Case Report

Guided Superficial Enhanced Fluid Fat Injection (SEFFI) Procedures for Facial Rejuvenation: An Italian Multicenter Retrospective Case Reports

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Posted Date: 23 April 2023

doi: 10.20944/preprints202304.0775.v1

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Article

Guided Superficial Enhanced Fluid Fat Injection (SEFFI) Procedures for Facial Rejuvenation: An Italian Multicenter Retrospective Case Reports

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Abstract: Background**:** The ageing process starts in the center of the face, in the periocular region and around the mouth, with a combination of volume loss and tissue descent, wrinkles deepen, and loss of skin structure and quality. Recently, several studies proved the efficacy of therapies based on the autologous adipose tissue grafting that leverages the properties of stromal vascular fraction (SVF) and adipose derived mesenchymal stem cells (ADSCs) to accelerate the regenerative processes of the skin. This study aimed to verify the ability of the guided Superficial Enhanced Fluid Fat Injection (SEFFI) in the facial area to correct volume loss and skin aging and proved the very low rate of complications of this standardized procedure. Methods: we retrospectively collected data from 2,365 procedures performed in Italian centers between 2019 and 2021. Guided SEFFI was performed alone or combined with cosmetic treatments, including the use of hyaluronic acid filler, suspension threads, synthetic calcium hydroxylapatite, botulin toxin, and microneedling. Results: SEFFI was used alone in more than 60% of the patients, and in all face areas. In about one tenth of patients SEFFI was combined with botulin toxin treatment or hyaluronic acid filling. Other procedures were used more rarely. Ecchymosis in the donor or injection sites was the most frequent event, and yet observed in only 14.2% and 38.6% of patients, respectively. Conclusions: The SEFFI technique is standardized and minimally invasive, leading to very few complications. It can be a promising antiaging medical treatment that combines effectiveness, safety, and simplicity.

Keywords: facial rejuvenation; Stromal Vascular Fraction; adipose derived mesenchymal stem cells; autologous adipose tissue graft; Superficial Enhanced Fluid Fat Injection; clinical regeneration applications

 doi:10.20944/preprints202304.0775.v1

1. Introduction

Aging is a natural and biological occurrence. In middle aged patients from 45 to 55 years old, skin atrophy and volume loss, mostly associated with variable degrees of tissue ptosis, are the most significant factors playing a role [1].

As the skin ages, dysregulation of the stem cell population - which usually helps repair damaged tissue - may occur [2]. In addition to intrinsic (chronologic) aging, the skin may also experience an extrinsic aging process due to exposures to various environmental stressors like ultraviolet (UV) radiation, trauma, chemicals, smoking, and reactive oxidative species [3,4]. All these factors lead to an accumulation of DNA damage with consequent impairment of protein maturation, cell function, and normal physiology [2].

In the periocular region thinning of the eyebrows, deepening of the superior eyelid sulcus, along with infraorbital hollows are worsened by midface descent [5–8], whilst in the perioral region worsening of the naso-labial folds, marionette lines, and lip atrophy occur. Clinically, aging manifests as fine lines and wrinkles, loss of elasticity, dyschromia, epidermal thinning, and increased coarseness [3,9]. Volumetric loss of contour and angularity in the face are also visible due to tissue atrophy within the deep layer [10,11]. Regenerative therapy exploits the properties of the cells of stromal vascular fraction (SVF) of the adipose tissue to counteract these aging-associated changes.

However, regenerative medicine currently resorts to injecting adipose-derived stem cells (ADSCs) because of their characteristics and easy availability [12–16].

In the last years, several studies proved the efficacy of therapies based on the autologous grafting of adult mesenchymal stem cells to accelerate the healing and regenerative processes of the skin and mesenchymal tissues. Adult mesenchymal stem cells are pluripotent adult progenitor cells derived from embryonic connective tissue. ADSCs can perform their regenerative activity due to their intrinsic capability of transforming into cells of the mesenchymal and endothelial line, promoting tissue reparation (17,18].

The Stromal Vascular Fraction (SVF) of the adipose tissue contains many cells creating interrelated cell populations: adipocyte progenitors, pericytes, endothelial progenitor cells, and transit-amplifying cells [19]. ACS can secrete bioactive molecules that stimulate angiogenesis and have antifibrotic, antiapoptotic, and immunomodulatory properties [20–23].

Moreover, SVF/ ASCs induce the secretion of cytokine and growth factors which promote angiogenesis and, thus, revascularization of fat grafts [24,25].

Such characteristics of SVF/ASCs could account for some effects observed after adipose tissue implantation, such as improved skin trophism, accelerated closure of complex wounds or ulcers, and enhancement of skin appearance after damage from radiotherapy [26,27].

In 2015 one of the Authors [28] standardized the new tissue graft techniques named Superficial Enhanced Fluid Fat Injection (SEFFI) to achieve skin enhancement and volume restoration of the face: these techniques use to harvest adipose tissue using microcannula with small sideport holes (0.3-0.5 and 0.8) in a superficial adipose tissue layer (SAT) [29,30], aimed at grafting adipose tissue, including the SVFCs and ADSCs contained therein.

Since 2015 [17,28–34] several studies have been publishing that proved that using a special cannula with tiny side ports holes the adipose tissue can be harvested to select small cellular clusters that don't need any manipulation to reduce the clusters dimension and fluidify the tissue.

The absence of substantial manipulation guarantees the maximum viability and stemness of the harvested tissue [35,36].

Although SEFFI is a minimally invasive technique, it still requires surgical skill to collect the adipose tissue through a small skin hole and in the superficial subcutaneous plane.

In 2020 A. Gennai et al. [37] published a simplified, guided SEFFI procedure that allows to harvest the tissue in a safe and effective plane even without major surgical skills.

