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Computer Simulation of Cyclic Temperature Effect on Biological Tissue During the Destruction of Oncologic Tumors

The results of computer simulation of the temperature effect on biological tissue with oncologic neoplasms in cooling, heating modes, as well as their cyclic change are presented. A physical, mathematical, and computer model of biological tissue with oncologic neoplasms is constructed, with regard to thermophysical processes, blood circulation, heat exchange, metabolic processes, and phase transition. The change in temperature distributions over time in biological tissue with an oncologic neoplasm and a working tool depending on the geometry of the working tool and its temperature is studied. Computer optimization of the working tool is carried out and the design of a thermoelectric device for the destruction of oncologic neoplasms is developed.

Keywords: thermoelectric device, cryodestruction, hyperthermia, cyclic temperature effect, computer simulation, biological tissue, tumor, cooling, heating.

Introduction

Oncologic diseases continue to be one of the leading causes of mortality in the world, which stimulates the development of new methods of their treatment [1, 2]. One of the

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promising areas is the use of thermoelectric devices for local destruction of oncologic neoplasms [3–6]. Such devices allow for both cooling and heating of the pathological area, which opens up wide opportunities for increasing the effectiveness of treatment by combining cryodestruction and hyperthermia.

Cryodestruction involves deep cooling of tissues, up to –50 °C, which causes irreversible damage to cellular structures [7–10]. Modern methods are implemented using cryoinstruments, mainly using liquid nitrogen [11, 12], which has a number of limitations, including the difficulty of ensuring a stable temperature, the risks of unwanted damage to healthy biological tissue, and logistical difficulties. Thermoelectric systems allow for precise temperature control according to a given cycle, are simple, reliable, and safe to use [13–17].

For effective cryodestruction, it is necessary to ensure an appropriate temperature regime [18]. When the temperature drops to –5 ÷ –10 °C, the process of crystal formation begins in the extracellular space, and at –15 ÷ –20 °C, intracellular ice is formed, which leads to cell death. The optimal cooling rate is (40–50) °C/min, while ultra-fast freezing (>100 °C/min) results in the formation of amorphous ice that does not cause cellular destruction. The thawing mode is also important: the best results are achieved at a rate of (10–12) °C/min. The use of multiple freeze-thaw cycles helps minimize damage to healthy tissues and increase the effectiveness of therapy.

Hyperthermia is an alternative method of destroying atypical cells by controlled overheating to (+43 ÷ +44) °C, which leads to selective damage to cancer cells due to lower efficiency of their heat dissipation [19–21]. In addition, hyperthermia enhances the effect of chemotherapeutic agents and radiation therapy, making it an effective addition to complex treatment.

A promising approach in oncology therapy is the combination of these two options for temperature effects on cancer. This allows for a comprehensive effect on affected cells: cryodestruction causes their mechanical damage through the formation of ice, and hyperthermia increases metabolic stress, increasing sensitivity to treatment. The use of thermoelectric devices for this purpose provides both modes of operation, cooling and heating, with precise control of temperature parameters, minimizing the risk of damage to healthy tissues. Due to the possibility of flexible temperature regulation, such devices open up new possibilities for personalized cancer therapy.

Therefore*, the purpose of the work* is computer-aided design and optimization of a thermoelectric device for cyclic temperature effect on biological tissue during the destruction of oncologic neoplasms.

1. Physical, mathematical and computer models of the device

Structurally, the device consists of a working tool surrounded by insulation, two thermoelectric modules with liquid heat exchangers installed on the hot side, a circulation pump that pumps water through the channels, a fan, and a liquid-air heat exchanger that cools the pumped liquid (Fig. 1). Since destruction requires achieving the lowest possible temperature values, it is advisable to use multi-stage thermoelectric modules characterized by an increased temperature difference ΔT_{max}.

