HYBRID ANALYTICAL NUMERICAL SOLUTION TO THE BIOHEAT TRANSFER EQUATION

A. V. Presgrave, R. O. C. Guedes, F. Scofano Neto
Departamento de Engenharia Mecânica e de Materiais
Instituto Militar de Engenharia
Praça General Tibúrcio 80
Rio de Janeiro, RJ, 22290-270
scofano@ime.eb.br

Abstract. *The bioheat transfer problem can be defined as the effect of blood flow on heat transfer in living tissue. Such physical situations have been examined for a long time but since direct measurements are extremely difficult to carry, there is a natural preference for mathematical models to study this phenomenon. The most commonly employed model for heat transfer within an organic tissue taking into account blood flow effects is the so-called Pennes bioheat equation. From a mathematical point of view, the Pennes model can be regarded as a standard heat diffusion equation together with an extra term that accounts for blood perfusion within the tissue. The main contribution of this work is to establish an analytical-numerical solution of a generalized bioheat transfer transient problem that accounts for a temperature dependent perfusion effect. This general solution is then applied to a specific situation related to the thermal balloon endometrial ablation treatment which is a modern and efficient medical procedure used in menorraghia therapy. The Generalized Integral Transform Technique is employed to analytically tackle the bioheat transfer equation. Finally, results are presented and compared to previously published data in the literature .*

Keywords*: bioheat, Pennes model, blood perfusion effect, eigenfuction expansion.*

1. Introduction

A series of modern procedures in medicine such as cancer treatments by hyperthermia, refractive surgeries employing lasers and cryosurgery based interventions for the cure of benign prostate hyperplasia, are fundamentally dependent on a previous knowledge of the temperature distribution of the affected tissues. Due to the difficulties of a direct temperature measurement in living tissues, the determination and the solution of the mathematical models for such bioheat transfer problems are desirable. A distinguishing feature of this particular form of heat transfer process is to assess the influence of the local blood perfusion through the vascular network on the temperature distribution. In many physiological processes, such as human thermoregulation and inflammation, a significant temperature difference is found between the tissue and the blood through which it flows and thus convective heat transfer occurs altering the temperature of both the tissue and the blood. As pointed out by Diller and Ryan (1998), this interaction relies on various parameters including the rate of perfusion and the vascular anatomy and pathology. The accurate determination of the rate of blood perfusion in a certain organic tissue is quite an involved matter as it is affected by many a series of effects such as physical activity, physiological stimulus and environmental conditions and over the years, numerous techniques have been established in order to carefully evaluate this parameter.

It is commonly agreed that the first work that describes the thermal interaction between an organic perfused tissue was advanced almost 60 years ago by Pennes (1948). Its main objective was to experimentally determine the radial temperature distribution in the forearm of nine unanesthetized human subjects. In his observations, Pennes noticed a temperature difference of three to four degrees between the skin and the interior of the arm, which he attributed to the effects of metabolism and to the heat transfer with the arterial blood perfused through the microvasculature. He then proposed a simple model to describe these two effects which were incorporated into the standard thermal diffusion equation. Over the years, alternative and more elaborate models that account for effects of vessel size, countercurrent heat exchange, combination of partial countercurrent exchange and bleed-off perfusion were proposed to describe the blood and tissue thermal interaction, Hartnett and Irvine (1992). However, it is interesting to notice while these more sophisticated models provide a larger depth in the analysis, they lack the generality and simplicity of the Pennes model. Therefore, it is no surprise that up to this day, this model is widely employed in bioheat transfer predictions (Azevedo, 2004, Presgrave, 2005, Chan, 1991).

