SENSITIVITY ANALYSIS OF TRANSIENT BIOHEAT TRANSFER DURING THERMAL INJURY FORMATION OF BIOLOGICAL TISSUE

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Abstract. The sensitivity analysis of the transient temperature field in the 2D tissue domain with respect to its thermophysical parameters is discussed. In particular, the influence of tissue specific heat, thermal conductivity, perfusion rate and metabolic heat source on the temperature distribution is considered. In order to determine the influence of variations of these parameters on temperature distribution, the direct approach of sensitivity analysis is applied. The algorithm of modeling of tissue injury withdrawal based on Arrhenius integral is also presented. At the stage of numerical realization the boundary element method is used. In the final part of paper the results obtained are shown.

Keywords: *bioheat transfer, tissue injury integral, tissue injury, sensitivity analysis*

Introduction

During the interaction between biological tissue and external, high-temperature impulse elevated temperature and tissue damage can dynamically alter thermo-physical properties of the tissue. Such processes are usually modeled by the so-called Arrhenius injury integral, in which the reaction rate increases exponentially with the temperature [1-4].

According to the Arrhenius formula, the damage of the tissue is irreversible. It follows that even in the case of a very small increase and lowering of temperature the tissue remains damaged. As a matter of fact, in the case of moderate temperature (37 to 45÷55°C) the only response of the tissue is dilatation of the blood vessels, without any thermal injury. Therefore, one can conclude that if the tissue destruction does not exceed some threshold value, the tissue has the ability to return to its native state. In the current paper the possibility of tissue damage withdrawal is taken into consideration by using of algorithm proposed in [4].

The course of the physical process is, as a rule, analyzed on the basis of a certain mathematical model. One of the problems connected with the application of such a model is the sensitivity of the solution with respect to the parameters appearing in the governing equations. The sensitivity information may be used,

among others, to analyze the influence of the change of parameters on the final solution of the problem being considered [5-8]. Additional tasks required to determine the sensitivity functions result from differentiation of the assumed equation describing bioheat transfer with respect to the parameter, which means that the number of additional sensitivity tasks corresponds to the number of parameters with respect to which the sensitivity analysis is performed [5, 9].

In this paper the tissue is regarded as a homogeneous domain with a perfusion coefficient dependent on tissue necrosis, while the remaining thermal parameters are regarded as constant values. So, the sensitivity analysis has been done with respect to thermal conductivity, volumetric specific heat, an initial perfusion rate, and a metabolic heat source.

The basic problems, but also the additional problems resulting from the sensitivity analysis, have been solved using the 1st scheme of boundary element method for transient heat diffusion [5, 10].

1. Governing equations

The transient heat transfer in the 2D homogeneous domain of biological tissue (Fig. 1) is described by the bioheat transfer equation in Pennes formulation [2]

$$\mathbf{x} \in \Omega: \quad c\dot{T} = \lambda T_{,ii} + c_B G_B \left(T_B - T\right) + Q_{met} \tag{1}$$

where λ [$\mathrm{Wm^{-1}K^{-1}}$] is the thermal conductivity, c [$\mathrm{Jm^{-3}K^{-1}}$] is the volumetric specific heat, G_B [($\mathrm{m^3}_{blood}$/s)/($\mathrm{m^3}_{tissue}$)], c_B [$\mathrm{Jm^{-3}K^{-1}}$] and T_B correspond to the perfusion coefficient, the volumetric specific heat of blood and the artery temperature respectively, Q_{met} [$\mathrm{Wm^{-3}}$] is the internal metabolic heat source while $T = T(\mathbf{x}, t)$ and $\dot{T}$ denotes a temperature and its time derivative [4, 6, 8].

