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Epidermal cooling during pulsed laser treatment of selected dermatoses

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ABSTRACT

The clinical objective in laser treatment of selected dermatoses such as port wine stain (PWS), hemangioma and telangiectasia is to maximize thermal damage to the blood vessels, while at the same time minimizing nonspecific injury to the normal overlying epidermis. "Dynamic" cooling of skin, whereby a cryogen is sprayed onto the surface for an appropriately short period of time (on the order of tens of milliseconds), may offer an effective method for eliminating epidermal thermal injury during laser treatment. We present theoretical and experimental investigations of the thermal response of skin to dynamic cooling in conjunction with pulsed laser irradiation at 585 nm. Computed temperature distributions indicate that cooling the skin immediately prior to pulsed laser irradiation with a cryogen spurt of tetrafluoroethane is an effective method for eliminating epidermal thermal injury during laser treatment of PWS. Experimental results show rapid reduction of skin surface temperature is obtained when using tetrafluoroethane spurts of 20-100 ms duration. Successful blanching of PWS without thermal injury to the overlying epidermis is accomplished.

Key words: cryogen, hemangioma, photothermolysis, port wine stain, telangiectasia, thermal injury, tetrafluoroethane

2. INTRODUCTION

Lasers have become important therapeutic tools for treatment of selected dermatoses such as port wine stain (PWS), hemangioma, and telangiectasia. The clinical objective in laser treatment of these dermatoses is to maximize thermal damage to the blood vessels, while at the same time minimizing nonspecific injury to the normal overlying epidermis¹⁻⁴. One approach to achieve this objective is to cool selectively the most superficial skin layers.

Cooling of skin using ice or chilled water in conjunction with laser irradiation has been used to prevent epidermal thermal injury⁵⁻⁷. Nevertheless, temperature distributions following sustained cooling (e.g., 15-60 s) by 0 °C ice at the skin surface show that in addition to cooling the epidermis, temperature of blood vessels is also reduced⁸. Thermal energy removed to protect the epidermis from injury will be offset by additional laser energy required to heat the blood vessels to a sufficiently high temperature for destruction.

With "dynamic" cooling, where a cryogen is sprayed on the surface of skin, the epidermis can be cooled selectively⁹⁻¹¹. For an appropriately short cryogen spurt duration (on the order of tens of milliseconds), the spatial distribution of cooling remains localized in the epidermis, while leaving the temperature of deeper vessels unchanged.

We present a theoretical study and experimental measurements of the thermal response of skin resulting from dynamic cooling and pulsed laser irradiation. Clinical implications for treatment of PWS and other dermatoses will be discussed.

3. THEORY

Temperature distributions within skin can be calculated by solving the one-dimensional heat conduction equation,

$$\frac{\partial^2 T}{\partial z^2} = \frac{1}{\alpha} \frac{\partial T}{\partial t} \quad (1)$$

where T (°C) is temperature, z (m) is distance into the skin (with origin at skin surface), t (s) is time, and α is thermal diffusivity ($1.1 \cdot 10^{-7} \text{ m}^2/\text{s}$)¹². The thermal boundary condition at the skin surface during dynamic cooling can be expressed as

$$-k \left. \frac{\partial T(z,t)}{\partial z} \right|_{z=0} = h[T_\infty - T(0,t)] \quad (2)$$

where k is the skin thermal conductivity of skin (0.45 W/mK)¹², h ($\text{W/m}^2\text{K}$) is the heat transfer coefficient, and T_∞ (°C) is temperature of the cryogen and/or cryogen-ice mixture (formed as a result of water condensation). Solution to the heat conduction equation (1) with boundary condition (2) is¹³

$$T_{cooling}(z,t) = (T_\infty - T_i) \{ \text{erfc}(\tilde{z}) - [e^{-\tilde{z}^2} \text{erfcx}(\tilde{h} + \tilde{z})] \} + T_i \quad (3)$$

Here $\text{erfcx}(x)$ is defined as $e^{x^2} \cdot \text{erfc}(x)$, where $\text{erfc}(x)$ is the complementary error function, $(1 - \text{erf}(x))$, T_i is the initial temperature of skin, $\tilde{z} = z/2\sqrt{\alpha t}$, and $\tilde{h} = (h/k)\sqrt{\alpha t}$.

