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## A two-temperature model for selective photothermolysis laser treatment of port wine stains

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### Abstract

Selective photothermolysis is the basic principle for laser treatment of vascular malformations such as port wine stain birthmarks (PWS). During cutaneous laser surgery, blood inside blood vessels is heated due to selective absorption of laser energy, while the surrounding normal tissue is spared. As a result, the blood and the surrounding tissue experience a local thermodynamic non-equilibrium condition. Traditionally, the PWS laser treatment process was simulated by a discrete-blood-vessel model that simplifies blood vessels into parallel cylinders buried in a multi-layer skin model. In this paper, PWS skin is treated as a porous medium made of tissue matrix and blood in the dermis. A two-temperature model is constructed following the local thermal non-equilibrium theory of porous media. Both transient and steady heat conduction problems are solved in a unit cell for the interfacial heat transfer between blood vessels and the surrounding tissue to close the present two-temperature model. The present two-temperature model is validated by good agreement with those from the discrete-blood-vessel model. The characteristics of the present two-temperature model are further illustrated through a comparison with the previously-used homogenous model, in which a local thermodynamic equilibrium assumption between the blood and the surrounding tissue is employed.

### Keywords

laser dermatology; port wine stains; two-temperature model; porous media; local thermal non-equilibrium; Monte-Carlo method

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## 1. Introduction

Port wine stain (PWS) birthmarks are congenital vascular malformations which occur in approximately 0.3% of newborns. PWS are composed of ectatic venular capillary blood vessels, with diameters ranging from 10 to 300  $\mu\text{m}$ , buried within healthy dermal tissue. PWS can be treated by the pulsed dye laser (PDL) based on the well-known theory of selective photothermolysis with hemoglobin serving as the target chromophore [1]. According to the theory, the PWS blood vessels can be thermally damaged selectively due to their preferential absorption of laser energy, as compared with normal skin tissues, which are minimally affected.

Numerical methods have been employed to simulate laser treatment of PWS [2–4]. Most existing models simplify the complex skin anatomy into a multi-layer structure. The Multi-Layer Monte Carlo method (MLMC) [5] was used to simulate light propagation within tissues and thus quantify light energy deposition [6–8]. Energy deposition can then be input into the bio-heat transfer equation as the energy source term. Solutions of the bio-heat equation yield temperature change of the skin tissues, from which thermal damage from a selected thermal injury model can be quantified [9].

Various skin models for laser treatment of PWS have been developed and can be roughly divided into two categories, the homogeneous model and the discrete blood vessel model. The homogeneous model refers to models that treat skin tissue with PWS as a homogeneous mixture of uniformly distributed blood and surrounding dermal tissue with a given blood volumetric fraction [6]. The optical and thermal properties of the homogenous mixtures are estimated based on the average of the corresponding properties of the two constituents, weighted by their volumetric fractions. Detailed anatomic structure of the blood has not been taken into account.

One critical shortcoming of the homogeneous model is that it fails to distinguish the difference in the temperature of the blood and the surrounding dermal tissue. According to the theory of selective photothermolysis, blood should be heated up preferentially by laser irradiation due to stronger absorption of the chosen wavelength by blood, compared with surrounding dermal tissue. It is therefore expected that the blood should have a temperature that is significantly higher than that of the surrounding dermal tissues, leading to a local thermodynamic non-equilibrium condition. The homogeneous model, however, assumes one temperature for both the targeted chromophores and surrounding tissues. In the case for PWS, such a local equilibrium assumption makes the homogeneous model undesirable.

Attention was then paid to direct simulation of laser heating of the blood vessels by applying so-called discrete blood vessel models [7, 8, 10]. PWS have complex anatomic structures, making modeling difficult. Early discrete models considered either a single blood vessel [7] or an array of blood vessels, regularly arranged within the dermis [8]. Multiple blood vessels randomly arranged within the dermis have also been taken into consideration [10]. The results concluded from these models have provided some quantitative information regarding selective blood vessel heating during laser treatment of PWS, and have been used in development of PWS laser treatment protocols.

The discrete models mentioned above assume that all blood vessels have a straight geometry and are parallel to the skin surface. Such an assumption significantly simplifies mathematical treatment of the problem. To make a more realistic PWS model, more complex structural models were attempted by Pfefer et al [11] who employed information about complex geometric configurations of PWS blood vessels obtained through biopsy. They also extended the Multi-Layer Monte-Carlo method to a Voxel-based three-dimensional method that could take into account the effect of the geometric complexity of the interface between dermal tissue and blood vessels [11]. Such a model could provide specific information regarding selective heating of blood vessels during PWS laser treatment. Unfortunately, we don't currently have imaging modalities that can map PWS blood vessels noninvasively, making this three-dimensional model impractical to use.

In this paper, we present a local thermodynamic non-equilibrium, two-temperature model for simulation of the thermal response of PWS to laser irradiation. We treat the PWS skin as a porous medium made of a tissue matrix buried with highly-absorbing chromophores (blood confined within the vessels). Two energy equations, one for the blood and the other for the dermal tissue, will be developed based on the local thermal non-equilibrium theory of porous media. We have shown that light propagation and energy absorption by skin tissue can still be treated by the well-developed Multi-Layer Monte-Carlo method, except that the energy deposition is modified to be separately scored in two phases respectively, which is consistent with the two-temperature model. We also show that the geometric configuration of the chromophore can be represented, as a first approximation, by the volumetric fraction of the chromophores and a length scale, i.e., the average diameter of the blood vessels within a PWS. An approximate relation is also developed to estimate the interfacial heat transfer between a blood vessel and surrounding tissue by solving a simplified one-dimensional transient heat conduction problem of a chromophore (blood vessel) within tissue. Finally, the present two-temperature model is compared with the discrete-blood-vessel model and homogenous model to illustrate the applicability of the present local thermal non-equilibrium model for laser dermatology.

## 2. Physical Model and Mathematical Description

### 2.1 Problem description and basic assumptions

In laser treatment of PWS, the pulsed laser beam with a chosen wavelength is fired from a handpiece and irradiates the skin surface. As the light penetrates into the tissue, it continuously scatters and is absorbed along the path. Two major chromophores that can absorb the laser light at the chosen wavelength are melanin in the basal layer of epidermis and hemoglobin (or deoxyhemoglobin) in the red blood cells within the blood vessels. The normal skin tissues are usually transparent to laser light at the chosen wavelength but do have a strong scattering effect. The laser energy absorbed by melanin and red blood cells in the blood vessels can be converted to thermal energy, raising the temperature of the epidermis and the blood within the blood vessels. A high blood temperature leads to the desired effect --- thermal damage to the walls of the blood vessels, while heating of the epidermis results in adverse effects. Due to the complexity of the anatomic structure of PWS and multi-physical and physiological reactions of the skin and blood under laser irradiation,

simplifications and assumptions have to be made in order to provide a mathematical description of this physical process. Major assumptions in this work are given as follows:

