Determination of thermal and physical properties of port wine stain lesions using pulsed photothermal radiometry

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ABSTRACT

A method for quantitative characterization of port wine stain (PWS) is presented. Pulsed photothermal radiometry (PPTR) uses a non-invasive infrared radiometry system to measure changes in surface temperature induced by pulsed radiation. When a pulsed laser is used to irradiate a PWS, an initial temperature jump (T-jump) is seen due to the heating of the epidermis as a result of melanin absorption. Subsequently, heat generated in the subsurface blood vessels due to hemoglobin absorption is detected by PPTR as a delayed thermal wave as the heat diffuses toward the skin surface. The time delay and magnitude of the delayed PPTR signal indicate the depth and thickness of the PWS. In this report, we present an initial clinical study of PPTR measurements on PWS patients. Computer simulations of various classes of PWS illustrate how the PPTR signal depends on the concentration of epidermal melanin, and depth and thickness of the PWS. The goal of this research is to provide a means of characterizing PWS before initiating therapy, guiding laser dosimetry, and advising the patient as to the time course and efficacy of the planned protocol.

1. INTRODUCTION

Port wine stain (PWS) is a congenital vasculopathy that occurs most commonly on the face and neck¹. The chief complication of PWS is psychological disability, particularly in young children. Personality development is adversely affected in a large percentage of patients due to the negative reaction of others to a "marked" person. PWS has been treated in the past with an array of therapeutic modalities including skin grafting, ionizing radiation, dermabrasion, cryosurgery, tattooing, and electrotherapy. All these methods have either unpredictable results or potentially serious complications, such as hypertrophic scarring.

The laser provided the first major advance in therapy for PWS and has been used extensively over the past two decades. Light of the appropriate wavelength and pulse width is preferentially absorbed by hemoglobin and converted to heat, causing thermal damage and thrombosis in the targeted vessels²,³. However, because of the complex nature of, and individual variability in the properties of human skin and PWS, optimal clinical results (i.e., significant blanching) are not always forthcoming⁴,⁵.

In this report, the application of pulsed photothermal radiometry (PPTR) to the clinical management of patients with PWS is described. The PPTR signal provides information on three key properties of the skin and PWS: (1) epidermal melanin concentration; (2) depth of the PWS; and (3) relative thickness of the PWS. It is obvious that a method that takes into consideration individual variations in the properties of both the skin and PWS, on a case by case basis, would have decided advantages in choosing the incident light dose for treatment over subjective criteria currently used, such as evaluating thresholds for purpura⁶.
The usefulness of the information provided by PPTR will be demonstrated in the following clinical situations commonly encountered: (1) thin, superficial or deep PWS with low epidermal melanin concentration; (2) thick, superficial or deep PWS with low epidermal melanin concentration; and (3) thick, superficial or deep, PWS with high epidermal melanin concentration.

2. PWS THERAPY AND PPTR

PPTR uses an infrared detector to measure changes in surface temperature induced by pulsed radiation. In practice, a pulsed laser is used to produce transient heating of the object under study and the subsequent temperature rise at the tissue surface creates an increase in infrared (blackbody) emission which is measured by a fast infrared detector. The time dependence of the decay of the blackbody emission signal can be used to map the spatial distribution of heat deposition in the tissue under study7,8,9.

Histopathological studies (Figure 1) of PWS show a normal epidermis overlying an abnormal plexus of dilated vessels in the upper dermis10. For the purposes of PPTR, PWS in human skin can be modeled as an absorbing surface layer (the epidermis which contains melanin) and a subsurface absorber (the blood vessels which contain hemoglobin). In the PWS model, if a pulsed light source (typically a laser) is used to irradiate the skin, an initial temperature jump (T-jump) will be seen due to the heating of the epidermis as a result of melanin absorption and is proportional to the melanin concentration (Figure 2). Subsequently, heat generated in the subsurface blood vessels due to hemoglobin absorption is detected by PPTR as a delayed thermal wave, which peaks to a maximum and then slowly decays, as the heat diffuses toward the skin surface. Measurement of the surface temperature as a function of time can indicate the depth of the PWS because the time required for the delayed thermal wave to be detected is proportional to $t^{1/2}$.

