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Sensitivity analysis and inverse problems in bio-heat transfer modelling

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In the paper the problems connected with numerical modelling of bio-heat transfer processes are discussed. The mathematical model of phenomena discussed bases on the Pennes equation, at the same time the steady and transient tasks are considered. The basic equation is supplemented by the adequate geometrical, physical, boundary and (in the case of transient heat transfer) initial conditions. In the first part of the paper the examples of direct solutions are discussed. Next the possibilities of sensitivity analysis applications in the domain of bio-heat transfer are presented. In the final part the selected solutions of inverse problems are shown. On the stage of numerical simulations both in the case of direct and inverse problems, as a rule, the different variants of the boundary element method have been used.

1. Governing equations

Heat transfer processes proceeding in the domain of biological tissue are described by the following Pennes equation [18, 60],

$$x \in \Omega: \quad c(T)\frac{\partial T(x,t)}{\partial t} = \nabla[\lambda(T)\nabla T(x,t)] + G\,c_B[T_B - T(x,t)] + Q_m\,, \tag{1}$$

where Ω is a tissue domain, c is a tissue volumetric specific heat, λ is a tissue thermal conductivity, G is a perfusion coefficient, c_B is a blood volumetric specific heat, T_B is an arterial blood temperature, Q_m is a metabolic heat source, T, x, t denote temperature, spatial co-ordinates and time.

If one considers the biological tissue freezing (e.g. cryosurgery treatment) then the right hand side of Eq. (1) must be supplemented by the term controlling the freezing process, namely [6, 10, 24, 25]

$$Q_f = L\frac{\partial f_S(x,t)}{\partial t}\,, \tag{2}$$

where L is a volumetric latent heat, f_S is a volumetric fraction of frozen state at the neigbourhood of considered point from tissue domain.

The basic assumption of such model of bio-heat transfer is that the tissue is supplied by the big number of small blood vessels. In the case of large vessels existence in the domain analyzed, Eq. (1) must be supplemented by the additional one concerning the vessel (or vessels) domain [38, 39, 54].

On the outer surface of the system the boundary conditions in general form

$$x \in \Gamma_0 : \quad \Phi\left[T(x,t), \frac{\partial T(x,t)}{\partial n}\right] = 0 \tag{3}$$

are given ($\partial T/\partial n$ denotes a normal derivative).

In the case of transient problems the initial condition

$$t = 0 : \quad T(x,0) = T_0(x) \tag{4}$$

is also known.

2. Examples of direct problems numerical solutions

2.1. Simulation of thermal processes in the skin tissue subjected to an external heat sources

The first example concerns the heating of skin subjected to an external heat source. The source is of duration t_0 and it generates on a skin surface the temperature $T(0,t)$. When the exposure ended, the cooling of skin surface proceeds according to the Newton formula (3rd kind boundary condition). The thermophysical parameters of successive skin layers (epidermis, dermis and sub-cutaneous region, Fig. 1) are different [42, 62]. The knowledge of heating (cooling) curves at the boundary points on the contact surfaces epidermis-dermis and dermis-sub-cutaneous region allow to predict the burn degree on the basis of so-called Henriques integrals [13, 14, 29, 31, 32].

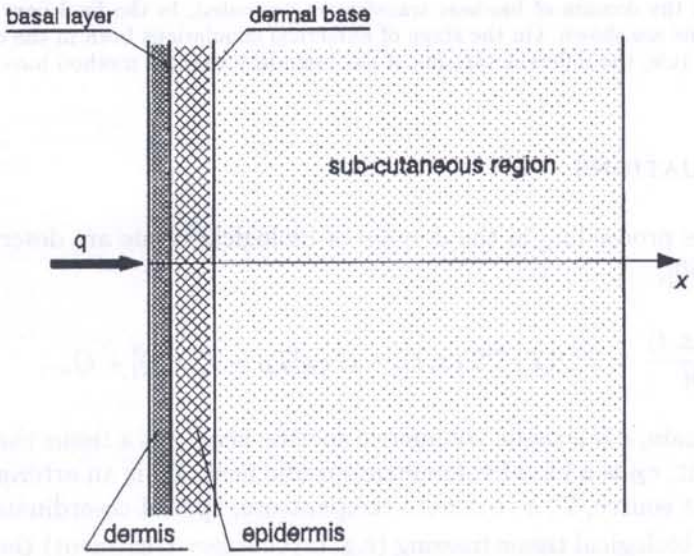

Fig. 1. Sub-domains of skin

Thermal damage of skin begins when the temperature at the basal layer (the interface between epidermis and dermis) rises above 44 [°C] (317 [K]) and Henriques found that the degree of skin damage could be predicted on the basis of the integrals

$$I_b = \int_0^t P_b(T_b) \exp\left(-\frac{\Delta E}{RT_b(\tau)}\right) \mathrm{d}\tau, \qquad I_d = \int_0^t P_d(T_d) \exp\left(-\frac{\Delta E}{RT_d(\tau)}\right) \mathrm{d}\tau, \tag{5}$$

where $\Delta E/R$ [K] is the ratio of activation energy to universal gas constant, P_b, P_d [1/s] are the pre-exponential factors and they are defined as follows,

$$P_b = \begin{cases} 0 & T_b < 317, \\ 1.43 \cdot 10^{72} & T_b \geq 317, \end{cases} \qquad P_d = \begin{cases} 0 & T_d < 317, \\ 2.86 \cdot 10^{69} & T_d \geq 317, \end{cases} \tag{6}$$

while T_b [K] and T_d [K] are the temperatures of basal layer and dermal base (the interface between dermis and underlying sub-cutaneous region), respectively. First degree burns are said to occur when the value of the burn integral is from the interval $0.53 < I_b \leq 1$, while the second degree burns when $I_b > 1$. Third degree burns are said to occur when $I_d \geq 1$.

So, in order to determine the values of integrals I_b and I_d the heating and next the cooling curves for the basal and dermal surfaces must be known. The problem can be solved using the numerical methods. Taking into account the geometry of multilayer domain Ω, the 1D task is considered and this simplification is sufficiently exact. So, the following system of Pennes equations is taken into account [14, 31–33, 35, 62],

$$x \in \Omega_e : \quad c_e \frac{\partial T_e(x,t)}{\partial t} = \lambda_e \frac{\partial^2 T_e(x,t)}{\partial x^2} + G_e c_B [T_B - T_e(x,t)] + Q_{me}\,, \tag{7}$$

where $e = 1, 2, 3$.

The mathematical model is supplemented by the following boundary-initial conditions

- the condition on the skin surface

$$x = 0 : \quad \begin{cases} T_1(x,t) = T_0 & t \leq t_0\,, \\ q_1(x,t) = -\alpha[T_1(x,t) - T^{\infty}] & t > t_0\,, \end{cases} \tag{8}$$

  where T_0 is the boundary temperature resulting from the contact between the skin surface and external heat source, t_0 is the duration of thermal pulse, $q_1(x,t)$ is the heat flux between the skin and environment after time t_0 (α is the heat transfer coefficient, while T^{∞} is the ambient temperature),

- the condition of ideal contact on the basal layer and dermal base

$$x = x_e : \quad \begin{cases} -\lambda_e \dfrac{\partial T_e(x,t)}{\partial x} & = -\lambda_{e+1} \dfrac{\partial T_{e+1}(x,t)}{\partial x}\,, \\ T_e(x,t) & = T_{e+1}(x,t)\,, \end{cases} \tag{9}$$

  where $e = 1, 2$,

- the condition on the external surface of sub-cutaneous region

$$x = x_3 : \quad T_3(x,t) = T_B\,, \tag{10}$$

- the initial condition

$$t = 0 : \quad T_1(x,0) = T_{10}(x), \quad T_2(x,0) = T_{20}(x), \quad T_3(x,0) = T_{30}(x), \tag{11}$$

  where T_{10}, T_{20} and T_{30} are the initial temperatures of successive sub-domains.

As it was mentioned on the stage of numerical computations the BEM (the first scheme of the BEM) has been used [2, 5, 21]. The details concerning this algorithm in the case of non-homogeneous domains can be found in [21, 29].

The input data used in presented below examples have been taken from [62]. The skin constitutes a composition of three layers of thicknesses $L_1 = 0.1$ [mm], $L_2 = 1$ [mm], $L_3 = 10$ [mm]. The initial temperature distribution is a parabolic one and at point corresponding to skin surface $T = 32.5$ [°C], while at point corresponding to the total skin thickness $T = T_B = 37$ [°C].

The solution presented concerns the heating determined by heat source generating the skin surface temperature $T_0 = 70$ [°C] during exposure time $t_0 = 2$ [s]. In Fig. 2 the cooling curves $T_b(t)$ and $T_d(t)$ are shown. It turned out that after the time 1.15 [s] the second degree burn takes place, but the third degree burn doesn't appear – Fig. 3.

