Physical background of Port Wine Stain vascular lesion treatment

Author:
Matija Milanič

Advisors:
dr. Boris Majaron
Prof. dr. Martin Čopič

Introduction

Nowadays cooperation of physics and medicine has become tighter as ever before. Physics provides medicine with new explanations, tools for diagnostics and treatment, but medicine gives physics insight in completely new world. There are countless areas of cooperation; just to name some of them: x-rays, NMR, CT, biomedical optics. The last one had great impact on modern surgery, diagnostics of eye diseases, cancer etc. In present text I am presenting the mechanisms of treatment of skin vascular disease, more precisely treatment of port wine stain (PWS) using laser irradiation.

Port wine stain is a congenital vascular malformation of the dermis. Since two thirds of these malformations occur on the face, PWS are a clinically significant problem.
In the past, PWS treatment has included cosmetic cover-up, skin grafting, ionizing radiation, dermabrasion, cryosurgery, tattooing and electrography, but none of these modalities provided cosmetically acceptable results. The development of lasers and their ability to selectively damage PWS blood vessels offered a promising treatment option.

PWS treatment is still a very active area of clinical research even after 40 years since laser irradiation was successfully used as a method of PWS treatment for the first time. The complexity of processes, intra-tissue photon transport, energy deposition, heat transport, physiological responses and the tissue structure diversity still contains a lot of unanswered questions and makes the problem of PWS treatment very interesting for physicists.

Physics of light interaction with tissue is quite complicated, but it is necessary tool for explanation of processes happening during laser treatment. The process depends on four parameters, which concern the properties of the laser beam that is incident on PWS, namely, the wavelength, spatial distribution of irradiance, pulse duration and spot diameter.

The aim of physics is to provide clinicians with optimal, previously named treatment parameters to meet the clinical goal of irreversible damage of the ectatic vessel walls without any damage to the other skin constituents.

Port wine stain birthmark

Port wine stain (lat. nevus flammeus) is a congenital vascular lesion that occurs in approximately 0.3 – 0.7 percent of individuals [1]. The lesion is irregularly shaped with prominent vessels that are present at birth and do not disappear with time. Generally, the malformation is confined to the subsurface layer of skin. Essentially, the deep vessels and capillaries are enlarged and dilated.

As a child grows, the area involved tends to increase in proportion to the increase in development and size of the child. As time goes on, progression of the malformation can occur and it can develop into a cosmetic disfigurement. With further aging, the color changes from pink to red and further to purple and nodular and papular type hemangiomas develop, causing increased disfigurement and irregularity of the skin texture.

Left untreated, port wine stains can cause problems. Children who have to deal with port wine stains have a potential possibility for significant psychological damage due to this cosmetic deformity. Hemorrhage and hypertrophy are common problems noted in adult years. Occasionally, infection is a problem.

The color of the port wine stain varies in hue from pink (Figure 1a) to red to purple. The shape is irregular and generally the distribution is unilateral. Most commonly, the face is involved but it may indeed incur at any cutaneous site.

Laser irradiation of PWS is the preferable treatment of the disease nowadays, because it gives best blanching and usually no scarring. Some other methods used in the past were tattooing, cryogenic treatment and surgical excision of PWS, but the result of treatments using these methods was far from satisfactory.

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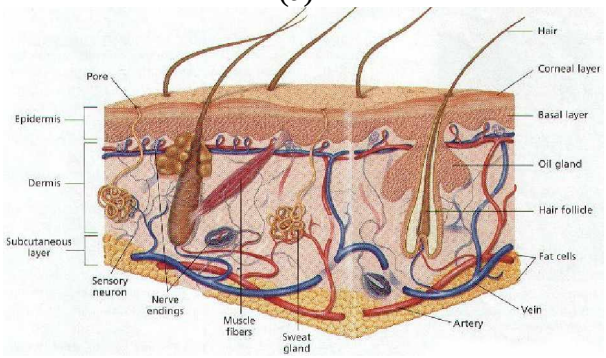
(b)



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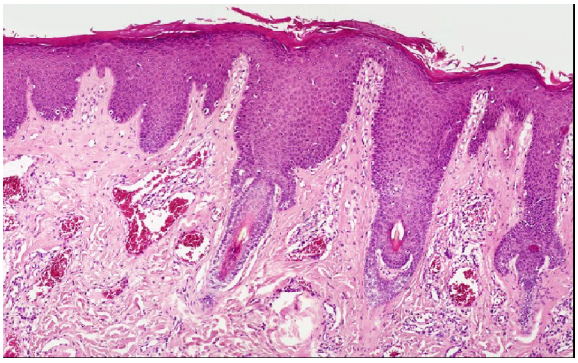


(d)

Fig. 1: (a) Picture of a child with PWS on his face (b) and of an adult with fully developed PWS lesion. (c) Healthy skin model with epidermis, dermis and upper layer of subcutaneous tissue. Usual inclusions are presented. (d) Histology of PWS skin. Dark stained layer is epidermis and light stained layer is dermis with prominent, ectatic vessels.

Human skin has two different layers (Figure 1c). The upper one is epidermis where melanocytes are located. Melanocites are cells with melanin dissolved in cytoplasm. Melanin is one of the most important natural cromophores in human body. Next layer is dermis, where blood vessels, nerval endings and a lot of other inclusions are found. Dermis consists mostly of collagen fibers. In the lumen of blood vessels are eritrocites with hemoglobin, which is next important human cromophore. Histology shows typical picture of PWS lesion. Most prominent are voluminous, ectatic blood vessels filled with eritrocites (Figure 1d).

