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SENSITIVITY ANALYSIS OF BIOLOGICAL TISSUE FREEZING PROCESS WITH RESPECT TO THE RADIUS OF SPHERICAL CRYOPROBE

Ewa Majchrzak
Grażyna Kałuża

Department for Strength of Materials and Computational Mechanics, Silesian University of Technology, Gliwice
e-mail: ewa.majchrzak@polsl.pl; grazyna.kaluza@polsl.pl

Application of the shape sensitivity analysis to the case of problems of the biological tissue freezing process is discussed. The freezing process described by a strongly non-linear bioheat transfer equation in which an additional term controlling the evolution of latent heat appears. Using the approach called 'the one domain method', one finally obtains a partial differential equation containing the substitute thermal capacity of tissue. The boundary and initial conditions determine the thermal interaction between the tissue and cryoprobe tip.
In the paper, we consider a spherical internal cryoprobe. In order to estimate the influence of cryoprobe geometry on the course of the process, the shape sensitivity analysis is applied. In particular, a direct approach is used (explicit differentiation method). The results of numerical modeling (the boundary element method is applied) allow one to formulate essential practical conclusions concerning the course of cryosurgery treatments.

Key words: freezing process, sensitivity analysis, boundary element method

1. Governing equations

From the mathematical point of view, the freezing process belongs to a group of moving boundary problems because the shape and dimensions of the frozen region are time-dependent. In the case of internal spherical cryoprobe application (Fig. 1), the following equation written in the spherical co-ordinate system should be taken into account

$$R_1 < r < R_2 : \qquad C(T)\frac{\partial T(r,t)}{\partial t} = \frac{1}{r^2}\frac{\partial}{\partial r}\Big[\lambda(T) r^2 \frac{\partial T(r,t)}{\partial r}\Big] \tag{1.1}$$

where $C(T)$ [J/(m^{3}K)] is the substitute thermal capacity per unit volume, $\lambda(T)$ [W/(mK)] is the thermal conductivity, T, r, t denote temperature, spatial co-ordinate and time. The courses of $C(T)$ and also $\lambda(T)$ are presented in Fig. 2 (Comini and Giudice, 1976; Majchrzak and Dziewoński, 2000).

