Mikołaj STRYCZYŃSKI[*1], Ewa MAJCHRZAK[1]

Chapter 3. MODELING OF ONCOLOGICAL HYPERTHERMIA USING DUAL-PHASE LAG EQUATIONS

3.1. Introduction

Oncological hyperthermia is a method of complementary treatment of neoplastic diseases which consists in the targeted application of thermal energy in the treatment of cancer. It is a method supporting chemotherapy and radiotherapy [1-4]. Modeling of hyperthermia allows one, among others, to determine the power density of external heating and the duration of the procedure, which will ensure the destruction of cancerous tissues.

In this work, a single blood vessel and surrounding biological tissue with a tumor region is considered. The temperature distribution is described by the system of dual-phase lag equations (DPL) [5-8] supplemented by the boundary and initial conditions. The effect of the heating technique (e.g. ultrasound, microwave, etc.) is taken into account by introducing the source function Q_{ext} into the equation describing the temperature distribution in the tumor region [9]. When the heating time t_{ext} is achieved, the source function Q_{ext} is equal to zero. The absorbed total energy density $Q_{ext}\, t_{ext}$ is kept constant, but different heating schemes (heating power density Q_{ext} and heating duration) are considered. The formulated problem is solved using the implicit scheme of the finite difference method. To estimate degree of the tumor destruction the Arrhenius integral is used [10-13].

[*] Corresponding author: mikolaj.stryczynski@polsl.pl, ul. Konarskiego 18a, 44-100 Gliwice, Poland.
[1] Faculty of Mechanical Engineering, Silesian University of Technology.

3.2. Mathematical model

A single blood vessel and surrounding biological tissue with a tumor region, as shown in Figure 3.1, is considered (axisymmetric problem).

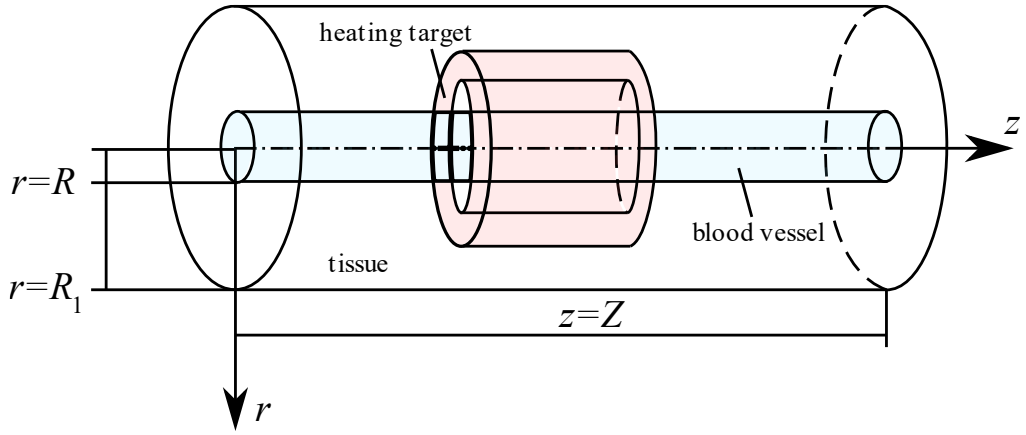

Fig. 3.1. Domain considered
Rys. 3.1. Rozpatrywany obszar

Blood temperature is described by the equation [5]

$$(r,z)\in\Omega_1:\quad c_b\rho_b\left(\frac{\partial T_b}{\partial t}+v\frac{\partial T_b}{\partial z}+\tau_{qb}\frac{\partial^2 T_b}{\partial t^2}+\tau_{qb}v\frac{\partial^2 T_b}{\partial t\partial z}\right)= \lambda_b\nabla^2 T_b+\tau_{Tb}\lambda_b\frac{\partial\left(\nabla^2 T_b\right)}{\partial t}+Q_{metb}+\tau_{qb}\frac{\partial Q_{metb}}{\partial t} \tag{1}$$

