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Investigation of Tissue Thermal Damage Process with Application of Direct Sensitivity Method

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Abstract: In the paper the numerical analysis of thermal processes proceeding in the biological tissue is presented. The tissue is subjected to the external heat flux and 2D problem is taken into account. In order to determine the influence of variations of thermophysical parameters of tissue on the value of Arrhenius injury integral the direct approach of sensitivity analysis is applied. On the basis of tissue damage fraction the thermal injury formation process is analysed. At the stage of numerical realization the boundary element method is used. In the final part of the paper the example of numerical simulation is shown.

Keywords: bioheat transfer, tissue injury integral, sensitivity analysis, boundary element method

1 Introduction

It is well-known that temperature elevation and thermal damage can dynamically change the thermal distribution during coagulation by altering thermophysical properties of biological tissue. Consequently, parameters applied in bioheat transfer model can be regarded as temperature-dependent or tissue damage-dependent. Special attention in this field is dedicated to the changes in perfusion that accompany necrosis. Such kind of processes are usually modeled by the so-called Arrhenius injury integral in which the reaction rate increases exponentially with the temperature.

Using the concept of the tissue injury integral, Henriques [1] proposed model of the skin burn prediction. This model has been later analysed and developed in many works, e.g. in Torvi et al. [2] and Majchrzak et al. [3, 4]. Oden et al. [5] as well as Zhou et al. [6] presented models concerning the tissue denaturation during laser irradiation. The problem of relation between degree of tissue damage and

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the value of perfusion coefficient has been analysed in Abraham et al. [7], who proposed the polynomial function modeling initially growth of blood flow caused by vasodilatation and decrease of perfusion as the value of injury integral increase. Glenn at al. [8] used the exponential function in order to investigate changes in value of scattering coefficient during laser – tissue interaction.

The main assumption of the Arrhenius formula is that the damage of tissue is irreversible, so even in the case of very little increase and lowering of temperature the tissue remain damaged. On the other hand, when the temperature is moderate, that is from 37˚C to 45–55˚C, the blood vessels in the tissue become dilated without being thermally damaged. Taking these two facts into account, in current paper special function based on approximation of Arrhenius integral and temperature was accepted in order to model withdrawal of tissue injury.

Knowledge of the temperature distribution, degree of the tissue injury and value of the perfusion coefficient allow ones to estimate the depth of the thermal damage as well as the value of the tissue damage fraction corresponding to respective zones in which different effects inducted by the thermal impulse occurred. It should be pointed out that knowledge of the depth of tissue necrosis could be significant information in some thermal therapies, such as prostate hyperplasia or cancer thermotherapy.

In the current paper the tissue is regarded as a homogeneous domain in which heat transfer is assumed to be transient and two-dimensional. Mathematical description of the processes proceeding in the tissue is based on the Pennes equation with perfusion coefficient dependent on tissue necrosis, while the remaining thermal parameters are regarded as constant values.

One of the problems connected with the application of mathematical 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 analyse the influence of the change of parameters on the final solution of the problem being considered. Such kind of problems have been analysed in Davies et al. [9] and Jasiński [10], while Majchrzak et al. [11] presented sensitivity analysis of the Henriques burn integrals mentioned above.

Additional tasks required to determine the sensitivity functions result from differentiation of the assumed equation describing heat transfer in biological tissue 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 done.

The basic problems, but also the additional problems resulting from the sensitivity analysis, have been solved using the 1^{st} scheme of boundary element method for

transient heat diffusion.

2 Mathematical model

The 2D domain of homogeneous biological tissue of rectangular shape (Fig. 1.) is considered, with boundary Γ_0 subjected to an irregular external heat impulse. The transient heat transfer in this domain is described by the Pennes equation in the form [1 – 11]

$$\mathbf{x} \in \Omega: \quad c\dot{T} = \lambda T_{,ii} + Q_V \tag{1}$$

where λ [$\mathrm{Wm^{-1}K^{-1}}$] is the thermal conductivity, c [$\mathrm{Jm^{-3}K^{-1}}$] is the volumetric specific heat, Q_V [$\mathrm{Wm^{-3}}$] is the internal heat source, while $T = T(\mathbf{x}, t)$ and $\dot{T}$ denotes a temperature and its time derivative.

