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The Effective Factors on Inconsistency of Theoretical Studies and Clinical Reports in Thermal Reactions

Sasan Soudi[1, *], Bahareh Khaksar Jalali[2], Sharifeh Shahi[2]

[1]Department of Medical Engineering, Faculty of Health and Medical Engineering Tehran Medical,Sciences Islamic Azad University, Tehran, Iran, S.Soudi@iautmu.ac.ir
[2]Laser and Biophotonics in Biotechnologies Research Center, Isfahan (Khorasgan) branch, Islamic Azad University, Isfahan, Iran

Abstract

In this paper, considering the damage equation, tissue heat transfer equations and also the Thermal damage time (TDT) of tissue at a specific temperature, the concept of selective photothermolysis has been studied in an organized and comprehensive way much better, more effective and closer clinical results to what is actually happening in reality. Because in laser-tissue thermal interactions therapies, the thermal relaxation time (TRT) of tissue and the choice of laser pulse width related to that are important parameters. On the other hand, the effect of the damage function and its related parameters on laser-tissue thermal interactions cannot be ignored, because they interfere with the analysis of the effectiveness of laser-tissue thermal reactions. Therefore, while examining the theory of topics related to selective photothermolysis, and clinical conditions affecting laser-tissue thermal interactions that lead to the phenomenon of selective photothermolysis have been investigated.

Keywords: Heat transfer equation, Selective Photothermolysis, Thermal damage time (TDT), Thermal relaxation time (TRT)
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1. Introduction

Since the advent of lasers in the medical treatments field and study of its effect on laser-tissue interaction, the concept of selective photothermolysis has particularly become important [1], [2]. One of the important parameters of selective photothermolysis, thermal relaxation time (TRT) is defined based on the appropriate and acceptable laser pulse width in the treatment and protection of healthy tissue around the target [1], [2], [3]. Equation (1) shows the numerical value of TRT in which d (mm) is the target diameter, α (mm^2/s) the thermal diffusion coefficient, k the geometric factor, and also the pulse length is expressed based on the target diameter [1] , [4], [5] (for example, k is 16 for the cylinders):

$$TRT = d^2/k\alpha \tag{1}$$

Numerous studies and experiments, including Altshuler et al., Have shown that it is incorrect to consider the pulse width based solely on the target diameter. Referring to blood vessels and hair follicles, they showed that even by selecting pulses several times larger than the target TRT, destruction is possible, so TRT cannot be the right criterion for treatment design [6]. This paradox is possible based on the equations of heat transfer to the tissue in the form of Equation (2), in which $\mathcal{T}_q$ represents the time delay in heat flux and $\mathcal{T}_T$ represents the time delay in creating a temperature difference in the tissue [4], [5], [6].

$$q(x,t+\mathcal{T}_q) = -k\nabla T(x,t+\mathcal{T}_T) \tag{2}$$

The more general state of Equation (2), which is the result of the quadratic Taylor expansion, is given in Equation (3).

$$\left(1+\mathcal{T}_q\frac{\partial}{\partial t}+\frac{\mathcal{T}_q^{\,2}}{2}\frac{\partial^2}{\partial t^2}\right)q = -\left(1+\mathcal{T}_T\frac{\partial}{\partial t}+\frac{\mathcal{T}_T^{\,2}}{2}\frac{\partial^2}{\partial t^2}\right)k\nabla T \tag{3}$$

On the other hand, the conservation of ***energy*** equation of regional equilibrium in tissue is expressed as Equation (4), in which T_b,

c_b, ρ_b, ω_b are temperature, specific heat capacity, density and rate of blood flow distribution, respectively. $q_m$is internal metabolic heat is produced and q_r external heat of source [4], [6].

$$q_r \rho c_{ᵬt}^{ᵬT} = -\nabla . q + \omega_b \rho_b c_b (T_b - T) + q_m \quad (4)$$

By using two equations (3) and (4) for the completed quadratic equation of heat transfer, Equation (5) is obtained. This equation will be simplified according to different conditions and tissues. For example, if the time delay is be short, quadratic or even first-order sentences $\mathcal{T}_q$ and $\mathcal{T}_T$ can be omitted. On the other hand, if the time delay is be large, fixed or first-degree sentences can also be ignored. For example, in homogeneous materials, where the time delay is very short (from in the order of 10^{-4}-10^{-8}), Taylor expansion sentences are omitted and Equation (1) will be obtained [4], [5], [6].