Figure 1. Histopathology of port wine stain.
During laser irradiation, absorption and deexcitation of the chromophore converts radiant energy into heat within the exposure field. The distribution of melanin and hemoglobin in combination with the subsurface laser irradiance determine the location of heat production and thermal damage as well as the depth of light penetration. The local heat generation, \( Q(z) \) (J/cm\(^3\)), equals the product of absorption coefficient, \( \mu_a \) (cm\(^{-1}\)), and radiant exposure, \( \Phi \) (J/cm\(^2\)):

\[
Q(z) = \mu_a(z)\Phi(z) \tag{1}
\]

The distribution of the temperature rise is given:

\[
T(z) = \frac{Q(z)}{\rho C} \tag{2}
\]

where \( \rho \) and \( C \) are the density and heat capacity of tissue, approximately 1.1 g/cc and 3.8 J/(g\(\cdot\)°C), respectively, which is typical for a 70-80% water content tissue. The value of \( \Phi(z) \) within the tissue depends on the radiant exposure delivered to the skin surface \( (\Phi_0) \), scattering of light in the dermis, and absorption by melanin in the epidermis and by hemoglobin in the PWS.

The predominant endogenous cutaneous chromophores absorbing light at the clinically relevant wavelengths of 577 or 585 nm are melanin and hemoglobin\(^1\). The ratio of the heat generation in the PWS \( (Q_{PWS}) \) to heat generation in the epidermis \( (Q_e) \) predicts the relative heating of the PWS with respect to the epidermis. Ideally, the clinical objective in a PWS patient undergoing laser therapy is to maximize this ratio \( (Q_{PWS} > Q_e) \), favoring thermal damage to the PWS, while at the same time minimizing damage to the overlying epidermis. Unfortunately, the overlying epidermal pigment layer represents a potential barrier through which the light must pass to reach the underlying blood vessels comprising the PWS.

In a lightly pigmented individual, some light is absorbed by melanin in the epidermis, but most is absorbed by the PWS in the dermis \( (Q_{PWS} > Q_e) \). If the targeted vessels are close to the surface, the subsurface laser fluence \( \Phi(z) \) is high enough to cause sufficient heat generation in the blood vessel to destroy the PWS. However, if the targeted vessels are deep within the skin, the subsurface light fluence may not be high enough to cause sufficient heat generation in the blood to destroy the PWS. Conversely, in a darkly pigmented individual, absorption of the laser light by epidermal melanin interferes with further transmission into the dermis, thus limiting absorption by...
hemoglobin in the PWS ($Q_{PWS} < Q_e$). In this case, the epidermal melanin pigment acts like a shield. The melanin causes localized heating in the epidermis and reduces the light reaching the blood vessels, thereby decreasing the amount of heat production in the targeted PWS, resulting in suboptimal blanching of the lesion.  

3. COMPUTER SIMULATIONS OF VARIOUS CLASSES OF PWS

Monte Carlo computer simulations that can specify tissue optical properties have been developed to model the propagation of light into multilayered tissues, such as skin. Histopathological studies show PWS compose, on the average, 5-15% of the dermis; therefore, in this model, PWS is considered as a mixture of 10% whole blood and 90% dermis, with average absorption and scattering properties. Table 1 lists the optical properties, absorption coefficient, $\mu_a$, and reduced scattering coefficient, $\mu_s'$, of the different tissue layers [$\mu_s'$ equals $\mu_s(1-g)$ where $\mu_s$ is the scattering coefficient and $g$ is the anisotropy of scattering]. For whole blood (45% hematocrit) at 577 nm, $\mu_a$ and $\mu_s'$ are assumed to be 325 and 8 cm$^{-1}$, respectively.

