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Thermal analysis in a triple-layered skin structure with embedded vasculature, tumor, and gold nanoshells

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ABSTRACT

Obtaining accurate temperature distributions in living tissue related to hyperthermia skin cancer treatment without using an intruding sensor is a challenge. Here, we report a mathematical model that can accurately determine the temperature distribution in the tumor region and surrounding normal tissue. The model is based on a modified Pennes' equation for the bioheat transfer in a 3-D triple-layered skin structure embedded with a vascular countercurrent network and a tumor appearing in the subcutaneous region. The vascular network is designed based on the constructal theory of multi-scale tree-shaped heat exchangers. The tumor is injected with gold nanoshells in order to be heated quickly. The proposed model is implemented numerically using a stable finite difference scheme. The method is demonstrated and tested by an example.

1. Introduction

In hyperthermia skin cancer treatment, the objective is the control laser heating of the tumor (target temperatures of 42–46 °C) so that the temperatures of the normal tissue surrounding the tumor remains low enough not to damage the normal tissue. However, it is not easy to obtain an accurate determination of the temperature field over the entire treatment region during clinical hyperthermia treatments, because the number of invasive temperature probes that can be used is limited due to the pain tolerances of the patients. Hence, it is important to determine the laser intensity and pattern of laser exposure for optimizing the temperature distribution in the treated region. The determinants of temperature distributions during thermal therapy include the power deposition pattern of the heating source, heat removal by conduction, and heat removal by blood flow forced convection.

There are many numerical and experimental methods developed based on the Pennes' bioheat transfer equation [1–22]. Among these, Liauh and Roemer [2] presented a semi-linear state and parameter estimation algorithm that decreases the total computational time between the temperature and the blood perfusion based on the Pennes' bioheat transfer equation (BHTE) in the hyperthermia temperature estimation problem. Huang [4] considered the heat transfer within a perfused tissue in the presence of a vessel. Payne [6] designed a phantom from the combination of the convective fin equation and the Pennes' BHTE, and developed a phantom model using an inverse technique applied to experimental data from a thin layer phantom to determine model parameters. Liu [8,9] modeled wave-like behaviors of bioheat transfer in a 1-D triple-layered skin structure which was solved by using a finite difference method. Sun et al. [10] developed a system that can treat tumor tissue and monitor the heating and cooling during the treatment by means of an invasive probe. The prediction of the temperature distribution in the tumor was modeled using the Pennes' equation. Dai and his colleagues [11–13] developed a domain decomposition method for solving the 3-D Pennes' BHTE in a triple-layered skin structure. In particular, Zeng et al. [14] developed a model for a 3-D triple-layered skin structure with a vascular countercurrent network that employed a modified Pennes' equation which accounts for thermal lag of the tissue where the vascular network is designed based on the constructal theory of multi-scale tree-shaped heat exchangers. Majchrzak and colleagues [15] developed a model based on the Pennes' equation to study the hyperthermia and hypothermia processes and to identify thermal parameters in a biological medium. Jamil and Ng [16] developed a model that predicts the leading factor for hyperthermia treatment using electromagnetic radiation in a single-layered human tissue structure with an embedded tumor based on the Pennes' equation. Randrianalisoa et al. [18] investigated effects of

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short-pulsed laser radiation transient heating of superficial human tissues. Majchrzak [19] modeled the dual-phase lag equation in a 3-D skin structure and obtained a solution numerically with an explicit finite difference method. Kumar and Srivastava [20] numerically investigated the influence of pulsatile blood flow on temperature distribution within the body of laser-irradiated biological tissue phantoms.

For hyperthermia cancer treatment, a recent advance is to inject golden nanoparticles into the tumor region in order to heat it up quickly [23–36]. Bayazitoglu and her colleagues [23–25] developed a model that used the finite difference time domain (FDTD) to calculate the heat distribution of nanoshells on a single layer of human biological tissue at varying particle distribution densities in different host mediums. Recently, they [26–28] have extended their study to the modeling and numerical investigation of nanoparticle assisted laser-induced thermotherapy for tumor and cancer treatments. Cai et al. [29] discussed the applications of gold nanoparticles in cancer nanotechnology. Pignol et al. [30] used the Monte Carlo method to predict gold nanoparticle radiosensitization needed to be lethal in a cell media on the nanoscale. Singh et al. [31] numerically studied the laser-induced hyperthermia of nanoshell mediated vascularized tissue. Lin et al. [32] also used the Monte Carlo method to model the effect of gold nanoparticles in response to multiple beam intensities to enhance the effect of proton beam therapy. Zunino et al. [33] developed a model that predicts the effect of nanoparticles in a tumor microenvironment in the form of temperature, by using the finite element method while taking into account the tumor's vascular system and heat transfer of the vascular system with the distribution of nanoparticles. Sazgarnia et al. [34] developed a model with gold nanoshells to predict the temperature distribution of a prostate with a tumor irradiated by a laser, which was solved numerically by the finite element method. Liu et al. [35] presented nanoscale optomechanical actuators for controlling mechanotransduction in living cells. Frieboes and Curtis et al. [36] evaluated the effects of drug-loaded gold nanoparticles in highly vascularized tumors, where the effect of the nanoparticles decreased tumor size in comparison to drug-free nanoparticles.

