Optimization of Multiprobe Cryosurgery

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This paper describes a general technique for optimizing cryosurgical procedures. The method, which is based on the simplex minimization algorithm, minimizes unnecessary freezing by optimizing various surgical parameters. The optimization procedure is illustrated using a simplified model of prostatic cryosurgery. In this illustrative case, the function to be minimized, F, defined as the volume of healthy tissue destroyed during complete freezing of the prostate, is assumed to depend on three parameters: the number of cryoprobes used, the freezing length per cryoprobe, and the cryoprobe diameter. Using an iterative procedure, the optimization algorithm first alters these parameters, then calculates F by solving a three-dimensional bioheat transfer model of multiprobe cryosurgery, and finally determines whether F is minimized. The iterative procedure continues until unnecessary freezing is minimized. For the model considered here, the optimization code indicates that unnecessary freezing during cryoprostatectomy is minimized using approximately 5 cryoprobes, each 7.5 mm in length and 4 mm in diameter.

Introduction

Cryosurgery utilizes freezing to destroy diseased tissue. Freezing is induced using a cryoprobe, a small, typically nitrogen-perfused hollow cylinder (diameters typically range from 2 to 10 mm), which is insulated everywhere, save the tip. Due to the cryoprobe's diminutive size, freezing is highly localized, and when directly monitored, is readily controlled. Cryosurgical procedures can use one or several probes, the number being determined by both the size of the diseased region and by the patient's ability to withstand surgical trauma. Cryosurgery has been used to treat a range of illnesses, both cancerous and benign (Flocks et al., 1972; Gage, 1982; Rubinsky et al., 1987; Onik, 1991; Onik et al., 1991a; Bischoff et al., 1992), and is generally of greatest utility in cases of local, nondiffuse pathological growth.

Since the introduction of cryosurgical techniques in human patients (Cooper and Lee, 1961), however, unintended perioperative destruction of healthy tissue has been a vexing problem that has, in many cases, limited the technique's application. Such unnecessary freezing can lead to a host of lethal or chronic complications (Debruyne and Kirkels, 1983). Generally, detrimental freezing is of concern when: (1) the diseased region is located close to critical organs or structures, and (2) when freezing cannot be accurately monitored.

At present, cryosurgical planning, i.e., selecting the number, size, location, and spatial orientation of the cryoprobes used in the procedure, is left to a surgeon's judgment. The planning phase is important first, for the reasons outlined above, and second, in high-risk cases where the patient for example, has a heart condition, is in a weakened state, has hemophilia, or is of advanced age. Visualization techniques, in particular ultrasonic monitoring (Onik, 1991; Onik et al., 1991a) allow relatively accurate control of freezing, and effectively widen the surgeon's margin for error during the planning phase. Nevertheless, since monitoring provides only two-dimensional information on an inherently three-dimensional process, and since cryoprobe movement is impossible once freezing has begun, unnecessary tissue destruction continues to be a problem.

Solving the problem of detrimental freezing, or at least *minimizing* healthy tissue destruction, clearly requires more than surgical judgment or reliance on visual monitoring. In this paper, we describe a method for planning cryosurgical procedures. The technique, which essentially quantifies the planning phase, minimizes unnecessary freezing by optimizing the number and size of cryoprobes used in the procedure.

The paper's purpose is to introduce and illustrate the optimization technique. Although the optimization procedure presented here is based on the multidimensional simplex minimization algorithm (Spendly et al., 1962), other minimization techniques may be more suitable in other applications. Similarly, the choice of surgical parameters to be optimized is not limited to those treated here. Rather, clinical applications will likely require that probe locations and orientations also be optimized. These points will be elaborated upon below. The optimization technique is illustrated using a simplified model of multiprobe *prostatic* cryosurgery.

Prostatic Cryosurgery. We choose prostatic cryosurgery for illustration since this procedure is widely used and since it provides a compelling example of the need for quantitatively based cryosurgical planning. We will focus on radical cryoprostatectomy in which the prostate is completely frozen.

