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Modeling and Simulation of Hyperthermia as Cancer Treatment

R. O. Olayiwola [*1], Olabiyisi, S. O. [2], O. A. Odebiyi [1], A. Ndanusa [1] and R. M. Momoh [1]
[1]Department of Mathematics and Statistics, Federal University of Technology, Minna, Nigeria.
[2]Department of Computer Science and Engineering, Ladoke Akintola University of Technology, Ogbomoso, Nigeria.

ABSTRACT

We study a one dimensional transient model for predicting temperatures in living tissues such as a prostate undergoing microwave heating. We show that temperature is non-decreasing function of time. The method of asymptotic expansion is used to decouple the system of partial differential equations, describing the problem under consideration, and an analytical solution of the reduced system is obtained using the method of eigenfunction expansion. The results are presented graphically and it is discovered that the heat transfer is significantly influenced by the parameters involved.

Keywords : *microwave heating, asymptotic expansion, bioheat, Maxwell's equations, hyperthermia treatment planning*

1. INTRODUCTION

Hyperthermia (or thermotherapy) is a cancer treatment that involves heating tumor cells within the body. Elevating the temperature of tumor cells results in cell membrane damage, which, in turn, leads to the destruction of the cancer cells.

Microwaves are a form of electromagnetic radiation; that is, they are waves of electrical and magnetic energy moving together through space [1]. Microwave energy is very effective in heating cancerous tumors, because tumors typically have high-water content [2]. Such tissue heats very rapidly when exposed to high-power microwaves. Furthermore, microwaves can be delivered to tissue by special-purpose antennas that are located adjacent to the patient's body. Depending on the tumor size and location in the body, one or more microwave antennas can be used to treat the tumor. When a microwave thermotherapy antenna is turned "on," body tissues with high-water content that are irradiated with significant amounts of microwave energy are heated [2]. This technology has found new applications in many industrial processes, such as those involving melting, smelting, sintering, dying and joining [3].

Hyperthermia treatment planning is an important therapeutic option in biomedical cancer medicine. It is a promising method to treat various types of cancer by heating the tumor to about 41^0C using electro-magnetic energy, thereby inducing preferential apoptosis of cancerous cells. It makes the tumor more susceptible to an accompanying radio or chemo therapy [4].

In the more recent literature, several authors have studied the microwave heating as cancer treatment. These include Olarewaju et al. [1] who employed shooting technique to explicitly construct the approximate solution of steady state reaction-diffusion equations with source term that arise in modeling microwave heating in an infinite slab with isothermal walls. El-dabe et al. [5] discussed the effects of microwave heating on the thermal states of biological tissues. Maxwell's equations and transient bioheat transfer equation were numerically calculated using finite difference method. Lu et al. [6] studied the simulation of the thermal wave propagation in biological tissues by dual reciprocity boundary element method. Marchant and Liu [7] considered the steady-state microwave heating of a finite one-dimensional slab. The temperature dependency of electrical conductivity and thermal absorptivity were assumed to be governed by the Arrhenius law, while both the electrical permittivity and permeability were assumed constant. They presented experimental evidence which indicates that the physical properties of material have power law dependence on temperature. Hill and Pincombe [8] presented a similarity solution to solve the microwave heating equation without studying the effect of convection due to the blood flow. They assumed that the electrical field decays exponentially with distance, that is, $|E|^2 = E_0^2 e^{-kx}$ for certain constants E_0 and k.

In this paper, we study a model for hyperthermia as a cancer treatment planning. As in [5], we assume that the tissue is homogeneous within each layer. We also assume that the thermal conductivity and heat capacity are constant. We shift and rescale the temperature so that 0 corresponds to the initial temperature of the tissue T_0. We examine the properties of solution and solve the Maxwell's equations and transient bioheat transfer equation analytically using asymptotic expansions.