where

$$\nabla^2 T_b=\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial T_b}{\partial r}\right)+\frac{\partial^2 T_b}{\partial z^2}=\frac{1}{r}\frac{\partial T_b}{\partial r}+\frac{\partial^2 T_b}{\partial r^2}+\frac{\partial^2 T_b}{\partial z^2} \tag{2}$$

and c_b is the specific heat of blood, ρ_b is the mass density of blood, λ_b is the thermal conductivity of blood, v is the blood flow velocity in the axial direction, τ_{Tb} is the thermalization time, $Q_{met\,b}$ is the metabolic heat source, while $T_b = T_b(r, z, t)$ is the blood temperature, r, z are the spatial coordinates and t denotes the time.

Temperature field in the tissue with a tumor is described by equation

$$(r,z)\in\Omega_2\cup\Omega_3:\ c\rho\left(\frac{\partial T}{\partial t}+\tau_q\frac{\partial^2 T}{\partial t^2}\right)=\lambda\nabla^2 T+\lambda\tau_T\frac{\partial\left(\nabla^2 T\right)}{\partial t}+Q+\tau_q\frac{\partial Q}{\partial t}+Q_{ext}+\tau_q\frac{\partial Q_{ext}}{\partial t} \tag{3}$$

where

$$Q=w_b c_b\left(T_a-T\right)+Q_{met} \tag{4}$$

and c is the specific heat, ρ is the mass density, λ is the thermal conductivity, τ_q is the relaxation time, τ_T is the thermalization time, w_b is the blood perfusion rate, T_a is the arterial blood temperature, Q_{met} is the metabolic heat source, Q_{ext} is the source function associated with the external heating (heating power density) and $T = T(r, z, t)$ is the tissue temperature. It should be noted that the same values of thermophysical parameters for tumor region and healthy tissue are assumed here.

Only the tumor sub-domain is heated, hence

$$(r,z)\in\Omega_3:\quad Q_{ext}=Q_{ext}\left(r,z,t\right)=\begin{cases}Q_0, & t\le t_{ext}\\ 0, & t>t_{ext}\end{cases} \tag{5}$$

where t_{ext} is the exposure time, while Q_0 is a constant value.

On the contact surface between blood vessel and biological tissue the continuity condition of temperature and heat flux is assumed

$$(r,z)\in\Gamma_c:\begin{cases}T_b=T\\ q_b=q\end{cases} \tag{6}$$

On the outer surface of the tissue the constant temperature (body core temperature) is accepted. For $z = 0$, $z = Z$ the no-flux conditions are assumed.

The initial conditions are also known [5]

$$\begin{aligned}&t=0:\quad T_b=T=T_p\\ &\left.\frac{\partial T_b}{\partial t}\right|_{t=0}=\frac{Q_{metb}}{c_b\rho_b},\quad \left.\frac{\partial T}{\partial t}\right|_{t=0}=\frac{w_bc_b\left(T_a-T_p\right)+Q_{met}}{c\rho}\end{aligned} \tag{7}$$

Tissue damage can be estimated on the basis of the so-called Arrhenius integral [13]

$$A\left(r,z,t^F\right)=P\int_0^{t^F}\exp\left(-\frac{E}{RT(r,z,t)}\right)\mathrm{d}t \tag{8}$$

where P is the pre-exponential factor, E is the activation energy, R is the universal gas constant (R = 8.314472), T is the temperature in Kelvin and t^F is the end time of analysis. A value of damage integral $A(r, z, t^F) = 1$ corresponds to a 63% probability of cell death at a specific point (r, z), while $A(r, z, t^F) = 4.6$ corresponds to a 99% probability of cell death at this point.

The problem formulated is solved using the implicit scheme of the finite difference method. The details are presented in [5-7].