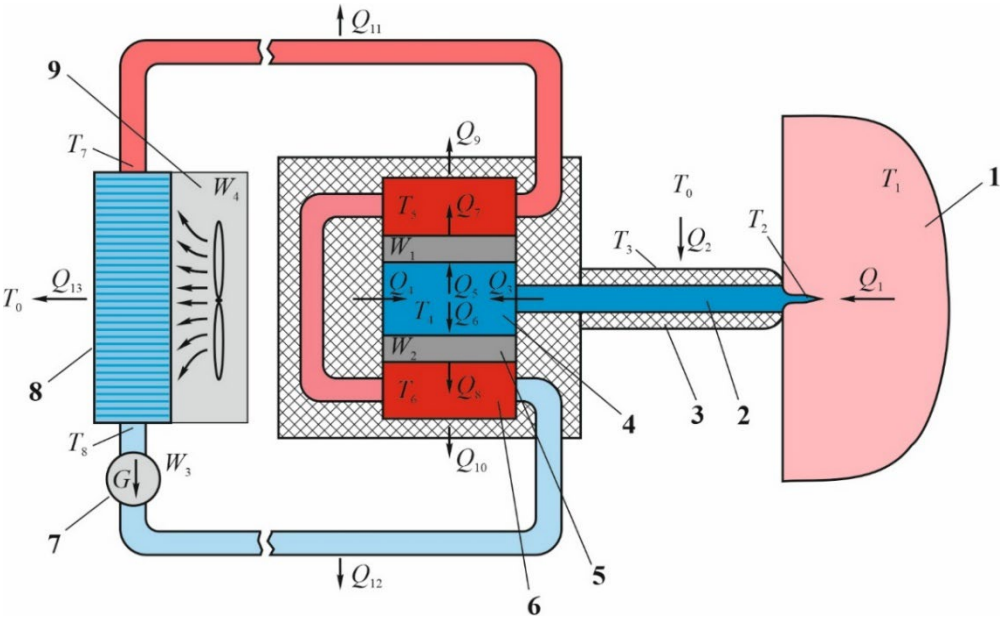

Fig. 1. Physical model of a thermoelectric device for the destruction of oncologic neoplasms (in cooling mode): 1 – biological tissue; 2 – working tool of the device; 3 – thermal insulation of the working tool; 4 – cold heat exchanger; 5 –thermoelectric modulesi; 6 – liquid heat exchangers; 7 – circulation pump; 8 – liquid-air heat exchanger; 9 – fan

Fig. 1 shows a physical model of a thermoelectric device for the destruction of oncologic neoplasms in cooling mode. Here: Q_1 – heat flow from the biological bed; Q_2 – heat exchange of the working tool with the environment through the side surface; Q_3 – heat flow from the working tool of the device to the cold heat exchanger in contact with the thermoelectric modules; Q_4 – heat inleak to the cold heat exchanger from the environment through the thermal insulation of the device; Q_5, Q_6 – heat flows removed by the thermoelectric modules from the cold heat exchanger; Q_7, Q_8 – heat flows removed from the thermoelectric modules by the liquid heat exchange system; Q_9, Q_{10} – heat exchange of the device with the environment through thermal insulation; Q_{11}, Q_{12} – heat exchange of liquid pumping hoses with the environment; Q_{13} – heat flow removed to the environment by the liquid-air heat exchanger; T_0 – ambient temperature; T_1 – temperature inside the biological tissue; T_2 – temperature of the tip of the working tool; T_3 – temperature of the side surface of the working tool; T_4 – temperature of the cold heat exchanger; T_5, T_6 – temperatures of the hot liquid heat exchangers; T_7, T_8 – temperatures at the inlet and outlet of the liquid-air heat exchanger.

In the case of using the heating mode, which requires changing the polarity of the electric current through the thermoelectric modules, the directions of the heat flows shown in Fig. 1 will change to opposite ones.

To find the temperature distributions in the structural elements of the device for tumor destruction and in the tumor itself, the Bioheat Transfer module of the Comsol Multiphysics platform was used, which allows simulating thermophysical processes in biological tissues with regard to blood circulation and metabolism [22–30]. The heat transfer equation in biological tissue in this case is given below:

$$\rho\, C_p \frac{\partial T}{\partial t} + \nabla(-\kappa \nabla T) = \rho_b\, C_b \omega_b (T_b - T) + Q_{met}, \quad (1)$$

where: ρ_b – blood density (kg/m^3); C_b – specific heat capacity of blood (J/kg·K); ω_b – blood perfusion rate (1/s), which in this case means (m^3/s)/m^3, and describes the volume of blood per second flowing through a unit volume of tissue; T_b – arterial blood temperature (K), equal to 310.15 K; Q_{met} – metabolic heat source (W/m^3).

