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# Analysis of nonablative skin resurfacing

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## ABSTRACT

Nonablative skin resurfacing is a dermatologic procedure utilizing pulsed laser irradiation and dynamic cooling to induce selectively a wound healing response in the papillary and upper reticular dermis. Using temperature measurements of human skin provided by pulsed photothermal radiometry immediately following laser irradiation ($\lambda$=1.32 μm), spatial distribution of thermal damage is predicted in response to various potential therapeutic laser-cryogen doses. Results of our analysis suggest that appropriate application of pulsed laser irradiation and cryogen spray cooling may be used to protect the epidermis and selectively confine thermal injury to the papillary and upper reticular dermis. Development of nonablative skin resurfacing will require understanding the relationship between the degree of dermal photocoagulation and the cutaneous wound healing response following laser irradiation.

## 1. INTRODUCTION

Laser-assisted skin resurfacing recently has emerged as a dermatologic procedure for reducing facial rhytides (i.e., wrinkles). In practice, a superficial layer of skin material is removed through an ablative mechanism frequently utilizing infrared radiation emitted from a $CO_2$ laser (10.6 μm). Recent investigations into the origin of the underlying mechanisms of laser ablative resurfacing procedures, however, indicate removal of skin material may not be the only process required for successful therapeutic outcome. In a histological study, Cotten et. al. noted reduction of human facial rhytides following $CO_2$ laser skin resurfacing may correspond to the formation of a new band of connective tissue formed in the papillary dermis.[1] The new tissue was composed of dense, compact collagen bundles oriented parallel to the skin surface. In addition, thickness of the new band of connective tissue strongly correlated to a corresponding measure of thermal denatured collagen. A light microscopic polarization sensitive histological study by Thomsen et. al., of rodent skin irradiated with laser parameters corresponding to a $CO_2$ resurfacing procedure in humans indicated thermal alteration of collagen fibrils in the dermis may occur at depths up to 250 μm.

Inasmuch as the $CO_2$ resurfacing technique partially relies on induction of a wound healing response following thermal injury in the superficial skin layers, a novel laser procedure utilizing "dynamic cooling" has been devised to protect the epidermis from damage while achieving thermal denaturation of proteins in the papillary and upper reticular dermis. In this procedure, the epidermis is rapidly cooled prior to pulsed laser irradiation by a short spurt of cryogen sprayed onto the skin surface.[2] Subsequent absorption of pulsed laser energy by water in skin results in a temperature increase in the papillary dermis sufficient to cause spatially selective protein thermal denaturation. Because skin temperature at superficial depths is decreased by dynamic cooling, thermal injury in the epidermis may be substantially reduced or eliminated.

The purpose of this study is to use temperature measurements provided by pulsed photothermal radiometry of human skin immediately following laser irradiation to predict the spatial distribution of thermal damage in response to various potential therapeutic laser-cryogen doses. Application of a non-negatively constrained conjugate gradient inversion algorithm[3] and model of dynamic cooling are used to predict the space-time temperature response of skin. Spatial distribution of thermal injury is computed at potential therapeutic laser-cryogen doses by application of a first-order rate

damage model.[4] Comparison of the predicted spatial distribution of thermal injury in skin with that observed in animal model studies is discussed.

## 2. METHODS AND MATERIALS

To evaluate the thermal response of human skin to laser irradiation without dynamic cooling, pulsed photothermal radiometry measurements (PPTR) are recorded[5] at seventy-one in-vivo test sites on volar forearm of human volunteers. The radiometric temperature change ($\Delta S(t)$) of an irradiated site is measured by collecting and focusing infrared emission from the skin onto a 1 $mm^2$ liquid nitrogen cooled HgCdTe detector sensitive in the 10-14 μm spectral region. An f/1, 25 mm diameter germanium lens configured for unit magnification is positioned 50 mm from the detector to give a 1 $mm^2$ square field at the skin surface. A silica multimode optical fiber (400 μm core diameter) is used to deliver pulsed laser radiation ($\lambda$=1.32 μm) emitted from the open tip onto the skin surface. Value of laser dosage (5-30 $Jcm^{-2}$) is determined for each irradiated skin site from independent measurements of the spot size (17-28 $mm^2$) and pulse energy (1-5.3 J).