2. Analysis

The Pennes bioheat equation mentioned earlier, can be described as an energy balance that takes into account the effects of the metabolism and the blood perfusion in an organic tissue. Thus, the transient temperature field of the tissue can be generally described as:

$$\rho C \frac{\partial T}{\partial t} = \nabla \bullet \left(k \nabla T \right) + q_{met} + q_{ext} + q_{per} \tag{1}$$

The first term on the right hand side of Eq.(1) is immediately recognized as the familiar heat diffusion term in the tissue. The next term, q_{met}, is the metabolic heat transfer rate per unit volume of tissue while q_{ext} is an external heat source which, for example, can be present in a case of microwave heat treatment. The last term, q_{per}, is the heat transfer rate per unit volume of tissue due to blood perfusion. Based on his own experimental evidence, Pennes (1948) stated that the thermal impact of the blood flow could be characterized by introducing an energy sink term which is proportional to the volumetric perfusion level, ω_b, and the difference between the local tissue temperature and that of the arterial blood, $\left(T - T_b \right)$ in such a way that:

$$q_{per} = -\rho_b C_b \varpi_b \left(T - T_b \right) \tag{2}$$

Accordingly, this analysis starts out by considering a sufficiently generalized two variable bioheat equation together with its appropriate boundary and initial conditions. Therefore, the problem to be analyzed is described as follows:

$$w(x) \frac{\partial T(x,t)}{\partial t} = \frac{\partial}{\partial x} \left[k(x) \frac{\partial T(x,t)}{\partial x} \right] - d(T) T(x,t) + P(x,t) , \quad x_0 < x < x_1 , \; t > 0 \tag{3}$$

$$T(x,0) = f(x) , \; x_0 \le x \le x_1 \tag{4}$$

$$\alpha_0 T(x_0,t) - \beta_0 k(x_0) \frac{\partial T(x_0,t)}{\partial x} = \phi_0(t) , \; t > 0 , \; \alpha_1 T(x_1,t) + \beta_1 k(x_1) \frac{\partial T(x_1,t)}{\partial x} = \phi_1(t) , \; t > 0 \tag{5,6}$$

An inspection of the above formulation reveals that a good variety of physical problems in bioheat transfer can be obtained by setting appropriate values to functions *w(x)*, *k(x)*, *d(T)*, *f(x)*, $\phi_0(t)$, $\phi_1(t)$ and to coefficients α_0, α_1, β_0 and β_1. Also, it is worth mentioning that in Eq. (3) the classical Pennes formulation is slightly modified in order to incorporate a temperature dependent perfusion coefficient , which is represented in the generic term $d(T)\,T(x,t)$.

The basic idea regarding the application of the Generalized Integral Transform Technique (Cotta 1993, Cotta 1998) is to express the potential *T(x,t)* as an eigenfuction expansion in the form:

$$T(x,t) = \sum_{i=1}^{\infty} A_i(t) \psi_i(x) \tag{7}$$

The auxiliary problem related to the determination of the eigenfunctions $\psi_i(x)$ is chosen to be:

$$\frac{d}{dx} \left[k(x) \frac{d\psi_i(x)}{dx} \right] + \mu_i^2 w(x) \psi_i(x) = 0 , \; x_0 < x < x_1 \tag{8}$$

$$\alpha_0 \psi_i(x_0) - \beta_0 k(x_0) \frac{d\psi_i(x_0)}{dx} = 0 , \; \alpha_1 \psi_i(x_1) + \beta_1 k(x_1) \frac{d\psi_i(x_1)}{dx} = 0 \tag{9,10}$$

Equation (8) together with its two boundary conditions is immediately recognized as a standard Sturm-Liouville problem and efficient algorithms, such as the “sign-count” method (Mikhailov and Ozisik, 1984), can be utilized in order to precisely evaluate the eigenvalues μ_i, its related eigenfuctions $\psi_i(x)$ and other desired eigenquantities such as, for example, the norm N_i. Furthermore, by applying the well established orthogonality property of this classical eigenvalue problem, it is possible to determine $A_i(t)$ such as:

$$A_i(t) = \frac{1}{N_i} \int_{x_0}^{x_1} w(x) \psi_i(x) T(x,t) dx \tag{11}$$

By inserting the above result in Eq. (7), it is a simple matter to determine the following inverse-transform pair :

$$\overline{T_i}(t) = \frac{1}{N_i^{1/2}} \int_{x_0}^{x_1} w(x)\psi_i(x)T(x,t)dx \;,\; T(x,t) = \sum_{i=1}^{\infty} \frac{1}{N_i^{1/2}} \psi_i(x)\overline{T_i}(t) \tag{12,13}$$