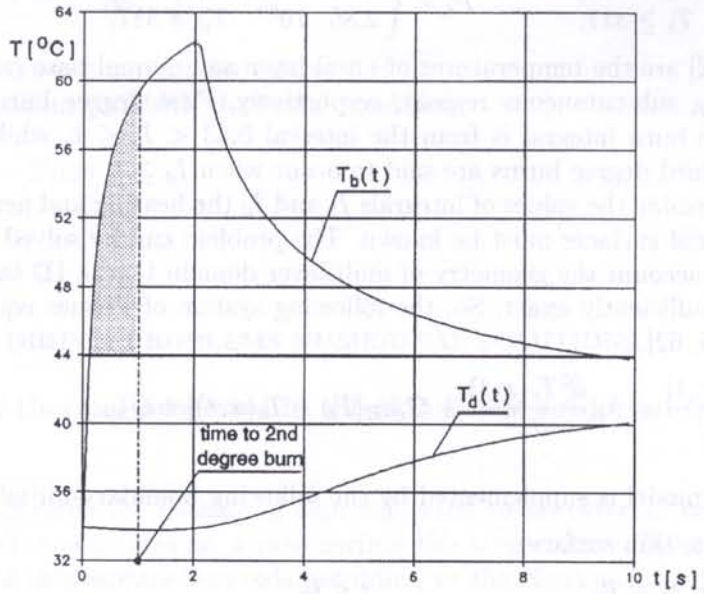

Fig. 2. Heating (cooling) curves ($T_0 = 70°\mathrm{C}$, $t_0 = 2$ s)

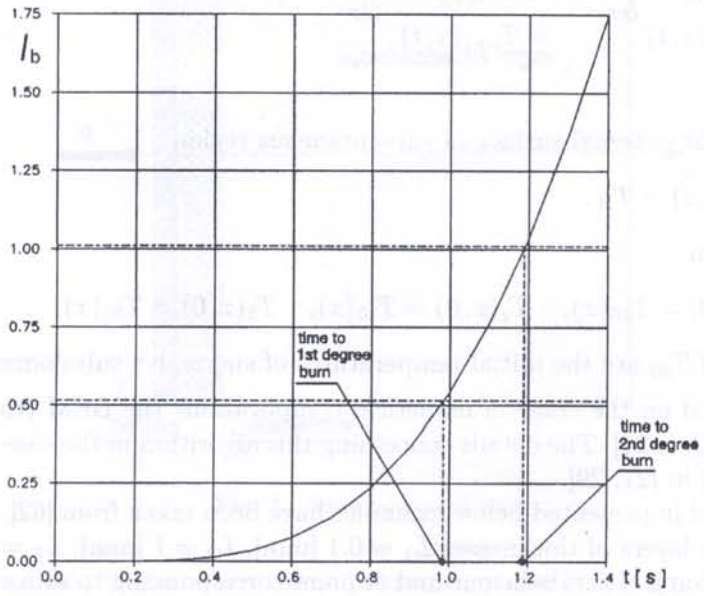

Fig. 3. Burn integral $I_b(t)$

2.2. Numerical simulation of freezing process

The well known phenomena, concerning the destructive effect of freezing on biological tissue, account for the broad application of cryogenic surgery. Tissue reactions to cryosurgical process depend on temperature changes and on rates of temperature changes caused by freezing probes. Below, the example of 2D solution (axially-symmetrical task) will be shown [11, 12, 23]. In order to solve the problem the mathematical model has been transformed to the enthalpy convention. On the stage of numerical computations the boundary element algorithm for parabolic equations has been used, while the 'non-linearities' of freezing and thawing mathematical description are taken into account by introduction of the numerical procedure called the alternating phase truncation method (APTM) [41, 61]. The basic energy equation describing the process is of the form (see: equations (1) and (2))

$$x \in \Omega: \quad c(T)\,\frac{\partial T(x,t)}{\partial t} = \nabla[\lambda(T)\,\nabla T(x,t)] + L\,\frac{\partial f_S(x,t)}{\partial t}\,. \tag{12}$$

One can see that the perfusion and metabolic heat sources are here neglected (they are essentially less than the term controlling the freezing process). If one assumes the knowledge of function f_S in the temperature interval $[T_2, T_1]$ (the beginning and the end of freezing) then

$$L\,\frac{\partial f_S(x,t)}{\partial t} = L\,\frac{\mathrm{d}f_S}{\mathrm{d}T}\,\frac{\partial T(x,t)}{\partial t} \tag{13}$$

and finally

$$x \in \Omega: \quad C(T)\,\frac{\partial T(x,t)}{\partial t} = \nabla[\lambda(T)\,\nabla T(x,t)] \tag{14}$$

where

$$C(T) = c(T) - L\,\frac{\mathrm{d}f_S}{\mathrm{d}T} \tag{15}$$

is called the substitute thermal capacity. Because the last equation concerns the whole tissue domain therefore this approach is known as the one domain method [19, 37, 51].

The volumetric physical enthalpy of tissue is defined as follows

$$H(T) = \int_{T_r}^{T} C(\mu)\,\mathrm{d}\mu \tag{16}$$

where T_r is an arbitrary assumed reference level. Introducing this function to Eq. (14) one obtains

$$x \in \Omega: \quad \frac{\partial H(x,t)}{\partial t} = \nabla[a(T)\,\nabla H(x,t)] \tag{17}$$

where $a = \lambda/C$ is the diffussivity coefficient.

The boundary and initial conditions should be also transformed to the enthalpy convention. The simple mathematical manipulations can be found, among others, in [21, 51].

In Figs. 4 and 5 the courses of $C(T)$ and $\lambda(T)$ [6] are shown. In order to use (on the stage of numerical computations) the standard BEM algorithm for linear parabolic equations the alternating phase truncation method (APTM) can be applied. The transition from t to $t+\Delta t$ requires the solving of three linear problems for the parameters corresponding to the natural state of tissue, intermediate phase and frozen region and after every loop the results are in a certain way corrected. The details of APTM can be found in [41].

The example presented below concerns the external cylindrical cryoprobe, the system considered is shown in Fig. 6. The surface of cryoprobe is in ideal thermal contact with a skin surface and the temperature of contact surface changes according to formula

$$x = 0: \begin{cases} T_b(t) = T_c - \nu_1 t\,, & t \le t_e\,, \\ T_b(t) = T_{\mathrm{end}} + \nu_2 t\,, & t_e < t < t_{\mathrm{end}}\,, \\ T_b(t) = T_c\,, & t \ge t_{\mathrm{end}}\,, \end{cases} \tag{18}$$

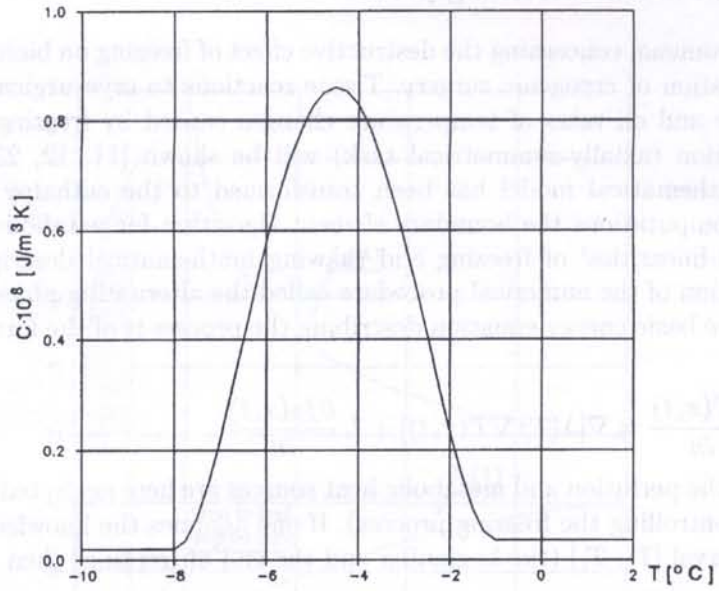

Fig. 4. Substitute thermal capacity

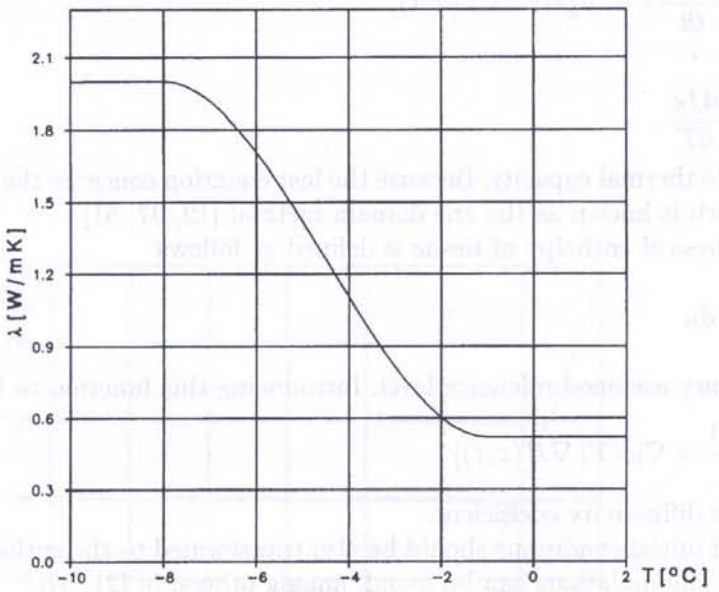

Fig. 5. Thermal conductivity of tissue

where T_c is the initial temperature of cryoprobe surface ($T_c = 37$ [°C]), v_1 is the cooling rate ($v_1 = 5$, 10, 15 [K/min]), v_2 is the heating rate ($v_2 = 30$ [K/min]), t_e is the time for which the temperature of skin surface reaches -63 [°C], while t_{end} is the time for which this surface reaches the initial temperature T_c.

