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METHOD FOR TAKING INTO ACCOUNT THE PHASE TRANSITION IN BIOLOGICAL TISSUE DURING COMPUTER-AIDED SIMULATION OF CRYODESTRUCTION PROCESS

The paper presents a method for taking into account the phase transition in biological tissue during computer-aided simulation of cryodestruction process. The physical, mathematical and computer models of biological tissue are constructed with regard to thermophysical processes, blood circulation, heat transfer, metabolic processes and the phase transition. As an example, we consider the case when there is a cooling element on the surface of biological tissue at a temperature of -50 ° C. The temperature and heat flux distributions in biological tissue are determined in cooling mode. The results obtained make it possible to predict the depth of freezing of biological tissue at a given temperature exposure. Bibl. 28, Fig. 7, Table. 1.
Key words: biological tissue, temperature exposure, cryodestruction, phase transition, computer simulation.

Introduction

It is well known in medical practice that temperature exposure is an important factor in the treatment of many diseases of the human body [1-3]. One of the promising areas is cryodestruction, i.e. a set of surgical treatment methods based on local freezing of the human body biological tissue. To perform cryodestruction, it is necessary to cool a certain part of the human body to a temperature of -50 ° C. Today, such cooling is realized with the help of special cryotools using liquid nitrogen [4 8]. However, the use of liquid nitrogen has a number of disadvantages, namely nitrogen does not provide cooling with the required accuracy of maintaining the temperature, and there are risks of overcooling with negative consequences. Moreover, liquid nitrogen is a very dangerous substance and requires proper care when used, and delivery of liquid nitrogen is not always available, which limits the possibility of using this method. This opens up prospects for the use of thermoelectric cooling for cryodestruction, which can be used for cooling to a temperature of (0 ÷ -80) ° C. Thermoelectric medical devices make it possible to precisely set the required temperature of the working tool, the time of temperature exposure on the corresponding part of the human body and provide a cyclic change of cooling and heating modes [1 – 2, 9 – 12].

Computer models of biological tissue created so far, on the surface of which there is a cooling element, make it possible to simulate thermophysical processes with regard to blood circulation, heat transfer and metabolic processes [13 19]. However, the existing computer models do not take into account the phase transition in biological tissue when it is cooled to a temperature below 0 ° C, which leads to errors in computer simulation of temperatures and heat fluxes.

Therefore, *the purpose of this paper* is to develop a method for taking into account the phase transition in biological tissue during computer simulation of the cryodestruction process.

Physical model

We constructed a physical 2*D* model with axial symmetry (Fig. 1) of the human body biological tissue 1 on the surface of which there is a cooling element 2. This model is a structure of two homogeneous rectangular bars and is characterized by the following thermophysical properties: thermal conductivity κ, specific heat C, density ρ, blood perfusion rate ω_b, blood density ρ_b, blood temperature T_b, specific heat of blood C_b, specific heat release Q_{met} due to metabolic processes and latent phase transition heat L (table 1). The corresponding section of biological tissue 1 is considered as a volumetric heat source q, where:

$$q = Q_{met} + \rho_b \cdot C_b \cdot \omega_b \cdot (T_b - T). \quad (1)$$

The geometric dimensions of biological tissue 1 are *a, b*, and, accordingly, of cooling element 2 - *c, d*. The temperatures at the boundaries of biological tissue 1 and cooling element 2 are T_1, T_2, T_3, T_4. The temperature inside biological tissue is T_1 = +37 ° C. The temperature of cooling element is T_4 = -50 ° C. The ambient temperature is T_5 = +22 ° C. The upper surface of biological tissue with temperature T_3 is in a state of heat exchange with the environment (coefficient of heat exchange α and emissivity ε) at temperature T_5. The lateral surface of biological tissue is adiabatically isolated.

