Title
Dynamic epidermal cooling in conjunction with laser treatment of port-wine stains: Theoretical and preliminary clinical evaluations

Journal
Lasers in Medical Science, 10(2)

ISSN
0268-8921

Authors
Anvari, Bahman
Milner, Thomas E
Tanenbaum, B Samuel
et al.

Publication Date
1995-06-01

DOI
10.1007/bf02150847

Lasers in Medical Science 1995, **10**:105–112

Dynamic Epidermal Cooling in Conjunction with Laser Treatment of Port-Wine Stains: Theoretical and Preliminary Clinical Evaluations

BAHMAN ANVARI[a,b], THOMAS E. MILNER[a,c], B. SAMUEL TANENBAUM[b], SOL KIMEL[d], LARS O. SVAASAND[e], J. STUART NELSON[a]

[a]*Beckman Laser Institute and Medical Clinic, Department of Surgery, University of California, Irvine, CA, USA*
[b]*Department of Engineering, Harvey Mudd College, Claremont, CA, USA*
[c]*Department of Physics, Harvey Mudd College, Claremont, CA, USA*
[d]*Department of Chemistry, Technion-Israel Institute of Technology, Haifa, Israel*
[e]*Division of Physical Electronics, University of Trondheim, Norwegian Institute of Technology, Norway*

Correspondence to Bahman Anvari, Beckman Laser Institute and Medical Clinic, 1002 Health Sciences Rd East, Irvine, CA 92715 USA

Paper received July 1995

Abstract. The clinical objective in laser treatment of port-wine stains (PWS) is to induce selective photothermolysis of subsurface blood vessels without damaging the overlying epidermis. This paper investigates the effectiveness of 'dynamic' cooling, where a cryogen is sprayed on the skin surface for an appropriately short period of time, to eliminate epidermal thermal injury during laser treatment of PWS. Comparative measurements of radiometric surface temperature from cooled and uncooled laser irradiated (585 nm) PWS sites, and theoretical predictions of temperature distributions within skin in response to dynamic cooling in conjunction with laser irradiation are presented. Rapid reduction of skin surface temperature and localization of cooling the epidermis are obtained when a cryogen is sprayed on skin prior to laser irradiation. Successful blanching of the PWS without thermal injury to the overlying epidermis is accomplished.

INTRODUCTION

Port-wine stains (PWS) are congenital vascular malformations characterized by ectatic vessels within dermis and occur in an estimated 0.3% of the newborn (1). Accompanying the potentially devastating psychological and social problems of PWS is hypertrophy of underlying soft tissue and bone in approximately two-thirds of patients, which further disfigures facial features (2).

Therapy of PWS has included skin grafting, ionizing radiation, tattooing and dermabrasion. However, none of these methods is considered to be successful and they are no longer considered viable treatment options. In recent years, flashlamp-pumped pulsed dye laser (FPPDL) irradiation of PWS has offered an alternative treatment modality, as the absorption of laser light by haemoglobin in PWS blood vessels results in irreversible thermal injury and subsequent destruction of cutaneous blood vessels (3). Successful clinical results (i.e. blanching of the PWS) without eschar formation have been reported in paediatric and adult patients (4–7).

Unfortunately, epidermal melanin which has a broad absorption spectrum, represents an 'optical shield' through which incident laser light must pass to reach the deeper PWS blood vessels. Non-specific absorption of laser light results in excessive heat generation that can cause irreversible epidermal thermal injury. The ideal laser treatment should, therefore, cause irreversible damage to the deep PWS blood vessels without damaging the overlying epidermis.

Cooling of skin using ice or chilled water in conjunction with laser irradiation has been used to prevent epidermal thermal injury (8–10). Temperature distributions in response to cooling can be calculated by solving the one-dimensional heat conduction equation:

0268–8921/95/020105+08 $12.00/0

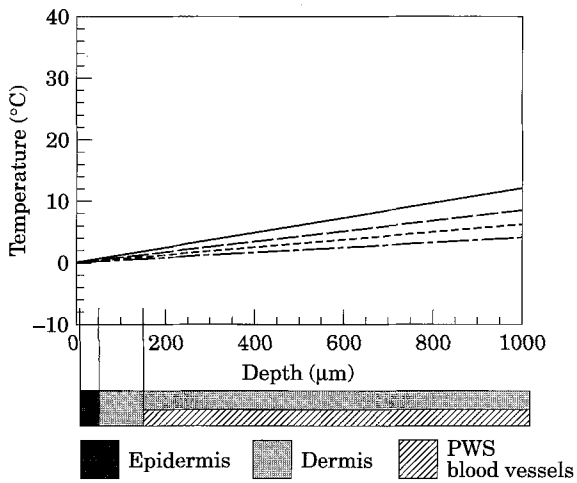

Fig. 1. Computed temperature distributions in response to a 0 °C constant surface temperature applied for 15 (———), 30 (– – –), 60 (· · ·) and 120 s (– · – ·).

