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SPECIAL TOPICS

Nonablative Laser and Light Rejuvenation

The Newest Approach to Photodamaged Skin

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For centuries, patients and physicians have sought a safe and effective method for treating skin changes associated with photoaging. Currently, a variety of modalities are used to treat facial rhytids, including dermabrasion, chemical peels, and laser skin resurfacing (LSR). Although these modalities are relatively effective for rhytid reduction, epidermal disruption or removal results in an open wound that places the patient at risk for bacterial, viral, and fungal infections. Abnormal or delayed wound healing may result in skin dyspigmentation and scarring. In addition, the wound resolves with significant erythema that often lasts for weeks or months and is cosmetically troubling to patients (**Figure 1**). The ideal method of skin rejuvenation would achieve optimal cosmetic improvement of photodamage while minimizing wound care and the risk of adverse effects.

Histologic evaluation of actinically damaged dermis demonstrates increased levels of glycosaminoglycan, which replaces damaged and disorganized collagen fibrils.[1] Elastic fibers are abundant, thickened, and tortuous. Because these histologic changes associated with wrinkles are primarily present in the dermis, epidermal disruption may not be necessary for rhytid improvement.[2]

Although the mechanisms of rhytid improvement after LSR remain incompletely understood, at least 2 involve dermal changes and could potentially be induced without epidermal disruption. First, traditional LSR results in dermal collagen denaturation, which stimulates fibroblastic collagen synthesis and deposition 100 to 400 µm below the skin surface.[3] Injured fibroblasts proliferate for the first 3 days and then migrate into the wound site, where they produce type I procollagen and other matrix molecules.[4] Partial collagen denaturation also stimulates a wound-healing reaction, accelerating collagen synthesis by fibroblasts and reabsorption of elastotic material. Thirty days after LSR, new deposition of collagen fibrils in parallel arrays is visible in the papillary dermis.[5] Ninety days after treatment there is an even more highly organized network of collagen and elastic fibers.

Heat-induced collagen contracture is a second probable mechanism of rhytid improvement after LSR. This temperature-induced reaction occurs at 63°C, when the intermolecular peptide bonds of the triple helix collagen molecule dissociate. This mechanism occurs particularly after carbon dioxide (CO_2) LSR, which creates a zone of thermal injury,[6] and it is also present to a lesser extent after Er:YAG LSR in which the injury is predominantly ablative because of the much higher absorption of its wavelength (2.94 µm) by tissue water.

To diminish the risks associated with traditional LSR, several approaches to nonablative laser or light skin rejuvenation have been investigated. Variable success has been achieved, but as yet no method has shown rhytid reduction comparable to that seen after CO_2 or Er:YAG LSR. In this article, factors relevant to the 2 key goals of nonablative skin rejuvenation—epidermal preservation and controlled dermal heating that induces

