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Recent Developments in Cutaneous Lasers

Maria Beatrice T. Alora, MD, and R. Rox Anderson, MD*

Wellman Laboratories of Photomedicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts 02144

INTRODUCTION

Laser surgery is one of the most rapidly advancing fields in medicine. In dermatology and ophthalmology, lasers now routinely provide the most precise form of surgery ever practiced, often for cosmetic goals. Consumer demand has generated intense interest from physicians and industry. This has led to the development of safer and more effective lasers with a wide range of applications.

The theory of selective photothermolysis, introduced by Anderson and Parrish in 1981, is the basis for many advancements in dermatological lasers [1]. It allows for highly localized destruction of light-absorbing "targets" in skin, with minimal damage to the surrounding tissue. To achieve selective photothermolysis, appropriate wavelength, exposure duration, and sufficient fluence are necessary. Various targets absorb at different wavelengths, and the wavelength of the laser should be absorbed more by the target structure than by surrounding structures. Light absorbed in the target structure is converted to heat, which immediately begins to diffuse away. In general, exposure duration should be shorter than or about equal to the thermal relaxation time of the target. Thermal relaxation time is the time it takes the target to cool significantly and is proportional to the square of the diameter of the target. Therefore, the thermal relaxation time of a small object is much shorter than that of large objects. A useful approximation is that the thermal relaxation time in seconds of a target is equal to the square of its diameter in millimeters. Thus, a 0.1-mm blood vessel cools significantly in about 0.01 sec (10 msec). Finally, sufficient energy must be delivered to cause the desired effect, destruction of the target. Fluence (energy/area) necessary for treatment is inversely proportional to the fraction of light absorbed by the targets. Thus, higher fluence is necessary when using weakly absorbed wavelengths, treating targets that contain less chromophore (the light absorbing substance), or targets that are deep within the skin. Clinically, selective photothermolysis involves ensuring that a maximum tissue-damaging temperature occurs only in the desired tissue targets. When treating dermal targets (blood vessels, tattoos, hair, etc.), light must pass through the epidermis. Epidermal injury is the most frequent cause of side effects in these settings.

A classic example of selective photothermolysis is the use of pulsed lasers in the treatment of port-wine stains (PWS). PWS consist of dilated venules in which the principal chromophore is oxyhemoglobin. The principal absorption peaks of oxyhemoglobin are in the blue–green–yellow portion of the visible range (418, 542, and 577 nm). In general, longer wavelengths penetrate more deeply into skin because of less scattering by dermal collagen, and the wavelengths 577–595 nm, within one absorption band of oxyhemoglobin, are well suited to target vessels in PWS. The first lasers designed for selective photothermolysis of PWS were pulsed dye lasers emitting pulses of about 1 msec duration. This pulse width corresponds to thermal relaxation time of vessels down to about 30 μm in diameter, typical for pediatric PWS. Laser light absorbed by hemoglobin is converted into heat, which damages the endothelium and surrounding vessel wall, followed by thrombosis, a vasculitis, and the removal of the abnormal venules [2]. The ideal pulse duration for PWS treatment is probably approximately 10 msec [3], and several laser systems are emerging that emit longer pulses.

*Correspondence to: R. Rox Anderson, MD, Wellman Laboratories of Photomedicine, Massachusetts General Hospital, Harvard Medical School, 50 Blossom Street, BHX 630, Boston, MA 02144-2696.

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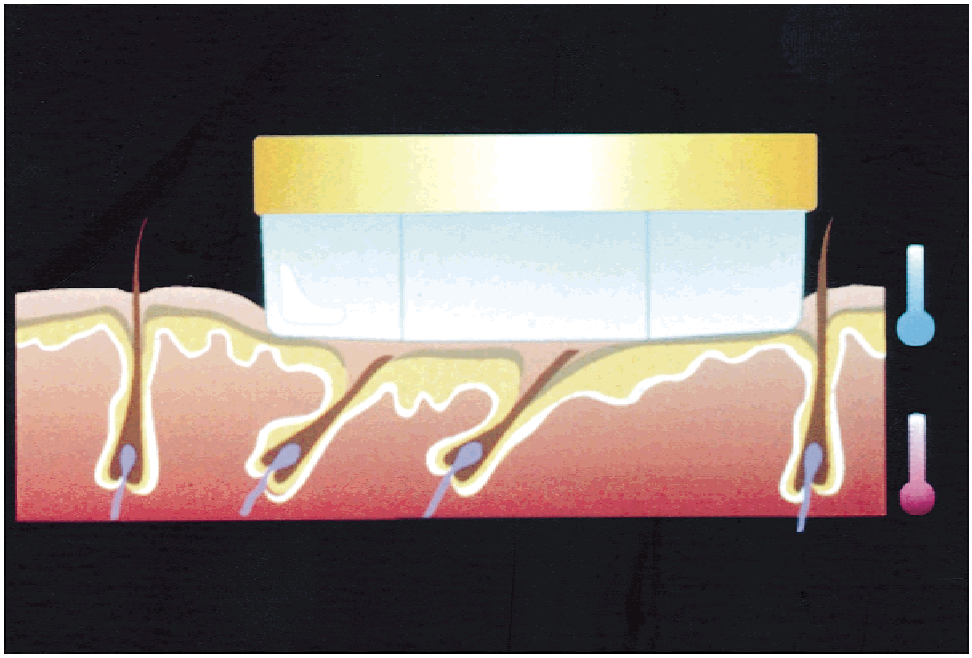

Fig. 1. The contact cooling handpiece of the Palomar E2000 (courtesy Palomar Medical Technologies, Lexington, MA).

