# A Small Artery Heat Transfer Model for Self-Heated Thermistor Measurements of Perfusion in the Kidney Cortex

G. T. Anderson

Department of Electronics and Instrumentation

The University of Arkansas at Little Rock

Little Rock, AR 72204.

J. W. Valvano

Department of Electrical and Computer Engineering

The University of Texas at Austin

Austin, TX 78712.

**Abstract**

*A small artery model (SAM) for self-heated thermistor measurements of perfusion in the canine kidney is developed based on the anatomy of the cortex vasculature. In this model interlobular arteries and veins play a dominant role in the heat transfer due to blood flow. Effective thermal conductivity, $k_{ss}$, is calculated from steady state thermistor measurements of heat transfer in the kidney cortex. This small artery and vein model of perfusion correctly indicates the shape of the measured $k_{ss}$ versus perfusion curve. It also correctly predicts that the sinusoidal response of the thermistor can be used to measure intrinsic tissue conductivity, $k_m$, in perfused tissue. Although this model is specific for the canine kidney cortex, the modeling approach is applicable for a wide variety of biologic tissues.*

**Nomenclature**

| | |
|---|---|
| A | steady state applied thermistor power (mW) |
| *A* | cross sectional area of blood vessels ($cm^2$) |
| a | thermistor radius, or vessel radius (cm) |
| B | sinusoidal applied thermistor power (mW) |
| C | steady state average temperature rise in thermistor (˚C) |
| c | specific heat (mW-sec/g-˚C) |
| $c_1,\ldots,c_7$ | empirically determined calibration coefficients |
| D | sinusoidal average temperature rise in thermistor (˚C) |
| f | frequency (Hz) |
| k | thermal conductivity (mW/cm-˚C) |
| l | distance from arteriole to venule (0.08 cm) |
| $L_e$ | vessel equilibration length (cm) |

| | |
|---|---|
| M | kidney cortex mass (g) |
| m | density of interlobular veins in kidney cortex ($1/cm^2$) |
| *m* | mass flow rate (g/sec) |
| n | density of interlobular arteries in kidney cortex ($1/cm^2$) |
| *n*(r) | number of blood vessels in a shell of tissue at radius r |
| P(t) | total power applied to thermistor (mW) |
| Q | distributed heat ($mW/cm^3$) |
| q | capillary contribution to Q ($mW/cm^3$) |
| r | radial distance from the center of the thermistor (cm) |
| S | kidney cortex cross sectional area ($cm^2$) |
| T | temperature difference $T - T_O$ (˚C) |
| t | time (sec) |
| *v* | velocity of blood (cm/s) |
| w | tissue perfusion (mL/100g-min, or $g/cm^3$-sec) |
| x,y,z | distance coordinates (cm) |
| $\alpha$ | thermal diffusivity ($cm^2$/sec) |
| $\beta$ | sinusoidal distributed power ($mW/cm^3$) |
| $\Gamma$ | steady state distributed power ($mW/cm^3$) |
| $\lambda$ | normalized bleed-off, 0 for none, 1 for complete |
| $\rho$ | density ($g/cm^3$) |
| $\varphi$ | phase delay (radians) |
| $\xi$ | normalized distance into cortex, 0 at medulla, 1 at capsule |
| $\Delta x, \Delta y, \Delta z$ | dimension of cubic control volume (cm) |
| $\Delta V$ | volume represented by a finite difference node ($cm^3$) |
| $\Delta T$ | average volumetric thermistor temperature rise (˚C) |
| $\sigma_\Sigma$ | coupling shape factor between tissue/vessels (2.5) |

| | |
|---|---|
| $\sigma_\Delta$ | coupling shape factor between two vessels (1.8) |

**Subscripts**

| | |
|---|---|
| a | arterial |
| b | thermistor bead |
| bl | blood or perfusate |
| eff | effective (KEFF model) or enhanced (W-J Model) |
| ext | external |
| i,j | finite difference indices |
| m | tissue medium (intrinsic) |
| met | metabolic |
| o | initial |
| perf | due to capillary perfusion |
| sin | from sinusoidally heated thermistor |
| ss | from steady-state heated thermistor |
| v | venous |
| ves | vessel |
| x,y,z | Cartesian directions |
| 0,1,2 | positive, central , negative face of a control volume |

**Introduction**

Although tissue perfusion is believed to be an important factor in many medical conditions (e.g., heart disease, vascular surgery, transplants, and cancer therapy), there is currently no widely accepted clinical method to quantify perfusion for a majority of applications. Self-heated thermistor techniques to measure perfusion have been investigated

in recent years (Chato 1968, Balasubramaniam 1977, Holmes 1980, Valvano 1984, Patel 1987, Anderson 1992). A thermistor is placed into a perfused tissue and a microcomputer based instrument is used to heat the thermistor with a predetermined power. The resultant temperature rise in the thermistor is then measured by the instrument. Both tissue thermal conduction and perfusion act to carry heat away from the thermistor. From the steady state temperature rise in the thermistor, an effective thermal conductivity of tissue, $k_{ss}$, is calculated. From the $k_{ss}$ calculation, perfusion can be extracted based on knowledge of the intrinsic tissue conductivity, $k_m$, and of the particular model of heat transfer due to perfusion that is used.

Currently there is little agreement as to what is the best mathematical model which describes the heat transfer due to perfusion. At least four different models have been used to describe the effects of perfusion on self-heated thermistors: the Pennes (1948) model, the Chen-Holmes model (Chen 1980, Holmes 1980, and Xu 1991), a KEFF model (Chen 1980, Roemer 1987, Patel 1987, and Valvano 1987) and the Weinbaum-Jiji model (Weinbaum 1985, Song 1987, Valvano 1990, Charny 1990, Xu 1991, Charny 1992). Some experimental data can be best described by the Pennes model (Valvano 1984), while other data supports the KEFF model (Patel 1987, Anderson 1988, Anderson 1989a). This paper examines the specific case of perfusion measured in the canine kidney cortex. A numerical model is developed that is based on the vasculature of the canine kidney cortex. This numerical model is then used to explain the effects of perfusion on a thermistor that is heated with a combination of steady state and sinusoidal power.

