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Mathematical modelling of dynamic cooling and pre-heating, used to increase the depth of selective damage to blood vessels in laser treatment of port wine stains

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Abstract. Based on the assumption that the maximum irradiance allowed during laser treatment of port wine stains is limited by the temperature rise at the dermoepidermal junction, we theoretically investigated how much the irradiance could be increased by dynamically cooling the skin surface. The heat condution equation was solved numerically in cylindrical coordinates using a skin model composed of four layers. The laser-light absorption was calculated using Monte Carlo simulations. The transient thermal behaviour of the skin was modelled when cooling with water at a temperature of 0 °C and with liquid nitrogen at a temperature of −196 °C. With cooling, an increase in the maximum irradiance by a factor of 2.3–3.6 was theoretically permitted depending on the irradiation time, wavelength and mode of cooling. The corresponding increase in vessel selective damage depth was predicted to be 0.4–0.5 mm.

A new concept for increasing the depth of vessel selective damage is introduced where the initial temperature profile of the skin is reshaped by using not only surface cooling but also laser irradiation. By pre-irradiating the skin with near-infrared light without selective absorption by the tissue chromophores in conjunction with surface cooling, a maximum temperature at a depth of 1 mm from the dermoepidermal junction was theoretically achieved. A subsequent 0.1 s pulse from a frequency doubled Nd:YAG laser is theoretically shown to selectively destroy vessels up to a depth of 0.8 mm from the dermoepidermal junction. By pre-heating at 1064 nm and treating at 532 nm in conjunction with surface cooling, the theoretical results indicate that the Nd:YAG laser can compete in effectiveness with the flashlamp-pumped dye laser in the treatment of port wine stains.

1. Introduction

Port wine stains are due to a congenital vascular disorder characterized by a large number of ectatic blood vessels in the dermis (Barsky *et al* 1980). Often situated in the face the port wine stains, ranging in colour from light pink to dark blue–purple, can have a substantial impact on the patient's psychological status (Pickering *et al* 1990). Laser treatments of port wine stains have shown good results (Tan 1992). The ectatic blood vessels have been selectively and irreversibly destroyed while leaving the overlying epidermis and the surrounding dermis intact. The selectivity is primarily based on the higher absorption of the laser light by oxyhaemoglobin as compared with melanin and other skin constituents. In order to exploit this favourable difference in absorption, short laser pulses must be employed (Lahaye and van Gemert 1985, Svaasand *et al* 1985). By using short pulses, the heat deposited in the blood vessels is prevented from dissipating to other tissue structures. A vessel selective damage down to 1.2 mm from the dermoepidermal junction, using the flashlamp-pumped dye laser emitting submillisecond pulses, has been reported (Tan *et al*

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1990). One disadvantage of using this type of laser is the purpura developing immediately after the treatment which however fades gradually over about one week (Sheehan-Dare and Cotterill 1993).

Continuous wave (cw) and 'quasi-continuous' lasers such as the argon ion laser, the cw dye laser, the frequency doubled Nd:YAG laser (KTP laser) and the copper vapour laser are also used to treat port wine stains (Wheeland 1995). The frequency doubled Nd:YAG laser and the copper vapour laser are 'quasi-continuous' as they emit nanosecond pulses at a repetition rate of 5–15 kHz, that is, one pulse every 67–200 μs. However, as the thermal relaxation time of a blood vessel is typically in the millisecond range, these lasers can, for this application, be considered as cw lasers (Parrish and Deutsch 1984). Due to the relatively low output powers of the cw lasers, an irradiation time of approximately 100 ms is required in order to deliver enough energy to destroy the enlarged vessels. During this time the heat produced after light absorption in the epidermis as well as in the blood vessels will diffuse into the dermis and can cause non-specific diffuse dermal damage resulting in scarring.

Even the Nd:YAG laser at 1064 nm has been used in the treatment of port wine stains. At this wavelength there exists no blood selective absorption and the treatment relies on diffuse dermal coagulation (van Gemert and Welch 1987). Due to the greater penetration depth in the skin of light from the Nd:YAG laser as compared with light from the other above-mentioned lasers, deep dermal damages can be achieved (Rosenfeld *et al* 1988).

Theoretically, the ideal laser parameters are a wavelength between 577 and 585 nm (Lahaye and van Gemert 1985, Verkruysse *et al* 1993), a beam spot size larger than 1 mm in diameter (Keijzer *et al* 1991) and an irradiation time of 1–10 ms (Lahaye and van Gemert 1985, van Gemert *et al* 1986). The optimal wavelength range has been calculated from the difference in light absorption between epidermal melanin and oxyhaemoglobin of blood. Additionally, the wavelength of preference is influenced by the amount of blood present in the dermis (van Gemert *et al* 1995). The beam spot size should be the largest possible. Too small a spot diameter will result in a diminished fluence at the vessel wall owing to photon scattering out of the beam. An irradiation time between 1 and 10 ms will allow heat diffusion within the heated vessels in order to coagulate the entire vessel lumen. Also, during a millisecond pulse heat diffusion from the heated epidermis to the underlying dermis will be limited. None of the clinically used lasers fulfils all three of the criteria mentioned above. The flashlamp-pumped dye laser, which has proved to produce the best results, has a shorter than optimal pulse length ($\sim$ 0.4 ms). The cw dye lasers have too low output powers, resulting in longer than optimal irradiation times. Due to the low power, the spot size must also be chosen significantly smaller than the optimal size.

The argon ion laser and the frequency doubled Nd:YAG laser emit non-optimal wavelengths in addition to suffering from the disadvantages common to all cw lasers. The light from these two lasers is absorbed to a substantially greater degree in the epidermis as compared with light at 577–585 nm (van Gemert *et al* 1992). However, in a recent theoretical study by van Gemert *et al* (1995), it was shown that the wavelength of the light from the frequency doubled Nd:YAG laser at 532 nm can be the optimal wavelength with a certain degree of blood in the dermis. The study was based solely on the degree of light absorption of blood, disregarding epidermal absorption. Therefore, if the 'iron heater' effect from the epidermis could be manipulated by cooling the skin surface, the frequency doubled Nd:YAG laser could turn out to be an interesting alternative for treating port wine stains.

