

NONLINEAR BEHAVIOR AND THERMAL DAMAGE OF THERMAL LAGGING IN CONCENTRIC LIVING TISSUES SUBJECTED TO GAUSSIAN DISTRIBUTION SOURCE

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ABSTRACT: The effects of thermal lagging with high-order became essential to describe non-equilibrium heating in tissues. This paper studies the temperature rise behavior in living tissues theoretically during the treatment by magnetic tumor hyperthermia based on the non-linear form of the dual-phase-lag model. Experimentally, it was found that the concentration of magnetic particles is in Gaussian distribution through the radial direction when magnetic fluid is injected into the living tissue space. Hence, the governing partial differential equation in concentric spherical space is solved in the Laplace transform domain. Some comparisons between the non-linear and linear effects of phase-lag time's parameters on bio-heat transfer have been studied and discussed. The thermal damage quantity for the tumor has been calculated with different values of the phase-lag times. The results show that the non-linear and linear effects of phase-lag times on bio-heat transfer have significant effects on the tumor, the tissue, and the thermal damage quantity.

Keywords: Nonlinear Behavior; Thermal Lagging; Thermal Damage; Living Tissue; Gaussian distribution Source

1. INTRODUCTION

Hyperthermia (also called thermal therapy or thermotherapy) is a kind of medical treatment in cancer therapy; it is elevated body temperature to 40–44 C. Hyperthermia is used with radiation therapy and chemotherapy to treat cancer [1]. Cells in these areas are often cell cycle arrest and so most resistant to growth prohibiting drugs. It remains unclear whether these cells are sensitive to heat damage; moreover, heat can motivate vascularization and increase oxygenation of the tissue, thermotherapy make cancer cells more motivate to radiation or harm other cancer cells that radiation cannot damage [2, 3]. These studies have been certain in a number of clinical studies [4, 5] which indicate that elevation of the temperature within a tumor has a cytotoxic influence on radio resistant cells when heated to temperatures above 42 C. There is a variety of techniques [3, 6] to increase the temperature within the human body. Hyperthermia for the processing of cancer is under study, including all body hyperthermia, partial or regional hyperthermia, and local hyperthermia. In several biologists studying the behavior of bio-heat transfer in tissues during magnetic fluid hyperthermia management, the distribution of the magnetic particles was always regarded as homogenous in a limited spherical domain [7-11]. Furthermore, Salloum et al. [12]

experimentally evaluated magnetic nan-ofluid transport and heat distribution stimulated by commercially available magnetic nanoparticles injected into the extracellular area of biological tissue using agarose gel with porous structures alike to human tissue. Pennes model [13] described temperature distribution in the living biological tissues. The connection between [14] arterial blood and the heat transfer in a living tissue are taken. The model known as the bioheat equation remains used today. Pennes inserted a medium response term to the basic heat equation that accounts for the mitigating effect of blood flow. This convective term depicts heat transport by means other than propagation. Wissler [15] explicated the validity of Pennes' model connected to normal thermal distribution in living tissue. supposed mixed boundary conditions in resting tissue, Pennes' model strictly describes the decay of temperature from the core of the body to the surface [14]. The Pennes bio-heat transfer equation (PBT) is based on the classical Fourier's law, taken into account a blood perfusion term, which is proportionate to the volumetric rate of blood perfusion and the difference between the average arterial blood and tissue temperatures. Pennes bio-heat model is true only if when the venous blood flows from the capillary bed to the main supply vein, its temperature remains the same as the tissue temperature disregard the size of the vessel and the

flow rate. Youssef modified the theory of heat conduction in deformable bodies which have been investigated by Chen and Gurtin, which depends upon two distinct temperatures, the conductive temperature and the thermodynamic temperature [16]. For time-independent situations, the difference between these two temperatures is proportional to the heat supply, and in the absence of any heat supply, the two temperatures are identical. Youssef considered the non-Fourier's heat conduction based on one relaxation time. Youssef applies the two-temperature heat conduction in many applications [17-21]. In this work, two-temperature bio-heat transfer equations based on second-order effects in thermal lagging was introduced and used to discuss the variation of temperature in a laser-irradiated biological tissue.