1. The skin tissue containing PWS is assumed to be a multi-layered skin model composed of a normal multi-layer skin matrix with the PWS blood vessels superposed on the matrix, see Fig. 1. The multi-layer skin matrix is simplified as a two-layered geometry, consisting of two parallel planar layers, which are the epidermal layer and the dermal layer without including any subcutaneous fat. The undulations of the skin surface at the epidermal-dermal interface are considered to be planar. Additional anatomic structures of normal skin tissue including nerve endings, sweat glands, oil glands and hair follicles are ignored. Melanin in the epidermis is an important light absorber and is included by inserting a melanin-filled basal layer at the bottom of the epidermal layer. The melanin particles are assumed to be homogeneously distributed in the basal layer of the epidermis, simulating the situation of un-tanned skin [12]. The PWS blood vessels, on the other hand, are buried in the dermis below a small superficial portion of uninvolved dermis and are assumed to be spread out and mixed with the dermal tissue, forming a PWS layer in the skin model.
2. The skin tissue is assumed to be a multi-layer turbid medium with light scattering and absorption occurring within the layers. Reflection and refraction take place at the interfaces between layers. The well-known radiative transport equation can be used to describe such light propagation. As a first approximation, all optical properties of the tissues are assumed to be constant and uniform within a given component and/or a layer. The radiative transport equations can be solved with the well-developed MLMC method [5].
3. Blood perfusion and metabolic heat generation are not included in the energy equations because of the short pulse of the laser irradiation used. Early works demonstrated that these effects were small, compared with the heat due to laser energy absorption [13]. As a first approximation, no phase change of blood is considered when the blood temperature is higher than the boiling point of water.
4. The composite melanin-filled basal layer in the epidermis is a homogeneous mixture of melanin particles and normal epidermal tissue. A local thermodynamic equilibrium condition is assumed within the mixture during the process of laser treatment of PWS so that both melanin and the epidermal tissues have the same temperature. Such an assumption is justified since the thermal relaxation time of melanin particles (in nanoseconds) is much shorter than the pulse duration of the laser irradiation (in milliseconds) during treatment of PWS.
5. The PWS layer is treated as a porous medium with blood vessels buried within the matrix of normal dermal tissues. Due to selective absorption of the laser energy by the blood, the layer is assumed to be at a local thermodynamic non-equilibrium condition, i.e., the blood within the vessels and the surrounding dermal tissue would have different temperatures. It is further assumed that the two energy equations of porous media, derived based on the volume averaging technique, can be employed to solve the macroscopic average temperatures of the two phases.

Of the five assumptions mentioned earlier, 1–4 are common practice and have been widely employed in the literature [7, 14]. The local thermodynamic non-equilibrium condition in the PWS layer is introduced for the first time in laser PWS modeling. We have demonstrated that such a condition is consistent with the principle of selective photothermolysis [1].

## 2.2 Governing equations and boundary conditions

With the above assumptions, the two normal epidermal and dermal layers are single-phase homogeneous media with constant and uniform thermal and optical properties. However, the basal layer with melanin and the PWS layer are two-phase mixtures. The macroscopic energy equations derived based on the volume averaging technique are employed for the two mixtures, but one is under local thermodynamic equilibrium condition and the other is under local non-equilibrium. In the case of local equilibrium, one-energy equation is used with the properties of the mixture as the weighted averaging of the two components [14]. In the case of local non-equilibrium, however, two energy equations, one for each phase, were used [15, 16]. The energy equations for each layer are given below:

Epidermis without melanin ( $0 < z < z_{\text{epi/basal}}$ )

$$\rho_{ec} \frac{\partial T_e}{\partial t} = \nabla (k_e \nabla T_e) + \frac{Q_e}{t_p} \quad (1)$$

Basal layer with melanin ( $z_{\text{epi/basal}} < z < z_{\text{basal/der}}$ )

$$[\varepsilon_m (\rho c)_m + (1 - \varepsilon_m) (\rho c)_e] \frac{\partial \bar{T}_{\text{basal}}}{\partial t} = \nabla [(\varepsilon_m k_m + (1 - \varepsilon_m) k_e) \nabla \bar{T}_{\text{basal}}] + \frac{Q_{\text{basal}}}{t_p} \quad (2)$$

Dermis without blood ( $z_{\text{basal/der}} < z < z_{\text{der/PWS}}$ )

$$\rho_d c_d \frac{\partial T_d}{\partial t} = \nabla (k_d \nabla T_d) + \frac{Q_d}{t_p} \quad (3)$$

PWS layer ( $z_{\text{der/PWS}} < z < z_k$ )

$$\varepsilon_b \rho_b c_b \frac{\partial \bar{T}_b}{\partial t} = \nabla (\varepsilon_b k_b \nabla \bar{T}_b) - h_{bd} a_{bd} (\bar{T}_b - \bar{T}_d) + \frac{\varepsilon_b Q_b}{t_p} \quad (4)$$

$$(1 - \varepsilon_b) \rho_d c_d \frac{\partial \bar{T}_d}{\partial t} = \nabla ((1 - \varepsilon_b) k_d \nabla \bar{T}_d) + h_{bd} a_{bd} (\bar{T}_b - \bar{T}_d) + \frac{(1 - \varepsilon_b) Q_d}{t_p} \quad (5)$$

where the energy deposition  $Q$  is only true during the pulse duration,  $T$  represents the local temperature in the single phase medium and  $\bar{T}$  represents the intrinsic volume-averaged temperature of the given phase in the mixture:

$$\bar{T}_i = \frac{1}{V_i} \int_{V_i} T_i dV \quad (6)$$

where  $V$  is the volume and  $V_i$  is the volume of the phase  $i$  within the chosen representative element volume (see Fig. 1) and the subscript  $i$  represents melanin (m), epidermal tissue (e), blood (b), or dermal tissue (d), respectively. For the basal layer in the epidermis, the two average temperatures,  $\bar{T}_e$  and  $\bar{T}_m$ , are equal due to the assumption of local thermodynamic equilibrium:

$$\bar{T}_{\text{basal}} = \bar{T}_e = \bar{T}_m \quad (7)$$

where  $\bar{T}_{\text{basal}}$  is the average temperature in the melanin-filled basal layer. Here the thermal and the optical properties of the mixture can be obtained by the weighted average of each component.

The two volume fractions,  $\varepsilon_m$  and  $\varepsilon_b$ , in the two mixtures are defined within a given representative elementary volume (REV),  $V_{\text{REV}}$  (see Figure 1), in the melanin-filled basal layer and PWS layer respectively, by the following expressions:

$$\begin{aligned} \varepsilon_m &= V_m / V_{\text{REV, basal}} \\ \varepsilon_b &= V_b / V_{\text{REV, PWS}} \end{aligned} \quad (8)$$

where  $V_{\text{REV}}$  is:

$$\begin{aligned} V_{\text{REV, basal}} &= V_m + V_e && \text{for the basal layer} \\ V_{\text{REV, PWS}} &= V_b + V_d && \text{for the PWS layer} \end{aligned} \quad (9)$$

For the PWS layer, a local thermodynamic non-equilibrium condition leads to a two-temperature model, i.e., an average temperature  $\bar{T}_b$  for the blood and an average temperature  $\bar{T}_d$  for the normal dermal tissue surrounding the blood vessels. Due to strong absorption of laser light by the blood, the two temperatures, i.e.,  $\bar{T}_b$  and  $\bar{T}_d$ , should be significantly different during laser irradiation. Therefore, two energy equations should be written for each, as Eqs. (4) and (5).

It should be noticed that in the present skin model, dermal tissue is continuous within the entire dermal region. Therefore, the temperature of the dermal layer ( $T_d$ ) without PWS and the temperature of dermal tissue ( $\bar{T}_d$ ) within the PWS layer should be continuous at the interface of the two layers. However,  $\bar{T}_d$  within the PWS represents a volume-averaged value, since the local temperature of the dermal tissues fluctuates greatly due to the existence of the blood vessels.

