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Thermophysical Properties of Swine Myocardium

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This paper presents the experimental technique and results for the thermal conductivity, thermal diffusivity, and density of swine myocardial tissue. These properties were measured for freshly excised tissue. Thermal properties were measured using a self-heated thermistor probe, while the density was measured using a water displacement method. Thermistor probes were inserted into the tissue of interest and were used to supply heat within the tissue as well as to monitor the temperature rise in the tissue. An empirical calibration procedure was used to measure the properties of the tissue at different temperatures. The measurement instrument was first calibrated against agar-gelled water and glycerol at each temperature. The measurements were made at temperatures of 25, 37, 50, 62, and 76°C. The uncertainty in the measurement ranges from 2% at lower temperatures to about 5% at higher temperatures ($T > 50$°C). The properties of the tissue depend significantly on the water content. At temperatures higher than 50°C, there is significant water loss from the tissue during the procedure. The water loss is found to vary exponentially with the increase in temperature relative to ambient. Consequently, there is a decrease in the thermal conductivity values with increasing temperature. This decrease, however, is not as much as one would expect from the water loss data. A hypothesis to explain the relationships among water loss, cell damage, and thermal properties is proposed.

KEY WORDS: density; myocardium; swine; thermal conductivity; thermal diffusivity.

1. INTRODUCTION

Thermal probe techniques are used frequently to determine the thermal conductivity and the thermal diffusivity of biomaterials [1–10]. These

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techniques utilize a thermistor bead both as a heat source and a temperature sensor to measure the thermal properties of the biomaterials. Various thermal diffusion probe techniques have been developed since Chato's [1] first practical use of the thermal probe. Physically, for all of these techniques, heat is introduced to the tissue at a specific location and is dissipated by conduction through the tissue and by convection with the blood perfusion,.

Thermal probes are constructed by placing a miniature thermistor at the tip of a plastic catheter. The volume of tissue over which the measurement occurs depends on the surface area of the thermistor and the heating protocol. Electrical power is delivered to a spherical thermistor positioned invasively within the tissue of interest. The tissue is assumed to be homogeneous within 1 cm^3 around the probe. The electrical power and the resulting temperature rise are measured by a microcomputer-based instrument. Thermal properties are derived from temperature and power measurements using equations that describe heat transfer in the integrated probe/tissue system.

The following five issues make the determination of thermal properties of biomaterials a technically challenging task. First, tissue heat transfer includes conduction, convection, radiation, metabolism, evaporation, and phase change. It is difficult but necessary to decouple these different heat transfer mechanisms. The accuracy of the thermal probe measurements depends on a realistic thermal model. Second, the mechanical and thermal interactions between the probe and the tissue are complex, and must be properly modeled to achieve accurate measurements. When the probe is inserted into living tissue, a blood pool may form around the probe because of the mechanical trauma. Tissue damage due to probe insertion may also occur *in vitro*. Third, the tissue structure is quite heterogeneous within each sample. Thus, the probe (which returns a single measurement value) measures a spatial average of the tissue properties surrounding the active elements. Unfortunately, the spatial average is very nonuniform [8]. The probe is most sensitive to the tissue immediately adjacent to it. It is important to control this effective measurement volume. If the effective volume is too small, then the measurement is highly sensitive to the mechanical/thermal contact between the probe and the tissue. If the effective volume is too large, then the measurement is sensitive to the outer boundary conditions at the surface of the tissue sample. Fourth, there is a significant sample-to-sample and species-to-species variability. One must be careful when extrapolating results obtained in one situation to different conditions. Fifth, tissue handling is critical. Thermal properties are dependent on temperature and water content [4, 9, 10]. Blood flow, extracellular water, and local metabolism are factors which strongly affect heat transfer

in living tissue but are difficult to determine or control experimentally. Once a tissue dies, if handled improperly, there will be significant water fluxes, which will affect tissue thermal properties. Tissues should be stored in a slightly hypertonic saline buffer to minimize tissue water loss or gain.

Accurate measurements of thermal properties are required in order to develop realistic transient thermal models. These models assume importance with increasing use of hyperthermia and therapeutic procedures based on heat delivery. Accurate properties are required to simulate techniques like radiofrequency, microwave, laser, and ultrasound therapies on tissues. The properties presented in this paper will be used to generate thermal models for radiofrequency cardiac ablation in swine myocardium.

