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Journal

IEEE Journal on Selected Topics in Quantum Electronics, 5(4)

ISSN

1077-260X

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Publication Date

1999-07-01

DOI

10.1109/2944.796330

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Estimation of Internal Skin Temperatures in Response to Cryogen Spray Cooling: Implications for Laser Therapy of Port Wine Stains

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Abstract—In many port wine stain (PWS) patients, successful clearing is not achieved even after multiple laser treatments because of inadequate heat generation within the targeted blood vessels. Use of higher radiant exposures has been suggested to improve lesion clearing, but risk of epidermal injury due to nonspecific absorption by melanin increases. It has been demonstrated that cryogen spray cooling (CSC) can protect the epidermis from nonspecific thermal injury during laser treatment of PWS. Inasmuch as epidermal melanin concentration and blood vessel depth vary among patients, evaluation of internal skin temperatures in response to CSC is essential for further development and optimization of treatment parameters on an individual patient basis. We present internal temperature measurements in an epoxy resin phantom in response to CSC and use the results in conjunction with a mathematical model to predict the temperature distribution within human skin for various cooling parameters. Measurements on the epoxy resin phantom show that cryogen film temperature is well below the cryogen boiling point, but a poor thermal contact exists at the cryogen-phantom interface. Based on phantom measurements and model predictions, internal skin temperature reduction remains confined to the upper 400 μm for spurt durations as long as 200 ms. At the end of a 100 ms spurt, our results show a 31 °C temperature reduction at the surface, 12 °C at a depth of 100 μm , and 4 °C at a depth of 200 μm in human skin. Analysis of estimated temperature distributions in response to CSC and temperature profiles obtained by pulsed photothermal radiometry indicates that a significant protective effect is achieved at the surface of laser irradiated PWS skin. Protection of the epidermal basal layer, however, poses a greater challenge when high radiant exposures are used.

Index Terms—Cutaneous hypervascular lesions, dermatology, refrigerant, selective thermal injury, skin model.

I. INTRODUCTION

LIGHT EMITTED from a flashlamp-pumped pulsed dye laser (FLPPDL) at wavelength of 577 or 585 nm is currently used to treat port wine stains (PWS). However, only a small percentage of patients (10%–20%) obtain 100% fading of their PWS lesions even after receiving multiple laser treatments [1], [2]. The principal reason for poor clinical results is insufficient heat generation within the PWS blood vessels. The 7–10 J/cm² radiant exposure, and 0.45–0.5-ms pulse duration employed with the FLPPDL may be insufficient to produce and sustain the critical core temperature necessary to destroy large PWS vessels. Additionally, further complications arise in patients with darker pigmentation who cannot be treated due to absorption of incident light by epidermal melanin.

Various investigators have suggested use of higher laser fluences and/or longer laser exposure times to produce irreversible injury of large PWS vessels [3]–[5]. Such increased dosimetry will also result in greater heat generated within the epidermis which can lead to complications such as hypertrophic scarring, atrophy, induration, or dyspigmentation.

One method to protect the epidermis during laser irradiation is to spray the skin with a short cryogen spurt (on the order of milliseconds). Cryogen spray cooling (CSC) of the skin surface has been shown to protect the epidermis from nonspecific thermal injury during laser treatment of PWS at current laser parameters while still allowing photocoagulation of targeted blood vessels [6]–[11]. However, the application of CSC to protect the epidermis during application of higher radiant exposures than those currently used requires further investigation. In addition, knowledge of internal skin temperature distribution in response to CSC is essential for optimization of treatment parameters on individual patient basis.

Inasmuch as making internal temperature measurements within human skin is not conducted easily, we utilize an epoxy resin phantom for depth resolved measurements and use these experimental results in conjunction with a heat transfer mathematical model to predict internal temperatures within human skin. To deduce these temperatures, knowledge of heat transfer coefficient at the surface is essential. We estimate this parameter by two methods: 1) fitting the measured subsurface temperature in the epoxy resin phantom with the heat transfer model and 2) fitting the radiometric temperature measurements on human skin with a heat transfer-infrared radiometry model. Based on the estimated value of the surface heat transfer

Manuscript received January 11, 1999; revised April 27, 1999. This work was supported in part by the Whitaker Foundation Biomedical Engineering Research under Grant 96-0235, in part by the National Science Foundation under Grant BES-9896101, in part by the Institute of Heart, Lung and Blood under Grant IR15-HL581215-01, and in part by Institute of Arthritis and Musculoskeletal and Skin Disease at the National Institutes of Health under Grant RIS-AR43403-01 and Grant IR01-AR43419.