In brief, prostatic diseases are either cancerous or benign, and primarily afflict middle-aged and elderly males. Prostate cancer, in various stages of development, is very prevalent, being found in approximately 30 percent of all males over 50 and over 90 percent of males over the age of 85 (Franks, 1977). Complications often include partial to complete blockage of the urinary tract and/or anal canal, pain during urination or bowel movement, and chronic pain in the pelvic and/or spinal regions. Benign prostatic hyperplasia is a related disease, characterized by nonmalignant enlargement of the prostrate, and having symptoms similar to prostate cancer.

Although cryosurgery has been used to treat prostatic diseases, the procedure has not been completely accepted, largely due to difficulties in monitoring the extent of freezing (Onik, 1991). In particular, the surgeon must ensure that both the urethra and the rectum are not damaged, since a number of postoperative complications can otherwise result (e.g., urinary incontinence, urinary tract infection, urethral stenosis, rectal fistula, sphincter damage, and death). As noted above, even relatively accurate visualization techniques do not solve the problem, since it is difficult to monitor the complete three-dimensional freezing front.

Prior Work. A limited number of studies have applied optimization and/or minimization techniques to biological heat transfer problems. For example, Rubinsky and Shitzer (1978)

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solved a one-dimensional inverse Stefan problem, which determined the boundary heat flux leading to maximum tissue destruction during cryosurgery. Dulikravich and Hayes (1988) reported a technique in which tissue survival during cryopreservation was maximized by optimizing exterior cooling rates. Clegg et al. (1988) reported recent work on an inverse method for predicting three-dimensional temperature distributions during hyperthermic treatments. The method simultaneously determined an unknown blood perfusion distribution and the temperature field by minimizing the total difference between known and iteratively calculated temperatures. Although related studies have been carried out in the above areas (Madison et al., 1987; Clegg and Roemer, 1989), it appears that no work has been reported on optimizing multiple probe cryosurgery or on minimizing unnecessary freezing during cryosurgery.

Since the present optimization program utilizes a three-dimensional simulation of multiprobe cryosurgery, it is of interest to discuss briefly prior analytical and numerical simulations of cryosurgical freezing. A number of one- and two-dimensional models of cryoprobe-induced freezing have been reported. For example, Cooper and Trezek (1970, 1971) used one-dimensional analytical models to examine the effect of probe shape on the freezing process. Budman et al. (1986) employed both analytical and numerical models in order to compare predicted freezing characteristics with freezing observed experimentally. Bischoff et al. (1992) developed a one-dimensional numerical model of lung tumor cryosurgery. Other analytical and numerical investigations of cryosurgical heat transfer include those of Staub and Storey (1967) and Comini and Del Giudice (1976). It appears that no three-dimensional simulations of multiple probe cryosurgical freezing have been reported.

Simplex Technique

In this section we first describe the simplex algorithm and then apply it to optimize cryosurgery. The multidimensional downhill simplex method (Spendly et al., 1962; Nelder and Mead, 1965), is a direct search minimization technique that utilizes simple geometric concepts to determine function minima.

Given a function, F, of K variables, p_i $(i=1, 2, \ldots, K)$, we seek a local minimum of F in K-space. The minimization process begins with the construction of a K-dimensional simplex (where for example, a simplex in two dimensions is a triangle, or in three dimensions, a tetrahedron). This initial construction is accomplished by evaluating F at $K+1$ points, $x_1, x_2, \ldots, x_{K+1}$, where each point, $x(p_1, p_2, \ldots, p_K)$, corresponds to a different set of independent variables. We imagine that each point x corresponds to a vertex, and that the set of all $K+1$ vertices defines a K-dimensional simplex. Once the simplex is thus constructed, the values of F at all $K+1$ vertices are compared. The vertices v_h and v_s, at which F assumes its largest and smallest values, $F_{\max}$ and $F_{\min}$, respectively, are then identified. The crux of the simplex method is to displace v_h to a new point, $x^*(p_1, p_2, \ldots, p_K)$, such that

$$F(x^*) < F_{\max} \tag{1}$$

Once x^* is found, a new vertex, v^*, is placed there, and the simplex is reconstructed using the K unchanged vertices and v^*.