For each recorded PPTR signal ($\Delta S(t)$), the one-dimensional spatial distribution of the initial temperature increase in skin ($\Delta T_L(z,t=0^+)$) immediately following pulsed laser irradiation is computed by application of a non-negatively constrained conjugate gradient inversion algorithm;[6] $\Delta S(t)$ and $\Delta T_L(z,t=0)$ are related by a Fredholm integral equation of the first kind (Eq. 1A).

$$\Delta S(t) = (C_d \mu_a / 2) \int_{z=0}^{z=\infty} \Delta T_L(z,0) \cdot \exp\left(-\frac{z^2}{4Dt}\right) \left[ \operatorname{erfcx}(u_-) + \operatorname{erfcx}(u_+) - \frac{2h_{as}}{h_{as} - \mu_a} \left( \operatorname{erfcx}(u_+) - \operatorname{erfcx}(u_1) \right) \right] \quad \textbf{(1A)}$$

Here, $\mu_a$ is the infrared absorption coefficient of skin at the detected wavelength(s), and $C_d$ is a proportionality constant determined by the detection system. Additionally, $\operatorname{erfcx}(u)=\exp(u^2)\cdot\operatorname{erfc}(u)$ is the exponential complementary error function and $u_{\pm,1}$ are functions (Eq. 1B) of space (z), time (t), thermal diffusivity of skin (D), and heat transfer coefficient ($h_{as}$) of the air-skin boundary.

$$u_\pm = \mu_a \sqrt{Dt} \pm z / 2\sqrt{Dt} \qquad u_1 = h_{as} \sqrt{Dt} + z / 2\sqrt{Dt} \quad \textbf{(1B)}$$

Spatial temperature distribution immediately following cryogen spray cooling ($\Delta T_c(z,t=0)$, Eq. 2A) has been extensively investigated experimentally and theoretically by Anvari et. al.,[2]

$$\Delta T_c(z, t + t_c) = (T_\infty - T_o) \left\{ \operatorname{erfc}(\tilde{z}) - \left[ \exp(\tilde{h}_c^2 + 2\tilde{h}_c \tilde{z}) \ \operatorname{erfc}(\tilde{h}_c + \tilde{z}) \right] \right\} \quad \textbf{(2A)}$$

$$\tilde{z} = z / \sqrt{D(t + t_c)} \qquad \tilde{h}_c = (h_c / k) \sqrt{D(t + t_c)} \quad \textbf{(2B)}$$

Here, $-t_c < t \le 0$, where $t_c$ is the spray cooling time, $T_\infty$ is the temperature of the cryogen-ice mixture on the skin (e.g., $T_\infty$= -10 °C), and $T_o$ is the initial skin temperature. Immediately following pulsed laser irradiation, we assume a heat loss coefficient $h_{as}$ at the air-skin boundary so that the spatial distribution of the initial temperature increase ($\Delta T(z,t=0)$) is a superposition (Eq. 3) of responses.

$$\Delta T(z, t = 0) = \Delta T_L(z, t = 0) + \Delta T_c(z, t = 0) \quad \textbf{(3)}$$

Knowledge of the thermal diffusivity (D) of human skin[7] together with the spatial distribution of the initial temperature increase ($\Delta T(z,t=0)$) allows computation of the space-time evolution of the thermal profile (Eq. 4, $\Delta T(z,t)$),

$$\Delta T(z,t) = \frac{1}{(4\pi Dt)^{1/2}} \int_{z'=0}^{z'=\infty} \Delta T(z',0) \cdot \left\{ \begin{array}{c} \exp\left[(z - z')^2 / 4Dt\right] + \exp\left[(z - z')^2 / 4Dt\right] \cdot \\ \left[1 - h_{as} \sqrt{4\pi Dt} \ \exp(u^2) \ \operatorname{erfc}(u)\right] \end{array} \right\} \quad \textbf{(4)}$$