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Publisher Item Identifier S 1077-260X(99)07538-3.

coefficient and the predicted internal temperatures during a cryogen spurt, we estimate the effect of CSC on the initial temperature distribution within PWS skin in response to laser irradiation.

II. MODEL THEORY

A. Heat Transfer

We assume a semi-infinite medium (either skin or epoxy resin) is cooled by spraying the surface with liquid cryogen. Since the lateral dimensions of the cooled surface ($\approx 1\text{--}1.5$ cm in practice) are much larger than the thickness of interest in the medium (≈ 1 mm), temperature distribution may be computed by solving the one-dimensional (1-D) heat conduction equation:

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

where $T(z, t)$ ($^\circ\text{C}$) is the medium temperature in response to CSC, $z(m)$ is distance into the medium (with origin at the medium surface), $t(s)$ is time, and $\alpha(m^2 \cdot s^{-1})$ is the medium thermal diffusivity.

A Robin boundary condition at the medium surface is implemented:

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

where $k(W \cdot m^{-1} \cdot K^{-1})$ is the thermal conductivity, T_∞ ($^\circ\text{C}$) is the temperature of the cryogen film in contact with the medium surface, and $h(W \cdot m^{-2} \cdot K^{-1})$ is the heat transfer coefficient at the cryogen film-medium interface. Here h is the overall surface heat transfer coefficient (corresponding to the symbol H given in Carslaw and Jaeger [12]) which may or may not include surface convection. As $h \rightarrow \infty$, thermal resistance at the interface diminishes and a perfect contact between the two media is achieved; conversely, as $h \rightarrow 0$, thermal resistance becomes infinite. Since both T_∞ and h are unknown, experimental measurements are performed in this study to determine their value (as described in Section III).

Solution to (1) with boundary condition (2) is [12]:

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

where,

$$\text{erfcx}(x) = \exp(x^2)\text{erfc}(x) \quad (4a)$$

$$\tilde{h} = \frac{h\sqrt{\alpha t}}{k} \quad (4b)$$

$$\tilde{z} = \frac{z}{2\sqrt{\alpha t}}. \quad (4c)$$

In the above expressions, T_i is medium initial temperature prior to cooling, and $\text{erfc}(x)$ is the complementary error function ($1 - \text{erf}(x)$).

B. Infrared Radiometry

Since we used infrared radiometry in human skin to correlate with temperatures from an epoxy resin phantom, we also present the model used for estimation of radiometric temperatures in skin.

Radiometric measurements are dependent on both the temperature distribution below the surface and the infrared properties of skin in the detected spectral bandwidth ($3\text{--}5 \mu\text{m}$ in this study). The change in radiometric temperature, $\Delta S(t)$ ($^\circ\text{C}$), due to cooling is computed by integrating the infrared emission over all depths [13]:

$$\begin{aligned} \Delta S(t) = & C\mu_{\text{film}} \int_{-l(t)}^0 [T(z, t) - T_i] \\ & \times \exp\{-\mu_{\text{film}}[z + l(t)]\} dz \\ & + C\mu_{\text{skin}} \int_0^\infty [T(z, t) - T_i] \\ & \times \exp[-\mu_{\text{film}}l(t) - \mu_{\text{skin}}z] dz. \end{aligned} \quad (5)$$

Here, we assume that the presence of an infrared attenuating cryogen film [thickness, $l(t)$] contributes to the measured radiometric temperature change. Infrared attenuation coefficients of skin and cryogen film are denoted as μ_{skin} and μ_{film} (m^{-1}), respectively. C is a proportionality constant determined by the infrared detection system.