Displacement of v_h can occur in one of three ways: reflection, contraction, or expansion. Following Nelder and Mead (1965), a reflection projects v_h to a point x^* such that

$$x^* = (1+\alpha)x^o - \alpha x^h \tag{2}$$

where $x^h(p_1, p_2, \ldots, p_K)$ is the point defining v_h, $x^o(p_1, p_2, \ldots, p_K)$ is the centroid of all remaining vertices (not including v_h), and α is a positive constant called the reflection coefficient. To illustrate, in a three-dimensional space, in which the simplex is a tetrahedron, a reflection would project v_h through the centroid of the opposing tetrahedral face. The new simplex in this case would be a somewhat inverted image of the original tetrahedron. If a reflection results in $F_{\min} < F(x^*) < F_{\max}$, then x^* is taken as the new vertex, and the simplex is reconstructed. In the event that $F(x^*) < F_{\min}$, then we have happened onto a region of decreasing F, and thus attempt an *expansion* to a new point $x^{**}(p_1, p_2, \ldots, p_K)$, where x^{**} is given by

Nomenclature

c = specific heat, W s/(kg K)
d_p = probe diameter, mm
$F = F(n_p, l_p, d_p)$ = volume of healthy tissue frozen, mm^3
$F*$ = (volume of extraprostatic tissue frozen)/(volume of prostate) * 100 percent
h = heat transfer coefficient, W/(m^{2}K)
k = thermal conductivity, W/(mK)
l_p = probe heat transfer length, mm
n_p = number of probes
p = variable in the minimization problem
Q = metabolic heat source term, W/m^3
t = time, s
t_o^c, t_o^f = time required to completely freeze prostate on $25\times25\times25$ and $49\times49\times49$ node grids, respectively
T = temperature, K
T_i = initial temperature of prostate and extraprostatic tissue, K
v = coordinate point of a vertex on a K-dimensional simplex
w = blood perfusion, ml/(g min)
x, y, z = Cartesian coordinates, m
x = coordinate point in K-space
α = thermal diffusivity, m^2/s; also reflection coefficient
β = contraction coefficient
γ = expansion coefficient
ϵ = minimization convergence tolerance
ρ = density, kg/m^3

Subscripts

a = arterial
b = blood
f = frozen
h = high value
i, j, k = grid indices for x, y, and z directions; also index for optimization variables
ln = liquid nitrogen
max = maximum
min = minimum
p = probe
s = small value
u = unfrozen
∂ = denotes boundary

Superscripts

c = coarse grid
f = fine grid
h = high value
I = iteration number
o = centroid
s = small value
$'$ = primary test point
$**$ = secondary test point

$$x^{**} = (1-\gamma)x^o + \gamma x^h \tag{3}$$

Here, γ, the expansion coefficient, is greater than 1. If $F(x^{**}) < F_{\min}$, then the expansion is successful and a new simplex is constructed using x^{**}. However, if $F(x^{**}) > F_{\min}$, then the expansion is not taken, and the new simplex is constructed using x^*.

It may happen that reflection of x^h to x^* simply leads to another function maximum, i.e.,

$$F(x^*) > F(x_i)$$

where x_i denotes either the set of all vertex points or the set of all vertex points, save x^h. In either case, a *contraction* is called for. A contraction begins by first comparing $F(x^*)$ with $F(x^h)$ $(=F_{\max})$. If $F(x^*) < F_{\max}$, then a new vertex is placed at x^*, while no change is made if $F(x^*) > F_{\max}$. Given this new temporary simplex, x^h is then displaced to x^{**}, where

$$x^{**} = (1-\beta)x^o + \beta x^h \tag{4}$$

Here, β, the contraction coefficient, satisfies $0 < \beta < 1$. The contraction is successful and x^{**} is taken as a new vertex if $F(x^{**}) < \min(F_{\max}, F(x^*))$. Otherwise, we have to construct a completely new simplex by contracting all vertices around the current minimum point at $x^s(p_1, p_2, \ldots, p_K)$ (where $F(x^s) = F_{\min}$). This latter procedure is accomplished by moving each vertex point, x_1, to the point $(x_i + x^s)/2$.

