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ANALYTICAL SOLUTION OF THE THREE-DIMMENSIONAL TRANSIENT PENNES' BIOHEAT EQUATION USING GREEN'S FUNCTIONS CONSIDERING BLOOD PERFUSION AND METABOLISM

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Abstract. *Bioheat transfer is an important tool to understand the thermal behavior of living organisms, aiding in diagnosis of diseases and infections and surgical procedures involving cryogenic and ablation methods. To model such phenomena, the classic heat diffusion equation must be altered, including blood perfusion and metabolism effects that are inherent in living tissues. In this sense, Pennes proposed an equation that models blood perfusion as proportional to the difference between the internal and external temperatures of a living tissue and includes metabolism as a source term. Such terms make it difficult to obtain an analytical solution, leading many authors to numerical methods, due to inhomogeneities and source terms. In the present work, an analytical solution of a three-dimensional and transient problem is obtained, taking into account the presence of metabolism and perfusion in a phantom tissue sample exposed to a convective medium via Green's functions. It helps, for example, the use of diagnostic techniques based on thermal imaging, allowing the analysis of inclusions influence that can simulate the presence of a tumor.*

Keywords: *bio-heat transfer, analytical solution, Pennes' equation, Green's Functions*

1. INTRODUCTION

The heat transfer modeling in biological structures is important to comprehend the behavior of an organ and/or complex organism of interest in response to external effects like burning injuries or other types of heat flux like laser beams or cancer thermal treatments, and to analyze the possibility of an infection or tumor and its influence. In this way, the Fourier heat conduction equation was modified by Harry H. Pennes to model heat transfer problems in human tissues. Pennes (1948) proposed, from the energy balance in a human forearm, the following equation:

$$\nabla \cdot (k \nabla T) + \omega_b \rho_b c_b (T_a - T) + Q_m = \rho c \frac{\partial T}{\partial t} \tag{1}$$

where ρ, c and k are, respectively, the specific mass [kg·m^{-3}], the specific heat [J·kg^{-1}·°C^{-1}] and the thermal conductivity of the tissue [W·m^{-1}·°C^{-1}], ω_b is the blood perfusion rate [mL·mL^{-1}·s^{-1})], ρ_b is the blood specific mass [kg·m^{-3}], c_b the blood specific heat [J·kg^{-1}·°C^{-1}], Q_m the heat generation term due to metabolism [W·m^{-3}], t the time [s], T_a the arterial temperature and $T = T(x, y, z, t)$ the temperature distribution in the domain, both in [°C].

Biothermal engineering can be broadly described as dealing with issues of bioheat transfer and the effects of thermal energy in biological systems. This field of engineering study is necessary, for example, to understand biological design, prediction of an organism response to various thermal environments, development of thermal safety standards for consumer and industrial products, advance of thermal therapies for human diseases, development of protective garments for human working in extreme temperatures (Chato & Lee, 1997). Other practical applications in biothermal engineering are athletic performance, cell behavior and cancer development, thermal therapies that may include hyperthermia therapy, cryosurgery, heat therapy for healing, non-invasive image-guided ultrasonic surgery, thermal constraints in tissue engineering, implants and biomaterials.

Even though Eq. (1) is broadly used, it is important to emphasize that, to describe all the energy transfer of a living organism with itself and the environment, the physical model must take in count effects of conduction, convection, radiation and the metabolic processes that are inherent. Another import effect that cannot be overlooked is the blood transport inside the body, called blood perfusion, assumed proportional to the difference between the tissue and the internal temperatures (Pennes hypothesis). In this way, a model that takes all those terms and easy to be applied in

common bio-engineering situations is difficult, and possibly impossible, to solve analytically, once determining the boundary conditions correctly, and the coupled effect of variables and their powers and derivatives contribute to the complexity of the model.

Many authors have been solving and studying the bioheat transfer problem numerically as Zhao *et al.* (2005), that used finite differences in a one-dimensional problem of hyperthermia; Deng & Liu (2002) used Monte Carlo approach to solve a tumor analysis problem; Silva (2004) discuss the bioheat problem in eye caused by retinal implants using finite volume method and treating the eye-surface as a two-dimensional model; Yang *et al.* (2007) expanded the classic Pennes' equation (Eq. (1)) including water evaporation during heat, modifying the metabolic term and solving using the finite element method.