2. MODEL FORMULATION

Following Christen et al. [4], modelling and simulation of the thermal behavior of the tissue exposed to the non-ionizing radiation is an essential component of hyperthermia

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treatment planning. The simulation relies on physical models for the electric fields generated by the the applicator, Maxwell's equations:

$$\varepsilon\frac{\partial E}{\partial t}+\frac{\partial H}{\partial x}+\sigma E=0 \tag{1}$$

$$\mu_c\frac{\partial H}{\partial t}+\frac{\partial E}{\partial x}=0 \tag{2}$$

and a model for temperature distribution within the patient's tissue, Penne's "bio-heat" equation (first introduced by Pennes [9])

$$\rho c_p\frac{\partial T}{\partial t}=\frac{\partial}{\partial x}\left(k\frac{\partial T}{\partial x}\right)-\rho_b c_b\omega_b\left(T-T_b\right)+Q(T)|E|^2 \tag{3}$$

Here, following Marchant and Liu [7], we assumed the body heating coefficient to be in the form:

$$Q(T)=(T-T_0)^n \tag{4}$$

The initial and boundary conditions were formulated as follows:
Initial condition:

At $t=0$ and $\forall\ x$

$$T=(T_b-T_0)\frac{x}{L}+T_0,\ E=\frac{E_0x}{L},\ H=\frac{H_0x}{L},\ T_b>T_0 \tag{5}$$

Boundary conditions:

$$\left.\begin{aligned}&T|_{x=0}=T_0, && E|_{x=0}=0, && H|_{x=0}=0\\ &T|_{x=L}=T_c, && E|_{x=L}=H_0, && H|_{x=L}=H_0,\ T_c>T_0\end{aligned}\right\}, \tag{6}$$

where T is tissue temperature, T_b is the temperature of blood, T_c is core temperature, T_0 is the initial temperature of tissue, Q is the body heating coefficient, ρ is density of tissue, ρ_b is density of blood, k is thermal conductivity of tissue, c_p is the specific heat of tissue, c_b is the specific heat of blood, ω_b is blood perfusion rate (blood perfusivity), t is time, x is space coordinate, E is electric field, H is magnetic field, L is distance from skin surface to body core, μ_e is magnetic permeability, ε is electric permittivity, σ is electrical conductivity, E_0 is electric field in the free space upon the tissue, H_0 is magnetic field in the free space upon the tissue, n is positive integer number.

3. METHOD OF SOLUTION

3.1 Non-dimensionalisation

We scale the length by using $L=\frac{\alpha}{\nu}$ and the time by using $t^*=\frac{L}{\nu}$, where $\nu=\frac{\mu}{\rho}$ is the kinematic viscosity, μ viscosity of tissue and $\alpha=\frac{k}{\rho c_p}$ the effective thermal diffusivity . We introduce dimensionless variables for space and time,

$$x'=\frac{x}{L},\qquad t'=\frac{t}{t^*} \tag{7}$$

We also introduce dimensionless variables for temperature, electric field and magnetic field;

$$\theta=\frac{T-T_0}{T_b-T_0},\qquad \phi=\frac{E}{E_0},\qquad \psi=\frac{H}{H_0}, \tag{8}$$

where T_0 is the initial temperature of the porous medium and $C_f^0,\ C_{ox}^0$ are the initial fuel concentration and initial oxygen mass fraction, respectively; $\eta^*,\ t^*,\ p^*,\ \rho^*$ are reference values for space, time, pressure and density, respectively.
Using (4) and (5), with these dimensionless variables, and after dropping the prime, the system (1) – (3) become

$$\frac{\partial\psi}{\partial t}+\mu_0\frac{\partial\phi}{\partial x}=0 \tag{9}$$

$$\frac{\partial\phi}{\partial t}+\in\frac{\partial\psi}{\partial x}+\sigma_1\phi=0 \tag{10}$$

$$\frac{\partial\theta}{\partial t}=\frac{\partial^2\theta}{\partial x^2}+\omega(1-\theta)+\beta|\phi|^2\theta^n \tag{11}$$

together with initial and boundary conditions

$$\left.\begin{aligned}&\psi(x,0)=x, && \psi(0,t)=0, && \psi(1,t)=1\\ &\phi(x,0)=x, && \phi(0,t)=0, && \phi(1,t)=1\\ &\theta(x,0)=x, && \theta(0,t)=0, && \theta(1,t)=\theta_c\end{aligned}\right\}, \tag{12}$$

