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RHEOLOGICAL FACTOR IN THE THERMAL PROBLEM OF SHF HYPERTHERMIA TREATMENT. 3. HETEROGENEOUS BIOLOGICAL TISSUE

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This article studies the influence of the rheological factor on the temperature field in heterogeneous biological tissue under local SHF hyperthermia treatment and optimization of this procedure by rational choice of the emitter power to ensure maximum theraupetic temperatures in the tumor.

Heat transfer modeling in living biological tissue under heating conditions is the subject of many investigations (see, e.g., [7-12]).

Among them is the important problem of local hyperthermia and, in particular, heating of a tumor tissue to theraupetic temperatures at prescribed depths without injuring normal biological tissue at other depths.

The analysis in [1, 2] of the influence of different simulation factors on the degree of heating of a homogeneous biological tissue is not exhaustive and does not prove the possibility (or impossibility) of solving this problem. A real biological tissue is substantially inhomogeneous; the emergence of a tumor in it causes such processes, for instance, as a change of blood flow in a local hyperthermia process. We will consider the possibilities of solving the above problem by using different strategies (procedures) of heating, in particular, with respect to a flat multilayer biological tissue in the case of a one-dimensional steady-state problem. The statement of the thermal problem in this case is analogous to Eqs. (1)-(3) in [1]; however, the conditions at the inner and outer boundaries of the biological tissue must be supplemented with the conjugation conditions (equality of temperatures and heat fluxes) at the layer boundaries. For instance, the problem in dimensionless form is as follows:

$$\left.\begin{aligned}
&\Theta'' - B_k^2\,\Theta_k + R_k \exp(aLx) = 0\,,\\
&\Theta_0'\,|_{x=0} = \mathrm{Bi}\,(1 + \Theta_0\,|_{x=0})\,,\\
&\Theta_k'\,|_{x=x_k} = (\lambda_{k+1}/\lambda_k)\,\Theta_{k+1}'\,|_{x=x_k}\,,\quad k = 0, 1, \ldots, n-2\,,\\
&\Theta_k\,|_{x=x_k} = \Theta_{k+1}\,|_{x=x_k}\,,\ k = 0, 1, \ldots, n-2\,,\\
&\Theta_{n-1}\,|_{x=1} = 0\,.
\end{aligned}\right\} \qquad (1)$$

where k is the layer number (0 pertains to the outer layer, $n-1$ indicates an inner layer);

$$B_k^2 = \frac{w_b\, c_b\, L^2}{\lambda_k}\,;\quad R_k = \frac{\rho_k\, sPL^2 \exp(-ad)}{\lambda_k\,(T_0 - T_s)}\,;\quad \mathrm{Bi} = \frac{\alpha L}{\lambda_0}\,.$$

The general solution of the problem is

$$\Theta_k(x) = C_k \exp(-B_k x) + D_k \exp(B_k x) + E_k \exp(aLx)\,, \qquad (2)$$

where

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TABLE 1. Geometric and Hemodynamic Parameters of the Problem

Layer No.	Biological tissue	Thickness, mm	Mass velocity of blood, kg/(m^3·sec)	
			variant 1	variant 2
0	Skin	2	5	5
1	Fat	5	5	5
2	Muscle	13	5	5
3	Actively growing tumor layer	2	8	8
4	Tumor core	6	5	0
5	Actively growing tumor layer	2	8	8
6	Muscle	20	5	5

TABLE 2. Thermophysical Parameters of the Problem

Biological tissue	Skin	Fat	Muscle	Tumor (layers 3-5)
Thermal conductivity, W/(m·K)	0.376	0.450	0.642	0.502
Density, kg/m^3	1000	850	1050	1050

$$E_k = \frac{R_k}{B_k^2 - (aL)^2}, \quad (B_k \neq |aL|),$$

and the coefficients C_k and D_k are found from the boundary and conjugate conditions by solving the resultant system consisting of $2n$ linear algebraic equations:

$$SG = R, \tag{3}$$

where

$$g_{2j} = C_j, \quad g_{2j+1} = D_j, \quad j = 0, 1, \ldots, n-1; \quad S_{00} = -(B_0 + \mathrm{Bi}),$$

$$S_{01} = B_0 - \mathrm{Bi}, \quad S_{0k} = 0, \quad 1 < k < 2n-1; \quad S_{2n-1,k} = 0, \quad k < 2n-2,$$

$$S_{2n-1,2n-2} = \exp(-B_{n-1}), \quad S_{2n-1,2n-1} = \exp(B_{n-1}),$$

$$S_{i,j} = -B_k \exp(-B_k, x_k), \quad S_{i,j+1} = B_k \exp(B_k x_k), \quad S_{i,j+2} = B_{k+1}(\lambda_{k+1}/\lambda_k) \times$$