In Fig. 7 the part of the results is presented. The boundary temperatures of cryoprobe are marked by the heavy lines. The cooling and heating curves for the points $x = 0$, 5, 10, 15, 20 [mm] (axis of symmetry) are also shown. The others problems of freezing process numerical simulation are discussed in papers [10–12, 23–25, 37, 47–49].

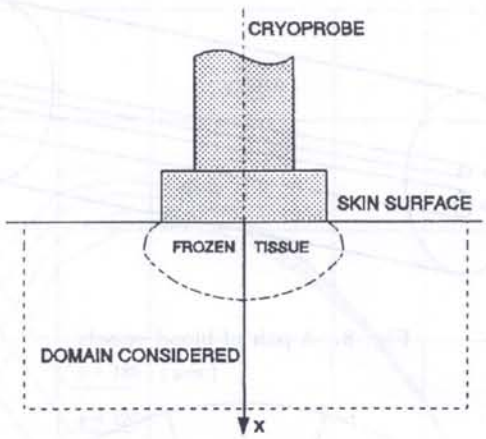

Fig. 6. Domain considered

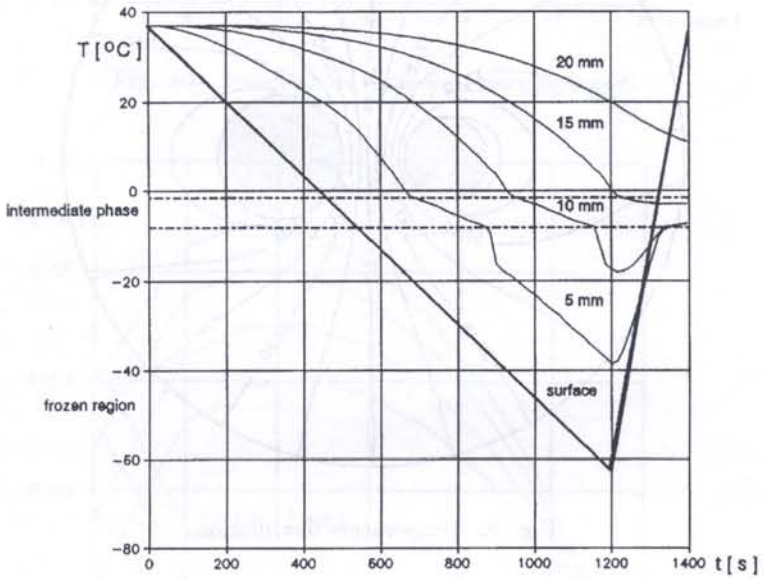

Fig. 7. Cooling and heating curves for $v_1 = 5$ [K/min]

2.3. Thermal interactions between blood vessels and tissue

The problem of heat exchange between blood vessel and biological tissue is very interesting, first of all, from the scientific point of view. As was mentioned, the Pennes equation has been found under the assumption that the tissue is supplied by the big number of small vessels. The large vessel and its interactions with the tissue must be treated separately. For example, if one considers the lateral section of domain in which the pair of vessels (artery and vein) is located (the domain in which the thermal interactions take place corresponds to the so-called Krough cylinder [22, 56] — Fig. 8) then on the contact surfaces between vessels and tissue the additional boundary conditions must be assumed (in the form of Robin ones). The steady state problem is, as a rule, considered at the same time the blood temperatures in both vessels are different. The heat transfer coefficients appearing in the Robin boundary conditions correspond to the Nusselt number equals 4 [56]. Below, the example of such problem solution is presented [22, 56]. It is obtained for the following input data: artery radius $R_1 = 0.2$ [mm], vein radius $R_2 = 0.3$ [mm], Krough cylinder radius $R = 1.5$ [mm], distance between vessels $D = 0.3$ [mm]. In Fig. 9 the temperature distribution in the rest conditions (metabolic heat source $Q_m = 245$ [W/m^3]) is shown.

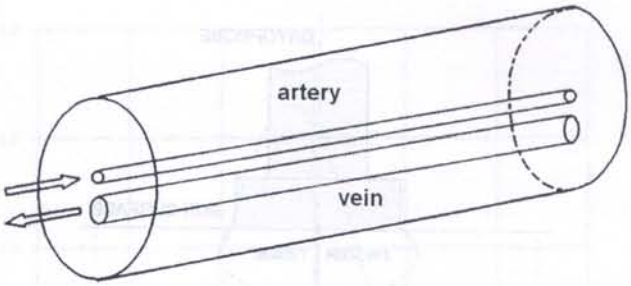

Fig. 8. A pair of blood vessels

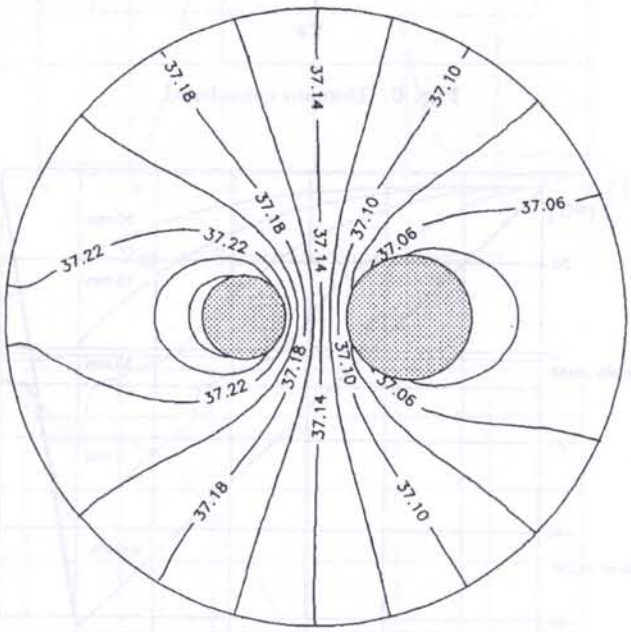

Fig. 9. Temperature distribution

The more complex problem depends on the modelling of heat transfer in the system considered under the assumption that the blood temperature changes along the vessel. For the tissue domain the Pennes equation is accepted, while the change of blood temperature results from the following equation (see: [38, 39]),

$$c_B w F \frac{\mathrm{d}T_B(z)}{\mathrm{d}z} + \alpha P[T_B(z) - T(R_1, z)] = 0, \tag{19}$$

at the same time

$$z = 0: \quad T_B(0) = T_{B0}\,. \tag{20}$$

In Eq. (19) the blood temperature corresponding to co-ordinate r is uniform, this means $T_B(r,z) = T_B(z)$, while w is the blood velocity, F is the vessel lateral section, P is the vessel periphery, α is the heat transfer coefficient between blood and tissue, $T(R_1, z)$ is the vessel wall temperature. The coupling of the Pennes equation and Eq. (19) results from the boundary condition given on the vessel wall. On the stage of numerical modelling the algorithm being the composition of the BEM (tissue) and finite differences method (vessel) has been applied.

Presented below results concern the single vessel ($R_1 = 0.2$ [mm]), tissue radius equals $R = 10R_1$, vessel length $Z = 0.18$ [m]. Two models have been considered [26]. In the first version the blood

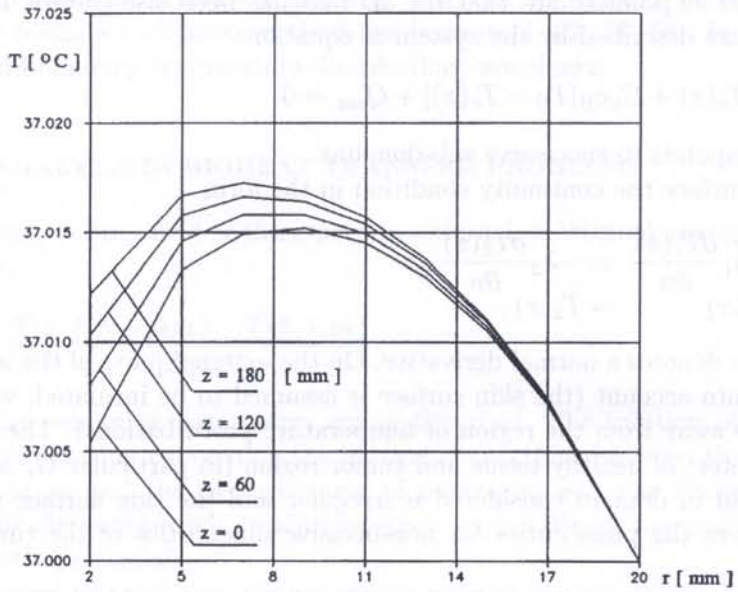

Fig. 10. Temperature profiles (traversing vessel)

