The impact of thermal wave characteristics on thermal dose distribution during thermal therapy: A numerical study

Tzu-Ching Shih

Department of Medical Radiology Technology, China Medical University, Taichung, Taiwan

Hong-Sen Kou

Department of Mechanical Engineering, Tatung University, Taipei, Taiwan

Chihng-Tsung Liauh

Department of Mechanical Engineering, Kun Shan University of Technology, Tainan, Taiwan

Win-Li Lin^{a)}

Institute of Biomedical Engineering, National Taiwan University, Taipei, Taiwan

and Medical Engineering Research Division, National Health Research Institutes, Miaoli, Taiwan

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The aim of this study was to investigate the effects of the propagation speed of a thermal wave in terms of the thermal relaxation time on the temperature/thermal dose distributions in living tissue during thermal therapies. The temperature field in tissue was solved by the finite difference method, and the thermal dose was calculated from the formulation proposed by Sapareto and Dewey [Int. J. Radiat. Oncol. Biol. Phys. **10**, 787–800 (1984)]. Under the same total deposited energy, for a rapid heating process the time lagging behavior of the peak temperature became pronounced and the level of the peak temperature was decreased with increasing the thermal relaxation time. When the heating duration was longer than the thermal relaxation time of tissues, there was no significant difference between the thermal dose distributions with/without considering the effect of the thermal relaxation time. In other words, when the heating duration is comparable to or shorter than the thermal relaxation time of tissue, the results of the wave bioheat transfer equation (WBHTE) are fully different from that of the Pennes' bioheat transfer equation (PBHTE). Besides, for a rapid heating process the dimension of thermal lesion was still significantly affected by perfusion, because this is what is predicted by the WBHTE but not by the PBHTE, i.e., the wave feature of the temperature field cannot fully be predicted by the PBHTE. © 2005 American Association of Physicists in Medicine. [DOI: 10.1118/1.2008507]

Key words: thermal relaxation time, wave bioheat transfer equation, thermal dose

I. INTRODUCTION

The Pennes' bioheat transfer equation (PBHTE) (1948),¹ as shown in Eq. (1), is widely used to solve the temperature field in living tissue for a given absorbed power deposition during thermal therapies

$$\rho_t c_t \frac{\partial T}{\partial t} = \nabla \cdot (k \nabla T) + W_b c_b (T_a - T) + Q, \quad (1)$$

where ρ_t is the tissue density, c_t is the specific heat of tissue, k is the thermal conductivity of tissue, W_b is the blood perfusion rate, c_b is the specific heat of blood, T_a is the arterial temperature, T is the tissue temperature, and Q is the absorbed power density. The heat conduction term of the Pennes' model is based on the Fourier's theory, $q = -k \nabla T$, that implies the immediate energy diffusion at infinite propagation speed in the medium. For most heating processes, this assumption is suitable. In some situations such as very low temperature, very high heat flux or very short heating duration, however, the Fourier's heat conduction theory breaks down.^{2–12} This is because the wave nature of heating processes becomes pronounced in these situations. Using the method of characteristics, Wiggert analyzed the case of a

step change in the heat flux at the boundary surface of a semi-infinite medium to illustrate the effect of finite heat propagation velocity.⁹ Moreover, Vick and Özisik investigated the wave characteristics of heat propagation in a semi-infinite medium containing volumetric energy sources.¹⁰ Based on their observation, it was found that thermal behavior in some situations cannot be predicted by the classical linear or nonlinear diffusion theory because it allows for the immediate diffusion of heat as soon as the energy is released, without considering the effect due to a relaxation time or start up time. In addition, the experimental results of Mitra *et al.* indicate that the wave nature of heat transfer is slow enough in processed meat (Bologna).¹¹

Considering the finite thermal propagation speed, Cattaneo² and Vernotte³ formulated a modified unsteady heat conduction equation as follows:

$$q(\vec{r}, t) + \tau \frac{\partial q(\vec{r}, t)}{\partial t} = -k \nabla T(\vec{r}, t), \quad (2)$$

where q is the heat flux, $\vec{r}$ is the position vector, and τ is the thermal relaxation time. Physically, the thermal relaxation time τ represents the time delay between the heat flux vector

TABLE I. Parameters used in simulation.