Where

$$\in=\frac{H_0t^*}{\varepsilon LE_0},\quad \sigma_1=\frac{\sigma t^*}{\varepsilon},\quad \mu_0=\frac{E_0t^*}{\mu_e LH_0},$$

$$\omega=\frac{\rho_b c_b\omega_b t^*}{\rho c_p},\quad \beta=\frac{(T_b-T_0)^{n-1}|E_0|^2t^*}{\rho c_p}$$

3.2 Properties of Solution

Theorem 1: Let $\beta=0$ and $\omega=1$ in (11). Then $\frac{\partial\theta}{\partial t}\geq 0$.

In the proof, we shall make use of following Lemma of Kolodner and Pederson [10].

Lemma (Kolodner and Pederson [10]) Let $u(x,t)=0\left(e^{\alpha|x|^2}\right)$ be a solution on $R^n\times[0,t)$ of the differential inequality

$$\frac{\partial u}{\partial t}-\Delta u+K(x,t)u\geq 0$$

where K is bounded from below. If $u(x,0)\geq 0$, then $u(x,t)\geq 0$ for all $(x,t)\in R^n\times[0,t_0)$.

Proof of Theorem 1: Let $\beta=0$ and $\omega=1$ in (11). We obtain

$$\frac{\partial\theta}{\partial t}-\frac{\partial^2\theta}{\partial x^2}+\theta=1$$

Differentiating with respect to t, we have

$$\frac{\partial}{\partial t}\left(\frac{\partial\theta}{\partial t}\right)-\frac{\partial^2}{\partial x^2}\left(\frac{\partial\theta}{\partial t}\right)+\frac{\partial\theta}{\partial t}=0$$

Let

$$u=\frac{\partial\theta}{\partial t}$$

Then

$$\frac{\partial u}{\partial t}-\frac{\partial^2 u}{\partial x^2}+u=0$$

This can be written as

$$\frac{\partial u}{\partial t}-\frac{\partial^2 u}{\partial x^2}+K(x,t)u=0,$$

where

$$K(x,t)=1$$

Clearly, K is bounded from below. Hence by Kolodner and Pederson's lemma $u(x,t)\geq 0$ i.e., $\frac{\partial\theta}{\partial t}\geq 0$. This completes the proof.

Theorem 2: Let $\beta=0$ and $\omega=1$ in (11). Then $\theta(x,t)\geq 0$ for $(x,t)\in(0,\infty)\times(0,t_0),\ t_0>0$.

Proof: Let $\beta=0$ and $\omega=1$ in (11). We obtain

$$\frac{\partial\theta}{\partial t}-\frac{\partial^2\theta}{\partial x^2}+\theta=1$$

That is

$$\frac{\partial\theta}{\partial t}-\frac{\partial^2\theta}{\partial x^2}+\theta\geq 0 \quad\text{since}\quad 1>0$$

This can be written as

$$\frac{\partial\theta}{\partial t}-\frac{\partial^2\theta}{\partial x^2}+k(x,t)\theta\geq 0\ ,$$

where

$$k(x,t)=1$$

Hence, by Kolodner and Pederson's lemma $\theta(x,t)\geq 0$. This completes the proof.

3.3 Analytical Solution

Here, we consider Equations (9) – (11) when $n=1$. We now seek to solve the system of equations (9) – (11) asymptotically in the limit $\in\to 0$. So, we write

$$\left.\begin{aligned}\psi&=\psi_0+\in\psi_1+h.o.t.\\ \phi&=\phi_0+\in\phi_1+h.o.t.\\ \theta&=\theta_0+\in\theta_1+h.o.t.\end{aligned}\right\}\qquad(13)$$

where $h.o.t.$ read "higher order terms in $\in$. In our analysis we are interested only in the first two terms.