2. FORMULATION OF THE PROBLEM

In a magnetic fluid hyperthermia, magnetic particles are injected into at the center of tumor surrounded by the normal tissue and radially diffuse from the injected point in Gaussian distribution [12]. For excitation of an alternating magnetic field, magnetic particles become the space-dependent heating sources in the tissue. For $t > 0$, the heat is transferring in the radius direction symmetrically. The small tumor is regarded as a solid sphere with the radius R [7-11]. The temperature distribution in the tumor $0 \leq r \leq R$ and normal $R \leq r < h$ tissues is the function of the distance r from the center of the sphere and time t .

Youssef proposed the two-temperature model to differentiate between the conductive temperature and the dynamical temperature as:

$$q_i(r, t + \tau_{qi}) = -K_i \nabla T_i^c(r, t + \tau_{Ti}), \quad i = 1, 2, \quad (1)$$

$$T_i^c(r, t) - T_i^D(r, t) = \beta_i \nabla^2 T_i^c(r, t), \quad i = 1, 2. \quad (2)$$

Where $i = 1$ for $0 \leq r \leq R$ and $i = 2$ for $R \leq r < h$,

β_i is a non-negative parameter which is called two-temperature parameter, T_i^c is the conductive temperature, T_i^D is the dynamical temperature, K the heat conductivity, q the heat flux, and t is the time, τ_q, τ_T are the phase-lag time parameters of the heat flux and the temperature gradient, respectively. In general, the relaxation times τ_q, τ_T take a minimal value, while in the biological materials this parameter is more significant.

The energy conservation equation of bio-heat transfer is described in the context of the two-temperature model as:

$$\rho_i C_i \frac{\partial T_i^D(r, t)}{\partial t} = -\nabla \cdot q_i(r, t) - w_{bi} C_b \rho_b (T_i^D(r, t) - T_0) + (q_{mi}(r, t) + q_{ri}(r, t)), \quad i = 1, 2 \quad (3)$$

The term $w_{bi} C_b (T_i^D(r, t) - T_0)$ expresses the heat caused by convection within the tissue per unit mass of the tissue and it is considered to be homogenous and $T_0 = 37^\circ C$ is the reference temperature of the tissue and the tumor.

The second order Taylor series of the DPL model can be rewritten as

$$\left(1 + \tau_{qi} \frac{\partial}{\partial t} + \frac{\tau_{qi}^2}{2} \frac{\partial^2}{\partial t^2}\right) q(r, t) = -K_i \left(1 + \tau_{Ti} \frac{\partial}{\partial t} + \frac{\tau_{Ti}^2}{2} \frac{\partial^2}{\partial t^2}\right) \nabla T_i^c(r, t), \quad i = 1, 2 \quad (4)$$

Consequently, it gives

$$\left(1 + \tau_{qi} \frac{\partial}{\partial t} + \frac{\tau_{qi}^2}{2} \frac{\partial^2}{\partial t^2}\right) \nabla \cdot q(r, t) = -K_i \left(1 + \tau_{Ti} \frac{\partial}{\partial t} + \frac{\tau_{Ti}^2}{2} \frac{\partial^2}{\partial t^2}\right) \nabla^2 T_i^c(r, t), \quad i = 1, 2 \quad (5)$$

A high order differential equation of bio-heat transfer is obtained from equation (3) as:

$$K_i \left(1 + \tau_{Ti} \frac{\partial}{\partial t} + \alpha_i \frac{\tau_{Ti}^2}{2} \frac{\partial^2}{\partial t^2}\right) \frac{1}{r^2} \frac{\partial}{\partial r} \left(r^2 \frac{\partial T_i^c(r, t)}{\partial r}\right) = \left(1 + \tau_{qi} \frac{\partial}{\partial t} + \alpha_2 \frac{\tau_{qi}^2}{2} \frac{\partial^2}{\partial t^2}\right) \left[\frac{\rho_i C_i \frac{\partial T_i^D(r, t)}{\partial t}}{w_{bi} \rho_b C_b (T_0 - T_i^D(r, t))} - \frac{q_{mi}(r, t) - q_{ri}(r, t)}{r} \right], \quad i = 1, 2. \quad (6)$$

where the values of the coefficients α_1 and α_2 are $\alpha_1 = \alpha_2 = 0.0$ for DPL type I equation, $\alpha_1 = 1.0, \alpha_2 = 0.0$ for DPL type II equation, and $\alpha_1 = \alpha_2 = 1.0$ for DPL type III equation.