Symbol	Definition	Value	Units
ρ_t, ρ_b	Density of tissue and blood	1050	kg m^{-3}
c_t, c_b	Specific heat of tissue and blood	3770 ^a	$\text{J kg}^{-1} \text{ } ^\circ\text{C}^{-1}$
k_t, k_b	Thermal conductivity of tissue and blood	0.5 ^a	$\text{W m}^{-1} \text{ } ^\circ\text{C}^{-1}$
τ	Thermal relaxation time	0, 2, ^b 8, 16 ^c	s
W_b	Blood perfusion rate	0, ^{d,e} 5, ^e 10, ^e 20 ^f	$\text{kg m}^{-3} \text{ s}^{-1}$
T_a	Arterial temperature	37	$^\circ\text{C}$
Q	Absorbed power density	Variable	W cm^{-3}

^aSee Ref. 23.^bSee Ref. 14.^cSee Ref. 11.^dIt is common in cryogenic surgery; see Ref. 19.^eThese values are commonly found in heart tumors; see Ref. 32.^fSee Ref. 28.

and the temperature gradient. That is, the heat flow does not start instantaneously, but grows gradually with a thermal relaxation time τ , after applying a temperature gradient. When τ is equal to zero, Eq. (2) becomes the Fourier heat conduction equation. The order of the thermal relaxation time is about 10^{-8} – 10^{-12} s for the homogeneous substance.^{4,6,8,13} These very short relaxation times would be correct for objects of molecular dimensions. For typical biological molecules, the energy fluctuation rate is of the order of 10^{11} per second.¹³ The thermal relaxation time is proportional to the radius squared of the homogeneous substance volume. The relationship between the thermal relaxation time and the radius has been established for biological systems excited by electric fields.¹³ Most biological materials that contain cells, superstructures, liquids, and solid tissue are nonhomogeneous, so that their thermal relaxation times are long. The finite propagation speed of the thermal wave is equal to $\sqrt{k_t/\rho_t c_t \tau}$ where k_t is the thermal conductivity of tissue, ρ_t is the tissue density, c_t is the specific heat of tissue, and τ is the thermal relaxation time.^{11,14} Furthermore, Mitra *et al.* observed experimentally that τ in processed meat (Bologna) was found to be approximately 16 s.¹¹ While τ equals 16 s and the values of tissue properties are chosen as in Table I, the finite propagation speed of thermal wave in processed meat is about $0.088\,85\text{ mm s}^{-1}$. Moreover, Kaminski determined experimentally that the τ values for nonhomogeneous inner structure materials, ranged from 10 to 50 s.¹² By simulating the nonhomogeneous biological material as a porous medium under the same boundary conditions used in one of the Mitra *et al.*'s experiments,¹¹ Xu and Liu found that the wave-like heat transfer conduction in the bologna meat can be caused by the propagation of water in the porous medium due to thermal expansions and pressure gradients applied to the meat during measurements.¹⁵ They explained that the mechanism of the observed phenomena may be attributed to the thermal nonequilibrium between solid and liquid in the biological material rather than the pure conduction. Xu and Liu also concluded that the living tissue possesses the characteristics of the multiphase porous medium, which may demonstrate some wave nature in its temperature response to an instantaneous heating under certain conditions.¹⁵ How-

ever, Tilahun *et al.*¹⁶ and Herwig and Beckert¹⁷ questioned for the experimental results of Mitra *et al.*¹¹ and Kaminski.¹² They failed to reproduce the experimental results of Mitra *et al.* and Kaminski, and further concluded that the thermal lag effect can be explained by the Fourier heat conduction rather than the wave behavior. Furthermore, Chato and Lee suggested heat transfer in living tissue should modify the standard heat conduction equation (PBHTE) into a wave equation by the inclusion of a second order time derivative of temperature.¹⁸ This model indicates that the thermal energy (i.e., temperature disturbance) propagates much slower in animal tissues than in “engineering” materials and it also allows temperature oscillations. By using the dual reciprocity boundary element method, Lu *et al.* reported that some thermal wave effects of changing power on bioheat transfer in biological tissues cannot be explained by the PBHTE.¹⁹