Four considerations must be addressed while developing a heat transfer model. First, one must have a clear specification of the objective of the model. In this paper, the model is used to examine the relationships between self-heated thermistor measurements and perfusion in the canine kidney cortex. Second, the model must carefully adhere to realistic anatomy and physiology. One should make simplifying assumptions because they

are realistic, and not just because they allow a solution to be found. Third, before formulating a model, it is important to define the volume of interest. The length scale of model in this paper is determined by the steady state temperature field around a thermistor. The temperature field around a 0.15 cm diameter thermistor extends to about 0.5 cm. Fourth, it is critical to verify the model with carefully acquired experimental data.

**Vascular Anatomy of the Canine Kidney Cortex**

Figure 1 outlines the blood vessels in the kidney cortex. Perfusion rates in the kidney are among the highest found in mammalian organs due to its filtration and reabsorption functions. The glomeruli function to retain cells in the circulation and also allow filtration of fluid into the tubular space. Blood enters the kidney through the renal artery, which branches into several interlobar arteries that run between the lobes of the kidney up to the cortex. At this point they bend and run parallel to the medulla - cortex interface as arcuate arteries. Off of these arcuate arteries branch interlobular arteries, which run up through the cortex approximately parallel to one another and perpendicular to the kidney surface. Glomeruli branch off of the interlobular arteries at regular intervals. Efferent arterioles leave the glomeruli and lead to a dense postglomeruli capillary network. The venous side of the circulation mirrors the arterial side with two exceptions. A substantial superficial venous network lies near the capsule that connects all lobes of the kidney. Also, large veins that run through the interlobular axes supplement the drainage through the interlobular veins.

Vascular casts of the canine kidney cortex were obtained to get the numerical data required to construct an accurate perfusion model. Three canine kidneys were excised and the renal arteries and veins were cannulated. The kidneys were cleared with a mannitol-saline perfusate for 30 minutes. Degassed microfil silicone rubber (Canton Bio-medical Products, Boulder, CO) was slowly injected over a period of about 30 seconds. The first

kidney cast was made with both the arteries and veins by injecting 15 mL into the renal artery, and stopping when the silicone appeared in the renal vein. The second cast was made of just the arteries by injecting 8 mL into the renal artery. The last cast was made of just the veins by injecting 8 mL into the renal vein. After injection, the kidneys were refrigerated for 24 hours. 1 mm slices were made at various angles. The tissue slices were soaked in increasing concentrations (25%, 50%, 75%, 95%, 100%) of ethyl alcohol, each for 24 hours. A methyl salicylate soak was then used to clear the tissue from the casts. Experimentally, the thermistors are located in the center of the cortex which is about 0.5 cm from the surface. Therefore, it is at this kidney location that the vascular statistics were collected.

Figure 2 is a typical x-z section showing the interlobular venules. The major heat carrying vessels in the cortex are the interlobular arterioles and venules. These vessels run predominately perpendicular to the kidney surface with only occasional branching. Figure 3 is a typical x-y section showing the interlobular venules. There were 34 interlobular arterioles counted in an area of 0.58 $cm^2$ ($n \approx 60$ interlobular arterioles/$cm^2$.) There were 313 interlobular venules counted in an area of 4.12 $cm^2$ ($m \approx 82$ interlobular venules/$cm^2$.) Interlobular arterioles have a radius, a, of about 0.003 cm in the center of the cortex and a length of about 1 cm. The majority of artery-vein countercurrent pairs exist in the cortex near the medulla. In the center of the cortex, there are few artery-vein countercurrent pairs. The interlobular arterioles and veins are typically at least several vessel diameters apart. In contrast to our finding in the canine kidney, Xu *et al.* (1991) found many artery-vein countercurrent pairs in the porcine kidney cortex.

The fluid velocity can be estimated from the total kidney perfusion, w. The vessel density, n, is taken as the average of n and m. The 6000 is necessary to convert the perfusion units mL/100g-min into the velocity units of cm/sec.

$$v = \frac{w \quad M}{6000\,\pi\, a^{\,2}\, S\, \frac{n+m}{2}} \approx 0.083\, w \qquad (1)$$

The Peclet number can be calculated from the velocity.

$$Pe = \frac{2\ a\ v}{\alpha_{bl}} \approx 4\, v \approx 0.332\, w \qquad (2)$$

| | | |
|---|---|---|
| $c_{bl}$ | Specific heat | 4000 mW-sec/g-˚C |
| $k_{bl}$ | Thermal conductivity | 6 mW/cm-˚C |
| $\alpha_{bl}$ | Thermal diffusivity | 0.0015 $cm^2$/sec |
| $\rho_{bl}$ | Density | 1 g/$cm^3$ |

Table 1. Parameters of the saline perfusate.

| | | |
|---|---|---|
| a | Interlobular vessel radius | 0.003 cm |
| $k_m$ | Tissue thermal conductivity | 5 mW/cm-˚C |
| l | Arteriole/venule distance | 0.08 cm |
| L | Length of the vessel | 1 cm |
| M | Kidney cortex mass | 50 g |
| n | Vessel density | 71 vessels/$cm^2$ |
| S | Surface area at center of the cortex | 50 $cm^2$ |
| $\alpha_m$ | Tissue thermal diffusivity | 0.00125 $cm^2$/sec |

Table 2. Typical parameters of the alcohol-fixed kidney cortex.