Cooling of the skin prior to laser treatment of port wine stains has been tried clinically (Gilchrest *et al* 1982, Dréno *et al* 1985). However, in those studies ice cooling was conducted 2–5 min before the treatment, resulting in a homogenous decrease in

skin temperature. By specifically lowering the temperature of the epidermis, a higher irradiance could be applied without producing damage to the dermis due to heat conduction. Preliminary calculations by Lahaye and van Gemert (1985) suggested that the depth of vessel specific damage could be increased from 0.2 mm to 0.5 mm when cooling with water during a 100 ms laser treatment at 577 nm. Svaasand *et al* (1995) have treated port wine stains using the flashlamp-pumped dye laser in conjunction with dynamic surface cooling and have obtained improved results with respect to dermal scarring. However, the issue of dynamic cooling needs to be further evaluated. In the present study, the effect of dynamic cooling of the skin surface on the maximum depth of vessel selective damage is theoretically investigated. Two modes of cooling are considered: water cooling and liquid nitrogen cooling. The results are used to compare the wavelengths of 532 nm and 577 nm for two different irradiation times which simulate the flashlamp-pumped dye laser and the cw laser.

The benefit of further reshaping the temperature profile of the skin prior to the laser treatment pulse is also theoretically investigated in this study. The reshaping is done by using deeply penetrating near-infrared light, with non-specific absorption by the tissue chromophores, in conjunction with surface cooling. In this way the maximum skin temperature can be forced deep into the tissue (Svaasand *et al* 1985). A subsequent laser pulse at a wavelength with selective blood absorption can then more easily coagulate deep-lying vessels as the temperature rise required to reach the coagulation limit is diminished. This pre-heating mode of application could be interesting to augment the treatment efficiency of the Nd:YAG laser, using the light at 1064 nm for pre-heating and the light at 532 nm for treatment.

2. Method

The temperature of the skin is governed by the following bioheat equation

$$\rho c \frac{\partial T}{\partial t} = \nabla(\lambda\ \nabla T) + Q_s \tag{1}$$

where T is the tissue temperature (K), ρ is the tissue density (kg m^{-3}), c is the specific heat of the tissue (J kg^{-1} K^{-1}) and λ is the thermal conductivity of the tissue (W m^{-1} K^{-1}). The time is represented by t (seconds) and Q_s is the external heat-source term (W m^{-3}) representing the laser light absorption. In the above expression, the metabolic heat generation as well as the heat exchange due to perfusion have been neglected, which is reasonable for short investigation times (Welch *et al* 1980, Jain 1983). The assumption that the thermal influence of the perfusion is negligible was also confirmed by model calculations. The details of the calculations are accounted for in section 3.

The laser light absorption in the tissue was modelled using the Monte Carlo method (Wilson and Adam 1983). The Monte Carlo method implies the trace following of a large number of single photons in the tissue, resulting in the distribution of absorbed photons. The light absorption in tissues with a layered structure of different optical properties can be modelled straightforwardly. For the simulations, the computer code developed by Wang and Jacques (1992) was used. The photon paths of 3.0×10^6 individual photons were simulated in the tissue. From the Monte Carlo simulations, the distribution of absorbed photons was given in a matrix in cylindrical coordinates for a 3 mm diameter beam with a 'top hat' intensity profile, irradiating the skin surface at normal incidence. The skin was modelled as a four-layer slab consisting of a 60 μm thick epidermis, an upper dermal layer of variable thickness overlying a 100 μm blood layer, and a lower dermal layer extending

down to 2560 μm (figure 1). The input parameters for the Monte Carlo simulations were the absorption coefficient, μ_a (cm^{-1}), the scattering coefficient, μ_s (cm^{-1}), the anisotropy factor, g (dimensionless), assuming a Henyey-Greenstein scattering phase function, and the refractive index of tissue, n (dimensionless), equal to 1.38 (Jacques and Prahl 1987). In table 1, the Monte Carlo input parameters used for 532 nm and 577 nm are shown (Verkruysse *et al* 1993). The thermophysical parameters used for the different layers are shown in table 2 (Sekins and Emery 1982, Wilson and Spence 1988).

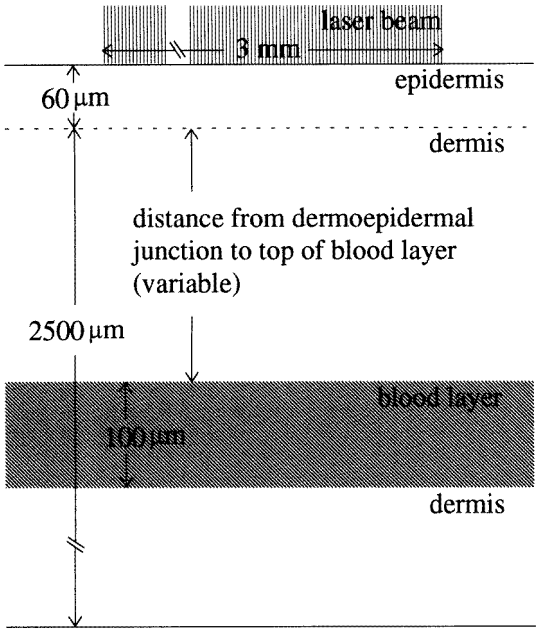


Figure 1. Skin modelled as composed of four layers.

