Bioheat transfer in a spherical biological tissue: a comparison among various models

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Abstract. The investigation of bioheat transfer is a difficult issue because it entails a mixture of many mechanisms to take into account, such as thermal conduction in tissues, convection and blood perfusion, metabolic heat generation, vascular structure, changing of tissue properties depending on physiological condition and so on. This topic has a key role to predict accurately the temperature distribution in tissues, especially during biomedical applications. In this paper, different bioheat transfer models are resumed and compared. The biological tissue is modelled as a porous sphere and liver tissue properties are used. Governing equations are averaged over a Representative Elementary Volume (REV) of the living tissue. Transient bioheat equations based on models like, for example, Pennes model, Local Thermal Non-Equilibrium equations (LTNE model), are employed. In the employed equations, radiative heat transfer is also considered. Governing equations with the appropriate boundary conditions are solved with the finite-element code COMSOL Multiphysics®. The effects of hyperthermia on the living tissue are included with a source term in the tissue energy equation. Results are presented in terms of temperature profiles in the biological tissue; the aim is to appreciate differences due to the various bioheat models.

Nomenclature

| Symbol | Description |
|--------|-------------|
| a      | volumetric transfer area, m⁻¹ |
| cₚ     | specific heat, J kg⁻¹ K⁻¹ |
| d      | diameter of blood vessel, m |
| h      | heat transfer coefficient, W m⁻² K |
| I₀     | intensity of radiation, W m⁻² |
| k      | thermal conductivity, W m⁻¹ K⁻¹ |
| kᵣ     | “radiative” thermal conductivity, W m⁻¹ K⁻¹ |
| n      | refractive index |
| qᵣ     | radiative heat flux, W m⁻² |
| Q      | power density, W m⁻³ |
| t      | time, s |
| T      | temperature, K |
| u      | velocity, m s⁻¹ |
| R      | external radius of the sphere, m |
| r      | heating zone radius, m |
| r,z    | spatial coordinates, m |

Greek symbols

| Symbol | Description |
|--------|-------------|
| β      | extinction coefficient, m⁻¹ |
| ε      | porosity |
| ρ      | density, kg m⁻³ |
| σ      | Stefan-Boltzmann constant, W m⁻² K⁻⁴ |
| ω      | blood perfusion rate, s⁻¹ |

Subscripts

| Symbol | Description |
|--------|-------------|
| a      | arterial |
| b      | blood |
| dis    | dispersion |
| ext    | external |
| f      | fluid |
| v      | venous |
| Pennes | pertinent to the Pennes’ model |
1. Introduction

Bioheat transfer is a difficult issue because it entails a mixture of many mechanisms to take into account, such as thermal conduction in tissues, convection and blood perfusion, metabolic heat generation, vascular structure, changing of tissue properties depending on physiological condition and so on. This topic has a key role to accurately predict the temperature distribution in tissues, especially during biomedical applications.

Hyperthermia is a human body situation caused by a lack of thermoregulation, in which the temperature goes beyond its normal values. Hyperthermia can be caused by natural reasons, as in fever, or it can be induced. Induced hyperthermia is a solution for many diseases [1]. For example, heat can be applied to destroy cancer cells, as in radiofrequency or microwave ablation [2 - 5]. With this technique, an antenna is placed into a tissue, and necrosis is induced by applying a certain thermal dose. Other examples are radiofrequency cardiac ablation, in which heat is used to destroy abnormal conduction pathways through the myocardium caused by arrhythmia [6, 7], or laser angioplasty [8-11], in which heat is employed for cardiovascular diseases.

When designing engineering tools for biomedical applications, modelling has a primary role, because of the difficulty of carrying out experiments, due to ethical reasons and small phenomena scale. Many models have been proposed through the years to describe heat transfer in biological tissues. This paper is an overview of some of the most relevant models used through the years. Four models (Pennes [12], Local Thermal Equilibrium [13], Local Thermal Non-Equilibrium [14] and Nakayama and Kuwahara [15]) are applied on spherical human tissue, in order to determine temperature profiles. Heating is supplied to the tissue by a spherical internal heating source. Various geometrical and fluid-dynamics conditions are analyzed, together with an analysis on radiative effects in the semi-transparent medium. The scope is to compare such models to appreciate when differences are significant, and results are presented in terms of temperature profiles in the biological tissue.