**Sinusoidal Heating Technique**

Valvano (1987) proposed a method to simultaneously measure intrinsic and effective thermal conductivity's in perfused tissue. In this technique the thermistor is heated with a combination of steady state and sinusoidal power.

$$P = A + B \sin(2\pi ft) \tag{3}$$

The resulting thermistor temperature rise is fitted to the following equation using linear regression.

$$\Delta T = C + D \sin(2\pi ft + \varphi) \tag{4}$$

Tissue thermal conductivity is calculated from the *steady state* response using the following analytic equation (Balasubramaniam 1977, Valvano 1984).

$$k_{ss} = \frac{1}{c_1 + c_2 \frac{C}{A}} \tag{5}$$

Tissue thermal conductivity is calculated from the *sinusoidal* response using the following empirical equation (Valvano 1987, Anderson 1988).

$$k_{sin} = \frac{1}{c_3 + c_4 \frac{D}{B}} \tag{6}$$

Coefficients $c_1$ - $c_4$ are experimentally determined by operating the thermistor probe in two media of known thermal conductivity's. Analytical and experimental studies show that $k_{ss}$

depends on tissue thermal conductivity and perfusion (Balasubramaniam 1977, Valvano 1984, Patel 1987, Anderson 1992). In these experiments, $k_{ss}$ is either linearly related to the perfusion rate or has an increasing slope with increasing perfusion rate. The shape of this response is dependent on the organ and the magnitude of perfusion. This variability suggests that no one model will be appropriate for all situations.

Analytical solution to the sinusoidally-heated thermistor (Valvano 1991) show that the sinusoidal response, D/B, is sensitive to both tissue conductivity, and tissue diffusivity. Equation 6 can be used to measure tissue conductivity if the density times the specific heat is similar for both tissue and calibration medium (which is true for kidney cortex and water).

It is the hypothesis of this technique that the sinusoidal heating frequency can be chosen such that the sinusoidal conductivity, $k_{sin}$, is independent of perfusion, and hence can be used to measure intrinsic thermal conductivity, $k_m$. Experimental results in alcohol-fixed canine kidneys have shown that $k_{sin}$ will be independent of perfusion rate if the sinusoidal heating frequency is fast enough (Anderson 1988, 1989a, 1989b, 1992). $k_{sin}$ measured with thermistors of 0.25 and 0.076 cm diameters heated with a sinusoidal period of 20 seconds is independent of perfusion rate. If the heating frequency is reduced below 0.05 Hz, the measured $k_{sin}$ is either linearly related to perfusion or has an increasing slope with increasing perfusion rate. Conversely, if the heating period is faster than 0.05 Hz, then $k_{sin}$ is an accurate measure of intrinsic thermal conductivity, $k_m$.

**Thermal Models**

Thermistor techniques to measure perfusion are based on solutions to a bioheat equation. The general form of the bioheat equation is given below.

$$\rho_m c_m \frac{\partial T_m}{\partial t} = k_m \quad {}^2T_m + Q_{perf} + Q_{ext} + Q_{met} + Q_{ves} \tag{7}$$

$Q_{met}$, the metabolic heat generation can be ignored if it is spatially and temporally uniform or is much smaller than $Q_{ext}$, the self-heated thermistor source. $Q_{ext}$ can be a steady state, transient, or a combination of steady state and periodic sources.

**Pennes Model.** Pennes (1948) suggested a model in which the net heat transfer from blood to tissue was proportional to the temperature difference between the arterial blood entering the tissue and the venous blood leaving the tissue. When most researchers apply the Pennes model, they assume that the temperature of venous blood is in equilibrium with the local tissue temperature, and that the arterial blood is constant. These two assumptions yield the familiar term:

$$Q_{perf} = w\, c_{bl}\, (T_a - T) \tag{8}$$

where perfusion is expressed in g/cm$^3$-sec. Charny (1990, 1992) showed that the bleed-off from the largest countercurrent vessels can be described by the Pennes equation. These bleed-off vessels in muscle tissue can be as large as 300 µm. For a self-heated thermistor, perfusion is then related to $k_{SS}$ by (Balasubramaniam 1977):

$$w = \frac{(k_{ss} - k_m)^2}{k_m\, c_{bl}\, a^2} \tag{9}$$

where a is the radius of the spherical thermistor. Finite element analysis was used to calculate $k_{sin}$ using Equation 6. The response of the Pennes model to a sinusoidal heat source is shown in Figure 4. Calculated $k_{sin}$, which depends only on the sinusoidal components of applied power (B) and thermistor temperature (D), decreases as sinusoidal

heating period decreases. At heating periods less than or equal to 10 seconds, calculated $k_{sin}$ is the same as the true intrinsic tissue conductivity. This demonstrates the feasibility of using $k_{sin}$ to measure $k_m$ in the presence of perfusion. The dashed line in Figure 4 is an extrapolation of $k_{sin}$ to the steady state value (or $k_{ss}$) of 6.25 mW/cm-˚C for the Pennes model.

The assumptions in the Pennes equation have been criticized by Chato (1980), Chen (1980), and Weinbaum (1985). Chato and Chen suggested that arterial blood equilibrates with the local tissue temperature before it reaches the capillary bed. Weinbaum proposed that the countercurrent heat exchange between parallel arterial and venous vessels is an important factor in blood-tissue heat exchange.

**KEFF Model.** Patel (1987) and Roemer (1989) proposed an effective conductivity models to describe the heat transfer from a thermistor due to perfusion. In Patel's model the perfusion term is approximated by:

$$Q_{perf} \approx \frac{w \Delta^2 c_{bl} \nabla^2 T_m}{6} \tag{10}$$

where $\Delta$ is a vague heuristically defined quantity called the "measurement length" of the thermistor. Perfusion and intrinsic tissue conductivity are lumped together. The effective thermal conductivity of the tissue is defined by

$$k_{eff} = k_m + \frac{w \Delta^2 c_{bl}}{6} \tag{11}$$

Patel (1987) and Valvano (1987) assumed that the measured steady state conductivity ($k_{ss}$) equaled this effective conductivity ($k_{eff}$). This assumption motivated the following empirical relation.

$$w = c_7 (k_{ss} - k_m) \tag{12}$$

where $c_7$ is a calibration coefficient determined by taking measurements in media of known perfusion.