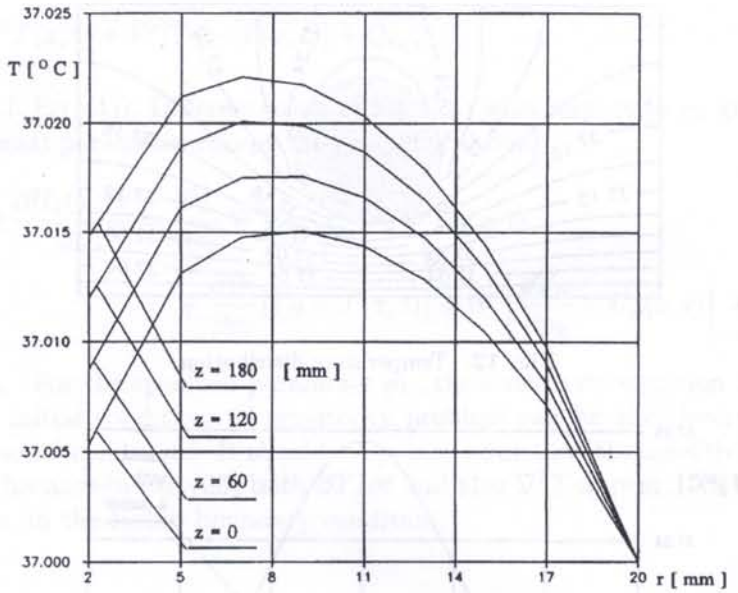

Fig. 11. Temperature profiles (supplying vessel)

temperature in the Pennes equation has been assumed to be constant end equal to blood temperature for $z = 0$ (traversing vessel), while in the second model the blood temperature in the Pennes equation was equal to $T_B(z)$ (supplying vessel).

In Figs. 10 and 11 the solutions obtained for different values of co-ordinate z are shown. One can see that differences between two models considered are visible.

2.4. Temperature distribution in the tissue with a tumor

The last example of direct problem numerical solution concerns the heterogeneous system healthy tissue - tumor region [17]. In particular, the results concerning the 2D problem will be presented [40,

43, 55] but, it should be pointed out, that the 3D task has been also solved. Thermal processes in domain considered are described by the system of equations

$$x \in \Omega_e : \quad \lambda_e \nabla^2 T_e(x) + G_e c_B [T_B - T_e(x)] + Q_{me} = 0 \tag{21}$$

where $e = 1, 2$ corresponds to successive sub-domains.

On the contact surface the continuity condition in the form

$$x \in \Gamma_{12} : \quad \begin{cases} -\lambda_1 \dfrac{\partial T_1(x)}{\partial n} & = -\lambda_2 \dfrac{\partial T_2(x)}{\partial n} \\ T_1(x) & = T_2(x) \end{cases}, \tag{22}$$

is given, where $\partial/\partial n$ denotes a normal derivative. On the external parts of the boundary the no-flux condition is taken into account (the skin surface is assumed to be insulated, while the other parts of the boundary are away from the region of temperature perturbations). The essential differences between the parameters of healthy tissue and tumor region (in particular G_e and Q_{me}) cause that the temperature field in domain considered is irregular and the skin surface temperature is non-homogeneous. It gives the possibilities for non-invasive diagnostics of the tumor presence in the tissue domain.

As the example, the solution of the following task will be presented [45]. The tissue of dimensions 0.06×0.03 [m] with a tumor of radius $R = 0.0075$ [m] and center $(0.03, 0.015)$ is considered. The

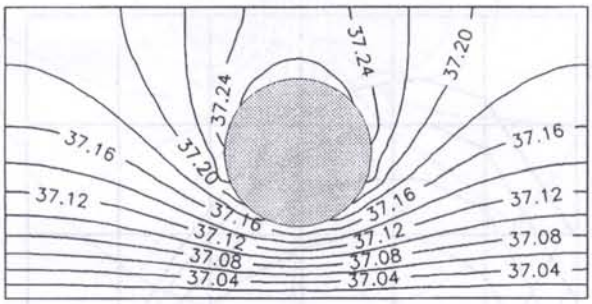

Fig. 12. Temperature distribution

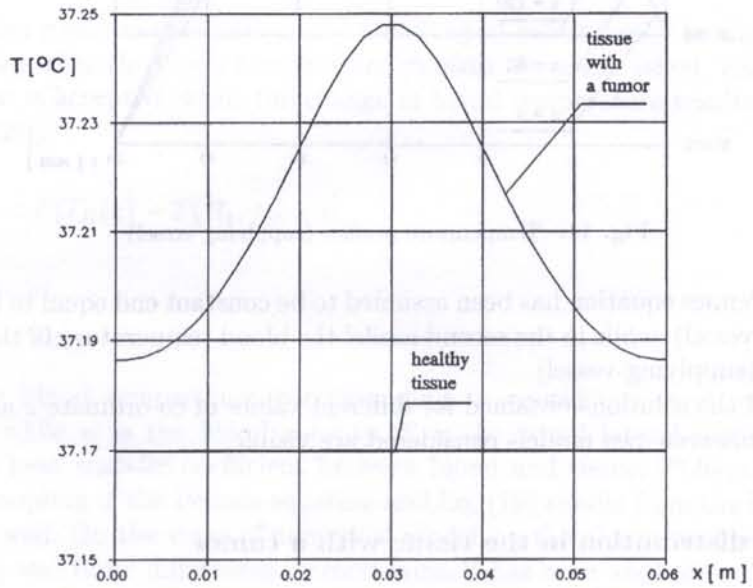

Fig. 13. Skin surface temperature

thermal parameters of sub-domains are taken from [17]. On the stage of numerical simulation the multiple reciprocity boundary element method has been used [22, 57, 58]. In Figs. 12 and 13 the results (internal and boundary temperature distribution) are shown.

3. Sensitivity analysis in bioheat transfer problems

The sensitivity of temperature field with respect to external or internal parameters $p_1, p_2, \ldots, p_n$ is defined as follows,

$$U_k(x,t) = \lim_{\Delta p_k \to 0} \frac{T(x,t,p_k+\Delta p_k) - T(x,t,p_k)}{\Delta p_k}, \tag{23}$$

at the same time the remaining parameters are undisturbed. The solution of sensitivity problem gives the essential information concerning the mutual connections between the steady or transient temperature distribution and the perturbations of parameter p_k. The sensitivity model can be constructed using the direct approach or adjoined one [7–9, 15]. Below the first version of sensitivity analysis will be shortly presented.

If the direct approach is used then the equations determining the thermal processes in domain considered must be differentiated with respect to parameter p_k analyzed. Let us consider the Pennes equation for the constant values of thermal parameters,

$$c\frac{\partial T(x,t)}{\partial t} = \lambda \nabla^2 T(x,t) + W[T_B - T(x,t)] + Q_m, \tag{24}$$

where $W = Gc_B$ (c.f. Eq. (1)). Differentiation of Eq. (24) with respect to p_k gives (here p_k denotes the internal or external parameter except the geometrical one)

$$\frac{\partial c}{\partial p_k}\frac{\partial T(x,t)}{\partial t} + c\frac{\partial U_k(x,t)}{\partial t} = \frac{\partial \lambda}{\partial p_k}\nabla^2 T(x,t) + \lambda \nabla^2 U_k(x,t) + \frac{\partial W}{\partial p_k}[T_B - T(x,t)] + W\left[\frac{\partial T_B}{\partial p_k} - U_k(x,t)\right] + \frac{\partial Q_m}{\partial p_k} \tag{25}$$

where $U_k = \partial T/\partial p_k$. For the specified parameter p_k, the sensitivity equation is simpler, of course. The boundary and initial conditions of sensitivity problem can be also determined by the differentiation of basic model conditions. It should be pointed out that the sensitivity model is coupled with the basic one, because in Eq. (25) both $\partial T/\partial t$ and also $\nabla^2 T$ appear. The same situation takes place, among others, in the Robin boundary condition.

3.1. Sensitivity analysis in thermal processes in the system tissue — blood vessel

The problem concerns the mutual connections between the temperature and capacity of metabolic heat source in the tissue domain. In order to estimate the changes of tissue and blood temperatures due to the change of this source the sensitivity analysis with respect to the Q_m has been done. Using the direct approach the following mathematical model is constructed (c.f. Section 2.3)

$$\begin{aligned}
&\lambda \nabla^2 U(r,z) + 1 + Gc_B[U_B^* - U(r,z)] = 0,\\
&r = R_1: \quad -\lambda \frac{\partial U(r,z)}{\partial r} = \alpha[U(R_1,z) - U_B(z)],\\
&r = R_2: \quad U = 0,\\
&z = 0,\ z = Z: \quad \frac{\partial U}{\partial z} = 0,
\end{aligned} \tag{26}$$

while for the blood sub-domain

$$c_B w F \frac{\mathrm{d}U_B(z)}{\mathrm{d}z} + \alpha P[U_B(z) - U(R_1, z)] = 0,$$
$$z = 0: \quad U_B(0) = 0, \tag{27}$$

where

$$U(r,z) = \frac{\partial T(r,z)}{\partial Q_m}, \qquad U_B(z) = \frac{\partial T_B(z)}{\partial Q_m} \tag{28}$$

are the sensitivity functions and $U_B^* = 0$ for supplying vessel, $U_B^* = U_B(z)$ for traversing vessel.

