On the physics of laser-induced selective photothermolysis of hair follicles: Influence of wavelength, pulse duration, and epidermal cooling

Lars O. Svaasand
Norwegian Univeristy of
   Science and Technology
NO-7491 Trondheim, Norway
   and
University of California
Beckman Laser Institute
1002 Health Sciences Road East
Irvine, California 92612
E-mail: svaasand@fysel.ntnu.no

J. Stuart Nelson
University of California
Beckman Laser Institute
1002 Health Sciences Road East
Irvine, California 92612

Abstract. The physical basis for optimization of wavelength, pulse duration, and cooling for laser-induced selective photothermolysis of hair follicles in human skin is discussed. The results indicate that the most important optimization parameter is the cooling efficiency of the technique utilized for epidermal protection. The optical penetration is approximately the same for lasers at 694, 755, and 800 nm. The penetration of radiation from Nd:yttrium–aluminum–garnet lasers at 1064 nm is, however, somewhat larger. Photothermal damage to the follicle is shown to be almost independent of laser pulse duration up to 100 ms. The results reveal that epidermal cooling by a 30–80-ms-long cryogen spurt immediately before laser exposure is the only efficient technique for laser pulse durations less than 10 ms. For longer pulse durations in the 30–100 ms range, protection can be done efficiently by skin cooling during laser exposure. For laser pulses of 100 ms, an extended precooling period, e.g., by bringing a cold object into good thermal contact with the skin for about 1 s, can be of value. Thermal quenching of laser induced epidermal temperature rise after pulsed exposure can most efficiently be done with a 20 ms cryogen spurt applied immediately after irradiation. © *2004 Society of Photo-Optical Instrumentation Engineers.* [DOI: 10.1117/1.1646174]

Keywords: cryogen spray cooling; contact cooling; air cooling; ruby laser; alexandrite laser; gallium–aluminum–arsenide laser diodes; neodymium–yttrium–aluminum–garnet laser.

Paper 014011 received Apr. 8, 2003; revised manuscript received Jun. 20, 2003; accepted for publication Jul. 1, 2003.

1 Introduction

The laser has many inherent properties that contribute to its ability to affect a specific therapeutic outcome. Most important, from a clinical point of view, are the properties of emitted wavelength and pulse duration. If the clinical objective is to cause selective destruction of a specific chromophore, the wavelength chosen should match the absorption of the targeted chromophore relative to other optically absorbing molecules.

Given that one goal of treatment is the precise control of thermal energy, the pulse duration of laser irradiation is just as important as optical and tissue factors.

Laser-induced selective photothermolysis has been used with promising results on many cutaneous targets, ranging from destruction of tattoo pigment granules, removal of ectactic port wine stain blood vessels, and to destruction of hair follicles.[1–6] Simultaneously, the upper pigmented layer of the skin, i.e., the epidermis, must be protected to avoid scarring and dyspigmentation. Epidermal preservation has been accomplished with several cooling techniques, such as contact cooling, cryogen spray cooling and cooling by forced airflow. The optimal cooling technique is dependent on laser pulse duration, as efficient cooling must be done immediately be-

fore laser exposure (precooling) for laser pulses shorter than about 10 ms, whereas cooling during laser exposure (parallel cooling) might be necessary for longer pulses. Finally, quenching of the temperature rise by cooling immediately after laser exposure is also of value (postcooling).[7,8]

This paper will focus on the physics of problems encountered in selective destruction of hair follicles in human skin. A variety of different lasers have been used for this purpose, ranging from ruby lasers ($Cr:Al_2O_3$) at a wavelength of 694 nm, alexandrite lasers ($Cr:BeAl_2O_4$) at 755 nm, gallium–aluminum–arsenide (GaAlAs) diode lasers around 800 nm to Nd:yttrium–aluminum–garnet (YAG) lasers ($Nd:Y_3Al_5O_{12}$) at 1064 nm. The pulse duration is usually dependent on the specific laser system, and pulses of 1–100 ms are typically used in the clinic. In order to facilitate extrapolation of the results in this paper to other wavelengths and pulse durations, the presentation will, as much as possible, be based on analytical solutions of the heat transfer equations.

2 Light Propagation in Skin

Light propagation in human skin in the 600–1100 nm wavelength region is strongly dominated by scattering and can therefore be adequately approximated by optical diffusion theory[9]

Address all correspondence to Lars O. Svaasand. Tel: 47-73-594-421; Fax: 47-73-591-441; E-mail: svaasand@fysel.ntnu.no.
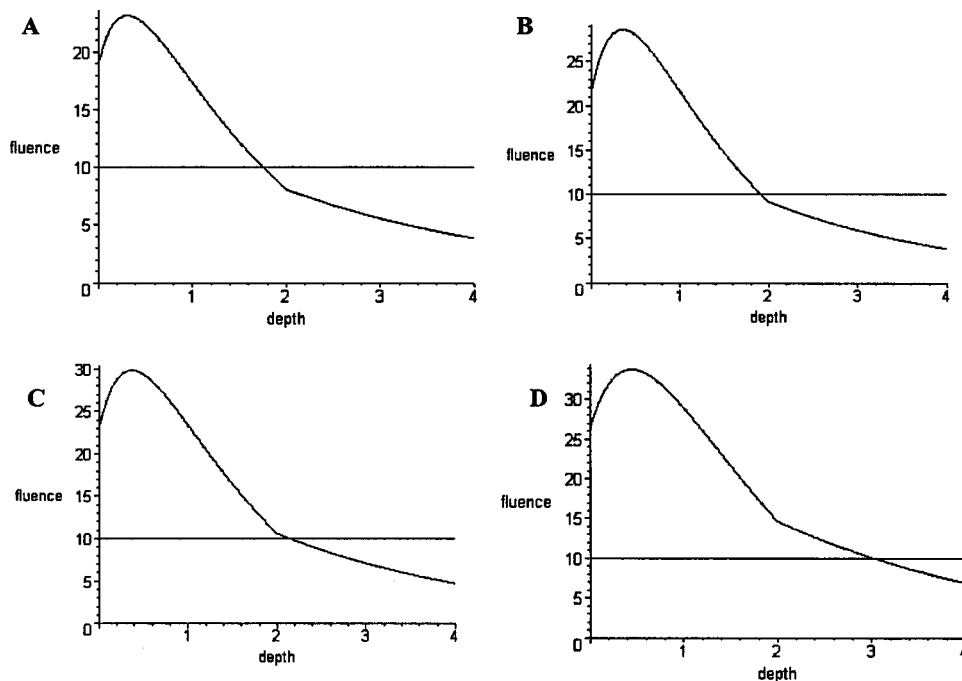
Fig. 1 Spatial distribution of diffuse light in moderately pigmented human skin (Fitzpatrick II-III) at four different wavelengths. Fluence (*in situ*) in J/cm^2, depth in mm. Radiant exposure (incident fluence) 10 J/cm^2 (indicated by horizontal line). A: 694 nm, B: 755 nm, C: 800 nm, D: 1064 nm.