Although the KEFF model predicts the linear response of measured $k_{ss}$ to perfusion (Anderson 1988), it does not predict the ability of the sinusoidal response, $k_{sin}$, to measure intrinsic thermal conductivity in the presence of perfusion. The KEFF model indicates that perfusion will have exactly the same influence on a thermistor heated with steady state and sinusoidal power.

**Weinbaum-Jiji (W-J) Model.** A three layer model for peripheral tissue was developed by Jiji *et al.* (1984) and extended by Song *et al.* (1987.) The W-J equation can be used only if equilibration length is smaller than the actual vessel length (Baish 1986, Qi 1990.) Equation 1 states that a perfusion of 100 mL/100g-min results in a velocity of about 8.3 cm/sec (Valvano 1990). For the 1 cm interlobular arteries and veins,

$$\varepsilon = \frac{L_e}{L} = \frac{\pi a^2 \rho_{bl} c_{bl} v}{k_m \sqrt{\sigma_\Delta \sigma_\Sigma}\, L} \approx 0.09 \tag{13}$$

Weinbaum and Jiji show that the unidirectional capillary flow from the artery to the vein creates a convective heat source which is small compared to the $u\, \partial T/\partial z$ heat transfer in the interlobular arteries. The W-J equation can be found in their 1985 paper:

$$\frac{1}{r}\frac{\partial}{\partial r}\left(r\, k_m \frac{\partial T}{\partial r}\right) + \frac{\partial}{\partial z}\left(k_{eff} \frac{\partial T}{\partial z}\right) = \rho_m c_m \frac{\partial T}{\partial t} \tag{14}$$

The enhanced conductivity was obtained as

$$k_{eff} = k_m + \frac{\pi^2}{4\ \sigma\ k_m}\ n\ a^2\ k_{bl}^2\ Pe^2 \approx 5 + 0.00114\ w^2 \qquad (15)$$

where the units of perfusion are mL/100-g-min and $\sigma$ is given by

$$\sigma = \frac{\pi}{\cosh^{-1}\left(\frac{l}{2a}\right)} \approx 3.33 \qquad (16)$$

The directional cosine terms have been dropped because of the parallel vessel structure in the kidney cortex. Because the major function of the kidney is filtration, the metabolic heat term is small compared to the flow term. In the alcohol-fixed kidney there is no metabolism. Thus, the metabolic heat term is also neglected. The arteriole and venule inlet temperatures are assumed to be $T_0$. Experimentally this is obtained by placing the alcohol-fixed kidney in a temperature controlled water bath. Thus, the only temperature perturbation is caused by the self-heated thermistor. Because Equ. 15 incorporates blood perfusion, the W-J approach automatically includes the bleed-off source effect.

The steady state and sinusoidal temperatures the thermistor with a 0.08 radius are plotted versus distance from the thermistor in Fig. 5. The size of this thermistor approximated the one used in the actual kidney experiments. The effective measurement volume is defined to be the tissue volume with a temperature rise above 0.1˚C. Table 3 shows that the steady state field includes many vessels, while the sinusoidal field contains only a few. The sinusoidal temperature field increases as the excitation frequency decreases (Valvano 1987.) The fact the sinusoidal temperature field only crosses about 4 arterioles and 6 venules and that $\varepsilon$ is 0.3 dictates that the W-J equation can not be used to study the sinusoidal response. Indeed, it is this small measurement volume which allows

the sinusoidal response to predict $k_m$ in the presence of perfusion. Thus, a new model which incorporates explicit vessels must be developed to simulate the transient response of the thermistor.

| | Symbol | Steady state | Sinusoidal |
|---|---|---|---|
| Distance to 0.1˚C | r | 0.5 cm | 0.15 cm |
| Length scale | $L_t = 2r$ | 1cm | 0.3 cm |
| Equilibration length | $L_e/L$ | 0.09 | 0.09 |
| Equilibration length | $L_e/L_t$ | 0.09 | 0.3 |
| Effective volume | $4/3\ \pi r^3$ | 0.5 $cm^3$ | 0.014 $cm^3$ |
| Surface area crossed | $\pi r^2$ | 0.79 $cm^2$ | 0.071 $cm^2$ |
| Vessels crossed | $(n+m)\ \pi r^2$ | 110 | 10 |

Table 3. Equilibration length and measurement volume.

**Small Artery Model (SAM)**

To reconcile the differences between experimental data and predicted results based on the Pennes and KEFF models, a more realistic thermal model is required. The interlobular arteries are approximately parallel to each other in the cortex. In addition, the capillary structure of the cortex is very dense. There are approximately 50 interlobular arteries and 82 interlobular venules per 1 $cm^2$ of kidney surface area. The artery/vein separation is typically several vessel diameters, although there doesn't seem to be any consistent spacing between the arteries and veins. According to the analysis of Chato (1980),

$$Gz = \frac{Re\ Pr\ d}{L} = \frac{2 \bullet 25 \bullet 0.006cm}{1cm} = 0.3 \qquad (17)$$

such a vessel will have a Graetz number of about 0.3. Thus, the fluid in the vessel will be in equilibrium with the tissue temperature within 120 μm of entering the vessel.