Consider the following functions:

$$\theta_i(r, t) = r(T_i^c(r, t) - T_0), \quad i = 1, 2 \quad (7)$$

$$\varphi_i(r, t) = r(T_i^D(r, t) - T_0), \quad i = 1, 2.$$

Hence,

$$K_i \left(1 + \tau_{Ti} \frac{\partial}{\partial t} + \alpha_i \frac{\tau_{Ti}^2}{2} \frac{\partial^2}{\partial t^2}\right) \left(\frac{\partial^2 \varphi_i(r, t)}{\partial r^2}\right) = \left(1 + \tau_{qi} \frac{\partial}{\partial t} + \alpha_2 \frac{\tau_{qi}^2}{2} \frac{\partial^2}{\partial t^2}\right) \left[\frac{\rho_i C_i \frac{\partial \theta_i(r, t)}{\partial t}}{w_{bi} \rho_b C_b \theta_i(r, t)} + \frac{r q_{mi}(r, t) - r q_{ri}(r, t)}{r q_{mi}(r, t) - r q_{ri}(r, t)} \right], \quad i = 1, 2. \quad (8)$$

$$\theta_i(r, t) = \varphi_i(r, t) - \beta_i \frac{\partial^2 \varphi_i(r, t)}{\partial r^2}, \quad i = 1, 2. \quad (9)$$

Assume the following spatial heating source

$$q_{ri}(r, t) = q_0 H(t) e^{-(r^2/r_0)}, \quad (10)$$

where r_0 is a parameter which determines how far the diffusion of the injected magnetic particles occurs and q_0 determines the maximum strength of the spatial heating source at the injection site. The function $H(t)$ is Heaviside unit step function

Applying Laplace transform for equation (8) and (10) defined as:

$$\bar{f}(s) = \int_0^\infty f(t) e^{-st} dt, \quad (11)$$

The following initial conditions will be used:

$$\varphi_i(r, t)|_{t=0} = \theta_i(r, t)|_{t=0} = \frac{\partial \varphi_i(r, t)}{\partial t} \bigg|_{t=0} = \frac{\partial \theta_i(r, t)}{\partial t} \bigg|_{t=0} = 0. \quad (12)$$

Thus,

$$\frac{\partial^2 \bar{\varphi}_i}{\partial r^2} - \lambda_i^2 \bar{\varphi}_i = -f_i r, \quad i = 1, 2, \quad (13)$$

$$\text{where} \quad \lambda_i^2 = \frac{h_{qi}(\rho_i C_i s + w_{bi} C_b \rho_p)}{K_i h_{ri} + \beta_i h_{qi}(\rho_i C_i s + w_{bi} C_b \rho_p)},$$

$$f_i = \frac{\bar{q}_{mi} + h_{qi} \bar{q}_{ri}}{[K_i h_{ri} + \beta_i h_{qi}(\rho_i C_i s + w_{bi} C_b \rho_p)]},$$

$$h_{ri} = \left(1 + s \tau_{ri} + \alpha_1 \frac{s^2 \tau_{ri}^2}{2}\right), \quad h_{qi} = \left(1 + s \tau_{qi} + \alpha_2 \frac{s^2 \tau_{qi}^2}{2}\right),$$

$$\bar{q}_{ri}(r, s) = \frac{q_0}{s} e^{-(r^2/r_0)}, \quad \bar{q}_{mi} = \frac{q_{mi}}{s}.$$

The general solution of the differential equation (13) takes the form

$$\bar{\varphi}_1(r, s) = c_{11} e^{-\lambda_1 r} + c_{12} e^{\lambda_1 r} + \frac{f_1}{\lambda_1^2} r, \quad 0 \leq r \leq R, \quad (14)$$

and

$$\bar{\varphi}_2(r, s) = c_{21} e^{-\lambda_2 r} + c_{22} e^{\lambda_2 r} + \frac{f_2}{\lambda_2^2} r, \quad R \leq r < h. \quad (15)$$

