

Acne vulgaris scars: a review of disease mechanisms, market trends, and emerging technologies

Abstract

Acne vulgaris is a chronic inflammation of the pilosebaceous glands that affects approximately 85% of adolescents. After healing, acne scars may remain due to skin damage during the healing process of active acne. These scars can be categorized as atrophic or hypertrophic/keloidal. Atrophic scars can be further classified as ice-pick, boxcar, or rolling. According to Grand View Research, the global topical scar treatment market is expected to grow significantly from 2025 to 2030, with a Compound Annual Growth Rate (CAGR) of 11.9%. Current treatment options for acne scars include ablative and non-ablative lasers, chemical peels, skin fillers, microneedling, thread lifting, dermabrasion, and platelet-rich plasma. Clinical trials are also exploring innovative technologies, such as combinations of polynucleotides with hyaluronic acid, topical insulin, and Alexandrite lasers. Additionally, preclinical research studies are exploring growth factor and exosome treatments. There remains an urgent need for acne scar treatments specifically tailored for patients with darker skin tones.

Keywords: acne scars, atrophic scars, laser treatment, collagen remodeling, combination therapy, tissue engineering

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Abbreviations: CAGR, compound annual growth rate; PIH, post-inflammatory hyperpigmentation; AHAs, alpha-hydroxy acids; BHAs, beta-hydroxy acids; TCA, trichloroacetic acid; HA, hyaluronic acid; PMMA, polymethylmethacrylate; RF, fractional radiofrequency; PLLA, poly-L-lactic acid; PDO, polydioxanone; PRP, platelet-rich plasma; PRF, platelet-rich fibrin; EGF, epidermal growth factor; rhEGF, recombinant human epidermal growth factor; CGF, concentrated growth factors; SVF, stromal vascular fraction; MSCs, mesenchymal stem cells; ASCE, adipose tissue stem cell-derived exosomes; PN-HPT, polynucleotide highly purified technology

Introduction

Acne vulgaris is a chronic inflammation of the pilosebaceous glands that affects approximately 85% of adolescents.¹ While primarily impacting adolescents, acne can persist into adulthood in 12–14% of cases and is the reason for 30% of dermatological appointments.^{2,3} Out of 37 studies with a total of 23,649 patients, the prevalence of acne scars was found to be 47%.⁴ In addition, 34% of 723 acne scar patients reported that their scars had a major impact on their wellbeing.⁵ As a result of acne scars, patients felt ashamed, embarrassed, anxious, and socially isolated.⁶ Acne scars appear most frequently in people with severe acne, which can lead to a significant reduction in their quality of life.

Acne occurs most frequently in areas with greater concentrations of pilosebaceous glands, typically on the face, back, and chest.³ Acne can be characterized by open and closed comedones, pustules, papules, and cysts.⁶ Causes for acne include increased sebum production, elevated levels of androgens, abnormal keratinization of pilosebaceous glands, Propionibacterium acnes proliferation, and an inflammatory response of innate immune cells (Figure 1B).³ Increased dairy and sugar consumption have also been shown to be proacnegenic, but it may be dependent on sex, ethnicity, and cultural dietary habits (Figure 1A).⁷ Androgens, such as testosterone, control sebaceous gland size and sebum secretion and underscore acne development.³ Acne can have a

significant impact on mental health with adolescents and adults with acne reporting higher rates of anxiety, low self-worth, and depression than those without acne.⁸

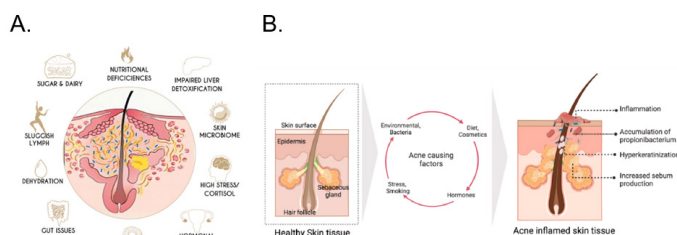


Figure 1 Main cause of acne. A) Etiology of acne B) Healthy vs. Acne inflamed skin.^{3,7}

The image shows a chart of the main causes of acne. Part B contrasts healthy and acne inflamed skin.