In this study, we present data retrospectively collected by ten physicians who carried out more than 2,300 guided SEFFI procedures in various anatomic locations of the face and for diverse indications between 2019 and 2021.

 doi:10.20944/preprints202304.0775.v1

2. Materials and Methods

The Adipose Tissue Harvesting Procedure

This study is a retrospective analysis of the data obtained from 2,365 healthy patients of whom 2,123 were females aged on average 49.2 years old (range 38-65 years) and 242 were males aged on average 47.0 years old (range 41-53 years). Patients were treated in 10 different professional centers for aesthetic physicians and surgeons with the SEFFI technique performed with SEFFILLER™ medical device between 2019 and 2021. There were no gender or age exclusion criteria in this retrospective study.

The follow up of the cases was between 4 and 6 months in any center.

Adipose tissue was harvested from patients after informed consent was obtained under the Declaration of Helsinki guidelines. All procedures were performed in private Italian medical centers, so international review board approval was not required.

The SEFFI harvesting technique has been previously described [37].

Briefly, the procedure was performed under local anesthesia using the microperforated cannula with 0.8 mm side portholes mounted inside the unique patented guide (Figure 1).

Figure 1. The guide with syringe and cannula. The guide is meant to standardize the adipose tissue harvesting procedure.

The superficial adipose tissue (SAT) was collected with a gentle back-and-forth fan movement throughout the sampling area. The harvesting areas were mainly the abdomen, trochanteric, hip, and others. The guide is addressed to standardize the procedure and guarantee that tunneling is performed in the subcutaneous adipose tissue adjacent to the dermis (SAT), particularly rich in mesenchymal and vascular stem cells and at the same plane for all samples [20,38] (Figure 2).

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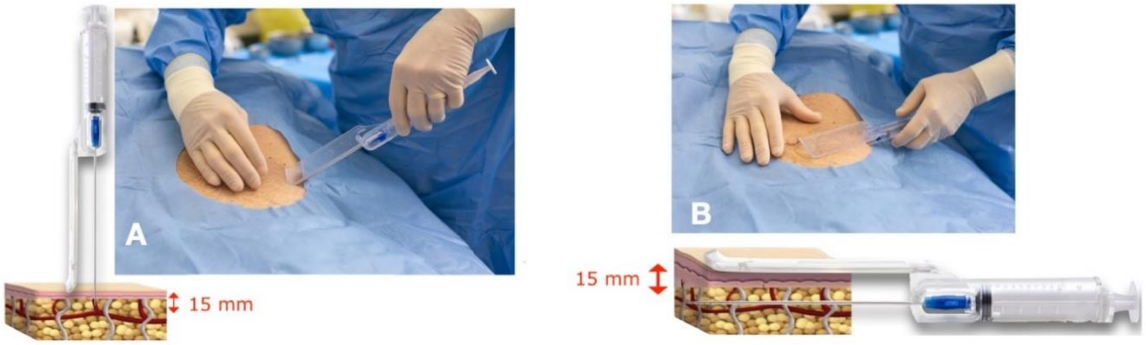

Figure 2. The guide allows the cannula to penetrate under the skin no more than 15 mm and to collect superficial adipose tissue (SAT) at 15mm of depth.

The harvested adipose tissue was transferred into the reservoir syringes. The reservoir syringes were filled up with a saline solution, cupped, and left in a vertical position for a few minutes to let the content stratify by the force of gravity in three layers: oil, tissue, and washing liquid in the bottom of the reservoir syringe (Figure 3).

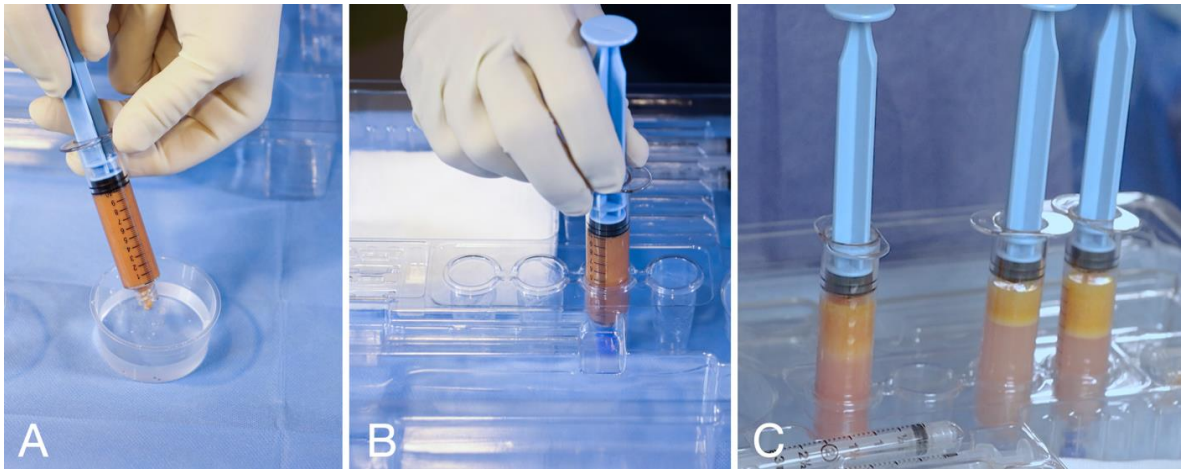

Figure 3. A: the reservoir syringe is filled with saline solution and capped. B: the reservoir syringe is placed in the syringe holder in vertical position for decanting C: after few minutes of decanting, the tissue is separated from washing liquid. The washing liquid will be discharged.

The washing liquid was discharged, and the tissue was ready to be prepared for the injection. The face areas have different skin and subcutaneous thicknesses; hence, it is essential to inject the proper fluidity of the tissue superficially without any risk of visibility and lumpiness. It's possible to reduce further the clusters' dimensions to obtain different degrees of fluidity; with the SEFFI technique, it's possible to achieve this further clusters reduction with an emulsification procedure by connecting the two syringes of 10 ml through a transfer provided in the device and performing some passages of the tissue from one syringe to the other (Figure 4).

