Superficial Enhanced Fluid Fat Injection (SEFFI) to Correct Volume Defects and Skin Aging of the Face and Periocular Region

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Abstract

Background: Although recent research on micro fat has shown the potential advantages of superficial implantation and high stem cell content, clinical applications thus far have been limited.

Objectives: The authors report their experience with superficial enhanced fluid fat injection (SEFFI) for the correction of volume loss and skin aging of the face in general and in the periocular region.

Methods: The finer SEFFI preparation (0.5 mL) was injected into the orbicularis in the periorbital and perioral areas, and the 0.8-mL preparation was injected subdermally elsewhere in the face.

Results: The records of 98 consecutive patients were reviewed. Average follow-up time was 6 months, and average volume of implanted fat was 20 mL and 51.4 mL for the 0.5-mL and 0.8-mL preparations, respectively. Good or excellent results were achieved for volume restoration and skin improvement in all patients. Complications were minor and included an oil cyst in 3 patients. The smaller SEFFI quantity (0.5 mL) was well suited to correct volume loss in the eyelids, especially the deep upper sulcus and tear trough, whereas the larger SEFFI content was effective for larger volume deficits in other areas of the face, including the brow, temporal fossa, zygomatic-malar region, nasolabial folds, marionette lines, chin, and lips.

Conclusions: The fat administered by SEFFI is easily harvested via small side-port cannulae, yielding micro fat that is rich in viable adipocytes and stem cells. Both volumes of fat (0.5 mL and 0.8 mL) were effective for treating age-related lipoatrophy, reducing facial rhytids, and improving skin quality.

Level of Evidence: 4

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Skin atrophy and volume loss are major factors involved in facial aging, contributing to the formation of facial rhytids, skeletonization, and pseudo-descent of the midface. Early signs of facial aging affect the periorcular region and include thinning of the eyebrows, deepening of the superior sulcus, development of infraorbital hollows, and atrophy of the Oculofacial Plastic Surgeon at Assaf Harofhe Medical Center in Zerifin, Israel.

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midface. Similar changes occur in the perioral region, contributing to the development of nasolabial folds, marionette lines, and lip atrophy. Some volume changes can be iatrogenic; for example, overaggressive blepharoplasty may lead to hollowing of the upper and/or lower eyelids. Other volume deficits may have a constitutional basis and be evident since adolescence or early adulthood.1

Restoring facial volume is often achieved with autologous fat transfer, as popularized by Coleman.2 However, this technique has limitations such as unpredictable fat survival and substantial risk of visible lumps. Consequently, many authors have been focusing their efforts on micro fat grafting.2-12 Reported advantages of micro fat grafting include enhanced safety in the periorcular area,4-6 ability to inject the fat superficially using syringe needles,3,4,7,8 and higher content of stem cells.9

The newer micro fat preparations consist of collagenase digestion or manual emulsification of the fat, upon completion of the traditional harvesting technique.4,5 However, strict legal limitations regulate the use of collagenase in humans, and manual centrifugation negatively affects adipocyte viability. Hence, we propose a novel technique in which “micro” side-port cannulae are used to harvest “micro” fat, obviating further post-harvest processing. The resulting fat, rich in stem cells and viable adipocytes, is subsequently enhanced and rendered fluid by adding autologous platelet-rich plasma (PRP) and then injected superficially with syringe needles. We have named this micro fat-grafting technique “superficial enhanced fluid fat injection” (SEFFI) and, in this preliminary study, was applied in a large series of patients.

METHODS

The study population comprised 98 consecutive patients, treated between January 2013 and January 2014, all of whom provided informed consent. Area(s) of injection, size and quantity of implanted fat, and needle size were documented for each patient. After treatment, the charts of all patients were reviewed, and a standardized protocol for fat harvesting and preparation was established prospectively.

The SEFFI technique was originally conceived of by one of the authors (A.G.) and was subsequently standardized by the 2 senior surgeons (A.G. and F.P.B.), who performed all procedures in 1 of 2 centers. Since the study was carried out in the private practices of the senior authors, international review board approval was not requested. The study was conducted in accordance with tenets of the Declaration of Helsinki.

