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# UNCERTAINTY IN TEMPERATURE MEASUREMENTS DURING CRYOSURGERY

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**Summary**: Temperature sensors are routinely applied in cryosurgery for the purpose of recording the thermal history of the cryotreated tissue. The temperature data is compiled to evaluate the freezing front propagation and to correlate the thermal history with the resulting cryoinjury. The current study arises from efforts to quantify the uncertainty in temperature measurements during cryosurgery due to heat conduction of the temperature sensor, which heats the point of measurement and interferes with the temperature field.

Keywords: Temperature Measurements, Uncertainty, Cryosurgery, Mathematical Analysis

## Introduction

Thermocouples are perhaps the most commonly used instruments for temperature measurements, with the possible exception of the glass thermometer for medical applications. They are inexpensive, small in size, simple to use, and remarkably accurate when used with an understanding of their peculiarities (1).

For medical applications, the thermocouple wires can be inserted into a standard syringe needle, or similar metallic tubing, and the thermocouple junction located adjacent to the needle's tip, forming a "temperature sensing needle", which is also known as a "thermocouple needle". The thermocouple needle enables a simple and convenient means of temperature sensor localization, which can be applied straightforwardly or guided by some imaging technique such as ultrasound. The thermocouple needle, used singly or as one of an array, is routinely applied in cryosurgery for the purpose of recording the thermal history (2-4,6). The temperature data from the cryoprocedure is compiled to evaluate the freezing front propagation and to correlate the thermal history with the resulting cryoinjury, seeking to define the so-called "lethal temperature".

The thermocouple needle is manufactured from metallic materials, such as stainless-steel, which have typical thermal conductivity and thermal diffusivity values of at least one order of magnitude higher than those of the surrounding biological tissues (see Table 1 for comparison). Higher thermal conductivity value represents higher ability of the material to conduct heat, and higher thermal diffusivity value represents faster thermal response of the material to a sudden temperature change. These differences in thermophysical properties introduce thermal interaction between the sensor and the sensed phenomenon, causing an increased heat flow along the thermocouple needle, which affects the temperature field in the vicinity of the sensor. Thus, the sensed temperature differs from the temperature that would have existed at the same location in the absence of the sensor. This temperature difference is generally not known and causes uncertainty in measurements, where the term uncertainty is used with respect to an undisturbed system (with no temperature sensor). The current study arises from efforts to quantify the uncertainty in thermocouple needle measurements during cryosurgery due to the phenomenon of heat conduction by the thermocouple needle. While this study deals with one source of uncertainty in temperature measurements, there are other sources which contribute to the uncertainty in measurements, such as electrical amplifiers, analog to digital converters, surrounding temperature compensation, the presence of electrical/magnetic fields, uncertainty in sensor localization, etc. (1,7).

## Analysis

It is assumed in this study that the heat transfer in the cryotreated tissue is governed by the classical bioheat equation:

$$C\frac{\partial T}{\partial t} = k\nabla^2 T + \dot{w}_b C_b (T_b - T) \tag{1}$$

where C is the specific heat of the tissue, T is the tissue temperature, t is the time, k is the thermal conductivity, $T_b$ is the blood temperature, $\dot{w}_b$ is the blood perfusion rate, and $C_b$ is the specific heat of blood (Fig.1). The specific heat of the tissue is taken as an effective property, including the latent heat effect in the phase transition temperature range. It follows that the integral of the effective specific heat with respect to the temperature, within the phase transition temperature boundaries, yields the latent heat (8).

Cryosurgery is performed with a large variety of cryoprobe shapes and dimensions. Flat-surface cryoprobes are typically applied for superficial treatments, while cylindrical cryoprobes are commonly applied in minimally invasive procedures. In order to study the most severe case of uncertainty, and in order to simplify the actual three-dimensional heat transfer process to a two-dimensional problem, the current analysis is focused on temperature measurements in perpendicular to a flat-surface cryoprobe, as schematically shown in Fig. 2.

With respect to Fig. 2, the thermocouple needle is located perpendicular to a flat cryoprobe surface at a distance, L, which is typically in the range of up to 25 mm. For the purpose of the numerical solution, a thermal insulation boundary condition is assumed at a distance B from the cryoprobe surface:

$$\frac{\partial T}{\partial z}(r, B) = 0 \tag{2}$$

The justification for this assumption, together with some insight regarding the practical values of B, are dealt with in the results and discussion section.

