Sensitivity analysis of bioheat transfer in human eye during laser irradiation with regard to the thermophysical and optical parameters

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Abstract

In the paper the numerical analysis of thermal processes proceeding in the human eye due to a laser irradiation is presented. The sensitivity analysis with respect to thermophysical and optical parameters of successive layers of eye is also done. The direct approach of sensitivity analysis is applied. Perfusion rate in the retina is treated as dependent on tissue injury which is estimated on the basis of Arrhenius integral. At the stage of numerical realization the boundary element method is used. In the final part of paper the results obtained are shown.

Keywords: heat transfer, biomechanics, sensitivity, boundary element method

1. Introduction

The most vulnerable to damage by laser irradiation organ in human body is the eye. Depending on the laser wavelength and impulse parameters like power, beam diameter or exposure time laser could cause many results in structures of the eye. One of the wide studied phenomenon is the thermal damage of the retina – a light sensitive tissue lining the inner surface of the eye on which the optics of the eye create an image of the visual world. One can say that retina serves much the same function as the film in a camera [2, 14].

During laser irradiation a unique structure of the blood vessels existing in the retina could be destroyed. This effect is used in some medical treatment as e.g. diabetic retinopathy. On the other hand, damage of the blood vessels could be effect of wide spread use of lasers in various devices or in some more and more frequent incidents like intentionally dazzling of plane pilots.

The eye is roughly spherical organ (Figure 1). The anterior transparent surface of the eye is the cornea that covers iris, pupil and anterior chamber. Together with the lens, the cornea focuses light rays to the back part of the eye and provides 2/3 of the eye's focusing power. The iris is pierced by a variable circular opening, the pupil, which can vary in diameter from 1.5 to 10 [mm] [17].

Both the aquenous as the vitreous humors are transparent, colourless, gelatinous mass with different concentration of NaCl, which bathe the lens. The aquenous humor maintains the intraocular pressure and carries away waste products from metabolism of the ocular tissue. Although the vitreous is in contact with the retina and helps to keep it in place by pressing it against the choroid, it doesn't adhere to the retina except in three places: around the anterior border of the retina, in the macula and at the optic nerve disc. The choroid serves to nourish the retina.

It should be pointed out that in the eye the special focalization mechanism exists, which causes that laser beam entering into the eye will be focused to a very small retinal image. The result of this is that the effective irradiation of the retina may be as 10^5 that of the irradiation at the cornea anterior surface [14].

In order to consider the changing of blood vessels structure in the retina the well - known Arrhenius concept of the injury integral could be applied. In this approach, the reaction rate increases exponentially with the temperature and affects the values of the tissue parameters [1, 17].

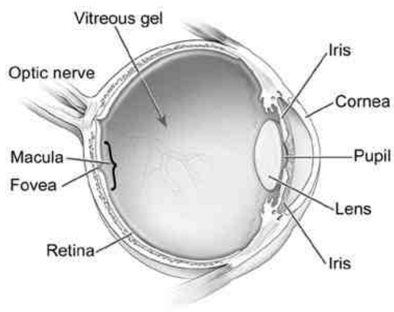

Figure 1: Human eye [18]

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 analyze the influence of the change of parameters on the final solution of the problem being considered [4, 5, 8, 9].

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 [11 - 13].

In this paper the eye is regarded as a multi - layer domain with perfusion rate coefficient in retina dependent on tissue injury integral, while the remaining thermal and optical parameters are regarded as the constant values. The sensitivity analysis has been performed with respect to the thermal conductivity, volumetric specific heat and absorption coefficient of all sub - domains and for initial perfusion rate and focalization rate of the retina.

The basic problem and also the additional problems resulting from the sensitivity analysis have been solved using the first scheme of boundary element method for transient heat diffusion [3, 10].

* This work is supported by the research grant N N501 3667 34 from the Polish Ministry of Science and Higher Education

2. Governing equations

The human eye is divided into five layers, i.e. cornea Ω_1, aquenous humor Ω_2, lens Ω_3, vitreous humor Ω_4 and retina Ω_5. These sub - domains are described by thermophysical parameters, this means the thermal conductivity λ_e [$\text{Wm}^{-1}\,\text{K}^{-1}$] and the specific heat per unit of volume c_e [$\text{Jm}^{-3}\,\text{K}^{-1}$], where e identifies successive layers (Figure 2) [2, 7].

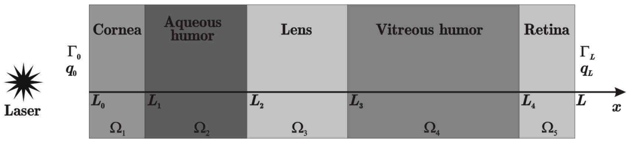

Figure 2: Model considered

The one - dimensional transient bioheat transfer in the domain of eye is described by the following system of equations [2, 6 - 8, 11 - 13]

$$x \in \Omega_e: \quad c_e \dot{T}_e = \lambda_e T_{e,ii} + Q_{Ve} \tag{1}$$

where Q_{Ve} [Wm^{-3}] are the internal heat sources containing the components connected with the perfusion, metabolism and lasers. According to the physiological properties of the human eye the metabolic heat sources for all sub - domains are assumed to be equal zero, while perfusion heat sources are defined as [1, 6, 7]