$$\mathbf{j}_o = -\kappa_o \, \text{grad} \, \varphi \qquad (1)$$

and

$$\text{div} \, \mathbf{j}_o = -\frac{1}{c} \frac{\partial \varphi}{\partial t} - \mu_a \varphi + q_o , \qquad (2)$$

where $\mathbf{j}_o$ is the diffuse photon flux vector, φ is the optical fluence rate and t is the time. The optical diffusion constant is denoted κ_o, c is the velocity of unscattered light, μ_a is the optical absorption constant and q_o is the source density for diffuse light. The diffusion constant can also be expressed in terms of scattering parameters

$$\kappa_o = \frac{1}{3(\mu_s(1-g) + \mu_a)} \approx \frac{1}{3\mu_s'}, \qquad (3)$$

where μ_s is the scattering coefficient, g is the scattering anisotropy factor and $\mu_s' = \mu_s(1-g)$ is the reduced scattering coefficient.

Equations (1) and (2) can be combined

$$\nabla^2 \varphi - \frac{1}{\chi_o} \frac{\partial \varphi}{\partial t} - \frac{\varphi}{\delta^2} = -\frac{q_o}{\kappa_o}, \qquad (4)$$

where the $\chi_0 = c/3\mu_s'$ is the optical diffusivity and $\delta = \sqrt{1/3\mu_s'\mu_a}$ is the optical penetration depth.

The first term in Eq. (4), i.e., the spatial term, is of equal importance as the second temporal term when the characteristic spatial dimensions d and corresponding temporal dimension t satisfy the condition

$$\frac{1}{d^2} \sim \frac{1}{\chi_o t_d}. \qquad (5)$$

Thus, the optical diffusion time t_d for light diffusing over distance d is given by $t_d \sim d^2/\chi_o$. The diffusion time over millimeter distances in human skin with a reduced scattering coefficient $\mu_s' \sim 3 \times 10^3$ m^{-1} and light velocity $c \sim 2 \times 10^8$ m/s is thus on the order of picoseconds. The temporal terms in Eqs. (2) and (4) are therefore of no importance for laser pulses in the micro- and millisecond domain, and the light distribution can be determined without these terms.

The spatial distributions of diffuse light in human skin at various wavelengths are shown in Fig. 1. The fluence rate in regions just below the skin surface is a factor of 2–3 times larger than the radiant exposure due to optical backscattering, but decays exponentially with increasing depth in distal regions. The value of diffusion theory is limited in regions close to the surface because the isotropic distribution is not fully developed, as there will be contributions from both unscattered and partially scattered light. However, the approximation is satisfactory for depths larger than the reciprocal scattering coefficient, which is about 40 μm in upper layers of human skin.

Figure 1 is based on a three-layer model of human skin with a 100-μm-thick epidermis and a subcutaneous layer of fat deeper than 2 mm. The wavelength dependence of melanin absorption in expressed by $\mu_{a,\text{mel}} = \mu_{a,\text{mel},694 \text{ nm}}(694/\lambda)^{3.48}$ where λ is wavelength in nanometers and $\mu_{a,\text{mel},694 \text{ nm}}$ is the reference value at 694 nm.[10] The epidermal melanin absorption at 694 nm is $\mu_{a,\text{mel}} = 1000$ m^{-1}.[9] The dermal/subcutaneous melanin absorption due to hair follicles is $\mu_{a,\text{mel}} = 50$ m^{-1}. The absorption coefficient of blood with an average of 80% oxygenation and hematocrit $Hc = 0.41$ is 316, 396, 419 and 304 m^{-1} at 694, 755, 800 and 1064 nm, respectively. The first three values are taken from the literature for wavelengths up to 1000 nm.[11] The value at 1064 nm has been

extrapolated from those values. The blood volume fraction is taken as 2% in the dermis and subcutaneous fat and zero in the epidermis. An additional absorption coefficient of $\mu_a = 25$ m^{-1}, which accounts for nonblood and nonmelanin related absorption, is used at 694, 755 and 800 nm. This coefficient is increased to $\mu_a = 35$ m^{-1} at 1064 nm because of increased water absorption at this wavelength.[12] The scattering coefficients used are inversely proportional to wavelength, i.e., $\mu_s = \mu_{s,577\,nm}(577/\lambda)$ where the reference value at 577 nm is $\mu_{s,577\,nm} = 25\,000$ m^{-1} for the epidermis and dermis and $\mu_{s,577\,nm} = 10\,000$ m^{-1} for subcutaneous fat.[9] The anisotropy factor is taken as $g = 0.85$ for all wavelengths.[9]

These calculations reveal that the fluence rate at 694, 755 and 800 nm wavelengths is equal to the radiant exposure at depths up to about 2 mm, whereas at 1064 nm this depth increases to 3 mm. However, it should be noted that these depths are dependent on parameters such as scattering, melanin- and blood content, which might vary significantly on an individual patient basis as well as from site to site on the same patient.

3 Follicular Temperature Rise

The spatial and temporal temperature distribution $T(r,t)$ of a uniformly heated sphere embedded in an infinitely large medium with identical thermal properties is expressed in Eq. (6) It is assumed that the sphere is in perfect thermal contact with the surroundings, i.e., the heat transfer coefficient at the interface is infinitely large. The initial uniform ambient temperature is denoted T_n[13,14]

$$T(r,t) = \frac{\mu_{a,b}\psi\chi}{\tau_p\kappa} \sum_{n=1}^{2} (-1)^{n-1} \Bigg[\Bigg\langle [t-\tau_p(n-1)]$$

$$\times \Bigg\{ 1 - \frac{1}{r} \Bigg[2a\Bigg(i^2\,\mathrm{erfc}\Bigg(\frac{a-r}{2\sqrt{\chi[t-\tau_p(n-1)]}}\Bigg)$$

$$+ i^2\,\mathrm{erfc}\Bigg(\frac{a+r}{2\sqrt{\chi[t-\tau_p(n-1)]}}\Bigg)\Bigg)$$

$$- 4\sqrt{\chi[t-\tau_p(n-1)]}$$

$$\times \Bigg(i^3\,\mathrm{erfc}\Bigg(\frac{a-r}{2\sqrt{\chi[t-\tau_p(n-1)]}}\Bigg)$$