Substituting the expression for temperature distribution (3) into (6), we obtain the predicted radiometric temperature change due to CSC:

$$\begin{aligned} \Delta S(t) = & C(T_\infty - T_i) \left\{ \left[\frac{1 - \exp[-\mu_{\text{film}}l(t)]}{\tilde{\mu}_{\text{skin}} \text{erfcx}(\tilde{h}) - \tilde{h} \text{erfcx}(\tilde{\mu}_{\text{skin}})} \right] \right\} \\ & \quad (6) \end{aligned}$$

where $\tilde{\mu}_{\text{skin}} = \mu_{\text{skin}}\sqrt{\alpha_{\text{skin}}t}$.

III. MATERIALS AND METHODS

A. Internal Temperature Measurements in an Epoxy-Based Skin Phantom

A skin phantom was constructed by creating a solid block of an epoxy resin (EP30, Master Bond Inc., Hackensack, NJ) with four micro-thermocouples embedded at known subsurface positions. Thermal diffusivity of the epoxy resin had a manufacturer's reported value of $0.7 \cdot 10^{-7} m^2 \cdot s^{-1}$, within 36% of that for skin ($1.1 \cdot 10^{-7} m^2 \cdot s^{-1}$ [14]). We confirmed the thermal diffusivity value for the epoxy resin by means of a technique that utilizes self-heated thermistors [15]. Additionally, we confirmed the epoxy specific heat capacity by using a standard dual scanning calorimetry technique ($1650 \text{ J/kg}\cdot\text{K}$). Since skin is a multilayer structure, variations in thermal properties among various components (i.e., epidermis and dermis) occur. However, the main differences between epidermal and dermal properties result from the low water content in the *stratum corneum* whose thickness is only a fraction of the epidermis in most areas of skin. We believe

Fig. 1. Microthermocouple placement within epoxy resin phantom. Four $30\text{-}\mu\text{m}$ bead thermocouples were positioned at depths of 20, 90, 200, and $400\text{ }\mu\text{m}$ within the phantom. A fifth thermocouple was placed on the phantom surface to measure the cryogen film temperature.

that the value indicated above for the thermal diffusivity of skin, based on reported thermal conductivity of whole human skin [14], can be used as a good approximation in a simplified single-layer model, recognizing that a more complex multilayer model would be more accurate. It is also important to mention that for the short cryogen spurt durations used in this study (20–200 ms), undesirable phase change in tissue water (e.g., freezing) is not expected, and the absence of water in the phantom should not affect extrapolation of results to human skin.

Type K thermocouples (Chromega-Alumega, Omega Engineering, Inc., Stamford, CT), with a wire diameter of $12.7\text{ }\mu\text{m}$ and a sensing bead of $30\text{ }\mu\text{m}$ were used for temperature measurements. The thermocouples were carefully positioned and fixed on a thin epoxy resin slab under direct visualization through a dissecting microscope. The slab with attached thermocouples was later placed in a specially constructed Teflon mold which was filled with liquid epoxy resin. The epoxy resin with embedded thermocouples was allowed to cure for 72 h, resulting in a solid block with a front face of $6\text{ cm} \times 6\text{ cm}$ and a depth of 4 cm. The four thermocouples were positioned at the following depths: 20, 90, 200, and $400\text{ }\mu\text{m}$ (as measured from the epoxy resin front surface to the bead centers) (Fig. 1). The uncertainty in thermocouple positions due to microscope measurement error was $\pm 5\text{ }\mu\text{m}$. In addition to the four embedded subsurface thermocouples, a fifth thermocouple (same type and size) was placed on the epoxy resin phantom surface to measure cryogen film temperature. When sprayed directly with a cryogen spurt, the response time of the thermocouples (to 67%) was 1.5–2 ms, with a nearly 100% response in 3 ms.

The thermocouple wires from the phantom were connected to an external 14-bit A/D converter (instruNet Direct-Sensor-to-Data Acquisition system, Omega Engineering Inc., Stamford, CT) and a PCI controller card plugged into a computer. The system software was set to a sampling rate of 1 kHz for

Fig. 2. Schematics of the instrumentation used for (a) thermocouple measurements in response to CSC of epoxy phantom and (b) radiometric temperature measurements of skin in response to CSC and laser therapy.

each of the six input channels used (five for the thermocouples and one for the injector trigger signal).