For a relatively large value of h (e.g., $40 \text{ kW/m}^2\text{K}$), corresponding to a liquid-vapor phase transition⁹, and $T_\infty = -10 \text{ °C}$, calculated values of temperatures within skin show that large temperature reductions ($30\text{-}35 \text{ °C}$) are obtained in a relatively short time ($5\text{-}100 \text{ ms}$) and the cooling remains localized to the epidermis (Fig. 1).

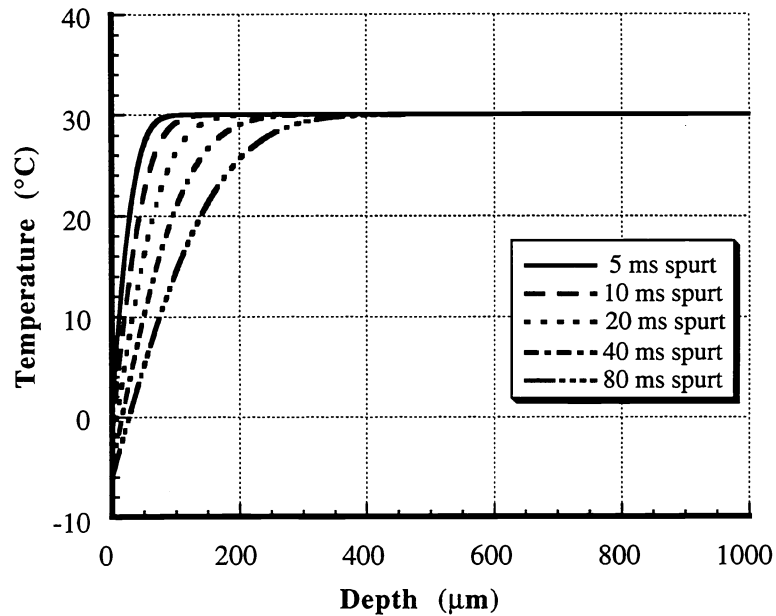


Fig. 1. Computed temperature distributions in response to tetrafluoroethane spurts of various durations.

We model the effect of laser irradiation by assuming an instantaneous deposition of energy that induces temperature increases at skin locations where light is absorbed by a) melanin within epidermis, and b) blood within vessels. This simplified representation of conversion of laser energy into heat generation does not explicitly account for the distribution of laser light within skin¹⁴⁻¹⁶. However, we assume laser induced initial temperature distributions that are consistent with predicted temperature rises based on pulsed photothermal radiometry (PPTR) of PWS lesions¹⁷.

We assume that at $t=t_{laser}$, the time when laser energy is deposited, the instantaneous temperature rise due to light absorption by melanin is constant over the epidermis, and that the temperature distribution within a blood layer decreases exponentially with depth by an effective blood absorption coefficient, μ_a^{blood} (m^{-1}), for a dermis composed of fractional blood volume, f_{vol} . Laser induced temperature rises in one-dimension are given by

$$\Delta T(z, t_{laser}) = \begin{cases} \Delta T_{0,epidermal} & \text{for } z_1 \leq z \leq z_2 \\ \frac{\Delta T_{0,blood}}{f_{area}} e^{-\mu_a^{blood}(z-z_3)} & \text{for } z_3 \leq z \leq z_4 \\ 0 & \text{for all other } z \end{cases} \quad (4)$$

where positions z_1 and z_2 define the interval over which epidermal melanin absorption takes place (e.g., 10 and 50 μm , respectively), z_3 and z_4 define the interval where blood absorption takes place (e.g., 150 μm and 800 μm , respectively), $\Delta T_{0,epidermal}$ ($^{\circ}C$) is the epidermal temperature rise due to melanin absorption, $\Delta T_{0,blood}$ is the average temperature rise at the most superficial dermal-blood interface (z_3), and f_{area} is fractional vascular area in a plane parallel to skin-air interface. f_{area} is related to fractional vascular volume, f_{vol} , as $f_{area} \approx (f_{vol})^{2/3}$ and is assumed to be independent of depth.