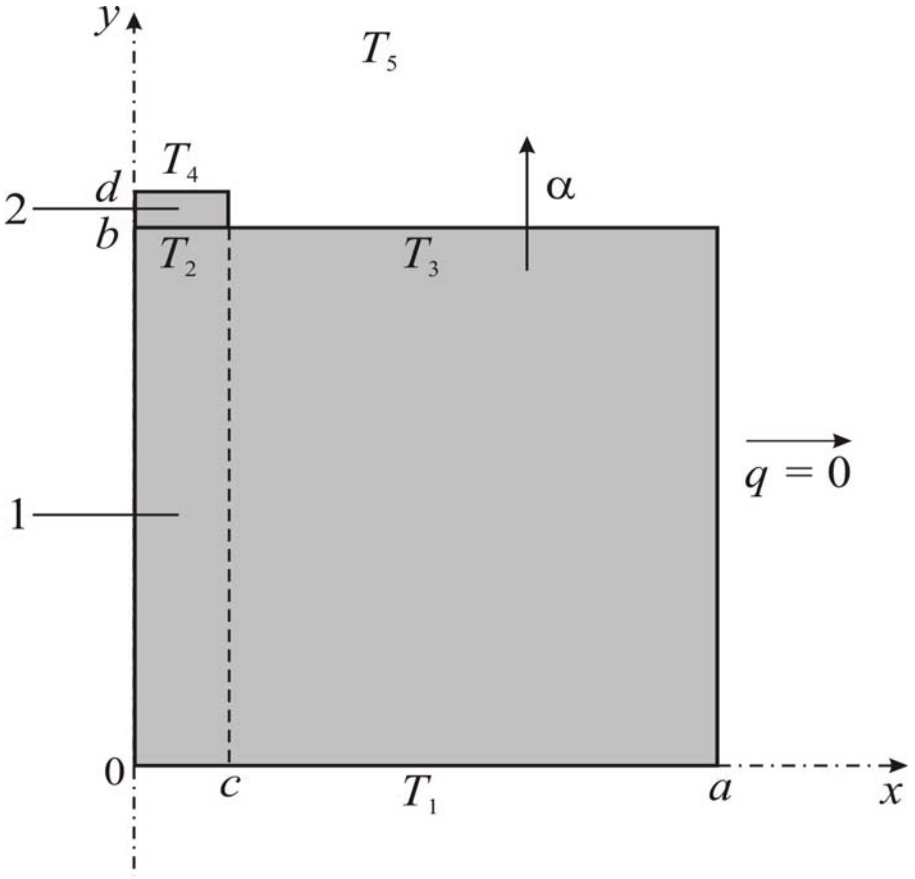

Fig.1. Physical 2D model with axial symmetry:
1 – biological tissue, 2 – cooling element.

Table 1.

Thermophysical properties of the human body biological tissue in normal [20-25] and frozen states [26, 27]

Thermophysical properties of biological tissue	Value	Measurement units
Heat capacity of normal biological tissue (C_1)	3600	J/m^3 ·°C
Heat capacity of frozen biological tissue (C_2)	1800	J/m^3 ·°C
Blood heat capacity (C_b)	3600	J/m^3 ·°C
Blood density (ρ_b)	1000	kg/m^3
Thermal conductivity of normal biological tissue (κ_1)	0.5	W/m ·°C
Thermal conductivity of frozen biological tissue (κ_2)	2	W/m ·°C
Latent heat of phase transition (L)	$250 \cdot 10^3$	J/m^3
Blood temperature (T_b)	37	°C
Upper temperature of phase transition (T_1)	-1	°C
Lower temperature of phase transition (T_2)	-8	°C
Blood perfusion in biological tissue (ω_b)	0.0005	ml/s·ml
Metabolism in biological tissue (Q_{met})	4200	W/m^3

Mathematical model

In general, the heat transfer equation in biological tissue is given by [20-27]:

$$C \cdot \frac{\partial T}{\partial t} = \nabla \cdot (\kappa \cdot \nabla T) + \rho_b \cdot C_b \cdot \omega_b \cdot (T_b - T) + Q_{met}, \quad (2)$$

where C, κ are specific heat and thermal conductivity of biological tissue, ρ_b is blood density, C_b is specific heat of blood, ω_b is blood perfusion, T_b is blood temperature, T is temperature of biological tissue; Q_{met} is heat which is released due to metabolic processes.

The term on the left side of equation (2) is the rate of change of thermal energy contained in a unit volume of biological tissue. The three terms on the right side of this equation represent, respectively, the rate of change of thermal energy due to thermal conductivity, blood perfusion, and heat metabolism.

The equation of heat transfer in biological tissue (2) is solved with the corresponding boundary conditions. The temperature on the surface of cooling element is T_4 = -50°C. The temperature inside

biological tissue is T_1 = + 37 ° C. The lateral surfaces of biological tissue are adiabatically isolated (q = 0), and the upper surface is in a state of heat exchange (heat transfer coefficient α and emissivity ε) with the environment at a temperature of T_5.

$$q(x,y,t)\Big|_{\substack{c\le x\le a\\ y=b}} = \alpha\cdot(T_5 - T_3) + \varepsilon\cdot\sigma\cdot(T_5^4 - T_3^4)\,, \tag{3}$$

where α is coefficient of convective heat exchange of the surface of biological tissue with the environment, ε is emissivity, σ is the Boltzmann constant, T_3 is temperature of biological tissue surface, T_5 is ambient temperature (T_5=+22°C).

At the initial time t = 0 s, it is believed that the temperature in the entire volume of biological tissue is T = +37 ° C, that is, the initial conditions for solving equation (2) are as follows:

$$T(x,y,0) = T_b. \tag{4}$$

As a result of solving the initial boundary value problem (2) - (4), the temperature distributions $T\ (x,\ y,\ t)$ and heat fluxes in biological tissue are determined at an arbitrary time. As an example, in this paper we consider a case in which the temperature of cooling element is T_4 = -50 ° C. However, it should be noted that the proposed method allows considering cases where the temperature of cooling element $T_f(t)$ changes in any temperature range or according to a predetermined function.

During the freezing, the cells will undergo a phase change at the freezing point, with the loss of latent heat of the phase transition (L) occurring and the temperature in these cells will not change. The phase transition in biological cells occurs in the temperature range (-1 ÷ -8) ° C. The properties of biological tissue in normal and frozen states are shown in Table 1. In the temperature range (-1 ÷ -8) ° C, when cells are frozen, the latent heat of the phase transition is absorbed, which can be simulated by adding an appropriate value to the heat capacity [26, 27].

When biological tissue is frozen, the vessels in the capillaries are narrowed to freeze all blood in the capillaries, and the value tends to zero. In addition, the cells will not be able to generate metabolic heat when frozen and Q_{met} will be zero at a temperature below zero.

