Published in final edited form as:

J Biomech Eng. 2009 July ; 131(7): 074506. doi:10.1115/1.3127260.

A Generic Bioheat Transfer Thermal Model for a Perfused Tissue

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Abstract

A thermal model was needed to predict temperatures in a perfused tissue, which satisfied the following three criteria. One, the model satisfied conservation of energy. Two, the heat transfer rate from blood vessels to tissue was modeled without following a vessel path. Three, the model applied to any unheated and heated tissue. To meet these criteria, a generic bioheat transfer model (BHTM) was derived here by conserving thermal energy in a heated, vascularized, finite tissue and by making a few simplifying assumptions. Two linear, coupled differential equations were obtained with the following two variables: tissue volume averaged temperature and blood volume averaged temperature. The generic model was compared to the widely employed, empirical Pennes' BHTM. The comparison showed that the Pennes' perfusion term $wC_p(1-\epsilon)$ should be interpreted as a local vasculature dependent heat transfer coefficient term. Suggestions are presented for further adaptations of the general BHTM for specific tissues using imaging techniques and numerical simulations.

Introduction

Several diagnostic and therapeutic protocols require the determination of in vivo temperatures to plan and optimize the protocols [1–5]. To manage computational costs, temperatures in a tissue embedded with 'small' (< 1 mm in diameter) more frequent blood vessels are determined using approximate thermal models known as the bioheat transfer models (BHTMs) [6–8]. Temperatures in the 'large' (vessel diameter ≥ 1 mm), less frequent blood vessels are determined using the exact thermal model the convective energy equation (CEE) [9].

Several BHTMs have been presented before. Many of them have been proposed based on intuition with undefined and empirical parameters and variables [10–14]. Lack of a formal derivation made it difficult to relate the parameters and variables of these BHTMs to in vivo temperatures and parameters (e.g., blood flow, blood vasculature geometry, thermal properties of tissue and blood vessels). This made implementation and interpretation of the BHTMs and their results controversial and less reliable [15].

Other BHTMs have been derived by conserving thermal energy in a heated, vascularized, finite tissue. However, to model the heat transfer rate from blood vessels to tissue, several of these derived BHTMs assumed local thermal equilibrium (i.e., the tissue and blood volume averaged temperatures were equal to each other) [15–22]. The assumption of the local thermal equilibrium is, in general, not valid in a heated tissue [23–27]. Rest of the derived BHTMs used parameters that required following paths of thermally important vessels [18,20,28,29]. Blood vessels smaller than ≤ 500 μm in diameter are difficult to image in vivo [7,30]. Thus, following paths of thermally important vessels ≤ 500 μm is difficult. Excellent reviews for several of the above BHTMs were presented in [31,32].

Several BHTMs have been derived by conserving thermal energy in a heated, vascularized, finite tissue and using volume averaging theorem of the theory of porous media.[33–36] Use of the volume averaging theorem introduced unknown, spatially varying continuous vector functions to relate the local, point-wise variation in the averaged variables and parameters to volume averaged variables and parameters. The determination of the unknown vector formulations requires the complete, continuous vascular tree.

This paper presents a basic and general BHTM formulation that satisfied the following three criteria. One, the model satisfied conservation of energy. Two, the heat transfer rate from blood vessels to tissue was modeled without following vessel paths. Three, the model applied to any unheated and heated tissue.

Mathematical Derivation of a Generic Bioheat Thermal Model

General Derivation

A finite, vascularized, heated tissue was considered. It was assumed that blood stayed in vasculature and everything surrounding the blood was tissue. Conserving energy for a point in the tissue and blood resulted in the following convective energy equation (CEE) [9]. Note that the velocity of tissue u_T was zero in equation (1).

$$(\rho C_p)_i \left[\frac{\partial T_i}{\partial t} + u_i \cdot \nabla T_i \right] = \nabla \cdot k_i \nabla T_i + \dot{Q}_i''', i=T, Bl \quad (1)$$

Equation (1) was integrated over the tissue and blood sub-volumes, separately. Both equations are presented below.

$$\int_{V_i} (\rho C_p)_i \left[\frac{\partial T_i}{\partial t} + u_i \cdot \nabla T_i \right] dV = \int_{V_i} (\nabla \cdot k_i \nabla T_i) dV + \int_{V_i} \dot{Q}_i''' dV, i=T, Bl \quad (2)$$