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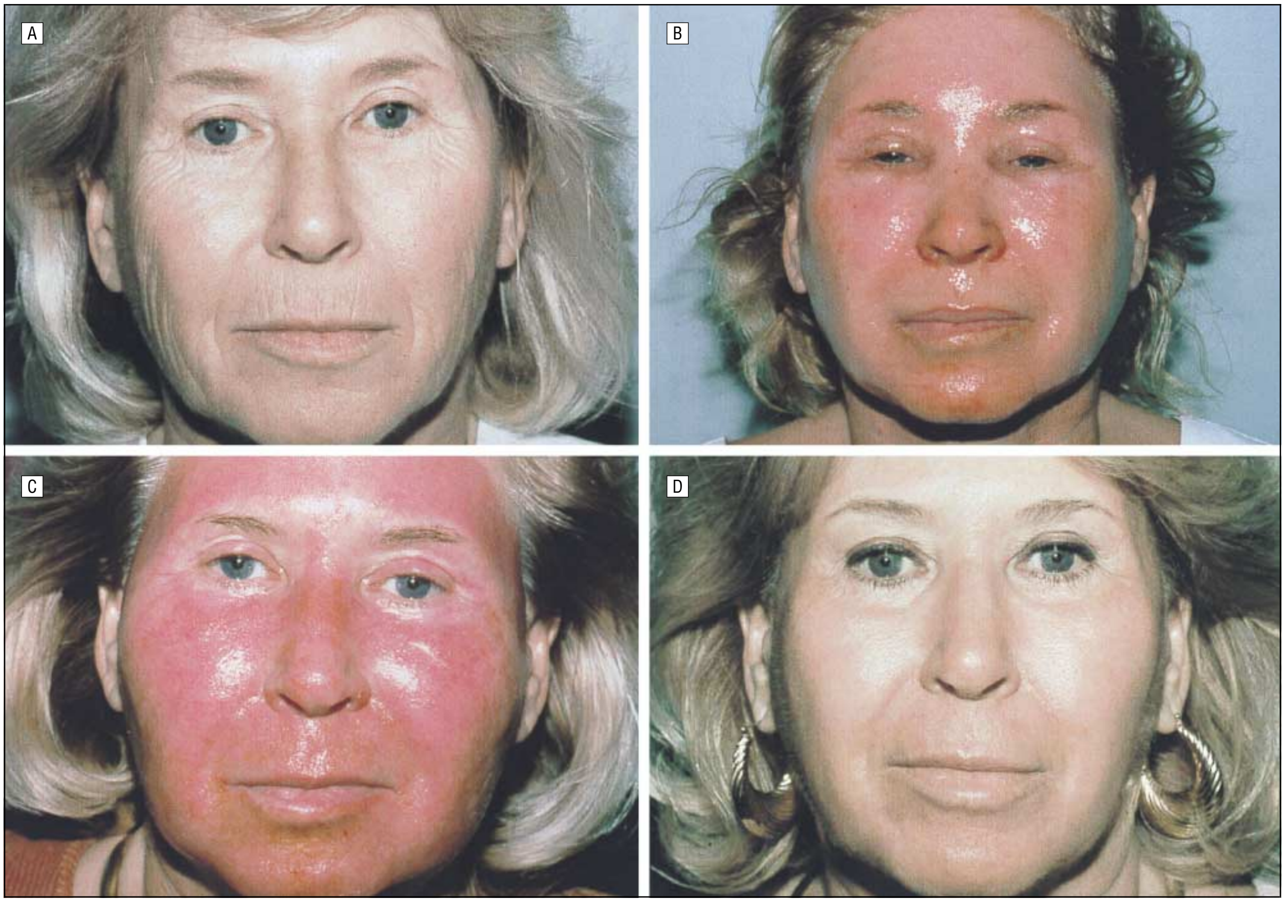

Figure 1. A 50-year-old woman with photodamaged skin before treatment (A) and 1 day (B), 1 week (C), and 1 month (D) after traditional carbon dioxide laser skin resurfacing.

fibroblast stimulation and collagen contracture—are discussed. In addition, methods of nonablative skin rejuvenation studied to date are reviewed.

EPIDERMAL PRESERVATION

Sparing of the epidermis during nonablative laser or light rejuvenation has been achieved by 4 main methods: (1) use of wavelengths that reduce epidermal thermal injury, (2) use of selective epidermal cooling, (3) distribution of delivered energy over multiple pulses, and (4) focusing of the laser energy to the desired depth.

Wavelength selection is an important factor in determining the degree of epidermal thermal injury. Epidermal melanin represents an "optical barrier" through which light must pass to reach the targeted dermal depth. Absorption of laser energy by melanin not only reduces the light dose reaching the dermis but also causes localized epidermal heating, potentially resulting in irreversible thermal damage or even ablation of the epidermis. Thus, wavelengths suitable for nonablative skin rejuvenation must have low melanin absorption, which favors the choice of longer-wavelength light (ie, mid- and near-infrared over visible wavelength light).