Eq. (1) is supplemented by boundary conditions:

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

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

$$\mathbf{x} \in \Gamma_c: \quad q(\mathbf{x},t) = 0 \tag{3}$$

and the initial distribution of temperature is also known

$$t = 0: \quad T(\mathbf{x},t) = T_p \tag{4}$$

The component Q_V comprises the information of the internal heat sources is described as

$$Q_V = Q_{perf} + Q_{met} = c_B G_B (T_B - T) + Q_{met} \tag{5}$$

where 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, while Q_{met} [$\mathrm{Wm^{-3}}$] is the internal metabolic heat source.

2.1 Tissue injury

According to the necrotic changes in tissue, the blood perfusion coefficient is defined as [7]

$$G_B = G_B(\theta) = G_{B0} f(\theta) \tag{6}$$

where G_{B0} is the initial perfusion coefficient, $f(\theta)$ is assumed as the polynomial one in the form

$$f(\theta) = \sum_{j=1}^{3} m_j \theta^{j-1} \tag{7}$$

where θ corresponds to the tissue injury integral [7, 8, 10]:

$$\theta(\mathbf{x}) = \int_0^{t^F} A \exp\left[-\frac{E}{RT}\right] dt \tag{8}$$

where A is the pre-exponential factor [s $^{-1}$], E is the activation energy [J mole^{-1}], R is the universal gas constant [J mole^{-1}K^{-1}], t^f is the time for which the tissue injury integral is calculated while the criterion for tissue necrosis is:

$$\theta(\mathbf{x}) \geq 1 \tag{9}$$

Additionally on the basis of the integral above the damage fraction $F_D$is calculated [5, 8]:

$$F_D(\mathbf{x}) = 1 - \exp(-\theta) \tag{10}$$

The damage of the tissue calculated on the basis of the Arrhenius integral (8) is irreversible. In order to consider that tissue could get back to its native state after the thermal impulse is ceased, the injury of tissue at point $\mathbf{x}$ selected from the domain, for time t^f is calculated according to the following algorithm:

1. if $\theta^{f-1}(\mathbf{x}) \geq \theta_{rec}$then item 2, else item 3,
2. equation (8), go to item 9,
3. if $T^f(\mathbf{x}) \geq T^{f-1}(\mathbf{x})$then item 2, else item 4,
4. if $\theta^{f-1}(\mathbf{x}) = 0$then item 5, else item 6,
5. $\theta^f(\mathbf{x}) := \theta^{f-1}(\mathbf{x})$, go to item 9,
6. if coefficients of function $\theta_{app}(\mathbf{x}, T)$are defined then item 7, else item 8,
7. $\theta^f(\mathbf{x}) := \theta_{app}(\mathbf{x}, T^f)$, go to item 9,
8. approximation: definition of coefficients of function $\theta_{app}(\mathbf{x}, T)$, go to item 7,
9. end of algorithm.

The value described as θ_{rec} is defined as the recovery threshold. If the injury integral achieves the value equal or greater than θ_{rec} then injury of the tissue becomes irreversible. The function denoted as $\theta_{app}(\mathbf{x}, T)$ is introduce in order to modeling of the withdrawal of the tissue injury. In current paper it is assumed as the linear function, and approximation using function $\theta_{app}(\mathbf{x}, T)$ has been done between (T^0, θ^0) and (T^{f-1}, θ^{f-1}) for selected points of domain considered, separately.

2.2 Sensitivity analysis – direct approach

To determine the influence of thermophysical parameters on the value of injury integral, the direct approach of sensitivity analysis has been applied [12].

According to the rules of direct method the injury integral is differentiated with respect to the thermophysical parameter p_s, where $p_s = \lambda$, c, G_{B0} or Q_{met} [13]. So, the variation of θ is as follows (c.f. Eq. (8))

$$\frac{\partial \theta}{\partial p_s} = \int_0^{t^F} A \frac{EU^s}{RT^2} \exp\left[-\frac{E}{RT}\right] dt \tag{11}$$

where

$$U_s = \frac{\partial T}{\partial p_s} \tag{12}$$

is the sensitivity function.