Let

$$\mu_0 = \in a_0, \qquad \beta = \in b_0 \tag{14}$$

We obtain the equations for ψ_0, ψ_1, ϕ_0, ϕ_1, θ_0, θ_1 in the form

$$\frac{\partial \psi_0}{\partial t} = 0,\ \psi_0(x,0) = x,\ \psi_0(0,t) = 0,\ \psi_0(1,t) = 1 \tag{15}$$

$$\frac{\partial \phi_0}{\partial t} + \sigma_1 \phi_0 = 0,\ \phi_0(x,0) = x,\ \phi_0(0,t) = 0,\ \phi_0(1,t) = 1 \tag{16}$$

$$\frac{\partial \theta_0}{\partial t} = \frac{\partial^2 \theta_0}{\partial x^2} + \omega(1-\theta_0), \quad \theta_0(x,0) = x, \quad \theta_0(0,t) = 0, \quad \theta_0(1,t) = \theta_c \tag{17}$$

$$\frac{\partial \psi_1}{\partial t} + a_0 \frac{\partial \phi_0}{\partial x} = 0, \quad \psi_1(x,0) = 0, \quad \psi_1(0,t) = 0, \quad \psi_1(1,t) = 0 \tag{18}$$

$$\frac{\partial \phi_1}{\partial t} + \frac{\partial \psi_0}{\partial x} + \sigma_1 \phi_1 = 0, \quad \phi_1(x,0) = 0, \quad \phi_1(0,t) = 0, \quad \phi_1(1,t) = 0 \tag{19}$$

$$\frac{\partial \theta_1}{\partial t} = \frac{\partial^2 \theta_1}{\partial x^2} - \omega\theta_1 + \beta|\phi_0|^2 \theta_0, \ \theta_1(x,0) = 0, \quad \theta_1(0,t) = 0, \quad \theta_1(1,t) = 0 \tag{20}$$

Then, using method of eigenfunction expansion, we obtain the solution for $\psi(x,t)$, $\phi(x,t)$ and $\theta(x,t)$ as

$$\psi(x,t) = x + \frac{\mu_0}{\sigma_1}\left(e^{-\sigma_1 t} - 1\right) \tag{21}$$

$$\phi(x,t) = xe^{-\sigma_1 t} + \frac{\in}{\sigma_1}\left(e^{-\sigma_1 t} - 1\right) \tag{22}$$

$$\theta(x,t) = \theta_c x + \left(A\left(1-e^{-ct}\right) + Be^{-ct}\right)\sin n\pi x + \sum_{n=1}^{\infty}\sum_{n=1}^{\infty}\left(\frac{D\left(e^{-2\sigma_1 t} - e^{-ct}\right)}{c_2} + \sum_{n=1}^{\infty} F\left(\frac{A\left(2\sigma_1 e^{ct} - ce^{2\sigma_1 t} + c_2\right)e^{-c_1 t}}{\sigma_1 c_2} + \frac{B\left(e^{-ct} - e^{-c_1 t}\right)}{2\sigma_1}\right)\right)\sin n\pi x, \tag{23}$$

where

$$A = \frac{2\omega\left(1 + (-1)^n(\theta_c - 1)\right)}{cn\pi}, \quad B = \frac{(-1)^n(\theta_c - 1)}{n\pi},$$

$$D = \frac{2\beta\theta_c\left(6 - n^2\pi^2\right)(-1)^n}{n^3\pi^3}, \quad c = \omega + n^2\pi^2,$$

$$F = \frac{2\beta\left(3 + 2n^2\pi^2 - 6(-1)^{2n}\right)}{12n^2\pi^2}, \quad c_1 = 2\sigma_1 + c,$$

$$c_2 = c - 2\sigma_1$$

4. RESULTS AND DISCUSSION

Under certain conditions, we have shown that $\theta(x,t)$ is non-decreasing function of time. The transient temperature profiles are presented in Figures 1- 8. Figure 1 displays the graph of $\theta(x,t)$ against t for different values of ω. Figure 2 displays the graph of $\theta(x,t)$ against x for different values of ω. Figures 1 and 2 reveal the effect of variation of blood perfusion rate ω on the tissue and it is seen that transient temperature increases with increasing of blood perfusion rate.