Most attempts at nonablative skin rejuvenation thus far have used such longer wavelengths with low (650-1100 nm) or intermediate (1.3-1.8 μm) tissue water absorption to deposit laser energy nonselectively in the dermis. Alternatively, wavelengths that target oxyhemoglobin, such as 585 nm, can be used to heat blood vessels present primarily at the desired dermal depth, ie, 100 to 400 μm below the skin surface. Subsequent heat conduction to adjacent perivascular collagen leads to the histologic changes described at the beginning of this article.

Epidermal protection during nonablative laser or light rejuvenation can also be provided by using selective epidermal cooling, which has emerged as an important adjunct to laser dermatologic surgery; it has been adapted for use in several clinical indications. Currently, the 2 most commonly used methods of selective epidermal cooling are cryogen spray cooling (CSC) and contact cooling (CC).

Nelson et al[7-9] developed CSC in 1994 as a form of dynamic cooling adapted for use with laser therapy of subsurface hypervascular lesions. A millisecond spurt of cryogenic liquid is applied to the skin surface immediately before pulsed laser exposure. The cryogen evaporates and the superficial skin temperature is reduced as a result of supplying the latent heat of vaporization, providing an efficient and effective method of selective epidermal cooling. Tetrafluoroethane, a nontoxic, nonflammable, Food and Drug Administration–approved freon substitute that has been demonstrated to be a safe and effective cooling agent,[10] is currently the cryogen of choice for CSC. In contrast, CC is based on conduction of heat

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from skin into a cold solid material. This is best achieved with a sapphire window, which has high thermal conductivity,[11] chilled with circulating water.

With both systems, skin temperature reductions depend primarily on initial coolant temperature and cooling time. One difficulty with the use of CC for nonablative skin rejuvenation is that the targeted collagen in the upper dermis is relatively superficial (<400 μm). As a result, localization of cooling in the epidermis requires short cooling times (10-100 ms) and low coolant temperatures (<0°C), which are much easier to obtain with CSC than with CC.[12]

The third method of epidermal preservation is distribution of delivered energy over multiple laser pulses. This approach has been used to drive deeper into the skin the thermal effect of some lasers, which would usually result in epidermal ablation. When multiple laser or light pulses are delivered at low fluence, the superficial tissue temperature rise relaxes rapidly between pulses as heat is conducted deeper into the skin. As a result, heat does not accumulate in the superficial skin layers, thereby minimizing epidermal damage. In deeper dermal tissue, the deposited heat accumulates owing to slower temperature relaxation in this region. Mathematical modeling has indicated that repetitive irradiation at low fluences can create significant dermal collagen coagulation with minimal epidermal damage, even with the strongly absorbed Er:YAG laser radiation.[13,14]

A fourth method of epidermal preservation is focusing of the laser energy to the desired depth. Biolase Technology Inc (San Clemente, Calif) developed a proprietary handpiece that focuses the light to the desired depth in the dermis. When used with a 980-nm diode laser and air cooling of the skin surface, this handpiece allows deep penetration of the light into the dermis while minimizing epidermal thermal injury.[15]

Traditional CO_2 and Er:YAG LSR offer the patient not only rhytid reduction but also improvement in epidermal atypia and melanocyte maldistribution, which present clinically as skin roughness and dyspigmentation. Although elimination of epidermal injury will significantly diminish the risks associated with traditional LSR, some of the cosmetic benefits of epidermal rejuvenation may also be lost. However, relatively low-risk adjuvant treatments, including tretinoin, glycolic acids, microdermabrasion, and light chemical peels, could be used to address such textural and pigmentary changes in patients undergoing nonablative skin rejuvenation.

In summary, several methods of epidermal preservation have been suggested to achieve nonablative laser or light skin rejuvenation. Often, 2 or more of the described methods have to be used to achieve optimal results.