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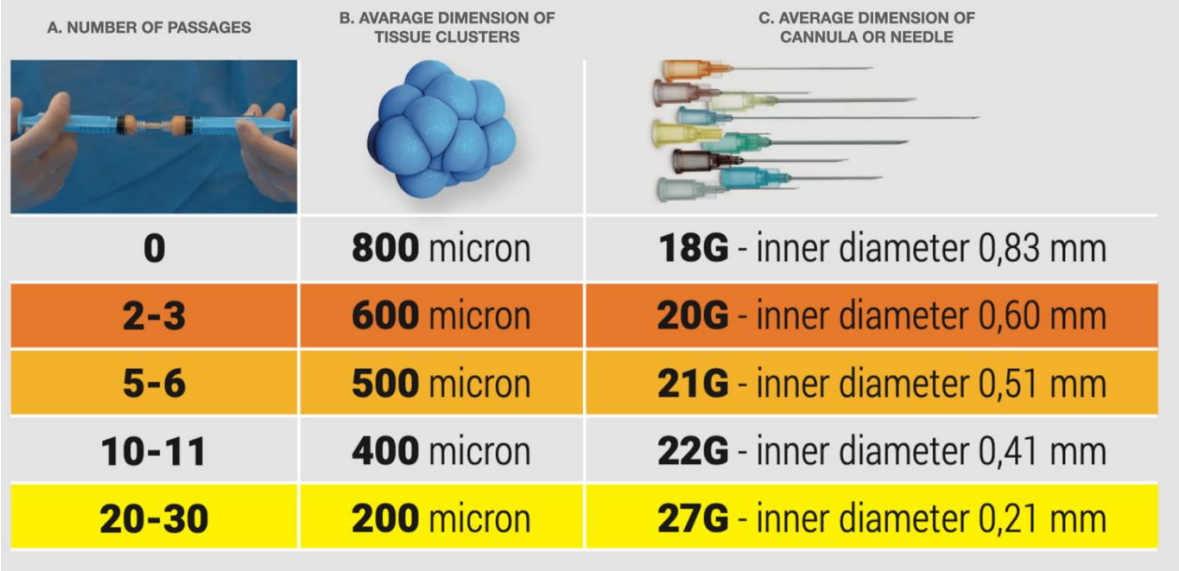

Figure 4. A: Number of tissue passages from one syringe to another trough the transfer without any filter B: average dimension of tissue cluster after the passages C: average dimension of cannula or needle using to inject the tissue.

The fresh micro fragmented adipose tissue obtained with the SEFFI technique doesn't need any further substantial manipulation due to the small dimension of harvested clusters with the SEFFI cannula with 0.8 mm side port holes; the only light manipulation (passaging from one syringe to another) should be performed in case of needs increasing fluidity to treat very delicate areas of the face.

Guided SEFFI Single treatment

The tissue was transferred to smaller syringes. The injection is achieved with a micro cannula of 20G or 21G in the very superficial subcutaneous layer. The goal of the treatment is "to sow" micro fragmented adipose tissue in the very superficial subcutaneous layer (Figure 5).

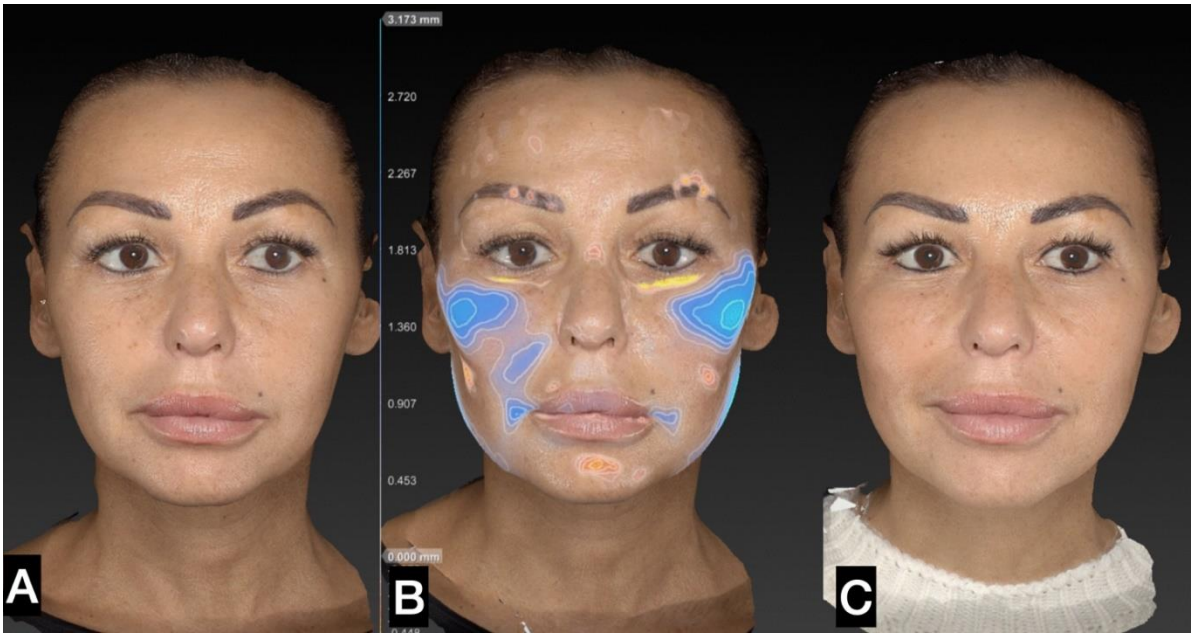

Figure 5. A: 46-yrs old woman pretreatment guided SEFFI single treatment. B: Treated face area Blue ones. C: post 45 days.