Apply the boundary and the continuity conditions

$$\bar{\varphi}_1(r, s)|_{r=0} = 0, \quad \bar{\varphi}_1(R, s) = \bar{\varphi}_2(R, s), \quad \frac{K_1}{r} \frac{\partial \bar{\varphi}_1(r, s)}{\partial r} \bigg|_{r=R} = \frac{K_2}{r} \frac{\partial \bar{\varphi}_2(r, s)}{\partial r} \bigg|_{r=R}, \quad \bar{\varphi}_2(r, s)|_{r=h} = 0. \quad (16)$$

The following system of linear equations has been deduced:

$$c_{11} + c_{12} = 0, \quad (17)$$

$$e^{-\lambda_1 R} c_{11} + e^{\lambda_1 R} c_{12} - e^{-\lambda_2 R} c_{21} - e^{\lambda_2 R} c_{22} = \left(\frac{f_2}{\lambda_2^2} - \frac{f_1}{\lambda_1^2}\right) R, \quad (18)$$

$$-\lambda_1 K_1 e^{-\lambda_1 R} c_{11} + \lambda_1 K_1 e^{\lambda_1 R} c_{12} + \lambda_2 K_2 e^{-\lambda_2 R} c_{21} - \lambda_2 K_2 e^{\lambda_2 R} c_{22} = \left(\frac{f_2}{\lambda_2^2} - \frac{f_1}{\lambda_1^2}\right) R, \quad (19)$$

$$c_{21} e^{-\lambda_2 h} + c_{22} e^{\lambda_2 h} = -\frac{f_2}{\lambda_2^2} h. \quad (20)$$

Solving equations (17-20) completing the solution in the Laplace transform domain.

3. THE THERMAL DAMAGE

The Arrhenius burn integration induced by Henriques and Moritz is widely used. Their results showed that progressively decreasing temperatures could produce a burn injury of standard threshold severity as the thermal insult period is logarithmically increased. They conducted two different experiments, which involved boundary conditions of constant temperature and constant heat flux in computing the time-temperature relationship at the dermal-epidermal junction. They worked out the solution of the Fourier heat conduction equation for a semi-infinite body to model the transfer of heat through the skin. Based on their observation, Moritz and Henriques proposed that skin damage could be represented as a chemical rate process, which is calculated by using a first order Arrhenius rate equation. Whereby damage is related to the rate of protein denaturation $\kappa(T)$ and exposure time t at a given absolute temperature T . The measure of thermal damage Ω was introduced, and its rate $\kappa(T)$ were postulated to satisfy:

$$\kappa(T) = \frac{d\Omega}{dt} = A \exp\left(-\frac{E_a/\eta}{T}\right), \quad (21)$$

which leads to

$$\Omega = A \int_0^t \exp\left(-\frac{E_a/\eta}{T}\right) dt, \quad (22)$$

where A is a material parameter (frequency factor); E_a is the activation energy; η is the universal gas constant. Equation (37) indicates that a reaction proceeds faster with larger values of T or A for the same E_a , or with smaller values of E_a for the same value of A . The constants A and E_a are usually obtained experimentally. After the pioneering work of Henriques and Moritz, many researchers have also proposed some other models, but most of them have a similar format. There are only differences in the coefficients used in the burn damage integral, which are mainly due to the different experimental databases used to define the models and the different emphasis

when analyzing the burn process where

$$T_i^c(^{\circ}C) = \frac{\varphi_i}{r} + T_0 + 237.$$

4. NUMERICAL INVERSION OF THE LAPLACE TRANSFORM

To determine the distribution $\varphi_i(r, t)$ of each layer, a Riemann-sum approximation method will be used to obtain the numerical results in which, any function in Laplace domain can be inverted to the time domain as:

$$Z(t) = \frac{e^{\varepsilon t}}{t} \left[\frac{1}{2} \bar{Z}(\varepsilon) + \operatorname{Re} \sum_{n=1}^N (-1)^n \bar{Z} \left(\varepsilon + \frac{in\pi}{t} \right) \right], \quad (23)$$

