The Effects of Intense Pulsed Light (IPL) on Blood Vessels Investigated by Mathematical Modeling

Wolfgang Bäumler, PhD,¹* Emre Vural, MD,^{2,3} Michael Landthaler, MD,¹ Francesco Muzzi,⁴ and Gal Shafirstein, PhD²

¹Department of Dermatology, University of Regensburg, Regensburg, Germany

²Department of Otolaryngology-Head and Neck Surgery, Vascular Anomalies Center Arkansas Children's Hospital, University Arkansas for Medical Sciences. Little Rock. Arkansas

³Division of Otolaryngology-Head and Neck Surgery, John McClellan VA Hospital, Little Rock, Arkansas ⁴DEKA Mela, Calenzano, Italy

Background and Objectives: Intense pulsed light (IPL) sources have been successfully used for coagulation of blood vessels in clinical practice. However, the broadband emission of IPL hampers the clinical evaluation of optimal light parameters. We describe a mathematical model in order to visualize the thermal effects of IPL on skin vessels, which was not available, so far.

Study Design/Materials and Methods: One IPL spectrum was shifted towards the near infrared range (near IR shifted spectrum: NIRSS) and the other was heavily shifted toward the visible range (visible shifted spectrum: VSS). The broadband emission was separated in distinct wavelengths with the respective relative light intensity. For each wavelength, the light and heat diffusion equations were simultaneously solved with the finite element method. The thermal effects of all wavelengths at the given radiant exposure (15 or 30 J/cm²) were added and the temperature in the vessels of varying diameters (60, 150, 300, 500 μ m) was calculated for the entire pulse duration of 30 milliseconds.

Results: VSS and NIRSS both provided homogeneous heating in the entire vessel. With the exception of the small vessels (60 μ m), which showed only a moderate temperature increase, all vessels exhibited a temperature raise within the vessel sufficient for coagulation with each IPL parameter. The time interval for effective temperature raise in larger vessels (diameter $>60~\mu$ m) was clearly shorter than the pulse duration. In most instances, the vessel temperature was higher for VSS when compared to NIRSS.

Conclusions: We presented a mathematical model capable of calculating the photon distribution and the thermal effects of the broadband IPL emission within cutaneous blood vessels. Lasers Surg. Med. 39:132–139, 2007. © 2006 Wiley-Liss, Inc.

INTRODUCTION

Broadband light emission of intense pulsed light (IPL) sources have been successfully used in dermatology for the treatment of various skin conditions including vascular disorders [1-6]. The mechanism of action of lasers in the treatment of vascular disorders is related to their selective absorption by hemoglobin within the blood vessels. The absorbed light energy is converted to heat, which coagulates the blood when it exceeds 70° C [7]. This well-known process has been first described by Anderson and Parrish as selective photothermolysis, and it forms the basis for laser treatment of cutaneous vascular disorders [8].

The mechanism for selective photothermolysis with IPL in the treatment of cutaneous vascular disorders should be similar to lasers. However, unlike lasers, the IPL simultaneously delivers multiple wavelengths of light within the range of 500 to 1,000 nm at different intensities. In essence, an IPL irradiation could be considered as a virtual application composed of more than 500 lasers emitting different wavelengths and radiant exposures (J/cm^2) of light at the same time. The radiant exposure of each virtual laser is proportional to the intensity of each wavelength in the IPL spectrum. The temperature generated within the blood vessel strongly depends on the IPL spectral distribution as well as the radiant exposure and pulse duration.

The optimal parameters for selective photothermolysis in laser treatments have been widely published by using mathematical models simulating selective photothermolysis [9-13]. However, no model exists in order to correlate the IPL spectrum to the temperature distribution within blood vessels. Establishing a mathematical model for IPLrelated selective photothermolysis may help to improve the treatment of cutaneous vascular disorders in clinical setting and may lead to the development of new IPL systems for optimal treatment of cutaneous vascular disorders.

