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# Emerging Innovations in Acne Management: A Focus on Non-Pharmacological Therapeutic Devices

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## ABSTRACT

Acne is a chronic inflammatory condition affecting the sebaceous glands, with approximately 80% of individuals experiencing it at some point in their lives. Among adolescents, the incidence is reported to exceed 85%. The disease can significantly impact both physical and emotional aspects of a person's quality of life, leading to permanent scarring, poor self-image, depression, and anxiety. The standard first-line treatment for acne vulgaris includes conventional pharmacological approaches such as keratolytics, topical or oral antibiotics, retinoids, and hormonal agents. However, these treatments are not universally effective due to patient noncompliance, adverse drug effects, and the emergence of antibiotic resistance in *Cutibacterium acnes*, often resulting in high rates of recurrence. Consequently, non-pharmacological therapies have been developed as safe and effective alternatives or supplements to pharmacological treatment. These non-pharmacological approaches can serve as standalone treatment modalities, adjuncts to pharmacological therapy, or maintenance treatments. Current literature lacks comprehensive data on the classification of these non-pharmacological treatment options. This paper aims to provide a brief overview of recent research on the practical applications and potential mechanisms of non-pharmacological therapies for both acne and acne scars. Through elucidating the distinct mechanisms and therapeutic roles of these treatments, we aim to assist dermatologists and other healthcare providers in formulating more effective disease management strategies, thereby encouraging further research in this area.

**Keywords:** Acne; Acne Scar; Mechanism; Energy-Based Device

## INTRODUCTION

Acne is a prevalent inflammatory dermatological condition that predominantly emerges during puberty, affecting over 95% of adolescent males and 85% of adolescent females. Approximately 12% to 14% of these cases persist into adulthood.[1] A lasting and significant consequence of acne is scarring, which is experienced by up to 95% of affected individuals; around 30% of these scarring cases are severe.[2]

The ramifications of acne and its associated scars extend beyond cosmetic concerns, exerting a considerable psychological and societal toll. They have been implicated in a range

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of mental health issues, including anxiety, depression, social isolation, and even suicidal tendencies.[3] The pathophysiology of acne involves four key elements: abnormal sebum production and composition, altered keratinization within the pilosebaceous duct, the presence of *Cutibacterium acnes* bacteria, and inflammation.[4] The etiology of acne scarring lies in a disrupted wound healing process, instigated by cutaneous inflammation. This disruption results in an imbalance between extracellular matrix degradation and collagen synthesis.[5] The consequence is either an overproduction of collagen, leading to hypertrophic or keloid scars, or a collagen deficit, resulting in the more commonly observed atrophic scars.[2]

Management options for acne and its scars depend on the clinical manifestations and include both pharmacologic and non-pharmacologic treatments, such as the utilization of energy-based devices (EBDs) and chemical peels.[6-9] Treatment efficacy for individual lesions may vary based on characteristics like color and depth. A multimodal approach has been suggested to offer potential benefits over monotherapy.[8]

This study aimed to review pertinent literature and provide updated information on non-pharmacologic treatments for acne and acne scars.

## EBDs FOR ACNE AND ACNE SCARS

In terms of technology, EBDs are classified into several categories: laser-based, light-based, electromagnetic energy-based, ultrasound-based, cryolipolysis, suction-based, and plasma EBDs.

This review focuses on the application of EBDs in treating acne and acne-related conditions. Specifically, we divide these devices into two main categories: those primarily used for active acne and those used for addressing erythema, pigmentation, and scarring associated with acne. **Table 1** summarizes the types, mechanisms, and effects of energy-based devices (EBDs)

**Table 1.** Energy-based devices for active acne

| Device | Mechanism of action | Efficacy | Side effects | Reference |
|---|---|---|---|---|
| Visible light (blue light) | Generates ROS and NO, targeting bacterial porphyrins and promoting anti-inflammatory effects | Reduces inflammatory lesions; improved lipid profiles; optimal efficacy at 100 mW/cm$^2$ for 20 minutes over five days | Inconsistent impact on wound healing; depends on energy density | 10-14 |
| Visible light (red light) | Deeper penetration targeting sebaceous glands; stimulates fibroblasts for wound repair | Comparable efficacy to blue light with fewer adverse reactions; 76% improvement with combination therapy | Minimal adverse reactions | 15-20 |
| IPL | Broadband light absorbed by chromophores, reducing sebaceous gland activity and inflammation | Effective for PIE and PIH; reduced sebaceous gland size and TNF-α expression | Transient erythema, mild discomfort | 21-24 |
| PDT | Photosensitizers induce ROS formation, leading to apoptosis and reduced inflammation | Equally effective as daylight PDT with lower ALA concentrations; fewer adverse effects | Photosensitivity, restricted penetration depth, discomfort during procedure | 25-28 |
| PTT | Gold nanoshells absorb light, heating sebaceous glands and inducing focal thermolysis | Efficient reduction in acne severity; effective for recurrent acne and enlarged pores | Minimal local inflammatory side effects, mild discomfort | 29-33 |
| Microneedle RF | Generates thermal heat in the dermis to stimulate collagen production and modulate sebaceous gland activity | 20.86% reduction in acne lesions in clinical trials; effective for active acne and pores | Mild erythema; no serious adverse events reported | 34-39 |
| 1,450 nm diode laser | Thermal coagulation of sebaceous lobules via mid-dermis heating | 40–83% lesion count reduction; long-term remission rate > 70% | PIH minimized with brief cooling and low fluence methods | 40-44,46,47 |
| 1,726 nm diode laser | Spectral selectivity for sebaceous glands; localized heating | 52–56% inflammatory lesion reduction in 4–12 weeks; long-term ILC reduction (97%) | Mild discomfort; no serious device-related adverse effects | 48-50 |