An axi-symmetric heat transfer process is assumed around the thermocouple needle, which is presented in a cylindrical domain having an outer radius $R_0$. The radius $R_0$ is chosen such that the temperature distribution on the outer surface of the domain is not affected by the presence of the thermocouple needle:

$$\frac{\partial T}{\partial r}(R_0, z) = 0 \tag{3}$$

Thus, the temperature distribution at $r = R_0$ (in z direction) is one-dimensional in nature, and is affected only by the cryoprobe surface temperature, the boundary condition described in Eq. (2), and the transient response of the tissue. Practically, the boundary condition described in Eq. (3) can be easily satisfied by taking the radius $R_0$ to be greater than ten times the diameter D of the thermocouple needle.

The heat transfer in the thermocouple needle can be described by the ordinary heat conduction equation:

$$C\frac{\partial T}{\partial t} = k\nabla^2 T \tag{4}$$

Equations (1)-(4) are solved explicitly, using a finite differences numerical scheme as suggested in (8). For clarification purposes only, the numerical scheme is present here in brief, independent of the coordinate system:

$$T_{i,j,k}^{p+1} = \frac{\Delta t}{\Delta V_{i,j,k}\left[C_{i,j,k} + (\dot{w}_b C_b)_{i,j,k}\Delta t\right]}\sum_{l,m,n}\frac{T_{l,m,n}^p - T_{i,j,k}^p}{R_{l,m,n-i,j,k}} + \frac{C_{i,j,k}T_{i,j,k}^p - (\dot{w}_b C_b)_{i,j,k}\Delta t\, T_b}{C_{i,j,k} + (\dot{w}_b C_b)_{i,j,k}\Delta t} \tag{5}$$

where i,j,k are the spatial indexes of the numerical grid; p is the time level; $\Delta t$ is the time interval; $\Delta V$ is the volume associated with the specific grid point; l,m,n are the indexes of all the neighboring grid points to the specific grid point i,j,k; and $R_{l,m,n-i,j,k}$ is the thermal resistance to heat flow from the grid point l,m,n to the grid point i,j,k. The thermal resistance to heat flow, R, is dependent on the chosen coordinate system. This numerical scheme is conditionally stable with the stability criterion:

$$\Delta t \le \left[\frac{\Delta V_{i,j,k}\ C_{i,j,k}}{\sum_{l,m,n}(1/R_{l,m,n-i,j,k})}\right]_{\min} \tag{6}$$

Further discussion with regard to stability criteria and solution efficiency is given in (8).

The problem has been solved for the following parameters: (a) an initial uniform temperature of 37°C; (b) a constant cooling rate of 200°C/min at the cryoprobe surface down to the liquid nitrogen boiling temperature, -196°C, followed by a constant temperature of -196°C thereafter; (c) the phase transition occurs over the temperature range of 0 down to -22°C; (d) the thermophysical properties outside of the phase transition temperature range are constant as listed in Table 1; (e) the effective specific heat within the phase transition range includes a latent heat effect of 300 MJ/m$^3$-°C; (f) the thermal conductivity is linearly dependent on temperature within the phase transition temperature range, between the two extreme values listed in Table 1 (also shown in Fig. 1); (g) the heating effect of blood perfusion, $\dot{w}_b C_b$, has a maximal value of 40,000 W/m$^3$-°C at 37°C, and decays linearly to 0 at 0°C.

The thermocouples copper-constantan or iron-constantan are commonly used in cryogenic temperatures. Although the thermocouple needle contains constantan and copper or iron wires, which have significantly higher thermal conductivity than that of stainless-steel, the heat capacity of the stainless steel needle is much higher than that of the thermocouple wires (the heat capacity is the production of the volumetric specific heat and the volume).

Therefore, the thermocouple needle is assumed to have the uniform average thermophysical properties of stainless-steel: thermal conductivity of 50 W/m-°C and specific heat of 3.6 $MJ/m^3$-°C. Further discussion with regard to this assumption is given below. It is noted that the thermal conductivity of metals increases significantly with the decrease in temperature within cryogenic temperature range (Table 1).

**Results and Discussion**

Thermocouple needle diameters chosen for the current study were of 16, 21, and 30 gauge (equal to 1.65, 0.8, and 0.3 mm, respectively), representing the typical spectrum of diameters for cryosurgical applications; see (10) for example. Results are discussed for two representative cases of L = 2 and L = 10 mm.

The axial temperature distribution along the thermocouple needle and the corresponding temperature distribution in the absence of the thermocouple needle, are shown in Figs. 3-5. Results are presented for the instances in which a thermocouple needle's tip reaches 0, -22, and -45°C, where the first two temperatures are the upper and lower boundaries of phase transition temperature range, respectively, indicating the interfaces' location. The temperature of -45°C is assumed to be the upper boundary below which maximal cryodestruction is achieved (the so-called "lethal temperature"). The latter assumption is taken for the purpose of uncertainty analysis below the phase transition temperature range only, bypassing the discussion with regard to the actual value of this temperature, which is known to be affected by many factors (5). Figure 6 shows two-dimensional temperature fields around the thermocouple needle for the special case of D = 21 gauge and L = 2 mm, which is also addressed in Fig. 4(a).