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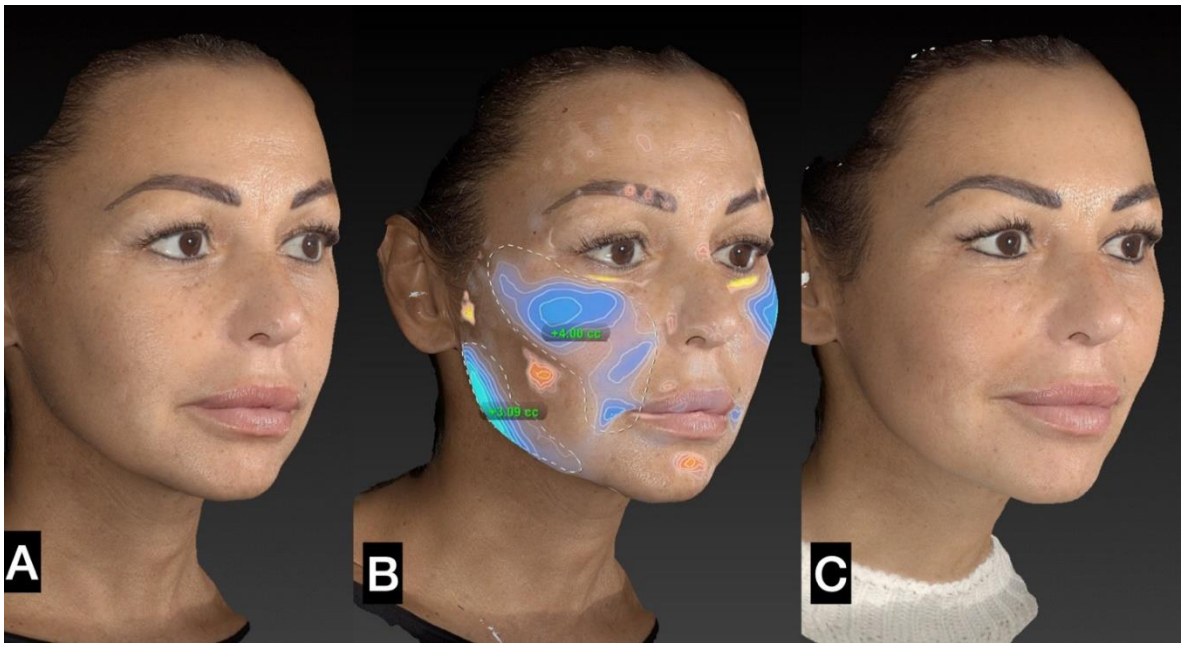

Figure 6. A: pretreatment right side guided SEFFI single treatment B: treated area and amount of tissue injected C: post treatment 45 days.

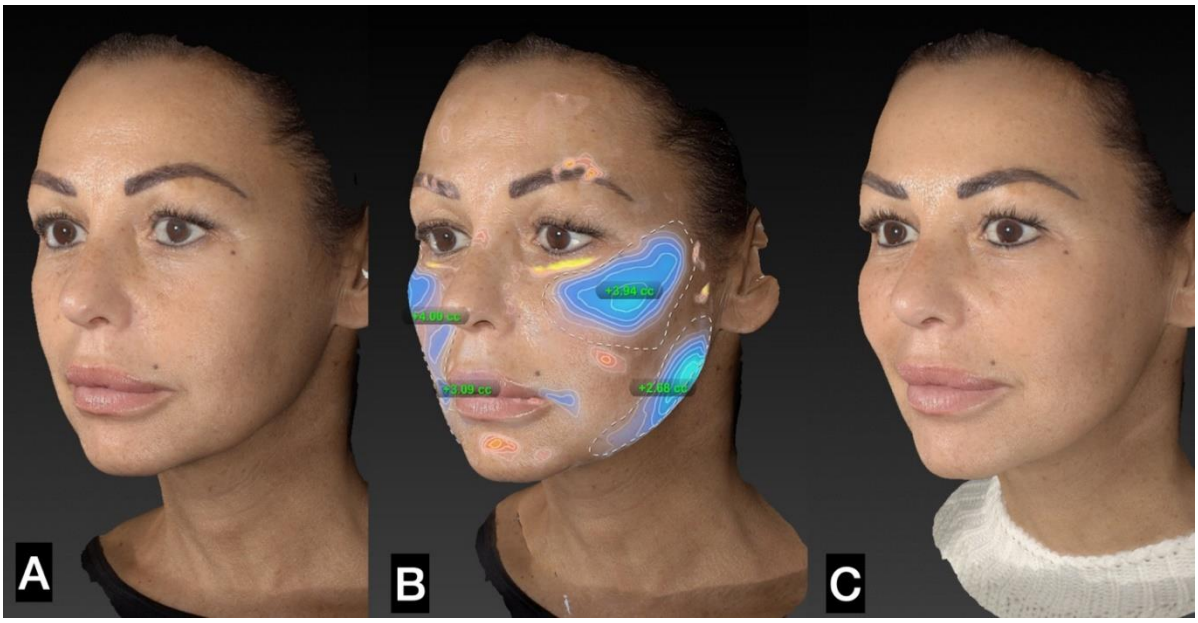

Figure 7. A pretreatment left side guided SEFFI single treatment B: treated area and amount of tissue injected. C: post treatment 45 days.

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Figure 8. A,C: 56-yrs old woman pretreatment guided SEFFI single treatment B,D: post treatment 4 months.

Figure 9. A,C: 31-yrs old woman pretreatment guided SEFFI single treatment B,D: post treatment 6 months.

The periocular area is the only area where Authors suggest injecting tissue in the submuscular plane [31,38,39] (Figures 10 and 11).

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Figure 10. A: 32-yrs old woman with deep inferior sulcus in the eyelid. B: single SEFFI guided treatment.

