Effective Treatments of Atrophic Acne Scars

MAYA VALESKA GOZALI, MD; BINGRONG ZHOU, MD, PhD; DAN LUO, MD, PhD

Department of Dermatology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China

ABSTRACT

Atrophic scarring is often an unfortunate and permanent complication of acne vulgaris. It has high prevalence, significant impact on quality of life, and therapeutic challenge for dermatologists. The treatment of atrophic acne scars varies depending on the types of acne scars and the limitations of the treatment modalities in their ability to improve scars. Therefore, many options are available for the treatment of acne scarring, including chemical peeling, dermabrasion, laser treatment, punch techniques, fat transplantation, other tissue augmenting agents, needling, subcision, and combined therapy. Various modalities have been used to treat scars, but limited efficacy and problematic side effects have restricted their application. In order to optimally treat a patient's scar, we need to consider which treatment offers the most satisfactory result. There are also promising procedures in the future, such as stem cell therapy. In this article, the authors review the different treatment options of atrophic acne scars while reducing or avoiding the side effects and complications. (*J Clin Aesthet Dermatol.* 2015;8(5):33–40.)

cne is a common condition that affects up to 80 percent of the adolescent population to some degree or another.¹⁻⁸ It is caused and characterized by multiple factors including Propionibacterium acnes activity, increased sebum production, androgenic stimulation, follicular hypercornification, lymphocyte, macrophage and neutrophil inflammatory response, and cytokine activation.8-11 Inflammatory acne lesions can result in permanent scars.9 Scarring occurs early in acne and may affect some 95 percent of patients with this disease, relating to both its severity and delay before treatment.⁶ Acne scars can be classified into three different types : atrophic, hypertrophic, or keloidal. Atrophic acne scars are the most common type.^{1,3,12} The pathogenesis of atrophic acne scarring is most likely related to inflammatory mediators and enzymatic degradation of collagen fibers and subcutaneous fat.1 The most basic and practical system divides atrophic acne scars into three main types: ice pick, rolling, and boxcar scars.¹³⁻¹⁵ A number of treatments are available to reduce the appearance of scars. Treatment of acne scars must be individually directed for each patient depending on the types of scars present.

CHEMICAL PEELS

Chemical peeling is the process of applying chemicals to the skin to destroy the outer damaged layers,^{9,16,17} thus accelerating the normal process of exfoliation.^{9,16} Different agents have different depths of penetration, and therefore, chemical peels can be divided into four different groups based on the histologic level of necrosis that they cause. The classification of peeling agents are listed in Table 1.^{18,19}

Glycolic acid. Glycolic acid is the most commonly used alpha hydroxyl acid as a peeling agent.^{16,20,21} It can be used as a daily skin care product in low concentrations of 5 to 15 percent. Greater concentrations of 30 to 70 percent are used for chemical peels.¹⁶ The higher the concentration, the deeper the peel they produce. Glycolic acid acts by thinning the stratum corneum, promoting epidermolysis, and dispersing basal layer melanin. Glycolic acids are systemically safe and nontoxic and produce superficial peels capable of significant effects, but with few complications. They are also well-tolerated by patients. The best results achieved for acne scars include five sequential sessions of 70% glycolic acid every two weeks.⁹

The advantages of glycolic acid are very mild erythema, mild desquamation, and short postoperative period. The disadvantages are penetration often not uniform, mandatory neutralization, and high risk of overpeel if time of application is too long or the skin is inflamed.²²

Trichloroacetic acid (TCA). TCA can be used in different concentrations; 10% to 20% TCA is used for superficial peels, whereas 35% is used as a medium-depth

Clinical...Aesthetic

33

DISCLOSURE: The authors report no relevant conflicts of interest. **ADDRESS CORRESPONDENCE TO:** Bingrong Zhou; E-mail: bingrong.2002@163.com

TABLE 1. Classification of peeling agents				
DEPTH OF PENETRATION	HISTOLOGIC LEVEL	PEELING AGENTS		
Very superficial	Destruction of the stratum corneum without creating a wound below the stratum granulosum	 Glycolic acid, 30% to 50%, applied briefly (1 to 2 minutes) Jessner solution, applied in 1 to 3 coats TCA 10%, applied in 1 coat 		
Superficial	Destruction of part or all of the epidermis, anywhere from the stratum granulosum to the basal cell layer	 Glycolic acid, 50% to 70%, applied for a variable time (2 to 20 minutes) Jessner solution, applied in 4 to 10 coats TCA, 10% to 30% 		
Medium depth	Destruction of the epidermis and part or all of the papillary dermis	 Glycolic acid 70%, applied for a variable time (3 to 30 minutes) TCA, 35% to 50% Augmented TCA (CO₂ plus TCA 35%; Jessner solution plus TCA 35%; glycolic acid 70% plus TCA 35%) 		
Deep	Destruction of the epidermis and papillary dermis, extending into the reticular dermis	Phenol 88%Baker-Gordon phenol formula		

peel. Concentrations higher than 35% are not recommended because the results are less predictable and the potential for scarring is higher.^{9,20} The application of TCA to the skin causes epidermal cellular necrosis and necrosis of collagen in the papillary to upper reticular dermis, depending on the concentration of TCA.^{10,23,24}