2. Geometry and properties

The transient temperature of a biological tissue during hyperthermia treatment with different models of bioheat equations is analyzed. The vascular structures of tissue have been supposed to be uniformly distributed in order to consider the physical model as a uniform porous medium. The entire computational domain is taken to be a sphere with a radius of 3.10 cm, and the heating zone within the biological tissue is a centrally located sphere with a radius of 0.62 cm, as shown in figure 1. All the blood vessels are assumed to be straight in the blood flow direction and to merge in the porous medium, and both the entrance blood and the boundary temperatures are equal to 37 °C. In addition, the thermal properties of tissue and blood are isotropic, and the heat transfer coefficient and blood velocity are supposed to be constant throughout the domain.

Furthermore, metabolic heat generation is neglected because it is much smaller than the power density released during hyperthermia treatment.

Figure 1. Schematic diagram of the calculation domain.
In this study a vessel diameter of 15 μm and an intervessel distance of 140 μm are considered to yield an estimated porosity of 0.01 [16] and two values of porosities (0.005 and 0.05) are selected. The relationship between volumetric heat transfer areas and diameters of blood vessels is given by Yuan [16], and resumed in Table 1, in which the different blood velocities related to the sizes of the vessels are included, according to the literature [17-19].

| Volumetric transfer area \(a\) \(m^2 m^{-3}\) | \(\varepsilon=0.005\) | \(\varepsilon=0.05\) |
|---|---|---|
| \(d=8\) μm \(\left(\nu=0.07\) cm s\(^{-1}\)\) | 2500 | 25000 |
| \(d=20\) μm \(\left(\nu=0.3\) cm s\(^{-1}\)\) | 1000 | 10000 |
| \(d=30\) μm \(\left(\nu=0.4\) cm s\(^{-1}\)\) | 667 | 6667 |
| \(d=50\) μm \(\left(\nu=2\) cm s\(^{-1}\)\) | 400 | 4000 |
| \(d=100\) μm \(\left(\nu=3\) cm s\(^{-1}\)\) | 200 | 2000 |
| \(d=140\) μm \(\left(\nu=3.4\) cm s\(^{-1}\)\) | 143 | 1429 |

Thermal properties of tissue and blood are chosen according to the work by Kou et al. [20]. Thermal conductivities of tissue and blood are 0.5 W m\(^{-1}\) K\(^{-1}\), densities of tissue and blood are 1050 kg m\(^{-3}\), and specific heat capacities of tissue and blood are 3770 J kg\(^{-1}\) K\(^{-1}\). To notice that the common input parameters are considered the same for the different models, because the paper is focused on the comparison among the different bioheat equations and not on the sensitivity of the models to the input parameters. However, it could be interesting to consider this analysis in further works. Moreover, two heating conditions are assumed: 2 s heating with a power density of 50 x 10\(^6\) W m\(^{-3}\) and 50 s heating with a power density of 2 x 10\(^6\) W m\(^{-3}\). The absorbed power density of blood is estimated to be one-tenth of that of tissue [21].

3. Mathematical models

Here the different four bioheat models applied to the porous biological sphere are described in detail. They are: the Pennes bioheat equation, the Local Thermal Non-Equilibrium equations (LTNE model), the Local Thermal Equilibrium equation (LTE model), and the three-energy equation model.