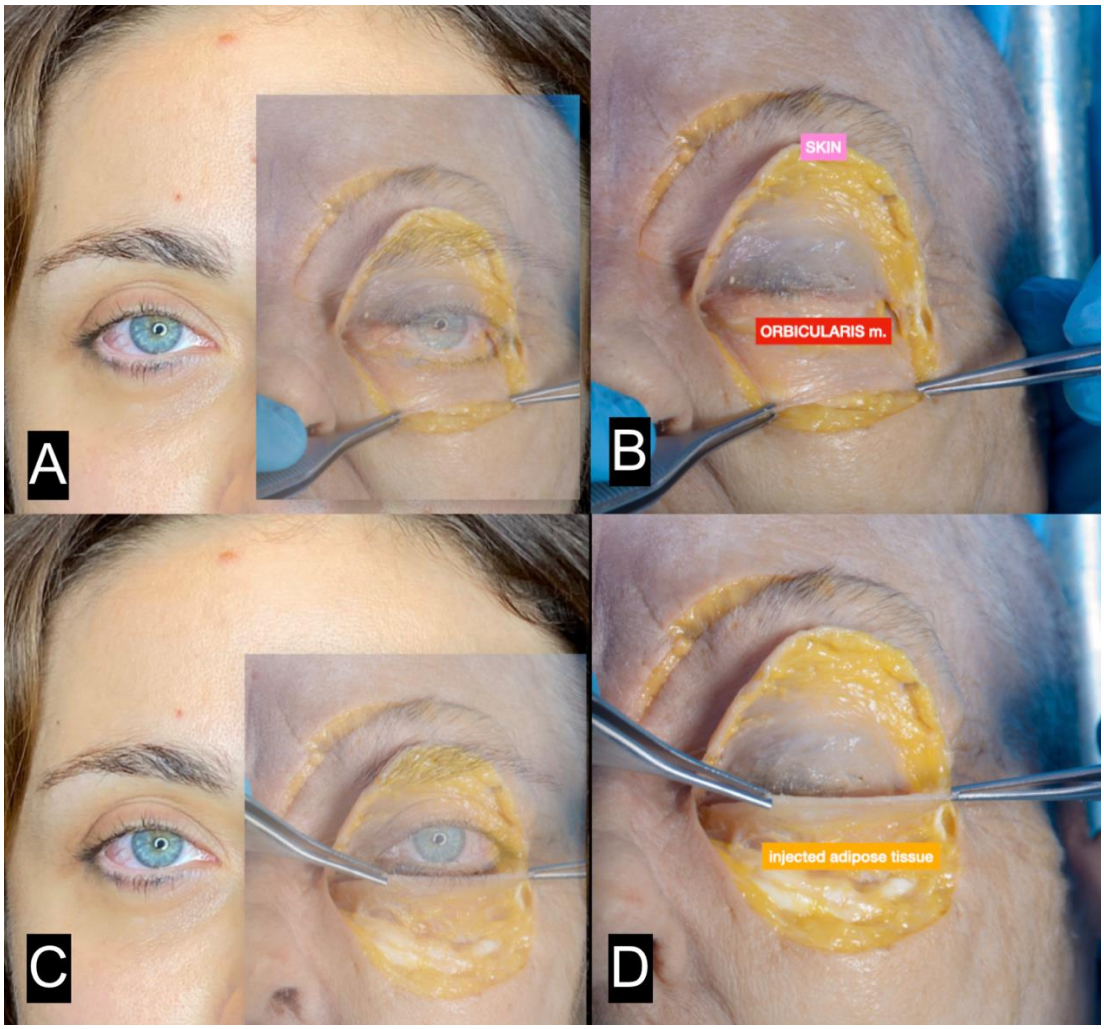

Figure 11. A: the patient of the Figure 10A with superimposed in transparency image from cadaver dissection: the skin is elevated. B: cadaver dissection: the orbicularis muscle is exposed. C: the patient of the Figure 10A with superimposed in transparency image from cadaver dissection: the orbicularis muscle is elevated. D: cadaver dissection: the injected tissue is exposed.

Guided SEFFI and Hyaluronic Acid

The combined treatments of guided SEFFI and Hyaluronic Acid (HA) are performed to enhance the volume of the face in a particular area such as malar, zygomatic, and jawline areas: in this case, the HA injection is performed before and more profound of the guided SEFFI. In the previous study, some AA proved that the combination of guided SEFFI and HA is available for the autologous ready-to-use treatment of human skin aging, which can be obtained without pre-treatment of enzymes and yields a highly homogeneous MSC population. The combination of SEFFI fresh tissue with HA product can be exploited to counteract the loss of volume and skin aging of the human face and body: examples of critical aesthetic areas of aging are the wrinkles around the mouth, loss of volume of the malar fat pad, tear trough periocular area, and hands and neck wrinkles. The non-expanded autologous fat product SEFFI with HA may pave the way to novel approaches and paradigms in facial rejuvenation within the context of personalized autologous regenerative medicine [40–42] (Figure 12).

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Figure 12. A,C: 43-yrs old woman pretreatment. B,D: post treatment 6 months: cross linked Hyaluronic Acid (HA) 1ml injected in the deep subcutaneous plane in each malar and zygomatic area, combined with guided SEFFI 5ml injected in the superficial subcutaneous plane in the same area in the same session.

Guided SEFFI and suspension threads

The three main factors in facial aging are volume loss, skin aging, and tissue descent. The combination of guided SEFFI and suspension threads is a facial rejuvenation treatment meant to restore volume, regenerate the skin, and reposition the superficial tissue. When the guided SEFFI and threads are performed in the same area, the procedure involves completing before the guide SEFFI, and after three weeks, it's possible the position of threads; in case the site is different (for example the guided SEFFI in malar zygomatic, perioral and periocular areas and suspension threads in the jawline area) it's possible to combine the two treatment in the same session. AA proved that in a retrospective analysis of a 232 cases series of patients seeking rejuvenation of the lower frame of the face (jowls and jawline), the combination of these medical techniques is promising medical treatments of mild to moderate facial laxity with a fast recovery and very low complications rate [43] (Figure 13).