B. Cryogen Spray Cooling of Epoxy Phantom

1,1,1,2 Tetrafluoroethane (Refrigerant 134a; National Refrigerants, Inc., Rosenhayn, NJ) (boiling point $\approx -26\text{ }^{\circ}\text{C}$ at 1 atm), an environmentally compatible, nontoxic, chlorofluorocarbon substitute [16]–[18] was used as the test cryogen. The refrigerant, contained in a pressurized steel canister, was delivered by an electronically controlled standard automobile fuel injection valve [Fig. 2(a)]. The refrigerant is maintained at liquid phase in the steel canister at room temperature by a pressure of $\approx 6\text{ atm}$. The refrigerant is atomized in liquid droplets upon exiting from the injector nozzle and its temperature instantaneously drops to its boiling point as it is suddenly exposed to atmospheric pressure. At the surface of

the phantom, a spot of approximately 1 cm in diameter was cooled by the spurt. The cryogen spurt duration, τ (20–100 ms), was controlled by a programmable digital delay generator (DG535, Stanford Research Systems, Sunnyvale, CA). Internal temperatures in the epoxy resin in response to CSC were measured as described in the previous section. The surface heat transfer coefficient was estimated by fitting the measured subsurface temperatures to the mathematical model for heat transfer described earlier.

C. Radiometric Temperature Measurements on PWS Patients

Radiometric surface temperature measurements were performed on three PWS patients undergoing laser therapy at the Beckman Laser Institute and Medical Clinic. The patients gave informed consent to participate in the study, approved by the University of California Medical Institutional Review Board (IRB). The experimental setup for radiometric measurements, CSC application, and laser delivery is shown in Fig. 2(b). Measurements were performed on PWS sites in response to CSC without laser irradiation, laser irradiation without CSC, and CSC immediately preceding laser irradiation.

Emission in the 3–5- μm spectral range was collected with an InSb infrared focal plane array (IR-FPA) camera (Model AE 4128, Amber Engineering Inc., Goleta, CA) configured for unit magnification. The camera system, which was externally triggered by the digital delay generator, acquired 1000 infrared emission images per second, each image consisting of 64×64 pixels. The infrared signal collected by each detector element in the focal plane array was digitized with a 12-bit A/D converter and stored in a computer. The infrared detection system was calibrated for temperature changes above and below the ambient value (23 °C). Average pixel values over a circular region (≈ 1 mm diameter; 800 pixels) were measured as a function of the surface temperature of: 1) an aluminum block coated with highly emissive ($\epsilon \approx 0.97$) black paint (TC-303 black, GIE Corp., Provo, UT) and heated by a resistive element from 23 °C to 75 °C and 2) a thermoelectric cooler (ITI FerroTec, Chelmsford, MA) coated with the same black paint, and cooled to –10 °C. Simultaneously, a surface mount precision thermistor (8681, Keithley Instruments, Cleveland, OH) measured the temperatures of the aluminum block and thermoelectric cooler.

Cryogen spurt duration was fixed at 40 ms in all cases. Prior to CSC of skin sites, the temperature of the cryogen spurt at the skin location was measured by means of a type K thermocouple (127- μm wire, 300- μm bead, Omega Engineering, Stamford, CT). PWS sites were irradiated with a FLPPDL (585-nm 0.45-ms pulse) (Candela Laser Corp., Wayland, MA) at $D = 7$ or 10 J/cm^2 radiant exposure. With $D = 7 \text{ J/cm}^2$, laser irradiation was performed either with or without cooling. With $D = 10 \text{ J/cm}^2$, all sites except two were irradiated in conjunction with CSC. The laser spot diameter was fixed at 5 mm.

Pulsed photothermal radiometry (PPTR) [19]–[23] of non-cooled irradiated sites was utilized in conjunction with a 1-D inversion algorithm [21] to estimate the unknown initial space dependent temperature increase in response to laser

Fig. 3. Example of epoxy resin internal temperatures in response to a 100-ms R-134a cryogen spurt.

irradiation. In the algorithm, a 1-D integral equation relates the measured radiometric temperature increase to the initial thermal profile in PWS immediately following laser pulse application. The 1-D integral equation is approximated as a linear matrix problem in which the initial thermal profile in PWS and a kernel function are represented by discrete vector and matrix quantities, respectively. A nonnegatively constrained conjugate gradient solution is used to estimate the profile. The skin emissivity within the detection bandwidth was assumed to be 1, which approximates closely reported values of 0.95–0.98 [24]–[26].