Healthy tissue

Sebaceous glands play a prominent role in the initiation of acne development.⁹ These glands are found within hair follicles over the entire surface of the body, aside from the palms and soles of the feet. Sebaceous glands are the most concentrated on the face, back, scalp, and chest, but are most numerous on the face.^{9,10} These glands are located in the dermis and typically develop alongside hair follicles. The sebaceous gland taken together with the hair follicle is known as a pilosebaceous unit (Figure 2).¹¹ Sebaceous glands have an acinar structure and sebocytes turn over once every 14 days, producing 1mg/10 cm² of sebum every 3 hours.⁹ The typical person has a film of facial sebum that can be greater than 4 μm thick.¹⁰ While the number of sebaceous glands is constant throughout a person's life, their size can increase with age, especially at the time of adolescence. This hypertrophy of sebaceous glands can be associated with the development of acne.¹¹

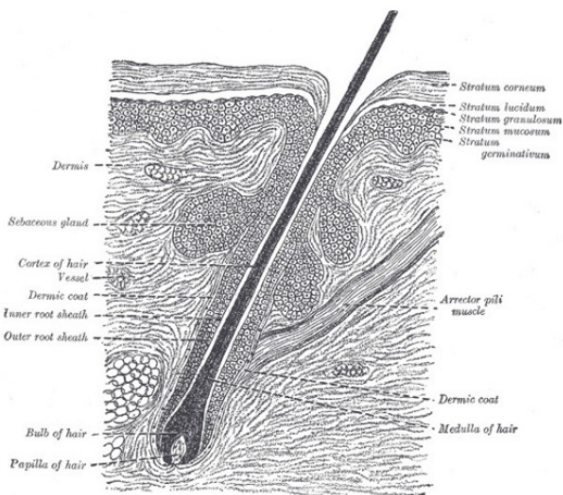


Figure 2

Figure 2 Pilosebaceous unit in healthy tissue.¹¹

The image shows a healthy pilosebaceous unit made up of the hair follicle and sebaceous gland located deep within the dermis.

Sebaceous glands are responsible for maintaining the integrity of the skin barrier by producing the holocrine secretion called sebum, which consists of squalene, cholesterol, triglycerides, and fatty acids.¹² The sebaceous glands empty sebum into the hair canal which reaches the skin surface through a wicking action of the hair shaft. Sebum is essential for the function and structure of the skin, given that it provides 90% of surface lipids.¹¹ The production of sebum is essential for maintaining skin lubrication and homeostasis.⁹ Sebum lubricates the hair and skin and can make them impermeable to water. Sebum also plays a role in the transportation of antioxidants and defends against the environment.¹¹ Other functions of sebum that are still being explored are protection against sunburn and maintenance of the skin biofilm.¹⁰ Androgens and other endocrine hormones regulate sebum secretion and can stimulate cell proliferation and lipogenesis.¹¹ During puberty, androgens are produced at a higher rate and lead to increased sebum production.⁹ Sebum lipids are also involved with the activation of macrophages and enhanced phagocytosis.¹³

Disease tissue

The development of acne is associated with the inflammation of the pilosebaceous unit and an overall disruption of the skin barrier.¹⁴ The overproduction of androgens is also associated with the development of acne.⁹ High levels of androgen production can result in sebum plugs, which result in closed and open comedones.¹¹ The chronic inflammatory response associated with acne can stimulate the activation of fibrosis-related cytokines and scar tissue formation.¹⁵

These permanent scars can be graded based on their severity and categorized as macular, mild, moderate, or severe (Figure 3).³ After healing, acne scars may persist due to damage to the skin, such as the abnormal degradation of facial collagen. An autopsy performed on patients' backs revealed that the development of acne scars could be associated with a stronger and longer inflammatory reaction at the pilosebaceous gland. They identified a strong relationship between the severity and duration of inflammation and acne scar formation.³ Another study identified three risk factors associated with developing acne scars: positive family history of acne, male gender, and acne severity.⁴

Grades of Post Acne Scarring	Level of disease	Clinical features
1	Macular	These scars can be erythematous, hyper- or hypopigmented flat marks. They do not represent a problem of contour like other scar grades but of color.
2	Mild	Mild atrophic or hypertrophic scars that may not be obvious at social distances of 50 cm or greater and may be covered adequately by makeup or the normal shadow of shaved beard hair in men or body hair if extrafacial, but is still able to be flattened by manual stretching of the skin (if atrophic).
3	Moderate	Moderate atrophic or hypertrophic scarring that is obvious at social distances of 50 cm or greater and is not covered easily by makeup or the normal shadow of shaved beard hair in men or body hair if extrafacial, but is still able to be flattened by manual stretching of the skin (if atrophic).
4	Severe	Severe atrophic or hypertrophic scarring that is evident at social distances greater than 50 cm and is not covered easily by makeup or the normal shadow of shaved beard hair in men or body hair if extrafacial and is not able to be flattened by manual stretching of the skin.

Figure 3 Qualitative scarring grading system.⁴

The image shows a tabular overview of the grades of post acne scarring. The levels of acne vulgaris are macular, mild, moderate, and severe.