Since the 120 μm equilibration length is small compared to the 1 cm vessel length, it is assumed that the temperature of the fluid in such vessels is in equilibrium with the local tissue temperature. Consider one artery in a control volume of tissue $\Delta x\,\Delta y\,\Delta z$ (see Figure 6). Let $A_a$ be the cross sectional area of the artery and $v_a$ be the average velocity of fluid in the artery. For the above system, heat transfer due to the interlobular artery takes place in the z direction only. Similar to Equation 19a of Weinbaum and Jiji (1985), the heat transfer per unit volume at node z1 is:

$$q_a = n v_a A_a \rho_{bl} c_{bl} \frac{(T_{z0} - T_{z1})}{\Delta z} \approx n v_a A_a \rho_{bl} c_{bl} \frac{dT^+}{dz} \qquad (18)$$

As a volume of blood travels through the interlobular arteries, a portion of it feeds off into afferent arterioles leading to the glomeruli associated with each artery. Some of the blood traveling in the interlobular arteries continues through the cortex until it reaches a subcapsular zone characterized by a profuse network of large arterioles, capillaries and superficial veins (Beeuwkes, 1971). It is thought that the efferent arterioles of these terminal interlobular arteries can open and close to control the distribution of blood in the kidney (Brenner, 1986). Several of the interlobular arteries continue through the cortex to supply the capsule, and a few of these continue to run on the outside of the kidney and anastomose with the arterial supply of perirenal fat and areolar tissue. The bleed-off of blood from the interlobular arteries can be modeled in equation (18) as a change in the arterial flow, $v_a A_a$. It is assumed that the bleed-off is linearly related to the length of the artery, with the average flow of the artery occurring at the midpoint along its length

($\xi$=0.5). Let $F_{a\text{-}avg}$ be the average flow of a typical interlobular artery in the center of the cortex. We define a bleed-off term, $\lambda$, such that $F_{a\text{-}avg}(1+\lambda)$ equals the arterial flow at the corticomedullary junction and $F_{a\text{-}avg}(1-\lambda)$ equals the arterial flow out of the cortex into the sub-capsular region. The flow of an interlobular artery at any point in the cortex can therefore be described by $F_{a\text{-}avg}[1 + \lambda - 2\lambda\xi]$, where $\xi$ is the normalized distance into the cortex such that $\xi = 0$ at the corticomedullary junction and $\xi = 1$ at the capsule. For complete bleed off, $\lambda$=1 and the flow is $F_{a\text{-}avg}[2 - 2\xi]$. If there are n arteries per unit area in the kidney cortex, then the number of arteries in the control volume $\Delta x\,\Delta y\,\Delta z$ is $n \bullet \Delta x \bullet \Delta y$. Similar to Equation 19a of Weinbaum and Jiji (1985), the heat transfer from the volume due to the artery becomes:

$$q_a = nF_{a\text{-}avg}[1 + \lambda - 2\lambda\xi]\,\rho_{bl}\,c_{bl}\,\frac{(T_{z0} - T_{z1})}{\Delta z} \approx nF_{a\text{-}avg}[1 + \lambda - 2\lambda\xi]\,\rho_{bl}\,c_{bl}\,\frac{dT^{+}}{dz} \qquad (19)$$

Similarly, if there are m veins per unit area in the kidney cortex, the heat transfer from a similar control volume $\Delta x\,\Delta y\,\Delta z$ due to the veins is:

$$q_v = mF_{v\text{-}avg}[1 + \lambda - 2\lambda\xi]\,\rho_{bl}\,c_{bl}\,\frac{(T_{z2} - T_{z1})}{\Delta z} \approx mF_{v\text{-}avg}[1 + \lambda - 2\lambda\xi]\,\rho_{bl}\,c_{bl}\,\frac{dT^{-}}{dz} \qquad (20)$$

The coefficients $(nF_{a\text{-}avg}[1+\lambda-2\lambda\xi]\rho_{bl}c_{bl})$ and $(mF_{v\text{-}avg}[1+\lambda-2\lambda\xi]\rho_{bl}c_{bl})$ can be derived from knowledge of the perfusion rate and kidney anatomy. Although there may be local variations in the velocity of arterial and venous blood, for the whole kidney $nF_{a\text{-}avg} = mF_{v\text{-}avg}$.

For this situation, the contribution due to conduction is much greater than the contribution due to capillary perfusion (Weinbaum and Jiji 1985). Thus, the heat transfer due to the capillary network will have little effect on the overall heat transfer rate in this model.

**Finite Difference Implementation**

A two dimensional axisymmetric finite difference code was implemented to model the effects of the interlobular arteries and veins on a self-heated thermistor probe (see Figures 7 and 8). A cylindrical thermistor with a radius of a = 0.045 cm and a height of 0.09 cm was centered in tissue with a conductivity of 5 mW/cm-˚C. The cylindrical tissue had a radial dimension of 0.5 cm and a height of 1 cm. There were 50 by 100 equally spaced nodes, 40 of which were in the thermistor and 20 nodes of which were on the thermistor/tissue interface. Interlobular arteries and veins were each confined to discrete shells of 0.01 cm thickness. In a given shell, the vessels were lumped with the tissue so that the shell had uniform heat transfer properties. Arterial shell to arterial shell spacing was 0.1 cm, as was venous shell to venous shell spacing. Spacing between arterial and venous shells was 0.05 cm. The number of arteries or veins in a given shell was proportional to the shell area in the r plane, and the overall density of both arteries and veins was $50/cm^2$ of tissue in the r - $\varphi$ plane.

Actual thermistor probe are constructed with metal lead wires and include protective glass or epoxy coverings. Valvano and Hayes (1985) developed a detailed finite element model of the thermistor probe including the metal wires, the prolate ellipsoid thermistor shape, and a glass shell around the active thermistor bead. The numerical results show the 40 gauge wires can be neglected. The results also show that the complex probe acts similar to a simple spherical bead with a new effective bead radius and effective bead thermal properties. Hence, the simple spherical bead model is used in this study.