Clinical studies were made on PWS patients to better understand the etiology of the disease and to improve its treatment. Here are presented some results of histology study made by Barsky et al [2] on 100 PWS patients. They found that on average, the number of vessels decreased with depth of the skin, but the percent of dermal area composed of vessels (vascular

area) had maximum between 200 μm and 400 μm and the mean vessel diameter was between 50 – 80 μm (Figure 2).

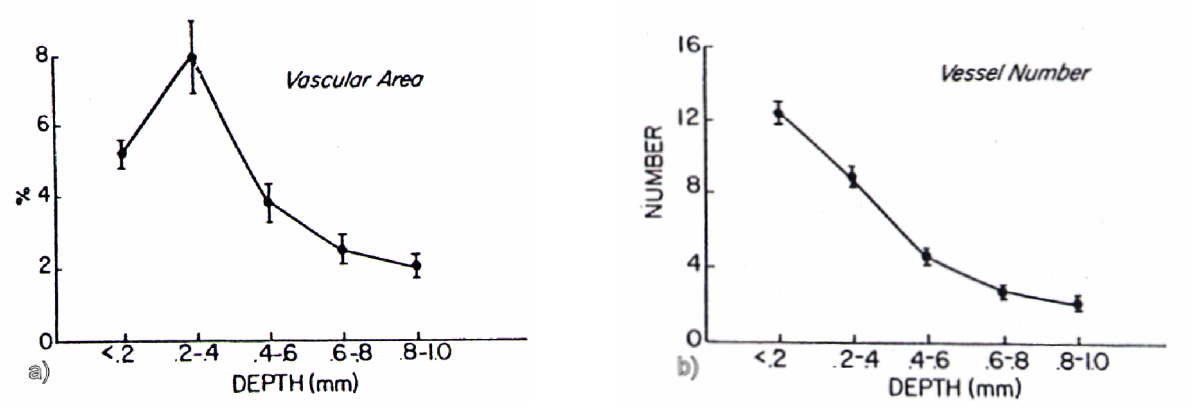


Fig. 2 a, b: Vascular area and vessel number dependence on skin depth [2].

An important break-through in PWS treatment was the idea of selective photothermolysis, first suggested by Anderson and Parish (1981). In case of selective phototermolysis irreversible injury must happen only to the blood vessels without damaging other skin constituents. This can be achieved by choice of the irradiation wavelength at which the target absorber (hemoglobin in the vessels) absorbs the laser light much better than other non-target skin constituents.

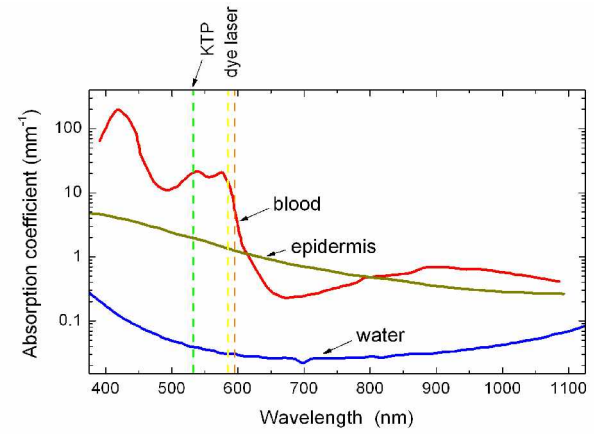


Fig. 3: Absorption spectra for different tissue constituents.

Skin, just like all the tissues, contains large a portion of water (75%-90%), therefore the absorption coefficient of normal skin has the similar course as absorption coefficient of pure water (Figure 3). Optical window with low water absorption is between 400 and 1100 nm, according to selective photothermolysis demand of low absorbance in skin constituents other than hemoglobin.

Tissue optics

When light irradiates the skin, part of light gets reflected and part of it gets into the skin and travels through it. During light traveling two processes happen: light absorption and light scattering.

The absorbed light is mostly dissipated as a heat within the medium. There are many compounds in biological tissue which absorb light radiation, collectively known as tissue cromophores, each of which has its own unique spectrum. Besides water important biological cromophores are hemoglobin (blood) in its various forms, lipids which exists in the form of triglycerids (neutral fats) and phospholipids (main component of cell membranes) and cytochrome c oxidase, the terminal protein in the electron transport chain within the inner mitochondrial membrane.

Next process is scattering of light, which affects the direction of light traveling. Media where scattering is important process is called turbid media.

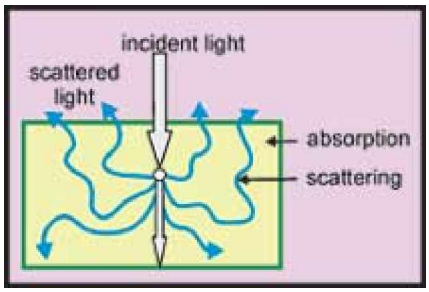
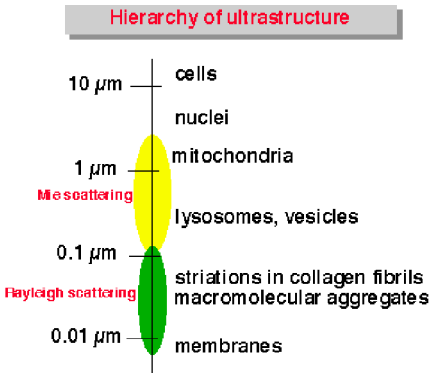


Fig. 4: Schematically presented processes of light absorption and scattering in tissue.

We can explain tissue scattering by Rayleigh and Mie theories. Scattering by particles small in diameter compared to the wavelength of the incident light is known as Rayleigh scattering. The most important aspect of Rayleigh scattering is its wavelength-dependence: scattering varies with the inverse fourth power of the wavelength of the illuminated light.