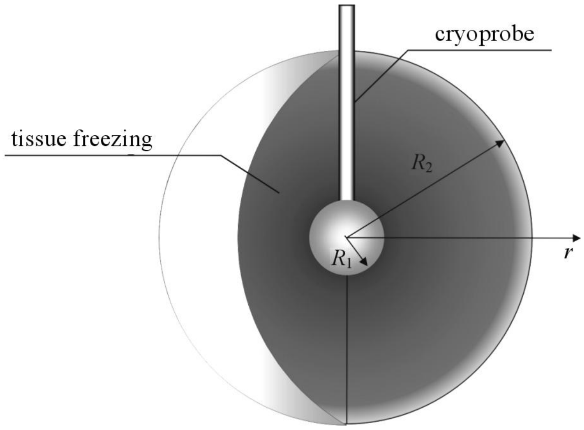

Fig. 1. Spherical cryoprobe

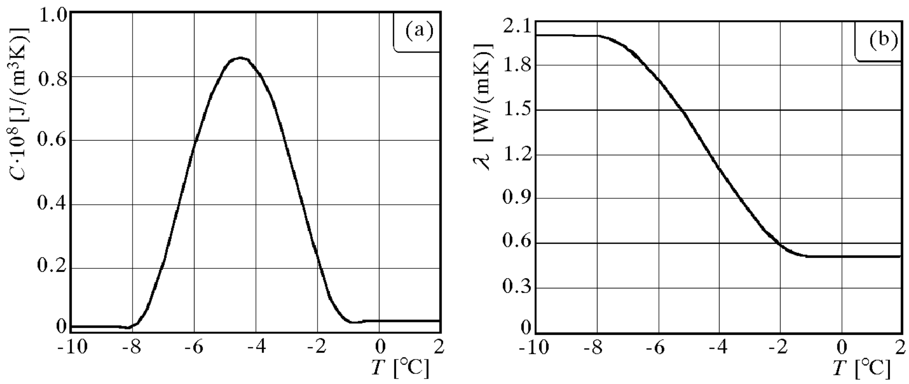

Fig. 2. (a) Substitute thermal capacity; (b) thermal conductivity

Equation (1.1) is supplemented by the following boundary conditions

$$\begin{cases} r = R_1 : \quad T(r,t) = T_c \\ r = R_2 : \quad \dfrac{\partial T(r,t)}{\partial r} = 0 \end{cases} \tag{1.2}$$

and initial condition

$$t = 0 : \qquad T(r,t) = T_0 \tag{1.3}$$

where R_1 is the cryoprobe radius, R_2 is the conventionally assumed external radius of the domain considered, T_c is the temperature of the cryoprobe surface, T_0 is the initial temperature of the tissue.

In order to use the boundary element method, linearization of the problem discussed must be introduced. Here, the artificial heat source method is applied (Majchrzak and Mochnacki, 1996). This method requires transformation of the governing equations and boundary-initial conditions by the introduction of Kirchhoff's function, namely

$$V(T) = \int_{T_r}^{T} \lambda(\mu)\, d\mu \tag{1.4}$$

where T_r is an arbitrary assumed reference level.

Using this function, we can transform governing equations (1.1), (1.2), (1.3) to the form

$$\varPhi[T(V)]\frac{\partial V(r,t)}{\partial t} = \frac{1}{r^2}\frac{\partial}{\partial r}\Big[r^2\frac{\partial V(r,t)}{\partial r}\Big] \tag{1.5}$$

where (cf. Fig. 3)

$$\varPhi[T(V)] = \frac{C[T(V)]}{\lambda[T(V)]} \tag{1.6}$$

Boundary and initial conditions (1.2), (1.3) should be also transformed and then

$$\left\{\begin{array}{ll} r = R_1 : & V(r,t) = V_c \\ r = R_2 : & \dfrac{\partial V(r,t)}{\partial r} = 0 \\ t = 0 : & V(r,t) = V_0 \end{array}\right. \tag{1.7}$$

where $V_c = V(T_c)$, $V_0 = V(T_0)$.

2. Sensitivity analysis

In order to estimate the influence of the cryoprobe radius on the course of the freezing process, a sensitivity model is constructed. Using the concept of material derivative (Dems, 1987; Kleiber, 1997) one can write

$$\frac{\mathrm{D}V}{\mathrm{D}b} = \frac{\partial V}{\partial b} + \frac{\partial V}{\partial r}v \tag{2.1}$$

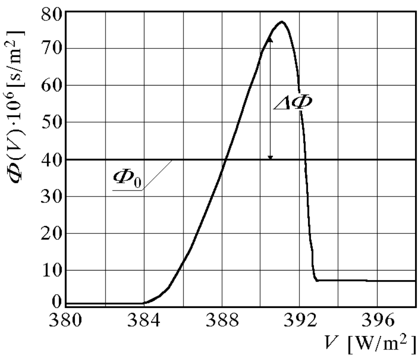

Fig. 3. Course of the function $\Phi[T(V)]$

where $v = v(r, b)$ is the velocity associated with the design parameter $b = R_1$.
Equation (1.5) can be written in the form

$$\Phi[T(V)]\frac{\partial V}{\partial t} = \frac{\partial^2 V}{\partial r^2} + \frac{2}{r}\frac{\partial V}{\partial r} \tag{2.2}$$

Using the direct approach of sensitivity analysis (Dems, 1987; Kałuża, 2005; Kleiber, 1997), equation (2.2) is differentiated with respect to the shape parameter b, namely

$$\frac{\mathrm{D}\Phi[T(V)]}{\mathrm{D}b}\frac{\partial V}{\partial t} + \Phi[T(V)]\frac{\mathrm{D}}{\mathrm{D}b}\Big(\frac{\partial V}{\partial t}\Big) = \frac{\mathrm{D}}{\mathrm{D}b}\Big(\frac{\partial^2 V}{\partial r^2}\Big) + 2\frac{\mathrm{D}}{\mathrm{D}b}\Big(\frac{1}{r}\frac{\partial V}{\partial r}\Big) \tag{2.3}$$