In all cases, SEFFI was performed concurrently with cosmetic surgery procedures including minimal-incisions vertical endoscopic lift (MIVEL), necklift, and primary or revisional blepharoplasty. For upper blepharoplasty procedures, the authors removed skin only, and excised the medial fat pad if it had been visible pretreatment when the patient was upright. For lower blepharoplasties, fat was either repositioned or excised through a transconjunctival approach. When indicated, a mini-pinch skin excision was added. In revisional blepharoplasty for lower lid retraction, lateral canthoplasty and transconjunctival lower retractor release were performed. Platysmaplasty was performed with necklifts: a Gore-Tex band (W.L. Gore & Associates, Newark, DE) was affixed to the platysma under the mandible line medially, tightened to the mastoid laterally, and the redundant retro-auricular skin was removed. No patient underwent dissection of the anterior superficial musculaponeurotic system dissection, and no pre-auricular skin was removed. Follow-up duration ranged from 4 months to 1 year (average, 6 months).

Fat Preparation

Fat aspiration was performed while the patient was under general anesthesia or monitored intravenous sedation. Our standardized protocol was utilized. Cold Ringer’s lactate solution (500 mL) was mixed with lidocaine (500 mg), sodium bicarbonate (5 mEq) and epinephrine (0.5%), then injected into the selected donor site. Manual aspiration of the fat was performed with a 10-mL syringe mounted alternatively with 2 different multi-perforated side-port cannulae. Both cannulae were 20 cm long and 2 mm in diameter. Side-port size was either 0.5 mm or 0.8 mm (Figure 1). Preferred harvesting sites were the suprapubic region, hip, pretrochanteric region, and inner aspect of the knee.

Figure 1. The side-port cannulas utilized in SEFFI harvesting (center, 0.8 mm; right, 0.5 mm) are significantly smaller than the traditional Coleman cannula (left, 2 × 3 mm).
After the aspiration syringe was filled, the fat was mixed with cold Ringer’s solution to rinse the anesthetic from the fat and to facilitate fat precipitation. The syringe was then capped and maintained in a dark environment, under a sterile cloth, to reduce the possibility of light oxidation of adipocytes. The 0.5- and 0.8-mL fat samples were kept in separate, labeled syringes.

The fat was centrifuged for 1 minute at 2000 rpm, with an estimated gravitational force of 448 g. PRP was obtained by drawing blood from the patient directly into four 4.5-mL citrate-containing Vacutainer tubes and was centrifuged at 1000 rpm for 2 minutes. In a sterile syringe, the concentrated PRP was mixed with the fat to obtain a final concentration of 10% of the total fat harvested. The end result of this process is an enhanced, fluid fat that can be injected with the needle of a small syringe under minimal digital pressure (Supplementary Video 1). (All videos cited in this article are available at www.aestheticsurgeryjournal.com.) The appropriate needle size was established for each patient by determining the smallest gauge that allowed easy flow under minimal pressure. This facilitated uniform distribution of the fat.

**Fat Injection**

The finer (0.5-mL) SEFFI fat was administered via multiple 1-mL syringes mounted with 23-gauge needles at the level of the superficial orbicularis of the upper eyelid sulcus, brow, lower eyelid, tear trough, and infraorbital hollows (Supplementary Videos 2 and 3), and subdermally in the perioral area (Supplementary Video 4). Small visible bulges that occasionally formed in the eyelids at the time of injection were flattened by digital pressure.

SEFFI 0.8 mL was administered subdermally, using 3-mL syringes mounted with 20-gauge needles, into the temporal fossa, brow, malar mound, zygomatic arch, and mandible line (Supplementary Video 5). In the lips, it was injected into the orbicularis.

**Histologic Analysis**

Fat harvested with cannulae of 3 different-sized ports (0.5 mm, 0.8 mm, and 2 mm) was examined histologically after centrifugation and mock injection. Hematoxylin and eosin stains demonstrated mature viable adipocytes, with intact cell walls and visible nuclei equally represented in the 3 different-sized specimens. A well-represented stromal component was noted between adipocytes, without signs of cell necrosis (Figure 2). The adipocyte size ranged from 0.03 mm to 0.13 mm and was independent of the size of the harvesting cannula.

**Figure 2.** High-power-field (original magnification × 40) hematoxylin and eosin stains of the 3 quantities of harvested fat (A, 0.5 mL; B, 0.8 mL; C, 2 mL [from Coleman cannula]) demonstrate mature adipocytes with features of vitality (intact cell walls with visible nuclei) and without signs of cell necrosis. (D) Healthy stromal component between adipocytes. A normal microvascular pattern is visible in all specimens.
Cell Cultures

The same fat samples were transferred into a sterile tube and washed twice in phosphate-buffered saline (PBS). A collagenase I solution in PBS was added, and the samples were incubated at 37°C for 20 minutes while shaking. Following incubation, the digested samples were centrifuged at 1200 rpm for 5 minutes. Supernatant was discarded, and pellets were suspended in cell culture medium. Viability of the cell line’s stromal vascular fraction (SVF) of 3 lipoaspirates was tested with Alamar Blue (AbD Serotec, Oxford, UK). Finally, stem cell differentiation was performed on the 3 specimens as follows: the SVF cells were seeded onto a 24-multiwell plate at a concentration of 25 000 cells/well and cultured in standard medium. The medium was replaced by Adipogenic Induction Medium (Lonza, Walkersville, MD) and cultured for 21 days.