The governing equations for the finite difference model were:

$$\rho_b c_b \frac{\partial T_b}{\partial t} = k_b \left[ \frac{1}{r} \frac{\partial T_b}{\partial r} + \frac{\partial^2 T_b}{\partial r^2} + \frac{\partial^2 T_b}{\partial z^2} \right] + \frac{A + B \sin(2\pi f t)}{\frac{4}{3} \pi a^3} \quad \text{in the thermistor} \quad (21)$$

$$\rho_m c_m \frac{\partial T_m}{\partial t} = k_m \left[ \frac{1}{r} \frac{\partial T_m}{\partial r} + \frac{\partial^2 T_m}{\partial r^2} + \frac{\partial^2 T_m}{\partial z^2} \right] \quad \text{in the tissue} \quad (22)$$

$$\rho_m c_m \frac{\partial T_m}{\partial t} = k_m \left[ \frac{1}{r} \frac{\partial T_m}{\partial r} + \frac{\partial^2 T_m}{\partial r^2} + \frac{\partial^2 T_m}{\partial z^2} \right] + n(r) F_{a\text{-}avg} [1 + \lambda - 2\lambda\xi] \rho_{bl} c_{bl} \frac{(T_{i,j-1} - T_{i,j})}{\Delta V} \quad \text{in the arterial shell} \quad (23)$$

$$\rho_m c_m \frac{\partial T_m}{\partial t} = k_m \left[ \frac{1}{r} \frac{\partial T_m}{\partial r} + \frac{\partial^2 T_m}{\partial r^2} + \frac{\partial^2 T_m}{\partial z^2} \right] + m(r) F_{v\text{-}avg} [1 + \lambda - 2\lambda\xi] \rho_{bl} c_{bl} \frac{(T_{i,j+1} - T_{i,j})}{\Delta V} \quad \text{in the venous shell} \quad (24)$$

where $\Delta V$ is the control volume, $n(r)$ and $m(r)$ are number of interlobular arteries and veins in a shell of tissue at radius r . Temperature is assumed to be initially zero. Conservation of flux is applied as a boundary condition at the interface between the thermistor bead and tissue. No heat flux can occur at the r=0 boundary.

$$\frac{\partial T_b}{\partial r} = \frac{\partial T_m}{\partial r} = 0 \quad \text{at } r = 0 \quad (25)$$

In order to approximate infinite tissue one can assume the tissue temperature field far away from the thermistor follows a $1/r$ shape (where $r$ is in spherical coordinates) This $1/r$ shape satisfies $T + r\frac{\partial T}{\partial r} = 0$ Therefore the infinite tissue can be approximated by the mixed boundary conditions:

$$T_m + \frac{z^2 + r^2}{r} \frac{\partial T_m}{\partial r} = 0 \qquad \text{at } r = 0.5 \text{ cm} \qquad (26)$$

$$T_m + \frac{z^2 + r^2}{z} \frac{\partial T_m}{\partial z} = 0 \qquad \text{at } z = \pm 0.5 \text{ cm} \qquad (27)$$

Another way to justify these remote boundary conditions comes from the fact that a T=0 boundary condition will underestimate the true solution while a $\partial T/\partial x=0$ boundary condition will overestimate the true solution. Equations 26 and 27 are a combination of the two simple boundary conditions.

Table 4 shows effect of bleed-off on the calculations of $k_{ss}$ and $k_{sin}$. Perfusion was 100 mL/100g-min for each calculation. The results show small variations in the range of $\lambda=0$ (no bleed-off) to $\lambda=0.89$ (bleed-off of most of the flow), and a large effect for complete bleed-off ($\lambda=1$).

| bleed-off ($\lambda$) | $k_{ss}$ | $k_{sin}$ (2 sec) | $k_{sin}$ (20 sec) |
|---|---|---|---|
| 0 | 6.020 | 4.920 | 5.750 |
| 0.89 | 6.130 | 4.930 | 5.750 |
| 1 | 7.070 | 4.980 | 6.620 |

Table 4. Calculated conductivity (mW/cm-˚C) versus bleed-off at 100 mL/100g-min.

Figure 9 graphs measured steady state and sinusoidal conductivity versus perfusion rate for a thermistor heated with a sinusoidal periods of 2 and 20 seconds using the SAM with $\lambda=0.89$. Notice the positive second derivative for both the $k_{ss}$ and measured $k_{sin}$ (with a 20 second heating period) versus perfusion curves. By definition $k_m$ should be independent of perfusion, so that for a heating period of 20 seconds, the measured $k_{sin}$ (that derived from the sinusoidal response in Equation 6) is not a good indicator of tissue

intrinsic conductivity. For a heating period of 2 seconds, the measured $k_{sin}$ curve has a slightly negative slope, and is nearly independent of perfusion. In this case, measured $k_{sin}$ is a good indicator of tissue intrinsic conductivity.

**Discussion**

Figure 10 plots steady state thermal conductivity versus perfusion for various situations. The experimental data was measured in an alcohol-fixed canine kidney with a P60 thermistor (Anderson 1989a, 1989b, 1992). Each experimental point represents 20 measurements averaged at the same flow. The standard deviation for this average was less than 0.05 mW/cm-˚C. For each of the models, a steady state power (A=12 mW) is applied to a spherical thermistor (a=0.05 cm), and the volume average temperature within the thermistor bead (C) is calculated as a function of perfusion. The numerical model is first run with no flow at two intrinsic conductivies to get $c_1$ and $c_2$ in Equation 5. Then, the numerical model is run with various perfusion models. The steady state temperature rise within the thermistor (C) was determined for each perfusion. Equation 5 is used again to calculate the steady state thermal conductivity ($k_{ss}$). The Pennes response is derived from Equation 9. The KEFF response comes from Equation 11 where $\Delta$ is arbitrarily chosen to fit the experimental data. For the Weinbaum-Jiji response Equ. 15 was used to convert perfusion into z-direction enhanced conductivity. The W-J equations were then solved using a 2-D finite element model (Valvano 1990). For the W-J model, the steady state thermal conductivity ($k_{ss}$) as measured by the thermistor is similar in shape but smaller in magnitude as the W-J $k_{eff}$ (See Table 5). This is because the W-J $k_{eff}$ is the conductivity enhanced in only the z-direction, while the $k_{ss}$ is the conductivity enhanced in all directions. The SAM curve was derived from the finite difference solution to Equations 20-26.