$$Q_{Ve\,perf} = c_B G_{B0e}\, f(\theta)(T_B - T_e) \tag{2}$$

where c_B [$\text{Jm}^{-3}\text{K}^{-1}$] is the volumetric specific heat of blood, T_B is the blood temperature, G_{B0e} [(m^3 blood s^{-1})/(m^3 tissue)] is the initial blood perfusion rate and θ corresponds to the tissue injury integral [1, 6, 16, 17]

$$\theta(x) = \int_0^{t^F} A \exp\left[-\frac{\Delta E}{RT}\right] \mathrm{d}t \tag{3}$$

where A is the pre - exponential factor [s^{-1}], ΔE is the activation energy [J mole^{-1}] and R is the universal gas constant [J $\text{mole}^{-1}\cdot\text{K}^{-1}$]. In current work the function θ in equation (2) is assumed as a polynomial in a form [1]

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

where m_j are the coefficients.

Laser heat source is given by the formula [2, 7, 17]

$$Q_{Ve\,las} = \mu_{ae} \varphi_e I_0 \exp(-\mu_{ae} x) \tag{5}$$

where x is the spatial co - ordinate, μ_{ae} [m^{-1}] is the absorption coefficient, I_0 [Wm^{-2}] is the irradiance on the cornea anterior surface and φ_e denotes lens focalization rate ($\varphi_e \neq 1$ only in the retina sub - domain) [2, 7]

$$\varphi_5 = \frac{d_b^2}{d_r^2} \tag{6}$$

where

$$d_b = \begin{cases} d_p, & d_p \le d_c \\ d_c, & d_p > d_c \end{cases}, \quad d_r = 2.44 \frac{\lambda^* f}{d_b} \tag{7}$$

where d_c [m] is the laser beam diameter on the corneal anterior surface, d_p [m] is the pupil aperture diameter, d_r [m] is the retinal spot diameter, λ^* is the laser wavelength and f [m] is the focal distance of lens.

So, finally the source components in system of equations (1) are in the form [7]

$$Q_{Ve} = c_B G_{B0e}\, f(\theta)(T_B - T_e) + \mu_{ae} \varphi_e I_0 \exp(-\mu_{ae} x) \tag{8}$$

Equations (1) are supplemented by the following boundary - initial conditions:

- on cornea surface (external surface of the eye)

$$x \in \Gamma_0: \quad q_0 = \alpha_{amb}\left(T_1 - T_{amb}\right) + \varepsilon\sigma(T_1^4 - T_{amb}^4) + E \tag{9}$$

- on the retina surface (internal surface of the eye)

$$x \in \Gamma_L: \quad q_L = \alpha_s\left(T_5 - T_s\right) \tag{10}$$

- the ideal thermal contact between sub-domains

$$x \in \Gamma_{e,e+1} = \begin{cases} T_e = T_{e+1} \\ -\lambda_e T_{e,i} = -\lambda_{e+1} T_{e+1,i} \end{cases} \tag{11}$$

- the initial parabolic distribution of temperature

$$t = 0: \quad T = T_p \tag{12}$$

where α_{amb} [$\text{Wm}^{-2}\,\text{K}^{-1}$] is the convective coefficient between cornea and surroundings, α_s [$\text{Wm}^{-2}\text{K}^{-1}$] is the convective coefficient between sclera and ocular globe, T_{amb} [K] is the ambient temperature, T_s [K] is the sclera temperature, ε is the emissivity of cornea, σ [$\text{Wm}^{-2}\,\text{K}^{-4}$] is the Stefan - Boltzmann constant, E [Wm^{-2}] is the heat flux loss due to tear evaporation.

3. Sensitivity analysis

To determine the influence of thermophysical and optical parameters on temperature distribution in the retina sub - domain, the direct approach of sensitivity analysis has been applied [5, 8, 9].

According to the rules of direct method of sensitivity analysis, the equation (1) is differentiated with respect to the thermophysical or optic parameter p_s (λ_e, c_e, G_{B0e}, μ_{ae}, φ_e).

$$\begin{aligned} &\frac{\partial c_e}{\partial p_s}\dot{T}_e + c_e \frac{\partial \dot{T}_e}{\partial p_s} = \frac{\partial \lambda_e}{\partial p_s} T_{e,ii} + \lambda_e \frac{\partial T_{e,ii}}{\partial p_s} \\ &+ \frac{\partial}{\partial p_s}\left[c_B G_{B0e} f(\theta)\left(T_B - T_e\right)\right] + \frac{\partial}{\partial p_s}\left[\mu_{ae}\varphi_e I_0 \exp(-\mu_{ae} x)\right] \end{aligned} \tag{13}$$