Table 1: Optical properties of tissue layers

| Optical properties          | $\mu_a$ (cm$^{-1}$) | $\mu_s'$ (cm$^{-1}$) |
|----------------------------|---------------------|----------------------|
| Low epidermal melanin      | 3                   | 48                   |
| High epidermal melanin     | 10                  | 48                   |
| Dermis                     | 2                   | 48                   |
| PWS (10% blood, 90% dermis)| 34                  | 44                   |

PWS were classified into three categories based on the epidermal melanin concentration, and depth and thickness of the PWS (Table 2). Class I is defined as a thin 20-µm PWS with a low epidermal melanin concentration, and is divided into two subclasses: (A) superficial PWS (150-µm depth), and (B) deep PWS (300-µm depth). Class II is defined as a thick PWS with a low epidermal melanin concentration, and is divided into two subclasses: (A) superficial PWS, and (B) deep PWS. Class III is the same as Class II, except that the epidermal melanin concentration is 3-fold higher for the Class III PWS.

Table 2: Types of PWS in computer simulations

| Description     | CLASS I Low epidermal melanin Thin PWS | CLASS II Low epidermal melanin Thick PWS | CLASS III High epidermal melanin Thick PWS |
|-----------------|---------------------------------------|-----------------------------------------|-------------------------------------------|
| PWS at 150 µm   | I A                                   | IIA                                     | IIIA                                      |
| PWS at 300 µm   | I B                                   | IIB                                     | IIIB                                      |

Using a model that simulated a 1 J/cm$^2$, 400-µs laser pulse at 577 nm wavelength, computer simulations mapped the absorption of light within the skin. These constitute the heat source term for a thermal diffusion calculation combining the optical and thermal models for a 1-dimensional case to specify: (1) the internal temperature distribution of the irradiated skin as a function of depth, and (2) the heat flow to the surface and the surface.
temperature rise as a function of time\textsuperscript{16,17}. The latter calculation is directly comparable to the measured PPTR signal.

Results of the computer simulations for Classes I-III PWS are shown in Figures 3-5, respectively. The upper schematic drawings depict the amount of absorption due to the epidermis (60-µm thickness), dermis, and PWS for each of the three classes. The middle graph specifies the internal temperature distribution as a function of depth. The lower graph models the skin surface temperature rise as a function of time (PPTR signal).

Figure 3 shows the expected internal temperature distributions and surface temperatures for Class I (A and B) thin PWS with a low epidermal melanin concentration. The PWS at 150 and 300 µm depth are elevated to average temperatures of 12.5°C and 10°C, respectively, at the end of the laser pulse. The model represents the PWS as a monolayer with a 10% blood content, yielding the correct average light distribution for the entire PWS. However, individual blood vessels within the PWS would actually experience approximately a 10-fold greater temperature rise, or 125°C and 100°C for Class IA and IB, respectively. The surface temperature rise is characterized by an initial T-jump of only 2.7°C due to the low concentration of epidermal melanin, which immediately begins to decay. At ~60 ms, the heat deposited in the superficial PWS has reached the surface as a delayed thermal wave and produces a temperature rise of ~0.7°C followed by gradual cooling. At ~200 ms, the heat deposited in the deep PWS has reached the surface, but the temperature rise is small.

Figure 4 shows the expected internal temperature distributions and surface temperatures for Class II (A and B) thick PWS with a low epidermal melanin concentration. The internal temperature distributions illustrate that light cannot penetrate very deep into a thick PWS and most of the laser heating is confined to the most superficial 200-300 µm of the lesion. More dense PWS would allow even less light penetration. The internal temperature distributions of the Class II PWS are slightly higher than for the Class I example of Figure 3 because the thicker heated layer suffers less thermal relaxation during the 400-µs laser pulse than did the thin Class I PWS. The initial T-jump is greater when the PWS is deeper because the backscattered light, which is greater when the PWS is deeper, can also cause heating of the epidermal melanin. When the PWS is thick and superficial (IIA), there is a large delayed thermal wave producing an additional surface temperature rise of ~3°C that peaks at ~150 ms, and slowly cools thereafter. If the PWS is deep (IIB), the time for the delayed thermal wave to peak is delayed until ~500 ms and the additional temperature rise is only ~0.5°C.

