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# Temperature distribution in multi-layer skin tissue in presence of a tumor

Daipayan Sarkar, A. Haji-Sheikh, Ankur Jain *

*Mechanical and Aerospace Engineering Department, The University of Texas at Arlington, Arlington, TX 76019, USA*

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ABSTRACT

Analytical investigation of bioheat transfer is of significant importance for numerous medical applications, for example in thermally-driven treatments for cancer. While bioheat transfer has been investigated for a number of specific conditions, relatively less work exists on bioheat transfer in a multilayer structure, such as skin. This paper presents an analytical solution for the steady-state Pennes bioheat equation in a multi-layer structure. The temperature distribution in each layer is derived separately and interface temperature and heat flux compatibility conditions are used to determine the complete solution. This solution is used to analyze the effect of heat generation during thermal therapy on a tumor in skin, which is modeled as a five-layer structure. The model is capable of accounting for the effects of various therapeutic measures such as cryotherapy, laser treatment, etc. as well as various physical phenomena such as conduction, blood perfusion and metabolism. The model is used to analyze the effect of various physical parameters on the temperature distribution. This theoretical treatment, as well as the quantitative results presented here may help improve the fundamental understanding of bioheat transfer in a layered structure such as skin.



## 1. Introduction

Heat transport in tissues is an important physical phenomenon for both healthy and diseased tissue. A significant amount of research in bioheat transfer over the past few decades has led to an understanding of the governing dynamics of thermal transport in a tissue [1–3]. A number of thermal based therapeutic measures have been developed and adopted in practice, including laser surgery, cryotherapy, magnetic nanoparticle based hyperthermia and radio frequency ablation [4–9]. The design and optimization of these procedures has been aided by advancements in the understanding of bioheat transfer. Thermal transport in a biological system is sensitive to a number of critical parameters such as rate of metabolism, blood perfusion and space dependent heat generation in the presence of a tumor [2]. Hence, careful consideration should be given to all these properties and phenomena, when studying the nature of the temperature field in such systems.

Several models governing the flow of heat in tissues have been proposed. A classical model was presented by Pennes in 1948 [2], followed by several refinements and related models [3,10,11]. Detailed reviews of these bioheat transfer models are also available [12,13]. The Pennes model is used widely due to its simplicity, but it must be modified depending on unique attributes of the tissue under study. This model includes the effect of heat transfer in a biological body due to diffusion, advection, volumetric heat generation due to metabolism and spatial heating. Diffusion and transient thermal effects in any tissue are based on its thermophysical properties such as thermal conductivity, density and specific heat. The Pennes equation accounts for blood flow through an advection term, consisting of the thermophysical properties of blood along with the difference between the blood temperature and the local tissue temperature. Thermophysical properties of blood and various tissue have been measured using a variety of methods [14]. Some analytical work has been reported on solving the Pennes bioheat transfer equation for specific conditions. Deng et al. reported a closed form analytical solution for spatial and time dependent surface or volumetric conditions using the Green's function method [15]. Laplace transform was used to study the transient effects of sinusoidal heat flux on a one-dimensional semi-infinite tissue [4]. Mahjoob and Vafai developed an analytical model for a biological tissue, assuming a porous media with contributions due to conduction between tissue and vascular system, convective heat transfer between blood and tissue, heat generation due to metabolism and induced surface heat flux [16]. A dual layer biological media was also considered, and analytical solutions for

* Corresponding author. Tel.: +1 817 272 9338; fax: +1 817 272 2952.
*E-mail address:* jaina@uta.edu (A. Jain).

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**Nomenclature**

| | |
|---|---|
| $a$ | length of tissue, m |
| $b$ | location of each interface from datum, m |
| $c$ | specific heat of blood, J/kg-K |
| $C$ | series coefficient used in all sections |
| $d$ | thickness of layer, m |
| $D$ | series coefficient used in a solution for case in Section 2.2 |
| $g$ | volumetric heat generation, W/m$^3$ |
| $h$ | heat transfer coefficient, W/m$^2$-K |
| $k$ | thermal conductivity, W/m-K |
| $L$ | length of tumor region, m |
| $m$ | parameter defined in Eq. (2) |
| $q$ | heat flux, W/m$^2$ |
| $Q$ | heat transfer in resistor network, W |
| $T$ | temperature, °C |
| $x$ | spatial co-ordinate, m |
| $y$ | spatial co-ordinate, m |
| $\beta$ | eigen value in $y$, m$^{-1}$ |
| $\gamma$ | eigen value in $x$, m$^{-1}$ |
| $\delta$ | factor to determine location of tumor |
| $\Phi$ | source term used in a solution for case in Section 2.2 |
| $\Psi$ | source term used in all solutions |
| $Z$ | set of integers |