RESULTS

Cell Cultures and Stem Cell Differentiation

Alamar Blue testing demonstrated that SVF cells from the 3 samples had a similar growth rate and an equal tendency to differentiate into mature adipocytes after being placed in the induction medium. During the differentiation process into mature adipocytes, the cells derived from the smaller side-port cannulae showed a reduced tendency to form aggregates (Figure 3).

Clinical Results

During the study period, 98 consecutive patients underwent SEFFI (6 men, 92 women). The mean age was 51 years (range, 27-74 years). SEFFI was used in conjunction with surgical procedures such as MIVEL (n = 51), primary blepharoplasty (n = 35), necklift (n = 23), and revisional blepharoplasty (n = 12). Some patients underwent more than 1 concomitant procedure. Overall, the average volume of implanted fat was 71.4 mL (20 mL with the 0.5-mL injection, and 51.4 mL with the 0.8-mL injection) (Figure 4 and Table 1).

The main outcome measures were restoration of volume, reduction of facial rhytids, and improvement in skin quality. Because it was not always possible for patients to critically evaluate the combined effects of the primary procedure and the fat grafting, the senior authors performed an objective clinical assessment based on retrospective comparison of pretreatment and final posttreatment photographs. Each senior author performed an independent assessment of every patient in the study. Volume restoration was evaluated by the 2 senior authors in selected facial sites where the effect could be most visibly recognized (brow, upper sulcus, tear trough, cheeks, lips) and rated on a scale of 1 to 4.

Figure 3. Phase contrast microscopy of the 3 quantities of harvested fat (A, 0.5 mL; B, 0.8 mL; C, 2 mL [from Coleman cannula]). The tendency to form aggregates was lowest in the SVF cell line derived from the smallest side-hole cannulae (0.5 mm).
(1 = no effect, 2 = fair effect, 3 = good effect, 4 = excellent effect). Skin changes also were evaluated by the 2 senior authors: visible rhytid reduction and skin tone improvement were and rated on a similar scale of 1 to 4 (1 = no effect, 2 = fair effect, 3 = good effect, 4 = excellent effect). The 2 senior authors rated the results independently as good in 62 patients (63%) and excellent in 36 patients (37%). (Clinical photographs are shown in Figures 5-10.) Complications occurred in only 4 patients (overall incidence, 3.9%). All complications were minor. There were 3 cases of oil cyst: 2 were aspirated with a syringe and the other required surgical removal (Figure 7). Another patient experienced visible lumpiness.

**DISCUSSION**

Skin atrophy and volume loss are major contributors to facial aging. Thus, ideally, the face should be rejuvenated by restoring lost volume and improving skin quality simultaneously. Volume restoration is a key component of facial rejuvenation that is commonly treated by injection of commercial cosmetic fillers or autologous fat. Traditional fat grafting involves Coleman’s harvesting technique with 2-mm side-port cannulae, followed by distribution of a structural fat implant throughout the various dermal layers of the face, from deep through superficial. Disadvantages of traditional fat grafting include the risks of irregular fat accumulation, fat necrosis, and visible lumpiness. Because eyelid skin is usually thin, the periorbicular area is most susceptible to contour problems, and thus deep implantation of fat is recommended. In response to concerns such as these, many authors have recently focused on micro fat-grafting techniques. A major action of micro fat injection is improvement in the viability of adipocytes by disruption of fat lobules, which is contrary to Coleman’s thesis that preservation of the lobular structure is essential for fat survival. Moreover, Moscatello et al demonstrated that the greater surface area of the disrupted fat lobules on the recipient bed significantly improves fat survival after injection, confirming Nguyen’s similar findings in mice. Trepsat was the first to propose utilizing small side-port cannulae to harvest micro fat for implantation below the orbicularis oculi plane in the periorbicular region. More recently, various authors have proposed “ultra-micro” fat as a very superficial implant in the periorbicular and perioral areas. These newer techniques are based on fat harvesting with Coleman’s traditional cannula, followed by various modalities of fat processing to disrupt the large fat lobules harvested. Manual fat emulsification, as proposed by Tonnard et al and Stuzin, provides a nanofat solution rich in SVF and consequently adipocyte-derived stem cells (ADSCs), but devoid of viable adipocytes. Consequently, the indications of nanofat are reportedly limited to skin regeneration and do not include volume restoration.