Spatial distribution of thermal injury (I(z)) is computed at two potential therapeutic laser doses (25 $Jcm^{-2}$ and 30 $Jcm^{-2}$) by application of a first-order rate damage model (Eq. 5),

$$I(z) = 1 - \exp\left[ - \int_{t=0}^{t=\infty} A(T(z,t)) \exp\left(\frac{-E_A(T(z,t))}{RT(z,t)}\right) \, dt \right] \quad (5)$$

here, I(z) represents the fraction ($0 \leq I(z) \leq 1$) of denatured protein at depth z. Values for temperature dependent parameters [i.e., A(T(z,t)) and $E_A(T(z,t))$] in the damage integral (Eq. 5) were determined by Weaver and Stoll.[8] We summarize (Figure 1) the processing steps to compute the fraction of denatured protein (I(z)) from a measured PPTR signal ($\Delta S(t)$).

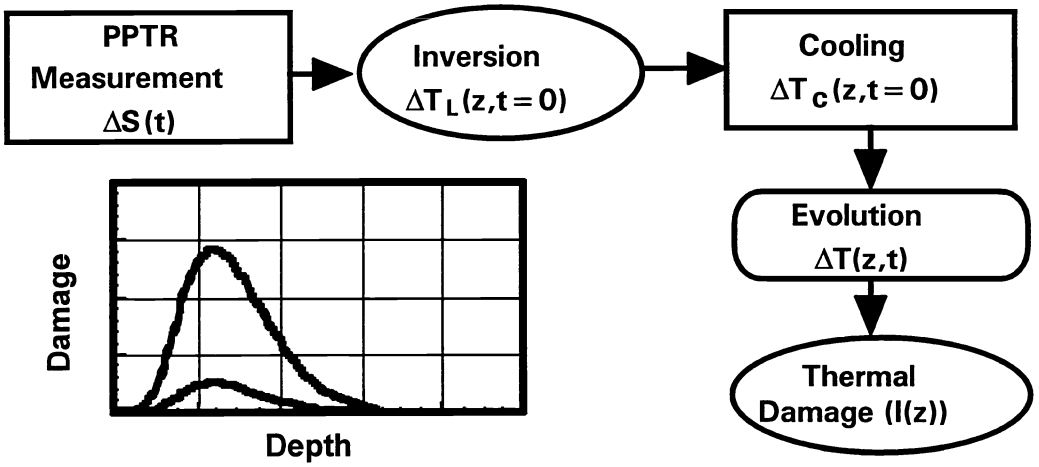


**Figure 1:** Steps to compute the fraction of denatured protein (I(z)) from a measured PPTR signal ($\Delta S(t)$).

## 3. RESULTS

PPTR signals recorded in response to pulsed laser irradiation indicate a rapid temperature increase followed subsequently by a slower monotonic decrease (Figure 2A). Application of the non-negatively constrained conjugate gradient inversion algorithm to the measured PPTR signal ($\Delta S(t)$) indicates a subsurface peak of the initial temperature increase with a monotonic decrease at deeper positions (Figure 2B). Magnitude of the temperature decay with increasing skin depth given by the inversion algorithm is greater than that predicted from simple diffusion theory; we believe the observed difference may be due to the use of one-dimensional models that do not correctly account for lateral propagation of photon or thermal flux.