Because (c.f. formula (2.1))

$$\frac{\mathrm{D}}{\mathrm{D}b}\Big(\frac{\partial V}{\partial r}\Big) = \frac{\partial}{\partial b}\Big(\frac{\partial V}{\partial r}\Big) + \frac{\partial}{\partial r}\Big(\frac{\partial V}{\partial r}\Big)v = \frac{\partial}{\partial r}\Big(\frac{\partial V}{\partial b}\Big) + \frac{\partial^2 V}{\partial r^2}v \tag{2.4}$$

and

$$\frac{\partial}{\partial r}\Big(\frac{\mathrm{D}V}{\mathrm{D}b}\Big) = \frac{\partial}{\partial r}\Big(\frac{\partial V}{\partial b} + \frac{\partial V}{\partial r}v\Big) = \frac{\partial}{\partial r}\Big(\frac{\partial V}{\partial b}\Big) + \frac{\partial^2 V}{\partial r^2}v + \frac{\partial V}{\partial r}\frac{\partial v}{\partial r} \tag{2.5}$$

therefore

$$\frac{\mathrm{D}}{\mathrm{D}b}\Big(\frac{\partial V}{\partial r}\Big) = \frac{\partial}{\partial r}\Big(\frac{\mathrm{D}V}{\mathrm{D}b}\Big) - \frac{\partial V}{\partial r}\frac{\partial v}{\partial r} \tag{2.6}$$

Next, the material derivative of the component $\partial^2 V/\partial r^2$ is calculated. From equation (2.1), one obtains

$$\frac{\mathrm{D}}{\mathrm{D}b}\Big(\frac{\partial^2 V}{\partial r^2}\Big) = \frac{\mathrm{D}}{\mathrm{D}b}\Big[\frac{\partial}{\partial r}\Big(\frac{\partial V}{\partial r}\Big)\Big] = \frac{\partial}{\partial r}\Big[\frac{\mathrm{D}}{\mathrm{D}b}\Big(\frac{\partial V}{\partial r}\Big)\Big] - \frac{\partial^2 V}{\partial r^2}\frac{\partial v}{\partial r} \tag{2.7}$$

this means

$$\frac{\mathrm{D}}{\mathrm{D}b}\Big(\frac{\partial^2 V}{\partial r^2}\Big)=\frac{\partial^2}{\partial r^2}\Big(\frac{\mathrm{D}V}{\mathrm{D}b}\Big)-2\frac{\partial^2 V}{\partial r^2}\frac{\partial v}{\partial r}-\frac{\partial V}{\partial r}\frac{\partial^2 v}{\partial r^2} \tag{2.8}$$

In a similar way, one finds

$$\frac{\mathrm{D}}{\mathrm{D}b}\Big(\frac{1}{r}\frac{\partial V}{\partial r}\Big)=\frac{1}{r}\Big[\frac{\partial}{\partial b}\Big(\frac{\partial V}{\partial r}\Big)+\frac{\partial}{\partial r}\Big(\frac{\partial V}{\partial r}\Big)v\Big]-\frac{1}{r^2}\frac{\partial V}{\partial r}v \tag{2.9}$$

Taking into account formula (2.1) and dependence (2.6), we have

$$\frac{\mathrm{D}}{\mathrm{D}b}\Big(\frac{1}{r}\frac{\partial V}{\partial r}\Big)=\frac{1}{r}\frac{\mathrm{D}}{\mathrm{D}b}\Big(\frac{\partial V}{\partial r}\Big)-\frac{1}{r^2}\frac{\partial V}{\partial r}v=\frac{1}{r}\frac{\partial}{\partial r}\Big(\frac{\mathrm{D}V}{\mathrm{D}b}\Big)-\frac{1}{r}\frac{\partial V}{\partial r}\frac{\partial v}{\partial r}-\frac{v}{r^2}\frac{\partial V}{\partial r} \tag{2.10}$$