Equation (1) was solved numerically using an explicit finite-difference technique assuming constant tissue thermophysical properties (Sturesson and Andersson-Engels 1995). The skin was modelled as a cylinder of a radius of 5.0 mm and a height of 2.56 mm. The lateral and bottom surfaces of the cylinder were located far from the laser-irradiated spot of a diameter of 3.0 mm at the upper surface, justifying the imposed isolation of the boundaries. The tissue was divided into a number of ring-shaped control volumes in a cylindrically symmetric matrix. The sizes of the control volumes were chosen to be $\Delta r = 250$ μm and $\Delta z = 5$ μm, representing the radial width and height of the control volumes, respectively. At the end of a small time step, the temperature of each control volume was iteratively calculated. The size of the time step chosen was calculated to ensure stability of the numerical solution (Sturesson and Andersson-Engels 1995). The initial temperature of the skin was set to 35 °C. Two different irradiation times were considered: 400 μs, representative of a flashlamp-pumped dye laser, and 100 ms, representative of a cw laser. The two wavelengths investigated were 532 nm and 577 nm. Cooling of the skin surface was performed by applying either water at a temperature of 0 °C or liquid nitrogen at a temperature of −196 °C. In the numerical model, one layer of cooling liquid of a thickness

of 5 μm was applied onto the skin surface. The thermal conductivities of water and liquid nitrogen were taken to be 0.56 W m^{-1} K^{-1} and 0.14 W m^{-1} K^{-1}, respectively. After each calculation step, the temperature of the cooling medium was preset to the original value. Without cooling, a heat convection coefficient of 25 W m^{-2} K^{-1}, the maximum expected for free convection from a flat plate (Incropera and De Witt 1990), was assumed to mathematically connect the ambient air at a temperature of 23 °C to the skin.

Table 1. Optical properties of skin.

Wavelength (nm)	Skin layer	Absorption coefficient μ_a (cm^{-1})	Scattering coefficient μ_s (cm^{-1})	Anisotropy factor g
532	Epidermis	23	530	0.775
	Dermis	2.4	240	0.775
	Blood	266	473	0.995
577	Epidermis	19	480	0.787
	Dermis	2.2	210	0.787
	Blood	354	468	0.995
800	All	1.7	175	0.852

To represent the tissue damage caused by the temperature rise following the laser irradiation, a damage integral based on an Arrhenius relationship was used:

$$\Omega(r,\, z) = A \int \exp \frac{-\Delta E}{RT(r,\, z,\, t)} \mathrm{d}t \tag{2}$$

where Ω represents the degree of coagulation (dimensionless), A is the frequency factor (s^{-1}), ΔE is the activation energy (J mol^{-1}), R is the universal gas constant, equal to 8.314 J mol^{-1} K^{-1}, and T is the tissue temperature (K). The values of A and ΔE for skin were taken from Henriques (1947) as $A = 3.1 \times 10^{98}$ s^{-1} and $\Delta E = 6.27 \times 10^5$ J mol^{-1}. When $\Omega = 0.7$, 50% of the tissue is assumed to be coagulated. This limit was taken to be the criterion for irreversible damage. The damage integral was calculated as a summation for each control volume after every time step. Damage first occurs on the axis of symmetry of the irradiating beam where the highest temperatures are reached. Thus, when referring to damage to a skin layer in this study, the damage on the axis of symmetry is implied. The maximum allowed irradiance during the laser treatment was evaluated as the lowest irradiance producing damage to the dermoepidermal junction. Using the maximum irradiance, the damage to a blood layer located at different depths was calculated. When the treatment resulted in a value of the damage integral greater than or equal to 0.7 at the top of the 100 μm thick blood layer, the layer was assumed to be damaged. By placing the blood layer at greater and greater depths, the maximum depth at which the top of the layer could be damaged, using the maximum irradiance, was evaluated. The distance between the dermoepidermal junction and the top of the most deeply located damaged blood layer was then taken to be the depth of vessel selective damage (see figure 1).

The new concept of pre-heating the skin by using deeply penetrating near-infrared light in conjunction with surface cooling in order to accomplish a more favourable baseline temperature was also investigated. This could be an interesting approach especially regarding the frequency doubled Nd:YAG laser as near-infrared light at 1064 nm is readily available. Due to the lack of values for optical properties of skin at 1064 nm, the reported values at 800 nm (Tuchin 1993), as shown in table 1, were utilized. In this wavelength region, the optical properties of skin become more homogenous for the different layers.

Melanin experiences an exponential decrease in the absorption coefficient between 550 nm and 800 nm (Boulnois 1987). Meanwhile, the absorption coefficient of oxyhaemoglobin, the other main skin chromophore, decreases by a factor of almost 100. Between 800 and 1064 nm the absorption coefficient of melanin still decreases exponentially while the absorption coefficient of blood is almost the same at 800 nm as at 1064 nm. The scattering coefficients of the epidermis, dermis and blood have values similar to each other and are less wavelength dependent (Tuchin 1993). As an approximation of the optical properties of skin at 1064 nm, it therefore seemed reasonable to use the optical properties of dermis at 800 nm for all layers.

3. Results

3.1. Surface cooling

Figure 2(*a*) shows the temperature as a function of time at different depths from the dermoepidermal junction when the skin surface was cooled with water. The initial skin temperature was 35 °C. For the cooling to be advantageous with respect to the subsequent laser treatment, a difference in temperature between the dermoepidermal junction and the location of the ectatic blood vessels should be achieved. The temperature difference between different depths and the dermoepidermal junction during water cooling is seen in figure 2(*b*). From the figure it can be concluded that there exist different optimal cooling times depending on the location of the blood vessels. With an exact timing of the pre-cooling, a difference in temperature of 14 °C between the dermoepidermal junction and a depth of 0.2 mm below, or a difference of 25 °C at a depth of 1 mm from the dermoepidermal junction, can be achieved. A cooling time of 1 s is predicted to produce almost optimal temperature differences throughout the skin with respect to the temperature at the dermoepidermal junction. Therefore, 1 s of water pre-cooling can be considered as a good approximation of the optimal cooling time before treating vessels at any depth.

When cooling with liquid nitrogen, the surface temperature can reach far below the freezing point of water and thereby damage the epidermis. By setting a safety temperature of 5 °C at the dermoepidermal junction, it is shown in figure 3 that the cooling time should be around 25 ms. With this mode of cooling, the temperature drop of the skin is limited to the epidermis, thereby creating a temperature difference of 30 °C between the dermoepidermal junction and the underlying skin.

