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Active Skin Cooling in Conjunction With Laser Dermatologic Surgery

J. Stuart Nelson, MD, PhD, Boris Majaron, PhD, and Kristen M. Kelly, MD

The clinical objective in the laser treatment of patients with specific dermatoses is to maximize thermal damage to the target chromophore while minimizing injury to the normal skin. Unfortunately, for some lesions, the threshold incident light dosage for epidermal injury can be very close to the threshold for permanent removal of the target chromophore, thus precluding the use of higher light dosages. An important method of overcoming the aforementioned problem is to selectively cool the most superficial layers of the skin. Although melanin absorption will result in heat production during laser exposure, cooling the epidermis can prevent its temperature elevation from exceeding the threshold for thermal injury. Spatially selective cooling can be achieved by active cooling using a cryogen spray or cold sapphire contact handpieces. These devices promote rapid and spatially selective epidermal cooling to low temperatures without affecting the target chromophore temperature before the laser pulse is delivered. Cooling has become an integral part in the emerging discipline of laser dermatologic surgery. Attend almost any academic dermatology conference and you are likely to find many lectures that relate to cooling during dermatologic laser surgery. Although cooling in conjunction with laser therapy has become the clinical standard for many laser procedures, considerable controversy surrounds this methodology. We present herewith an overview of currently used techniques for active cooling of human skin and explore their advantages and disadvantages in relationship to specific dermatoses amenable to laser therapy.

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DERMATOLOGIC laser surgery is regarded as one of the fastest growing areas in the emerging fields of photomedicine and biomedical optics. Lasers are now the treatment of choice for several dermatoses for which no reliable or effective modality was previously available. The evolution of the laser as a medical device for dermatologic surgery has been a process of continued improvement. As with any such device, the most efficacious and appropriate use requires an understanding of the basic photo-biological and photo-physical principles of laser tissue interaction as well as the properties of the laser itself. Research

has not only made it possible to elucidate the effects of a particular laser system but has also improved our understanding of the optical and thermal characteristics of human skin.

The laser has many inherent properties that contribute to its ability to effect a specific biological outcome. Most important, from a clinical point of view, are the properties of emitted wavelength and pulse duration. Before light can be absorbed, there must be some absorbing molecules in the tissue, generally referred to as chromophores. If the clinical objective is to cause selective destruction of a specific chromophore, the wavelength chosen should match the highest absorption of the targeted chromophore relative to other optically absorbing molecules. Additionally, the laser pulse should be suitably brief so that all light energy is uniformly invested in the target chromophore before much heat is lost to the surrounding tissue by thermal diffusion. In 1983, selective photothermolysis (SP) was introduced as a means of achieving targeted chromophore destruction by careful selection of wavelength and pulse duration.¹ If these properties are optimized, then a maximum transient temperature differential between the target and adjacent structures is achieved with high spatial selectivity.

Although therapeutic outcome in response to laser therapy has significantly improved for many patients, SP is not absolute. Unfortunately, when the absorption spectra of the predominant skin chromophores (hemoglobin, melanin, and water) are compared, there is a very limited range of clinically useful and technically practical wave-

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lengths that provide for the greatest differences between the absorptions by the target chromophore and all other competing chromophores.² Very often, much of the incident light is absorbed by unintended competing chromophores.

Although distributed throughout the epidermis, melanin is particularly concentrated in the 10- μm -thick basal layer which is typically located 50 to 100 μm below the skin surface. Epidermal melanin represents an optical barrier through which the light must pass to reach the underlying targeted chromophore. Except in the treatment of epidermal melanoses, absorption of light by the epidermis is unwanted because it reduces the light dose reaching the target and decreases the amount of heat produced in the target, which leads to suboptimal removal of the lesion.

Most importantly, melanin light absorption causes localized heating of the epidermis, which may, if not controlled, produce acute epidermal disruption or blistering and crusting and may lead to permanent complications such as scarring and dyspigmentation. Unfortunately, for some dermatoses, the threshold incident light dosage for epidermal injury can be very close to the threshold for permanent removal of the target, thus precluding the use of higher light dosages, which would be more effective. For patients with darker skin (types IV through VI), who have a higher concentration of epidermal melanin, it is difficult to treat many lesions amenable to laser therapy using visible or near-infrared wavelengths (below 1,200 nm), because of an increased risk of epidermal damage.

Direct absorption of incident light by epidermal melanin is not the only factor contributing to elevated skin surface temperatures during laser exposure. For example, diffuse backscattered light in combination with Fresnel (total internal) reflection at the skin surface can increase the epidermal fluence several times above the incident light dosage. Such optical effects can lead to increased epidermal melanin absorption and higher skin surface temperatures, contributing to further skin damage. Finally, the heat loss from human skin in contact with air is insignificant, because air is an excellent thermal insulator. Heat initially generated in the irradiated target subsurface chromophores diffuses toward the skin surface, where it is trapped at the air-skin interface. As a consequence, heat builds up near the skin surface and

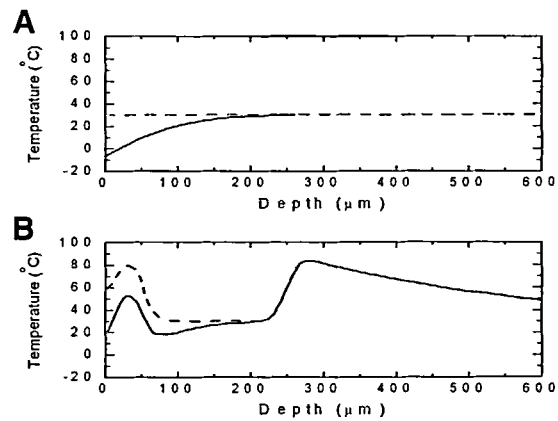


Fig 1. Spatial temperature distribution versus depth in PWS skin in response to (A) a 40-ms cryogen spurt before the laser pulse; and (B) immediately after pulsed laser exposure with (—) and without (---) precooling. Note spatial selectivity of the epidermal temperature reduction in response to CSC in (A). Although melanin absorption results in heat production in (B), if the skin is precooled before laser exposure by CSC, the laser-induced temperature elevation will not exceed the threshold for epidermal damage (60° to 65°C). Second temperature peak in (B) at 250 μm is attributable to light absorption by PWS blood vessels and not affected by epidermal precooling.

results in an elevated surface temperature that persists for a long time after laser exposure. Eventually, slow heat loss at the skin surface (due to natural convection, radiation, and evaporation) and thermal diffusion into the dermis with subsequent cooling by blood perfusion, eliminate the heat buildup near the surface, but this may take several seconds.