Acne scars can be categorized as either atrophic or hypertrophic/keloidal (Figure 4). These two acne scar types depend on whether the scar is associated with a net loss or gain of collagen. Atrophic scars are associated with a loss of collagen, while hypertrophic/keloidal scars are associated with a gain of collagen. Out of patients who experience acne scars, 80-90% of people have atrophic scars or scars associated with a loss of collagen.³ Atrophic acne scars are caused by inflammation of the pilosebaceous gland that destroys deep dermal structures. This inflammation is followed by the abnormal synthesis/degradation of collagen and tissue contraction and frequently results in skin indentation. The three classifications of atrophic scars based on their shapes and depths are ice-pick, rolling, and boxcar. Ice-pick scars are the most common, accounting for 60-70% of atrophic acne scars.³ Ice-pick scars are characterized by a “V” shape. They have a surface width of usually less than 2mm and usually extend to the deep dermis tissue (Figure 5). Boxcar scars make up 20-30% of atrophic scars and have a “U” shaped cross-section. The surface opening and bottom are wider for rolling scars than ice-pick scars. Lastly, rolling scars comprise 15-25% of atrophic scars and are wide with a diameter greater than 4mm and a soft edge. In rolling scars, the dermis and subcutaneous tissue has a wavy “M” appearance.¹ In contrast to atrophic scars, hypertrophic and keloidal scars are characterized by decreased collagenase activity and excess collagen deposition. Hypertrophic scars are pink, raised, and firm with hyalinized collagen bundles that remain within the borders of the original injury. Keloids form red/purple nodules and papules that proliferate beyond the original wound borders. These are characterized by thick bundles of hyalinized acellular collagen.³

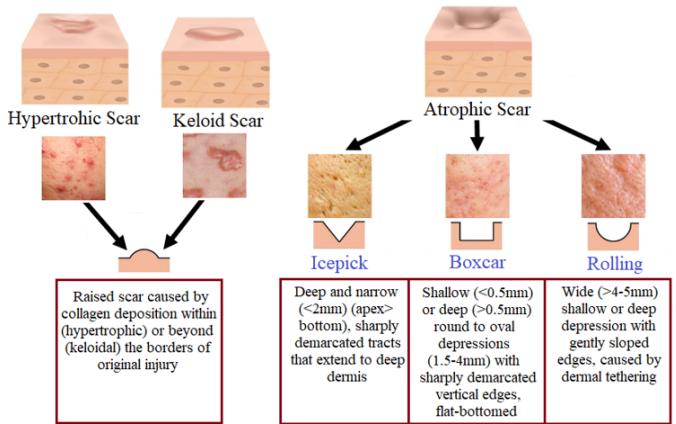


Figure 4 Types of acne scars: atrophic and hypertrophic/keloid scars.⁵⁵

The image shows the three different types of acne scars: hypertrophic, keloid, and atrophic. Atrophic acne scars can be further separated into icepick, boxcar, and rolling scars.

Acne Scars Subtype	Clinical Features
Icepick	Icepick scars are narrow (<2 mm), deep, sharply margined epithelial tracts that extend vertically to the deep dermis or subcutaneous tissue.
Rolling	Rolling scars occur from dermal tethering of otherwise relatively normal-appearing skin and are usually wider than 4 to 5 mm. Abnormal fibrous anchoring of the dermis to the subcutis leads to superficial shadowing and a rolling or undulating appearance to the overlying skin.
Boxcar Shallow <3 mm diameter >3 mm diameter	Boxcar scars are round to oval depressions with sharply demarcated vertical edges, similar to varicella scars. They are clinically wider at the surface than icepick scars and do not taper to a point at the base.
Deep <3 mm diameter >3 mm diameter	They may be shallow (0.1–0.5 mm) or deep (≥0.5 mm) and are most often 1.5 to 4.0 mm in diameter.

Figure 5 Clinical features of each atrophic acne scar subtype.¹

The image shows a tabular overview of the clinical features of each atrophic scar subtype.

Market size, products, and companies

The prevalence of acne is estimated to be 9.4% worldwide.¹⁶ Acne mainly impacts adolescents, with a peak incidence at ages 15-20 years. This is also fairly consistent throughout the world⁹. Acne scarring can also be dependent on ethnicity since acne scarring and PIH (post-inflammatory hyperpigmentation) occur more frequently for people of color. Additionally, atrophic scarring is also more common in Hispanic and African American women versus other ethnicities.¹⁶ Despite unfamiliarity with acne scar solutions, 86% of patients in a Nigerian study claimed that they were willing to pay for scar treatment. This study demonstrated a global interest in effective acne scar treatments.¹⁷

According to Grand View Research, the global topical scar

treatment was estimated at USD 1.69 billion in 2024 and is expected to grow at a Compounded Annual Growth Rate (CAGR) of 11.9% from 2025 to 2030 (Figure 6A). This market growth is expected due to increased concern regarding appearance and technological advancements. Atrophic scars dominated the market with a revenue share of 37.15% in 2024 and are anticipated to experience the fastest growth due to the rising prevalence in acne scars. Retail pharmacies held the largest market share (40.30%) in 2024 due to government support and industry consolidation (Figure 6B). The online distribution channel is projected to witness the fastest growth from 2025 to 2030 due to increased consumer preference for convenience.¹⁸