Assuming that the laser pulse is sufficiently short (e.g., $\approx 450 \mu s$) so that there is no significant heat diffusion during irradiation, epidermal temperature rise at the end of the laser pulse is computed as¹⁸

$$\Delta T_{0,epidermal} = \frac{E_0 \mu_a^{epidermal}}{\rho c} \left[1 + 2 \frac{1+r_i}{1-r_i} R_d \right] \quad (5)$$

where E_0 (J/m^2) is the incident laser fluence, $\mu_a^{epidermal}$ (m^{-1}) is the epidermal absorption coefficient, ρ is the density (kg/m^3), c is the specific heat ($J/kg \text{ } ^{\circ}C$), r_i is the averaged internal reflectance at the air/tissue interface, and R_d is the diffuse reflectance resulting from light that enters the tissue, is scattered, and subsequently reemerges from the tissue, and can be approximated as¹⁹

$$R_d = e^{-7\delta\mu_a^{epidermal}} \quad (6)$$

From diffusion theory, the optical penetration depth, δ , is calculated as

$$\delta = \frac{1}{\sqrt{3\mu_a[\mu_a + \mu_s(1-g)]}} \quad (7)$$

where μ_s (m^{-1}) is the scattering coefficient, and g is the anisotropy factor.

We calculate $\Delta T_{0,blood}$ in a similar manner as $\Delta T_{0,epidermal}$ except that we assume no diffuse reflectance at dermis-blood interface so that

$$\Delta T_{0,blood} = \frac{E(z=z_3)\mu_a^{blood}}{\rho c}, \quad (8)$$

and estimate $E(z=z_3)$ by assuming that incident fluence, E_0 , attenuates according to δ^{-1} within the epidermis and dermis before reaching the dermis-blood layer.

Solution of equation (1) with the boundary condition (2), and initial temperature distribution (4) is obtained by superposition of the thermal response due to cooling, and laser-induced epidermal and blood temperature changes:

$$\begin{aligned} \Delta T(z, t > t_{laser}) &= \Delta T_{cooling}(z, t > t_{laser}) \\ &+ \Delta T_{epidermal}(z, t > t_{laser}) + \Delta T_{blood}(z, t > t_{laser}) \end{aligned} \quad (9)$$

where $\Delta T_{cooling}$ is obtained by subtracting T_i from the expression given for $T_{cooling}$ in equation (3), and²⁰

$$\begin{aligned} \Delta T_{epidermal}(z, t > t_{laser}) &= \Delta T_{0,epidermal} \left\{ \frac{1}{2} [\operatorname{erf}(\tilde{Z}_i - \tilde{Z}) - \operatorname{erf}(\tilde{Z}_i + \tilde{Z})] \right. \\ &\left. - e^{-(\tilde{z}+\tilde{z}_i)^2} \operatorname{erfcx}(\tilde{H} + \tilde{Z} + \tilde{Z}_i) \right\}_{\substack{\tilde{z}_i=\tilde{z}_2 \\ \tilde{z}_i=\tilde{z}_1}}, \end{aligned} \quad (10)$$

$$\begin{aligned} \Delta T_{blood}(z, t > t_{laser}) &= \frac{\Delta T_{0,blood}}{f_{area}} e^{2\tilde{M}\tilde{Z}_3} \left\{ \frac{e^{\tilde{M}^2}}{2} [e^{-2\tilde{M}\tilde{Z}} \operatorname{erf}(\tilde{Z}_i - \tilde{Z} + \tilde{M}) \right. \\ &+ \frac{\tilde{M} + \tilde{H}}{\tilde{M} - \tilde{H}} e^{2\tilde{M}\tilde{Z}} \operatorname{erf}(\tilde{Z}_i + \tilde{Z} + \tilde{M})] \\ &\left. + \frac{\tilde{H}}{\tilde{M} - \tilde{H}} e^{-(\tilde{z}_i+\tilde{z})^2-2\tilde{M}\tilde{z}_i} \operatorname{erfcx}(\tilde{Z}_i + \tilde{Z} + \tilde{H}) \right\}_{\substack{\tilde{z}_i=\tilde{z}_4 \\ \tilde{z}_i=\tilde{z}_3}} \end{aligned} \quad (11)$$