Up to date, modeling the laser heating in a 3-D triple-layered skin tissue where the tumor is injected by nanoparticles with a nearby countercurrent vascular network has not been seen. For this purpose, the present study develops a mathematical model that can accurately determine the temperature in the tumor region and surrounding normal tissue. Our model is based on a modified Pennes' equation for the bioheat transfer in a 3-D triple-layered skin structure embedded with a vascular countercurrent network and a tumor appearing in the subcutaneous region. The vascular network is designed based on the constructal theory of multi-scale tree-shaped heat exchangers. The tumor is injected with golden nanoshells in order to be heated quickly. The proposed model is then solved numerically using a stable finite-difference scheme. Such research may provide an useful tool for optimizing laser irradiation to kill the tumor while keeping the damage to the surrounding healthy tissue to a minimum during the hyperthermia cancer treatment. Our preliminary idea and outline for this study with not yet obtaining numerical results was presented in the 2015 Constructal Law Conference held in Italy in May 2015 and was included in the conference proceedings, which appeared in a special issue in International Journal of Heat and Technology [37]. The present article not only improves the model by considering the thermal lag of heat flux on the skin surface and a different thermal lag in the tumor than in the healthy tissue, but also completes the study with computational procedure and numerical results.

The organization of the rest of the text is given as follows. In Section 2, the bioheat transfer model for thermal analysis in a 3-D triple-layered skin structure with a countercurrent vascular network with an embedded tumor and nanoshells in the subcutaneous region is presented. In Section 3, we propose a finite difference method and computational procedure for solving the model. In Section 4, we test the method by an example.

2. Mathematical model

2.1. Network design

For simplicity, we consider the skin tissue to be a rectangular structure embedded with a seven-level countercurrent vascular network, which is a highly branching and hierarchical network as described in [38], under the tumor region in the subcutaneous layer. The tumor region is assumed to locate directly below the dermis layer, as shown in Fig. 1. It should be pointed out that only large blood vessels can be seen in the subcutaneous tissue because the significance of the blood vessel in light propagation is dependent on the relative diameter of the blood vessel to the mean free path (MFP, i.e., the reciprocal of the total attenuate coefficient of light in tissue) of photon in tissues. If the vessel diameter is much less than the photon MFP, the contribution of these vessels to the light distributed can be collectively represented by a continuum model [40]. Therefore, we combine the tissue and capillary blood vessels together and use one heat transfer equation for both the capillary beds and tissue. Furthermore, the dermis is very sparingly supplied with capillaries and the capillary beds of skin lying immediately below the epidermis, and thus, the contribution of these small vessels to the heat transfer can be ignored [39,40]. In Fig. 1, the red[1] color dendritic network represents arteries while the blue color dendritic network represents veins, where all are considered as slender cuboids for simplicity. Levels of arteries are designed such that the first-level artery runs from right to left along the x-coordinate; the second-level artery branches from the left end of the first-level artery and flows along the y-coordinate; the third-level artery has two vessels branching from the two ends of the second-level artery, and flowing along the z-coordinate; there are four fourth-level arteries branching from the four ends of the third-level arteries, which flow along the x-coordinate; the fifth-level artery has eight arteries branching from the eight ends of the fourth-level arteries, and so on. The vein network has the same number of blood vessels as its counterpart artery in corresponding levels.

In sum, there are 128 blood vessels in total in the considered skin structure. Although the orthogonal structure of blood vessels (Fig. 1) is a special design, the constructal-design literature has shown convincingly [41,42] that when the complexity of the tree is as high as in the present model, the volume averaged flow perfusion properties (such as the permeability) do not change if the details of the tree architecture change. The tree flow architecture is robust, and this is why the use of assumed structures in the numerical modeling of previously untractable 'complex' flow structure has a real opportunity for advances.

To determine the diameters of the blood vessels on each level, we follow the constructal theory of multi-scale tree-shaped heat exchangers [41–44] and assume that the diameters of arteries are decreasing by a constant ratio γ between successive levels of branched vessels, given by [44],

$$\gamma = \frac{NL_b^{m+1}}{NL_b^m} = \frac{NW_b^{m+1}}{NW_b^m} = 2^{-\frac{1}{3}}, \quad m = 1, \ldots, 6, \tag{1}$$

where NL_b^m and NW_b^m are the length and width of the cross section of a blood vessel in level m, respectively. The length of a blood vessel is

[1] For interpretation of color in Fig. 1, the reader is referred to the web version of this article.