The main technical challenge in mathematical modeling of multiple light wavelengths (as in IPL) is the need to

DOI 10.1002/lsm.20408

^{*}Correspondence to: Dr. Wolfgang Bäumler, Department of Dermatology, University of Regensburg, 93042 Regensburg, Germany. E-mail: baeumler.wolfgang@klinik.uni-regensburg.de

Accepted 17 August 2006 Published online 25 October 2006 in Wiley InterScience (www.interscience.wiley.com).

include the effect of various optical parameters such as absorption, scattering coefficient, and anisotropy factor on the light propagation in tissue. Since these properties are unique for every wavelength, they cannot be averaged. Thus, the modeling of IPL propagation in tissue must be simultaneously performed for each wavelength composing the IPL spectrum. In order to achieve this, we modified our mathematical model of selective photothermolysis of portwine stains used in a previous study [14]. This model utilized finite element methods to solve the diffusion approximation of light tissue interaction and was successfully shown in animal model to be well correlated with clinical outcomes [14-16]. In the current study, we investigated the applicability of mathematical modeling for selective photothermolysis to multiple wavelengths in a simultaneous fashion.

MATERIALS AND METHODS

The mathematical model, which has been discussed in detail in a previous study, was modified to simulate selective photothermolysis for two IPL spectra [14]. Using similar skin geometry, we calculated the temperature distributions within four different size of blood vessels (60, 150 300, and 500 μ m in diameter) for IPL radiant exposures of 15 and 30 J/cm² and pulse time of 30 milliseconds, all of which are typical IPL parameters currently used in clinical practice.

In order to determine the temperature distributions within the tissue, the heat and optical diffusion equations were solved simultaneously using the finite element method (FEM) by the aid of commercially available software (Femlab 3.1, Comsol, Burlington, MA). The model was created based on an IPL applicator with an area of 40×8 mm, whereas only half of the applicator width (4 mm) was used in the model due to symmetry (Fig. 1). The blood vessels used for calculations were located at the depth of 1.2 mm and were surrounded by other blood vessels to simulate a more realistic scenario.

Photon Distribution in IPL Spectra

In order to apply the diffusion approximation principle to our modeling, the respective IPL spectrum was divided into a certain number of sampling points regarding the emission peaks of the curve. The exact location and relative intensity of each peak were calculated by finding the center of gravity within the range that is bound between two circles representing the background level (see Fig. 2). The relative intensity I_{λ} for each wavelength λ is the area under each peak of a specific wavelength.

The light intensity, $P(t)_{\lambda}$ of the IPL emission for each wavelength λ is:

$$P(t)\lambda = \frac{I\lambda}{\sum_{\lambda=m}^{\lambda=m} I\lambda} \cdot P(t) \text{IPL}$$
(1)

The sum of all "*m*" peaks yields the total power of the IPL spectrum in the range of 500 to 1,000 nm. We modeled the

Capillaries, 10 & 20 µm Capillaries, 10 & 20 µm Test Vessel 25 3 35 1 2 3 4 5 6 6.5

IPL Irradiated Zone

Fig. 1. Schematic geometrical model of a cross section of normal skin that was used in the IPL simulation. It consists of a thin epidermal layer and a dermis containing different blood vessels of different diameters. The blood vessels can be positioned by the computer at different positions in the dermis. This model includes the test vessel used for modeling (depth 1.2 mm) showing a vessel diameter of 60, 150, 300, or 500 μ m). The symmetry axis is at distance 0 from the center. The irradiated zone in the figure is equivalent to the half width of short edge length of an IPL applicator (8×40 mm).

emission spectrum of two typical xenon flash lamps that are used in IPL sources (DEKA, Calenzano, Italy) showing a cutoff at 500 and 1,000 nm of wavelengths. Thus, the emission ranged from 500 to 1,000 nm exhibiting two different spectral distributions. One spectrum was shifted towards the near infrared range (i.e., near IR shifted spectrum, NIRSS) and the other was heavily shifted toward the visible range (i.e., visible shifted spectrum VSS).