In the frozen state the properties of biological tissue will have the following values (5)-(8):

$$C = \begin{cases} C_1 & T \ge -1°C \\ \dfrac{L}{-1-(-8)} + \dfrac{C_1 + C_2}{2} & -8°C \le T \le -1°C \\ C_2 & T \le -8°C \end{cases} \tag{5}$$

$$\kappa = \begin{cases} \kappa_1 & T \ge -1°C \\ \dfrac{\kappa_1 + \kappa_2}{2} & -8°C \le T \le -1°C \\ \kappa_2 & T \le -8°C \end{cases} \tag{6}$$

$$Q_m = \begin{cases} 4200 & T \ge -1°C \\ 0 & -8°C \le T \le -1°C \\ 0 & T \le -8°C \end{cases} \tag{7}$$

$$\omega_b = \begin{cases} 0,0005 & T \geq -1°C \\ 0 & -8°C \leq T \leq -1°C \\ 0 & T \leq -8°C \end{cases} \quad (8)$$

Computer model

A computer model of biological tissue was created with a cooling element on its surface. Comsol Multiphysics software package [28] was used to build the computer model, which enables simulating thermophysical processes in biological tissue taking into account blood circulation, heat exchange, metabolism processes and phase transition.

The distribution of temperatures and heat fluxes in biological tissue was calculated by the finite element method, the essence of which is that the object under study is divided into a large number of finite elements and in each of them a function value is searched that satisfies given second-order differential equations with the corresponding boundary conditions. The accuracy of solving the formulated problem depends on the level of partitioning and is ensured by the use of a large number of finite elements [28].

As an example, Figs.2 - 3 show the distributions of temperature and isothermal surfaces in the bulk of the human body biological tissue on the surface of which there is cooling element at a temperature of T = -50°C.

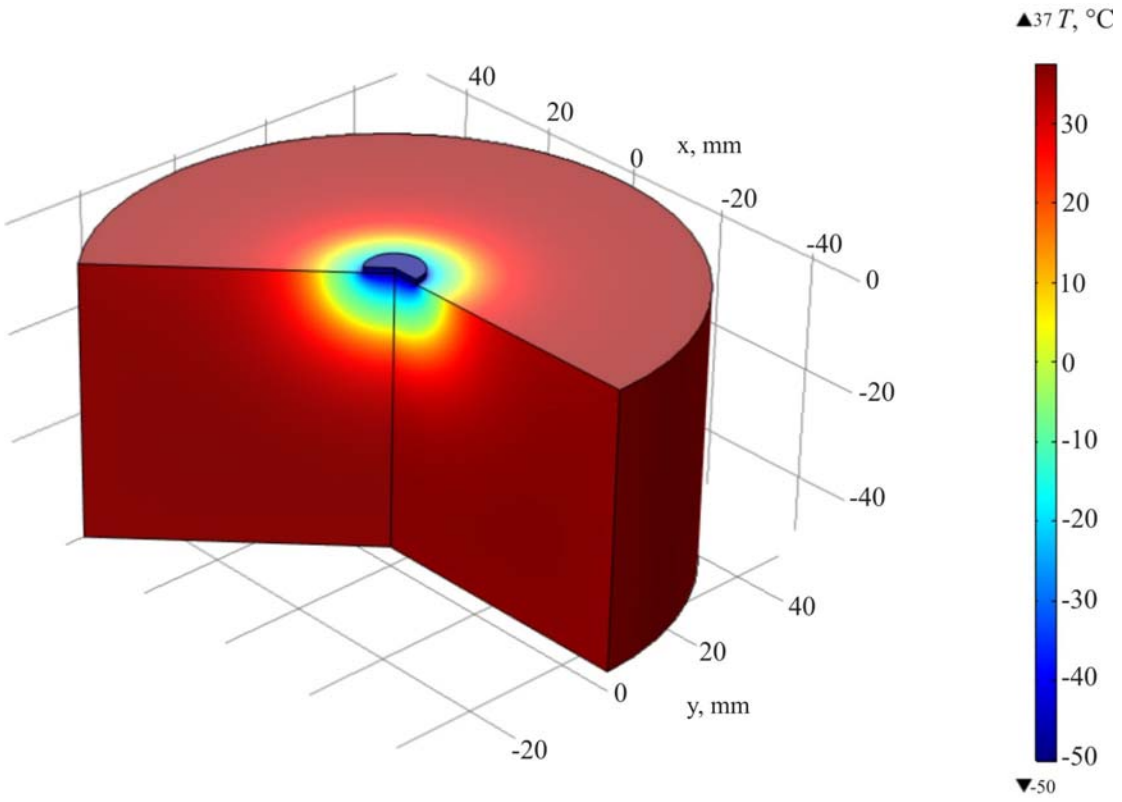

Fig.2. Temperature distribution in the bulk of biological tissue on the surface of which there is a cooling element at a temperature of T = -50°C.