Globally, the topical scar treatment for acne scars market is experiencing steady growth in China, Latin America, and in the Middle East and Africa (MEA) (Figure 6C). The increasing prevalence of acne scars has heightened the demand for topical treatments in China since approximately 7.1% of Chinese adolescents suffer from acne scars. In Brazil, the topical scar market is also experiencing growth because of increasing beauty consciousness and a high value on aesthetics. Due to an increased interest in Saudi Arabia, the Saudi government has been investing in dermatological research. Currently, the companies that hold the greatest share in the topical scar treatment market and dictate market share are Lumenis, Merz Pharmaceuticals LLC, Sonoma Pharmaceuticals Incorporated, and Cynosure Lutronic (Table 1).¹⁸

Table 1 Acne scar key players and their products

Name of Company	Year founded	Location	Products	Reference
Lumenis	1991	Israel	UltraPulse: 10,600 nm CO ₂ fractional or full ablative laser, deepest penetration with lowest energy, shortest pulses per energy level	I a, 2a
Cynosure Lutronic	1991	USA	RevLite SL: 1064nm and 532nm wavelengths for non-ablative skin resurfacing. PicoSurePro: delivers 755nm energy in picoseconds	I b, 2d, 2c, 2d
The Ordinary	2016	USA	Icon: Er:Glass 1540nm laser for acne scar removal	I c, 2e
Dermalure	2007	USA	AHA 30% + BHA2% peeling solution to improve skin texture	I d, 2f
SkinCeuticals	1994	USA	10%-50% TCA medium-depth facial peel	I e, 2g
Bellafill	2006	USA	Smart TCA Peel with 15% TCA and 3% glycolic acid	I f, 2h
Cutera	1998	USA	Polymethylmethacrylate (PMMA) microspheres suspended within bovine collagen	I g, 2i
VIOLA Threads	2019	Korea	Secret RF: fractional radiofrequency microneedling system	I h
Allergan Aesthetics	2013	USA	FDA-cleared polydioxanone (PDO) threads for tissue suspension	I i, 2j
Crown Aesthetics	2012	USA	DiamondGlow: dermabrasion treatment that exfoliates, extracts, and infuses	I j, 2k
Merz Aesthetics	1908	USA	ProGenPRP: Kit for preparation of autologous platelet rich plasma (PRP)	I k, 2l
Sonoma Pharmaceuticals Incorporated	1999	USA	Merderma Advanced Scar Gel: contains allantoin to protect the skin	I l, 2m
			Regenacyn: Hypochlorous acid and silicone scar gel for infection control and promoting wound healing	

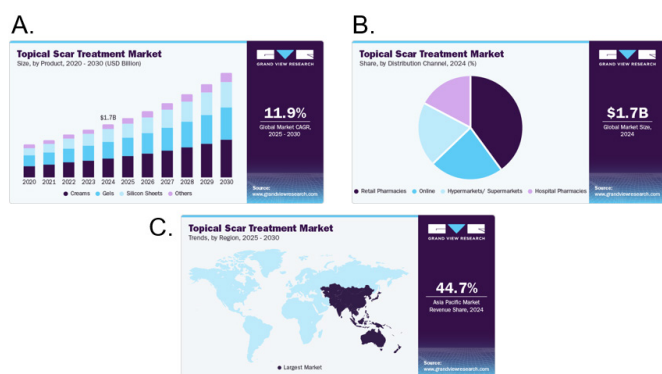


Figure 6 Topical scar global market analysis A) Topical scar market growth and CAGR B) Topical scar market share by distribution channel C) Topical scar treatment market by region.¹⁸

The image shows the growth of the topical scar market from 2020-2030 and the share of the topical scar treatment market by distribution channel. Part C depicts the topical scar treatment market trends per region.

Existing products

Fractional laser

The current gold standard for treating depressed acne scars is an ablative CO₂ fractional laser which has been in use since the 1980s.^{6,19} There are two categories of established lasers to treat acne: ablative and non-ablative fractionated lasers. Ablative lasers use high heat to vaporize the skin, accelerate tissue removal, and create scars following treatment.¹ The most established ablative laser is the 10600 nm CO₂ laser which emits light in the infrared spectrum to create microscopic treatment zones. These microscopic treatment zones activate re-epithelialization and new collagen formation. Pulsed-action lasers are also implemented to improve laser precision and depth of skin ablation.⁶ When using 10600 nm CO₂ lasers to treat atrophic scars in Asian patients, it was found that 3 treatment sessions led to up to 80% improvement and minimal adverse effects (Figure 7).²⁰ In an experiment where Asian patients received three treatments of the lasers, the clinical effective rate was 68.4% (21). This suggested that 10600 nm CO₂ lasers could improve mild to moderate acne scars. Key companies that produce these lasers are Lumenis and Cynosure.¹⁸ Lumenis offers various devices with adjustable healing zone volume, spot size, and depth for optimal treatment (1a) (Figure 8). Despite the effectiveness of the 10600 nm CO₂ laser, this method is often accompanied by side-effects, including edema, pigmentation, and edema.¹