The following equation (3) was obtained by applying Green's divergence theorem to the first terms on the left hand side (LHS) and right hand side (RHS) of equation (2).

$$\begin{aligned} \int_{V_i} (\rho C_p)_i \frac{\partial T_i}{\partial t} dV - \int_{V_i} T_i \nabla \cdot (\rho C_p u)_i dV &= \int_{S_{out-i}} [(-k_i \nabla T_i) - (\rho C_p)_i u_i T_i] \cdot n_{out-i} dS \\ &+ \int_{S_{j-i}} (-k_i \nabla T_i) \cdot n_{j-i} dS + \int_{V_i} \dot{Q}_i''' dV \end{aligned} \quad (3)$$

where, $i = j = T, Bl$ and $i \neq j$.

Assuming a) constant density and specific heat and b) incompressibility for the blood in the averaging blood volume, the second term on the LHS reduced to zero due to conservation of mass. (Note that this term was zero for a tissue since $u_T = 0$). Thus, equation (3) was simplified as follows.

$$\int_{V_i} (\rho C_p)_i \frac{\partial T_i}{\partial t} dV = \int_{S_{out-i}} [(-k_i \nabla T_i) - (\rho C_p)_i u_i T_i] \cdot n_{out-i} dS + \int_{S_{j-i}} (-k_i \nabla T_i) \cdot n_{j-i} dS + \int_{V_i} \dot{Q}_i''' dV \quad (4)$$

where, $i = j = T, Bl$ and $i \neq j$.

In equation (4), the first term on the RHS represented the energy gained by the i^{th} control volume from adjacent control volumes. In other words, this term represented the energy gained by a tissue (or blood) sub-volume from adjacent tissue (or blood) sub-volumes. The second term on the RHS represented the energy gained from the interaction between the tissue and blood sub-volumes in the vascularized tissue volume.

Next, normalizing equation (4) by volume V_i the following general form of the new BHTM (equation (5)) was obtained. This form satisfied the energy equation and was valid for any unheated and heated tissue. Note that equation (5) represented two equations; one for tissue and another for blood.

$$\langle (\rho C_p)_i \rangle_i \frac{\partial \langle T_i \rangle^i}{\partial t} = \frac{1}{V_i} \left[\int_{S_{out-i}} [(-k_i \nabla T_i) - (\rho C_p)_i u_i T_i] \cdot n_{out-i} dS + \int_{S_{j-i}} (-k_i \nabla T_i) \cdot n_{j-i} dS \right] + \langle \dot{Q}_i''' \rangle^i \quad (5)$$

where, $i = j = T, Bl$ and $i \neq j$ and

$$\langle (\rho C_p)_i \rangle_i \frac{\partial \langle T_i \rangle^i}{\partial t} \equiv \frac{1}{V_i} \int_{V_i} (\rho C_p)_i \frac{\partial T_i}{\partial t} dV \quad (6)$$

Simplifications

The following simplifications were made to obtain a simplified BHTM.

$$\frac{1}{V_i} \int_{S_{out-i}} (-k_i \nabla T_i) \cdot n_{out-i} dS \equiv C_{il} \nabla \cdot k_i \nabla \langle T_i \rangle^i \quad (7)$$

$$\frac{1}{V_i} \int_{S_{j-i}} (-k_i \nabla T_i) \cdot n_{j-i} dS \equiv \frac{(US)_{j-i}}{V_i} (\langle T_j \rangle^j - \langle T_i \rangle^i) \quad (8)$$

where, $i = j = T, Bl$ and $i \neq j$, and

$$\int_{S_{out-i}} [(-k_i \nabla T_i)] \cdot n_{out-i} dS \ll \int_{S_{out-i}} [-(\rho C_p)_i u_i T_i] \cdot n_{out-i} dS, i=Bl \quad (9)$$

$$\frac{1}{V_i} \int_{S_{out-i}} [-(\rho C_p u T)_i] \cdot n_{out-i} dS \equiv C_{i2} \nabla \cdot (P C_p < T_i >^i), i=Bl \quad (10)$$

$$\text{where, } P \equiv \frac{1}{V_{Bl}} \int_{V_{Bl}} (\rho u)_{Bl} dV$$

The first simplification (equation (7)) was similar to the simplification proposed by other investigators [18, 19, 29]. This simplification needs to be verified numerically and experimentally in vascularized tissues. A new, to be determined parameter C_{i1} was introduced in equation (7) to keep the simplification general.