In Eqs. (4) and (5),  $h_{bd}$  and  $a_{bd}$  are the interfacial heat transfer coefficient and the interfacial area per unit volume, respectively. Both of them have to be determined separately from supplemental models, i.e., a closure problem to be discussed in detail in section 2.3 below. It is of interest to note that if one assumes  $\bar{T}_b = \bar{T}_d$ , i.e., local thermodynamic equilibrium Eqs. (4) and (5) can be combined together to form a one-temperature equation, i.e., the classical homogenous model widely used in the early stage of the field [6]:

$$[\varepsilon_b(\rho c)_b + (1 - \varepsilon_b)(\rho c)_b] \frac{\partial \bar{T}_{PWS}}{\partial t} = \nabla \cdot [(\varepsilon_b k_b + (1 - \varepsilon_b) k_d) \nabla \bar{T}_{PWS}] + \frac{\varepsilon_b Q_b + (1 - \varepsilon_b) Q_d}{t_p} \quad (10)$$

where  $\bar{T}_{PWS}$  is the average temperature of the PWS layer.

The definitions of other variables in the above equations are listed in the nomenclature, and will not be repeated here.

On the skin surface ( $z=0$ ), a convection heat transfer condition is used to describe the cooling effect of the environment:

$$k_e \left. \frac{\partial T_e}{\partial z} \right|_{z=0} = h_a [T_e(r, 0, t) - T_a] \quad (11)$$

where  $T_a$  is the temperature of the environment, and  $h_a$ , treated as a constant, stands for the convective heat transfer coefficient between the skin surface and air.

At the interface between the PWS layer and the dermal layer without blood ( $z_{der/PWS}$ ), a zero flux condition is used for  $\bar{T}_b$  and a continuum condition is used for  $\bar{T}_d$ :

$$\left\{ \begin{array}{l} \left. \frac{\partial \bar{T}_b}{\partial z} \right|_{z=z_{der/PWS}} = 0 \\ \left. \frac{\partial \bar{T}_d}{\partial z} \right|_{z^+=z_{der/PWS}} = \left. \frac{\partial \bar{T}_d}{\partial z} \right|_{z^-=z_{der/PWS}} \end{array} \right. \quad (12)$$

Adiabatic conditions are adapted for other three boundaries.

### 2.3 Closure problem for the two-temperature model of the PWS layer: estimation of the interfacial heat transfer ( $h_{bd}$ and $a_{bd}$ )

Equations (4) and (5) represent macroscopic energy transport of a porous medium based on the average temperature of each phase, with the effect of the detailed microscopic-level transport of energy within the mixture lumped into two new variables.  $h_{bd}$  and  $a_{bd}$ .  $h_{bd}$  represent the rate of local energy exchange at the blood-vessel interfaces, while  $a_{bd}$  is the specific interfacial area. Therefore, the values of these two new variables depend on the detailed size and anatomic structure of the blood vessels in the PWS. Mathematically, there is a closure problem to provide the quantitative relation for  $h_{bd}$  and  $a_{bd}$  for any given PWS.

In the literature of porous media, significant efforts have been made to estimate  $h_{bd}$  for various porous media [15–18], but the majority of these studies targeted a liquid filled with porous solid media. Such work demonstrated that the interfacial heat transfer coefficient depended on the geometry, the size and the volumetric fraction of the solid phase. For fast transient heating due to laser absorption,  $h_{bd}$ , should really be a function of both the time and temperature differences between the blood and surrounding tissues. To solve this transient problem, we have to go back to the specific blood vessel configuration. However, PWSs are malformations of venous capillaries with fairly complex shapes and sizes [19–22]



and it is very difficult to predict the heat transfer between blood and dermis in a real PWS. As a first approximation in this study, we simplify the irregularly distributed PWS blood vessels as parallel tubes, and regularly distributed in dermis with the same diameter  $d_b$  (which can be thought as an average diameter of blood vessels). In this way, the dermis containing PWS blood vessels can be recognized as repeating unit cells composed of normal tissue and a single blood vessel. Thermal analysis can then be made in this unit cell to provide quantitative information of interfacial heat transfer between the blood and surrounding dermal tissue. Both transient and quasi-steady conditions have been considered. The details of the problem settings and solutions are given in the Appendix. The analysis provides non-dimensional heat transfer relationships that can be used to evaluate the interfacial heat transfer coefficient during and after laser irradiation, as summarized below for a case in which  $\varepsilon_b = 6\%$ :

$$Nu_{bd} = \frac{h_{bd}d_b}{k_t} = \begin{cases} 3.92141 \exp\left(-\frac{\Delta\bar{\theta}}{0.05132}\right) + 2.69397 \exp\left(-\frac{\Delta\bar{\theta}}{0.00705}\right) + 1.42507 & t^* \leq t_p^* \\ \frac{4}{\frac{\ln 2}{K_{bd}} + \frac{1-\varepsilon_b^{1/2}}{2\varepsilon_b^{1/2}}} & t^* > t_p^* \end{cases} \quad (13)$$

where  $d_b$  is the diameter of the blood vessels,  $K_{bd} = k_b/k_d$  is the ratio of the thermal conductivities of the blood and the dermal tissues.  $t^* = \alpha_b t/d_b^2$  and  $t_p^* = \alpha_b t_p/d_b^2$  are the non-dimensional time and laser pulse duration, respectively, with  $t_p$  the dimensional laser pulse duration and  $\alpha_b$  the thermal diffusivity of the blood, and  $\Delta\bar{\theta}$  is the non-dimensional temperature difference, defined as follows:

$$\Delta\bar{\theta} = \frac{\bar{T}_b - \bar{T}_d}{Q_b d_b^2 / 4k_b} \quad (14)$$

Within such a uniform cell, the specific interfacial area  $a_{bd}$  can be simply written as:

$$a_{bd} = 4\varepsilon_b/d_b \quad (15)$$

It is then evident that the information for both diameter ( $d_b$ ) and the volumetric fraction ( $\varepsilon_b$ ) of the blood are needed to carry out any quantitative analysis with the present two-temperature model.

## 2.4 Multi-Layer Monte Carlo method for light propagation and energy deposition

The radiative transport equation for light propagation in the skin model is solved by the Monte Carlo method. The Monte Carlo method used here is the so-called MLMC, developed by Wang et al [5]. However, some modifications have to be conducted to make it consistent with the present two-temperature model for laser heating of PWS.