Figure 5 shows the expected internal temperature distributions and surface temperatures for Class III (A and B) thick PWS with a high epidermal melanin concentration. Class III is the same as Class II except that the epidermal melanin concentration is now 3-fold higher. The internal temperature distributions show that both the superficial and deep PWS are heated slightly less than the Class II examples, but still there is significant heating. However, the heating of the skin surface due to epidermal melanin is about 3-fold greater than the Class I or II examples, producing a large initial T-jump at the end of the laser pulse. The initial T-jump is greater when the PWS is deeper as described above in Figure 4. The elevated melanin concentration dominates the surface temperature rise, causing a high initial T-jump that only slowly decays. The delayed thermal wave temperature rises due to the superficial and deep PWS lesions are similar to those in Class II A and B, but the rises are lower because of the shielding by epidermal melanin.

In summary, the initial T-jump in the PPTR signal indicates the epidermal melanin concentration. The time for the arrival of the delayed thermal wave peak temperature rise due to the absorption of light by the subsurface vessels indicates the depth of the PWS. The magnitude of the delayed temperature rise indicates the thickness of the PWS, but since light has limited penetration into the large PWS, there is an upper limit to how much the thickness of the PWS can increase the PPTR signal. Both the thickness and depth of the PWS influence the magnitude of the temperature rise. When the epidermal melanin concentration is high, the amount of light reaching the PWS will decrease. Therefore, the T-jump due to the heated melanin dominates the signal and the delayed thermal wave from the PWS becomes less obvious.
Figure 3: Class I PWS. This is a thin PWS that is either superficial (A, 150 μm) or deep (B, 300 μm) with a low epidermal melanin concentration. The top schematic shows the relative amounts of absorption for the epidermis, dermis, and PWS (see Table 1). The middle graph shows the initial internal temperature distribution at the end of the 400-μs laser pulse. The lower graph shows the surface temperature rise as a function of time after the pulse. In this class, neither the epidermis nor the thin PWS cause much surface temperature rise, but they are measurable.
Figure 4: Class II PWS. This is a thick PWS that is either superficial (A, 150 μm) or deep (B, 300 μm) with a low epidermal melanin concentration. The heat deposited in the thick PWS causes a significant delayed temperature rise as the heat diffuses to the surface. Note that the deep PWS causes a more delayed and much lower temperature rise than the superficial PWS.

Figure 5: Class III PWS. This is a thick PWS like the Class II PWS example, but the melanin in the overlying epidermis is increased 3-fold. The immediate surface temperature rise is much more pronounced. Note that the delayed temperature rises due to the PWS lesions are less obvious due to the dominant signal from the epidermis.
4. CLINICAL TRIAL

4.1. Subjects:

Subjects for this study were recruited from the population of patients currently undergoing PWS therapy at the Beckman Laser Institute and Medical Clinic, University of California, Irvine. All subjects had an admission history taken, including laser treatments prior to the study, and a limited physical examination (skin type and assessment of PWS depth and involvement). Full details of the procedure, possible side effects, risks, and complications were explained to each participant before informed consent was sought and documented on the standard University of California, Irvine consent form. Permission for the study was obtained from the Institutional Review Board (IRB) Human Subjects Review Committee at the University of California, Irvine.