$$\frac{\partial^2 T}{\partial z^2} = \frac{1}{\alpha}\frac{\partial T}{\partial t} \tag{1}$$

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 (taken to be 1.1×10^{-7} m^2 s^{-1}) (11). Assuming that the air–skin interface is maintained at a constant temperature when applying ice at the surface, solution to equation (1) is (12):

$$T_{cooling}(z,t) = (T_\infty - T_i)erfc(\tilde{z}) + T_i \tag{2}$$

where $T_{cooling}$ (°C) is the resulting temperature after cooling at $t=0$, T_i is the initial skin temperature (assumed to be 30 °C), T_∞ is the temperature of the medium (e.g. ice; $T_\infty = 0$ °C) in contact with the skin surface, $ercf(x)$ is the complementary error function ($1 - erf(x)$), and:

$$\tilde{z} = \frac{z}{2\sqrt{\alpha t}} \tag{3}$$

Although prevention of epidermal thermal injury has been reported when using these cooling methods (8, 9), temperature distributions following sustained cooling (i.e. 15–120 s) by 0 °C ice at the skin surface show that in addition to cooling the epidermis, temperature of PWS blood vessels are similarly reduced (Fig. 1). Thermal energy removed to protect the epidermis from injury will be offset by additional laser energy required to heat the PWS to a sufficient temperature for blood vessel destruction. A suitable cooling method should therefore cool the epidermis selectively without changing the temperature of deeper PWS blood vessels.

With 'dynamic' cooling, the epidermis can be cooled selectively. When a cryogen is sprayed on the skin surface for an appropriately short period of time (of the order of tens of millisecond), the cooling remains localized in the epidermis (13–15). A thermal boundary condition at the skin surface during dynamic cooling can be expressed as:

$$-k\left.\frac{\partial T(z,t)}{\partial z}\right|_{z=0} = h[T_\infty - T(0,t)] \tag{4}$$

where k is thermal conductivity of skin (taken to be 0.45 W m^{-1} K^{-1}) (11), h (W m^{-2} K^{-1}) is the heat transfer coefficient, and T_∞ (°C) is temperature of the cryogen and/or cryogen-ice (formed as a result of water condensation) mixture. The solution to the heat conduction equation (1) with boundary condition (4) is (12):

$$T_{cooling}(z,t) = (T_\infty - T_i)\{erfc(\tilde{z}) - [e^{\tilde{z}^2} erfcx(\tilde{h} + \tilde{z})]\} + T_i \tag{5}$$

where $erfcx(x)$ is defined as $exp(x^2) \times erfc(x)$, and:

$$\tilde{h} = \frac{h}{k}\sqrt{\alpha t} \tag{6}$$

For a relatively large value of h (e.g. 40 kW m^{-2} K^{-1}), corresponding to a liquid–vapour phase transition (16), and $T_\infty = -10$ °C (e.g. temperature of a cryogen-ice mixture), calculated values of temperatures within skin show that large reductions (30–35 °C) are obtained in a relatively short time (5–100 ms) and cooling remains localized to the epidermis (Fig. 2).

The authors have investigated experimentally the effectiveness of dynamic cooling to eliminate epidermal thermal injury by inducing a rapid and large surface temperature decrease at the skin surface. The authors present (1) infra-red radiometric measurements of skin temperature, (2) preliminary clinical results of dynamic cooling in conjunction with FPPDL for treatment of PWS, and (3) theoretical calculations of temperature distributions within skin in response to dynamic cooling and pulsed laser irradiation.

MATERIALS AND METHODS

1,1,1,2 tetrafluoroethane (R134a, cryogen's name in accordance with National Institute of

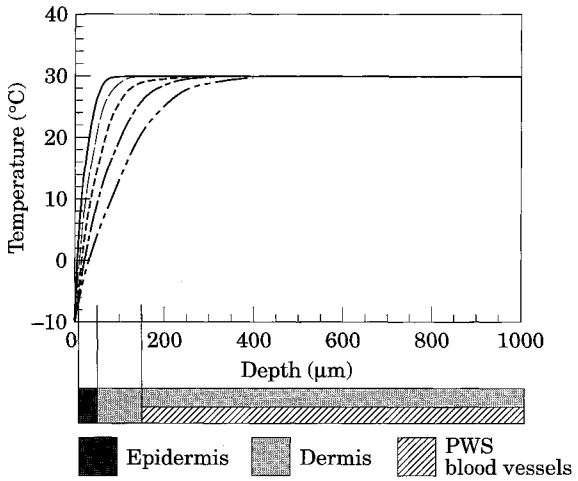

Fig. 2. Computed temperature distributions in response cryogen spurt durations of 5 (———), 10 (– – –), 20 (· · ·), 40 (– · – · ·) and 80 ms (– · · · –).