An important method of overcoming the aforementioned problem is to selectively cool the most superficial layers of the skin. In general, all cooling methods require bringing a cold medium (gas, liquid, or low-temperature solid) in contact with the skin surface. The epidermis is protected as long as it is prevented from sustaining an elevation of temperature that is above its threshold for denaturation (60° to 65°C) for a prolonged period of time in response to laser exposure. Although melanin absorption will result in heat production, if the skin is precooled, the temperature elevation will not exceed the threshold for epidermal damage (Fig 1).

The concept of cooling the skin to protect the epidermis during laser treatment was first sug-

gested almost 20 years ago. Since that time, researchers have used various cooling strategies for epidermal protection. Gilchrest et al³ evaluated the application of ice before argon laser treatment of port-wine stain (PWS) birthmarks. Welch et al⁴ investigated the use of a freon spray to reduce thermal damage in porcine skin during continuous argon and neodymium:yttrium aluminum garnet (Nd:YAG) laser irradiations. Although these first attempts at cooling the skin during laser treatment indicated that a reduction in epidermal injury could be achieved, neither proved entirely satisfactory or, most importantly, led to an improved therapeutic response.

Both approaches failed because the cooling medium was applied to the surface for a prolonged period of time, resulting in a near-steady-state temperature distribution within the skin. Therefore, in addition to cooling the epidermis, prolonged cooling also reduces the core temperature of the targeted chromophores and leads to suboptimal removal of the lesion. Any increase in the threshold fluence for epidermal damage achieved by cooling is largely offset by the increase in the incident light dose required to heat the targeted chromophores to a temperature sufficient for permanent photocoagulation. Spatially selective (and much more effective) cooling can be achieved by dynamic cooling with a cryogen spray^{5,6} or by using cold sapphire contact handpieces.⁷ These devices promote rapid and spatially selective epidermal cooling to low temperatures without affecting the target chromophore temperature before the laser pulse is delivered.

The anatomic depth of the cooling depends primarily on the cooling time—the duration of contact between the cold medium and the skin surface. For example, the epidermis is cooled in tens of milliseconds while deeper bulk skin cooling is achieved after several seconds of cooling. Ideally, from a clinical point of view, the optimal parameters for skin cooling should be selected on an individual patient basis and depending on the epidermal thickness and depth of the target chromophores. Several studies to determine the depth of target chromophores in human skin using fast infrared detectors to measure the temporal behavior of the infrared radiant emission following laser exposure have been described.⁸⁻¹⁴

The rate of heat removal depends on the thermal properties of the cold medium, skin, temper-

ature of the cooling medium, and the interface at the medium/skin surface. To achieve optimal heat transfer from the skin to the cold medium, the thermal contact between the two should be perfect. The ultimate extent of cooling depends primarily upon the temperature of the cooling medium.

For practical implementation of cooling in the clinical management of patients receiving laser therapy, the following general guidelines can be drawn: (1) for superficial target chromophores (eg, PWS blood vessels or collagen during nonablative laser skin resurfacing), a large temperature gradient at the skin surface is required, which can be achieved by good thermal contact with a very cold cooling medium for short cooling times; (2) for deeper target chromophores (eg, hair follicles), thermal contact is not critical, prolonged cooling times are permissible, and higher temperatures in the cooling medium might be advantageous to prevent cryoinjury.

The first and intuitively simple objective of skin cooling is to increase the threshold for epidermal damage. So long as the epidermis is prevented from reaching a temperature that is above its threshold for denaturation (60° to 65°C) in response to laser exposure, the epidermis and upper dermis can be preserved. The second objective of cooling is to permit the use of higher-incident light dosages for the treatment of resistant lesions. Multiple treatments at low light doses will not achieve and sustain the critical temperatures necessary to destroy irreversibly some targets, regardless of the number of treatments performed. The third objective is the treatment of patients with all skin types. For patients with darker skin (types IV through VI), it is not possible to treat lesions without cooling at a sufficiently high therapeutic light dosage without cooling attributable to epidermal damage. The fourth objective is reduction of pain and post-treatment swelling or edema.^{5,15} Pain reported by patients receiving laser therapy has been described as a “hot pinprick” or “elastic band snapping against the skin.” The discomfort level is energy-dependent, increasing with higher light doses, and varies with the sensitivity of the treated anatomic site. Tolerance decreases with decreasing patient age. For all patients, particularly children, the pain and distress associated with laser therapy are significantly reduced by skin cooling. Pain reduction following laser exposure by pa-

tients when using skin cooling can be explained by 2 intuitive hypotheses: (1) the maximum skin surface temperature achieved is lower on cooled sites than on noncooled sites; and (2) the heat sink created below the skin surface continues to remove trapped heat at the air-skin interface. Therefore, the temperature of the postirradiated epidermis decreases more rapidly with skin cooling.

METHODS AND MECHANISMS OF ACTIVE COOLING

Several different methods have been developed for cooling human skin in conjunction with laser therapy. All approaches use a precooled medium, which can be either solid, liquid, or gas, brought into contact with the skin surface. Deeper skin layers are cooled by heat diffusion toward the cooled surface, with subsequent transfer to the cooling medium.

The rate of heat transfer across the interface between the skin and cooling medium depends primarily on the temperature difference between the 2 adjacent materials, as well as on other parameters, specific to each cooling method. Under most conditions, the heat transfer rate (ie, heat flux) is roughly proportional to the temperature difference between the 2 materials. Therefore, cooling efficiency using any method can be adequately characterized by the proportionality constant, termed heat transfer coefficient, regardless of the physical mechanisms involved (conductive, convective, or radiative heat transfer).