The influence of lowering the epidermal temperature on the maximum allowed irradiance was investigated by defining that damage to the dermoepidermal junction was the limiting factor. An irradiance resulting in a value of the damage integral equal to 0.7 at the dermoepidermal junction was considered to be the maximum irradiance. Two different irradiation times were investigated: 400 μs, representative of treatment with a flashlamp-pumped dye laser, and 100 ms, representative of a cw laser. The beam diameter was 3.0 mm. Water cooling was started 1.0 s before the laser treatment to continue thereafter. Liquid nitrogen cooling was applied 25 ms before the laser pulse. To prevent damage to the skin surrounding the treatment area, the liquid nitrogen cooling ceased just as the laser treatment begun and the non-cooling boundary condition was then applied. In table 3, the maximum irradiances are shown for the two investigated wavelengths. With cooling, the threshold irradiance was found to increase by a factor of 2.3–3.6 depending on the irradiation time. The two values apply to the 400 μs and 100 ms irradiation times, respectively. Nitrogen cooling proved to be best for the 400 μs pulse. During this short irradiation time, heat conduction is minimal and the more favourable initial temperature created by the nitrogen

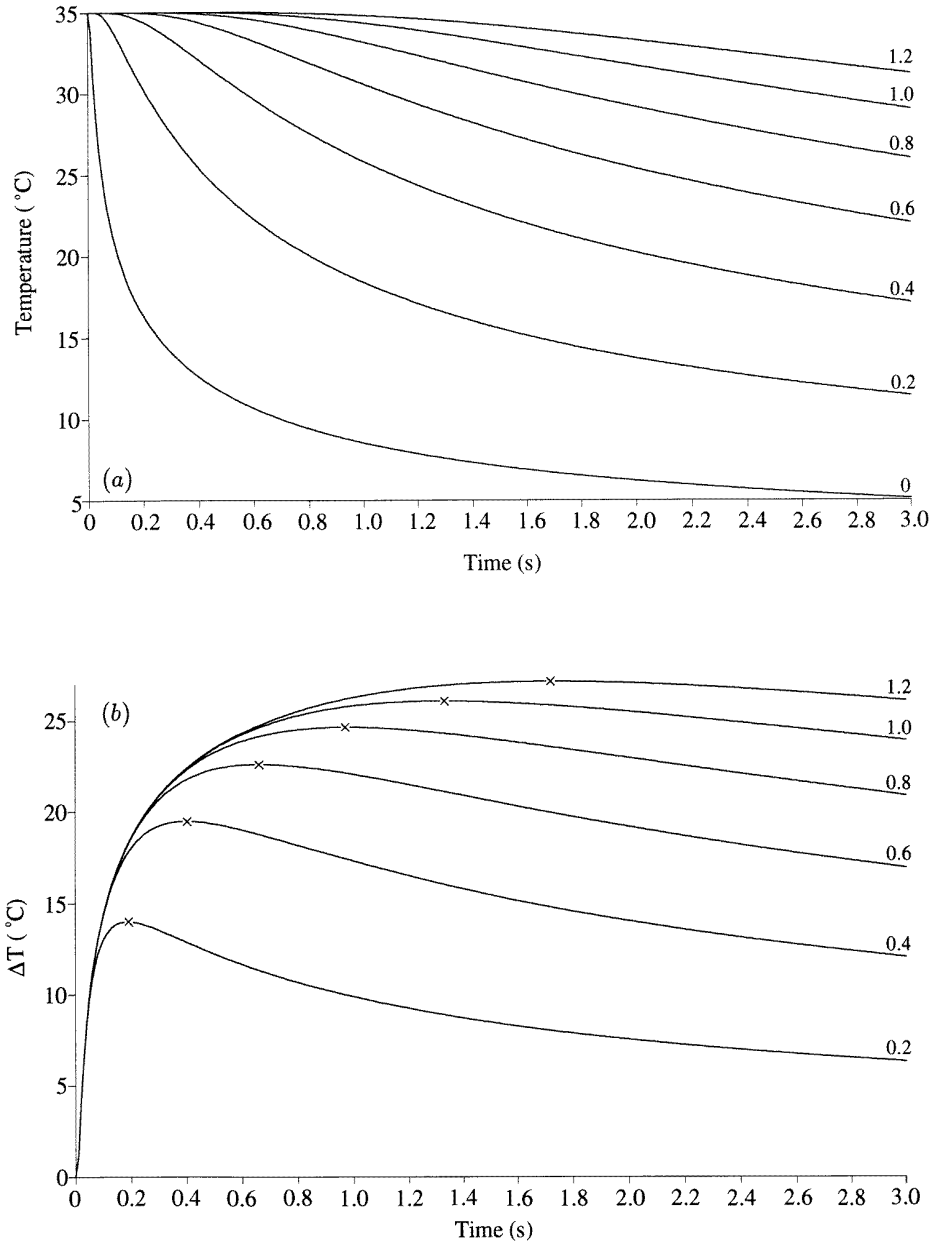


Figure 2. (*a*) The temperature of the skin during 0 °C water cooling. The values on the curves signify the distance from the dermoepidermal junction (mm). (*b*) Temperature differences between the temperature at the dermoepidermal junction and that at different depths below the junction during water cooling. The depths from the junction (mm) are indicated by the values on the curves. Crosses mark the maximum difference in temperature.

cooling makes this mode of cooling better than water cooling. However, water cooling proved to be the best choice when irradiating for 100 ms. This was due to the restriction