For the model presented in Eq. (1), if an analytical solution is possible, it impacts in the analysis of the bioheat transfer problem, according to Yue, Zhang & Yu (2004), once the results can be obtained exactly and show lower dependence of the dimensions, and could be used as validation patterns to numerical solutions. For Chato & Lee (2007), other frontiers in the analytical field are: characterization of tissue thermal properties, description of vascular perfusion architecture for different organs, and better understanding of the heat generation terms.

2. MATHEMATICAL MODEL

Based on Pennes' model, Eq. (1), constant thermal properties will be considered and, the metabolic term, Q_m, will be added to a possible heat generation term, $Q_E(x, y, z, t)$, called $g(x, y, z, t)$, to summarize both effects. So, in a three-dimensional orthogonal and Cartesian coordinate system, Eq. (1) turns to

$$\frac{1}{\alpha}\frac{\partial T}{\partial t} = \frac{\partial^2 T}{\partial x^2} + \frac{\partial^2 T}{\partial y^2} + \frac{\partial^2 T}{\partial z^2} + \frac{\omega_b \rho_b c_b}{k} \cdot (T_a - T) + \frac{g(x, y, z, t)}{k} \tag{2}$$

where $a = k/(\rho c)$ is the thermal diffusivity of the tissue domain.

From the Cartesian model in Eq. (2), it is possible to describe the behavior of a phantom tissue sample with dimensions indicated as $L \times a \times b$, submitted to an external heat flux $q_0 = q_o(t)$ at the surface $(x = 0)$ and in an environment with temperature T_∞ and convective heat transfer coefficient h. In this way, the initial and boundary conditions can be supposed as

$$T(x, y, z, 0) = T_0 \tag{3}$$

$$-k\frac{\partial T}{\partial x}\bigg|_{x=0} = q_0 \text{ and } T = T_a, \text{at } x = L \tag{4}$$

$$-k\frac{\partial T}{\partial y}\bigg|_{y=0} = h\left(T_\infty - T|_{y=0}\right) \text{and} -k\frac{\partial T}{\partial y}\bigg|_{y=a} = h\left(T|_{y=a} - T_\infty\right) \tag{5}$$

$$-k\frac{\partial T}{\partial z}\bigg|_{z=0} = h\left(T_\infty - T|_{z=0}\right) \text{and} -k\frac{\partial T}{\partial z}\bigg|_{z=b} = h\left(T|_{z=b} - T_\infty\right) \tag{6}$$

2.1. Analytical solution

To obtain the analytical solution of the problem composed by the Eqs. (2) to (6) via Green's Functions, a change in variables must made. Suppose $W(x, y, z, t)$ such as

$$W(x, y, z, t) = [T(x, y, z, t) - T_a]\exp(\lambda t) \tag{7}$$

where

$$\lambda = M^2 \alpha \ , \ M^2 = \frac{\omega_b \rho_b c_b}{k} \tag{8}$$

which brings to

$$\frac{1}{\alpha}\frac{\partial W}{\partial t} = \frac{\partial^2 W}{\partial x^2} + \frac{\partial^2 W}{\partial y^2} + \frac{\partial^2 W}{\partial z^2} + \frac{g(x,y,z,t)\exp(\lambda t)}{k} \tag{9}$$

and the solution will be of the type (see Cole *et al.* (2010):

$$W(x,y,z,t) = \frac{\alpha}{k}\int_{\tau=0}^{t}\int_{x'=0}^{L}\int_{y'=0}^{a}\int_{z'=0}^{b} G \cdot g(x,y,z,t)\exp(\lambda\tau) + \frac{\alpha}{k}\int_{\tau=0}^{t}\int_{y'=0}^{a}\int_{z'=0}^{b} q_0 \exp(\lambda\tau)G\big|_{x'=0} dz'dy'd\tau +$$
$$+ \frac{\alpha h(T_\infty - T_a)}{k}\left[\int_{\tau=0}^{t}\int_{x'=0}^{L}\int_{z'=0}^{b} \exp(\lambda\tau)G\big|_{y'=0} dz'dx'd\tau + \int_{\tau=0}^{t}\int_{x'=0}^{L}\int_{y'=0}^{a} \exp(\lambda\tau)G\big|_{z'=0} dy'dx'd\tau\right] \tag{10}$$

