



Acne Scars: Multimodal Treatment with Surgical Subdermal Plane Dissection, Microfragmented Adipose Tissue Infiltration and Deep CO2 Laser Resurfacing. Our Clinical Experience in 15 Clinical Cases Treated

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Abstract

Background: Acne vulgaris is a common dermatological condition with an estimated prevalence of 70 to 87% in the general population; post-acne scars are equally common conditions with an estimated prevalence of 11 to 14% in the general population and cause a major impact on patients' quality of life with an important negative psychological impact.

Currently, there is no single treatment that can guarantee satisfactory results in the treatment of permanent scars, but the use of multiple therapeutic modalities in combination and with a synergistic effect allows to obtain a better outcome. From this assumption of combining different treatments but with a synergistic effect in the remodeling of acne scars, our study was born. We decided to evaluate the results obtained with 3 techniques that have proven to be complementary in our experience: surgical plane dermoabrasion and their surgical preparation with a cannula and/or 18G needle, infiltration of microfragmented autologous adipose tissue and treatment with fractionated CO2 laser in deep resurfacing mode.

Surgical dermoabrasion of the subcutaneous plane from the dermal plane using a cannula needle allows to free the tissue from the adhesions responsible for the scarring retraction and to prepare the correct plane for infiltration with microfragmented adipose tissue.

Treatment with microfragmented adipose tissue allows, through the action of stem cells and derived secretion factors, to stimulate collagen synthesis, neoangiogenesis and fibroblast migration.

Finally, treatment with fractionated CO2 laser with deep resurfacing induces the synthesis of new collagen through the activation of cutaneous fibroblasts or growth factors.

Materials and methods: We recruited 15 patients who we treated at our center (12 women and 3 men, age range between 19 and 54 years, 8 with Fitzpatrick phototype II and 7 with Fitzpatrick phototype III) with atrophic acne scars (boxcar, rolling and icepeak).

Patients with active acne, active medical treatment, or patients who had undergone other treatments such as chemical, mechanical or laser resurfacing in the 12 months prior to the study were excluded.

All patients were reassessed in the postoperative period at 3, 6, 9 and 12 months and were photographed using a standardized digital camera with the same lighting.

The efficacy of the improvement of the scar was evaluated with the ECCA score (échelle d'évaluation clinique des cicatrices d'acné), to which the patients were subjected to every medical check-up.

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We also analyzed the subjective perception of patients and their satisfaction through the IGA scale (Investigator's Global Assessment). All treated patients expressed their feedback during the final follow-up visit using a 5-point scale corresponding to different degrees of improvement (grade 0=no improvement, 1=1–25% improvement, 2=26–50% improvement, standard scale for 75% improvement and 4=76–100% improvement).

We recorded the overall duration of patient downtime, defined as a period that significantly affected their quality of relationships and work activity.

Results: A significant reduction in the ECCA score was observed from the first postoperative visit in 12 treated cases and subsequently in all cases at the final follow-up visit.

According to the IGA scale at the final follow-up visit, 12 patients achieved grade 3 improvements and three patients achieved grade 2. At the final follow-up visit, all patients had a reduction in the volume of the atrophic scar, the average pore volume and the skin roughness.

The mean duration of patient downtime was 4.5 days. 11 patients experienced treatment-related side effects such as post-treatment pain, erythema, edema and dryness that resolved within 4 days. No patient healed with the appearance of new scars or other permanent events.

Conclusion: The use of adipose tissue in regenerative medicine associated with plane dermoabrasion and ablative CO2 laser represents a valid strategy not only in terms of clinical efficacy, but also of safety in the treatment of acne scars. Furthermore, the use of microfragmented adipose tissue allows for the reduction of post-procedural side effects (edema, inflammation, pain, dryness) with a much faster return to regular daily activities and consequently greater patient satisfaction.