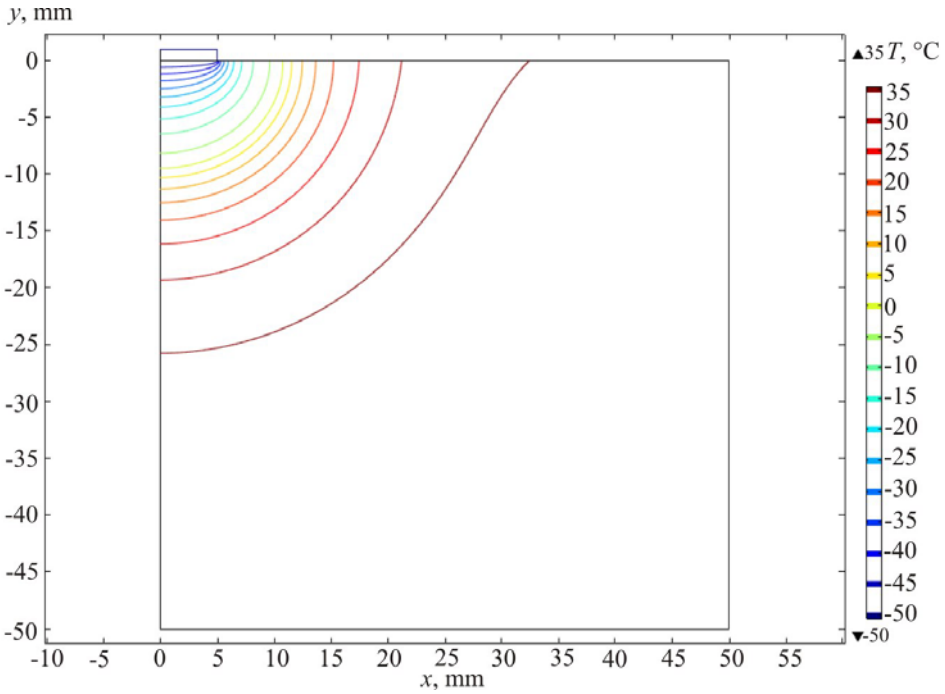

Fig. 3. Isothermal surfaces in the bulk of biological tissue on the surface of which there is a cooling element at a temperature T = -50°C.

Computer simulation results

Fig. 4 shows temperature distribution in the section of biological tissue on the surface of which there is a cooling element at temperature T = -50°C at time moment t = 500 s. In this case, l_1 is temperature level T = -8°C and l_2 is temperature level T = -1°C.

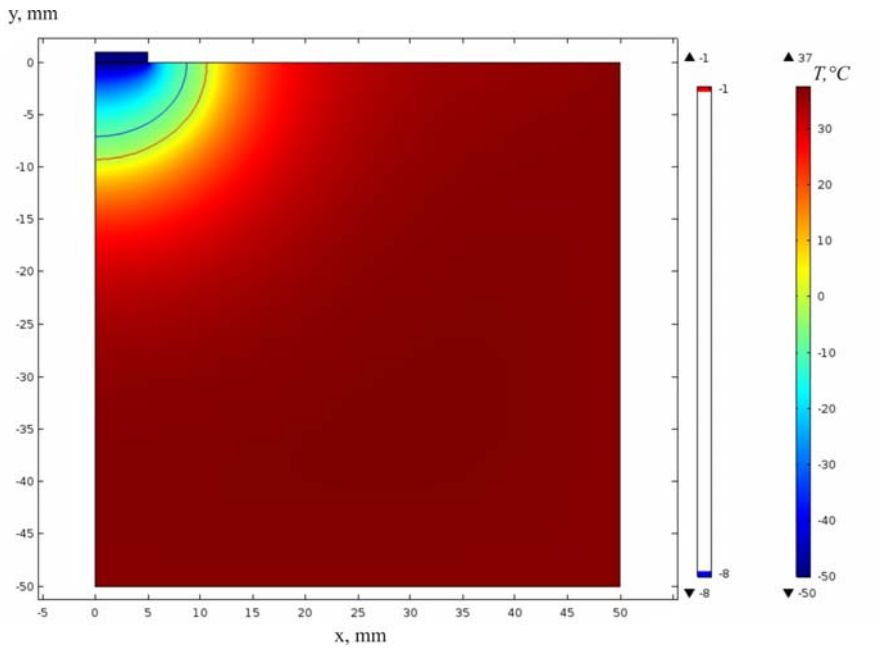

Fig. 4. Temperature distribution in the section of biological tissue on the surface of which there is a cooling element at a temperature T = -50°C at time moment t = 500 s:
l_1 – temperature level T = -8°C and l_2 is temperature level T = -1°C.

Fig. 5 shows the dependence of the motion of phase transition zone (crystallization zone of biological tissue) on the time of temperature exposure. From Fig.5 it is seen that maximum freezing depth of biological tissue is about $l \approx 10$ mm at a temperature of cooling element T = -50°C.

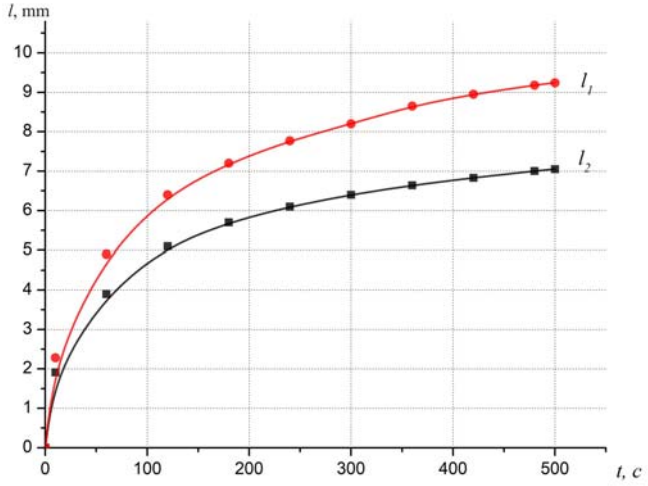

Fig. 5. Dependence of the motion of phase transition zone (crystallization zone of biological tissue) on the time of temperature exposure at a cooling element temperature T = -50°C: l_1 – temperature level T = -8°C and l_2 – temperature level T = -1°C.