$$\left(1 + \mathcal{T}_T \frac{ᵬ}{ᵬt} + \frac{\mathcal{T}_T^2}{2} \frac{ᵬ^2}{ᵬt^2}\right) k \nabla^2 T = \left(1 + \mathcal{T}_q \frac{ᵬ}{ᵬt} + \frac{\mathcal{T}_q^2}{2} \frac{ᵬ^2}{ᵬt^2}\right) [\rho c_{ᵬt}^{ᵬT} - \omega_b \rho_b c_b (T_b - T) - q_m - q_r] \quad (5)$$

2. Discussion

In cases where the spot size of laser beam is larger than the thickness of irradiated tissue, a one-dimensional model of Equation (5) can be used, so Equation (6) is obtained [2], [5], [7]:

$$\left(1 + \mathcal{T}_T \frac{ᵬ}{ᵬt} + \frac{\mathcal{T}_T^2}{2} \frac{ᵬ^2}{ᵬt^2}\right) k \frac{ᵬ^2}{ᵬ\chi^2} T = \left(1 + \mathcal{T}_q \frac{ᵬ}{ᵬt} + \frac{\mathcal{T}_q^2}{2} \frac{ᵬ^2}{ᵬt^2}\right) [\rho c_{ᵬt}^{ᵬT} - \omega_b \rho_b c_b (T_b - T) - q_m - q_r] \quad (6)$$

Equation (6), the laser heat source is defined by q_r as bellow and depends on the laser radiation $\Phi(x)$ [2], [5], [8]:

$$q_r = \mu_a \Phi(x) \quad (7)$$

On the other hand, the thermal damage parameter Ω is defined as Equation (8), in which c_0 and c_d are the tissue protein concentration and the demolished protein concentration, respectively. Accordingly, when the demolished proteins reach 63%, the value of the damage parameter will be equal to 1, which means that the tissue is completely damaged [2], [5], [7]:

$$\Omega = ln(\frac{c_0}{c_0 - c_d}) \quad (8)$$

In addition, Ω can be expressed based on the damage function of Equation (9), in which A is the repetition factor and E is the activation energy [2], [5], [6], [8].

$$\Omega = A \int_{t_i}^{t_f} \exp(-\frac{E}{RT})\, dt \quad (9)$$

If T as tissue temperature is be a function of living tissue blood flow, the effect of propagation rate on tissue heat transfer needs more attention. In this case, the heat transfer equation through conduction can be shown as Equation (10) from Equation (2) [5], [6]:

$$-\nabla q = k \nabla^2 T \quad (10)$$

Since the heat exchange of blood and convection flow in Equation (5) are expressed by the expression $\omega_b \rho_b c_b (T_b - T)$, when the tissue temperature is higher than the arterial temperature, the blood diffusion will have a cooling function [5], [6], [9], [10]. Thus, at first (the first seconds) the heat energy carried by the blood flow is small. Therefore, surface temperatures for different values of ω_b are no obvious difference, but over time, the difference in cooling performance of blood flow increases. The heat energy carried by blood is proportional to the rate of blood flow so as a result the temperature decreases with the rate of blood flow [10], [11]. Therefore, the temperatures obtained from each of the linear and nonlinear equations are almost similar, but the occurrence of slight differences will cause more serious thermal damage [5], [7], [9]. This indicates that thermal damage in living tissue is very sensitive to temperature. Metabolic heat produced and blood flow are important parameters in living tissue. Blood flow can have a significant effect on increasing temperature [9], [10]. Experiments have shown that the damage parameter of the nonlinear heat equation is larger than the other one. The reason is the effects of the second order of delay times $(\mathcal{T}_T{}^2 . \mathcal{T}_q{}^2)$ on increasing tissue temperature [9], [10]. The values of physical-thermal parameters of tissue and blood that are mentioned in the previous equations are given in Table (1).

Table.1.
Values of physical-thermal parameters of tissue and blood [5]

physical-thermal parameters of tissue	***physical-thermal parameters of blood***
K = 0.628 w/m. K	ρ_b= 1.06 × 10^3 kg/m^3
ρ = 1000 kg/m^3	c_b = 3860 J/ kg.K
c = 4187 J/ (kg.K)	ω_b= 1.87 × 10^{-3} m^3/ m^3
	T_b = 37 ^{o}c

In solving heat transfer equations, all the parameters that are effective during this process must be considered simultaneously and in an organized manner.

The heterogeneous structure of biological tissue causes the resulting energy flux to be asynchronous with its generating factor (temperature changes); this delay time must be considered in solving and interpreting the equations [5], [12].

The resultant of the input and output energies leads to an increase in temperature at the target point. These energies depend on several factors such as tissue blood flow, tissue type, heat source and its physical parameters [7], [8].

Conduction, convection and radiation are all kinds of heat transfer methods that depend on the type, location and size of the target and after identifying the effective energy transfer method, all analyzes should be expressed based on that [5], [13], [14], [15].