<table>
<thead>
<tr>
<th>Facial Region</th>
<th>Average Volume (mL)</th>
<th>Plane/Muscle of Injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brows and upper sulcus</td>
<td>3</td>
<td>Orbicularis oculi</td>
</tr>
<tr>
<td>Inferior orbit hollow</td>
<td>1.8</td>
<td>Orbicularis oculi</td>
</tr>
<tr>
<td>Tear trough</td>
<td>1.9</td>
<td>Subdermal</td>
</tr>
<tr>
<td>Perioral area</td>
<td>3.3</td>
<td>Subdermal</td>
</tr>
<tr>
<td>Malar and zygomatic areas</td>
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<td>Subdermal</td>
</tr>
<tr>
<td>Lips</td>
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<td>Orbicularis oris</td>
</tr>
<tr>
<td>Chin</td>
<td>3.5</td>
<td>Mentalis</td>
</tr>
<tr>
<td>Temporal fossa</td>
<td>3.8</td>
<td>Subcutaneous</td>
</tr>
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Figure 4. SEFFI distribution pattern for different areas of the face, based on numeric data in Table 1. The sites that received 0.5 mL appear in yellow, and those injected with 0.8 mL appear in red.

Youn et al reported on infradermal injection of collagenase-digested fat into the eyelids to correct periocular dark circles. However, this procedure is time-consuming, and there are strict legal restrictions on its utilization in humans because
enzymatic digestion also may affect normal collagen in the injection sites.

In a previous article, we reported our preliminary experience with fat harvested through a 1-mm side-port cannula and implanted superficially with sharp needles; this technique yielded excellent results in our series.\(^3\)

SEFFI is superior to traditional fat-grafting techniques in various ways. Research by Trepsat\(^6\) demonstrated that SEFFI micro fat is 50% finer and can be injected into the superficial orbicularis oculi plane with a small syringe needle. This is important because the smaller the fat lobules, the more superficially the fat can be implanted, which reduces the risk of visible irregularities in very delicate areas of the face. Since the SEFFI fat exits the syringe as a paste, temporary volume-related bulges can be easily redistributed with digital massage, similar to the routine practice performed when calcium hydroxylapatite is injected into the periocular region.\(^1\) Unlike ultra-micro fat\(^4,5\) SEFFI does not require further fat processing other than enhancement with PRP after standard rinsing and centrifugation. In other words, SEFFI fat does not require chemical digestion or manual emulsification to reach its final composition. The small size of the fat lobules harvested is determined at the outset by the small size of the side ports. Since the adipocytes are much smaller in relation to the size of the side ports, their integrity is preserved and they can effectively provide volume correction, as demonstrated in our current case series. This is in contrast to the study by

Figure 5. (A) Pretreatment view of this 29-year-old woman with constitutional tear trough deformity who underwent SEFFI to the lower eyelids combined with a skin-only upper blepharoplasty. (B) One year after treatment, significant improvement was observed in both tear troughs. (C) Side-by-side comparison of the left side of the face: left view, pretreatment; right view, posttreatment “mirrored” left-sided image.
Tonnard et al.4 in which their “no-fat” solution acted only as a regenerative substrate to improve skin quality. SVF contains ADSCs, preadipocytes, and hematopoietic, endothelial, and smooth muscle cells that are involved in prolonging fat graft survival and providing skin regeneration.15,16 Trivisonno et al.9 demonstrated that harvesting fat with a microcannula carried a 2-fold increase in ADSC content compared with traditional harvesting cannulae. Phase contrast microscopy of the SEFFI fat showed an abundance of SVF, concordant with the findings of Trivisonno et al.9

New evidence supports the role of PRP-enhanced fat grafting for skin regeneration, increased fat-graft survival, and improved wound cosmesis.17-20 Techniques to enhance fat grafts with additional vascular-associated progenitor cells continue to evolve.21 Hence, we combined the SEFFI stem cells of double origin (the ADSCs and the blood line-derived PRP) to provide a potentially more powerful effect on skin regeneration, which likely contributed to the clinical improvement in facial rhytids and skin quality observed in our patients. PRP also