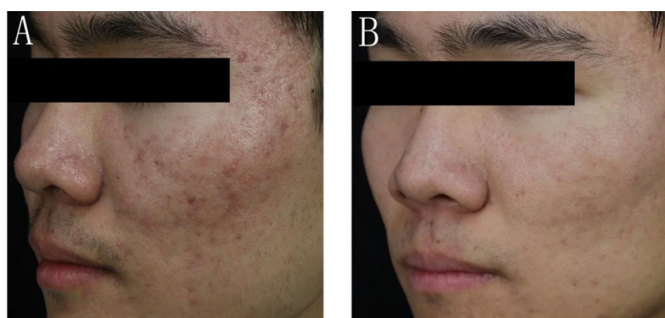


Figure 7 Treatment of Acne Scars with 10600 nm CO₂ Lasers A) Pre-treatment B) Post-treatment.²⁰

The image shows the before and after appearance of a patient's acne scars after treatment with a 10600 nm CO₂ laser.

	ActiveFX™ Treat fine lines, texture & dyschromia	DeepFX™ Treat wrinkles & acne scars	TotalFX™ Combine superficial & deep fractional effects	SCAR FX™ Treat deep, conspicuous and complex lesions
Adjustable Healing Zone Volume				
Spot Size	1.3mm	0.2mm	1.3mm & 0.2mm	0.2mm
Depth				
Scanner	ActiveFX (CFG)	DeepFX	ActiveFX (CFG) & DeepFX	DeepFX

Figure 8 Lumenis ultrapulse configurations for treating scars.^{2a}

This image shows the various spot sizes, healing zones, and scanners available for the UltraPulse laser scar treatment from Lumenis.

Non-ablative lasers divide the beam of the laser in weak light spots that act on the skin. This causes water in the tissue to absorb energy from the laser and form columnar, microthermal zones (MTZs), while the layer between the MTZs remains intact.^{1,22} This can lead to repair mechanisms that stimulate collagen regeneration. The primary non-ablative lasers in use are pulsed dye lasers (PDL), which have wavelengths ranging from 585 nm to 600 nm. These lasers stimulate collagen resynthesis and increase the number of collagen fibers.¹ In a study of 24 subjects who received three sessions of a 675 nm non-ablative laser, all patients experienced a significant improvement in their acne scars (Figure 9).²³



Figure 9 675 nm non-ablative laser improves skin texture.²³

This image shows a patient before (a,b) and after (c,d) three sessions of a 675 nm non-ablative laser device treatment.

Chemical peel

In addition to laser treatment, chemical peeling can be utilized for skin rejuvenation and induce the production of new collagen fibers. Acid substances, such as alpha-hydroxy acids (AHAs), beta-hydroxy acids (BHAs), and trichloroacetic acids (TCAs) can act as chemical peeling agents.¹ These acids coagulate proteins on the surface of the skin and damage the living cells of the epidermis, which leads to exfoliation of the cells and the production of collagen fibers.⁶ Chemical peels are becoming widely accessible with superficial or light peels (AHAs and BHAs) dominating the majority of the chemical peel market (Figure 10).²⁴ For example, the AHA 30% + BHA 2% Peeling Solution from The Ordinary is a very popular at-home exfoliating solution available at the low price of only \$11.40 USD

(2e) If improperly used, chemical peels can cause skin irritation and redness, especially if combining AHAs with other skin treatments.²⁵ For example, in the Philippines, the Food and Drug Administration (FDA) warned the public not to purchase the AHA 30% + BHA 2% Peeling Solution from The Ordinary due to the danger of chemical burns.²⁶ For deeper atrophic scars, peeling agents such as TCA are required and are typically administered in a dermatology office.¹ Key companies driving the TCA market include Dermalure which offers TCA ranging from 10-50% and SkinCeuticals which offers a TCA restorative masque and a TCA peel with 15% TCA and 3% Glycolic Acid.^{1d,1e,2f,2g,27}

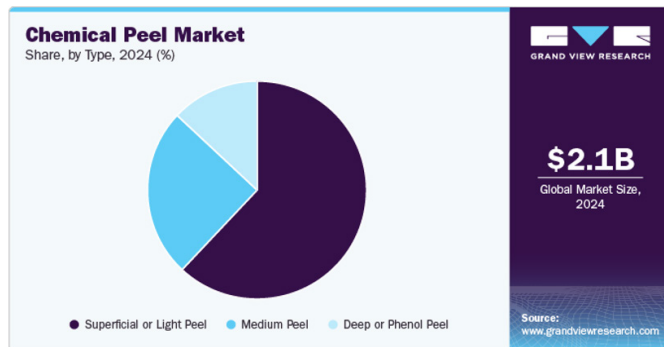


Figure 10 Chemical peel market share by type.²⁴

This image shows the share of the chemical peel market by type and the global market size.