Because (cf. (1) and (8))

$$T_{e,ii} = \frac{1}{\lambda_e}\left[c_e \dot{T}_e - c_B G_{Be} f(\theta)\left(T_B - T_e\right) - \mu_{ae}\varphi_e I_0 \exp(-\mu_{ae} x)\right] \tag{14}$$

so

$$\begin{aligned} &c_e \dot{U}_e^s = \lambda U_{e,ii}^s - \frac{\partial c_e}{\partial p_s}\dot{T}_e \\ &+ \frac{1}{\lambda_e}\frac{\partial \lambda_e}{\partial p_s}\left[c_e \dot{T}_e - c_B G_{B0e} f(\theta)\left(T_B - T_e\right) - \mu_{ae}\varphi_e I_0 \exp(-\mu_{ae} x)\right] \\ &+ \frac{\partial}{\partial p_s}\left[c_B G_{B0e} f(\theta)\left(T_B - T_e\right)\right] + \frac{\partial}{\partial p_s}\left[\mu_{ae}\varphi_e I_0 \exp(-\mu_{ae} x)\right] \end{aligned} \tag{15}$$

where

$$U_e^s = \frac{\partial T_e}{\partial p_s} \tag{16}$$

while

$$\dot{U}_e^s = \frac{\partial U_e^s}{\partial t}, \quad U_{e,i}^s = \frac{\partial T_{e,i}}{\partial p_s} \tag{17}$$

After the mathematical manipulations one can write the equation for additional sensitivity problem as [8]

$$x \in \Omega_e: \quad c_e \dot{U}_e^s = \lambda_e U_{e,ii}^s + Q_{Ve}^s \tag{18}$$

where Q_{Ve}^s is the sensitivity source function

$$\begin{aligned} Q_{Ve}^s = & \left[\frac{k_e}{\lambda_e} \frac{\partial \lambda_e}{\partial p_s} - c_B f(\theta) \frac{\partial G_{B0e}}{\partial p_s} - c_B G_{B0e} \frac{\partial f(\theta)}{\partial p_s} \right] (T_e - T_B) \\ & - k_e U_e^s + \left(\frac{c_e}{\lambda_e} \frac{\partial \lambda_e}{\partial p_s} - \frac{\partial c_e}{\partial p_s} \right) \dot{T}_e \\ & + I_0 \exp(-\mu_{ae} x) \left[\frac{\partial \mu_{ae}}{\partial p_s} \varphi_e (1 - \mu_{ae}) + \frac{\partial \varphi_e}{\partial p_s} \mu_{ae} \right] \end{aligned} \tag{19}$$

where $k_e = c_B G_{B0e} f(\theta)$ and the derivative of function $f(\theta)$ with respect to parameter p_s is as follows

$$\frac{\partial f(\theta)}{\partial p_s} = m_2 \frac{\partial \theta}{\partial p_s} + 2 m_3 \theta \frac{\partial \theta}{\partial p_s} \tag{20}$$

while the variation of θ is calculated as (c.f. equation (3))

$$\frac{\partial \theta}{\partial p_s} = \int_0^{t^F} A \frac{\Delta E U^s}{R T^2} \exp\left[-\frac{\Delta E}{R T} \right] \mathrm{d}t \tag{21}$$

Equation (18) is supplemented by boundary conditions in the form

$$x \in \Gamma_0: \quad Q_0 = U_1^s \left(\alpha_{amb} + 4 \varepsilon \sigma T_1^3 \right) - \frac{1}{\lambda_1} \frac{\partial \lambda_1}{\partial p_s} q_0 \tag{22}$$

$$x \in \Gamma_L: \quad Q_L = \alpha_s U_5^s - \frac{1}{\lambda_5} \frac{\partial \lambda_5}{\partial p_s} q_L \tag{23}$$

$$x \in \Gamma_{e,e+1}: \begin{cases} U_e^s = U_{e+1}^s \\ \dfrac{1}{\lambda_e} \dfrac{\partial \lambda_e}{\partial p_s} q_e + Q_e^s = \dfrac{1}{\lambda_{e+1}} \dfrac{\partial \lambda_{e+1}}{\partial p_s} q_{e+1} + Q_{e+1}^s \end{cases} \tag{24}$$

where

$$q_e = -\lambda_e T_{e,i} n_i, \quad Q_e^s = -\lambda_e U_{e,i}^s n_i \tag{25}$$

and the initial one

$$t = 0: \quad U^s = 0 \tag{26}$$

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

$$\Delta T_e = \sqrt{\sum_{s=1}^{n} \left(\frac{\partial T_e}{\partial p_s} \Delta p_s \right)^2} \tag{27}$$

Moreover, the maximal intervals of temperature changes during the process analyzed are determined on the basis of Taylor formula

$$T_e(x, t, p_s \pm \Delta p_s, p_s) = T_e(x, t, p_s) \pm \frac{\partial T_e}{\partial p_s} \Delta p_s \tag{28}$$

and after some manipulations

$$\Delta T_e = 2 \frac{\partial T_e}{\partial p_s} \Delta p_s = 2 U_e^s \Delta p_s \tag{29}$$

where

$$\Delta T_e = T_e(x, t, p_s + \Delta p_s, p_s) - T_e(x, t, p_s - \Delta p_s, p_s) \tag{30}$$

4. Boundary element method

The basic and also the additional problems resulting from the sensitivity analysis have been solved using the 1st scheme of the BEM for 1D transient heat diffusion. So, we consider the following equations ($e = 1, 2, \ldots, 5$, $x \in (L_{e-1}, L_e)$) [3, 10, 15]

$$c_e \dot{F}_e = \lambda_e F_{e,ii} + S_e \tag{31}$$

where $F_e = F_e(x, t)$ denotes the temperature T_e or functions U_e resulting from the sensitivity analysis, $S_e = S_e(x, t)$ are the source functions described by equation (8) for the primary problem or by equation (19) for the sensitivity problems with respect to p_s.