Figure 13. A,C: 47-yrs old woman pretreatment. B,D: post treatment 6 months: suspension threads in the jawline combined with guided SEFFI injected in the malar zygomatic and temporal area.

Guided SEFFI and microneedling

Photoaging and smoke are the leading causes of superficial wrinkles, particularly in the perioral area ("barcode wrinkles"); skin microneedling is a technique that accelerates the process of skin regeneration through the creation of numerous microinjuries which emerge when skin is deeply punctured with very tiny needles. The procedure evokes various reactions, divided into three major

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phases: inflammation, proliferation, and remodeling. It activates platelet growth factors which are responsible for the stimulation of fibroblasts to produce collagen and elastin. Treatment can be performed using different devices, all equipped with needles of various lengths, since skin microneedling stimulates the synthesis of significant rebuilding and structural skin elements [44].

Moreover, several studies have analyzed in vitro actions of AD-MSCs against photoaging's effects, thanks to their migratory activity, paracrine actions, and related in vivo–ex vivo outcomes. AD-MSCs act against skin photoaging in vitro via activation of dermal fibroblast proliferation, antioxidant effect, and matrix metalloproteinases (MMPs) reduction [45,46].

In light of this evidence, some AA of this study proposed the combination of guided SEFFI and microneedling to treat superficial skin wrinkles, particularly in the perioral area and chin. The combination of these treatments was performed in the same session: guided SEFFI was carried out as the first procedure, followed some microneedling treatments (5-8 treatments weekly) (Figure 14).

Figure 14. A,C: 49-yrs old woman pretreatment. B,D: perioral post treatment 12 months: 2 guide SEFFI (every 6 months); any guided SEFFI was followed by 6 microneedling treatments.

Guided SEFFI and botulin toxin

Gaze rejuvenation is crucial in face antiaging treatment; the periocular area plays a fundamental role in the beauty and youthful aspect of the face. The main factors involved in gaze aging are dynamic wrinkles, the lowering of the eyebrow tails, the loss of volume, and skin aging of the periocular area.

Many AA proved the effect of the botulin toxin to reduce both the periocular dynamic wrinkles and the lift of the eyebrow tail [47–49].

Moreover, Bernardini et al. [30] proved the regenerative and volumizing effect of the SEFFI technique in the periocular area.

The micro fragmented adipose tissue injection involved a very fluid tissue. The injection was performed under the orbicularis muscle by microcannula with a relatively slow retrograde technique; before the tissue injection, an anesthetic solution with adrenaline (1: 100,000) was administrated under the orbicularis muscle. In this study, the botulin toxin was administrated ten days before the guided SEFFI procedure.

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Guided SEFFI and carboxytherapy

Carboxytherapy is a medical technique during which a sterile gas—carbon dioxide—is injected into the subdermal tissue. The utility of carbon dioxide injections has enhanced the practical relevance of carboxytherapy as a method for managing multiple disorders. Carboxytherapy provides an attractive aesthetic option in skin rejuvenation, atrophic scars, striae distensae (stretch marks), cellulite-fibrolipodystrophy adhesions after liposuction, and certain types of alopecia**.** The proposed mechanisms of action include increasing the blood supply, reopening closed capillaries, dilating pre-capillary vessels, increasing oxygen levels through the Bohr effect, which consists of a shift of the oxygen dissociation curve to the right, as a result of hypercapnia, decreasing oxygen consumption, increasing CO_2 in the tissues, and decreasing the affinity of hemoglobin affinity for oxygen [50,51].

In light of these effects, some AA of this study combined the tissue injection with carboxytherapy to combine the regenerative effect with the enhancement of tissue oxygenation. The two treatments were combined in the same section, and the Carboxytherapy was carried out (as a single procedure) 4 times every seven/ten days after the first combined treatment.

Guided SEFFI and Calcium Hydroxylapatite

Facial aging is a multifactorial and three-dimensional process involving volume loss, sagging, and skin alterations like elastosis. Every anatomical component of the face is affected. The combination of guided SEFFI and calcium hydroxyapatite has proven effective for a natural result of reharmonization of the face, especially in the scope of the duration of the results. The procedure foresees (T0) the treatment of the temporal, malar, zygomatic, preauricular, mandibular angle and marionette area with 3 ml of calcium hydroxyapatite diluted 1:1 or with hyperdilution 1:2 with physiological solution, to determine neocollagenogenesis, the production of elastic and angiogenesis of which both has extensive literature [52–54].

The implant is accomplished using 38 mm 27G or 50 mm 25G cannulas on the supraperiosteal and subcutaneous or subdermal plane [55]. After two weeks (T1), the SEFFI treatment uses approximately 20-24 ml of adipose tissue. The implant is performed on the subcutaneous and subdermal plane using 25G or 22G 50mm cannulas. Integrating these two medical techniques determines an excellent natural and balanced result and a notable duration over time (Figure 15).

Figure 15. A,C: 39-yrs old woman pretreatment. B,D: post treatment 16 months: 1 treatments of Calcium Hydroxylapatite filler (1.5 ml diluted 1:1 with saline solution) malar area followed by guided SEFFI 18 ml full face.

Guided SEFFI and Endolift

The TAR Autologous Regenerative Therapy in association with the Interstitial Laser Lifting 1470 nm with optical fiber: the perfect match in the treatment of facial aging.

Autologous Regenerative Therapy TAR exploits the regenerative potential of micro fragmented adipose tissue naturally rich in stromal vascular fraction (SVF), progenitor cells (ADSCs) and growth factors (GF).

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The harvest of adipose tissue is carried out through a device that allows the TAR to be performed on an outpatient basis in a simple, standardized and safe way. The procedure includes three phases, guided extraction of the adipose tissue, decantation and grafting, with maximum availability and cell vitality. The use of a cannula with micro-holes allows to harvest of already fluid adipose tissue which does not require further manipulation and can be injected with a micro-cannula (20-22G) into the SMAS and into the dermal layers of the face.