3.3. Results of computations

The thermally significant blood vessel of dimensions R = 0.001 m, Z = 0.02 m is considered. The blood flow velocity is equal to v = 0.2 m/s. The heating target volume is specified as 0.0015 m ≤ r ≤ 0.0025 m and 0.005 ≤ z ≤ 0.015. The following values of thermophysical parameters are assumed: thermal conductivities λ_b = 0.488 W/(mK), λ = 0.5 W/(mK), specific heats c_b = 3770 J/(kgK), c = 4000 J/(kgK), mass densities ρ_b = 1060 kg/m^3, ρ = 1000 kg/m^3, metabolic heat sources $Q_{\text{met b}} = Q_{met}$ = 245 W/m^3, blood perfusion rate w_b = 0.5 kg/(m^{3}s), arterial blood temperature T_a = 37°C [5], relaxation times $\tau_{qb} = \tau_q$ = 3 s and thermalization times $\tau_{Tb} = \tau_T$ = 1 s [8]. The initial temperature of tissue and blood is equal to T_p = 37°C, on the outer surface of the tissue the boundary temperature equals 37°C. The following parameters in the Arrhenius integral (8) are assumed: $P = 3.1 \cdot 10^{98}$ 1/s, $E = 6.28 \cdot 10^5$ J/mol [9].

The absorbed total energy density $Q_{ext}\, t_{ext}$ is kept constant as $240 \cdot 10^6$ J/m^3, but different heating schemes are taken into account: Q_{ext} = 120 MW/m^3, t_{ext} = 2 s; Q_{ext} = 60 MW/m^3, t_{ext} = 4 s; Q_{ext} = 30 MW/m^3, t_{ext} = 8 s and Q_{ext} = 20 MW/m^3, t_{ext} = 12 s). The computations were performed until t^F = 20 s.

3.3.1. Temperature distribution

In Figures 3.2–3.5 the temperature distribution after 20 s is shown. As can be seen, the method of heating the tumor affects the temperature distribution in the tissue.

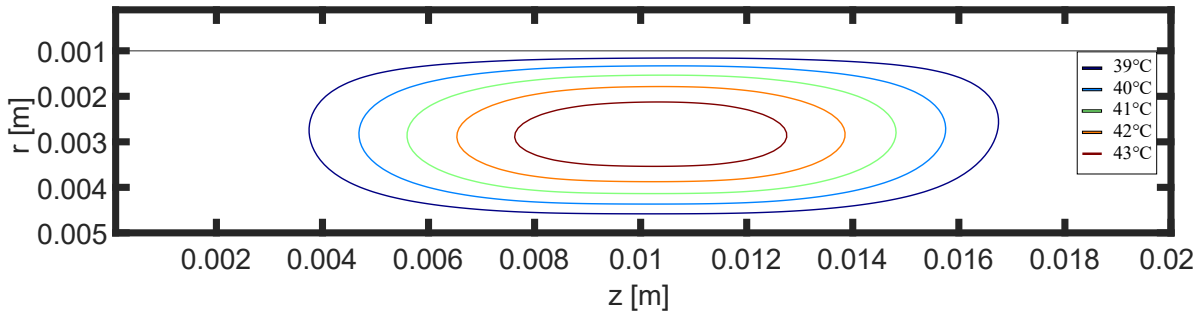

Fig. 3.2. Temperature distribution after 20 s (Q_{ext} = 120 MW/m^3, t_{ext} = 2 s)
Rys. 3.2. Rozkład temperatury po 20 sekundach (Q_{ext} = 120 MW/m^3, t_{ext} = 2 s)