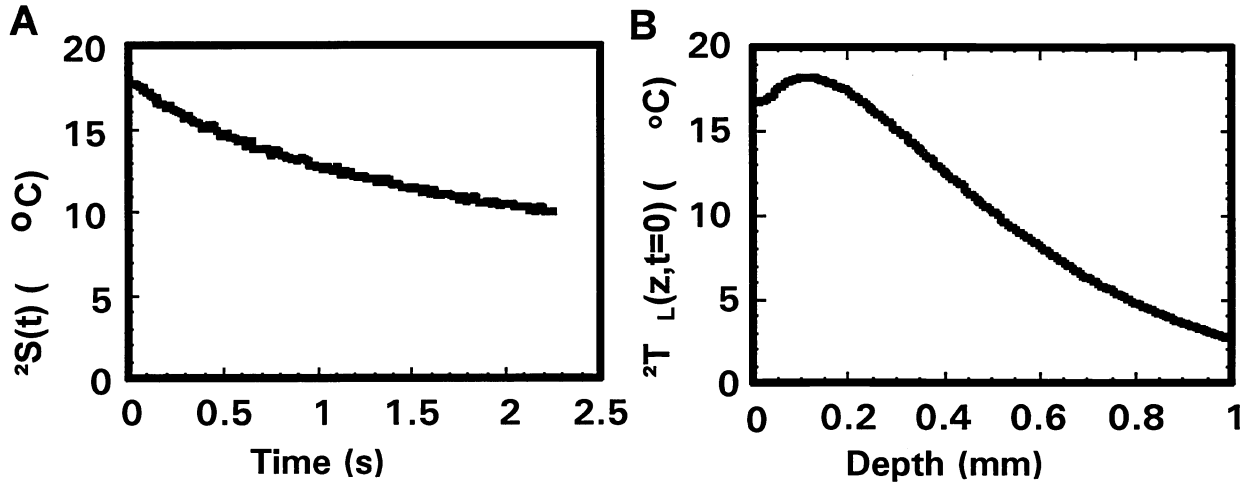


**Figure 2:** (A) Example measured PPTR signal ($\Delta S(t)$) with incident light dose D=13.6 $Jcm^{-2}$; (B) Computed initial spatial temperature distribution ($\Delta T_L(z,t=0)$) immediately following pulsed laser irradiation, subsurface peak at z=0.13 mm.

The peak temperature increase ($\Delta S_{peak}$) from recorded PPTR signals is plotted (Figure 3) versus the corresponding laser dose for each in-vivo skin test site. The recorded data suggest $\Delta S_{peak}$ varies linearly with increasing dose. Linear least squares analysis of the recorded data gives a slope of 1.2 ($^oCJ^{-1}cm^2$).

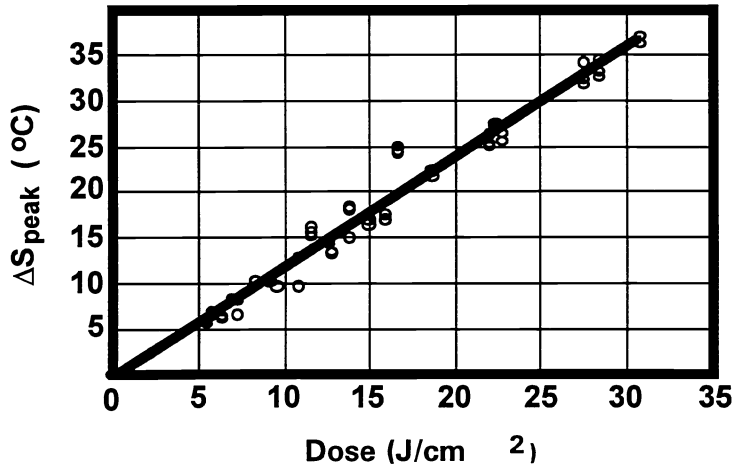


**Figure 3:** Peak temperature increase ($\Delta S_{peak}$) from recorded PPTR signals at corresponding laser dose. Solid line is linear least squares fit to recorded data points.

Each computed initial spatial temperature distribution ($\Delta T_L(z,t=0)$) determined by application of the non-negatively constrained conjugate gradient inversion algorithm is extrapolated to values corresponding to potential therapeutic laser doses of 25 and 30 ($Jcm^{-2}$) by a simple multiplicative factor.

