Numerical simulation of cryosurgery in biological tissue with developed circulatory system

K E Shilnikov$^{1,2}$ and M B Kochanov$^1$

$^1$Department of applied mathematics, National Research Nuclear University "MEPhI", Russia
E-mail: shilnikov.k@yandex.ru

Abstract. This paper is devoted to the modeling of the cryogenic impact on biological tissue with a developed circulatory system: large blood vessels, dense distributed small vessels and capillaries penetrating the tissue. The case of cryogenic destruction of a cancer tumor localized near a large artery is considered. The paper presents a direct numerical simulation of the temperature distribution evolution in biological tissue including the calculation of blood flow parameters in a vessel. The mathematical model is based on the Pennes bioheat transfer model with enthalpy modification and the quasi-one-dimensional hemodynamic model of blood flow in arteries, taking into account local changes in the elastic properties of the vessel walls due to strong cooling of adjacent tissue. A numerical algorithm based on explicit finite-volume approximation of the heat transfer model and the hybrid characteristic scheme (after splitting the equation with respect to physical processes) for numerical solution of hyperbolic systems is developed in order to simulate cryosurgery for the tumor near the artery. The main focus of the paper is a numerical study of the circulatory system parameters’ influence on the shape of the final distribution of the cellular necrosis zone. We study the dependence of the necrosis front penetration depth on the perfusion power which characterizes the density of capillary distribution, the peak and background rates of blood flow in the artery, the diameter of the blood vessel and the thickness of its walls.

1. Introduction
During the last decades cryosurgery has become a competitive approach for human cancer treatment [1–3]. Taking into account the risk of relapse and undesired destruction of healthy tissue the prediction of the cryosurgery results is very important [4]. The cryosurgical treatment is based on the tissue necrosis effect caused by the impact of extremely low temperatures on tumor tissue [5–8]. In case of the cryotip based cryosurgery necrosis effect is caused by the freezing front propagation from the tips of cryoneedles in the tissue. Current paper is concerned with the direct numerical simulation of the temperature distribution evaluation in biological tissue near the large artery including the calculation of the blood flow parameters in a vessel. The mathematical model is based on the Pennes bioheat transfer model with enthalpy modification [9,10] and the quasi-one-dimensional hemodynamic model of blood flow in arteries [11,12]. The influence of circulatory system parameters such as vessel wall thickness, blood flow speed and capillary blood perfusion rate is numerically studied.
2. Mathematical model

For the numerical modeling of the cryosurgery on the tumor near the artery a cylindrical computational region $D_1$ with height $Z = z_2 - z_1$ was considered:

$$D_1 = \left\{ r \in \mathbb{R}^3 \mid R_1 < r < R_2, 0 < \phi \leq 2\pi, z_1 < z < z_2, r \in D_3 \right\}.$$ 

Here $R_2$ is an outer radius of the computational region. $R_1$ is a radius of the artery $\hat{D}_{00}$. A middle section of the computational region orthogonal to the cylinder axis is shown in figure 1. $D_2 \subset D_1$ is a tumor zone and $D_3$ marks the position of the cryotip. The enthalpy modified Pennes model [9] was used in order to describe the cryogenic heat transfer in the target tissue:

$$\hat{C} \frac{\partial T}{\partial t} = - \text{div} Q_F + \omega_b C_b (T_c - T),$$

$$Q_F = -k \nabla T, \quad r \in D_1,$$

$$\hat{C}(T) = \frac{dH(T)}{dT}, \quad H(T) = \begin{cases} C_T, & T \leq T_1 \\ F(T), & T_1 < T < T_2 \\ H_2 + C_T, & T \geq T_2 \end{cases},$$

$$H_1 = C_T T_1, \quad H_2 = H_1 + (C_1 + C_2) \frac{T_2 - T_1}{2} + L,$$

$$F(T) = \left[ C_2(T_2 - T_1) + H_1 - H_2 \right] \frac{(T - T_1)^2(T - T_2)}{(T_1 - T_2)^3} + H_2 \frac{T - T_1}{T_2 - T_1}$$

$$+ \left[ C_1(T_2 - T_1) + H_1 - H_2 \right] \frac{(T - T_1)(T - T_2)^2}{(T_1 - T_2)^3} - H_1 \frac{T - T_2}{T_2 - T_1}.$$

Here $C, T, k, \omega_b, C_b, T_c, L$ are the effective heat capacity, temperature, thermal conductivity of biological tissue, perfusion rate, heat capacity, temperature of blood in capillaries penetrating the biological tissues and latent heat of phase transition, correspondingly. Numerical values of the parameters used in the model are presented in table 1. The thermal conductivity coefficient $k$ is linearly interpolated within an interval of $T \in (T_1, T_2)$, where $T_1$ and $T_2$ are the corresponding temperature values at the beginning and at the end of the phase transition process.

