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ANALYSIS OF NONLINEAR RADIATIVE MICROWAVE HEATING OF HYPERTHERMIA TUMOR CELLS THERAPY IN A POROUS MEDIUM

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Abstract. This work examines the theoretical analysis of the nonlinear thermal radiation therapy that involves microwave heating of the hyperthermia tumor cell. The heat transfer is carried out in a porous medium and is time dependent. Non-dimensionalized variables and quantities were used as the main modeled equations alongside the Dirichlet boundary conditions for physical interpretation. The dimensionless equation accurately predicts the blood temperature distributions within the tissues, by using stable and unconditional convergent finite difference of semi-implicit type. Tumor cells death occurred due to increased cells sensitivity to non-linear thermal radiation and blood flow emanating from the hyperthermia treatment. The results showed that applying high metabolic heat of $3.97X10^5 Wm^{-3}$ on tumor cells have a therapeutic effect.

Keywords: hyperthermia treatment; bioheat transfer; breast cancer; radiation; biological tissue.

2010 AMS Subject Classification: 65M06, 65M50,65M60, 74F10,80A32.

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1. INTRODUCTION

Cancer is a multifaceted life threatening disease that affects millions of people worldwide. Cancer can be caused by both internal (DNA damage, hormone imbalance) and external factors (tobacco smoking, alcohol consumption, carcinogenic substances) Oke *et al.* [2]. According to World Health Organisation (WHO), cancer is the second and leading cause of morbidity in both developing and developed countries. Tumor cells result from dysfunctional and unregulated cell division and can become malignant or metastasize to other areas of the body thereby making them evasive to treatment [4]. The most prevalent cancer toes, in millions, globally includes; lung (2.09 million cases), colorectal (1.80 million cases), prostate (1.28 million cases), skin (1.04 million cases), stomach (1.03 million cases) and breast (2.09 million cases) cancer [3]. Several factors are known to predispose females to breast cancer, among which is hormonal imbalance for most breast cancer cases [5]. Several mathematical models have evolved to study the effect of high heat and blood perfusion in living tissues after the introduction of ”pennes” bioheat equation over decades ago [6]. The equation was used by Lopez *et al* to evaluate tissue temperature during microwave ablation of breast cancer therapy. This experiment was validated when temperature was calculated in an ex-vivo swine breast tissue and in a breast phantom while using dielectric properties similar to human tissues [7]. Although this equation has been widely accepted and used for various biological and medical applications, the major weakness has been the use of assumptions. For instance, its assumption of uniform perfusion rate, without considering the direction of blood flow as well as anatomical and physiological features of the circulatory network system [7]. Nakayama and kuwahara used the modified two-equation bioheat model in a local non-equilibrium condition to incorporate blood perfusion term within two sub-volume equations for the vascular and extravascular space [8]. Hyperthermia is the administration of different heat sources, such as radio-frequency, microwave, magnetically excitable thermo-seeds, and infra-radiation by oncologists to treat benign and malignant tumors xu et al[9]. Besides chemotherapy and surgery, hyperthermia is another clinical approach to for cancer treatment. Hyperthemia employs the use of high heat[upto 45^0C] that destroys tumor cells but causes minimal damage to normal tissues van der Zee [12]. Habash *et al.* [10,11] studied temperature level and time duration of hyperthermia therapy.

According to Yang *et al.* [13] the modified Pennes biostat equation gave a more accurate prediction of tissue temperature when used to ascertain tissue temperature during an ex-vivo microwave ablation in bovine liver. Furthermore, Bhownik *et al.* [14], postulated that heat transfer in multilayer tissue requires multiple mechanism involving conduction, convection, blood perfusion and diffusion in micro-vascular cells. In general, there are three fundamental bioheat transfer models such as Pennes bioheat transfer model [6], thermal wave bioheat transfer model [15,16] and dual phase-lag bioheat transfer model, Tzou [17]. The mechanism of heat decomposition and consequently, increase in temperature in biological tissues during microwave heating was considered by Adegbile *et al.* [18]. Microwaves have been found useful in medical therapy as a means of heat deposition in hyperthermic treatment [19]. It was discovered and reported that tumor cells are destroyed through heat deposition in tissue at a given time.