The material derivative of the component $\partial V/\partial t$ is also calculated

$$\frac{\mathrm{D}}{\mathrm{D}b}\Big(\frac{\partial V}{\partial t}\Big)=\frac{\partial}{\partial b}\Big(\frac{\partial V}{\partial t}\Big)+\frac{\partial}{\partial r}\Big(\frac{\partial V}{\partial t}\Big)v=\frac{\partial}{\partial t}\Big(\frac{\partial V}{\partial b}+\frac{\partial V}{\partial r}v\Big)=\frac{\partial}{\partial t}\Big(\frac{\mathrm{D}V}{\mathrm{D}b}\Big) \tag{2.11}$$

From equation (2.2), it results that

$$\frac{\partial^2 V}{\partial r^2}=\varPhi[T(V)]\frac{\partial V}{\partial t}-\frac{2}{r}\frac{\partial V}{\partial r} \tag{2.12}$$

Using formulas (2.8), (2.10) and (2.11), equation (2.3) takes form

$$\begin{aligned}\varPhi[T(V)]\frac{\partial U(r,t)}{\partial t}&=\frac{\partial^2 U(r,t)}{\partial r^2}+\frac{2}{r}\frac{\partial U(r,t)}{\partial r}+\\&-\Big(2\varPhi[T(V)]\frac{\partial v}{\partial r}+\frac{\mathrm{D}\varPhi[T(V)]}{\mathrm{D}b}\Big)\frac{\partial V(r,t)}{\partial t}+\Big(\frac{2}{r}\frac{\partial v}{\partial r}-\frac{\partial^2 v}{\partial r^2}-\frac{2v}{r^2}\Big)\frac{\partial V(r,t)}{\partial r}\end{aligned} \tag{2.13}$$

where

$$U(r,t)=\frac{\mathrm{D}V(r,t)}{\mathrm{D}b} \tag{2.14}$$

is the sensitivity function, while

$$\frac{\mathrm{D}\varPhi[T(V)]}{\mathrm{D}b}=\frac{1}{\lambda^2[T(V)]}\Big(\frac{dC}{dT}-\frac{d\lambda}{dT}\varPhi[T(V)]\Big)U(r,t) \tag{2.15}$$

Boundary and initial conditions (1.7) are also differentiated with respect to b

$$\begin{cases} r=R_1: & \dfrac{\mathrm{D}V}{\mathrm{D}b}=\dfrac{\mathrm{D}V_c}{\mathrm{D}b}=0\\[2ex] r=R_2: & \dfrac{\mathrm{D}q}{\mathrm{D}b}=-\dfrac{\mathrm{D}}{\mathrm{D}b}\Big(\dfrac{\partial V}{\partial r}\Big)=-\dfrac{\partial}{\partial r}\Big(\dfrac{\mathrm{D}V}{\mathrm{D}b}\Big)+\dfrac{\partial V}{\partial r}\dfrac{\partial v}{\partial r}=0\\[2ex] t=0: & \dfrac{\mathrm{D}V}{\mathrm{D}b}=\dfrac{\mathrm{D}V_0}{\mathrm{D}b}=0\end{cases} \tag{2.16}$$

this means

$$\begin{cases} r = R_1,: & U(r,t) = 0 \\ r = R_2\ : & W(r,t) = 0 \\ t = 0\ : & U(r,t) = 0 \end{cases} \tag{2.17}$$

where

$$W(r,t) = -\frac{\partial U(r,t)}{\partial r} \tag{2.18}$$

In equation (2.13), the velocity field $v(r,b)$ associated with the design parameter $b = R_1$ is defined as follows

$$v = v(r,b) = \frac{R_2 - r}{R_2 - b} \tag{2.19}$$

It should be pointed out that the additional problem (c.f. equations (2.13), (2.17)) connected with the sensitivity function $U(r,t)$ is coupled with the basic one (c.f. equations (1.5), (1.7)) by the functions $V(r,t)$ and $\Phi[T(V)]$.