Computer simulation was used to determine the dependence of the freezing depth of biological tissue on temperature at different time intervals (Fig. 6) and on the time of temperature exposure at a cooling element temperature T = -50 ° C (Fig. 7).

Figs. 6 and 7 show that at t = 60 s the biological tissue is cooled to a temperature of T = 10 ° C at a depth of l ≈ 4 mm, and at t = 180 s - at a depth of l ≈ 5 mm and at t = 480 s - at a depth of l ≈ 7 mm.

It is established that with increasing temperature exposure, a deeper cooling of biological tissue is attained. That is, with prolonged temperature exposure (T = -50 ° C), destruction of the corresponding section of biological tissue can be achieved.

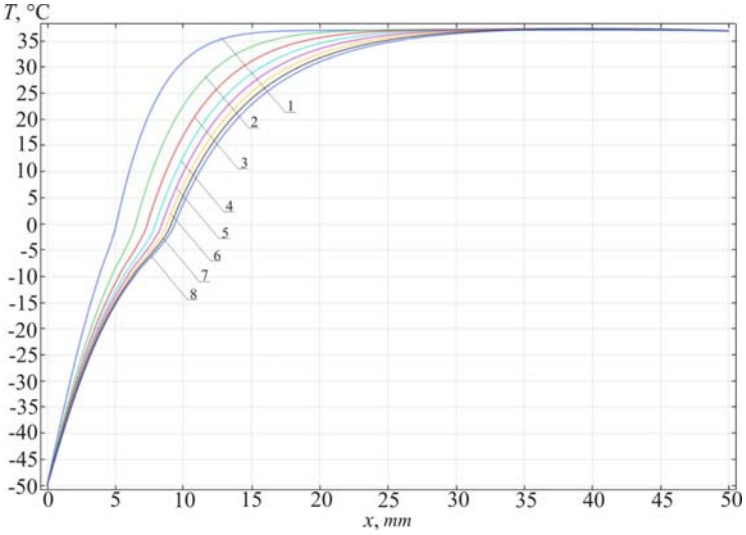

Fig.6. Temperature distribution in biological tissue at different time moments of temperature exposure: 1 – t = 60 s; 2 – t = 120 s; 3 – t = 180 s; 4 – t = 240 s; 5 – t = 300 s; 6 – t = 360 s; 7 – t = 420 s; 8 – t = 480 s.

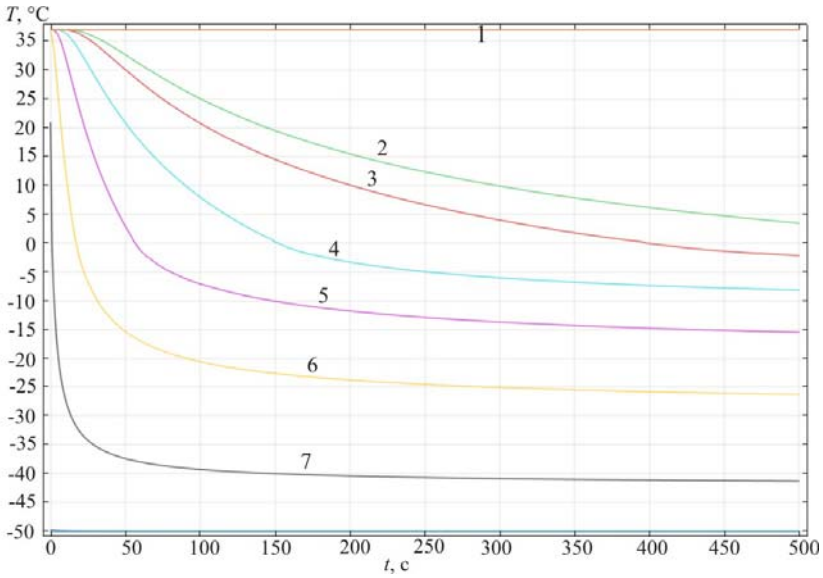

Fig. 7. Time dependence of temperature at different depth h of biological tissue at cooling element temperature T = -50°C: 1 – h = 0; 2 – h = 1 mm; 3 – h = 3 mm; 4 – h = 5 mm; 5 – h = 7 mm; 6 – h = 9 mm; 7 – h = 10 mm.

Thus, a technique was developed for taking into account the phase transition in biological tissue during computer –aided simulation of cryodestruction process, which makes it possible to predict the results of local temperature effect on biological tissue and to determine the temperature and heat flux distributions at any given time with a predetermined arbitrary time function of change in the temperature of cooling element $T_f(t)$.

It should be noted that the obtained results make it possible to predict the depth of freezing of biological tissue at a given temperature exposure, taking into account the phase transition to achieve the maximum effect during cryodestruction.