where

$$\tilde{Z} = \frac{z}{2\sqrt{\alpha(t-t_{laser})}}, \quad \tilde{M} = \mu_a^{blood} \sqrt{\alpha(t-t_{laser})}, \quad \text{and} \quad \tilde{H} = \frac{h}{k} \sqrt{\alpha(t-t_{laser})}. \quad (12)$$

Without tissue cooling, we assume an insulated boundary condition (i.e., $h = 0$ in equation (2)). The thermal response will then be given by superposition of laser-induced epidermal and blood temperature changes only, where²⁰

$$\Delta T_{epidermal}(z, t > t_{laser}) = \frac{\Delta T_{0,epidermal}}{2} \left\{ \operatorname{erf}(\tilde{Z}_i - \tilde{Z}) + \operatorname{erf}(\tilde{Z}_i + \tilde{Z}) \right\}_{\substack{\tilde{z}_i=\tilde{z}_2 \\ \tilde{z}_i=\tilde{z}_1}} \quad (13)$$

and

$$\begin{aligned} \Delta T_{blood}(z, t > t_{laser}) &= \frac{\Delta T_{0,blood}}{2f_{area}} e^{2\tilde{M}\tilde{Z}_3+\tilde{M}^2} \left\{ e^{-2\tilde{M}\tilde{Z}} \operatorname{erf}(\tilde{Z}_i - \tilde{Z} + \tilde{M}) \right. \\ &\left. + e^{2\tilde{M}\tilde{Z}} \operatorname{erf}(\tilde{Z}_i + \tilde{Z} + \tilde{M}) \right\}_{\substack{\tilde{z}_i=\tilde{z}_4 \\ \tilde{z}_i=\tilde{z}_3}}. \end{aligned} \quad (14)$$

Assuming $E_0 = 5 \text{ J/cm}^2$ and substituting optical properties of skin at 585 nm ²¹ into equations (5) and (8), $\Delta T_{0,epidermal} = 60 \text{ }^\circ\text{C}$, and $\Delta T_{0,blood} / f_{area} = 70 \text{ }^\circ\text{C}$. Calculated temperature distributions indicate that cooling remains localized within the epidermis, when using a cryogen (tetrafluoroethane; R134a) spurt duration of 20 ms, while temperature of the deeper blood vessels is unaffected. Peak epidermal temperature 1 ms after deposition of laser energy is reduced by approximately $25 \text{ }^\circ\text{C}$ (Fig. 2a). At 100 ms, heat generated in blood vessels diffuses to the skin surface and cooling of skin results in an overall temperature reduction within the epidermis (Fig. 2b).

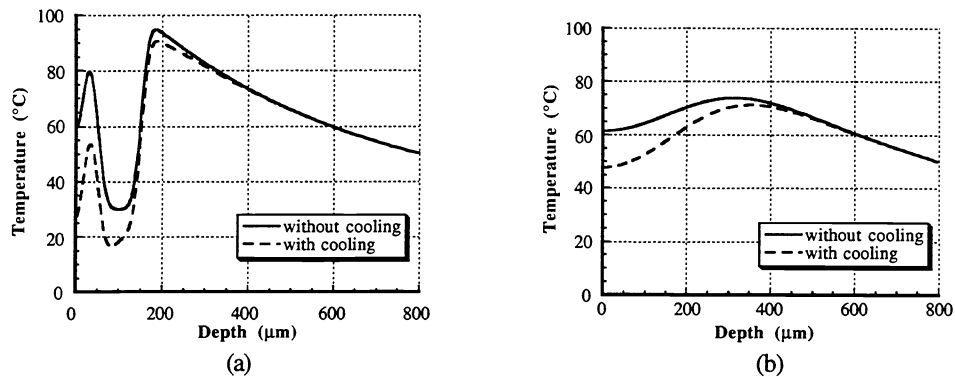


Fig. 2. Computed temperature distributions with no cooling and 20 ms pre-cooling with tetrafluoroethane: (a) 1 ms, (b) 100 ms after laser irradiation.