TCA application to the skin causes protein denaturation, the so-called keratocoagulation, resulting in a readily observed white frost.⁹ The degree of the frosting correlates with the depth of solution penetration. Level 1 is speckled white frosting with mild erythema and corresponds to superficial penetration.^{16,20} This should heal after 2 to 4 days of light flaking . Level 2 is characterized by an even whitecoated frost with background erythema. This degree of frosting is usually desirable for medium-depth peels, a fullthickness epidermal peel that heals after about five days. Level 3 is solid white opaque frost with little or no background erythema,^{16,18,20} the peel has extended to the papillary dermis, and this takes up to seven days to heal.¹⁶

The advantages of TCA are low cost, uniformity of application, and the fact that penetration can be easily evaluated by the color of frost. The disadvantages include stinging and burning sensation during the application, high concentrations not recommended in skin types V to VI, and potential for hypo/hyperpigmentation.²²

Jessner's solution. Jessner's solution is used for light peels alone or in preparation for a TCA peel.¹⁶ The preparation is made from salicylic acid, 14g; resorcinol, 14g; lactic acid (85%), 14g; and ethanol to 100mL.^{9,16,21} The

Jessner's solution was found effective in destroying the epidermal barrier by breaking up individual epidermal cells. 18

The depth of the peel depends on the number of coats of solution applied. A very superficial Jessner's peel results in faint erythema, which may be associated with a light powdery-looking whitening of the skin surface. Level 1 created with 1 to 3 coats of Jessner's solution is very superficial and only causes mild flaking of the skin for 1 or 2 days or none at all. A level 2 peel is created with the application of more than 4 to 10 coats of the solution. There is increased erythema and some pinpoints of true white frosting. There is mild-to-moderate burning and stinging, which lasts for 15 to 30 minutes. In the next 1 to 3 days, a mild red-brown discoloration develops, and the skin feels tight. Exfoliation then follows for 2 to 4 days, with moderate flaking. Further coats of Jessner solution create a level 3 peel, where there is prominent erythema and increased areas of frosting associated with a moderate amount of stinging. At this level, exfoliation usually lasts 8 to 10 days, and there might be actual peeling apart from the dry flaking of the skin.

Different patients may require different number of coats to achieve the same level of peel. This is because penetration of the solution depends on a number of factors, including the preparation of the skin, the thickness of the corneum, and the sensitivity of the skin. The advantages of Jessner's solution are that the peel is very superficial and safe and rarely goes deeper than one would expect. Disadvantages include erythema and discoloration.¹⁶

Pyruvic acid. Pyruvic acid is an alpha-ketoacid and an effective peeling agent. It presents keratolytic, antimicrobial, and sebostatic properties as well as the ability to stimulate new collagen production and the formation of elastic fibers. The use of 40 to 70% pyruvic acid has been proposed for the treatment of moderate acne scars.⁹

The advantages of pyruvic acid are homogeneous penetration with uniform erythema, mild desquamation, short postoperative period, and the ability to be used in all skin types. Disadvantages include intense stinging and burning sensation, mandatory neutralization, and pungent and irritating vapors for the upper respiratory mucosa.²²

Salicylic acid. Salicylic acid is one of the best peeling agents for the treatment of acne scars.⁹ It is a beta hydroxyl acid agent,^{9,20,21} which removes intercellular lipids that are covalently linked to the cornified envelope surrounding keratinized cells.^{9,21} The most efficacious concentration for acne scars is 30% in multiple sessions, 3 to 5 times, every 3 to 4 weeks. The side effects of salicylic acid peeling are mild and transient. These include erythema and dryness. Persistent postinflammatory hyperpigmentation or scarring are very rare.⁹

The advantages of salicylic acid are established safety profile in all skin types, formation of white precipitate to verify if application is homogeneous, and an anesthetic effect that is useful in combination peelings. The disadvantage of salicylic acid is intense stinging and burning sensation.²²

CROSS technique/dot peeling. Using a high strength of the peeling agent TCA, the CROSS technique (chemical reconstruction of skin scars)^{7,10,23} has been found to be useful as a simple office procedure. It is best suited to treat ice pick or small boxcar scars.³

The CROSS technique entails stretching the skin and using a fine wooden toothpick to apply 65 to 100 percent TCA to the bottom of the ice pick scar, which leads to destruction of the epithelial tract. This is followed by collagenization in the healing phase and filling up of the depressed ice pick scar. It causes momentary, mild, tolerable burning on application, and no anesthesia is required. Collagen formation may take 2 to 3 weeks and can continue up to 4 to 6 weeks. On average, about 25 percent improvement of scars takes place with one session. The procedure may be repeated two or three times at intervals of 2 to 4 weeks.¹⁷ The advantage of the CROSS technique is that since the adjacent normal tissue and adnexal structures are spared, healing is more rapid with a lower complication rate.^{17,25,26}