Conclusion

1. A technique was developed for taking into account the phase transition in biological tissue during computer-aided simulation of the cryodestruction process, which makes it possible to predict the results of local temperature effect on biological tissue and to determine the temperature and heat flux distributions at any given time with a predetermined arbitrary time function of change in the temperature of cooling element $T_f(t)$.
2. Physical, mathematical and computer models of biological tissue on the surface of which there is a cooling element at a temperature of T = -50°C have been created with regard to thermophysical processes, blood circulation, heat transfer, metabolic processes and phase transition.
3. Using computer simulation, the distribution of temperature and heat fluxes inside the biological tissue was determined in cooling mode at a cooling element temperature T = 50 °C. The dependence of the freezing depth of biological tissue on the temperature of cooling element and the time of temperature exposure was established. The maximum freezing depth of biological tissue was determined, which is $l \approx$ 7-10 mm at a cooling element temperature T = 50 °C.

References

1. Anatychuk L.I. (1979). *Termoelementy i termoelektricheskiie ustroistva. Spravochnik [Thermo-*

elements and thermoelectric devices. Reference book]. Kyiv: Naukova Dumka [in Russian].
2. Kolenko E.A. (1967). *Termoelektricheskiie okhlazhdaiushchiie pribory [Thermoelectric cooling devices. 2nd ed.* Leningrad: Nauka [in Russian].
3. Anatychuk L.I., Denisenko O.I., Kobylianskyi R.R., Kadeniuk T.Ya., Perepichka M.P. (2017). Modern methods of cryotherapy in dermatological practice. *Klinichna ta eksperymental'na patologiia - Clinical and experimental pathology*, XVI, (59), 150-156.
4. Denkov V. (1988). At the edge of life. Moscow: Znaniie [Russian transl.]
5. Maruyama S., Nakagawa K., Takeda H. (2008). The flexible cryoprobe using Peltier effect for heat transfer control. *Journal of Biomechanical Science and Engineering*, 138-150.
6. Kochenov V.I. (2000). *Kriokhirurgicheskaia profilakticheskaia onkologiia [Cryosurgical preventive oncology]*. Nizhnii Novgorod [in Russian].
7. Kochenov V.I. (2003). *Kriologicheskaia profilakticheskaia onkologiia: kratkoie uchebnoie I metodicheskooie posibiie dlia vrachei i studentov [Cryological preventive oncology: brief educational and methodological manual for doctors and students]*. 2nd revised ed. Nizhnii Novgorod [in Russian].
8. Kochenov V.I. (1982). Adhesive effect in cryosurgery. *Abstract in the International Abstract Journal*, IV, 8.
9. Moskalyk, I.A., Manyk O.M. (2013). On the use of thermoelectric cooling in cryodestruction practice. *J.Thermoelectricity*, 6, 84-92.
10. Anatychuk L.I., Denisenko O.I., Kobylianskyi R.R., Kadeniuk T.Ya. (2015). On the use of thermoelectric cooling in dermatology and cosmetology. *J.Thermoelectricity*, 3, 57-71.
11. Moskalyk I.A. (2015). On the use of thermoelectric devices in cryosurgery. *Physics and Chemistry of the Solid State,* 4, 742-746.
12. Kobylianskyi R.R., Kadeniuk T.Ya. (2016) Pro perspektyvy vykorystannia termoelektryky dlia likuvannia zakhvoriuvan shkiry kholodom [On the prospects of using thermoelectricity for treatment of skin diseases with cold]. *Naukovy visnyk Chernivetskogo universitetu: zbirnyk naukovykh ptrats. Fizyka. Elektronika - Scientific Bulletin of Chernivtsi University: Collection of Scientific Papers. Physics. Electronics,* 5, 1, 67 – 72 [in Ukrainian].
13. Anatychuk L.I., Vikhor L.M., Kotsur M.P., Kobylianskyi R.R., Kadeniuk T.Ya. (2016). Optimal control of time dependence of cooling temperature in thermoelectric devices. *J.Thermoelectricity*, 5, 5-11.
14. Anatychuk L.I., Kobylianskyi R.R., Kadeniuk T.Ya. (2017). Computer simulation of local thermal effect on human skin. *J.Thermoelectricity*, 1, 69-79.
15. Anatychuk L.I., Vikhor L.M., Kobylianskyi R.R., Kadeniuk T.Ya. (2017). Computer simulation and optimization of the dynamic operating modes of thermoelectric device for treatment of skin diseases. *J.Thermoelectricity*, 2, 44-57.
16. Anatychuk L.I.., Vikhor L.M., Kobylianskyi R.R., Kadeniuk T.Ya., Zvarich O.V. (2017). Computer simulation and optimization of the dynamic operating modes of thermoelectric device for reflexotherapy. *J.Thermoelectricity*, 3, 68-78.
17. Anatychuk L.I., Vikhor L.M., Kobylianskyi R.R., Kadeniuk T.Ya. (2017). Computer simulation and optimization of the dynamic operating modes of thermoelectric device for cryodestruction. *Physics and Chemistry of the Solid State*, 18 (4), 455-459.
18. Anatychuk L., Vikhor L, Kotsur M., Kobylianskyi R., Kadeniuk T. (2018). Optimal control of time dependence of temperature in thermoelectric devices for medical purposes. *International Journal of Thermophysics 3*9:108. https://doi.org/10.1007/s10765-018-2430-z.