Determining the scattered field patterns from particles that are of the same size or large compared to the wavelength of the illuminating light is an enormously complex task, due to the significant phase difference between the scattered wavelets which must be taken into consideration. Mie theory describes both absorption and scattering by a spherical particle of arbitrary radius and refractive index. The scattering in this case is most intense in the forward direction. Rayleigh scattering is just a limit of Mie scattering for small scattereres.

The light in tissue is scattered by ultrastructure of the tissue. Scattering on cell membranes, vesicles, collagen fibers is described by Rayleigh scattering, but scattering on mitochondria, nuclei and cells is described by Mie scattering. Photons are most strongly scattered by those structures whose size matches the light wavelength.



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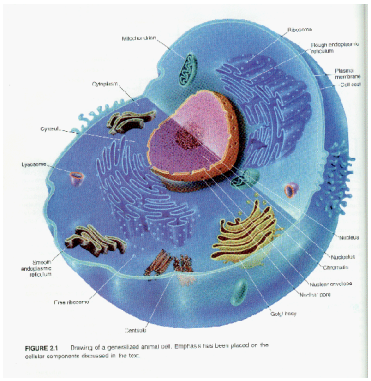


(b)

Fig. 5: (a) The size range of tissue ultrastructure which affects visible and IR light by Mie and Rayleigh scattering. (b) Scheme of cell with typical organelles: nucleus, mitochondria, enendoplasmaic reticulum, vesicles etc.

Characteristic parameters of scattering and absorption processes in tissue are scattering and absorption coefficients, which are defined such that, when a photon propagates over infinitesimal distance ds, the probability for absorption or scattering is $\mu_a ds$ and $\mu_s ds$ respetively. The sum of both coefficients is called total attenuation coefficient μ_t.

$$\mu_t = \mu_a + \mu_s \tag{1}$$

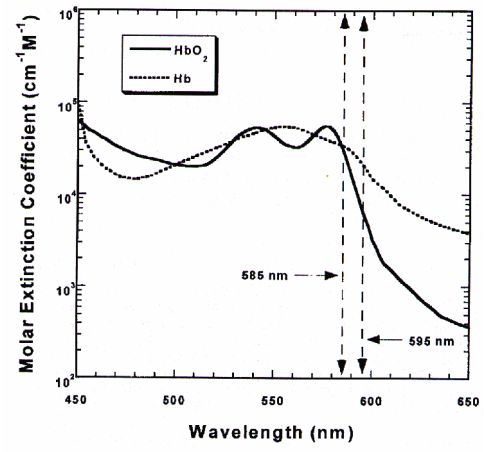
Let us examine the case when collimated light enters into tissue. A collimated laser beam normal to the surface has a small portion of light reflected at the surface, and the remaining light is attenuated in the tissue by absorption and scattering according to Beer's law

$$I(z) = I_0 \cdot e^{-\mu_t z} \tag{2}$$

The penetration depth δ of the collimated beam is defined as the mean free path for absorption or scattering event. Thus, the collimated penetration depth is calculated as the reciprocal of the attenuation coefficient

$$\delta = \frac{1}{\mu_t} \tag{3}$$

In skin the most important cromophores in visible and near IR spectra are hemoglobin in blood and melanin. Hemoglobin can be in two states, without oxygen binded (20-30% in venous blood), and with four oxygen molecules binded (100% in arterial blood). The absorption of light by blood is highly dependent on wavelength and oxygenation as illustrated in Figure 6a. The absorption coefficient of melanin decreases monotonically with increasing wavelength in visual part of spectra (Figure 6b).



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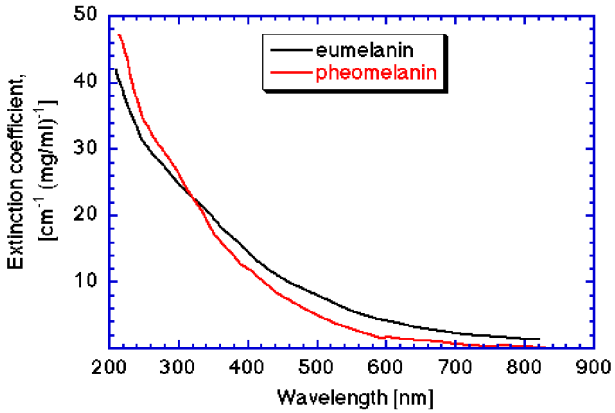

(b)

Fig. 6: (a) Absorption coefficient of oxy- (HbO_2) and deoxyhemoglobin (Hb) as a function of wavelength [5]. (b) Absorption of melanin as a function of wavelength (eumelanin in epidermis).

Let us define phase function *p*. On encountering a scattering event particle within a homogenous medium, photons traveling in a direction **s** are scattered into a new direction **s'**. The new directions generally do not occur with equal probability and can be described by the phase function *p*, which is probability distribution for scattering angle. The phase function in case of isotropic scattering has a constant value, $1/4\pi$. The mean cosine of the scattering angle θ, the angle between the incident **s** and scattered **s'** directions, is known as anisotropy factor (g):

$$g = \int_{4\pi} p(\theta) \cdot \cos\theta \cdot ds' = \langle \cos(\theta) \rangle \tag{4}$$