The next step is to rewrite the original problem in terms of the transformed potential $\overline{T_i}(t)$. This task is accomplished through a series of mathematical operations which are briefly discussed now. Initially, the governing partial differential equation is operated on with $\frac{1}{N_i^{1/2}} \int_{x_0}^{x_1} \psi_i(x)\, dx$. Secondly, the Sturm-Liouville equation is multiplied by $\frac{1}{N_i^{1/2}} \int_{x_0}^{x_1} \theta(x,t)\, dx$ .These results are added and the boundary conditions of both the original and auxiliary problems are employed to furnish:

$$\frac{d\overline{T_i}(t)}{dt} + \mu_i^2 \overline{T_i}(t) = \overline{g_i}(t) - \frac{1}{N_i^{1/2}} \int_{x_0}^{x_1} d(T)\psi_i(x)T(x,t)dx \tag{14}$$

The first term on the right-hand side of the above formulation is related to the non-homogeneous terms that are present in the boundary condition and in the source term of the generalized bioheat equation. Thus

$$\overline{g_i}(t) = \Omega_{1i}\phi_1(t) + \Omega_{0i}\phi_0(t) + \overline{P_i}(t) \tag{15}$$

where the coefficients Ω_{0i} and Ω_{1i} together with the transformed source term $\overline{P_i}(t)$ are given by

$$\Omega_{1i} = \frac{1}{N_i^{1/2}} \left[\frac{\psi_i(x_1) - k(x_1)\dfrac{d\psi_i(x_1)}{dx}}{\alpha_1 + \beta_1} \right],\; \Omega_{0i} = \frac{1}{N_i^{1/2}} \left[\frac{\psi_i(x_0) + k(x_0)\dfrac{d\psi_i(x_0)}{dx}}{\alpha_0 + \beta_0} \right] \tag{16,17}$$

$$\overline{P_i}(t) = \frac{1}{N_i^{1/2}} \int_{x_0}^{x_1} \psi_i(x)P(x,t)dx \tag{18}$$

Clearly, no further generalization is possible without prescribing the functional relationship between the perfusion term and the temperature field. Here, in accordance with Rai *et al*. (1999a, 1999b), we assume that the blood perfusion and the temperature field are linked in the form:

$$d(T) = d_0(x) + d_1(T) = d_0(x) + \gamma\, T(x,t) \tag{19}$$

Inserting the above result in Eq. (14) and making use of the transform relation, Eq(13), we have:

$$\frac{d\overline{T_i}(t)}{dt} + \mu_i^2 \overline{T_i}(t) = \overline{g_i}(t) - \sum_{j=1}^{\infty} A_{ij}\overline{T_j}(t) - \gamma \sum_{j=1}^{\infty} \sum_{k=1}^{\infty} B_{ijk}\overline{T_j}(t)\overline{T_k}(t) \tag{20}$$

where coefficients A_{ij} and B_{ijk} are given by:

$$A_{ij} = \frac{1}{N_i^{1/2}} \frac{1}{N_j^{1/2}} \int_{x_0}^{x_1} d_0(x)\psi_i(x)\psi_j(x)dx \;,\; B_{ijk} = \frac{1}{N_i^{1/2}} \frac{1}{N_j^{1/2}} \frac{1}{N_k^{1/2}} \int_{x_0}^{x_1} \psi_i(x)\psi_j(x)\psi_k(x)dx \tag{21,22}$$

The formulation is completed by transforming the initial condition of the original problem, Eq(4). This is easily accomplished by making use of relation (12) which yields:

$$\overline{T}_i(0) = \frac{1}{N_i^{1/2}} \int_{x_0}^{x_1} w(x)\psi_i(x) f(x) dx = \bar{f}_i \tag{23}$$

An inspection of the above system of ordinary differentials equations suggests that a fully analytical solution does not appear to be possible due to the non-linear coupled nature of these equations. Consequently, numerical solutions must be employed to solve the truncated version of system (20). Due to its stiff nature, such equations are better solved by utilizing numerical subroutines such as DGEAR found in the IMSL package (IMSL,1999). Once the solution is determined, the inverse expression is employed to find the transient temperature field.

3. Application, Results and Discussion

The ideas outlined above were tested for a series of physical cases relevant to the bioheat transfer field. Transient temperature distributions in the human skin subjected to an intense heating and the selective cooling for treating an ischemic brain were studied, among other cases. Also, on a more fundamental level, the mathematical aspects of the proposed methodology solution were carefully assessed. Generally speaking, in all the cases considered, the convergence rates of the engenfuction expansions was found to be fast (N < 30) even for situations where the temperature dependent perfusion coefficient was high (Presgrave, 2005).