19. Anatychuk L.I., Vikhor L.M., Kobylianskyi R.R., Kadeniuk T.Ya. (2018). Kompiuterne modeliuvannia lokalnogo temperaturenogo vplyvu na shkiru liudyny v dynamichnomu rezhymi [Computer simulation of local temperature effect on human skin in the dynamic mode]. *Visnyk Natsionalnogo universitetu "Lvivska Politechnica". Physical and mathematical sciences – Bulletin of National university "Lvivska Politechnica." Physical and mathematical sciences.* Lviv: Lvivska Politechnical Publ., 898, 78-82.
20. Pennes H.H. (1948). Analysis of tissue and arterial blood temperatures in the resting forearm *J. Appl. Physiol*. 1(2), 93 – 122.
21. Jiang S.C., Ma N., Li H.J. and Zhang X.X. (2002). Effects of thermal properties and geometrical dimensions on skin burn injuries. *Burns* 28, 713 – 717.
22. Cetingul M.P., Herman C. (2008). Identification of skin lesions from the transient thermal response using infrared imaging technique. *IEEE*, 1219 – 1222.
23. Ciesielski M., Mochnacki B. and Szopa R. (2011). Numerical modeling of biological tissue heating. Admissible thermal dose. *Scientific Research of the Institute of Mathematics and Computer Science* 1 (10), 11 – 20.
24. Filipoiu Florin, Bogdan Andrei Ioan and Carstea Iulia Maria (2010). Computer-aided analysis of the heat transfer in skin tissue. *Proceedings of the 3rd WSEAS Int. Conference on Finite Differences - Finite Elements - Finite Volumes - Boundary Elements,* 53 – 59.
25. Carstea Daniela, Carstea Ion and Carstea Iulia Maria Carstea (2011). Interdisciplinarity in computer-aided analysis of thermal therapies. *WSEAS Transactions on Systems and Control*, 6 (4), 115 – 124.
26. Deng Z.S., Liu J. (2005). Numerical simulation of selective freezing of target biological tissues following injection of solutions with specific thermal properties. *Cryobiology*, 50, 183-192.
27. Han Liang Lim, Venmathi Gunasekaran. Mathematical modeling of heat distribution during cryosurgery // https://isn.ucsd.edu/last/courses/beng221/problems/2011/project10.pdf.
28. COMSOL Multiphysics User's Guide (2018). COMSOLAB.

Submitted 21.03.2019

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МЕТОДИКА ВРАХУВАННЯ ФАЗОВОГО ПЕРЕХОДУ В БІОЛОГІЧНІЙ ТКАНИНІ ПРИ КОМП'ЮТЕРНОМУ МОДЕЛЮВАННІ ПРОЦЕСУ КРІОДЕСТРУКЦІЇ

У роботі наведено методику врахування фазового переходу в біологічній тканині при комп'ютерному моделюванні процесу кріодеструкції. Побудовано фізичну, математичну та комп'ютерну моделі біологічної тканини з врахуванням теплофізичних процесів, кровообігу, теплообміну, процесів метаболізму та фазового переходу. Як приклад, розглянуто випадок, коли на поверхні біологічної тканини знаходиться охолоджуючий елемент при температурі - 50°С. Визначено розподіли температури і теплових потоків у біологічній тканині в режимі охолодження. Отримані результати дають можливість прогнозувати глибину промерзання біологічної тканини при заданому температурному впливі. Бібл. 28, рис. 7, табл. 1.
Ключові слова: біологічна тканина, температурний вплив, кріодеструкція, фазовий перехід, комп'ютерне моделювання.

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В работе приведена методика учитывания фазового перехода в биологической ткани при компьютерном моделировании процесса криодеструкции. Построены физическая, математическая и компьютерная модели биологической ткани с учетом теплофизических процессов, кровообращения, теплообмена, процессов метаболизма и фазового перехода. Как пример, рассмотрен случай, когда на поверхности биологической ткани находится охлаждающий элемент при температуре - 50 С. Определенно распределения температуры и тепловых потоков в биологической ткани в режиме охлаждения. Полученные результаты дают возможность прогнозировать глубину промерзания биологической ткани при заданном температурном влиянии. Библ. 28, рис. 7, табл. 1.
Ключевые слова: биологическая ткань, температурное влияние, криодеструкция, фазовый переход, компьютерное моделирование.

References

1. Anatychuk L.I. (1979). *Termoelementy i termoelektricheskiie ustroistva. Spravochnik [Thermoelements and thermoelectric devices. Reference book]*. Kyiv: Naukova Dumka [in Russian].
2. Kolenko E.A. (1967). *Termoelektricheskiie okhlazhdaiushchiie pribory [Thermoelectric cooling devices. 2nd ed.* Leningrad: Nauka [in Russian].
3. Anatychuk L.I., Denisenko O.I., Kobylianskyi R.R., Kadeniuk T.Ya., Perepichka M.P. (2017). Modern methods of cryotherapy in dermatological practice. *Klinichna ta eksperymental'na patologiia - Clinical and experimental pathology*, XVI, (59), 150-156.
4. Denkov V. (1988). At the edge of life. Moscow: Znaniie [Russian transl.]
5. Maruyama S., Nakagawa K., Takeda H. (2008). The flexible cryoprobe using Peltier effect for heat transfer control. *Journal of Biomechanical Science and Engineering*, 138-150.