In the MLMC method, the photon propagation through the multi-layer skin is calculated using the absorption and scattering coefficients, together with a random number  $\xi$ :

$$\Delta s = -\ln(\xi)/\mu_t \quad (16)$$

where  $s$  is the free path length,  $\mu_t$  is the attenuation coefficient of the layer which is the sum of the absorption coefficient  $\mu_a$  and scattering coefficient  $\mu_s$ . Here we need to mention that, for the mixed layers (basal layer of the epidermis and PWS), the average absorption coefficient  $\mu_a$  and the scattering coefficient  $\mu_s$  of the mixture are weighted averages based on the local volumetric fraction of melanin or blood, respectively. Thus, in the melanin-filled basal layer, we have:

$$\mu_{a, \text{basal}} = \varepsilon_m \cdot \mu_{a, m} + (1 - \varepsilon_m) \cdot \mu_{a, e} \quad (17)$$

$$\mu_{s, \text{basal}} = \varepsilon_m \cdot \mu_{s, m} + (1 - \varepsilon_m) \cdot \mu_{s, e} \quad (18)$$

In addition, in the PWS layer, it is necessary to consider the optical screening effect of the blood vessels [23]. Following Milanic et al [24] a correction factor  $C$ , related to the absorption coefficient of the blood and the diameter of the blood vessels, can be introduced to account for such an effect. We have:

$$\mu_{a, \text{PWS}} = \varepsilon_b \cdot C \cdot \mu_{a, b} + (1 - \varepsilon_b) \cdot \mu_{a, d} \quad (19)$$

$$\mu_{s, \text{PWS}} = \varepsilon_b \cdot C \cdot \mu_{s, b} + (1 - \varepsilon_b) \cdot \mu_{s, d} \quad (20)$$

After each absorption event, the photon is scattered, and a new propagation direction is then generated which can be predicted according to the probability of distributions of the deflection (polar) angle and azimuthal angle at each interaction site (based on the anisotropy index,  $g$ ). In the mixed layers, the average anisotropy index,  $g$ , of the mixture is again weighted based on the local volumetric fraction:

For the basal layer with melanin:

$$g_{\text{basal}} = \varepsilon_m \cdot g_m + (1 - \varepsilon_m) \cdot g_e \quad (21)$$

For the PWS layer with blood:

$$g_{\text{PWS}} = \frac{\varepsilon_b \cdot C \cdot \mu_{s, b} \cdot g_b + (1 - \varepsilon_b) \cdot \mu_{s, d} \cdot g_d}{\varepsilon_b \cdot C \cdot \mu_{s, b} + (1 - \varepsilon_b) \cdot \mu_{s, d}} \quad (22)$$

here again the screening effect of large blood vessels is accounted for by the same correction factor,  $C$ .

In the present MLMC simulation, the weight method is used in scoring the absorption of light energy at a given location [5]. After each scattering event, a fraction of the photon weight would be absorbed at the end location of each path. The initial photon energy is set to be a unit and reduced after each absorption event. The absorbed fraction ( $\mu_a/\mu_t$ ) of the photon energy is scored in the absorption array,  $A$ , for a given location. With sufficient

photon propagation, the light fluence,  $F$ , in each layer, within a representative volume element can be calculated as follows:

$$F = \frac{E \cdot \pi r_p^2}{\mu_{a,i} t_p} \cdot \frac{A}{N \cdot V_{REV}}, \quad i=e, \text{ basal d and PWS} \quad (23)$$

where  $r_p$  is the laser spot size (cm),  $t_p$  the laser pulse duration (s),  $N$  the photon number,  $V_{REV}$  the volume of the REV, and  $E$  the incident laser fluence. The details of the MLMC method can be found elsewhere [5].

The known light fluence distribution within tissue,  $F$ , can be converted to the energy deposition by multiplying the light absorption coefficient of a given layer:

$$Q_i = \mu_{a,i} F \quad i=e, \text{ d, basal} \quad (24)$$

where the subscript  $i$  represents the epidermal layer and the dermal layer or the basal layer. In Eq. (24) a volume averaged absorption coefficient has to be used for a mixed layer.

In the PWS layer, it is necessary to evaluate the volumetric heat generation for both phases separately, consistent with the present two-temperature model (Eqs. (4) and (5)). A modification of the energy scoring has also been applied to obtain the energy deposition for each phase:

$$\begin{aligned} Q_b &= \mu_{a,b} F \\ Q_d &= \mu_{a,d} F \end{aligned} \quad (25)$$

## 2.5 Numerical method

The above mathematical equations constitute a multi-region, two-dimensional axial-symmetric transient heat conduction problem for pulsed heat generation. The problem is numerically solved by a finite-volume method with a uniform grid. The solution procedure includes the following steps:

1. Solve photon weight deposition ( $A$ ) and the laser fluence ( $F$ ) for each control element by using the MLMC method, with an in-house Monte-Carlo code.
2. For a given volume fraction of blood within the PWS layer, solve the transient heat conduction equation of a unit cell to evaluate the interface heat transfer coefficient,  $h_{bd}$ . For each time step,  $h_{bd}$  at each location is estimated from Eq. (13) based on the known  $T_b$  and  $T_d$ .
3. Solve the nodal temperature equations with an implicit time scheme by the tri-diagonal matrix algorithm (TDMA) with block correction.

The validity of the MLMC code and the temperature code has been extensively tested based on simple cases found in the literature [25]. The dense grid is used to generate the grid-independent solutions.

### 3. Results

To illustrate the basic characteristics of the present two-temperature model, the above mathematical equations are solved for a case of clinical interest. We choose a laser wavelength of 585 nm, typical for modern pulsed dye lasers [19]. The beam diameter of a flat hat-beam profile is chosen as 6 mm [10]. The thickness of each layer is 50  $\mu\text{m}$  for the epidermal layer without melanin, 10  $\mu\text{m}$  for the melanin-filled basal layer with a melanin volumetric fraction of 25%, 90  $\mu\text{m}$  dermal layer without blood, and 850  $\mu\text{m}$  PWS layer filled with 80  $\mu\text{m}$  blood vessels with volumetric fraction of 6% [10]. The initial skin temperature is assumed to be at 33  $^{\circ}\text{C}$ . The ambient temperature  $T_a$  is set to be 25  $^{\circ}\text{C}$ . The convective heat transfer coefficient between the skin surface and air  $h_a$  is assumed to be 10  $\text{W}/\text{m}^2\text{K}$  [10]. The optical properties of the epidermis, melanin, dermis, and blood at this wavelength are listed in Table 1.

#### 3.1 Thermal characteristics of the two-temperature model and comparison with the discrete blood vessel model

Figure 2 shows a spatial view of the calculated temperature of the skin matrix (a) and the blood (b) in the PWS layer at the end of the 1.5 ms laser irradiation. Figure 2a shows that there is a high temperature spike in the melanin-filled basal layer, much higher than that of the melanin-free epidermis and dermis. At the same time, within the PWS layer, a high peak blood temperature followed by quick decrease can be observed in Fig. 2b. Comparing Fig. 2b with Fig. 2a, as one would expect, the blood shows a significantly higher temperature than that of the surrounding dermal tissue.

The temperature distribution in the skin matrix (Fig. 2a) and the blood (Fig. 2b) can be plotted, as shown in Fig. 3 that plots the temperature distribution of each layer along the tissue depth ( $z$ ) at the center of the beam spot. Figure 3 shows a sharp temperature spike,  $T_{\text{basal}}$ , caused by epidermal melanin heating, can be observed in the melanin-filled basal layer. In the PWS layer, however, significant differences in the calculated temperatures between the blood ( $\bar{T}_b$ ) and the tissue ( $\bar{T}_d$ ) indicate that the present two-temperature model can correctly reflect the selective heating of blood under laser irradiation.

A quantitative comparison can be made between the present two-temperature model and the discrete-blood-vessel model. The latter was proposed by Tunnell et al [10] who employed a discrete-blood-vessel model that was made of randomly distributed parallel cylindrical blood vessels with diameter of 80  $\mu\text{m}$ . The result of Fig. 4 shows such a comparison immediately after 1.5 ms and 585 nm laser irradiation. The colorful background in Fig. 4 is a two-dimensional view of a three dimensional temperature presentation taken from Tunnell et al that shows significant overlapping of temperature curves for neighboring blood vessels. As one can see, in the epidermal layer, the calculated temperature by the present model is almost the same as that calculated by Tunnell et al. For a PWS, the prediction of two-temperature model envelops the 2-D temperature field of blood vessels by Tunnell et al. The good agreement shown in Fig. 4 for the two different models validates the present two-temperature model.