2. EXPERIMENTAL METHODS

2.1. Thermal Properties

In this technique, the instrument first measures the baseline tissue temperature, T_0. Then an electronic feedback circuit, shown in Fig. 1, applies a variable voltage in order to maintain the average thermistor temperature at a predefined constant value, T_h. The feedback circuit drives the thermistor resistance, R_h, to equal the set resistance R_{set}. The applied thermistor power includes a steady-state and a transient term.

$$P(t) = A + Bt^{-1/2} \tag{1}$$

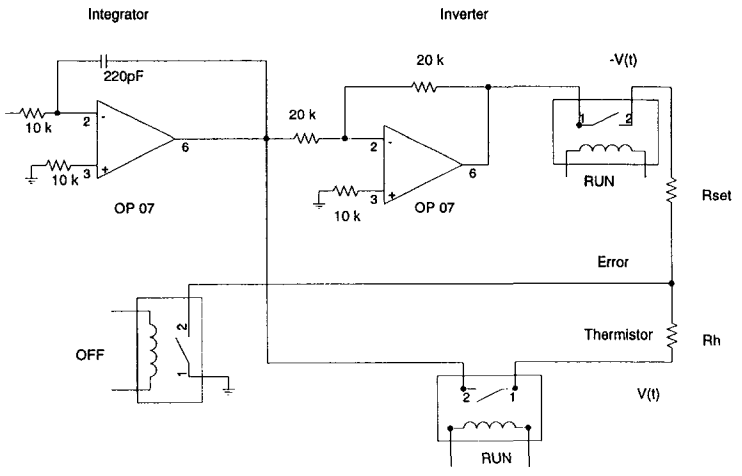

Fig. 1. Electronic feedback circuit used to heat thermistor to a constant temperature.

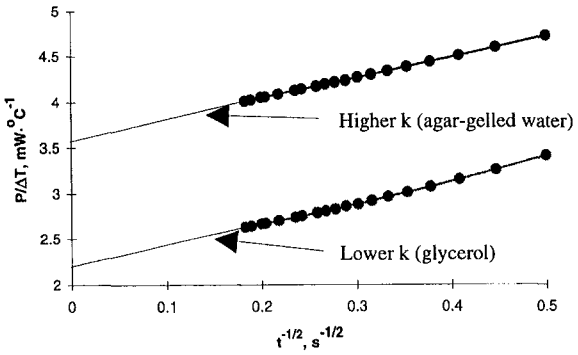

Fig. 2. Typical $P/\Delta T$ versus time$^{-1/2}$ data for the constant-temperature heating technique.

The applied power, $P(t)$, varies during the 30-s transient. Linear regression is used to calculate the steady-state and transient terms, A and B, in (1). Figure 2 shows some typical responses. The steady-state response ($t \to \infty$) is a measure of the thermal conductivity. The transient response (slope) indicates the thermal diffusivity.

In order to measure the thermal conductivity and thermal diffusivity, the relationship between the applied thermistor power, P, and the resulting thermistor temperature rise, $\Delta T(t) = T_h - T_0$, must be known. In the constant-temperature method, the ΔT is constant. The thermistor bead is treated as a sphere of radius a embedded in a homogeneous medium. Balasubramaniam and Bowman [2] developed the relationship used to measure thermal conductivity (k_m) assuming no perfusion:

$$k_m = \frac{1}{(4\pi a\, \Delta T/A) - (0.2/k_b)} \tag{2}$$

where k_b is the thermal conductivity of the spherical thermistor bead. A similar equation allows the measurement of thermal diffusivity from the transient response, again assuming no perfusion [4]:

$$\alpha_m = \left[\frac{a}{\sqrt{\pi}\, B/A(1 + 0.2(k_m/k_b)}\right]^2 \tag{3}$$

Rather than using the actual probe radius (a) and probe thermal conductivity (k_b), the following empirical equations are used to calculate thermal properties:

$$k_m = \frac{1}{(4\pi c_1\, \Delta T/A) - (0.2/c_2)} \tag{4}$$

and

$$\alpha_m = \left[\frac{c_3}{\sqrt{\pi}\, B/A(1 + 0.2(k_m/c_4)} \right]^2 \tag{5}$$

The coefficients c_1, c_2, c_3, and c_4 are determined by calibrating the probe in two materials of known thermal properties. Typically agar-gelled water (5 g of agar in 500 ml of water) and glycerol are used as thermal standards. This calibration is performed at the same temperatures at which the thermal property measurements will be performed with the same experimental conditions (ΔT, time of heating, and sample size).