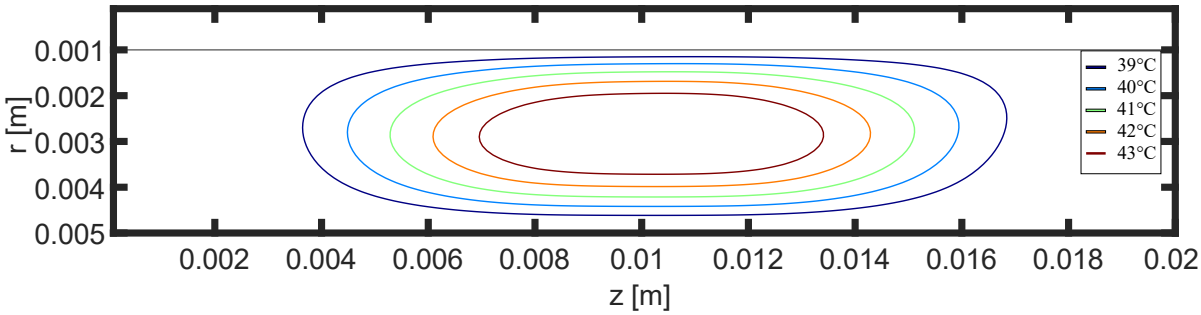

Fig. 3.3. Temperature distribution after 20 s (Q_{ext} = 60 MW/m^3, t_{ext} = 4 s)
Rys. 3.3. Rozkład temperatury po 20 sekundach (Q_{ext} = 60 MW/m^3, t_{ext} = 4 s)

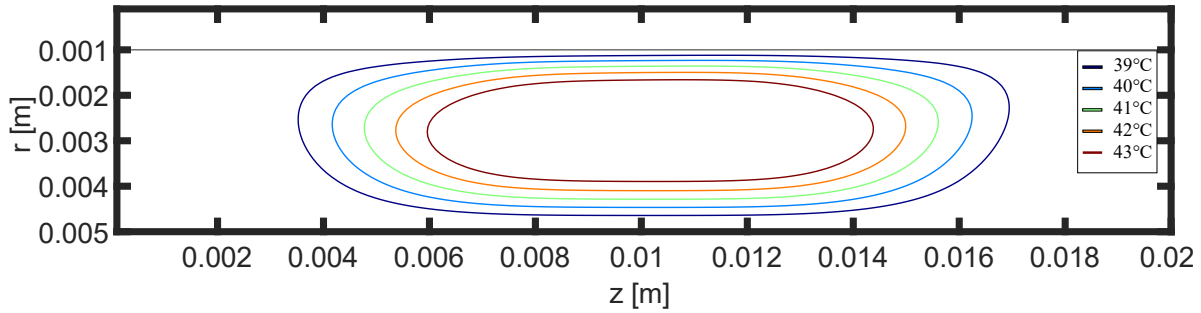

Fig. 3.4. Temperature distribution after 20 s (Q_{ext} = 30 MW/m^3, t_{ext} = 8 s)
Rys. 3.4. Rozkład temperatury po 20 sekundach (Q_{ext} = 30 MW/m^3, t_{ext} = 8 s)

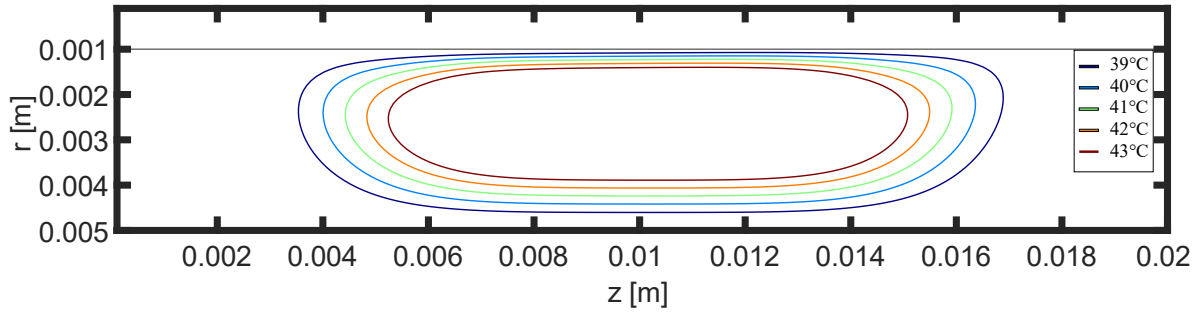

Fig. 3.5. Temperature distribution after 20 s (Q_{ext} = 20 MW/m^3, t_{ext} = 12 s)
Rys. 3.5. Rozkład temperatury po 20 sekundach (Q_{ext} = 20 MW/m^3, t_{ext} = 12 s)