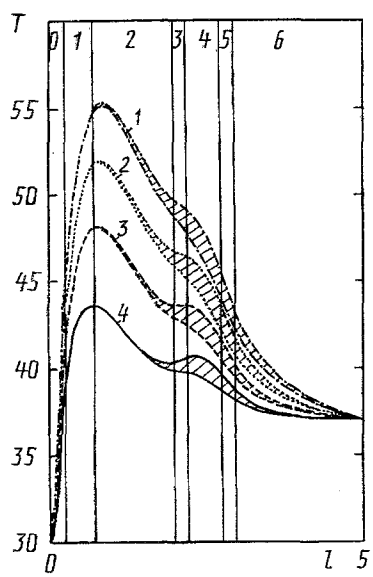
$$\times \exp(-B_{k+1} x_k), \quad S_{i,j+3} = B_{k+1}(\lambda_{k+1}/\lambda_k) \exp(B_{k+1} x_k), \quad j = [i/2],$$

$$i = 2k+1, \quad 0 \leq k < n-1;$$

the remaining $S_{i,j} = 0$;

$$r_0 = \mathrm{Bi}(1 + E_0) - aL E_0, \quad r_{2n-1} = -E_{n-1} \exp(aL), \quad r_{2k+1} = (E_{k+1} \lambda_{k+1}/\lambda_k -$$

$$- E_k) aL \exp(aLx_k), \quad r_{2k+2} = (E_{k+1} - E_k) \exp(aLx_k), \quad k = 0, 1, \ldots, n-2.$$



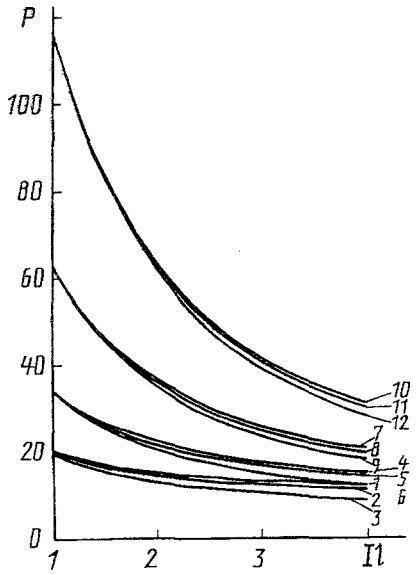


Fig. 1. Temperature distribution in the multilayer flat biological tissue in the presence and absence of blood flow in the tumor core (upper and lower curves, respectively, confining the hatched regions): 1, Il = 1; 2, Il = 2; 3, Il = 3; 4, Il = 4. T, °C; l, cm.

Fig. 2. Optimal power as a function of the Il'yushin parameter. P, W.

The temperature fields were calculated by formula (2) with the coefficients C_k and D_k determined from solutions of the system of equations (3), for two variants given in Table 1. The thermophysical characteristics of the biological tissues were taken from [3] (see Table 2).

The blood flow in a steady thermal state was evaluated by the formula from [1]:

$$\frac{w_b}{w_{b\,in}} = \left(\frac{R}{R_{in}}\right)^3 \frac{Il_{in}}{Il}. \tag{4}$$

The relative change of the Il'yushin parameter was within 1 to 4 ($Il_{in} = 1$ and R/R_{in} was assumed to be unity for a tumor and 1.5 for normal biological tissue).

Figure 1 shows the calculated temperature distributions with respect to the tissue depth for both variants at Il = 1, 2, 3, 4.

As is seen, the presence of the necrosis core in the tumor causes a rather small temperature rise which is most pronounced at the center of the tumor (1.2 deg at Il = 1; 1.5 deg at Il = 2; 1.7 deg at Il = 3, and 1.8 deg at Il = 4).

The temperature is maximum, as in the case of a homogeneous biological tissue, near the surface (at depths from 0.7 to 1.0 cm). One may observe substantial nonuniformity of the temperature distribution with respect to depth, which is in proportion to the increasing Il'yushin parameter. This means that in this instance the Il'yushin parameter also exerts a significant effect.

For other combinations of the parameters, the temperatures will, naturally, have different values. However, the situation, as a rule, develops as in Fig. 1: a considerable part of the biological tissue is highly superheated, while the tumor (or part of it) is heated only to temperatures beyond the theraupetic range.

This example illustrates that it is necessary to optimize only those parameters that may be changed in a local hyperthermia process, thus making the procedure highly effective. In the hyperthermia procedure considered (attaining stationary temperatures) such parameters include the power of the SHF emitter P and the cooling intensity Bi of the external surface of a biological tissue (skin).