ROS = reactive oxygen species, NO = nitric oxide, IPL = intense pulsed light, PIE = postinflammatory erythema, PIH = postinflammatory hyperpigmentation, TNF-α = tumor necrosis factor-α, PDT = photodynamic therapy, ALA = aminolevulinic acid, PTT = photo-thermal therapy, RF = radiofrequency, ILC = inflammatory lesion counts.

**Table 2.** Energy-based devices for acne scars, PIH, and postinflammatory erythema

| Device | Mechanism of action | Efficacy | Side effects | Reference |
|---|---|---|---|---|
| 585/595 nm PDL | Stimulates dermal remodeling and collagen synthesis, reduces inflammation via increased TGF-β | Improvement in acne erythema, scarring, and active acne lesions; effective with low-fluence protocols | Purpura, transient erythema | 50-52,54 |
| 532 nm KTP laser | Selective photothermolysis of blood vessels; photoactivation of porphyrins targeting *C. acnes* | Reduces acne lesions and sebum secretion; effective for pigmented lesions and scars | Mild erythema, transient pigmentation changes | 5,53,56,57 |
| Microneedle RF | Combines microneedling-induced injuries and RF energy to promote collagen remodeling | Significant scar depth reduction; improvements in skin texture and pore appearance | Pain, erythema, localized swelling | 36,60-63 |
| Nonablative and ablative fractional lasers | Promote collagen biosynthesis and dermal remodeling via thermocoagulation | Effective for acne scars and pores; minimal downtime with nonablative lasers | PIH (reduced with proper parameter settings) | 64-68 |
| Fractional picosecond lasers | Induce dermal remodeling through laser-induced optical breakdown and plasma generation | Superior improvement in scars and skin texture compared to nonablative lasers; high patient satisfaction | Minimal downtime; rare cases of transient erythema | 69-71 |
| 1,064 nm Nd:YAG laser | Deep dermal penetration for pigmentation disorders and scar tissue; reduces sebum secretion | Simultaneous improvements in acne scars, pigmentation, and texture | Localized discomfort; rare transient pigmentation changes | 72-74 |
| Ultrasound | Induces thermal injuries for collagen remodeling; enhances transdermal drug delivery | Improves hydration, reduces erythema and fibroblast growth; beneficial for keloid and hypertrophic scars | Mild localized heating effects | 75-80 |

PIH = postinflammatory hyperpigmentation, PDL = pulsed dye lasers, TGF-β = transforming growth factor-β, RF = radiofrequency.

used for active acne treatment. **Table 2** provides an overview of the EBDs applied for acne scars and postinflammatory conditions, including their mechanisms and therapeutic effects.

## EBDs primarily used for active acne

### *Visible light*

Phototherapy utilizing visible light, particularly blue light with a wavelength range of 400–500 nm, has been extensively employed for acne treatment. The key physiological mechanisms activated by blue light involve the generation of reactive oxygen species (ROS) and nitric oxide. These contribute to angiogenesis promotion, anti-inflammatory effects, and direct antimicrobial activity.[10] The effectiveness of blue light is contingent upon specific chromophores such as opsins, flavins, porphyrins, and nitrosated proteins. Studies have shown that exposure to blue light leads to the photoexcitation of bacterial porphyrins in *C. acnes* colonies, resulting in the production of singlet oxygen and subsequent bacterial destruction.[11,12] Research by Ding et al.[13] demonstrated that skin surface lipidomics can reveal a correlation between lipidomic profiles and acne grades in adolescents. Further, significant alterations in skin surface lipids were observed following blue light treatment, indicating potential changes in lipid content and distribution.[13] The literature presents some contradictions regarding blue light's impact on wound healing. A recent study found that low energy densities (< 20 J/cm$^2$) of blue light stimulated various cell types and proteins involved in the healing process by reducing pro-inflammatory cytokines and increasing growth factors. Conversely, high energy densities (20.6–50 J/cm$^2$) were found to significantly inhibit cell proliferation, migration, and metabolism.[10] Nakayama et al.[14] reported optimal efficacy for blue light treatment when irradiation was administered at 100 mW/cm$^2$ for 20 minutes over five consecutive days in a mouse model. Consequently, this treatment protocol could be beneficial for treating acne with high levels of inflammation on a daily basis until improvement is noted.

