TISSUE TEMPERATURE SIMULATION IN CRYOSURGERY

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A method is described for simulating tissue temperature in cryosurgery by numerical solution of a heat-conduction problem with a mobile phase interface. The results are compared with experiment.

Information can be obtained on the probability of cell death in a given tissue volume in cryosurgery by reference to the temperature distribution, the cooling rate, and the growth rate of the frozen zone [1-3]. Input data in the design of cryosurgery systems are provided by the temperature and characteristic dimension of the working tip, since these largely control the above characteristics. Also, it is necessary to know the heat flux from the tissue. These characteristics can be determined by physical or mathematical simulation, which is intended to forecast the results of cryosurgery and to provide design data for instruments and for the cryogenic support.

One of the traditional ways of simulating thermal conditions in cryosurgery is to solve the heat-conduction problem for a two-phase system with a mobile boundary between the frozen and unfrozen parts. Factors peculiar to biological objects have to be incorporated, such as the heat S_b supplied by the blood flow and the metabolic heat production S_m [4]. A major condition for obtaining reliable information in such simulation is adequate accuracy in the numerous input data: ρ, c, λ, ρ', c', λ', m_b, c_b, S_m, l; however, such data as yet have not been properly classified, and there are many discrepancies even in qualitative features of the published data. For instance, in [1] we find references to [5,6] concerning the assumption that the blood flow rate m_b is constant. On the other hand, in the calculations of [7] we find that S_m and S_b are taken as dependent on temperature [8], and it has also been shown [7] that neglect of this factor can result in up to 20% error in the result for the radius of the frozen zone. Also, the values of S_m and S_b may be influenced by the response of the organism, but the data are taken from experiments [6, 8] that do not reflect the specific features of local cryosurgery. As a consequence, the results of [2, 7], which were derived by numerical solution of the Stefan's problem [9] for a biological system, are to be viewed as qualitative and cannot be used with confidence in forecasting, or even as input data in the design of cryosurgery instruments. A preliminary analysis indicates that this is particularly important in the determination of heat fluxes to instruments at the start of operation, when the fluxes are largest, since these fluxes must be the ones for which the instruments are designed to operate.

Any quantitative characterization of freezing requires a formulation in which the input data are of minimal volume and reflect a single integral characteristic of the living tissue, since there are very severe experimental difficulties in determining numerous quantities. An appropriate integral factor is the law followed by the boundary of the frozen zone, as this is fairly easy to establish in some cases of practical importance [10], particularly with regard to appropriate accuracy in the measurements. The heat-conduction problem for a two-phase biological system [7] then splits up into two subsystems of equations, each relating to one phase only.

An advantage of this approach to local cryosurgery is that the simulation need be conducted only for the frozen zone, because the necrotic zone is usually smaller than the latter [3]. This means that the number of input quantities is reduced from 10 to 4 (ρ, c, λ, $R(t)$), and therefore there is a reduction in the overall error introduced by the error in the input data. That is, use of measured $R(t)$ for the boundary conditions enables one to test the assumption that the temperature distribution is quasistationary, particularly as this may be derived by approximate analytical solution [11].

Another advantage of the formulation with a known law of motion for the interface is

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that it is possible to determine the blood flow rate $\dot{m}_b$, especially the values characteristic of cryosurgery.

We now consider the application to a case of practical importance, viz., where the working tip is a hemisphere of radius r_0. If the law followed by the boundary of the frozen zone is known [10] along with the thermophysical parameters ρ, c, and λ, then the following equation has to be solved to determine the temperature distribution and the heat flux in the frozen region:

$$\rho c(T)\frac{\partial T}{\partial t}=\frac{1}{r^\nu}\frac{\partial}{\partial r}r^\nu\lambda(T)\frac{\partial T}{\partial r} \tag{1}$$

subject to the boundary conditions

$$\begin{gathered} r=r_0,\quad T=T_0(t),\\ r=R(t),\quad T=T_c=\text{const}, \end{gathered} \tag{2}$$

where ν = 0, 1, 2 correspond to planar, cylindrical, and spherical cases.

The function $T_0(t)$ is put as

$$T_0(t)=\begin{cases} T_k'+(T_c-T_k')\dfrac{t_0'-t}{t_0'}, & 0<t\leqslant t_0'\\ T_k'-(T_k'-T_k)\dfrac{t-t_0'}{t_0-t_0'}, & t_0'\leqslant t\leqslant t_0\\ T_k=\text{const}, & t>t_0 \end{cases} \tag{3}$$

on the basis of the observed temperature of the tip.