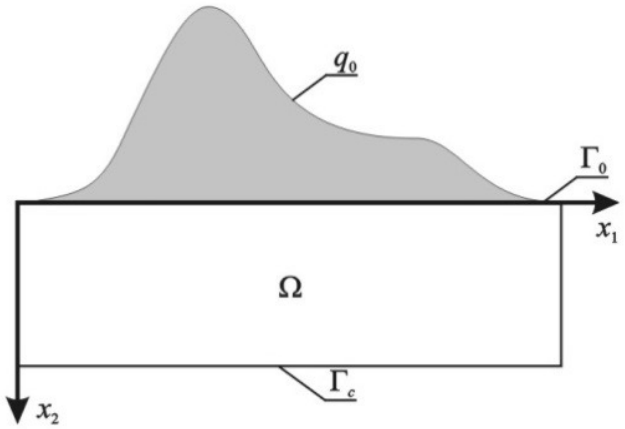

Fig. 1. Domain considered

Equation (1) is supplemented by boundary condition along the external boundary of the tissue Γ_0 in the form:

$$\mathbf{x} \in \Gamma_0 : \quad \begin{cases} q(\mathbf{x},t) = q_0, & t \le t_{exp} \\ q(\mathbf{x},t) = \alpha(T - T_{amb}), & t > t_{exp} \end{cases} \tag{2}$$

where q_0 [Wm^{-2}] is the known boundary heat flux, α [Wm^{-2}K^{-1}] is the convective heat transfer coefficient and T_{amb} is the temperature of surroundings, while t_{exp} is the exposure time. On the remaining parts of the boundary Γ_c the non-flux condition is accepted, and the initial distribution of temperature is also known.

In order to perform the conditions of non-controlled case of high temperature - biological tissue interaction, the heat flux along boundary Γ_0 is assumed to be the irregular one. The distribution of the heat flux is visible in Figure 1 and it is described by the polynomial function of 7th degree [4].

According to the necrotic changes in tissue, the blood perfusion coefficient is defined as [2]

$$G_B = G_B(\theta) = G_{B0} f(\theta) \tag{3}$$

where G_{B0} denotes the initial perfusion coefficient while $f(\theta)$ denotes the polynomial function in the form

$$f(\theta) = \sum_{j=1}^{3} m_j \theta^{j-1} \tag{4}$$

where m_j are the coefficients and θ is the Arrhenius injury integral [2, 3, 6]:

$$\theta(\mathbf{x}) = \int_0^{t^F} A \exp\left[-\frac{\Delta E}{RT}\right] \mathrm{d}t \tag{5}$$

In equation (5) A is the pre-exponential factor [s^{-1}], ΔE is the activation energy [J mole^{-1}] and R is the universal gas constant [J mole^{-1}K^{-1}], $[0,t^F]$ is the considered time interval, while the criterion for tissue necrosis is [2, 3]:

$$\theta(x) \ge 1 \tag{6}$$

The assumption of the tissue injury integral is that the damage of the tissue is irreversible. In order to consider that the tissue could get back to its native state after the thermal impulse is ceased, the following algorithm is proposed (Fig. 2).

Let us assume that for the time interval $[0, t^F]$ being under consideration and divided into F subintervals $[t^{f-1}, t^f]$ (where $f = 1,2\ldots F$), the values $T^0(\mathbf{x}) \ldots T^f(\mathbf{x})$ as well as $\theta^0(\mathbf{x})\ldots\theta^{f-1}(\mathbf{x})$ at the point $\mathbf{x} \in \Omega$ are known. At the same time the recovery threshold θ_{rec} is accepted.

If the injury integral at the point **x** for time t^f achieves the value equal to or greater than θ_{rec} then the injury of the tissue becomes irreversible. Otherwise the function denoted as $\theta_{app}(\mathbf{x}, T)$ is introduced in order to model the withdrawal of the tissue injury. In current paper it is assumed as the linear one between (T^0, θ^0) and (T^{f-1}, θ^{f-1}).

$$\theta_{app}(\mathbf{x}, T) = b_1 + b_2 T \tag{7}$$

For the time t^{f+1}, if $T^{f+1} < T^f$ and $\theta^f < \theta_{rec}$ again the function θ_{app} defined for time t^f is used [4].