At first, the time grid must be introduced

$$0 = t^0 < t^1 < \ldots < t^{f-1} < t^f < \ldots < \infty \tag{32}$$

with constant time step $\Delta t = t^f - t^{f-1}$.

The 1st scheme of boundary element method for equation (31) and transition $t^{f-1} \to t^f$ leads to the following equations (for successive layers of the eye - $e = 1, 2, .., 5$)

$$\begin{aligned} & F_e(\xi, t^f) + \left[\frac{1}{c_e} \int_{t^{f-1}}^{t^f} F_e^*(\xi, x, t^f, t) J_e(x, t^f) \, \mathrm{d}t \right]_{x=L_{e-1}}^{x=L_e} \\ & = \left[\frac{1}{c_e} \int_{t^{f-1}}^{t^f} J_e^*(\xi, x, t^f, t) F_e(x, t^f) \, \mathrm{d}t \right]_{x=L_{e-1}}^{x=L_e} \\ & + \int_{L_{e-1}}^{L_e} F_e^*(\xi, x, t^f, t^{f-1}) F_e(x, t^{f-1}) \, \mathrm{d}x \\ & + \frac{1}{c_e} \int_{L_{e-1}}^{L_e} S_e(x, t^{f-1}) \int_{t^{f-1}}^{t^f} F_e^*(\xi, x, t^f, t) J_e(x, t^f) \, \mathrm{d}t \, \mathrm{d}x \end{aligned} \tag{33}$$

where F_e^* are the fundamental solutions given by formulas

$$F_e^*(\xi, x, t^f, t) = \frac{1}{2\sqrt{\pi a_e (t^f - t)}} \exp\left[-\frac{(x - \xi)^2}{4 a_e (t^f - t)} \right] \tag{34}$$

while ξ is the point in which the concentrated heat source is applied, $a_e = \lambda_e / c_e$, $J_e(x, t^f) = -\lambda_e F_{e,i} n_i$

The heat fluxes resulting from fundamental solutions are equal to

$$\begin{aligned} J_e^*(\xi, x, t^f, t) & = -\lambda_e F_{e,i}^* n_i \\ & = \frac{\lambda_e (x - \xi)}{4\sqrt{\pi} \left[a_e (t^f - t) \right]^{3/2}} \exp\left[-\frac{(x - \xi)^2}{4 a_e (t^f - t)} \right] \end{aligned} \tag{35}$$

Assuming that

$$t \in [t^{f-1}, t^f]: \quad \begin{cases} F_e(x, t) = F_e(x, t^f) \\ J_e(x, t) = J_e(x, t^f) \end{cases} \tag{36}$$

one obtains the following form of equations (33)

$$F_e(\xi,t^f)+g_e(\xi,L_e)J_e(L_e,t^f)-g_e(\xi,L_{e-1})J_e(L_{e-1},t^f) \\ =h_e(\xi,L_e)F_e(L_e,t^f)-h_e(\xi,L_{e-1})F_e(L_{e-1},t^f)+p_e(\xi)+z_e(\xi) \tag{37}$$

where

$$h_e(\xi,x)=\frac{1}{c_e}\int_{t^{f-1}}^{t^f} J_e^*\,\mathrm{d}t=\frac{\mathrm{sgn}(x-\xi)}{2}\mathrm{erfc}\left(\frac{|x-\xi|}{2\sqrt{a_e\Delta t}}\right) \tag{38}$$

and

$$g_e(\xi,x)=\frac{1}{c_e}\int_{t^{f-1}}^{t^f} F_e^*\,\mathrm{d}t \\ =\frac{\sqrt{\Delta t}}{\sqrt{\pi}\lambda_e c_e}\exp\left[-\frac{(x-\xi)^2}{4a_e\Delta t}\right]-\frac{|x-\xi|}{2\lambda_e}\mathrm{erfc}\left(\frac{|x-\xi|}{2\sqrt{a_e\Delta t}}\right) \tag{39}$$

while

$$p_e(\xi)=\int_{L_{e-1}}^{L_e} F_e^*(\xi,x,t^f,t^{f-1})F_e(x,t^{f-1})\,\mathrm{d}x \\ =\frac{1}{2\sqrt{\pi a_e\Delta t}}\int_{L_{e-1}}^{L_e}\exp\left[-\frac{(x-\xi)^2}{4a_e\Delta t}\right]F_e(x,t^{f-1})\,\mathrm{d}x \tag{40}$$

at the same time

$$z_e(\xi)=\int_{L_e-1}^{L_e} S_e(x,t^{f-1})g_e(\xi,x)\,\mathrm{d}x \tag{41}$$

For $\xi\rightarrow L_{e-1}^+$ and $\xi\rightarrow L_e^-$ for each sub - domain considered one obtains the system of equations

$$\begin{bmatrix} g_e(L_{e-1},L_{e-1}) & g_e(L_{e-1},L_e) \\ g_e(L_e,L_{e-1}) & g_e(L_e,L_e)\end{bmatrix}\begin{bmatrix} J_e(L_{e-1},t^f) \\ J_e(L_e,t^f)\end{bmatrix}= \\ \begin{bmatrix} h_e(L_{e-1}^+,L_{e-1}) & h_e(L_{e-1}^+,L_e) \\ h_e(L_e^-,L_{e-1}) & h_e(L_e^-,L_e)\end{bmatrix}\begin{bmatrix} F_e(L_{e-1},t^f) \\ F_e(L_e,t^f)\end{bmatrix}+ \\ \begin{bmatrix} p_e(L_{e-1}) \\ p_e(L_e)\end{bmatrix}+\begin{bmatrix} z_e(L_{e-1}) \\ z_e(L_e)\end{bmatrix} \tag{42}$$