$$- i^3\,\mathrm{erfc}\Bigg(\frac{a+r}{2\sqrt{\chi[t-\tau_p(n-1)]}}\Bigg)\Bigg)\Bigg]\Bigg\}$$

$$\times h[t-\tau_p(n-1)] \Bigg\rangle h(a-r)$$

$$+ \Bigg\langle \frac{2[t-\tau_p(n-1)]a}{r}$$

$$\times \Bigg\{ \Bigg(i^2\,\mathrm{erfc}\Bigg(\frac{r-a}{2\sqrt{\chi[t-\tau_p(n-1)]}}\Bigg)$$

$$+ i^2\,\mathrm{erfc}\Bigg(\frac{r+a}{2\sqrt{\chi[t-\tau_p(n-1)]}}\Bigg)$$

$$- \frac{2\sqrt{\chi[t-\tau_p(n-1)]}}{a}$$

$$\times \Bigg[i^3\,\mathrm{erfc}\Bigg(\frac{r-a}{2\sqrt{\chi[t-\tau_p(n-1)]}}\Bigg)$$

$$- i^3\,\mathrm{erfc}\Bigg(\frac{r+a}{2\sqrt{\chi[t-\tau_p(n-1)]}}\Bigg)\Bigg]\Bigg\}$$

$$\times h[t-\tau_p(n-1)] \Bigg\rangle h(r-a) \Bigg] + T_n, \tag{6}$$

where ψ, r and t are the fluence, distance from the center of the sphere, and time from onset of the laser pulse. The radius of the melanin containing spherical follicle bulb is given by a, laser pulse duration is τ_p, and $\mu_{a,b}$ is the optical absorption coefficient of the follicle. The function $h(x)$ is the Heaviside step function defined by $h(x) = 0$ when $x < 0$ and $h(x) = 1$ when $x > 0$, and $i^n\,\mathrm{erfc}(x)$ is the n'th integral of the complementary error function, defined as, $i^n\,\mathrm{erfc}(x) = \int_x^\infty i^{n-1}\,\mathrm{erfc}(\xi)d\xi$, where $i^0\,\mathrm{erfc}(x) = \mathrm{erfc}(x)$ is the complementary error function.

When light depletion occurs in the follicle, i.e., when the optical penetration depth $\delta = 1/\mu_{a,b}$ is less than or equal to the radius, $\mu_{a,b}$ in Eq. (6) can be substituted by an effective average value $\mu_{a,b,\mathrm{eff}}$ expressing the absorption coefficient averaged over an entire sphere, i.e., the average absorbed energy density is $\mu_{a,b,\mathrm{eff}}\psi$[14]

$$\mu_{a,b,\mathrm{eff}} = \frac{3}{8} \frac{(1+2\mu_{a,b}a)e^{-2\mu_a a} + 2\mu_{a,b}^2 a^2 - 1}{\mu_{a,b}^2 a^3}. \tag{7}$$

Equation (7) reduces to $\mu_{a,\mathrm{eff}} \Rightarrow \mu_a$ when light depletion is negligible. When light depletion is predominant $\mu_{a,\mathrm{eff}}$ becomes $3/4a$, which corresponds to complete absorption of incident light. Equation (7), which is exact for a collimated beam, is an acceptable approximation in highly scattering media such as human skin where the light distribution is more isotropic.

Temperature distributions inside a 300-nm-diam light absorbing follicle as well as in nonabsorbing surrounding perifollicular layers are shown in Fig. 2 for four different laser pulse durations 0.3, 3, 30 and 300 ms. The 3 ms pulse is typically used for alexandrite lasers at 755 nm, whereas 30 ms is frequently used for gallium–aluminum–arsenide diode lasers at 800 nm. The parameters selected in this figure refer to melanin absorption at 755 nm. Fluence values corresponding to 30 J/cm^2 at 755 nm are 25, 35 and 80 J/cm^2 for, respectively, 694, 800 and 1064 nm. Figures 2(A), 2(B), 2(C) and 2(D) give the temperature distributions for 0.3, 3, 30, and 300 ms laser pulses, respectively. Temperature distributions for the 0.3, 3 and 30 ms pulses reveal that the threshold for damage, as indicated by the 65°C isotherm, extends about 50 μm outside the follicle. In the case of 0.3 and 3 ms pulses very little heat diffuses out of the follicle during the laser pulse. However, heat diffusion out of the follicle continues after the laser
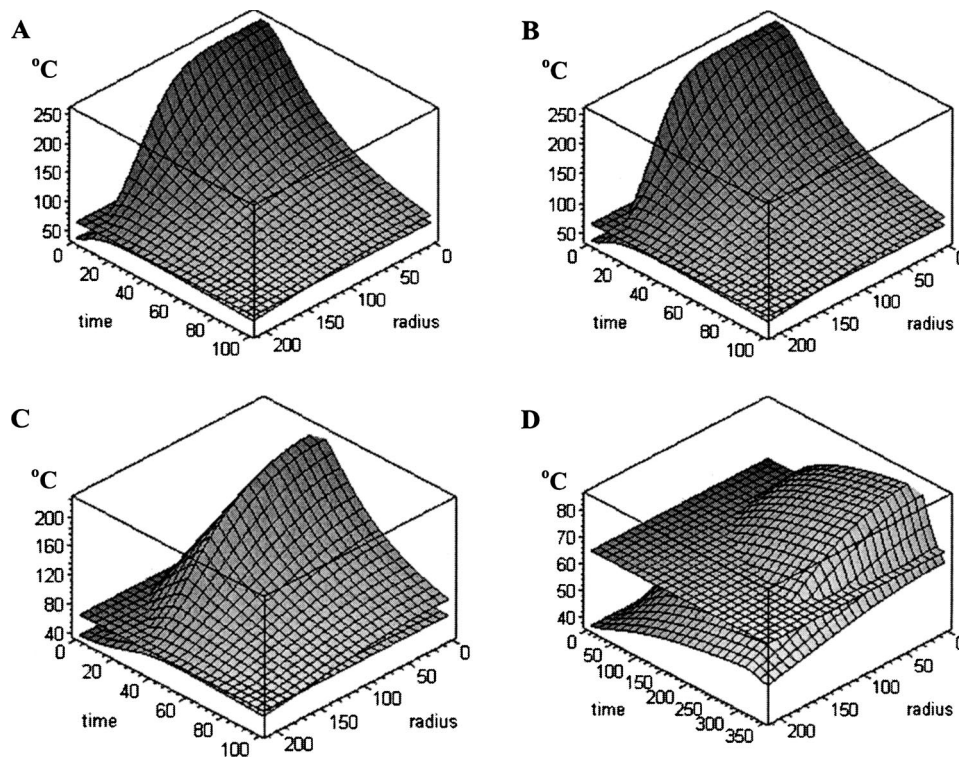
Fig. 2 Temperature in °C (vertical axis) in and around a 300 μm diam follicular bulb versus time (ms) and distance (radius) from center (μm) for four different pulse durations. Absorption coefficient $\mu_{a,mel}$=3500 m^{-1} ($\mu_{a,mel,eff}$=2500 m^{-1}) and fluence (*in situ*) ψ=30 J/cm^2. A: 0.3 ms, B: 3 ms, C: 30 ms, D: 300 ms.