The model represents a volume of biological tissue with isotropic thermal properties. Inside the tissue, a needle made of a material with high thermal conductivity is placed, fixed on a rod made of the same material. The rod is surrounded by thermal insulation, which is in a state of heat exchange with the surrounding environment. The temperature at the end of the rod is given.

The boundary condition in the region far from the probe, where the temperature should be the same as body temperature, is 37 °C. During the freezing process, the cells will undergo a phase change at the freezing point, with losses of latent heat of phase transition and the temperature in these cells will not change. The phase transition in biological cells occurs at temperatures from –1 to –8 °C. The tissue properties used in the computer simulation are given in Table 2.

In the temperature range of –1 ÷ –8 °C, when cells are frozen, the latent heat of the phase transition is absorbed, which can be modeled by adding the corresponding value to the heat capacity.

Table 2

Properties of biological tissue [25–30]

Parameter name	*Units of measurement*	*Parameter value*
Heat capacity of frozen tissue	MJ/m^3 °C	1.8
Heat capacity of thawed tissue	MJ/m^3 °C	3.6
Heat capacity of blood	MJ/m^3 °C	3.6
Thermal conductivity of thawed tissue	W/m^3 °C	0.5
Thermal conductivity of frozen tissue	W/m^3 °C	2
Latent heat of phase transition	MJ/m^3	250
Body temperature	°C	37
Lower temperature of phase transition	°C	–8
Upper temperature of phase transition	°C	–1
Blood perfusion in healthy tissue	ml/s/ml	0.0005
Blood perfusion in tumor	ml/s/ml	0.002
Metabolism in normal tissue	W/m^3	4200
Metabolism in tumor	W/m^3	42000

When biological tissue is frozen, the capillaries constrict until all the blood in the capillaries freezes, and the value of ω_b approaches zero. In addition, cells will not be able to generate metabolic heat when frozen, and Q_{met} will be zero at temperatures below zero.

2. Computer simulation results

To study the system's entry into steady-state mode, as well as the cyclic change in the temperature of the working tool, computer simulation of the non-stationary mode of operation of the device was carried out. Figs. 2–4 show the change in temperature distributions in the working tool and biological tissue over time for cooling and heating modes. The distributions shown are obtained for the case of a working tool with the following geometric dimensions: rod diameter 8 mm, rod length 40 mm, insulation thickness 5 mm, needle length 7 mm, needle diameter 2 mm.