Red light therapy (620–660 nm) is less effective in activating porphyrins but offers deeper skin penetration, thereby targeting sebaceous glands directly and exerting anti-inflammatory effects through the release of cytokines from macrophages. Subsequently, these cytokines stimulate fibroblast proliferation and the production of growth factors, thereby facilitating

wound repair processes.[15,16] A comparative study by Li et al.[17] showed that red and blue light therapies displayed comparable efficacy in treating mild-to-moderate acne vulgaris, particularly inflammatory lesions. Red light therapy had the added advantage of causing fewer adverse reactions than blue light.[17] Papageorgiou et al.[18] reported an average 76% improvement in inflammatory lesions when treated with a combination of blue and red light, as compared to benzoyl peroxide or blue light alone. Additional research indicates that combined blue and red light LED phototherapy is a safe, effective, and painless treatment for acne lesions.[19,20]

*Intense pulsed light (IPL)*

IPL systems operate based on principles similar to lasers: light energy is absorbed by specific target cells containing chromophores within the skin. This energy is then converted into heat, causing damage to the target area. Unlike lasers, IPL systems utilize broadband light (560–1,200 nm) and often employ filters to fine-tune energy output for treating specific areas. This approach enhances penetration without requiring excessive energy levels and allows for the targeting of specific chromophores. The absorption of red and blue light can activate porphyrins, reducing the growth of *C. acnes*. Additionally, endogenous chromophores in the skin absorb the broad spectrum light emitted by IPL, resulting in damage to the blood vessels supplying the sebaceous glands and consequently reducing gland size and/or function. Barakat et al.[21] observed a microscopically significant reduction in inflammation through the downregulation of tumor necrosis factor-α and a reduction in sebaceous gland size in acne vulgaris lesions post-IPL treatment.[22] IPL has also proven effective and safe for treating acne-related postinflammatory erythema (PIE) and postinflammatory hyperpigmentation (PIH).[23] A prospective study demonstrated that narrow-spectrum vascular filters (530–650 nm and 900–1,200 nm) used in IPL treatment resulted in more effective treatment of PIE, along with greater patient satisfaction and a lower rate of acne relapse, than did broad-spectrum treatment.[24]

*Photodynamic therapy (PDT)*

PDT employs photosensitizing agents in conjunction with low-level lasers to induce the rapid formation of ROS. The ROS subsequently triggers cellular apoptosis, necrosis, or immunogenic cell death through lipid peroxidation and DNA damage, as well as induces local immune responses and microvascular damage.[25,26] PDT offers several advantages and disadvantages for the treatment of skin conditions. Advantages of PDT include: 1) Precise targeting: PDT allows for the selective ablation of abnormal or damaged skin cells without harming adjacent healthy tissues. this selectivity is particularly advantageous for skin condition treatments. 2) Minimally invasive nature: being a generally non-invasive treatment, PDT often results in shorter recovery periods and less scarring. 3) Simultaneous treatment: multiple lesions can be addressed in a single session. However, PDT also has limitations, such as restricted penetration depth, light sensitivity, pain or discomfort during the procedure, the necessity for multiple treatment sessions, and limited accessibility based on geographic location and healthcare resources. The interval between the application of the photosensitizing agent and the initiation of light treatment, termed the “incubation” or “activation” period, may vary according to several factors. These factors include the specific photosensitizing agent employed, the condition under treatment, and the established treatment protocol. Daylight PDT, which forgoes the incubation period and relies on natural sunlight, has been reported as an effective and well-tolerated alternative for acne treatment.[27] While the concentration of aminolevulinic acid used in conventional PDT is typically 20%, daylight PDT employs significantly lower concentrations, such as 6% or 1.5%. A split-face clinical trial comparing conventional red-light PDT with daylight PDT found the latter to be equally effective, with fewer adverse effects and shorter downtime.[28]


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*Photo-thermal therapy (PTT)*

PTT is a minimally invasive therapeutic approach that has garnered significant interest in recent years. The technique primarily relies on the activation of photosensitizing agents via electromagnetic radiation, such as radio frequency, microwaves, pulsed lasers in the near-infrared spectrum, or visible light, to convert this energy into heat.

Previous studies have demonstrated the potential efficacy of gold nanoshell-mediated PTT for treating recurrent acne. Advantages of this approach include negligible systemic toxicity, minimal local inflammatory side effects, rapid and efficient reduction in acne severity, and sustained therapeutic benefits due to the targeting of sebaceous glands (**Fig. 1**). In investigations involving gold nanoshell-mediated PTT, optical imaging identified gold microparticles appearing as hyperreflective columns within hair follicles, a feature absent in the surrounding skin of both healthy participants and acne patients.[29] Post-laser exposure analyses, including reflectance confocal microscopy (RCM) and histology, indicated selective perifollicular tissue changes.[30] After administering the nanoshells into the follicles and glands, wiping away superficial nanoshells from the skin surface, and exposing the skin to near-infrared laser, these localized nanoshells absorb light, become heated, and induce focal thermolysis of the sebaceous glands. Human clinical studies have confirmed the effectiveness of ultrasonically delivered silica-gold nanoshells in disrupting sebaceous glands without causing collateral skin damage.[31] Topically applying gold salt itself directly reduced the activity of the NLRP3 inflammasome in a mouse model, indicating a potential anti-acne effect.[32]

Interestingly, chronic recurrent acne has been linked to the presence of enlarged facial pores. A recent case report has documented the efficacy and safety of gold nanoshell-mediated PTT as a treatment modality for enlarged facial pores.[33]

*Microneedle radiofrequency (RF)*

RF technology emits low-frequency electromagnetic waves that generate thermal heat in the dermis, subsequently stimulating collagen production, elastin formation, and neovascularization, all crucial elements in the healing process.[34] The therapeutic efficacy of microneedle RF in treating active acne can be attributed to multiple factors.

