Thermal Relaxation Times in Biological Tissues Subjected to Pulsed Laser Irradiation

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There are several expressions for calculating thermal relaxation time in tissues subjected to laser irradiation. Physically this time constant represents the time required for the temperature rise in a heated region of tissue to drop to a factor of $e^{-1}$. In this study, we conduct combined radiation and heat conduction simulations to obtain this time constant for several different tissues, and compare the results with other mathematical expressions used for determining the thermal relaxation time. The scattering effect and surface convection are considered. A new thermal relaxation time expression is introduced in which its value is two times of the thermal relaxation time used in the literature. It is found that the results predicted by this new expression match better with the predictions based on the peak temperature decaying.

Nomenclature

\begin{align*}
C_p &= \text{specific heat capacity} \\
c &= \text{speed of light} \\
D &= \text{beam width} \\
G &= \text{incident radiation} \\
h &= \text{heat transfer coefficient} \\
I &= \text{radiation intensity} \\
N &= \text{number of total incident pulses.} \\
\text{OPD} &= \text{optical penetration depth} \\
\vec{q} &= \text{heat flux vector} \\
t &= \text{time} \\
T &= \text{temperature} \\
\tau_p &= \text{laser pulse width} \\
T_\infty &= \text{ambient temperature} \\
w &= \text{angular weight} \\
x, y &= \text{coordinates} \\
\alpha &= \text{thermal diffusivity} \\
\delta &= \text{characteristic length} \\
\xi, \eta &= \text{directional cosines} \\
\omega &= \text{scattering albedo} \\
\Phi &= \text{phase function} \\
\rho &= \text{density} \\
\sigma_a &= \text{absorption coefficient} \\
\sigma_e &= \text{extinction coefficient} \\
\sigma_s' &= \text{reduced scattering coefficient} \\
\tau &= \text{thermal relaxation time} \\
\theta &= \text{non-dimensional temperature}
\end{align*}

Superscript

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I. Introduction

Since the advent of lasers in 1960s, many practical and potential applications have been investigated. Among them, medical laser surgery and/or treatment certainly belong to the most significant advances of the past several decades. Nowadays, clinical laser is widely used in laser microsurgery,\textsuperscript{1} nonablative dermal remodeling,\textsuperscript{2} tissue fusion,\textsuperscript{3} and photodynamic therapy,\textsuperscript{4} etc. The general goal among these applications is to provide proper heat to a targeted region of tissue while minimizing the collateral thermal damage. There is an increasing demand for effective and safe laser applications in medicine.

The degree and extent of tissue thermal damage depends on many factors. These factors include the maximum temperature reached and the exposure time as well as the mechanical stress applied on the tissue during heating. The amount and rate of heat deposition, coupled with the properties of the tissue and the surrounding medium govern the thermal response at both the microscopic and macroscopic scales. The response is typically modeled by the bio-heat equation.\textsuperscript{5} For irradiation times less than about 5 sec, the influence of blood perfusion plays a minor role.\textsuperscript{6} When blood perfusion is neglected, the governing equation is merely a heat conduction equation, in which the rate of thermal energy storage within a volume must equal the local volumetric absorbed laser energy rate minus the local volumetric losses of heat flux by diffusion. A combined heat radiation and conduction modeling can predict the temperature field and time history, and the data can be used for evaluating the laser parameters. In reality, nevertheless, simpler models are always preferred for guiding the selection of laser input parameters.

The classic theory of selective photothermolysis proposed by Anderson and Parrish\textsuperscript{1} is generally adopted to determine the appropriate laser pulse width. A common practice is that the irradiation duration is less than the thermal relaxation time of the target tissue to minimize thermal damage.\textsuperscript{5,7} Time constants in heat conduction problems have been intensively studied. Furzikov\textsuperscript{8} mathematically expressed the thermal relaxation time as follows

\[ \tau = \delta^2/(4\alpha), \]

where \(\delta\) is a characteristic length and \(\alpha\) is the thermal diffusivity. \(\delta\) is either the optical penetration depth of the incident radiation (for axial conduction) or the Gaussian beam radius at \(e^{-2}\) (for radial conduction). van Gemert and Welch\textsuperscript{6} considered a parallel circuit of axial and radial heat conduction with corresponding time constants \(\tau_z\), \(\tau_r\), respectively; and suggested

\[ \frac{1}{\tau_0} = \frac{1}{\tau_z} + \frac{1}{\tau_r}, \]

According to Eq. (2), the overall time constant is smaller than the smallest individual time constant \(\tau_z\) or \(\tau_r\). It is worth mentioning that \(\tau_z\) and \(\tau_r\) derived by van Gemert and Welch\textsuperscript{6} are virtually identical to Eq. (1) although the numerical factors are slightly different.