Figure 3 displays the graph of $\theta(x,t)$ against t for different values of σ_1. Figure 4 displays the graph of $\theta(x,t)$ against x for different values of σ_1. From Figures 3 and 4 it is evident that temperature distribution decreases with increasing of electrical conductivity parameter σ_1.

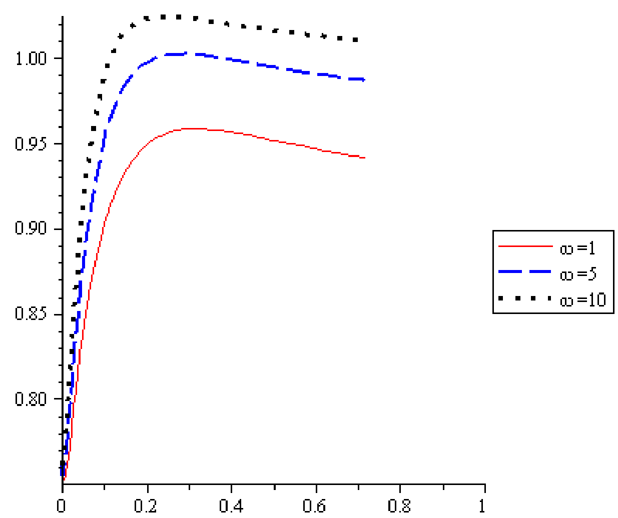

Figure 1: Plots of temperature $\theta(x, t)$ against time t for different values of ω and $\beta = 2$, $\epsilon = 0.0025$, $\sigma_1 = 1$, $\theta_c = 1.5$, $x = 0.6$, $\mu_0 = 1$

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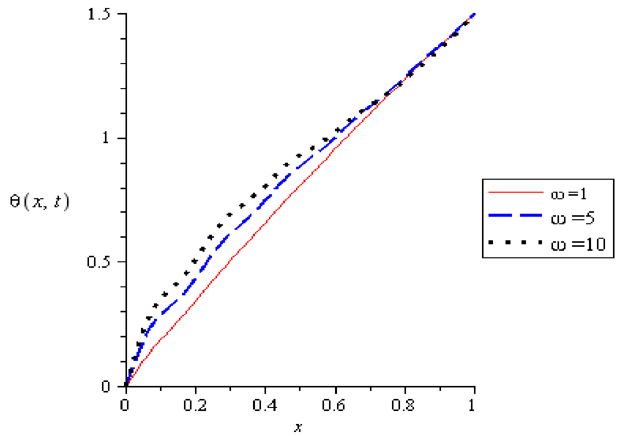

Figure 2: Plots of temperature $\theta(x, t)$ against spece coordinate x for different values of ω and
$\beta = 2,\ \epsilon = 0.0025,\ \sigma_1 = 1,\ \theta_c = 1.5,\ t = 0.4,\ \mu_0 = 1$

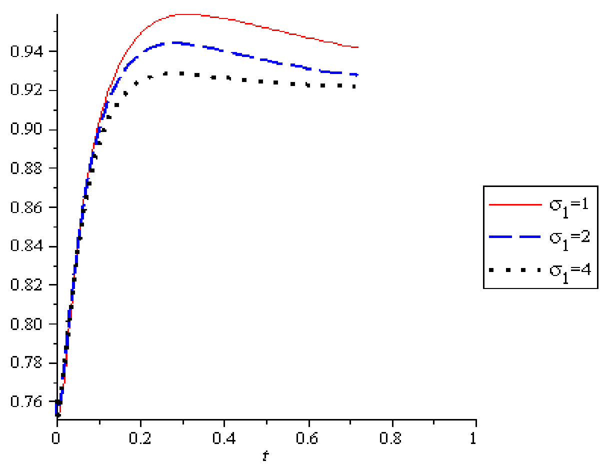

Figure 3: Plots of temperature $\theta(x, t)$ against time t for different values of σ_1 and $\beta = 2,\ \epsilon = 0.0025,\ \omega = 1,\ \theta_c = 1.5,\ x = 0.6,\ \mu_0 = 1$