The second simplification (equation (8)) defined the thermal interaction between a tissue and the embedded vasculature using the tissue and blood volume averaged temperatures and a heat transfer coefficient. Note that the heat transfer coefficient was different from conventional heat transfer coefficients since it was defined based on the volume averaged temperatures. Conventional heat transfer coefficients were defined using a tissue boundary temperature and a mixed mean blood temperature. To compute these new heat transfer coefficients, Shrivastava et al. derived Poisson conduction shape factors (PCSFs) for heated tissues embedded with one and two vessels using the area averaged tissue temperature and vessel boundary temperatures [37–40]. Poisson conduction shape factors for tissues embedded with more than two vessels are needed. Additionally, a quantification of Nusselt number is desired, which is defined based on the volume averaged blood temperature and the vessel wall temperature.

Regarding an appropriate number of thermally important vessels to be considered in an averaging volume to obtain US values, Xu et al. demonstrated that 1–3 vessels of diameter $\geq 50\mu\text{m}$ were present in every 1 mm^2 of a perfused kidney tissue in a pig. [41]. Similar studies are needed for other organs including human organs.

The third simplification (equation (9)) was justifiable since the convective term was at least ~ 10 times larger than the conductive term. This could easily be verified using the following values for the blood: $k = 0.5\text{ W/(mK)}$, $\rho = 1000\text{ kg/m}^3$, $C_p = 4180\text{ J/(kg K)}$, $u = 100\text{ D m/s}$, vessel diameter $D \geq 10\text{ }\mu\text{m}$, tissue length scale $\sim O(1\text{ mm})$ [42, 43].

The fourth simplification (equation (10)) was similar to the simplification proposed by equation (7). This simplification needs to be verified numerically and experimentally in vascularized tissues. A new, to be determined parameter C_{i2} was introduced in equation (10) to keep the simplification general.

Further, note that P was defined as a blood volume averaged vector mass flux in an averaging perfused tissue volume. This definition was appropriate for an averaging tissue volume with ≤ 1.0 thermally significant vessel. Xu et al. reported vessel number density of ≤ 1.6 per mm^2 for vessels with diameter $\geq 100\text{ }\mu\text{m}$ in a pig kidney cortex. In most of the cortex ($\sim 76\%$), the vessel number density was ≤ 1.0 . Less than 30% of the vessels were found paired [41]. For averaging perfused tissue volumes with two or more, arbitrarily flowing thermally important vessels; a new, more appropriate definition of P may need to be identified. Next, the constant C_{Bl2} should be evaluated using numerical simulations and experiments such that equation (10) was always satisfied. The new P should be defined such that it could be spatially and temporally quantified using imaging methods.

With the above simplifications implemented the following simplified BHTM was obtained. Equations (11) and (12) were coupled equations. Equation (11) was valid for the tissue sub-volume. Equation (12) was valid for the blood sub-volume.

$$\langle \rho C_p \rangle_T \frac{\partial \langle T_T \rangle^T}{\partial t} = C_{T1} \nabla \cdot k_T \nabla \langle T_T \rangle^T + \frac{(US)_{Bl-T}}{V_T} (\langle T_{Bl} \rangle^{Bl} - \langle T_T \rangle^T) + \langle \dot{Q}_T \rangle^T \quad (11)$$

$$\langle \rho C_p \rangle_{Bl} \frac{\partial \langle T_{Bl} \rangle^{Bl}}{\partial t} = C_{Bl2} \nabla \cdot (P C_p \langle T_{Bl} \rangle^{Bl}) + \frac{(US)_{Bl-T}}{V_{Bl}} (\langle T_T \rangle^T - \langle T_{Bl} \rangle^{Bl}) + \langle \dot{Q}_{Bl} \rangle^{Bl} \quad (12)$$

Note that in equation (12) the local perfusion P and the blood volume V_{Bl} were unknown. These values should be determined for different tissue types using imaging methods; e.g., magnetic resonance imaging, Positron emission tomography, ultrasound, etc [44–47]. Alternatively, the local perfusion P can be estimated by developing geometric vascular network maps and assuming mean blood flow of ~ 100 (diameter of vessel) m/s [42]. The tissue volume V_T can be estimated as the difference between the imaging voxel volume and blood volume.

