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RHEOLOGICAL FACTOR OF BLOOD FLOW IN SHF-LOCAL HYPERTHERMIA. "RHEOMED" PROJECT

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Different physicomathematical models of SHF hyperthermia, viz., local, regional, and extracorporal, are considered. All biothermal problems within the "Rheomed" project are solved analytically and numerically in conjugate formulations. Among the main advantages of the project is a new universal model of nonisothermal perfusion that is based on temperature-time superposition.

Thermal effects on a living biotissue are commonly found and used in a great number of applications: in medicine, agriculture, space, aquanautics, military science, everyday life, under tropic and polar conditions, etc. Blood flow is also known to have a fundamental role in the formation of temperature fields inside a living body. In local superheating of some object, e.g., a malignant tumor, arterial blood passing through it carries away a portion of heat supplied from without to venous beds, and the local temperature of such biotissue will be determined mainly by the intensity of the blood flow. Here the blood flow rate is determined by both rheological properties of blood and hemodynamic factors of vessels. However, strange as it may seem, we did not succeed in finding any publications about the role, contribution, and influence of a rheological factor on the development and setting of temperature fields in a living biotissue. At the same time, the nonlinear viscoplastic behavior of normal blood that is described by the Casson equation of a rheological state has been known for more than 35 years [1]

$$\sqrt{\left(\frac{\Delta pR}{2L}\right)} = \sqrt{\tau_0} + \sqrt{\left(\mu_p \frac{du}{dr}\right)}. \tag{1}$$

Here Δp is the pressure drop in a blood vessel; τ_0 is the blood yield limit (plasticity); μ_p is the parameter of blood plasticity; du/dr is the change in rate across a blood vessel; and R and L are the radius and length of a vessel.

The Casson rheogram was included in all medical manuals and reference books.

The rheological parameters τ_0 and μ_p depend, to a known extent, on hematocrit, content of fibrinogens, albumins, and globulins in blood [2, 3]. A more general rheological law for blood, which we suggested almost 30 years ago [4], is also valid for pathological blood (diabetes, asthma, cancer, nephritis, ischemia, etc.). It has the form

$$\sqrt[n]{\left(\frac{\Delta pR}{2L}\right)} = \sqrt[n]{\tau_0} + \sqrt[m]{\left(\mu_p \frac{du}{dr}\right)}. \tag{2}$$

The parameters of plastic (n) and viscous (m) nonlinearities are positive and not necessarily integers. In the general case, in contrast to (1), $n \neq m$. For instance, for moderately serious ischemia $n \approx 2$, $m \approx 3$.

Thus, a fundamentally new idea was developed: to construct a physicomathematical biothermal model which allows for the effect of the rheological factor of blood flow on temperature fields in a living biotissue heated from without [5, 6]. The project based on this idea was financed by the Fundamental Research Fund of Belarus over three years. For its implementation, in 1992 the association "Rheomed" was organized, initially consisting of 15 specialists: thermophysicists, mathematicians, medical personnel, hemorheologists, and oncologists.

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As an object of theoretical experimental studies we selected a very acute problem of local SHF hyperthermia, which is widely used all over the world and especially in Belarus at the Belarusian Scientific-Research Institute of Oncology and Medical Radiology due to the efforts of Professors N. N. Aleksandrov, S. Z. Fradkin, and E. A. Zhavrid [7, 8].

Below we present the conclusions that generalize the data of original analytical and numerical calculations and experiments (rheological, thermophysical, medical laboratory and clinical) performed within the framework of the "Rheomed" project. Most of them are included in [9-22]. We emphasize the most important results, which are the following:

- a new physicomathematical model and the corresponding formulation of a conjugate biothermal problem are created that include the equation of the rheological state of blood, nonisothermal hemodynamics, and also a strong temperature-time dependence of perfusion and vascular stasis;
- an original automated rheoviscometer "Rheomed" R-10 is constructed for blood rheometry in a "jerky" (stepwise) mode of deformation, which is similar to pulse in blood vessels. A previously unknown conservativeness of rheograms is revealed for blood of oncology patients in a narrow sub- and superlethal temperature range ($41.5-43^{\circ}C$);
- laboratory and clinical measurements of basic parameters of blood of animals and oncology donors are conducted before and after hyperthermic (HT) procedures. An acceptable agreement is found between our calculations and experiments;
- a universal model of nonisothermal perfusion is suggested and tested. The model is based on temperature-time superposition and quite adequately describes the rheokinetics of a local blood flow, including retardation of perfusion response to the change in the local temperature of biotissue;
- parameters of various regimes of local HT, viz., constant and pulsating powers of the field at different frequencies (2450, 915, 450 MHz), constant temperature of the tumor, different intensities of skin cooling, dimensions of tumors, depths of their location, etc., are quantitatively determined and estimated;
- it is suggested to compare the results of calculations of these therapeutic regimes and to estimate the efficiency of HT procedures using a new definition of a thermal dose;
- from the inverse problem of HT, rational laws are found to control emitter power for creating and maintaining a priori assigned temperatures that damage a tumor but not normal biotissues;
- a new rheological model of an equivalent porous medium (EPM) is suggested and tested. The model allows for morphology of the microcirculation system of a blood flow and the generalized rheological equation of the state of blood as a nonlinear viscoplastic medium and also for the contribution of the Fahraeus–Lindquist effects to heat transfer and rheohemodynamics, and colmatage- and-suffosion phenomena in blood filtering through EPM;
- an attempt is undertaken to create a stable tissue permeable phantom for modeling transfer processes in HT;
- two versions of the problem of regional heat transfer in extracorporal normothermia and hyperthermia are solved and analyzed; the results of calculations are compared to the data of special experiments: laboratory and clinical;
- a rather general approach to the problem of optimal control over the power source is developed;
- transition processes in normal and tumoral biotissues after imposition and removed of SHF field and also under the regulation of its power (linear, pulse, stepwise) are studied;
- programs are developed to calculate the choice of the most efficient regimes of local SHF hyperthermia for treating oncology patients and also to regulate the power of the emitter, which provide automatic attainment of the prescribed therapeutic temperature;
- the effect of electromagnetic hyperthermia on the state of homeostasis in the "tumor-organism" system (hematological status, hemocoagulation status, state of peripheral hemodynamics) is estimated on the basis of extensive clinical studies;
- the changes in hemodynamics, blood rheology and also rates of the growth of tumors for animals during long-lasting arterial hypotension under the effect of hypotensive drugs (medical and soluble in blood polymers) are studied under laboratory conditions.

Total report data of the association "Rheomed" for 1992-1994 are:

◇ Total length of reports for 3 years: 250 + 434 +351 = 1035 typed pages + Supplement to the final report 343 typed pages;

◇ Tables: 40 + 43 + 45 = 128;

◇ Figures: 96 + 104 + 59 = 259;

◇ Reference sources: 319 + 268 + 183 = 770;

◇ Papers, published and presented for publication: 10 + 13 + 5 = 28 (including international publications: 1 + 2 = 3);

◇ Registered inventions: 1 (1993) + 1 (1994) = 2;

◇ Reports: 3 + 6 + 16 = 25 (incliding those made abroad: 4 + 9 = 13).

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