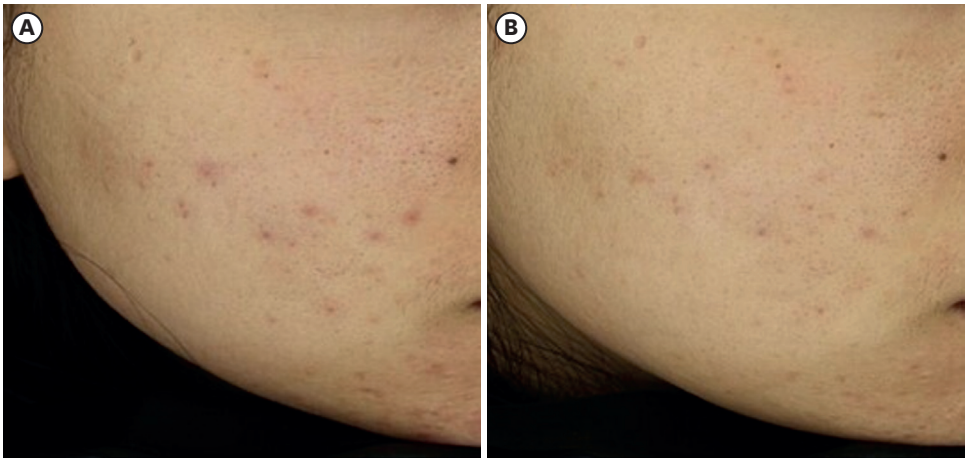


**Fig. 1.** Representative clinical images demonstrating the effects of photothermal therapy. Before treatment (**A**) and after photo-thermal therapy treatment (**B**). Improvement in the acne lesions. The figures are published under agreement of the patient.


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- Reduction of inflammation: thermal heat generated by RF has been shown to attenuate the inflammation often associated with active acne.[35] Inflammation is a critical contributor to the formation and persistence of acne lesions. A study by Hernández-Bule et al.[36] demonstrated that RF stimulation led to decreased production of interleukin-8 and RANTES while increasing levels of monocyte chemoattractant protein-1, without notably altering other chemokines such as macrophage inflammatory protein-1.[36] Seok et al.[37] investigated the effectiveness of IPL, RF, and a combination of both on cultured *C. acnes* strains using an induced rabbit ear model. They found that RF significantly reduced papule volume, while IPL exhibited an immunomodulatory effect. A synergistic effect was observed when both treatments were applied in combination.

- Regulation of sebaceous glands: RF energy has the potential to modulate the activity of sebaceous glands in the skin, an important consideration in the management of acne. Targeted intervention at the sebaceous gland level is essential for effective treatment, particularly in cases of severe histological inflammation like acne conglobata. In such instances, a unipolar single needle with partial insulation has shown efficacy. The length of the insulation is designed to align with the depth of the sebaceous gland. This approach offers an alternative mechanism for acne improvement, distinct from laser treatments, as supported by clinical literature. A prospective, randomized, controlled clinical trial involving 63 patients with moderate to severe facial acne assessed the effectiveness of a single microneedle RF device. The device demonstrated significantly greater efficacy in reducing acne lesions compared to simple needling, as evaluated through the reduction rate and the number of acne lesions at a 12-week follow-up. Specifically, the mean reduction rate was 20.86 ± 81.37% in the treatment group and −5.13 ± 75.21% in the control group ($P$ = 0.03). Importantly, no serious adverse events were reported.[38] Moreover, multi-needle fractional RF devices, commonly used for enhancing dermal conditions like acne scarring and pore treatment, can also be adapted for treating active acne lesions. Effective treatment can be achieved by optimizing parameters such as conduction time, intensity level, and needle depth to establish an appropriate ablative injury zone for the lesion.[38,39]

*1,450 nm diode laser*

Given the anatomical distribution of sebaceous glands and water as the primary chromophore, wavelengths in the range of 1,300–1,800 nm have been extensively employed for acne treatment. Among these, the 1,450 nm wavelength has gained recent prominence. Monte Carlo simulations, which model light penetration and heat transfer, indicate that the penetration depth of this wavelength is 435 μm. Furthermore, thermal damage zones have been identified in the upper dermal layer in human studies.[40] Paithankar et al.[41] found that an infrared 1,450-nm diode laser led to thermal coagulation of the sebaceous lobule and its associated hair follicle by heating the mid-dermis in a rabbit ear model. At fluences lower than or equal to 14 J/cm$^2$, the extent of thermal injury and coagulation was less pronounced. Nevertheless, it was posited that the heat generated in the infundibulum and sebaceous lobules led to reduced sebaceous gland activity, which in turn resulted in fewer inflammatory acne lesions.[40,41] Several small, uncontrolled studies have reported that the 1,450 nm laser yields significant improvements in inflammatory acne, with lesion counts decreasing by 40% to 83%.[42-45] Moreover, a substantial long-term clinical remission rate exceeding 70% was observed 12 months post-treatment.[42] Politi et al.[46] reported that an integrated cooling-vacuum-assisted non-fractional 1,540 nm erbium:glass laser effectively treated 22 patients with mild-to-moderate acne vulgaris. This mid-infrared laser yielded favorable outcomes through its anti-inflammatory effects on acne and induction of neocollagenesis within