If the scattering is isotropic then *g* will be equal to 0. As the particle size increases, the intensity distribution increases in the forward direction and *p* for small angles is much higher than for all other angles. Therefore, the mean cosine tends towards a value of unity. Combining the scattering coefficient and the anisotropy factor gives the transport scattering coefficient

$$\mu_s' = (1-g)\mu_s \tag{5}$$

One can understand μ_s' as inverse of effective scattering length, which increases with increasing scattering anisotropy. From the definition of μ_s' follows the expression for the transport attenuation coefficient

$$\mu_t' = \mu_a + \mu_s' \tag{6}$$

Light scattered from collimated beam undergoes multiple scattering events as it propagates through the tissue. A rigorous description of this propagation is not possible, but the transport equation approach has proven to be effective. It relates the gradient of energy radiance *L* at point r and with direction **s** to losses owing to absorption and scattering and to gain owing to light scattered from all other directions **s'**. It can be written in the following form

$$\frac{dL(\mathbf{r},\mathbf{s})}{ds} = -\mu_t' L(\mathbf{r},\mathbf{s}) + \mu_s \int_{4\pi} p(\theta) L(\mathbf{r},\mathbf{s}') ds' \tag{7}$$

Important optical parameter for clinical use, fluence rate $\Phi(\mathbf{r})$, is derived from $L(\mathbf{r},\mathbf{s})$ by integration over solid angle.

From transport equation can be derived diffusion equation [3], which provides simplest analytical solutions for the photon fluence distribution. The diffusion approximation is generally valid far from sources and boundaries, in comparison to mean scattering length $1/\mu_s$', in highly scattering media, where $\mu_s >> \mu_a$. Although this condition may not be strictly true for a given light wavelength and tissue sample, the result derived from diffusion equation

in case of collimated beam normally irradiating a semi-infinite optical reduces to exponential law behavior when absorption dominates scattering:

$$\phi(z) = A \cdot \exp(-\mu_{eff} z) + B \cdot \exp(-\mu_t' z)$$
$$A = \frac{\phi_0 (9 + 6r)\mu_s' D}{(1 + r\sqrt{4\mu_a D})(1 - 9\mu_a D)}, B = \frac{-2\phi_0}{1 - 9\mu_a D} \quad (8)$$

$\mu_s'=\mu_s$ is reduced scattering coefficient, r is semi-empirical constant that depends on refractive indices, $D=[3(\mu_a+\mu_s')]^{-1}$ and $\mu_{eff}=(\mu_a/D)^{1/2}$ is the effective attenuation coefficient.

When no analytical model can be used, and that is usually the case, Monte Carlo simulation is the right tool to bring into use. MC simulation, for example, shows that fluence near the air-skin border exceeds the incident light radiant exposure (Figure 7) as a consequence of scattering.

Tissues have whitish look, which is partly because of scattering inside tissues. Inside the tissue scattering "de-collimate" the incident flux. Some of the scattered light undergoes multiple reflections and propagates in the backward direction. Backscattered light that reaches the tissue surface is either internally reflected or transmitted according to Fresnel's relation. Diffuse reflectivity is next contribution. Some of the incident light is speculary reflected according to Fresnel equation.

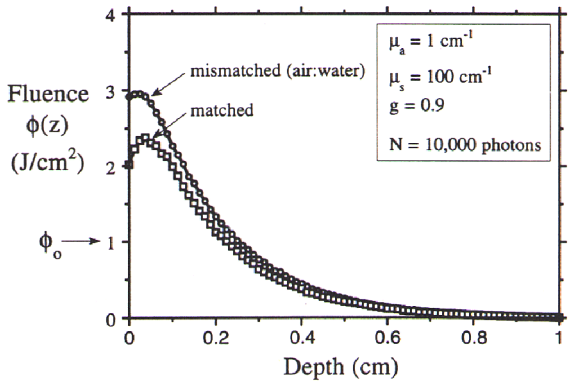

Fig. 7: One dimensional fluence distribution in an aqueous phantom tissue slab 1 cm thick (MC simulation). Two different boundary conditions were applied [3].

Incident light spot size

An important parameter that strongly influences the penetration depth of light in tissue is the laser beam spot diameter. For small spot diameters (Figure 8a), that is for diameters smaller than mean scattering length, scattering events carry a lot of photons out of the path of the collimated beam. The distribution of light consists of a narrow beam of collimated light surrounded by diffuse light. The result is a strong exponential attenuation with depth and a pronounced radial broadening of the beam.

For spot diameters much larger than the average photon scattering length(Figure 8b), a large fraction of scattered photons remain inside the beam volume as only the peripheral photons are scattered out of the beam. As a result, there is less radial beam broadening and attenuation with depth is weaker, approaching 1-D limit solution.

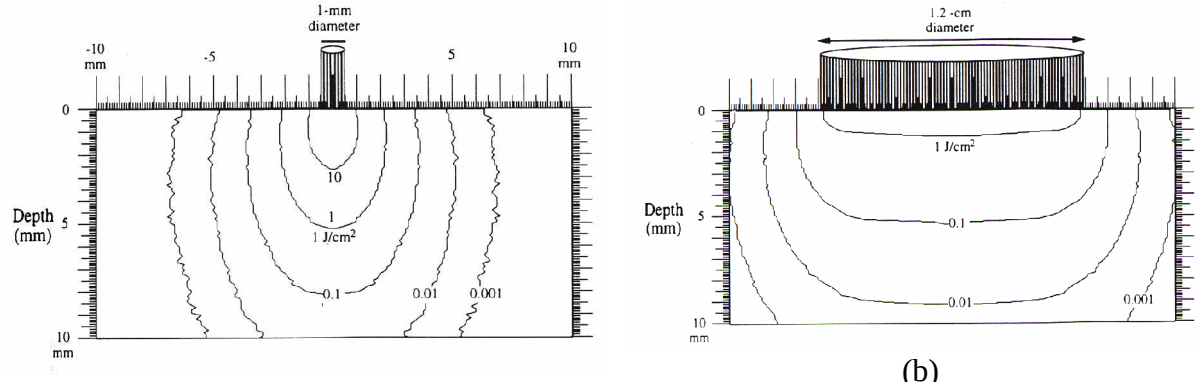

Fig. 8: Monte Carlo simulations scattering effect on beam broadening (a) in case of small spot and (b) in case of large spot [3].