Because calculation of the variation (11) requires knowledge of the sensitivity functions (12) the Pennes equation (1) also is differentiated with respect to the parameter p_s, so

$$\frac{\partial c}{\partial p_s}\dot{T} + c\frac{\partial \dot{T}}{\partial p_s} = \frac{\partial \lambda}{\partial p_s} T_{,ii} + \lambda \frac{\partial T_{,ii}}{\partial p_s} + \frac{\partial Q_V}{\partial p_s} \tag{13}$$

Because (c.f (1))

$$T_{,ii} = \frac{1}{\lambda}\left[c\dot{T} - Q_V\right] \tag{14}$$

so

$$c\dot{U}_s = \lambda U^s_{,ii} - \frac{\partial c}{\partial p_s}\dot{T} + \frac{1}{\lambda}\frac{\partial \lambda}{\partial p_s}\left[c\dot{T} - Q_V\right] + \frac{\partial Q_V}{\partial p_s} \tag{15}$$

where

$$\dot{U}_s = \frac{\partial \dot{T}}{\partial p_s}, \quad U^s_{,ii} = \frac{\partial T_{,ii}}{\partial p_s} \tag{16}$$

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

$$\mathbf{x} \in \Omega: \quad c\dot{U}_s = \lambda U^s_{,ii} + Q^s_V \tag{17}$$

where

$$\begin{aligned} Q^s_V = &\left[\frac{c_B G_{B0} f(\theta)}{\lambda}\frac{\partial \lambda}{\partial p_s} - c_B f(\theta)\frac{\partial G_{B0}}{\partial p_s} - c_B G_{B0}\frac{\partial f(\theta)}{\partial p_s}\right](T - T_B) \\ &-c_B G_{B0} f(\theta) U_s + \left(\frac{c}{\lambda}\frac{\partial \lambda}{\partial p_s} - \frac{\partial c}{\partial p_s}\right)\dot{T} - \frac{Q_{met}}{\lambda}\frac{\partial \lambda}{\partial p_s} + \frac{\partial Q_{met}}{\partial p_s} \end{aligned} \tag{18}$$

Eq. (17) is supplemented by boundary conditions in the form:

$$\mathbf{x} \in \Gamma_0: \quad \begin{cases} Q^s(\mathbf{x},t) = -\frac{1}{\lambda}\frac{\partial \lambda}{\partial p_s} q(\mathbf{x},t), & t \le t_{exp} \\ Q^s(\mathbf{x},t) = \alpha U^s - \frac{1}{\lambda}\frac{\partial \lambda}{\partial p_s} q(\mathbf{x},t), & t > t_{exp} \end{cases} \tag{19}$$

where

$$Q^s = -\lambda U^s_{,i} n_i \tag{20}$$

Finally, the change of injury integral due to the changes of the parameters p_s is estimated using the following formula

$$\Delta\theta(\mathbf{x}) = \sqrt{\sum_{s=1}^{n}\left(\frac{\partial \theta(\mathbf{x})}{\partial p_s}\Delta p_s\right)^2} \tag{21}$$

2.3 Numerical realization – boundary element method

The primary and also the additional problems resulting from the sensitivity analysis have been solved using the 1^{st} scheme of the BEM for 2D transient heat diffusion [14 - 18]. So, the following equation will be considered

$$\mathbf{x} \in \Omega: \quad c\dot{F} = \lambda F_{,ii} + S \tag{22}$$

where $F = F(\mathbf{x}, t)$ denotes the temperature or functions resulting from the sensitivity analysis (c.f. Eq. (1) and (17)), while $S = S(\mathbf{x}, t)$ is the source function (c.f. Eq. (5) and (18)).

For the time grid with constant time step Δt the boundary integral equation corresponding to transition $t^{f-1} \to t^f$ is of the form

$$\begin{aligned} &B(\xi)F(\mathbf{x},t^f) + \frac{1}{c}\int_{t^{f-1}}^{t^f}\int_{\Gamma} F^*(\xi,\mathbf{x},t^f,t)J(\mathbf{x},t)d\Gamma dt = \frac{1}{c}\int_{t^{f-1}}^{t^f}\int_{\Gamma} J^*(\xi,\mathbf{x},t^f,t)F(\mathbf{x},t)d\Gamma dt + \\ &\frac{1}{c}\int_{t^{f-1}}^{t^f}\iint_{\Omega} F^*(\xi,\mathbf{x},t^f,t^{f-1})F(\mathbf{x},t^{f-1})d\Omega + \frac{1}{c}\int_{t^{f-1}}^{t^f}\iint_{\Omega} S(\mathbf{x},t)F^*(\xi,\mathbf{x},t^f,t)d\Omega dt \end{aligned}$$