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atrophic scars.[46] In studies focused on Asian populations, both inflammatory and non-inflammatory acne lesions showed improvement. Additionally, the technology contributed to reduced sebum secretion and some improvement in skin texture. Notably, PIH, a concern particularly for Asians, was substantially mitigated when employing a brief cooling time combined with a low flow/multi-pass method.[47]

*1,726 nm diode laser*

The laser operating at a 1,726 nm wavelength exhibits spectral selectivity for sebaceous glands due to its narrow bandwidth at the specific absorption ratio peak.[48] Goldberg et al.[49] evaluated the safety and efficacy of this laser, equipped with contact cooling, in 17 adult patients who had mild-to-severe acne. Relative to baseline measurements, there was a statistically significant reduction in inflammatory lesion counts (ILC) ranging from 52% to 56% over a period of 4–12 weeks. Long-term follow-ups conducted 24 months post-treatment revealed a 97% reduction in ILC.[49] A prospective, open-label, single-arm study involving 104 subjects with moderate to severe acne corroborated these findings. The study found that three full-face treatments, each lasting 30 minutes, with the 1,726 nm laser were generally well-tolerated. Progressive post-treatment improvement persisted for at least 26 weeks. At least a 50% reduction in inflammatory acne was observed in 80% of the treatment population, and a 70% reduction in nodule count was noted at the 3-month follow-up visit. While no serious device-related adverse effects such as burns or blisters were reported, some participants did find the treatment to be mildly uncomfortable.[50]

## EBD is primarily used for addressing acne erythema, pigmentation, and scars as the main lesions

*585/595 nm pulsed dye lasers (PDL)*

PDL is primarily employed for the treatment of vascular lesions and rosacea.[51] In addition, it has applications in managing hypertrophic scars and keloids due to its ability to stimulate dermal remodeling and collagen synthesis.[50,51] Recent studies suggest that performing multiple PDL treatments at fluences low enough to prevent purpura may lead to a reduction in inflammatory acne.[52] Although earlier literature attributed the effects to a decrease in *C. acnes* population or sebum secretion, recent insights suggest anti-inflammatory effects and dermal remodeling, facilitated by a significant increase in transforming growth factor (TGF)-β, as more plausible mechanisms.[53] Numerous clinical studies have consistently reported not only a reduction in the number of acne lesions but also improvements in acne erythema and scarring alongside active acne.[5]

*532 nm KTP lasers*

The 532 nm KTP laser is predominantly employed for treating telangiectasia and rosacea, as well as various pigmentary disorders, with hemoglobin and melanin acting as the primary chromophores.[54,55] Recent studies have reported its efficacy in treating active acne, with the proposed mechanisms involving selective photothermolysis of blood vessels and photoactivation of porphyrins against *C. acnes* and sebaceous glands.[56] In studies focused on mild-to-moderate acne, split-face trials have confirmed reductions in both the number of lesions and sebum secretion, although further follow-up studies are warranted.[57] This laser technology also holds promise for treating patients with both pigmented lesions and acne or acne scars.

*Microneedle RF*

Both microneedling and RF are known to stimulate collagen production in the skin. The MFR device functions by generating RF thermal zones, avoiding epidermal injury in the


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process.[58,59] Prior research has demonstrated the transcription and expression of TGF-β persisting for a week following RF treatment. This is accompanied by neocollagenesis, marked by an increased expression of type I and III collagen as well as the upregulation of type I collagen mRNA within the affected tissue.[60] The synergistic action of microneedling-induced micro-injuries and RF energy facilitates the skin's natural wound healing mechanisms. A study by Hernández-Bule et al.[36] showed that the electrostimulation facilitated by RF led to the proliferation and/or migration of keratinocytes and fibroblasts. This was achieved through the modulation of intercellular adhesion proteins like β-catenin and E-cadherin, proteins that manage cell-to-substrate adhesion such as vinculin and p-FAK, matrix metalloproteinase-9, and additional proteins that control both processes, including MAP kinases p-p38, p-JUNK, and p-ERK1/2.[36] Fusano and Bencini[61] examined the in vivo morphological changes in atrophic acne scars following MFR treatment, using RCM and three-dimensional (3D) imaging. They treated a total of 11 patients with atrophic facial acne scars through four monthly MFR sessions. Assessments with 3D imaging and RCM were conducted both at baseline and one month following the final session. The study found that 3D imaging revealed significant improvements in the mean depth of the scars, while RCM showed collagen remodeling and the restoration of a reticular structure.[61] A recent randomized, single-treatment, split-face trial involving 15 patients with moderate to severe acne scars compared the efficacy of ablative fractional $CO_2$ laser (AFL) with microneedle RF. The results suggested that both AFL and microneedle RF were equally effective in improving skin texture affected by acne scars. However, AFL resulted in more noticeable local skin reactions, whereas microneedle RF was associated with greater pain.[62] Also, RF combined with IPL is shown to effectively treat moderate to severe acne.[63]