In Figure 3.6 the temperature courses at the central point of tumor are presented. In the case of short heating duration the temperature rises faster and reaches higher values compared to the longer heating time.

3.3.2. Arrhenius integral

Figures 3.7–3.10 illustrate the distribution of Arrhenius integral after 20 seconds for various heating schemes. Dashed lines correspond to the tumor region. Sub-domain between 1 and 4.6 corresponds to the [66% – 99%] probability of tissue destruction, while sub-domain where Arrhenius integral is greater than or equal to 4.6 corresponds to the 99% probability of tissue destruction.

As can be seen, for heating scheme: Q_{ext} = 20 MW/m^3, t_{ext} = 12 s (Figure 3.9) the cancerous tissue is not destroyed. The most effective heating scheme is: Q_{ext} = 120 MW/m^3 and t_{ext} = 2 s (Figure 3.7).

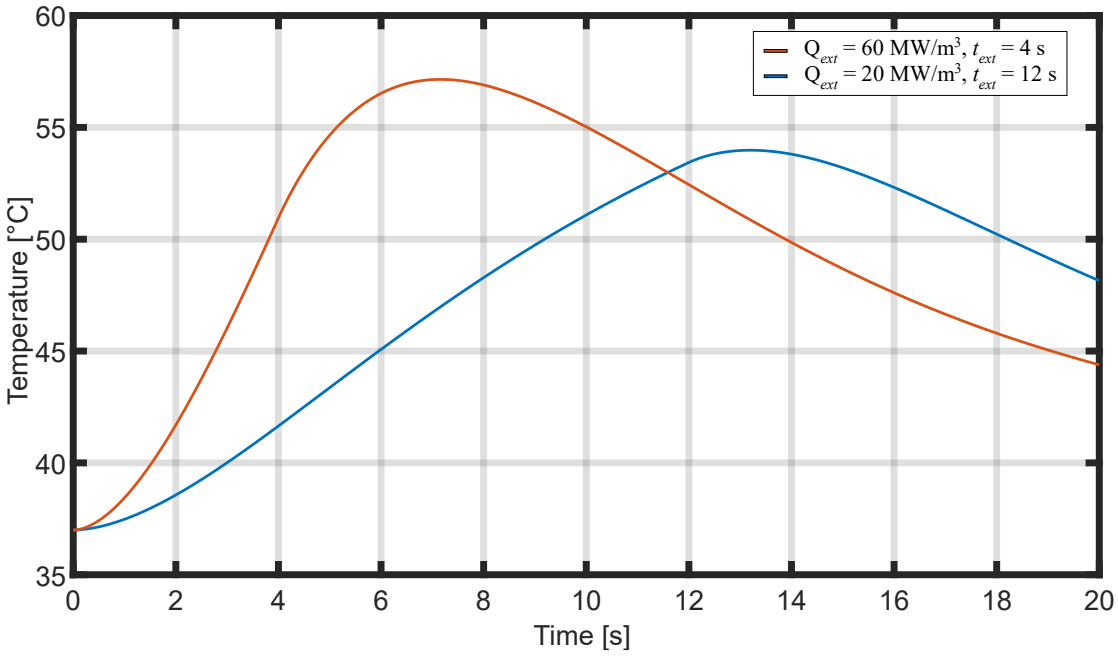

Fig. 3.6. Temperature history at the central point of tumor
Rys. 3.6. Przebieg temperatury w centralnym punkcie nowotworu