Deep peels (phenol). Deep peels may also be an option, but are more rarely used because of the downtime required for healing and the potential for complications and adverse events.¹² Deep peeling solutions penetrate the skin to the midreticular dermis and create maximal effect for production of new collagen. The solutions for deep peeling are composed of a combination of croton oil and phenol in various concentrations. Phenol peels have been the agent traditionally used, but may cause cardiac arrhythmia so patients require cardiac monitoring during the procedure.^{14,27}

Deep peels can improve atrophic acne scars, but require sedation and cardiovascular monitoring, are not recommended in skin types IV to VI, can cause cardiotoxicity, and can cause hypo/hyperpigmentation.²²

DERMABRASION/MICRODERMABRASION

Dermabrasion was the first major advance treatment of acne scarring.^{6,28} Dermabrasion and microdermabrasion are facial resurfacing techniques that mechanically ablate damaged skin in order to promote re-epithelialization. Although the act of physical abrasion of the skin is common to both procedures, dermabrasion and microdermabrasion employ different instruments with a different technical execution.9 Dermabrasion completely removes the epidermis and penetrates to the level of the papillary or reticular dermis,^{6,9,28} inducing remodeling of the skin's structural proteins. Microdermabrasion, a more superficial variation of dermabrasion, only removes the outer layer of the epidermis,^{9,29} accelerating the natural process of exfoliation. Both techniques are particularly effective in the treatment of scars and produce clinically significant improvements in skin appearance. Unlike dermabrasion, microdermabrasion can be repeated at short intervals, is painless, does not require anesthesia, and is associated with less severe and rare complications,²⁹ but it also has a lesser effect and does not treat deep scars.9 In addition, dermabrasion does not improve ice pick or deep boxcar scars optimally.2,12

LASER TREATMENT

Laser resurfacing is an effective treatment that is easier to use than other modalities.³⁰ Different types of laser, including nonablative and ablative lasers, are very useful in treating acne scars, except for deep ice pick scars.¹

Ablative lasers. Carbon dioxide (CO_2) laser. CO_2 laser resurfacing vaporizes tissue at a depth of 20 to 60µm and zones of thermal necrosis ranging another 20 to 50µm.³¹ Energy at 10.600nm wavelength is absorbed by both intracellular and extracellular water, causing rapid heating and vaporization of tissue.³²⁻³⁴ Dermal heating below the zone of ablation induces a wound-healing response,^{32,35} which causes collagen remodeling and heat-mediated tissue contraction. Re-epithelialization generally takes 5 to 10 days, and erythema may persist for months.³² Side effects may include dyschromia (hyper- or hypopigmentation),^{9,32,36} infection,^{37,38} lines of demarcation between treated and untreated areas,³² and scarring.³⁶⁻³⁸

Erbium: yttrium-aluminum-garnet (Er:YAG). Er:YAG emits a wavelength of 2940nm,^{39,40} is 10 times more selective for water than CO_2 laser due to its shorter wavelength, and reduces residual thermal damage.^{31,34,41} Er:YAG at 5J/cm vaporizes tissue at a depth of 20 to 25µm with an additional 5 to 10µm zone of thermal necrosis.³¹ The main difference is that energy from the Er:YAG laser more closely approximates the absorption peak of water (3,000nm), so virtually all the energy is absorbed in the epidermis and superficial papillary dermis. Thus, it has a

35

more superficial ablation profile and a smaller zone of thermal damage beneath the ablated layer,³² leading to shorter healing times and a lower rate of side effects.^{10,33,42} Re-epithelialization takes 4 to 7 days with Er:YAG.³¹

Plasma skin resurfacing. A new technology utilizes a nonlaser device to generate plasma, a cloud of electrons, from nitrogen atoms, and a spark of radiofrequency.³⁴ This technology uses pulses of ionized nitrogen gas to deliver heat energy directly to the skin.^{32,33,43} The epidermis initially is left intact, only later to shed as healing is completed.³⁴ Roughly 10 days after treatment, fibroblasts depositing new collagen and elastin fibers can be seen. Side effects are rare and can include temporary hyperpigmentation, erythema, edema, epidermal de-epithelialization, infection, and scarring.³²

Nonablative lasers. Nonablative skin remodeling systems have become increasingly popular for the treatment of acne scars because they decrease the risk of side effects and the need for postoperative care.^{9,44} These nonablative lasers are designed to spare the epidermis and stimulate the dermis to produce new collagen.⁴⁵

Neodymium: yttrium-aluminum-garnet (Nd: YAG) laser. The Nd:YAG laser is used on patients with darker or more sensitive skin. These lasers cool the surface of the epithelium while also penetrating the deeper layers of the skin with infrared wavelengths. These wavelengths target the underlying water and collagen without disrupting the epidermal layer.⁴² Thermal damage serves as the stimulus for inflammatory mediator release, fibroblast activation, neocollagenesis, and dermal remodeling.46 The Nd:YAG laser requires more sessions (3–5 treatments per month for several months), but a patient can expect to see a 40- to 50percent improvement in the quality of their scarring.⁴² The results are long lasting and continue well beyond the last treatment, indicating ongoing collagen remodeling after completion of the laser treatment sessions.⁴⁷ This treatment offers significant advantages to patients in terms of its minimal recovery period and minimal risk of infectious and pigmentary complications.^{47,48}