Keywords: Acne vulgaris, Acne scars, Microfragmented adipose tissue, Dermoabrasion

Introduction

Acne has a prevalence ranging from 70% to 87% in the general population and the clinical condition persists into adulthood in 12%-14% of cases, often causing significant psychological and social consequences.¹⁻³ Severe acne scars can result in both physical and psychological distress, especially during adolescence, and can affect various areas of the body having a high concentration of pilosebaceous glands, particularly the face, back, and chest. Inflammatory acne lesions can lead to permanent scars, the severity of which is often correlated with the delay in diagnosis and treatment or with the ineffectiveness of the treatments applied.¹ Available literature demonstrates a strong correlation between the severity of acne and the presence of scars in the general population.⁴ The pathogenesis of acne is currently attributed to various factors, including increased sebum production, altered lipid quality in sebum, androgen activity, proliferation of *Propionibacterium acnes* (*P. acnes*) within the follicle, and follicular hyperkeratinization.^{1,5} The primary factor predisposing to acne development is increased sebum excretion by the sebaceous gland. Lipids produced by sebaceous glands play various roles in signal transduction and are actively involved in multiple biological pathways.^{1,6}

Additionally, fatty acids act as ligands for nuclear receptors such as PPAR receptors. Sebaceous gland lipids have both pro-inflammatory and anti-inflammatory properties, while the induction of 5-lipoxygenase and cyclooxygenase-2 pathways in sebocytes leads to the production of pro-inflammatory lipids.^{1,7} Furthermore, hormones such as androgens control sebaceous gland size and sebum secretion. Evidence suggests that androgens promote sebocyte proliferation in cell culture, while PPAR ligands are neces-

sary for differentiation and lipogenic activity.^{1,8} Keratinocytes and sebocytes can be activated by *P. Acnes* through TLR, CD14, and CD1 molecules.^{1,9} Pilosebaceous follicles in acne lesions are surrounded by macrophages expressing TLR2 on their surface. Activation of TLR2 leads to nuclear transcription factor activation and the production of cytokines/chemokines, pathognomonic phenomena in acne lesions. Additionally, *P. acnes* induces the release of IL-8 and IL-12 from TLR2-positive Monocytes.^{1,10} All these events stimulate intrafundibular inflammatory process, follicular rupture, and perifollicular abscess formation, which are directly responsible for the wound-healing process. Wound healing represents one of the most complex biological processes, involving soluble chemical mediators, extracellular matrix components, resident parenchymal cells such as keratinocytes, fibroblasts, endothelial cells, nerve cells, and infiltrating blood cells like lymphocytes, monocytes, and neutrophils, known as immunoinflammatory cells.¹

The acne healing process consists of three successive phases: inflammation, granulation tissue formation, and matrix remodeling.^{1,11,12} Scar formation can result from prolonged inflammation, altered collagen balance during granulation tissue formation, imbalances in matrix-degrading enzymes during the remodeling phase, or delayed treatment of acne lesions. Olanda et al. have performed clinical studies on biopsy samples from acne lesions in patients with and without scars to compare the two groups and highlight differences. They have found that the inflammatory reaction to the pilosebaceous gland was stronger and longer-lasting in patients with scars than in those without, and the inflammatory reaction was slower in patients with scars than in those who had not developed scars. Current literature shows a strong relationship between the severity and duration of inflammation and the development of

scars, suggesting that early treatment of inflammation in acne-involved lesions may be the best approach to prevent scar formation.^{1,13} There are two main types of acne scars, which differ in the presence of a net loss of collagen in one case (atrophic scars) and a gain of collagen in the other (hypertrophic scars). Atrophic acne scars are more common than keloids and hypertrophic scars, with a ratio of 3:1. The latter are subclassified based on their morphology into ice pick (60%-70%), boxcar (20%-30%), and rolling scars (15%-25%).¹⁴ Icepick scars are narrow (2mm), pinpoint, and deep scars and their opening is typically wider than the infundibulum that is deeper (V-shaped). Boxcar scars are round or oval scars with well-defined vertical edges; they tend to be wider on the surface than ice pick scars, do not have a tapered V shape but rather a U shape with a broad base. The depth of these scars can be different. Rolling scars are wider scars, ranging in size from approximately 4 to 5mm, giving the skin a wavy appearance (M-shaped). As these three different types of atrophic scars can be found in the same patient, various authors have proposed different classifications and scales. Goodman and Baron proposed a qualitative and quantitative scale^{15,16} that is simple and universally applicable.¹ It represents a useful tool for a quantitative global assessment of acne scars¹⁶ based on both scar type and scars quantity. This system, known as IGA scale (Investigator Global Assessment of Acne), assigns fewer points to mild and macular atrophic scars than to moderate and severe atrophic scores (macular or mildly atrophic: 1 point; moderately atrophic: 2 points; perforated or linear severe scars: 3 points; hypertrophic papular scars: 4 points).