SKIN COOLING

With the exception of epidermal pigmented lesions, melanin in the epidermis is an unwanted site for absorption of light. Thus, darkly pigmented skin is at high risk for epidermal injury during any laser treatment using visible or near-infrared wavelengths less than 1,200 nm [4]. All methods of cooling the skin consist of placing a cold medium in contact with the skin surface. The anatomic depth of cooling depends on contact time. For example, the epidermis is cooled in tens of milliseconds, the epidermis and papillary dermis are cooled in hundreds of millliseconds, and bulk skin cooling requires seconds of contact time. Cooling has several useful consequences. Epidermal cooling minimizes epidermal damage and allows for the delivery of fluences higher than would be normally tolerated. Cooling the upper dermis is also protective and relieves pain generally without reducing efficacy. The anatomic depth of cooling that is desired differs with different laser applications. For superficial PWS, epidermal cooling is desired. For deeper targets such as hair follicles or leg veins, epidermal plus upper dermis cooling is desirable. Bulk cooling is most useful when the targets are closely spaced to decrease the risk of dermal injury. For example, treatment of a dense beard using pulses longer than several milliseconds is a setting in which gross thermal injury of the dermis is a risk.

Cooling the skin before and during laser treatment has been practiced for at least 30 years, but advanced cooling techniques have been recently incorporated into various laser treatment systems. The simplest way for bulk skin cooling is by icing the area to be treated immediately before the procedure [5] or by applying a thin layer of a clear cold gel that absorbs heat. However, these are not very aggressive and offer limited protection. More effective cooling can be achieved by cold sapphire contact handpieces (e.g., EpiWand, Palomar Medical Technologies, Lexington, MA; ChillTip, Coherent, Inc., Palo Alto, CA; CLO Contact Cooling System, Cool Laser Optics, Westborough, MA) that are held against the skin surface (Fig. 1). The −10°C to +10°C sapphire cools the epidermis before, during, and after the laser pulse, permits beam coupling into the skin, and can provide a convergent beam that maximizes light penetration to the deeper dermis. With gentle pressure, such contact devices can also be used to compress the skin, thereby decreasing the distance light must travel to reach dermal targets such as hair follicles.

Dynamic cooling (DCD, Candela Laser Corporation, Wayland, MA) uses a cryogen, tetrafluoroethane (HFC 134), sprayed on the skin surface through a controlled solenoid valve (Fig. 2). This cryogen has a boiling point of −26°C and is an environmentally compatible, nontoxic, nonflammable freon substitute. The cryogen spurt duration ranges between 20 and 100 msec, followed by

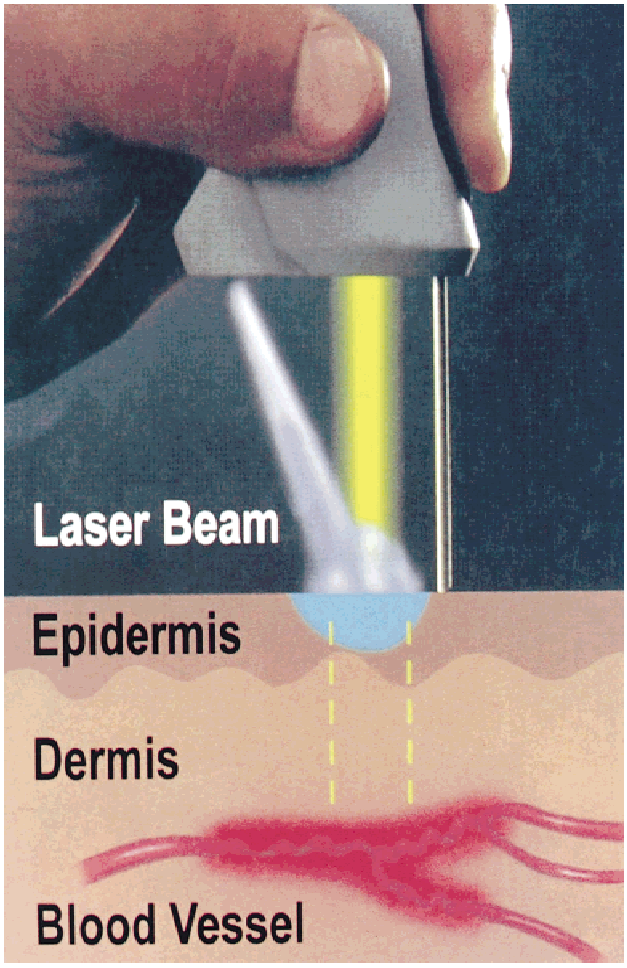

Fig. 2. The dynamic cooling device emits short bursts of cryogen several milliseconds before the laser pulse (courtesy Candela Laser Corporation, Wayland, MA).

a 0–500-msec delay before delivery of the pulse. Cryogen spray cooling provides rapid, aggressive epidermal cooling and is ideal for vascular targets such as PWS, which may be blanched by contact cooling devices [6,7].