Diode laser. The 1450nm diode laser in the infrared spectrum targets the water in the upper dermis, remodels the skin's underlying collagen, and promotes formation of new collagen.⁸ An increase in collagen synthesis and deposition was noted until six months after treatment with this laser.³⁴ Side effects are usually minimal and can include postoperative erythema, edema, and hyperpigmentation.^{8,40}

Fractional photothermolysis (FP). Although improvement was noted with nonablative lasers, the results obtained were not as impressive as the results from those using ablative laser. For this reason, a new concept in skin laser therapy,^{9,49} called FP, has been designed to create microscopic thermal wounds to achieve homogeneous thermal damage at a particular depth within the skin.⁵⁰⁻⁵² Fractional photothermolysis system selectively damages the dermal tissue to induce a wound-healing response that affects the stimulation of prolonged neocollagenesis without damage to the epidermis in order to overcome the problems associated with laser resurfacing, dermabrasion,

36

and chemical peeling.⁵³ Efficacy of treatment for patients with diverse morphology of scars was noted, ranging from ice pick to boxcar and rolling scars.⁵⁴ Treated zones are completely healed within 24 hours compared with two weeks for ablative laser resurfacing.⁵⁵

The benefits of this system are less downtime and side effects compared to the conventional ablative laser and an increased efficacy of tissue regeneration compared to the nonablative methods.^{56,57}

Pinpoint irradiation technique. Pinpoint irradiation technique accompanied by needling is as effective as FP in the treatment of atrophic acne scars.^{53,58} It often induces microscopic thermal wounds to achieve skin rejuvenation treatment for ice pick acne scars. In pinpointed irradiation, no complications could be seen as those with ordinary laser resurfacing and the downtime is shortened to 3 to 6 days. All irradiated points on the face were small dry macules of ablated epithelium, which could be gently removed with a topical antibiotic cream after a day. The color of the treated scar area was back to pink or normal within 2 to 4 days. Also, postoperative hyperpigmentation did not occur;⁵⁸ this could be because there was no overlapped irradiation, no massive damage, and the time interval between each shot was relatively long.⁵³

RADIOFREQUENCY (RF)

Radiofrequency is nonionizing electromagnetic radiation with a frequency range between 3 and 300GHz. With the fractional bipolar RF device, the RF current flows through the skin between the electrode-pin rows. It generates fractional deep dermal heating in the region of the electrode matrix to induce skin injury and then elicits a wound healing response, stimulating the remodeling of dermal collagen. More recently, fractional bipolar RF, based on the principle of "sublative rejuvenation," which causes low epidermal disruption with high dermal remodeling, has been introduced to improve the efficacy and reduce the side effects of FP. The fractional bipolar RF device was also able to improve acne scars significantly.⁵⁹

PUNCH TECHNIQUES

Punch excision. Punch or elliptical excision to the subcutaneous level is preferred for ice pick scars^{1,12,14,60} and also deep boxcar scars.² Punch excision removes a pitted scar with a straight-walled disposable or hair transplant punch that is slightly larger than the scar being addressed.^{6,28} The goal is to trade a larger, deeper scar for a smaller, linear closure that will hopefully be less noticeable and possibly fade with time.¹⁰ Although excisional procedures are an effective one-time treatment, a major disadvantage is that only the scars that are treated have a chance of improving. It does little for the surrounding textural irregularity or discoloration that is frequently seen in a field of acne scars.³

Punch elevation. Punch elevation combines the techniques of punch excision and grafting without the risk of skin color or texture mismatch.^{2,12} This limits its use to shallow and deep boxcar scars.² After the scar has been

isolated from the surrounding skin, it is elevated enough to be slightly raised against the bordering tissue.^{6,28} Retraction of the grafted tissue occurs during the healing phase, resulting in a leveled surface.^{2,12}

Punch replacement grafting. This is probably the best of these techniques for sharp-walled or deep ice pick scars. It is quite a painstaking technique as often 20 or more replacement grafts are required in a single session, but it is usually worthwhile as it will often yield the best results for difficult sharply defined scars. The scar is discarded and is replaced with a slightly larger full-thickness skin graft, usually from the postauricular area. Some of the grafts will heal in the same level of skin surface and some will be elevated.^{6,28}

FAT TRANSPLANTATION

Fat is close to the ideal augmentation material in that it is cheap, readily available, and incapable of being rejected or causing allergic or other adverse tissue reactions.^{9,28,61} The technique consists of two phases: procurement of the graft and placement of the graft. The injection phase with small parcels of fat implanted in multiple tunnels allows the fat graft maximal access to its available blood supply. Most acceesscarred patients achieve maximum results about three months after the procedure.^{6,28}

OTHER TISSUE AUGMENTING AGENTS

many new and older autologous, There are nonautologous biologic, and nonbiologic tissue augmentation agents that may be used for atrophic scar contour correction.^{6,9} Soft-tissue fillers are effective in treating patients with rolling acne scars.¹ Fillers for acne scarring can be utilized in two ways. First, fillers can be injected directly under individual scars for immediate improvement. Second, volumizing fillers, such as poly-L lactic acid (PLLA) or calcium hydroxylapatite, can be delivered to areas where laxity of skin or deep tissue atrophy is accentuating the appearance of acne scars.^{1,3} Injectable PLLA is a biocompatible, biodegradable, synthetic polymer hypothesized to elicit the endogenous production of fibroblasts and, subsequently, collagen.⁵