3.1 The Pennes’ bioheat equation

The bioheat equation developed in 1948 by Harry Pennes [12] is based on an experimental analysis of human forearm. Pennes’ model is a modified form of the transient heat conduction equation, including the effect of blood perfusion and metabolic heat generation rate on heat transfer within the living tissue. This model has been widely used by many researchers for numerous biological and medical applications, but it shows some shortcomings because of its simplicity; in fact, it does not take into account the blood flow direction, neglecting also important anatomical features of the circulatory network system such as the artery-vein countercurrent arrangement. Besides Pennes’ model considers only the venous blood stream as the one equilibrated with the tissue. In this case, as mentioned before, metabolic heat generation is neglected because it is much smaller than the power density released during hyperthermia treatment. The Pennes’ bioheat equation, considering the external heat source and neglecting the metabolic heat source, can be written as:

\[
\left(\rho c_p\right)_t \frac{\partial T}{\partial t} = \nabla \cdot \left( \kappa \nabla T \right) + \left(\rho c_p\right)_b a_{\text{Pennes}} (T_a - T_b) + Q_{\text{ext}}
\]

where \(t\) is the time and \(T\) is the temperature, the subscripts \(t\), \(b\) and \(a\) stand for tissue, blood, and arterial blood, respectively, \(\rho\) is the density, \(c_p\) is the specific heat, \(\kappa\) is the thermal conductivity, \(a_{\text{Pennes}}\) is mean
blood perfusion rate, that is selected to be 0.0036 s\(^{-1}\) for all cases [22], and \(Q_{\text{ext}}\) is the heat generation due to hyperthermia treatment. The blood temperature is assumed to be uniform throughout the tissue and it is taken as body temperature equal to 37 °C. The tissue temperature \(T_t\) is equal to 37 °C at the boundary of the sphere \(R=3.10\) cm and at the starting time \(t=0\) s.

3.2 The Local Thermal Non-Equilibrium equations (LTNE)
In 1998, Roetzel and Xuan [14] introduced a two-equation bioheat model that considers the heat transfer in porous media. They modelled the biological tissue by dividing it into two different regions, namely, the tissue region and the blood region (i.e. solid phase consists of muscle, vascular tissues and other solid compounds, while the fluid phase is made up by the blood flow that streams), without considering local thermal equilibrium between the two media and introducing an equivalent effective thermal conductivity in the energy equations of blood and tissue. Furthermore they proposed an interfacial convective heat transfer term instead of perfusion one. Based on the study of Yuan [16], the value of the heat transfer coefficient is selected to be 170 W m\(^{-2}\) K\(^{-1}\) for all cases. Considering the conservation of energy to the tissue and blood, the simultaneous differential equations can be formulated as follows.

For the tissue phase:

\[
(1-\varepsilon)(\rho c_p) \frac{\partial T_t}{\partial t} = (1-\varepsilon)k_t \nabla^2 T_t + h\alpha(T_b - T_t) + (1-\varepsilon)Q
\]  

(2)

For the blood phase:

\[
\varepsilon(\rho c_p)_b \left( \frac{\partial T_b}{\partial t} + \mathbf{u}_b \cdot \nabla T_b \right) = \varepsilon k_b \nabla^2 T_b + h\alpha(T_t - T_b) + \varepsilon Q_b
\]  

(3)

where \(T_t\) and \(T_b\) are temperatures averaged over the tissue and blood volumes, \(\varepsilon\) is the porosity, \(h\) is the heat transfer coefficient, \(\mathbf{u}_b\) is the blood velocity vector, \(a\) is the volumetric transfer area between tissue and blood, and \(Q\) is the absorbed power density.

The initial and boundary conditions are:

\[T_t(t,R,z) = 37 \degree\text{C at } R=3.10\text{ cm};\]
\[T_t(0,r,z) = T_b(0,r,z) = 37 \degree\text{C}\]

3.3 The Local Thermal Equilibrium equation (LTE)
When the Local Thermal Equilibrium hypothesis is maintained, the temperature of the tissue is the same of the blood temperature \((T_t=T_b=T)\), thus the equations (2) and (3) can be combined into a single equation as follows:

\[
\left[(1-\varepsilon)(\rho c_p)_t + \varepsilon(\rho c_p)_b + \varepsilon(\rho c_p)_b \mathbf{u}_b \cdot \nabla T\right] = \left[(1-\varepsilon)k_t + \varepsilon k_b\right] \nabla^2 T_t + (1-\varepsilon)Q_t + \varepsilon Q_b
\]  

(4)

The initial and boundary conditions are the same of the LTNE model.