3. Method of solution

The basic problem and the additional one have been solved using a combined variant of BEM (Brebbia and Dominiguez, 1992; Kałuża, 2005; Majchrzak, 2001) supplemented by the artificial heat source procedure (Majchrzak and Mochnacki, 1996).

Let us consider the following equation

$$\Phi[T(V)]\frac{\partial F(r,t)}{\partial t} = \frac{1}{r^2}\frac{\partial}{\partial r}\Big[r^2\frac{\partial F(r,t)}{\partial r}\Big] + R(r,t) \tag{3.1}$$

where for the basic problem $F(r,t) = V(r,t)$, $R(r,t) = 0$ (cf. equation (1.5)), while for the additional problem $F(r,t) = U(r,t)$ and (cf. equations (2.13), (2.15))

$$\begin{aligned} R(r,t) = {} & \frac{2\Phi[T(V)]}{R_2 - b}\frac{\partial V(r,t)}{\partial t} + \frac{1}{\lambda^2[T(V)]}\Big(\frac{d\lambda}{dT}\Phi[T(V)] - \frac{dC}{dT}\Big)U(r,t)\frac{\partial V(r,t)}{\partial t} + \\ & -2\Big[\frac{1}{r(R_2 - b)} + \frac{R_2 - r}{r^2(R_2 - b)}\Big]\frac{\partial V(r,t)}{\partial r} \end{aligned} \tag{3.2}$$

Using the artificial heat source method ((Majchrzak and Mochnacki, 1996) the function $\Phi[T(V)]$ is expressed as a sum of two components, which entails a constant part Φ_0 and a certain increment $\Delta\Phi[T(V)]$, see Fig. 3

$$\Phi[T(V)] = \Phi_0 + \Delta\Phi[T(V)] \tag{3.3}$$

Equation (3.1) can be written in the form

$$\Phi_0 \frac{\partial F(r,t)}{\partial t} = \frac{1}{r^2}\frac{\partial}{\partial r}\Big[r^2 \frac{\partial F(r,t)}{\partial r}\Big] + S(r,t) \tag{3.4}$$

where

$$S(r,t) = R(r,t) - \Delta\Phi[T(V)]\frac{\partial F(r,t)}{\partial t} \tag{3.5}$$

is the source function (capacity of internal heat sources).

The essential feature of equation (3.4) consists in the fact that leaving out the last term, we obtain a linear form of energy equation. The calculation of the source function requires the introduction of a certain iterative procedure (Majchrzak and Mochnacki, 1996).

In order to solve equation (3.4), BEM using discretization in the time domain is applied (Brebbia and Dominiguez, 1992; Kałuża, 2005; Majchrzak, 2001). At first, the time derivative appearing in equation (3.4) is substituted by a differential quotient

$$t \in [t^{f-1}, t^f] : \qquad \frac{\partial F(r,t)}{\partial t} = \frac{F(r,t^f) - F(r,t^{f-1})}{\Delta t} \tag{3.6}$$

and then equation (3.4) takes form

$$\frac{\partial}{\partial r}\Big[r^2 \frac{\partial F(r,t^f)}{\partial r}\Big] - \frac{\Phi_0}{\Delta t} r^2 F(r,t^f) + \frac{\Phi_0}{\Delta t} r^2 F(r,t^{f-1}) + r^2 S(r,t^f) = 0 \tag{3.7}$$