The rate of heat extraction from human skin is limited by the stratum corneum, which has a very low thermal conductivity because of its low hydration level.¹⁶ A very thin (<10 μm) and low viscous topical hydrating gel can increase stratum corneum conductivity and thus enhance "natural" cooling of skin after laser exposure by means of convection, radiation, and evaporation at the surface. The cool gel also extracts heat from the skin through conduction, but the amount of heat removed is limited, as the temperature difference is not maintained by a secondary cooling mechanism. Such "passive" cooling reduces heat buildup near the skin surface after laser exposure, but cannot provide the spatial selectivity required for enhanced epidermal protection during laser exposure. Hydrating gel can be used also in com-

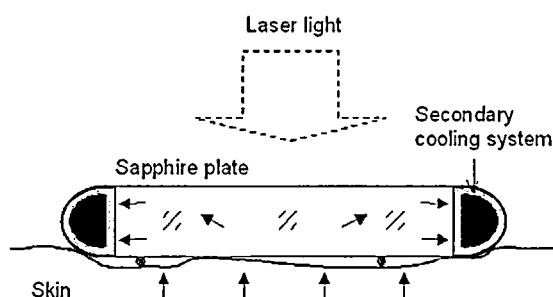


Fig 2. Schematic of CC of human skin. Arrows indicate heat flow from the skin into the sapphire plate.

ination with "active" or "dynamic" cooling methods.

Contact Cooling

Contact cooling (CC) of human skin is achieved by heat conduction into an adjacent precooled solid body, usually in the form of an optically transparent plate, kept at constant temperature by a secondary cooling system (using chilled water, liquid cryogen, or thermoelectric coolers). Therapeutic laser exposure is delivered through the plate, which is pressed against the patient's skin (Fig 2).

Contact cooling can be efficient, especially when a highly conductive material, such as sapphire, is used for the cooling plate. However, an ideal thermal contact between the skin and plate, sometimes assumed in theoretical analyses of CC,¹⁷ only applies to 2 materials in "very intimate contact, such as a soldered joint."¹⁸ In practice, the rate of heat extraction with CC is inevitably impaired by the thermal resistance of the interface or intervening layer between the skin and plate.¹⁹⁻²¹ When CC is used clinically, a layer consisting of air or bubbles, hair, fatty acids, water, thick (>20 μm) hydrating gel, anesthetic cream, or other substances may impede the direct contact between the skin surface and cooling plate.

Recent experimental data (Fig 3) indicate that the cooling rate, as measured at the basal layer of in vivo human skin using a sapphire plate cooled to -4°C , is significantly slower compared to that of the commercial cryogen spray cooling (CSC) device (DCD; Candela, Wayland, MA).²² When the plate was cooled to a much lower temperature (-27°C), the cooling rate was comparable to that of the CSC device.¹⁷ Therefore, cooling plate tem-

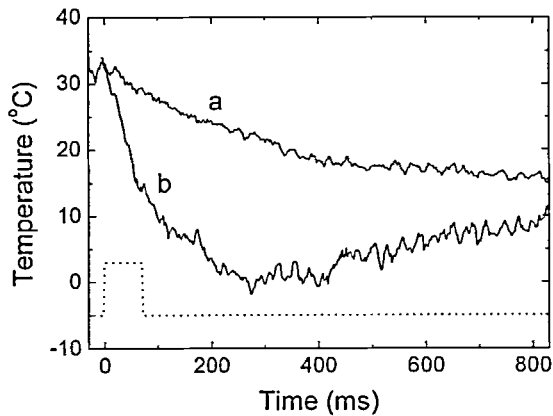


Fig 3. Epidermal basal layer temperature versus time in response to (a) CC with a -4°C sapphire plate incorporated into the Coherent Light-Shear laser; and (b) CSC with an 80-ms cryogen spurt from the Dynamic Cooling Device incorporated into the Candela GentleLASE laser. Note slower cooling rate with (a) CC compared with (b) CSC. (Data courtesy of Karl Pope, PhD, Candela Laser Corporation, Wayland, MA.)

peratures below the freezing point of skin (-5° to 0°C) are necessary to achieve effective heat extraction and high spatial selectivity. Such plate temperatures pose a considerable risk of irreversible skin injury (frostbite) because of lack of automated control over the cooling time. Consequently, the steep temperature gradients, required for optimal spatial selectivity in laser therapy of resistant PWS, may be very difficult to achieve in a safe manner with CC.

In the laboratory, the heat transfer coefficient between a sapphire plate (at 6° to 12°C) and an epoxy phantom was found to vary between 2,000 and $10,000\text{ W/m}^2\text{K}$.¹⁹ When CC is used clinically, the quality of thermal contact can vary with factors as diverse as force/pressure applied by the operator,²⁰ elasticity of treated skin and underlying tissue, density and thickness of hair, and, especially, on the type and amount of substances present on the skin surface (sweat, hydrating/lubricating gel, anesthetic cream). Therefore, to significantly increase the light dosage without risk of epidermal thermal damage or frostbite, it is critically important to have control of the induced epidermal cooling.²⁰

Further, water condensate from the environment freezes on the sapphire plate at temperatures below 0°C and builds up a layer of frost. Uncon-

trolled scattering of the incident laser light can affect the dose delivered for therapy and presents a potential risk to the operator, paramedical personnel, or patient. Similar concerns may be raised also with respect to transient freezing of the superficial epidermal layers using such an aggressive cooling regime.