From the therapeutic viewpoint, the high-intensity short-duration heating scheme can efficiently produce an appropriate thermal dose distribution during thermal therapies.^{20,21} In addition, reducing the overall treatment time is important for ultrasound thermal therapy, especially when the treatment target volume is large.^{22,23} These mean that a rapid heating scheme with a good strategy is essential for tumor thermal therapy in the future. However, the wave nature of heat transfer in living tissue may play an important role during rapid heating, such as thermal ablation/thermal surgery when using high-intensity focused ultrasound or radiofrequency ablation. Therefore, in this study a wave bioheat transfer equation (WBHTE) is explored to investigate the relationship between the thermal relaxation time and the thermal lesion during thermal therapies.

II. METHODS

A. Temperature field calculation

Considering the heat propagation problem with a finite speed, the WBHTE can be obtained by employing Eq. (2) into energy balance equation as follows:

FIG. 1. Schematic illustration of a heating cube studies for the temperature/equivalent thermal dose at 43 °C distributions.

$$\rho_t c_t \left(\frac{\partial T}{\partial t} + \tau \frac{\partial^2 T}{\partial t^2} \right) = \nabla \cdot (k \nabla T) + \tau \left(-W_b c_b \frac{\partial T}{\partial t} + \frac{\partial Q}{\partial t} \right) + W_b c_b (T_a - T) + Q. \quad (3)$$

By assuming all the thermal properties taken as constants, the finite difference method applied to the earlier partial differential equations and then derived the finite difference equation as

$$\begin{aligned} & \rho_t c_t \left[\frac{T_{i,j,k}^{n+1} - T_{i,j,k}^n}{\Delta t} + \tau \frac{T_{i,j,k}^{n+1} - 2T_{i,j,k}^n + T_{i,j,k}^{n-1}}{(\Delta t)^2} \right] \\ &= k \left[\frac{T_{i+1,j,k}^n - 2T_{i,j,k}^n + T_{i-1,j,k}^n}{(\Delta x)^2} + \frac{T_{i,j,k+1}^n - 2T_{i,j,k}^n + T_{i,j,k-1}^n}{(\Delta y)^2} \right. \\ & \quad \left. + \frac{T_{i,j,k+1}^n - 2T_{i,j,k}^n + T_{i,j,k-1}^n}{(\Delta z)^2} \right] \\ &+ \tau \left(-W_b c_b \frac{T_{i,j,k}^{n+1} - T_{i,j,k}^n}{\Delta t} + \frac{Q_{i,j,k}^{n+1} - Q_{i,j,k}^n}{\Delta t} \right) \\ &+ W_b c_b (T_a - T_{i,j,k}^n) + Q_{i,j,k}^n. \end{aligned} \quad (4)$$

Rearranging Eq. (4), the explicit finite difference equation gives

$$\begin{aligned} T_{i,j,k}^{n+1} = & C_1 T_{i,j,k}^n + C_2 T_{i+1,j,k}^n + C_3 T_{i-1,j,k}^n + C_4 T_{i,j+1,k}^n \\ & + C_5 T_{i,j-1,k}^n + C_6 T_{i,j,k+1}^n + C_7 T_{i,j,k-1}^n + C_8 T_{i,j,k}^{n-1} \\ & + C_9 Q_{i,j,k}^{n+1} + C_{10} Q_{i,j,k}^n + C_{11}, \end{aligned} \quad (5)$$

where

$$C_0 = \frac{\rho_t c_t}{\Delta t} + \frac{\tau \rho_t c_t}{(\Delta t)^2} + \frac{\tau W_b c_b}{\Delta t},$$

$$C_1 = \left[\frac{\rho_t c_t}{\Delta t} + \frac{2\tau \rho_t c_t}{(\Delta t)^2} - \frac{2k}{(\Delta x)^2} - \frac{2k}{(\Delta y)^2} - \frac{2k}{(\Delta z)^2} + \frac{\tau W_b c_b}{\Delta t} - W_b c_b \right] / C_0$$

$$C_2 = \frac{k}{(\Delta x)^2} / C_0, \quad C_3 = \frac{k}{(\Delta x)^2} / C_0,$$