VASCULAR LASERS

One of the first lesions successfully treated with lasers was the vascular malformation. The argon laser was one of the first lasers available. However, because this is a relatively low-power continuous wave (CW) laser, exposure times were in general too long for selective photothermolysis, and nonselective heating of surrounding structures occurred, resulting in dermal injury and an unacceptably high risk of scarring. The development of pulsed dye lasers specifically for PWS during the 1980s heralded a new treatment for cutaneous vascular lesions. The first commercially available device, with a wavelength of 585 nm and pulse width of 450 sec, is safe and effective for PWS [8,9], hemangiomas [10], facial telangiectasia from rosacea and other causes [11,12], and for some angiogenic lesions such as scars [13] and warts [14]. Risk of scarring is less than 1% and occurs more often on the neck than on any other site. Despite these successes, deep lesions with larger blood vessels such as leg telangiectasia and a sizeable fraction of PWS remain difficult to treat. The short, strongly absorbed pulses from pulsed dye lasers cause vaporization of blood, local rupture of microvessels, and purpura. Purpura is often cosmetically unacceptable and often lasts for 7–10 days. Pulsed dye lasers with longer wavelengths (595 and 600 nm) and a pulse width of 1.5 msec are now available (Scleroplus, Candela Laser Corporation; PhotoGenica VLS, Cynosure, Inc., Chelmsford, MA) and appear to be somewhat more effective, although they nonetheless cause purpura. The longer wavelengths have the advantage of deeper penetration, whereas the longer pulse duration is closer to the thermal relaxation time of somewhat larger vessels (1–10 msec), thus being able to target larger-diameter vessels including leg telangiectasia [15]. For most vascular lesions, a pulse duration about equal to the thermal relaxation time of the offending vessels is probably ideal, although a study using a 4-msec 595-nm pulsed dye laser found that it was ineffective in treating leg telangiectasia [16]. In general, lasers have failed to rival the efficacy of sclerotherapy for leg veins. Cryogen spray cooling is available with some pulsed dye lasers and offers the option of safe higher-fluence treatment to achieve greater efficacy.

Several pulsed 532-nm lasers are available that deliver at pulse widths of 1–100 msec (e.g., CBDiode, Continuum Biomedical, Dublin, CA; Aura KTP, Laserscope, San Jose, CA; Versapulse, Coherent, Inc.). The 532-nm output is derived by creating the second harmonic of a Nd:YAG laser generating at exactly twice this wavelength, 1,064 nm. Because hemoglobin has a strong absorption band at 532 nm, this green wavelength is also effective for treating vascular lesions [17]. An advantage of this group of lasers is that, with their long and tunable pulse widths, one can avoid rupturing the target vessels, thus avoiding postoperative purpura. After treatment, most patients develop some erythema and swelling, which usually resolves within 24 hr. Purpura-free treat-

ment is favored by adult patients even if the final efficacy is less than with pulsed dye lasers [18]. Vascular lesions composed of larger-diameter vessels, such as adult PWS and leg telangiectasia that may be resistant to pulsed dye laser treatment, are sometimes responsive to these longer pulse width devices. It has been shown that multiple pulses are often required [19]. A disadvantage of this group of lasers is that 532 nm is well absorbed by melanin, thereby increasing somewhat the risk of epidermal damage in darkly pigmented individuals.

Oxyhemoglobin and reduced hemoglobin have wide but useful absorption bands in the near-infrared spectrum (700–1,200 nm). Alexandrite and diode lasers at wavelengths near 755 and 800 nm, respectively, are also being used for leg veins. Their longer wavelength is absorbed less by melanin, thus allowing increased penetration of light into dermis, but hemoglobin absorption is also far less at these wavelengths. Millisecond Nd:YAG lasers that emit laser light at 1,064 nm have also recently become available. Because this wavelength is weakly absorbed by melanin but has equivalent absorption in blood compared with the alexandrite and diode lasers, 1,064 nm can penetrate deeper and is useful for leg veins.

Despite promising progress, the present concensus is that laser treatment of leg veins is best used in patients with contraindications, fear of sclerotherapy, small vessels too technically challenging for sclerotherapy, or vessels resistant to sclerotherapy.