The interstitial laser lifting wavelenght 1470 is a mini invasive procedure which involves the use of 200-300micron optical fibers (OF). Like a luminous path, the OF cross the dermal layers transmitting laser radiant energy in the near infrared. Through a process of redensification and dermal retraction it allows to treat skin laxity, harmonize and redefine the profiles of the face.

The two methods are combined during the same treatment session. Dermal retraction lines, fan-shaped, are created from the pre-tragal region towards the cheek and along the profile of the jaw (200 joules per side) with 200- or 300-micron optical fiber. Subsequently, the fluid fat graft is taken from the trochanteric region which, after washing with a few cc of saline solution, is grafted multilayer in full face with a 20G cannula (8cc per side).

The integration of the two methods promotes the metabolic functions of the extracellular matrix, improves vascularization and amplifies the response of fibroblasts to neo-collagenesis. The results, progressively visible after two weeks, show a global rejuvenation of the face in terms of skin tightening and skin quality (Figure 16).

Figure 16. A,C: 50-yrs old woman pretreatment. B,D: post treatment 4 months: guided SEFFI 16 ml full face, followed by endolift fiber 300-micron flat tip, Ton50, Toff75, pulse mode, 500 joule lower third of the face, and 150 loule neck.

3. Results

In this study, we analyzed the results obtained from a total of 2,365 patients: of these, the vast majority (2,123 patients, 89.8%) were female, with a mean age of 49.2 years (range 38-65 years); the remaining 242 male patients (10.2% of the total patients) had a mean age of 37.6 years (range 41-53 years).

Table 1 reports the details of the fat harvesting sites and collected volumes using the guided SEFFI techniques. Fat tissue was gathered from the abdomen in more than 50% of treated patients. Trochanteric was also a frequently selected area (in about one-third of patients). Interestingly, the harvesting procedure from these two areas allowed us to obtain the same amount of tissue (27.1 ml). Hip was less frequently selected for the harvesting procedure, with a slightly lower yield (22.6 ml). The knee was also chosen as a collection site, yet more rarely, as the amount of liquid obtainable was lower than that obtained from the other harvesting areas.

Table 1 also reports the details of the injection sites and inoculated volumes using the guided SEFFI techniques. Most patients (81.4%) were treated in more than one site of the face; in particular, the procedure involved the whole face in almost one-quarter of patients (23.6%). The injection was

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performed in a single region of the face in only 18.6% of patients, and the malar-zygomatic area was the most frequently selected site as a single administration (9.9% of patients).

Table 1. Details of fat harvesting and injections sites with the SEFFI technique. The number in parenthesis indicate the percentage of the number of treated patients/total number of patients (N = 2,365). The column of the left side of the table reports the mean volume of tissue harvested and injected per patient.

FAT HARVESTING	Involved area	Number of patients (%)	Average harvested volume (ml)
	Abdomen	1231 (52.1)	27.1
	Trochanteric	761 (32.4)	27.1
	Hip	296 (12.6)	22.6
	Knee	67 (2.8)	6.8
	Other	3 (0.1)	2.1

SEFFI INJECTION	Injection area	Number of patients (%)	Average injected volume (ml)
Single area	Periocular	63 (2.7)	1.4
	Temporal	5 (0.2)	1.1
	Malar-zygomatic	233 (9.9)	4.4
	Perioral/lip	34 (1.4)	1.3
	Jawline	91 (3.8)	2.8
	Other	14 (0.6)	5.2
	Total	**440 (18.6)**	
Combined areas	Full face	557 (23.6)	14.8
	Two areas	561 (23.7)	5.1
	Three areas	639 (27.0)	2.8
	Four areas	246 (10.4)	8.3
	Total	**1925 (81.4)**	

Table 2 illustrates the types of aesthetic treatments performed using the SEFFI alone or combined with other procedures. The guided SEFFI procedure was portrayed as a single procedure in more than 60% of the cases and involved all the face areas. About one-tenth of patients had the fat graft combined with the botulin toxin treatment or hyaluronic acid filling; fewer patients underwent the other combined procedures.

Table 2. Details of the types of TAR procedures performed using the SEFFI techniques. The column of the left side of the table indicates the percentage of treated patients (N. total of patients =2,365).

TAR PROCEDURES		Number of procedures	Percentage of patients
Single procedure		1,484	62.7
Combined procedures	Botulin toxin	295	12.5
	Hyaluronic acids	233	9.9
	Threads	122	5.2
	Microneedling	85	3.6
	Calcium Hydroxylapatite	65	2.7
	Carboxytherapy	51	2.6
	Endolift	24	1.0
	Others	0	0
	Total	**875**	**37.0**

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Table 3 illustrates the adverse events at the donor and injection sites of treated patients.

The rate of complications was low: only ecchymosis was the most common complication occurring both in the donor site and injection site (14.2% and 38.6%, respectively).

In the donor site, other complications occurred very infrequently, such as hematoma or skin irregularities lasting more than 20 days, experienced by only 1.3 and 0.2% of patients, respectively.

Table 3. Summarized details of complications occurred in the donor and injection sites of patients who underwent the aesthetic rejuvenation treatment using the SEFFI technique.

Site of complications	Type of complications	Number of events	Percentage of patients
DONOR SITE	Ecchymosis	336	14.2
	Hematoma	31	1.3
	Prolonged erythema (> 48 hours)	0	0
	Skin necrosis	0	0
	Prolonged edema (> 20 days)	0	0
	Infection	0	0
	Fat necrosis	0	0
	Telangiectasias	0	0
	Skin irregularities (> 20 days)	5	0.2
	Embolism	0	0
	Other	0	0
INJECTION SITE	Ecchymosis	914	38.6
	Hematoma	18	0.8
	Prolonged erythema (> 48 hours)	0	0
	Skin necrosis	0	0
	Prolonged edema (> 5 days)	14	0.6
	Infection	1	<0.1
	Fat necrosis	0	0
	Telangiectasias	0	0
	Activation of acne	0	0
	Visibility	2	0.1
	Skin irregularities (> 48 hours)	1	<0.1
	Blindness	0	0
	Asymmetry	3	0.1
	Other	0	0

4. Discussion

Since 2001, Coleman [56] has studied a procedure that uses autologous fat tissue to restore facial volume. Autologous adipose tissue was believed to be the ideal filler, delivering natural filling in a safe and easy procedure [56].

