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Thermal Conductivity and Diffusivity of Biomaterials Measured with Self-Heated Thermistors

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This paper presents an experimental method to measure the thermal conductivity and thermal diffusivity of biomaterials. Self-heated thermistor probes, inserted into the tissue of interest, are used to deliver heat as well as to monitor the rate of heat removal. An empirical calibration procedure allows accurate thermal-property measurements over a wide range of tissue temperatures. Operation of the instrument in three media with known thermal properties shows the uncertainty of measurements to be about 2%. The reproducibility is 0.5% for the thermal-conductivity measurements and 2% for the thermal-diffusivity measurements. Thermal properties were measured in dog, pig, rabbit, and human tissues. The tissues included kidney, spleen, liver, brain, heart, lung, pancreas, colon cancer, and breast cancer. Thermal properties were measured for 65 separate tissue samples at 3, 10, 17, 23, 30, 37, and 45°C. The results show that the temperature coefficient of biomaterials approximates that of water.

KEY WORDS: heart; kidney; liver; thermal conductivity; thermal diffusivity.

1. INTRODUCTION

The purpose of this paper is to present an experimental method with which to measure the temperature variations in the thermal conductivity and thermal diffusivity of biomaterials. The technique of Balasubramaniam and Bowman [1] and Valvano et al. [2] has been extended to allow accurate thermal-property measurements over the temperature range of 3 to 45°C. The second objective of this paper is to present thermal-property data measured in human, dog, pig, and rabbit tissues.

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2. SIGNIFICANCE

The understanding of heat-transfer mechanisms occurring in biomaterials requires the accurate knowledge of tissue thermal properties. For example, thermal models of localized hyperthermia as a therapeutic modality must have accurate thermal-property values in order to generate valid results. Models of the burn-injury process also require accurate thermal properties. The encouraging application of cryoprotective agents in tissue preservation has generated a need for precise measurements under hypothermic conditions. The temperature range of 3 to 45°C for property evaluation was chosen so that the results could be applied to hypothermic as well as hyperthermic situations.

3. THEORY OF OPERATION

3.1. Background

Self-heated thermistors have been used widely for the measurement of thermal properties and tissue perfusion. Chato [3] was the first to solve the bio-heat equation for the time-dependent perfused-tissue response to a heated thermistor. Balasubramaniam and Bowman [1] extended the thermal model to include a spatial variation of temperature within the spherical thermistor. Jain [4] developed a thermal model which included a passive glass shell surrounding the active heated thermistor. Valvano et al. [2] obtained a closed-form transient solution which improved the accuracy of the thermal-diffusivity measurements. Holmes and Chen [5] developed a measurement technique which heated the thermistor with a pulse of power and monitored the temperature decay. Hayes and Valvano [6] used finite elements to validate the thermal-conductivity measurements with a realistic thermistor geometry and electrical heating pattern. Valvano et al. [7] modified the technique to obtain a noninvasive probe by placing the thermistor on the surface of an insulating barrier.

The essence of the thermal probe is a spherical thermistor which is inserted into the tissue of interest. The thermistor is first used in a passive mode to measure the baseline tissue temperature, T_s. Electrical power, Q, is the applied to the thermistor at a transient rate to hold the thermistor temperature constant at T_h. $Q(t)$ is monitored as a function of time, t, during a 20-s heating interval. The electrical power is dissipated by thermal conduction from the probe into the tissue. Solution of the time-dependent probe–tissue coupled thermal model allows the simultaneous measurement of tissue thermal conductivity and thermal diffusivity. Discussion of the thermal model and its solution can be found in the literature [2, 6].

An analog feedback circuit is used to apply electrical power in the thermistor bead at a rate sufficient to maintain the volume-average thermistor temperature at T_h. The time varying power can be characterized by a steady-state term, P, and a transient term, S.