The optical penetration depth (OPD) is defined as the depth where the fluence rate drops to \(e^{-1}\) of its original radiance.\textsuperscript{5} For purely absorbing media, \(OPD = 1/\sigma_a\) according to Beer’s law. Because of the difficulty in the analysis of radiation heat transfer in absorbing and scattering turbid media like biological tissues, most of the previous researches\textsuperscript{6-8} used Beer’s law to represent the laser radiation transfer and the scattering effect was neglected. For absorbing and scattering media, a corrected OPD can be defined as \(OPD = 1/(\sigma_a + \sigma_s)\). Nowadays, great progress has been made in the numerical solution of radiation heat transfer participating media and the importance of accurate radiation analysis is being well recognized. The authors considered the modeling of transient laser radiation transfer in tissues using the discrete ordinates method\textsuperscript{9,12} The OPD can then be accurately predicted by the numerical method and used to estimate time constants.

On the other hand, the thermal relaxation time can be physically interpreted as the time required to estimate the temperature rise \((T - T_{base})\) in a heated region of tissue to decrease to \(e^{-1}\) of its peak value \((T_{peak} - T_{base})\).\textsuperscript{7} Thus, one can obtain a thermal relaxation time based on the decay of the temperature at the laser spot. Certainly this time
constant can incorporate the influence of a realistic tissue surface condition (free convection or forced cooling). While $\tau$ in Eq. (1) or (2) has no such an advantage. Nowadays, Cryogen spray cooling\(^{13}\) has become more and more popular in a laser surgery procedure to minimize thermal damage.

The purpose of this study is twofold: (1) to investigate the influence of radiation scattering on the prediction of OPD and thermal relaxation time; and (2) to compare time constants predicted by different models under various conditions.

II. Mathematical Formulation

Consider a collimated laser pulse incidence upon a two-dimensional (2-D) biological tissue shown in Fig. 1. The local temperature response of the tissue within a short time period is formulated as

$$\rho C_P \frac{\partial T(x,y,t)}{\partial t} = -\nabla \cdot \vec{q}_{rad}(x,y,t),$$

where $\nabla \cdot \vec{q}_{rad}(x,y,t)$ is the divergence of radiation heat flux due to laser radiation absorption and can be calculated by

$$\nabla \cdot \vec{q}_{rad}(x,y,t) = \sigma_e (4\pi I_b - G),$$

where $I_b$ is the black body emissive intensity of the tissue which is negligible because the tissue can be treated as a cold medium as compared to the large flux of laser beam. The incident radiation, $G$, is a direction-integrated radiation intensity and can be obtained by the summation of angle-discretized radiation intensity.

To calculate the radiation intensity $I_l^i$ in a discrete ordinate, the time-dependent equation of radiation transfer (ERT) in discrete-ordinate format is introduced:

$$\frac{1}{c} \frac{\partial I_l^i}{\partial t} + \xi_l^i \frac{\partial I_l^i}{\partial \xi} + \eta_l^i \frac{\partial I_l^i}{\partial \eta} + \sigma_e I_l^i = \sigma_e S_l^i, \quad l = 1, 2, 3, ..., n$$

where $\xi_l^i$ and $\eta_l^i$ are the directional cosines, $\sigma_e$ is the extinction coefficient that is the sum of the absorption and scattering coefficients, and $S_l^i$ is the radiative source term from the laser radiation that can be expressed as

$$S_l^i = (1 - \omega) I_b + \frac{\omega}{4\pi} \sum_{i=1}^n w^i \Phi i^i I_l^i + S_c^i, \quad l = 1, 2, 3, ..., n$$

Here, the scattering albedo is $\omega = \sigma_s / \sigma_e$ and the scattering phase function is $\Phi(s^i \rightarrow s^f)$. A quadrature set of $n$ discrete ordinates with the appropriate angular weight $w^i$ ($i = 1, 2, ..., n$) is used. The laser source in Eq. (6) is the driving force of the transient radiation heat transport and can be expressed as

$$S_c^i = \frac{\omega}{4\pi} I_c (\xi_c \xi_l^i + \eta_c \eta_l^i),$$

where the unit vector of $(\xi_c, \eta_c)$ represents the collimated laser incident direction. The incident laser sheet with a Gaussian profile can be expressed by