PIGMENTED LESIONS

Q-switching is a process that produces extremely high-power (typically 10–100 MW), extremely short (typically 1–50 nsec) pulses. A variety of Q-switched lasers (pulsed dye, 510 nm; frequency doubled Q-switched Nd:YAG, 532 nm; Q-switched ruby, 694 nm; Q-switched alexandrite, 755 nm; and Q-switched Nd:YAG, 1,064 nm) have been available for over a decade that selectively destroy pigmented lesions and tattoos. Extremely fast heating of melanin or tattoo pigment granules occurs, approximately 10 billion°C/sec, which both fractures these submicrometer particles and kills the cells that contain them [20]. Therefore, Q-switched laser pulses are ideal for targeting pigmented cells. They effectively treat epidermal lesions such as lentigenes [21–23], dermal lesions such as nevus of Ota [24,25], and tattoos [26–31]. Simple lentigenes usually respond to a single treatment, whereas several treatments are often necessary to treat lesions such as nevus of Ota. Café-au-lait macules can often be lightened with these Q-switched laser systems, but results are variable and recurrence is common [32–34]. Melasma generally gets worse after Q-switched laser treatments [35]. There have been reports of success in using a long-pulsed ruby laser for treating congenital nevi [36], but close monitoring is necessary because residual nests of nevus cells are present that are not clinically visible. Although laser treatment of congenital nevi may offer hope for patients with unresectable, disfiguring lesions, patients need to be counseled that the malignant potential of the residual nevus cells is unknown. Some clinicians are using Q-switched lasers for treating flat, benign-appearing nevi and have achieved significant clinical improvement after multiple treatments [37]. Conversely, Q-switched and normal-mode ruby lasers have been used for treating benign, atypical, and congenital nevi, and results have shown that one or two treatments with either laser do not produce complete removal of a lesion clinically or histologically [38]. Some surgeons routinely perform erbium resurfacing before treating dermal lesions and tattoos with one of the Q-switched lasers to allow increased penetration of laser light, but there is no firm clinical evidence to support this idea.

Before the development of pulsed lasers, therapeutic options for tattoo removal were limited to dermabrasion, CO_2 laser ablation, and surgical excision, all of which resulted in scarring. Q-switched lasers safely and effectively remove many tattoo ink colors. The exact mechanism for laser removal of tattoos is largely unknown. Proposed mechanisms include lymphatic removal of laser-ruptured particles, rephagocytosis of laser-altered pigment particles, and/or transepidermal elimination via a scale crust. Other mechanisms include pyrolytic chemical alteration of the pigment particle and fibrosis, which alters the dermal scattering coefficient, resulting in obscuring of deeper pigment [39].

Because of the different colors of ink, one laser cannot remove all the colors present in colored tattoos. Red ink is better removed by green laser pulses (short pulsed dye or frequency doubled Q-switched Nd:YAG laser), whereas black and green ink is better removed by the Q-switched ruby and alexandrite lasers. None of the available lasers effectively remove yellow ink. Because of its low

melanin absorption, the Q-switched Nd:YAG laser at 1,064 nm is probably more useful when treating dark-skinned individuals. Permanent or prolonged hypopigmentation can result after laser treatment, particularly with the Q-switched ruby laser, which limits its use in dark-skinned individuals. Irreversible ink darkening of cosmetic skin-color tattoos can occur with any of these high-energy, short-pulsed lasers, which can result in dramatic and cosmetically disastrous change of some white, pink, flesh-toned, and light-brown tattoo inks [40]. Reduction of tattoo ink containing ferric oxide (Fe_2O_3, "rust") to ferrous oxide (FeO, "jet black") by laser exposure appears to be the mechanism. The darkening appears within several seconds of the laser treatment and does not clear spontaneously, although it may respond to repeated laser treatments. Sunblock from the area to be treated should be removed because many of these products contain metal-containing oxides and salts (such as titanium dioxide) that may be flammable after exposure to high-energy Q-switched laser pulses.

In patients receiving parenteral gold, one concern is blue-gray discoloration (localized chyrisiasis) of the treated area that may develop after any short-pulsed Q-switched laser treatment. Physicochemical alterations in dermal gold deposits after exposure to laser light may cause an increase in optical scattering of incident visible light and depression of diffuse reflectance in the longer (red) wavelengths, resulting in blue discoloration [41]. Local allergic or granulomatous reactions and anaphylactoid reactions may also occur from laser-induced release of tattoo antigens.

Limitations of currently available lasers are the inability to remove yellow ink, a risk of hypo- or depigmentation, especially among darker individuals, and the incomplete removal of many tattoos. Also, to achieve satisfactory results, most tattoos require 6–12 treatments, with amateur tattoos requiring fewer treatments that professional tattoos. Several studies have recently shown that picosecond (10^{-12} sec) pulses are more effective for tattoo treatment [42–44]. However, these lasers are expensive to build, and none are currently available for use in the clinics. Tattoo removal with the best technology available is still disappointing in many cases. After a series of expensive and painful treatments, approximately one-third of patients still have residual, laser-altered tattoos.

RESURFACING

The carbon dioxide laser, at 10,600-nm wavelength, has been the workhorse of dermatologic lasers for many years. Conventional CW CO_2 lasers deposit energy in the upper 20 μm of skin because of the strong absorption by water and typically leave 0.2–1 mm of residual thermal damage, which achieves hemostasis. The depth of residual injury depends on laser exposure and other factors [45]. However, this is also responsible for prolonged wound healing and a high incidence of scarring. Conventional CW CO_2 lasers have been used effectively for ablation of warts, actinic cheilitis, and other benign epidermal lesions.