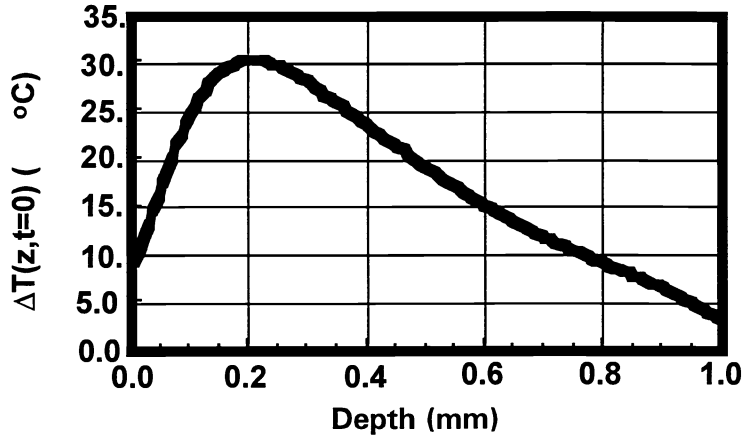


**Figure 4:** Computed initial temperature increase ($\Delta T(z,t=0)$) following pulsed laser irradiation ($D=25$ Jcm$^{-2}$) and cryogen spray cooling ($t_c=40$ ms, $T_\infty=-10$ °C, and $h_c=40$ kWm$^{-2}$).

The initial temperature increase ($\Delta T(z,t=0)$) due to pulsed laser irradiation and cryogen spray precooling ($t_c=40$ ms, $T_\infty=-10$ °C, and $h_c=40$ kWm$^{-2}$) is determined by superposing $\Delta T_L$ and $\Delta T_C$ (Figure 4). The combined effect of pulsed laser irradiation and cryogen spray cooling selectively reduces temperature of the epidermis while creating a peak subsurface increase at $z=0.2$ mm.

Determination of thermal damage distribution (I(z)) following pulsed laser irradiation and cryogen spray cooling requires computation of $\Delta T(z,t)$. Computation of $\Delta T(z,t)$ at three time points (Figure 5) indicate thermal energy diffuses into the epidermis and deeper positions in the skin.

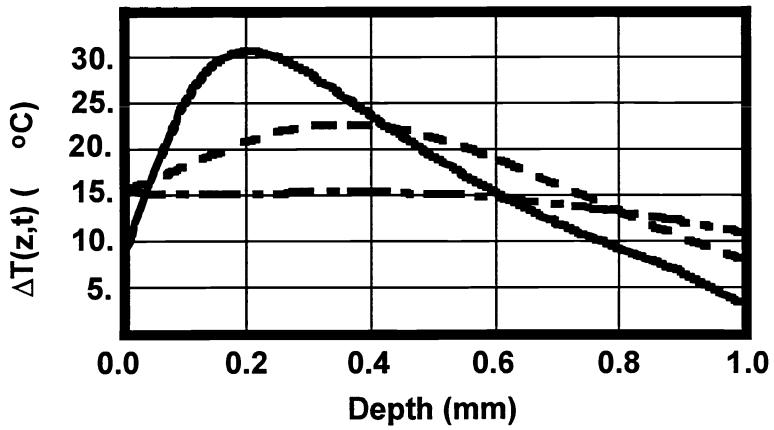


**Figure 5:** Temperature distribution in the skin at three times following pulsed laser irradiation ($D=25.0$ Jcm$^{-2}$) and cryogen spray cooling ($t_c=40$ ms, $T_\infty=-10$ °C, and $h_c=40$ kWm$^{-2}$): t=0 s(_____), t=0.35 s (_ _ _ _), and t=1.4 s (_ . _ . _ . _).

Spatial distribution of thermal injury (I(z)) was computed using the damage integral analysis discussed above (Eq. 5). Mean fraction of denatured protein (Figure 6) was determined by averaging each I(z) for for each irradiated skin site at potential therapeutic doses, $D=25$ Jcm$^{-2}$ and 30 Jcm$^{-2}$.