$$I_c(x,y) = I_{c0} \exp[-4 \ln 2 \times [(t - x / c) / t_p - 1.5]^2] \times \exp[-2(2 y / D - 1)^2] \times \exp(-\sigma_c x),$$

$$0 \leq t \leq 3t_p.$$
In which \( I_{e0} \) is the amplitude of the laser radiation intensity and can be adjusted to let the tissue reach a pre-assumed maximum temperature \( T_{\text{ref}} \) at the laser spot center. \( T_{\text{ref}} \) can be expressed by

\[
T_{\text{ref}} = T_i + \int_0^{3t_p} N \sigma_e I_e(x = 0, y = D/2, t) dt / \rho C_p
\]

where \( T_i \) is the initial tissue base temperature, and \( N \) is the number of total incident laser pulses.

The temperature is then nondimensionalized as

\[
\theta = \frac{T - T_i}{T_{\text{ref}} - T_i}.
\]

In the present study, we consider pulsed laser irradiation in a short time period, say 1 ms. Within this time period, there are many short pulses. After that, the laser is turned off and the medium experiences merely heat diffusion from the irradiation region to the surrounding region without external heat generation. This process is governed by the heat conduction equation as follows:

\[
\rho C_p \frac{\partial \theta(x, y, t)}{\partial t} = k \left( \frac{\partial^2 \theta}{\partial x^2} + \frac{\partial^2 \theta}{\partial y^2} \right),
\]

where \( k \) is the thermal conductivity.

For the calculation of heat conduction, the non-dimensional temperature is initially zero except in the path of the collimated laser incidence. Equation (1), coupled with the radiation heat transfer modeling is employed for finding the initial temperature distribution along the laser path. The boundary conductons are specified below.

\[
\theta(x, y, t) = 0, \text{ for } y = 0, y = W, \text{ or } x = L
\]

\[
-k \frac{\partial T}{\partial x} = h (T_w - T), \text{ for } x = 0
\]

For the analysis of radiation heat transfer, reflection and refraction governed by Snell’s law and Fresnel equation, respectively, are considered at the tissue-air interface. At the rest boundaries, diffuse reflection is considered. For details, please refer to our recent publications.\(^{9,11}\)

The following lists several assumptions we adopted when we set up the present model:

1. Thermal radiation emission from the tissue is neglected inside the tissue and on tissue surface.
2. The tissue optical and thermal properties are thermally stable and constant during the heat transfer processes.
3. Thermal evaporation and phase change of tissue are not considered.
4. The heating of tissue by short-pulsed irradiation is treated by local volumetric method assuming thermal equilibrium. The abrupt electron temperature rise during an ultrashort time period is neglected.

In the present study, we consider a 2-D tissue model in Cartesian coordinates system. Thus, \( \tau_x \) and \( \tau_y \), in Eq. (2) are replaced by \( \tau_{1x} \) and \( \tau_{1y} \), respectively. \( \tau_{1x} \) is determined by the optical penetration depth; while \( \tau_{1y} \) is dependent on the beam width. Here we use two different thermal relaxation time definitions. The first one is an inversely averaged time constant defined as

\[
\frac{2}{\tau_1} = \frac{1}{\tau_{1x}} + \frac{1}{\tau_{1y}}
\]

The second one is the time required for the peak temperature rise \( \theta_{\text{peak}} \) (=1) at the laser spot center to decrease to \( e^{-1} \). We denote this thermal relaxation time as \( \tau_2 \) and evaluate \( \tau_2 \) from time-dependent simulation of
combined laser radiation and heat conduction. $\tau_2$ has a better physical interpretation than $\tau_1$. Further, $\tau_2$ is influenced by the convective boundary condition at tissue-air interface.

To solve the time-dependent equation of the radiation transfer, the transient discrete ordinates method (TDOM) based on $S_{10}$ scheme is employed. The tissue geometry is divided by a uniform grid system of $200 \times 200$. The solid angle is divided by a quadrature set of $n = 120$ discrete ordinates. Details of the numerical schemes have been intensively described and evaluated in our recent publications, thus, they are not repeated here.

The fully explicit scheme is adopted to solve the heat conduction equation. The grid size is chosen the same as the radiation transfer problem and the time step is selected as 0.001 sec. The calculation was stable. The simulation was examined by analytical heat conduction solutions and the results were satisfactory.