Carbon dioxide laser resurfacing has been performed for more than 20 years. It has been very popular for 5 years because of new technology and clinical development. By using the same thermal-confinement principles for selective photothermolysis, residual thermal damage from CO_2 lasers may be minimized. One can vaporize a thin layer of skin and leave only 50–150 μm of residual thermal damage by using pulses that are shorter than the thermal relaxation time (1 msec) of the directly heated (20 μm) layer in which absorption occurs [46]. This can be achieved in two ways. High-energy, short-pulsed lasers (e.g., Ultrapulse, Coherent, Inc.) produce high power at very short pulse durations (<1 msec), resulting in maximal vaporization with minimal diffusion of thermal energy. Another way is by using a focused CW CO_2 beam with a rapid beam scanner system that moves the laser spot at constant velocity (e.g., Silktouch/Feathertouch, ESC-Sharplan Lasers, Inc., Allendale, NJ) in a pattern that covers the treatment site at a dwell time of less than 1 msec. One can achieve similar clinical results with either system. Erbium:YAG (Er:YAG) lasers have been more recently developed for resurfacing. The Er:YAG emission wavelength of 2,940 nm is the most strongly absorbed of any wavelength by H_2O, 16 times greater than that for CO_2 laser light. Shallower skin penetration of 1 μm versus 20 μm for CO_2 laser light allows more precise ablation with less thermal damage.

When performed by a skilled operator on ideal candidates, laser resurfacing produces excellent results with minimal risks [47–50]. It allows for precise control of the amount of tissue to be removed. However, when improperly used, it may produce disastrous results such as scarring. Delayed hypopigmentation appearing 6 months

after laser resurfacing has been described after CO_2 laser treatments, which ranges from pale skin to white, depigmented skin. It may be a mismatch between the pale new skin of the resurfaced area and the surrounding photodamaged areas. Aside from photoaging, resurfacing has been used to treat acne scars [51–53], scars resulting from other causes, actinic cheilitis [54–55], actinic keratoses, xanthelasmas, and other epidermal lesions. One disadvantage of CO_2 laser resurfacing is the prolonged healing time. Although reepithelialization occurs within 7 days, erythema may last more than 6 weeks. Er:YAG resurfacing has been promoted as having shorter healing times. However, when depths equal to that of carbon dioxide laser resurfacing are achieved, healing times appear to be similar. Also, it does not appear to produce the same amount of skin tightening as carbon dioxide laser resurfacing. Some laser surgeons perform one to two passes with the Er:YAG laser after carbon dioxide laser resurfacing to remove thermally damaged tissue and consequently decrease healing time. An advantage of Er:YAG laser resurfacing over carbon dioxide laser resurfacing is that pigmentary changes are less common, making it beneficial for highly pigmented individuals [56]. A disadvantage of Er:YAG laser treatment is that the thermal damage it produces is insufficient to coagulate blood vessels, resulting in pinpoint bleeding during and sometimes after treatment. Newer Er:YAG lasers have longer pulse widths that produce greater thermal damage and perhaps more collagen contraction, new collagen formation, and better hemostasis.

"Subsurfacing" (a word we have coined in the present report to describe an upside-down skin burn) has recently become available. With this technique, cryogen spray or other cooling methods cool the epidermis so that only the dermis reaches high temperatures when exposed to a penetrating laser wavelength, such as the 1,320-nm line of Nd:YAG (CoolTouch, Laser Aesthetics, Auburn, CA). After treatment, patients experience erythema and edema lasting several hours. Multiple treatments with 4–6-week intervals are necessary. A potential advantage of this method is that wound care is unnecessary, but minor improvements in rhytides have been achieved with current technology [57]. Because most patients with photoaging have both epidermal and dermal changes, many would probably benefit more from either laser resurfacing or chemical peels in addition to subsurfacing.

HAIR REMOVAL

Laser hair removal is presently one of the most requested laser procedures. Most commercially available devices (e.g., long-pulsed ruby, alexandrite, and pulsed diode lasers) target melanin, thus making them most effective and safe for fair-skinned individuals with dark-colored hair. Temporary alopecia of pigmented hair is easy to obtain with all of these lasers, even at lower fluences. Even blonde hair is temporarily removed, with a growth delay of up to several months after treatment. Some of these lasers have been shown, at high fluences and large exposure spots, to produce long-lasting hair removal. For the first long-pulsed ruby laser (694 nm; Epilaser, Palomar Medical Technologies, Inc.) and for a high-energy diode array laser (800 nm; LightSheer, Coherent, Inc.), long-term controlled studies using quantitative hair counts have been reported [58,59]. A recent multicenter study used a long-pulse ruby laser with sapphire skin cooling (Epilaser, Palomar Medical Technologies) given in up to six treatments over 1 year, with blind evaluation of clinical results 6 months after the final treatment, in 153 patients, most of whom had brown hair [60]. The majority were graded with greater than 75% hair loss, and about one in 10 had complete laser-induced hair loss. In a previous study, a small number of subjects were followed for 2 years after ruby laser treatment; long-term, partial hair loss occurred in four of 12. None had growth recovery beyond 6 months after treatment [61]. Fluence-dependent long-term efficacy has been reported after diode laser treatment. Alexandrite laser combined with spray cooling (Gentlelase, Candela Laser Corporation) and an intense pulsed xenon lamp (EpiLight, ESC, Yokneam, Israel) appears to have similar fluence-dependent results, but quantitative long-term follow-up is still limited [62,63]. In addition to fluence, exposure spot size is an important factor to achieve hair removal because large spot sizes produce greater optical intensity deep in the dermis. For these high-energy devices, multiple treatments, spaced at least 1 month apart, are additive, with 15–35% long-term hair loss after each laser treatment when sufficient fluences are used. Among the different body sites treated, it appears that the chest and axilla respond best. Aside from producing long-lasting hair removal, improvement of acne and pseudofolliculitis barbae has been noted. It is likely that other follicular disorders can be treated effectively by these systems.