A further comparison between the present two-temperature model and the discrete-blood-vessel model is made at two time points after laser irradiation in Fig. 5 that shows a comparison of the temperature distributions for various tissue depths at 5 ms (a) and 10 ms (b) post-laser irradiation. Both Figs. 5a and 5b demonstrate fairly good agreement between our two-temperature model and Tunnell's discrete model. Although the two-temperature model shows a slower cooling rate than that predicted by the discrete model (Fig. 5a), agreement between the two models becomes better at 10 ms and the subsequent period after laser irradiation (Fig. 5b). This discrepancy between the two models may result from inaccurate treatment of the interfacial heat transfer ( $a_{bd}h_{bd}$ ) between the blood vessels and the surrounding tissues in the two-temperature model.

### 3.2 Comparison with the homogeneous PWS model

The present two-temperature model has many common features compared with the traditional homogeneous model used in early modeling of PWS laser treatments [6]. Both models ignore the detailed anatomic structure of the PWS blood vessels and treat the irregularly distributed blood vessels as homogeneously distributed blood in the dermis. However the early homogeneous model assumed a local thermodynamic equilibrium between the blood in the blood vessel and the surrounding dermal tissue, and employed an average temperature for both blood and dermal tissue. As a result, the homogeneous model was eventually replaced by discrete blood vessel models [7, 14]. The present two-temperature model removes the assumption of local thermodynamic equilibrium and considers the temperature difference between the blood and the dermal tissue. Such a model presents a more realistic view of laser treatment of PWS.

The importance of considering local non-equilibrium in the PWS layer is demonstrated by comparing the results from the present two-temperature model with that from the traditional homogeneous model (Eq. 10), as shown in Fig. 6 that shows the temperature distribution for various tissue depths calculated by the homogeneous model and the two-temperature model, respectively. As we can see from the figure, the temperature predictions by the present model are as exact as the homogeneous model in the epidermis ( $0 < z < Z_{\text{mel-epi/der}}$ ) and dermis without blood ( $Z_{\text{mel-epi/der}} < z < Z_{\text{der/blood}}$ ) as the thermodynamic equilibrium condition can be achieved in both layers. In dermis containing PWS ( $Z_{\text{der/blood}} < z < Z_k$ ) and at the selected wavelength and pulse duration, the two-temperature model predicts that the calculated average temperature of the blood ( $\bar{T}_b$ ) is much higher than that of the dermis ( $\bar{T}_d$ ) due to the distinct selective heating of blood over the surrounding dermis. However, with the homogenous model, only an average temperature for the blood and dermis ( $\bar{T}_{\text{PWS}}$ ) can be calculated, as the local thermodynamic equilibrium condition was employed. The average temperature of the PWS layer is lower than the blood temperature and higher than the dermal temperature calculated by the two-temperature model.  $\bar{T}_{\text{PWS}}$  is related to the volumetric fraction of the blood, which in this study was selected to be 6%. As a result, the average temperature is closer to the dermal temperature.

The dynamic temperature variations in the laser spot center at dermal skin depth of 150  $\mu\text{m}$ , as predicted by the two-temperature and homogenous models, are shown in Fig. 6b. As we can see from the figure, in the two-temperature model, the blood and surrounding dermal

tissue temperatures can be predicted simultaneously. During laser heating, the blood temperature ( $\bar{T}_b$ ) increases quickly due to selective energy absorption at the selected wavelength. At the same time, dermal temperature ( $\bar{T}_d$ ) increases little during laser heating. After laser heating, as a result of heat conduction, energy absorbed by the blood would conduct to the surrounding dermis and, as a result, blood temperature gradually decreases and dermal temperature slowly increases simultaneously (volumetric fraction of the dermis is much larger than the blood). With a homogeneous model, however, only one average temperature ( $\bar{T}_{PWS}$ ) can be predicted for the blood and dermis, which is higher than the dermal temperature and lower than the blood temperature. During laser heating, the average temperature gradually increases as a result of energy absorption by blood. After the laser irradiation, the average temperature gradually decreases. As time goes on (e.g. 20 ms after the laser pulse), a local thermodynamic equilibrium condition is achieved between the blood and the surrounding dermal tissue and, as a result, the blood temperature predicted by the two-temperature model is almost equal to the dermal tissue temperature and the average temperature predicted by the homogeneous model.

#### 4. Discussion (a separate discussion is added here)

A discrete blood vessel model has been commonly used to calculate the thermal process during laser treatment of PWS [7, 10, 14]. Such a model could provide an exact solution of detailed temperature distributions within the blood vessels as well as surrounding tissues to laser heating. However, the results are only valid if the blood vessels of PWS lesions are straight parallel cylinders, as assumed in the discrete blood vessel model. The local thermodynamic non-equilibrium heat transfer theory of porous media has already been used to model the flow and heat transfer in blood perfused biological tissue accounting for the thermal non-equilibrium induced by blood perfusion [26–28]. The porous media heat transfer theory employs fewer assumptions compared to other bio-heat transfer models [27]. In this study, however, for the first time we present how the local thermodynamic non-equilibrium heat transfer theory can be implemented to model laser treatment of PWS accounting for the thermal non-equilibrium between blood and peripheral tissue induced by selective photothermolysis.

Without detailed anatomic structure, the complex geometric configuration of PWS blood vessels is quantified by a typical length scale such as the local average blood vessel diameter and local volumetric fraction of blood vessels. Two volume-averaged temperature values, one for the blood temperature and the other for the temperature of healthy dermal tissues surrounding the vessels, are defined in the REV. Two energy equations for blood and surrounding dermal tissue are constructed based on the local thermodynamic non-equilibrium heat transfer theory. Both the selective light energy absorption of the blood and interfacial heat transfer between the blood and the surrounding tissue are included in the present two-temperature model. The model provides an average behavior of selective laser heating of the blood as described by the theory of selective photothermolysis. Mathematically, the two-temperature model is less complicated in terms of coding and computation and requires less PWS blood vessel micro-structure information, compared with the discrete-blood-vessel model. The advantage of the two-temperature model over the

discrete model becomes even more significant as the geometric configuration of a real PWS becomes more complex.

To accurately estimate the thermal history within skin during laser treatment of PWS, however, quantitative information for the interfacial heat transfer between the blood and surrounding tissue is essential in the present two-temperature model. In the literature of porous media, significant efforts have been made to estimate  $h_{bd}$  for various porous media [15–18]. But the majority of these analyses are for steady state flow problems. In the present two-temperature model, a simplified treatment is employed by simplifying irregularly distributed PWS blood vessels as repeating unit cells composed of normal tissue and single blood vessel parallel tubes. A transient heat conduction problem is solved in the single cell for the interfacial heat transfer coefficient. Our assumptions deviate somewhat from clinical reality because PWSs are blood vessel malformations with fairly complex shapes and sizes [19–22]. However, we provide a reasonable approximation of the evaluated situations. Further work will be performed to solve the closure problem for the two-temperature model in a more realistic manner.

Our two-temperature model can also be applied to provide an accurate description of other laser dermatologic surgery such as the short-pulse laser heating process for removal of pigmented lesions, where a strong non-equilibrium exists between melanin and the surrounding tissue, leading to a large temperature difference. However, due to the small size of melanin particles and the large number of these particles within the skin, traditional methods are not accurate as they can only simulate the situation of a single melanin particle [29]. We will apply this model to other dermatologic surgery indications in the near future.