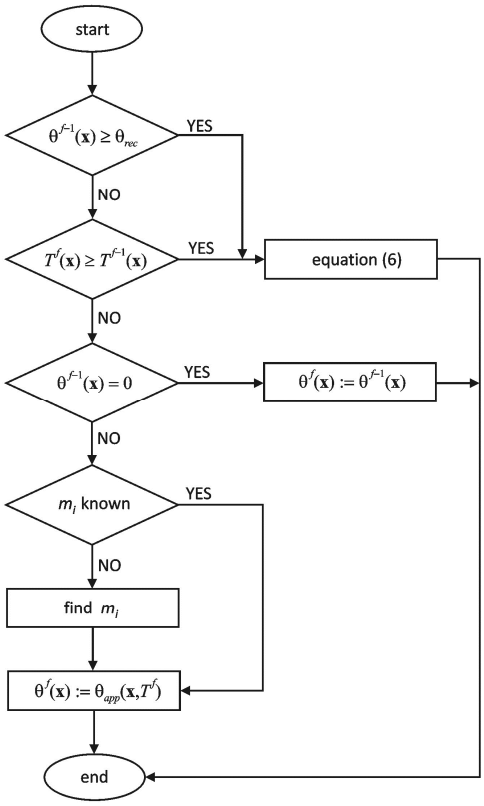

Fig. 2. The algorithm of tissue injury calculation

2. Sensitivity analysis

In order to determine the influence of thermophysical parameters on the temperature distribution in tissue domain, the direct approach of sensitivity analysis has been applied [7, 9].

According to the rules of direct method equation (1) is differentiated with respect to thermophysical parameter p_s, where $s = \lambda, c, G_{B0}$ or Q_{met} [5, 6]

$$\frac{\partial c}{\partial p_s}\dot{T} + c\frac{\partial \dot{T}}{\partial p_s} = \frac{\partial \lambda}{\partial p_s}T_{,ii} + \lambda\frac{\partial T_{,ii}}{\partial p_s} + \frac{\partial}{\partial p_s}\left[c_B G_{B0} f(\theta)\left(T_B - T\right)\right] + \frac{\partial Q_{met}}{\partial p_s} \tag{8}$$

After the mathematical manipulations one can write the equation for an additional sensitivity problem as

$$\mathbf{x} \in \Omega: \quad c\dot{U}^s = \lambda U^s_{,ii} + Q^s_V \tag{9}$$

where

$$U^s = \frac{\partial T}{\partial p_s} \tag{10}$$

denotes the sensitivity function of the parameter p_s, while [7]

$$\dot{U}^s = \frac{\partial U^s}{\partial t}, \quad U^s_{,ii} = \frac{\partial T_{,ii}}{\partial p_s} \tag{11}$$

The source component Q^s_V of the equation (9) is in the form

$$\begin{aligned} Q^s_V = &\left[\frac{k}{\lambda}\frac{\partial \lambda}{\partial p_s} - \frac{k}{G_{B0}}\frac{\partial G_{B0}}{\partial p_s} - \frac{k}{f(\theta)}\frac{\partial f(\theta)}{\partial p_s}\right]\left(T - T_B\right) \\ &-kU^s + \left(\frac{c}{\lambda}\frac{\partial \lambda}{\partial p_s} - \frac{\partial c}{\partial p_s}\right)\dot{T} - \frac{Q_{met}}{\lambda}\frac{\partial \lambda}{\partial p_s} + \frac{\partial Q_{met}}{\partial p_s} \end{aligned} \tag{12}$$

where

$$k = c_B G_{B0} f(\theta) \tag{13}$$

and the derivative function $f(\theta)$ with respect to parameter p_s is as follows

$$\frac{\partial f(\theta)}{\partial p_s} = m_2\frac{\partial \theta}{\partial p_s} + 2m_3\theta\frac{\partial \theta}{\partial p_s} \tag{14}$$

while the variation of θ is calculated as (cf. equation (5))

$$\frac{\partial \theta}{\partial p_s} = \int_0^{t^F} A\frac{\Delta E U^s}{RT^2}\exp\left[-\frac{\Delta E}{RT}\right]\mathrm{d}t \tag{15}$$