Skin-filling

Another mainstream method for treating atrophic acne scars is skin-filling treatment. This involves injecting material into the acne scar area to elevate the skin. Common skin fillers include hyaluronic acid (HA) and exogenous collagen. Since HA is naturally produced by the body, it is very biocompatible and has low allergenicity.²⁸ Longterm, HA activates fibroblasts to increase collagen synthesis. Twelve patients with moderate to severe acne scarring underwent microinjections of 20mg/mL HA into depressed acne scars. Immediate visual improvement was observed in all lesions and the procedure was well tolerated (Figure 11).²⁸ Exogenous bovine or porcine collagen can be directly injected into the dermis to restore volume loss. In comparison to HA fillers, exogenous collagen has greater potential for allergenicity and must be tested before injection. Bellafill is a FDA-approved filler with polymethylmethacrylate (PMMA) microspheres suspended into a bovine collagen gel.²⁹ PMMA is a biocompatible polymer used in cranial plates and bone cement since 1975.³⁰ In a clinical trial over the course of 4 years and involving 212 patients, 99% of patients reported that they were satisfied with improvement.²⁹ For a semi-permanent effect on rolling scars, Poly-L-lactic acid (PLLA) can be injected to stimulate fibroblasts to produce collagen (1). PLLA has been reported to sustain the correction of rolling acne scars for up to 4 years.¹

Microneedling

Microneedling (MN) can also be used for acne scar treatment by creating hundreds of tiny holes to stimulate healthy skin regeneration. This tiny damage can increase collagen deposition, promote growth factors synthesis, and reduce inflammatory reactions. In a randomized clinical trial of 20 healthy adults, mean scar scores were significantly lower in the treatment group compared with the baseline at 6 months.³¹ While MN therapy is effective for treating rolling and boxcar scars,

there was no significant observed effect on ice-pick scars.¹ A key player in MN therapy is Cutera's FDA-cleared Secret RF which is a fractional radiofrequency (RF) microneedling system (Figure 12).^{1g,2i,32} Cutera offers two sizes of treatment tips, 25 and 64 pin, for precision and efficiency.²ⁱ

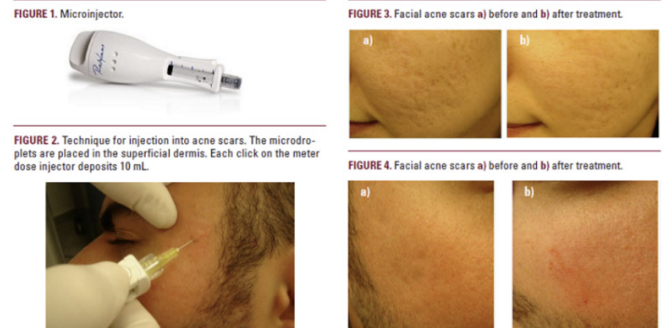


Figure 11 Microinjection of hyaluronic acid fillers for acne scars.²⁸

This image shows the process of injecting hyaluronic acid fillers and skin before and after treatment.

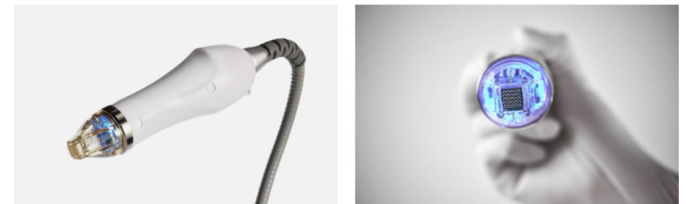


Figure 12 Cutera secret rf microneedling device.²ⁱ

This image shows the cutera secret RF microneedling device from a front and side view.

Thread lifting

Thread lifting is another minimally invasive approach for treating acne scars by inserting absorbable, barbed threads beneath facial skin. These threads can suspend underlying tissues and stimulate collagen synthesis via fibroblast activation.¹ Significant clinical improvement was observed in 23 of 24 patients treated with a microneedling pen device.³³ In the United States, VIOLA Threads manufactures FDA-cleared polydioxanone (PDO) threads to suspend tissue and promote collagen synthesis (Figure 13).^{1h} VIOLA Threads offers sixteen different products with varying needle length/thickness and thread length for different body areas.^{1h}



Figure 13 VIOLA threads polydioxanone (PDO) products (1h)

This image shows the eight PDO thread products that VIOLA Threads offers.