There are many tissue augmentation agents that have been used in the past, but nowadays, because of the high incidence of side effects, the recommended material to use is hyaluronic acid.⁹ Hyaluronic acid derivatives potentially offer improved longevity of correction and reduced risk of immunogenicity and hypersensitivity.⁶² There are also indications that native hyaluronic acid promotes cell proliferation and extracellular matrix synthesis and modulates the diameter of the collagen fibers.⁶³

NEEDLING

Skin needling also called collagen induction therapy^{1,61} or needle dermabrasion is the technique of rolling a device comprising a barrel studded with hundreds of needles, which create thousands of micropunctures in the skin to the level of the papillary to mid-dermis.^{1,26} With this technique, the rolling is usually continued until bruising occurs, which initiates the complex cascade of growth factors that finally results in collagen production.^{4,9,26} Results generally start to be seen after about six weeks, but the full effects can take at least three months to occur and, as the deposition of new collagen takes place slowly, the skin texture will continue to improve over a 12-month period.⁹ The optimal scars to treat with skin needling are the same as fractional laser resurfacing—rolling acne scars and superficial boxcar scars.^{1,4}

Compared to other resurfacing procedures, this technique has many advantages. First, it is purposed to be safe in all skin types and to carry the lowest risk of postinflammatory hyperpigmentation when compared to laser resurfacing, chemical peels, or dermabrasion.^{1,9} Second, the treatment does not result in a line of demarcation between treated and untreated skin. Third, the recovery period of 2 to 3 days is significantly shorter than other resurfacing procedures. Finally, needling is much less expensive to incorporate into a practice compared with a fractional laser or dermabrasion.¹

SUBCISION (SUBCUTANEOUS INCISIONLESS SURGERY)

Subcision is a procedure in which a needle is inserted under the skin and passed in multiple directions. Subcision is best utilized for rolling acne scars^{3,60,64} that have normal quality of skin at the base of each scar; it is less effective for treating boxcar and ice pick scars.³ The mechanisms of scar improvement are releasing fibrotic strands underlying scars, organization of blood in the induced dermal pocket, and connective tissue formation in the area.^{28,61,64}

The advantages of this innovative method include the following: easy to apply, inexpensive, short down-time, applicable for various skin types (I–IV), no significant complications, and remarkable and persistent improvement in short time without injury to the skin surface. The disadvantages include pain at the time of subcision in some cases, bruising, transient discoloration, hemorrhagic papule and pustule, hypertrophic scar, necessity of frequent suctioning sessions, and recurrence.⁶⁴

COMBINED THERAPY

There is a new combination therapy for the treatment of acne scars. The first therapy consists of peeling with TCA, followed by subcision, the process by which there is separation of the acne scar from the underlying skin, and finally fractional laser irradiation. The efficacy and safety of this method was investigated for the treatment of acne scars. The duration of this therapy is 12 months. Dot peeling and subcision were performed twice 2 to 3 months apart and fractional laser irradiation was performed every 3 to 4 weeks. There were no significant complications at the treatment sites.⁹ It would appear that triple combination therapy is a safe and very effective combination treatment modality for a variety of atrophic acne scars.^{9,55}

The current study could be added to recent research welcoming the relative new comer platelet-rich plasma (PRP) to the dermatologic field. PRP is an autologous

37

TABLE 2. Procedures to select by lesion type of scars				
TREATMENT	ICE PICK SCARS	ROLLING SCARS	BOXCAR SCARS	
Chemical peels TCA CROSS technique	++ ++	- -	++ ++	
Dermabrasion/microdermabrasion	+	-	+	
Laser Ablative and nonablative laser Fractional photothermolysis	- ++	++ ++	++ ++	
Punch techniques Punch excision Punch elevation Punch replacement grafting	++ - ++	- - -	+ ++ -	
Tissue augmenting agents	+	++	+	
Needling	-	++	++	
Subcision	+	++	+	
++ = Effective, + = less effective, - = not effective				

concentration of human platelets contained in a small volume of plasma. It provides further evidence of the potential benefits that the use of PRP offers as an adjuvant to CO_2 laser in the treatment of atrophic acne scars. The superiority of the combination was clearly evident in several aspects, including the rapidity and degree of improvement of the acne scars, fewer side effects, and shorter downtime.⁶³

STEM CELL THERAPY

38

Epidermal substitute is made by adding epidermal cells to a scaffold to form a composite skin with some biological activity. Cells in these substitutes have a relatively weak ability to proliferate and self-renew, which affects the outcome of repair. However, the seed cells of the dermal substitute are mainly fibroblasts. Although fibroblasts are easy to obtain and grow relatively quick, their function is simple and they do not encourage the development of skin appendages. This problem might be resolved effectively if the dermal substitute is used to cover the wound with a population of epidermal stem cells.⁶⁵