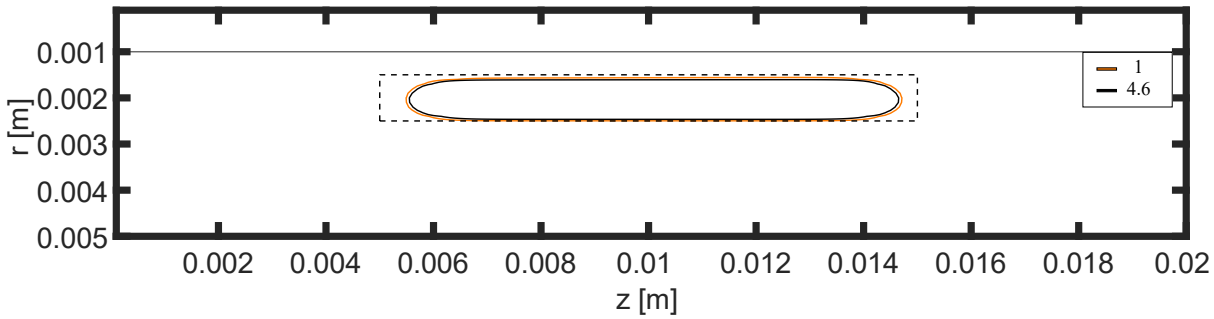

Fig. 3.7. Arrhenius integral distribution after 20 s (Q_{ext} = 120 MW/m^3, t_{ext} = 2 s)
Rys. 3.7. Rozkład całki Arrheniusa po 20 sekundach (Q_{ext} = 120 MW/m^3, t_{ext} = 2 s)

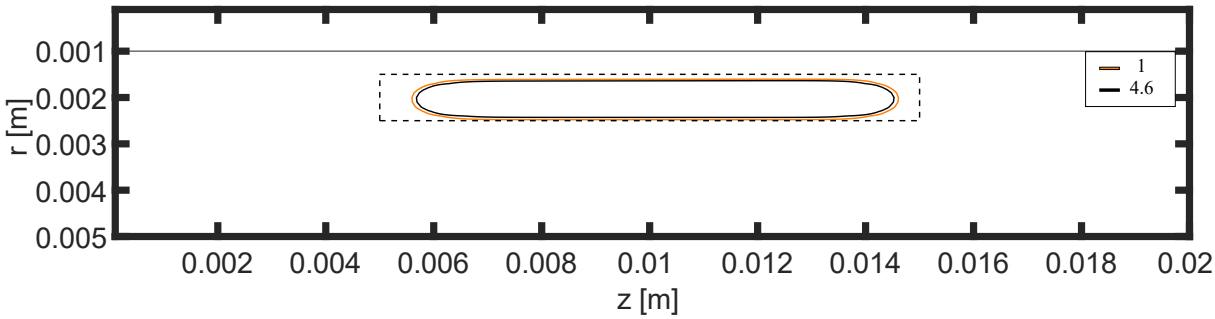

Fig. 3.8. Arrhenius integral distribution after 20 s (Q_{ext} = 60 MW/m^3, t_{ext} = 4 s)
Rys. 3.8. Rozkład całki Arrheniusa po 20 sekundach (Q_{ext} = 60 MW/m^3, t_{ext} = 4 s)