III. Results and Discussion

For simplicity, we consider a square tissue with $L = W = 13.416$ mm. The optical properties of the considered tissues are listed in Table 1. The thermal properties are assumed as the tissue is composed with 70% water, $\alpha = 0.142$ mm$^2$/s, and $\rho C_p = 3.52 \times 10^6$ J/(m$^3$·K); if they are not otherwise specified. In the present study the reference temperature is $T_{ref} = 65$ °C, and the base temperature is $T_{base} = T_i = 37$ °C. The ambient temperature is $T_{\infty} = 23$°C, and $h$ is the heat transfer coefficient. If not specified, the convective heat transfer coefficient is selected as $h = 20$ W/m$^2$K.

In Fig. 2, the fluence variations along the optical axis are shown at 1 ms time instant for different optical properties of tissue. For the fully absorbing media ($\sigma_a = 0.1$ mm$^{-1}$ or $\sigma_a = 1.0$ mm$^{-1}$), $\sigma_s' = 0$ and the numerical results are compared with the analytical solutions. An excellent agreement was found. Usually scattering in tissue is very strong, particularly in the near-infrared wavelength. We consider the model tissue with two different scattering coefficients (i.e., $\sigma_s' = 1.3$ mm$^{-1}$ or $\sigma_s' = 2.6$ mm$^{-1}$). It is seen that the fluence drops faster with increasing scattering coefficient. Since OPD is the length for a fluence drop to a factor of $e^{-1}$, the OPD can be measured from Fig. 2. With the presence of scattering, OPD decreases. In particular, the scattering effect is substantial for small absorption tissue. For example, the OPD is 10 mm for the case of $\sigma_a = 0.1$ mm$^{-1}$ when only absorption is considered; while it is less than 2 mm when the scattering effect is added. Thus, both absorption and scattering effects must be incorporated in the calculation of OPD.
The optical penetration depth for absorbing and scattering tissue may be approximated as

\[ \text{OPD} = 1 \left( \frac{1}{\sigma_a + \sigma_s'} \right). \]  

(15)

In Fig. 3, the OPDs estimated from this approximation are compared with the measurements through complete numerical modeling. It is seen that Eq. (15) is a very good approximation when the scattering coefficient is weaker than the absorption coefficient. On the other side, when the absorption coefficient is small and the absorption is much weaker than the scattering, Eq. (15) should not be adopted.

In Fig. 4, the actual fluence variation in the y-axis on the tissue-air interface is investigated. We compare the original incident beam variance with those at 1 ms with different scattering coefficients. The absorption coefficient is fixed at \( \sigma_a = 0.1 \text{mm}^{-1} \). At 1 ms, radiation equilibrium has been achieved. It is seen that the scattering influences the fluence profile in the y-axis as well. It slows down the fluence variation in the y-direction and results in an increase in the fluence width. However, this influence is not as strong as that in the OPD. Thus, one may still use the original beam radius to represent the characteristic length in the radial direction.

In the followings we define the beam half width at \( e^{-1} \) (\( W_L \) in Fig. 4) for estimating \( \tau_{1y} \) and use the numerically calculated OPD for analyzing \( \tau_{1x} \). Figure 5 shows the thermal relaxation times under various optical properties. Clearly \( \tau_{1x} \) is influenced by the radiation heat transfer, while effect of radiation transfer on \( \tau_{1y} \) is only obvious for very small absorption with strong scattering. With increasing absorption, \( \tau_{1x} \) decreases exponentially. With large absorption coefficient, the variation of thermal relaxation time against the scattering is small.

Figure 6 shows the temporal temperature profiles at several locations for a human dermis tissue. The corresponding optical properties\(^\text{15}\) are \( \sigma_a = 0.27 \text{mm}^{-1} \) and \( \sigma_s' = 3.55 \text{mm}^{-1} \). It is seen that the temperature drops rapidly at the center of laser spot (\( x = 0, y = 0.5W \)). The dropping speed decreases with increasing distance. The solid black marks represent where the temperature in a heated location of the tissue decreases to \( e^{-1} \) of its peak value. The times in the marks are then the thermal relaxation times at the selected locations based on the physical interpretation. It is seen that thermal relaxation time at the laser spot center is the smallest one; and this time is selected as \( \tau_2 \) in the present study. The peak temperature at the laser spot center is also the maximum temperature of the tissue resulted from the irradiation.
As afore-mentioned, the convective heat transfer condition at the tissue-air interface will affect the value of $\tau_2$. To investigate this effect, several values of $h$ are selected and the temporal temperature profiles at the laser spot center are compared in Fig. 7. Two types of tissue are chosen: dermis tissue and heart tissue (endocardium). We assumed same thermal properties for the both tissues. Obviously, the thermal relaxation time with higher $h$ shows smaller value because part of the heat is released by the convection. Larger convective heat transfer rate provides more rapid cooling performance. The effect of surface convection on the heart tissue is more pronounced than on the dermis tissue. The radiation coefficients of the dermis tissue are larger than those of the heart tissue; thus, radiation effect predominates in the dermis tissue.