Through this process of reflection, expansion, and contraction, the simplex method eventually drives the simplex to a region of K-space, where F has a local minimum. As the minimum is approached, the vertices begin to approach one another and a criterion can be employed to signal convergence. Here, convergence is assumed to occur if the following condition holds (Press et al., 1981):

$$|F_{\max} - F_{\min}| / |F_{\max} + F_{\min}| < \epsilon \tag{5}$$

where ϵ is a specified tolerance.

Optimizing Cryosurgery. For our illustration, the function to be minimized, F, is the volume of healthy extraprostatic tissue destroyed during the freezing process:

F = volume of healthy tissue destroyed during cryosurgery

We assume that this function depends on three independent variables ($K=3$): the number of probes (n_p), the probe diameter (d_p), and the probe active length (l_p), or

$$F = F(n_p, l_p, d_p) \tag{6}$$

As explained below, we fix the location and orientation of all n_p cryoprobes rather than determining these parameters through minimization. This latter simplification greatly reduces the problem's scope, shrinking the parameter space from $6n_p + 3$ to three dimensions (where the $6n_p + 3$ dimensions correspond to 3 n_p coordinates fixing n_p reference points on n_p probes, 3 n_p corresponding direction cosines, and 3 probe parameters, n_p, l_p, d_p).

Following Nelder and Mead (1965) α, γ, and β are given the values 1.0, 2.0, and 0.5.

Heat Transfer Model

Heat transfer within a blood perfused tissue is modeled by the bioheat transfer equation (Pennes, 1948):

$$\rho c_p \frac{\partial T}{\partial t} = \nabla \cdot [k \nabla T] - \rho_b \cdot w c_b (T - T_a) + Q \tag{7}$$

where ρ is the tissue density, c_p is the tissue specific heat, k is the tissue thermal conductivity, w is the blood perfusion, c_b is the blood specific heat, ρ_b is the blood density, T_a is the arterial blood temperature, and Q is the metabolic heat generation. Although the validity of this model has recently been questioned by several investigators (see, e.g., Chen, 1980), it nevertheless predicts heat transfer well within first and second-generation vascular regions, and captures temperature profiles within third-generation vascular regions, which agree reasonably well with comprehensive theoretical predictions (Charny et al., 1990).

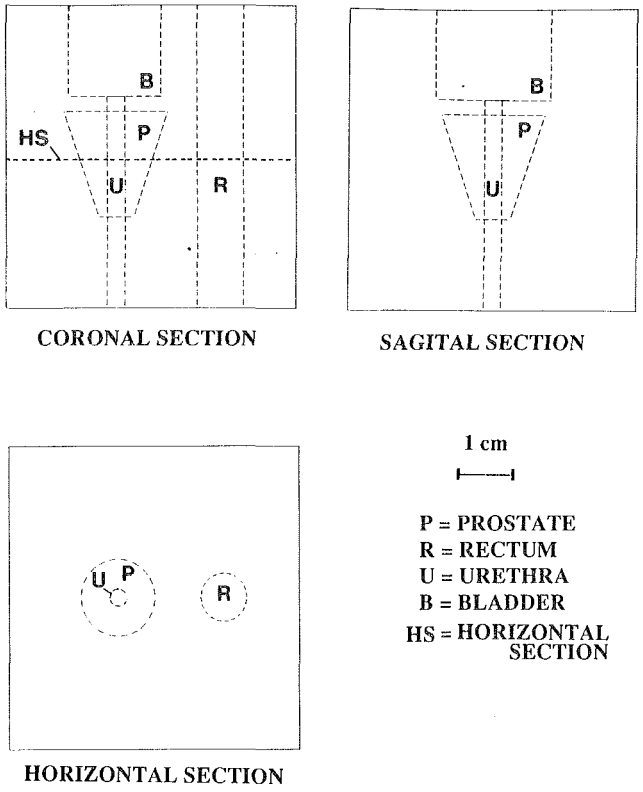

Fig. 1 Geometry of prostate region; horizontal plane bisects the tissue domain

The boundary conditions and initial condition for the problem are as follows. At the surface of each cryoprobe, the normal flux is given as