As presented in the analysis section and Table 1, the thermal conductivity and thermal diffusivity values of the thermocouple needle are of at least one order of magnitude higher than those of the surrounding tissues. This causes the thermocouple needle to conduct heat from warmer to colder areas of the tissue. Hence, the thermocouple needle tends to lower the local temperature in warmer areas and to elevate the local temperature in colder areas. In Fig. 3(a) for example, it can be seen that, indeed, the temperatures in the vicinity of the thermocouple needle's tip (solid line) are higher than those far distant from the thermocouple needle (dashed line). This difference is maximal at the thermocouple needle's tip, which increases in the range of 20 to 28°C when the tip's temperature decreases in the range of 0 to -45°C, respectively. This temperature difference at a tip temperature of -45°C is illustrated in Figs. 3(a), 4(a), and 5(a). In general, this temperature difference at the thermocouple needle's tip decreases with the decrease of the thermocouple needle diameter and with the increase of the distance between the tip and the cryoprobe surface, as listed in Table 2.

The major interference of the thermocouple needle with the temperature field of the surrounding tissue can be seen in Fig. 6. With respect to Fig. 6(c), following an imaginary line at a constant distance of 2 mm from the cryoprobe surface (which is at z = 0), one can observe a rapid temperature increase when moving towards the thermocouple's tip. The temperature difference between the two ends of this imaginary line, at r = 0 and r = ∞, is the same temperature difference as that illustrated in Fig. 4(a).

The thermocouple needle is sometimes used to evaluate the freezing front location. More specifically, it is used to indicate the instant at which the freezing front passes the location of the temperature sensor. The time periods, from the beginning of the cryoprocedure up to the instant at which a specific temperature is sensed at the thermocouple needle's tip, are listed in Table 3. For example, consider a case in which an indication is desired at the instant at which some point at a distance of 10 mm from the cryoprobe is cooled down to -45°C. Table 3 reveals that this will happen after 160 seconds (D = 0), however, thermocouple needles in diameters of 30, 21, and 16 gauge, will indicate this temperature in a delay of 13, 35, and 65 seconds, respectively. In general, this error is within the range of 20% to 45% for the cases studied here.

Special attention has been given to the temperature at the tip of the thermocouple needle up to this point in the discussion. It has been shown that the difference between the measured temperature and the temperature that would have existed at the same location in the absence of the thermocouple needle, is maximal at the tip. However, the junction of the thermocouple, i.e. the point at which the temperature is measured, is always at some unknown short distance from the needle's tip. Hence, the temperature difference values discussed above are the upper boundary of the expected temperature difference. At this point the discussion shifts from an exact temperature difference to an uncertainty interval, i.e. the maximal possible value that the above temperature difference may have.

The orientation of the thermocouple needle plays an important role in the analysis of uncertainty. Figure 6 shows the major effect of the thermocouple needle placed parallel to the maximal temperature gradient, e.g., perpendicular to the isotherms. Furthermore, one may predict that placement of the thermocouple needle parallel to the isotherms will result in a minor effect on the temperature distribution in general, and on the uncertainty in measurement in particular (note that the heat flow along an isotherm is zero by definition). Unfortunately, the frozen region is egg-shaped in minimally invasive procedure, and the thermocouple needle cannot be placed parallel to the isotherms. However, special care should be taken to ensure that the thermocouple is not placed radial to a cryoprobe (not perpendicular to the isotherms). From this consideration, again, the calculated values presented above give the upper boundary of the uncertainty interval.

One may speculate that the heating effect of blood perfusion would play an important role in the uncertainty analysis. Although results are presented for the case of maximal blood perfusion only, numerical simulations were repeated for the case of no blood perfusion as well. Only minor differences were observed between these two general cases, which cannot indicate a significant change in uncertainty. In general, the case with blood perfusion shows somewhat higher intervals of uncertainty.

We now return to the mathematical analysis. The two boundary conditions assumed in Eqs. (2) and (3) still remain unjustified. From Fig. 5, for example, it can be seen that the temperature at $z = -15$ mm has not changed from its initial value up to the instant for which the temperature distribution is presented. In such a case, where a boundary condition of zero heat flux was chosen, and no temperature change was observed at the same location, the domain is said to behave like a semi-infinite domain from heat transfer considerations in the same direction. Thus, the boundary condition at $z = B$ serves the numerical solution only, but does not affect the resulting temperature field (a value of $B = 50$ mm was taken for all numerical simulations). The boundary condition at $r = R_0$ is handled similarly, where the temperature gradients in the radial direction can be observed in Fig. 6 (note that the outer radius, $R_0$, is much larger than the radius of the field presented in this figure).

