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BIOMEDICAL SCIENCES: INNOVATIONS OF THE FUTURE

MATHEMATICAL MODELING OF TEMPERATURE DISTRIBUTION IN MALIGNANT TUMORS THAT ARE HETEROGENEOUS BY BLOOD STREAM

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The study of the thermal properties of tumors shows that blood perfusion as the most important biomechanical parameter corresponding to the conversion coefficient in the biothermal equation depends not only on the type of neoplasm, but is largely determined by its size, and is variable by section of the tumor [1-5]. Uneven perfusion of blood by the volume of the tumor was confirmed by the researchers [4-7]. Such differences are explained by the choice of different types of tumors by different researchers, different stages of their development [5, 8] and, above all, they prove the validity of the previously stated requirement for a differentiated hyperthermia strategy with respect to each tumor.

The center of the tumor has poorly expressed blood flow, up to its absence, whereas the growing front of the neoplasm is highly perfused even in comparison with normal tissue [5, 8]. The heterogeneity of the thermal properties of tumors appears, apparently, for metabolic heat [2]. Naturally, different values of the maximum intensity of the blood flow and the specific power of the thermal source acting on the tissue within one neoplasm lead to unequal values of other thermal coefficients entering into the biothermal equation.

In connection with the established fact of different values of the maximum intensity of blood flow along the cross-section of malignant tissue, a more accurate thermal model of the tumor is a layered tumor, with each layer characterized by its maximum intensity of blood flow. The number of such layers usually does not exceed five [4]. These layers correspond to: 1) a necrotic zone; 2) a necrotic zone with long capillaries; 3) a stabilized zone with a pronounced microcirculation system; 4) a growing tissue; and 5) a normal tissue. For theoretical calculations of thermal fields inside a malignant neoplasm, the number of layers should not be increased to four or more, since such calculations and cumbersome analytical formulas can make it difficult to understand the qualitative picture. Three-layered and often two-layer models of heterogeneous tumors virtually completely reflect the real heterogeneous distribution of blood flow by their volume [9]. This is based on the fact that each layer is characterized by its set of values of thermal properties, which determine the nature of energy absorption from the external source of the field supplied from outside.

Since the main mechanism of heat transfer for biological tissue is associated with the blood flow, it is obvious that for local hyperthermia, the layered recording of different values of the maximum intensity of the blood flow that largely reflects the various properties of the tumor should lead to appreciable differences in temperature distributions over the tissue section, compared with the medium with homogeneous thermal and perfusion properties [8, 10].

For a tumor heterogeneous by blood flow for heated biological tissue, for each layer (i) of the tumor, we can write:

$$\frac{d^2T_i}{dr^2}+\frac{2}{r}\cdot\frac{dT_i}{dr}-\beta_i^2T_i+\frac{P_i}{k_t}=0$$

where, $T_i = T - T_a$; T is the temperature of all layers of the tumor; T_a is temperature of the tumor layer at the arterial end of the capillary; k_t is the thermal conductivity of biological tissue, r is the size of the heated part of the tumor; P_i is the specific power of all thermal sources acting on the tumor, including external ones; β is a coefficient that depends on the size of the tumor, the thermal conductivity and density of the tumor layers, the volume-averaged blood flow, specific heat and blood density.

Based on the three-layer model of malignant neoplasm (i = 3), the boundary conditions can be chosen, for example, as follows:

$$\begin{cases} r = 0, \xrightarrow{\beta} T_i \prec \infty \\ r = r_1, \xrightarrow{\beta_1} T_1 = T_2 \\ r = r_1, \xrightarrow{\beta_2} k_{t1} T_1' = k_{t2} T_2' \\ r = r_2, \xrightarrow{\beta_{2,3}} T_2 = T_3 \\ r = r_2, \xrightarrow{\beta_3} k_{t2} T_2' = k_{t3} T_3' \\ r = r_3, \xrightarrow{\beta_{3,2,1}} T_3' = \dfrac{hR}{k_m}\left[\widetilde{T} - T_3\right] \end{cases}$$

where, $\widetilde{T} = T_s - T_a$, T_s is the ambient temperature; R is the characteristic size of the heated tissue; h is the heat transfer coefficient in each of the layers of the heterogeneous tumor (respectively 1, 2, 3). The solution of the formulated problem can be obtained analytically. Obviously, for clinical applications of local hyperthermia, the temperature value at the center of the tumor should not exceed 45 [5, 8, 11]. Calculations from the formulas obtained by us show that the thermal fields are sensitive to the characteristic size of the malignant neoplasm. It is established [4] that the growing highly perfused layer of the tumor is approximately constant in thickness during the entire evolution of the malignant neoplasm. This means that such a layer is a part of its volume that is constantly decreasing during the growth of the tumor. Consequently, the energy density of the external heat source is inversely proportional to the size of the tumor. Since the volume of the latter grows with the increase in the radius of the tumor, the total energy required to heat the tissue, in contrast, must be directly proportional to the size of the neoplasm's [8]. The management of local hyperthermia requires consideration of the size of the tumor heterogeneous by the bloodstream, the efficiency of the heating process depends on the properties of the layer into which the energy of the external heat source is supplied, within rather narrow limits. Therefore, local hyperthermia requires the development of a graph of the distribution of temperature fields in order to predict specific temperatures that should not exceed the limits of the established values that have a therapeutic effect.

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