The traditional concept of stem cell therapy comprises the isolation of stem cells from patients, propagation and differentiation *in vitro*, and subsequent re-injection of autologous cells into the patient. An alternative approach that could be easier includes local activation and recruitment of endogenous stem cells to the site of defect for new tissue regeneration. This may occur in response to certain agents that can promote the proliferation and differentiation of stem cells.⁶⁶ The mechanisms for stem cell delivery to improve wound healing are intravenous or subcutaneous injection, but the mechanism through this is currently still not clearly understood.⁶⁷

The role of epidermal stem cells in contributing to homeostatic maintenance of the skin and wound repair has been well acknowledged for many years.⁶⁸ Stem cell therapy has emerged as a promising new approach in almost every medical problem.⁶⁶ Stem cells found in our body are undifferentiated or nonspecific cells without having any tissue-specific structure that have the potential to become other, more specialized types of cells.⁶⁷ Stem cells demonstrate two defining features, namely self-renewal and multipotency, and are instrumental for renewal, regeneration, and repair.⁶⁵ Stem cells have the ability to renew themselves as well as differentiate into specialized cell types.⁶⁷

CONCLUSION

A variety of effective treatments of atrophic acne scars have been developed. Each of these procedure has a different role in treating acne scars, with some modalities being better suited for certain scar types than others. Individual scars can vary widely in type and depth, with different treatment approaches that can be seen in Table 2. If multiple procedures were combined, then many types of scars and fine textural irregularities would likely be improved to a degree that could not be obtained by each procedure alone. The varying morphology of acne scars, especially when multiple types of scars are found in the same patient, suggests the need for combination therapy to provide the most effective treatment. Stem cell therapy might have the potential as a promising therapy for atrophic acne scars in the future.

ACKNOWLEDGMENT

This work was supported by a grant from the China National Natural Science Foundation (81000700 and 81171518) science project from traditional Chinese medicine Bureau of Jiangsu Province (LZ11084) and Jiangsu National Natural Science Foundation (BK2012877) and the Priority Academic Program Development of Jiangsu Higher Education Institutions (PAPD).

REFERENCES

- 1. Fife D. Practical evaluation and management of atrophic acne scars: tips for the general dermatologist. J Clin Aesthet Dermatol. 2011;4:50–57.
- Jacob CI, Dover JS, Kaminer MS. Acne scarring: a classification system and review of treatment options. J Am Acad Dermatol. 2001;45:109–117.
- 3. Fife D, Zachary CB. Combining techniques for treating acne scars. *Current Dermatology Reports.* 2012;1:82–88.
- Fabbrocini G, Fardella N, Monfrecola A, et al. Acne scarring treatment using skin needling. *Clin Exp Dermatol.* 2009;34:874–879.
- Sadove R. Injectable poly-L lactic acid: a novel sculpting agent for the treatment of dermal fat atrophy after severe acne. *Aesthetic Plast Surg.* 2009;33:113–116.
- 6. Goodman GJ. Postacne scarring: a review of its pathophysiology and treatment. *Dermatol Surg.* 2000;26:857–871.
- Fabbrocini G, Cacciapuoti S, Fardella N, et al. CROSS technique: chemical reconstruction of skin scar method. *Dermatol Ther*. 2008;21:S29–S32.
- Nouri K, Ballard CJ. Laser therapy for acne. *Clin Dermatol.* 2006;24:26–32.
- Fabbrocini G, Annunziata MC, D'Arco V, et al. Acne scars: pathogenesis, classification and treatment. *Dermatol Res Pract*. 2010;2010:893080.
- 10. Rivera AE. Acne scarring: a review and current treatment modalities. *J Am Acad Dermatol*. 2008;59:659–676.
- Bagatin E, Guadanhim LRDS, Yarak S, et al. Dermabrasion for acne scars during treatment with oral isotretinoin. *Dermatol Surg.* 2010;36:483–489.
- 12. Thiboutot D, Gollnick H. New insights into the management of

acne: an update from the Global Alliance to Improve Outcomes in Acne Group. *J Am Acad Dermatol.* 2009;60:S1–S50.