In the IPL modeling, we first calculated the photon distribution for each specific wavelength λ , and thereafter combined the solutions to calculate the thermal field. The two-dimensional time-dependent diffusion equation for each wavelength is given by

$$\frac{\partial}{\partial t}\Phi^{\lambda}(x,z,t) - \nabla(\alpha_{n}^{\lambda}\nabla\Phi^{\lambda}(x,z,t)) = c_{n}^{\lambda}\mu_{\mathbf{a},n}^{\lambda}\Phi^{\lambda}(x,z,t) \qquad (2)$$

$$a_n^{\lambda} = \frac{c_n}{3(\mu_{a,n}^{\lambda} + (1 - g^{\lambda})\mu_{s,n}^{\lambda})}$$
(3)

 $\Phi^{\lambda}(x,z,t)$ is the photon fluence rate $[P_n/m^2 \text{second}] P_n$ is the number of photons for each wavelength used in the simulation, α_n^{λ} is the optical diffusion coefficient $[m^2/\text{second}]$ of tissue *n* (epidermis, dermis, or blood) absorption, $\mu_{a,n}$ and $\mu_{s,n}$ are the linear absorption and scattering coefficients [1/m], *g* is the optical anisotropy factor, and c_n is the speed of light. The right term of Equation (2) represents the reaction rate or the absorbed energy in the epidermis (n = e), dermis (n = d), or red blood cells (n = b).



 $rac{(1-r_r)P(t)\lambda c_0}{hv^\lambda}\Big| z=0, 0\leq x\leq 4mm=-lpha_n^\lambda
abla \Phi^\lambda(x,z,t)$ (4) t>0

 v^{λ} is the frequency of light at each wavelength λ , h is the Planck's constant (6.62×10^{-34} Js). The reflection factor, r = 0.1 is the ratio between the light reflected from the tissue and IPL power output, whereas c_0 is the speed of light in a vacuum (3×10^8 m/second). It was assumed that the photons at each wavelength propagated in tissue according to the corresponding optical properties such as scattering and absorption, and the respective values were taken from the literature [17] that has been improved by a recent article [18].

With respect to surface boundary conditions, the flux of photons at the skin surface (epidermis) at every wavelength

The corresponding heat transfer equation is:

~**m**

$$\rho_n C(T)_n \frac{\partial T}{\partial t} - \nabla (k_n \nabla T) = \rho_n C(T)_n v_p (T_v - T) + \sum_{\lambda=1}^{\lambda=m} \mu_{\mathbf{a},n}^{\lambda} \Phi^{\lambda}(x, z, t) h v^{\lambda}$$
(5)

where *T* is the temperature as a function of time (*t*) and space (x, z), k_n [W/mK] is the thermal conductivity of the epidermis (n = e), dermis (n = d), or blood (n = b). ρ_n [kg/m³] is the density, $V_{\text{F},n}$ is the volume fraction of the chromophores inside the tissue, and $C(T)_n$ [J/kgK] is the temperature-dependent specific heat capacity of epidermis, dermis, or blood, including the latent heat of evaporation. The blood perfusion v_p was $18.73 m_b/\text{kgs}$, where m_b is the mass of blood per kilogram tissue.

The photon distribution and the temperature in tissue were calculated for both emission spectra using pulse duration of 30 milliseconds, and a radiant exposure of 15 or 30 J/cm^2 . The modeling was performed for vessels 60, 150, 300, or $500 \ \mu\text{m}$ at a depth of 1.2 mm.

The dependency of the optical parameters on each wavelength composing IPL spectrum complicates mathematical modeling of light tissue interaction for IPL, as compared to monochromatic lasers. The emission of an IPL shows a broadband spectrum of several hundreds of nanometer [1]. This would require the calculation of photon propagations for each single wavelength within the IPL spectrum, which may take significant amount of time to accomplish, even for one set of parameters. Therefore, we decided to perform our modeling of IPL only for distinct positions within the spectrum, which are marked with green lines in Figures 2. The length of the lines represents the respective contribution to the optical power of the total IPL emission. The respective absorption coefficients at these wavelengths are shown in Figure 2c.

The two IPL spectra used in our modeling are shown in Figure 2. The first spectrum is shifted towards the near infrared range NIRSS (Fig. 2a) and the second spectrum is shifted toward the visible range VSS (Fig. 2b). These two spectra may represent the full bandwidth of IPL used in clinical practice [1-6]. It is obvious that the VSS spectrum

Fig. 2. The two IPL spectra that are used for the modeling with the spectrally resolved intensity of the NIRSS (**a**) and the VSS (**b**), the respective absorption coefficients are shown in (**c**). The respective IPL spectrum was cut into pieces yielding small bands. The width (wavelength interval) of each band is marked by two small circles on the spectral course. The middle of each wavelength interval (sampling points) shows the relative intensity I_{λ} for each wavelength λ_1 to λ_m (green lines).