4. EXPERIMENTAL PROCEDURE

1,1,1,2 tetrafluoroethane (b.p. $\approx -26^\circ\text{C}$) (AlliedSignal Inc., Morristown, NJ), an environmentally compatible, non-toxic, non-flammable refrigerant was used as a test cryogen. Cryogen was contained in a pressurized steel canister and delivered through an electronically controlled standard fuel injection valve positioned 4 cm away from skin at an angle of approximately 30° with respect to the normal axis to the surface (Fig. 3). Duration of the cryogen spurt and the timing between cryogen delivery and laser irradiation were controlled with a programmable digital delay generator (DG535, Stanford Research Systems, Sunnyvale, CA).

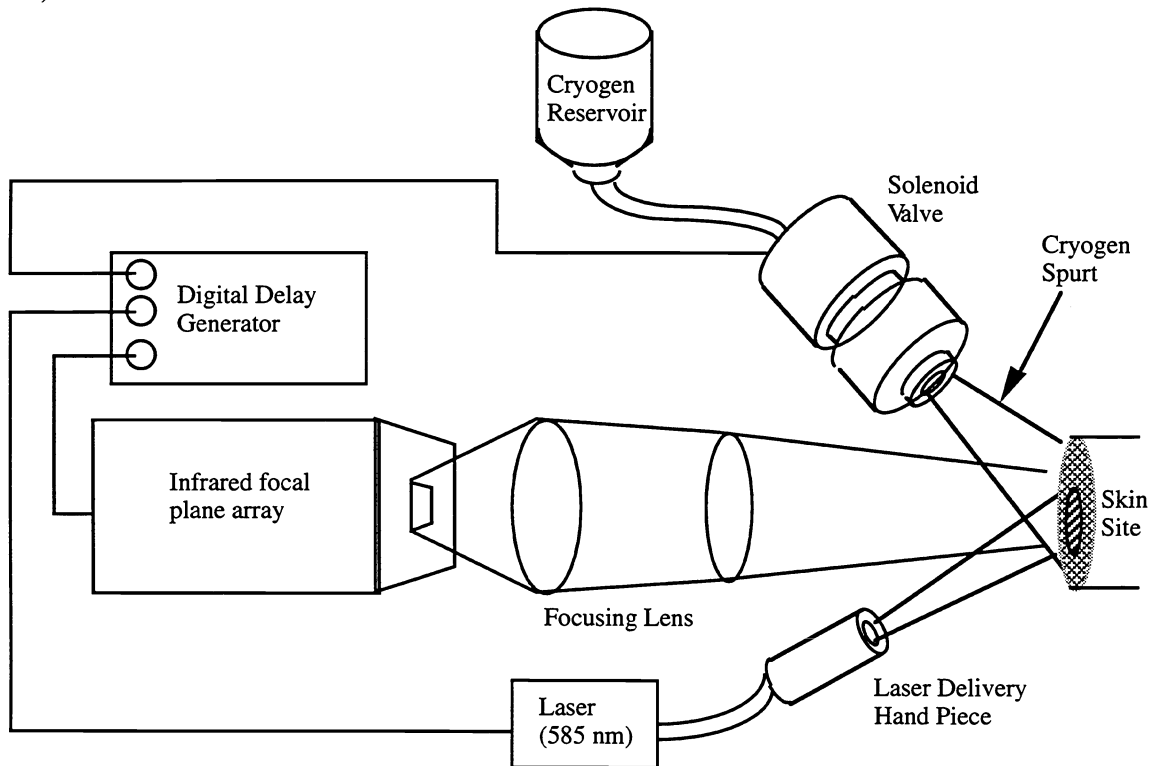


Fig. 3. Schematic of experimental set-up for dynamic cooling in conjunction with skin irradiation while measuring the radiometric surface temperature.