where Re is the real part and i is imaginary number unit. For faster convergence, numerous numerical experiments have shown that the value of ε satisfies the relation $\varepsilon t \approx 4.7$ Tzou. The value of $\frac{\varphi_i(r, t)}{r}$ at $r = 0$ is undefined value and it must be replaced by its limit as $\lim_{r \rightarrow 0} \frac{\varphi_i(r, t)}{r}$ and by using L'Hôpital's rule as:

$$\left. \frac{\varphi_i(r, t)}{r} \right|_{r=0} = \lim_{r \rightarrow 0} \frac{\varphi_i(r, t)}{r} = \left. \frac{d\varphi_i(r, t)}{dr} \right|_{r=0}. \quad (24)$$

5. NUMERICAL RESULTS AND DISCUSSION

To simulate the thermal response within a small spherical tumor of radius $R = 0.005$ m and its surround tissue, the thermal material properties of the tumor and the tissue are provided in Table1. The volumetric heat capacity of blood is $\rho_b C_b = 4.18 \times 10^6$ J / m³ / K and the spatial heating source is specified with $q_0 = 6.15 \times 10^6$ W / m³, $r_0 = 0.75 \times R$ and $h = 4.0 \times R$.

Table1: Properties of Tumor-Tissue Model

Parameter	Unit	Tumor	Tissue
K	W / m K	0.778	0.642
ρ	kg / m ³	1660	1000
C	J / kg K	2540	3720
w_b	m ³ / s / m ³	0.0064	0.0064
T_0	°C	37	37
q_m	W / m ³	29000	450
x	m	0.005	0.02
β	m ⁻²	0.000001	0.000001

Figure 1 shows the heat conduction increment along the distance range of tumor $0.0 \leq r \leq R = 0.005$ and of tissue $R = 0.005 \leq r \leq h = 0.02$ at the instant time $t = 20$ s and $\tau_r = 5.0$ s, $\tau_q = 15.0$ s. DPL type I, II, III for the one-temperature and two-temperature model, respectively, have been represented in this figure to discuss the effect of the two temperature parameter on the conductive temperature increment. The two-temperature parameter β has significant effect where the conductive temperature increment decreases in the context of the two-temperature model for the three DPL types. The non-linear effects of τ_r^2 , τ_q^2 are very significant.

The heat conduction temperature increment is greater in the context of DPL type III than DPL type I and Type II. The non-linear term of τ_q^2 plays a vital role to increase the heat conduction temperature increment in the context of the one-temperature model and the two-temperature model. In the tumor space, the heat conduction temperature increment in the context of DPL type III is greater than DPL type I and DPL type I is greater than DPL type II. In the tissue space, the three types are much closed based on one-temperature parameter while they are coinciding based on the two-temperature model.

The difference values of the heat conduction increment in the context of the one-temperature model and the two-temperature model are greater in the tumor space than its values in the tissue space because the positions $0 \leq r \leq R$ are in the range of the heating source. Figures 2-4 show the heat conduction increment of DPL type I, II, and III, respectively, in the context of the one-temperature model and two-temperature model, respectively.

The non-linear effects of τ_r^2 , τ_q^2 are significant. The heat conduction temperature increment is greater in the context of the one-temperature model than the two-temperature model. The non-linear term of τ_q^2 plays a vital role to increase the heat conduction temperature increment in the context of the one-temperature model while it has a limited role in the context of the two-temperature model. In the tumor space, the heat conduction temperature increments when $\tau_r = 15.0$ s, $\tau_q = 30.0$ s is greater when $\tau_r = 10.0$ s, $\tau_q = 20.0$ s, and then $\tau_r = 5.0$ s, $\tau_q = 10.0$ s, while the three cases are coinciding in the context of the two-temperature model. In the tissue space, the three types are much closed based on one-temperature parameter while they are coinciding based on the two-temperature model.

The difference values of the heat conduction increment in the context of the one-temperature model and the two-temperature model are greater in the tumor space than its values in the tissue space because the positions $0 \leq r \leq R$ are in the range of the heating source. Figures 5-7 show the heat conduction increment of DPL type I, II, and III, respectively, in the context of the one-temperature model and two-temperature model, respectively. The non-linear effects of τ_r^2 , τ_q^2 are significant.