$$C_4 = \frac{k}{(\Delta y)^2} / C_0, \quad C_5 = \frac{k}{(\Delta y)^2} / C_0,$$

$$C_6 = \frac{k}{(\Delta z)^2} / C_0, \quad C_7 = \frac{k}{(\Delta z)^2} / C_0,$$

$$C_8 = - \left[\frac{\tau \rho_t c_t}{(\Delta t)^2} \right] / C_0, \quad C_9 = \frac{\tau}{\Delta t} / C_0,$$

$$C_{10} = \left(1 - \frac{\tau}{\Delta t} \right) / C_0, \quad C_{11} = W_b c_b T_a / C_0.$$

The temperature distribution can be calculated by solving Eq. (5). If considering the change of tissue properties during

FIG. 2. The comparison of the temperature profiles at the center of the heating cube between the present numerical solution and the exact solution (See Ref. 27) for three heating schemes and with the blood perfusion rate $W_b = 0.5 \text{ kg m}^{-3} \text{ s}^{-1}$. The solid and dashed lines represented the exact solution (See Ref. 27) and the present numerical solution, respectively. (a) Case I; (b) case II; and (c) case III.

TABLE II. Values of the three different heating schemes.

	Case		
	I	II	III
Absorbed power density Q (W cm^{-3})	50	10	2
Heating duration t_h (s)	2	10	50
Total absorbed energy density (J cm^{-3})	100	100	100

heating treatment, the derivation of the WBHTE would become more complex and its solution would be difficult to obtain. In some studies on ultrasound surgery, they can successfully treat a $10 \times 10 \times 10 \text{ mm}^3$ tumor tissue.^{23–26} Hence, a heating cube was assumed to be of dimensions $10 \times 10 \times 10 \text{ mm}^3$ in the present study, as shown in Fig. 1. For numerical simulation, the initial temperatures of inside and outside of a heating cube and its surrounding tissue were set to 37°C . Note that the heating power was uniformly and completely absorbed in tissue in the simulation. For a simple case with τ equals zero, the quantitative comparison of temperature profiles at the center of a heating cube between the present numerical solution and the exact solution (Kou *et al.*) is shown in Fig. 2.²⁷ Even with the three different heating schemes, the temperature profile of the present numerical solution is agreeable with the exact solution (Kou *et al.*).²⁷ In addition, for high intensity applications (such as high-intensity focused ultrasound surgery), where the temperature of coagulation necrosis is typically 50 – 100°C ,^{28,29} herein the heating power schemes are chosen as in Table II.

B. Thermal dose calculation

The accumulated thermal dose induced by the thermal therapies depends upon not only the heating temperature level but also the heating duration. Sapareto and Dewey³⁰ determined that the clinical application of the thermal isoeffect dose concept in which different heating modalities for different times at different temperatures are converted into equivalent minutes at 43°C (EM_{43}). As suggested by Sapareto and Dewey,³⁰ the thermal dose formulation is given by

$$EM_{43} = \int R^{T-43} dt, \quad (6)$$

where $R=4$ for $37^\circ\text{C} < T < 43^\circ\text{C}$, $R=2$ for $T \geq 43^\circ\text{C}$, T is temperature, and t is time. Using magnetic resonance imaging thermometry and dosimetry, McDannold *et al.* observed that the minimal necrosis of muscle tissue occurred for 0.5–30 equivalent min at 43°C , the moderate damage occurred for 60–240 min, and the severe damage occurred for more than 240 min.³¹ In this study the threshold value for 100% necrosis is 240 min for thermal surgeries.

III. RESULTS AND DISCUSSION

Figures 3(a) and 3(b) show the transient profiles of temperature and thermal dose at the center point of a heated cube, respectively, with the three different thermal relaxation

FIG. 3. Effects of three different thermal relaxation times on the transient temperature and thermal dose profiles at the central point within a heated cube for $W_b = 0.5 \text{ kg m}^{-3} \text{ s}^{-1}$ and the heating case II in Table II. The solid lines represent the PBHTE (i.e., $\tau = 0$ s) and the dashed or dotted lines represent the WBHTE (i.e., $\tau = 8$ s and 16 s). (a) The temperature profiles; (b) their corresponding equivalent thermal dose at 43°C profiles.