Many researchers like [19-22] have carried out investigation on hyperthermia therapy. In their studies, the effect of surface cooling and blood flow on the temperature distribution of tissues during microwave heating was examined. Kritikos *et al.* [21] investigated the differential temperature rise in a spherical region, stimulating a potential hot-spot in a central region of the head. Fourier transform method was used to solve the problem and the result shows that the temperature rise for a large man's head is small. Hill and Pincombe [19] reported on similarity temperature profiles for microwave heating of a half space and power law exponential micro physical property. In the mathematical formulation, the differential equation was solved numerically to obtain the solution to the transient state problems. Furthermore, El-dabe *et al.* [23] discussed the thermal state of the biological tissue when incident with microwaves. The study considered one dimensional multilayer model and analyzed it using Maxwell equations coupled with bioheat model. Adegbile and Ogunmoyela [24] examined the effect of spatial and temperature dependent blood perfusion on the temperature field of biological tissue during microwave heating. Their solutions revealed the possibility of multiple results when blood perfusion is temperature dependent. Popoola and Ayeni [25] investigated the multiplicity of solutions of a boundary value problem arising from the theory of microwave heating of cancerous tumor. In their study, shooting techniques was used to prescribe an initial gradient results in the existence of a unique solution.

Following the above studies, most of the authors neglected the effect of nonlinear thermal radiative heat flux and permeability of the porous media of the biological tissues. However, the present study is interested in examining the hyperthermia therapy and nonlinear thermal radiative heat flux intensity effects on the tissues with permeability of the porous media. The study is basically done for moderate temperature hyperthermia treatment of cancer in critical situation and characterized analytically to establish a more accurate prediction of blood temperature distributions within the tissues. Checking through the literature, it is worth remarking that the effects of variations in blood heat conductivity, porosity, radiation, heat source and blood perfusion on temperature distribution during microwave heating of hyperthermia therapy is an open question; and hence, this study.

2. MATHEMATICAL FORMULATION

During hyperthermia therapy, the initial body tissue is considered to have a temperature $T_0 = 37^0C$ is heated by some external heat source. The mechanism of the living tissues heat transport involves a combination of metabolic heat generation, tissues heat conduction, blood perfusion and convection. Taking the local heat equilibrium (between tissue and blood), Pennes [6] presented a model for the blood arterial temperature, which remain the same all through the tissue, while the local tissue temperature is equal to the temperature of the blood venous. Follow from [23], the heat equation is expressed as

$$\rho_b C_{pb}\frac{\partial \bar{T}}{\partial \bar{t}} = K_b\frac{\partial^2 \bar{T}^2}{\partial \bar{y}^2} + \omega_b\rho_b C_b\left(T_b - \bar{T}\right) + Q\left(\bar{T}\right)|E|^2. \tag{1}$$

Additionally, the benefit of considering the theory of porous media in bioheat transport formulation is as a result of some assumptions, as related to different formulated bioheat transfer models reported in [2,26,27]. Hence, the one-dimensional transient radiative heat balance equation to the study takes the form:

$$\rho_b C_{pb}\frac{\partial \bar{T}}{\partial \bar{t}} = \frac{\varepsilon}{k} + K_b\frac{\partial^2 \bar{T}}{\partial \bar{y}^2} - \frac{\partial q}{\partial \bar{y}} + Q_m\left(\bar{T} - T_0\right) + \omega_b\rho_b C_b\left(T_b - \bar{T}\right). \tag{2}$$

Subject to the following boundary conditions:

$$\bar{T}(\bar{y},0) = 37^0C, \qquad \bar{T}(0,\bar{t}) = 37^0C, \qquad \bar{T}(a,\bar{t}) = 45^0C. \tag{3}$$

From figure 1, the hyperthermia is grouped into three categories, which are (i) long term low hyperthermia temperature ($T \leq 41^0C$ for 6-72hrs), (ii) moderate hyperthermia temperature ($41 < T < 46^0C$ for 15-60 mins) and (iii) thermal ablation or high hyperthermia temperature ($T \geq 46^0C$ for 4-6 mins). Thermo-therapy depends on the heat volumetric intensity source to various hyperthermia kinds. The site of tumor cells determines the types of hyperthermia to be used whether regional hyperthermia, localized hyperthermia or whole body hyperthermia (WBH) in the therapeutic clinical application to treat the tumor cells [10,11,28]. For localized hyperthermia, high temperature is required during the treatment of small area where the cancer cells are located in the body. In regional hyperthermia, the therapy is applied to the large area of the whole tissues or organ but in whole body hyperthermia, the therapy is applied with a special technique to treat metastatic cancerous cells when it spreads throughout the body.

