

SENSITIVITY ANALYSIS OF BIOLOGICAL TISSUE DAMAGE WITH RESPECT TO THE PARAMETERS OF THE HYPERTHERMIA PROCESS

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1. Introduction

Hyperthermia in addition to radiotherapy and chemotherapy, plays an important and significant role in modern oncology. The essence of this method of treatment focuses on the thermal sensitivity of living cells. In a certain temperature range, between 40 and 45°C, healthy cells remain untouched, while pathological cells are destroyed. However, exceeding the temperature of 45°C (temperature above 45°C is known as thermoablative) may cause irreversible changes, both in healthy and cancerous tissues [1]. Therefore, a very important problem during hyperthermia treatment is to predict and accurately control the temperature in the target area and the time of heating, in order to minimize the possibility of overheating and damage the healthy tissues. From the point of view of the possibility of supporting thermotherapeutic techniques, it is important to examine the impact of individual parameters occurring in the mathematical model on the degree of tissue destruction. Therefore, it is necessary to estimate, based on the sensitivity analysis methods, which parameter has the greatest effect on the computations results.

2. Method of solution

The mathematical model describing the process of biological tissue destruction primarily involves the equation of the bioheat transfer (the Pennes equation), tissue destruction model (the Arrhenius scheme), internal source functions (the source component related to perfusion or metabolism) and external source function (resulting from the interaction of the electric field).

The heat transfer process in biological tissue is described by a system of Pennes equations [2]

$$(1) \quad X \in \Omega_e : \quad c_e \rho_e \frac{\partial T_e(X)}{\partial t} = \lambda_e \nabla^2 T_e(X) + k_e [T_B - T_e(X)] + Q_{met e} + Q_e^E$$

where $e=1, 2$ denotes the healthy tissue and tumor, respectively, $X=\{x_1, x_2, x_3\}$ are the spatial co-ordinates, t denotes time, ρ_e [kg/m³] 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 [W/(m³K)] is the perfusion rate, T_B is the supplying arterial blood temperature, $Q_{met e}$ [W/m³] is the metabolic heat source and Q_e^E is an external heat source due to the electric heating.

Using the quasi-static formulation, the electric field intensity \mathbf{E} (V/m) inside the tissue for 3D problem can be calculated as follows [3, 4] (φ_e [V] is an electric potential)

$$(2) \quad \mathbf{E}_e(X) = -\nabla \varphi_e(X)$$

The heat generation Q_e^E due to the electric heating is defined as follows

$$(3) \quad Q_e^E(X) = \frac{\sigma_e}{2} |\mathbf{E}_e(X)|^2$$

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

To estimate the degree of tissue destruction the Arrhenius integral, which describes the relationship between temperature and tissue damage, is used [5]

$$(4) \quad Arr(X, t^f) = \int_0^{t^f} A \exp \left[-\frac{\Delta E}{RT(X, t)} \right] dt$$

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, $T(X, t)$ denotes a temperature at the point considered, while $[0, t^f]$ is the time interval considered. It is assumed that the thermal tissue damage is irreversible and total when $Arr(X, t^f) \geq 1$. In this case the probability of the cell's damage is equal to 63%. If the Arrhenius integral value exceeds 4.63 the probability of cell destruction is equal to 99%

The task was solved by means of finite element method using the MSC Marc/Mentat software.

4. Results of computations

The 3D domain of biological tissue (approx. by cylinder) with tumor (approx. by sphere) which is located at the center of healthy tissue has been considered (c.f. Figure 1a). Figure 1b presents the distribution of Arrhenius integral after 2400 seconds (electric potential $U=17[V]$, time step $\Delta t=1s$). In fact, this figure should be treated as an illustration of the shape of the thermal damage of tissue. The sensitivity analysis of the temperature field and the degree of tissue destruction will be performed due to the geometric and physical parameters of the analyzed process.

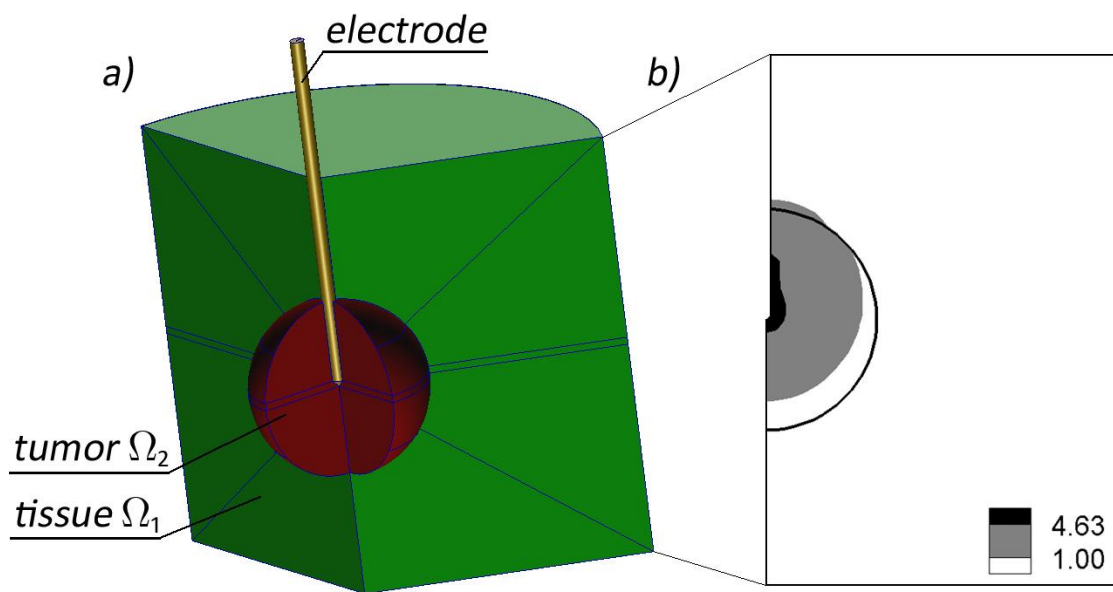


Fig. 1. a) The healthy and tumor tissues with the internal electrode b) Arrhenius integral distribution

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