We now return to the assumed thermophysical properties of the thermocouple needle. One may argue that the chosen average thermophysical properties of the thermocouple needle are too high or too low, and, therefore, the results presented above are questionable. The thermal diffusivity of the biological tissues is so low, with respect to metals, that it dictates the time scale of the heat transfer process. Furthermore, the latent heat effect of freezing is so significant that it dictates the time scale of the bioheat transfer process. Therefore, infinite thermal conductivity and thermal diffusivity values could have been chosen for the thermocouple needle without significantly affecting the results.

One possible way of decreasing the uncertainty in measurements is to use a plastic needle for the construction of the thermocouple needle. Plastics have typical thermal conductivity of about one fifth of that of unfrozen tissues and negligible thermal conductivity with respect to that of frozen tissues, Table 1. With the plastic needle setup, the only cross-section of higher thermal conductivity is that of the thermocouple wires, while the plastic needle provides the stiffness. The analysis of a plastic needle case remains to be done.

Uncertainty in measurements is also associated with the quality of the thermocouple materials and of the peripheral equipment used to translate the thermocouple output to temperature values. Uncertainty intervals due to the quality of the materials are provided by the manufacturer and are typically in the range of ±0.1 to ±0.5°C. Uncertainty intervals due to the quality of peripheral equipment are typically smaller than ±0.1°C. Therefore, the uncertainty in measurements during cryosurgery due to heat conduction along the thermocouple needle overwhelms uncertainties from these other sources.

Finally, uncertainty due to temperature sensor localization is addressed. For the purpose of the current stage of the discussion, a temperature sensor of an infinitesimal diameter is assumed, i.e. no uncertainty due to heat conduction is now involved. The temperature gradients in the vicinity of the thermocouple needle's tip, when the tip experiences temperatures in the range of 0 down to -45°C, are 30 and 15°C/mm at the distances of 2 to 10 mm from the cryoprobe surface, respectively, as can be seen from Fig. 5 for example (dashed lines). This means that a reasonable localization error of 1 mm will result in uncertainty intervals of 30 and 15°C in measurements when the measurement point is at the distances of 2 and 10 mm from the cryoprobe surface, respectively. It appears that the uncertainty due to localization error decreases as the distance from the cryoprobe surface increases. It can be concluded that the uncertainty interval will increase with the increase of the cryoprobe cooling rate, and especially in short distances from the cryoprobe surface. It can further be concluded that a 1 mm error in thermocouple needle localization, on the one hand, and heat conduction by a 21 gauge thermocouple needle on the other hand, will introduce uncertainty intervals of the same order of magnitude (see also Table 2).

An alternative way of reducing heat conduction and decreasing the localization error has been suggested (9), in which the needle and the thermocouple are not rigidly connected. Using this technique, the needle is used to deliver the thermocouple junction to some specific location, and the needle is withdrawn before the beginning of the operation. Extremely thin thermocouple wires of 0.1 mm are used here. However, since in this form of application the thermocouple junction no longer has a fixed location in space, some imaging device is required to complete the operation.


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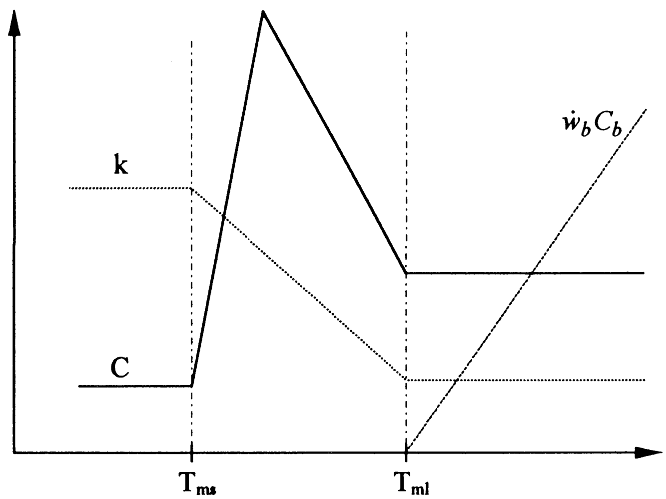



Figure 1: Schematic representation of the assumed thermal effect of blood perfusion, $\dot{w}_b C_b$, thermal conductivity, k, and specific heat, C. The lower and upper boundaries of phase transition temperature range are $T_{ms}$ and $T_{ml}$, respectively.