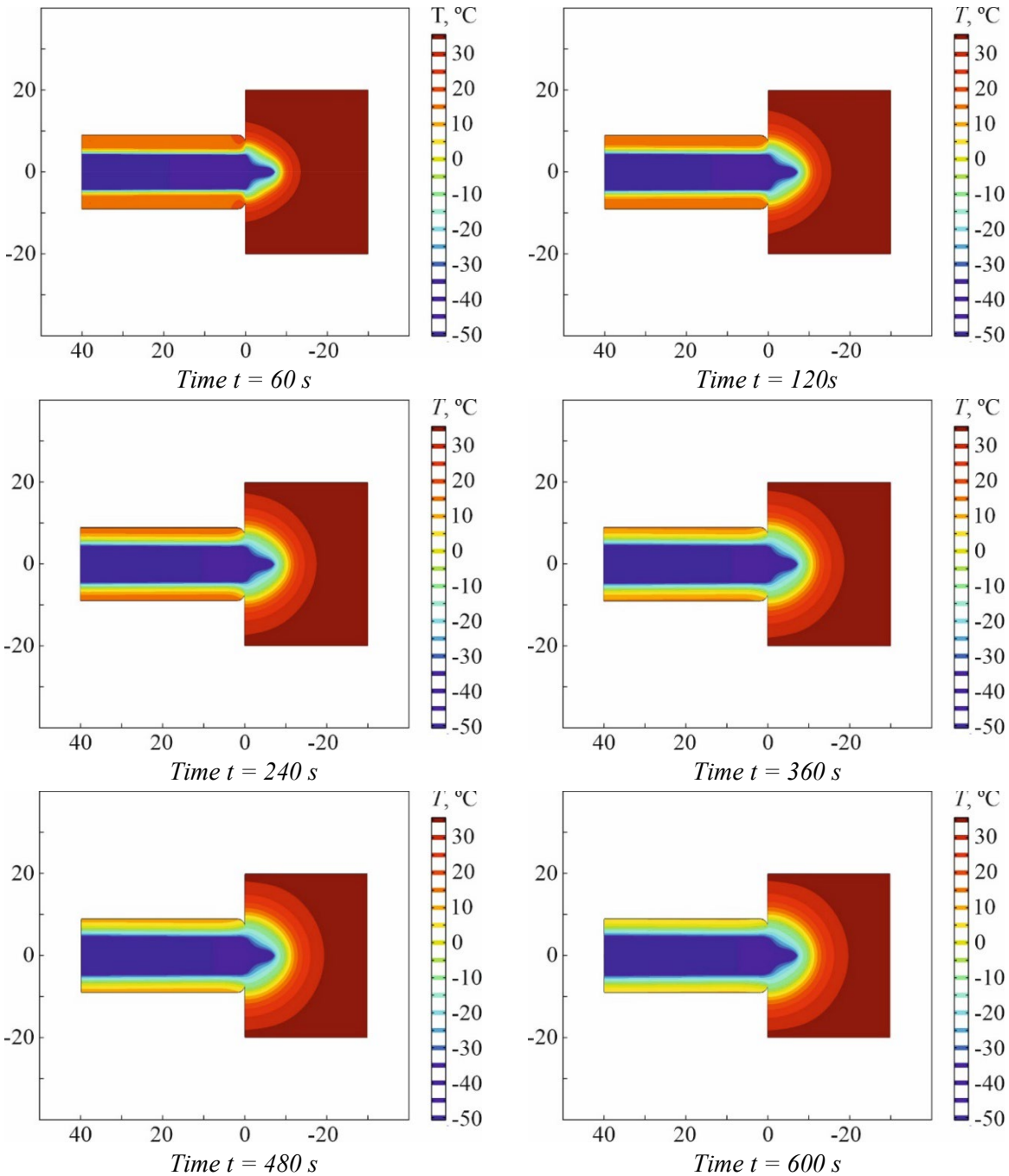

Fig. 2. Dynamics of changes in the temperature distribution of biological tissue under the action of a device for the destruction of oncologic neoplasms in cooling mode