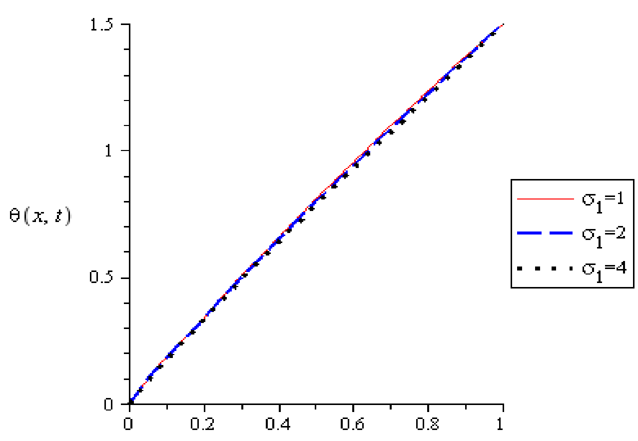

Figure 4: Plots of temperature $\theta(x, t)$ against space coordinate x for different values of σ_1 and
$\beta = 2,\ \epsilon = 0.0025,\ \omega = 1,\ \theta_c = 1.5,\ t = 0.4,\ \mu_0 = 1$

Figure 5 displays the graph of $\theta(x,t)$ against t for different values of β. Figure 6 displays the graph of $\theta(x,t)$ against x for different values of β. Figures 5 and 6 show the relation between the electric field in the free space parameter β and the temperature distribution. It is seen that temperature distribution increases as β increases.

Figure 7 displays the graph of $\theta(x,t)$ against t for different thickness of skin x. It is seen that temperature distribution increases with the increasing of skin thickness. Figure 8 displays the graph of $\theta(x,t)$ against x for different time t. It is seen that temperature distribution of tissue increases as time t increases.

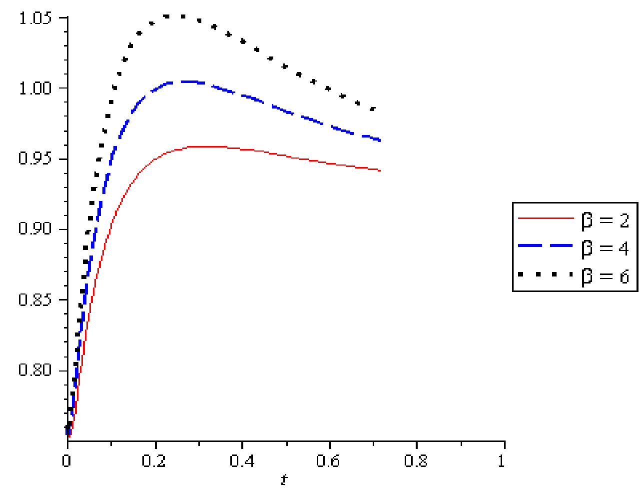

Figure 5: Plots of temperature $\theta(x, t)$ against time t for different values of β and $\sigma_1 = 1,\ \epsilon = 0.0025,\ \omega = 1,\ \theta_c = 1.5,\ x = 0.6,\ \mu_0 = 1$