$$k \frac{\partial T}{\partial n} = h_p (T - T_p) \tag{8a}$$

The tissue temperature at the boundary of the problem domain is fixed at a constant value:

$$T_\partial = T_o \tag{8b}$$

while the initial temperature within the domain is given as a function of position:

$$T(x, y, z, t=0) = G(x, y, z) \tag{8c}$$

Assumptions

Since this work is designed to illustrate a cryosurgical optimization technique, simplified heat transfer and physiological models are used. The assumptions are as follows:

1 The shapes of the major structures lying within the problem domain are simplified. Specifically, we idealize the three-dimensional bounding surfaces of the prostrate, urethra, bladder, and rectum as being composed of intersecting circular cylinders, circular conic sections, and planes. Refer to Fig. 1. Likewise, cryoprobes are idealized as simple circular cylinders.

2 Differences in tissue thermophysical properties are not accounted for, and all properties, save thermal conductivity, are assumed to be temperature independent. Thermal conductivity assumes one constant value in the frozen phase, and another constant value in the unfrozen phase. These simplifications neglect tissue density variations and the temperature dependence of various properties (e.g., specific heat, thermal

conductivity). A simulation that accurately accounts for tissue geometry, property inhomogeneities, and temperature dependencies will require a much larger computational effort.

3 Due to the overwhelming influence of the cryoprobes on tissue heat transfer (Anderson et al., 1988), metabolic heat release is neglected.

4 During prostatic cryosurgery, the bladder is flushed with warm solution in order to prevent bladder freezing. This procedure is simulated by maintaining the bladder at 310 K.

5 In order to simulate a recently developed technique in which a heated fluid is introduced into the urethra through the urinary tract (Onik et al., 1991a), we assume that the temperature on the centerline of the urethra is fixed at a characteristic temperature of 310 K. All other temperatures within the urethra are allowed to vary, and are determined as part of the overall solution.

6 For the initial condition, the operating area, save the bladder and the urethra, is precooled to 285 K. The urethra's initial temperature and the bladder's fixed temperature are 310 K.

Following Clegg et al. (1988), we employ approximate representative tissue properties in the calculations. Property and parameter values are as follows (Vanderby et al., 1988; Bischoff et al., 1992): $c_p = c_b = 4300$ W s/(kgK), $\rho = \rho_b = 1000$ kg/m^3, $w = 100$ ml/(100 g min), $k_f = 2.25$ W/(m/K), $k_u = 0.63$ W/(mK), $T_a = 310$ K, $T_p = 83$ K, $h_p = 500$ W/(m^{2}K).

Optimization Study Simplifications

The program begins by incrementing the number of cryoprobes from some initial number (e.g., 0). For n_p cryoprobes, the prostrate is divided into n_p equiangular subregions about a given reference axis. In order to reduce the scope of the minimization problem, we specify the position and orientation of all n_p probes by placing each cryoprobe (of given radius and length) at the centroid of each subregion, with its long axis parallel to the urethra's long axis (see Fig. 1). The latter simplification is consistent with the fact that the preferred orientation for cryoprobe application during most operations is somewhat parallel to the urethra. The former simplification should provide spatially uniform freezing since our idealized prostate is symmetric about the urethra. In general, when the object to be frozen lacks symmetry, then probe placement may have to be determined through minimization.