Standards and Technology; b.p. $\simeq -26$ °C) (ICE KLEA, Wilmington, DE), 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 surface normal (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).

PWS sites of individuals (informed consent was sought and documented on standard University of California, Irvine consent form) were pre-cooled with R134a and irradiated with a FPPDL (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 ($\simeq$7 mm in diameter) on the skin surface and irradiation was carried out immediately following cryogen delivery.

Infra-red emission from skin was collected with a 128 × 128 InSb fast infra-red focal plane array (IR-FPA) (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 camera system acquired 217 images of radiometric temperature per second and was triggered by the digital delay generator. The infra-red signal collected by each detector element in the IR-FPA was digitized with a 3.2 MHz 12-bit (0–4095) A/D converter, and stored in a computer for later analysis.

Radiometric surface temperatures is dependent on the spectral range (bandwidth) over which the measurements are made. To investigate the effect of the infra-red detection bandwidth, a HgCdTe single element detector (MDD-10E0-S1, Cincinnati Electronics, Mason, OH), optically filtered by a 7–11 μm bandpass filter, was used to measure the radiometric surface temperature of normal skin when sprayed with R134a. The detector was placed at the focal plane of a 25 mm diameter f/1 Ge lens configured for unit magnification. Infra-red emission was modulated (3.5 kHz) by a mechanical chopper and synchronously detected by a lock-in amplifier (SR850, Stanford Research Systems, Sunnyvale, CA). Radiometric signals were recorded on a digital oscilloscope (DSA601, Tektronix, Beaverton, OR) for further analysis.

Calibration of the infra-red signal was performed by measuring the pixel value of IR-FPA or the lock-in amplifier output voltage as a function of surface temperature of an aluminium block coated with highly emissive ($\varepsilon \simeq 0.97$) black paint (TC-303 black, GIE Corp, Provo, UT) and heated by a resistive element. The surface temperature of the aluminium block was measured using a precision thermistor (8681, Keithley, Cleveland, OH) attached to the block.

RESULTS

Radiometric surface temperature profiles recorded with the IR-FPA camera in response to laser irradiation of different PWS sites with and without pre-cooling are displayed in Fig. 4. Measurements represent average skin surface temperatures in a 2 mm diameter (13 pixels) circular region. Immediate radiometric temperatures in response to laser fluences 5–10 J cm^{-2} are 50–78 °C without cooling [Fig. 4(a)].

Radiometric measurements show rapid temperature reductions to 12–17 °C when the skin is pre-cooled with 20–80 ms R134a spurts [Fig. 4(b)]. Immediate radiometric temperature increase in response to a laser fluence of 10 J cm^{-2} is 24–34 °C lower than those obtained without cooling. Reductions in immediate temperature increase in response to laser irradiation may be attributed to the infra-red emission from the cryogen/ice mixture on the skin surface and/or laser light attenuation