 L_{λ} is given by

exhibits more power in the spectral range of 500 to 700 nm as compared to NIRSS.

RESULTS AND DISCUSSION

Two-Dimensional Temperature Distributions

The temperature in the two-dimensional section of the skin was calculated for each spectrum and two examples are displayed in Figure 3. In Figure 3a, the temperature is shown for the NIRSS at the end of 30-millisecond pulse duration using a radiant exposure of 15 J/cm². The test vessel had a diameter of 300 μ m and it exhibited a homogeneous heating in its entirety with an approximate maximal temperature of 80°C in its core. The temperature outside the vessels in the dermis is elevated to a certain



Fig. 3. The resulting temperature at the end of 30 milliseconds pulse duration is shown as a virtual two-dimensional cut using a radiant exposure of 15 J/cm^2 in a test vessel with the diameter of 300 μ m. NIRSS results in a steeper temperature gradient within the test vessel (**top**). The VSS emission leads to a more homogeneous heating in the same test vessel (**bottom**).

degree and this might be partly due to heat transfer from the hot vessels and partly due to direct heating of dermis, since part of the NIRSS photons ($\lambda > 900$ nm) can be readily absorbed by the bloodless dermis.

In Figure 3b, the temperature is shown for the VSS at the end of 30-millisecond pulse duration using a radiant exposure of 15 J/cm². The test vessel had a diameter of $300 \,\mu\text{m}$. In addition, with the VSS, the test vessel exhibited homogeneous heating in its entirety but the temperature was slightly less when compared to the NIRSS. This is probably due to decreased proportion of infrared photons in this spectrum, which resulted with less direct heating of the dermis than NIRSS and more comparable heating with pulsed dye lasers [14].

Effects of Vessel Size

The effects of IPL parameters on vessel diameter of 60, 150, 300, and 500 μ m were studied. The temperature at the top, center, and bottom portion of each blood vessel was calculated for IPL based on the temperature gradients within blood vessels found in a previous study [14]. It was postulated that coagulation of blood would occur at temperatures higher than 70°C [7]. In Figure 4, temperature measurements in various size vessels are shown for NIRSS and VSS at both radiant exposures.

The temperature values for the top portions of the vessels increased as the vessel diameter increased from 60 μ m to 150 μ m and yielded comparable values for 300 μ m and 500 μ m vessels. Neither NIRSS nor VSS revealed a sufficient temperature increase in order to coagulate various size vessels using 15 J/cm² of radiant exposure. However, coagulation at the top portions of vessels occurred using the higher radiant exposure of 30 J/cm² at both spectra, except for the vessel diameter of 60 μ m. The VSS generated higher temperatures as compared to NIRSS and this was attributed to the high absorption coefficient of hemoglobin for most of the wavelengths covered by VSS ranging from 500 to 650 nm.

The temperature, at the center portions of the vessels exceeded the needed temperature for blood coagulation in the vessels with 150 μ m, 300 μ m, and 500 μ m diameter for both spectra and radiant exposures. Again, the IPL parameters used in the modeling hardly matched the criteria of a sufficient coagulation temperature in the vessel with 60 μ m diameter.

Finally, it was observed that effective coagulation was difficult to achieve at the bottom portions of the vessels, regardless of the vessel size or IPL parameters. When using the radiant exposure of 15 J/cm², temperature values of about 50°C were calculated, which is equivalent to only a moderate warming effect at the bottom portions of the vessels.

Based on these findings, it seems to be very unlikely to coagulate small vessels ($60 \mu m$) using the given IPL spectra at radiant exposures less than 30 J/cm^2 . This is probably due to the limited amount of chromophores (hemoglobin) in such small vessels, which is similar to modeling using



Fig. 4. The temperature inside the vessels for different vessel diameters. The results are shown for the top, center, and bottom portions of the vessels at the end of the pulse duration (30 milliseconds). For both spectra, radiant exposures of 15 J/cm^2 and 30 J/cm^2 were used with pulse duration of 30 milliseconds.

pulsed dye lasers at 585 or 595 nm [14]. Effects such as hypobaric pressure [19] or dermal blood volume fraction [20] play a significant role. Additionally, the cooling of a vessel by heat diffusion into the dermis has a major impact on the temperature in the vessel and the thermal damage. The cooling of a vessel during and after laser irradiation depends on the volume–surface ratio of each vessel and therefore on the vessel size. The smaller the vessel diameter, the faster is the cooling and the smaller is the thermal damage inside the vessel. This has been discussed when modeling the treatment of large vessels with Nd:YAG laser at 1,064 nm [16].