Incident light wavelength

To come as close as possible to the clinical goal which is to ensure selective vessel damage one must assure that the temperatures of ectatic blood vessels rise by a greater extent than the temperature of other cutaneus structures. This imposes finding laser wavelengths that are absorbed more by blood than by melanin and collagen. At the same time, the laser light must penetrate sufficiently deep that it reaches deeper ectatic vessels.

An exact analysis of the effect of wavelength on the dermal depth of vascular injury requires detailed simulations of fluence rate, temperature and damage, where MC simulations are used. Firstly a criterion must be established, which tells us when selective vascular damage happens. One of the criterions used by physicists [4] is that the heat production at the top of the red blood cells in the capillary lumen must be greater than heat production at the epidermis-dermis interface. Such criterion is established because we don't want to exceed threshold for epidermal damage.

$$\phi(z=0,\lambda)\cdot\mu_{a,e}(z=0,\lambda)\leq\phi(z=z_v,\lambda)\cdot\mu_{a,bl}(\lambda) \qquad (9)$$

The criterion will be of use for initial analysis of vessel damage dependence on light wavelength. Consider the simplest possible skin model, composed of two layers, a 60 μm thick epidermis and semi-infinite dermis (Figure 9) with a single blood vessel inside. The fluence rate below the center of the beam Φ(z), where z is the depth from the skin surface, is calculated for an uniform radial distribution of diameter 3 mm [4]. To carry out the simulation, optical parameters for each wavelength are needed. They are presented in Table 1.

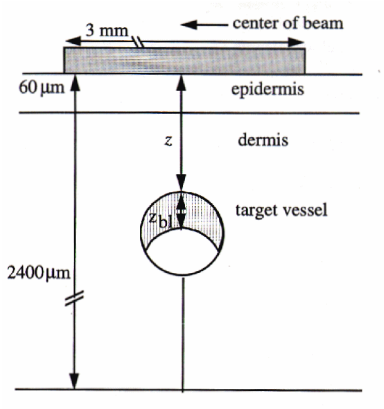

Fig.9: Skin model used in Monte Carlo simulation [4]

Wavelength (nm)	Absorption Coefficient (mm^{-1})	Scattering Coefficient (mm^{-1})	Anisotropy Factor
Blood			
415	300.0	48.0	0.995
500	11.5	47.5	0.995
532	26.6	47.3	0.995
545	33.0	47.2	0.995
560	20.0	47	0.995
577	35.4	46.8	0.995
585	19.1	46.7	0.995
590	6.9	46.6	0.995
Epidermis			
415	3.30	80	0.743
500	2.40	59	0.760
532	2.30	53	0.775
545	2.00	50	0.780
560	1.9	49	0.785
577	1.9	48	0.787
585	1.9	47	0.790
590	1.9	46	0.800
Dermis			
415	0.35	32.0	0.743
500	0.26	25.5	0.760
532	0.24	24.0	0.775
545	0.23	23.0	0.780
560	0.22	22.0	0.785
577	0.22	21.0	0.787
585	0.22	20.5	0.790
590	0.22	20.0	0.800

Table 1: Optical properties of the skin [4]

Figure 10 gives maximum depth of vascular injury as a function of wavelength using proposed damage criterion. The first curve shows the maximal depth where damage to vessel happened in bloodless dermis case, but that is not correct. In normal, but even more in PWS dermis, there are many other vessels. Therefore the absorption coefficient of dermis must be corrected in the way that it incorporates effect of blood vessels in vicinity [4]. The parameter used for correction is average vascular area as percentage of all dermis area. The result is a considerable reduction in the depth of vascular injury, even for small quantity of blood (1-2% for healthy dermis, but 2-10% for PWS dermis). From Figure 10 follows that optimal wavelengths for PWS treatment are 575-590 nm in yellow spectra.

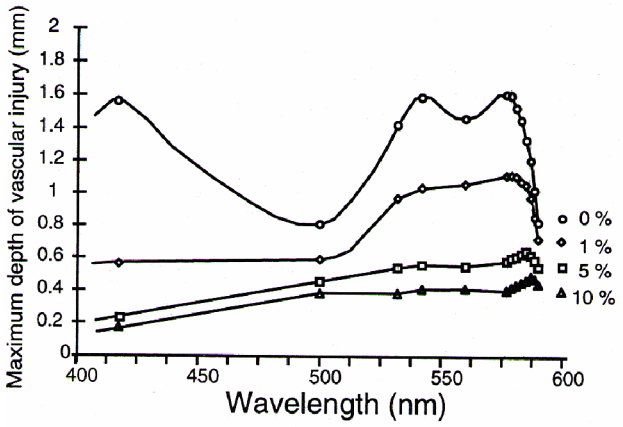

Fig. 10: The maximum depth of vascular injury as a function of wavelength. Results for four different vascular areas are presented [4].

Next, 2D MC simulation was made for 577 nm, 585 nm and 590 nm light and deposited energy in vessel lumen and in epidermis layer was observed [3]. A two-layer skin model was used and a vessel with diameter of 120 µm was placed 250 µm deep. It is obvious

from Figure 11 that shadowing effect is present inside the vessel. There are sharp peaks of deposited energy along the vessel wall in both cases, which are more prominent for the shorter wavelength.