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

Initially ($t = 0$), it is assumed that the probe and tissue are in equilibium at temperature T_s. In the heating mode, the volume-average thermistor temperature is fixed at T_h. Thus, the temperature rise is

$$\Delta T = T_h - T_s \tag{2}$$

The steady-state solution of the thermal model can be used to calculate the thermal conductivity of the tissue, K:

$$K = \frac{1}{a\Delta T/P + b} \tag{3}$$

where a and b are calibration coefficients incorporating the geometry and thermal properties of the thermistor [6]. The transient solution of the thermal model can be used to calculate the thermal diffusivity of the tissue, α:

$$\alpha = \left[\frac{c}{S/P(1 + dK)}\right]^2 \tag{4}$$

where c and d are calibration coefficients also incorporating the geometry and thermal properties of the thermistor.

3.2. Thermistor-Probe Design

A number of factors are relevant in the design of the thermistor probe. The objective is a minimally invasive device which is accurate and durable. A large probe is desired to increase the effective volume of measurement, reduce the effect of thermal contact, improve the accuracy, and increase the durability. Finite-element studies show that the effective volume of measurement in the tissue is 5 to 10 thermistor radii [6, 7]. A small probe is desired to reduce the invasiveness and improve the time response of the probe. As a compromise of these factors, glass-encapsulated spherical thermistors with a radius of about 0.05 cm were used in this study. Figure 1 shows a typical probe inserted into tissue. The thermistor, which actually has a prolate spheroid geometry, is epoxied to the tip of a plastic catheter. The probe is inserted into the tissue so that at least 1 cm^3 of tissue

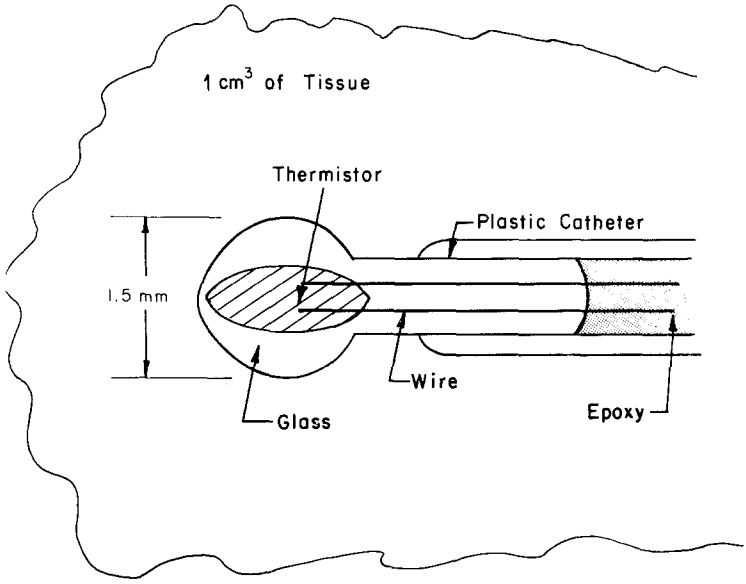

Fig. 1. Thermistor probe.

surrounds the thermistor. Since biologic tissue is highly anisotropic, it is assumed that the thermal properties measured by the probe represent a volume average for about 1 cm^3 of tissue.

3.3. Instrumentation

A constant current source, a linear amplifier, and a 14-bit A/D converter are used to measure the thermistor resistance, R, during the sensing mode. The feedback circuit, shown in Fig. 2, is used to supply the electrical power during the heating mode. The fixed resistance, R_{set}, is a microcomputer-controlled precision potentiometer. The integrator will increase or decrease the voltage, V, across the thermistor until the thermistor resistance, R, matches the fixed resistance, R_{set}. The applied temperature step, ΔT, is established with the microcomputer by adjusting the potentiometer value, R_{set}. An inverse log function is used to calculate the thermistor temperature, T, from the thermistor resistance by

$$T = \frac{1}{H_0 + H_1 \ln R + H_3 (\ln R)^3} \tag{5}$$

where T is the temperature in K and H_0, H_1, and H_3 are calibration coefficients. Equation (5) is used during the sensing mode to calculate T_s. Since