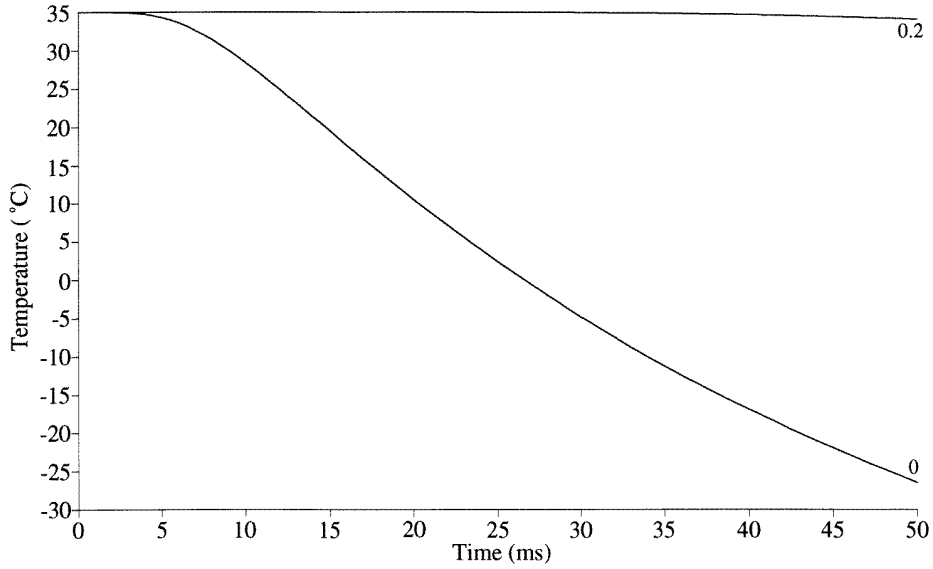


Figure 3. Temporal behaviour of the skin temperature when cooling with liquid nitrogen at −196 °C. The values on the curves signify the distance from the dermoepidermal junction (mm).

imposed on the nitrogen cooling to end just before the laser pulse, assuming a direct and complete evaporation of the nitrogen. Water cooling was continued throughout and after the treatment, enabling heat from the hot epidermis to diffuse into the water layer during and after the laser pulse.

Table 2. Thermophysical properties of skin.

	Conductivity λ (W m^{-1} K^{-1})	Specific heat c (kJ kg^{-1} K^{-1})	Density ρ (kg m^{-3} $\times$ 10^{-3})
Epidermis	0.21	3.6	1.2
Dermis	0.53	3.8	1.2
Blood	0.55	3.6	1.1

Using the maximum irradiances in table 3, the maximum depth of vessel selective damage was calculated. The calculated damage depths from the dermoepidermal junction are shown in table 4. With cooling, the depth of vessel selective damage was predicted to increase from 0.9 mm to 1.3 mm using a 400 μs pulse at 577 nm. After a 100 ms pulse, the depth of vessel damage increased from 0.2 mm to 0.7 mm. With an irradiation wavelength of 532 nm and a 100 ms pulse, no vessel specific damage was predicted. Water cooling made it possible to reach a depth of 0.5 mm when irradiating at 532 nm for 100 ms.

3.2. Surface cooling in conjunction with pre-heating using near-infrared light

In order to obtain complete fading of port wine stains, a vessel selective damage down to $\sim$ 1 mm from the dermoepidermal junction should be achieved (Tan *et al* 1990). Using

Table 3. Calculated threshold irradiances.

Wavelength (nm)	Irradiation time	Irradiance (J cm^{-2})		
		No cooling	Water cooling	Nitrogen cooling
532	400 μs	4.7	9.4	10.9
577	400 μs	5.3	10.7	12.3
532	100 ms	5.1	18.4	11.1
577	100 ms	6.0	20.4	12.5

Table 4. Calculated depths of vessel selective damage.

Wavelength (nm)	Irradiation time	Depth (mm)		
		No cooling	Water cooling	Nitrogen cooling
532	400 μs	0.6	0.9	1.0
577	400 μs	0.9	1.2	1.3
532	100 ms	—	0.5	0.4
577	100 ms	0.2	0.7	0.5

cw lasers, it has not been clinically possible to reach this depth, which our simulations also suggest (table 4). In order to increase the depth of vessel selective damage towards 1 mm using cw lasers, we theoretically investigated how the initial skin temperature, that is, the skin temperature before the laser treatment pulse, could be reshaped to yield an even more favourable temperature profile than obtained using dynamic cooling alone. If the temperature inside the skin could be raised from the baseline temperature while keeping the epidermis cold, two advantageous effects would be attained. First, lowering the epidermal temperature would permit an increased irradiance, as shown above. Second, if the temperature gap between the temperature of the blood vessel to be treated and the coagulation limit ($\sim 70\,^{\circ}$C) is decreased, the heat delivered during a 100 ms pulse will not diffuse away as quickly as otherwise, and less energy deposition is required to damage the blood vessel. To achieve a selective temperature rise inside the skin, surface cooling in conjunction with laser irradiation can be used. In order to have the maximum tissue temperature located as deeply as possible, a penetrating wavelength should be chosen. The 1064 nm light from the Nd:YAG laser is one of the most tissue penetrating laser wavelengths. Therefore, the above described method should be practically feasible for the Nd:YAG laser using the 1064 nm light for pre-heating and the 532 nm light for treatment.

Due to the lack of values for the optical properties of skin at 1064 nm, the optical properties of dermis at 800 nm were used to simulate the light distribution within the skin. Cooling of the skin was first performed with water at a temperature of $0\,^{\circ}$C during 1 s. After this time the calculations resulted in a $26\,^{\circ}$C difference in temperature between the dermoepidermal junction and 1 mm below the junction, yielding a favourable temperature profile. A 3 mm diameter laser spot with a 'top hat' intensity profile at 800 nm was then directed to the skin surface. A number of combinations of laser powers and irradiation times was tested in order to achieve an optimal temperature difference between the dermoepidermal junction and 1 mm below. The limiting factor is that no damage to the skin is allowed. Too short an irradiation time will not affect the temperature at 1 mm from the dermoepidermal junction selectively while a too long irradiation time will produce damage. After an