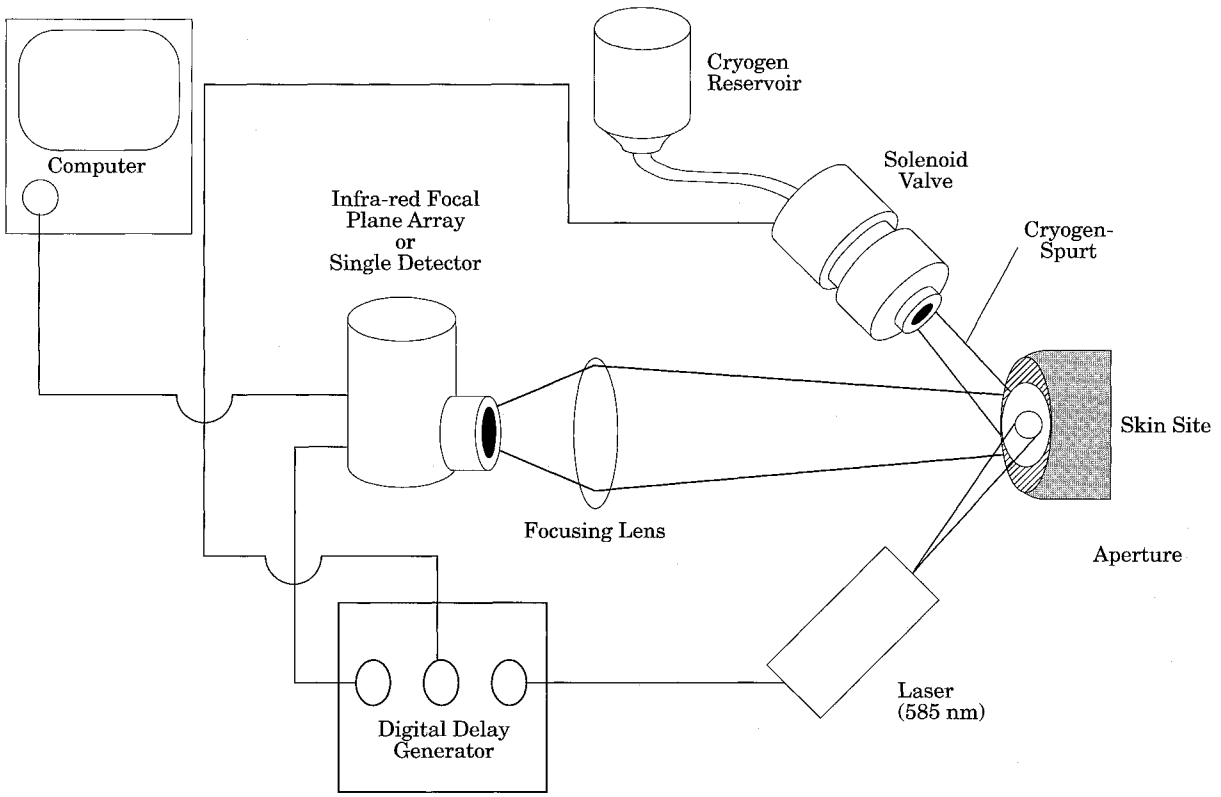

Fig. 3. Experimental set-up for dynamic cooling in conjunction with laser irradiation of skin, and measurement of radiometric surface temperature.

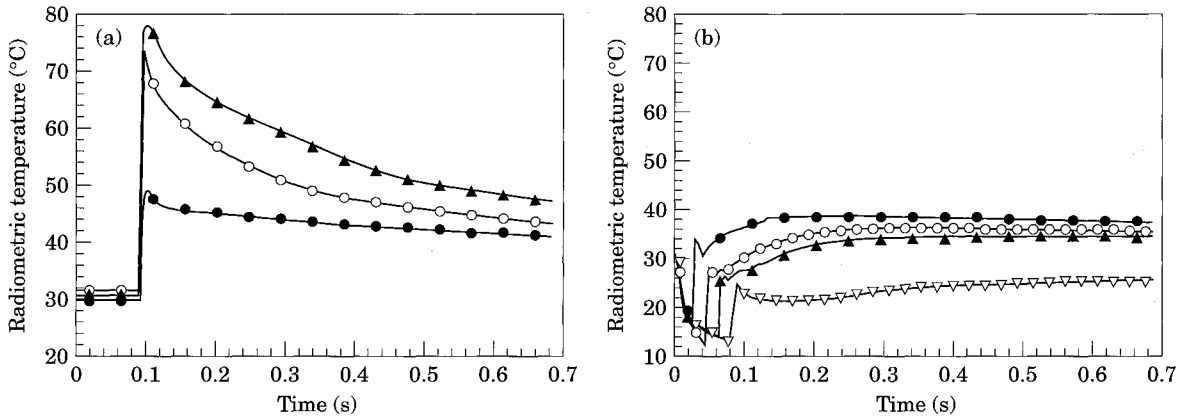

Fig. 4. Radiometric surface temperatures of different PWS sites measured with IR–FPA camera (sensitive in 3–5 μm spectral range) from (a) non-cooled sites in response to incident laser fluences of 5 (—●—), 8.5 (—○—), and 10 (—▲—) J cm^{-2}, (b) cooled sites with spurt durations 20 (—●—), 40 (—○—), 60 (—▲—), and 80 ms (—▽—) and a laser fluence of 10 J cm^{-2}.

through it. Measurements of transmitted laser light through the cryogen/ice mixture on synthetic dry collagen films (Colla-Tec, Plainsboro, NJ) showed 10–15% reduction in light tranmission through films that were sprayed for 5–100 ms as compared with those that were not sprayed.

Radiometric surface temperatures using the HgCdTe single element detector (sensitive in 7–11 μm spectral bandwidth) in response to spray cooling the skin with R134a for 20–100 ms show larger temperature drops (Fig. 5) when compared with similar measurements made by the IR-FPA at 3–5 μm spectral bandwidth. Measured radiometric temperature is dependent on the infra-red properties of the cryogen/ice mixture and skin in the detection bandwidth. The change in radiometric temperature, $\Delta S(t)$, can be expressed as (13):