times for heating case II. Without considering the effect of thermal relaxation (PBHTE), the temperature increased during heating before reaching peak temperature and decayed immediately after the power was turned off. Under the same total absorbed energy density 100 J cm^{-3} , the peak temperature predicted by the PBHTE (i.e., $\tau = 0$ s) was always higher than that by the WBHTE (i.e., $\tau > 0$ s). The temperatures from all cases converged around 45°C . When τ was equal to 0 s (i.e., the PBHTE), the temperature increased during the heating duration (0–10 s) and reached the peak around 62°C , and decayed after the power was turned off. Due to the finite speed of wave propagation, the peak temperature predicted by the WBHTE occurs with a time lag. This time lag causes a longer thermal dissipation (i.e., cooling by the heat conduction of tissue and by the blood perfusion) period of peak temperature, so that the peak temperature calculated by the PBHTE is higher than that by the WBHTE. Moreover, this implies that the temperature predicted by the PBHTE becomes higher and, hence, the accumulation of the thermal dose is also overestimated. The level of the accumulative thermal dose depends primarily on the peak temperature. As shown in Fig. 3(b), the thermal dose by the PBHTE ($\tau = 0$ s) was over two times higher than the one by the WBHTE ($\tau = 16$ s). When the heating duration is shorter than

FIG. 4. The development of the temperature distributions for heating case I, with the thermal relaxation time $\tau = 16$ s and the blood perfusion rate $W_b = 0.5 \text{ kg m}^{-3} \text{ s}^{-1}$. (a) $t = 3$ s; (b) $t = 12$ s; (c) peak temperature, 59.84°C , occurred at $t = 51$ s; (d) $t = 60$ s; (e) four rhythmic thermal wave with the equal amplitude at $t = 84$ s; (f) $t = 90$ s; (g) $t = 120$ s; and (h) $t = 180$ s.

the thermal relaxation time of tissue consequently, the thermal dose may be overestimated by using the PBHTE.

Figure 4 displays the development of temperature distributions on the X - Y plane for heating case I ($Q = 50 \text{ W cm}^{-3}$ and $t_h = 2$ s) and with the blood perfusion rate $W_b = 0.5 \text{ kg m}^{-3} \text{ s}^{-1}$. At the early stage, the temperature increased with time and then reached the peak temperature about 59.8°C at $t = 51$ s as shown in Fig. 4(c). As shown in Fig. 4(d), the temperature distribution decayed with time. At $t = 84$ s as shown in Fig. 4(e), the temperature distribution has four summits with the same amplitude. A similar thermal wave behavior can be seen in Lu *et al.*'s results,¹⁹ but they did not consider the heating source and the perfusion term. It is known that this wave feature of the temperature distribution cannot fully be predicted by the PBHTE. When the time was at $t = 90$ s, the amplitude of four summits of the temperature distribution became smaller, as shown in Fig. 4(f). Moreover, this wave phenomenon of the temperature distribution can be distinctly observed only when the thermal relaxation time is longer than the heating duration. With the

thermal dissipation affected by the blood perfusion and the tissue heat conduction, the temperature distribution finally became flat at $t = 180$ s as shown in Fig. 4(h).

Figure 5 shows the effects of thermal relaxation time and heating scheme on the final thermal dose distribution. For a rapid heating ($Q = 50 \text{ W cm}^{-3}$ and $t_h = 2$ s) and for the PBHTE ($\tau = 0$ s), $EM_{43} = 240$ min contour fully covered the desired heating region except the four corners. The region of thermal lesion of $\tau = 16$ s was 64% less than that of $\tau = 0$ s, as shown in Fig. 5(a). Furthermore, Fig. 5(b) shows that the thermal doses at the center point of heated cube go up to $EM_{43} \cong \sim 9 \times 10^4$ and $\sim 1 \times 10^4$ for the PBHTE ($\tau = 0$ s) and the WBHTE ($\tau = 16$ s), respectively. By using the heating scheme II ($Q = 10 \text{ W cm}^{-3}$ and $t_h = 10$ s), the result demonstrates that the thermal dose level predicted by the PBHTE ($\tau = 0$ s) was at least five times greater than that predicted by the WBHTE ($\tau = 16$ s) for a rapid heating, as shown in Fig. 5(d). Figure 5(f) illustrates that for a longer heating ($Q = 2 \text{ W cm}^{-3}$ and $t_h = 50$ s), there was a small difference of