IV. RESULTS

A. Internal Temperatures in the Epoxy Phantom Due to CSC and Estimation of Surface Heat Transfer Coefficient

An example of thermocouple measurements in the epoxy resin phantom is shown in Fig. 3. The phantom was sprayed with a 100-ms cryogen spurt with the injector nozzle positioned 60 mm away from the surface. The cryogen film temperature on the epoxy resin surface was –44 °C during the spurt, well below the cryogen boiling point (–26 °C), indicating that the droplets cool substantially as they travel from the injector to the target. Note that the temperature measured by the thermocouple located 20 μm below the epoxy surface is approximately –14 °C at the end of the spurt, 30 °C above the cryogen film temperature. Liquid cryogen remains on the epoxy resin surface for ≈ 335 ms following spurt termination (≈ 435 ms from beginning of the spurt). Additional cooling of the thermocouple positioned on the surface occurs as cryogen adheres to the thermocouple bead for a longer time (up to ≈ 780 ms).

Computed and measured temperatures within the epoxy resin in response to a 100 ms cryogen spurt are presented in Fig. 4. Due to temperature averaging within the thermocouple bead, the effective measuring depth for each thermocouple was within $\pm 5 \mu\text{m}$ of the bead center. The depths used in the model were 20, 90, 200, and 400 $\mu\text{m} \pm 5 \mu\text{m}$. The curves for 400 μm depth are not shown because no change was observed from baseline during the 100-ms spurt. By fitting the measured temperature curve at 20 μm depth, the surface heat transfer coefficient (h) at the cryogen film–epoxy resin

Fig. 4. Theoretical versus measured internal temperatures in epoxy resin phantom in response to a 100-ms cryogen spurt.

Fig. 5. Theoretical versus measured radiometric surface temperature on PWS skin in response to a 40-ms cryogen spurt.

interface was estimated at $2400 \text{ W} \cdot \text{m}^{-2} \cdot \text{K}^{-1}$. Using the same h value, excellent agreement (within 5%–10%) was obtained between predicted and measured temperatures at depths of 90, 200, and 400 μm . The temperature of the cryogen film, measured by the thermocouple placed on the phantom surface, was -44°C .

B. Prediction of Skin Internal Temperatures in Response to CSC

To determine if the estimated value of h at the cryogen film–epoxy resin interface was consistent with that for human skin, we measured the radiometric surface temperature on skin of PWS patients in response to CSC and compared it with predictions by the heat transfer-infrared radiometry model using the same h . In the model, we used the reported value of $1.1 \cdot 10^{-7} \text{ m}^2 \cdot \text{s}^{-1}$ for thermal diffusivity of skin [14]. Infrared absorption coefficients of human skin and cryogen film were both fixed at 20000 m^{-1} , consistent with infrared absorption curves for water and cryogen in the IR-FPA camera spectral range. Based on previous interferometric estimations on a mirror surface [13], a cryogen film thickness of 14 μm was used. Comparison between predicted and measured radiometric temperatures on human skin during CSC with a 40-ms cryogen spurt is presented in Fig. 5. The good agreement between predicted and measured values indicates that the h value obtained for the epoxy resin phantom is valid for human skin. Similar agreement was obtained in each

Fig. 6. Predicted internal temperatures in human skin in response to a 200-ms cryogen spurt.

patient participating in this study by only varying the cryogen film thickness within a 13–15- μm range in the model.

Using the thermal diffusivity of skin and the estimated h value we predict human skin internal temperatures in response to CSC. Predicted temperatures are presented in Fig. 6 for a spurt duration as long as 200 ms. Temperature reductions of 31°C at the surface, 12°C at a depth of 100 μm , and 4°C at a depth of 200 μm are predicted for human skin, at the end of a 100 ms spurt. Temperature reductions of 38°C at the surface, 21°C at 100 μm , and 10°C at 200 μm are predicted at the end of a 200 ms spurt. A temperature reduction of only 1.5°C is predicted at a depth of 400 μm for this spurt duration.