where $G = G(x,y,z,t|x',y',z',\tau)$ is the Green function associated to the boundary conditions with the respectively Green function that describes the type of effects in each direction, first type (1), second type (2) and third type (3) (Fernandes, 2009):

$$G = G_{X21} \cdot G_{Y33} \cdot G_{Z33} \tag{11}$$

with

$$G_{X21} = \frac{2}{L}\sum_{m=1}^{\infty} \exp\left[\frac{-\beta_m^2 \alpha(t-\tau)}{L^2}\right]\cos\left(\beta_m \frac{x}{L}\right)\cos\left(\beta_m \frac{x'}{L}\right) \tag{12}$$

$$G_{Y33} = \frac{2}{a}\sum_{n=1}^{\infty}\left\{\exp\left[\frac{-\beta_n^2 \alpha(t-\tau)}{a^2}\right]\left[\beta_n \cos\left(\beta_n \frac{y}{a}\right) + B_1 \sin\left(\beta_n \frac{y}{a}\right)\right]\left[\beta_n \cos\left(\beta_n \frac{y'}{a}\right) + B_1 \sin\left(\beta_n \frac{y'}{a}\right)\right]\times\right.$$
$$\left.\times\frac{\beta_n^2 + B_1}{\beta_n^2 + B_1^2 + B_1}\right\} \tag{13}$$

$$G_{Z33} = \frac{2}{b}\sum_{p=1}^{\infty}\left\{\exp\left[\frac{-\beta_p^2 \alpha(t-\tau)}{b^2}\right]\left[\beta_p \cos\left(\beta_p \frac{z}{b}\right) + B_2 \sin\left(\beta_p \frac{z}{b}\right)\right]\left[\beta_p \cos\left(\beta_p \frac{z'}{b}\right) + B_2 \sin\left(\beta_p \frac{z'}{b}\right)\right]\times\right.$$
$$\left.\times\frac{\beta_p^2 + B_2}{\beta_p^2 + B_2^2 + B_2}\right\} \tag{14}$$

where the eigenvalues in Eqs. (12), (13) and (14) are, respectively, given by

$$\beta_m = \pi\left(m - \frac{1}{2}\right) \tag{15}$$

$$\beta_n \tan\beta_n = B_1 = \frac{ha}{k} \tag{16}$$

$$\beta_p \tan\beta_p = B_2 = \frac{hb}{k} \tag{17}$$

Considering the heat source term as combination of the metabolic rate and an abnormal effect, $Q_E(t)$, in a known region $R = [x_1, x_2] \times [y_1, y_2] \times [z_1, z_2]$, with $0 < x_1 < x_2 < L, 0 < y_1 < y_2 < a$ and $0 < z_1 < z_2 < b$, the solution of the problem proposed will be

$$W = \frac{\alpha}{k}I_1 + \frac{\alpha}{k}I_2 + \frac{ah}{k}I_3 + \frac{ah}{k}I_4 \tag{18}$$

defining

$$G^* = \frac{8}{Lab}\cos\left(\beta_m \frac{x}{L}\right)\cos\left[\beta_n\left(1-\frac{y}{a}\right)\right]\cos\left[\beta_p\left(1-\frac{z}{b}\right)\right]\left(\frac{\beta_n^2 + B_1^2}{\beta_n^2 + B_1^2 + B_1}\right)\left(\frac{\beta_p^2 + B_2^2}{\beta_p^2 + B_2^2 + B_2}\right) \tag{19}$$

$$I_x = \frac{L\sin\beta_m}{\beta_m} \ , \ I_y = \frac{a\sin\beta_n}{\beta_n} \ \text{and} \ I_z = \frac{b\sin\beta_p}{\beta_p} \tag{20}$$