CSC

The main cooling mechanism of CSC is rapid evaporation of cryogen, which extracts latent heat from the surrounding environment (Fig 4). The only cryogenic compound currently approved by the Food and Drug Administration for use in dermatology is tetrafluoroethane (TFE; $\text{C}_2\text{H}_2\text{F}_4$, also known as R134a). TFE has a boiling point at -26°C , which results in a much higher evaporation rate and, consequently, faster heat extraction when compared to chilled water sprays.²³ On release from a pressurized container, liquid cryogen is atomized into a fine spray and directed toward the skin surface a few centimeters away. During flight, spray droplets cool rapidly because of cryogen evaporation. Therefore, the droplet temperature when impinging on the skin surface is typically between -40° and -60°C , depending primarily on the distance to the skin surface²⁴⁻²⁶ and atomizer nozzle design.^{26,27} As a result, CSC provides a rapid, large, and spatially selective epidermal temperature reduction. Reported values of the effective heat transfer coefficient during the CSC spurt have varied (for different atomizers, spraying distances, and atmospheric conditions): 2,400,^{28,29} 1,600 to 3,100,³⁰ 10,000,³¹ and $40,000\text{ W/m}^2\text{K}$.^{19,32}

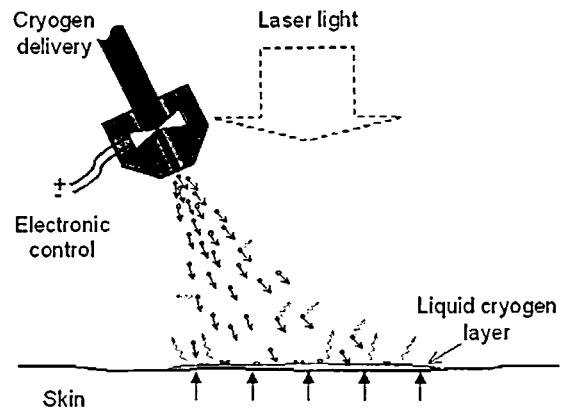


Fig 4. Schematic of CSC of human skin.

Theoretical considerations predict that the most efficient cooling occurs when the mass flux of sprayed cryogen matches the evaporation rate at the skin surface. Heat conducted from deeper skin layers is converted directly into latent heat of evaporating cryogen droplets. When the spray flux exceeds the evaporation rate at the surface, a layer of liquid cryogen builds up on the skin surface.³² Under such conditions, heat must be transported from the skin to the site of evaporation through the cryogen layer, via conduction and forced convection. The additional thermal barrier imposed by this liquid layer reduces the cooling rate.³³

Our studies have shown the ability of larger and faster droplets, produced by less atomizing spray nozzles, to minimize or prevent formation of the liquid cryogen layer, leading to increased cooling rates especially for spurts longer than 40 to 50 ms.^{28,31} These results have recently been confirmed through measurements of the heat transfer coefficient under steady-state conditions.²⁷ However, because the more forceful impact of such sprays induced some patient discomfort, as well as inferior localization of the cooled area,³¹ other approaches need to be explored to enhance the heat extraction rate with CSC.

The cryogen spurt duration and the delay between spurt termination and the laser pulse can be controlled electronically, which results in predictable cooling with reproducible spatial selectivity. This approach provides an unparalleled safety margin with respect to the prevention of undesirable thermal injury by the laser pulse or frostbite attributable to cooling. Consequently, significantly higher light dosages can be used with CSC, leading to expedited lesion clearing without adverse effects.

A layer of liquid cryogen can remain on the skin surface long after spurt termination,^{28,29} as is the case also with the commercially available CSC device.^{17,31} Consequently, cooling continues for a much longer period of time than the actual user-specified spurt duration. The temperature of this layer approaches the boiling temperature of TFE (-26°C).^{28,29} After laser exposure, this layer rapidly evaporates, and thus removes part of the heat generated in the irradiated chromophores.

A layer of frost has been observed to form on the skin surface during and after the cryogen spurt (Fig 5). Experiments studying CSC in a controlled atmosphere have proven conclusively that this

frost forms primarily by condensation of atmospheric vapor on the cooled surface. The potential implications of such frost are similar to those discussed above with regard to CC. It has been our experience that observable frost forms on human skin only after the liquid cryogen layer has retracted. This occurs approximately 100 ms after the end of a 40-ms cryogen spurt from the commercial CSC device, long after the therapeutic laser pulse is completed. However, the latent heat released in condensation of water vapor on the cooled surface significantly reduces the cooling rate (unpublished data). If required, frost formation could be minimized by flushing the treated area with a dry gas, such as nitrogen.

It has often been speculated that, under certain conditions, a thin layer of cryogen vapor might form between the skin surface and liquid cryogen, owing to vigorous cryogen evaporation at the immediate skin surface (Leidenfrost effect). To our knowledge, there is no evidence that documents this effect with commercial or experimental CSC devices.

Air Cooling

Human skin can also be cooled by air precooled to temperatures as low as -30°C and blown onto or across the surface (Fig 6). Despite the low air temperature used, this cooling method is characterized by the lowest cooling rate, since the heat transfer coefficient for forced convection in gas typically ranges between 25 and $250\text{ W/m}^2\text{K}$.³⁴ As a result, long cooling times (on the order of several seconds) are necessary to induce significant temperature reductions in the basal layer. Because of the deep penetration of heat diffusion resulting from such long cooling times, the final outcome is inevitably general ("bulk") cooling of the entire skin, with minimal spatial selectivity. Obviously, this technique offers only minimal protection against laser-induced epidermal damage.

One clinical benefit of air cooling might be pain reduction, as the heat dissipated from the chromophores during laser exposure should be removed from the skin surface considerably faster than by natural convection at the skin surface, heat diffusion deeper into the skin, and by blood perfusion. Further, the thermal gradient maintained by air cooling would cause a larger fraction of dissipated heat to diffuse toward the skin surface, away from the deeper heat sensors.