(23)

In equation (23) F^* is the fundamental solution:

$$F^*(\xi,\mathbf{x},t^f,t)=\frac{1}{4\pi a(t^f-t)}\exp\left[-\frac{r^2}{4a(t^f-t)}\right] \tag{24}$$

where r is the distance from the point under consideration $\mathbf{x}$ to the observation point ξ, while

$$J^*(\xi,\mathbf{x},t^f,t)=-\lambda F^*(\xi,\mathbf{x},t^f,t)_{,i}n_i \tag{25}$$

and $B(\xi)$ is the coefficient from the interval (0, 1).

If the constant elements with respect to time are used then the boundary integral equation (23) takes form

$$\begin{aligned}&B(\xi)F(\mathbf{x},t^f)+\int\limits_{\Gamma}J(\mathbf{x},t^f)g(\xi,\mathbf{x})d\Gamma=\int\limits_{\Gamma}F(\mathbf{x},t^f)h(\xi,\mathbf{x})d\Gamma+\\&\iint\limits_{\Omega}J^*(\xi,\mathbf{x},t^f,t^{f-1})F(\mathbf{x},t^{f-1})d\Omega+\iint\limits_{\Omega}S(\mathbf{x},t^{f-1})g(\xi,\mathbf{x})d\Omega\end{aligned} \tag{26}$$

where

$$h(\xi,\mathbf{x})=\frac{1}{c}\int\limits_{t^{f-1}}^{t^f}J^*(\xi,\mathbf{x},t^f,t)dt \tag{27}$$

and

$$g(\xi,\mathbf{x})=\frac{1}{c}\int\limits_{t^{f-1}}^{t^f}F^*(\xi,\mathbf{x},t^f,t)dt \tag{28}$$

In numerical realization the following discrete form of the equation (26) is considered

$$\sum_{j=1}^{N}G_{ij}J_j^f=\sum_{j=1}^{N}H_{ij}F_j^f+\sum_{l=1}^{L}P_{il}F_l^{f-1}+\sum_{l=1}^{L}Z_{il}S_l^{f-1} \tag{29}$$

where

$$G_{ij}=\int\limits_{\Gamma_j}g(\xi^i,\mathbf{x})d\Gamma_j \tag{30}$$

and

$$H_{ij} = \begin{cases} \int\limits_{\Gamma_j} h(\xi^i, \mathbf{x}) d\Gamma_j, & i \neq j \\ -0.5, & i = j \end{cases} \tag{31}$$

while

$$P_{il} = \iint\limits_{\Omega_l} T^*(\xi^i, \mathbf{x}, t^f, t^{f-1}) d\Omega_l \tag{32}$$

and

$$Z_{il} = \iint\limits_{\Omega_l} g(\xi^i, \mathbf{x}) d\Omega_l \tag{33}$$

The system of equations (29) can be written in the matrix form, namely

$$\mathbf{G} \cdot \mathbf{q}^f = \mathbf{H} \cdot \mathbf{T}^f + \mathbf{P} \cdot \mathbf{T}^{f-1} + \mathbf{Z} \cdot \mathbf{Q}_{\mathbf{V}}^{f-1} \tag{34}$$

After the determining the "missing" boundary values of temperatures and heat fluxes, the values of temperatures at the internal points ξ^i for time t^f are calculated using the formula ($i = N+1, ..., N+L$):

$$F_i^f = \sum_{j=1}^{N} H_{ij} F_j^f - \sum_{j=1}^{N} G_{ij} J_j^f + \sum_{l=1}^{L} P_{il} F_l^{f-1} + \sum_{l=1}^{L} Z_{il} S_l^{f-1} \tag{35}$$

