International Journal of Thermal Sciences 130 (2018) 507–517

Contents lists available at ScienceDirect

International Journal of Thermal Sciences

journal homepage: www.elsevier.com/locate/ijts

Identification of the degree of tumor destruction on the basis of the Arrhenius integral using the evolutionary algorithm

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ARTICLE INFO

Keywords:
Arrhenius scheme
Bioheat transfer
Evolutionary algorithm
Finite element method
Hyperthermia
Thermal ablation

ABSTRACT

The article presents the mathematical modeling of the artificial hyperthermia process caused by the action of electric field. The increase in the tissue temperature causes, as one knows, the destruction of the cancer tissue. To estimate the degree of damage of the tumor tissue the Arrhenius scheme has been used. In the paper the inverse problem consisting in the simultaneous identification of the exposure time of the electric field and the parameters controlling the process of tissue damage is solved using the evolutionary algorithm. As a parameter of the fitness function for the evolutionary algorithm, the Arrhenius integral which determines the degree of tissue destruction is applied.

The electric field is induced by an internal applicator placed inside the biological tissue attacked by the cancer. The mathematical description is based on the Pennes equations (for the temperature field) and the Laplace equations (for the electric field). Electro-thermal coupling is taken into account by means of an additional internal heat source occurring in the bioheat transfer equation. On the stage of numerical computations, the evolutionary algorithm coupled with the finite element method is used.

1. Introduction

Oncological hyperthermia using artificial hyperthermia methods is a dynamically developing method of complementary treatment of cancer, which involves the targeted use of thermal energy. Its essence consists in a controlled, local temperature increase of the area of pathological changes. Oncological hyperthermia is used primarily in the combination with chemotherapy and radiotherapy. Such an approach increases the effectiveness and force of the treatment. Artificial raising of body temperature is not a new method, it has been known in medicine many years ago.

Hyperthermia occurs when the body produces or absorbs greater heat than warmth given to the environment. Such a process can be induced by the medical devices. In this type of treatments, the local hyperthermia (interstitial) and whole body hyperthermia (systemic) can be distinguished. The local hyperthermia is a method in which the heat is applied only to the tumor region (locally), while the whole body hyperthermia focuses mainly on activating the entire immune system. In particular, the fever stimulates the patient's immune system to destroy cancer cells and causes increased immune responses in the whole body [1].

The methods of the artificial hyperthermia treatment use the laser impact e.g. Ref. [2–5], the electric field e.g. Ref. [6–13], the microwaves e.g. Ref. [14–17] or the ultrasounds e.g. Refs. [18,19]. From the point of view of the local hyperthermia treatment, it is important not only to heat the tumor to the proper temperature, but also to estimate the degree of its destruction. One of the methods of tissue destruction degree estimation is the Arrhenius integral [20] – [23], which describes the relationship between the local temperature and the tissue damage. So, the tissue temperature should be increased to 42–46 °C, because at the temperatures above 42 °C the process of necrosis of living cells begins. Temperatures above 45 °C are known as thermoablative. Prolonged exposure at such high temperature destroys the cells via coagulation necrosis [24,25]. The research have shown that the high temperatures can damage and kill the cancer cells, usually accompanied by a low risk of damage to healthy tissue [10]. As mentioned above, one of the methods of destroying cancerous tumors in healthy tissue is heating the malignant tissue to a critical temperature that kills cancer cells by means of electric field. The analyzed calculation example concerns local heating of the tumor by placing inside it a single-armed electric probe through which electric current flows. The current flow through the tip of the electrode allows to increasing the temperature to the expected value. The flowing electric current generates an electric field in the tissue. The electric field is the strongest in the immediate vicinity of the probe and in this way generates heating of the tissue.

Interstitial radiofrequency (RF) hyperthermia is clinically applied mainly for non-operable liver tumors, with increasing application to other organ sites like kidney, lung and bone. Most present devices use

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https://doi.org/10.1016/j.ijthermalsci.2018.05.015
Received 12 February 2018; Received in revised form 9 May 2018; Accepted 9 May 2018

radiofrequency current to heat tumor tissue surrounding the applicator, which is introduced into the tumor [26].

In this article, the state of artificial hyperthermia is caused by the interaction of the electric field induced by the internal applicator. The geometrical 2D model is defined as an axially-symmetrical one (Fig. 1) [10,27,28]. Due to the necessity of solving a very large number of direct problems during the process of identification, it was decided to simplify the geometry of the analyzed area to the axisymmetric form. This operation allowed the transition from the 3D model into a 2D model, but oriented in the cylindrical coordinate system. After the application of the electrode, a low-voltage current is generated (max. 35 V) [10]. Additionally, in order to properly focus the heat energy in the tumor region the magnetic nanoparticles to this sub-domain are introduced, which enable accumulation of heat in the desired place. Such magnetic particles must have the appropriate magnetic properties and biological compatibility. Until now, iron oxides such as Fe_3O_4 (magnetite) and γ-Fe_2O_3 (maghemite) are the most investigated [9]. It is essential, of course, the proper selection of the process parameters (the electric potential, the number of nanoparticles, the size of applicator active part, the exposure time of electrical interactions).

To estimate these parameters, the solution of inverse problem is applied and the method based on the evolutionary algorithm is used. On the other hand, the direct problem for the assumed set of parameters is solved using the finite element method. In this way the intensity of electric field and temperature distribution can be found. The values of thermophysical and electrical parameters used for numerical calculations refer to the liver.