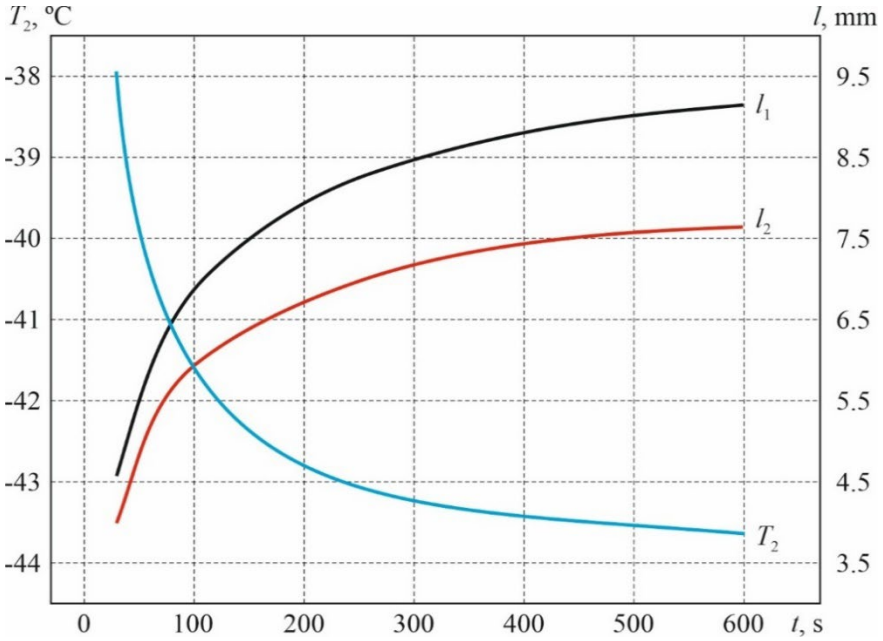

Fig 3. Time dependences of the needle temperature (T_2) and freezing depth (l_1 – distance to the isotherm with a temperature of – 1 °C, l_2 – distance to the isotherm with a temperature of – 8 °C)

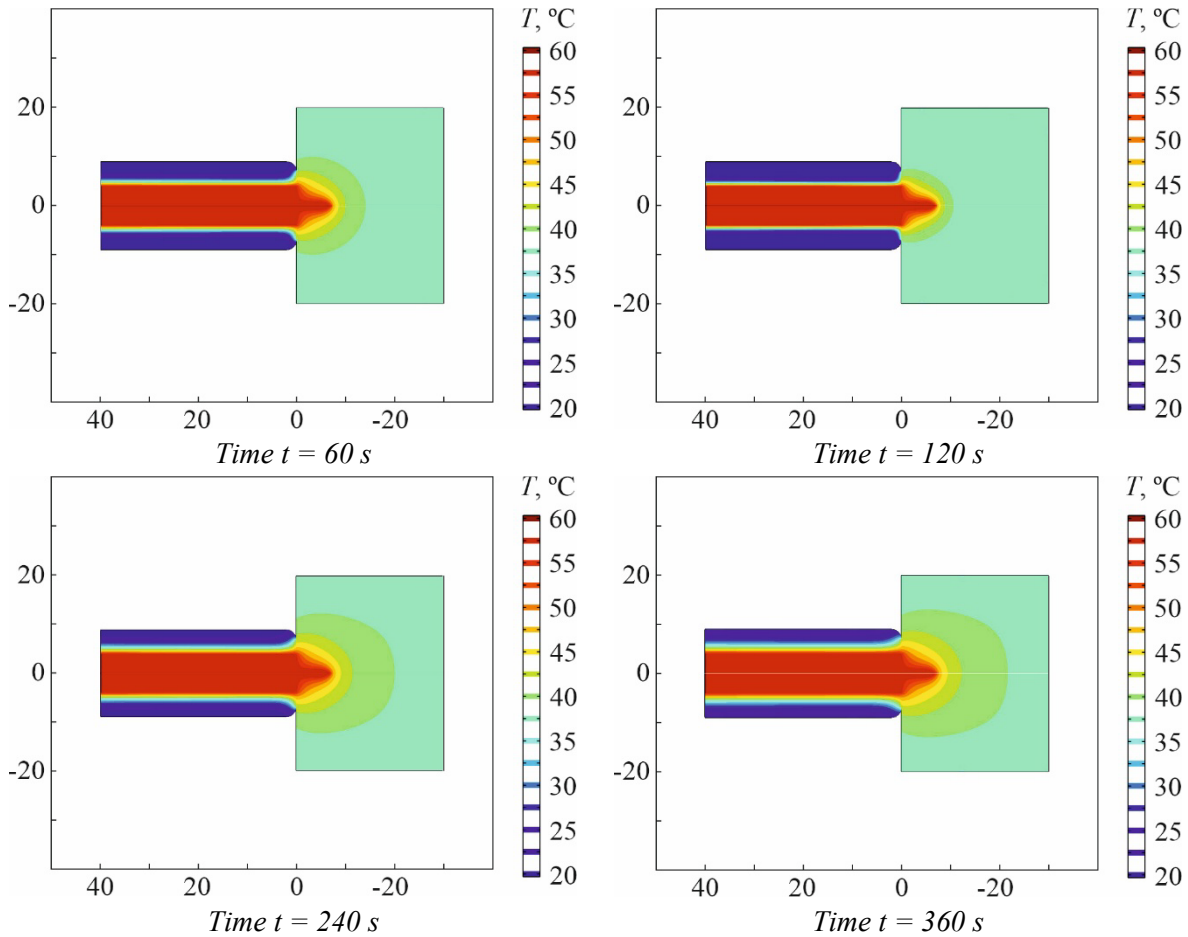

Fig. 4. Dynamics of changes in the temperature distribution of biological tissue under the action of a device for the destruction of oncologic neoplasms in heating mode