- LaTowsky B, MacGregor JL, Dover JS, Arndt KA. Prevention and treatment of scars. In: Alam M, ed. *Evidence-Based Procedural Dermatology*. Springer; 2012:149–177.
- Bhatia N, David CV, Hazany S, Samrao A. Acne scarring. In: Zeichner JA, ed. Acneiform Eruptions in Dermatology: A Differential Diagnosis. New York: Springer; 2014:237–243.
- Beasley K, Dai JM, Brown P, et al. Ablative fractional versus nonablative fractional lasers—where are we and how do we compare differing products? *Current Dermatology Reports*. 2013;2:135–143.
- 16. Clark E, Scerri L. Superficial and medium-depth chemical peels. *J Clin Dermatol.* 2008;26:209–218.
- Khunger N. Facial peels. In: Giuseppe MASaAD, ed. Cosmetic Surgery. Berlin Heidelberg; 2013:147–166.
- 18. Monheit GD. Chemical peels. Curr Probl Dermatol. 2001:65–79.
- Hassan KM, Benedetto AV. Facial skin rejuvenation: ablative laser resurfacing, chemical peels, or photodynamic therapy? Facts and controversies. *Clin Dermatol.* 2013;31:737–740.
- 20. Landau M. Chemical peels. Clin Dermatol. 2007;26:200-208.
- Starling J, Karimpour DJ. Nonlaser superficial resurfacing techniques: superficial chemical peel and microdermabrasion. In: Alam M, ed. *Evidence-Based Procedural Dermatology*. Springer; 2012:301–316.
- 22. Padova MPD, Tosti A. Types of chemical peels: advantages/disadvantages, an illustrated algorithm. In: Tosti A, Grimes PA, Padova MPD, eds. *Color Atlas of Chemical Peels*. Berlin Heidelberg: Springer; 2012:3–6.
- 23. O'Daniel TG. Multimodal management of atrophic acne scarring in the aging face. *Aesthetic Plast Surg.* 2011;35:1143–1150.
- Yug A, Lane JE, Howard MS, Kent DE. Histologic study of depressed acne scars treated with serial high-concentration (95%) trichloroacetic acid. *Dermatol Surg.* 2006;32:985–990; discussion 90.
- Lee JB, Chung WG, Kwahck H, Lee KH. Focal treatment of acne scars with trichloroacetic acid: chemical reconstruction of skin scars method. *Dermatol Surg.* 2002;28:1017–1021.
- Leheta T, El Tawdy A, Abdel Hay R, Farid S. Percutaneous collagen induction versus full-concentration trichloroacetic acid in the treatment of atrophic acne scars. *Dermatol Surg.* 2011;37:207–216.
- Landau M. Deep chemical peels for post-acne scarring. In: Tosti A, Grimes PA, Padova MPD, eds. *Color Atlas of Chemical Peels*. Berlin Heidelberg: Springer; 2011:149–157.
- 28. Goodman GJ. Post acne scarring: a review. *J Cosmet Laser Ther*. 2003;5:77–95.
- Fernandes M, Pinheiro NM, Crema VO, Mendonca AC. Effects of microdermabrasion on skin rejuvenation. J Cosmet Laser Ther. 2014;16:26–31.
- Hsiao PF, Lin YC, Huang CC, Wu YH. Efficacy and safety of a single treatment using a 10,600nm carbon dioxide fractional laser for mild-to-moderate atrophic acne scars in Asian skin. *Dermatologi Sinica*. 2013;31:59–63.
- Harithy Ra, Pon K. Scar treatment with lasers: a review and update. *Current Dermatology Reports*. 2012;1:69–75.
- 32. Bogle MA, Yadav G, Arndt KA, Dover JS. Wrinkles and acne scars: ablative and nonablative facial resurfacing. In: Raulin C, Karsai S,

Clinical ... Aesthetic

39

eds. Laser and IPL Technology in Dermatology and Aesthetic Medicine. Berlin Heidelberg: Springer; 2011:289-297.

- Alexiades-Armenakas MR, Dover JS, Arndt KA. The spectrum of laser skin resurfacing: nonablative, fractional, and ablative laser resurfacing. J Am Acad Dermatol. 2008;58:719–737; quiz 38–40.
- Goldberg DJ. Laser Therapy. In: *Therapy of Skin Disease*. Berlin Heidelberg: Springer; 2010:93–104.
- 35. Kauvar ANB, Warycha MA. Wrinkles and acne scars: fractional ablative lasers. 2011:307–318.
- Kim S. Clinical trial of a pinpoint irradiation technique with the CO2 laser for the treatment of atrophic acne scars. J Cosmet Laser Ther. 2008;10:177–180.
- Anolik R, Geronemus RG. Complications of fractional laser. In: Management of Complications of Cosmetic Procedures. Berlin Heidelberg: Springer; 2012:23–35.
- Metelisa AI, Alster TS. Fractioned laser skin resurfacing treatment complications: a review. *Dermatol Surg.* 2010;36:299–306.
- 39. Tanzi EL, Alster TS. Treatment of atrophic facial acne scars with a dual-mode Er:YAG laser. *Dermatol Surg.* 2002;28:551–555.
- Tanzi EL, Lupton JR, Alster TS. Lasers in dermatology: four decades of progress. J Am Acad Dermatol. 2003;49:1–31; quiz 31–34.
- Cho SI, Kim YC. Treatment of atrophic facial scars with combined use of high-energy pulsed CO₂ laser and Er:YAG laser: a practical guide of the laser techniques for the Er:YAG laser. *Dermatol Surg.* 1999;25:959–964.
- Bitar GJ, Patel P, Craig L. Scar management. In: Prendergast PM, Shiffman MA, eds. *Aesthetic Medicine*. Berlin Heidelberg: Springer; 2011:277–288.
- Gonzales MJ, Sturgill WH, Ross EV, Uebelhoer NS. Treatment of acne scars using the plasma skin regeneration (PSR) system. *Lasers Surg Med.* 2008;40:124–127.
- 44. Schweiger ES, Sundick L. Focal Acne Scar Treatment (FAST), a new approach to atrophic acne scars: a case series. *J Drugs Dermatol.* 2013;12:1163–1167.
- 45. Carniol PJ, Vynatheya J, Carniol E. Evaluation of acne scar treatment with a 1450-nm midinfrared laser and 30% trichloroacetic acid peels. Arch Facial Plast Surg. 2005;7:251–255.
- Bellew SG, Lee C, Weiss MA, Weiss RA. Improvement of atrophic acne scars with a 1320nm Nd:YAG laser: retrospective study. *Dermatol Surg.* 2005;31:1218–1222.
- Friedman PM, Jih MH, Skover GR, et al. Treatment of atrophic facial acne scars with the 1064nm Q-switched Nd:YAG laser. *Arch Dermatol.* 2004;140:1337–1341.
- 48. Chan HH, Lam LK, Wong DS, et al. Use of 1,320nm Nd:YAG laser for wrinkle reduction and the treatment of atrophic acne scarring in Asians. *Lasers Surg Med.* 2004;34:98–103.
- Vejjabhinanta V, Patel SS, Nouri K. Laser for scars. In: Nouri K, ed. Lasers in Dermatology and Medicine. London: Springer; 2011:45–51.
- Goerge T, Peukert N, Bayer H, Rutter A. Ablative fractional photothermolysis—A novel in skin resurfacing. *Medical Laser Application.* 2008;23:93–98.
- 51. Hedelund L, Haak CS, Togsverd-Bo K, et al. Fractional CO₂ laser resurfacing for atrophic acne scars: a randomized controlled trial with blinded response evaluation. *Lasers Surg Med.*