DERMAL HEATING

No matter which method of epidermal preservation is used, successful nonablative skin rejuvenation can only be achieved if the goal of concomitant rhytid reduction is accomplished. As described in the introduction, the mechanisms of rhytid improvement after traditional LSR remain incompletely understood; however, dermal thermal injury resulting in collagen denaturation, fibroblast stimulation, and subsequent neocollagen formation is believed to be most important. To develop nonablative rejuvenation procedures with results comparable to traditional LSR, neocollagen formation should be induced in (and, most likely, confined to) a zone approximately 100 to 400 μm from the skin surface,[12] which contains most of the solar elastoses in photodamaged skin.

Thermal injury during laser or light treatment results from heat generated by absorption of photon energy. The depth of thermal injury depends on the penetration depth of the radiation used, which dictates the temperature distribution resulting from the light-tissue interaction.[4] To maximize heating in a subsurface tissue layer it is useful to select radiation with an optical penetration depth that matches the targeted tissue depth. In spectral regions where absorption dominates over scattering, the optical penetration depth is approximated by the reciprocal of the absorption coefficient at the selected optical wavelength. If the targeted dermal depth is 100 to 400 μm below the skin surface, the absorption coefficient should be approximately 25 to 100 cm^{-1}. Wavelengths from 1.3 to 1.8 μm best fit this need, which currently limits the selection of light sources to the 1.32- and 1.44-μm Nd:YAG lasers, the 1.54-μm Er:Glass laser, and the recently developed 1.45-μm diode laser.

Because deposited heat is redistributed within tissue by the process of heat diffusion, the ultimate depth of thermal injury is affected not only by the optical penetration of the selected wavelength but also by several other factors, including deposited energy, pulse duration, focal characteristics of the light, and, if multiple pulses are used, the repetition rate and number of pulses. Although discussion of such a multitude of variables is beyond the scope of this article, their effect must be considered in development of novel nonablative skin rejuvenation methods.

Application of various epidermal cooling modalities during nonablative skin rejuvenation is another factor that may affect the depth of thermal injury. As mentioned in the previous section, short cooling times will confine temperature reductions to the superficial layers of skin, and the greatest temperature drop will occur in the epidermis, whereas longer cooling times will result in a deeper zone of cooled skin.[12] In addition, the cooling rate depends on the quality of thermal contact and the temperature difference between the skin and the cooling medium.[12]

CURRENT METHODS OF NONABLATIVE SKIN REJUVENATION

Q-Switched 1064-nm Nd:YAG Laser

The Q-switched Nd:YAG laser was used in one of the first attempts at nonablative skin rejuvenation. Using a 3-mm spot size and fluence of 5.5 J/cm^2 for treatment of perioral or periorbital rhytids, Goldberg and Whitworth[16] achieved rhytid improvement comparable to ablative LSR in 3 of 11 patients and some improvement in 6 of 11 patients. However, the treatment resulted in pinpoint bleed-

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ing, and in some patients erythema persisted for up to 3 months after the procedure. A subsequent study by Newman et al[17] used the Q-switched Nd:YAG laser in combination with topical carbon suspension to provide a chromophore target. This procedure used lower fluences (2.5 J/cm^2) and resulted in an average of 25% rhytid improvement in 12 patients after 4 treatments, without epidermal disruption. Small areas of transient hypopigmentation were reported in 2 patients with type VI skin, but this complication was eliminated in later treatments by using lower fluences.

Pulsed-Dye Laser

There have been anecdotal reports of wrinkle reduction in patients who had vascular lesions treated with the pulsed-dye laser. Zelickson et al[18] treated 20 patients and documented clinical improvement in 90% of patients with mild to moderate wrinkles and 40% of those with moderate to severe wrinkles after one pulsed-dye laser (Photogenica V; Cynosure, Chelmsford, Mass, or model SPTL-1b; Candela, Wayland, Mass) treatment at 585 nm using a 7- or 10-mm spot size and fluence of 3.0 to 7.6 J/cm^2. However, significant purpura and swelling lasting for 1 to 2 weeks occurred in all patients.