Moreover, our findings support the results of clinical studies. Using IPL, a better clearance was observed in patients treated for visible teleangiectatic vessels when compared to patients with diffuse erythema composed of much smaller vessels [1]. It is also reported that shorter wavelengths (530–750 nm) of IPL, which is comparable to our VSS yielded better vessel clearance than longer wavelengths (555–950 nm) of IPL, which comparable to our NIRSS. This finding correlates with our modeling results, which revealed higher temperature values for VSS as compared to NIRSS.

Because of the high absorption coefficient of hemoglobin in the visible part of the spectrum, the temperature at the top or center portions of the vessel were generally higher for the VSS as compared to the NIRSS. Nevertheless, the temperature in the center portion of the large vessels ($300 \ \mu\text{m}$, $500 \ \mu\text{m}$) was higher by using NIRSS and the radiant exposure of 15 J/cm². The longer wavelengths of NIRSS penetrate the large vessels and come across a thick layer of light absorbing hemoglobin. This combination may lead to an effective delivery of thermal energy in these large vessels, at least for the radiant exposure of 15 J/cm². At the bottom portions of the vessels, the NIRSS causes similar or even higher temperatures, except for the small vessel diameters.

Effects of Heating

When using pulsed dye lasers for vessel diameters in the range of 10 to 500 μ m (e.g., port wine stains), typically very short pulse durations of less than 10 milliseconds are applied. In fact, sufficient heating of the vessels can be achieved within tenths of milliseconds with a pulse duration as short as 0.45 milliseconds, while cooling down may require time intervals up to 20 milliseconds [14].

Heating process of the vessels using IPL is shown in Figure 5, where the temperature values represent the values of the center portions of the vessels. It is clear that the temperature increases slowly by time and saturates at very low levels for the vessels with 60-µm diameter. Using radiant exposures of 15 J/cm^2 , the maximal value is almost achieved after 10 milliseconds and it remains nearly constant for the following 20 milliseconds of the pulse duration. It is obvious that the long pulse duration cannot provide a temperature sufficient to provide coagulation in the small vessel. Therefore, shortening the pulse duration and increasing the power of IPL emission would be



necessary in order to coagulate smaller vessels, as proven for pulsed dye lasers [14].

For medium caliber vessels with a diameter of 150 μ m, the temperature increases by time and the effective temperature for ablation is reached after about 20 milliseconds by using a radiant exposure of 30 J/cm². To achieve similar results, the pulse duration might be shortened by 10 milliseconds. When using 15 J/cm², the temperature also increases but at a lower level. Using a low radiant exposure, the pulse duration seems to be appropriate for a sufficient coagulation temperature, which may take place at the end of IPL pulse (30 milliseconds).

For larger caliber vessels with a 300 μ m or 500 μ m diameter, the temperature increases linearly by time and the values saturate at high levels ranging from 90 to 100°C using a radiant exposure 30 J/cm². The saturation is due to the latent heating of water within the blood. Since the coagulation temperature is achieved after about 15 milliseconds, the pulse duration might be shortened by 50%. When using 15 J/cm², the full pulse duration is required for a sufficient coagulation temperature.

Regarding the two different IPL spectra, VSS yields higher temperature values in the small vessels (60 μ m, 150 μ m) during the entire course of pulse duration as compared to NIRSS. Interestingly, NIRSS provides a faster heating in larger vessels (300 μ m, 500 μ m) as compared to VSS, but generates only a minor maximal temperature value, except for 500 μ m vessel at 15 J/cm². The use of NIRSS leads to a steeper gradient of temperature within the vessel (see Fig. 3) causing a rapid outflow of heat energy from the center portion of the vessels towards their walls. This would decrease the temperature in the center portions of these vessels.

