development and use of cannulas for fat injection, but the technique still failed to achieve widespread adoption. The following decades saw a decline in fat grafting, highlighted by Peer's[12] historic observation that half of fat graft volume was lost in the first year with mostly fibrous tissue remaining. As a result of his experiments, Peer concluded that revascularization was necessary for fat graft survival and that a larger number of small aliquots fared better than a large single graft because of enhanced surface area. Even with these groundbreaking observations, the first major efforts to apply his findings did not come until the 1980s.

Challenged by the poor results of contemporary techniques, Ellenbogen[13] developed a method of mincing fat into 4- to 6-mm "pearls" before placing them directly into the recipient bed. Using this method, he was able to achieve success with acne pitting, facial wrinkles, scars, and chin augmentation. Even though Ellenbogen initially reported good results using his technique, he later retracted his previous claims and concluded that the fat did not have long-term survival with his mincing technique.[14] Around the same time, Illouz[15] and Fournier[16,17] described using unprocessed liposuction for fat transplantation. However, resorption was even worse than with traditional fat transfer, creating a necessity for substantial overcorrection and limiting adoption.[18] This led Chajchir and Benzaquen[19] to develop several handling strategies, including removing oil and blood before reinjection. However, it was not until Coleman developed a meticulous, standardized means of processing and injecting lipoaspirate, termed lipostructure, that fat grafting became widely used in aesthetic surgery.[1–3,20–22]

ADIPOSE STEM CELLS

Adipose Stem Cells History and Biology

In 2001, Zuk and colleagues[23,24] described a population of multipotent mesenchymal stem cells present in lipoaspirate that were similar to bone marrow mesenchymal stem cells. These adipose-derived stem cells (ASCs) have since become one of the most widely used stem cell populations in regenerative medicine because of ease of harvest and diverse differentiation capacity.[25] ASCs have the capacity to differentiate to mesoderm derivatives, including fat, cartilage, muscle, and bone. Furthermore, they can be induced to form endodermal and ectodermal tissue types, including skin epithelium, neural cells, hepatocytes, and pancreatic islets.[25–27] In addition to their differentiation capacity, ASCs are also involved with paracrine signaling for angiogenesis, immunomodulation, and tissue regeneration.[28–30]

Isolating Adipose Stem Cells

ASCs reside in the perivascular compartments of adipose stroma. As a result, stromal dissociation is necessary to liberate enough cells for practical use. This is most often achieved by enzymatic digestion with collagenase followed by lysis of red blood cells.[31] The resulting stromal vascular faction (SVF) contains a diverse progenitor cell population, which includes ASCs, pericytes, endothelial progenitor cells, and transit amplifying cells. To isolate ASCs, the SVF is plated on tissue culture plastic where ASCs adhere preferentially. In addition to collagenase digestion, several nonenzymatic approaches, including washing and mechanical separation, are also described for SVF isolation but are less widely used.[32–40] Numerous point-of-care devices have been developed to harvest the SVF, but they generally use similar enzymatic or mechanical digestion strategies.[41]

Clinical Use of Adipose Stem Cells: Cell-Assisted Lipotransfer

ASC or SVF-enriched fat grafts were first reported by Moseley and colleagues[42] in 2006 based on unpublished work by Llull in 2005. The technique was more formally described by Matsumoto and colleagues[43] shortly thereafter and termed "cell-assisted lipotransfer" (CAL). Numerous preclinical animal studies have since demonstrated improvements in fat graft volume with CAL,[44] leading to the initiation of human trials.

To date, two randomized controlled trials have been conducted in humans. Koh and colleagues[45] assessed ASC-enriched microfat grafts in 10 patients with Parry-Romberg hemifacial atrophy and found that volume retention improved substantially in the group receiving CAL (47% resorption in control subjects vs 21% in CAL). Similarly, in a triple-blind RCT of 10 patients, Kolle and