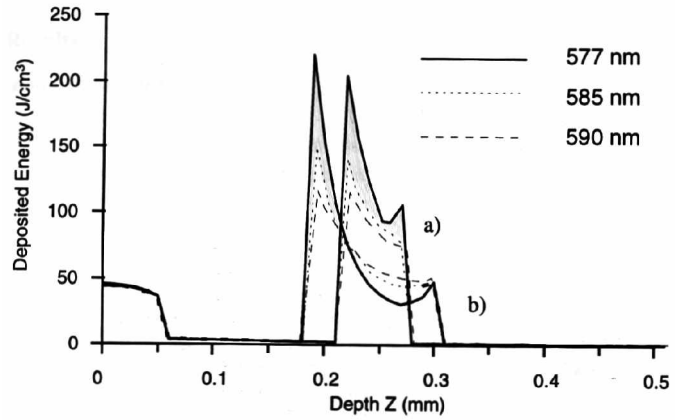

Fig. 11: Deposited energy for 577 nm, 585 nm and 590 nm wavelengths [4].

Next, ratio *f* between total deposited energy in vessel at 585 nm and at 577 nm was calculated for vessels with different diameters placed at the same depth (Figure 12).

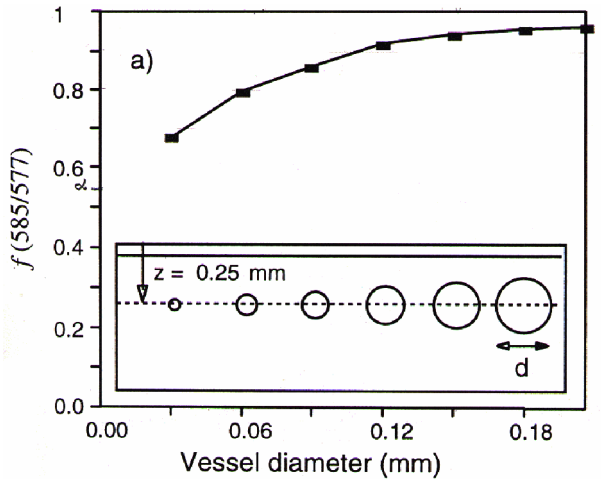

Fig.12: Ratio between the total deposited energy at 585 nm to that at 577 nm as a function of vessel diameter d at constant vessel depth z=250 nm [4].

There exist two limits of energy deposition inside the vessel lumen, which follows from previous results. In case of small, optically thin vessels, energy deposition is proportional to μ_a. In contrast, in large vessels there exists shadowing regime and energy is deposited mostly close to the vessel walls. The deposited energy in large vessels do not depend on wavelength much, which follows from ratio *f* (Figure 12). Therefore one would think of the energy deposition inside the vessel, that it is mostly irrelevant which wavelength is being used. But again longer wavelength is preferred because it is necessary to avoid extreme vessel injury, which is the consequence of explosive vaporization, due to prominent peaks of deposited energy close to the vessel wall.

An analytical model which incorporates correction factor due to discrete vessels in dermis was applied to different geometrical models of PWS [6]. Results of that study indicate that 585-590 nm wavelengths are best for treatment in patients with large and deep PWS vessels, but 577-580 nm wavelengths are optimal to treat young children with light-colored PWS, featuring smaller and shallower vessels.

Incident light pulse duration

After photonic transport phase of PWS treatment, heat diffusion from vessel lumen to surrounding dermis comes. The pulse duration governs the spatial confinement of the heat within the targeted vessel. The pulse duration t_p should be compatible with the diameter d of the vessel and about equal to the thermal relaxation time τ_d for that dimension ($\tau_d=d^2/16D$, where D is thermal diffusivity). τ_d is the time required for the instaneus temperature rise, generated inside the target after exposure to the laser pulse, to decrease by 50%. Taking $D=1.4\ 10^{-7}$ m^2/s, corresponding to water, typical values for τ_d are 0.2 ms for d=20 μm and 4.5 ms for d=100 μm. If $\tau_p>\tau_d$, most of heat diffuses outside the vessel during the laser exposure and the selectivity of photothermolysis is reduced, unwanted thermal damage to surrounding tissue is caused. A very short pulse, $t_p<<\tau_d$, will generate a high-peak intravascular temperature rise, leading to localized explosive vaporization of tissue water accompanied by acoustic transients, which will result in vessel rupture. In such cases, repair mechanisms may revascularize the tissue.

The effect of radial thermal diffusion out of the heated vessel into the surrounding tissue is best considered using diffusion equation. Diffusion is particularly relevant for small diameter vessels and long irradiation times, $t_p>>\tau_d$. As an approximation of diffusion equation we use following DE in exponential form [5], so that for t>t',

$$dQ(t,t') = dQ_A(t')e^{-(t-t')/\tau_d} \tag{10}$$

$dQ_A(t')$ denotes the incremental amount of optical energy absorbed in the exposed lumen during dt' at a time t'; dQ(t,t') denotes the corresponding heat after the time interval (t-t'). The heat remaining in the vessel at time t is found by integrating Eq. (10) over the duration of the laser pulse, $0<t'<t_p$. The result is

$$Q_t(t) = Q_A\left(\frac{\tau_d}{t_p}\right)\left(1-e^{-t/t_p}\right) = \Delta T(t)\rho c l \pi\left(\frac{d}{2}\right)^2, t \le t_p \tag{11}$$

Where ρc denotes average product of mass density and specific heat for the vessel; ΔT denotes temperature rise in the vessel lumen. In Figure 9 is plotted ΔT given by Eq. (11) for long-pulse irradiation (t_p=10 ms and fluence F=7 J/cm^2) and for short-pulse irradiation (t_p=0.45 ms and F=3 J/cm^2). The long-pulse exposure causes a monotonic temperature rise with d over the relevant range d<130 μm. In contrast, the temperature rise due to the short-pulse exposure reaches its maximum at a smaller diameter. Consequently, for a critical temperature rise (approximately ΔT=55 ˚C), Figure 13 indicates that the short-pulse exposure at F=3 J/cm^2 affects predominantly small diameter vessels, whereas the long-pulse exposure will damage larger diameter vessels.