In addition to heat equations, the injury function also plays an important role in treatment process. Therefore, the temporal dependence of the parameters introduced in Equation (9) cannot be ignored. In various articles, the dependence of the temperature required to cause irreversible damage on the residence time of the target tissue in the presence of radiation has been investigated, but temperature is not the only cause of irreversible damage to the tissue [5], [13], [14], [16]. For example, it takes one second to destroy the skin at $60°C$, while the same amount of damage occurs to the skin tissue at $70°C$ in 33 *(ms)* [1], [17]. Therefore, in laboratory and clinical studies, due to the inability of TRT to study and analyze tissue thermal processes, a parameter called thermal damage time (TDT) is considered. That taking the time required to change the nature of the protein at a certain temperature and eventually causing damage to the target tissue or protecting the adjacent tissue from damage, the defect caused by TRT is eliminated. Of course, this does not only mean deleting TRT, but also to correcting and supplementing it.

3. Conclusion

Many articles have been published based on the definition of TDT and based on this, and different treatment protocols have been proposed. Murphy *et all.*, expressed the pulse width based on the concept of TDT, considering its damage function and its unrelatedness to TRT. Also, they pay to express the positive role of pulse width in selecting pulses longer than what TRT introduces [1]. Based on all the previous work done and what has been done in the present article, can be briefly mentioned about the two concepts of TRT and TDT.

The concept of TRT states that if pulses longer than TRT are used, the target will not be damaged, and if the pulse length is shorter than TRT, the energy will be trapped in the target and the tissue will be damaged. This definition is based on the concept of selective photothermolysis and is as relevant as the target size [15].

Thermal damage time is the time when target tissue proteins are irreversibly damaged [16], which is related to the type of tissue and is defined based on Arrhenius variables [12]. Because in the treatment process, not only the destruction of the target tissue but also the protection of adjacent tissues is important. Protection of adjacent tissues almost by TRT and destruction of target tissue by TDT is done. Recent articles have shown that TDT can be much larger than TRT, meaning that it is not necessary to use the minimum pulse width defined by TRT for damage to target tissue. Numerous experiments have shown the effect of pulse width much larger than TRT. Especially in the treatment of small blood vessels where a short pulse width can cause injuries such as purpura. In fact, using a longer pulse will provide more energy flux to damage the target tissue by extra protecting the surrounding tissue.

In none of the articles, all the variables involved in treatment have been examined together, So far. Longer pulses are useful because they allow enough time to damage the protein at a lower temperature. That is, by using long pulses and of course at the right temperature, enough time can be given to the target tissue for the degradation process, and in addition, this long pulse can further protect the adjacent tissues against degradation. But the other point is that the adjacent tissues will also experience longer time at this temperature. In this case, how to increase the flux resulting from increasing the length of the radiation pulse, which can control the thermal effects due to long time in the adjacent tissue, is a matter that has not been studied.

It is clear that just as long pulses give the target tissue more opportunity to stay at the appropriate temperature for destruction, this time can also damage adjacent tissue. So, it is necessary to consider TDT for target tissue and TRT for adjacent tissue at the same time. In addition, the role of heat transfer methods and the effect of each of them in different tissues should be given more attention. For example, the effect of heat radiation on the skin is greater than blood and deep tissues. Table 2 summarizes the role of each heat transfer method in different tissues [1]. In general, a comprehensive theory that can fully demonstrate the role of all variables involved in the treatment process should be based on the thermal equation of the tissue, the physical and optical properties of the surrounding tissues, the Arrhenius constants, and the shape and size of the target tissue.

Table.2.

The importance of heat transfer modes in living systems [5], [14].

Conduction	Convection	Radiation	Tissue
main	-	-	Bone
mean	main	-	Blood vessels
-	main	main	Skin

Based on what has been shown in detail, the role of long pulses in creating the necessary and sufficient time to destroy the target cannot be considered, but ignored the possible destruction caused by longer time in the surrounding tissue. In some cases, it may be necessary to even investigate the role of radiation in stimulating Vasodilation centers of blood vessels and increasing blood flow (change ω_b due to heat intake) [5], [14]. It is also necessary to consider the effects of the qualitative heat transfer modes mentioned in Table (2) with precise quantities in the heat transfer equations and the damage function. There are also so many variables in the body that a specific numerical value cannot be considered. Even disease conditions, stress, and environmental factors should be considered in the precise determination of variables. Therefore, by stating all these effective but uncertain parameters, in the treatment process, the presented protocols are also associated with approximation, and here the physician's skill (knowledge and experience) and comprehensive viewpoints of the variables will play an important role to achieve an impressive result of treatment.

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