Graphs of temperature dependent regularized thermophysical quantities for healthy biological tissue and tumor tissue are shown in figure 2.
|                  | Healthy tissue | Tumor tissue |
|------------------|----------------|--------------|
|                  | $T > 272$ K    | $T < 265$ K  |
|                  | $T > 272$ K    | $T < 265$ K  |
| $C$, erg K$^{-1}$ cm$^{-3}$ | $3.16 \times 10^7$ | $1.80 \times 10^7$ | $3.89 \times 10^7$ | $2.01 \times 10^7$ |
| $k$, erg K$^{-1}$ cm$^{-1}$ s$^{-1}$ | $0.48 \times 10^5$ | $1.68 \times 10^5$ | $0.56 \times 10^5$ | $2.22 \times 10^5$ |
| $\omega_b C_b$, erg K$^{-1}$ cm$^{-3}$ s$^{-1}$ | $24.2 \times 10^4$ | 0 | $48.5 \times 10^4$ | 0 |

Table 1. Thermophysical parameters of healthy tissue and tumor tissue.

Figure 2. Plots of thermodynamic characteristics of a healthy (—— line) biological tissue and angioma (- - - - line).

For the numerical modeling of the blood flow in the artery the quasi-one-dimensional hemodynamic model was applied:

$$
\frac{\partial S}{\partial t} + \frac{\partial}{\partial z} (Su) = 0, \quad \frac{\partial u}{\partial t} + \frac{\partial}{\partial z} \left( \frac{u^2}{2} + \frac{1}{\rho_b} P(S) \right) = 0,
$$

$$
\frac{\partial T_b}{\partial t} + u \frac{\partial T_b}{\partial z} - k_b \frac{\partial^2 T_b}{\partial z^2} = q, \quad z \in \hat{D}_0, \quad 0 < t,
$$

$$
q(z, t) = \frac{2\sqrt{\pi}}{C_b \sqrt{S}} \int_{\partial D_{S(z)}} \frac{T|_{r=R_b} - T_b(z, t)}{h} dl,
$$

$$
\bar{k} = \frac{k_b(T_b(z, t)) + k(T|_{r=R_b})}{2}, \quad P(S) = P_0 + \alpha \left( 1 - \sqrt{\frac{S_0}{S}} \right).
$$

Here $S, u, P$ are the cross-sectional area of the vessel, the average cross-sectional velocity of blood flow and pressure, respectively. $T_b$ is the average temperature of blood in the vessel, $k_b = 0.56 \times 10^5$ erg K$^{-1}$ cm$^{-1}$ s$^{-1}$, $C_b = 4.212 \times 10^7$ erg K$^{-1}$ cm$^{-3}$ are thermal conductivity and heat capacity of blood. $\bar{k}$ is the average temperature of blood in the vessel, $\hat{D}_0$ is the interval of height variation along the vessel $\hat{D}_{00}$. $q(z, t)$ is the Newton's type heat exchange term describing averaged heat transfer between biological tissue and artery through the vessel wall with thickness of $h$. $S_0, \eta$ are the cross-sectional area of the vessel in the equilibrium state and the relative change in the cross-sectional area correspondingly. $\partial D_{S(z)}$ is the boundary of the vessel cross-section.
The initial and boundary conditions used in this paper are:

\[
T(r, t)_{t=0} = T_0, \quad T_b(z, t)_{t=0} = T_0, \quad u(z, t)_{t=0} = u_0, \quad S(z, t)_{t=0} = s_0,
\]

\[
T(r, t)_{r \in \partial D_1 \setminus (\partial D_0 \cup \partial D_3)} = T_0, \quad k \frac{\partial T}{\partial n}_{r \in \partial D_0} = -\theta(r; T, T_b) (T_{r=R_1} - T_b(z, t)),
\]

\[
T_b(z, t)_{z=z_1} = T_0, \quad S(z, t)u(z, t)_{z=z_1} = Q(t).
\]

On the active zone of the cryoprobe surface \( \Sigma_1 \subset \partial D_3 \) the Dirichlet boundary condition \( T(r \in \Sigma_1) = T_s(t) \) was used. We use the homogeneous Neuman boundary condition on the surface separating domain \( \Sigma_2 \subset \partial D_3 \) from \( D_1 \).