It is assumed that the baseline tissue temperature, T_0, is constant during the 30-s transient. Patel et al. [8] have shown that if the temperature drift, dT_0/dt, is larger than $0.1°C \cdot min^{-1}$, then significant errors will occur. The electronic feedback circuit forces T_h to a constant ($T_h = R_{set}$). Thus, if T_0 is constant, then ΔT does not vary during the 30-s transient.

The time of heating can vary from 10 to 60 s. Shorter heating times are better for small tissue samples and for situations where there is baseline tissue temperature drift. Another advantage of shorter heating times is the reduction in the total time required to make a single measurement. Longer heating times increase the measurement volume and reduce the effect of imperfect thermistor/tissue coupling. Typically, we use shorter heating times *in vivo* because it allows more measurements to be taken over the same time period. On the other hand, we use longer heating times *in vitro* because accuracy is more important than measurement speed.

Prior to running the instrument on the tissue, the uncertainty was tested using glycerol, water gelled with agar, and mixtures of glycerol and agar-gelled water. The uncertainty of the temperature measurement was less than 0.5%. The uncertainty of the thermal properties measurement technique was 2% at lower temperatures and 5% at temperatures higher than 50°C. A tissue's thermal properties are strongly affected by its constituents; in particular, water is a major factor. In addition, the internal structure of myocardial tissue may also affect thermal properties. Structurally, the myocardial fibers align along the contraction path. This heterogeneity may cause the thermal conductivity to have a directional component.

2.2. Density

The density measurements were performed using the water displacement method. The mass of tissue samples near 15 g was determined using an electronic scale (Ohaus; accuracy = 0.5%). They were then immersed in water and the weight of the water displaced was measured. The volume of

water displaced was obtained from the density of the water at that temperature (about 24°C). The uncertainty of this measurement technique was tested initially by measuring the volume of marbles. Ten marbles (approximately 1 cm in diameter) were used for this purpose. The volume measured using the water displacement method was tested against the volume measured using their diameter measurement. Since the marbles were not exactly spherical, the diameter of the marbles was measured at five different locations using a vernier calipers and the average diameter was used. The maximum variation in the diameter was found to be 0.015 cm. The uncertainty in the volume measurement was estimated to be 1.6%.

3. MEASUREMENTS

The swine heart tissue was obtained from a meat shop. Freshly excised heart was wrapped in plastic and stored in a cooler at about 5°C within 15 min after the death. The experiments were performed on the tissue on the same day. The following experimental protocol was used for all experiments. The left ventricle of the heart was cut into approximately cuboidal pieces of between 15 and 25 g. The left ventricle of the heart was always taken because it is easier to measure with the thicker muscle. The thermistor was inserted into the center of the tissue sample. The thermistor and tissue together were wrapped in two layers of plastic and then immersed in a flask of water. This flask was put in a water bath maintained at a constant temperature. The experiments were performed at 25, 37, 50, 62, and 76°C. Protein denaturation is expected at these higher temperatures. Nevertheless, this temperature range was chosen because it matches the temperatures that occur in therapeutic procedures. Three probes were used to measure the properties simultaneously in three fresh tissue samples obtained from the same swine heart. The properties presented are each an average of 10 measurements in a single tissue sample. Each experiment involved about 60 to 90 min of heating and another 60 min of the actual experiment for the 10 readings. The properties at 25°C were always measured as a control. The samples were weighed before the insertion of the thermistor into the sample and also after the experiment was completed. It was assumed that the weight loss in the tissue because of heating is due to the water loss. The water lost from the tissue, however, remained inside the plastic wrapper, which also prevented any water from entering the tissue from outside.

Density measurements were also performed simultaneously on fresh pieces of tissue. The tissue pieces were taken from the cooler, immediately weighed, and used in the experiment. The displacement method used water at room temperature.