*Fractional lasers ($CO_2$ fractional laser and pico-fractional laser)*

The 1,540 and 1,550 nm erbium glass lasers are predominantly employed for the treatment of wrinkles, scars, enlarged pores, and diminished skin elasticity by promoting nonablative dermal remodeling and collagen biosynthesis.[64] Compared to other lasers that target scarring, this laser technology is less invasive and is often selected for treating acne scars and pores owing to its minimal downtime.[65] Although its impact on acne itself remains a subject of debate, certain studies have indicated a decline in acne lesions following 3–5 treatments spaced 3–4 weeks apart.[66] Lasers operating at these wavelengths can penetrate deeply into the dermis and modulate sebaceous gland activity through thermocoagulation, providing a theoretical basis for their utility in acne management.[67] Given that more than 90% of acne cases are accompanied by some form of scarring, these lasers offer the potential for concurrent improvement of both conditions by tailoring the parameters to individual patients. Hwang et al.[68] demonstrated that $CO_2$ fractional laser is an effective and safe treatment for acne scars and wrinkles in Korean patients. The study showed that skin barrier damage and erythema resolved after treatment, with patients reporting "moderate or greater improvement" and high satisfaction.[68]

More recently, the use of fractional picosecond lasers has garnered attention. Fractional picosecond laser is known for its non-ablative mechanism to improve acne scars with minimal downtime.[69] These lasers facilitate dermal remodeling via the laser-induced optical breakdown mechanism, which generates plasma within the tissue and produces a cavity.[70] A study involving 25 patients with acne scars compared the safety and efficacy of fractional picosecond lasers and nonablative fractional lasers. Patients underwent four consecutive treatments at 3-week intervals on one side of their face and were monitored for 8 weeks subsequent to the final treatment. The results indicated that those treated with the


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fractional picosecond laser demonstrated superior outcomes in both acne scar improvement and overall evaluation by researchers compared to those treated with nonablative fractional lasers. Notably, patients undergoing treatment with the fractional picosecond laser reported greater satisfaction in terms of pore reduction and skin texture enhancement. Histological analyses corroborated these findings, revealing a significant augmentation in collagen, elastic fibers, and the dermal matrix throughout the dermal layer.[71]

*1,064 nm Nd:YAG lasers*

The 1,064 nm wavelength exhibits significant penetration depth, enabling effective heat transfer to the dermal layer while minimizing epidermal damage. This characteristic makes it particularly useful for treating pigmentation disorders and scar tissue.[72] Recent studies have also demonstrated its efficacy in treating active acne, noting reductions in sebum secretion and inflammation.[73] Various pulse durations—including Q-switched, quasi-long, and long pulses—can be employed to treat acne, and the technique can be augmented by the use of carbon particles for targeted treatment of the sebaceous glands.[74] Given that many patients present with multiple skin issues, such as acne, enlarged pores, irregular skin texture, and pigmentation, optimizing treatment parameters can yield simultaneous improvements across these conditions.

*Ultrasound*

Ultrasound has been extensively utilized in treating various skin conditions, such as cutaneous wounds, inflammatory skin disorders, and aesthetic concerns.[75] This form of energy targets both dermal and subdermal tissues, inducing thermal injuries that promote collagen remodeling. As a result, ultrasound treatment leads to the lifting and tightening of skin.[76] Although limited studies have specifically addressed ultrasound's efficacy in acne treatment, it is more commonly used as a monitoring device during treatment. Recent preclinical and clinical investigations have, however, pointed to its potential as a therapeutic tool. For example, impulse mode dual-frequency ultrasound operating at 1/3 MHz administered once a week for four weeks demonstrated efficacy and safety in enhancing skin hydration and reducing erythema among acne patients.[77] Ultrasound technology has also been employed for transdermal drug delivery, with typical skin penetration enhancements ranging between 1 and 10 folds. Acoustic cavitation serves as the primary mechanism for enhancement in both low-frequency and high-frequency sonophoresis.[78] Moreover, ultrasound can function as part of a multimodal approach to treating acne scars.[79] Trelles and Martínez-Carpio[80] reported that the combination of unipolar fractional ablative RF and ultrasonic dermal injections of bioactive compounds through perforated acoustic pressure microchannels led to a reduction in acne scars. Additionally, keloid and hypertrophic scars, which are common byproducts of the acne healing process, can also be addressed through ultrasound treatment. A recent study demonstrated a significant reduction in fibroblast growth and extracellular matrix deposition without adversely affecting cell viability or adhesion, suggesting these effects were mediated by nonthermal mechanisms. The findings indicate that ultrasound could serve as a beneficial therapeutic approach for scar reduction.

## CHEMICAL PEELS

Chemical peeling is a common procedure in medical aesthetics and has a long history of application. Chemical peels are categorized based on their penetration depth, as shown in **Table 3**. Superficial peels are primarily used to treat acne, owing to their ability to dissolve comedones and exert anti-inflammatory effects.