C. CSC in Conjunction With Laser Irradiation of PWS

Radiometric surface temperature measurements were performed on PWS patients during laser irradiation. Measured radiometric signals on PWS sites in response to 7 and 10 J/cm^2 radiant exposures are presented in Fig. 7(a). Measurements correspond to two separate irradiated sites on the same patient without CSC. A 1-D inversion algorithm [21] was used to compute the unknown initial space dependent temperature increase from the radiometric measurements [Fig. 7(b)]. Temperature within the epidermis peaks at a depth of approximately 75–80 μm . The respective temperatures at this location in response to 7 and 10 J/cm^2 radiant exposures are 63 and 76°C , respectively. In the layer of blood vessels, the respective peak temperatures are 46°C and 53°C . These last peak values correspond to the respective average temperature at a depth of 510 μm , and are not temperature of individual vessels. PWS vessels are shown distributed in depth from 400 to 800 μm .

Predicted temperature distributions within skin in response to CSC alone (100 ms spurt), laser irradiation alone (10 J/cm^2), and laser irradiation immediately following CSC are presented in Fig. 8. The temperature distribution in response to laser irradiation with CSC was obtained by superposition of the other two distributions. The temperature distribution resulting from such superposition indicates that, by applying CSC immediately before laser irradiation, considerable temperature reduction is obtained at the epidermal surface ($z = 0$), but less dramatic effect is obtained at depths of 75–100 μm . For a 100-ms spurt, CSC does not reduce the laser induced temperature

(a)

(b)

Fig. 7. (a) Pulsed photothermal radiometry signals from PWS sites irradiated with 7 and 10 J/cm² radiant exposures. (b) Temperature profiles within skin obtained by 1-D inversion of the radiometric signals.

increase in the layer of PWS vessels (400–600 μm below the skin surface in this patient). When laser irradiation is applied in conjunction with CSC, the epidermal peak temperature induced by the laser pulse is expected to cool rapidly, as radiometric surface temperature measurements indicate. In Fig. 9, radiometric surface temperatures measured at four separate PWS sites are presented. In two sites, CSC was used without laser irradiation. In the other two sites, a 10-J/cm² radiant exposure was applied in conjunction with CSC. The radiometric surface temperature is reduced immediately following the laser pulse due to presence of the cryogen film on the surface. No surface temperatures above 30 °C are recorded during or following application of the laser pulse. This is in contrast with Fig. 7(a), where much slower temperature reduction (heat dissipation) occurs following the pulse because of an insulating skin surface.

V. DISCUSSION

Adequate clearing of PWS lesions is not achieved in many patients with currently used irradiation parameters even after multiple laser treatments. Irreversible thermal injury of many enlarged blood vessels is not achieved because of insufficient heat generation therein. Increased heat deposition in the vessels can be obtained with the use of higher laser fluence or longer laser pulse duration, but excessive heating of the epidermis due to melanin absorption must be avoided. CSC can protect the epidermis from nonspecific thermal

Fig. 8. Predicted temperature profiles within skin in response to CSC alone (100 ms spurt), laser irradiation alone (10 J/cm²), and laser irradiation immediately following CSC. The temperature distribution in response to laser irradiation with CSC was obtained by superposition of the other two distributions.

Fig. 9. Measured radiometric surface temperatures in response to 40-ms R-134a cryogen spurts at four separate PWS sites, with laser irradiation at 10-J/cm² radiant exposure in two sites, and no laser irradiation in the other two sites.

injury during laser treatment of the PWS while still allowing photocoagulation of targeted blood vessels [6]–[11]. Since epidermal melanin concentration and blood vessel depth vary among patients, evaluation of internal skin temperatures in response to CSC is essential for further development and optimization of treatment parameters on an individual patient basis. In this study, we have measured internal temperatures in an epoxy resin phantom in response to CSC and used the results in conjunction with a mathematical model to predict the temperature distribution within human skin. Effect of CSC on skin temperature induced during laser therapy of PWS has also been assessed.