Using Rosseland diffusion approximation for radiation [29-31, 35]

$$q = \frac{-4\sigma}{3\delta}\frac{\partial T^4}{\partial \bar{y}} = -\frac{4\sigma}{3\delta}(T \times T \times T \times T), \tag{4}$$

Here, δ is the mean coefficient absorption and σ is constant Boltzmann-Stefan. For radiative heating of hyperthermia, the heat radiation is absorbed or scattered after a short moves. A diffusion term is introduced into the energy equation (4), which was formulated according to the energy conservation theory. It is taken that the heat variation in the blood flow is not sufficiently small. Hence, Taylor series expansion and simplification of heat flux radiation by T^4 about T_0 may not be realistic. Therefore, implicit differentiation will be used for the simplification of equation (4), which is then introduced in the energy equation (2). The energy modified equation becomes

$$\rho_b C_{pb}\frac{\partial \bar{T}}{\partial \bar{t}} = K_b\frac{\partial^2 \bar{T}}{\partial \bar{y}^2} - \frac{\partial}{\partial \bar{y}}\left(-\frac{4\sigma}{3\delta}4\bar{T}^3\frac{\partial \bar{T}}{\partial \bar{y}}\right) + \frac{\varepsilon}{k} + \omega_b\rho_b C_b(T_b - \bar{T}) + Q_m(\bar{T} - T_0). \tag{5}$$

The radiation term in equation (5) when divided by heat capacity C_{pb} and differentiated becomes

$$\frac{\partial}{\partial \bar{y}}\left(\frac{4\sigma}{3\delta}4\bar{T}^3\frac{\partial \bar{T}}{\partial \bar{y}}\right) = \frac{16\sigma}{3\delta}\bar{T}^3\frac{\partial^2 \bar{T}}{\partial \bar{y}^2} + \frac{16\sigma}{3\delta}\frac{\partial \bar{T}}{\partial \bar{y}}\frac{\partial \bar{T}^3}{\partial \bar{y}}. \tag{6}$$

Therefore, equation (5) takes the form

$$\rho_b C_{pb}\frac{\partial \bar{T}}{\partial \bar{t}} = K_b\frac{\partial^2 \bar{T}}{\partial \bar{y}^2} + \frac{16\sigma}{3\delta}\bar{T}^3\frac{\partial^2 \bar{T}}{\partial \bar{y}^2} + \frac{16\sigma}{3\delta}\frac{\partial \bar{T}}{\partial \bar{y}}\frac{\partial \bar{T}^3}{\partial \bar{y}} + \frac{\varepsilon}{k} + \omega_b\rho_b C_b(T_b - \bar{T}) + Q_m(\bar{T} - T_0). \tag{7}$$

Meanwhile, considering $\theta = \frac{\bar{T}-T_0}{T_b-T_0}$,

It is essential to note that θ could not be successfully used for the parametrize and non-dimensionalize $\bar{T}^3$ and $\frac{\partial \bar{T}^3}{\partial \bar{y}}$ in the thermal radiation. We shall now proceed to simplify, parametrize and non-dimensionalize the term without using Taylor series expansion.

Hence, by simplification, $\theta = \frac{\bar{T}-T_0}{T_b-T_0} \Longrightarrow \bar{T} = [\theta(\theta_w - 1)+1]T_0$ such that $\theta_w = \frac{T_b}{T_0}$.