## 5. Conclusion

In this paper, a two-temperature model for laser surgery of PWS is created by treating PWS as a porous medium made of a tissue matrix buried with the blood in the dermis and following the local thermal non-equilibrium theory of porous media. The thermal model includes two energy equations, one for the blood and the other for non-absorbing tissues. A relation of non-dimensional heat transfer coefficient and non-dimensional time difference have been developed for interfacial heat transfer between the blood and the tissue by performing a numerical analysis in a unit cell with simplified blood vessel geometry. The technique has been also devised in applications of the MLMC method for laser propagation and energy deposition within a two-phase PWS layer. The calculated results of the present two-temperature model have demonstrated clearly that the local thermal non-equilibrium occurring during laser treatment of PWS is consistent with the theory of selective photothermolysis. The present model may provide a new way to numerically simulate laser treatment of PWS.

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## Appendix: Calculation of Normalized Interfacial Heat Transfer Coefficient Nubd between the Blood and Normal Tissue

Here we e construct a microscopic heat transfer unit cell to calculate the interfacial heat transfer coefficient,  $h_{bd}$ , between the blood and the surrounding dermal tissue for transient heating during and after laser irradiation. It is further assumed that the size of the blood vessels is small, and as a result, the assumption of uniform heating within the blood with a rate of heat generation,  $Q_b$ , can be employed. Cylindrical geometry for PWS blood vessels is assumed as one-dimensional heat transfer.

In each unit cell, the energy equations can be written in terms of the blood (b) and the surrounding dermal tissue (d), respectively:

$$\rho_b c_b \frac{\partial T_b}{\partial t} = \frac{k_b}{r} \frac{\partial}{\partial r} \left( r \frac{\partial T_b}{\partial r} \right) + Q_b \quad 0 \leq r \leq \frac{d_b}{2} \quad (\text{A.1})$$

$$\rho_d c_d \frac{\partial T_d}{\partial t} = \frac{k_d}{r} \frac{\partial}{\partial r} \left( r \frac{\partial T_d}{\partial r} \right) + Q_d \quad \frac{d_d}{2} < r \leq \frac{d_k}{2} \quad (\text{A.2})$$

where  $d_b$  is the diameter of the blood vessels and  $d_k$  is the equivalent diameter of the microscopic unit cell, with  $d_k = d_b / \varepsilon_b^{1/2}$ . Equations (A.1) and (A.2) can be non-dimensionalized with the length ( $d_b/2$ ), the character time ( $\tau = d_b^2 / \alpha_b$ ), and the characteristic temperature difference ( $\Delta T = Q_b d_b^2 / (4k_b)$ ):

$$\frac{\partial \theta_b}{\partial t^*} = \frac{1}{(r^*)} \frac{\partial}{\partial r^*} \left( (r^*) \frac{\partial \theta_b}{\partial r^*} \right) + 1 \quad 0 \leq r^* \leq 1 \quad (\text{A.3})$$

$$\frac{\partial \theta_d}{\partial t^*} = \frac{1}{\alpha_{bd} (r^*)} \frac{\partial}{\partial r^*} \left( (r^*) \frac{\partial \theta_d}{\partial r^*} \right) + \frac{Q_d}{Q_b} \quad 1 < r^* \leq \frac{1}{\varepsilon^{1/2}} \quad (\text{A.4})$$

where  $\alpha_b$  is the thermal diffusivities of the blood and  $\alpha_{bd}$  is the ratio of the thermal diffusivities of the blood and the dermal tissues.

The corresponding boundary conditions become:

$$r^* = 0, \quad \frac{\partial \theta_b}{\partial r^*} = 0 \quad (\text{A.5})$$

$$r^* = 1, \quad \begin{cases} \theta_b(1, t^*) = \theta_d(1, t^*) \\ K_{bd} \frac{\partial \theta_b}{\partial r^*} \Big|_{r^*=1} = \frac{\partial \theta_d}{\partial r^*} \Big|_{r^*=1} \end{cases} \quad (\text{A.6})$$

$$r^* = \frac{1}{\varepsilon^{1/2}}, \quad \frac{\partial \theta_d}{\partial r^*} = 0 \quad (\text{A.7})$$



It is assumed that the entire micro-volume is initially at a uniform temperature so the initial condition becomes:

$$t^*=0 \quad \theta_b(r^*, 0) = \theta_d(r^*, 0) = 0 \quad (\text{A.8})$$

The interfacial heat transfer coefficient,  $h_{bd}$ , between the blood and the surrounding tissue is defined based on the heat transfer between the blood and the surrounding tissue and the mean temperatures of the chromophores and the tissue. A non-dimensional form is given as follows:

$$Nu_{bd} = \frac{h_{bd}d_b}{k_d} = \frac{-2 \left. \frac{\partial \bar{\theta}_d}{\partial r^*} \right|_{r^*=1}}{\bar{\theta}_b - \bar{\theta}_d} \quad (\text{A.9})$$

where the dimensionless mean temperatures of the blood ( $\bar{\theta}_b$ ) and the dermal tissue ( $\bar{\theta}_d$ ) are defined as follows:

$$\bar{\theta}_b = \frac{1}{2} \int_0^1 r^* \theta_b dr^* \quad (\text{A.10})$$

$$\bar{\theta}_d = \frac{1}{2} \left( \frac{1}{\varepsilon_b^{1/2}} - 1 \right) \int_1^{1/\varepsilon_b^{1/2}} r^* \theta_d dr^* \quad (\text{A.11})$$

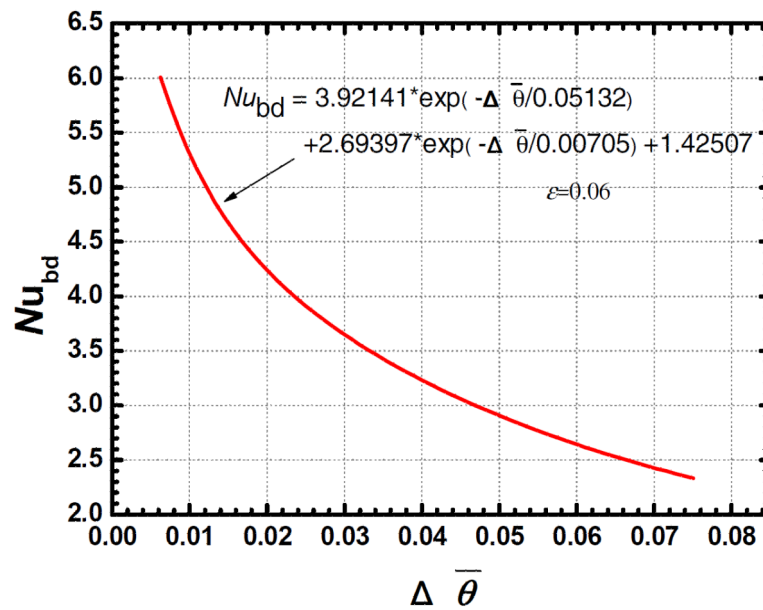
For a given chromophore and its volumetric fraction ( $\varepsilon_b$ ), the above problem can be solved numerically. The results provide a relationship between  $Nu_{bd}$  and dimensionless temperature difference  $\Delta \bar{\theta} = \bar{\theta}_b - \bar{\theta}_d$ . Figure A1 shows the typical  $Nu_{bd}$  for cylindrical blood vessels. The curve can be numerically fitted to a mathematical relationship that can be used to estimate  $h_{bd}$  in Eqs. (4) and (5) for the two-temperature model simulation.