exposure. The maximum extent of the damage zone occurs 40 ms after laser exposure. In the case of a 30 ms pulse, heat diffuses out of the follicle during the pulse, and damage zone extends to slightly less than 50 μm after 45 ms. Maximal selective damage to follicle is obtained when the laser pulse duration permits heat to diffuse from the light absorbing follicle bulb through the outer root sheath and into the stem cells located in the bulge area. Thus, damage to perifollicular structures is expected to be much the same for 0.3–30 ms pulse durations. The most significant difference is that the follicle bulb itself will be heated to a higher temperature in the case of the 0.3 and 3 ms pulses, as compared to 30 ms.

Heating of the follicle bulb itself above 100°C will, of course, result in vapor formation and carbonization, but the absorbed thermal energy must subsequently diffuse into the surrounding perifollicular regions. This assumption, which is very reasonable for pulse duration in the range of 0.3–100 ms, is not necessarily valid for Q-switched lasers with nanosecond pulses where plasma formation and subsequent acoustic shock wave generation might occur.

The temperature distribution for laser pulses longer than 100 ms behaves, however, quite differently as illustrated in Fig. 2(D) for a 300 ms pulse. Diffusion out of the follicle during the laser pulse is now quite significant; the maximum temperature in the follicle center is only 85°C, and no damage occurs in perifollicular structures. This implies that in order to obtain an identical damage zone for a 300 ms pulse as for 0.3–30 ms pulses the fluence must be increased by about 70%.

4 Skin Cooling Techniques

The clinical objective of laser therapy is to maximize thermal damage to target chromophores while minimizing injury to overlying skin. A valuable method to overcome this problem is to cool selectively the superficial layers of the skin during laser therapy, which prevents thermal injury despite some melanin absorption.

Rapid and spatially selective epidermal cooling can be achieved by active skin cooling. So long as the epidermis is prevented from reaching a temperature in response to laser exposure that is above its threshold for denaturation (60–65°C), the epidermis and upper dermis can be preserved. The second objective is to permit the use of higher light dosages for treatment of laser resistant lesions. The third objective is the treatment of patients with all skin types. For patients with darker skin types (Fitzpatrick IV–VI), it is not possible to treat lesions without cooling due to epidermal damage with a sufficiently high light dosage. The fourth objective is reduction of pain and posttreatment swelling or edema.

Several different methods have been developed for epidermal cooling in conjunction with laser therapy. Most methods utilize a precooled medium brought in contact with the skin surface. Deeper skin layers are cooled by heat diffusion toward the cooled surface with subsequent transfer to the cooling medium. The rate of heat transfer across the interface between the skin and cooling medium depends on the tem-

perature difference and thermal contact between the two adjacent materials.

Contact cooling of human skin is achieved by heat conduction into an adjacent precooled solid body, usually an optically transparent plate, kept at constant temperature (-10 to $+4°C$) by a cooling system. Laser exposure is delivered through the plate, which is pressed against the patient's skin. Contact cooling can be very efficient especially when a highly conductive material, such as sapphire, is used for the cooling plate. However, in practice, the thermal resistance at the interface of the intervening layer between the skin and plate inevitably impairs the rate of heat extraction with contact cooling. Air, bubbles, hair or other substances may impede the direct contact between the skin surface and cooling plate.

Human skin can also be cooled by precooled air blown onto or across the surface at temperatures as low as $-30°C$. Despite the low air temperature used, air cooling is characterized by the lowest cooling rate since the heat transfer coefficient is very low. As a result, long cooling times (on the order of several seconds) are necessary to induce significant temperature reductions in the basal layer. Therefore, the final outcome is inevitably general ("bulk") cooling of the entire skin with minimal spatial selectivity.

Rapid and spatially selective epidermal cooling can be achieved by cryogen spray cooling (also referred to as dynamic cooling). Tetrafluoroethane (R-134a), which has a boiling point of $-26°C$ at atmospheric pressure, is the only cryogenic compound currently approved by the Food and Drug Administration for use in dermatologic laser surgery. This cryogen is a nonflammable, nontoxic, and nonchlorinated ($C_2H_2F_4$) environmentally compatible Freon substitute. Liquid cryogen is "atomized" into a fine spray and directed toward the skin surface.

Heat transport in skin can be expressed by the so-called bio-heat equation

$$\mathbf{j} = -\kappa \operatorname{grad} T \tag{8}$$

and

$$\operatorname{div} \mathbf{j} = -\rho C \frac{\partial T}{\partial t} - \rho_b C_b \frac{T_a - T}{\tau} + q_m + q_a, \tag{9}$$

where $\mathbf{j}$ is the heat flux vector, κ is thermal conductivity and T is temperature, respectively. The specific heat per unit volume of skin is denoted by ρC, where ρ is the specific gravity and C is the specific heat per unit mass. The corresponding quantities for blood are $\rho_b C_b$, ρ_b and C_b, respectively. Time is given by t, T_a is arterial blood temperature, and τ is the blood perfusion time, i.e., the reciprocal blood perfusion rate. The rate of heat generated per unit volume of tissue by ambient metabolic processes is denoted q_m, and q_a is the corresponding value for absorption of laser power, i.e., $q_a = \mu_a \varphi$. The ambient metabolic heat corresponds, however, to a temperature of less than 0.1 K, which is orders of magnitudes less that the required temperature rise of 30–40 K obtained during laser-assisted hair removal. Equations (8) and (9) can be combined

$$\nabla^2 T - \frac{1}{\chi} \frac{\partial T}{\partial t} - \frac{1}{\chi} \frac{T}{\tau} = -\frac{T_a}{\chi \tau} - \frac{q_m}{\kappa} - \frac{q_a}{\kappa}, \tag{10}$$

where the specific heat of blood is assumed to be equal that of tissue. The quantity $\chi = \kappa/\rho C$ is the thermal diffusivity. The blood perfusion time is typically $\tau = 2000\text{-}2500$ s in skin and subcutaneous fat. Thus, the contribution of blood perfusion to skin cooling during $1\text{-}100$ ms laser pulses is negligible. The thermal diffusion time t_{dt}, which follows from the first two terms in Eq. (10), i.e., $t_{dt} \sim d^2/\chi$, is, however, quite comparable with laser pulse durations longer than 10 ms, e.g., for a $50\text{-}100\text{-}\mu$m-thick epidermis the diffusion time is in the range of $t_{dt} \sim 20\text{-}80$ ms ($\chi = 1.2 \times 10^{-7}$ m^2/s).[15]