By virtue of the condition $R(0) = r_0$, the problem of (1) and (2) is of the type without initial conditions [9]; in particular, for $T_0(t) \equiv T_k$, c, λ — const and $R(t) \sim t^{1/2}$ the problem in the planar case (ν = 0) has a self-modeling solution [12]. In numerical analysis, the initial temperature distribution is defined for some sufficiently small time interval t_Δ:

$$t=t_\Delta,\quad T=T_i(r),\quad r_0\leqslant r\leqslant R(t_\Delta). \tag{4}$$

As a rule, $T_i(r)$ is taken as a linear distribution, because preliminary calculations have shown that the exact choice of $T_i(r)$ influences the solution only for the early period, viz., the first 5 or 6 time steps. For convenience, the following change of variable is also made: $x = (r - r_0)/(R(t) - r_0)$. Then (1) and (2) become

$$\rho c(T)\frac{\partial T}{\partial t}=\frac{1}{(R-r_0)^2}\frac{\partial}{\partial x}\lambda(T)\frac{\partial T}{\partial x}+\frac{\partial T}{\partial x}\left\{\rho c(T)\dot{R}+\frac{2\lambda(T)}{r_0+x(R-r_0)}\right\}\frac{1}{R-r_0}, \tag{5}$$

$$\begin{gathered} x=0,\quad T=T_0(t),\\ x=1,\quad T=T_*=\text{const}, \end{gathered} \tag{6}$$

and the region of integration is transformed to the rectangle $\{t_\Delta\leqslant t\leqslant t_{max},\ 0\leqslant x\leqslant 1\}$; Eq. (5) and boundary condition (6) are rendered dimensionless before proceeding further, with the characteristic time taken as $t_* = (c_0\rho r_0^2)/\lambda_0$, where c_0 and λ_0 are the characteristic values of the specific heat and thermal conductivity in $c(T) = c_0 + gT$ and $\lambda(T) = \lambda_0 - bT$.

The numerical solution was based on a net difference having a uniform step of h_x in the coordinate but a variable time step of h_t; the process is essentially nonstationary at the start, so a relatively small time step is used for that range. The process is only slightly nonstationary at later times, so a larger time step can be used, which saves computer run time. The exact step size was derived from trial calculations and was such that any further reduction in the step size did not alter the result by more than 1%.

The derivatives in the equations were approximated by an inexplicit scheme:

$$\frac{\partial T}{\partial t}\simeq\frac{T_i^{n+1}-T_i^n}{h_t},\quad \frac{\partial T}{\partial x}\simeq\frac{T_{i+1}^{n+1}-T_{i-1}^{n+1}}{2h_x},$$

$$\frac{\partial}{\partial x}\lambda(T)\frac{\partial T}{\partial x}\simeq\frac{\lambda(T_{i+1/2}^{n+1})(T_{i+1}^{n+1}-T_i^{n+1})-\lambda(T_{i-1/2}^{n+1})(T_i^{n+1}-T_{i-1}^{n+1})}{h_x^2}.$$

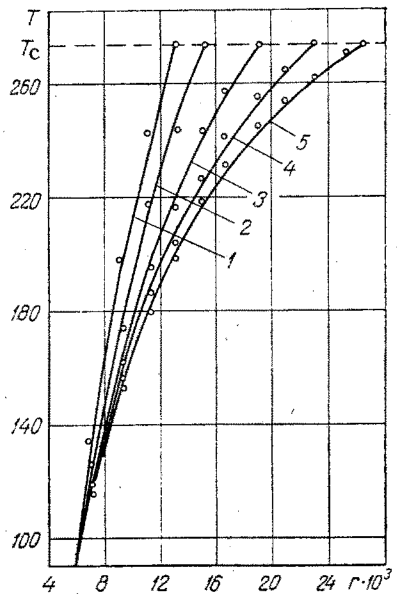

Fig. 1

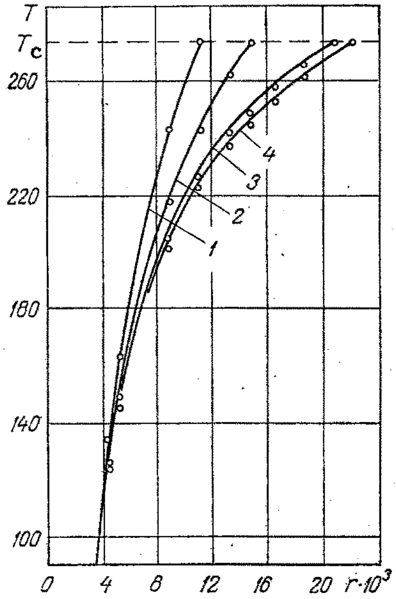

Fig. 2

Fig. 1. Temperature T (°K) in the frozen zone as a function of radius r, m; $r_0 = 6 \cdot 10^{-3}$ m; $T_k' = 93$°K; $T_k = 88$°K; $t_0' = 8$ sec; $t_0 = 60$ sec; $R(t) - r_0 = 0.602 \cdot 10^{-3}\ t^{0.5899}$, $0 \le t \le 79.53$; $R(t) - r_0 = 1.69 \cdot 10^{-3}\ t^{0.3537}$, $79.53 \le t \le 393.38$; $R(t) - r_0 = 3.017 \cdot 10^{-3}\ t^{0.2570}$, $393.38 \le t \le 1800$; 1) t = 66 sec; 2) correspondingly 114; 3) 300; 4) 760; 5) 1800.