2. Method of solution

2.1. Arrhenius scheme

To estimate the degree of tissue destruction the Arrhenius integral [20–23] [28,29] which describes the relationship between temperature and tissue damage is used

$$Arr(r,\ z,\ t) = \int_0^{t^f} A \exp\left[-\frac{\Delta E}{RT(r,\ z,\ t)}\right] \mathrm{d}t \tag{1}$$

where $R = 8.3143$ J/(mol·K) is the universal gas constant, ΔE [J/mol] is the activation energy, A [1/s] is the pre-exponential factor, $T(r, z, t)$ denotes a temperature at the point considered, while $[0, t^f]$ is the time interval considered, where t^f is the time of the end of the analysis.

The parameters A and ΔE are determined experimentally. For example, Table 1 summarizes the values of the above parameters for different types of tissues [30,31].

It is assumed that the thermal tissue damage is irreversible and total

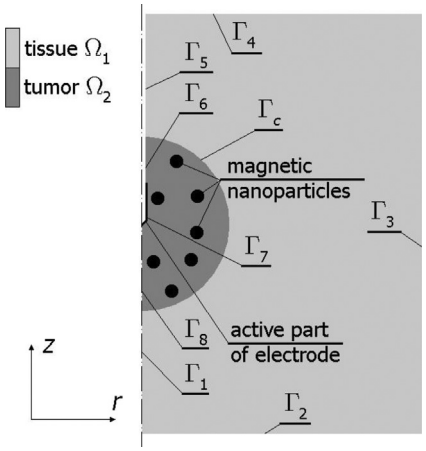

Fig. 1. The healthy tissue and the tumor region with internal electrode.

Table 1
The parameters A and ΔE for different tissue types [30,31].

Tissue type	A [1/s]	ΔE [J/mol]
Liver	$7.39 \cdot 10^{39}$	$2.58 \cdot 10^5$
Skin	$1.80 \cdot 10^{51}$	$3.27 \cdot 10^5$
Tissue with the capillaries	$1.98 \cdot 10^{106}$	$6.67 \cdot 10^5$
Aorta	$5.60 \cdot 10^{63}$	$4.30 \cdot 10^5$
Breast	$1.18 \cdot 10^{44}$	$3.02 \cdot 10^5$

when

$$Arr(r,\ z,\ t) \geq 1 \tag{2}$$

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% [31].

2.2. Inverse problem

The aim of investigations is to determine the electric potential U of the active part of electrode, the length L_{apoe} of the active part of electrode and the exposure time t_{exp} of the electric field action.

The functional (fitness function) S is defined as follows

$$S = \sum_{f=1}^{F} \sum_{i=1}^{M} \left(Arr_i(r,\ z,\ t) - Arr_i^h(r,\ z,\ t)\right)^2 \rightarrow \mathrm{MIN} \tag{3}$$

where $Arr_i(r, z, t)$ are the nodal values of Arrhenius integral (Eq. (1)) located inside the tumor and resulting from the numerical solution of the direct problem for assumed values of U, L_{apoe} and t_{exp}, M is the number of nodes located inside the tumor, F is a number of time steps. The $Arr_i^h(r, z, t)$ is a postulated value of the Arrhenius integral and it has been assumed either as 1 or 4.63 (see Chapter 2.1).

To check the correctness and effectiveness of the evolutionary algorithm coupled with the FEM, the direct problem corresponding to the known values of the identified parameters has been solved. The obtained value of $Arr_i^h(r, z, t)$ played a role of the expected value, and finally the identified parameters of U, L_{apoe} and t_{exp} were found.

The evolutionary algorithm (EA) operates on the chromosomes population. Each chromosome contains the genes [32–35]. The chromosome containing the information about the identified parameters is of the form

$$\mathbf{p} = [U \quad L_{apoe} \quad t_{exp}]^{\mathrm{T}} \tag{4}$$

where U, L_{apoe} and t_{exp} are the genes. The genes representing the possible solutions are obtained during the appropriate operations of the evolutionary algorithm, within the constraints

$$U^L \leq U \leq U^H,\ L_{apoe}^L \leq L_{apoe} \leq L_{apoe}^H,\ t_{apoe}^L \leq t_{exp} \leq t_{apoe}^H \tag{5}$$

where L and H denote the minimum and maximum values of the limitations imposed on the identified parameters.

In Table 2, the parameters of evolutionary algorithm used at the stage of computations are collected.

The evolutionary algorithm starts with an initial population. This population consists of N chromosomes $\mathbf{p}^n$, $n = 1, 2, \ldots, N$, generated in random way – Fig. A1. Each value of the gene, during creation of the start population, was determined with continuous uniform distribution. Every gene is taken from the feasible domain. For the assumed values of $\mathbf{p}^n$, $n = 1, 2, \ldots, N$, the direct problems described in the next chapter are solved. The next stage is an evaluation of the fitness function (3) for every chromosome $\mathbf{p}^n$ and the selection process is employed. The selection is performed in the form of ranking selection or the tournament selection and the evolutionary operators (mutation, crossover and cloning) are applied. In this way the next population is created. The process is repeated until one finds the chromosome, for which the value of the fitness function is equal to zero, or after the achieving the