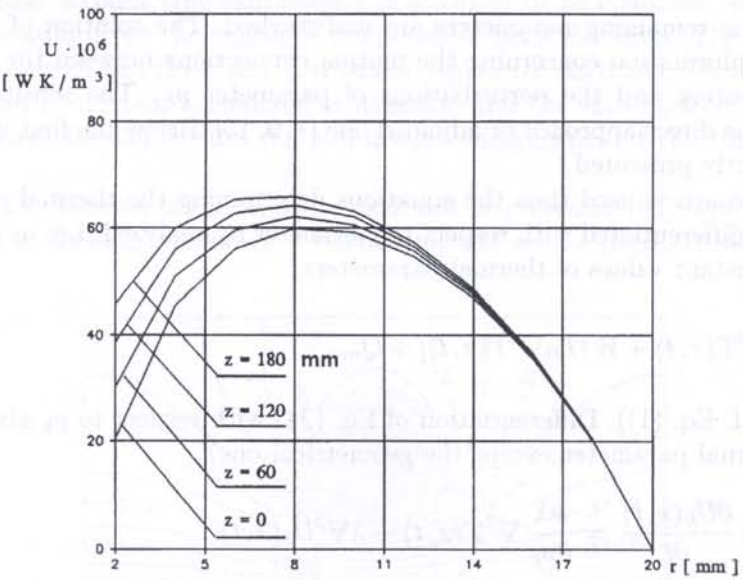

Fig. 14. Distribution of function U (traversing vessel model)

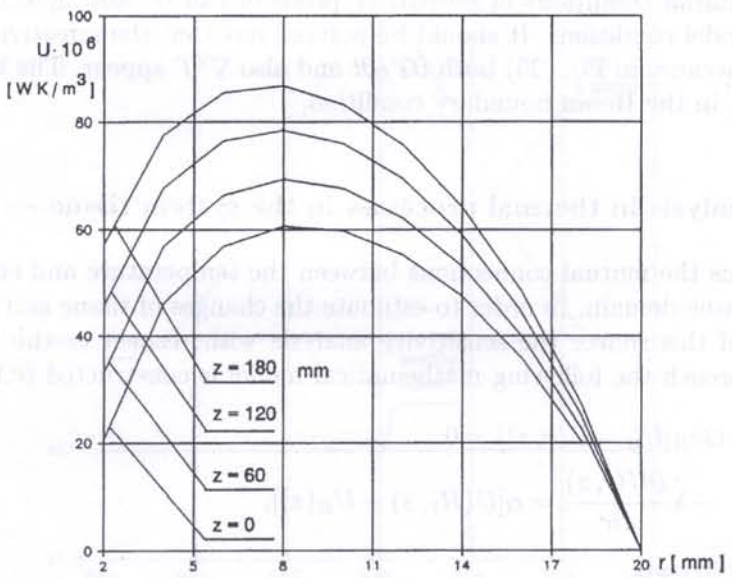

Fig. 15. Distribution of function U (supplying vessel model)

The basic problem and additional one connected with the sensitivity analysis have been solved using the hybrid algorithm [26]. For the tissue sub-domain the boundary element method has been applied, while for the blood sub-domain the finite difference method has been used. The methods have been coupled by the condition given at the vessel wall, at the same time the iterative process has been applied.

As the example the blood vessel of radius $R_1 = 0.0002$ [m] is considered. The external radius of domain is assumed as $R = 10R_1$, while $Z = 0.18$ [m]. The following input data have been introduced: $\lambda = 0.5$ [W/(mK)], $Q_m = 250$ [W/m^3], $G = 0.002$ [1/s], $c_B = 4.134 \cdot 10^6$ [J/(m^{3}K)], $w = 0.01$ [m/s], $P/F = 2/R_1$ [1/m], the Nusselt number $Nu = \alpha 2R_1/\lambda = 4$ ($\alpha = 500$ [W/(m^{2}K)]). The blood temperature T_{B0} equals 37°C, the tissue temperature equals $T(R, z) = 37$°C.

Figures 14 and 15 illustrate the distribution of sensitivity function in the radial direction and different values of z. One can notice that the sensitivity distributions are visible different for supplying and traversing vessel models. In particular, in the case of supplying vessel the sensitivity function $U = \partial T/\partial Q_m$ in surrounding tissue domain is higher than in the case of traversing vessel.

3.2. Sensitivity analysis of bioheat transfer in 2D tissue domain subjected to an external heat source

Below, the sensitivity analysis of transient temperature field in the tissue domain with respect to its thermal parameters is discussed [52]. The biological tissue is subjected to the external heat source and 2D problem is taken into account [30]. Contrary to the model presented in Section 2.1 the skin tissue is treated as the homogeneous domain. The distribution of external heat flux is shown in Fig. 16.

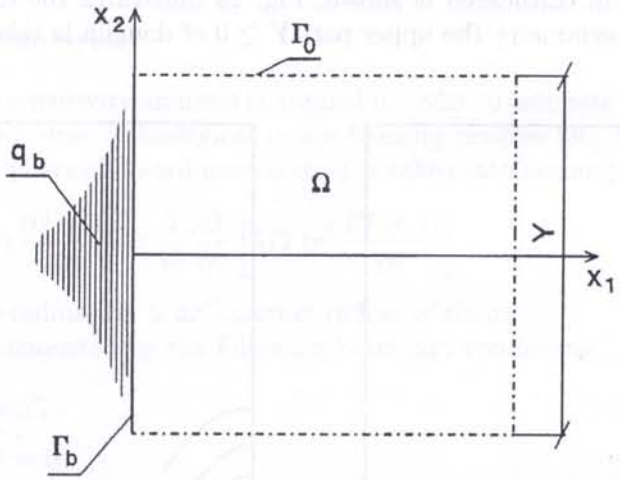

Fig. 16. Domain considered

The Pennes equation (1) is supplemented by the following boundary conditions,

$$x \in \Gamma_b: \begin{cases} q = q_b & t \le t_b, \\ q = 0 & t > t_b, \end{cases} \tag{29}$$

where q_b is the known boundary heat flux, t_b is the exposure time. The distribution of the boundary heat flux q_b is described by the polynomial of 4th degree, in particular

$$q_b(x_2) = -10^4 + 8 \cdot 10^8 x_2^2 - 1.28 \cdot 10^{13} x_2^4, \qquad x_2 \in \left[-\frac{Y}{4}, \frac{Y}{4}\right]. \tag{30}$$

Along the remaining part of the boundary $q_b = 0$. The initial condition is also given.

The sensitivity model concerning the tissue thermal conductivity is of the form

$$\begin{cases} x \in \Omega: & c\dfrac{\partial U_1}{\partial t} = \lambda \nabla^2 U_1 + \dfrac{c}{\lambda}\dfrac{\partial T}{\partial t} - WU_1\,, \\ x \in \Gamma_0: & V_1 = 0, \\ x \in \Gamma_b: & V_1 = -\dfrac{1}{\lambda} q_b\,, \\ t = 0: & U_1 = 0\,, \end{cases} \tag{31}$$

where $V_1 = -\lambda\, \partial U_1/\partial n$. The similar models can be formulated for the others parameters of process considered.

Very essential application of the sensitivity analysis results from the following considerations. Let us assume that the primary and additional problems have been solved for parameters λ_0, c_0, W_0, in other words we know the distribution of temperature field and functions U_k in domain Ω at optional time t. If we want to find the solution of primary problem for the new values of parameters $\lambda = \lambda_0 \pm \Delta\lambda$, $c = c_0 \pm \Delta c$, $W = W_0 \pm \Delta W$, we can use the Taylor formula, this means

$$T(x,\, t,\, \lambda_0 \pm \Delta\lambda,\, c_0 \pm \Delta c,\, W_0 \pm \Delta W) = T(\lambda_0, c_0, W_0) \pm \sum_k U_k\,(x, t, \lambda_0, c_0, W_0)\,\Delta p_k\,. \tag{32}$$

In this way the basic solution can be quickly transformed to the new one.

As the example the 2D domain of skin shown in Fig. 16 is considered. The external boundary of tissue Γ_b is subjected to the heat flux given by formula (30), the duration of this flux $t_b = 5$ [s]. The depth of domain considered is equal to 10 [mm], while $Y = 20$ [mm] (c.f. Eq. (30)). The basic thermophysical parameters of tissue equal $c_0 = 3.35 \cdot 10^6$ [J/m^{3}K], $\lambda_0 = 0.75$ [W/mK], $W_0 = 5000$ [W/m^{3}K]. The initial temperature of skin: $T_0 = 37$[°C]. In Fig. 17 the temperature distribution in the domain considered is shown, Fig. 18 illustrates the distribution of sensitivity function U_1. Due to the symmetry the upper part $Y \geq 0$ of domain is taken into account.