4.2. PPTR Apparatus:

Construction of the PPTR instrument followed the work of Anderson\textsuperscript{18}. A Candela model SPTL-1 (Wayland, MA) pulsed dye laser operating at a wavelength of 577 nm was coupled into an optical fiber and routed to the apparatus (Figure 6). The fiber terminus was imaged by a lens onto an aperture through which the skin site received laser radiation. The surface temperature was measured using a HgCdTe detector (New England Research Center model MPC11-2-A1; Sudbury, MA) having a surface area of 2 X 2 mm that was cooled to 77°K. A germanium lens was used to image a 2-mm-diameter area in the center of the 5-mm diameter spot of laser irradiance onto the detector. This ensured that the optical/thermal diffusion problem was 1-dimensional (dependent only on depth) and therefore amenable to a 1-dimensional analysis. A 7.5 μm longpass filter was placed in front of the detector to block any stray visible and near infrared light. Since the detector is a photoconductor whose resistance changes with IR illumination, it was connected as one arm of a Wheatstone bridge. The signal across the bridge was then amplified using a differential amplifier with response to DC. This was a high-gain, low-noise amplifier with a bandwidth of 2.5 kHz, optimized for the detection of the delayed thermal waves. The signal was acquired by the digital oscilloscope (Tektronix DSA 601; Beaverton, OR) connected to a Macintosh PC using the GPIB interface. A data acquisition and instrument program, LabVIEW (National Instruments; Austin, TX) was used to control the GPIB interface.

Figure 6. Schematic diagram of the PPTR instrument.
The system was calibrated by measuring the temperature of two objects: (1) a graphite block at 25°C and (2) a human forearm at 31°C. A quartz temperature probe (Hewlett-Packard Model 10023A; Palo Alto, CA) was used to verify the temperature measurements. Both these objects behave as black bodies in the 10 μm infrared wavelength range measured by the HgCdTe detector. Although the PPTR signal is proportional to $T^4$, for T-jumps of a few degrees, the relationship between the PPTR signal and temperature is approximately linear.

4.3. Results:

Examples of PPTR signals obtained from representative patients having Class I-III PWS are shown in Figures 7-9, respectively. The PPTR measurements have been converted to skin surface temperature rises. Figure 7(a) is a Class IA thin, superficial PWS with a low epidermal melanin concentration, as evidenced by an initial T-jump of only 0.5°C. Because of the superficial location of the PWS, a prominent delayed thermal wave appears ~ 100 ms after delivery of the laser pulse. Figure 7(b) shows the result obtained from a Class IB PWS that is deeper than the previous example. Here, although the delayed thermal wave is not evident, heat deposited in the deeper PWS has kept the surface at an elevated temperature relative to normal skin.

Figure 7. Class I PWS: (a) thin, superficial; (b) thin, deep.

Figure 8(a) is a Class IIA thick, superficial PWS with a low epidermal melanin concentration. There is a small T-jump due to the melanin, followed by the appearance of a large delayed thermal wave that peaks ~ 250 ms after the laser pulse is delivered. Even after 800 ms, the skin surface has only cooled slightly from its maximum temperature, indicating that a large amount of heat was deposited in the PWS. When the PWS is deeper (Class IIB), the magnitude of the delayed thermal wave is attenuated, as shown in Figure 8(b).

Figure 8. Class II PWS: (a) thick, superficial; (b) thick, deep.
Figure 9(a) is a Class IIIA thick, superficial PWS with a high epidermal melanin concentration. The initial T-jump due to epidermal melanin absorption is 2.5°C, higher than for Class I and II examples. Because the PWS is superficial, the delayed thermal wave appears 100 ms after the laser pulse is delivered. When the PWS is deeper, as shown in Figure 9(b) for Class IIIB, the delayed thermal wave is attenuated. When the epidermal melanin concentration is high, the amount of light reaching the PWS decreases. Therefore, the T-jump due to the heated epidermal melanin dominates the signal, and the delayed thermal wave from the PWS becomes less obvious.

Figure 9. Class III PWS: (a) thick, superficial; (b) thick, deep.

5. DISCUSSION

During the initial consultation, prior to beginning laser PWS therapy, the patient and family want answers to two very important questions:

1. How many treatments will be required to achieve optimal fading of the PWS?
2. Can the PWS be treated without damaging the normal skin?