Equation (11) and (12) together with equations (7–10) presented a generic BHTM framework. To develop the BHTM completely for a given organ and application, all the parameters in equations (11) and (12) should be estimated based on a real vasculature of the organ, physiological conditions, and expected variation in those physiological conditions for that application in the organ. This is so since vessel-tissue heat transfer rates and thermally important vessels are strong functions of the relative distribution of the vessels of different diameters and blood flow rates in an organ. [27, 37–40] Subject to subject variation may also need to be quantified. However, this variation may not be significant for a given organ and application. Shrivastava et al. measured unique, normalized temperature contours in porcine brains under RF heating conditions relevant for ultra-high field magnetic resonance imaging applications. [3] Sensitivity study needs to be performed on the relative importance of different parameters in predicting temperatures. Further, confidence intervals and error estimates in predicting temperatures need to be determined. Once all the associated parameters are determined, the use of the general BHTM adapted for a given organ and application will provide reasonably accurate volume averaged temperature field without solving for the point-wise true temperature field in a vascularized tissue. The tissue volume V_T should be determined on a case by case basis to establish the relationship between the values of all parameters and the local vascular geometry and blood perfusion rate.

Next, the new BHTM requires the diameter of the vessels, locations, flow rate in the vessels for each averaging voxel volume. These pieces of information are needed to compute US and P values for each averaging volume and can be obtained using current imaging methods. However, the model does not require the path of the vessel from one averaging volume to others. The effect of the vessel eccentricity on the vessel-tissue heat transfer rate and Poisson Conduction Shape Factors was found relatively less compared to the effect of the vessel radius. [37–40] Following a certain vessel and building an imaging based vascular tree is challenging. The model presents a way to obtain temperatures by circumventing the need for knowing a continuous vascular tree.

A continuous vascular tree is required to develop confidence intervals and error estimates everywhere in an organ. Since building a continuous vascular tree is challenging, discrete temperature measurements need to be performed to estimate confidence intervals and error

estimates. 'C' parameters and their sensitivities can be estimated using artificial, physiologically realistic, numerical networks.

Comparison with the Pennes' Bioheat Model

Pennes' bioheat model was presented in equation (13).

$$(\rho C_p)_T \frac{\partial T_T}{\partial t} = \nabla \cdot k_T \nabla T_T + w C_p (1 - \varepsilon) (T_{Bl} - T_T) + \dot{Q}_T''' \quad (13)$$

Traditionally, it was assumed that 1) this model was a point wise differential equation; and 2) the model solved for a point wise tissue temperature T_T assuming blood as an infinite heat sink at temperature T_{Bl} . However, validity of this model as a point wise true differential equation has been questioned on physical as well as theoretical grounds [15]. Volume averaged nature of the Pennes' equation was suggested by several previous researchers to provide the Pennes' equation with physical and theoretical validity; e.g., [18,29].

Simplicity and superior performance of the Pennes' bioheat model compared to other BHTMs has always been puzzling for a 'physically and theoretically invalid' model. A comparison of this equation with the newly developed equation (11) explained the reason for the better performance of the Pennes' BHTM (Table 1) [48, 49]. Note that the basic form of equation (13) and equation (11) was similar. Further, note that the Pennes' $w C_p (1 - \varepsilon)$ term was optimized to reduce the error between measured and modeled temperatures. This would be equivalent to obtaining $(US)_{T-Bl}/V_T$ values by optimization. Large deviations between Pennes' BHTM predictions and the absolute temperature field in a vascularized tissue could be explained by the absence of an equation for modeling the blood temperature variation in the Pennes' BHTM [12, 50].

Comparing equations (11) and (13), the two equations quantified the blood-tissue heat transfer rate terms differently. In equation (11) the blood-tissue heat transfer rate term was quantified on the walls of the blood vessels. In equation (13) the blood-tissue heat transfer rate term was quantified on the inlet and the outlet of the blood vessels. Thus, for steady state cases and $\varepsilon = 0$ in the Pennes' equation the blood-tissue heat transfer rate terms of the two equations were equal to each other. For transient cases, the blood-tissue heat transfer rate term of equation (11) was more appropriate compared to the Pennes' term with $\varepsilon = 0$. The introduction of the adjustable, unknown equilibration parameter ε allowed the Pennes' blood-tissue heat transfer rate term to be appropriately equated to the heat transfer rate term of equation (11).