PWS sites of individuals (informed consent was sought and documented on standard University of California, Irvine forms) were pre-cooled with tetrafluoroethane and irradiated using a flashlamp-pumped pulsed dye laser (585 nm) (Candela Laser Corp., Wayland, MA) immediately following cryogen spurt delivery. The laser spot size (5 mm diameter) was concentric with the sprayed area (≈ 7 mm in diameter) on the skin surface and irradiation was performed immediately following cryogen delivery.

Infrared emission from skin was collected with a 128x128 InSb fast infrared focal plane array (IR-FPA) camera system (Amber Engineering Inc., Goleta, CA). A bandpass filter (3-5 μm) was positioned near the cold stop of the IR-FPA to reduce background fluctuations and, hence, increase signal to noise ratio. The IR-FPA acquired 217 images of radiometric temperature per second and was triggered by the digital delay generator. The infrared signal collected by each detector element in the IR-FPA was digitized with a 3.2 MHz 12-bit A/D converter, and then downloaded to a magneto-optic disk storage device for analysis.

Calibration of the infrared signal was performed by measuring the pixel value of the IR-FPA as a function of surface temperature of an aluminum block coated with highly emissive ($\epsilon \approx 0.97$) black paint (TC-303 black, GIE Corp., Provo, UT) heated by a resistive element. The surface temperature of the aluminum block was measured using a precision thermistor (8681, Keithley, Cleveland, OH) attached to the block.

5. RESULTS AND DISCUSSION

Radiometric surface temperature profiles recorded with the IR-FPA camera in response to laser irradiation of PWS sites with and without pre-cooling are displayed in Fig. 4. Measurements represent average skin surface temperatures in a 2 mm diameter circular region. Immediate radiometric temperatures in response to laser fluences 5-10 J/cm^2 and without cooling are 50-78 $^\circ\text{C}$ (Fig. 4a).

Radiometric measurements show rapid temperature reductions to 12-17 $^\circ\text{C}$ when skin is pre-cooled with 20-80 ms tetrafluoroethane spurts (Fig. 4b). Instantaneous radiometric temperatures in response to a laser fluence of 10 J/cm^2 , delivered immediately following the cryogen spurt, are 24-34 $^\circ\text{C}$, lower than those obtained from uncooled PWS sites. Reductions in instantaneous temperature increase in response to laser irradiation may be attributed to infrared emission from the cryogen-ice mixture remaining on the skin surface, and some attenuation of laser light through the mixture. Our measurements, using dry synthetic collagen films (Colla-Tec, Plainsboro, NJ) as a skin model, have shown laser light attenuation of approximately 15% through the cryogen sprayed on the collagen film.

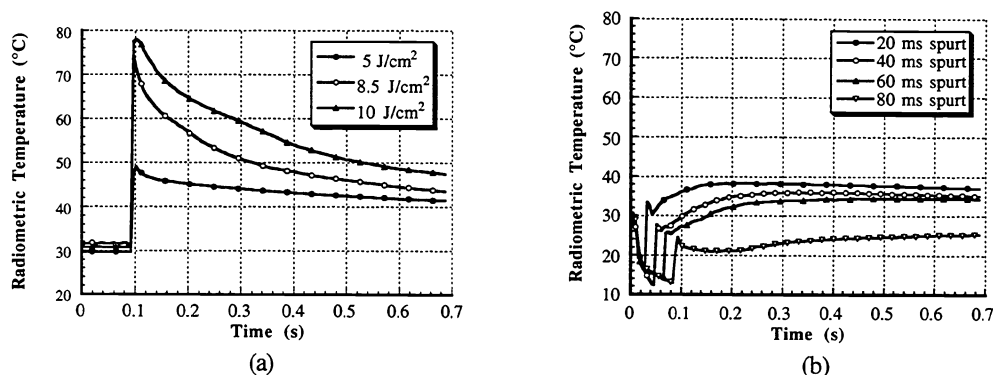


Fig. 4. Radiometric surface temperatures measured with the IR-FPA camera from (a) non-cooled sites in response to various incident fluences, (b) cooled sites with various spurt durations and an incident laser fluence of 10 J/cm^2 .