or

$$\begin{bmatrix} g_{11}^e & g_{12}^e \\ g_{21}^e & g_{22}^e\end{bmatrix}\begin{bmatrix} J_e(L_{e-1},t^f) \\ J_e(L_e,t^f)\end{bmatrix}=\begin{bmatrix} h_{11}^e & h_{12}^e \\ h_{21}^e & h_{22}^e\end{bmatrix}\begin{bmatrix} F_e(L_{e-1},t^f) \\ F_e(L_e,t^f)\end{bmatrix}+ \\ \begin{bmatrix} p_e(L_{e-1}) \\ p_e(L_e)\end{bmatrix}+\begin{bmatrix} z_e(L_{e-1}) \\ z_e(L_e)\end{bmatrix} \tag{43}$$

Using the conditions (11) for direct problem or conditions (24) for sensitivity problems, the equations (43) for particular sub - domains are joining together into one final system of equations written in the form

$$\mathbf{AX}=\mathbf{B} \tag{44}$$

where

$$\mathbf{B}=\mathbf{P}+\mathbf{Z}+\mathbf{W}+\mathbf{C} \tag{45}$$

Taking into account the boundary conditions (9) and (10) for the basic problem (problem concerning information about the temperature) and the conditions (22) and (23) for the sensitivity problems, the elements of matrixes in equation (44) are defined as follows:

- Matrix **A (**only non - zero elements**):**
  - for e = 1, i = 1, 2

$$a_{i,2}=g_{i,2}^e \\ a_{i,3}=-h_{i,2}^e \tag{46}$$

  - for e = 2, 3, 4; i = 1, 2; j = 1, 2

$$a_{2e+i-2,2e+2j-4}=g_{ij}^e \\ a_{2e+i-2,2e+2j-3}=-h_{ij}^e \tag{47}$$

  - for e = 5, i = 1, 2

$$a_{2e+i-2,2e-2}=g_{i,1}^e \\ a_{2e+i-2,2e-1}=-h_{i,1}^e \\ a_{2e-1,2e}=\alpha_s g_{12}^e-h_{12}^e \\ a_{2e,2e}=\alpha_s g_{22}^n-h_{22}^n \tag{48}$$

  - for the basic problem, e = 1, i = 1, 2

$$a_{i,1}=g_{i,1}^e \tag{49}$$

  - for the sensitivity problems, e = 1, i = 1, 2

$$a_{i,1}=g_{i,1}^e\left[\alpha_{amb}+4\sigma\varepsilon_{amb}T_e^3(0,t^f)\right]-h_{i,1}^e \tag{50}$$

- Vectors **P** and **Z**, e = 1,2,…,5:

$$p_{2e-1}=p_e(L_{e-1}) \\ p_{2e}=p_e(L_e) \tag{51}$$

and

$$z_{2e-1}=z_e(L_{e-1}) \\ z_{2e}=z_e(L_e) \tag{52}$$

- Vector **W**:
  - for i = 3, 4,…,8

$$w_i=0 \tag{53}$$

  - for the basic problem

$$w_1=g_{11}^1\left[\alpha_{amb}T_{amb}-\sigma\varepsilon\left[T_1^4(0,t^{f-1})-T_{amb}^4\right]-E\right] \\ w_2=g_{21}^1\left[\alpha_{amb}T_{amb}-\sigma\varepsilon\left[T_1^4(0,t^{f-1})-T_{amb}^4\right]-E\right] \\ w_9=\alpha_s g_{12}^5 T_s \\ w_{10}=\alpha_s g_{22}^5 T_s \tag{54}$$

  - for the sensitivity problems

$$w_1=\frac{1}{\lambda_1}g_{11}^1\frac{\partial\lambda_1}{\partial p_s}q_1(0,t^f) \\ w_2=\frac{1}{\lambda_1}g_{21}^1\frac{\partial\lambda_1}{\partial p_s}q_1(0,t^f) \\ w_9=\frac{1}{\lambda_5}g_{12}^5\frac{\partial\lambda_5}{\partial p_s}q_5(L,t^f) \\ w_{10}=\frac{1}{\lambda_5}g_{22}^5\frac{\partial\lambda_5}{\partial p_s}q_5(L,t^f) \tag{55}$$

- Vector **C**:

- for the basic problem, i = 1, 2,…10:

$$c_i = 0 \tag{56}$$

- for the sensitivity problems, e = 2, 3, 4

$$\begin{aligned} c_{2e+1} &= g_{11}^{e+1}\left(\frac{1}{\lambda_{e+1}}\frac{\partial\lambda_{e+1}}{\partial p_s} - \frac{1}{\lambda_e}\frac{\partial\lambda_e}{\partial p_s}\right) q_{e,e+1}(L_e, t^f) \\ c_{2e} &= g_{21}^{e+1}\left(\frac{1}{\lambda_{e+1}}\frac{\partial\lambda_{e+1}}{\partial p_s} - \frac{1}{\lambda_e}\frac{\partial\lambda_e}{\partial p_s}\right) q_{e,e+1}(L_e, t^f) \end{aligned} \tag{57}$$