The thermal relaxation times in a brain tissue (gray matter) with varying beam width are compared in Fig. 8. It is observed that with increasing beam width the thermal relaxation time $\tau_{1y}$ increases quickly, but the change in $\tau_{1x}$ is trivial. The predicted $\tau_1$ and $\tau_2$ are between the values of $\tau_{1x}$ and $\tau_{1y}$. Most importantly, the values of $\tau_1$ and $\tau_2$ match each other very well when the beam width is less than 6 mm. Since $\tau_0$ is half of $\tau_1$, the difference between $\tau_0$ and $\tau_2$ will be large. The use of $\tau_0$ as the thermal relaxation time as previous researchers suggested is then not supported by the results of $\tau_2$.

Table 2 lists the predicted thermal relaxation times based on the four definitions for several biological tissues.

### IV. Conclusion

The transient temperature response upon short-pulsed laser irradiation is numerically investigated. The emphasis was placed on the comparisons of thermal relaxation times based on different definitions. The scattering effect should not be overlooked in the determination of the optical penetration depth based on the simulation evaluations. A new expression of $\tau_1$ is introduced and found to closely match with the prediction of $\tau_2$ which is based on the peak temperature decaying with moderate heat convection conditions. Thus, $\tau_1$ is recommended for use as the thermal relaxation time to be determined by the optical and thermal properties of tissue, coupled with the laser input parameters. $\tau_2$ has better physical meaning in representing the thermal relaxation time and can incorporate the realistic surface cooling condition. However, the determination of $\tau_2$ requires for a complete modeling or experimental measurement.
Figure 6. Transient temperature response at several selected locations and measurement of $\tau_2$.

Figure 7. Influence of surface convection on transient temperature response and $\tau_2$. 
Table 1. Optical and thermal properties of several selected human tissues.

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Wavelength (nm)</th>
<th>Absorption (mm⁻¹)</th>
<th>Reduced Scattering (mm⁻¹)</th>
<th>Diffusivity α (mm²/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human dermis</td>
<td>633</td>
<td>0.27</td>
<td>3.55</td>
<td>0.142</td>
</tr>
<tr>
<td>Caucasian</td>
<td>632.8</td>
<td>0.052</td>
<td>4.1</td>
<td>0.135</td>
</tr>
<tr>
<td>Human aorta</td>
<td>1060</td>
<td>0.007</td>
<td>0.367</td>
<td>0.14</td>
</tr>
<tr>
<td>Human heart</td>
<td>630</td>
<td>0.32</td>
<td>2.07</td>
<td>0.133</td>
</tr>
<tr>
<td>Human liver</td>
<td>635</td>
<td>0.035</td>
<td>12.214</td>
<td>0.142</td>
</tr>
<tr>
<td>Human brain</td>
<td>810</td>
<td>0.002</td>
<td>0.7</td>
<td>0.142</td>
</tr>
</tbody>
</table>

Table 2. The predicted thermal relaxation times for the several human tissues.

<table>
<thead>
<tr>
<th>Beam width D (mm)</th>
<th>1.0</th>
<th>2.5</th>
<th>5.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thermal Relaxation Time (sec)</td>
<td>$\tau_{1x}$</td>
<td>$\tau_{1y}$</td>
<td>$\tau_1$</td>
</tr>
<tr>
<td>Dermis</td>
<td>0.59</td>
<td>0.66</td>
<td>0.62</td>
</tr>
<tr>
<td>Aorta</td>
<td>1.15</td>
<td>0.92</td>
<td>1.02</td>
</tr>
<tr>
<td>Endocardium</td>
<td>22.37</td>
<td>0.64</td>
<td>1.24</td>
</tr>
<tr>
<td>Liver</td>
<td>0.89</td>
<td>0.67</td>
<td>0.79</td>
</tr>
<tr>
<td>Gray matter</td>
<td>2.95</td>
<td>0.55</td>
<td>0.92</td>
</tr>
<tr>
<td>Uterus</td>
<td>0.51</td>
<td>0.69</td>
<td>0.59</td>
</tr>
<tr>
<td>Breast</td>
<td>9.75</td>
<td>0.82</td>
<td>1.50</td>
</tr>
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Figure 8. Comparison of thermal relaxation times predicted by different models.
References