The heat conduction temperature increment is greater in the context of the one-temperature model than the two-temperature model. The non-linear term of τ_q^2 and the time t are playing vital roles to increase the heat conduction temperature increment in the context of the two models. The difference values of the heat conduction increment in the context of the one-temperature model and the two-temperature model are greater in the tumor space than its values in the tissue space because the positions $0 \leq r \leq R$ are in the range of the heating source.

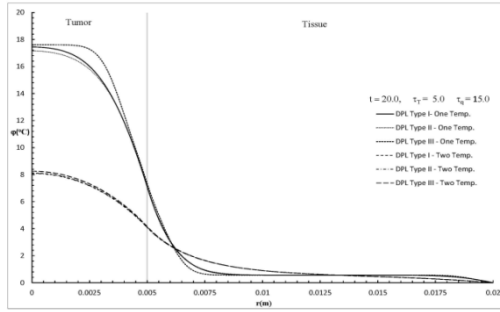


Fig. 1: The heat conduction increment with different DPL types

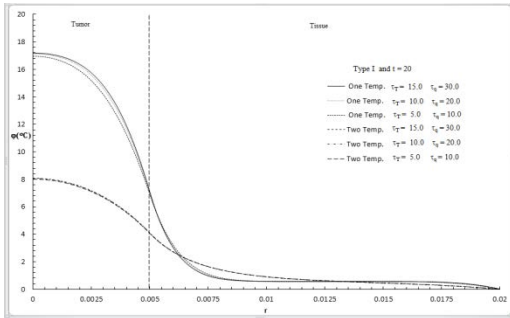


Fig. 2: The heat conduction increment of DPL type I

Figures 8-10 shows the thermal damage of DPL type I, II, and III, respectively, in the context of the one-temperature model and two-temperature model, respectively. The line passing through the damage $\Omega = 1.0$ separates between the irreversible damage

above and the reversible damage below. The non-linear effects of τ_r^2 , τ_q^2 are significant. The thermal damage is greater in the context of the one-temperature model than the two-temperature model. The non-linear term of τ_q^2 and the position r are playing vital roles to increase or decrease the heat thermal damage in the context of the two models. The only one case that has irreversible damage occurred when $\tau_q > \tau_r$ for the one-temperature model and the two-temperature model and all the other cases when $\tau_q < \tau_r$ and $\tau_q = \tau_r$ has reversible damage to the two models.

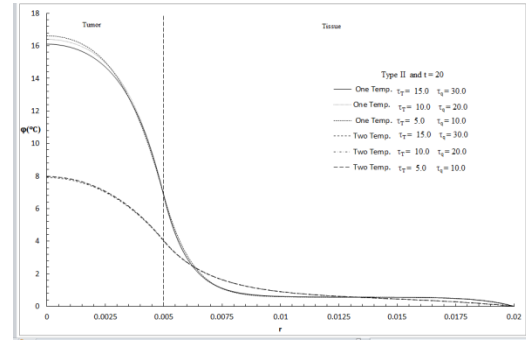


Fig. 3: The heat conduction increment of DPL type II

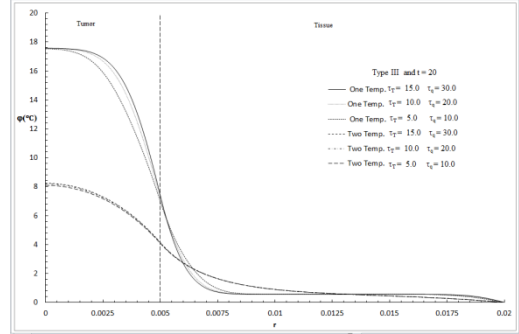


Fig.4: The heat conduction increment of DPL type III

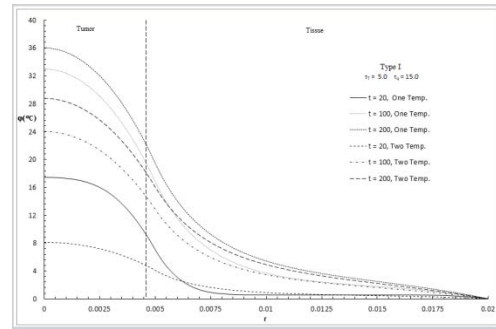


Fig. 5: The heat conduction increment of DPL type I at a different time and various r

The one-temperature model offers irreversible damage quantity more than the two-temperature parameter. The DPL type III offer irreversible damage quantity more than the DPL type I and then the DPL type II offers the smallest irreversible damage quantity.