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**Table 3.** Peeling agents categorized by depth of peel

| Chemical peel | Superficial | Medium-deep | Deep |
|---|---|---|---|
| SA | O | | |
| GA | O | | |
| Jessner's solution | O | O (in combination with TCA or multiple applications) | |
| Resorcinol | O | O (when included in Jessner's solution and used in combination with TCA) | |
| TCA | O (10–25%) | O (25–50%) | O (> 50%) |
| Lactic acid | O | | |
| SM | O | | |
| Beta-lipohydroxy | O | | |

SA = salicylic acid, GA = glycolic acid, TCA = trichloroacetic acid, SM = salicylic acid-mandelic acid combination.

## Salicylic acid (SA) peel

SA is an organic compound characterized by the formula $HOC_6H_4COOH$. It serves both as a precursor and a metabolite of aspirin (acetylsalicylic acid). SA is a type of beta-hydroxy acid (BHA) and a frequent component in acne treatment formulations. Typically used at a concentration of 30%, SA easily penetrates the epidermis due to its affinity for skin cells. It loosens the cohesion among keratinocytes and facilitates the exfoliation of dead skin cells, making it effective against comedonal acne. Additionally, SA is capable of penetrating sebaceous glands, thereby reducing sebum production. It also exhibits anti-inflammatory properties that ameliorate acne erythema and are effective against inflammatory acne. Treatment with SA has been shown to downregulate sebocyte lipogenesis via the AMPK/SREBP-1 pathway and to suppress inflammation through the nuclear factor-κB pathway in human SEB-1 sebocytes.[81] Various studies indicate that SA can also reduce acne-induced pigmentation.[82,83] Previously, the concurrent use of oral isotretinoin with SA peels was discouraged due to overlapping mechanisms and the potential for severe dryness and irritation. However, recent findings suggest that SA, being a superficial peel, can be safely administered alongside oral isotretinoin for treating acne.[84,85] Traditional SA formulations have poor water solubility, leading to their dissolution in alcoholic solutions, which can irritate the skin and potentially result in low patient compliance. A newly developed form, supramolecular SA (SSA), is a water-soluble complex that allows for the alcohol-free delivery of SA, reducing skin irritation. The application of 30% SSA has been shown to modify the skin microenvironment and microbiota in acne patients, improving their symptoms.[86] Moreover, a sequential treatment involving 30% SSA followed by 1,565-nm NAFL has been reported to yield significant improvements in acne and pore size.[87]

## Glycolic acid (GA) peel

GA, the smallest alpha-hydroxy acid (AHA), is commonly used at concentrations ranging from 25–30% to 70%. It is particularly effective against comedo-type acne, targeting the corneosome and keratinocytes to enhance their breakdown and reduce their cohesiveness, thereby inducing desquamation. Additionally, GA promotes the enzymatic activity within the epidermis, leading to both epidermolysis and exfoliation. Takenaka et al.[88] found that GA at concentrations of 30–35 vol% demonstrated antibacterial activity against *C. acnes* and significantly reduced *C. acnes* concentrations on the cheeks of individuals with acne vulgaris in a clinical trial.[89] Recent research also indicates that GA possesses strong antibacterial activity against *C. acnes*, particularly at acidic pH levels between 3 and 4.5, making it suitable for over-the-counter formulations.[90]

While generally considered safe, GA can cause skin irritation, particularly at concentrations of 10% or higher. Additionally, GA may increase susceptibility to sun damage, so the use of sunscreen is advised during treatment.


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### Trichloroacetic acid (TCA)

TCA induces coagulation of skin proteins, resulting in the exfoliation of superficial layers and stimulating collagen synthesis in deeper skin strata.[91] Although it is more effective in treating acne scars rather than active acne, it shows promise as a therapeutic option. A comparative study evaluating the efficacy and safety of a 25% TCA peel versus a 30% SA peel in treating mild-to-moderate acne vulgaris found the 25% TCA to be similarly effective, although the SA peel was noted to have better safety and tolerability.[92] The "chemical reconstruction of skin scars" technique using TCA has been proven effective for treating acne scars, although it requires specialized expertise.[93] Another recent study reported that localized application of 90% TCA using a cosmetic brush applicator was both safe and effective in treating boxcar and polymorphic acne scars.[94]

### Jessner's solution

Jessner's solution comprises equal concentrations of 14% resorcinol, 14% SA, 14% lactic acid, and 14% ethanol. The penetration depth is directly related to the number of applications; thus, adjusting the number of coats can control it. A comparative clinical study investigating the efficacy of 30% SA peel and JS in treating acne vulgaris and postacne hyperpigmentation in individuals with skin of color found both treatments to be equally effective.[95] A medium-depth chemical peel that combines Jessner's solution with a subsequent application of 35% TCA has been shown to be a safe and effective approach for the treatment of acne scars, even in patients with a darker skin tone.[96] However, it should be noted that resorcinol can occasionally act as a contact allergen and may cause pigmentation issues, particularly in individuals with dark skin.[97]