Using IPL for the treatment of rosacea in clinical practice, a radiant exposure of about 30 J/cm² is applied at pulse durations of about 5 milliseconds [21]. In another study, the radiant exposure and the cut-off filter is changed for different vessels sizes. For small vessels, a radiant exposure of 30 J/cm² is applied and up to 56 J/cm² for large vessels using multiple pulses. The pulse duration was about 5 milliseconds using triple pulses [22]. Bjerring et al [1] show a table of pulse durations and radiant exposures when using IPL for different vessels sizes. For teleangiectasia, he recommends pulse durations of 15 to 30 milliseconds and a radiant exposure of 11.5 to 22 J/cm², whereas for diffuse erythema (small vessels) a pulse duration of about 5 to 12 milliseconds and a radiant exposure of about 9 to 17 J/cm².

In our modeling, we used pulse duration of 30 milliseconds and depending on the vessel size, the maximum temperature is achieved after 10 to 20 milliseconds. This supports the clinical findings of Bjerring et al. [1], who used long pulse durations at moderate radiant exposures.

Fig. 5. The course of the temperature in the center of the vessels for the different vessel diameters 60 μ m, 150 μ m, 300 μ m, or 500 μ m. For both spectra, radiant exposures of 15 J/ cm² and 30 J/cm² were used with pulse duration of 30 milliseconds (end of pulse).



Effects of Wavelength

In order to investigate the inradiant exposure of wavelength distribution on the photothermal action, the temperature was calculated for each wavelength within the respective spectrum (Fig. 6). There is a major contribution of the shorter wavelengths for effective heating of smaller vessels ($60 \mu m$ and $150 \mu m$) using VSS. For larger vessels ($300 \mu m$ and $500 \mu m$), there is not much difference between individual wavelengths, although the photothermal effect is slightly more pronounced for longer wavelengths. For NIRSS, the contribution to the thermal effects is more evident for longer wavelengths regardless of the vessel diameter. In the future, we will investigate the radiant exposure of different cut-off filters on the thermal action in blood vessels.

CONCLUSION

We present a mathematical model for selective photothermolysis of IPL, which may help for developing optimal IPL systems or parameters for dermatological applications. Although mathematical modeling is an excellent tool that helps to identify the optimal parameters for satisfactory clinical outcomes; it cannot replace clinical studies.

Moreover, the temperature achieved in the different vessel sizes are not due to the light energy applied to the sin surface but to the light energy absorbed in the hemoglobin inside the vessel. Due to the broadband emission, IPL light consists of many different wavelengths. However, the absorption coefficient shows a substantial variation when going from 500 to 1,000 nm. Thus, the absorbed light energy depends critically on the distribution of photon energies of the IPL emission, that is, it depends on the spectral shape of the IPL emission. For a monochromatic laser light, beside pulse duration and radiant exposure, the laser wavelength is important for selective photothermolysis and efficacy of the treatment.

Regarding the broadband emission of IPL, not a single wavelength but different photons with different energies and wavelengths are responsible for the thermal effects in the vessels. In contrast to lasers, the clinical outcome of different studies using a certain pulse duration and radiant exposure are only comparable if the same spectral shape of IPL has been used. Consequently, using IPL for blood vessels coagulation, the specification of pulse duration, radiant exposure, and cut-off filter is not sufficient without any information about the spectral shape of light emission.

This article should encourage physicians to evaluate modeling findings in clinical practice performing clinical studies.

Fig. 6. The contribution of the different bands to the temperature in the vessel. The results are displayed for the different vessel diameters $60 \ \mu m$, $150 \ \mu m$, $300 \ \mu m$, or $500 \ \mu m$. For both spectra, a radiant exposure $30 \ J/cm^2$ was used with pulse duration of 30 milliseconds.