4. RESULTS AND DISCUSSION

Table I gives the thermal conductivity of the swine myocardium while Table II gives the data on the thermal diffusivity. Figures 3 and 4 give the plots of the data. Figure 5 shows the water loss from the tissue due to heating. The density data are given in Table III. Figure 6 gives the plots of the density of different tissues in the myocardium.

Analysis of variance of the data at a 5% level of significance showed that the thermal conductivity does not change with temperature. The variation in thermal diffusivity is also not significant at the 5% level. There was no significant difference at the 5% level among the density of tissue taken from the left ventricle, the right ventricle, and the interventricular septum.

The water loss in the tissue is exponentially related to the temperature difference from ambient, increasing to 27% at 76°C as shown in Fig. 5. There is no corresponding decrease in conductivity as one would expect. This can be explained if we consider the tissue as a multiphase system with cell structures suspended in extracellular fluid. Initially, the effective conductivity of the tissue is a result of the thermal conductivity of the extracellular water and the thermal conductivity of the cell structures. As the tissue sample is heated, the extra cellular water comes out of the tissue. The cell structures, however, stay intact until the temperature goes above 50°C. At higher temperatures, tissue started losing its color. It became very pale

Table I. Thermal Conductivity ($mW \cdot cm^{-1} \cdot K^{-1}$) of Myocardial Tissue

	T (°C)				
	25	37	50	62	76
	5.23	5.14	5.17	4.39	5.24
	5.07	5.12	4.75	3.30	4.29
	5.30	5.21	5.61	5.67	4.83
	5.43	5.54	4.22	4.16	5.89
	4.68	5.35	4.93	5.33	5.23
	5.25	5.08	4.84	5.70	5.39
	5.27	5.48	4.42	5.11	4.75
	5.28	4.57	4.93	4.99	3.25
	5.86	5.76	5.52	5.03	2.69
	4.78	5.10	5.88	5.30	5.28
	4.75	5.35	5.35	4.67	5.60
	4.92	6.02	5.60	5.49	4.68
Mean	5.15	5.31	5.1	4.93	4.76
SD	0.33	0.37	0.51	0.70	0.95

Table II. Thermal Diffusivity ($cm^2 \cdot s^{-1}$) of Myocardial Tissue

	T (°C)				
	25	37	50	62	76
	0.00151	0.00170	0.00165	0.00159	0.00167
	0.00154	0.00147	0.00203	0.00235	0.00249
	0.00143	0.00165	0.00151	0.00169	0.00166
	0.00146	0.00143	0.00116	0.00191	0.00229
	0.00159	0.00160	0.00176	0.00167	0.00173
	0.00141	0.00178	0.00179	0.00163	0.00185
	0.00165	0.00149	0.00235	0.00143	0.00185
	0.00132	0.00206	0.00179	0.00170	0.00199
	0.00141	0.00144	0.00147	0.00143	0.00062
	0.00168	0.00179	0.00160	0.00180	0.00167
	0.00154	0.00156	0.00173	0.00161	0.00173
	0.00164	0.00138	0.00171	0.00169	0.00192
Mean	0.00152	0.00161	0.00171	0.00171	0.00179
SD	0.00012	0.00020	0.00031	0.00025	0.00047

at 76°C, shrunk, and became hard. These changes in tissue due to denaturing of proteins in the cell structures were similar to earlier-documented [11] effects of heating on tissues. Proteins in their native state are characterized by a number of hydrogen bonds. As the temperature increases, these hydrogen bonds break and the proteins start unfolding. These conformational changes in the proteins make their structure straight-chained and

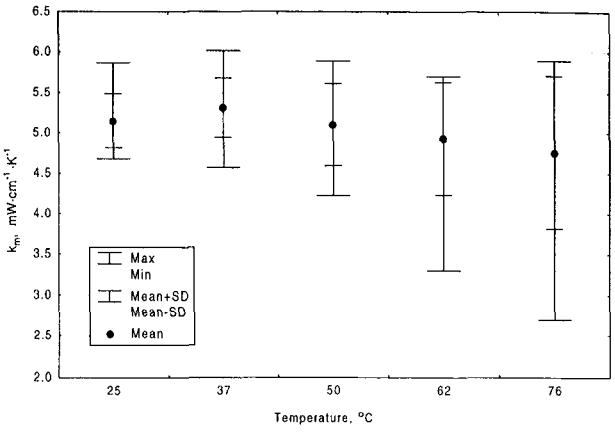

Fig. 3. Thermal conductivity of myocardial tissue.