extensive theoretical testing of different combinations of irradiation times and laser powers, we found that a good combination was an irradiation time of 1 s with a power of 4.1 W. Surface cooling with water was applied throughout the irradiation. After an additional 1 s of cooling the temperature distribution was predicted to be as shown in figure 4, yielding a temperature difference of 36 °C between the dermoepidermal junction and 1 mm below. The calculated temporal behaviour of the temperature at different depths during this pre-treatment is seen in figure 5(*a*). The difference in temperature between different depths and the dermoepidermal junction is shown in figure 5(*b*). Figure 5(*c*) schematically shows the time intervals during which the water cooling and the pre-heating are applied. The figure also shows at what time the treatment pulse is to be applied. A steep rise in the temperature difference occurs after the near-infrared laser has been switched off (after 1 s of irradiation). This is due to the faster cooling of the superficial skin as compared with the deeper lying structures. The maximum skin temperature during the pre-heating never exceeded 60 °C so the calculated damage to the skin inflicted by this pre-treatment was negligible. At this stage, the validity of the assumption that the thermal influence of the blood perfusion can be neglected was tested. The mathematical expression of the perfusion as described by Pennes (1948), where the perfusion acts like a heat sink/source, was incorporated into the model. The value of the blood perfusion rate, which was assigned to the tissue below the epidermal layer, was chosen to be a factor of two greater than the maximum normal skin blood perfusion rate which is found in the face and is equal to 70 ml (100 g)$^{-1}$ min^{-1} (Sekins and Emery 1982). In the epidermal layer, which is devoid of blood vessels, the perfusion rate was set to zero. When simulating with blood perfusion, the calculated temperatures after the entire pre-treatment (cooling, pre-heating and cooling) were found to deviate by less than 0.5 °C from the temperatures obtained in the calculations neglecting the perfusion (results not shown). Thus, neglecting the perfusion can be considered to be a reasonable assumption.

Using the temperature distribution as shown in figure 4 as the initial temperature of the skin, a 100 ms pulse at 532 nm yielded a maximum allowed irradiance and a depth of vessel selective damage of 17.1 J cm^{-2} and 0.8 mm, respectively. In figure 6, the resulting skin temperature distribution immediately after the 100 ms treatment pulse is shown. The maximum depth of vessel selective damage using the Nd:YAG laser thus approaches what can be expected from a treatment with a flashlamp-pumped dye laser at 577 nm without cooling. Most striking is the increase in the depth of vessel selective damage with the pre-treatment as compared with direct application, where no vessel selective damage was predicted. For comparison, the same pre-treatment as above was applied before a 100 ms pulse at 577 nm. The maximum irradiance was found to be 19.1 J cm^{-2} and the depth of vessel selective damage was 1.0 mm. The results are summarized in table 5.

4. Discussion

4.1. Flashlamp-pumped dye lasers

The present study theoretically investigates to what extent dynamic surface cooling influences the vessel selective damage depth by allowing an increase in irradiance. Simulating a flashlamp-pumped dye laser at 577 nm, the calculations showed that by cooling the skin with liquid nitrogen 25 ms before the laser pulse permitted an increase in irradiance by a factor of 2.3 which would result in an increase in the depth of vessel selective damage from 0.9 mm to 1.3 mm. In the model, the liquid nitrogen cooling ceased after 25 ms even if prolonged application at the irradiation spot would be preferable. This boundary condition

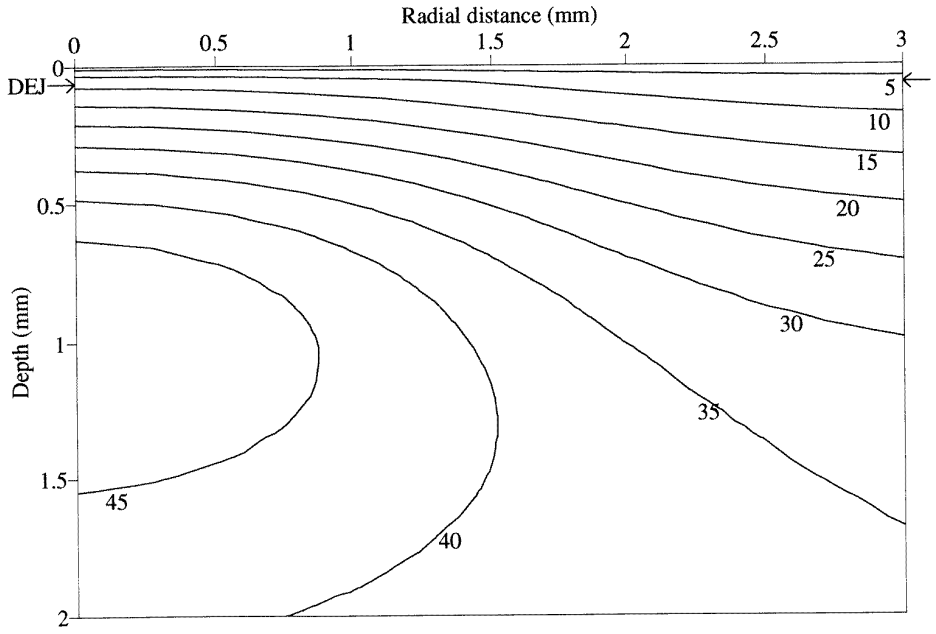


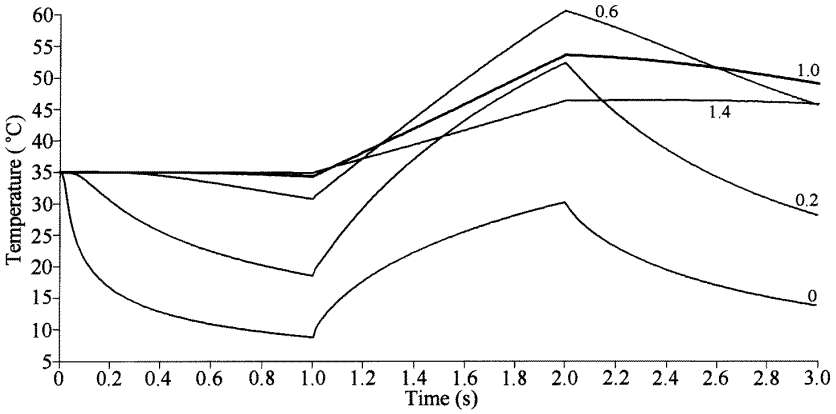
Figure 4. The resulting temperature distribution of the skin after pre-treatment of 1 s of water cooling followed by 1 s of combined cooling and near-infrared irradiation followed by 1 s of cooling. The values on the curves signify the temperature (°C). The position of the dermoepidermal junction (DEJ) is indicated by arrows. As the temperature is cylindrically symmetric, only half of the distribution is shown.

was chosen in order to protect any cooled surrounding area of untreated skin. Cooling with water was predicted to be slightly less efficient (damage depth 1.2 mm). Clinically it may prove difficult to apply the liquid nitrogen in the step like fashion of short duration used in the calculations. Water cooling could however easily be applied using ice or by holding a glass cuvette with circulating water to the skin. Due to the calculated small advantage and the apparently great practical disadvantages of using nitrogen cooling as compared with water cooling, cooling with water seems to be the clinically best mode of cooling.