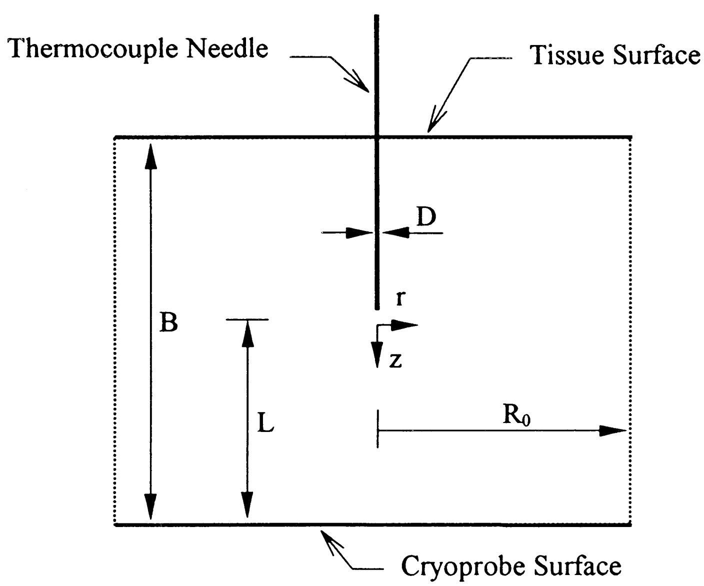



Figure 2: Schematic view of the heat transfer problem in a cylindrical domain representing biological tissues surrounding a thermocouple needle.

Table 1: Typical thermophysical properties of biological tissues, metals, and plastics

| | Biological Tissues | Stainless-Steel | Copper | Iron | Plastics (average) |
|---|---|---|---|---|---|
| Thermal Conductivity, W/m-°C | 0.5 T ≥ 0°C<br>2.0 T ≤ -22°C | 15 - 72 | 386 T= 0°C<br>407 T= -100°C | 73 T= 0°C<br>87 T= -100°C | 0.1 |
| Thermal Diffusivity, $m^2/s \times 10^7$ | 1.4 T ≥ 0°C<br>11.1 T ≤ -22°C | 42 - 203 | 1125 T= 0°C<br>1186 T= -100°C | 204 T= 0°C<br>244 T= -100°C | |
| Specific Heat, $MJ/m^3$-°C | 3.6 T ≥ 0°C<br>1.8 T ≤ -22°C | 3.60 | 3.43 | 3.57 | |

Table 2: Temperature difference between the thermocouple needle's tip and the temperature that would have existed at the same location in the absence of the thermocouple needle. Values are given for tip temperature range of 0 down to -45°C.

| Distance from the thermocouple needle, mm | Thermocouple needle diameter, gauge (mm) | | |
|---|---|---|---|
| | 16 (1.65) | 21 (0.8) | 30 (0.3) |
| 2 | 35 - 44°C | 20 - 28°C | 11 - 12°C |
| 5 | 35 - 39°C | 21 - 25°C | 11 - 12°C |
| 10 | 27 - 28°C | 16 - 19°C | 5 - 6°C |

Table 3: Time, in seconds, needed for the thermocouple needle's tip to reach the temperatures of 0, -22, and -45°C. The thermocouple needle diameter D is given in gauge, where 16, 21, and 30 gauges equal 1.65, 0.8 and 0.3 mm, respectively. D = 0 represents the case in the absence of a thermocouple needle.

| Tip Temperature | L = 2 mm | | | | L = 5 mm | | | | L = 10 mm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | D=16 | D=21 | D=30 | D=0 | D=16 | D=21 | D=30 | D=0 | D=16 | D=21 | D=30 | D=0 |
| T = 0°C | 39 | 36 | 32 | 28 | 67 | 63 | 60 | 55 | 132 | 125 | 116 | 108 |
| T = -22°C | 47 | 43 | 39 | 35 | 75 | 72 | 67 | 63 | 168 | 151 | 137 | 128 |
| T = -45°C | 57 | 52 | 47 | 43 | 99 | 85 | 77 | 71 | 225 | 195 | 173 | 160 |