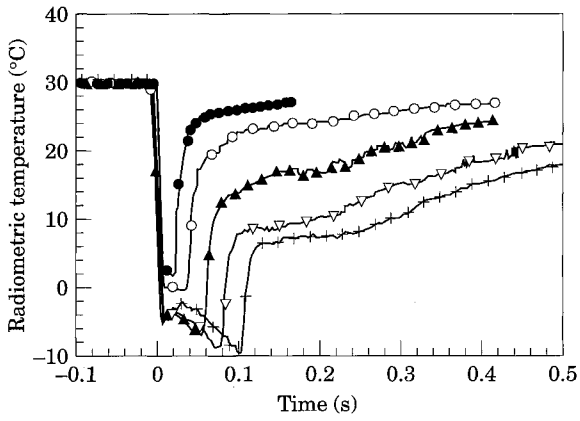

Fig. 5. Radiometric surface temperatures measured with HgCdTe single element detector (sensitive in 7–11 μm spectral range) in response to cryogen spurt durations 20 (—●—), 40 (—○—), 60 (—▲—), 80 (—▽—), and 100 ms (—+—).

$$\Delta S(t) = \mu_{mix} \int_{-l}^{0} [T(z,t) - T_i] exp[-\mu_{mix}(z+l)]dz + \mu_{skin} \int_{0}^{\infty} [T(z,t) - T_i] exp[-\mu_{mix} l - \mu_{skin} z]dz \quad (7)$$

where l is the thickness of the cryogen/ice mixture on skin surface, and μ_{mix} and μ_{skin} (m^{-1}) represent the infra-red attenuation by the mixture and skin, respectively.

As the infra-red attenuation of the cryogen/ice mixture increases, a greater contribution to the radiometric signal originates from the mixture [(first term in equation (7)] and the radiometric temperature approaches that of the mixture. Conversely, as the infra-red attenuation of the mixture approaches zero, the detected signal originates entirely from skin [second term in equation (7)].

Inasmuch as water is the major constituent of skin, μ_{skin} may be approximated as 40 m^{-1} and 60 m^{-1} in the 3–5 and 7–11 μm spectral regions, respectively (17, 18). Therefore, contributions to the infra-red signal originate from approximately the uppermost 30 and 15 μm of skin when using the IR-FPA and the HgCdTe detector, respectively.

Photographs of uncooled sites (top rows) taken 10 min [Fig. 6(a)] and 10 days [Fig. 6(b)] after laser exposure (10 J cm^{-2}) show blistering, indicative of thermal injury to overlying epidermis, and eschar formation, indicative of epidermal denaturation and necrosis. No surface textural changes are noted where the skin was pre-cooled for 40 ms [Figs 6(a) and 6(b), bottom two rows]. Photographs taken 6 months after laser irradiation show blanching of the cooled sites, indicating that laser photothermolysis of PWS blood vessels did occur [Fig. 6(c)].

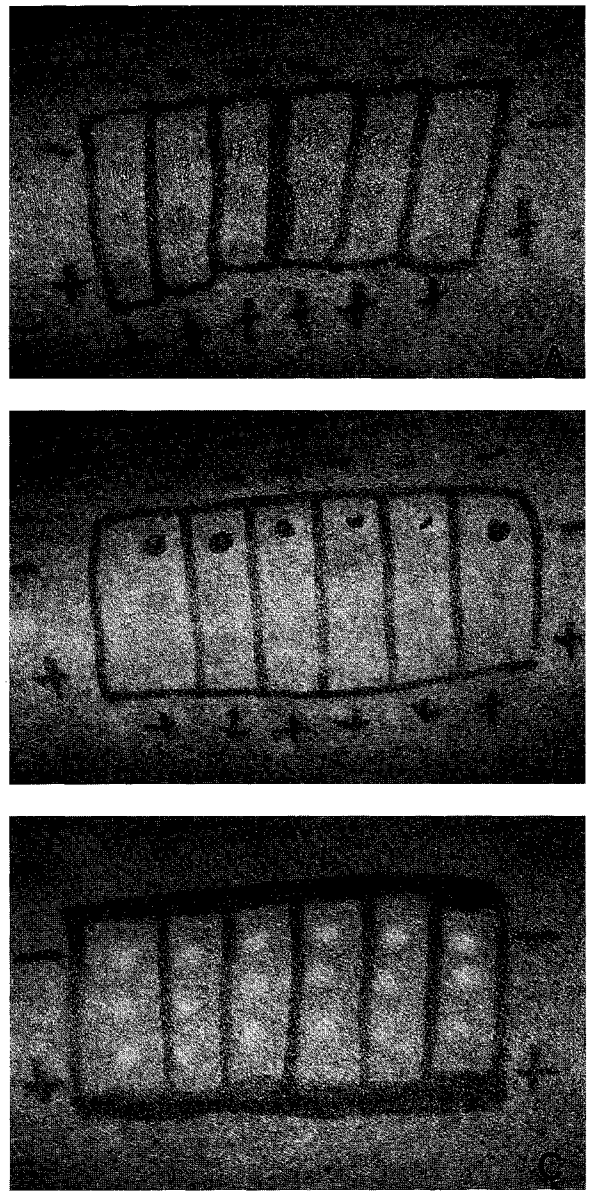

Fig. 6. Photographs of uncooled (upper row) and cooled (spurt duration of 40 ms) (lower two rows) PWS sites at (a) 10 min, (b) 10 days, and (c) 6 months after laser irradiation at 10 J cm^{-2}.