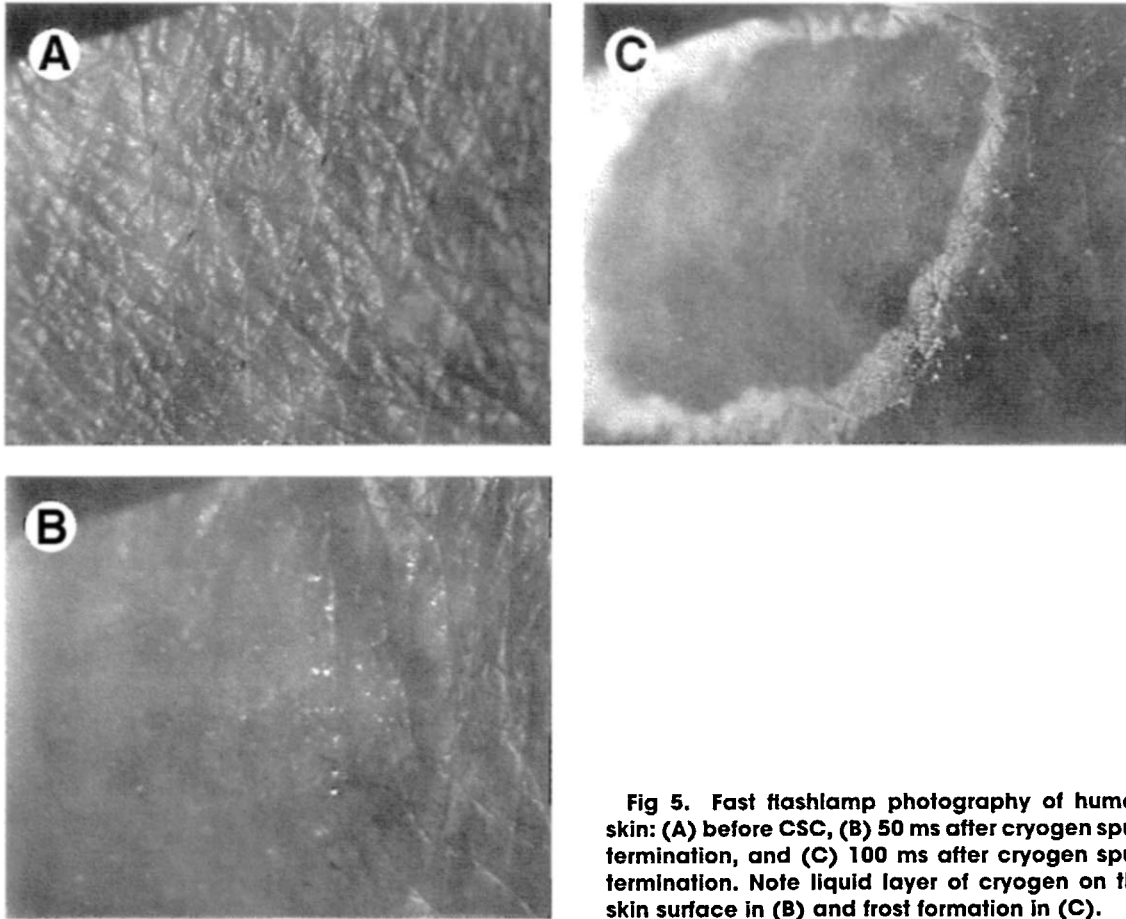


Fig 5. Fast flashlamp photography of human skin: (A) before CSC, (B) 50 ms after cryogen spurt termination, and (C) 100 ms after cryogen spurt termination. Note liquid layer of cryogen on the skin surface in (B) and frost formation in (C).

TIMING CONSIDERATIONS FOR ACTIVE SKIN COOLING

Because all methods affect only the skin surface, cooling of deeper skin layers relies on the process of heat diffusion. The depth of skin influenced by

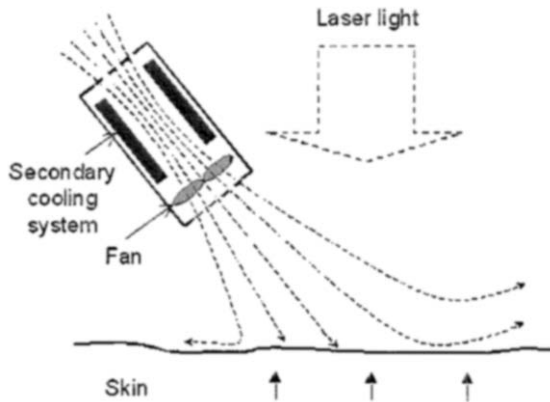


Fig 6. Schematic of AC of human skin.

cooling depends on the cooling time and the quality of thermal contact (represented by the heat-transfer coefficient). The latter can be assumed constant for a particular cooling device, and to be on the same order of magnitude for both CSC and CC under optimal conditions. Therefore, the strategies of optimal timing during cooling-assisted laser therapy depend primarily on the target chromophores' depth. The commercial CSC device, DCD by Candela, offers a wide range of spurt durations (20 to 100 ms) and delays (10 to 500 ms) before the laser pulse is delivered. Here, we discuss in more detail 2 clinical procedures in which cooling in conjunction with laser therapy is the clinical standard: PWS therapy and laser hair removal (LHR). Most arguments presented for PWS apply also to nonablative laser skin resurfacing, which aims at coagulating dermal collagen 100 to 200 μm below the epidermal-dermal junction while minimizing thermal injury to the epidermis.

PWS LASER THERAPY

Port-wine stain is a clinical entity with a superficial target chromophore. In most cases, the highest temperatures in laser irradiated PWS occur 200 to 400 μm below the skin surface.^{8,14,28,29,35-37} Therefore, very short (tens of milliseconds) precooling times are used to avoid unwanted cooling of the target PWS blood vessels. The need for very high spatial selectivity favors using CSC, which offers very precise control of the precooling time and higher heat transfer rates as compared to CC or air cooling.

As described above, a layer of liquid cryogen remains on the skin surface long after spurt termination from the commercial CSC device. Therefore, cooling persists long after the user-specified spurt duration. This is the rationale for inserting a delay between cryogen spurt termination and the laser pulse. If, for example, it takes approximately 60 ms to cool the basal layer (to a depth of 100 μm with a negligible temperature decrease at the target chromophore depth of 300 μm), a 30-ms spurt can be used in combination with a 30-ms delay before laser exposure. Such a cooling regime offers significant epidermal protection and permits safe use of higher light dosages, leading to improved PWS blanching.³⁸

However, because cooling attributable to the evaporating liquid layer on the skin surface is less efficient than during the spurt (unpublished data), higher spatial selectivity can be achieved by cryogen spurt durations of 50 to 60 ms combined with minimizing the delay before the laser pulse is delivered.^{39,40} This is a much better approach to treatment of resistant PWS, which require higher light dosages. Moreover, the optimal duration of such a prolonged spurt has been found less sensitive to epidermal thickness and target depth, compared with the optimal laser pulse delay after a shorter spurt.⁴¹ This is an important clinical advantage, as PWS geometry varies on an individual patient basis.⁴²

Spatial selectivity of cooling may be further increased by using even longer spurt durations (above 100 ms).⁴¹ While the temperature of the target chromophores may be affected by such prolonged cooling times—somewhat contrary to the original concept of dynamic cooling—the temperature reduction achieved in the basal layer is predicted to be significantly greater. This offers more

epidermal protection against thermal damage, even when the light dose is increased to compensate for minor precooling of the targets. However, because the epidermis is cooled more aggressively in this regime, the risk of frostbite must be carefully evaluated before spurts longer than 100 ms are used clinically. Spurt durations of up to 100 ms have often been used in our clinic, with no evidence of frostbite.