Numerical Method

Three-Dimensional Freezing Simulation. The optimization algorithm requires that the three-dimensional heat transfer problem defined by Eqs. (7) and (8) be solved every time n_p, l_p, or d_p is altered during minimization. A number of techniques exist for treating unsteady phase change problems (see, e.g., Crank, 1984). Here, we employ the finite difference enthalpy method (Lunardini, 1981) with an Euler forward integration scheme. The problem domain corresponds to a cubic volume 5 cm on a side, slightly offset from the center of the prostate. A mesh of 43 nodes in each coordinate direction (79507 total nodes) is employed for the calculations discussed here. The three-dimensional freezing simulation was checked for grid independence by comparing solutions on $25 \times 25 \times 25$ and $49 \times 49 \times 49$ node meshes. A comparison of temperature fields at the time of complete prostatic freezing, t_o, indicated a maximum relative temperature difference, Δ, of 4.2 percent, where

$$\Delta = \max\left(\frac{|T_i^f - T_I^c|}{T_i^f}\right)$$

Here, T_i^f and T_I^c denote corresponding nodal temperatures on the fine and coarse grids, respectively. (Note, the indices i and I have different values in each mesh but refer to the temperature at the same location within the problem domain. The comparison was carried out using the parameter combination $(n_p, l_p, d_p) = (5, 6.0$ mm, 2.5 mm).) The relative difference in freezing times for this comparison case,

$$\frac{|t_o^f - t_o^c|}{t_o^f}$$

was 3.4 percent. The time step used with the $43 \times 43 \times 43$ mesh was 0.005 s.

Optimization Algorithm. At the beginning of the program, an initial simplex is constructed by guessing four different combinations of (n_p, l_p, d_p). The associated F's are determined by executing the three-dimensional freezing simulation four times. Once the initial simplex is constructed, the optimization program uses the following iterative procedure to minimize F:

1 The current simplex is altered by displacing v_h to a new point in parameter space such that $F_{\max}$ becomes smaller. As described above, movement of v_h is accomplished by (*i*) reflection, (*ii*) reflection followed by expansion, (*iii*) contraction, or (*iv*) complete contraction around the current minimum.

2 Each time v_h is moved to a candidate point in parameter space, the corresponding F is calculated by inputing the $n_p l_p d_p$ coordinates of the candidate point into the freezing simulation. (The simulation is capable of modeling freezing due to variable numbers of probes, each of variable length and diameter.) Thus, each *permanent* displacement of v_h requires at least one simulation run (in the case of a reflection), and as many as three runs (in the case of a complete contraction). Note that the simplex procedure generally displaces v_h to points in parameter space where n_p is nonintegral. Thus, once the simplex procedure determines a candidate point, then the corresponding value of n_p is rounded to the nearest integer prior to use in the freezing simulation. Similarly, the l_p and d_p values determined by each v_h displacement are altered to coincide with the nearest gridlines prior to use in the simulation.

The simplex is iteratively altered until a local minimum in F is located, as indicated by the inequality in Eq. (5).

Results and Discussion

Freezing Characteristics. The qualitative features of the freezing process are depicted in Figs. 2–4, in the case when $n_p = 5$, $l_p = 6.0$ mm, and $d_p = 2.5$ mm. The location of the freezing front is shown in the coronal, sagittal, and horizontal planes at various stages of freezing. The iceballs propagate preferentially in the radial direction and gradually grow into one another as the prostate approaches complete freezing. Although the sagittal isotherm maps appear to show complete freezing within the urethra, the coronal and horizontal sections reveal that this is not the case. Instead, freezing within the urethra occurs predominantly on its distal edges and is inhibited in the central region due to the imposed constant temperature boundary condition on the centerline (see assumption 5 above). Freezing is also inhibited near the constant-temperature bladder (assumption 4), and consistent with clinical observations, freezing remains confined to the immediate vicinity of the probes. Prostatic freezing decreases at an approximately exponential rate under the above conditions ($n_p = 5$, $l_p = 6.0$ mm, $d_p = 2.5$ mm), with a time constant on the order of 0.05 s^{-1}. Note that in Fig. 4, the cryoprobes appear to be square due to the coarseness of the grid. Note too that the horizontal plane shown in Fig. 4 bisects the tissue domain as shown in Fig. 1.