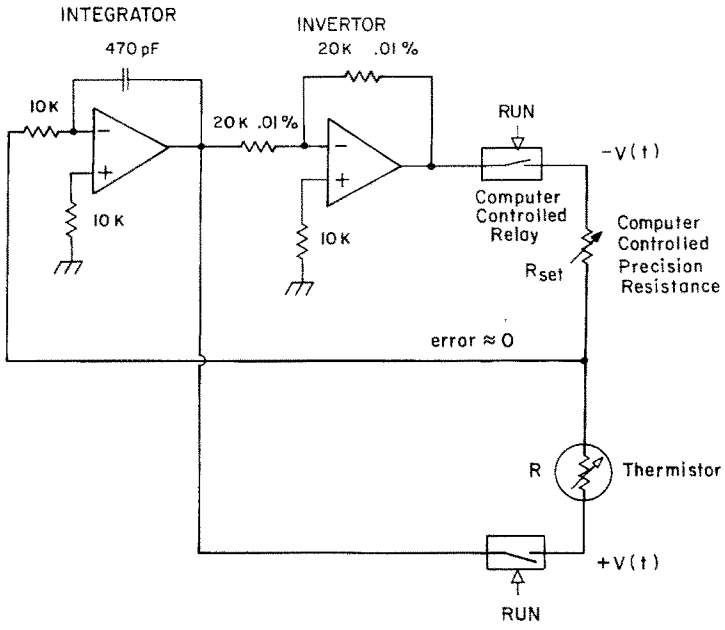

Fig. 2. Feedback circuit used to heat the thermistors.

$R = R_{set}$ during the heating mode, Eq. (5) can also be used to calculate T_h. The voltage, V, is measured at 2 Hz during the heating mode to obtain an expression for the transient energy dissipation.

$$Q(t) = V(t)^2/R_{set} \tag{6}$$

3.4. Measurement Protocol

First, the initial temperature, T_s, is determined using the current source in conjunction with Eq. (5). The value of R_{set} is then chosen so that ΔT will be as close to 4°C as possible. The actual ΔT is calculated with Eqs. (2) and (5). The feedback circuit is activated to cause heating for 20 s, and $V(t)$ is measured every 0.5 s. $Q(t)$ is calculated at each point in time using Eq. (6). P and S are calculated by fitting the 4- to 18-s $Q(t)$ data to Eq. (1) using linear regression. Figure 3 shows a plot of the power versus time$^{-1/2}$ data measured using a Thermometrics R55DA102M thermistor placed in agar-gelled water. Thermal conductivity and thermal diffusivity are calculated from Eqs. (3) and (4). The probe–tissue thermal system is allowed to reach equilibrium (requiring about 5 min) and the above procedure is repeated a total of 10 times.

