skin elasticity measurements, and photographs were conducted at baseline, 1, 3, 6, and 12 months. Mean skin thickness (as shown by ultrasonography) and skin elasticity showed ($P < .001$) increases at each time point. Subjective physician and subject evaluations indicated improvement, high subject satisfaction, and minimal adverse effects.

Laser Lipolysis and Fat Removal

Selective fat destruction with laser has proven difficult, largely secondary to the depth of fat relative to the penetration depth of the laser. Three wavelengths, 915 nm, 1210 nm, and 1720 nm, show favorable ratios of light absorption relative to water; however, the ratios are less than 1.5, such that selectivity is marginal. Surface cooling improves the likelihood of achieving a temperature gradient between superficial water (dermis) and subcutaneous fat.[25,26] Articles reporting fat destruction showed that long (several seconds) irradiation times are required for adequate fat heating; the long heating times and inevitable heating of tissue water are associated with considerable pain.[27]

The Food and Drug Administration approval in October 2006 of a 1064-nm Nd:YAG laser lipolysis system (Deka, Cynosure, Westford, MA) triggered an influx of manufacturers to market Nd:YAG and diode devices emitting laser radiation between 920 nm and 1320 nm, as advantages were claimed for each of the frequencies. A combination of frequencies (980-nm diode and 1064-nm Nd:YAG laser) was used by Mordon et al[28] in 2007 in a mathematical model that suggested for the first time that heat generated by the interaction of laser light energy with the tissue rather than the biophysical effects of a particular wavelength produced fat destruction, which facilitated a focused approach in developing the efficiency of lipolysis devices. Skin tightening appears to occur at dermal temperatures of 48°C-50°C without inducing burning injury to the epidermis. Corresponding external temperatures that balance safety and a good lipolytic effect were found to be in the range of 38°C-41°C. However, a search for the optimal laser frequency in inducing lipolysis and/or skin tightening, including 924, 968, 980, 1064, 1319, 1320, 1344, and 1440 nm, has not identified a single optimal frequency that would achieve simultaneously both goals and would satisfy both efficiency and safety criteria. For example, irradiation of fat tissue with 924 nm has the highest selectivity for melting of adipose cells, but not as good of a skin-tightening effect.[29]

Acne

Destruction of the sebaceous glands should deprive the acne-prone follicle of the fuel that feeds the acne fire. Like fat, sebum enjoys preferential light absorption at 915 nm, 1210 nm, and 1720 nm. The more superficial location of the glands compared with the subcutaneous fat layer permits a more favorable scenario for selective heating. With optimized parameters, selective sebaceous gland heating can be achieved. Future trials should uncover those settings that create a practical device for "sebum"-based acne clearing.

PDT in acne continues to be improved. Drawbacks to therapy include long incubation times and phototoxicity. Various methods have been used to decrease these side effects, many of which are from epidermal PpIX formation. Cooling the epidermis can suppress both singlet O_2 formation as well as suppress the conversion of ALA to PpIX.

Another way to suppress epidermal damage is to inhibit surface fluorescence by photobleaching the epidermis using low-power density blue light. In this way, PpIX is converted to photoproducts. Sakamoto et al[30] introduced this new concept with ALA to enhance the ratio of sebaceous gland to epidermal fluorescence and phototoxicity. They discovered that low-level light exposure during the period of ALA metabolism prevents accumulation of porphyrins and can be used to selectively inhibit epidermal porphyrins. Because light prevents accumulation of the photosensitizer, they called this phenomenon "photoinhibition" of PDT or "i-PDT." They studied PpIX in cultured human keratinocytes, and in vivo in Yorkshire swine, by measuring porphyrin accumulation, cell lethality, and inflammatory responses when inhibitory red (635 nm) or blue (420 nm) light was delivered during metabolism after topical ALA application. Subsequent exposure to high-fluence red light was then used to activate a PDT reaction. i-PDT was compared split-face with conventional PDT in a patient with recalcitrant acne. They found, in an irradiance-dependent manner, that low threshold levels of blue light (60-100 $\mu W/cm^2$) suppressed porphyrin accumulation in vitro and in vivo, with a corresponding decrease in inflammation after PDT. i-PDT produced much less inflammation, yet a similar benefit in deeper targets compared with conventional PDT.

Pixilated Radiofrequency

The increasing use of radiofrequency (RF) devices as laser "surrogates" is expected. RF devices are typically less expensive to manufacture than their laser counterparts and can perform some tasks as well as light. They can only act as substitutes for laser where water is the target, as RF devices offer none of the selective absorption for HgB and melanin as do wavelength-specific lasers. We recently studied a pixilated RF device that creates plasmas at the skin surface (Fig. 1) (Pixel RF, Alma lasers, Buffalo Grove, IL). The microwounds are similar to that produced by fractional CO_2 lasers (Fig. 2). The device is equipped with a roller that delivers wounds at a specific pitch. Multiple passes are delivered to achieve a final wound density sufficient to improve acne scarring, wrinkles, and/or striae (Fig. 3).