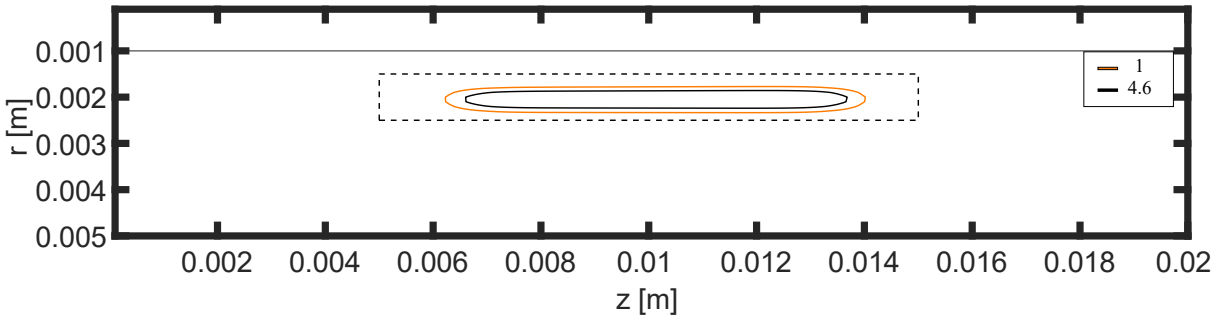

Fig. 3.9. Arrhenius integral distribution after 20 s (Q_{ext} = 30 MW/m^3, t_{ext} = 8 s)
Rys. 3.9. Rozkład całki Arrheniusa po 20 sekundach (Q_{ext} = 30 MW/m^3, t_{ext} = 8 s)

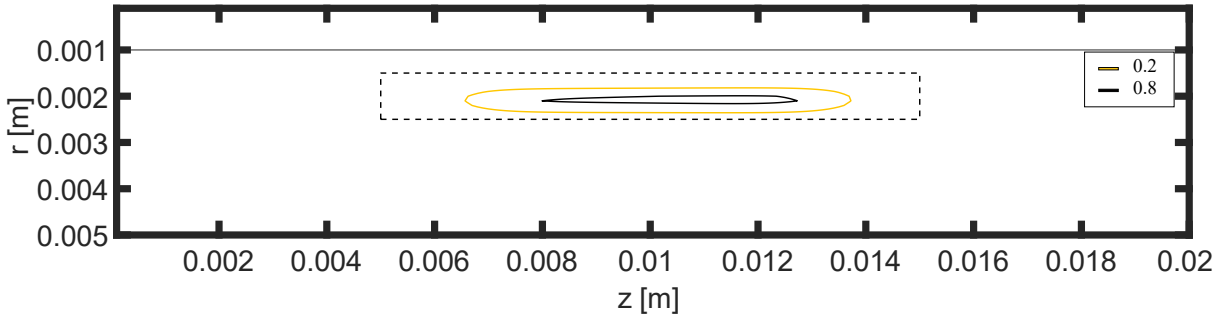

Fig. 3.10. Arrhenius integral distribution after 20 s (Q_{ext} = 20 MW/m^3, t_{ext} = 12 s)
Rys. 3.10. Rozkład całki Arrheniusa po 20 sekundach (Q_{ext} = 20 MW/m^3, t_{ext} = 12 s)

3.4. Conculsions

The single blood vessel surrounded by the biological tissue with a tumor has been considered. Different heating schemes of tumor, it means heating power density Q_{ext} and heating duration t_{ext}, under the assumption that the total energy density Q_{ext} t_{ext} is constant, have been taken into account. The blood and tissue temperature fields have been described by the dual-phase lag equations supplemented by appropriate boundary and initial conditions. The problem has been solved by implicit scheme of finite difference method.

The calculations carried out showed that a short heating time and high heating power density guarantee successful tumor destruction.

Acknowledgements

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Abstract

In the paper a single blood vessel and surrounding biological tissue with a tumor region is considered. The blood and tissue temperature fields are described by the dual-phase lag equations supplemented by appropriate boundary and initial conditions. The degree of destruction of tumor was estimated on the basis of the so-called Arrhenius integrals. The problem was solved using the implicit scheme of the finite difference method. The main purpose of the work is to analyze various heating schemes (power density and heating duration t_{ext}) and to investigate which of the schemes is more effective in order to destroy the tumor tissue: short heating time and high power density, or long heating time and low power density. It turned out that the first of these options is more effective.

Keywords: oncological hyperthermia, dual-phase lag equation, finite difference method, Arrhenius integral.