- Vector **X**:

- for e = 1, 2, …,4

$$\begin{aligned} x_{2e} &= J_e(L_e, t^f) \\ x_{2e+1} &= F_e(L_e, t^f) \end{aligned} \tag{58}$$

- for e = 1

$$x_1 = F_e(0, t^f) \tag{59}$$

- for e = 5

$$x_{10} = F_e(L, t^f) \tag{60}$$

After solving the system of equations (44), the values of unknown heat fluxes can be found on the basis of formulas (9) and (10) for the basic problem (concerning the temperature information), while for the sensitivities problems on the basis of (22) and (23). Additionally:

$$Q_{e+1}^s = Q_e^s - \left(\frac{1}{\lambda_{e+1}}\frac{\partial\lambda_{e+1}}{\partial p_s} - \frac{1}{\lambda_e}\frac{\partial\lambda_e}{\partial p_s}\right) q_{e,e+1} \tag{61}$$

Next, the values of function $F_e(\xi, t^f)$ at the internal points $\xi \in (L_{e-1}, L_e)$ are determined using the following equations

$$\begin{aligned} F_e(\xi, t^f) &= g_e(\xi, L_{e-1}) J_e(L_{e-1}, t^f) - \\ & g_e(\xi, L_e) J_e(L_e, t^f) + h_e(\xi, L_e) F_e(L_e, t^f) - \\ & h_e(\xi, L_{e-1}) F_e(L_{e-1}, t^f) + p_e(\xi) + z_e(\xi) \end{aligned} \tag{62}$$

5. Results of computations

As an example, the solution of 1D problem has been taken into account. The eye was subjected to a single pulse of the ruby or Nd:YAG laser irradiation.

The data concerning the successive sub - domains of eye are collected in the Tables 1 and 2 [2, 7].

The focal distance of lens is f = 1.7 [cm] and the parameters for the blood are the following: $G_{B0e} = 0$ for e = 1,…,4, G_{B05} = 0.00125 [(m^3 blood s^{-1})/(m^3 tissue)], c_B = 3.9962 [MJm^{-3}K^{-1}], T_B = 37 ºC, while the parameters appearing in the Arrhenius injury integral are equal to: $A = 1\cdot10^{44}$ [s^{-1}], $\Delta E = 2.93\cdot10^5$ [J mole^{-1}] and R = 8.314 [J mole$^{-1}\cdot$K^{-1}] and the coefficients appearing in the $f(\theta)$ function (c.f. equation (4)) are as follows [1, 17]:

$$\begin{aligned} 0 < \theta \le 0.1: &\quad m_1 = 1, \quad m_2 = 25, \quad m_3 = -260, \\ 0.1 < \theta \le 1: &\quad m_1 = 1, \quad m_2 = -1, \quad m_3 = 0, \end{aligned} \tag{63}$$

The values of these coefficients for the interval from 0 to 0.1 respond to the increase of perfusion rate caused by vasodilatation, while for interval from 0.1 to 1 they reflect blood flow decrease as the vasculature begins to shut down (thrombosis).

For both kind of laser the power was assumed as P = 1 [mW]. Because laser beam diameter on the corneal anterior surface is equal to d_c = 1 [mm], so the laser irradiation I_0 = 1273[Wm^{-2}]. The remaining parameters connected with the eye and lasers are presented in Table 3.

Table 1: Values of parameters for sub - domains

	λ_e [Wm^{-1} K^{-1}]	c_e [MJm^{-3} K^{-1}]	$L_e - L_{e-1}$ [mm]
Cornea	0.58	4.3869	0.6
Aqueous humor	0.58	3.997	3
Lens	0.4	3.15	4
Vitreous humor	0.603	4.178	15
Retina	0.628	4.19	0.1

Table 2: Values of absorption coefficient for sub - domains

	μ_{ae}[m^{-1}]	
	Nd:YAG laser	Ruby laser
Cornea	113	124
Aqueous humor	35	8.4
Lens	43.5	9.5
Vitreous humor	20	2
Retina	10000	44000

Table 3: Parameters of lasers and eye

	Nd:YAG laser	Ruby laser
λ^* [nm]	1064	694.3
d_p [mm]	8.9	7.3
φ_5	531.38	1206
t_{ex} [s]	0.08	0.02

In the boundary condition (c.f. equation (9) and (10)) the following values of parameters have been assumed: α_{amb} = 10 [Wm^{-2} K^{-1}], α_s = 65 [Wm^{-2} K^{-1}], T_{amb} = 25 ºC, T_s = 37 ºC, ε = 0.975, $\sigma = 5.67\cdot10^{-8}$ [Wm^{-2} K^{-4}], E = 40 [Wm^{-2}].

The initial distribution of temperature has been assumed as the parabolic one between 33.6 ºC at the corneal anterior surface and 37 ºC at the posterior surface of retina.

The successive layers of the eye have been divided into 20, 50, 50, 150 and 20 linear elements, respectively, time step is equal to Δt = 0.002 [s].