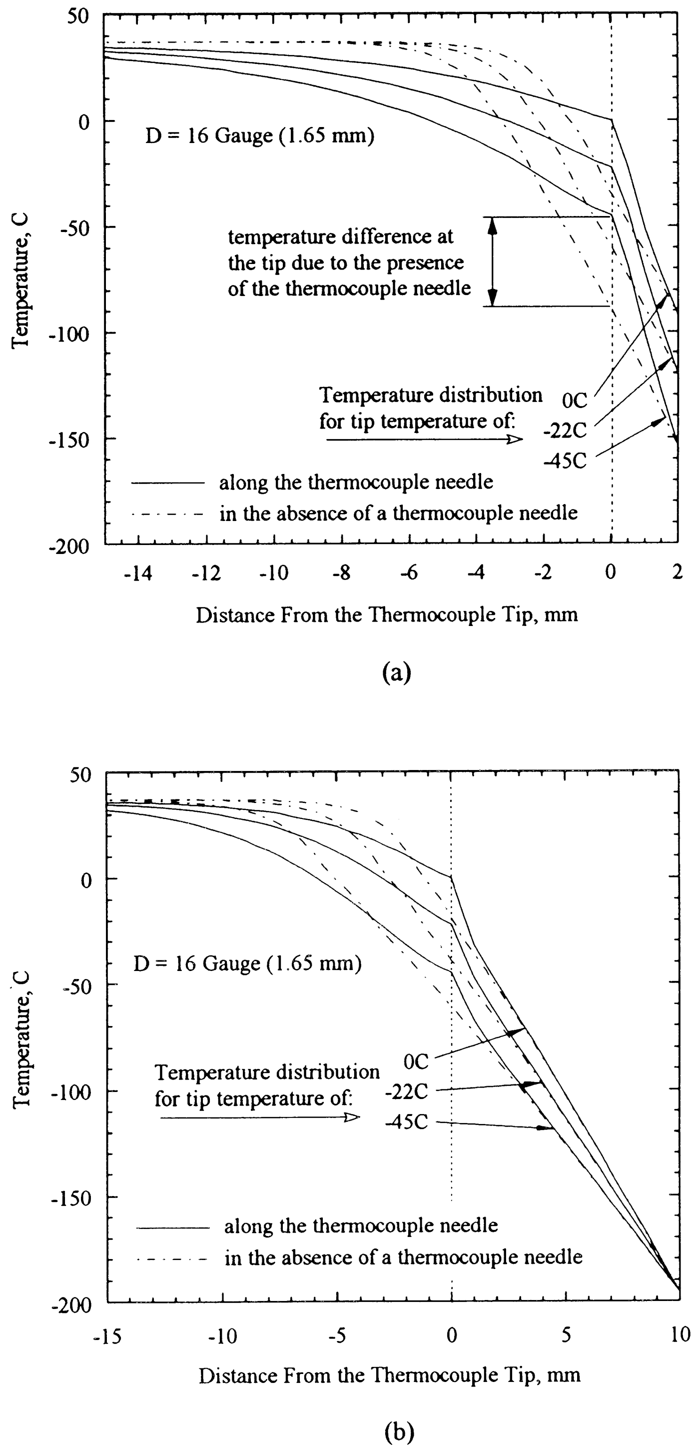
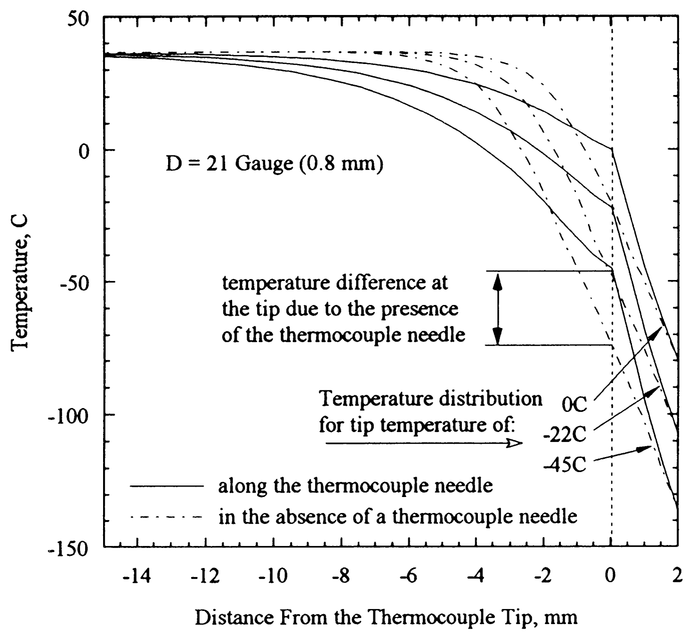
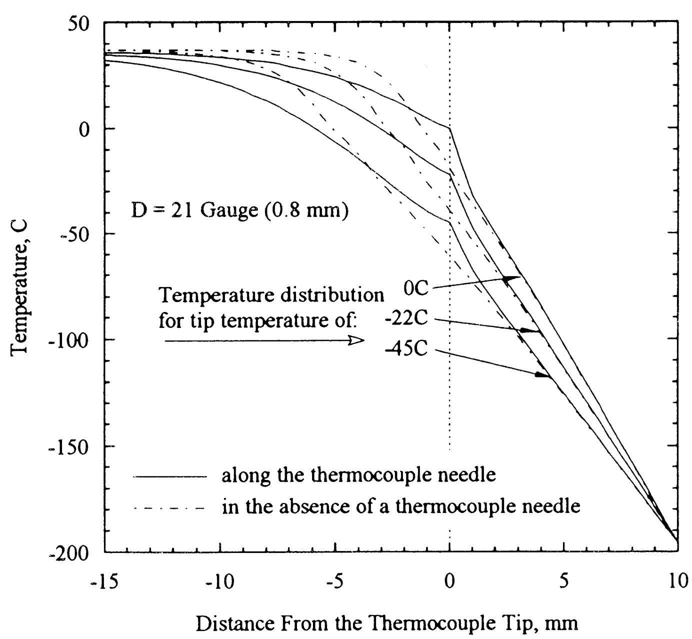