REFERENCES

- Bjerring P, Christiansen K, Troilius A, Dierickx C. Facial photo rejuvenation using two different intense pulsed light (IPL) wavelength bands. Lasers Surg Med 2004;34(2):120– 126.
- 2. Bedewi AF. Hair removal with intense pulsed light. Lasers Med Sci 2004;19(1):48–51.
- 3. Dierickx CC. Hair removal by lasers and intense pulsed light sources. Dermatol Clin 2002;20(1):135-146.
- 4. Troilius A, Troilius C. Hair removal with a second generation broad spectrum intense pulsed light source—A long-term follow-up. J Cutan Laser Ther 1999;1(3):173–178.
- 5. Gold MH, Bell MW, Foster TD, Street S. One-year follow-up using an intense pulsed light source for long-term hair removal. J Cutan Laser Ther 1999;1(3):167-171.
- Raulin C, Werner S, Hartschuh W, Schonermark MP. Effective treatment of hypertrichosis with pulsed light: A report of two cases. Ann Plast Surg 1997;39(2):169-173.
- Black JF, Barton JK. Chemical and structural changes in blood undergoing laser photocoagulation. Photochem Photobiol 2004;80:89–97.
- 8. Anderson RR, Parrish JA. Selective photothermolysis: Precise microsurgery by selective absorption of pulsed radiation. Science 1983;220(4596):524-527.
- 9. Kimel S, Svaasand LO, Hammer-Wilson MJ, Nelson JS. Influence of wavelength on response to laser photothermolysis of blood vessels: Implications for port wine stain laser therapy. Lasers Surg Med 2003;33(5):288-295.
- Lucassen GW, Verkruysse W, Keijzer M, van Gemert MJ. Light distributions in a port wine stain model containing multiple cylindrical and curved blood vessels. Lasers Surg Med 1996;18(4):345-357.
- Pfefer TJ, Barton JK, Smithies DJ, Milner TE, Nelson JS, van Gemert MJ, Welch AJ. Modeling laser treatment of port wine stains with a computer-reconstructed biopsy. Lasers Surg Med 1999;24(2):151-166.
- van Gemert MJ, Lucassen GW, Welch AJ. Time constants in thermal laser medicine: II. Distributions of time constants and thermal relaxation of tissue. Phys Med Biol 1996; 41(8):1381-1399.

- Verkruysse W, Lucassen GW, de Boer JF, Smithies DJ, Nelson JS, van Gemert MJ. Modelling light distributions of homogeneous versus discrete absorbers in light irradiated turbid media. Phys Med Biol 1997;42(1):51-65.
- 14. Shafirstein G, Baumler W, Lapidoth M, Ferguson S, North PE, Waner M. A new mathematical approach to the diffusion approximation theory for selective photothermolysis modeling and its implication in laser treatment of port-wine stains. Lasers Surg Med 2004;34(4):335–347.
- Babilas P, Shafirstein G, Baumler W, Baier J, Landthaler M, Szeimies RM, Abels C. Selective photothermolysis of blood vessels following flashlamp-pumped pulsed dye laser irradiation: In vivo results and mathematical modelling are in agreement. J Invest Dermatol 2005;125(2):343-352.
- Boumler W UH, Hartl A, Landthaler M, Shafirstein G. Optimal parameters for the treatment of leg veins using Nd:YAG lasers at 1064 nm. Br J Dermatol 2006;155:364– 371.
- 17. Welch AJ, van Gemert MJ. Optical-Thermal Response of Laser-Irradiated Tissue. New York: Plenum Press. 1995.
- Faber MJ, Aalders MC, Mik EG, Hooper BA, van Gemert MJ, van Leeuwen TG. Oxygen saturation-dependent absorption and scattering of blood. Phys Rev Lett 2004; 93(2):28102.
- Aguilar G, Franco W, Liu J, Svaasand LO, Nelson JS. Effects of hypobaric pressure on human skin: Implications for cryogen spray cooling (part II). Lasers Surg Med 2005; 36(2):130-135.
- Svaasand LO, Aguilar G, Viator JA, Randeberg LL, Kimel S, Nelson JS. Increase of dermal blood volume fraction reduces the threshold for laser-induced purpura: Implications for port wine stain laser treatment. Lasers Surg Med 2004;34(2):182– 188.
- Schroeter CA, Haaf-von Below S, Neumann HA. Effective treatment of rosacea using intense pulsed light systems. Dermatol Surg 2005;31(10):1285-1289.
- Clementoni MT, Gilardino P, Muti GF, Signorini M, Pistorale A, Morselli PG, Cavina C. Facial teleangectasias: Our experience in treatment with IPL. Lasers Surg Med 2005; 37(1):9–13.