3 Results of computations

The domain of rectangular shape (c.f. 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 [($\mathrm{m^3_{blood}/s}$)/($\mathrm{m^3_{tissue}}$)] , 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: $A = 3.1 \cdot 10^{98}$ [$\mathrm{s^{-1}}$], $E = 6.27 \cdot 10^5$ [J $\mathrm{mole^{-1}}$], R = 8.314 [J $\mathrm{mole^{-1}K^{-1}}$] and θ_{rec} = 0.05, and the coefficients appearing in the $f(\theta)$ function are as follows (c.f. (7)):

$$\begin{array}{lll} 0 < \theta \leq 0.1: & m_1 = 1, & m_2 = 25, \quad m_3 = -260 \\ 0.1 < \theta \leq 1: & m_1 = 1, & m_2 = -1, \quad m_3 = 0 \end{array} \tag{36}$$

The values of these coefficients for the interval from 0 to 0.1 respond to the increase of perfusion coefficient caused by vasodilatation, while for interval from 0.1 to 1

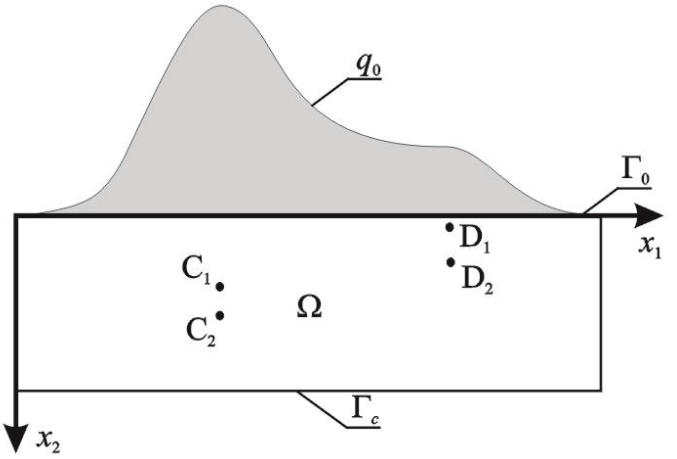

Figure 1: Domain considered

they reflect blood flow decrease as the vasculature begins to shut down (thrombosis).

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

The co-ordinates of the points are (c.f. 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).

Fig. 2 shows the courses of temperature while Fig. 3 illustrates the courses of injury integral θ at selected points of the domain considered. At two of these points, this means C_1 and D_1, the value of injury integral is above the recovery threshold θ_{rec}. At point C_1 the maximal temperature about 70˚C causes that the value of injury integral is much greater than 1 (as a matter of fact the value is much greater than 10, what corresponds to the value of F_D greater than 0.99), so the tissue is fully damaged in this point while at point D_1 the value of injury integral is 0.168 (with maximal temperature about 55˚C), which determines partly damaged tissue. Arrhenius integral value at points C_2 and D_2 hadn't reached the recovery threshold, so the functions θ_{app} (see algorithm in chapter 2.1) are defined for the stage of lowering temperature.

In Fig. 4 the perfusion coefficient G_B courses at selected points of the domain considered are presented. On the basis of these results one can say that the injury integral at selected points of the domain has influence on the value of perfusion