2012;44:447-452.

- Marqa MF, Mordon S. Laser fractional photothermolysis of the skin: numerical simulation of microthermal zones. J Cosmet Laser Ther. 2014;16(2):57–65.
- Mohammed G. Randomized clinical trial of CO₂ laser pinpoint irradiation technique with/without needling for ice pick acne scars. J Cosmet Laser Ther. 2013;15:177–182.
- Tierney EP, Kouba DJ, Hanke CW. Review of fractional photothermolysis: treatment indications and efficacy. *Dermatol Surg.* 2009;35:1445–1461.
- 55. Kang WH, Kim YJ, Pyo WS, Park SJ, Kim JH. Atrophic acne scar treatment using triple combination therapy: dot peeling, subcision and fractional laser. J Cosmet Laser Ther. 2009;11:212–215.
- 56. Alster TS, Tanzi EL, Lazarus M. The use of fractional laser photothermolysis for the treatment of atrophic scars. *Dermatol Surg.* 2007;33:295–299.
- Magnani LR, Schweiger ES. Fractional CO₂ lasers for the treatment of atrophic acne scars: a review of the literature. J Cosmet Laser Ther. 2014;16(2):48–56.
- 58. Ahmed R, Mohammed G, Ismail N, Elakhras A. Randomized clinical trial of CO(2) LASER pinpoint irradiation technique versus chemical reconstruction of skin scars (CROSS) in treating ice pick acne scars. *J Cosmet Laser Ther.* 2014;16:8–13.
- 59. Rongsaard N, Rummaneethorn P. Comparison of a fractional bipolar radiofrequency device and a fractional erbium-doped glass 1,550-nm device for the treatment of atrophic acne scars: a randomized split-face clinical study. *Dermatol Surg.* 2014;40:14–21.
- Sardana K, Manjhi M, Garg VK, Sagar V. Which type of atrophic acne scar (ice-pick, boxcar, or rolling) responds to nonablative fractional laser therapy? *Dermatol Surg.* 2014;40:288–300.
- Goodman GJ, Baron JA. The management of postacne scarring. Dermatol Surg. 2007;33:1175–1188.
- Jemec GBE, Jemec B. Acne: treatment of scars. J Clin Dermatol. 2004;22:434–438.
- 63. Gawdat HI, Hegazy RA, Fawzy MM, Fathy M. Autologous platelet rich plasma: topical versus intradermal after fractional ablative carbon dioxide laser treatment of atrophic acne scars. *Dermatol Surg.* 2014;40:152–161.
- 64. Harandi SA, Balighi K, Lajevardi V, Akbari E. Subcision-suction method: a new successful combination therapy in treatment of atrophic acne scars and other depressed scars. J Eur Acad Dermatol Venereol. 2011;25:92–99.
- 65. Shen Y, Dai L, Li X, et al. Epidermal stem cells cultured on collagen-modified chitin membrane induce in situ tissue regeneration of full-thickness skin defects in mice. *PLoS One.* 2014;9:1–14.
- 66. El-Hadidy MR, El-Hadidy AR, Bhaa A, Asker SA, Mazroa SA. Role of epidermal stem cells in repair of partial-thickness burn injury after using Moist Exposed Burn Ointment (MEBO[®]) histological and immunohistochemical study. *Tissue Cell.* 2014;46(2): 144–151.
- Oni G, Lequeux C, Cho MJ, et al. Transdermal delivery of adipocyte-derived stem cells using a fractional ablative laser. *Aesthet Surg J.* 2013;33:109–116.
- 68. Senoo M. Epidermal stem cells in homeostasis and wound repair of the skin. *Adv Wound Care*. 2013;273–282. ●