Figure 3: Temperature distribution perpendicular to the cryoprobe surface for a thermocouple needle diameter of 16 gauge (1.65 mm), located at distances of (a) 2 mm and (b) 10 mm from the cryoprobe surface. The solid lines represent the axial temperature distribution along the thermocouple needle, for tip temperatures of 0, -22, and -45°C, whereas the dashed lines represent the temperature distributions at the same instances in the absence of the thermocouple needle (undisturbed system).

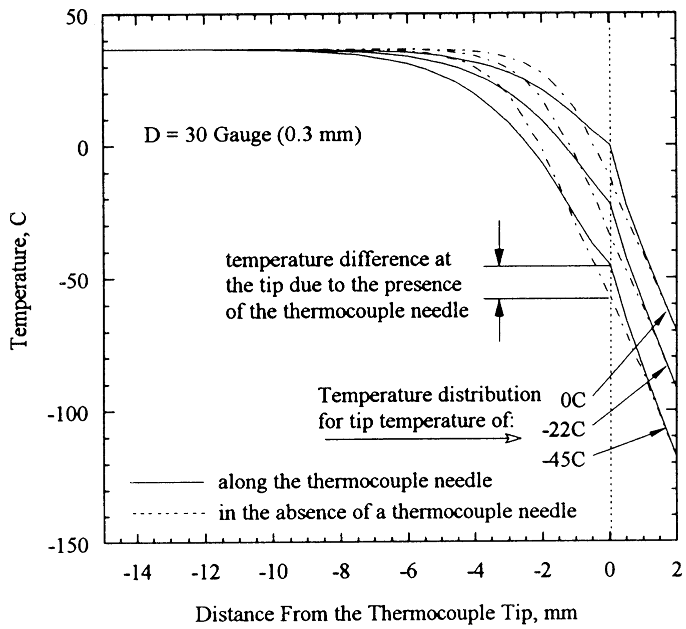



(a)

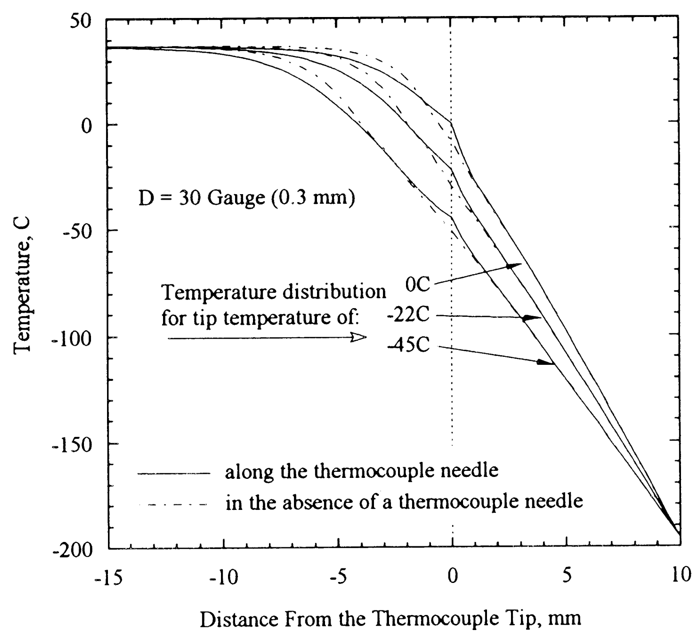



(b)

Figure 4: Temperature distribution perpendicular to the cryoprobe surface for a thermocouple needle diameter of 21 gauge (0.8 mm), located at distances of (a) 2 mm and (b) 10 mm from the cryoprobe surface. The solid lines represent the axial temperature distribution along the thermocouple needle, for tip temperatures of 0, -22, and -45°C, whereas the dashed lines represent the temperature distributions at the same instances in the absence of the thermocouple needle (undisturbed system).