| Velocity (cm/sec) | Perfusion (mL/100g-min) | W-J $k_{eff}$ (mW/cm-˚C) | $k_{ss}$ (mW/cm-˚C) |
|---|---|---|---|
| 0 | 0 | 5.00 | 5.00 |
| 2 | 22 | 5.55 | 5.11 |
| 4 | 44 | 7.21 | 5.54 |
| 6 | 66 | 9.97 | 6.16 |
| 8 | 88 | 13.83 | 6.92 |

Table 5. Weinbaum-Jiji $k_{eff}$ (Equation 15) and thermistor $k_{ss}$ (Equation 5).

Experimental measurements in the canine kidney indicate that the Pennes model of perfusion correctly predicts that intrinsic conductivity can be measured in perfused tissue independent of the perfusion rate, but incorrectly predicts that $k_{ss}$ is related to the square root of perfusion. The KEFF model (Patel 1987, Valvano 1987, Roemer 1989) predicts that $k_{ss}$ is linearly related to perfusion, as is seen in some measurements, but is unable to explain why $k_{sin}$ can be used to determine intrinsic thermal conductivity in the presence of perfusion. The Weinbaum-Jiji model correctly determines the shape of the $k_{ss}$ data, but can not be used to model the sinusoidal response of the thermistor because the equilibration length is large compared to the vessel length.

The new perfusion model (SAM) based on the interlobular arteries and veins in the kidney predicts that the slope of the $k_{ss}$ versus perfusion curve will increase with increasing perfusion rate. Published experimental data agree with this prediction (Anderson 1987, 1989a, 1989b, 1992), although the extent of the upswing in $k_{ss}$ slope varies greatly between different measurements. One explanation for this might be the distance between

the thermistor and the arteries and veins will vary depending on where the thermistor is placed in the kidney. The SAM can easily be implemented in 3-D, which may be necessary to correctly adjust all these factors. Other factors that would affect the slope of the $k_{ss}$ versus perfusion curve include artery to vein spacing, vessel density, and artery and vein distribution. The small artery model of kidney perfusion also correctly predicts that $k_{sin}$ can be used to determine intrinsic thermal conductivity in the presence of perfusion by choosing the correct sinusoidal heating period.

The finite difference code used to develop the small artery model of perfusion assumed that arteries were 0.005 cm from the thermistor surface. Other finite difference codes were developed varying the probe to vessel separation, and the results were similar to the case presented in this paper.

This thermal model has been developed specifically for thermistors placed in the canine kidney cortex. This type of model is appropriate for any study of local tissue heat transfer ($\approx 1\ cm^3$.) The development steps can be repeated to create thermal models for other tissues. An advantage of the small artery model comes from the fact that actual physical dimensions are utilized and the heat transfer equations are developed from basic principles. If the arterioles run next to the venules in the tissue, it may be necessary to include counter-current heat exchange term. In the liver, the capillaries (or sinusoids) are larger and more dense. In this situation, capillary perfusion may be important. A three dimensional numerical implementation will be required if symmetry is not present.

## Conclusions

The small artery model (SAM) was developed based on the anatomy of the kidney cortex vasculature. It correctly predicts the shape of the $k_{ss}$ versus perfusion curve and the ability to measure $k_m$ *in vivo* by choosing the correct sinusoidal heating period of the

thermistor. Although this model is specific for the canine kidney cortex, the modeling approach is applicable for a wide variety of biologic tissues.

## Acknowledgments

This research was funded by a grants from the Whitaker Foundation, NIH grant GM31931-01A3, and Texas Advanced Technology Program #003658-570.

## References

Anderson, G.T., Valvano, J.W., Santos, R.R., 1992, "Self-Heated Thermistor Measurements of Perfusion", *IEEE Transactions on Biomedical Engineering*, Vol. 39(9), pp. 877-885.

Anderson, G.T., 1989a, "An Interlobular Artery and Vein Based Model for Self-Heated Thermistor Measurements of Perfusion in the Canine Kidney Cortex", Ph.D. Dissertation, The University of Texas at Austin, Austin, Texas.

Anderson, G.T., 1989b, "An Interlobular Artery and Vein Based Model for Self-Heated Thermistor Measurements of Perfusion in the Canine Kidney Cortex", ASME Winter Annual Mtg., San Francisco, HTD Vol. 126, BED Vol. 12, pp. 29-35.

Balasubramaniam, T.A., Bowman, H.F., 1977, "Thermal Conductivity and Thermal Diffusivity of Biomaterials: A Simultaneous Measurement Technique", *J. of Biomechanical Engineering*, Vol. 99, pp. 148-154.

Baish, J.W., Ayyaswamy, P.S., and Foster, K.R., 1986, "Heat Transport Mechanisms in Vascular Tissues: A Model Comparison", *J. of Biomech. Eng.*, Vol. 108, pp. 324-331.

Brenner, B. M., *et al.*, 1986, "The Renal Circulations", *The Kidney*, W. B. Saunders Pub., Brenner and Rector Ed., pp. 93-123.

Beeuwkes, R., 1971, “Efferent Vascular Patterns and Early Vascular-Tubular Relations in the Dog Kidney,” *Am. J. Physiol.* , Vol. 221, pp. 1361-1374.