The multiplication factor for these types of lesions is based on the numerical range, from one to ten scars, the multiplier is 1; for 11-20 scars, it is 2; for more than 20, it is 3. Dreno introduced the ECCA scale (Echelle d'Evaluation Clinique des Cicatrices d'Acne), designed for clinical practice with the goal of standardizing scar treatment discussions. It is based on the addition of individual scar types and their wideness. Specific scar types and their associated weighting factors were as follows: atrophic scars with a diameter of less than 2mm: 15; U-shaped atrophic scars with a diameter of 2-4mm: 20; M-shaped atrophic scars with a diameter of more than 4mm: 25; superficial elastolysis: 30; hypertrophic scars lasting less than 2 years: 40; hypertrophic scars lasting more than 2 years: 50.

A semiquantitative evaluation of the number of each of these scar types was then determined using a four-point scale, where 0 indicates no scars, 1 indicates less than five scars, 2 indicates between five and 20 scars, and 3 indicates more than 20 scars. With this method, the relative extent of each scar type was calculated. The total score can range from 0 to 540. Hypertrophic scars and keloids are associated with excessive collagen deposition and reduced collagenase activity. Hypertrophic scars are typically pink,

raised, and hard, with a predilection for the upper chest, shoulder, and earlobe. Onset is usually 4-8 weeks after injury and is followed by growth for 6-12 months before plateauing. Mature hypertrophic scars are often asymmetrical and can regress slowly over years.¹ Various treatments are available for acne scars, including chemical peels, dermabrasion, microdermabrasion, microneedling, fractional lasers, dermal fillers, and surgical interventions such as punch excision, subcision, and autologous fat transfer. Combination therapy with several of these modalities is often required for optimal results.

In this article, we present a multimodal treatment approach for acne scars, involving surgical subdermal plane dissection, microfragmented adipose tissue infiltration, and deep CO2 laser resurfacing. We share our experience in 15 clinical cases treated with this approach.

Material and Methods

In this study we treated 15 patients (12 females and 3 males) with an age range of 19 to 54 years old. Among the treated patients, 8 had Fitzpatrick skin type II, and 7 had Fitzpatrick skin type III, all presenting with atrophic acne scars (boxcar, rolling, and icepick).

Patients with active acne, ongoing treatment with Isotretinoids, or those who had undergone other treatments (such as chemical, mechanical, or laser resurfacing) in the preceding 12 months were excluded from the study. We treated all the patients at Image Regenerative Clinic in Milan, and the procedure was performed in the surgical theatre. The treatment team consisted of an experienced surgeon, a laser therapy specialist, an anesthetist, and a professional nurse.

Prior to the setup of a sterile field and disinfection of the areas affected by acne scars using 2% Chlorhexidine, conscious sedation (slow-drip Midazolam) combined with local anesthesia using Lidocaine was administered. Subsequently, a meticulous surgical detachment of the subdermal plane from the dermal plane in the areas affected by acne scarring was performed. This procedure allowed for the release of subdermal tissue from scar adhesions and was carried out using an 18G needle or a 20G cannula. Later, manual liposuction was performed with a disposable 13G diameter liposuction cannula after infiltration with a solution of physiological saline (500ml + 1ml adrenaline) mixed with Klein's solution (physiological saline 250ml + 30cc Lidocaine 2% + 1ml adrenaline). The amount of adipose tissue harvested varied (ranging from a minimum of 60cc to a maximum of 300cc) and was carefully evaluated and weighed by the medical team in relation to the number and extent of acne scars to be treated.