(a)




(b)

Figure 5: Temperature distribution perpendicular to the cryoprobe surface for a thermocouple needle diameter of 30 gauge (0.3 mm), located at distances of (a) 2 mm and (b) 10 mm from the cryoprobe surface. The solid lines represent the axial temperature distribution, along the thermocouple needle, for tip temperatures of 0, -22, and -45°C, whereas the dashed lines represent the temperature distributions at the same instances in the absence of the thermocouple needle (undisturbed system).

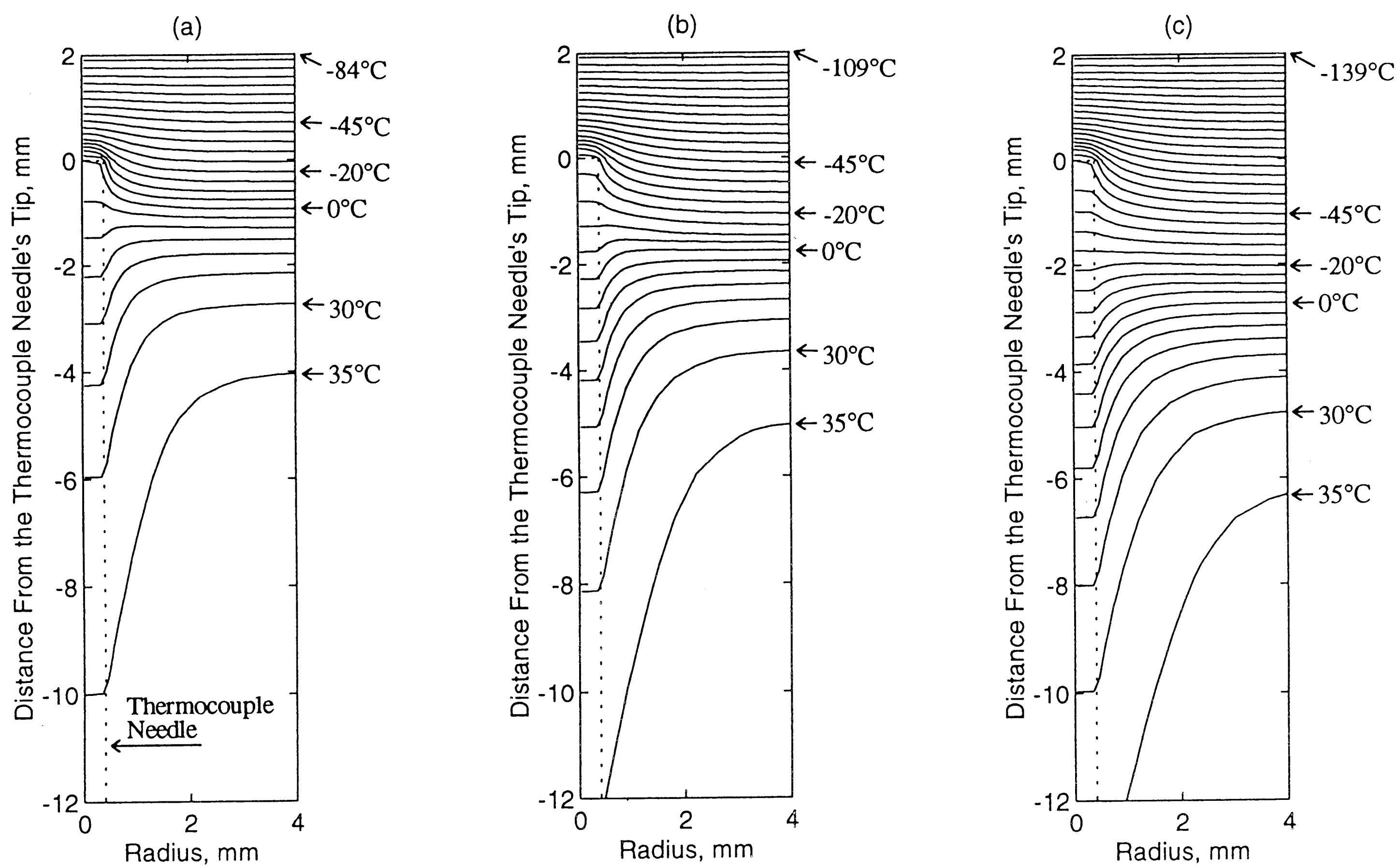



Figure 6: Temperature fields around a thermocouple needle having a diameter of 21 gauge (0.8 mm), located at a distance of 2 mm from the cryoprobe surface, when the tip senses the temperature of (a) 0°C, (b) -22°C, and (b) -45°C. The temperature difference between every two adjacent isotherms is 5°C. The dotted lines represent the thermocouple needle's contour.