Fig. 2. Temperature T (°K) in the frozen zone as a function of radius r, m; $r_0 = 3.5 \cdot 10^{-3}$ m; $T_k' = 93$°K; $T_k = 88$°K; $t_0' = 10$ sec; $t_0 = 60$ sec; $R(t) - r_0 = 0.687 \cdot 10^{-3}\ t^{0.5565}$, $0 < t \le 69.36$; $R(t) - r_0 = 1.714 \cdot 10^{-3}\ t^{0.3408}$, $69.36 \le t \le 789.39$; $R(t) - r_0 = 3.072 \cdot 10^{-3}\ t^{0.2532}$, $789.39 \le t \le 1200$; 1) t = 78 sec; 2) 250; 3) 800 sec; 4) 1200.

Here T_i^n is the temperature in layer n at point i and $T_{i\pm1/2} = {}^1/_2(T_{i\pm1} + T_i)$; the difference equations for layer n + 1 were solved by fitting, and the nonlinearity arising from the temperature dependence of the specific heat and thermal conductivity was handled by iteration. The initial approximations for c(T) and λ(T) were derived from the temperature for the previous time layer. The temperature gradients are fairly high (up to 80°K/mm), so ∂T/∂r was represented in second-order form in determining q_0:

$$\left.\frac{\partial T}{\partial r}\right|_{r=r_0} \simeq \frac{-1.5T_k + 2T_{k+1} - 0.5T_{k+2}}{h_x}.$$

No exact values were available for the thermophysical parameters of the frozen tissue, so the values appropriate for ice [13] were used.

The measurements on R(t) for the entire range $r_0 \le r \le R_{max}$, could be fitted to t = $t = a_1 \mathrm{sh}[a_2 + (R + a_3)]$ in a comparatively small number of cases to give a maximum error of about 0.4–0.5 mm for the initial instant; however, the process is maximally nonstationary at this time, and the errors in determining q_0 were then more than 14%. For this reason, R(t) was put as $R - r_0 = ft^m$ for three successive time intervals, whose limits were defined automatically by least-squares fitting by computer. Then the maximum error of approximation for the initial instant was 0.15 mm, which corresponded to the limiting experimental error. Test calculations show that the errors in determining T(r), q_0, and q arising from the discontinuity in R on going to the second segment were then, respectively, not more than 0.04, 0.25, and 2.6%. The calculations for the start of the third segment gave lower values for these quantities, because the nonstationary component is then very slight.

Figures 1 and 2 show results on the temperature distributions along with measurements made by the method of [10] on dog leg muscle.

In these experiments, the surface of the tissue was insulated from the environment by a

TABLE 1. Frozen-Zone Temperatures Computed from the Quasistationary Equation and by Simulation

t=6,5	$r\cdot10^3$, m	6,00	6,21	6,49	6,82	7,03	7,73	7,89	8,01
	T_{cal}, °K	122,91	139,57	162,21	187,20	202,42	252,57	264,23	273,0
	T_{qs}, °K	122,91	138,68	159,35	183,42	198,69	250,79	263,33	273,0
t=8,17	$r\cdot10^3$, m	6,00	6,18	6,37	6,55	7,01	7,52	8,03	8,26
	T_{cal}, °K	88	103,61	119,02	134,24	171,76	212,57	253,73	273,0
	T_{qs}, °K	88	102,77	118,13	132,52	168,91	209,55	252,25	273,0
t=29,85	$r\cdot10^3$, m	6	6,26	6,70	7,06	7,67	8,55	9,52	10,32
	T_{cal}, °K	88	102,13	124,40	141,23	168,96	205,70	243,43	273,0
	T_{qs}, °K	88	101,74	123,72	140,69	167,77	204,13	242,06	273,0

TABLE 2. Comparison of q_0 Computed Precisely and from the Quasistationary Equation

t, sec	0	8,05	15,88	31,57	60,38	121,08	300,58	896,24	1528	1800
T_k, °K	273	93,02	92,25	90,74	88	88	88	88	88	88
$R\cdot10^3$, m	6,00	8,04	9,07	10,61	12,76	15,25	18,81	23,30	25,84	26,70
$q_0^{cal}\cdot10^{-4}$, $\frac{W}{m^2}$	0	42,68	31,08	24,48	20,49	17,72	15,73	14,35	13,83	13,70
$q_0^{qs}\cdot10^{-4}$, $\frac{W}{m^2}$	0	40,11	30,54	24,06	20,14	17,59	15,66	14,37	13,89	13,76

50-mm layer of foam polystyrene, which was sufficient to give the system spherical symmetry.