The presence of a liquid cryogen layer on the skin surface after spurt termination constitutes de facto cooling during and after the laser exposure. The potential benefits of such “parallel” and postcooling in combination with PWS therapy have not been investigated systematically apart from an isolated report.³⁶ On one hand, it seems plausible that, owing to the strong nonlinear temperature dependence of tissue denaturation rate,⁴³ most thermal damage to the epidermis and, especially the basal layer, occurs during the transient temperature rise immediately following laser irradiation. On the other hand, application of postcooling might be useful in reducing the pain associated with PWS therapy.

In the future, optimization of CSC treatment parameters on an individual patient basis may be possible. Noninvasive imaging modalities, such as optical coherence tomography (OCT), optical Doppler tomography (ODT),^{44,45} pulsed photothermal radiometry (PPTR),^{8,10,14,35,37} or ultrasound, would have to provide fast and accurate determinations of epidermal thickness and target depth for practical clinical use.

LASER HAIR REMOVAL

Laser hair removal (LHR) differs from PWS therapy in several important aspects.²¹ First, the target chromophores (primarily melanin-rich hair shafts) are located much deeper in human skin (bulb at 2 to 7 mm and bulge at approximately 1.5 mm). Because of the limited optical penetration depth even at the long wavelengths (7,690 nm) typically used, significantly higher light doses must be applied to deposit sufficient energy at greater depths. Second, longer laser pulses (up to 100 ms) can be used to allow for heat diffusion from the absorbing shaft into the surrounding follicular epithelium. At such long pulse durations, the temperature peak in the basal layer and near the skin surface is reduced, which helps protect the epidermis from nonselective thermal injury.

A direct consequence of the deeper target chromophore location is that prolonged cooling times can be used without compromising spatial selectivity. For example, the skin temperature at the bulge (depth of 1.5 mm) is not affected after 1 second of CC using a sapphire plate.¹⁷ The requisite cooling times can therefore be prolonged and do not need to be controlled as precisely as in PWS therapy, which makes CC an attractive alternative to CSC for use in conjunction with LHR. With most commercial CC devices, the operator must decide on and manually apply an appropriate delay between the start of cooling and laser pulse delivery.

Higher light dosages, as compared with PWS therapy, are required for successful LHR. Therefore, for adequate epidermal protection, low cooling temperature and good thermal contact with skin are still required. Because the quality of thermal contact between the CC plate and skin varies widely in clinical use, automated adjustment of the laser pulse delay on a site-to-site basis using on-line control of epidermal cooling is very important—not to ensure sufficient spatial selectivity of cooling, but to prevent epidermal injury due to freezing.²⁰ Such an automated timing device is now available from Palomar Inc (Burlington, MA).

One advantage of using CC in conjunction with LHR is that it allows for active cooling during exposure. Significant benefit from such “parallel” cooling is achieved primarily with laser pulse durations of 100 ms and longer, the clinical benefit of which is still controversial. It is likely that similar “parallel” cooling could be obtained with CSC using more aggressive precooling and/or postcooling. Although some concerns have been raised about the possible effect of a liquid cryogen layer on the incident laser light dosage, it has been determined that less than 3% of the pulse energy (alexandrite laser, 755 nm) is lost on passage through this layer using the commercial CSC device.⁴⁶

Although the superior cooling efficiency and precise control of timing featured by CSC are not imperative for LHR, it is certainly an equally effective technology. Therefore, the choice of cooling method for LHR is influenced by factors such as safety, ease of use (ergonomics), and cost.

CLINICAL STUDIES

To date, the benefits of skin cooling in conjunction with laser therapy have been demonstrated

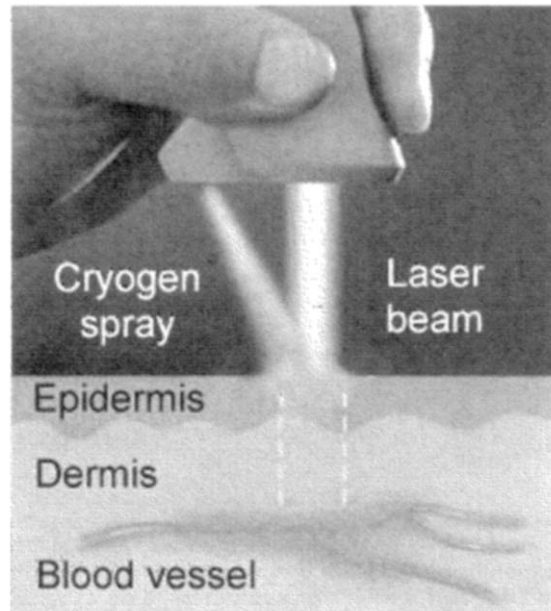


Fig 7. When a cryogen spurt is applied to the skin surface for an appropriately short period of time (tens of milliseconds), cooling remains localized to the epidermis while leaving the temperature of the deeper targeted blood vessels unchanged. (Courtesy of Candela Laser Corp, Wayland, MA.)

for the following clinical indications: PWS, facial telangiectasias, hemangiomas, LHR, and nonablative laser skin resurfacing.