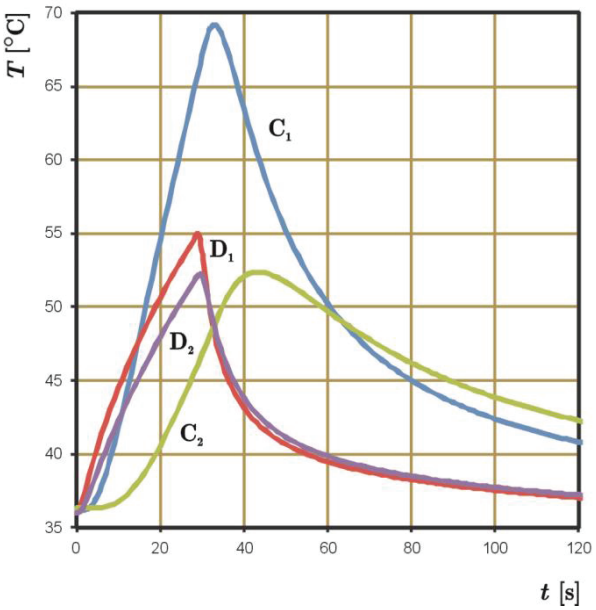

Figure 2: Courses of temperature

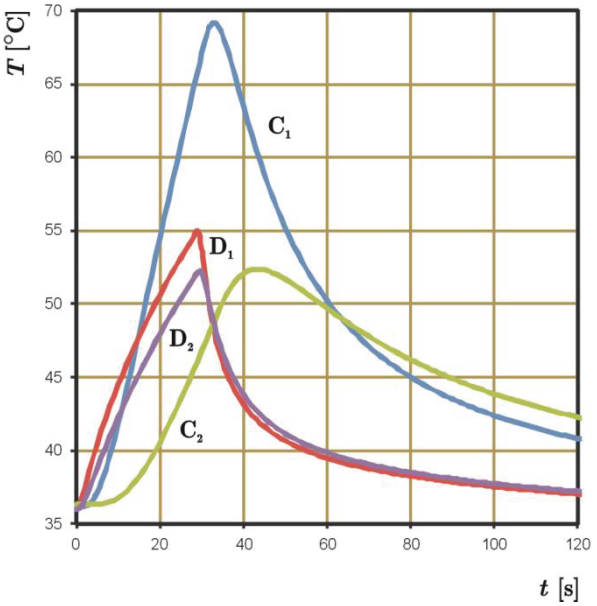

Figure 3: Courses of injury integral θ

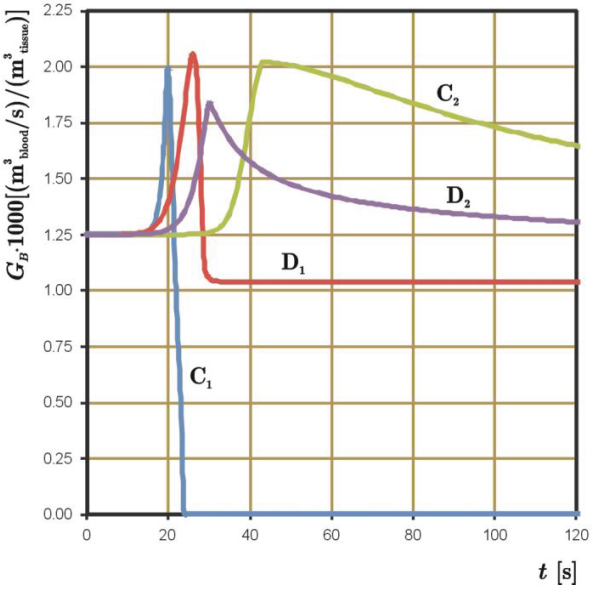

Figure 4: Courses of perfusion coefficient G_B

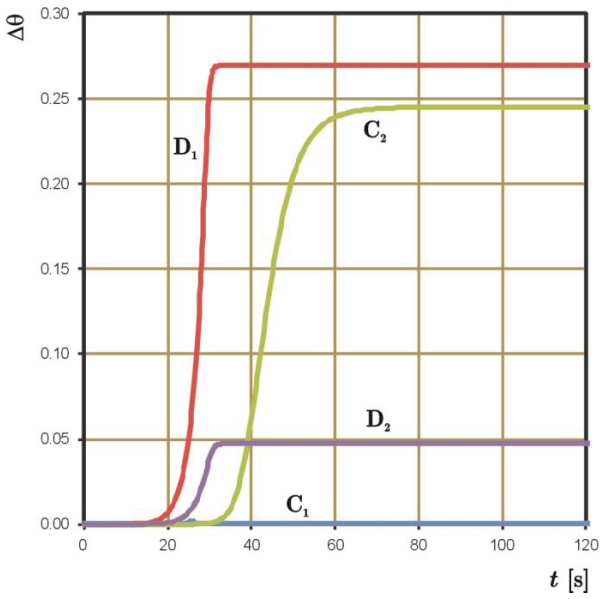

Figure 5: Changes of injury integral due to the changes of parameters p_s

coefficient G_B. Both the effect of vasodilatation as well as shutting down the vasculature is clearly visible. According to the necrotic changes in the tissue domain the perfusion coefficient is changing, decreasing to zero for the region in which the injury integral is equal or greater than 1. At the points C_2 and D_2 the value of perfusion coefficient decreases to the initial value in accordance with decreasing of injury integral value. At point C_2 the tissue returns to the healthy state after 383 seconds, while at point D_2 – after 197 seconds.