When treating PWS patients with relatively high epidermal melanin concentration, cooling with tetrafluoroethane may not be sufficient to prevent epidermal thermal injury (19). For an incident laser fluence of 10 J cm^{-2} and a R134a spurt duration of 20 ms, radiometric surface temperature profiles measured with the IR-FPA from PWS sites indicate increased laser-induced initial temperature rises by

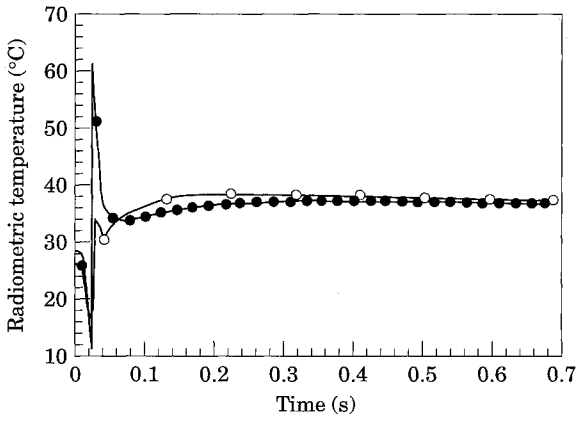

Fig. 7. Radiometric surface temperatures measured with IR-FPA camera for PWS patients with relatively low (—○—) and high (—●—) epidermal melanin concentrations, and in response to a cryogen spurt duration of 20 ms and a laser fluence of 10 J cm-2.

approximately 35 °C when the epidermal melanin content is high (Fig. 7). Cryogens with lower boiling points than that of R134a may prove useful in eliminating epidermal thermal injury when melanin concentration is high.

DISCUSSION

Selective cooling of epidermis during laser treatment of PWS can be achieved with dynamic cooling. Temperatures within skin in response to pre-cooling with a cryogen spurt, and pulsed laser irradiation can be calculated as:

$$T(z,t>t_{laser})=\Delta T_{cooling}(z,t>t_{laser})+\Delta T_{epidermal}(z,t>t_{laser})+\Delta T_{PWS}(z,t>t_{laser})+T_i \quad (8)$$

where t_{laser} is the time at which the laser energy is deposited (cooling starts at $t=0$), $\Delta T_{cooling}$ (°C) is the induced temperature change due to the cryogen spurt, and $\Delta T_{epidermal}$ and ΔT_{PWS} (°C) are induced temperature changes due to instantaneous absorption of laser light by epidermal melanin and haemoglobin PWS blood vessels, respectively.

Assuming that immediately after the laser pulse the temperature increase within the epidermis, $\Delta T_{0,epidermal}$, is constant over a finite depth, and that the spatial temperature distribution within PWS blood vessels decreases exponentially with depth with an effective blood absorption coefficient, μ_a^{blood} (m^{-1}) (assumed to be 1900 m^{-1}, corresponding to 10% fractional vascular volume within dermis) (20), explicit expressions for $\Delta T_{cooling}$, $\Delta T_{epidermal}$, and ΔT_{PWS} become (21):

$$\Delta T_{cooling}(z,t>t_{laser})=\frac{\Delta T_s e^{-\tilde{Z}^2}}{2}[erfcx(\tilde{K}+\tilde{Z})+erfcx(\tilde{K}-\tilde{Z})], \quad (9)$$

$$\Delta T_{epidermal}(z,t>t_{laser})=\frac{\Delta T_{0,epidermal}}{2}\{erf(\tilde{Z}_i-\tilde{Z})+erf(\tilde{Z}_i+\tilde{Z})\}_{\tilde{Z}_i=\tilde{Z}_1}^{\tilde{Z}_i=\tilde{Z}_2} \quad (10)$$

and:

$$\Delta T_{PWS}(z,t>t_{laser})=\frac{\Delta T_{0,PWS}}{2}e^{2\tilde{M}\tilde{Z}_3+\tilde{M}^2}\{e^{-2\tilde{M}\tilde{Z}}erf(\tilde{Z}_i-\tilde{Z}+\tilde{M})+e^{2\tilde{M}\tilde{Z}}erf(\tilde{Z}_i+\tilde{Z}+\tilde{M})\}_{\tilde{Z}_i=\tilde{Z}_3}^{\tilde{Z}_i=\tilde{Z}_4} \quad (11)$$

where $\Delta T_{0,PWS}$ is the temperature at the most superficial dermal–PWS interface at $t=t_{laser}$, and:

$$\tilde{K}=\kappa\sqrt{\alpha(t-t_{laser})},\ \tilde{Z}=\frac{z}{2\sqrt{\alpha(t-t_{laser})}},\ \tilde{M}=\mu_a^{blood}\sqrt{\alpha(t-t_{laser})} \quad (12)$$

where κ (m^{-1}) is a parameter used in fitting equation (5) with an exponential function. Non-dimensional intervals $[Z_1, Z_2]$ and $[Z_3, Z_4]$ define regions of light absorption by epidermal melanin and haemoglobin, respectively. In absence of cooling, the thermal response of skin is the superposition of epidermal and PWS heating given in equations (10) and (11), respectively.