6. Kochenov V.I. (2000). *Kriokhirurgicheskaia profilakticheskaia onkologiia [Cryosurgical preventive oncology]*. Nizhnii Novgorod [in Russian].
7. Kochenov V.I. (2003). *Kriologicheskaia profilakticheskaia onkologiia: kratkoie uchebnoie I metodicheskooie posibiie dlia vrachei i studentov [Cryological preventive oncology: brief educational and methodological manual for doctors and students]*. 2nd revised ed. Nizhnii Novgorod [in Russian].
8. Kochenov V.I. (1982). Adhesive effect in cryosurgery. *Abstract in the International Abstract Journal*, IV, 8.
9. Moskalyk, I.A., Manyk O.M. (2013). On the use of thermoelectric cooling in cryodestruction practice. *J.Thermoelectricity*, 6, 84-92.
10. Anatychuk L.I., Denisenko O.I., Kobylianskyi R.R., Kadeniuk T.Ya. (2015). On the use of thermoelectric cooling in dermatology and cosmetology. *J.Thermoelectricity*, 3, 57-71.
11. Moskalyk I.A. (2015). On the use of thermoelectric devices in cryosurgery. *Physics and Chemistry of the Solid State,* 4, 742-746.
12. Kobylianskyi R.R., Kadeniuk T.Ya. (2016) Pro perspektyvy vykorystannia termoelektryky dlia likuvannia zakhvoriuvan shkiry kholodom [On the prospects of using thermoelectricity for treatment of skin diseases with cold]. *Naukovy visnyk Chernivetskogo universitetu: zbirnyk naukovykh ptrats. Fizyka. Elektronika - Scientific Bulletin of Chernivtsi University: Collection of Scientific Papers. Physics. Electronics,* 5, 1, 67 – 72 [in Ukrainian].
13. Anatychuk L.I., Vikhor L.M., Kotsur M.P., Kobylianskyi R.R., Kadeniuk T.Ya. (2016). Optimal control of time dependence of cooling temperature in thermoelectric devices. *J.Thermoelectricity*, 5, 5-11.
14. Anatychuk L.I., Kobylianskyi R.R., Kadeniuk T.Ya. (2017). Computer simulation of local thermal effect on human skin. *J.Thermoelectricity*, 1, 69-79.
15. Anatychuk L.I., Vikhor L.M., Kobylianskyi R.R., Kadeniuk T.Ya. (2017). Computer simulation and optimization of the dynamic operating modes of thermoelectric device for treatment of skin diseases. *J.Thermoelectricity*, 2, 44-57.
16. Anatychuk L.I.., Vikhor L.M., Kobylianskyi R.R., Kadeniuk T.Ya., Zvarich O.V. (2017). Computer simulation and optimization of the dynamic operating modes of thermoelectric device for reflexotherapy. *J.Thermoelectricity*, 3, 68-78.
17. Anatychuk L.I., Vikhor L.M., Kobylianskyi R.R., Kadeniuk T.Ya. (2017). Computer simulation and optimization of the dynamic operating modes of thermoelectric device for cryodestruction. *Physics and Chemistry of the Solid State*, 18 (4), 455-459.
18. Anatychuk L., Vikhor L, Kotsur M., Kobylianskyi R., Kadeniuk T. (2018). Optimal control of time dependence of temperature in thermoelectric devices for medical purposes. *International Journal of Thermophysics 3*9:108. https://doi.org/10.1007/s10765-018-2430-z.
19. Anatychuk L.I., Vikhor L.M., Kobylianskyi R.R., Kadeniuk T.Ya. (2018). Kompiuterne modeliuvannia lokalnogo temperaturenogo vplyvu na shkiru liudyny v dynamichnomu rezhymi [Computer simulation of local temperature effect on human skin in the dynamic mode]. *Visnyk Natsionalnogo universitetu "Lvivska Politechnica". Physical and mathematical sciences – Bulletin of National university "Lvivska Politechnica." Physical and mathematical sciences.* Lviv: Lvivska Politechnical Publ., 898, 78-82.
20. Pennes H.H. (1948). Analysis of tissue and arterial blood temperatures in the resting forearm *J. Appl. Physiol*. 1(2), 93 – 122.
21. Jiang S.C., Ma N., Li H.J. and Zhang X.X. (2002). Effects of thermal properties and geometrical

dimensions on skin burn injuries. *Burns* 28, 713 – 717.
22. Cetingul M.P., Herman C. (2008). Identification of skin lesions from the transient thermal response using infrared imaging technique. *IEEE*, 1219 – 1222.
23. Ciesielski M., Mochnacki B. and Szopa R. (2011). Numerical modeling of biological tissue heating. Admissible thermal dose. *Scientific Research of the Institute of Mathematics and Computer Science* 1 (10), 11 – 20.
24. Filipoiu Florin, Bogdan Andrei Ioan and Carstea Iulia Maria (2010). Computer-aided analysis of the heat transfer in skin tissue. *Proceedings of the 3rd WSEAS Int. Conference on Finite Differences - Finite Elements - Finite Volumes - Boundary Elements,* 53 – 59.
25. Carstea Daniela, Carstea Ion and Carstea Iulia Maria Carstea (2011). Interdisciplinarity in computer-aided analysis of thermal therapies. *WSEAS Transactions on Systems and Control*, 6 (4), 115 – 124.
26. Deng Z.S., Liu J. (2005). Numerical simulation of selective freezing of target biological tissues following injection of solutions with specific thermal properties. *Cryobiology*, 50, 183-192.
27. Han Liang Lim, Venmathi Gunasekaran. Mathematical modeling of heat distribution during cryosurgery // https://isn.ucsd.edu/last/courses/beng221/problems/2011/project10.pdf.
28. COMSOL Multiphysics User's Guide (2018). COMSOLAB.

Submitted 21.03.2019