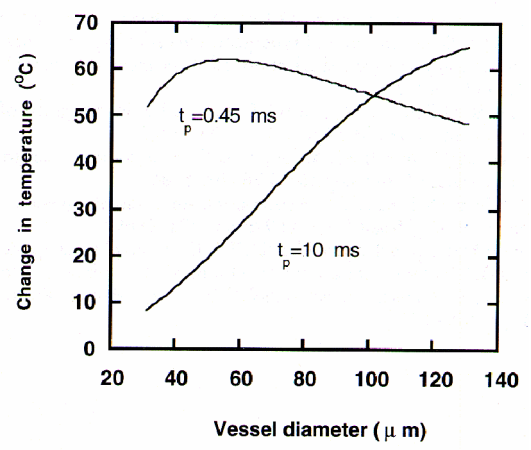

Fig. 13: Change in vessel temperature for short (0.45 ms) and long-pulse (10 ms) laser irradiation for different vessel diameters [5].

Recently new research presented results [7] that are inconsistent with previously described model of pulse length impact on vessel damage. Experiments were made irradiating chorioallantoic membrane, which is properly developed vascular membrane on the top of fertilized eggs, using pulsed dye laser at 595 nm wavelength and different pulse durations. Damage degree was determined by counting damaged vessels under optical microscope. Experiments showed no benefits of using longer pulses (Figure 14), not even for the largest vessels under investigation (120 μm). This is because fast thermal exchange due to convection in vessel lumen was neglected in previous model. Consequently modified relaxation time τ_d depends only on conduction through the vessel wall, which is assumed to have a thickness $\Delta d=0.1*d$. Therefore for optimal treatment of PWS it is proposed that t_p be between 0.1 ms and 1.5 ms. Differences between initial damage and total damage are due to physiological and biochemical processes which follow pure thermal damage to the vessel in initial phase.

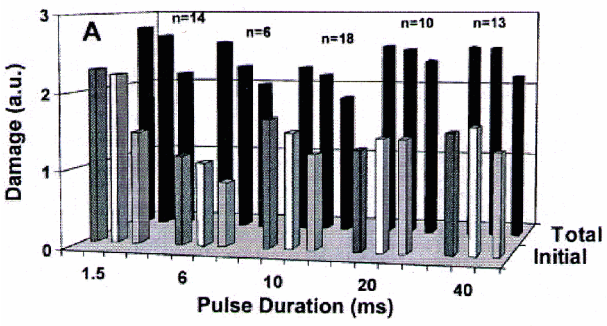

Fig. 14: Initial (1 min after pulse) and total damage (10-20 min after pulse) to CAM blood vessels (595 nm, 15 J/cm^2). First column represents small vessels (50 μm), second middle vessels (74 μm) and last big vessels (112 μm) [7].

Threshold radiant exposure

For PWS therapy it is important to know the damage threshold fluence sufficient to effect selective, irreversible thermal injury to vessel wall structures, without causing rupture of the

targeted vessel. The necessary fluence is difficult to establish from theoretical modeling, because of epidermal melanin absorption, multiple scattering events within the skin and the fact that blood vessels are located at different dermal depths. Because of all of this, results of animal model and clinical studies are still the most important.

An experiment was made on hamster skin vasculature as a mammalian skin model. KTP laser with 532 nm wavelength and 10 ms was used [8]. The purpose of experiment was to determine the average radiant exposure needed to cause permanent damage for different kinds of vessels. From the results (Figure 15) follows that arterioles have higher destruction threshold than venules, most probably because of thicker, muscular wall and the same holds for bigger vessels in comparison to smaller.

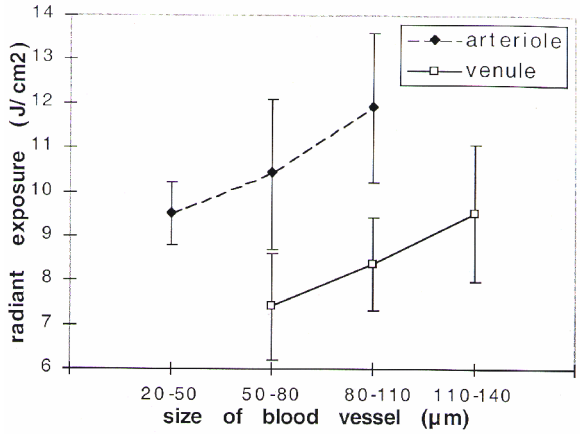

Fig. 15: Radiant exposure values for 50% probability of permanent vessel damage in a hamster model as a function of vessel type and size. Error bars represent 35-65% probability values [8].

