Mathematical modelling of the destruction degree of cancer under the influence of a RF hyperthermia

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Abstract

The article presents the numerical modeling of the phenomenon of artificial hyperthermia which is caused by the interaction of an electric field. The electric field is induced by the applicator positioned within the biological tissue with cancer. In addition, in order to estimate the degree of tumor destruction under the influence of high temperature an Arrhenius integral has been used. The distribution of electric potential in the domain considered is described by the Laplace system of equations, while the temperature field is described by the Pennes system of equations. These problems are coupled by source function being the additional component in the Pennes equation and resulting from the electric field action. The boundary element method is applied to solve the coupled problem connected with the heating of biological tissues.

Keywords: Arrhenius scheme, boundary element method, cancer ablation, RF hyperthermia

1. Introduction

Hyperthermia in addition to radiotherapy and chemotherapy, has an important and significant role in modern oncology. The essence of this method of treatment focuses on the thermal sensitivity of living cells [6]. Over a given temperature, between 40 and 45°C, normal cells remain unaffected, while the pathological cells are destroyed in the progressive effects of the necrosis and apoptosis phenomena [6]. However, exceeding 45°C can cause irreversible changes both in normal (healthy) and tumor tissues, because the temperature above 45°C as so-called thermoablative temperature. In this connection, a very important problem in the treatment by hyperthermia is to provide and control the temperature in the target area in order to minimize overheating and damage the normal tissues. For correct evaluate of the tissue destruction, it is not enough to exceed the assumed temperature at the cell. For this purpose, the Arrhenius integral value is calculated, which allows to estimate tissue damage.

2. Mathematical modelling

RF hyperthermia (RFH) represents coupled electro-thermal problems. In order to determine the intensity of the electric field the simplification known as the quasi-static approach can be taken into account, because the RFH uses low frequencies [1].

Using above mentioned approach, the electric field intensity **E** (V/m) inside the tissue for 2D problem can be calculated as follows [1, 4]

$$\mathbf{E}_e(X) = -\nabla\varphi_e(X) = -\left[\partial\varphi_e(X)/\partial x_1 \quad \partial\varphi_e(X)/\partial x_2\right]^{\mathrm{T}} \tag{1}$$

where e=1, 2 denotes the healthy tissue and tumor, respectively, X={x_1, x_2} and φ_e [V] is an electric potential, while the heat generation $Q_e^E(X)$ due to the electromagnetic heating for healthy tissue and tumor is defined as follows

$$Q_e^E(X) = \left[\sigma_e\left|\mathbf{E}_e(X)\right|^2\right]/2 = (\sigma_e/2)\sum_{i=1}^{2}\left(\partial\varphi_e(X)/\partial x_i\right)^2 \tag{2}$$

where σ [S/m] is an electrical conductivity.

The electric potential $\varphi_e(X)$ inside the healthy tissue Ω_1 and cancer Ω_2 (c.f. Figure 1) is described by the system of Laplace equations

$$X \in \Omega_e: \quad \nabla\left[\varepsilon_e(X)\nabla\varphi_e(X)\right] = 0 \tag{3}$$

where ε_e [C^2/(Nm^2)] is a dielectric permittivity of tissue.
For a heat transfer process in biological tissue the Pennes model has been proposed [5]

$X \in \Omega_e$:

$$c_e\rho_e\frac{\partial T_e(X)}{\partial t} = \lambda_e\nabla^2 T_e(X) + k_e\left[T_B - T_e(X)\right] + Q_{met\,e} + Q_e^E(X) \tag{4}$$

where t denotes time, ρ_e [kg/m^3] is the density, c_e [J/(kgK)] is the specific heat, λ_e [W/(mK)] is the thermal conductivity, T_e [K] is the temperature, $k_e = G_{Be}c_B$ [W/(m^{3}K)]is the perfusion rate (G_{Be} [1/s] is the perfusion coefficient, c_B [J/(m^{3}K)] is the volumetric specific heat of blood), T_B is the supplying arterial blood temperature and $Q_{met\,e}$ [W/m^3] is the metabolic heat source.

Differential equations which describe the electric (c.f. eq. (3)) and temperature (c.f. eq. (4)) fields are supplemented by appropriate boundary and conditions [4]. Equation (4) is also supplemented by the initial condition $T_0(X)$.

3. Arrhenius scheme

To estimate the degree of tissue destruction an Arrhenius integral [2] is used, which describing the relationship between temperature and tissue damage

$$Arr(X, t^f) = \int_0^{t^f} A\exp\left[-\frac{\Delta E}{RT(X,t)}\right]\mathrm{d}t \tag{5}$$

where R [J/(molK)] is the universal gas constant (R=8.3143), ΔE [J/mol] is the activation energy, A [1/s] is the pre-exponential factor, $T(X, t^f)$ denotes tissue temperature at the point considered, while [0, t^F] is the considered time interval [2].