## 5 Cooling Before Laser Exposure: Precooling

The thermal distribution in human skin during cooling prior to laser exposure can be expressed as[13,16]

$$T(x,t) = \left\{ \operatorname{erfc}\left(\frac{x}{2\sqrt{\chi t}}\right) - e^{\chi t H^2/\kappa^2 + Hx/\kappa} \right.$$
$$\left. \times \operatorname{erfc}\left(\frac{x}{2\sqrt{\chi t}} + \frac{H\sqrt{\chi t}}{\kappa}\right) \right\}(T_c - T_n) + T_n, \tag{11}$$

where x and t are depth from the skin surface and time after onset of the precooling, respectively. The cooling medium temperature is T_c, T_n is ambient skin temperature, and H is the heat transfer coefficient between coolant and skin surface.

The dependence of H on cooling efficacy is illustrated in Fig. 3, which illustrates the fractional temperature drop, i.e., $F = T/(T_n - T_c)$ versus time after onset of the precooling. Figures 3(A) and 3(B) show the value of F at the skin surface over ranges of $H = 10\text{-}1000$ W/m^2 K and $H = 1000\text{-}10\,000$ W/m^2 K, respectively. Typical values of H range from $H \sim 250$ W/m^2 K for forced air cooling, $H \sim 2000\text{-}5000$ W/m^2 K for contact cooling, and to $H \sim 6000\text{-}12\,000$ W/m^2 K for cryogen spray cooling.[8,16] Figure 3(A) shows that for forced air cooling with a typical value of $H = 250$ W/m^2 K the fractional drop is about $F = 0.1$ after 100 ms, increasing to $F = 0.25$ for the comparatively high value of $H = 1000$ W/m^2 K. The corresponding values for $H = 1000\text{-}10\,000$ W/m^2 K are shown in Fig. 3(B). The fractional value for contact cooling with the typical value of $H = 3000$ W/m^2 K is about $F = 0.5$ after 100 ms, whereas the value for spray cooling of $H = 10\,000$ W/m^2 K is $F = 0.8$ It should also be noted that the most rapid temperature drop is achieved with cryogen spray cooling, e.g., the fractional drop after 20 ms is $F = 0.6$ for cryogen spray cooling, $F = 0.3$ for contact cooling and less than $F = 0.04$ for forced air cooling. Moreover, the temperature of the cryogen spray, which can be as low as $-50°C$, is significantly lower than temperatures of about $0°C$ that can be used for contact cooling.

The fractional cooling values in the basal layer of the skin, i.e., the junction between epidermis and dermis, are given Figs. 3(C) and 3(D). Figure 3(C) shows that the value for forced air cooling of $H = 250$ W/m^2 K is about $F = 0.03$, whereas in Fig. 3(D) the corresponding values for contact cooling of $H = 3000$ W/m^2 K and cryogen spray cooling of $H = 10\,000$ W/m^2 K are about $F = 0.2$ and $F = 0.4$, respectively.
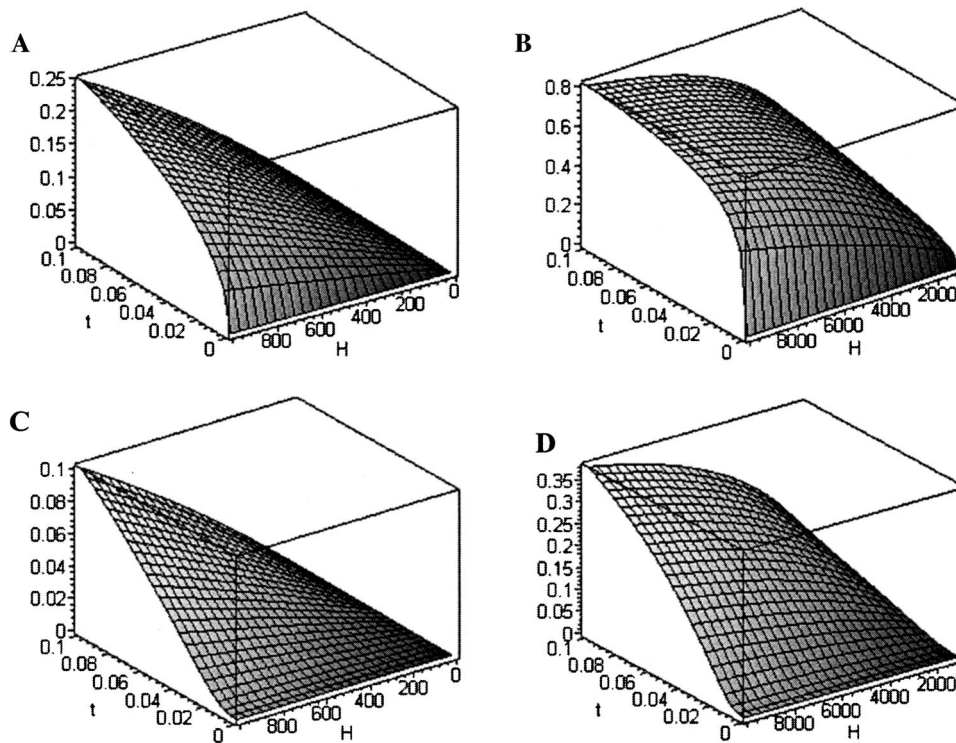
Fig. 3 Fractional temperature drop at skin surface and basal layer versus time t (s) after the onset of precooling and heat transfer coefficient H (W/m^2 K). $\chi = 1.2 \times 10^{-7}$ m^2/s, $\kappa = 0.4$ W/m K (see Ref. 15). A: Skin surface, $H = 10$–1000 W/m^2 K, B: skin surface, $H = 1000$–$10\,000$ W/m^2 K, C: basal layer ($d_e = 100$ μm), $H = 10$–1000 W/m^2 K, D: basal layer ($d_e = 100$ μm), $H = 1000$–$10\,000$ W/m^2 K.

