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GENERAL HYPERTHERMIA – CURRENT STATUS OF THE CONCEPTUAL-THEORETICAL BASIS

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Different approaches to the physicomathematical description of the thermophysics and rheodynamics of blood flow in living, externally heated biotissues are considered, analyzed, and compared. Our own model is suggested that allows for the influence of the rheological factor on the spatial-temporal evolution of temperature and hydrodynamic fields in normal and tumor biotissues subjected to the effect of shf electromagnetic fields.

1. Analysis of Basic Concepts of the Theory of Heat Transfer in Living Biotissues. With the development of computers and improvement of numerical techniques many difficulties disappeared in the solution of complex, especially nonlinear multifactor boundary-value problems by analytical, more often approximate, methods. Two approaches are used in theoretical hyperthermia: compartmental and with distributed parameters. The first is used in calculations of general hyperthermia (GHT) and is based on mental sectioning of a human body by integral balances of heat, mass, and momentum for each section (compartment). The sections are divided into individual, as a rule, cylindrical layers (subcompartments) with a number from 2 to 6. Spatial constancy and continuity of all properties and parameters are assumed for each layer (skin, fat, muscles, bone, tumor, large blood vessels). On this basis the temperature field in a subcompartment (layer) is already described by the differential biothermal equation (BTE)

$$\rho c \frac{\partial T}{\partial t} = \nabla (\lambda \nabla T) + q_{\text{con}} + q_{\text{met}} + q_{\text{v}} . \tag{1}$$

The method of distributed parameters is used in calculations of local and regional hyperthermia and is based on biothermal equations of different types. In this approach it is most difficult to express the convective component in an analytical form. The so-called purely convective perfusion formulation

$$q_{\text{con}} = \eta \omega \rho_{\text{b}} c_{\text{b}} (T_{\text{a}} - T) \tag{2}$$

is used most often. Here ω is the perfusion (the rate of blood microcirculation in individual living biotissue, sec^{-1}), η is the efficiency of heat transfer between biotissue and venous blood ($0 \le \eta \le 1$), $\eta = 1$ corresponds to total thermal equilibrium.

Expression (2) describes a convective heat flux as the difference between the thermal energies supplied to biotissue by arterial blood and carried away from biotissue by venous blood.

There is a nonconvective purely diffusion formulation of the biothermal equation:

$$\rho c \frac{\partial T}{\partial t} = \nabla (\lambda_{\text{eff}} \nabla T) + q_{\text{met}} + q_{\text{v}} . \tag{3}$$

The effective coefficient of thermal conductivity λ_{eff} characterizes the combined effect of the molecular and molar components of heat transfer. This formulation implicitly assumes full leveling of the temperatures of biotissue and blood in capillaries, which is not always correct.

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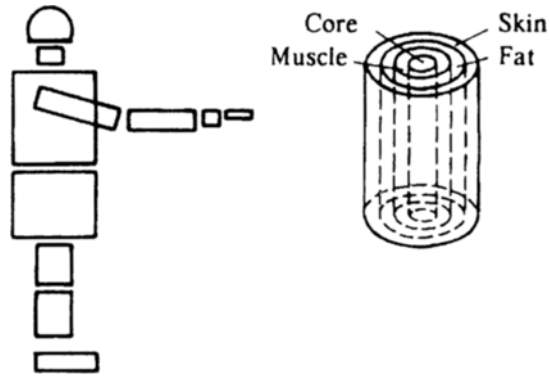

Fig. 1. Eleven-compartment thermal model of a man (Huckaba and Tam).

2. Our Own Model. At present we are developing one more approach. Living biotissue is considered to be some effective capillary-porous medium (EPM) the architectonics of which (diameter, length, sinuosity of capillaries) is similar to biotissue. The network of finest capillaries is modeled by one tube that has the same volume and hemodynamic resistance as the network. The diameter of this tube is expressed in terms of the size, geometry, and permeability of the pores. When the diameter and length of the equivalent tube are found, well-known classical dimensionless relations for convective heat transfer of the type