3.4 The three-energy equation model
In 2008, Nakayama and Kuwahara [15] developed a generalized two-equation bioheat models for vascular and extravascular space in local thermal non-equilibrium condition and they incorporated blood perfusion term within the two sub-volume equations. Then they extended the two-equation model to three-equation model to consider the effect of heat transfer in closely spaced countercurrent artery-vein pair, illustrated in figure 2. The three equations are derived for arterial blood phase, venous blood phase and tissue phase distinctively with three different temperatures as follows.
Figure 2. Schematic view of countercurrent heat exchange.

For the arterial blood phase:

$$\varepsilon_a (\rho c_p)_f \frac{\partial T_a}{\partial t} + \varepsilon_a (\rho c_p) u_a \cdot \nabla T_a = \left[ \varepsilon_a k_f + \varepsilon_a k_{dis,a} \right] \nabla^2 T_a - a_a h_a (T_a - T) - \omega_a (\rho c_p)_f T_a + \varepsilon_a Q_b \tag{5}$$

For the venous blood phase:

$$\varepsilon_v (\rho c_p)_f \frac{\partial T_v}{\partial t} + \varepsilon_v (\rho c_p) u_v \cdot \nabla T_v = \left[ \varepsilon_v k_f + \varepsilon_v k_{dis,v} \right] \nabla^2 T_v - a_v h_v (T_v - T) - \omega_v (\rho c_p)_f T_v + \varepsilon_v Q_b \tag{6}$$

For the tissue phase:

$$(1-\varepsilon) (\rho c_p) \frac{\partial T}{\partial t} = (1-\varepsilon) k \nabla^2 T + a_a h_a (T_a - T) + a_v h_v (T_v - T) + (\rho c_p)_f (\omega_a T_a + \omega_v T_v) + (1-\varepsilon_a - \varepsilon_v) Q_t \tag{7}$$

The subscripts t, a, v, represent tissue, arterial and venous blood, respectively, while $k_{dis}$ is the thermal dispersion conductivity, which can be estimated according to the relationship in [23]:

$$k_{dis} = \frac{3 \varepsilon_a \left[ (\rho c_p)_f \right]^2 |u|}{14 a_a h_a} \tag{8}$$

Following the studies of Nakayama et al [15, 24], some assumptions have to be considered:

- $\varepsilon_a = \varepsilon_v$ and $a_a + a_v = a_t$
- $a_a h_a = a_v h_v$
- $u_a = u_v$
- $\omega_a = -\omega_v$