It should also be noted that efficient cooling at some given depth, d, requires that H is larger than the thermal admittance of the cooled layer, i.e., $\kappa/d > H$. In the case of a 100-μm-thick epidermis, this requirement corresponds to $H > 4000$ W/m^2 K, which is fully satisfied by cryogen spray cooling, marginally satisfied by contact cooling, but not satisfied at all for forced air cooling. It is therefore not possible to obtain selective cooling of the epidermis with air cooling of the skin surface as such cooling implies that not only the epidermis, but also the entire dermis will be cooled, e.g., a heat transfer coefficient of $H = 250$ W/m^2 K corresponds to cooling depth of about 1.6 mm ($d \sim \kappa/H \Rightarrow 1.6$ mm). This is also a slow process and the required precooling period will be about 20 s ($t_{dt} \sim d^2/\chi = \kappa^2/H^2/\chi \Rightarrow 20$ s).

6 Cooling During Laser Exposure: Parallel Cooling

Provided that epidermal absorption is predominant, the thermal distribution in human skin during laser exposure can be expressed

$$T(x,t) = T_n + \int_0^t \frac{\mu_{a,e}\psi\chi}{\kappa\tau_p}\left\{ \mathrm{erf}\left(\frac{x}{2\sqrt{\chi(t-\tau)}}\right)\right.$$
$$\left. - \mathrm{erf}\left(\frac{x-d_e}{2\sqrt{\chi(t-\tau)}}\right) + A\left(\mathrm{erf}\left(\frac{x}{2\sqrt{\chi(t-\tau)}}\right)\right.\right.$$
$$\left.\left. - \mathrm{erf}\left(\frac{x+d_e}{2\sqrt{\chi(t-\tau)}}\right)\right)\right\} d\tau, \quad (12)$$

where $\mu_{a,e}$ is the epidermal optical absorption coefficient, ψ is the *in situ* epidermal optical fluence, τ_p is pulse duration and d_e is epidermal thickness.

The value of the dimensionless parameter $A = -1$ corresponds to no heat loss at the skin surface, and $A = 0$ corresponds to the case where during passive cooling heat diffuses from the skin into a thick layer of aqueous gel deposited over the surface.

The corresponding expression for active skin surface cooling can be written

$$T(x,t) = T_n + \int_0^t \frac{\mu_{a,e}\psi\chi}{\kappa\tau_p}\left\{ \mathrm{erf}\left(\frac{x}{2\sqrt{\chi(t-\tau)}}\right)\right.$$
$$- \mathrm{erf}\left(\frac{x-d_e}{2\sqrt{\chi(t-\tau)}}\right) + \left(\mathrm{erf}\left(\frac{x}{2\sqrt{\chi(t-\tau)}}\right)\right.$$
$$\left.\left. - \mathrm{erf}\left(\frac{x+d_e}{2\sqrt{\chi(t-\tau)}}\right)\right)\right\} d\tau + (T_s - T_n)\mathrm{erfc}\left(\frac{x}{2\sqrt{\chi t}}\right),$$
$$(13)$$

where T_s is the skin surface temperature. In the case of ideal thermal contact, corresponding to $H \to \infty$, T_s will be equal to that of the cooling medium. This condition requires a value of H much larger than the thermal admittance of 4000 W/m^2 K, which corresponds to a 100-μm-thick epidermis.

The thermal distributions with and without cooling during laser exposure are illustrated in Fig. 4. The laser fluence is selected such that the epidermal temperature during a 100 ms

A

B

C

D
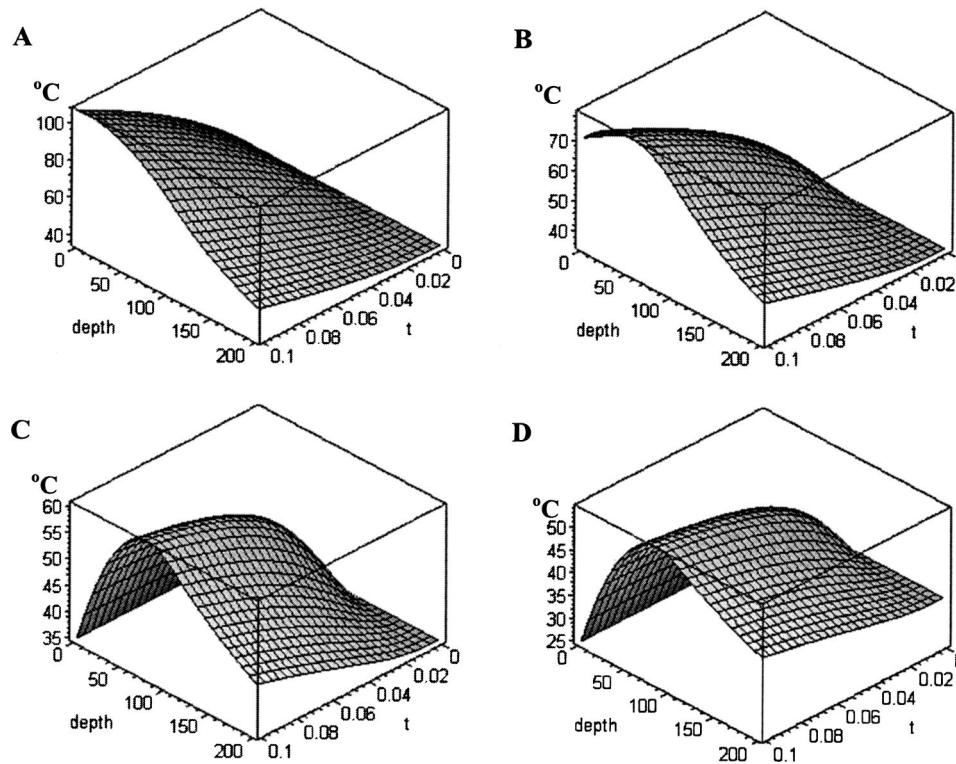
Fig. 4 Skin temperature in °C (vertical axis) with cooling during laser exposure versus depth (μm) and time t (s). $\mu_{a,e}=1000$ m^{-1}, ψ $=35$ J/cm^2, $\tau_p=100$ ms, $d_e=100$ μm, $T_n=35$°C. A: No heat loss at surface, B: a thick layer of aqueous gel covers the exposed surface, C: skin surface kept at $T_s=35$°C, D: skin surface kept at $T_s=25$°C.

laser pulse just reaches above the boiling point of water. The thermal distribution in the absence of any heat loss at the skin surface is shown in Fig. 4(A). The temperature is highest at the skin surface and drops down to 70°C in the basal layer. Passive surface cooling, such as when covering the skin with a thick layer of aqueous gel, is shown in Fig. 4(B). The maximum temperature rise, which now occurs in the middle of the epidermis, is reduced to 80°C, and the temperature in the basal layer about 60°C.