$$\mathrm{Nu_b} = A\,\mathrm{Re_b^{0.5}Pr_b^{0.25}} \tag{4}$$

or in terms of dimensional characteristics

$$\frac{\alpha_b d_{eqv}}{\lambda_b} = A\sqrt{\left(\frac{4\rho_b Q_b}{\pi d_{eqv}\mu_b}\right)}\ \sqrt[4]{\left(\frac{\mu_b c_b}{\lambda_b}\right)}$$

are written. Here α_b is the coefficient of convective heat transfer of blood; μ_b is the blood viscosity; d_{eqv} is the diameter of the equivalent channel; Q_b is the blood flow rate through biotissue (cross section of the equivalent tube); $\mathrm{Nu_b}$, $\mathrm{Re_b}$, $\mathrm{Pr_b}$ are the dimensionless Nusselt, Reynolds, and Prandtl numbers for blood.

3. Critical Notes. Both models, BTE and EPM, are, to a certain extent, physically incorrect since the blood flow velocity and the heat fluxes are inherently vectors, whereas the mathematical models considered are scalar. Whereas for large blood vessels (veins, arteries) one can take into account the direction of blood flow and the spatial orientation of the velocity vector, for microcirculation it is practically impossible to indicate them unambigously. In principle, for this purpose tensor descriptions are applicable that considerably complicate mathematical simulation due to uncertainty in the determination of a large number of material constants in all directions rather than due to the labor-consuming and cumbersome nature of the system of biothermal equations. Ineffective attempts to realize this idea are known [1]. Moreover, both BTE and EPM used in local approximations either ignore the presence of large blood vessels or replace them by effective microcirculational ones. Furthermore, in real living biotissue both large and small arterial channels adjoin with similar venous ones that have a different temperature. Two additional processes of heat transfer arise, one between channel vessels and the other between blood vessels and biotissue surrounding them. Both processes lend themselves to be included in a general physicomathematical model of BTE (or EPM).

4. Compartmental Physicomathematical Models of General Hyperthermia. Figure 1, taken from the report of the scientific group "Rheomed" [2], schematically shows a plane model of Huckaba and Tam that consists of eleven compartments – one spherical and ten cylindrical, with paired limbs being represented as a single entity: head, neck, forearm, hand, arm, fingers, chest, abdomen, thigh, shin, foot. An individual compartment (depot) of blood is added to them. The subcompartments are: skin, fat, muscles, a central region (core) (for limbs bone serves as the core). It is important to note that this scheme supposes spatial uniformity of temperature within the limits of each subcompartment. Temperature changes only in time and from compartment to compartment. Moreover,

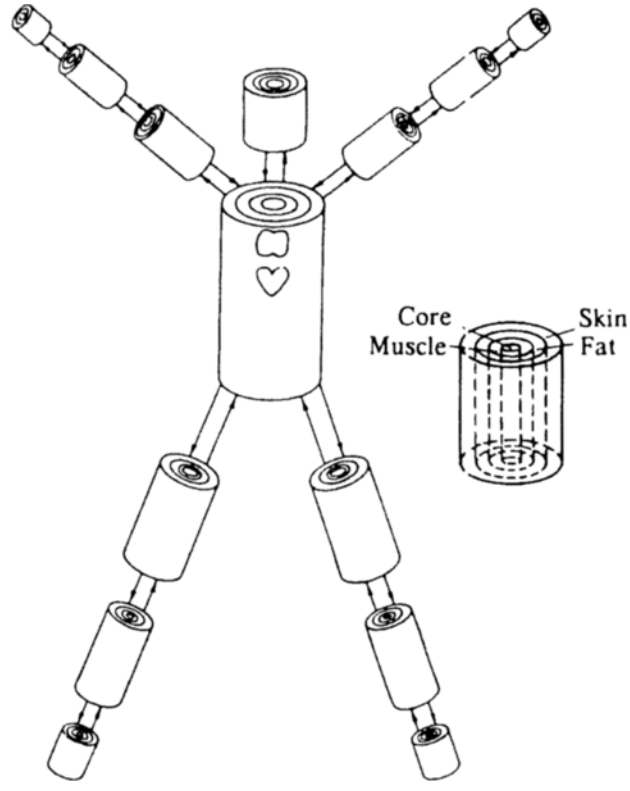

Fig. 2. Fourteen-compartment thermal model of a man (Shitzer).