The following variables and quantities are then introduced into equation (7)

$$y = \frac{\bar{y}}{a},\ t = \frac{\bar{t}}{a^2},\ \theta = \frac{(\bar{T}-T_0)}{(T_b-T_0)},\ \bar{T} = [\theta(\theta_w-1)+1]T_0,\ \theta_w = \frac{T_b}{T_0}. \tag{8}$$

Substituting the quantities of equation (8) into equations (3) and (7) to obtain

$$\frac{\partial \theta}{\partial t} = \alpha\frac{\partial^2\theta}{\partial y^2} + \frac{1}{R}\left([\theta(\theta_w-1)+1)^3\frac{\partial^2\theta}{\partial y^2} + \frac{3}{R}[1+(\theta_w-1)\theta]^2(\theta_w-1)\frac{\partial\theta}{\partial y}\frac{\partial\theta}{\partial y} - (\gamma-\lambda)\theta + (\beta+\gamma),\right. \tag{9}$$

The corresponding boundary conditions becomes

$$\theta(y,0) = 37^0C, \qquad \theta(0,t) = 37^0C, \qquad \theta(1,t) = 45^0C, \tag{10}$$

where $\alpha = \frac{K_b}{\rho_b C_{pb}}, \beta = \frac{a^2\varepsilon}{k\rho_b C_{pb}(T_b-T_0)}, \gamma = a^2\omega_b, \lambda = \frac{a^2 Q_m}{\rho_b C_{pb}}$, and $R = \frac{4\sigma T_b^3}{\delta K_b}$ are the dimensionless parameters.

3. MAIN RESULTS

The unsteady state solution for equation (9) together with equation (10) are obtained using a numerical method. The numerical scheme used for the radiative microwave hyperthermia therapy equation is the finite difference of semi-implicit technique as in [32-34]. At time level of intermediary, the method assumes an implicit terms $(\xi + N)$ in [0,1]. To take a several time step, ξ is assumed a value of 1. In fact, for the complete implicit, the computational technique used in this study is taken to be applicable for any time steps estimate. The discretarization of the equation is done on a linear mesh Cartesian with unvarying grid on which the finite differences are defined. Spatial derivatives of the first and second is approximated with the second order central differences, the conformation equation to the grids point are employed for the boundary conditions integration. The semi-implicit method for the hyperthermia component is expressed as:

(11)
$$\frac{(\theta^{(N+1)}-\theta^{(N)})}{\Delta t}=\alpha\theta_{yy}^{(N+\xi)}+\frac{1}{R}\left(([\theta(\theta_w-1)]+1)^3\right)^{(N)}\theta_{yy}^{(N+\xi)}-(\gamma-\lambda)\theta^{(N)}+(\beta+\gamma)+$$
$$\frac{3}{R}(\theta_w-1)\left([1+(\theta_w-1)\theta]^2\theta_y\theta_y\right)^{(N)}.$$

The equation for $\theta^{(N+1)}$ gives:

(12)
$$-r\theta_{j-1}^{N+1}+(1+2r+\varphi\Delta t)\theta_j^{N+1}-r\theta_{j+1}^{N+1}=\alpha\left(\theta^{(N)}+\Delta t(1-\xi)\theta_{yy}^{(N)}\right)-\Delta t(\gamma-\lambda)\theta^{(N)}+$$
$$\frac{1}{R}\Delta t(1-\xi)\left(([\theta(\theta_w-1)+1)^3\right)^{(N)}\theta_{yy}^{(N)}+\frac{3}{R}\Delta t(1-\xi)(\theta_w-1)\left([1+(\theta_w-1)\theta]^2\theta_y\theta_y\right)^{(N)}$$
$$+\Delta t(\beta+\gamma),$$

where $r=\xi\Delta t/\Delta y^2$ and all time derivatives finite difference forward technique are taken. The method of solution for $\theta^{(N+1)}$ diminishes to the inverse tri-diagonal matrices.

The method was checked for consistence when $\xi=1$ to encourage huge time steps consideration that is of order 1 in time precise and order 2 in space. As firstly taken, the values of time step is satisfied by the method. The analysis is done with the aid of Maple 18 software.

4. Results and Discussion

A transient single-dimensional multilayer bioheat for temperatures prediction in living biological tissue during microwave heating has been investigated using numerical scheme of solution after a linearization. The computational analysis has been made by using MAPLE 18 software and the figures depicting the results are conferred. The thermophysical typical characteristics of heat transport in biological tissue with tissue metabolic heat source and boundary conditions are examined. The following reference parameters value inline with the related studies are used in finite domain to compute the heat distribution in the tissues: $C_{pb}=3500JKg^{-1}K^{-1}, \rho_b=1060Kgm^{-3}, T_0=37^0C, \omega_b=0.00125Kgs^{-1}, K_b=0.24Wm^{-1}K^{-1}$ and $T_b=45^0C$ [11,13]. The finer even mesh for the unsteady solutions takes ($\Delta y=0.0001$ with $\Delta t=0.001$) are display in Fig 2a. The Figure portray a transient rises in the heat distribution until it reaches a steady state. Fig 2b illustrate the time of obtaining steady state heat distribution for various values of terms. That is, the state of achieving no difference in the temperature

distribution, the maximum temperature is recorded at $\theta_{max} = 44.977$.