Subsequently, adipose tissue microfragmentation was infiltrated into the pre-established subdermal plane using an 18G needle

or a 20G infiltration cannula. Patients were then treated with a fractional CO2 laser with parameters set at 15-23W, stack 2, and 500nm spacing on critical areas, and 12-16W on less damaged areas. Finally, patients were treated with a dermaroller with 3mm micro-needles and microfragmented adipose tissue, which was put into absorption.

All patients were reassessed at 3, 6, 9, and 12 months post-operation and were photographed in standardized conditions, in the same position, and under the same lighting. The effectiveness of aesthetic improvement of acne scars was assessed using the ECCA score (Clinical Evaluation Scale of Acne Scars) at each visit. The patient's subjective perception of the treatment and their satisfaction were evaluated through the IGA scale performed at the final follow-up visit. Finally, the overall duration of patient downtime, defined as the period significantly affecting their quality of life and work activity, was recorded.^{17,18}

The Lipogems® System

The literature demonstrates how application of adipose-derived stem cells (ASCs) has synergistic effects in enhancing responses to CO2 laser treatment and reducing adverse effects, thanks to its potential to accelerate tissue regeneration and wound healing.¹⁹ The combination of laser treatment and autologous adipose tissue infiltration in the treatment of acne scars is an effective but also quite impactful protocol for the patient, made possible through the use of ASCs, which induce rapid healing following post-laser ablation by providing multiple anti-inflammatory and regenerative growth factors.^{20,21} ASCs activate fibroblast properties, such as promoting migration, proliferation, and collagen synthesis,^{22,23} thus accelerating the healing of soft tissue wounds with extracellular matrix remodeling.^{24,25} It has been over a century since the first definition of stem cells as ancestral germ line cells,^{26,27} and since then, a significant number of studies have been published regarding their potential and application in regenerative medicine and surgery. In vitro and in vivo experimental studies have shown that human MSCs can differentiate into various cellular subtypes, such as osteoblasts, chondrocytes, myocytes, and adipocytes. Increasing attention is being paid to MSCs derived from human and animal adipose tissue due to their abundance and ease of access. These multipotent cells can also differentiate into mature adipocytes, chondrocytes, osteoblasts, myocytes, hepatocytes, neuronal cells, and endothelial cells as suggested by in vitro, ex vivo, and in vivo evidence,^{26,28,29} and this potential can be used to regenerate damaged tissues. Furthermore, MSCs secrete a variety of bioactive molecules that act paracrinally to trigger and support angiogenic, antifibrotic, anti-apoptotic, and immunomodulatory responses in the target tissue.^{26,30,31} Adipose-derived stem cells also promote skin lesion repair without scarring by regulating the ratios of collagen type III and type I, transforming

growth factor (TGF)- β 3:TGF- β 1, matrix metalloproteinase 3: tissue inhibitor of metalloproteinase-1, and by regulating fibroblast differentiation to mitigate scar formation.²³ Recent literature has shown that adipose-derived stem cells can increase de novo ceramide synthesis to rebuild the skin barrier.²¹ In recent years, numerous studies have focused their attention on technical improvement and maximization of the therapeutic effects of the traditional adipose tissue transfer technique. Various protocols have demonstrated greater tissue vitality and a lower percentage of contaminants in washed and filtered adipose tissue within a closed system. Among these new findings, Lipogems® technology plays an emerging role. The Lipogems® system commercially available belongs to the class II of medical devices and is intended to produce a sort of natural implantable bioreactor. This technology reduces the size of adipose tissue, which clusters together through gentle mechanical forces, eliminating oily impurities and dead cells, mechanically and intra-operatively providing microfragmented adipose tissue in a short time without expansion and/or enzymatic treatment.^{32,33} Throughout the entire procedure, the processed fat is subjected only to mild mechanical forces without any detrimental effects on the integrity of the stromal vascular niche and the tissue itself because the device is carefully pre-filled with a physiological solution to avoid the presence of air during all steps. The resulting product has been shown to possess reparative properties, particularly when injected into inflamed and ischemic tissues,^{32,34} due to its ability to induce vascular stabilization and inhibit various macrophage functions involved in inflammation.^{32,35}