The thermal distributions with active cooling during laser exposure are shown in Figs. 4(C) and 4(D). Figure 4(C) represents a very moderate cooling where the skin surface is kept at ambient skin temperature ($T_n=35$°C), and Fig. 4(D) represents a more aggressive surface cooling to $T_s=25$°C. The maximum epidermal temperature is for both these cases well below a temperature that can result in epidermal damage.

It is, however, important to point out that efficient parallel cooling can only be obtained when the laser pulse duration is comparable or larger than the thermal relaxation time of the epidermis, i.e., 20-80 ms. This is illustrated in Fig. 5, which shows the temperature rise versus depth for four different laser pulse durations ranging from 0.1 to 100 ms. The laser fluence and optical absorption are the same as those used in the Fig. 4 examples, and the cooling is assumed to keep the skin surface temperature constant at $T_s=5$°C. The effect of parallel cooling is negligible for laser pulse durations of τ_p $=0.1$-1 ms, as shown in Figs. 5(A) and 5(B). Cooling during a 10 ms laser pulse is of marginal value as shown in Fig. 5(C), whereas it can be very efficient for longer pulses as shown in Fig. 5(D) for 100 ms laser exposure.

In conclusion, parallel cooling is of little or no value for pulse duration less than 10 ms, whereas it can be quite important for pulses in the range of 30–100 ms, which are frequently used for hair removal with laser diodes.[14]

7 Cooling After Laser Exposure: Postcooling

Some commercial laser systems equipped with cryogen spray cooling utilize a short cryogen spurt immediately after laser exposure. Postcooling will quench thermal buildup below the skin surface during the laser pulse, and thereby diminish epidermal damage. Quenching of the epidermal temperature buildup can be expressed[13]

$$
\begin{aligned}
T(x,t)=T_n+&\int_0^{d_e}\left\{\frac{e^{-(x-x_1)^2/4\chi t}+e^{-(x+x_1)^2/4\chi t}}{2\sqrt{\pi\chi t}}\right.\\
&-\frac{H}{\kappa}e^{\chi t H^2/\kappa^2+H(x+x_1)/\kappa}\left.\operatorname{erfc}\left(\frac{x+x_1}{2\sqrt{\chi t}}+\frac{H\sqrt{\chi t}}{\kappa}\right)\right\}\\
&\times(T_{\max}-T_n)dx_1+\int_0^t\frac{\chi H}{\kappa}\left\{\frac{e^{-x^2/4\chi(t-\tau)}}{\sqrt{\pi\chi(t-\tau)}}\right.\\
&-\frac{H}{\kappa}e^{\chi(t-\tau)H^2/\kappa^2+Hx/\kappa}\operatorname{erfc}\left(\frac{x}{2\sqrt{\chi(t-\tau)}}\right.\\
&\left.\left.+\frac{H\sqrt{\chi(t-\tau)}}{\kappa}\right)\right\}(T_c-T_n)d\tau,\qquad(14)
\end{aligned}
$$
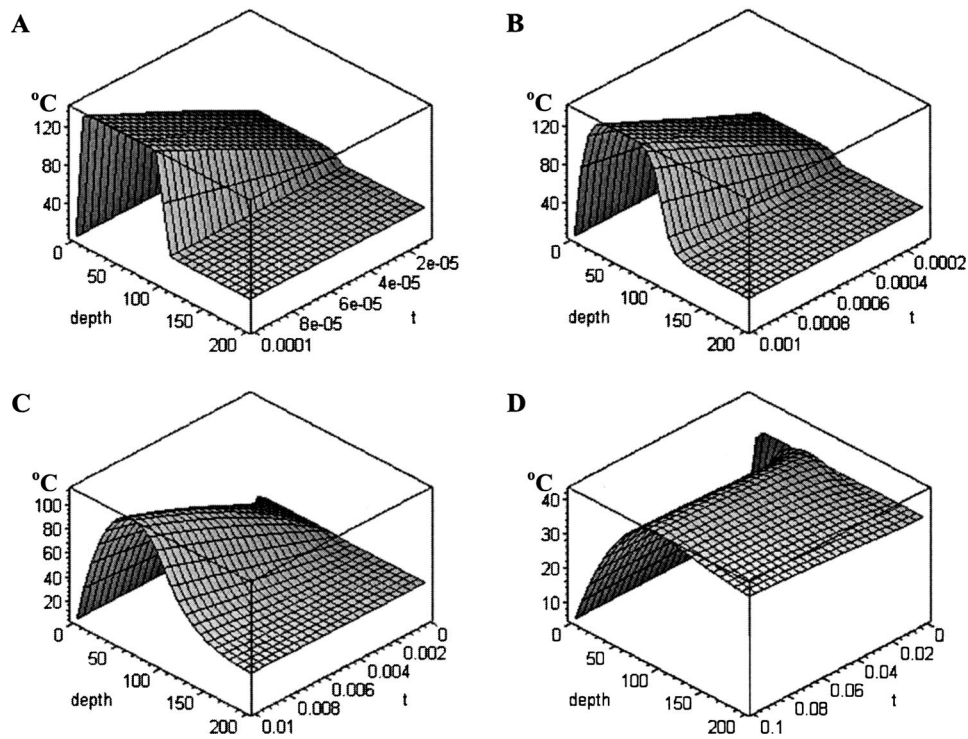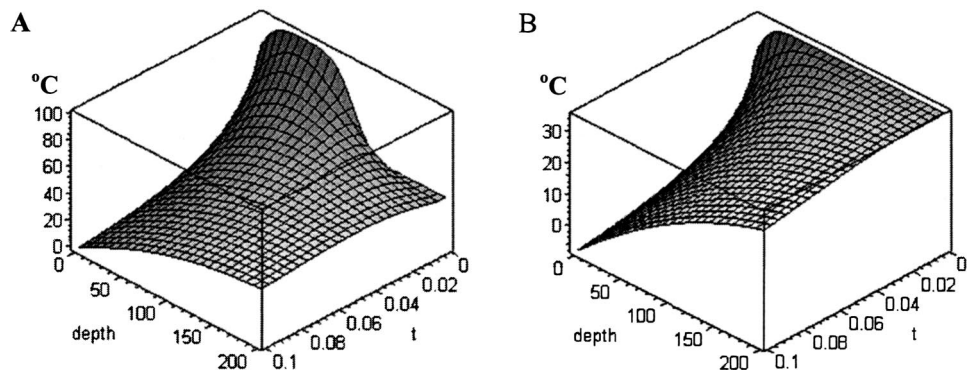
Fig. 5 Skin temperature in °C (vertical axis) with cooling during laser exposure versus depth (μm) and time t (s) for four different pulse durations. $\mu_{a,e} = 1000$ m^{-1}, $\psi = 35$ J/cm^2, $d_e = 100$ μm, $T_n = 35$°C, $T_s = 5$°C. A: 0.1 ms, B: 1 ms, C: 10 ms, D: 100 ms.

where x and t are, respectively, the depth from the skin surface and time after the onset of cooling. The temperature rise in the epidermis immediately after laser exposure is given by T_{max}.