Here, we illustrate the analysis carried out in the previous section by addressing the endometrial ablation heat transfer problem. This therapy is a highly efficient office-based medical procedure designed to treat menorrhagia, which is a condition associated with excessive menstrual bleeding. Prior to the development of this therapy, dysfunctional bleeding of the uterus was typically treated by hysterectomy, which is a drastic solution involving high costs. The main advantage of endometrial ablation over hysterectomy is a decreased recovery time together with a lack of surgical complications such as wound healing. (Bucksee *et al*, 1998).

The device consists of a latex balloon filled with sterile 5% dextrose in water which is attached to the end of a 16 cm long plastic catheter. This balloon is inserted into the uterus while conforming to the shape of the uterine cavity and the fluid is maintained at a constant pressure, typically in the rage of 160 to 180 mm Hg. A heating element inside the balloon raises the fluid temperature up to an operating value usually around 87 °C and, consequently, heat is transferred to the inside surface of the uterus producing a burn injury. The main purpose of this heating operation is to completely coagulate the endometrium, which is the inner lining of the uterus, and most studies claim that a treatment time of 8 minutes is said to be effective (Baldwin *et al*, 2001).

Thus, it seems that an knowledge of the transient temperature field in the uterus wall is desirable in order to accurately predict the effects of the endometrial ablation therapy. Here, we follow closely the assumptions presented in the mathematical model of Baldwin *et al* (2001). Accordingly, the uterine cavity is taken to be a planar structure which is heated along a single direction. The initial temperature field of the uterus is assumed to be uniform and equal to the body core temperature (37 °C), which is also the arterial blood temperature within the tissue, T_b. It is a well–known fact that the uterus wall is composed of three distinct layers, the endometrium (1-4 mm thick), the myometrium (15-24 mm thick) and the serosa (approx. 1 mm thick) but our mathematical model treats the uterus wall as a single layer on the grounds that the thickness of both the endometrium and serosa are very thin compared to that of the myometrium. We also assume that, due to the almost perfect contact of the balloon with the uterus wall, a prescribed temperature situation is achieved and so the temperature of the endometrium layer is assumed to be equal of that of the fluid inside the balloon, $T_{bal} = 87^{\circ}C$. It is interesting to notice that in the study of Baldwin *et al*.(2001) the uterus was treated as a semi-infinite medium. In our present simulations, we substitute this boundary condition with the more realistic assumption that the heat transfer at the serosa layer of the uterus is negligible. With these ideas in mind, the transient temperature field $T(x,t)$ along the uterus wall is assumed to follow the ensuing mathematical model:

$$\rho C \frac{\partial T(x,t)}{\partial t} = k \frac{\partial^2 T(x,t)}{\partial x^2} + \omega_b \rho_b c_b \left(T_b - T(x,t)\right) + q_{met} \quad 0 < x < l\ ,\ t > 0 \tag{24}$$

$$T(x,0) = T_b\ ,\ 0 \le x \le 1 \tag{25}$$

$$\frac{\partial T(0,t)}{\partial x} = 0\ ,\ t > 0\ ,\ T(l,t) = T_{bal}\ ,\ t > 0 \tag{26,27}$$

By taking the dimensionless variables for the temperature field, space position and time

$$\theta = \frac{T - T_{bal}}{T_b - T_{bal}},\ X = \frac{x}{l},\ \tau = \frac{k\,t}{\rho\, C\, l^2} \tag{28,29,30}$$

the problem can be rewritten as follows:

$$\frac{\partial \theta(X,\tau)}{\partial \tau} = \frac{\partial^2 \theta(X,\tau)}{\partial X^2} - P_f \theta(X,\tau) + G\ ,\ 0 < X < 1\ ,\ \tau > 0 \tag{31}$$

$$\theta(X,0) = 1\ ,\ 0 \le X \le 1 \tag{32}$$

$$\frac{\partial \theta(0,\tau)}{\partial X} = 0\ ,\ \tau > 0\ ,\ \theta(1,\tau) = 0\ ,\ \tau > 0 \tag{33,34}$$

where P_f and G are respectively the dimensionless perfusion coefficient and metabolic rate:

$$P_f = \frac{\rho_b C_b \omega_b l^2}{k},\ G = \frac{q_{met} l^2}{k\left(T_b - T_{bal}\right)} + P_f \tag{35,36}$$