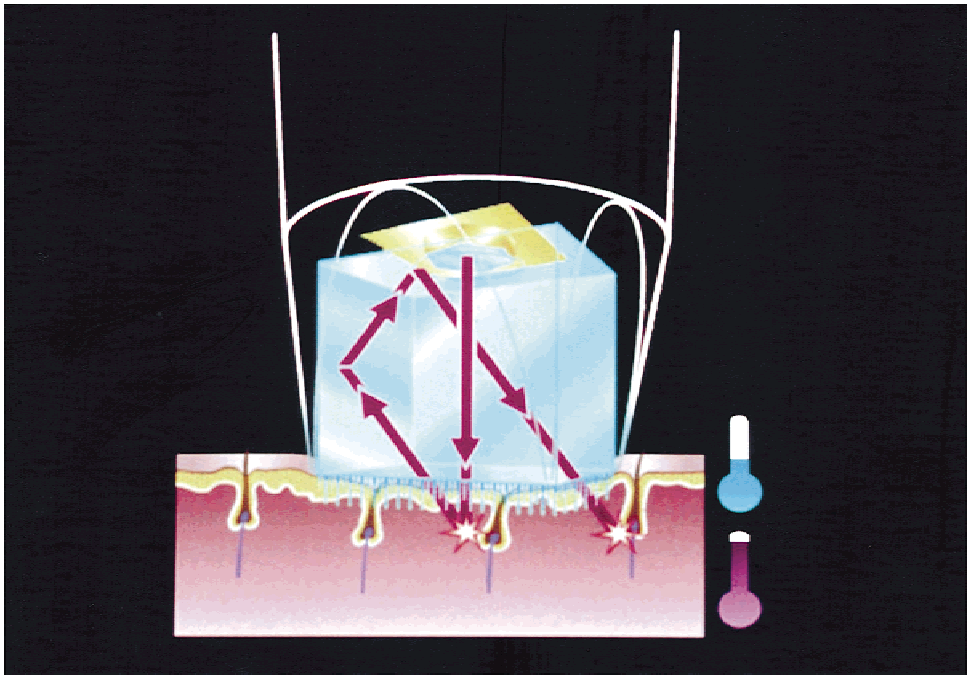

Fig. 3. Photon recycling reflects scattered light back into the skin (courtesy Palomar Medical Technologies, Lexington, MA).

The first cleared laser hair removal technique approved by the U.S. Food and Drug Administration employs the application of an India-ink–like carbon suspension followed by exposure to a Q-switched Nd:YAG laser. This has the advantage of being fast and safe with dark or light hair and with dark or light skin. However, no long-lasting results have been shown [64], and the technique has largely been replaced by lasers that combine skin cooling and high fluences to produce long-term removal of pigmented hair. The technology for laser hair removal is quickly advancing, driven by competition for faster, more effective, and less expensive devices. New lasers have been introduced that allow faster treatment times and allegedly greater epidermal protection. Currently available systems include normal-mode ruby (694 nm), normal-mode alexandrite (755 nm), pulsed diode (800 nm), and Nd:YAG (1,064 nm) lasers. Because all of these use follicular melanin as the target chromophore, all of them pose a risk for darker-skinned individuals. The diode and Nd:YAG lasers have the advantage of having a longer wavelength with somewhat better optical penetration, and the diode laser has an advantage of cooling during long pulses (30 msec) to better protect dark skin.

The hair shaft is produced by rapidly dividing matrix stem cells located in the deepest portion of the hair follicle, 2–7 mm below the skin surface. This matrix is probably the best target for temporary hair removal. However, pluripotential epithelial stem cells located near the insertion of the arrector pili muscle, in the area known as the bulge, about 1–1.5 mm deep, can regenerate an entire follicle. It was recently reported that growth phase of hair at the time of treatment does not affect the sensitivity for permanent hair loss, which strongly suggests that the bulge is the important target for permanent hair loss [65]. At present, it is unknown whether the bulge, dermal papilla, or both have to be destroyed to achieve permanent hair removal.

Permanent hair removal results both from degeneration of follicles and miniaturization of coarse terminal hair follicles to velluslike hair follicles, whereas temporary hair removal results mainly from induction of telogen [66].