### 3. Numerical algorithm

A finite volume explicit scheme for indexed convex grids \([13, 14]\) is used for the numerical modeling of the tissue freezing problem:

\[
C_{ijk}^n T_{ijk}^{n+1} - T_{ijk}^n V_{ijk} = - \left\{ \sum_{l=1}^6 (Q_F)_l \right\}^{n}_{ijk} + \omega_b C_b (T_c - T_{ijk}^n) V_{ijk}.
\]  \( (3) \)

Here \( \{(Q_F)\}_l^{n}_{ijk} \) is the heat flux through the \( l \)-th face of the cell \( v_{ijk} \) (of volume \( V_{ijk} \)) on the \( n \)-th time layer and \( F_{ijk}^n = F(r_{ijk}, t^n) \), where \( r_{ijk} \) is the center of the cell \( v_{ijk} \). Heat fluxes through faces are calculated by means of the estimations for the space derivatives of the temperature field. For the improvement of applied scheme stability the flux relaxation approach \([15, 16]\) is used. \( (1) \) is modified in following manner:

\[
\hat{C} \frac{\partial T}{\partial t} = - \text{div} \, Q + \omega_b C_b (T_c - T),
\]

\[
Q + \tau_r \frac{\partial}{\partial t} Q = Q_F.
\]  \( (4) \)

Here \( Q_F = -\kappa \nabla T \) is Fourier flux, \( \tau_r \sim \tau \) is the stabilizing parameter \([17, 18]\). Thus the following estimation for the heat flux can be obtained:

\[
Q^n = DQ^{n-1} + (1 - D)Q_F^n, \quad D = e^{-\frac{r}{\tau_r}}.
\]

Taking into account the heat equilibrium state of the tissue before beginning of the freezing process, the trivial initial conditions for the fluxes are used.

For the numerical computation of the hemodynamical part of the model the process decomposition method is applied. Finite difference approximation of the hyperbolical part is given by the hybrid characteristic scheme \([19]\) with Fedorenko type switching analyzer \([20]\). Reaction-diffusion part is approximated directly.

### 4. Numerical results

The angioma is present in model as a sphere with the radius of 0.75 cm. The distance between the center of the sphere and the axis of the vessel is 0.75 cm. The center of the sphere is located on a straight line passing through the origin and the cryotip that is located on a radial beam in the \( z = 0 \) plane. The active zone of the cryoprobe tip has a fixed square cross-section of 0.02 cm\(^2\) and length of \( l_c = 0.5 \) cm. The frontal part of the tip is located 0.35 cm away from the vessel wall.

Note that the cryoprobe parameters are corresponded to the parameters of industrial cryotips already used during the cryosurgery procedures. In our model the parameters are based
on the parameters of Endocare cryoprobes. The protocol of the cryosurgery procedure was 
\[ T_s(t) = \max(310 - t, 77.4) \text{ K}, \] corresponding to the constant cooling rate 1 K per second.

Preliminary numerical experiments showed that in order to obtain the results that correspond to the error of the order of 1 °C, it is sufficient to use a rather coarse grid (grid step \( \approx 1 \) mm).

The amount of blood entering the artery is
\[ Q(t) = Q_1 + Q_0 e^{-10^3(t \text{ mod } 1 - 0.5)^2}, \]
where \( Q_1 \) is the background flow, \( Q_0 \) is the flow associated with heartbeats.

The basic values of the parameters used in the process of numerical modeling are presented by the following set of values: \( h = 1 \) mm, \( R_1 = 3 \) mm, \( Q_1 = 3 \) ml s\(^{-1}\) and \( Q_0 = 15 \) ml s\(^{-1}\).

Figure 4(b) presents a graph of the phase transition boundary at \( z = 0 \) through \( t = 300 \) s after the beginning of cryogenic exposure. For convenience of comparison, all the results of numerical simulation obtained below are given at the same time \( t = 300 \) s at \( z = 0 \). Figure 3 shows two orthogonal sections (\( z = 0 \) and \( y = 0 \)) of phase transition boundary. Also it shows two iso-surfaces of temperature at \( t = 265 \) K and \( t = 272 \) K that correspond to the temperature interval of phase transition.