Equation (9) is supplemented by boundary conditions in the form

$$\mathbf{x}\in\Gamma_0:\quad \begin{cases} Q^s(\mathbf{x},t)=-\dfrac{1}{\lambda}\dfrac{\partial\lambda}{\partial p_s}q(\mathbf{x},t), & t\le t_{exp} \\ Q^s(\mathbf{x},t)=\alpha U^s-\dfrac{1}{\lambda}\dfrac{\partial\lambda}{\partial p_s}q(\mathbf{x},t), & t>t_{exp} \end{cases} \tag{16}$$

where

$$Q^s=-\lambda U^s_{,i}n_i \tag{17}$$

and the initial one

$$t=0:\quad U^s=0 \tag{18}$$

The change of temperature due to the changes of the parameters p_s can be estimated using the following formula

$$\Delta T=\sqrt{\sum_{s=1}^{n}\left(\frac{\partial T}{\partial p_s}\Delta p_s\right)^2} \tag{19}$$

3. Results of computations

The basic and also additional problems resulting from the sensitivity analysis have been solved using the 1st scheme of the boundary element method for 2D transient heat diffusion [5, 10].

The domain of rectangular shape (cf. Fig. 1) of dimensions 0.05×0.015 m is considered. The interior of domain has been divided into 6000 internal constant cells, while the external boundary into 320 constant elements.

In computations, the following values of tissue parameters have been assumed: λ = 0.3 $\mathrm{Wm^{-1}K^{-1}}$, c = 3.647 $\mathrm{MJm^{-3}K^{-1}}$, G_{B0} = 0.00125 $(\mathrm{m^3}_{blood}/\mathrm{s})/(\mathrm{m^3}_{tissue})$, Q_{met} = = 245 $\mathrm{Wm^{-3}}$, while for the blood c_B = 3.9962 $\mathrm{MJm^{-3}K^{-1}}$ and T_B = 37°C. The parameters of Arrhenius injury integral are: $A = 3.1\cdot10^{98}$ $\mathrm{s^{-1}}$, $E = 6.27\cdot10^5$ J $\mathrm{mole^{-1}}$, R = 8.314 J $\mathrm{mole^{-1}K^{-1}}$ and θ_{rec} = 0.05, and the complete form of perfusion coefficient definition (cf. equations (3) and (4)) is [4]:

$$G_B(\theta)=\begin{cases} G_{B0}, & \theta=0 \\ \left(1+25\theta-260\theta^2\right)G_{B0}, & 0<\theta\le 0.1 \\ \left(1-\theta\right)G_{B0}, & 0.1<\theta\le 1 \\ 0, & \theta>1 \end{cases} \tag{20}$$

The values of coefficients for the interval from 0 to 0.1 respond to the increasing of the perfusion coefficient caused by vasodilatation up to the value $\theta = 0.05$ (maximum of the function) and the beginning of the narrowing of blood vessels (between 0.05 and 0.1). The interval 0.1 to 1 they reflect blood flow decrease as the vasculature is going to shut down [2].

In the boundary condition (cf. equation (2)) the following values of parameters have been assumed: $\alpha = 10\ \mathrm{Wm^{-2}K^{-1}}$ and $T_{amb} = 20°\mathrm{C}$, maximal value of the heat flux q_0 is assumed as $20\ \mathrm{kWm^{-2}}$ while the exposure time is 30 seconds. The time step $\Delta t = 1$ s.

The co-ordinates of the points are (cf. Fig. 1): C_1 (0.01575, 0.001875), D_1 (0.03475, 0.000625), C_2 (0.01575, 0.003125) and D_2 (0.03475, 0.000875).

As it was previously mentioned, the sensitivity analysis has been performed with regard to thermal conductivity, volumetric specific heat, initial perfusion coefficient and metabolic heat source. It is assumed that for all parameters $\Delta p_s = 0.1 p_s$.