Next, the weighted residual criterion is applied

$$\begin{split}\int\limits_{R_1}^{R_2} \Big\{ \frac{\partial}{\partial r}\Big[r^2 \frac{\partial F(r,t^f)}{\partial r}\Big] - \frac{\Phi_0}{\Delta t} r^2 F(r,t^f) + \\ + \frac{\Phi_0}{\Delta t} r^2 F(r,t^{f-1}) + r^2 S(r,t^f)\Big\} F^*(\xi,r)\, dr = 0\end{split} \tag{3.8}$$

where ξ is the observation point and $F^*(\xi,r)$ is the fundamental solution

$$F^*(\xi,r) = \frac{1}{2r\xi}\sqrt{\frac{\Delta t}{\Phi_0}}\Big[\exp\Big(-|r-\xi|\sqrt{\frac{\Phi_0}{\Delta t}}\Big) - \exp\Big(-|r+\xi|\sqrt{\frac{\Phi_0}{\Delta t}}\Big)\Big] \tag{3.9}$$

After mathematical transformations of criterion (3.8), one obtains

$$
\begin{aligned}
&F(\xi, t^f) + \Big[r^2 F^*(\xi, r) J(r, t^f)\Big]_{r=R_1}^{r=R_2} = \Big[r^2 J^*(\xi, r) F(r, t^f)\Big]_{r=R_1}^{r=R_2} + \\
&+\frac{\Phi_0}{\Delta t}\int_{R_1}^{R_2} r^2 F(r, t^{f-1}) F^*(\xi, r)\, dr + \int_{R_1}^{R_2} r^2 S(r, t^f) F^*(\xi, r)\, dr
\end{aligned}
\tag{3.10}
$$

where

$$
\begin{aligned}
&J^*(\xi, r) = -\frac{\partial F^*(\xi, r)}{\partial r} = \frac{1}{r} F^*(\xi, r) + \\
&+\frac{1}{2r\xi}\Big[\operatorname{sgn}(r-\xi)\exp\Big(-|r-\xi|\sqrt{\frac{\Phi_0}{\Delta t}}\Big) - \operatorname{sgn}(r+\xi)\exp\Big(-|r+\xi|\sqrt{\frac{\Phi_0}{\Delta t}}\Big)\Big]
\end{aligned}
\tag{3.11}
$$

and

$$
J(r, t^f) = -\frac{\partial F(r, t^f)}{\partial r} \tag{3.12}
$$

Equation (3.10) can be written in the form

$$
\begin{aligned}
&F(\xi, t^f) + R_2^2 F^*(\xi, R_2) J(R_2, t^f) - R_1^2 F^*(\xi, R_1) J(R_1, t^f) = \\
&= R_2^2 J^*(\xi, R_2) F(R_2, t^f) - R_1^2 J^*(\xi, R_1) F(R_1, t^f) + P(\xi) + Z(\xi)
\end{aligned}
\tag{3.13}
$$

where

$$
\begin{aligned}
P(\xi) &= \frac{\Phi_0}{\Delta t}\int_{R_1}^{R_2} r^2 F(r, t^{f-1}) F^*(\xi, r)\, dr \\
Z(\xi) &= \int_{R_1}^{R_2} r^2 S(r, t^f) F^*(\xi, r)\, dr
\end{aligned}
\tag{3.14}
$$

For $\xi \to R_1^+$ and $\xi \to R_2^-$, one obtains the following system of equations

$$
\begin{aligned}
&\begin{bmatrix} -R_1^2 F^*(R_1, R_1) & R_2^2 F^*(R_1, R_2) \\ -R_1^2 F^*(R_2, R_1) & R_2^2 F^*(R_2, R_2) \end{bmatrix} \begin{bmatrix} J(R_1, t^f) \\ J(R_2, t^f) \end{bmatrix} = \\
&= \begin{bmatrix} -R_1^2 J^*(R_1^+, R_1) - 1 & R_2^2 J^*(R_1^+, R_2) \\ -R_1^2 J^*(R_2^-, R_1) & R_2^2 J^*(R_2^-, R_2) - 1 \end{bmatrix} \begin{bmatrix} F(R_1, t^f) \\ F(R_2, t^f) \end{bmatrix} + \begin{bmatrix} P(R_1) \\ P(R_2) \end{bmatrix} + \begin{bmatrix} Z(R_1) \\ Z(R_2) \end{bmatrix}
\end{aligned}
\tag{3.15}
$$