![Figure 3. The two orthogonal sections (z = 0 and y = 0) of phase transition boundary at t = 300 s.](image)

Firstly, the effect of blood perfusion on the propagation of the freezing front was investigated. From figures 4(c) and 4(d) it can be seen that an increase of the perfusion coefficient \( \omega_b C_b \) leads to a decrease of the volume of the area that has been frozen. The shape of the area is preserved.

A decrease of wall thickness (see figure 4(e)) leads to an increase of heat flow through the vessel wall. Thus, the leading edge of the phase transition is located at a greater distance from the vessel wall. When the vessel wall thickness is doubled (see figure 4(f)) the vessel wall is cooled to lower temperatures.

The change of cross-sectional area (figures 4(g) and 4(h)) has little effect on the volume of the frozen part of the tissue. The shape of the frozen area adjacent to the vessel slightly varies due to a small change in the curvature radius of the vessel wall.

A change in the flow parameters (an increase of the background flow rate and amplitude of the peak velocity) does not lead to noticeable changes, the phase transition front is not distinguishable in the graphs.
5. Conclusion

The direct numerical simulation of the temperature distribution evolution in biological tissue near a large artery and the calculation of the blood flow in the artery were made.

The mathematical model of heat transfer process in tissue is based on the Pennes model with enthalpy modification. To describe the blood flow in the artery the quasi-one-dimensional hemodynamic model is used. The model takes into account local changes in the elastic properties of the vessel wall during strong cooling of the adjacent biological tissue.

The proposed model was simulated via numerical algorithm based on explicit finite-volume method and the hybrid characteristic scheme (after splitting the equation with respect to physical processes) for numerical solution of hyperbolic system.

The influence of circulatory system parameters such as vessel wall thickness, blood flow speed and capillary blood perfusion rate is numerically studied. It is shown that capillary blood perfusion, artery size and the thickness of its walls can cause valuable changes in tissue necrosis propagation when the influence of blood flow speed is negligible.

Acknowledgments

This work is supported by the Russian Science Foundation under grant No.18-71-00108.

References

[1] Gdal-On M and Gelfand Y A 1998 Ophthal. Surg. Lasers 29 969–73
[2] Grunder W, Goldammer A, Schober R and Vitzthum H E 2003 Z. Med. Phys. 13 203–7
[3] Baust J, Gage A A, Ma H and Zhang C 1997 Cryobiology 34 373–84
[4] Stanczyk M and Telega J J 2003 Acta Bioeng. Biomech. 5 3–22
[5] Mazur P 1963 J. Gen. Physiol. 47 347–69
[6] Toner M, Cravalho E G and Karel M 1990 J. Appl. Phys. 67 1582–93
[7] Zhao G, Takamatsu H and He X 2014 J. Appl. Phys. 115 144701
[8] Devireddy R V, Smith D J and Bischof J C 2002 J. Heat. Transf. 124 365–74
[9] Pennes H H 1948 J. Appl. Physiol. 1 93–122
[10] Shilnikov K E, Kudryashov N A and Gaiur I Y 2017 J. Phys. Conf. Ser. 937 012048
[11] Vassilevski Y V, Salamatova V Y and Simakov S S 2015 Comp. Math. Math. Phys. 55 1567–78
[12] Olufsen M S, Peskin C S, Kim W Y, Pedersen E M, Nadim A and Larsen J 2000 Ann. Biomed. Eng. 28 1281–99
[13] Shilnikov E V 2014 Viscous gas flow simulation based on QGD equations system on non-orthogonal index
  grids Preprints of Keldysh Institute of Applied Mathematics RAS, 33
[14] Kudryashov N A and Shilnikov K E 2016 Math. Models Comput. Simul. 8 680–8
[15] Chetverushkin B N, Shilnikov E V and Davydov A A 2013 Adv. Eng. Softw. 60 42–7
[16] Chetverushkin B N and Shilnikov E V 2010 Proceedings of the II International Conference on Engineering
  Optimization, EngOpt-2010 (Lisbon)
[17] Myshetskaya E E and Tishkin V F 2015 Comp. Math. Math. Phys. 55 1270–5
[18] Chetverushkin B N 2013 Math. Mod. and Comp. Simul. 5 266 – 79
[19] Magomedov K M and Kholodov A S 1969 USSR Comp. Math. Math. Phys. 9 158–76
[20] Fedorenko R F 1963 USSR Comp. Math. Math. Phys. 2 1355–65