Dermabrasion

A more invasive, surgical approach to improve acne scars is dermabrasion. Dermabrasion involves the controlled abrasion of

the epidermis and dermis typically using a grinding wheel. This can induce reepithelialization, repigmentation, and collagen synthesis.¹ Dermabrasion allows a practitioner to selectively plane off “hilltops” surrounding atrophic scars, which is very effective for deeper ice-pick scars.³⁴ While dermabrasion allows for the removal of deeper scars, penetrating the skin too deep in the dermis can lead to new scar formation. This emphasizes the need for identifying innovative and less invasive technologies.³⁴ A leading FDA-cleared device in the dermabrasion market is DiamondGlow by Allergan Aesthetics (Figure 14).^{11,2j} This device utilizes a three-in-one treatment to exfoliate the skin with diamond tips, extract debris with high-powered suction, and infuse serums into the skin for long-lasting effects.^{2j}



Figure 14 DiamondGlow dermabrasion treatment.^{2j}

This image shows the use of DiamondGlow from Allergan Aesthetics on patient's face.

Platelet-rich plasma

Platelet-rich plasma (PRP) has also emerged as a novel therapeutic for the management of acne scars. Within PRP, there are highly concentrated platelets, inflammatory cells, and substantial levels of proteins. These proteins consist of epithelial growth factor (EGF), platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), transforming growth factor beta (TCF-Beta), and adhesion molecules (fibrin, fibronectin, and vitronectin). These proteins have been demonstrated to promote proliferation and tissue regeneration, which could be utilized with the PCP approach.³⁶ One study compared the use of Platelet-rich-fibrin (PRF) and PRP on reducing atrophic acne scars. Out of 30 patients who received both treatments on either side of their faces, acne scars were significantly reduced on both sides. According to a grading scale and patient satisfaction, the therapeutic response was significantly higher in the PRF group than the PRP group.³⁷ The current gold standard is the FDA-cleared ProGen Kit from Crown Aesthetics (Figure 15).^{1j, 2k} A small amount of blood is drawn from a patient, placed into a sterile container, spun down to separate the platelets from the blood sample, and injected into the patient (2k). Since the PCP is derived from the patient, there is minimal risk for an immune reaction (2k).

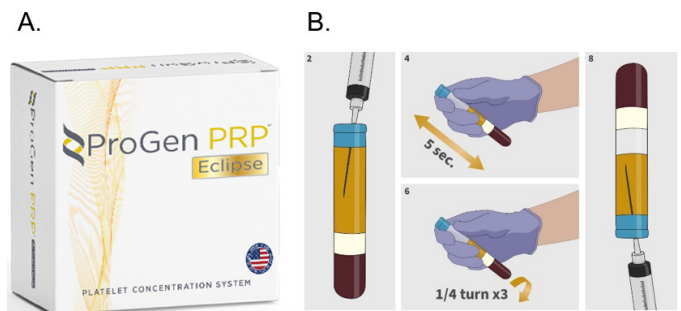


Figure 15 ProGen platelet rich plasma (PRP) Kit A) Extraction Kit B) Extraction of PRP from Centrifuged Blood (2k)

This image shows the ProGen PRP eclipse kit and the instructions for the extraction of PRP from centrifuge tubes included in the kit.

Products in clinical trials

The majority of acne scars clinical trials that are recruiting/not yet recruiting are biologic, combination products.³⁸ One clinical trial is evaluating the efficacy and safety of a medical device that combines Polynucleotide Highly Purified Technology (PN-HPT) and hyaluronic acid (HA) to treat atrophic acne scars. Polynucleotides are naturally occurring DNA molecules that can be extracted from trout gonads and used as temporary fillers. Further, the synergistic effect of PN-HPT and HA on pain control and fibroblast proliferation may have an influence on acne scar reduction.⁴⁰ The treatment plan consists of four treatments at two-week intervals.³⁹ Another clinical trial is currently investigating the impact of stromal vascular fraction (SVF) enriched PRP on acne.⁴¹ SVF cells have been shown to be effective in combination with fat in improving scar tissue. Autologous fat injections have also been used independently of SVF to repair soft tissue defects.⁴² Another clinical trial is exploring nano-fat grafting combined with CO₂ laser resurfacing versus solely nano-grafting for the treatment of atrophic acne scars, which emphasizes that combination products may be the future of acne scar reduction.^{43,44} Further, another clinical trial intends to explore a combination of traditional acne scar reduction strategies by comparing microneedling with autologous PRP and microneedling with topical insulin.⁴⁵ The transdermal delivery of topical insulin is known to stimulate collagen production and promote growth factor synthesis.⁴⁶

Most of the active clinical trials for acne scars involve new laser treatment techniques. One clinical trial aims to evaluate the safety and efficacy of using an Alexandrite laser for the treatment of acne scars on Fitzpatrick Type V (dark brown) and Type VI skin (deeply pigmented).⁴⁷ There is also a clinical trial evaluating the efficacy of the AVAVA MIRIA Laser Skin System treatment on acne scars. The improvement of acne scars will be evaluated at one-, two-, and six-month timepoints.⁴⁸ Another clinical trial is currently exploring the non-ablative ER:Glass 1540 nm laser to treat both acne vulgaris and acne scars. This laser would work by deeply penetrating the skin to reduce sebum production and promote collagen production.⁴⁹