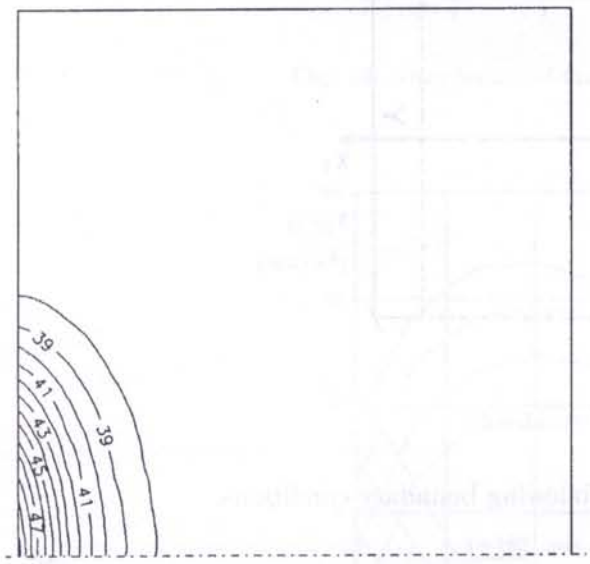

Fig. 17. Temperature distribution (5 s)

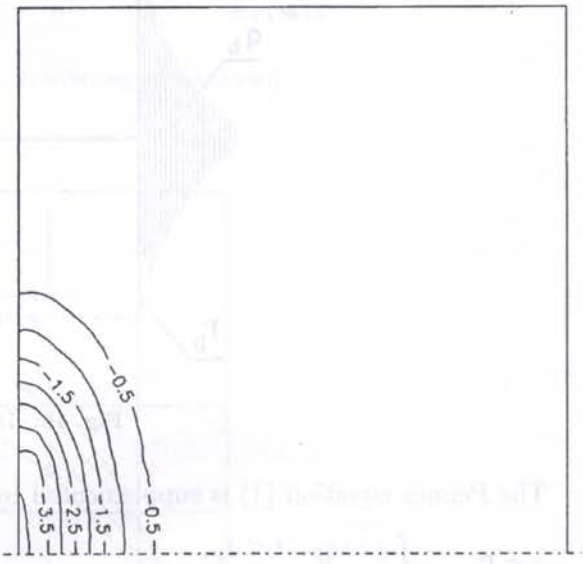

Fig. 18. Distribution of function U_1 (5 s)

The numerical computations show that in the case of example discussed the values of U_2 and U_3 are very small and the temperature field in skin is almost independent of c and W.

In Fig. 19 the heating curves at points A and B from the domain Ω are shown. The successive cooling curves concern the basic solution ($\lambda = 0.75$ [W/mK]) and the solutions for $\lambda = 0.5$ and

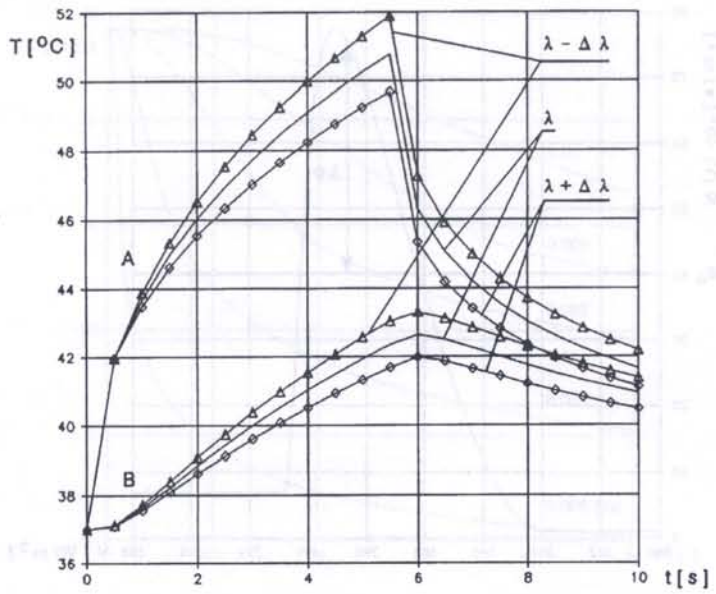

Fig. 19. Heating (cooling) curves at points A (0,0.33) and B (1,1) [mm]

$\lambda = 1$, in other words $\Delta\lambda = 0.25$. The results obtained using the sensitivity analysis and formula (32) are marked by the full lines, the results found directly – by the symbols. It should be pointed out that they are practically the same.

3.3. Shape sensitivity analysis

In this section the shape sensitivity analysis is applied in order to estimate the influence of spherical cryoprobe radius on the course of biological tissue freezing process [36, 50]. So, the following 1D equation written in the spherical co-ordinate system is taken into account (see Eq. (14)),

$$R_1 < r < R_2 : \quad C(T)\frac{\partial T(r,t)}{\partial t} = \frac{1}{r^2}\frac{\partial}{\partial r}\left[\lambda(T) r^2 \frac{\partial T(r,t)}{\partial r}\right] \tag{33}$$

where R_1 is a cryoprobe radius, R_2 is an external radius of tissue.

Equation (33) is supplemented by the following boundary conditions,

$$\begin{cases} r = R_1 : & T(r,t) = T_c\,, \\ r = R_2 : & \dfrac{\partial T(r,t)}{\partial r} = 0\,. \end{cases} \tag{34}$$

and initial one,

$$t = 0 : \quad T(r,t) = T_0, \tag{35}$$

where T_c is the temperature of cryoprobe surface, T_0 is the initial temperature of tissue.

Taking into account the possibilities of standard BEM algorithm it is convenient to transform the basic model using the Kirchhoff transformation

$$V(T) = \int_{T_r}^{T} \lambda(\mu)\mathrm{d}\mu \tag{36}$$

and then

$$\Phi[T(V)]\frac{\partial V(r,t)}{\partial t} = \frac{1}{r^2}\frac{\partial}{\partial r}\left[r^2 \frac{\partial V(r,t)}{\partial r}\right] \tag{37}$$

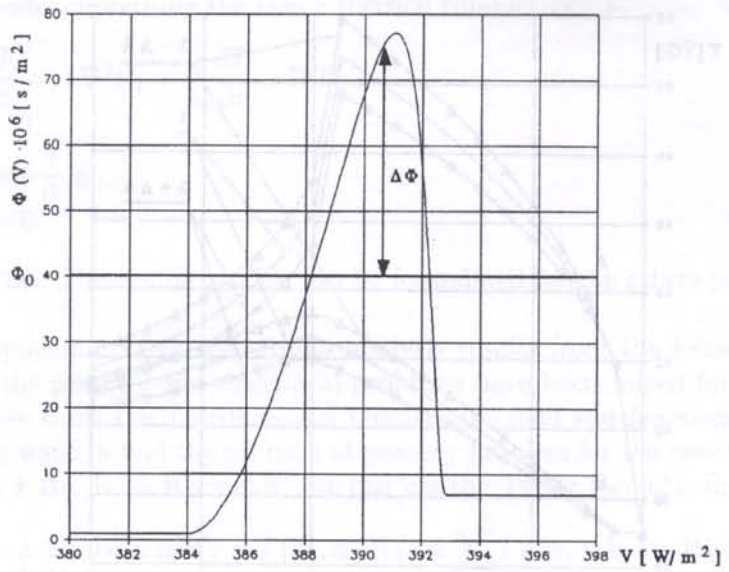

Fig. 20. Course of function $\Phi[T(V)]$

where (c.f. Fig. 20)

$$\Phi[T(V)] = \frac{C[T(V)]}{\lambda[T(V)]} \,. \tag{38}$$

The new boundary and initial conditions result directly from Eq. (36).

In order to estimate the influence of cryoprobe radius on the course of freezing process the sensitivity model is constructed. Using the concept of material derivative,

$$\frac{\mathrm{D}V}{\mathrm{D}b} = \frac{\partial V}{\partial b} + \frac{\partial V}{\partial r} v \,, \tag{39}$$

where $v = v(r, b)$ is the velocity associated with design parameter $b = R_1$, one finally obtains (after rather complex mathematical manipulations) the following shape sensitivity equation,

$$\begin{aligned} \Phi[T(V)] \frac{\partial U}{\partial t} &= \frac{1}{r^2} \frac{\partial}{\partial r} \left(r^2 \frac{\partial U}{\partial r} \right) - 2\Phi[T(V)] \frac{\partial v}{\partial r} \frac{\partial V}{\partial t} \\ &\quad - \frac{1}{\lambda^2[T(V)]} \left(\frac{\mathrm{d}C}{\mathrm{d}T} - \frac{\mathrm{d}\lambda}{\mathrm{d}T} \Phi[T(V)] \right) U \frac{\partial V}{\partial t} + \left(\frac{2}{r} \frac{\partial v}{\partial r} - \frac{\partial^2 v}{\partial r^2} - \frac{2v}{r^2} \right) \frac{\partial V}{\partial r} \,, \end{aligned} \tag{40}$$

where $U = U(r, t) = \mathrm{D}T/\mathrm{D}b$. The boundary–initial conditions are also differentiated with respect to b and then

$$\begin{aligned} r = R_1 : &\quad U(r, t) = 0, \\ r = R_2 : &\quad \frac{\partial U(r, t)}{\partial r} = 0, \\ t = 0 : &\quad U(r, t) = 0. \end{aligned} \tag{41}$$

The velocity field $v(r, b)$ associated with design parameter $b = R_1$ (see Eq. (40)) is defined as follows,

$$v = v(r, b) = \frac{R_2 - r}{R_2 - b} \,. \tag{42}$$

On the stage of numerical realization both in the case of basic problem and additional one the BEM algorithm supplemented by artificial heat source method [21, 41] has been used.