This present formulation is a special case of the more general problem discussed in the previous section. Thus, the inversion-transform pair is immediately found to be:

$$\overline{\theta}_i(t) = \frac{1}{N_i^{1/2}} \int_0^1 w(X) \psi_i(X) T(X,\tau) dX\ ,\ \theta(X,\tau) = \sum_{i=1}^{\infty} \frac{1}{N_i^{1/2}} \psi_i(X) \overline{\theta}_i(\tau) \tag{37,38}$$

while the auxiliary eigenvalue problem is taken as:

$$\frac{d^2 \psi_i(X)}{dX^2} + \mu_i^2 \psi_i(X) = 0\ ,\ 0 < X < 1 \tag{39}$$

$$\frac{d\psi_i(0)}{dX} = 0\ ,\ \psi_i(1) = 0 \tag{40,41}$$

The system of ordinary differential equations for the transformed temperature field together with its initial conditions is:

$$\frac{d\overline{\theta}_i(\tau)}{d\tau} + \left(\mu_i^2 + P_f\right)\overline{\theta}_i(\tau) = G\ \bar{f}_i \tag{42}$$

$$\overline{\theta}_i(0) = \frac{1}{N_i^{1/2}} \int_0^1 \psi_i(X) dX = \bar{f}_i \tag{43}$$

Given the particular nature of this problem, a fully analytical solution for the transformed temperature field can be obtained and is given by:

$$\overline{\theta}_i(\tau) = \bar{f}_i\ e^{-\left(\mu_i^2 + P_f\right)\tau} + \frac{G\,\bar{f}_i}{\mu_i^2 + P_f}\left(1 - e^{-\left(\mu_i^2 + P_f\right)\tau}\right) \tag{44}$$

Finally, the application of the inverse relation, Eq. (38) , is used to determine the transient temperature of the uterus wall.

Typical values for the physical parameters necessary for the simulations were employed in order to determine the temperature field (Presgrave, 2005). When dealing with physiological properties, it is expected some variation on an individual basis. Nonetheless, the literature suggests that it is reasonable to adopt invariant values of the density and specific heat of the uterus ($\rho = 1060\, kg/m^3$, $C = 3600\, J/kg\ K$) and the blood ($\rho_b = 1080\, kg/m^3$, $C_b = 3500\, J/kg\ K$).

Also, the thermal conductivity of the uterus exhibits a weak dependence with respect to the temperature and therefore it can also be assumed equal to $k = 0.56 W/m\ ^{\circ}C$. Basically, the blood perfusion rate, ω_b, and the tissue metabolic heat generation, q_{met}, are the two main parameters that exhibit a fairly large fluctuation. It is also naturally expected that the uterus wall thickness varies from patient to patient but the simulations presented here were carried out by considering a fixed mean value of 20 mm. Table (1) shows the relevant dimensional and dimensionless parameters selected for the simulations reported in this contribution.

Table 1. Dimensional and Dimensionless Values for the Endometrial Ablation Problem

$\omega_b \left[m_b^3/m^3\ s\right]$	$q_{met} \left[W/m^3\right]$	P_f	G
0.0	170	0.0000	0.2244
0.0014	170	3.7800	3.7776
0.0028	170	7.5600	7.5576
0.0056	170	15.1200	15.1176
0.0028	0.0	7.5600	7.5600
0.0028	5540	7.5600	7.4809