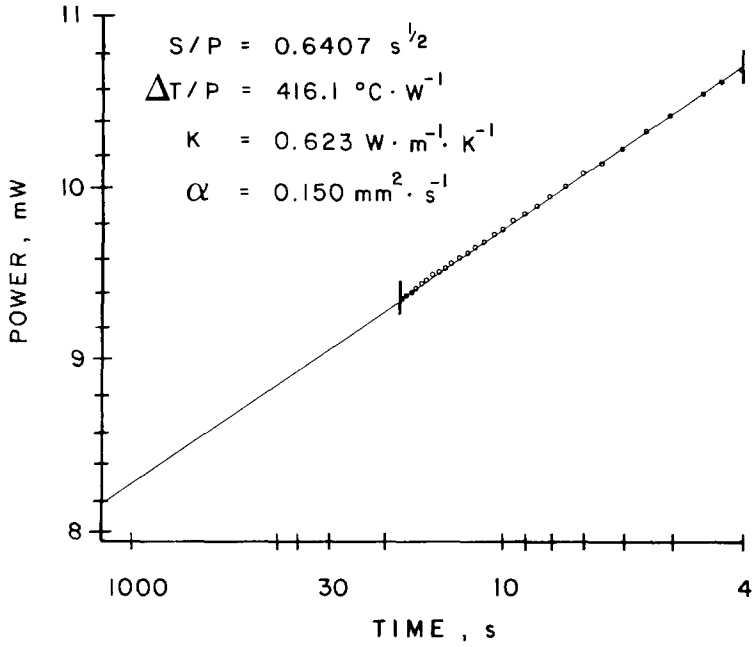

Fig. 3. Thermistor power versus time$^{-1/2}$.

A number of factors are relevant in the choice of heating interval. Within a few milliseconds after the power is applied, the electrical feedback circuit establishes the desired volume-average temperature, but the temperature rise is concentrated inside the thermistor. After a few seconds, the temperature wave has crossed the thermistor glass coating and has entered the tissue. Steady state occurs within a few minutes. At each point in time, the response of the thermistor is a function of the thermal properties of the thermistor, the glass coating, the probe–tissue interface, and the tissue, but the relative importance of these factors changes with time. A long heating interval is desired to increase the effective volume of measurement and to improve the statistics of the linear regression. A short heating interval is desired to reduce the time between measurements. Experimental results show no statistical difference among measurements made with 20-, 30-, 60-, and 120-s heating intervals. The relative importance of the tissue thermal properties to the thermistor response is small during the earlier portion of the heating period. Thus, the linear regression is started at 4 s to reduce the errors due to an imperfect thermal contact between the probe and the tissue.

Reference studies were performed in a gel solution consisting of 1 g of agar mixed with 100 g of water. The gel acted to eliminate natural convec-

tion-driven flows in water which would have biased the calibration experiments. Experiments with 0.5, 1, 2, and 5 g of agar powder per 100 g of water show no measurable difference in thermal properties. Hence, the thermal properties of water are used for the agar gel.

4. CALIBRATION PROCEDURES

4.1. Temperature Calibration

In order to measure temperature, the resistance versus temperature characteristics of the thermistor are required. Simultaneous measurements are obtained of resistance, by the microcomputer intrumentation, and temperature, by a precision thermometer (Hewlett Packard HP2804A), at 1°C increments from 0 to 45°C. A chi-square nonlinear regression is used to calculate H_0, H_1, and H_3 from the calibration data for each thermistor.

4.2. Thermal-Conductivity and Thermal-Diffusivity Calibration

In order to measure thermal properties, the coefficients a, b, c, and d in Eqs. (3) and (4) must be determined. Agar-gelled water and glycerin are used as thermal standards. Each probe is heated 10 times in each liquid at temperatures of 3, 10, 17, 23, 30, 37, and 45°C. Equations (3) and (4) are used to calculate a, b, c, and d for each probe at each temperature. Linear interpolation is used to measure thermal properties at any temperature between 3 and 45°C. In order to achieve accurate results, it is important to perform the tissue measurements with the same protocol as the calibrations. It is also important to have reliable thermal property standards with which to calibrate the instrumention. Water and glycerin are suitable substances because their thermal properties are well defined and they approximate tissue [8].

5. ESTIMATION OF ERROR

It is imperative to estimate the error in any measurement technique. The R_{set} resistor has a precision of 7 bits, a resolution of 10 Ω, a range of 500 to 3000 Ω, and an accuracy of 0.1 Ω. The resistance measurement has an accuracy of 0.1 Ω. The temperature resolution is 0.003°C. Because of the drift in the thermistor resistance versus temperature coefficients, the absolute temperature accuracy is only 0.02°C. Since a single thermistor is used to measure both T_s and T_h, the accuracy of ΔT is dependent on the temperature resolution of T_s and T_h. Thus, the accuracy of ΔT is 0.006°C.

The voltage accuracy of 1.22 mV corresponds to a power accuracy of 0.005 mW or 0.1 %.