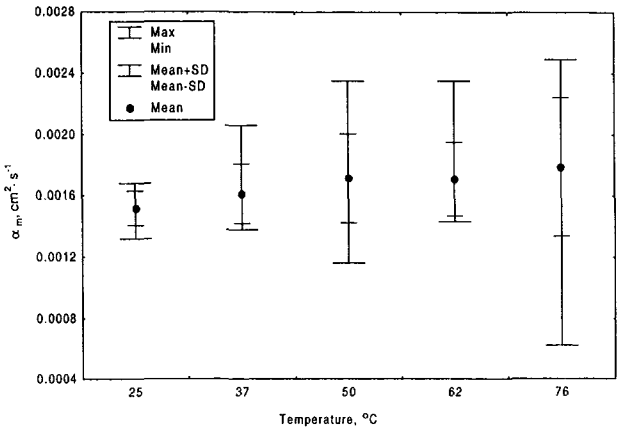

Fig. 4. Thermal diffusity of myocardial tissue.

increase their degrees of freedom. These changes could result in an increase in their thermal conductivity. It is known that there is an increase in the specific heat capacity of proteins in their native state as the temperature increases [12]. The dominant effects, however, occur at the cellular level. At temperatures above 50°C, the cells collapse and the cell membrane ruptures, releasing the water into the extracellular space. This enhances the conductivity of the tissue sample. The process is briefly explained below.

Figure 7a shows a drawing of the cardiac tissue as seen through a microscope. The myocardial tissue has cell structures connected by dark bands of intercalated disks [13, 14]. These disks are thickened opposing

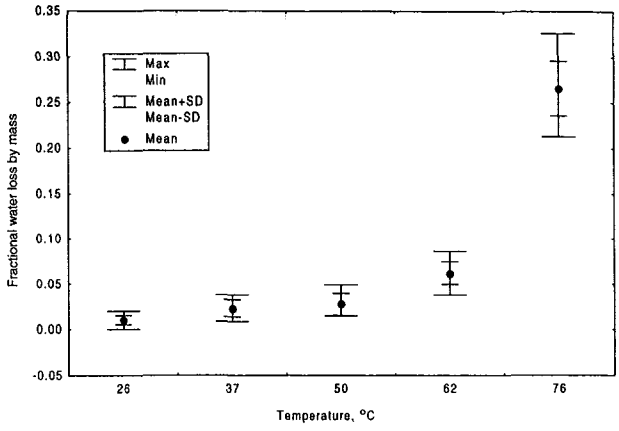

Fig. 5. Water loss to heating.

Table III. Density ($g \cdot cm^{-3}$) of Myocardial Tissue at 24°C

	Left ventricle	Right ventricle	Septum
	1.08	1.11	1.13
	1.04	1.05	1.13
	1.07	1.15	1.09
	1.05	1.15	1.10
	1.05	1.06	1.03
	1.09	1.06	1.03
	1.09	1.10	1.11
	1.03	1.08	1.06
	1.04	1.04	1.04
Mean	1.06	1.09	1.08
SD	0.02	0.04	0.04

cell membranes. Figure 7b shows a hypothetical drawing of damaged cardiac muscle showing gaps in the cell membranes. The tissue water in combination with these cell structures is responsible for the net resistance to the heat flux.