At 694 nm, 30–80% of incident light is reflected and scattered from the skin. The reflection coefficient depends on the ratio of optical scattering to optical absorption. This ratio reaches a maximum in the red/near-infrared spectrum and is higher for light skin than for dark skin. Recycling of reflected "wasted" photons is possible by incorporating a reflective coating into the laser handpiece that reflects scattered light back into the skin (Fig. 3). This technique is available with a new ruby laser (E2000, Palomar Medical Technologies) and allows for a very large spot size (20 × 20 mm) and faster treatment of large skin areas.

Pulse duration has a major influence on laser hair removal. Submicrosecond (Q-switched) pulses produce isolated pigment cell injury, which

can cause leukotrichia [67], but have not been shown to cause long-term hair removal. There is also emerging evidence that pulse width affects the size of hair follicles that respond with long-term hair loss, in a manner consistent with the theory of selective photothermolysis. The best example is lack of long-term hair removal of fine hairs by pulses much longer than their thermal relaxation time. A 100-μm-diameter hair follicle containing a 50-μm hair shaft has a thermal relaxation time of about 10 msec. Such a follicle will escape injury from pulses somewhat longer than 10 msec by cooling during the laser pulse itself. Using longer pulse durations has several advantages, but it allows for better heat diffusion to the stem cells surrounding the hair shafts. The epidermis is better spared if pulses longer than about 10 msec are combined with contact cooling.

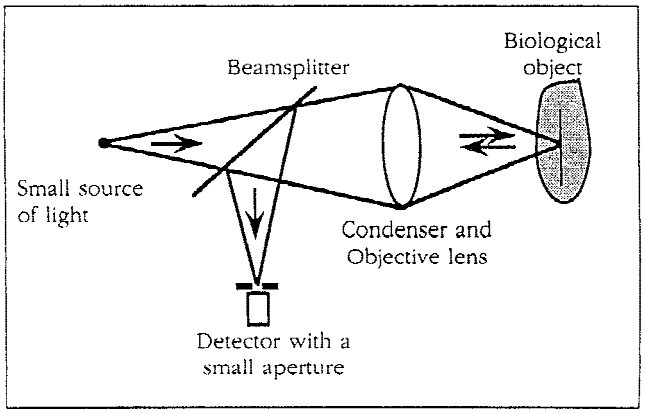

Fig. 4. Schematic representation of a confocal microscope (reproduced from Rajadhyaksha M, Zavislan JM. Confocal reflectance microscopy of unstained tissue in vivo. Retinoids 1998;14:26–30) with permission from Mediscript Limited.

EXCIMER LASERS

Ultraviolet B (UVB) phototherapy has been used for decades for the treatment of psoriasis, with excellent efficacy and safety records. The XeCl excimer laser emits light in the UVB range (308 nm). An advantage of laser phototherapy may be that unaffected skin need not be exposed to UV radiation, such that higher fluences of UV can be given to plaques of psoriasis. A preliminary study has shown that this laser safely and effectively clears psoriasis at shorter treatment times and in fewer number of treatments than standard phototherapy units [68]. With appropriate delivery systems, psoriasis on areas that are difficult to reach such as the scalp may potentially be treated. Other narrowband-UVB responsive conditions such as eczema and mycosis fungoides may benefit from this modality.

CONFOCAL MICROSCOPY AND OPTICAL COHERENCE TOMOGRAPHY

Confocal microscopy is a novel, noninvasive tool that allows for real-time imaging of human and animal tissue in vivo or freshly biopsied (ex vivo) without the fixing, sectioning, and staining necessary for routine histology. A confocal microscope consists of a tightly focused source of light that illuminates a small spot within the biologic specimen. Reflected or fluorescent light from the illuminated spot is then imaged onto a detector through a small pinhole aperture. The light source, illuminated spot, and detector aperture are placed in conjugate focal planes and thus are said to be confocal to each other (Fig. 4). The diameter of the detector aperture is matched to that of the illuminated spot through the intermediate optics. Because a small spot is illuminated and then detected through a small aperture, only the plane in focus within the specimen is imaged, thus allowing imaging of thin slices of tissue (optical sectioning) with high axial resolution and high contrast. Confocal microscopy provides fast, high-resolution imaging of live human skin cytology including epidermis, microvascular blood flow, and inflammatory cells (Fig. 5). Potential clinical applications include imaging skin lesions and their margins before biopsy, diagnosis of lesions without biopsy, or detection of margins in freshly excised tumors. Research applications include directly observing cellular and nuclear morphology of tissue, cell-to-cell interactions, wound healing and tissue regeneration, effects of UV light, responses to irritant and allergic agents, photoaging, microcirculation, fungal infections, and delivery of drugs [69–73].

Optical coherence tomography is a promising diagnostic method that uses low-coherence interferometry to produce a two-dimensional image of optical scattering from internal tissue microstructures in a way that is analogous to ultrasonic pulse-echo imaging. Cross-sectional images of the human skin can be obtained in vivo with a lower spatial resolution than confocal microscopy, i.e., ~15 μm. With a penetration depth of 0.5–1.5 mm, morphologic changes in the stratum corneum, epidermis, and papillary dermis can be visualized. However, single cells and subcellular structures cannot be studied. This technique is potentially useful for noninvasive diagnosis of bullous skin diseases and skin tumors [74].