*Subscripts/superscripts*

| | |
|---|---|
| $bl$ | blood |
| $f$ | effect of flux boundary condition in superimposed solution |
| $j$ | layer |
| $n$ | number of terms |
| $p$ | number of terms |
| $r$ | resistor network solution |
| $s$ | effect of source in superimposed solution |
| $t$ | tumor region |
| $sur$ | surface |
| $\infty$ | ambient |
| $*$ | set of integers ($Z$) including zero, $\{0,1,2,3,\ldots\}$ |
| $+$ | set of integers ($Z$) excluding zero, $\{1,2,3,\ldots\}$ |

two specific cases were discussed [17]. An analytical study of an axisymmetric tissue-vascular system is used to analyze the effect due to the radiofrequency ablation treatment due to volumetric heat generation in the tissue region due to a heater probe [9]. The application of Pennes equation to magnetic fluid hyperthermia has been studied, where a theoretical solution is presented for a spherical tumor surrounded by a thin shell of magnetic nanoparticles [7]. An analytical model was proposed to investigate the rate of cell destruction during a freeze–thaw cryosurgical procedure, in order to minimize damage to healthy cells [5]. Steady state temperature distribution in a one dimensional cylindrical tissue has been developed for human limbs [18]. Steady state thermal penetration depth has been derived analytically using method based on Laplace transforms [19]. Analytical solution based on the Laplace transforms is used to solve a two-dimensional Pennes bioheat equation for both Fourier and non-Fourier heat conduction effects for a cylindrical skin tissue [20].

In addition to such analytical models, numerical solutions have also been developed for scenarios where temperature solutions are difficult to determine explicitly. Steady state temperature in breast cancer was studied numerically through user-defined functions to account for blood perfusion and metabolism [21]. An investigation of minimum invasive methods such as microwave thermal therapy was performed both numerically and experimentally, *in vivo* and *in vitro*, to determine the extent of the tissue injury [22]. Temperature solution in a system with time-dependent spatial heating has been studied numerically [23]. The cooling of human brain and neck in emergency medical situations has been studied using finite element simulations [24]. In a recent finite element based analysis, an alternating magnetic field is applied to ferrofluids to generate heat inside a tumor. The Pennes bioheat equation was coupled with Maxwell's equation in the finite element model to calculate the input parameters such as the magnetic flux intensity [25]. A finite difference model of the Pennes bioheat equation was used to study the effects of cryofreezing using the immersed boundary method [26]. Skin surface cooling based on optical window contact cooling, cryogenic spray cooling are considered for the Pennes bioheat equation and Weinbaum–Jiji bioheat model. Combined conduction and radiation effects are considered in Pennes equation and the temperature field in the multilayer tissue structure is computed numerically [27].

Finally, a number of experimental investigations of bioheat transfer in tissue have also been reported. The different theories involved with hyperthermia treatment were verified by performing experiments on a large bovine kidney by turning it into tissue phantom using alcohol fixation technique [28]. Most of these papers investigate therapy of cancerous tissue, including electroporation-based chemotherapy [6,29,30], magnetic nanoparticle based heating [7,8], etc. In a recent study, a high resolution microcomputed tomography imaging system has been used to investigate the concentration and distribution of injected nanoparticles. Also nanoparticle induced volumetric heat generation rate was measured experimentally [8]. Several studies on estimating the thermal damage potential due to Joule heating and the importance of considering the multilayer nature of skin tissue have also been presented [6,31,32]. In a related work, detection of shape, size and depth of a melanoma lesion by applying a cold stimulus at the surface has been reported [33]. In addition, an extension to Pennes bioheat equation is made to include the effect of water evaporation during in the tissue during laser heating. A source term is added to the Pennes bioheat equation to account for the energy required for evaporation process to occur, based on which, a relationship for effective specific heat is derived. Experiments on a liver tissue along with numerical solutions are presented to illustrate the effect of water evaporation from the tissue [34].

Techniques for temperature field computation during such procedures continue to be critical for design and optimization of present and future therapies. Unique bioheat transfer phenomena may be expected in skin due to its unique multi-layer structure and the resulting heterogeneity in thermophysical properties and biotransport parameters in the transverse direction. Recognition of the multi-layer nature of the skin – and the resulting bioheat transfer characteristics – is important for analyzing thermal effects in the presence of, and in treating skin lesions and cancers. While some work has been presented in understanding bioheat transfer in skin [4,13], the present literature lacks analytical solutions of Pennes bioheat equation for a multilayer structure. Analytical solutions for multilayer structures have been proposed for other engineering applications [35–38], however, bioheat transfer in a multilayer structure presents additional challenges due to the complicated nature of the governing equation. This paper presents the