plane symmetry does not make it possible to include in the analysis any organ affected by tumor (kidney, lungs, stomach, etc.). For all 44 subcompartments the equations of nonstationary heat balance are written in the form

$$\begin{bmatrix}\text{Accumulation}\\ \text{of thermal energy}\\ \text{in a subcompartment}\end{bmatrix} = \begin{bmatrix}\text{Heat of}\\ \text{subcompartment}\\ \text{metabolism}\end{bmatrix} + \begin{bmatrix}\text{Conductive heat}\\ \text{transfer of adjacent}\\ \text{subcompartments}\end{bmatrix} - \\ - \begin{bmatrix}\text{Heat entrainment}\\ \text{by blood flow from}\\ \text{a compartment}\end{bmatrix} - \begin{bmatrix}\text{Heat transfer}\\ \text{to environment}\end{bmatrix} \tag{5}$$

For the central blood depot the following intrinsic energy balance is formed:

$$\begin{bmatrix}\text{Accumulation}\\ \text{of thermal energy}\\ \text{in the depot}\end{bmatrix} = \begin{bmatrix}\text{Heat supplied}\\ \text{to the depot by}\\ \text{venous blood}\end{bmatrix} - \begin{bmatrix}\text{Heat carried}\\ \text{away from the}\\ \text{depot by arterial blood}\end{bmatrix} \tag{6}$$

After substitution of material properties, parameters, and characteristics this system of 45 differential equations is solved numerically. As a result the spatial-temporal evolution of temperature fields in a human body with general and regional hyperthermia is determined.

5. Shitzer Three-Dimensional Models. In a series of works by A. Shitzer [4-7] an interesting development and improvement of the GHT model is given in the form of a 14-compartment axisymmetric model (Fig. 2). An important advantage of this model is a more rigorous analysis of the geometry of the temperature fields in the subcompartments in the radial and azimuthal directions. Thus, the asymmetry of external effects of the environment or the source of electromagnetic radiation is taken into account. The Shitzer model includes, although in a simplified form, the variability of the temperature of large blood vessels in the heat balances: heat transfer between arteries and veins and thermal interaction between large blood vessels and biotissues surrounding them are taken into account. Moreover, thermal interconnection between different compartments via the system of blood circulation is envisaged.

Division of the entire blood vessel system into two groups is an important step forward. The first encompasses large channels where arteries and veins in a counterflow exchange heat with each other and with biotissues (predominantly muscular) surrounding them. The second involves fine capillaries where blood flow is much slower than in arteries and veins. Consequently, the time of residence of each portion of the blood in the capillaries will be large and sufficient to reach thermal balance with the blood vessel walls.

The mathematical formulation of the thermal balances for each subcompartment in cylindrical coordinates has the form

$$\rho_i c_i \frac{\partial T_i}{\partial t} = \lambda_i \left[\frac{1}{r} \frac{\partial}{\partial r} \left(r \frac{\partial T_i}{\partial r} \right) + \frac{1}{r^2} \frac{\partial^2 T_i}{\partial \varphi^2} \right] + q_{\text{met}i} + \omega_{\text{b}i} c_{\text{b}i} (T_{\text{a}i} - T_i) +$$

$$+ \alpha_{\text{a}i} (T_{\text{a}i} - T_i) + \alpha_{\text{v}i} (T_{\text{a}i} - T_i) + \alpha_{\text{v}i} (T_{\text{v}i} - T_i) . \tag{7}$$

The left-hand side of the balance describes accumulation of thermal energy (time variation of heat content in biotissue), the right-hand side expresses, respectively, radial and azimuthal changes in the heat fluxes, metabolism heat, heat transfer by microcirculation (perfusion), heat convecttion in an artery, heat transfer between an artery and a vein, and heat transfer through a vein.

The boundary conditions are

$$\left. \frac{\partial T}{\partial r} \right|_{r=0} = 0 \; - \; \begin{array}{l} \text{axial symmetry of the temperature profile} \\ \text{(adiabatic thermal regime in the} \\ \text{near-axis region)} , \end{array}$$

$$q|_{r=R_0} = - \lambda \frac{\partial T}{\partial r} = \alpha (T - T_{\text{env}}) + q_{\text{rad}} + q_{\text{sw}}|_{r=R_0} \; - \; \text{boundary condition of the third kind on the wall} . \tag{8}$$

Here α is the coefficient of convective heat exchange with the environment; q_{rad} is the radiation heat flux on the blood vessel wall; q_{sw} is the heat of sweating, which depends on the quantity of liberated sweat and also on the temperature and humidity of the surrounding air. The local coefficients of heat exchange of blood vessels (arteries and veins) with each other and with biotissues surrounding them, α_{a} and α_{v}, depend on the volume of blood in the blood vessels and the dimensions (volume) of the compartment. Thermal interaction (conjunction) of neighboring (contacting) compartments is realized through blood vessels.