To graphically compare the new BHTM and the Pennes' BHTM, a one-dimensional (1-D), steady state case with no source term and uniform properties was considered. The problem description in a non-dimensional form is presented below.

$$\frac{d^2 \theta_T}{d\xi^2} + \frac{\gamma}{1 - \beta} (\theta_{Bl} - \theta_T) = 0 \quad (14)$$

$$\lambda \frac{d\theta_{Bl}}{d\xi} + \frac{\gamma}{\beta} (\theta_T - \theta_{Bl}) = 0 \quad (15)$$

and,

$$\theta_T|_{\xi=0}=0, \theta_T|_{\xi=1}=1, \text{ and } \theta_{Bl}|_{\xi=0}=0.5, \text{ with } C_{T1}=1=C_{Bl2}, \gamma=5\pi, \beta=10\%, C_{T1}=1=C_{Bl2}$$

$$\text{where, } \theta_i = \frac{\langle T_i \rangle^i - \langle T_T \rangle^T|_{x=0}}{\langle T_T \rangle^T|_{x=L} - \langle T_T \rangle^T|_{x=0}}, \xi = \frac{x}{L}, \gamma = \frac{(US)_{Bl-T}}{V_T + V_{Bl}} \frac{L^2}{k_T}, \beta = \frac{V_{Bl}}{V_T + V_{Bl}}, \lambda = \frac{|P|C_p L}{k_T}$$

To simulate the Pennes' equation the non-dimensional blood temperature was assumed to stay constant at 0.5 in the simplified, non-dimensional, 1-D equation (14). Results demonstrated the effect of spatially varying blood temperature on the tissue temperature (Figure 1). As the perfusion approached infinity ($\lambda > 1000$ in the 1-D simulations) the solution of the new BHTM approached the solution of the Pennes' equation, as it must.

Summary

A new bioheat thermal model has been derived to predict temperatures in a vascularized tissue. The model satisfied the following three criteria: 1) conservation of energy; 2) the heat transfer between blood and tissue was modeled without following a vessel path; and 3) model was applicable to both an unheated and heated tissue. The new model provided the much needed theoretically rigorous framework using which future adaptations of the model for specific organs and tissue types can be performed to predict accurate temperatures.

Acknowledgments

R01 CA94318, R01 EB0000895, R01 CA94200, C06 RR12147, C06 RR17557, BTRR - P41 RR08079, R01 EB006835, R01 EB007327, P41 RR08079, and the Keck foundation.

Nomenclature

C_p	specific heat (J/(kg.K))
D	vessel diameter (m)
k	thermal conductivity (W/(m.K))
L	characteristic length of an imaged voxel
n_{i-j}	normal vector from i to j
P	Perfusion vector (kg/(m ² .s))
$\dot{Q}'''$	power (W/m ³)
S_{i-j}	surface area between volume i and j (m ²)
T	temperature (K)

U	heat transfer coefficient
t	time (s)
u	velocity (m/s)
V	volume (m ³)
w	Pennes' perfusion term
Bl	blood
T	tissue
β	blood volume over imaged voxel volume
ε	Pennes' equilibration term (0–1)
λ	ratio of the energy carrying capacity of the blood and tissue
ρ	density (Kg/m ³)
θ	non-dimensional temperature
ξ	non-dimensional length

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Figure 1.
A comparison between the new BHTM and the Pennes' BHTM in a uniform, one dimensional, unheated tissue.

Table 1

Comparison between the generic BHTM and the empirical Pennes' BHTM

	Generic BHTM	Pennes' BHTM
No. of equations	Two coupled differential equations; one for tissue another for blood	One; for tissue alone.
Thermal model type	Derived	Empirical
Tissue temperature variable	$\langle T_T \rangle^T$	T_T
Transient term for tissue	$\langle \rho C_p \rangle_T^T \frac{\partial \langle T_T \rangle^T}{\partial t}$	$(\rho C_p)_T \frac{\partial T_T}{\partial t}$
Thermal conduction term for tissue	$C_{Ti} \nabla \cdot k_T \nabla \langle T_T \rangle^T$	$\nabla \cdot k_T \nabla T_T$
Blood-tissue heat transfer rate term for tissue	$\frac{(US)_{Bl-T}}{V_T} (\langle T_{Bl} \rangle^{Bl} - \langle T_T \rangle^T)$	$w C_p (1 - \varepsilon) (T_{Bl} - T_T)$
Power term for tissue	$\langle \dot{Q}_T \rangle^T$	$\dot{Q}_T$