A water/glycerin mixture is used to determine the accuracy of the thermal-conductivity and thermal-diffusivity measurements. The thermal properties of the mixture, K_{mix} and α_{mix}, can be calculated from the mass fraction, p [9].

$$K_{mix} = pK_g + (1-p)K_w + 1.4\,p(p-1)(K_w - K_g - 0.2) - 0.0014\,p(p-1)(T-20) \tag{7}$$

$$\alpha_{mix} = p\alpha_g + (1-p)\alpha_w \tag{8}$$

where K_g and K_w are the thermal conductivity ($W \cdot m^{-1} \cdot K^{-1}$) of glycerin and water, respectively, α_g and α_w are the thermal diffusivity ($mm^2 \cdot s^{-1}$) of glycerin and water, respectively, and T is the mixture temperature (°C). The uncertainty in both the thermal conductivity and the thermal diffusivity is about 2%. The reproducibility is 0.5% for the thermal-conductivity measurement and 2% for the thermal-diffusivity measurement.

6. RESULTS

The tissue samples were always chosen to have a volume larger than 1 cm^3. Samples were removed immediately postmortem from the dogs, rabbits, and pigs. The human tissues were removed at autopsy, placed in saline, and refrigerated. Thermal properties of the human tissues were measured 1 to 2 days after the autopsy. The human cancer tissues were removed at biopsy and measured within 24 h.

A thermistor was gently inserted into each individual tissue specimen; the tissue–probe system was then wrapped in a plastic sheet and placed into a temperature-controlled water bath. Thermal conductivity and thermal diffusivity were measured 10 times each at temperatures of 3, 10, 17, 23, 30, 37, and 45°C. Table I presents a summary of 3780 measurements in 65 tissue samples. The first two columns identify the tissue. The third and fourth columns specify the number of tissue samples and the total number of measurements. Linear regression was used to fit the measurements of each type of tissue to the following equations.

$$K = K_0 + K_1 T \tag{9}$$

$$\alpha = \alpha_0 + \alpha_1 T \tag{10}$$

The coefficients K_0 and K_1 are shown in columns 5 and 6. The correlation coefficient is displayed in column 7. Complementary thermal-diffusivity data are shown in columns 8–10.

Table I. Summary of Thermal-Conductivity and Thermal-Diffusivity Measurements (a Total of 3780) Represented by Linear Functions According to Eqs. (9) and (10), Respectively[a]