Figures 3a and 3b depict the impact of variation in the values of the heat conductivity on the temperature distributions. It is seen that a rise in the thermal conductivity value increases the heat distribution in the system when $\lambda = 0.5$ but decreases when the value of $\lambda = 2$. This is because an increase in α causes a rise in the thickness of energy boundary layer when $\lambda = 0.5$ and thereby increase the average temperature within the tissue but at $\lambda = 2$ the thermal layers get thinner and heat is able to diffuse away from the heated surface. Figures 3c and 3d depict the response of porosity parameters β on the temperature fields. It is noticed that the temperature distributions rises as the porosity term is enhanced $\lambda = 0.5$ minimum and $\lambda = 2$ maximum value occurred. The reason for this behaviour is that the porosity term enhances heat distribution which in turn provides an additional support to the blood flow in the tissue. An increase in the temperature distribution leads to fast destroying of tumor cell and in turn encourages the hyperthermia tumor cells therapy.

The effect of radiation parameter R on the temperature profiles is shown in Figures 4a and 4b. It is noticed from the figures that a rise in the radiation term the microwave temperature that is directed towards the tumor cells. Whenever there is increase in λ the rate of microwave heating reduces thereby decreases hyperthermia tumor cells therapy. It is seen that as the value of R increases, there is corresponding increase in the temperature profiles at $\lambda = 0.5$ and $\lambda = 1$ this due to an increase in the rate at which heat gets to the tumor cell. As a result, the therapy improve recovery as the tumor cell get destroyed. Figures 4c and 4d illustrate the variation in the temperature field in relation to the blood perfusion parameter γ. Figure 4c is linear in nature especially when $\lambda = 0.5$ and maximum temperature is obtained as γ increases. However, it simply means increase in the blood perfusion rate causes an increase in the temperature of the biological tissue at $\lambda = 0.5$ and $\lambda = 1$. Hence, the hyperthermia tumor cells therapy is improved.

Figures 5a and 5b denote the influence of variational increase in the metabolic heat source λ on the heat field. Metabolic heat generation in the tissue is utilized for active heat transfer via membrane pumps, chemical reaction requiring energy, such as muscular work, glucose glycogen formation and amino acid proteins production. Almost all metallic energy utilized in these

processes is transformed into heat in the biological tissue. It is seen that enhancing the values of λ increases the heat field at $\alpha = 2$ and $\gamma = 0.004$, which results in the death of cancerous cells and the enhancement of the hyperthermia tumor cells therapy.

5. CONCLUSION

Radiative microwave heating presents a new way to treat cancerous tumors by hyperthermia with minimal or no damage to surrounding tissues, by using Pennes' bioheat model to compute the energy distribution, due to the model simplicity. However, its major setback is that it does not account for the blood flow direction due to the non-directional perfusion term in its model. The porosity and permeability in this case describe the tissue direction of blood flow, but it needs a reasonable amount of heat through a porous medium. The different values of λ significantly affected the heat field at the targeted area of the tumor cell during treatment as well as radiative heat flux in the prediction and control of heat at targeted area in treatment process of tumor cells. As the values of heat source metabolic parameter is enhanced, the heat at targeted region is also encouraged, thus, helping the therapy treatment process. The boundary conditions influence on the energy transfer profile is reflected on the thermal conductivity with the outer surface high heat that is being influenced by the cooling pad.

Finally, rigorous mathematical analysis can help in controlling heat during hyperthermia treatment. Therefore, it is believed that hyperthermia treatment, based on radiative microwave heating of bioheat transfer model, is essential in clinical or medical practice and Oncologist expert should embrace it for alternative treatment because it is affordable.

Conflict of Interests

The author(s) declare that there is no conflict of interests.