and considering Q_E as constant, it is possible to write

$$I_1 = Q_m \sum_{m=1}^{\infty}\sum_{n=1}^{\infty}\sum_{p=1}^{\infty} \frac{G^* Lab I_x I_y I_z [\exp(\lambda t) - \exp(-\gamma \alpha t)]}{\alpha(\lambda + \gamma)} + Q_E \sum_{m=1}^{\infty}\sum_{n=1}^{\infty}\sum_{p=1}^{\infty}\left\{\frac{G^* Lab [\exp(\lambda t) - \exp(-\gamma \alpha t)]}{\alpha \beta_m \beta_n \beta_p (\lambda + \gamma)} \times \right.$$
$$\left. \times \left[\sin\left(\beta_m \frac{x_2}{L}\right) - \sin\left(\beta_m \frac{x_1}{L}\right)\right]\left\{\sin\left[\beta_n\left(1-\frac{y_1}{a}\right)\right] - \sin\left[\beta_n\left(1-\frac{y_2}{a}\right)\right]\right\}\left\{\sin\left[\beta_p\left(1-\frac{z_1}{b}\right)\right] - \sin\left[\beta_p\left(1-\frac{z_2}{b}\right)\right]\right\}\right\} \tag{21}$$

$$I_2 = q_0 \sum_{m=1}^{\infty}\sum_{n=1}^{\infty}\sum_{p=1}^{\infty} \frac{G^* ab I_y I_z [\exp(\lambda t) - \exp(-\gamma \alpha t)]}{\alpha(\lambda + \gamma)} \tag{22}$$

$$I_3 = (T_\infty - T_a)\sum_{m=1}^{\infty}\sum_{n=1}^{\infty}\sum_{p=1}^{\infty} \frac{G^* Lb I_x I_z [\exp(\lambda t) - \exp(-\gamma \alpha t)]}{\alpha(\lambda + \gamma)} \tag{23}$$

$$I_4 = (T_\infty - T_a)\sum_{m=1}^{\infty}\sum_{n=1}^{\infty}\sum_{p=1}^{\infty} \frac{G^* La I_x I_y [\exp(\lambda t) - \exp(-\gamma \alpha t)]}{\alpha(\lambda + \gamma)} \tag{24}$$

3. RESULTS AND DISCUSSIONS

To discuss and analyze the presence of a possible tumor, simulated as an abnormal heat source in the tissue domain, numerical results considering that the tissue is excited by an external heat flux at the surface, numerical probes were defined across the center plane, called σ–plane, of the domain, as illustrated in Fig. 1.

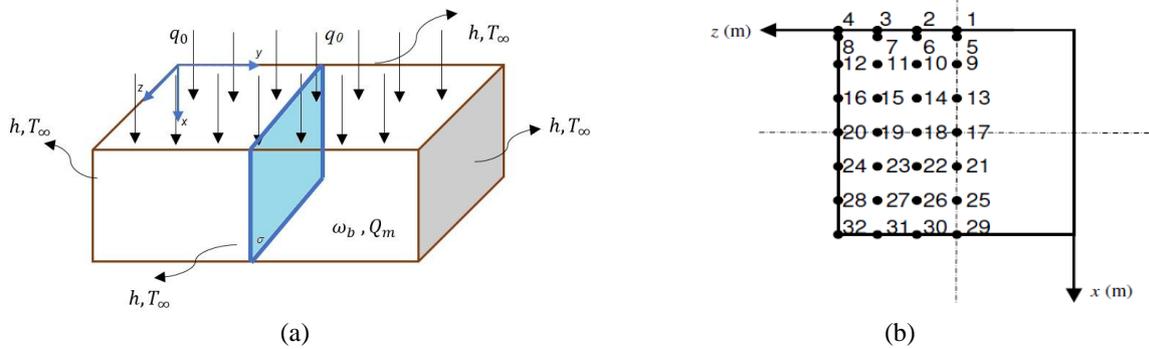Figure 1. (a) Definition of the σ–plane. (b) Probes for temperature analysis.

For the problem proposed, thermal properties of the tissue were considered as constant and thermal rates were assumed in a safety-band for thermal treatments (Holmes, 1997), enumerated in Table 1.

In this way, in a common thermography image, only the surface is shown. So, just probes 1 to 4 (see Fig. (1b)) are emphasized. Comparing both situations: a healthy tissue and a sick (morbid) one.

Table 1. Tissue properties and boundary conditions.