We consider now the possibilities of optimization with respect to the relative part of the tumor heated to theraupetic temperatures (the effectiveness function) by choosing the corresponding emitter power at different (but

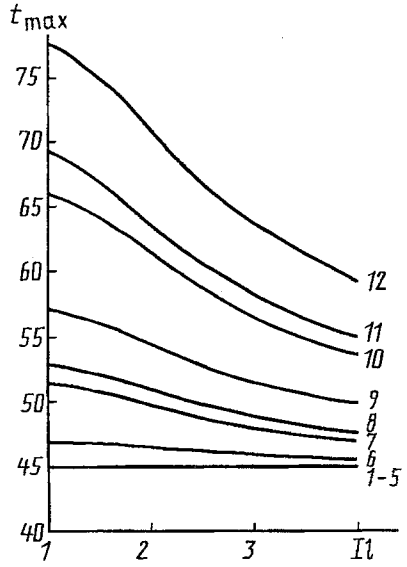


Fig. 3. Maximum heating of the biological tissue under optimal treatment conditions at different values of the viscoplasticity parameter. t_{max}, °C.

recorded) Bi and Il values. We use the same geometric, thermophysical, and hemodynamic parameters of the model as in the above problem but different depths of tumor localization (the center of its core), namely, 1.5, 2.0, 2.5, and 3.0 cm. The blood flow in the core is assumed equal to 0.

Thus, we write problem (1) with the additional condition

$$\varepsilon_0 (\text{Il}, P, \text{Bi}) :: = \frac{1}{l_2 - l_1} \int_{l_1}^{l_2} \psi_0 (l, \text{Il}, P, \text{Bi})\, dl = \max, \tag{5}$$

where l_1, l_2 are the coordinates of the lower and upper boundaries,

$$\psi_0 (l) = \begin{cases} 0, \ \Theta (l) < \Theta^*_{\min} \text{ or } \Theta (l) > \Theta^*_{\max}, \\ 1, \ \Theta^*_{\min} \le \Theta (l) \le \Theta^*_{\max}; \end{cases}$$

$$\Theta^*_{\min} = \frac{t^*_{\min} - t_0}{t_0 - t_s}; \quad \Theta^*_{\max} = \frac{t^*_{\max} - t_0}{t_0 - t_s}.$$

As earlier, we assume that $t^*_{\min} = 42°C$, $t^*_{\max} = 45°C$ is the theraupetic temperature range. The optimal power, at which ε_0 is at its maximum, is calculated by the Hooke-Jeeves method [4] (for the determination of the total minimum of the function ε_0 (Il, P, Bi). Prior to determining the effectiveness function, we calculated the temperature distribution by formulas (2), (3) using some coordinate network whose density was chosen such as to ensure a calculation error in ε_0 of not greater than 10^{-4}. The results of numerical modeling are given in Figs. 2-5. The numbers of the lines in the figures correspond to the following combinations of skin cooling intensities Bi and localization depths l_c of the center of the tumor core:

Bi	l_c, cm			
	1.5	2.0	2.5	3.0
4000	1	4	7	10
60	2	5	8	11
12	3	6	9	12

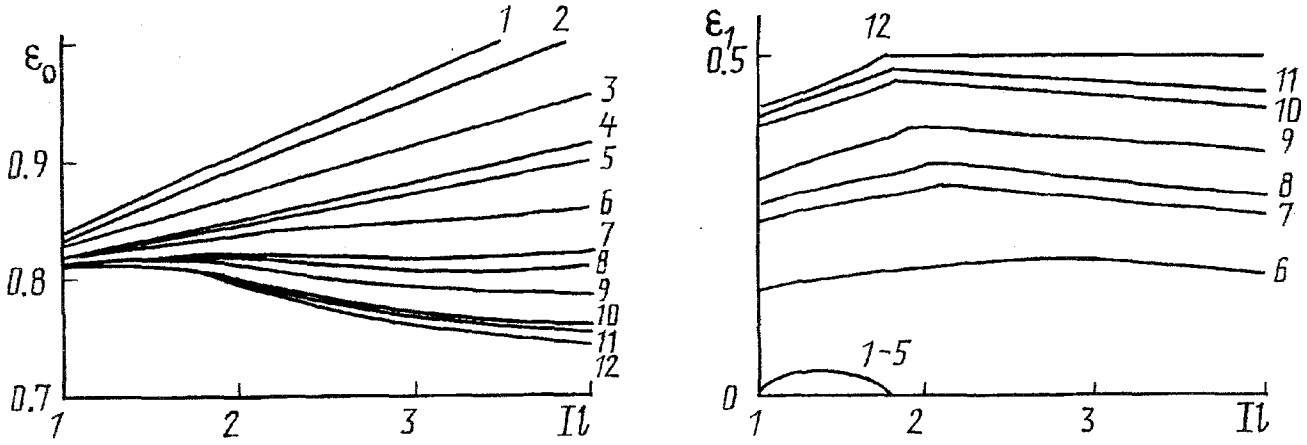


Fig. 4. Maximum degree of tumor heating to the theraupetic temperatures as a function of the Il'yushin parameter.