Species	Tissue	m	n	K_0 ($W \cdot m^{-1} \cdot K^{-1}$)	K_1 ($W \cdot m^{-1} \cdot K^{-1} \cdot °C^{-1}$)	r	α_0 ($mm^2 \cdot s^{-1}$)	α_1 ($mm^2 \cdot s^{-1} \cdot °C^{-1}$)	r
Dog	Renal pelvis	2	120	0.4930	0.001055	0.40	0.1334	0.00052	0.92
Dog	Renal medulla	4	250	0.5065	0.001298	0.71	0.1305	0.00063	0.63
Dog	Renal cortex	7	390	0.4905	0.001280	0.86	0.1333	0.00039	0.56
Dog	Myocardium	4	220	0.4869	0.001332	0.86	0.1296	0.00058	0.67
Dog	Pancreas	2	140	0.4790	0.000849	0.65	0.1287	0.00062	0.41
Pig	Renal cortex	3	190	0.4967	0.001176	0.93	0.1284	0.00039	0.90
Pig	Myocardium	3	200	0.4841	0.001333	0.84	0.1270	0.00051	0.88
Pig	Pancreas	1	70	0.4700	0.000194	0.68	0.1530	0.00130	0.99
Pig	Lung	1	60	0.2339	0.002216	0.97	0.0695	0.0008	0.87
Pig	Liver	2	130	0.4981	0.000800	0.88	0.1240	0.00053	0.94
Pig	Spleen	2	130	0.4863	0.001267	0.91	0.1257	0.00042	0.93
Rabbit	Kidney	1	70	0.4945	0.001345	0.99	0.1311	0.00027	0.95
Rabbit	Liver	1	60	0.4668	0.002601	0.99	0.1370	0.00178	0.91
Rabbit	Lung	1	70	0.3080	0.002395	0.99	0.1071	0.00082	0.95
Human	Renal pelvis	1	70	0.4795	0.001923	1.00	0.1329	0.00011	0.85
Human	Renal medulla	2	140	0.4994	0.001102	0.91	0.1278	0.00055	0.95
Human	Renal cortex	5	310	0.4989	0.001288	0.88	0.1266	0.00055	0.85
Human	Myocardium	6	340	0.4925	0.001195	0.80	0.1289	0.00050	0.83
Human	Pancreas	3	140	0.4365	0.002844	0.62	0.1391	0.00084	0.66
Human	Lung	2	140	0.4071	0.001176	0.69	0.1192	0.00031	0.86
Human	Liver	4	210	0.4692	0.001161	0.80	0.1279	0.00036	0.92
Human	Spleen	2	80	0.4913	0.001300	0.97	0.1270	0.00047	0.94
Human	Fat of spleen	1	60	0.3431	−0.000254	−0.48	0.1321	−0.00002	−0.08
Human	Cerebral cortex	2	90	0.5043	0.000296	0.43	0.1283	0.00050	0.80
Human	Adenocarinoma of the breast	3	100	0.4194	0.003911	0.60	0.1617	−0.00049	−0.19
Human	Colon cancer	1	10	0.5450	(at 19°C)		0.1340		

[a] The quantity m is the number of specimens, n is the number of measurements, and r is the correlation coefficient of the linear regression of thermal properties to temperature.

7. DISCUSSION

There was considerable variation in the thermal properties from tissue to tissue, from species to species, and even within tissues from the same donor. However, the temperature coefficients of the tissue thermal properties consistently matched the temperature coefficient of water. To illustrate this point, the thermal properties of water taken from Touloukian et al. [8] were fit to a linear equation over the range 0 to 45°C.

$$K = 0.5652 + 0.001575\ T \tag{11}$$

$$\alpha = 0.1339 + 0.000473\ T \tag{12}$$

where K is in $W \cdot m^{-1} \cdot K^{-1}$, α is in $mm^2 \cdot s^{-1}$, and T is in °C. A linear regression of the data to temerature was performed on all tissues except lung, fat, and cancer, which displayed thermal properties significantly different from those of the remaining tissues. The results show that the thermal conductivity of tissue is lower than that of water, while the temperature dependence approximates that of water. The thermal diffusivity of tissue matched the thermal diffusivity of water well for both the magnitude and the temperature coefficient.

$$K = 0.4882 + 0.001265\ T, \qquad r = 0.642 \tag{13}$$

$$\alpha = 0.1304 + 0.000519\ T, \qquad r = 0.510 \tag{14}$$

where K is in $W \cdot m^{-1} \cdot K^{-1}$, α is in $mm^2 \cdot s^{-1}$, and T is in °C.

The thermophysical properties of living tissue are significantly affected by blood flow [1–7]. Therefore, an understanding of the heat transfer in living tissue must account for the influence of blood perfusion. The data presented in this paper were taken *in vitro* and, hence, do not include perfusion effects. Another limitation of this data set is that once the tissue is removed from its supply of nutrients, it begins degeneration. The samples measured were therefore altered to an undetermined degree from their state *in vivo*. One key problem in the *in vitro* measurement of thermal properties is caused by the salt imbalance between the tissue and the bath solution. Significant water flux can occur if there is a salt gradient, and it is thus important to maintain the tissue in an isotonic solution. The decay process can also be reduced by decreasing the time between the sacrifice of the animal and the thermal measurements. The human tissues were refrigerated to retard deterioration. The cumulative degeneration process together with the anisotropic properties of tissue may account for much of the variability found in the data.

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