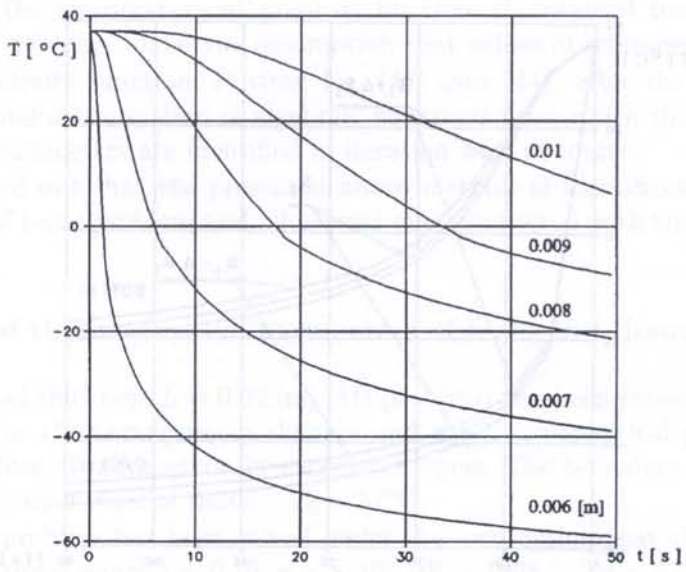

Fig. 21. Cooling curves

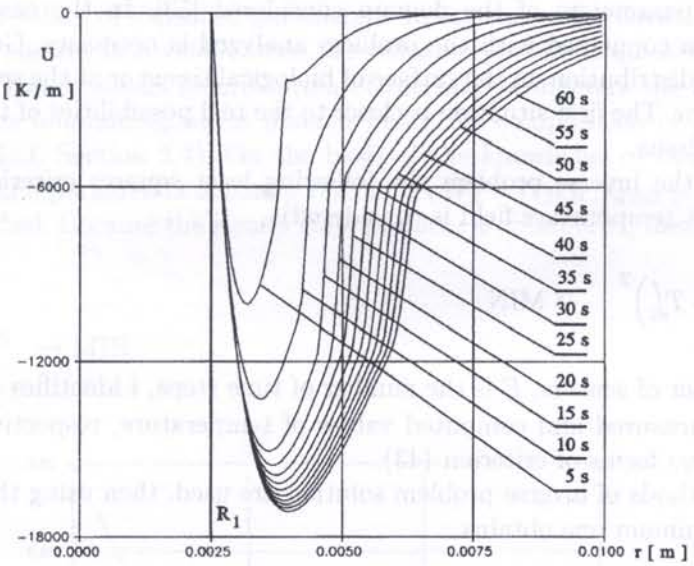

Fig. 22. Distribution of function $U = \mathrm{D}V/\mathrm{D}b$ for 5, ..., 60 [s]

As the example we consider the cryoprobe of diameter $R_1 = 0.005$ [m] and surface temperature $-90°$C. The external radius of domain: $R_2 = 0.025$ [m]. Initial temperature of tissue: $T_0 = 37°$C. The cooling curves obtained for these input data are shown in Fig. 21.

In Fig. 22 the distribution of sensitivity function $U = \mathrm{D}V/\mathrm{D}b$ in the domain considered for times 5, 10, 15, ..., 60 [s] is presented. Figure 23 presents the results obtained for disturbed cryoprobe radius ($\Delta R_1 = 0.1R_1$), in this place the Taylor formula has been used.

4. Inverse problems

Inverse problems [1, 3, 4, 16, 59] in bioheat transfer, as a rule, usually concern the identification of thermal parameters appearing in Pennes equation [20, 34, 44, 46] boundary or initial conditions [27,

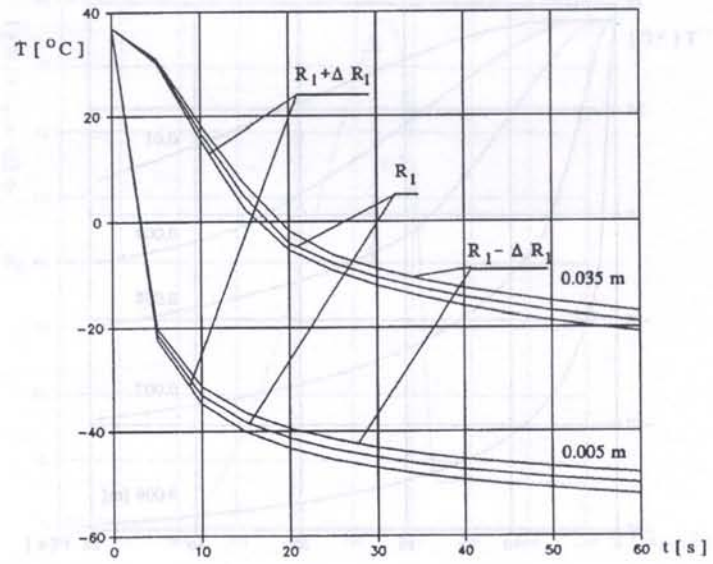

Fig. 23. Heating curves at the points $r = 0.0035$ [m] and $r = 0.005$ [m] ($\Delta R_1 = 0.1R_1$)

28] and geometrical parameters of the domain considered [53]. In the case of inverse task the additional information connected with the problem analyzed is necessary. Generally it is assumed that the temperature distribution on the surface of biological tissue or at the selected points from the tissue interior is known. The first situation is closer to the real possibilities of thermal measurements in the case of living tissue.

In order to solve the inverse problem the following least squares criterion can be taken into account (the transient temperature field is considered)

$$S = \sum_{f=1}^{F} \sum_{i=1}^{M} \left(T_i^f - T_{di}^f \right)^2 \quad \rightarrow \text{MIN} \tag{43}$$

where M is the number of sensors, F is the number of time steps, i identifies the position of sensor, T_{di}^f, T_i^f denote the measured and computed values of temperature, respectively. In literature one can find also the others forms of criterion (43).

If the gradient methods of inverse problem solution are used, then using the necessary condition of functional (43) minimum one obtains

$$\frac{\partial S}{\partial p_k} = 2 \sum_{f=1}^{F} \sum_{i=1}^{M} \left(T_i^f - T_{di}^f \right) \left. \frac{\partial T_i^f}{\partial p_k} \right|_{p_k = p_k^s} = 0, \tag{44}$$

where p_k denotes the unknown parameter, $k = 1, 2, \ldots, K$, while p_k^s is an arbitrary assumed value of the parameter p_k ($s = 0$ corresponds to start point, $s = 1, 2, \ldots, S$ correspond to the successive iterations).

Function T_i^f is expanded in a Taylor series

$$T_i^f = \left(T_i^f \right)^s + \sum_{k=1}^{K} \left. \frac{\partial T_i^f}{\partial p_k} \right|_{p_k = p_k^s} \left(p_k^{s+1} - p_k^s \right) \tag{45}$$

or

$$T_i^f = \left(T_i^f \right)^s + \sum_{k=1}^{K} \left(U_{ki}^f \right)^s \left(p_k^{s+1} - p_k^s \right), \tag{46}$$

where $(T_i^f)^s$ denotes the temperature at point x_i for time t^f obtained from the solution of the basic boundary-initial problem under the assumption that values of unknown parameters p_k equal p_k^s, $(U_{ki}^f)^s$ is the sensitivity function. Putting Eq. (46) into (44), after the simple mathematical manipulations, one obtains the system of algebraic equations from which the unknown parameters can be found. These parameters are identified in iteration way, of course.

It should be pointed out that the presented above method of identification requires for every iteration the solving of basic problem and additional ones connected with the sensitivity functions.

4.1. Identification of thermophysical parameters of biological tissue

Domain of skin tissue of thickness $L = 0.02$ [m] (1D problem) has been considered (c.f. Fig. 1) [34]. The tissue is treated as the homogeneous domain and the thermophysical parameters of domain are equal to mean values of parameters for successive layers. The boundary heat flux equals $q_b = 6000$ [W/m^2], initial temperature of tissue – $T_0 = 37$°C.

At first the direct problem has been solved under the assumption that the thermophysical parameters of biological tissue equal $\lambda = 0.75$, $c = 3 \cdot 10^6$, $W = 1998.1$, $T_B = 37$°C, $Q_m = 420$. On the stage of inverse problem formulation it is assumed that the thermal conductivity λ is unknown (the remaining parameters are given) or the volumetric specific c is unknown. On the basis of knowledge of time-dependent course of temperature on the skin surface the inverse problems have been solved. In Figs. 24 and 25 the values of identified parameters during successive iterations for different initial values of λ and c are shown. It is visible, that the iteration process is quickly convergent.