CSC has been incorporated into Candela's (Wayland, MA) SPTL1b, ScleroPLUS and, more recently, V-Beam pulsed-dye lasers for treatment of hypervascular skin lesions (Fig 7). The largest study to date³⁹ on the benefits of CSC in conjunction with laser exposure was a retrospective review of 196 patients with head or neck PWS birthmarks treated with the SPTL1b pulsed dye laser. The objective of this study was to compare the efficacy and safety of noncooled and laser-treated (NC-LT) versus cryogen-spray-cooled and laser-treated (CSC-LT) patients with PWS birthmarks. Ninety-eight patients received NC-LT at light dosages of 5 to 7 J/cm². Subsequently, 98 patients received CSC-LT at light dosages of 8 to 10 J/cm². Cryogen parameters were a spurt duration of 50 ms and a delay time of 10 ms between cryogen delivery and laser irradiation. The primary efficacy measure was the quantitative assessment of the blanching response scores of the 2 treatment groups, on a blinded basis. Based on chi-square

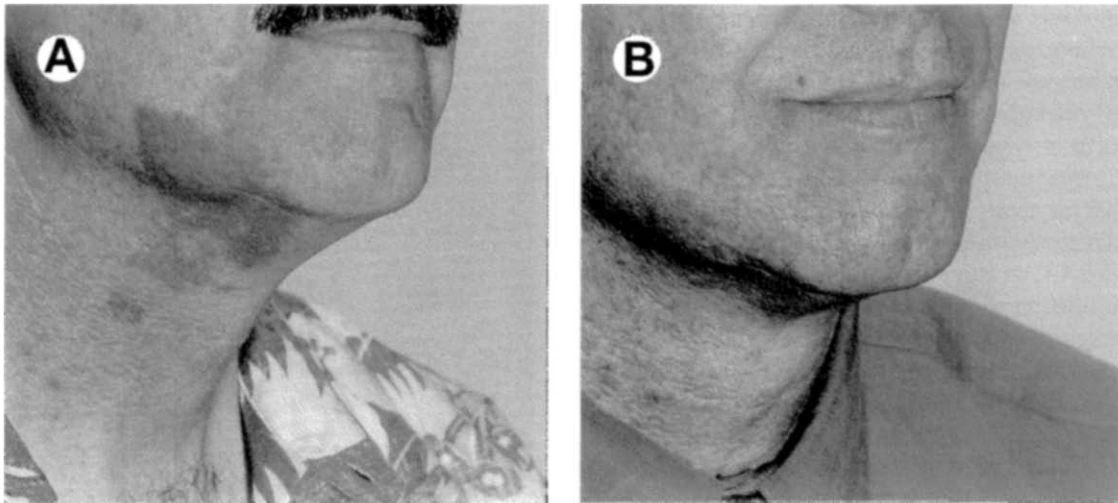


Fig 8. A 48-year-old white man with PWS of the right cheek and neck (A) before laser therapy and (B) 6 months after 3 laser treatments with CSC and the Candela ScleroPlus laser using energy densities of 11 to 14 J/cm². Result was evaluated as an excellent blanching response.

analysis, there were clinical, and statistically significant, differences in the blanching response scores favoring PWS receiving CSC-LT compared with the NC-LT group ($P < .001$). Permanent scarring was noted in 3.1% ($n = 3$) of patients in the NC-LT group. Permanent scarring was not observed in the CSC-LT treatment group. Transient hyperpigmentation was noted in 57% ($n = 56$) and 48% ($n = 47$) of patients in the NC-LT and CSC-LT groups, respectively. For both groups, transient hyperpigmentation resolved in all patients within 1 year. Two patients in the NC-LT group developed delayed permanent hypopigmentation. Permanent hypopigmentation was not observed in the CSC-LT group. In conclusion, CSC permitted the use of higher incident light dosages, leading to improved PWS clearance without producing complications such as permanent scarring or dyspigmentation (Fig 8).

CSC during PWS treatment has been shown to decrease the pain associated with laser therapy especially in patients with darker skin types.^{5,15,39} Excellent clearance without adverse effects has also been reported with the use of CSC for the treatment of hemangiomas, telangiectasia, and other vascular lesions.

Both CSC and CC devices have been incorporated into laser systems used for treating leg telangiectasia. Because of the increased hydrostatic pressure in these vessels, higher light dosages are required to achieve permanent photocoagulation,

making active cooling an essential component of patient treatment using lasers. While studies have demonstrated improvement in leg telangiectasia after laser therapy,⁴⁷⁻⁴⁹ patient results are highly variable, and a clinically significant incidence of hyper- and hypopigmentation has been reported.

CC has been incorporated into Coherent's VersaPulse (Santa Clara, CA) (VPW) laser for treatment of hypervascular skin lesions (Fig 9). The 532-nm VPW laser contains a hand-piece with an attachable chilled sapphire plate cooled by recirculating water. The VPW laser has been used for treatment of facial telangiectasias with good results and minimal side effects. Adrian and Tanghetti⁵⁰ treated 40 patients with facial telangiectasias and achieved greater than 75% clearance of 1.5-mm diameter or smaller vessels in all patients after 1 treatment. Most patients who underwent a second treatment achieved 90% to 100% clearance. Dummer et al⁵¹ reported 50% or greater blanching in 75% of PWS patients after 1 to 3 treatments with the VPW laser. No scarring or dyspigmentation occurred.

Cooling has also been incorporated into systems designed for LHR, which target melanin in the entire follicle. Such targeting requires the use of high fluences capable of heating a large volume of tissue and long pulse widths, on the order of milliseconds. The addition of cooling during LHR allows the safe use of the required higher fluences.²¹ The use of longer wavelengths and pulse

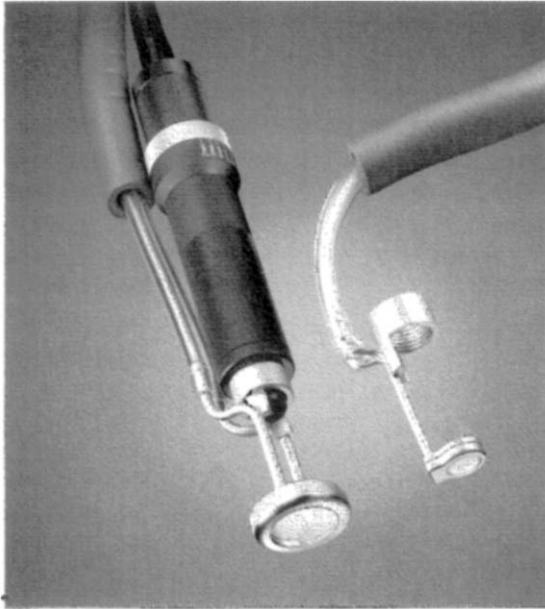


Fig 9. CC has been incorporated into the Coherent VersaPulse laser for the treatment of hypervascular skin lesions. (Courtesy of Coherent, Santa Clara, CA.)

widths helps to diminish epidermal melanin damage. However, epidermal cooling maximizes protection. Skin dyspigmentation as a result of epidermal melanin absorption is the most common adverse effect. Patients with darker skin types are at greatest risk for dyspigmentation.