In this model the convective heat transfer coefficients $ah$ considered in the LTNE equations, are replaced by the convection-perfusion terms, namely $(a_i h_i + (\rho c_p)_f \omega)$ [25]; furthermore, the perfusion rate $\omega$ should vary locally, unlike that of Pennes, but it is assumed that its local value is provided everywhere, and its value varies in the range from $2 \times 10^4$ s$^{-1}$ to $5 \times 10^4$ s$^{-1}$ [15], so in this paper the value of blood perfusion is selected to be $0.0005$ s$^{-1}$ for all cases, considering the value that reduces mostly the heat transfer coefficient; specifically, $h=156.1$ W m$^{-2}$ K$^{-1}$ in the worst case, for porosity $\varepsilon=0.005$ and blood velocity modulus $\nu=3.4$ cm/s. Also, for this bioheat model, the initial and boundary conditions are the same of those used for the models above.
4. Numerical approach and validation
The bioheat transient models have been implemented by using the finite-element commercial code COMSOL Multiphysics software. A 2D axissymmetric model has been used to minimize computational efforts and consequently computing time. The mesh chosen for all the models has 11746 triangular elements; thicker meshes have been tested on temperature profiles, but without particular improvements. As regards the transient solver, the absolute tolerance used is 0.001, the time stepping method is the intermediate BDF with initial and maximum steps of 0.001 s and 1 s respectively for the 50 s heating case. For the 2 s heating condition, the maximum step considered is 0.1 s. In order to validate the presented different mathematical models, simulation results of tissue temperature distributions at the centre of the sphere are then compared against the results obtained by Yuan [16], in which LTNE and LTE models are implemented for different conditions of porosity, blood velocities and heating conditions for a cubical tissue. In this work the sphere has the same volume of the Yuan’s cube, in order to have the same heating power density; moreover the properties of blood and tissue, the blood velocities and the heating conditions chosen in this work are identical in order to validate the results obtained in COMSOL. The LTNE and LTE models have been simulated in COMSOL for all porosities, blood velocities and heating conditions and they fit the results obtained by Yuan very well in all cases. In figure 3 only the extreme cases of LTNE equations have been presented, considering three blood velocities, i.e. figure 3(a) shows the results for $\varepsilon=0.005$, $Q_f=2 \times 10^6$ W m$^{-3}$ and the blood velocities $u=0.07$ cm s$^{-1}$, $u=0.4$ cm s$^{-1}$, $u=3.4$ cm s$^{-1}$; figure 3 (b) regards the outcomes for $\varepsilon=0.05$, $Q_f=50 \times 10^6$ W m$^{-3}$ and the same three blood velocities. An excellent agreement with literature data has been found.

![Figure 3. Temperature distributions of LTNE model compared with Yuan's LTNE equations: (a) $\varepsilon=0.005$, $Q_f=2 \times 10^6$ W m$^{-3}$; (b) $\varepsilon=0.05$, $Q_f=50 \times 10^6$ W m$^{-3}$.](image)

5. Results and discussion
In this section all the tissue temperatures at the central point of the sphere obtained from the simulations for the different analyzed bioheat models are presented and compared at the same blood velocities, considering four separate cases as described in figures 4-7.

Comparing figure 4 to figure 6 and figure 5 to figure 7, the first result to underline is that for all the models the maximum temperature increases in the case of shorter heating duration, but in this condition of quick heating the temperature drop rate occurs more rapidly than in the longer heating because of the enhanced heat transfer. Another common conclusion for all the models is that the temperature decreases with an increase in porosity because higher porosity means having more blood to carry the heat away from the tissue, see figure 4 vs. figure 5 and figure 6 vs. figure 7. Moreover the Peclet number, that is equal to $\varepsilon u \rho c_p 2R/k$, increases as the porosity increases too, so the advection term becomes more important than the conductive one and consequently the temperature decreases more quickly. Obviously this is not valid for the Pennes equation that is not referred to a porous medium.
Comparing LTNE and LTE models for the two porosities considered, they yield the same results for lower velocities, specifically for $u<0.4$ cm s$^{-1}$, which means that the LTE equation is suitable for predicting the temperature during hyperthermia treatment when the blood vessels distributed in the tissue have a diameter less than 30 μm (capillaries, arterioles and terminal arteries); for higher velocities (and consequently vessels diameters), the LTE model overrates the heat carried out by the blood flow; in particular, the increase of velocity corresponds to a decrease of the Stanton number, that is equal to $h/(\mu\rho c_p)$, so the LTNE equations have to be used. In addition, for the LTNE equations the tissue temperature drops as the blood velocity rises, until $u=2$ cm/s; for higher velocities, the temperature restarts to increase because the higher velocity is compensated by the growth of the volumetric transfer area $a$. These considerations on different velocities are not valid for the Pennes’ model, which does not take into account the blood velocity, but only the blood perfusion.