As an example of simultaneous identification of thermal parameters the following solution will be presented [46]. The non-homogeneous domain being the composition of skin tissue and tumor region is considered (c.f. Section 2.4). On the basis of the knowledge of skin surface temperature (see Fig. 13) the thermal parameters of tumor region λ_2, $W_2 = G_2 c_B$, Q_{m2} (c.f. Eq. (21)) have been simultaneously identified. Because the steady state problem is considered, therefore the criterion (43) takes a form

$$S = \sum_{i=1}^{M} (T_i - T_{di})^2 \rightarrow \text{MIN} \tag{47}$$

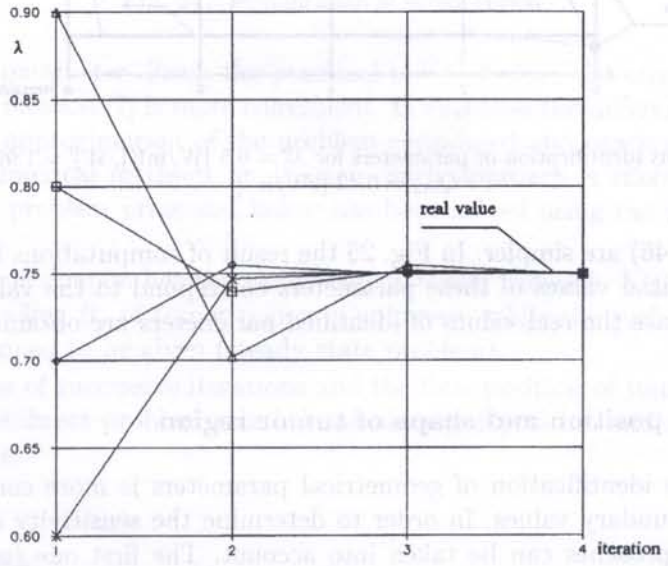

Fig. 24. Identification of λ

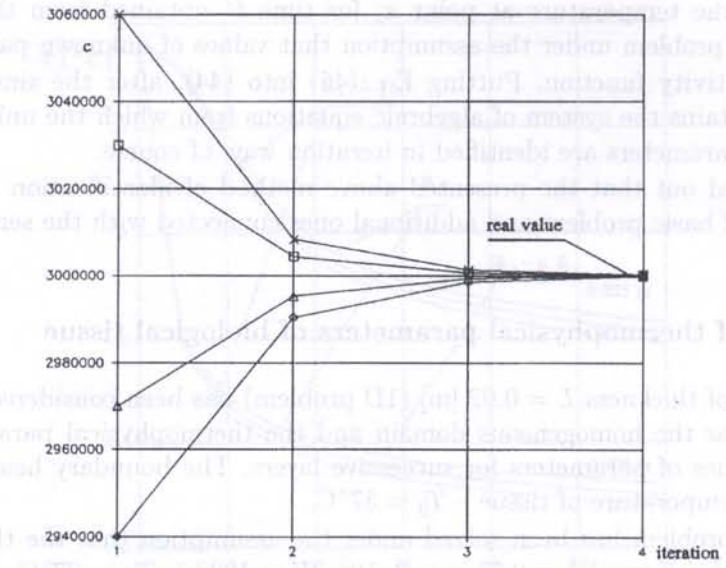

Fig. 25. Identification of c

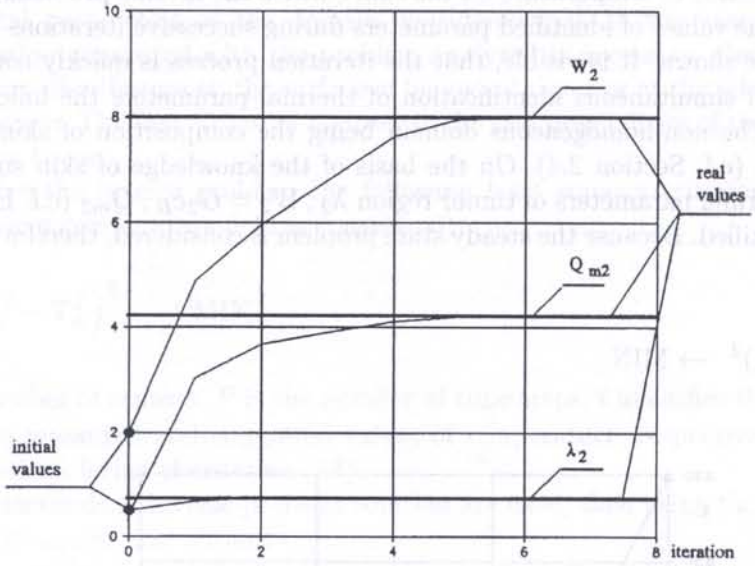

Fig. 26. Simultaneous identification of parameters for $\lambda_2^0 = 0.5$ [W/mK], $W_2^0 = 1.9981$ [KW/m^{3}K] and $Q_{m2} = 0.42$ [kW/m^3]

and the formulas (44)–(46) are simpler. In Fig. 26 the result of computations is shown. It should be pointed out that the initial values of these parameters correspond to the values λ_1, W_1, Q_{m1} for healthy tissue. In this case the real values of identified parameters are obtained after 5 iterations.

4.2. Identification of position and shape of tumor region

Generally speaking, the identification of geometrical parameters is more complex as the identification of internal or boundary values. In order to determine the sensitivity coefficients appearing in formula (46) two approaches can be taken into account. The first one (explicit differentiation method) consists in the application of material derivative and next the basic equations are differentiated in adequate way [7–9], similarly as in Section 3.3. It requires the knowledge of velocity

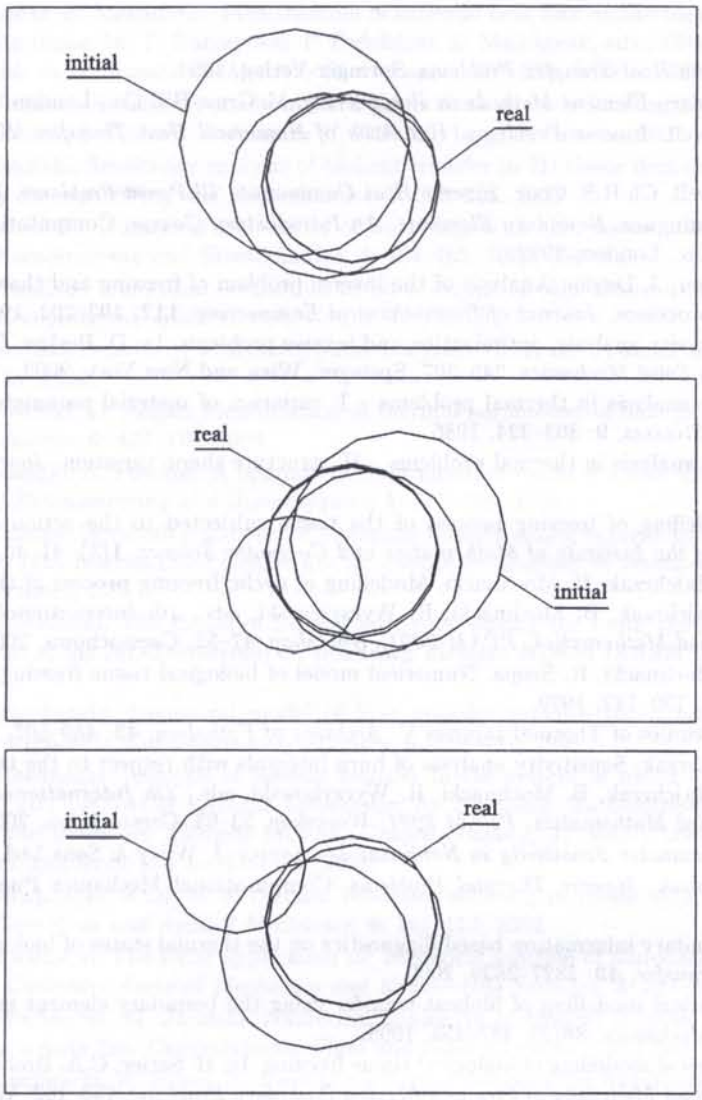

Fig. 27. Identification of tumor region

associated with shape parameter. From the practical point of view, the other approach called the implicit differentiation method [7] is more convenient. In this case the differentiation takes place on the stage of numerical approximation of the problem considered and concerns the system of equations resulting from numerical methods application. Such approach is effective in the case of the BEM application. The problem presented below has been solved using the implicit differentiation method.

The non-homogeneous domain healthy tissue–tumor region shown in Fig. 12 is considered. The position $(x_s\,,\,y_s)$ and radius R_s of tumor region is unknown, while the surface temperature distribution (Fig. 13) is assumed to be given (steady state problem).

In Fig. 27 the results of successive iterations and the final position of tumor region are marked. In comparison with the direct problem solution the identified position and shape of tumor region are practically the same.

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