Using another pulsed-dye laser system (Nlite; SLS Ltd, Llanelli, Wales), Bjerring et al[19] treated 30 patients at 585 nm with the following parameters: 350-μs pulse duration, 5-mm spot size, and fluence of 2.4 J/cm^2. Patients did not develop purpura or skin dyspigmentation, and procollagen III production was demonstrated. For Fitzpatrick class I, II, and III wrinkle groups, rhytid improvement at 6 months was judged to be 52%, 89%, and 79%, respectively, of that seen in previous CO_2 LSR studies.[20]

980-nm Diode Laser

As described in the "Epidermal Preservation" section, Muccini et al[15] used a specially designed optical handpiece that focused light in the dermis and served as a thermal conductor to remove heat from the epidermis. The handpiece was used with a 980-nm diode laser for nonablative skin rejuvenation in vitro on breast and facial skin and subsequently on 2 patients. Combined with cool air blown over the skin surface, this approach enabled epidermal preservation while inducing new collagen and elastin formation, which was evident 3 weeks after treatment. The depth of thermal injury averaged 750 μm when shallow and moderate probes were used and 1475 μm when a deeper-focusing probe was used. Such depths may be deeper than desired and might result in adverse clinical effects such as pitted scarring; therefore, further studies are needed to optimize this approach.

1.32-μm Nd:YAG Laser

Laser Aesthetics (Auburn, Calif) developed a 1.32-μm Nd:YAG laser used in combination with CSC for nonablative skin rejuvenation. A multicenter study[21] evaluated periorbital rhytid improvement in 35 adults after 3 treatments performed at 2-week intervals. Small but statistically significant clinical improvements were noted in the mild, moderate, and severe rhytid groups 12 weeks after the final laser treatment. A final assessment performed 24 weeks after the last treatment showed statistically significant clinical improvement in the severe rhytid group only (**Figure 2**). The procedure was safe, although 4 sites (5.6%) developed transient hyperpigmentation and 2 (2.8%) developed barely perceptible pinpoint pitted scars. Subsequent device improvements, including features that prevent laser irradiation if the cryogen spray fails to operate and a thermal sensor that rapidly reports skin temperatures (allowing optimal laser fluence adjustment), have improved the safety and efficacy of this approach.

Goldberg[22] recently used the same laser for full-face nonablative skin rejuvenation in 10 patients. Four treatments were performed in 16 weeks, and assess-

Figure 2. A 42-year-old woman with periorbital rhytides before treatment (A), immediately after nonablative skin rejuvenation using a 1.32-μm Nd:YAG laser in conjunction with cryogen spray cooling (B), and 6 weeks after nonablative laser skin resurfacing (C).

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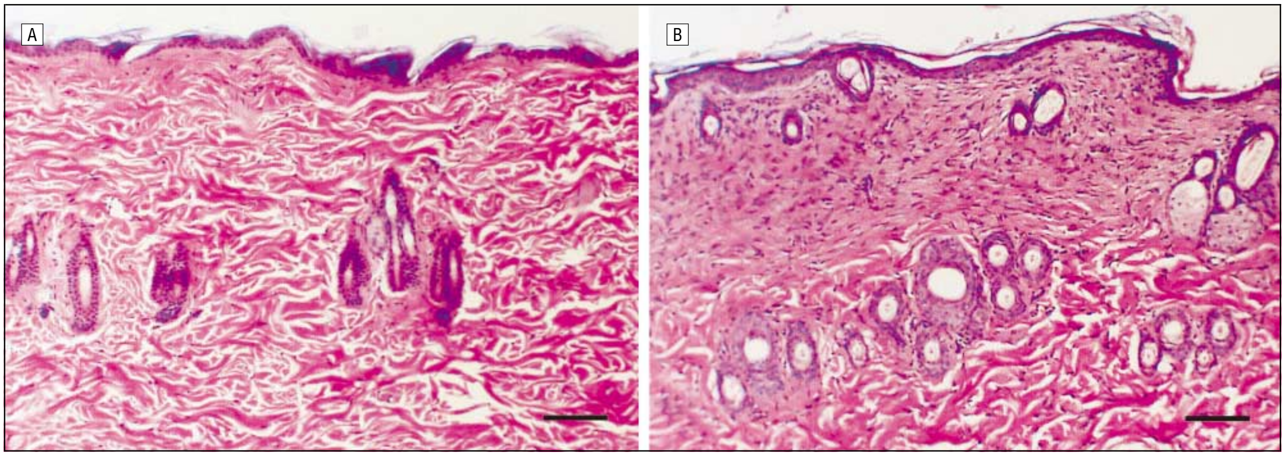