This result is illustrated in Fig. 6(A), which shows the temperature distribution versus depth and time after the onset of the postcooling. The cooling parameters selected are typical values for cryogen spray cooling with tetrafluoroethane. The heat transfer coefficient is taken as a moderate value for commercially available cryogen spray cooling systems, i.e., $H = 6000$ W/m^2 K. The calculation reveals than the epidermal temperature is quenched from 100 to 60°C within a cryogen spurt duration of 20 ms.

For comparison, the corresponding temperature for precooling with the same cryogen spray cooling system is given in Fig. 6(B). The entire 100-μm-thick epidermis is now cooled down to a temperature below 10°C within 100 ms. It should also be noted that these cooling parameters are conservatively chosen, as adiabatic expansion of cryogen gas reduces the cryogen droplet temperature significantly below the cryogen boiling point before impinging onto the skin surface, e.g., cryogen spray temperatures of $T_c = -50$°C and values for H up to 11 500 W/m^2 K have been reported.[16]

Fig. 6 Skin temperature in °C (vertical axis) during postcooling and precooling laser exposure versus depth (μm) and time t (s). $T_n = 35$°C, $T_c = -26.5$°C, $H = 6000$ W/m^2 K, $d_e = 100$ μm. A: Postcooling with epidermis heated to $T_{max} = 100$°C at time $t = 0$, B: precooling of skin at ambient temperature $T_n = 35$°C at time $t = 0$.

8 Conclusions

The present analysis shows that penetration of laser light in human skin is almost the same for lasers at 694, 755, and 800 nm, whereas light penetrates somewhat deeper for Nd:YAG lasers at 1064 nm. The required radiant exposure is, due to reduced melanin absorption in the near infrared, significantly larger for 1064 nm. However, since the target chromophore of the hair follicle, i.e., melanin, is the same as the competing chromophore in the epidermis, the probability for epidermal damage is expected to be about the same for all wavelengths under study.

Moreover, the analysis indicates that the efficacy of introducing damage to hair follicles in human skin is almost independent on laser pulse duration in the 0.3–100 ms region. The most important factor to ensure epidermal protection is to optimize skin cooling.

For laser pulses less than 10 ms, precooling with cryogen spray is the only efficient technique. In the case of 30–100 ms laser pulses, precooling of the skin by contact cooling for 0.5–1 s can provide adequate protection.[16] Precooling can also be performed by forced cooled air, but the cooling time must be on the order of 10–20 s, which results in an increased cooling depth down to 1.5 mm. However, this might be acceptable in the case of deep targets such as the hair follicles.

For 30–100 ms laser pulses, parallel cooling can be very efficient. Parallel cooling can be performed with continuous or intermittent cryogen spray during the laser pulse, by irradiating through a block of ice, or by bringing a chilled optically transparent window with high thermal conductivity, such as a sapphire plate, into good thermal contact with the skin. Passive cooling by depositing a thick layer of aqueous gel on the skin surface during laser exposure can also be of some value.

Finally, in the case of postcooling, which shortens the time that the epidermis remains at elevated temperatures, cryogen spray cooling is by far the most efficient. Here, a single short cryogen spurt of about 20 ms duration is sufficient to reduce the laser-induced epidermal temperature rise down to ambient values.

References

1. R. R. Anderson and J. A. Parish, "Selective photothermolysis. Precise microsurgery by selective absorption of pulsed radiation," *Science* **226**, 524–527 (1983).
2. W. W. Lou, A. T. Quintana, R. G. Geronemus, and M. C. Grossman, "Prospective study of hair reduction by diode laser (800 nm) with long-term followup," *Dermatol. Surg.* **26**, 428–432 (2000).
3. J. R. Lloyd and M. Mirkow, "Long-term evaluation of the long-pulsed alexandrite laser for the removal of bikini-hair at shortened intervals," *Dermatol. Surg.* **26**, 633–637 (2000).
4. E. V. Ross, Z. Ladin, M. Kreindel, and C. Dierickx, "Theoretical considerations in laser hair removal," *Dermatol. Clin.* **17**, 333–355 (1999).
5. G. B. Altshuler, R. R. Anderson, D. Manstein, H. H. Zenzie, and M. Z. Smirnov, "Extended theory of selective photothermolysis," *Lasers Surg. Med.* **29**, 416–432 (2001).
6. R. J. Ort and R. R. Anderson, "Optical hair removal," *Semin Cutan Med. Surg.* **18**, 149–158 (1999).
7. J. S. Nelson, T. E. Milner, B. Anvari, B. S. Tanenbaum, S. Kimel, L. O. Svaasand, and S. L. Jacques, "Dynamic epidermal cooling during pulsed laser treatment of port-wine stain. A new methodology with preliminary clinical evaluation," *Arch. Dermatol.* **131**, 695–700 (1995).
8. J. S. Nelson, B. Majaron, and K. M. Kelly, "Active skin cooling in conjunction with laser dermatologic surgery," *Semin Cutan Med. Surg.* **19**, 253–266 (2000).
9. L. O. Svaasand, L. T. Norvang, E. J. Fiskerstrand, E. K. S. Stopps, M. W. Berns, and J. S. Nelson, "Tissue parameters determining the visual appearance of normal skin and port-wine stains," *Lasers Med. Sci.* **10**, 55–65 (1995).
10. http://omlc.ogi.edu/spectra/melanin/mua.html
11. http://omlc.ogi.edu/spectra/hemoglobin/summary.html
12. http://omlc.ogi.edu/spectra/water/data/kou93b.dat
13. H. S. Carslaw and J. C. Jaeger, *Conduction of Heat in Solids*, Clarendon, Oxford (1959).
14. E. J. Fiskerstrand, L. O. Svaasand, and J. S. Nelson, "Hair removal with long pulsed diode lasers; a comparison between two systems with different pulse structures," *Lasers Surg. Med.* **32**, 399–404 (2003).
15. F. A. Duck, *Physical Properties of Tissue*, Academic, London (1990).
16. L. O. Svaasand, L. L. Randeberg, G. Aguilar, B. Majaron, S. Kimel, E. J. Lavernia, and J. S. Nelson, "Cooling efficiency of cryogen spray during laser therapy of skin," *Lasers Surg. Med.* **32**, 137–143 (2003).