Radiometric surface temperatures are dependent on the infrared properties of cryogen-ice mixture and skin in the detection bandwidth. When using a HgCdTe single element detector (sensitive in the 7-11 μm spectral bandwidth), radiometric surface temperature reductions from 0 to -10 $^{\circ}\text{C}$ in response to 5-100 ms spurts of tetrafluoroethane have been reported^{8,9}.

Blistering, indicative of thermal injury to overlying epidermis, and eschar formation developed on the uncooled sites within 10 days following treatment. In comparison, there was no blistering on the cooled sites; blanching, indicative of laser photothermolysis of PWS blood vessels, did occur within six months following treatment.

Although successful blanching of PWS and elimination of epidermal thermal injury through dynamic cooling has been reported here and in previous studies^{8,10}, optimum cooling parameters (e.g., spurt duration, relative timing with respect to laser irradiation) need to be determined on an individual patient basis since density of melanosomes as well as depth of the PWS blood vessels vary considerably. For fluences in the range of 5-8 J/cm^2 in patients with intermediate melanin concentration (e.g., olive complexion) and superficial blood vessels (e.g., located at 150 μm below the surface), calculations of thermal response of skin to dynamic cooling and pulsed laser irradiation (at 585 nm) indicate that a tetrafluoroethane spurt duration of 20 ms applied prior to laser irradiation is sufficient to eliminate epidermal thermal injury without reducing the temperature of PWS blood vessels²⁰. For deeper blood vessels (e.g., located at 300 μm below the surface), tetrafluoroethane spurt durations up to 100 ms may be applied without cooling the PWS blood vessels.

For patients with high epidermal melanin concentration (e.g., black complexion) and superficial blood vessels, a tetrafluoroethane spurt duration of 20 ms is sufficient to eliminate epidermal thermal injury when the incident laser fluence is 5-6 J/cm^2 . Spurt durations up to 80 ms may be applied for deeper blood vessels. For larger fluences, cryogens with lower boiling points than tetrafluoroethane such as chlorodifluoromethane (R22; b.p. \approx -40 $^{\circ}\text{C}$), difluoromethane (R32; b.p. \approx -52 $^{\circ}\text{C}$), or trifluoromethane (R23; b.p. \approx -82 $^{\circ}\text{C}$) may be effective in eliminating epidermal thermal injury while allowing photothermolysis of PWS blood vessels²⁰.

Dynamic cooling may prove to be useful during laser treatment of other dermatoses such as hemangiomas. Due to the relatively deep tissue penetration at 1064 nm, Nd:YAG laser has been used to coagulate bulky hemangiomas²²⁻²³. Nevertheless, ulceration of the epidermis and papillary dermis, the end result of which is scarring, remains a major concern²⁴. Dynamic cooling during continuous Nd:YAG laser irradiation may be a method by which the epidermal layer and papillary dermis can be protected. Studies are currently underway in our laboratory to further investigate the potential of dynamic cooling in conjunction with laser treatment of hemangiomas.

6. CONCLUSIONS

Dynamic cooling induces rapid and localized temperature reductions in skin. Calculations indicate that for appropriate cryogen spurt durations, cooling only affects the superficial epidermis and not the deeper blood vessels. Preliminary clinical results in PWS patients show successful blanching of PWS and elimination of epidermal thermal injury. Further clinical studies are required to optimize the cooling parameters in conjunction with laser irradiation for improved treatment of port wine stains and other selected dermatoses on an individual patient basis.

7. ACKNOWLEDGMENTS

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