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Nomenclature

$\rho_b =$**:** Density of blood, $\left(Kgm^{-3}\right)$

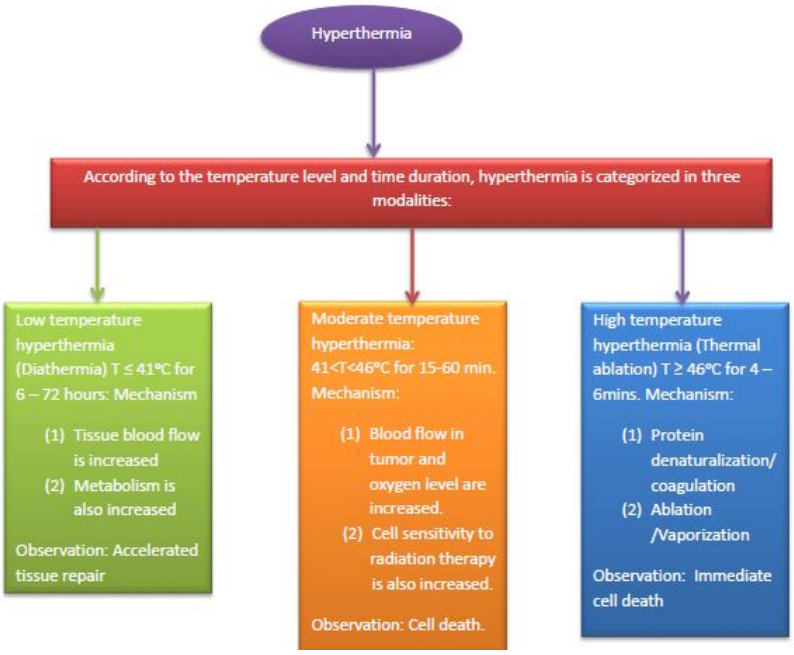


FIGURE 1. **Types of the hyperthermia [14]**

C_{pb} =: Specific heat at constant pressure, $\left(JKg^{-1}\,(^oC)^{-1}\right)$

K_b =: Blood heat conductivity, $\left(Wm^{-1}K^{-1}\right)$

ω_b =: Rate of blood perfusion volumetric $\left(Kgs^{-1}\right)$

T_b =: Blood arterial temperature, (^oC)

T =: Local tissue temperature, (^oC)

k =: Permeability of the medium

ε =: Tissue Porosity term

T_o =: Reference temperature, $(T_b > T_o)$ (^oC)

Q_m =: Tissue metabolic heat source, $\left(Wm^{-3}\right)$

q =: Radiative heat flux, $\left(Wm^{-2}\right)$

R =: Radiation parameters

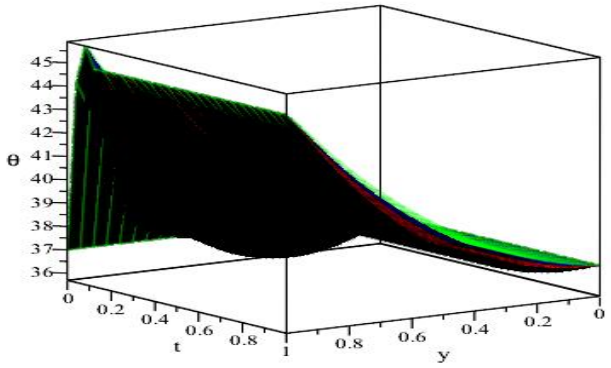
y =: space coordinate, (m)

t =: time, (s)

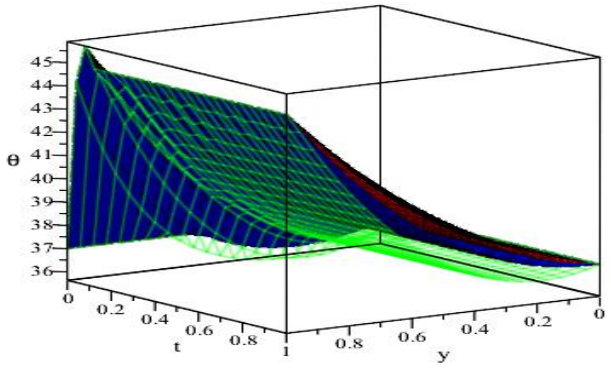
α =: Blood thermal conductivity terms

β =: Porosity parameters

γ =: Blood perfusion rate terms



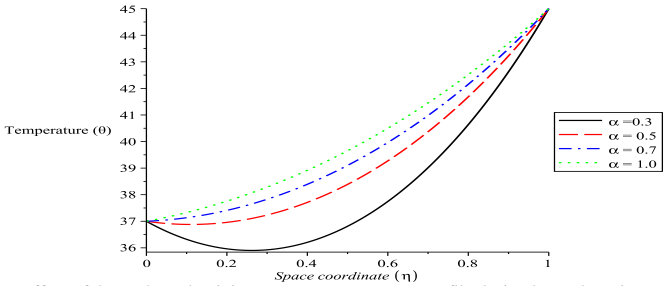
(a)