The illustrations show that the maximum discrepancy in the corresponding temperatures was ±4-5°K and may arise in particular from inaccuracy in the thermophysical parameters used in the calculations; similar calculations with λ = const, as in [2,7], gave deviations of up to 20°K from the measurements and therefore show that T dependence on λ must be incorporated in order to obtain accurate results.

It is of particular interest to compare the exact numerical solution with similar results obtained for the quasistationary case, where a substantially simplified analytical model is employed. Tables 1 and 2 compare the exact and quasistationary solutions for the temperature distributions and heat flux q_0. Such comparisons were made for the comparatively wide ranges 88°K < T_k < 170°K, 3.5 mm $\leq r_0 \leq 6$ mm and showed that the maximum discrepancies in the temperatures and heat fluxes occur for times t less than 10-15 sec and were, respectively, not more than 2 and 6%. These errors are quite acceptable for practical cryosurgery calculations.

If R(t) is known from experiment, the following equation can be solved [4] to determine the blood flow rate in the tissue:

$$\rho'c'\frac{\partial T}{\partial t} = \frac{1}{r^2}\frac{\partial}{\partial r}r^2\lambda'\frac{\partial T}{\partial r} + m_b c_b (T_a - T) + S_m \quad (7)$$

subject to the boundary conditions

$$r = R(t),\quad T = T_c = \text{const},\quad \lambda'\frac{\partial T}{\partial r} = q(t), \quad (8)$$

$$r = \infty,\quad T = T_a,$$

where q(t) is derived from the above solution for the frozen zone. For qualitative purposes, it is possible to assume [11] a quasistationary temperature distribution, with λ' = const and S_m = 0 [11], which then gives

$$m_b = \frac{\lambda'}{c_b}\left[\frac{q(t)}{\lambda'(T_a - T_c)} - \frac{1}{R(t)}\right]^2. \quad (9)$$

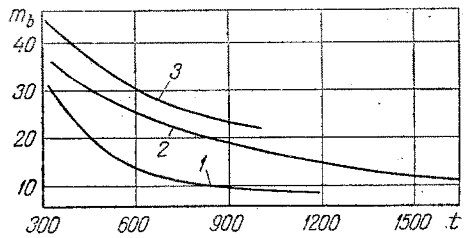

Fig. 3. Distribution of m_b, kg/m^3·sec, as a function of time t (sec) for local freezing of dog leg muscle: 1) r_0 = $3.5 \cdot 10^{-3}$ m, T_k = 88°K; 2) correspondingly $6 \cdot 10^{-3}$ m, T_k = 88°K; 3) $6 \cdot 10^{-3}$ m, T_k = 173°K.

Figure 3 shows results from (9), which indicate that m_b is substantially dependent on T_k, r_0, and t, which indirectly confirms that m_b is dependent on the tissue temperature [8]. The quantitative parameters characteristic of the local blood flow can be refined by numerical solution of (7) and (8), which provides a basis for more refined prediction by traditional techniques [2, 7].

This simulation method thus employs a single-phase heat-conduction equation with a mobile boundary, and it provides satisfactory accuracy in defining the major characteristics of the tissue while requiring much less input data than do traditional methods, while also demonstrating that the quasistationary solution is applicable for the frozen zone throughout the relevant range. Also, the method can be used to define the blood flow rate. In such a case, the measurements must include ones on the growth of the frozen zone, e.g., as determined at the surface of the tissue.

NOTATION

S_b, heat derived from blood flow; S_m, metabolic heat production; r_0, radius of tip; ρ, c, λ, density, specific heat, and thermal conductivity of frozen tissue; T, current temperature; t, time; r, instantaneous coordinate; R, radius of frozen zone; T_0, T_k', T_k, temperatures at tip; T_c, crystallization temperature; t_0', time needed for tip temperature to fall from T_c to T_k'; x, transformed coordinate; h_x, h_t, coordinate and time steps; i, n, coordinate node and time range, respectively; a_1, a_2, a_3, coefficients; sh, hyperbolic sine; q_0, q, heat-flux densities toward the immobile boundary (r_0) and from the mobile boundary (R); f, g, b, coefficients of proportionality; m, exponent; m_b, c_b, T_a, blood flow rate, specific heat, and temperature; ρ', c', λ', density, specific heat, and thermal conductivity of unfrozen tissue; l, latent heat of crystallization.

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