FIG. 5. Effects of three heating schemes on the contours of $EM_{43} = 240$ min and their corresponding thermal dose profiles along the x axis at $t = 180$ s, with four thermal relaxation times, 0, 2, 8, and 16 s with the blood perfusion rate $W_b = 5 \text{ kg m}^{-3} \text{ s}^{-1}$. (a)–(b) for heating case I; (c)–(d) for heating case II; (e)–(f) for heating case III.

thermal dose level between the thermal relaxation times $\tau = 0$ s and $\tau = 16$ s. For a rapid heating, the dimension of thermal lesion will be reduced by the increasing thermal relaxation time. When the thermal relaxation time remains constant, the dimension of thermal lesion will be decreased with a longer heating scheme under the same total power deposited energy.

To investigate the influence of the blood perfusion rate and the thermal relaxation time on thermal dose contour ($EM_{43} = 240$ min), the three heating schemes were investigated. For a rapid heating ($Q = 50 \text{ W cm}^{-3}$ and $t_h = 2$ s) as shown in Fig. 6(a), there was almost no difference for the dimension of thermal lesion predicted by the PBHTE ($\tau = 0$ s) even when the blood perfusion rates ranged from 0 to $20 \text{ kg m}^{-3} \text{ s}^{-1}$. While $\tau = 16$ s and the higher blood per-

fusion rate $W_b = 20 \text{ kg m}^{-3} \text{ s}^{-1}$, it is clear that the thermal dose was only about 100 min so that the contour of 240 equivalent min at 43°C did not exist, as shown in Fig. 6(b). By using the heating scheme II ($Q = 10 \text{ W cm}^{-3}$ and $t_h = 10$ s) and considering the blood perfusion rate $W_b = 20 \text{ kg m}^{-3} \text{ s}^{-1}$, the thermal lesion contour was still created (the PBHTE) as shown in Fig. 6(c). In contrast, the thermal dose contour ($EM_{43} = 240$ min) did not exist in Fig. 6(d) because in this case the heating duration was shorter than the thermal relaxation time. As for a longer heating (i.e., the heating duration was longer than the thermal relaxation time), the thermal lesion dimensions predicted by the PBHTE and by the WBHTE were nearly the same, as shown in Figs. 6(e) and 6(f).

FIG. 6. Effects of blood perfusion rates on the contours of $EM_{43} = 240$ min at $t = 180$ s. (a) and (b) for heating case I with $\tau = 0$ s and $\tau = 16$ s, respectively; (c) and (d) for heating case II with $\tau = 0$ s and $\tau = 16$ s, respectively; (e) and (f) for heating case III with $\tau = 0$ s and $\tau = 16$ s, respectively.

Most of the studies of thermal therapies ignore the wave effect for the heating process. These studies employing the model of PBHTE belong to a good approach offering a reasonable prediction of temperature field only for a longer heating process. Since the edges of a heated cube have the higher temperature gradient to diffuse the delivered energy, they become difficult to reach a desired therapeutic level. When the heating duration is shorter than the thermal relaxation time of tissue, it is observed that the use of the WBHTE predicts different but suitable results as compared to the use of the PBHTE.

IV. CONCLUSIONS

The thermal relaxation time of tissues will cause the delay of the appearance of the peak temperature during thermal

treatments. The lag behavior of the peak temperature would result in a lower thermal dose level. For a rapid heating (i.e., the heating duration is shorter than the thermal relaxation time of tissue), the temperature predicted by the PBHTE is higher than that of the WBHTE. For a rapid heating process, the WBHTE may provide an appropriate way for describing in the dimensions of thermal lesion during thermal treatments. In contrast, the difference of the dimensions of thermal lesion predicted between by the PBHTE and by the WBHTE will become smaller when the heating duration is longer than the thermal relaxation time of tissue.

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- ^{a)} Author to whom correspondence should be addressed. Electronic mail: winli@ntu.edu.tw
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