(b)

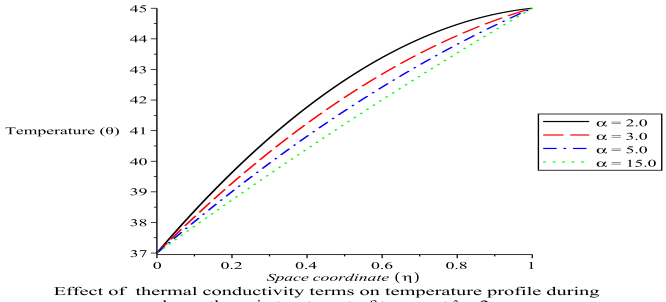
FIGURE 2. **Transient and steady state temperature profiles**

$\lambda =$**:** Heat source terms



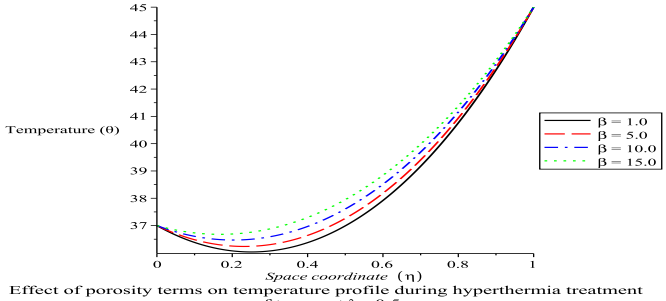
Effect of thermal conductivity terms on temperature profile during hyperthermia treatment of tumor at λ= 0.5

(a)



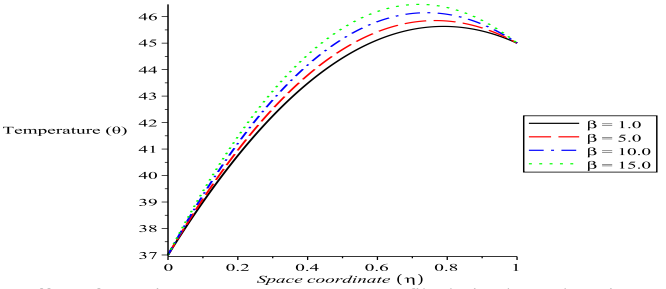
Effect of thermal conductivity terms on temperature profile during hyperthermia treatment of tumor at λ= 2

(b)



Effect of porosity terms on temperature profile during hyperthermia treatment of tumor at λ= 0.5

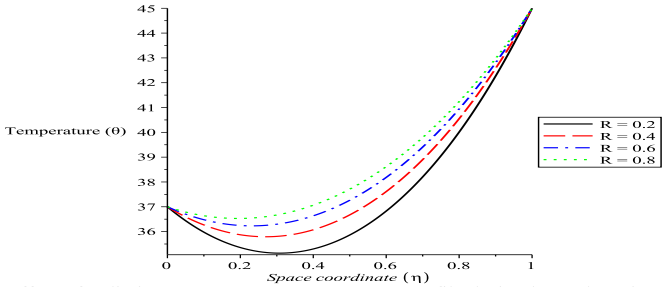
(c)



Effect of porosity terms on temperature profile during hyperthermia treatment of tumor at λ= 2

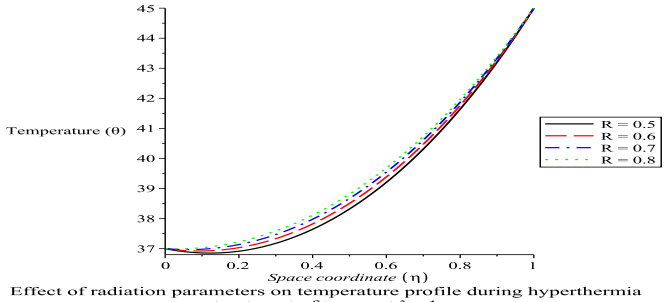
(d)