The epoxy resin phantom used in this study allowed controlled positioning of microthermocouples and provided a stable testing medium for CSC. The phantom also allowed estimation of the surface heat transfer coefficient that is critical for any quantitative determination of skin internal temperatures in response to CSC. Temperature measurements of the cryogen film over the epoxy resin surface and at a depth of 20 μm within the epoxy resin show a considerable temperature difference that indicates poor thermal contact at the cryogen film–epoxy interface. This poor thermal contact results in a low surface heat transfer coefficient when compared to typical

coefficients associated with liquid evaporation on a surface (phase change) [26], [27]. The temperature of the cryogen film measured at the epoxy resin surface, sprayed from a distance of 60 mm was -44°C , well below the cryogen boiling point; an indication that the cryogen droplets are significantly cooled as they evaporate in flight toward the target surface. Therefore, the temperature of the cryogen film over the surface is highly affected by spraying distance.

Once the surface heat transfer coefficient was estimated, temperatures predicted by the heat transfer model matched those measured by the thermocouples placed deeper in the epoxy resin (at 90, 200, and $400\text{ }\mu\text{m}$) within a few percent. In addition, the radiometric surface temperature measurements confirmed that the estimated value of the surface heat transfer coefficient at the cryogen-epoxy phantom interface was approximately the same as that for the cryogen-human skin interface.

With the cryogen used in this study (R-134a), temperature reductions of 31°C at the surface, 12°C at a depth of $100\text{ }\mu\text{m}$, and 4°C at a depth of $200\text{ }\mu\text{m}$ are predicted for human skin at the end of a 100-ms spurt. Further temperature reductions of 7°C at the surface, 9°C at $100\text{ }\mu\text{m}$, and 6°C at $200\text{ }\mu\text{m}$ are predicted when the spurt duration is increased to 200 ms. A temperature reduction of only 1.5°C is predicted at a depth of $400\text{ }\mu\text{m}$ for a spurt duration of 200 ms, and no temperature reduction is predicted for a 100-ms spurt. Based on temperature profiles induced by laser irradiation [Figs. 7(b) and 8], a cryogen spurt duration shorter than 100 ms may be inadequate to counteract the initial temperature increase at the epidermal basal layer when radiant exposures greater than 10 J/cm^2 are used. Since PWS capillaries may be very superficial ($\leq 200\text{ }\mu\text{m}$ [21], [23]) in many patients, spurt durations longer than 100 ms may result in undesirable cooling of the vessels. For deeper PWS blood vessels (i.e., $400\text{ }\mu\text{m}$ [28]), a 200-ms spurt duration appears desirable because temperature reduction at this depth is not expected.

The profiles presented in Fig. 7(b) provide important insight on internal skin temperatures that result from pulsed laser treatment of PWS. The two peaks in the curve of induced temperature rise correspond to light absorption at the epidermis and at the layer of highest blood vessel concentration. Irreversible damage to PWS vessels has been assumed to occur at an intravascular temperature of 80°C or higher [23], [29]. Based on the 1-D inversion of the radiometric temperature signals, the average temperatures within the targeted blood vessel layer are 46°C and 53°C immediately after the laser pulse for radiant exposures of 7 and 10 J/cm^2 , respectively [Fig. 7(b)]. Since the initial base temperature is assumed to be 30°C , the average temperature increase induced by the laser pulse in response to 7 and 10 J/cm^2 radiant exposures is 16 and 23°C , respectively. The temperature at individual blood vessels cannot be determined with the use of the 1-D inversion technique. However, since the density of PWS vessels in the dermis can be as low as 10% [20], [28], the temperature rise in individual vessels could be 5–10 times higher than the average temperature rise measured by the PPTR/1-D inversion method. The figure also indicates that PWS vessels are in this case

mainly distributed between 400 and $800\text{ }\mu\text{m}$ below the skin surface.