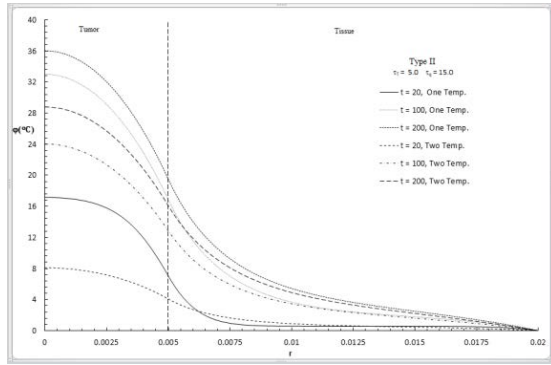


Fig.6: The heat conduction increment of DPL type II at a different time and various r

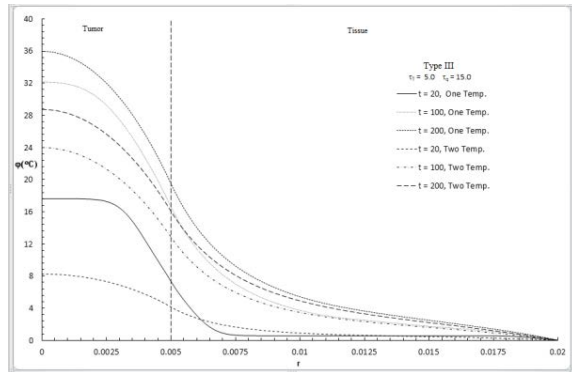


Fig. 7: The heat conduction increment of DPL type III at a different time and various r

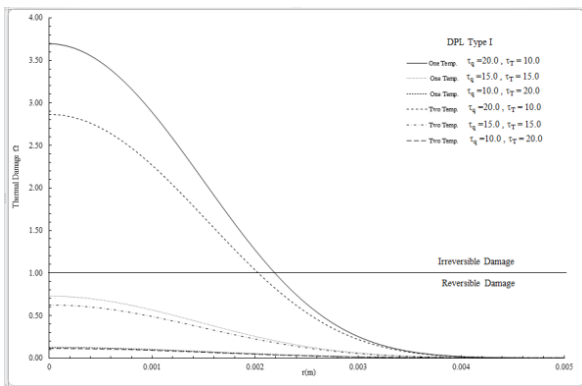


Fig.8: The thermal damage quantity of DPL type I of the tumor

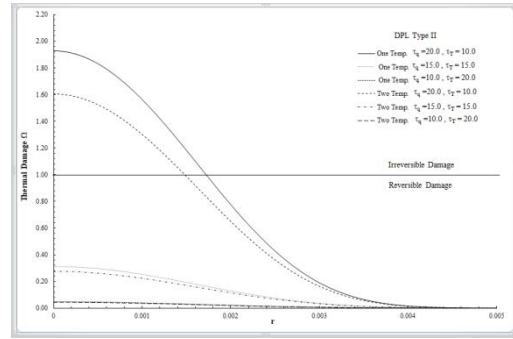


Fig. 9: The thermal damage quantity of DPL type II of the tumor

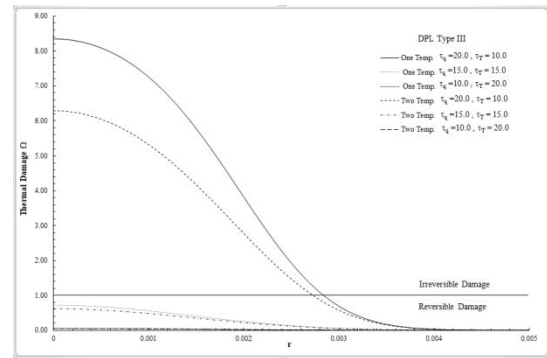


Fig. 10: The thermal damage quantity of DPL type III of the tumor

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