Sensitivity analysis has been done with regard to the thermal conductivity, volumetric specific heat and absorption coefficient of all sub - domains as well as with regard to the initial perfusion rate and the focalization rate of retina, that means the seventeen additional problems have been solved (n = 17). It is assumed that for all parameters $\Delta p_s = 0.1 p_s$.

In Figures 3 and 4 the curses of temperature at the anterior and posterior surface of retina for Nd:YAG as well as Ruby laser are presented. Next two figures concern results connected with the sensitivity analysis. Figures 5 and 6 show the changes of temperature at the anterior surface of retina due to the changes of parameters obtained on the basis of equation (27). The curves have been calculated for thermophysical parameters (λ_e, c_e, G_{B0e}) and optical parameters (μ_{ae}, φ_e) separately, and for both groups together.

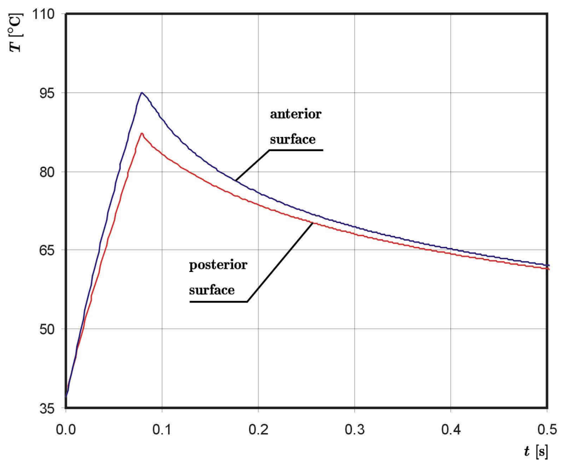

Figure 3: Temperature at the retina during Nd:YAG laser irradiation

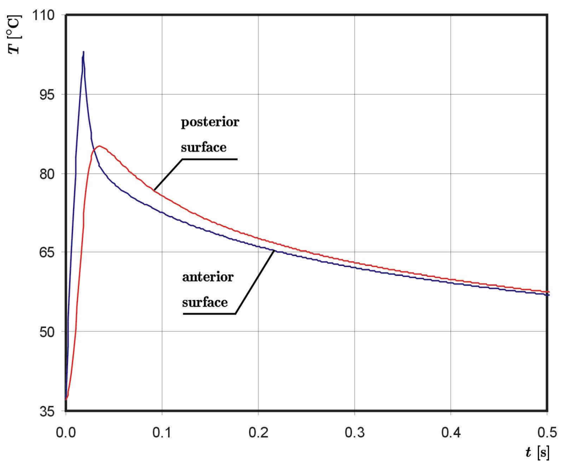

Figure 2: Temperature at the retina during ruby laser irradiation

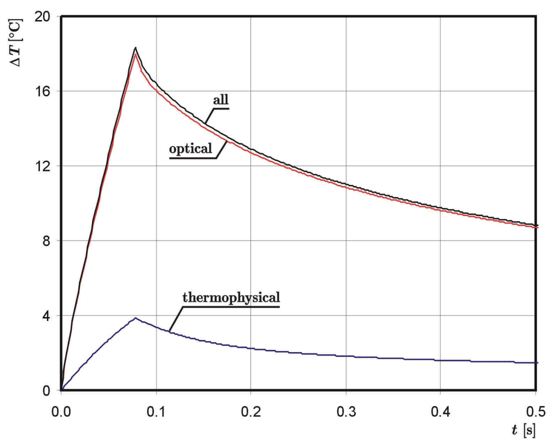

Figure 5: The change of temperature at the anterior surface of retina due to the changes of parameters (Nd:YAG irradiation)

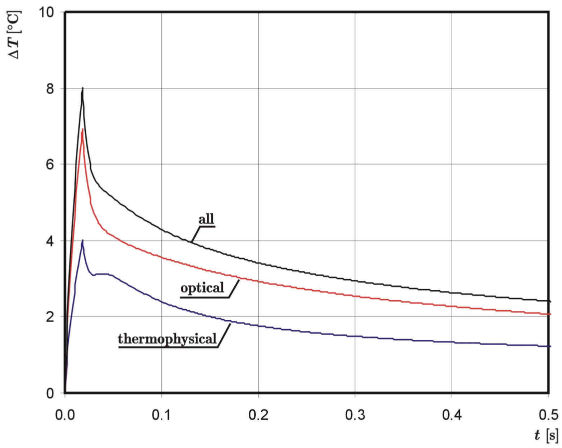

Figure 6: The change of temperature at the anterior surface of retina due to the changes of parameters (Ruby irradiation)

Figures 7 and 8 illustrate the maximal intervals of temperature at the retina calculated using the formula (29) during Nd:YAG and Ruby lasers irradiation, respectively. The numeration of parameters is presented in the Table 4.

Table 4: Numeration of parameters

Numeration	Parameters
s = 1, 2,..., 5	λ_s
s = 6, 7,..., 10	c_{s-5}
s = 11	G_{B05}
s = 12, 13,..., 16	μ_{as-11}
s = 17	φ_5

In Figure 9 the changes of maximal perfusion rate in retina during laser irradiation are presented. It should be pointed out that both initial increase of perfusion arising from vasodilatation as well as the fall connected with the damage of the retina's vasculature are clearly.