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The main objective of the Arrhenius scheme is, that thermal tissue damage is irreversible and total, and as a criterion of tissue damage is assumed that the value of the Arrhenius integral is set to [2]

$$Arr(X,t^f)\geq 1 \tag{6}$$

In this case (cf. eq. (6)) it is assumed that the probability of the cell's damage equal to 63%. If the Arrhenius integral value exceeds 4.63 the probability of cell destruction is equal to 99%.

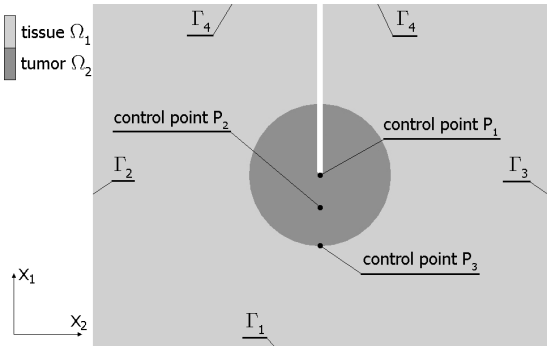

Figure 1: The healthy and tumor tissue with internal electrode

4. Boundary element method

In order to solve the equations describing the potential of electric field and the temperature field in the considered domains the 1st scheme of boundary element method has been applied [3]. The boundary integral equations corresponding to the equations (3) can be expressed as follows

$$B_e(\xi,\eta)\varphi_e(\xi,\eta)+\int_\Gamma \psi_e(X)\varphi_e^*(\xi,\eta,X)\mathrm{d}\Gamma = \int_\Gamma \varphi_e(X)\psi_e^*(\xi,\eta,X)\mathrm{d}\Gamma,\quad e=1,2 \tag{7}$$

while for temperature field (c.f. eq. (4))

$$B_e(\xi,\eta)T_e(\xi,\eta,t^f)+\frac{1}{c_e}\int_{t^{f-1}}^{t^f}\int_\Gamma T_e^*(\xi,\eta,X,t^f,t)q(X,t)\mathrm{d}\Gamma\mathrm{d}t = \frac{1}{c_e\rho_e}\int_{t^{f-1}}^{t^f}\int_\Gamma q_e^*(\xi,\eta,X,t^f,t)T(X,t)\mathrm{d}\Gamma\mathrm{d}t + \iint_\Omega T_e^*(\xi,\eta,X,t^f,t^{f-1})T(X,t^{f-1})\mathrm{d}\Omega + \frac{1}{c_e\rho_e}\int_{t^{f-1}}^{t^f}\iint_\Omega Q_e(X,t)T_e^*(\xi,\eta,X,t^f,t)\mathrm{d}\Omega\mathrm{d}t,\quad e=1,2 \tag{8}$$

where $Q_e=Q_{met\,e}+Q_e^E(X)$. The functions $\varphi_e^*(\cdot)$ and $T_e^*(\cdot)$ are the fundamental solutions.

5. Results of computations

The 2D domain of dimensions 0.12×0.16 [m] has been considered. The tumor region which is located at the center of healthy tissue (c.f. Figure 1) is approximated by circle (radius: 0.025 [m]). The electrical and thermophysical parameters are easy to find in many references e.g. [4]. In Figure 2 the temperature history at the control points P_i (i=1, 2, 3) obtained after the action of the internal electrode (electric potential U=17[V], analysis time t=3600s, time step Δt=1s) are shown, while in Figure 3 the Arrhenius integral courses at the control points are presented. Values of the parameters in the formula (5) are assumed as $\Delta E=2.58\cdot10^5$, $A=7.39\cdot10^{39}$.

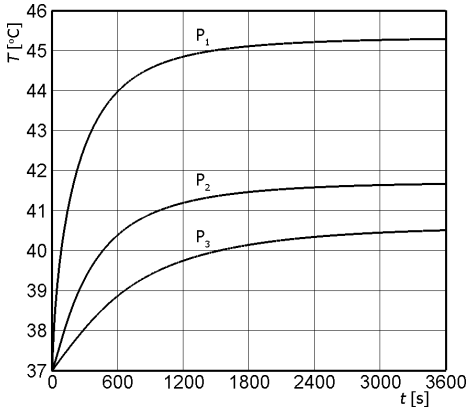

Figure 2: Temperature history at the control points (c.f. Fig. 1)

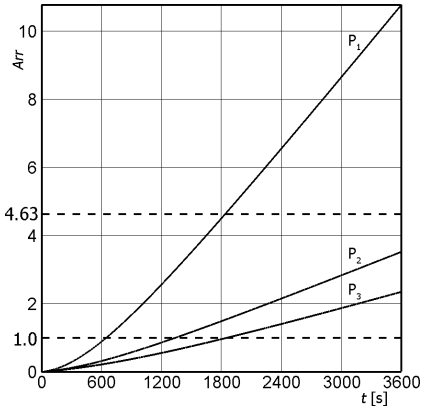

Figure 3: Arrhenius integral courses at the control points

It is clearly visible that the cells corresponding to the points P_1, P_2 and P_3 are destroyed with high probability after 600s, 1200s and 1800s, respectively (Arr>1). Simultaneously, after 1800s the cell at the point P_1 is definitely destroyed (Arr>4.63) (c.f. Figure 3).

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