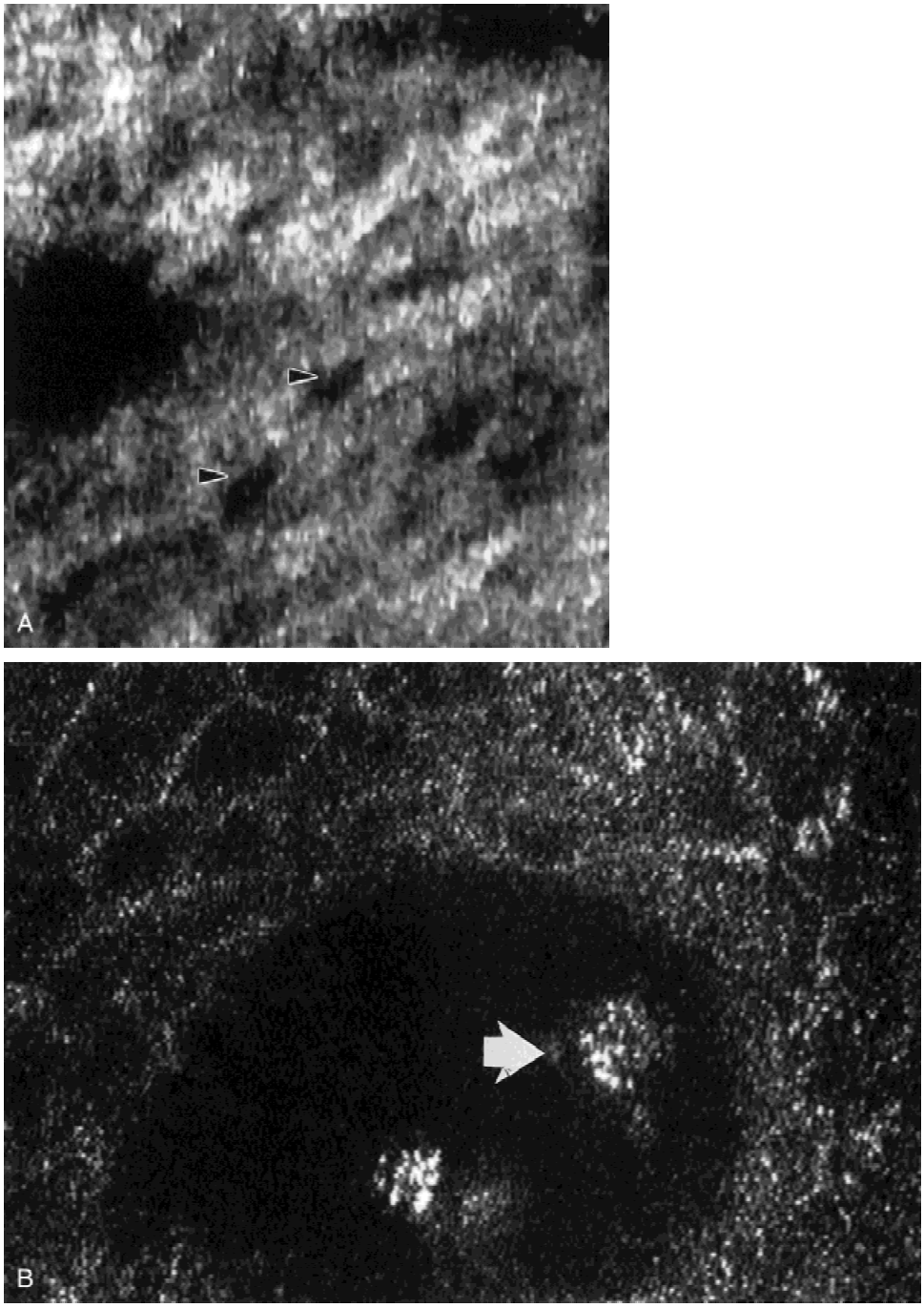

Fig. 5. **A:** Confocal images of a basal cell carcinoma shows atypical nuclei (arrow) with a nonanaplastic pattern (60×, 0.85 numerical aperture water-immersion objective lens; width = 170 μm). **B:** Acute allergic eczema to balsam of Peru shows the presence of a microvesicle containing inflammatory cells (arrow; 100×, 1.2 numerical aperture water-immersion objective lens; width = 150 μm) (courtesy Salvador Gonzalez, MD, and Milind Rajadhyaksha).

FUTURE DIRECTIONS

Although many advancements have been made in dermatologic uses of lasers and the device technology, there are still are many potential applications. Lasers could be used to target sebaceous glands, fat, sweat glands, cutaneous nerves, inflammatory cells, etc., and for treating dermatologic conditions such as acne vulgaris and hyperhidrosis. Future developments in optical imaging may allow noninvasive diagnosis of skin disorders. By combining optical diagnostics and laser treatment, robots capable of targeting not based on selective photothermolysis should be possible. Lasers in the future will be even more durable and compact. The final challenge and the final judgment of lasers in dermatology lie in their creative but responsible clinical use in medical practice.

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