In Fig. 7(b), peak epidermal temperatures immediately after the laser pulse are 63 and 76°C for 7 and 10 J/cm^2 radiant exposures, respectively. As epidermal temperature increases with increasing radiant exposure, the risk of severe thermal injury increases, even before the reported threshold temperature for melanosome explosion (110°C , [30]) is reached. Here, the choice of CSC parameters is critical. According to the results shown in Fig. 8, maintaining the peak temperature increase at the epidermal basal layer ($75\text{--}100\text{-}\mu\text{m}$ subsurface) below the threshold for epidermal damage presents the main challenge in application of CSC. Nevertheless, even without achieving a dramatic reduction of this peak temperature in the deep epidermis at the time of laser exposure, CSC accelerates its vanishing by increasing heat dissipation following the laser pulse, thereby reducing the risk of damage caused by persistence of high temperature over time. Further studies are needed to investigate the thermal events taking place after termination of the spurt and the effect of liquid cryogen remaining on the skin surface after pulsed laser irradiation.

It is important to point out that for the short spurt durations used in this study (20–200 ms), freezing of water within the skin is not expected. In addition, a temperature of only -1°C is predicted at the surface at the end of 100 ms. Although the predicted surface temperature drops to -8°C at the end of a 200 ms spurt, the temperature throughout most of the epidermis is predicted to remain above 0°C , reaching a minimum of $+9^{\circ}\text{C}$ at a depth of $100\text{ }\mu\text{m}$. Certainly, if longer spurt durations are to be used and lower temperatures are achieved, water freezing within the skin must be taken into account and latent heat release and thermal property changes need to be included in a mathematical model. Freezing of skin is undesirable and must be avoided since it will damage the epidermis that we are precisely trying to protect. The laser pulse, however, applied immediately after the cryogen spurt quickly raises the skin temperature above 0°C .

In previous studies [10], [11], [13], a mixture of cryogen and ice was believed to form over the skin surface during spurt application, the ice resulting from the fast freezing of water vapor in the ambient air. In our recent experiments applying CSC to the epoxy phantom and other materials, we have observed that ice forms over the surface only after the liquid cryogen film has completely evaporated. No ice deposits on the surface during the cryogen spurt. Therefore, the effects of ice formation have not been included in our model. Any future mathematical modeling of thermal events occurring after the spurt should take into account deposition of ice over the skin surface. In this case, however, the subsequently applied laser pulse and heat diffusing from deeper layers of the warm skin reduce the ice life time when compared to the case of ice formation over the epoxy phantom used in this study.

Improvements in cooling efficiency can be achieved by optimization of control variables, including selection of cryogen, choice of atomizer (injector), and variation of spraying distance. Cryogens R-404a and R-407c with boiling points of ≈ -48 and -43°C , respectively, can provide additional cooling when compared with R-134a [31]. An optimal spray-

ing distance can be defined for specific cryogen and atomizer to allow further cooling of the cryogen droplets by in-flight evaporation while still delivering sufficient amount of liquid to the skin surface. Further investigation on these control variables is important for optimization of CSC and improvement in patient treatment outcome when used in conjunction with laser irradiation.

VI. CONCLUSION

Internal temperature measurements in an epoxy resin phantom provide data for quantitative analysis of the thermal response of human skin to CSC. A mathematical model based on simple thermal diffusion theory can be used in conjunction with measurements in the phantom to predict internal skin temperatures. At the skin surface, cryogen temperature is significantly lower than the cryogen boiling point, but a high thermal resistance is present at the cryogen film-human skin interface. Estimated internal temperature distributions indicate that a significant protective effect at the surface of laser irradiated PWS skin is achieved with CSC. Protection of the epidermal basal layer, however, poses the greatest challenge when high radiant exposures are used. Predicted temperature distributions in response to CSC can be combined with temperature profiles obtained by 1-D inversion of radiometric surface temperatures to choose appropriate cooling parameters on an individual patient basis.

ACKNOWLEDGMENT

The authors would like to thank J. C. Yu for his contribution to the construction of the epoxy resin phantom and assistance with the cryogen experiments, L.-H. Liaw for her invaluable technical support, S. Telenkov and W. Verkruysse for their assistance with the infrared measurements and data analysis, Q. Liu and R. K. Meszlenyi for their assistance with heat capacity measurements of the epoxy resin, N. C. Bhavaraju for performing thermal conductivity and diffusivity measurements on the epoxy resin, D. Smithies for his help regarding use of proper parameters in the 1-D inversion algorithm, and S. Kimel for helpful discussions on cryogen thermodynamics.

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