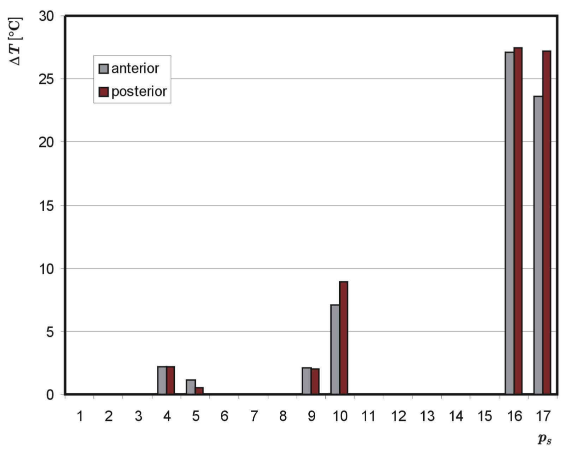

Figure 7: Maximal intervals of temperature at the retina during Nd:YAG irradiation

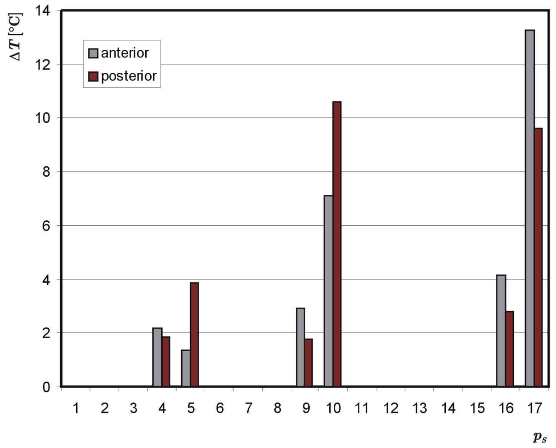

Figure 8: Maximal intervals of temperature at the retina during ruby irradiation

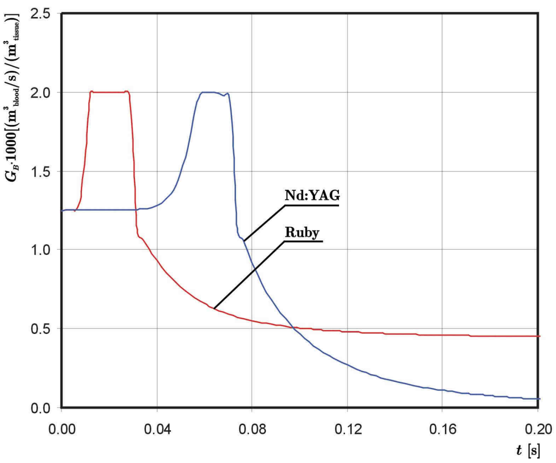

Figure 9: Maximal perfusion rate in the retina during laser irradiation

6. Final remarks

Both Nd:YAG as well as ruby laser irradiation have visible influence on the temperature in human retina. Temperature level depends on the laser parameter (power, beam diameter, wavelength, impulse duration) and also the parameters of the sub - domains.

Results of sensitivity analysis show that the optical parameters have dominant influence on the temperature (c.f. Figures 5 and 6). In the case of Nd:YAG irradiation the curve obtained only for optical parameters is very close to the curve for all parameters.

Taking into account the maximal intervals of temperature presented in the Figures 7 and 8 it could be stated that parameters, which changes have the most crucial impact on the temperature level are those for the vitreous humor and retina – thermal conductivity, volumetric specific heat for both of them and absorption coefficient and focalization rate for retina only. Values of the intervals for these parameters are presented in the Table 5.

The widest temperature intervals for both lasers have been noticed for focalization rate of the retina. It determines that the temperature level in the human eye is strongly dependent on the power and beam diameter of the laser as well as on the laser wavelength.

Table 5: Maximal wide of intervals for selected parameters

	Nd:YAG laser [°C]		Ruby laser [°C]	
	anterior	posterior	anterior	posterior
λ_4	2.22	2.19	2.19	1.87
λ_5	1.10	0.56	1.35	3.86
c_4	2.12	2.04	2.91	1.75
c_5	7.07	8.90	7.09	10.59
μ_{a5}	27.11	27.43	4.16	2.78
φ_5	23.60	27.16	13.24	9.60

The second most influencing parameter is the absorption coefficient (s = 16, c.f. Figure 7) for Nd:YAG laser irradiation while for ruby laser irradiation volumetric specific heat of vitreous humor (s = 10, c.f. Figure 8). The reason of this effect is that the Nd:YAG laser represents the irradiation in the infrared (1064 [nm]) band, while the ruby laser in visible region (694.3 [nm]). Consequently, the mechanism of absorption laser energy in both cases is slightly different, however in both the region absorption is dominated by melanin and haemoglobin.

It should be pointed out that the changes in perfusion rate coefficient have not visible effects in temperature level even though it is well - known that the laser irradiation has the influence on the value and degree of retinal vasculature destruction.

The proposed model is closer to the real conditions of thermal processes in the human eye, especially in the retina, than the classical Pennes equation with constant value of perfusion coefficient. Application of tissue injury integral in such a kind of problems seems to be quite a convenient tool to obtain additional information about the process considered. At the stage of sensitivity analysis the application of the adjoint approach is also possible.

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