Figure 3. A, Histologic section from a nonirradiated skin site (control). B, Four weeks after treatment with repetitive Er:YAG laser (10 pulses at 1.3 J/cm^2, 10 Hz), neocollagen formation extending to 250 μm deep is easily identified by tightly packed parallel collagen fibrils and an increased number of fibroblasts (regressive hematoxylin-eosin, original magnification ×100).

ments were made 6 months after the last treatment. Some improvement was reported in 6 patients, and substantial improvement was seen in 2. No patients showed complete improvement, and no adverse effects were reported. All patients demonstrated some new collagen formation 6 months after treatment.

Er:Glass Laser

Several researchers favor this laser because of its wavelength (1.54 μm), which is optimal for penetration to a depth of 100 to 400 μm in human skin. Furthermore, compared with other wavelengths with similar penetration depths, 1.54 μm has low melanin absorption, low tissue scattering, and relatively high water absorption. Mordon et al[4] recently used an Er:Glass laser in combination with a sapphire CC handpiece on the abdomen of male hairless rats. By using a pulse train mode (1.1 J/pulse, 15 or 30 pulses at 3 Hz), the investigators demonstrated epidermal preservation with dermal homogenization indicative of thermal injury and subsequent fibroblast proliferation. The depth of collagen coagulation was centered at 250 μm (15 pulses) or 300 μm (30 pulses) and averaged 200 μm thick.

Repetitive Low-Fluence Er:YAG Laser Irradiation

Majaron et al[23] exposed in vivo rat skin to 5 to 10 low-fluence (1.0-1.5 J/cm^2) Er:YAG pulses at 10 and 33 Hz, resulting in dermal collagen coagulation to a depth of approximately 250 μm. Subsequent neocollagen formation was noted histologically by a band of parallel collagen fibrils in the superficial dermis with a thickness of 100 to 250 μm (**Figure 3**).[24] These dermal changes were significant and closely approximated results seen after CO_2 LSR; however, although the epidermis was not completely ablated, moderate epidermal damage occurred. The addition of CSC before, or during and after, the sequence of laser pulses improved epidermal preservation but also significantly diminished the depth of collagen coagulation.

Intense Pulsed Light Sources

These are usually flashlamp devices that emit at wavelengths between 500 and 1200 nm. Absorption filters can be used to select appropriate wavelengths for irradiation. ESC Medical (Yokneam, Israel) has developed a device that delivers 3 to 90 J/cm^2 over multiple pulses through an 8×35-mm handpiece that can be precooled with a cooling collar. Goldberg and Cutler[25] used this device for nonablative skin rejuvenation and after 1 to 4 treatments reported some improvement in 16 of 30 patients and substantial improvement in 9 of 30. Three patients developed mild blistering, but no long-term adverse effects were reported. Improvement in irregular skin pigmentation and telangiectasia can also be achieved using this device.[26]

CONCLUSIONS

The risk-benefit ratio of skin rejuvenation procedures would be significantly improved by development of methods for preserving the epidermis. Clinicians and scientists have recently explored a variety of approaches in attempts to develop a method of nonablative laser or light skin rejuvenation. Such a method would ideally preserve the epidermis and at the same time achieve dermal coagulation and subsequent neocollagen formation significant enough to result in rhytid reduction comparable to that seen after traditional LSR. Variable treatment success has been achieved, but to date an optimal method of nonablative skin rejuvenation has not been demonstrated. Improved understanding of laser and light-tissue interactions is crucial for optimization of nonablative skin rejuvenation as research efforts continue.

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