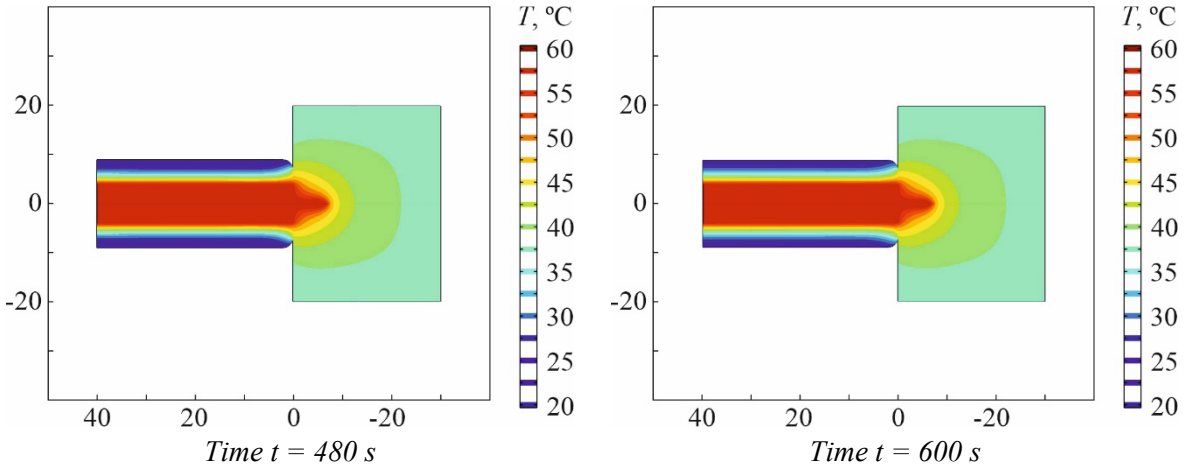

Fig. 4 (continued). Dynamics of changes in the temperature distribution of biological tissue under the action of a device for the destruction of oncologic neoplasms in heating mode

Fig. 5 shows the change in temperature over time at a point in biological tissue 5 mm away from the center of the needle. The shown dependences were obtained for the case of a working tool with the following geometric dimensions: rod diameter 8 mm, rod length 40 mm, insulation thickness 5 mm, needle length 7 mm, needle diameter 2 mm.