A further simplified form for  $Nu_{bd}$  can be derived for the case without internal heating, by assuming quasi-steady state one-dimensional heat conduction between the blood and the surrounding tissue. In this case, a simplified thermal circuit can be constructed as shown in figure A2 with the average temperatures of the blood and the surrounding dermal tissue located at the middle of region, respectively. Then one has:

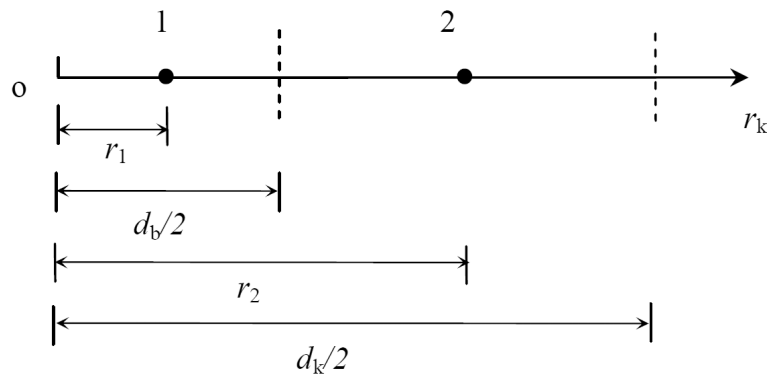
For a cylindrical chromophore:

$$Nu_{bd} = \frac{h_{bd}d_b}{k_b} = \frac{4}{\frac{\ln 2}{K_{bd}} + \frac{1 - \varepsilon_b^{1/2}}{\varepsilon_b^{1/2}}} \quad (\text{A.12})$$

Finally, we can combine the two cases mentioned earlier for the interfacial heat transfer during ( $t < t_p$ ) and after laser irradiation ( $t > t_p$ ), where  $t_p$  is the laser pulse duration, as given in Eq. (13) for a cylindrical blood vessel.



**Fig. A1.**  
Calculated  $Nu_{bd}$  vs  $\Delta\bar{\theta}$  for cylindrical blood vessels ( $\varepsilon_b=0.06$ ) during transient heating due to an internal heat source within the blood



**Fig. A2.**  
A thermal circuit for one-dimensional heat conduction between the blood and the surrounding dermal tissue

## Nomenclature

- A** Array to score light energy absorption
- a** Specific interfacial area
- c** Specific heat
- C** Correction factor for tissue optical properties in homogeneous layers
- d** Diameter

<b>E</b>	Incident laser fluence
<b>F</b>	Light fluence distribution within tissue
<b>g</b>	Anisotropy index
<b>h</b>	Heat transfer coefficient
<b>k</b>	Thermal conductivity
<b><math>K_{bd}</math></b>	The ratio of the thermal conductivities of the blood and the dermal tissues
<b>N</b>	Photon number
<b>Nu</b>	Non-dimensional heat transfer coefficient
<b>Q</b>	Volumetric heat generation due to laser energy absorption
<b>r</b>	Radial coordinate
<b>s</b>	Free path length of the photon
<b>T</b>	Temperature
<b><math>\bar{T}</math></b>	Volume-averaged temperature
<b>t</b>	time
<b>V</b>	Volume
<b>z</b>	Axial coordinate

### Greek symbols

<b><math>\alpha</math></b>	The thermal diffusivity
<b><math>\varepsilon</math></b>	Volumetric fraction of the chromophore
<b><math>\mu_a</math></b>	The absorption coefficient
<b><math>\mu_s</math></b>	The scattering coefficient
<b><math>\mu_t</math></b>	The attenuation coefficient
<b><math>\tau</math></b>	Normalized time
<b><math>\xi</math></b>	Random number

### Subscripts and superscripts

<b>a</b>	Air
<b>b</b>	Blood
<b>basal</b>	Basal layer of the epidermis
<b>basal/der</b>	Interface between the basal layer and the dermal layer
<b>bd</b>	Interface between the blood vessel and the dermis

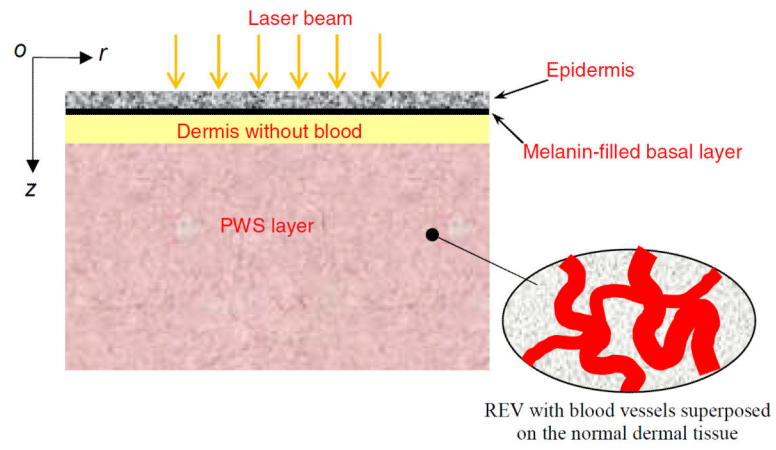
<b>d</b>	Dermis
<b>der/PWS</b>	Interface between the dermal layer and the PWS layer
<b>e</b>	Epidermis
<b>epi/basal</b>	Interface between epidermis without melanin and the basal layer
<b>k</b>	Bottom surface of the computation domain
<b>m</b>	Melanin
<b>p</b>	Pulse
<b>PWS</b>	The PWS layer
<b>REV</b>	representative elementary volume
<b>*</b>	Normalized

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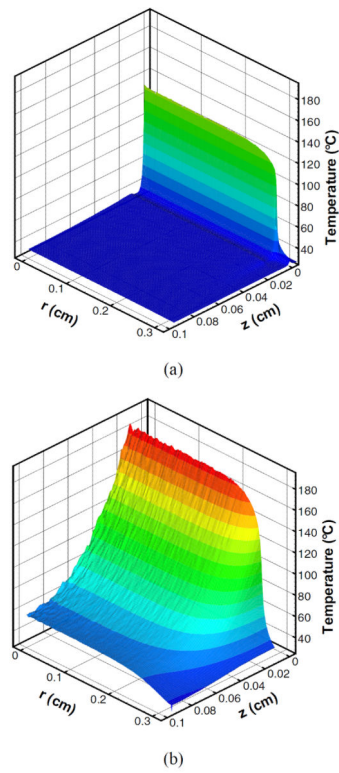
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- Local thermal non-equilibrium theory was adapted in field of laser dermatology
- Transient interfacial heat transfer coefficient between two phases is presented
- Less PWS blood vessel micro-structure information is requires in present model
- Good agreement between present model and classical discrete-blood-vessel model