from which the unknown boundary values $J(R_1,t^f)$, $F(R_2,t^f)$ are determined. Values of the function F at the internal points $\xi \in (R_1,R_2)$ are calculated using the formula

$$
\begin{aligned}
F(\xi,t^f) &= R_2^2 J^*(\xi,R_2)F(R_2,t^f) - R_1^2 J^*(\xi,R_1)F(R_1,t^f) + \\
&-R_2^2 F^*(\xi,R_2)J(R_2,t^f) + R_1^2 F^*(\xi,R_1)J(R_1,t^f) + P(\xi) + Z(\xi)
\end{aligned}
\tag{3.16}
$$

4. Results of computations

A cryoprobe of diameter $R_1 = 0.005\,\mathrm{m}$ has been considered. The surface temperature is assumed as $-90°\mathrm{C}$. The external radius of the tissue domain: $R_2 = 0.025\,\mathrm{m}$. The initial temperature of tissue $T_0 = 37°\mathrm{C}$. The domain of tissue has been divided into 600 linear internal cells, time step $\Delta t = 0.5\,\mathrm{s}$ and constant $\Phi_0 = 4 \cdot 10^7$ (see equation (3.4) and Fig. 3).

In Figure 4a, the temperature distribution in the tissue for times instants 5, 10, 15, ..., 60 s is shown. Figure 4b illustrates cooling curves at the points $r = 0.006$, 0.007, 0.008, 0.009 and 0.01 m. In Figure 5a, the distribution of the sensitivity function $U = \mathrm{D}V/\mathrm{D}b$ in the domain considered for instants 5, 10, 15, ..., 60 s is presented. Figure 5b shows courses of the function U at selected points in the tissue domain.

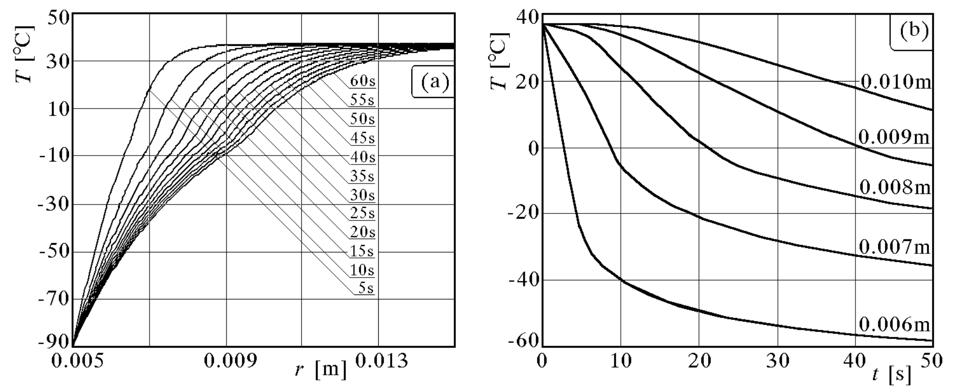

Fig. 4. (a) Temperature distribution; (b) cooling curves

The function $V(r,t,R_1)$ is expanded into Taylor series taking into account the first two components