Figure 3 shows the courses of the temperature as well as the courses of the injury integral θ. At two of these points, C_1 and D_1, the value of the injury integral is above the recovery threshold θ_{rec}. At the point C_1 the value of the injury integral is much greater than 1, so the tissue is fully damaged, while at the point D_1 the value of the injury integral is 0.168, which means partly damaged tissue. Arrhenius integral values at points C_2 and D_2 haven't reached the recovery threshold, so the functions θ_{app} are defined for the stage of lowering temperature.

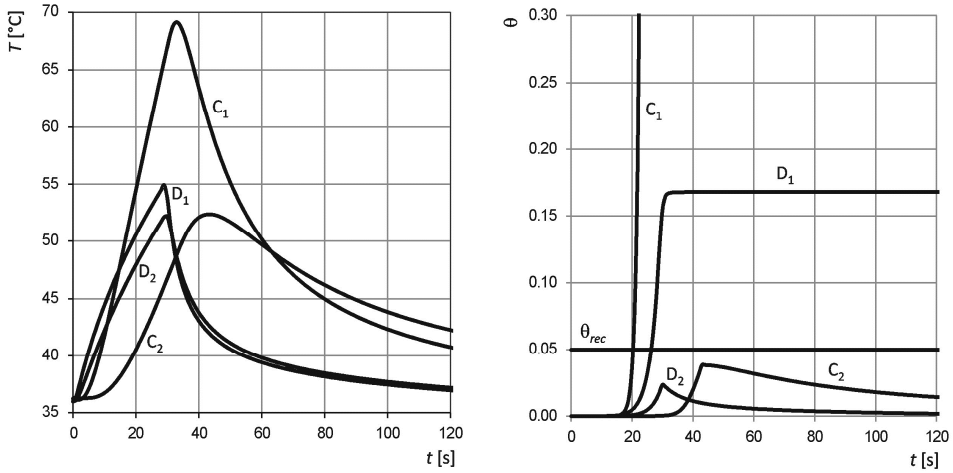

Fig. 3. Courses of temperature and the injury integral θ

The next two figures present the profiles of sensitivity function for successive thermophysical parameters of tissue. It turns out that 10% changes in parameters p_s values have effects mainly in the sensitivity functions of thermal conductivity λ

and volumetric specific heat. The maximal changes are noticed at the points C_1 and C_2.

The sensitivity function of the initial perfusion coefficient G_{B0} achieved a value much below 1°C (absolute value) while the values of sensitivities for metabolic heat source Q_{met} are practically negligible.

It should be pointed out that in each of the four cases, the courses of sensitivity functions at the points D_1 and D_2 were very similar.