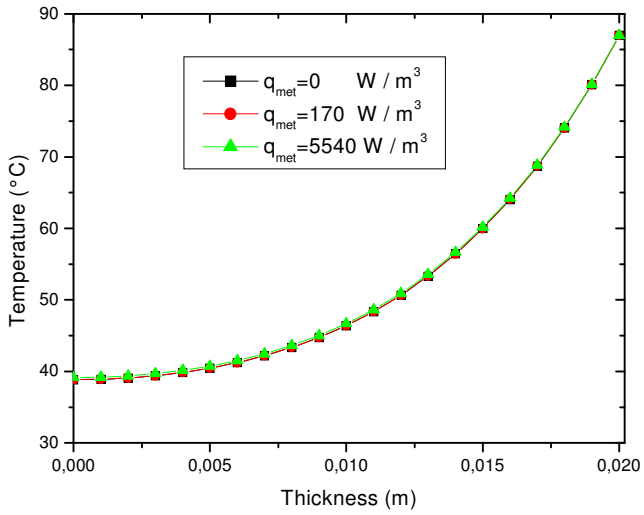

Figure 1. Spatial temperature distribution along the uterus wall for a 5 minute treatment, $\omega_b = 0.0028\, m_b^3/m^3\ s$.

An inspection of the above table illustrates certain features on the role of metabolic heat generation in the endometrial ablation problem. Although the literature suggests that a typical value of q_{met} for the uterus is $170 W/m^3$ we also conducted numerical tests for q_{met} equal to zero and $5540 W/m^3$ (Baldwin *et al.,* 2001). Except for $\omega_b = 0\, m_b^3/m\, s$, tab. (1) reveals that the difference between P_f and G is negligible suggesting that the heat rate due to the metabolism does not significantly affect the temperature field. This trend can be better illustrated in figs. (1) and (2) where we present the temperature distributions along the entire uterus wall at treatment times equal to 5 and 8 minutes. Indeed, these results show that the role of human metabolism is negligible in the determination of the temperature in the thermal ablation therapy. Moreover, fig.(2) compares the results of the present simulations with those of Baldwin *et al.*(2001). As expected, a good coincidence is achieved between the two models except for the regions close to the serosa layer where the boundary conditions differ. From these results we observe that the semi-infinite model underestimates the serosal temperature and this fact may be relevant to medical procedures. It is argued that one of the goals of a successful treatment is to establish a coagulative cell damage to a depth of 4 to 6 mm together with a minimal rise in the serosal temperature, Baldwin *et al.*(2001), but the semi-infinite model will always predict that the serosal temperature is equal to the uterus' initial condition. Figure (3) presents the transient temperature distribution for a few selected space positions and it is interesting to notice that the serosal temperature *T(0,t)* is indeed constant and equal to the body core temperature for the first three minutes of the ablation process. However, as more heat is added, the serosa

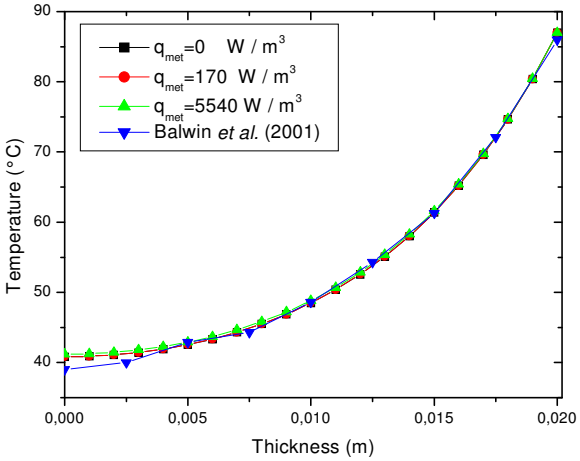

Figure 2. Spatial temperature distribution along the uterus wall for a 8 minute treatment, $\omega_b = 0.0028\, m_b^3 / m^3\, s$.

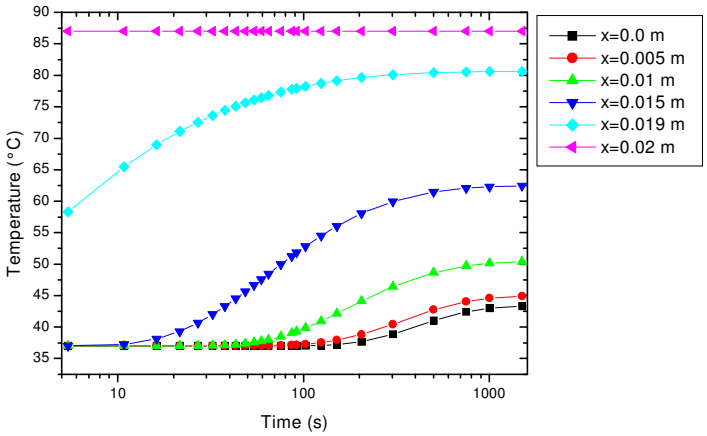

Figure 3. Transient temperature distribution along the uterus wall, $\omega_b = 0.0028\, m_b^3 / m\, s$, $q_{met} = 170 W / m^3$.