As regards the Nakayama three-energy equation model, the results are in good agreement with the LTNE model for the lowest porosity and both the heating conditions, while for $\varepsilon=0.05$ it yields higher temperatures than the LTNE ones, except for the highest velocity $u=3.4$ cm/s, when LTNE equations result in higher temperatures. However, this more complex model requires more detailed anatomical data compared to others, so its application could be useful only in particular case, such as when artery and vein temperatures have necessarily to be considered different.

To notice that typical values of tissue temperatures are higher than 55 °C because the goal of thermo ablation therapy is the necrosis of tumoral tissue, and actually this can be obtained with different combinations of input power and time of application depending also on the tumor dimension, for example from 32 W to 180 W for a total duration of the corresponding treatment of 15 min and 6 min as described in [26]. On the other hand, the surrounding healthy tissue has to be preserved and the medical probe usually cannot support temperatures higher than 120 °C, so it is preferable to not overcome 100 °C. For these reasons, the differences observed are important especially taking into account higher input powers and application times.
Figure 5. Tissue temperature distributions for $\varepsilon = 0.05$, $Q_t = 2 \times 10^6$ W m$^{-3}$ when heating time is 50 s: (a) $u = 0.07$ cm/s, (b) $u = 0.4$ cm/s, (c) $u = 2$ cm/s, (d) $u = 3.4$ cm/s.

Figure 6. Tissue temperature distributions for $\varepsilon = 0.005$, $Q_t = 50 \times 10^6$ W m$^{-3}$ when heating is 2 s: (a) $u = 0.07$ cm/s, (b) $u = 0.4$ cm/s, (c) $u = 2$ cm/s, (d) $u = 3.4$ cm/s.
Figure 7. Tissue temperature distributions for $\varepsilon=0.05$, $Q_t=50 \times 10^6$ W m$^{-3}$ when heating time is 2 s: (a) $u=0.07$ cm/s, (b) $u=0.4$ cm/s, (c) $u=2$ cm/s, (d) $u=3.4$ cm/s.

In addition, it is interesting to show the computational times of the different models simulations, more in particular, it has been chosen the most onerous case, which is referred to $Q_t=50 \times 10^6$ W m$^{-3}$ when heating time is 2 s, for $\varepsilon=0.05$, and $u=3.4$ cm s$^{-1}$. In this situation, using a 2.50 GHz Intel Core i7-4710MQ CPU and a 16 GB 799 MHz DDR3 RAM, the computational times for Pennes’ equation, LTE model, LTNE equations and three-energy equation model are 30’19'', 33’37'', 45’23'', and 59’50’’ respectively. These results confirm the simplicity of Pennes’ bioheat model, which is also the less onerous computationally, but in this case, it produces not accurate outcomes. In the other cases, the computational times are comparable to the Pennes’ ones, so it has not been reported.

6. Radiative heat transfer

Radiation effects on the biological medium considered in this paper can be analysed with two simplified approaches, the Rosseland diffusive approximation and the Beer-Lambert-Bouguer law; the first assumes the medium to be optically thick and allows to define a “radiative conductivity” as follows:

$$k_R = \frac{16n^2\sigma T^3}{3\beta}$$

(9)

where $n$ is the refractive index, assumed to be 1.4 [27], $\sigma$ is the Stefan-Boltzmann constant and $\beta$ is the extinction coefficient, considered equal to 5550 m$^{-1}$, according to the study of optical properties of ex vivo human tissues by Simpson et al. [28]. The Beer-Lambert-Bouguer law, instead, is a simplified form for the Radiative Transfer Equation in which the radiation is assumed to be collimated, and consequently the radiative heat flux divergence (heat source term for the governing equations) could be written as:

$$\nabla \cdot q_R = -\beta I_0 e^{-\beta r^2 + z^2}$$

(10)
where \( I_0 \) is the intensity of radiation measured in W m\(^{-2}\). Since one can assume that the energy irradiates from the internal sphere to the external (the internal sphere acts as a catheter with a spherical tip), the heat exchange area for the radiation contribution is the internal/external spheres contact surface area. This because if one assumes that the radiative source is pointwise, for \( r = 0 \) one can have an infinite value of the radiative source term in Eq. 10. For this reason, the tissue temperature is evaluated at \( r=0.62 \) cm in the model that accounts for the Beer-Lambert-Bouguer law and consequently it is compared with tissue temperature at \( r=0.62 \) cm for LTNE. Radiative contribution effects are presented in figure 8 for both Rosseland approximation and Beer-Lambert-Bouguer law. It is shown that in both cases the radiative contribution does not affect the tissue temperature in all the models considered and can be neglected, even in the case of the maximum temperature reached (i.e. for \( \varepsilon=0.005, Q_t = 50 \times 10^6 \) W m\(^{-3}\), \( u=0.07 \) cm/s and when heating time is 2 s).

7. Conclusions

The study of bioheat transfer is a challenging task because of the complexity of the involved phenomena. Modelling heat transfer in tissues has a key role because of the difficulty of carrying out experiments. In this paper some of the most relevant bioheat transfer models proposed through the years are applied on a spherical human tissue modelled as a porous medium, in order to compare them. This comparison is performed in terms of temperature profiles at equal conditions. More in detail, from the simplest to the most complex, the four models considered are the Pennes equation, the Local Thermal Equilibrium equation, the Local Thermal Non-Equilibrium equations and the three-equation model. By using the finite-element commercial code COMSOL Multiphysics software, the tissue temperature profiles versus time are presented for each model under different porosities, blood velocity, vessels diameters and heating conditions. Numerical results are validated by means of results from literature. According to the results, the Pennes’ model shows its inaccuracy due to its simplicity, while the LTE model is suitable to predict temperatures during hyperthermia therapy when the diameter of the blood vessels is less than 30 \( \mu \)m, which corresponds to the low blood velocity of 0.4 cm s\(^{-1}\). For higher velocities, and consequently vessels diameters, the LTE model overrates the heat carried out by the blood flow, so the LTNE equations have to be used to take into account interfacial convective heat transfer. As regards the Nakayama three-energy equation model, the results are in good agreement with the LTNE model for the lowest porosity and both the heating conditions, even if this model requires more detailed anatomical data compared to others, so its application could be useful only in particular case, such as when artery and vein temperatures have necessarily to be considered different. This means that the LTNE model is preferable.
Furthermore, for $\varepsilon=0.05$ the three-energy equation model yields higher temperatures than the LTNE ones, except for the highest velocity $u=3.4$ cm/s, when LTNE equations result in higher temperatures. Finally, radiative heat transfer effects have been analyzed by employing either Rosseland approximation or Beer-Lambert-Bouguer law, showing that radiation through biological tissues is negligible for the conditions herein presented. In conclusion, we can state that LTNE model is preferable because it is a good compromise between accuracy and complexity. For further developments, it is clear that these models will require more comparisons with experiments in order to understand which one is better depending on the application.