Fractional CO2 Ablative Laser

CO2 laser treatment is now an effective and widely used procedure for atrophic acne scars. This device operates at a wavelength of 10nm, which is absorbed by the water contained in intracellular fluids, allowing it to selectively heat and vaporize the superficial layers of the skin.³⁶ Through controlled heating of the collagen present within the dermis, the CO2 laser allows for the removal of fragmented collagen in the matrix and promotes the production of new collagen, resulting in an improvement in the aesthetic appearance of the scar. However, the use of this device is often associated with a high risk of complications and side effects such as prolonged erythema, hypopigmentation, post-inflammatory hyperpigmentation (PIH), especially in patients with darker skin types, and an extended healing and recovery time. This is why we evaluated the effectiveness of combined treatment and, in particular, the combination with microfragmented adipose tissue treatment. The ability to modulate the action of the CO2 laser through parameter settings allows for different treatment of various regions of the face depending on their involvement in the scarring process and tailoring the treatment based on the patient's type, phototype, and lesion char-

acteristics. Higher energy can be used for the treatment of significant acne scars, while lower energy and multiple passes can be used in less sensitive areas. On the other hand, high fluence and multiple passes should be avoided in more sensitive areas such as the eyelids and neck to reduce the risk of complications.

Results

The patients were followed up for several months after treatment, and the outcomes were assessed using the ECCA score and IGA scale. In 12 cases treated from the first postoperative visit, a reduction in the ECCA score (Clinical Evaluation Scale for Acne Scars) was observed. In the remaining cases, a decrease in the ECCA score was noted at the final follow-up visit.

According to the IGA scale (Investigator Global Assessment of Acne), which was presented to the patients at the final follow-up visit, 12 patients achieved grade 3 improvements, and three patients achieved grade 2 improvements. At the final follow-up visit, and through photographic comparison, all patients experienced a reduction in the volume of atrophic scars, average pore size, and skin roughness. The average patient downtime was 4.5 days. Side effects related to the treatment occurred in 11 patients, including post-treatment pain, erythema, edema, and dryness, all of which resolved within 4 days. No patients experienced the development of new scars or any other permanent events.

Discussion

The multimodal treatment approach presented in this study addresses the complex nature of acne scars by combining surgical dissection, adipose tissue infiltration, and laser resurfacing. Each component of the treatment plays a distinct role in scar improvement.

The Surgical Subdermal Plane Dissection releases fibrous bands that tether the scar to the underlying tissue, allowing for scar elevation. By dissecting the subdermal plane, the surgeon can improve the contour of the scar.

Afterwards, infiltrating microfragmented adipose tissue into the subdermal plane helps elevate the scars and provides a volumetric improvement of the scar area.

Laser resurfacing is essential for collagen remodeling and skin tightening. It helps improve skin texture and further enhances the appearance of the treated area.

This combination of techniques addresses both the loss of collagen and volume in atrophic scars, resulting in comprehensive scar improvement. The results are long-lasting, and patients experience minimal downtime.

Conclusion

The multimodal treatment involving surgical detachment of the dermal plane from the subdermal plane, infiltration with micro-

fragmented adipose tissue, and ablative fractional laser has proven to be effective in the treatment of acne scars, not only in terms of clinical efficacy but also in terms of treatment safety. Acne scars often negatively impact the patients' quality of life.

It is crucial to consider the characteristics of the scars, their extent, and plan tailored treatment approaches based on the patient and the characteristics of the lesions to be treated. The discussion of outcomes should be conducted between the physician and the patient to achieve an optimal result that meets the patient's expectations. The interaction between the physician and the patient is vital for establishing a trusting relationship and for monitoring post-procedural home care.

The use of regenerative medicine and microfragmented adipose tissue allows for the reduction of post-procedural side effects (edema, inflammation, pain, dryness) and a much quicker return to regular daily activities, resulting in greater patient satisfaction.

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Conflict of Interest

Authors declares that there is no conflict of interest.

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