In one study⁵² 85 patients were treated with a 3-ms alexandrite laser in combination with CSC. The mean fluence was 40.7 J/cm². Patients received 1 to 3 treatments to a test site that was compared with an untreated control site. Twelve months after the final laser treatment, sites that received a single treatment showed a mean hair count reduction of 41% and sites treated 3 times showed a corresponding reduction of 74%. Ten patients (12.3%) developed transient hyperpigmentation and 3 patients developed transient hypopigmentation. There were no cases of scarring or permanent skin dyspigmentation. Moreover, patients with darker skin types (III and IV) experienced no increase in pain during the procedure or subsequent complications.

CC has also been used successfully for LHR. Campos et al⁵³ studied a 3-ms ruby laser exposure in combination with a sapphire lens CC device for hair removal in 51 adults with Fitzpatrick skin

types I to IV. After a median follow-up of 8 months, 63% of patients had less than 25% hair regrowth. The best results were achieved with the use of higher fluences. Transient pigmentary change was noted in 29% of patients. No patients had scarring or permanent dyspigmentation.

Laser skin resurfacing for the treatment of rhytides, photo-damaged skin, and acne scars has received much attention from the media, patients, and physicians alike. However, both carbon dioxide and erbium:YAG laser skin resurfacing completely disrupt or remove the epidermis. The resulting open wounds contribute to significant patient cosmetic morbidity and require daily care to optimize healing. The concept of cooling in conjunction with nonablative laser skin resurfacing of rhytides by stimulating dermal collagen formation without epidermal injury was first described in 1997.⁵⁴

Laser Aesthetics (Auburn, CA) developed a 1,320-nm Nd:YAG laser that, in combination with CSC, is capable of stimulating tissue fibroblasts without epidermal injury. A multicenter study evaluated periorbital rhytid improvement in 35 adults after 3 nonablative laser treatments performed sequentially at intervals of 2 weeks.⁵⁵ Treatment fluences of 28 to 36 J/cm² were used with a 20 to 40 ms cryogen spray duration and a delay time of 10 ms between cryogen spray and laser irradiation. Small but statistically significant 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 improvement only in the severe rhytid group. The procedure was found to be relatively safe, with 4 sites (5.6%) developing transient hyperpigmentation and 2 sites (2.8%) developing barely perceptible pinpoint pitted scars. In conclusion, this study found that CSC is a safe and effective method of protecting the epidermis during nonablative laser treatment of facial rhytides, avoiding much of the morbidity associated with other resurfacing procedures. Another recently added device feature may help to improve treatment results. During the study, it was determined that blistering was more likely to occur when the skin surface temperature exceeded 50°C immediately after laser exposure. Skin temperature measurements during laser exposure documented substantial interpatient and even site-to-site inpatient variability. The optimal skin surface temperature immediately after pulsed laser exposure appears to range between

42° and 47°C. A thermal sensor has been built into the hand-piece to measure the skin surface temperature before treatment and then immediately after pulsed laser exposure. By measuring the temperature increase in response to the first few laser pulses, the clinician will be better able to choose the optimum light dosage: one that will sufficiently increase the skin temperature to achieve therapeutic results, but not exceed the epidermal threshold for blistering of 50°C.

Cynosure (Chelmsford, MA) has developed a steady-state cooling device termed SmartCool, which uses convective rather than contact or evaporative cooling. A continuous flow of air, chilled to at least -4°C, is delivered to the treatment area before, during, and after laser exposure. An advantage of cold air-cooling is the low operating cost. In addition, no substrate is applied to the skin, and thus, optical scattering of the incident laser light is not an issue. However, it is unlikely that this method is as efficacious as CSC or CC. Hammes et al⁵⁶ treated 166 patients with vascular lesions, tattoos, or hypertrichosis using lasers plus the SmartCool device and reported decreased treatment pain. Three percent of patients disliked the cold air device because of respiratory or ocular problems during facial treatment, pain from the cold air current, or noise. Further studies will be required to explore the potential of this relatively new cooling method to assess its clinical utility.

CONCLUSIONS

The development of skin cooling methodology has definite implications for patients receiving laser therapy as follows:

1. Cooling permits safe and effective laser treatment by increasing the threshold for epidermal damage. The epidermis is protected as long as it is prevented from sustaining an elevation of temperature that is above its threshold for denaturation (60° to 65°C)

for a sustained period of time, in response to laser exposure.

2. Cooling permits the use of higher-incident light doses for the treatment of resistant lesions.
3. Cooling permits the treatment of patients with all skin types.
4. For all patients, particularly children, pain and distress associated with laser therapy are significantly reduced by cooling.

For practical implementation of cooling in the clinical management of patients receiving laser therapy, the following general conclusions can be drawn (1) for superficial target chromophores (eg, PWS blood vessels or collagen during nonablative laser skin resurfacing), a large temperature gradient at the skin surface is required, which can be achieved by good thermal contact with a very cold cooling medium for short cooling times; (2) for deeper target chromophores (eg, hair follicles), thermal contact is not critical, prolonged cooling times are permissible, and higher temperatures in the cooling medium might be advantageous to prevent cryoinjury.

Presently, all patients receiving laser therapy are treated according to the clinical judgment of their physicians without consideration given to individual variations in the biophysical, structural, optical, and thermal properties of human skin and the target chromophores. Epidermal melanin concentration and target chromophore depth vary on an individual patient basis and even from site to site on the same patient. Ideally, cooling parameters should be selected from knowledge of the temperature increase in epidermal melanin immediately after laser exposure and the target chromophore's depth. In the future, the development of remote optical, thermal, and acoustic sensing techniques should permit selection of the optimal cooling parameters on an individual patient basis, throughout an extended treatment protocol.

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