layer experiences a slight temperature rise, reaching approximately $41.3^{\circ}C$ at the end of the 8 minute treatment. It is worth mentioning the high temperature differences along the endometrium layer, $15 < x < 20\, mm$, indicating that this region is subjected to a elevated heat flux. Also of interest is the fact that the thermal endometrial balloon therapy should be simulated as a transient process since for times greater than the prescribed treatment time, 480 s, the inner layers of the uterus still experience a small temperature rise.

Figures 4 and 5 examine the role of the perfusion coefficient at the uterus wall for selected time intervals. In the initial stages of the endometrial ablation procedure, fig. 4 shows that only the endometrium is somewhat affected by a variation of the perfusion coefficient. However, as time increases the temperature distribution becomes increasingly dependent upon the value of ω_b . Also, consistent with its role as a sink term, the higher the perfusion coefficient, the lower the temperature levels become. For example, if perfusion effects are not taken into account, $\omega_b = 0$, the serosal temperature at the end of the treatment, fig (5), is around $47^{\circ}C$. This temperature can drop to $40^{\circ}C$ if the normal uterine blood perfusion rate of $0.0028\, m_b^3 / m^3\, s$ is employed. Such trends illustrate the need of accurate measurements of the perfusion coefficient.

4. Conclusions

In this paper we have advanced a hybrid analytical-numerical solution for a generalized bioheat transfer equation which is flexible enough to accommodate a series of relevant physical situations and boundary conditions. The solution methodology is based on the Generalized Integral Transform Technique where through means of an auxiliary eigenvalue problem, an integral transform pair is established and used to transform the original temperature field into a series of coupled ordinary differential equations for the transformed potential field. These ideas were applied to study the temperature fields of the thermal balloon endometrial ablation process. The simulations revealed that the metabolic heat generation plays a minor role in this problem in the while variations of the perfusion coefficient significantly affect the temperature distribution especially at time intervals towards the end of the treatment.

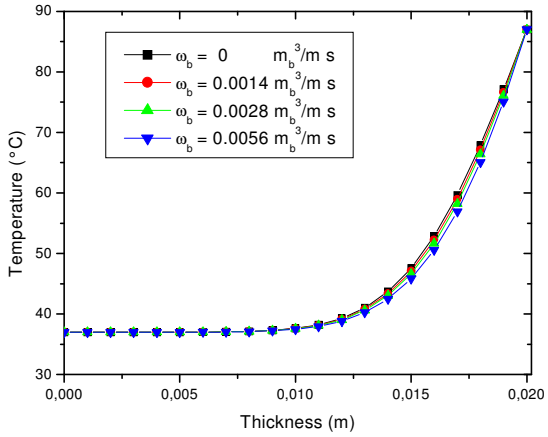

Figure 4. Spatial temperature distribution along the uterus wall for a 1 minute treatment, $q_{met} = 170 W/m^3$.

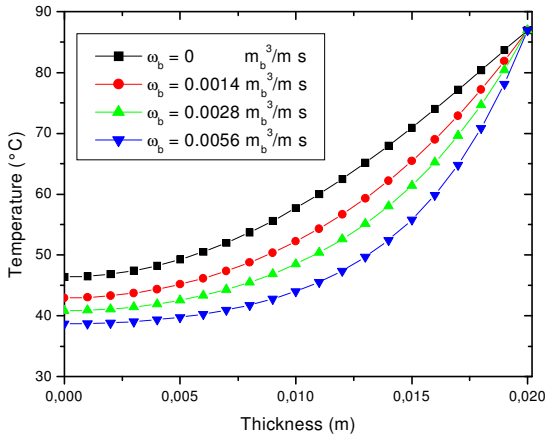

Figure 5. Spatial temperature distribution along the uterus wall for a 5 minute treatment, $q_{met} = 170 W/m^3$.

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7. Responsibility notice

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