In contrast to the well-known propositions of Wissler [8] about the constancy of the temperature and velocity of blood in large blood vessels of a compartment, Shitzer assumes the temperature to be variable along the blood vessel length according to the linear additive law

$$T_{\text{b.out}} = \beta_{\text{b}} \widetilde{T}_{\text{b}} - (1 - \beta_{\text{b}}) T_{\text{b.in}} . \tag{9}$$

Here $\widetilde{T}_{\text{b}}$ is the mean temperature of blood in a blood vessel; β_{b} is a numerical coefficient; $T_{\text{b.out}}$ and $T_{\text{b.in}}$ are the temperatures at the outlet and inlet of a blood vessel, respectively.

The field of dimensionless temperatures in each subcompartment is described by the generalized differential equation

$$\frac{\partial \Theta_i}{\partial \tau} = \gamma_i \beta_i \left[\frac{\partial^2 \Theta_i}{\partial \xi^2} + \frac{1}{\xi} \frac{\partial \Theta_i}{\partial \xi} + \frac{1}{\xi^2} \frac{\partial^2 \Theta_i}{\partial \varphi^2} \right] + q_i X_i + (W_i + U_{\text{a}i}) \times$$

$$\times X_i (\Theta_{\text{a}i}) - \Theta_i) + U_{\text{v}i} X_i (\Theta_{\text{v}i} - \Theta_i) \tag{10}$$

with the boundary conditions

$$\left. \frac{\partial \Theta_i}{\partial \xi} \right|_{\xi=0} = 0 ,$$

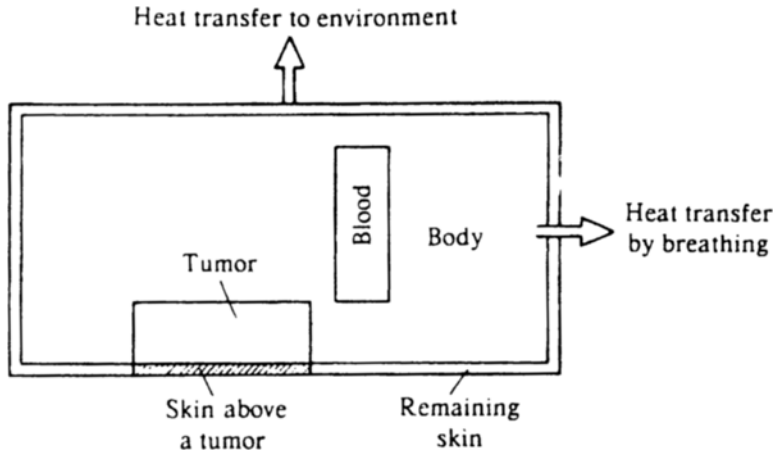

Fig. 3. Five-compartment thermal model of a man (Jain).

$$\left.\frac{\partial \Theta_i}{\partial \xi}\right|_{\xi=1} = \mathrm{Nu}_{\mathrm{con}i}\,(\Theta_{\mathrm{env},i} - \Theta_i) + \mathrm{Nu}_{\mathrm{sw}i} + \mathrm{Nu}_{\mathrm{rad}}\,(\Theta_{\mathrm{rad}i} - \Theta_i)\,. \tag{11}$$