Description	Values	Description	Values
L (x-length)	0.03 m	T_∞ (air temperature)	25°C
a (y-length)	0.03 m	k (tissue thermal conductivity)	$5 \cdot 10^{-1}$ W·m^{-1}·°C^{-1}
b (z-length)	0.03 m	ω_b (blood perfusion rate)	$5 \cdot 10^{-4}$ s^{-1}
ρ (tissue specific mass)	$1 \cdot 10^3$ kg·m^{-3}	h_0 (air convective coefficient)	10 W·m^{-2}·°C^{-1}
ρ_b (blood specific mass)	$1 \cdot 10^3$ kg·m^{-3}	Q_m (metabolic rate)	$3,38 \cdot 10^4$ W·m^{-3}
c (tissue specific heat)	4.2 kJ·kg^{-1}·°C^{-1}	Q_E (abnormal heat source)	$5 \cdot 10^3$ W·m^{-3}
c_b (blood specific heat)	4.2 kJ·kg^{-1}·°C^{-1}	q_o (heat flux at the surface)	5 W·m^{-2}
T_a (core temperature)	37°C		

Analyzing Figs. (2) to (4) it is possible to conclude that the presence of a tumor, contributing to the generation term, increase the point temperature, what can contribute to an abnormal metabolic rate that is characteristic of diseases associated in skin.
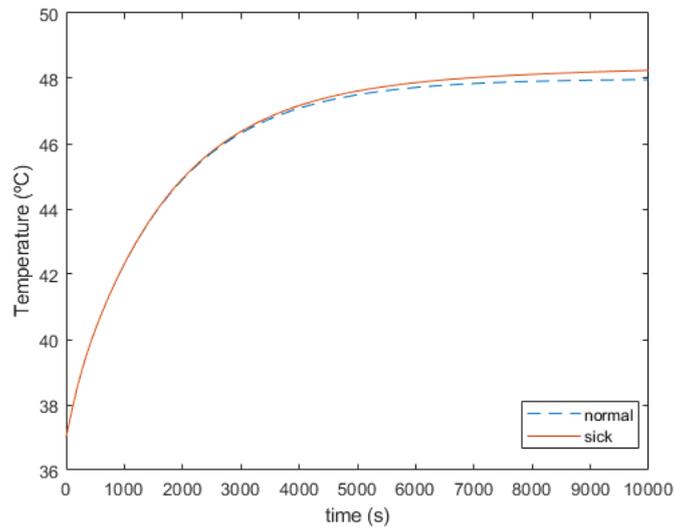

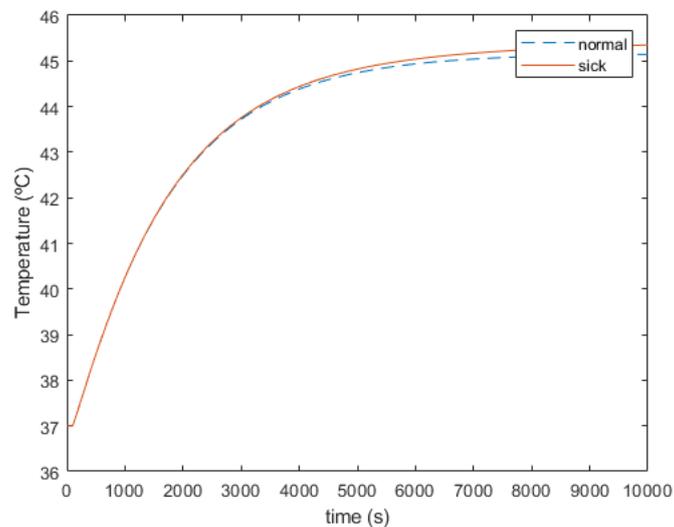Figure 2. Temperature behavior at probe 1 (center of the surface).

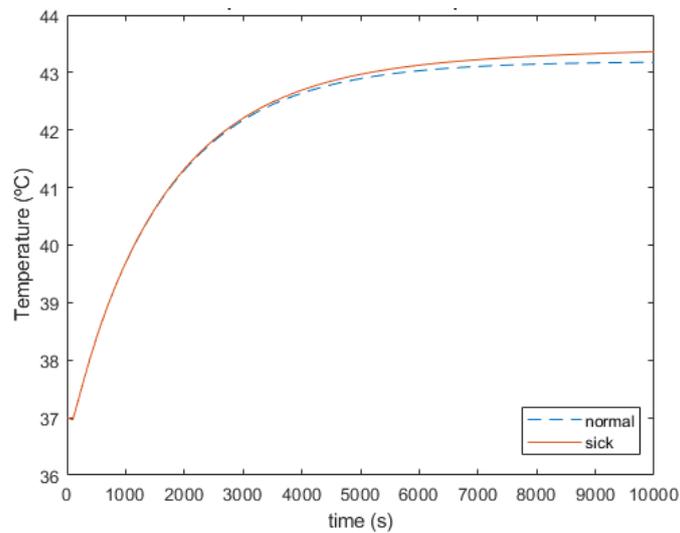Figure 3. Temperature behavior at probe 4.