Pre-clinical products

Emerging therapies for acne scarring rely on biologic substances for anti-inflammatory and anti-fibrotic effects. Growth factors, such as epidermal growth factors (EGF), have recently been shown to reduce skin scarring by inhibiting the inflammatory response. This is especially true when growth factors are combined with other FDA-cleared therapies.¹ In one study, 15 patients with atrophic acne scars received CO₂ laser treatment and then were randomly assigned to

receive either recombinant human epidermal growth factor (rhEGF) or a placebo on one side of their face. Following treatment, both the CO₂ and CO₂ + rhEGF sites exhibited significant improvements in the appearance of acne scars. On the rhEGF treated side, a significant decrease in pore number and epidermal pigment area was observed, as well as an increase in epidermal thickness and collagen fibers.⁵⁰ In another combination study, subcision was combined with concentrated growth factors (CGF) to investigate the effect of these therapies on acne scar treatment. Subcision is a minimally invasive procedure of severing fibrous bands beneath dermal scars to promote tissue regeneration and elevate the depressed scars. CGF is a platelet concentrate product that is obtained through the centrifugation of blood and can have a greater tissue regeneration effect when compared to PCP (51). From a study of patients, they demonstrated that the combination of subcision of CGF injection is more effective than using subcision alone (Figure 16).⁵¹

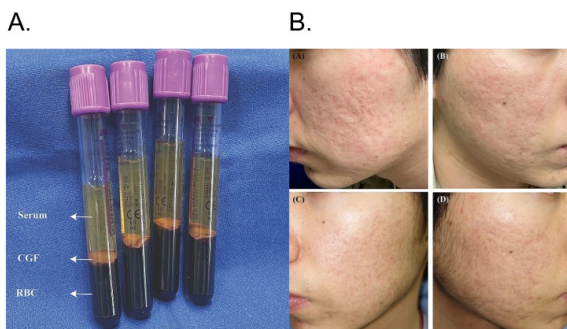


Figure 16 Concentrated Growth Factor (CGF) Preparation and Before and After Results A) Three Distinct Layers of Centrifuged Blood 2) Before and After Six Months of Subcision and CGF Injection Treatment.⁵¹

This image shows centrifuged blood with the CGF layer and a patient's face before (A,B) and after (C,D) subcision and CGF injection treatment.

Another developing therapy for acne scars is the use of human adipose tissue stem cell-derived exosomes (ASCE) to combat the downside of mesenchymal stem cells (MSCs).⁵² While MSCs can promote wound healing, they can also lead to tumor formation, which emphasizes the need for a safer alternative.⁵³ Studies have shown that MSC-derived exosomes carry the essential properties of MSCs, suggesting that they may have regenerative properties without the risk. In a study of 25 Korean subjects, ASCE treated patients achieved a significantly greater improvement than the control patients at the final follow-up visit after 6 weeks (Figure 17). Some adverse effects of the exosome treatment included pain, erythema, and dryness [Appendix](#).⁵²

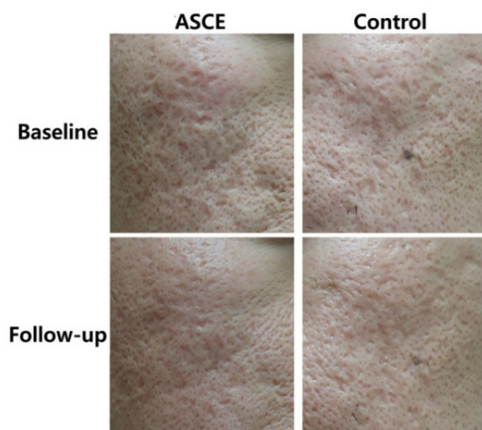


Figure 17 Control and adipose tissue stem cell derived exosomes (ASCE) at Baseline and 6 weeks after 3 treatment sessions.⁵² This image shows the baseline and follow-up of skin treated with 3 sessions of ASCE.

Conclusion and future considerations

Based on current pre-clinical and clinical studies, combination therapies appear to be the future direction for acne scar treatment. Combined approaches can utilize the complementary effects of different treatment methods to produce results that are superior to a single therapy. Currently, the most researched combination therapies are laser and PRP injections, MN and subcision, and PRP with 50% TCA.¹ There is a strong and urgent need for research into acne scar treatments specifically tailored for patients with darker skin tones. While chemical peels and laser treatments may be effective for lighter skin types, these therapies are associated with risks (dyspigmentation and hypertrophic scarring) that disproportionately impact patients with darker skin.⁵⁴ This urgency is further demonstrated by the large number of active clinical trials for acne scars that focus specifically on patients with darker skin, such as the Alexandrite laser.⁴⁷

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Conflict of interest

Authors declare that there is no conflict of interest.

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