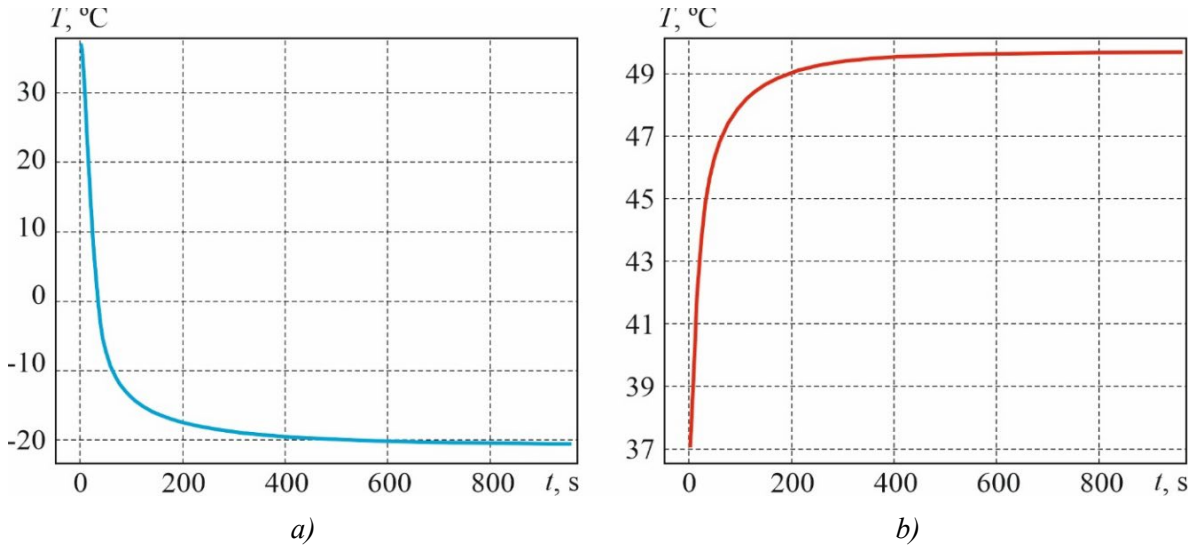

Fig. 5. Time dependence of tumor temperature at a point 5 mm from the center of the needle: a – cooling mode; b – heating mode

Fig. 6 shows an example of the time dependences of the temperature on the cold sides of the thermoelectric modules (curve 1), the needle (curve 2), and in the tumor at a distance of 5 mm from the center of the needle (curve 3) under cyclic cooling and heating.

Thus, we can conclude that using the proposed design of the device for the destruction of oncologic neoplasms, it is possible to implement a cyclic effect of temperature, and the created computer model allows predicting the results of temperature effects on biological tissue and selecting a design for a specific treatment method.

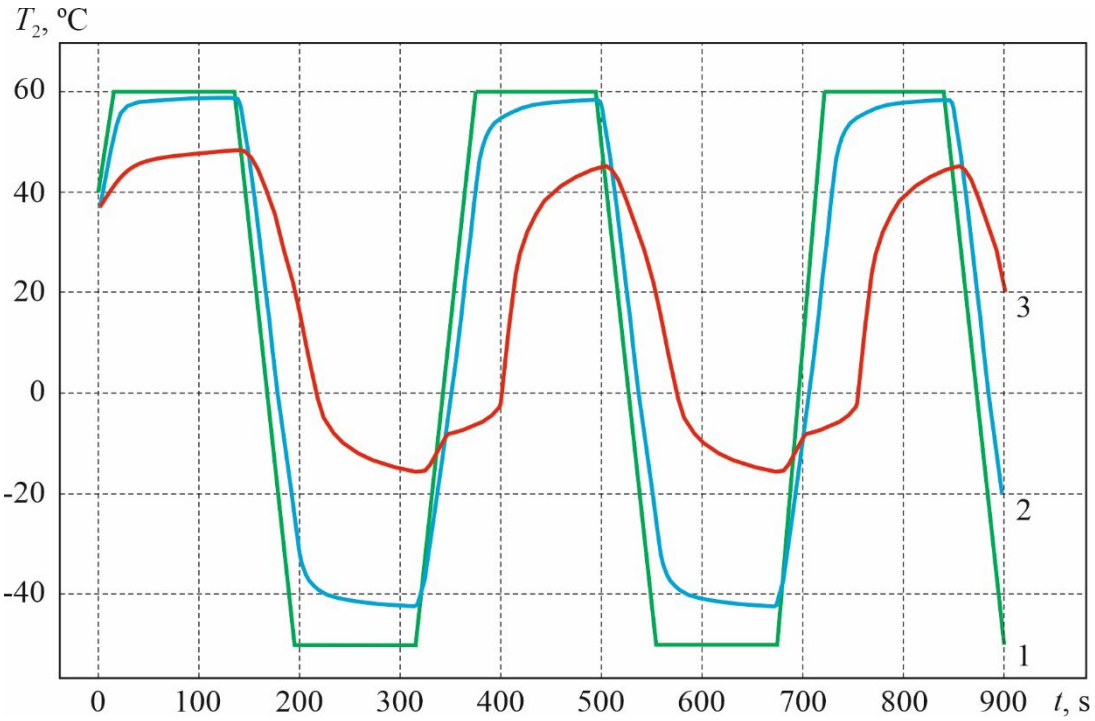

Fig. 6. Cyclic effect of cooling and heating on the tumor. 1, 2, 3 – time dependences of the temperature on the cold sides of the thermoelectric modules, the needle and in the tumor at a distance of 5 mm from the center of the needle

Based on the calculations, a thermoelectric device design was developed, the external appearance of which is shown in Fig. 7. The device contains: a copper rod 2, a copper plate 6, which is placed between two thermoelectric cooling modules 5, 7 and two liquid heat exchangers 4, 8.