Results of Optimization Procedure. For the purpose of illustration, and due to the computational expense (on the order of 10 to 20 min cpu time on the Cray X-MP), we only consider two different sets of initial parameter combinations. The results from the two optimization runs are given in Tables 1 and 2. As shown in the tables, ϵ equals 0.1 in the first test case

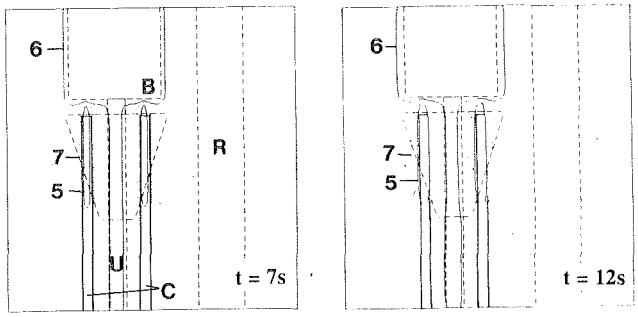

Fig. 2 Isotherms in coronal plane when $n_p = 5$ probes, $l_p = 6.0$ mm, $d_p = 2.5$ mm; isotherm spacing = 40 K

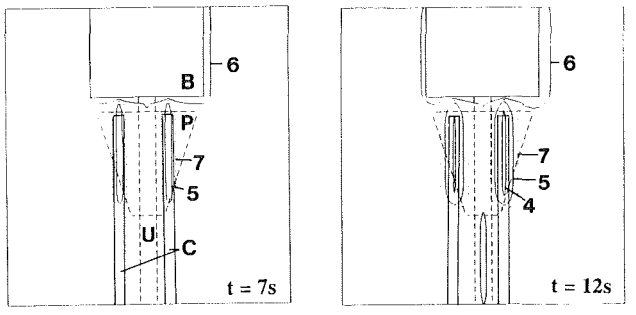

Fig. 3 Isotherms in sagittal plane when $n_p = 5$ probes, $l_p = 6.0$ mm, $d_p = 2.5$ mm; isothermal spacing = 40 K

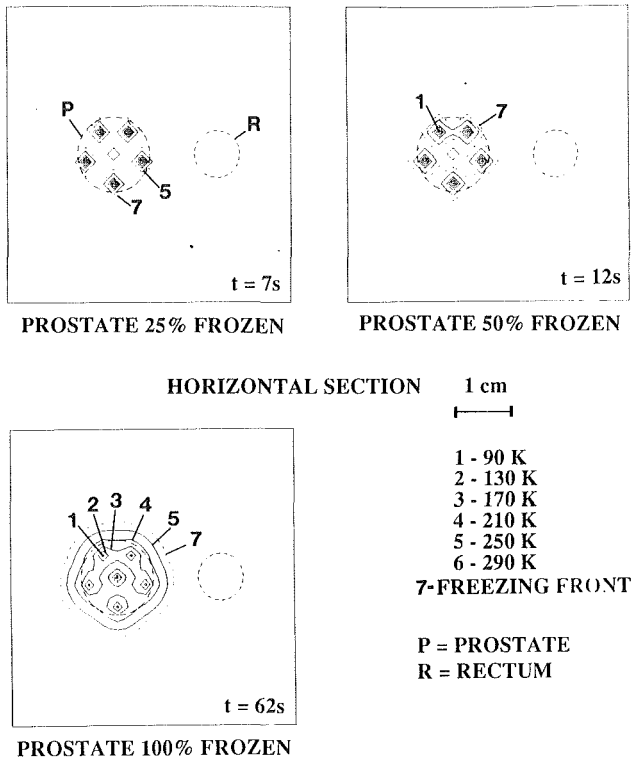

Fig. 4 Isotherms in horizontal plane (as defined in Fig. 1) when $n_p = 5$ probes, $l_p = 6.0$ mm, $d_p = 2.5$ mm; isotherm spacing = 40 K

and 0.01 in the second. Following construction of the initial simplex, the first test required three subsequent adjustments of the simplex to achieve convergence, while the second required 10 subsequent iterations. Note that in the tables, F^* is the volume of frozen extra-prostatic tissue divided by the volume of the prostate, determined at the time of complete prostatic freezing.