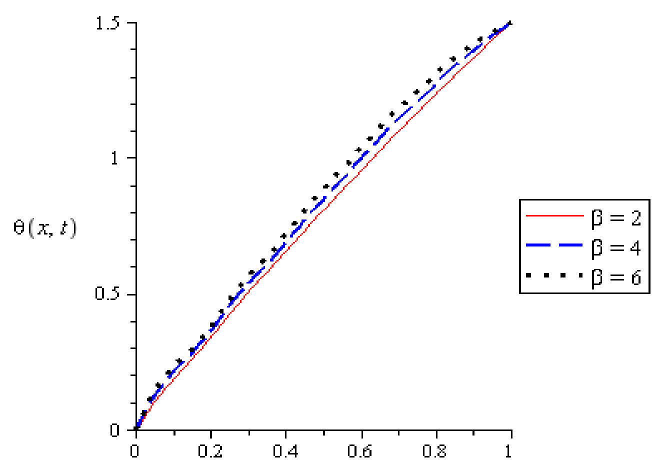

Figure 6: Plots of temperature $\theta(x, t)$ against space coordinate x for different values of β and
$\sigma_1 = 1,\ \epsilon = 0.0025,\ \omega = 1,\ \theta_c = 1.5,\ t = 0.4,\ \mu_0 = 1$

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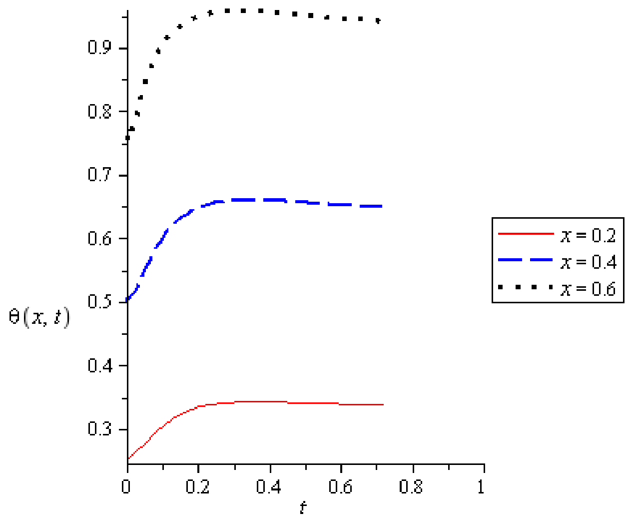

Figure 7: Plots of temperature $\theta(x, t)$ against time t for different thickness of skin x and

$\sigma_1 = 1$, $\epsilon = 0.0025$, $\omega = 1$, $\theta_c = 1.5$, $\beta = 2$, $\mu_0 = 1$

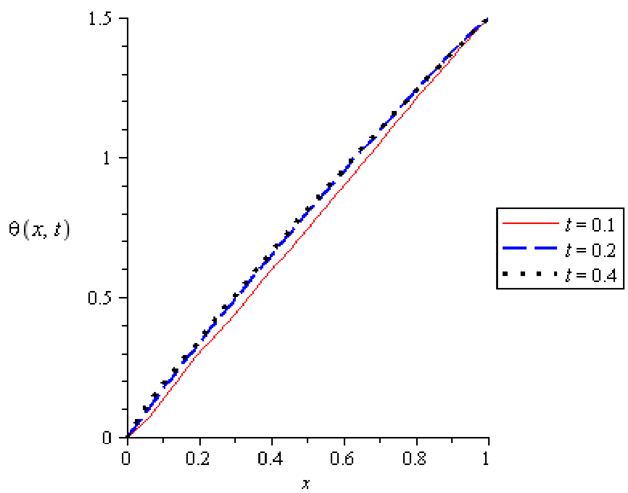

Figure 8: Plots of temperature $\theta(x, t)$ against space coordinate x for different time t and

$\sigma_1 = 1$, $\epsilon = 0.0025$, $\omega = 1$, $\theta_c = 1.5$, $\beta = 2$, $\mu_0 = 1$

5. CONCLUSION

For Maxwell's equations and transient bioheat equation describing the skin burn process resulting from the application of a high temperature heat source to a skin surface, analytical solution via asymptotic expansions and method of eigenfunction expansion has been presented. The governing parameters of the problem are the blood perfusion rate parameter (ω), electrical conductivity parameter (σ_1) and electric field in the free space parameter (β). The analytical method is used to search for transient state temperature profiles.

The behaviors of temperature distributions for different thermal properties of tissues have been illustrated. The heat transfer in the skin burn process is significantly influenced by the parameters involved. The applications of this problem have a great benefit in various branches of science especially in cancer therapy using microwave devices such as the thermocouple.

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