In Fig. 5 the changes of injury integral due to the changes of parameters p_s based on the sensitivity analysis are shown (c.f. Eq. (21)). It is visible that the 10% changes in parameters values cause the maximal changes in value of injury integral at points D_1 and C_2 (0.26 and 0.245 respectively). At point D_2 the changes are much smaller (up to 0.045), while there are almost no changes at point C_1 (point at which the tissue is fully damaged).

Analysis of the dynamics of tissue thermal injury formation process is based on the damage fraction F_D(c.f. Eq. (10)). Five intervals of values for F_D have been distinguished (for the sake of convenience denoted as tha):

- tha 1: [0, 0.01),
- tha 2: [0.01, 0.05),
- tha 3: [0.05, 0.63),
- tha 4: [0.63, 0.99),
- tha 5: ≥ 0.99.

The values in intervals are interpreted as:

- 0.01: up to this value the tissue is in its normal state so the value could be named as the border of thermally untouched tissue,
- 0.05: the border of vasodilatation – arise from the polynomial function for G_B(c.f. Eq. (36)); at this value of F_D the perfusion coefficient has maximum,
- 0.63: corresponds to the criterion of tissue necrosis (c.f. Eq. (9)),
- 0.99: could be treated as the criterion of complete tissue destruction.

In Fig. 6 the concept of tissue thermal injury formation analysis is presented. At first, the comparison of tha intervals achieved on element in domain considered for two successive time steps is made. Next, only elements which changed intervals are

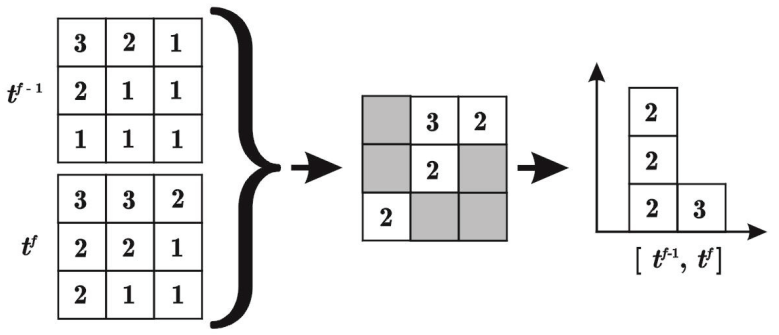

Figure 6: The concept of tissue thermal injury formation analysis

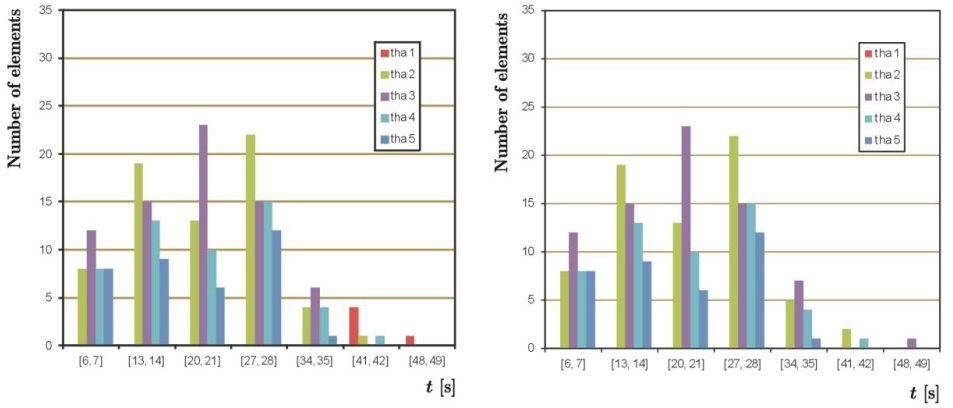

Figure 7: Number of elements achieving individual intervals (LHS – algorithm presented in chapter 2.1, RHS – Arrhenius injury integral (c.f. equation (8))

selected. Finally, bar chart with number of elements achieving individual interval is drawn.

The results obtained by this method are presented in Fig. 7. The results are shown for algorithm presented in chapter 2.1 as well as for the Arrhenius injury integral expressed by Eq. (8). One could see that for $t > t_{exp}$ some elements are classified into tha 1 accordingly to the process of recovery of tissue, while for $t < t_{exp}$ there are no differences. Additionally, these data could be very easy recalculated into cross-section area of the wound using the field of single internal element (for the geometrical grid assumed in the paper: 1.25×10^{-7} [m^2]).