The tissue can be modeled as a series-parallel combination of resistive networks. To keep the equations simple we will deal with a one-dimensional case. The tissue thermal resistance due to a single layer of cells in the tissue is given by Eq. (6).

$$R_m = R_{ecf} + R_{cm} + R_{icf} \tag{6}$$

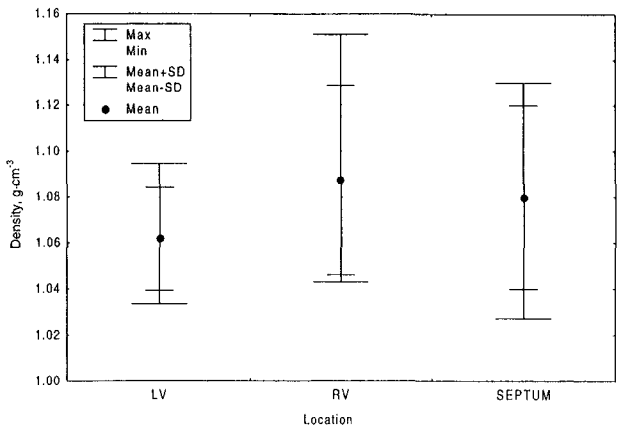

Fig. 6. Density of myocardial tissue. LV, left ventricle; RV, right ventricle.

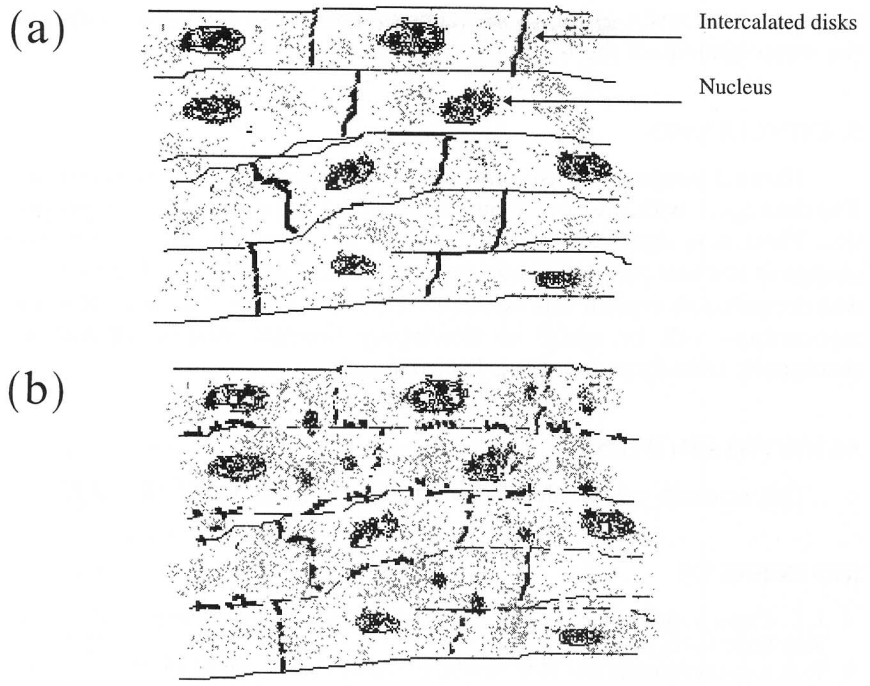

Fig. 7. (a) Drawing of myocardial tissue. (b) Hypothetical drawing of damaged myocardial tissue.

where R_{ecf} is the resistance of the extracellular fluid, R_{cm} is the resistance of the cell membrane, and R_{icf} is the resistance of the intracellular fluid. This structure of the tissue resistance remains until the temperature reaches about 50°C. Above 50°C, effects due to heating appear. The cell membrane ruptures, and consequently, there is a drop in the cell membrane resistance due to the gaps formed in the membrane. These gaps will be filled by fluid. Hence, the membrane resistance now will be as shown in Eq. (7).

$$R_{cm} = \frac{R_{gap} R_{cm}}{R_{gap} + R_{cm}} \tag{7}$$

where R_{gap} is the resistance of the gap formed due to the rupture of the cell membrane. This will be close to the R_{icf} and is very small. Thus, there is an overall reduction in the value of R_{cm}. This change in the structure results in a drop in the thermal resistance of the tissue and is more significant than the changes in the protein thermal resistance due to denaturation. The

thermal conductivity of the tissue remains unchanged even after a drop in the water content of the tissue by up to 27%.

5. CONCLUSION

Thermal property measurements in swine myocardium are presented. The data agree with previously published data [10] on the thermal properties. There was significant water loss from the tissue due to heating. The change in thermal properties was, however, not significant. A simple model was presented to explain this behavior. These properties measured in swine myocardium will be useful in developing thermal models for various therapeutic techniques involving heat delivery.

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