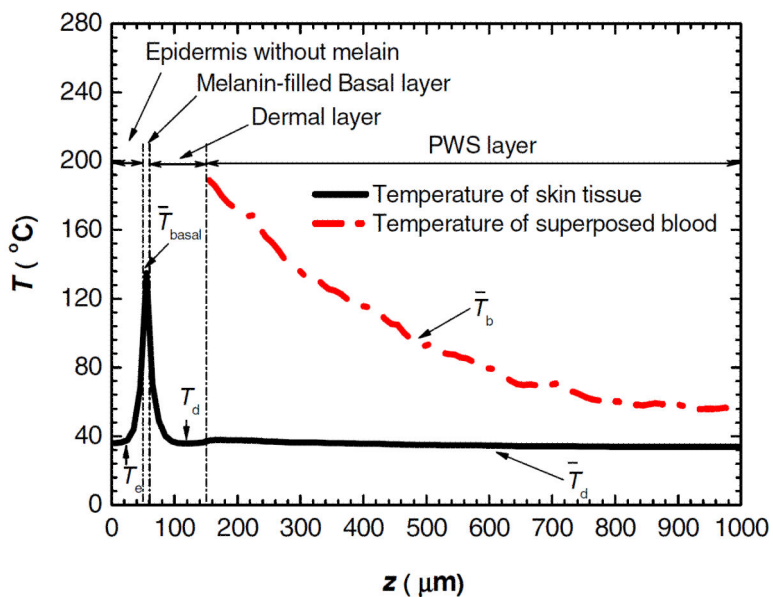


**Fig. 1.** Representative elementary volume (REV) for port wine stains in a four-layer skin model

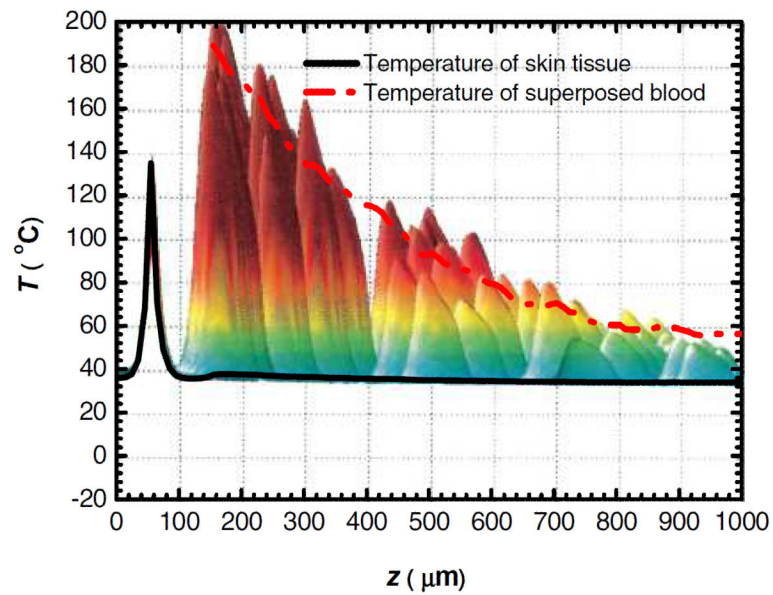


**Fig. 2.** Temperature distribution for the skin matrix (a) and the blood (b) immediately after laser irradiation. Blood vessel diameter ( $80\mu\text{m}$ ), blood volume fraction (6%), melanin fraction in epidermis (25%), laser wavelength (585nm), pulse duration (1.5ms), spot diameter (6 mm), and laser fluence ( $3.1\text{ J/cm}^2$ )

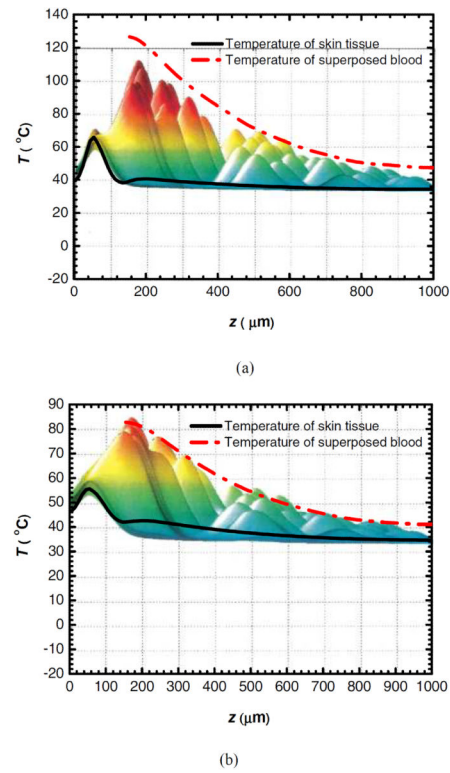




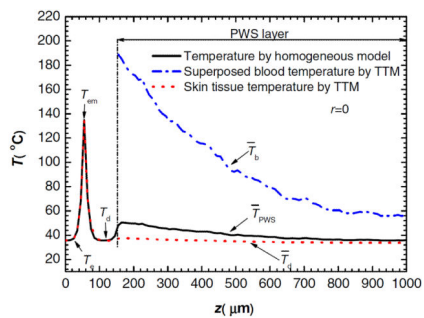
**Fig. 3.** Temperature distribution for various tissue depths immediately after laser irradiation. Blood vessel diameter ( $80\mu\text{m}$ ), blood volume fraction (6%), melanin fraction in epidermis (25%), laser wavelength (585nm), pulse duration (1.5ms), spot diameter (6 mm), and laser fluence ( $3.1\text{ J/cm}^2$ )



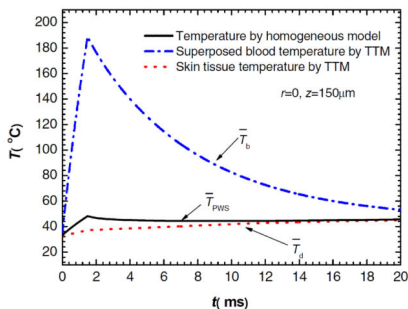
**Fig. 4.** Comparison of temperature distributions immediately after laser irradiation between the present two-temperature model (lines) and the discrete model of Tunnell et al [10]. Blood vessel diameter ( $80\mu\text{m}$ ), blood volume fraction (6%), melanin fraction in epidermis (25%), laser wavelength (585nm), pulse duration (1.5ms), spot diameter (6 mm), and laser fluence ( $3.1 \text{ J/cm}^2$ )



**Fig. 5.** Comparison of temperature distributions 5 ms (a) and 10 ms (b) after laser irradiation between the present two-temperature model (lines) and the discrete model of Tunnell et al [10]. Blood vessel diameter ( $80\mu\text{m}$ ), blood volume fraction (6%), melanin fraction in epidermis (25%), laser wavelength (585nm), pulse duration (1.5ms), spot diameter (6 mm), and laser fluence ( $3.1\text{ J/cm}^2$ )



(a)



(b)

**Fig. 6.** Comparison of temperature distributions along tissue depth (a) and dynamic variation (b) between the present two-temperature model (TTM) and the homogenous model. Blood vessel diameter ( $80\mu\text{m}$ ), blood volume fraction (6%), melanin fraction in epidermis (25%), laser wavelength ( $585\text{nm}$ ), pulse duration ( $1.5\text{ms}$ ), spot diameter ( $6\text{mm}$ ), and laser fluence ( $3.1\text{J}/\text{cm}^2$ )

**Table 1**

Thermal and optical properties of skin components [10]

Physical properties	Melanin	Blood	Dermis
Thermal conductivity, $k$ (KW/(m-K))	0.34	0.55	0.41
Specific heat, $c$ (J/(kg-K))	3.2	3.6	3.5
Density, $\rho$ (kg/m <sup>3</sup> )	1120	1060	1090
Absorption coefficient, $\mu_a$ (cm <sup>-1</sup> )	350	191	2.4
Scattering coefficient, $\mu_s$ (cm <sup>-1</sup> )	470	467	129
Anisotropy index, $g$	0.79	0.99	0.79