Calculated temperature distributions indicate that cooling remains localized within the epidermis while leaving temperatures of the deeper PWS blood vessels unaffected. For $\Delta T_{0,epidermal}=60$ °C and $\Delta T_{0,PWS}=70$ °C, peak epidermal temperature 1 ms after deposition of laser energy is reduced by approximately 25 °C [Fig. 8(a)]. At later times (100 ms), heat generated in PWS blood vessels diffuses to the skin surface and pre-cooling the skin results in an overall temperature reduction within the epidermis [Fig. 8(b)].

Although successful blanching of PWS and elimination of epidermal thermal injury through dynamic cooling has been demonstrated, optimum cooling parameters (e.g.

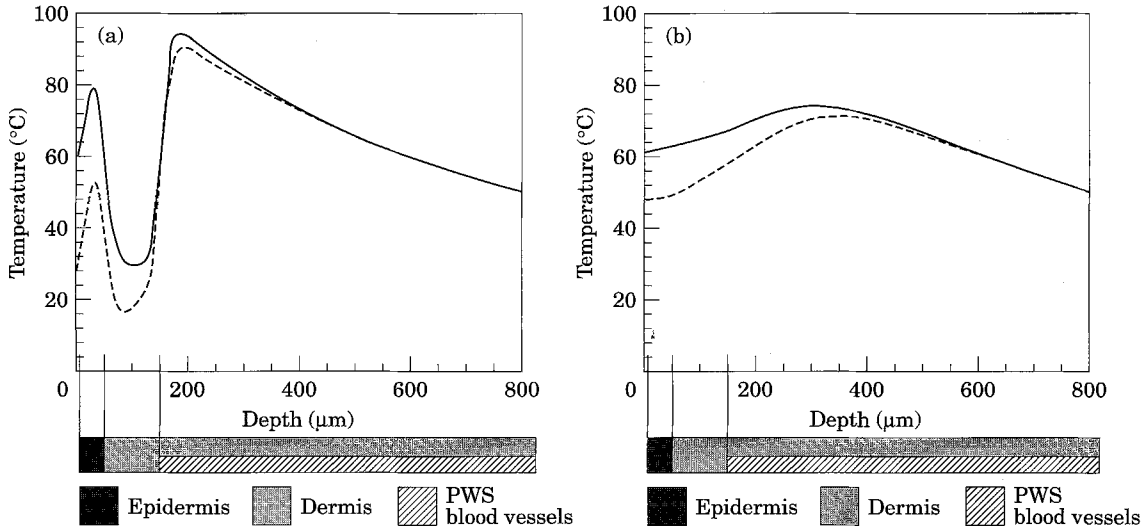

Fig. 8. Computed temperature distributions with no cooling (———), and 20 ms pre-cooling with R134a (– – –): (a) 1 ms, (b) 100 ms post laser irradiation.

spurt duration, relative interval with respect to laser irradiation time) need to be determined on an individual patient basis as density of melanosomes as well as depth of the PWS blood vessels vary considerably. Estimation of depth of PWS blood vessels may be obtained by analysis of time-resolved infra-red radiometric measurements (21) or similar diagnostic techniques (22).

Theoretical predictions of the thermal response of skin to dynamic cooling and pulsed laser irradiation (at 585 nm) indicate that a R134a spurt duration of 20 ms applied prior to laser irradiation is sufficient to eliminate epidermal thermal injury without reducing the temperature of PWS blood vessels when using 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) (19). For deeper blood vessels (e.g. located at 300 μm below the surface), calculations of temperature distributions indicate that R134a spurt durations up to 100 ms may be applied without cooling the PWS blood vessels.

For patients with high epidermal melanin concentrations (e.g. black complexion) and superficial blood vessels, theoretical calculations indicate that a R134a 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 fluences greater than those indicated here, cryogens with lower boiling points than R134a such as chlorodifluoromethane (R22; b.p. $\simeq -40$ °C), or difluoromethane (R32, b.p. $\simeq -52$ °C) may be effective to eliminate epidermal thermal injury and allow photothermolysis of PWS blood vessels. Studies are currently underway in the authors' laboratory to characterize the thermal response of skin to these cryogens, and optimize cooling parameters in conjunction with laser treatment of PWS and other selected vascular and pigmented dermatoses.