Another valuable advantage of the Shitzer model is an original choice of the parameters that make the system dimensionless: $T^* = Q_{\mathrm{b.bas}}/C_{\mathrm{bas}}\rho_{\mathrm{b}}c_{\mathrm{b}}$ is the nondimensionalizing temperature; $\Theta = T/T^*$ is the dimensionless temperature; $\tau = ta_{\mathrm{ch}}/R_{\mathrm{ch}}^2$ is the dimensionless time. Here $Q_{\mathrm{b.bas}}$ is the basic value of metabolism heat flux; C_{bas} is the basic value of heart discharge; $\xi = r/R_0$ is the dimensionless radial coordinate (R_0 is the radius of the outer surface of the compartment); φ is the dimensionless azimuthal coordinate; $X = \rho_{\mathrm{b}}c_{\mathrm{b}}/(\rho c)$ is the ratio of the heat capacities of blood and biotissue; $q_{\mathrm{met},i} = R_{\mathrm{ch}}^2 q_{\mathrm{met}}/(a_{\mathrm{ch}}\rho_{\mathrm{b}}c_{\mathrm{b}}\widetilde{T})$ is the dimensionless metabolism heat flux; $W_i = \gamma_i\beta_i w_{\mathrm{b}}/\rho_{\mathrm{b}}$ is the dimensionless velocity of blood flow in capillaries; w_{b} is the velocity of blood flow in capillaries.

The following additional conditions close system (10)-(11): a) for longitudinal temperature variations in arteries and veins (two relations); b) for heat transfer of large blood vessels (two relations); c) a continuity equation (one condition is mass conservation of blood in the body).

Basic parameters that are found from a numerical solution of the initial pseudostationary problem in the absence of hyperthermia and sweating and with a switched-off thermoregulatory system are used in the Shitzer approach. Here, the well-known dependences of measured physiological parameters, namely, metabolism and heart discharge of blood, on the age of the patient are used as the basic ones. In this way the basic characteristics (perfusional and metabolic) are calculated for all subcompartments. The Shitzer model with its high efficiency is still rather complex and cumbersome and requires a great amount of various input information.

6. Jain Rapid Model. The five-compartment Jain model [9] is rather promising for rapid estimation of the effect of GHT on a tumor lying slightly below the skin. The initial premise is as follows: if we are interested only in a tumor and its interaction with normal biotissues, then we can restrict ourselves to just a small number of compartments. According to the Jain model (Fig. 3), all normal biotissues of the body, except skin, are combined to one compartment. The remaining compartments are the tumor, the skin directly above the tumor, the remaining skin, and the central blood depot. To determine temperature gradients each compartment is divided into N subcompartments. Nonstationary heat balances (5) and (6) are written for all sections.

Different modifications and versions of the Jain model are used to calculate GHT as applied to a man and animals: rats, rabbits, pigs, dogs, and monkeys.

NOTATION

a, coefficient of thermal diffusivity; c, heat capacity; q, heat flux; r, radial coordinate; t, time; R, radius of a compartment; T, temperature; U, mean dimensionless coefficient of heat transfer in a blood vessel; λ, thermal conductivity; ρ, density; φ, azimuthal angle; Θ, dimensionless temperature. Subscripts: a, artery (arterial); bas,

basic value; v, vein (venous); ext, external; in, inlet; out, outlet; b, blood; con, convective; met, metabolic; sw, sweating; env, environment; ch, characteristic value; eqv, equivalent; w, wall; rad, radiation.

REFERENCES

1. A. Shitzer and R. C. Eberhart (eds.), Heat Transfer in Medicine and Biology. Analysis and Applications, New York (1985).
2. Report of the Scientific Group "RHEOMED" on the Research Study: "Rheological and Thermophysical Factors of Hyperthermia of Tumor Biotissues," Stage 2, Project BZ-222 of the Fundamental-Research Foundation of the Republic of Belarus, Minsk (1993).
3. Ch. E. Huckaba and H. S. Tam, in: Adv. Biomed. Eng., Pt. I, New York (1980), pp. 1-57.
4. A. Shitzer, NASA Tech. Mem. X62, 172 (1974).
5. A. Shitzer, in: Topics in Transport Phenomena (ed. C. Gutfinger), New York (1975), pp. 211-341.
6. A. Shitzer and M. K. Kleiner, J. Biomech. Eng., **102**, 162-169 (1980).
7. A. Shitzer and M. K. Kleiner, Bull. Math. Biology, **38**, 369-386 (1976).
8. E. H. Wissler, J. Biomech. Eng., **110**, 254-256 (1988).
9. R. K. Jain, in: Adv. Biomed. Eng., Pt. I, New York (1980), pp. 58-66.