Lasers for Infections

Recent evidence supports a role for lasers in certain infections, most notably onychomycosis.[31] Studies have shown that 42.5°C for 2 minutes is sufficient to inactivate *T rubrum* and other pathologic fungi. However, much of this work was done in culture plates and might not be extrapolated to a thickened dystrophic nail. Both long-pulsed and Q switch Nd:YAG lasers, as well as 1320-nm lasers, have been applied to nails.[32] Typically, sessions are carried out every 1-4 months, and nails are treated to a point

Figure 1 Roller RF device.

where the patient reports a "warm" sensation. Another laser uses 870 nm and 930 nm light.[33] They found that after 4- and 2-minute exposures (in the same office visit) which were carried out 4 times at roughly monthly intervals, 75% of the nail cultures had cleared. They used infrared (IR) thermometers to maintain temperature (T) at 102°F (39°C) at a laser power density of 1 W/cm^2. Other lasers have been applied, but no published peer-reviewed studies compare laser with conventional medical approaches. One popular system is the PinPointe laser, a device that uses 1064 nm to gently heat the nails. In the future, expect to see other light-based technologies that inactivate fungus and bacteria through photothermal or photochemical means.

Figure 2 Patient just after treatment with roller RF device—note microwounds about 200 μm in diameter.

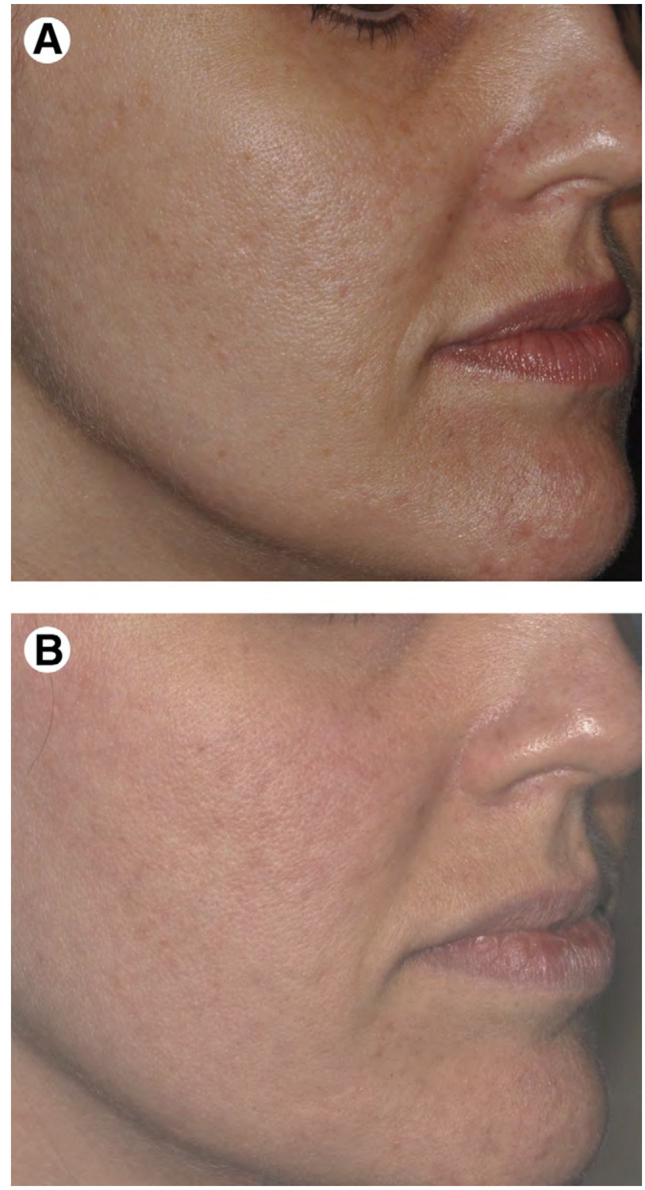

Figure 3 (A) Pretreatment RF pixel acne scar. (B) 3 months after 1 treatment.

Combining Medications and Laser

Nelson et al[34] have examined the role of angiogenesis-inhibiting drugs. They noted that PDL is the treatment of choice for PWS, but that in many cases, lesions remain resistant to laser treatment. They theorized that low therapeutic efficacy might be caused by revascularization of photocoagulated blood vessels owing to angiogenesis associated with the normal wound-healing response. Rapamycin, an inhibitor of mammalian target of rapamycin, effectively inhibits the growth of pathologic blood vessels. They developed a transgenic mouse model of pathologic angiogenesis with inducible overexpression of activated