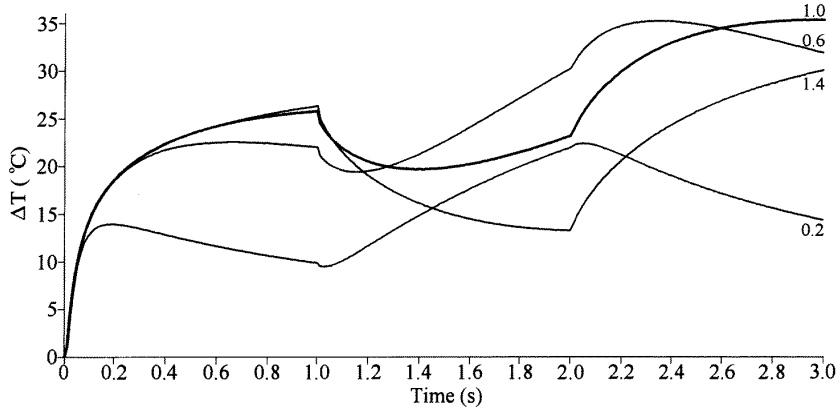
For comparison, even if not of practical interest, the wavelength at 532 nm was also investigated. At this wavelength the predicted vessel damage depth was 0.3 mm less than predicted at 577 nm for all modes of surface cooling.

The predicted irradiance of 5.3 J cm^{-2} for the laser treatment at 577 nm before any dermal damage occurred is in good agreement with the irradiances used for clinical treatment which are in the range of 5–7 J cm^{-2} (Tan 1992). Also, the predicted depth of vessel specific damage of 0.9 mm corresponds well with the reported damage depth of 0.72 mm (Tan *et al* 1990).

By modelling the blood vessels as a simple layer, a dense distribution of vessels is assumed. This implies that the light fluence at the centre of the beam, at the top of the blood layer, will be diminished as compared with the case when modelling a single small blood vessel. Some photons that would have been back scattered into the beam at the level of the blood layer when modelling a single vessel will instead be absorbed off axis



(*a*)



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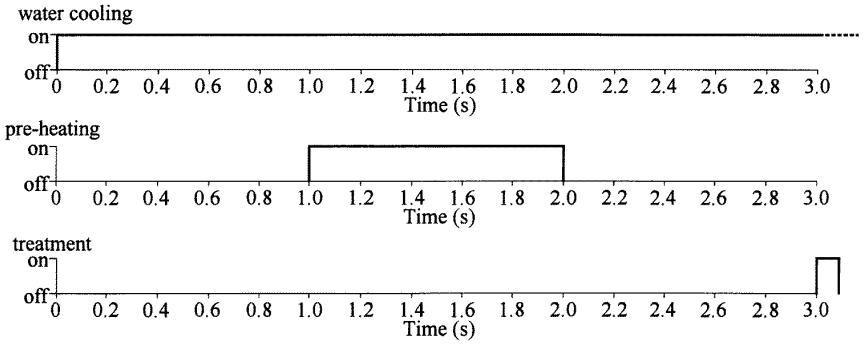

(*c*)

Figure 5. (*a*) The temporal behaviour of the temperature during pre-treatment at different depths from the dermoepidermal junction (mm) as indicated by the values on the curves. (*b*) Temperature differences during pre-treatment between the temperature of the dermoepidermal junction and different depths below the junction (mm) as indicated by the values on the curves. (*c*) A schematic representation of the pre-treatment showing when surface cooling and pre-heating are applied. The temporal position of the treatment pulse is also shown.

in the blood layer. This partly explains the much greater damage depths predicted by Verkruysse *et al* (1993) using a single-vessel model. The model presented in that study also included a diffuse dermal blood distribution overlying the target vessel. With a dermal blood concentration of 1–5%, the damage depth predicted by Verkruysse *et al* (1993) is equal to the damage depth obtained in the present study, indicating the physical significance of a layered model.

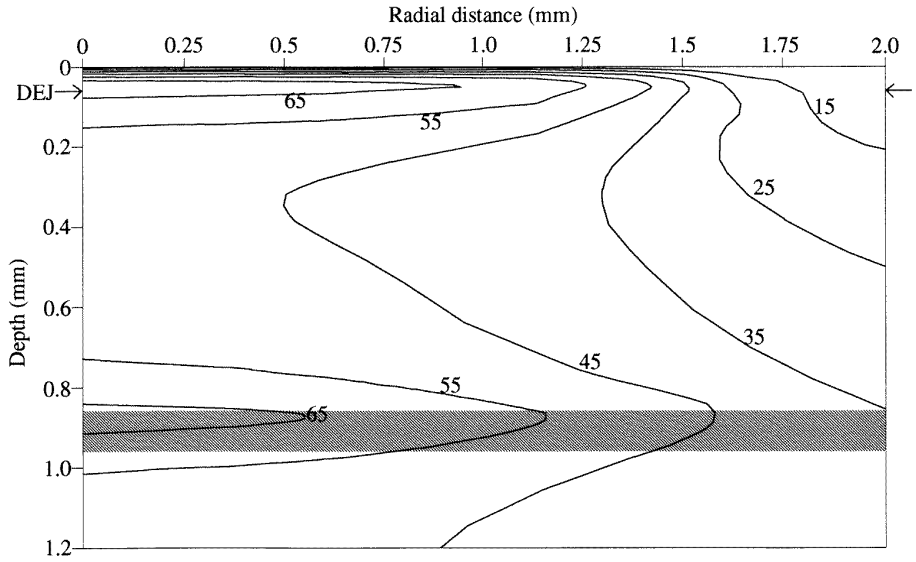

Figure 6. The resulting temperature distribution after treatment at 532 nm for 100 ms following the described pre-treatment. The spot size of the irradiating beam was 3.0 mm in diameter. The blood layer is represented by the hatched area, of which the top is located 0.8 mm from the dermoepidermal junction (i.e., 0.86 mm from the skin surface). The values on the curves signify the temperature (°C). The position of the dermoepidermal junction (DEJ) is indicated by arrows. As the temperature is cylindrically symmetric, only half of the distribution is shown.