From the tables, we see that convergence occurs approximately at the point where n_p, l_p, and d_p equal 5 probes, 7.5 mm, and 4.0 mm, respectively. We thus take this combination of probe parameters as the one that leads to minimal extra prostatic freezing. Interestingly, this point appears to be the approximate minimum for a fairly large region within n_p, l_p, d_p space, since a wide range of initial parameter combinations approach it.

Extension of Present Technique. In closing this section, we outline some of the general features associated with optimization problems and note possible modifications to the present application:

1 Other minimization techniques that appear to be suitable for the present problem include Powell's direct search method (Powell, 1964) and the simulated annealing technique (Press et al., 1986). In contrast, techniques requiring derivative calculations of F (e.g., the Davidon–Fletcher–Powell variable metric method and the Polak–Ribiere conjugate gradient method), may be inefficient.

2 Defining the function to be minimized is problem specific. For example, in the area of prostatic cryosurgery, it is sometimes important to minimize freeze damage to the seminal vesicles. In this case, the function to be minimized would be the amount of seminal vesicle freezing produced during cryosurgery.

3 Once a function is defined, all of the parameters on which it depends should be identified.

4 In order to reduce the scope of the minimization problem, some of these parameters might have to be specified in some way other than minimization. For example, in the problem treated here, we specified probe placement and probe orientation.

Table 1(*a*) Initial parameter values—Case 1 ($\epsilon = 0.1$)

Point	No. of Probes	Probe Dia. (mm)	Probe Length (mm)
1	3	2.80	6.50
2	4	3.20	7.00
3	5	3.60	7.50
4	6	4.00	8.00

Table 1(*b*) Parameter values and amount of frozen tissue at convergence

Point	No. of Probes	Probe Dia. (mm)	Probe Length (mm)	F^* (%)
1	6	4.06	8.08	71.5
2	5	3.60	7.50	75.5
3	5	3.60	7.50	75.5
4	6	4.00	8.00	71.5

Table 2(*a*) Initial parameter values—Case 2 ($\epsilon = 0.01$)

Point	No. of Probes	Probe Dia. (mm)	Probe Length (mm)
1	5	4.00	7.00
2	7	4.50	9.00
3	9	5.00	7.00
4	8	5.50	5.00

Table 2(*b*) Parameter values and amount of frozen tissue at convergence

Point	No. of Probes	Probe Dia. (mm)	Probe Length (mm)	F^* (%)
1	6	4.10	7.44	71.8
2	5	3.97	8.11	71.4
3	5	3.94	7.50	71.8
4	5	3.81	7.48	71.4

F^* is the volume of extra-prostatic tissue frozen at the time of complete prostatic freezing divided by the volume of the prostate (expressed as a percentage)

Conclusions

This paper presents a method for optimizing cryosurgical procedures. Although the method is illustrated using the particular case of complete cryoprostatectomy, the technique can be specialized to aid in planning other cryosurgical procedures, such as freezing of single or multiple tumors. For the present application, the approximate optimal parameter combination is $n_p = 5$ probes, $l_n = 7.5$ mm, and $d_p = 4.0$ mm.

Clinical application of this technique will require, at minimum, accurate biophysical models of the tissues being frozen, comprehensive bioheat transfer models that accurately account for blood perfusion, and efficient minimization algorithms capable of treating large numbers of parameters. Due to the highly localized nature of cryosurgical freezing, the size of the tissue domain considered could conceivably be reduced to a volume not much larger than the diseased region. This would clearly reduce the scope of the problem.

Acknowledgments

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