However, this technique had limitations, such as unpredictable fat survival and a substantial risk of visible lumps. Consequently, many authors have been focusing on micro fragmented adipose tissue graft, naturally rich in cells from SVF and ADSCs, as a valuable approach in the aesthetic rejuvenation treatment to give volumization and skin regeneration effects [16,56]. Reported advantages of micro fat grafting include enhanced safety in the periocular area [57], the ability to inject the fat superficially using syringe needles [21,57–59], and higher content of stem cells [20].

Many studies have demonstrated that the smaller the adipose clusters injected, the most superficial tissue harvesting and the better the results obtained [16,20,21].

Moreover, when small (0.3 to 0.8 mm) adipose tissue clusters are injected, the cellular blood irroration is improved along with the degree of engraftment [31]. Coleman [56] emphasized that when placing fat, it is imperative to maximize the surface area contact with surrounding tissue to

 doi:10.20944/preprints202304.0775.v1

ensure the grafted fat's proximity to the recipient's vasculature. Larger fat globules undergo central necrosis and volume loss and may result in oil cysts [59,60].

In the last years, regenerative antiaging medical treatment encountered great interest from physicians and appreciation from patients, as this medical procedure is a natural therapy for tissue ageing. It is not merely a cosmetic treatment; the results are natural without overfilled and fake effects. Many studies proved the benefits of injecting adipose tissue, SVF, ADSCs, and GF in aging tissue [61,62].

In light of this evidence, regenerative medical treatment is becoming the main procedure for curing aged tissue; many combined treatments with other aesthetic medical procedures, such as hyaluronic acid filler, suspension threads, synthetic calcium hydroxylapatite, botulin toxin, and microneedling, are under investigation to improve the results and safety. The rationale for combining treatments is to perform the aesthetic treatment in a tissue with increased trophism and better circulation.

In recent years, guided SEFFI has allowed regenerative treatment in many Italian aesthetic medical centers, and the number of patients who have undergone this treatment has been steadily increasing since 2019.

Thanks to the patented guide, the guided SEFFI guarantees to collect adipose tissue in a very superficial layer (SAT), which yields a higher amount of SVF cells [20,63].

Furthermore, it guarantees that the harvesting procedure is performed in a safe plane. The SEFFI cannula allows for collecting adipose tissue already in small cellular clusters avoiding any further mechanical manipulations while allowing high viability and stemness of the micro-fragmented adipose tissue [12,36].

The coding technique for the guided SEFFI use allowed physicians without surgical skills to perform the SEFFI technique in a coded, simple safe, and effective way. This treatment will enable physicians (and not only surgeons) to accomplish regenerative therapy in aesthetic medicine for antiaging treatment by exploiting the capacity of SVF, ADSCs, and GF naturally present in the adipose tissue [37].

In this study, we focused the attention on the safety of the guided SEFFI and combined procedures: the results proved that these procedures are safe in the light of evidence that the only minor complication was the appearance of ecchymoses in the site of donor and injection - which, by the way, is quite a rather event in all harvesting and injecting procedures. Besides, the rate of other complications could have been more neglectable. Moreover, it is essential to underline that the shallow rate of complications in the harvesting site is because the amount of tissue harvested is lower than that collected in other harvesting or liposuction procedures previously described by other authors [45,64–66].

In this study, we analyzed data obtained from more than 2,000 patients.

Regarding the harvesting area, we found that the abdomen was the first choice, as it was selected in 52% of patients, followed by the trochanteric site (in 32% of patients). Interestingly, the mean average amount of tissue collected from both sites was 27.1 ml. Thus, this procedure is minimally invasive and allows the collection of moderate amounts of tissue: therefore, it can be safely performed in a medical facility under local anesthesia. After tissue harvesting and washing, the injection treatment was carried out in the whole face in almost one-quarter of patients (23.6%). A single area treatment was performed in fewer patients (18.4%): the most frequently treated area was the malar-zygomatic site (9.6%), where the average amount of injected tissue was 4.4 ml per side.

In this study, the guided SEFFI was performed as a single treatment in almost two-thirds of patients (62.7%). Of the remaining 37% of patients who received combined treatments, botulin toxin, and hyaluronic acid were the most commonly selected techniques (used in 12.5% and 9.9% of patients, respectively).

Not less importantly, the study proved that the guided SEFFI procedure was accompanied by a low rate of complications. However, more analyses on the use of guided SEFFI combined with other cosmetic procedures are the subject of further studies to corroborate the encouraging findings obtained in the present study. The results of this work will be published soon.

CONCLUSIONS

The presented study proved that guided SEFFI alone or in combination with other facial rejuvenation techniques performed in medical facilities is a minimally invasive procedure with a shallow rate of complications. In light of this evidence, guided SEFFI proved to be a promising medical antiaging treatment that combines effectiveness, safety, and simplicity.

Author Contributions: Gennai A., Baldessin M., Melfa F., Bovani B., Camporese A., Claysset B, Colli M., Diaspro A., Russo R, Strano P. contributed in treating and collecting cases; Bollero D, Capparè G., Casadei A., Gallo G., Piccolo D., Salti G., Tesauro P. contributed in statistical analysis and writing the article.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki; all procedures were performed in private Italian medical centers, so international review board approval was not required.

Informed Consent Statement: Written informed consent has been obtained from the patients to publish this paper.

Conflicts of Interest: The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

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