CONCLUSIONS

Dynamic cooling provides an effective method for inducing rapid and localized temperature drops in skin. Theoretical calculations indicate that for appropriate cryogen spurt durations, cooling only affects the superficial epidermis and not the deeper PWS blood vessels during laser irradiation. Preliminary clinical results 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 on an individual patient basis.

ACKNOWLEDGEMENTS

This work was supported by Institute of Arthritis and Musculoskeletal and Skin Disease (1R29-AR41638-01A1

and 1R01-AR42437-01A1) at the National Institutes of Health, Whitaker Foundation Special Opportunity Grant, Biomedical Research Technology Program (R03-RR0698), Dermatology Foundation, DOE (DE-F6-3-91ER6122), ONR (N0014-91-0134), NIH (RR01192), Packard Foundation Grant, and the Beckman Laser Institute Endowment.

REFERENCES

1 Jacobs AH, Walton RG. The incidence of birthmarks in the neonate. *Pediatrics* 1976, **58**:218–22
2 Geronemus RG, Ashinoff R. The medical necessity of evaluation and treatment of port wine stains. *J Dermatol Surg Oncol* 1991, **17**:76–9
3 Anderson RR, Parrish JA. Selective photothermolysis: Precise microsurgery by selective absorption of pulsed radiation. *Science* 1983, **220**:524–7
4 Garden JM, Polla LL, Tan OT. The treatment of port-wine stains by the pulsed dye laser. *Arch Dermatol* 1988, **124**:889–96
5 Tan OT, Sherwood K, Gilchrest BA. Treatment of children with port-wine stains using the flashlamp-pumped dye laser. *N Engl J Med* 1989, **320**:416–21
6 Reyes BA, Geronemus RG. Treatment of port-wine stains during childhood with the flashlamp-pumped dye laser. *J Am Acad Dermatol* 1990, **23**:1142–8
7 Nelson JS, Applebaum J. Clinical management of port-wine stain in infants and young children using the flashlamp-pulsed dye laser. *Clin Pediatrics* 1990, **29**:503–8
8 Gilchrest BA, Rosen S, Noe JM. Chilling port-wine stains improves the response to argon laser therapy. *Plast Reconstr Surg* 1982, **69**:278–83
9 Dereno B, Patrice T, Litoux B, Barroere H. The benefit of chilling in argon laser treatment of port-wine stains. *Plast Reconstr Surg* 1985, **74**:42–5
10 Chess C, Chess Q. Cool laser optics treatment of large telangiectasia of the lower extremities. *J Dermatol Surg Oncol* 1993, **17**:74–80
11 Duck FA. *Physical Properties of Tissue. A Comprehensive Reference Book*. London: Academic, 1990
12 Carslaw HS, Jaeger JC. *Conduction of Heat in Solids*, 2nd edn. Oxford: Clarendon, 1959
13 Anvari B, Milner TE, Tanenbaum BS et al. Selective cooling of biological tissues: Application for thermally mediated therapeutic procedures. *Phys Med Biol* 1995, **40**:241–52
14 Nelson JS, Milner TE, Anvari B et al. Dynamic epidermal cooling during pulsed laser treatment of port-wine stain—a new methodology with preliminary clinical evaluation. *Arch Dermatol* 1995, **131**:695–700
15 Nelson JS, Milner TE, Anvari B et al. Dynamic epidermal cooling in conjunction with laser-induced photothermolysis of port-wine stain blood vessels. *Lasers Surg Med* (in press)
16 Incropera FP, Dewitt DP. *Fundamentals of Heat and Mass Transfer*, 2nd edn. New York: Wiley, 1981
17 Hale GM, Querry MR. Optical constants of water in the 200 nm to 200 μm wavelength region. *Appl Opt* 1973, **12**:555–63
18 Marechal Y. Infrared spectra of water. I. Effect of temperature and H/D isotopic dilution. *J Chem Phys* 1991, **95**:5565–73
19 Anvari B, Tanenbaum BS, Milner TE et al. A theoretical study of the thermal response of skin to cryogen spray cooling and pulsed laser irradiation: Implications for treatment of port wine stain birthmarks. *Phys Med Biol* 1995, **40**:1451–65
20 Verkruysse W, Pickering JW, Beek JF et al. Modelling the effect of wavelength on the pulsed dye laser treatment of port-wine stains. *Appl Opt* 1993, **32**:393–8
21 Milner TE, Goodman DM, Tanenbaum BS, Nelson JS. Depth profiling of laser heated chromophores in biological tissues using pulsed photothermal radiometry. *J Opt Soc Am A* 1995, **12**:1479–88
22 Long FH, Anderson RR, Deutsch TF. Pulsed photothermal radiometry for depth profiling of layered media. *Appl Phys Lett* 1987, **51**:2076–8

Key words: Epidermal thermal injury; Infra-red radiometry; Refrigerant; Selective cooling; Selective photothermolysis; Tetrafluoroethane; Vascular abnormalities; Port-wine stain