Table 5. The calculated maximum irradiance and depth of vessel selective damage after pre-treatment. Irradiation time, 100 ms.

Wavelength (nm)	Irradiance (J cm^{-2})	Damage depth (mm)
532	17.1	0.8
577	19.1	1.0

4.2. Continuous wave lasers

The maximum allowed irradiance predicted without surface cooling (5.1 J cm^{-2} at 532 nm, 6.0 J cm^{-2} at 577 nm) was for the cw lasers using a 100 ms pulse somewhat lower than the irradiances used clinically. In a study made by Mordon *et al* (1993), the threshold irradiance for clinical whitening was found to be between 9 and 12 J cm^{-2} for both the cw

dye laser at 577 nm and the frequency doubled Nd:YAG laser at 532 nm. Clinical whitening represents epidermal coagulation and excludes vessel selective damage and should thus be a similar endpoint of the treatment as the one used in this theoretical study. However, the predicted depth of vessel selective damage of 0.2 mm for irradiation at 577 nm for 100 ms is in good agreement with the reported 0.27 mm obtained with the copper vapour laser at 578 nm (Neumann *et al* 1993).

The frequency doubled Nd:YAG laser has been used in the treatment of port wine stains (Laffitte *et al* 1992) and treatment effects similar to the ones obtained using the argon ion laser have been reported (Apfelberg *et al* 1986), suggesting non-specific diffuse dermal coagulation (Neumann *et al* 1991). The clinical findings are in agreement with our theoretical results in that damage selective to vessels is not attainable with the frequency doubled Nd:YAG laser (table 4). A number of reasons, among those that the 532 nm wavelength may be just right for penetrating through a partially blood filled dermis (van Gemert *et al* 1995), warrants investigations of how to overcome the apparently greatest drawback of using the frequency doubled Nd:YAG laser, namely the epidermal heating. The light at 532 nm is absorbed by haemoglobin in equal amounts as light at 583 nm (van Gemert *et al* 1995). However, the epidermal absorption is greater at 532 nm than at 583 nm resulting in the relatively poor performance of the frequency doubled Nd:YAG laser.

Cooling the surface with water made it theoretically possible to selectively treat blood vessels up to a depth of 0.5 mm at 532 nm (table 4). When treating at 577 nm, water cooling was predicted to increase the maximum depth of vessel selective damage from 0.2 mm to 0.7 mm. A substantial increase in the vessel selective damage depth is thus predicted, encouraging to clinical trials.

For the cw lasers it was found that the maximum irradiance was highest when cooling with water. Heat conduction from the hot epidermis during and after the laser pulse made this mode of cooling more efficient than cooling with liquid nitrogen, where the cooling was assumed to end just before the laser pulse. However, even with surface cooling, the performance of the cw lasers was predicted not to be as good as the flashlamp-pumped dye lasers without cooling.

In order to increase the vessel selective damage depth we investigated the possibility of further reshaping the skin temperature profile before the treatment pulse by pre-irradiating the skin with near-infrared light in conjunction with surface cooling. Theoretically it was found that a temperature of $\sim 50\,^{\circ}\mathrm{C}$ could be achieved at a depth of 1 mm from the dermoepidermal junction without producing dermal damage while the temperature at the junction was $\sim 15\,^{\circ}\mathrm{C}$ (figure 4). By using a pre-irradiation time of as long as 1 s the temperature differences within the skin will be smoothed out due to heat conduction, which makes the assumption of homogenous optical properties of the skin less critical. A subsequent 100 ms laser pulse at 532 nm, with the allowed increase in irradiance plus the fact that the heat conduction process at the irradiated blood layer was slowed down due to the increased baseline temperature, resulted in a vessel selective damage depth of 0.8 mm. The predicted damage depth is comparable with the predicted damage depth of the flashlamp-pumped dye laser at 577 nm without cooling, which was found to be 0.9 mm. For comparison, by irradiating with light at 577 nm for 100 ms after the pre-treatment a damage depth of 1.0 mm was predicted. Another effect of the pre-treatment is that the induced temperature gradient in the skin prior to the treatment pulse will result in a more homogenous heating of vessels located at different depths more proximal than 1 mm from the dermoepidermal junction.

Using the wavelength at 1064 nm for pre-treatment in conjunction with water surface cooling and treating with the wavelength at 532 nm, our calculations suggest that the

Nd:YAG laser might prove to give competitive treatment results. Practically, this could be achieved using Nd:YAG lasers with frequency doubling which can be switched from emitting at 1064 nm to 532 nm in 1 s. In order to achieve efficient cooling throughout the treatment, a glass cuvette with circulating water could be used which would permit the pre-heating pulse and treatment pulse to be directed through the cuvette to the skin. Although a theoretically promising and a seemingly practically feasible technique, the clinical performance of the method still remains to be evaluated.

5. Conclusions

The present study has theoretically shown that the vessel selective damage depth obtainable with an Nd:YAG laser can be comparable with the damage depth produced by a flashlamp-pumped dye laser at 577 nm. By utilizing the near-infrared light at 1064 nm for pre-heating in conjunction with water surface cooling, a treatment pulse at 532 nm is theoretically shown to selectively treat blood vessels down to a depth of 0.8 mm from the dermoepidermal junction. The corresponding calculated depth using the flashlamp-pumped dye laser was 0.9 mm. Water cooling alone resulted in a calculated increase in the damage depth from zero to 0.5 mm when treating at 532 nm. The theoretical results presented in this study thus suggest that the performance of the Nd:YAG laser for treatment of port wine stains can be improved substantially.

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