$$
V(r,t,R_1 \pm \Delta R_1) = V(r,t,R_1) \pm U(r,t,R_1)\Delta R_1 \tag{4.1}
$$

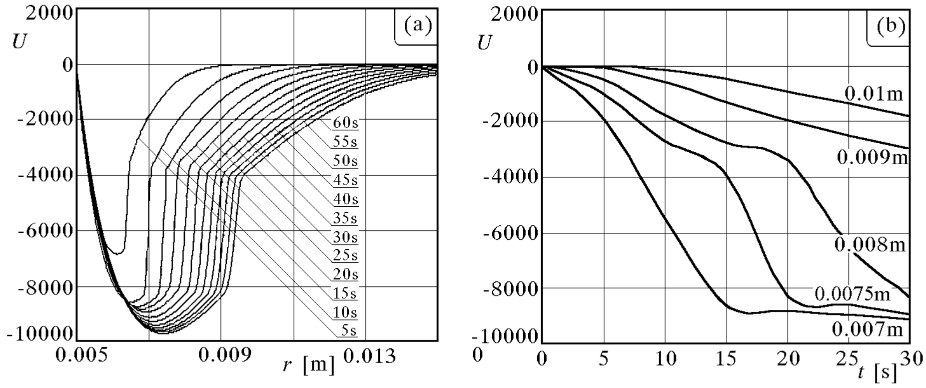

Fig. 5. (a) Distribution of the function $U = \mathrm{D}V/\mathrm{D}b$; (b) courses of the function U at selected points

Thus, using the solutions $V(r, t, R_1)$ and $U(r, t, R_1)$, it is possible to obtain solutions corresponding to cryoprobe radii $R_1 - \Delta R_1$ and $R_1 + \Delta R_1$. Figures 6 present results obtained this way on the assumption that $\Delta R_1 = 0.1 R_1$.

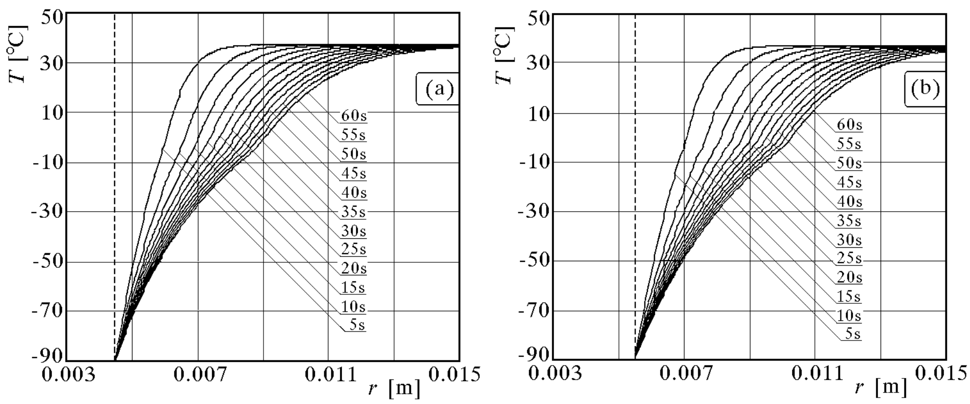

Fig. 6. (a) Temperature distribution for $R_1 - \Delta R_1$; (b) temperature distribution for $R_1 + \Delta R_1$

Summing up, the solutions to the basic and additional problem allow one (using the Taylor formula) to rebuilt the results obtained on the infinite number of other solutions corresponding to the changed cryoprobe radii. In this way, it is possible to analyze mutual connections between the radius of the cryoprobe and the course of freezing process proceeding in the tissue domain.

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Analiza wrażliwości procesu zamrażania tkanki biologicznej ze względu na promień kriosondy sferycznej

Streszczenie

Praca dotyczy zastosowania analizy wrażliwości kształtu w zagadnieniach modelowania procesu zamrażania tkanki biologicznej. Proces ten jest opisany silnie nieliniowym równaniem przepływu biociepła, w którym pojawia się dodatkowy składnik związany z wydzielaniem się utajonego ciepła zamrażania. Formalne przekształcenia wyjściowego równania opisującego proces prowadzi do równania różniczkowego, w którym występuje zastępcza pojemność cieplna tkanki (tzw. metoda jednego obszaru).

Odpowiednio przyjęte warunki brzegowe determinują oddziaływania termiczne między tkanką a końcówką kriosondy.

W pracy rozważa się sferyczną kriosondę wewnętrzną. W celu oszacowania wpływu geometrii kriosondy na przebieg procesu zamrażania wykorzystano podejście bezpośrednie analizy wrażliwości kształtu. Wyniki obliczeń numerycznych otrzymane za pomocą metody elementów brzegowych pozwoliły na sformułowanie wniosków przydatnych w praktyce kriochirurgicznej.

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