Figure 4. Temperature at lateral center (probe 20).

Figure 5 shows the influence of convection at the lateral of the domain. Once the heat rate is greater for the sick tissue, the convective effected is reduced and the temperature registered along time by probe 17 increases in comparison with a tissue with normal metabolism.
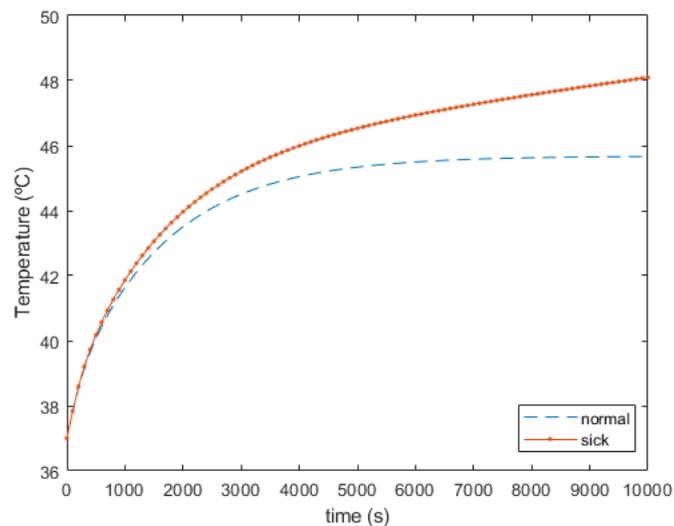

Figure 5. Temperature behavior at the center of the σ-plane (probe 17).

For all calculations, 200 eigenvalues were used, once it results in an error of order 10^{-8} when the process of intrinsic verification (Cole *et al.*, 2010). of the solution was conducted (Oliveira, 2018). In Figure 6, the steady-state temperature of the sick domain is presented, showing that the temperature at the surface has increased by the presence of the heat flux and the abnormal heat source. This model contribute for the development of non-invasive techniques in skin burn-injures and tumor diagnoses.

4. CONCLUSIONS

An analytical solution for a bioheat transfer in human tissue was presented considering metabolism and perfusion, and a possible presence of an abnormal heat source that simulate a tumor. The solution was conducted using the Green's function method. That consists in analyze the problem as a response to a perturbation in some position and time, and from this, get the temperature distribution in a domain. This technique has a great advantage because it allows intrinsic verification, all the results can be compared to well-known solutions to check its physical interpretation.

Once the analytical solution is provided, it is possible to predict the tissue behavior and interpret thermography results to diagnose if there is or not an abnormal behavior of the domain. Future works include modeling a three-

dimensional multi-layer body with the presence of living characteristics, approximating the model even more the model to reality.
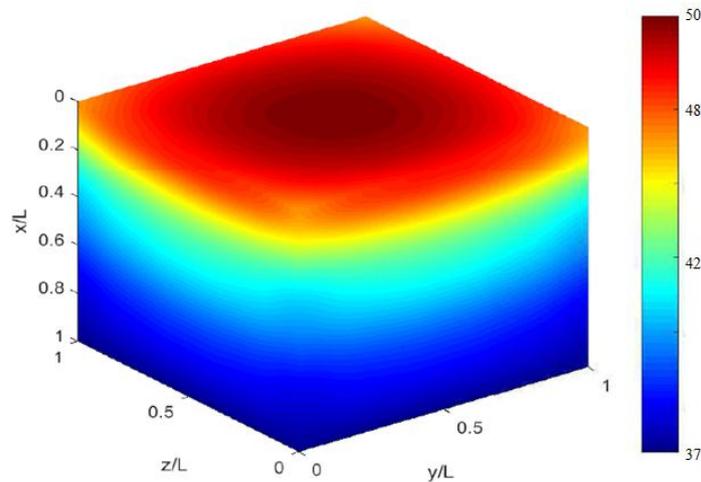

Figure 6. Steady state temperature for the morbid tissue (200 eigenvalues).

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6. RESPONSIBILITY NOTICE