FIGURE 3. **The effects of blood thermal conductivity and porosity on temperature profiles**



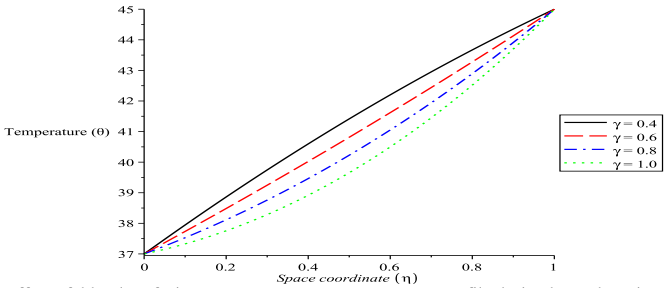
Effect of radiation parameters on temperature profile during hyperthermia treatment of tumor at λ= 0.5

(a)



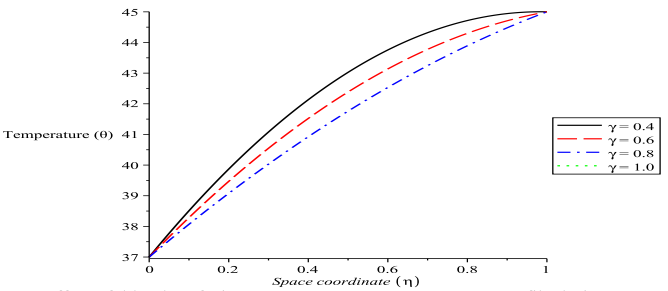
Effect of radiation parameters on temperature profile during hyperthermia treatment of tumor at λ= 1

(b)



Effect of blood perfusion rate parameters on temperature profile during hyperthermia treatment of tumor at λ= 0.5

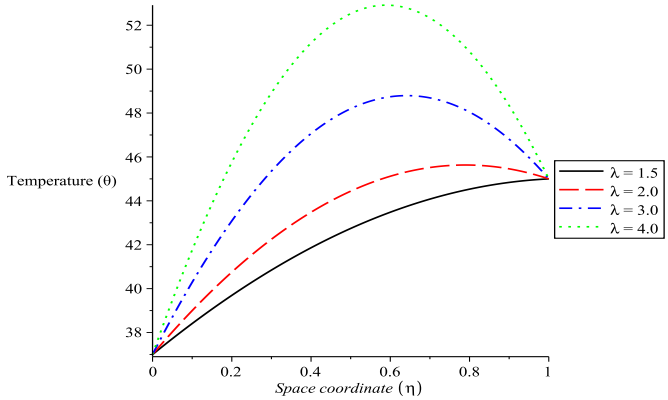
(c)



Effect of blood perfusion rate parameters on temperature profile during hyperthermia treatment of tumor at λ= 1

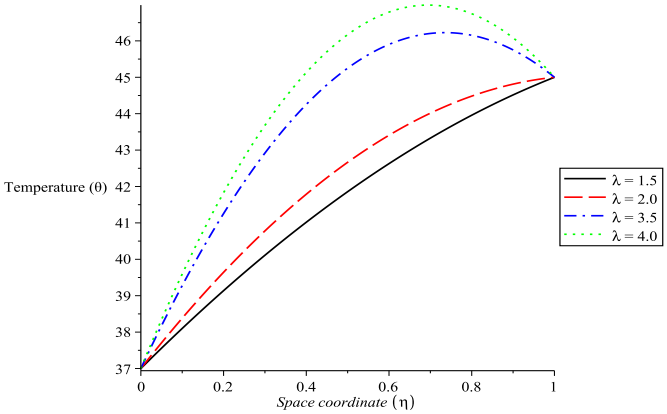
(d)

FIGURE 4. **The effects of radiation parameters and blood perfusion on temperature profiles**



Effect of heat source terms on temperature profile during hyperthermia treatment of tumor with default parameter values

(a)



Effect of heat source terms on temperature profile during hyperthermia treatment of tumor at α = 2

(b)

FIGURE 5. **The effects of heat source on temperature profiles**

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