Charny, C.K., Weinbaum, S., and Levin, R.L., 1990, “An Evaluation of the Weinbaum-Jiji Bioheat Equation for Normal and Hyperthermic Conditions”, *J. of Biomech. Eng.*, Vol. 112, pp. 80-87.

Charny, C.K., 1992, “Mathematical Models of Bioheat Transfer”, Advances in Heat Transfer, Vol. 22, pp. 19-155.

Chato, J.C., 1968, “A Method for the Measurement of Thermal Properties of Biologic Materials”, *Symposium on Thermal Problems in Biotechnology*, ASME, N.Y, LCN068-58741, pp. 16-25.

Chato, J.C., 1980, “Heat Transfer to Blood Vessels”, *J. of Biomechanical Engineering*, Vol. 102, pp. 110-118.

Chen, M.M., *et al.*, 1980, "Microvascular Contribution to Tissue Heat Transfer," *Annals of the NY Acad. of Sci.*, Vol. 335, pp. 137-150.

Holmes, K.R., Chen, M.M., 1980, "*In vivo* Tissue Thermal Conductivity and Local Blood Perfusion Measured with Heat Pulse-decay Method", *Advances in Bioeng.*, pp. 113-115.

Jiji, L.M., Weinbaum, S., Lemons, D.E., 1984, “Theory and Experiment for the Effect of Vascular Microstructure on Surface Tissue Heat Transfer,” *J. of Biomechanical Engineering*, Vol. 106, pp. 331-???.

Patel, P. A., Valvano, J. W., Pearce, J. A., Prahl, S. A., and Denham, C. R., 1987, “A Self-Heated Thermistor Technique to Measure Effective Thermal Properties from the Tissue Surface”, *Journal of Biomech. Eng.*, Vol. 109, pp. 330-335.

Pennes, H.H., 1948, “Analysis of Tissue and Arterial Blood Temperature in the Resting Human Forearm”," *J. of Applied Physiology*, Vol. 1, pp. 93-102.

Qi, Y., Wissler, E.H., 1990, "A Three-dimensional, Finite Element Analysis of Countercurrent Heat Transfer Between an Artery-Vein Pair and the Surrounding Tissue Cylinder", ASME Winter Annual Mtg., Dallas, HTD Vol. 147, pp. 43-50.

Roemer, R.B., Moros, E.G., and Hynyen, K., 1989, "A Comparison of Bio-Heat Transfer and Effective Conductivity Equation Predictions to Experimental Hyperthermia Data", ASME Winter Annual Mtg., San Francisco, HTD Vol. 126, pp. 11-15.

Song, W.J., Weinbaum, S., and Jiji, L.M., 1987, "A Theoretical Model for Peripheral Tissue Heat Transfer Using the Bioheat Equation of Weinbaum and Jiji", *J. of Biomech. Eng.*, Vol. 109, pp. 72-78.

Valvano, J.W., *et al.*, 1984, "The Simultaneous Measurement of Thermal Conductivity, Thermal Diffusivity and Perfusion in Small Volume of Tissue". *J. of Biomech. Eng.*, Vol. 106, pp. 192-197.

Valvano, J.W., and Hayes, L.J., 1985, "Transient Finite Element Analysis of Self-Heated Thermistors Placed in Perfused Tissue", ASME Winter Annual Mtg., Advances in Bioengineering, pp. 77-78.

Valvano, J.W., Badeau, A.F., and Pearce, J.A., 1987, "Simultaneous Measurement of Intrinsic and Effective Thermal Conductivity," *Heat Transfer in Bioengineering and Medicine*, ASME Winter Annual Mtg., Boston, HTD Vol. 95, BED Vol. 7, ed. Chato, Diller, Diller, Roemer, pp. 31-36.

Valvano, J.W., Nho, S., 1990, "A Weinbaum-Jiji Model of Steady State Heated Thermistors in the Canine Kidney Cortex", ASME Winter Annual Mtg., Dallas, HTD Vol. 147, pp. 51-57.

Valvano, J.W., Nho, S., 1991, "Tissue Thermal Diffusivity Measured with Sinusoidal Heated Thermistors," ASME Winter Annual Mtg., Atlanta, HTD Vol. 179, pp. 9-14.

Weinbaum, S., and Jiji, L., 1985, "A New Simplified Bioheat Equation for the Effect of Blood Flow on Average Tissue Temperature", *J. of Biomech. Eng.*, Vol. 107, pp. 131-139.

Xu, L.X., Chen, M.M., Holmes, K.R., and Arkin, H., 1991, "The Theoretical Evaluation of the Pennes, the Chen-Holmes and the Weinbaum-Jiji Bioheat Transfer Models in the Pig Renal Cortex", ASME Winter Annual Meeting, Atlanta, HTD-Vol. 189, pp. 15-22.

**List of Figures.**

Figure 1. Outline of the vasculature in the canine kidney cortex.

Figure 2. Cross section (x,z plane) of the venous vasculature of a canine kidney cortex.

Figure 3. Top view (x,y plane) of the venous vasculature of a canine kidney cortex.

Figure 4. Measured $k_{sin}$ vs. sinusoidal heating period for the Pennes model.

Figure 5. Steady state and sinusoidal temperature versus distance solved using finite element analysis with no perfusion.

Figure 6. An interlobular artery in a control volume of tissue $\Delta x\, \Delta y\, \Delta z$.

Figure 7. Top view of the 2-D finite difference implementation of the small artery model.

Figure 8. 2-D finite difference model showing placement of the thermistor, arteries and veins in tissue. Drawing is not to scale.

Figure 9. Numerically determined tissue conductivity versus perfusion rate.

Figure 10. Steady state thermal conductivity versus perfusion for various thermal models.