Moreover, it should be pointed out that the values of maximal changes of injury

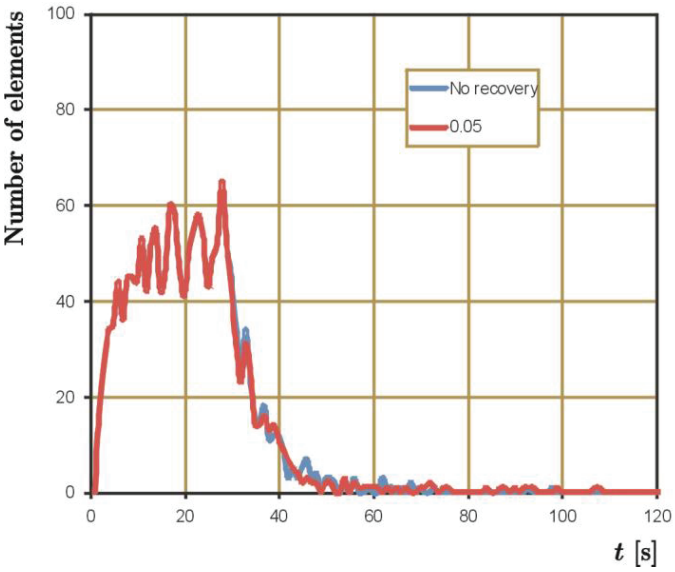

Figure 8: The thermal injury formation process

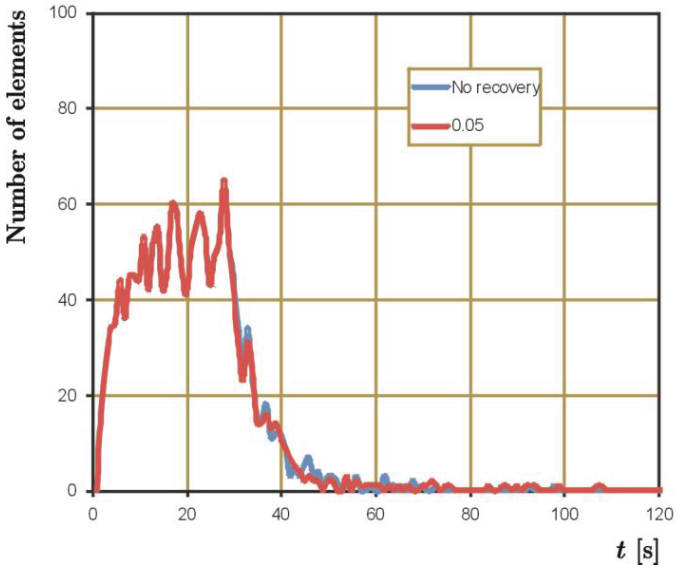

Figure 9: Proliferation of the thermal injury

integral at the points D_1, C_2, D_2 presented in Fig. 5 are crucial from the point of view of tha intervals. Depending on the value of injury integral (and in consequence on the damage fraction F_D) the points could be classified into different tha interval.

Summarizing the number of elements which swapped from one interval to another one in successive time intervals we can obtain knowledge of the dynamics of formation process and proliferation of the thermal injury. These results are presented in the Fig. 8 and Fig. 9. As previously, the results are shown both for algorithm presented in chapter 2.1 and the Arrhenius injury integral expressed by equation (8). Although the processes of formation for both cases presented in the picture are very similar, the differences of proliferation of thermal injury are clearly visible. Furthermore, there is difference in time of formation of the wound. From the thermal point of view the injury is formed within 96 seconds for Arrhenius injury integral and within 158 seconds for the algorithm of tissue injury calculation proposed in current paper.

4 Conclusions

The sensitivity analysis in combination with tha intervals and new algorithm of tissue injury calculation seems to be a quite convenient means of analysis of thermal injury formation process and could give more precise data about depth and cross-section area of injury. It could be very important especially in cases of controlled coagulation process like e.g. in some thermo therapies.

The proposed algorithm of tissue injury is closer to the real conditions of coagulation process in living tissue than the classical Pennes equation with constant values of thermal parameters; however, the thermal wave model of bioheat transfer could be also taken into account.

At the stage of sensitivity analysis use of the adjoint approach is also possible.

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