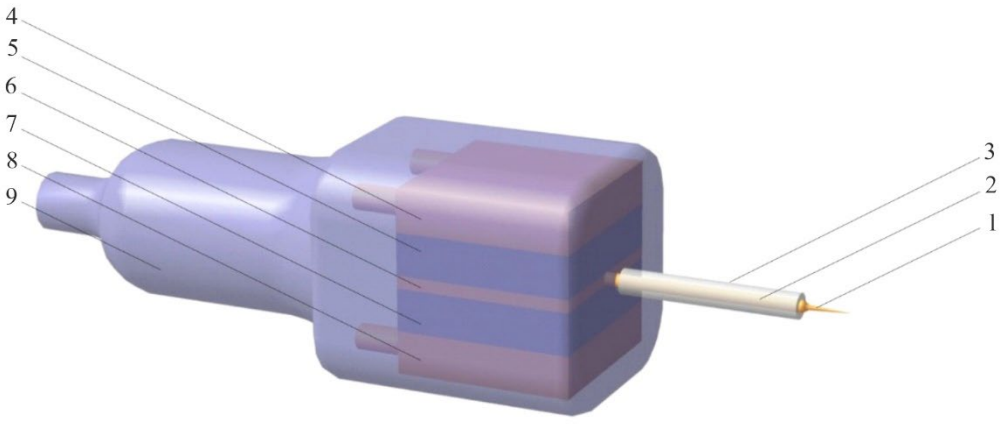

Fig. 7. Design of a thermoelectric device for the destruction of oncologic neoplasms: 1 – cooling needle; 2 – copper rod; 3 – thermal insulation; 4, 8 – liquid heat exchangers, 5, 7 – two-stage thermoelectric cooling modules; 6 – cold heat exchanger – copper plate; 9 – device body

Conclusions

1. A physical model of a thermoelectric device for local cyclic temperature effects on biological tissue during the destruction of oncologic neoplasms has been constructed. A method for computer calculation of such temperature effects has been developed, which allows obtaining time dependences of temperature distributions inside biological tissue and predicting the destruction limit at a certain point in time.
2. The change in temperature distributions over time in biological tissue with an oncologic neoplasm and the working tool in cooling and heating modes was investigated, and computer optimization of the working tool was performed.
3. It is shown that using the proposed design of the working tool for the destruction of oncologic neoplasms, it is possible to implement a cyclic effect of temperature on the tumor in the temperature range of the working tool from +50 to –40 ºC.

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Комп'ютерне моделювання циклічного температурного впливу на біологічну тканину при деструкції онкологічних новоутворень

Наведено результати комп'ютерного моделювання температурного впливу на біологічну тканину з онкологічним новоутворенням у режимах охолодження, нагріву, а також їх циклічної зміни. Побудовано фізичну, математичну і комп'ютерну моделі біологічної тканини з онкологічним новоутворенням із врахуванням теплофізичних процесів, кровообігу, теплообміну, процесів метаболізму та фазового переходу. Досліджено зміну з часом розподілів температури у біологічній тканині з онкологічним новоутворенням та робочому інструменті в залежності від геометрії робочого інструменту та його температури. Проведено комп'ютерну оптимізацію робочого інструменту та розроблено конструкцію термоелектричного приладу для деструкції онкологічних новоутворень.

Ключові слова: термоелектричний прилад, кріодеструкція, гіпертермія, циклічний температурний вплив, комп'ютерне моделювання, біологічна тканина, пухлина, охолодження, нагрів.

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