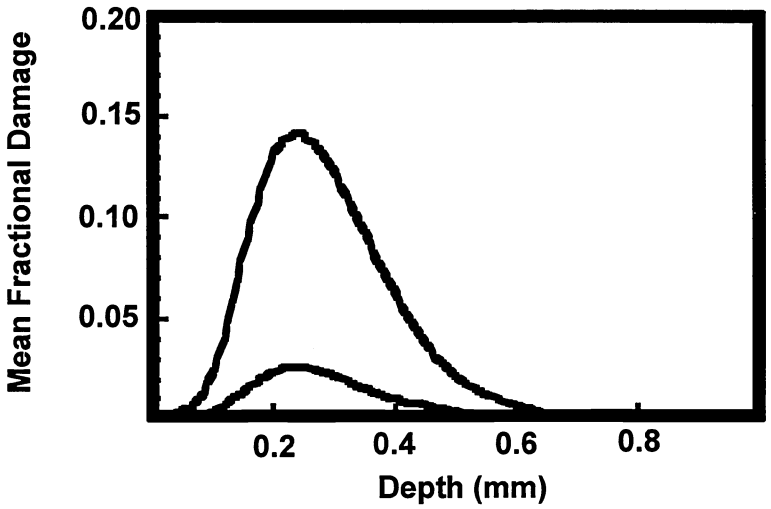


**Figure 6:** Computed mean fractional damage of denatured protein corresponding to incident laser dosse of 25 $Jcm^{-2}$ (Lower Curve) and 30 $Jcm^{-2}$ (Upper Curve).

Mean spatial distribution of thermal injury is concentrated in the papillary dermis approximately 0.25 mm deep. Increased laser dose (i.e., 30 $Jcm^{-2}$) results in a more extensive and greater fraction of denatured protein in superficial skin layers.

## 4. DISCUSSION

Results of our analysis suggest that appropriate application pulsed laser irradiation and cryogen spray cooling may be used to protect the epidermis and selectively confine the spatial distribution of thermal injury to the papillary and upper reticular dermis. Although a number of assumptions (e.g., one-dimensional model) in our analysis may compromise the numerical accuracy of the results, the ability to limit preferentially spatial distribution of thermal injury to the papillary dermis is supported by histological studies in a porcine skin model.[9] Furthermore, although the spatial distribution of thermal injury in skin may be confined in the papillary and upper reticular dermis, therapeutic efficacy of nonablative skin resurfacing is determined primarily by the cutaneous wound healing response.

Despite the advances that have been achieved in understanding the important cellular and biochemical processes involved in the cutaneous wound healing response,[10] many important questions remain. For example, changes in the wound healing response for various levels of dermal photocoagulation and accompanying damage to the skin microvasculature require additional study. Specifically, in nonablative skin resurfacing, dermal photocoagulation just above the thermal damage threshold will result in slightly increased levels of new collagen and proteoglycan synthesis. As the degree of dermal photocoagulation becomes greater, subsequent protein synthesis will also increase in order to replace greater quantities of thermally damaged tissue. One may not expect, however, that the degree of dermal photocoagulation may be arbitrarily increased in nonablative resurfacing procedures without increasing the risk of complications such as blistering, induration, or possibly skin sloughing. For example, increased levels of dermal photocoagulation may irreversibly damage and temporarily occlude the microvasculature in the papillary dermis resulting in a thick (~300 μm) region of necrotic tissue which can not be regenerated without sloughing.

Inasmuch as the primary advantage of nonablative skin resurfacing is reduced patient discomfort and simpler post-operative wound care, retaining the viability of at least a portion of the dermal microvasculature is important. Additional quantitative studies are required to ascertain accurate values of the scattering coefficient of the papillary and reticular dermis and the dependence of subsurface fluence on the numerical aperture of incident light. Inasmuch as the optical properties of skin vary between different sites and subjects, a subtherapeutic diagnostic temperature measurement in response to pulsed laser irradiation may be required to determine the appropriate cryogen-laser dosimetry. Most importantly, understanding the relationship between the degree of dermal photocoagulation and the subsequent cutaneous wound healing response is fundamental to: (1) predicting the limitations and clinical efficacy of nonablative skin resurfacing; and (2) optimizing the treatment for selected facial rhytides.

## ACKNOWLEDGEMENTS

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