Although no guarantee for complete removal of a PWS can ever be given, information obtained from non-invasive PPTR measurements can be helpful in advising the family as to the time course of the planned protocol. If the PPTR signal identifies a thin superficial PWS, the family can be informed that perhaps 1-2 treatments might be required for optimal fading. Conversely, if PPTR identifies a thick deep PWS, the family is informed that laser treatment may consist of multiple treatments, perhaps 5 or more. As these treatments would be administered at timed intervals of 2-3 months, a lengthy commitment on the part of the patient and family, perhaps several years, may be required.

Prior to the institution of laser PWS therapy, the physician should know the maximum incident light dose that may be delivered without damaging the normal epidermis. In turbid media such as skin, the T-jump is

\[ \Delta T = \frac{\mu_a \Phi_0}{\rho C} \left[ 1 + 2 \frac{1 + r_1}{1 - r_1} R_d \right] \tag{3} \]

where \( r_1 \) is the internal reflectance of diffuse radiation at the skin-air interface. \( R_d \) is the observed diffuse reflectance resulting from light that enters the tissue, is scattered, and subsequently reemerges from the tissue. By measuring \( \Delta T, \Phi_0, R_d \), and using approximate values for \( \rho C \) and \( r_1 \), the epidermal absorption coefficient, \( \mu_a \), can be determined. Although initial T-jump measurements can be made at subtherapeutic incident light doses, once \( \mu_a \) has been calculated, T-jumps at all incident light doses may be predicted using equation (3).
When the surface of the skin is irradiated by a laser pulse such that the temperature exceeds 70°C, the result is epidermal denaturation leading to necrosis. For temperatures in excess of 140°C, the result is explosive vaporization of the epidermis. The attending physician must avoid both such phenomena during laser PWS therapy, otherwise scarring or changes in the normal skin pigmentation will result. Consider a simple example to illustrate the principle in a patient with a normal skin surface temperature of 30°C. One Joule of laser energy delivered to the skin produces an initial T-jump of 8°C. Therefore, in order to keep the T-jump after laser irradiation less than 40°C, such that the epidermal temperature does not exceed 70°C, the threshold light dose for epidermal damage is 5 J/cm². This threshold will vary from subject to subject, and site to site. However, since temperature can be monitored on a pulse-by-pulse basis, immediate feedback will be provided to the physician by the PPTR measurement to indicate if damage to the epidermis is likely to occur.

Successful laser therapy becomes increasingly difficult when the lesion is deep, thick, or the epidermal melanin concentration is high. The physician who is faced with these situations must consider higher pulse energies to remove the PWS which may compromise the normal overlying epidermis. A risk/benefit decision must be made so that the physician can explain and justify the planned protocol to the patient and family. If higher pulse energies are contemplated, pre-operatively the patient and family are told that blistering and/or sloughing of the upper layers of the skin can be expected after laser treatment. However, because the PPTR measurements made in advance can predict this side effect, the patient and family are adequately prepared.

6. CONCLUSION

PPTR offers a means of documenting the character of a PWS skin site prior to laser treatment. The epidermal melanin concentration is specified, and the depth and thickness of the PWS is indicated. The initial T-jump in response to a modest diagnostic laser pulse informs the clinician about the anticipated skin surface temperature elevation in response to a therapeutic laser pulse.

Information provided by PPTR will allow clinical laser treatment of PWS in infants, young children and adults to be individualized, on a case by case basis. The technique will permit a much more scientific and safe approach to the selection of the laser parameters appropriate to the patient over the time course of the therapy. Presently, such lack of specificity in choosing the light dose for therapy is the primary reason for poor clinical results or complications, such as hypertrophic scarring or changes in the normal skin pigmentation, seen after laser therapy. The attending physician who uses PPTR measurements and the computer model prior to laser treatment will be in a position to anticipate, and minimize or avoid, epidermal damage.

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