### Lipohydroxy acid (LHA)

LHA is a BHA and a derivative of SA characterized by its higher molecular weight and an eight-carbon fatty chain attached to its benzene ring, which contributes to its enhanced lipophilic properties. These attributes may explain its unique advantages over other acids. In vitro and in vivo studies have demonstrated that LHA has lower skin penetration compared to other acids. It exhibits a good safety profile with less irritation compared to 10% GA and demonstrates efficacy similar to 30% SA.[98] Its pH is compatible with physiological skin pH, eliminating the need for neutralization and minimizing irritation and side effects. LHA specifically targets the upper epidermis and sebaceous glands and exhibits antibacterial, anti-inflammatory, anti-fungal, and comedolytic properties, making it well-suited for acne treatment.[99] Additionally, LHA has been shown to reduce melanosome clustering and epidermal pigmentation. Unlike AHAs, LHA has been found to increase the skin's resistance to ultraviolet -induced damage.[100]

### Others

Combination peels offer enhanced clinical outcomes while reducing the likelihood of adverse effects. The fractional cell regeneration (FCR) peel is formulated with niacinamide, arbutin, Centella asiatica, papain, and a complex of acids (mandelic acid, lactic acid, citric acid, SA) along with fractional prickle coral calcium. FCR treatment is versatile and can be applied to various body parts, including large acne-prone areas like the back and chest, as well as limbs affected by keratosis pilaris (**Fig. 2**).[101] A recent study found that a 40% mandelic acid peel exhibited efficacy comparable to that of a 30% SA peel, but with a more favorable safety profile and tolerability in cases of mild-to-moderate acne.[102] One significant advantage of mandelic acid is its comparatively mild impact on the skin relative to other AHAs, rendering it a suitable option for individuals with sensitive skin.


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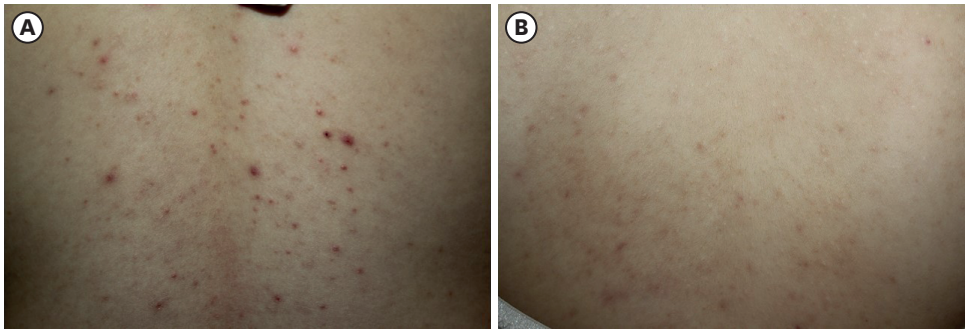


**Fig. 2.** Representative clinical images demonstrating the effects of fractional cell regeneration.
Before treatment (**A**) and after fractional cell regeneration treatment (**B**). Marked improvement in the keratosis pilaris lesions. The figures are published under agreement of the patient.

### Chemical peels for acne

Chemical peels serve as an effective treatment for active acne breakouts, atrophic acne scars, and hyperpigmentation. The literature indicates that these peels are beneficial for both non-inflammatory and inflammatory types of acne, though they have limited efficacy against nodular cystic acne. Comparative studies on the impact of peels on open and closed comedones are lacking. Expert opinion suggests that chemical peels are generally effective for acne management; however, it is inconclusive whether any specific peeling agent offers superior results.[103] Therefore, the selection of a peeling agent should take into account various factors such as the patient's skin type, morphology of the acne lesions, ratio of inflammatory to non-inflammatory lesions, skin barrier status, the presence of coexisting conditions like rosacea, and potential side effects.

While the exact mechanism of action in treating inflammatory acne lesions is not yet fully understood, initial exacerbation occurs in approximately 20% of cases, which tends to improve with successive treatments. Beyond their anti-acne properties, chemical peels offer additional benefits, including enhanced skin texture, pore reduction, sebum reduction, alleviation of PIH, and improved local drug penetration. These ancillary benefits can increase patient satisfaction and allow for the integration of chemical peels into multimodal treatment plans. Nonetheless, caution is advised due to potential side effects, such as redness, crusting, heightened photosensitivity, infections, herpes flare-ups, dyspigmentation, scarring, and acute exacerbation of acne. After undergoing a chemical peel, patients should minimize sun exposure and apply a broad-spectrum, non-comedogenic sunscreen. For cases of persistent or resistant active acne, adjunctive treatment with oral or topical medications may be necessary.

## CONCLUSION

Acne is a prevalent dermatological condition that often necessitates medical intervention. Isotretinoin and antibiotics are commonly prescribed treatments, but they present limitations such as teratogenic risks and potential for antibiotic resistance, respectively. Therefore, alternative approaches like EBD and chemical peeling have gained prominence.[104] Recent advancements focus on optimizing therapeutic outcomes while minimizing adverse effects through the synergistic use of cosmeceuticals with these treatment modalities. EBD and chemical peeling enhance the skin's absorption of active ingredients found in cosmeceuticals, which often possess moisturizing, soothing, regenerative, and anti-inflammatory properties.[105] These characteristics can ameliorate erythema and reduce


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the recovery period post-treatment, thereby sustaining long-term beneficial effects. Future research could explore diverse applications of EBD and chemical peeling in the comprehensive management of acne.

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