Clinical studies

First wavelength used for PWS treatment was 577 nm, because it is the wavelength of the hemoglobin absorption peak. Results were much better when compared to other treatment methods. Then other wavelengths were probed and it proved that 585 nm wavelength was even better, as physics explained due to dermis blood filtering. Later different groups of PWS patients were treated with other wavelengths (532 nm from KTP laser, 595 nm from dye laser) and in some cases results were better than in case of 585 nm. Therefore no common set of parameters could be prescribed which would be optimal for each patient. Each patient has a unique vascular pattern of PWS, which makes total clearing of PWS hard to achieve. Therefore changing parameters (wavelength, pulse duration, irradiance exposure) may additionally improve PWS blanching. Many clinical studies were done using different sets of parameters, but due to the lack of efficient modality to determine actual PWS pattern of individual patient, no real connection between PWS and treatment parameters can be found.

Most clinical studies were dealing with testing different wavelengths. One recent study presented results of PWS treatment of 15 patients using three different sets of parameters [9]: 585 nm/0.5 ms, 595 nm/0.5 ms and 595 nm/20 ms. The wavelength of 585 nm and pulse duration of 0.5 ms brought about the best results with an average clearing index (CI) of 2.7, measured on scale from 1 to 4, where 1 means nearly no improvement and 4 represents total

clearing of PWS. Treatment with 595 nm/20 ms gave CI 2.1 and 595 nm/0.5 ms CI 1.6. Therefore the best choice for initial treatment is 585 nm wavelength, but authors suggest that after 585 nm has been used for multiple treatments and a clearance plateau is reached, it can be beneficial to try other wavelengths and pulse durations, presumably because different vessels may respond.

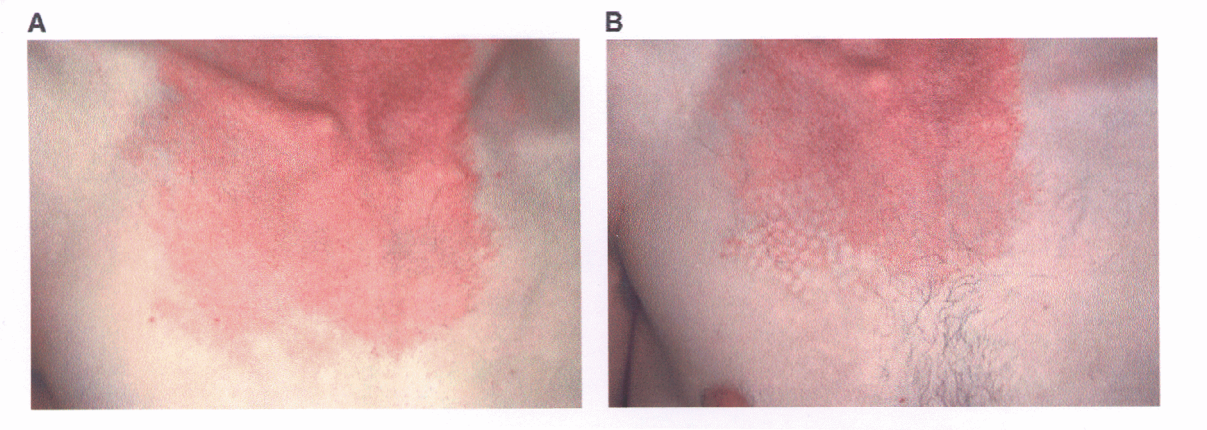

Fig. 13: A: PWS before treatment B: Four weeks after the treatment with 585 nm PDL. Right side: 585 nm/0.5 ms (CI=4), middle: 595 nm/0.5 ms (CI=1), left side: 595 nm/20 ms (CS=3) [9].

Another study tested influence of lower wavelength on success of PWS treatment on a group of PWS patients resistive to 585 nm wavelength treatment. Study was made on a group of 30 patients [10]. All of the patients had at least 5 treatments with 585 nm wavelength with less than 50% reduction of their PWS and had no further lightening from their last 585 nm treatment. Treatment was done using KTP laser with 532 nm wavelength, 1-50 ms pulse lengths and 18-24 J/cm^2. Overall, 16 patients showed more than 25% improvement, 25-50% improvement 11 patients and more than 50% 5 patients. Therefore the KTP laser can be used for further lightening of 585 nm resistant PWS.

Fig. 14: PWS on cheek showing substantial clearing in the hexagonal test sites (532 nm KTP) [9].

These and many other studies showed that there is a need for a modality which will enable individual patient PWS pattern determination. One technique is pulsed photothermal radiometry, which detects black-body radiation as a consequence of temperature rise in vessels after laser irradiation. Temperature profile and 3D vessel profile in skin can be reconstructed from detected radiometric signal. Patient-based PWS treatment is the challenge left to the future.

At least one additional technique that accompany described method of treatment must be mentioned, too. That is treatment of PWS in conjunction with cryogen spray cooling (CSC) [11]. Cryogen spurts were sprayed onto the PWS to cool down the epidermal layer of skin to prevent epidermal damage, which is common cause of post-treatment complications (scaring and purpura).

Conclusions

Laser treatment of PWS has greatly improved life quality of many patients. The advantage of lasers over other techniques is selective destruction of ectatic vessels using appropriate wavelength, namely orange light, where hemoglobin has its maximum.

Clinicians should use optimal treatment parameters to get best clearing of PWS. Most important parameters used in treatment are wavelength (most frequently used 585 nm and 595 nm, 532 nm), pulse length (0.5 - 25 ms), spot size (3 - 7 mm diameters) and radiant exposure (around 10 - 14 J/cm^2). But the same set of parameters is not optimal for every patient, because each of them has different skin structure, most importantly vessel pattern. That is why physical models try to find out, which parameters are best for certain type of skin and PWS characteristics (vessel site and depth distribution). Physics does not have an easy job, because of complex processes of light-tissue interactions, thermal diffusion and even unknown photobiochemical interactions. Therefore a lot of research has to be done to significantly improve laser treatment of PWS.

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