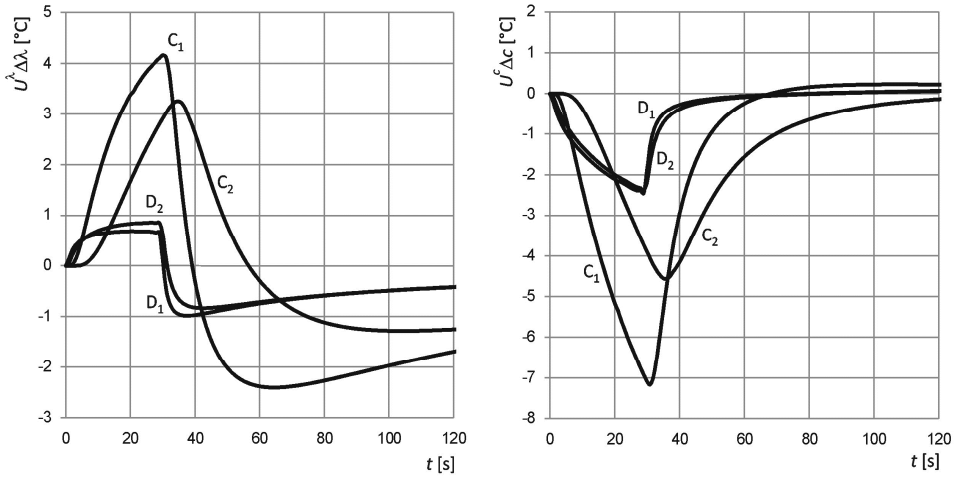

Fig. 4. Courses of sensitivity function of λ and *c*

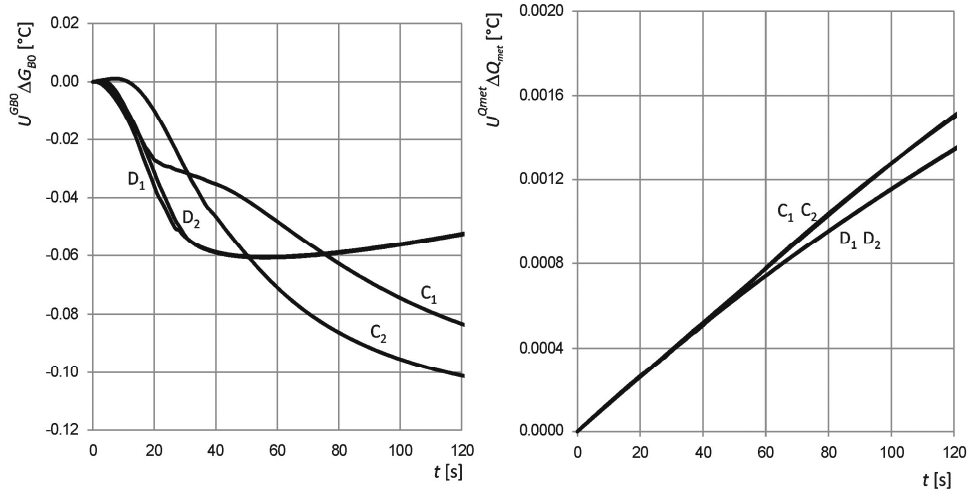

Fig. 5. Courses of sensitivity function of G_{B0} and Q_{met}

In the Figure 6 the changes of temperature due to the changes of parameters p_s are shown (cf. equation (19)). As for the single parameters the maximal changes are noticed at the points C_1 and C_2 (8.6 and 5.75°C respectively) as well as the courses at the points D_1 and D_2 are very alike (the changes up to 2.6°C).

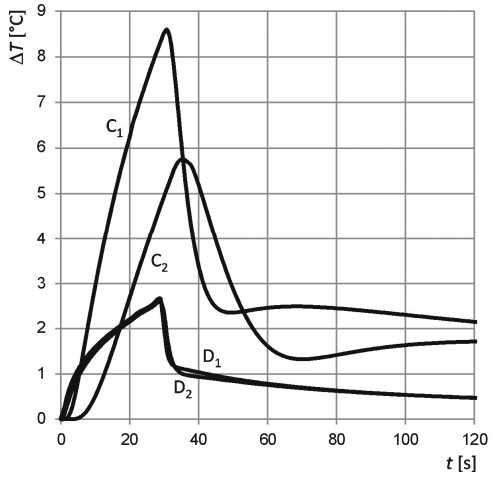

Fig. 6. Changes of temperature due to the changes of parameters p_s

4. Final remarks

The profiles of the sensitivity functions show that thermal conductivity and volumetric specific heat have the most substantial impact on temperature levels. It should be pointed out that for these two parameters maximal values of sensitivity function at the point C_1 (as well as at the points D_1 and D_2) are achieved about time when the external heat impulse is ceased while for the point C_2 the maximal values are reached a few seconds later. This is due to the necrotic zone around the point C_1. As it was written previously, the value of tissue injury integral at that point is much greater than 1, so it could be treated as the area of fully damaged tissue (cf. Fig. 3).

Application of the Arrhenius formulation in such a kind of problems seems to be quite a convenient tool to obtain additional information about the process considered. The proposed method of tissue injury calculation is closer to the real conditions of interaction between tissue and high-temperature impulse. Its main advantage is the possibility of estimation of the tissue recovery area, which could have an important part in the case of modelling of a fully controlled case of interaction, such as prostate hyperplasia or cancer thermotherapy.

It should be pointed out that the presented model could also be considered with phase change taken into account, similarly to that presented in [2]. At the stage of sensitivity analysis using the adjoint approach is also possible.

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