References
[1] Moros E 2012 Physics of thermal therapy: fundamentals and clinical applications (Boca Raton: CRC Press).
[2] Chu K F and Dupuy D E 2014 Thermal ablation of tumours: biological mechanisms and advances in therapy Nature Reviews Cancer 14 199-208.
[3] Diederich C J 2005 Thermal ablation and high-temperature thermal therapy: overview of technology and clinical implementation International journal of hyperthermia 21 745-53.
[4] Wang K, Tavakkoli F, Wang S and Vafai K 2015 Analysis and analytical characterization of bioheat transfer during radiofrequency ablation Journal of biomechanics 48 930-40.
[5] Rattanadecho P and Keangin P 2013 Numerical study of heat transfer and blood flow in two-layered porous liver tissue during microwave ablation process using single and double slot antenna International Journal of Heat and Mass Transfer 58 457-70.
[6] Yee R, Connolly S and Noorani H 2003 Clinical review of radiofrequency catheter ablation for cardiac arrhythmias The Canadian journal of cardiology 19 1273-84.
[7] González-Suárez A and Berjano E 2016 Comparative analysis of different methods of modeling the thermal effect of circulating blood flow during RF cardiac ablation IEEE Transactions on Biomedical Engineering 63 250-9.
[8] Karsch K R and Haase K K 1991 Coronary laser angioplasty: an update (Berlin: Springer-Verlag Berlin Heidelberg).
[9] Vincent G M, Fox J, Johnson M D, Strickland R, Garry S Land Hammond E 1990 Thermal laser probe angioplasty: Influence of constant tip temperature, plaque composition, and probe/vessel diameter ratio Lasers in surgery and medicine 10 420-6.
[10] Iasiello M, Vafai K, Andreozzi A, Bianco N and Tavakkoli F 2015 Effects of external and internal hyperthermia on LDL transport and accumulation within an arterial wall in the presence of a stenosis Annals of biomedical engineering 43 1585-99.
[11] Iasiello M, Vafai K, Andreozzi A and Bianco N 2016 Low-density lipoprotein transport through an arterial wall under hyperthermia and hypertension conditions–An analytical solution Journal of biomechanics 49 193-204.
[12] Pennes H H 1948 Analysis of tissue and arterial blood temperatures in the resting human forearm Journal of applied physiology 1 93-122.
[13] Vafai K 2015 Handbook of porous media (Boca Raton: CRC Press).
[14] Roetzel W and Xuan Y 1997 Bioheat equation of the human thermal system Chemical engineering & technology 20 268-76.
[15] Nakayama A and Kuwahara F 2008 A general bioheat transfer model based on the theory of porous media International Journal of Heat and Mass Transfer 51 3190-9.
[16] Yuan P 2008 Numerical analysis of temperature and thermal dose response of biological tissues to thermal non-equilibrium during hyperthermia therapy Med Eng & Phy 30 135-43.
[17] Crezee J and Lagendijk J J W 1992 Temperature uniformity during hyperthermia: the impact of large vessels Phys Med Biol 37 1321-37.
[18] Chato J C 1980 Heat transfer to blood vessels J Biomech Eng-T ASME 102 110-8.
[19] Weinbaum S and Jiji L M 1985 A new simplified bioheat equation for the effect of blood flow on local average tissue temperature J Biomech Eng-T ASME 107 131-9.
[20] Kou H S, Shih T C and Lin W L 2003 Effect of the directional blood flow on thermal dose distribution during thermal therapy: an application of a Green’s function based on the porous model Phys Med Biol 48 1577-89.

[21] Duck F A, Baker A C and Starrit H C 1998 Ultrasound in medicine London: Institute of Physics Publishing 57-88.

[22] Vera A and Leija L 2008 Microcoaxial Double slot antenna for interstitial hyperthermia: design, modeling and validation, in: International Conference on Advances in Electronics and Microelectronics ENICS2008 138-143.

[23] Yang C and Nakayama A 2010 A synthesis of tortuosity and dispersion in effective thermal conductivity of porous media International Journal of Heat and Mass Transfer 53 3222-30.

[24] Nakayama A, Sano Y and Yoshikawa K 2010 A rigorous derivation of the bioheat equation for local tissue heat transfer based on a volume averaging theory Heat Mass Transfer 46 739-46.

[25] Nakayama A, Kuwahara F and Liu W 2009 A Macroscopic Model for Countercurrent Bioheat Transfer in a Circulatory System Journal of Porous Media 12 289-300.

[26] Hoffmann R, Rempp H, Erhard L, Blumenstock G, Pereira P L, Claussen C D, Clasen S 2013 Comparison of four microwave ablation devices: an experimental study in ex vivo bovine liver Radiology 268 89-97.

[27] Tsenova V and Stoykova E 2003 Refractive index measurement in human tissue samples Proc. SPIE 5226 413-17.

[28] Simpson RC, Kohl M, Essenpreis M and Cope M 1998 Near-infrared optical properties of ex vivo human skin and subcutaneous tissues measured using the Monte Carlo inversion technique Phys Med Biol 43 2465–78.