Figure 6. (A) Pretreatment view of this 54-year-old woman who had undergone blepharoplasty to all 4 eyelids 10 years prior to presentation. Before SEFFI treatment, a deep superior sulcus was observed along with tear trough deformity, loose and wrinkled lower-eyelid skin, and skeletonization of the orbital rims. (B) Eleven months after SEFFI treatment performed in conjunction with MIVEL, removal of upper-eyelid skin and medial fat pad, and lower skin-pinch blepharoplasty. (C) Side-by-side pre- and posttreatment images of the left side of the face demonstrate that SEFFI restored volume to the superior sulcus, enhanced brow prominence, increased fullness in the temporal fossa, and “blended” the junction between the lower eyelid and cheek.
provides fluidity to the SEFFI fat, allowing easy egress from small-bore needles under minimal digital pressure. We believe that utilization of sharp needles rather than blunt cannulae is important, because only needles allow for precise placement of fat in superficial planes. However, we acknowledge that needles (vs blunt cannulae) may be associated with a higher risk of vascular complications. In our patients, this risk was minimized by retrograde injection under low pressure, and by prior infiltration of the injection sites with local anesthetic containing adrenaline. Moreover, we did not inject the areas associated with a high risk of vascular embolization, such as the glabella and the nose. We believe that more widespread distribution is possible with the SEFFI “fat paste” relative to the bulkier bolus injections of fat achieved by the traditional Coleman technique, and this contributes to the favorable safety profile.
Figure 8. (A) Pretreatment view of this 52-year-old woman who underwent SEFFI in conjunction with MIVEL, upper blepharoplasty (skin-only removal), and lower blepharoplasty with transconjunctival fat transposition and mini-pinch skin excision. (B) Eleven months after the procedures, improvement was observed in the central oval of the face, the periocular region, and the perioral regions. (C) These favorable outcomes are highlighted further by pre- and posttreatment comparison of the right side of the patient’s face.

Figure 9. (A) Pretreatment image of this 55-year-old woman who underwent SEFFI in conjunction with MIVEL and a necklift. Eyelid surgery was not performed. (B) One year later, good volume restoration was observed, as was reduction in rhytids and improvement of skin quality throughout the face.
Figure 10. (A, C, E) Pretreatment frontal and side views of this 65-year-old woman who underwent SEFFI, MIVEL, upper blepharoplasty, and a necklift. (B, D, F) One year after the procedures, the favorable impact of SEFFI on rhytids and skin quality was apparent throughout the face.
of SEFFI. In summary, we agree with the statement of Zeltzer et al\(^8\) that “fat grafting can be performed safely with a sharp needle.”

The current study has limitations that must be emphasized. Because of the prospective, non-randomized design, it may conceal a selection bias. Histologic analysis of the treated areas was not performed, and therefore the exact layer of fat implantation could not be determined. The methods to evaluate volume correction, rhytid reduction, and skin quality were not standardized and relied solely on the judgment of the 2 senior authors. Until a prospective double-blind study is conducted, the role of PRP enhancement to the SEFFI will remain speculative. Larger series with longer follow-up are needed to confirm the effectiveness and safety of the SEFFI technique and to rule out potential long-term complications related to superficial placement of fat. However, we believe that the 6-month posttreatment observation period in our study likely was sufficient for discovering the majority of complications that would occur long term in our patients.

**CONCLUSIONS**

This study demonstrates that SEFFI is a safe and effective method to correct volume loss and improve skin quality throughout the face, including the periorcular and perioral regions.

Because SEFFI fat is rich in viable adipocytes and stem cells, it may be utilized for volume augmentation as well as skin regeneration. The small size of its fat lobules allows for superficial implantation of viable adipocytes and minimizes the risk of visible lumps and other irregularities. It appears that superficial implantation is more volume-effective than deeper penetration, and it permits the delivery of stem cells and growth factors of double origin closer to the skin, where they are needed most. A significant advantage of SEFFI in the periorcular region is that, since the plane of implant (eg, pre-orbicularis) differs from that of surgical dissection (eg, retro-orbicularis), fat grafting can be performed in this area at the time of lower-eyelid surgery such as blepharoplasty. Both quantities of SEFFI fat (0.5 mL and 0.8 mL) were effective for increasing volume, reducing rhytids, and improving skin quality in treated areas.

**Supplementary Material**

This article contains supplementary material located online at www.aestheticsurgeryjournal.com.

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