Fig. 5. Relative part of the superheated biological tissue under optimal heating conditions as a function of the Il'yushin parameter.

As is seen in Fig. 2, the optimal power depends weakly on the skin cooling intensity. However, as follows from Figs. 5 and 3, with decreasing Bi number from 4,000 to 12, the part of the biological tissue that is heated to dangerous temperatures increases considerably, and simultaneously the value of its maximum heating increases markedly too. It is noteworthy that within the Il'yushin parameter range 1 to 4 the maximum level and range of change of all these parameters depend substantially on the depth of tumor localization and decrease in proportion to this depth.

Therefore, it is preferable to carry out the local hyperthermia treatment at as high a skin cooling intensity as possible. From the safety standpoint (biological tissue must not be heated to temperatures higher than 45°C), this procedure may be highly effective at the chosen parameters only for the tumors localized at depths of not greater than 2 cm for Bi $\geq$ 60.

Figures 2-4 also indicate the significant effect of the Il'yushin parameter on the optimal power, maximum heating, and degree of attaining the theraupetic temperature range in the tumor. For the tumors localized at depths of less than 2.5 cm the last parameter increases in proportion to the Il'yushin parameter, thus confirming the effectiveness of the local hyperthermia treatment at elevated Il'yushin parameters.

In [5, 6] it is noted that introduction of high-molecular dextrans (polysaccharides) into the animal's blood leads to pronounced aggregation of erythrocytes and increase in blood viscosity and yield point. Consequently, introduction of a dextran with molecular mass exceeding 40,000 into a tumor may cause an abrupt decrease in blood flow, thus creating more favorable conditions for attaining the theraupetic temperatures under conditions of local hyperthermia. If a dextran with molecular mass lower than 40,000 is introduced into the tumor (and/or the neighboring biological tissue), the elevated aggregation of erythrocytes, blood viscosity, and yield point decrease and, as a result, the initial blood flow may be restored.

The superheated part of the biological tissue, as seen in Fig. 5, changes insignificantly (not greater than by 27%) with increase in the Il'yushin parameter, attains its maximum in the range Il $\cong$ 2 and at Il > 2 continues to decrease monotonically.

Figures 2-5 also show that local hyperthermia treatment may be highly effective at the chosen parameters when the tumor is localized at small depths. The lower the depth of localization and the smaller the power level and optimal power range, i.e., the smaller the effect of the error in prescribing the Il'yushin parameter, the greater is the part of the tumor heated to the required temperatures (up to 100%), the smaller is the superheated part of the biological tissue (to 0%), and the lower is its maximum temperature. In the case where a tumor is deeply localized, this procedure is poorly effective (or not effective at all) and requires a radical change in treatment conditions, e.g., in the parameters of the SHF emitter antenna, heating, etc.

In conclusion we note that the results obtained characterize the effect of the rheological factor on local hyperthermia treatment only qualitatively. This is due not only to our considering the biothermal equation as applied to a plane (one-dimensional) problem but also to the extreme simplification of the dynamics of changing the blood flow intensity. The latter is connected with the fact that the relative change in the viscoplasticity parameter in expression (4) has been prescribed a priori disregarding the real change in hemodynamic (and, in particular, rheological) characteristics of the blood and microvascular system in proportion to heating of the biological tissue. Expression (4) describing the relative change in the mass velocity of the blood as a function of the relative change in the Il'yushin parameter is valid only when the coefficients m and n in the Shul'man equation do not change under the conditions of blood heating, i.e., $m = n = \text{const}$.

However, the rheological factor undoubtedly plays the predominant role from the viewpoint both of the temperature profiles attained in the local hyperthermia processes and their regulation by changing the external (controllable) parameters, in particular, the emitter power.

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NOTATION

k, number of the heterogeneous biological tissue layer; λ_k, thermal conductivity of the biological tissue; c_b, heat capacity of blood; ρ_k, biological tissue density; $w_{b\,in}$, initial mass velocity of blood; w_b, mass velocity of blood; T_s, temperature of the liquid cooling the skin; T_0, homeostatic temperature (37°C); α, skin-to-environment heat transfer coefficient; Bi, Biot number; s, a, b, c, d, antennna parameters; P, SHF emitter power; T, biological tissue temperature; l, depth; L, thickness of the heated biological tissue layer; l_c, localization depth of the center of the tumor core; θ_k, dimensionless temperature; x_k, relative depth; R_{in}, initial radius of the capillary; R, finite radius of the capillary; Il, rheological factor (Il'yushin parameter); Il_{in}, initial value of the Il'yushin parameter.

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