IMPROVING THE CLINICAL APPLICABILITY OF A NON-INVASIVE PERFUSION DETERMINATION TECHNIQUE

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ABSTRACT: *The development of a data management solution that is used for the collection, storage, and retrieval of numerical data in a clinical setting to infer perfusion through a non-invasive thermal method is the impetus for this study. The concept of a self-heated thermistor bead located between a kidney and adjacent tissue is analyzed to determine the efficacy of the procedure to infer perfusion after transplant surgery. This procedure is then analyzed to improve the clinical applicability of the method for physicians.*

Many important perfusion problems related to blood flow do not require a mathematical solution of the actual volume flow per unit time, but only require information as to whether flow has increased, decreased, or remained constant. This determination of tissue perfusion is of interest to medical professionals and engineers. Although a quantitative study is not necessary, the ability to determine tissue perfusion while adhering to stringent clinical requirements is always necessary in the engineering and medical environment.

A non-invasive technique to the organ is developed that will allow for the continuous qualitative and quantitative monitoring of blood perfusion in a kidney during postoperative periods utilizing an easily extracted thermistor probe. The continuous assessment of blood perfusion in the kidney may allow timely therapeutic maneuvers to correct any abnormality in blood flow and prevent graft thrombosis and loss.

The data obtained from implementing the continuous assessment of perfusion in the kidney can be converted from numerical values to graphical images. This allows the physician a means of comparing perfusion variations over time, determine perfuse or non-perfuse states, and evaluate real-time perfusion in an efficient manner.

Keywords: *perfusion, database management, bioengineering, heat transfer*

1. INTRODUCTION

Sufficient renal blood perfusion is extremely important to successful implantation of the kidney. If insufficient blood perfusion occurs, transplant surgeons have available some means of stimulating perfusion if the need is known. What is critical to this is a minimally invasive method of inferring the presence of satisfactory perfusion.

The objectives of this study are to analyze whether the presence of tissue perfusion in an organ can be assessed using a non-invasive self-heated thermal diffusion probe and to determine how to collect, store, and retrieve perfusion data to improve the clinical viability of the method. This involves thermal numerical modeling of the system and issues concerning database management of numerically determined or collected values.

The complications encountered with organ transplant procedures are greater than any other type of transplant surgery. The second most common transplant surgery in the United States is the kidney transplant (roughly over 9,000 cases per year). Kidney transplantation is a life saving procedure when it is done for those with end stage kidney disease. A patient can be treated with dialysis until a kidney donor can be found. The most common cause of kidney failure is diabetes.

Thus, measurement of tissue perfusion is of obvious importance in clinical situations such as the immediate post-operative period after renal transplantation. Currently, the duplex ultrasound and the nuclear medicine renal blood flow scan are the two most commonly used modalities for this purpose [1]. These modalities, however, do not provide continuous monitoring of renal blood flow.

Continuous monitoring, at least in theory, may allow timely therapeutic maneuvers to correct any abnormality in blood flow. The non-invasive method of blood perfusion determination has implications that affect a significant number of organ transplant procedures. The importance of being able to quantify perfusion after kidney transplant surgery aids the surgeon in making critical decisions concerning the type of anti-rejection protocols to utilize if perfusion problems are determined early post-operatively. It is of importance to have a method that is non-invasive to the organ in an effort to prevent the inducing of trauma in the organs in contact with the thermistor probe.

This paper presents a two-dimensional axisymmetric finite difference model for predicting heat dissipation and distribution through two adjacent biological media. The heat dissipation and distribution then can be collected, stored, and retrieved through the use of a data management system that will allow the physician to make timely decisions regarding perfusion states and appropriate medical intervention techniques.

2. RELATED WORK

The work is based upon previously explored thermal diffusion techniques that determined thermal conductivity, thermal diffusivity, and perfusion values. The thermistor bead is the most widely used device in concluding these values. The single bead thermistor technique was first used as a method to determine perfusion and thermal values [2]. A constant temperature, transient diffusion technique is employed in this research.

Combining the research done on thermal diffusion techniques and self-heated thermistors, it is determined that a single thermistor bead utilized as a heating and sensing source is applicable to this study. The thermistor bead is modeled as a continuous point source and sensing device located at the interface of the kidney and an adjacent medium. The thermistor bead functions as a sensing element when the collection of the basal temperature is necessary and as a heating element when it is desired to maintain an incremental fixed temperature above baseline values.

3. METHODOLOGY

A two-dimensional axisymmetric finite difference model for predicting blood perfusion is presented. The system consists of two semi-infinite bodies, the kidney (Region a) and a specified adjacent medium (Region b), and a spherical thermistor (Figure 1).

The adjacent region (Region b) is characterized with tissue properties different from those of the kidney (Region a). Two separate governing equations, one for the kidney and one for the adjacent medium are developed.

The initial temperature of the system is taken as the baseline temperature. At $t=0^+$, the temperature of the thermistor is increased by 0.5°C of the baseline temperature and a transient, constant temperature heating is imposed at the heat source surface. Heating is induced for a predetermined amount of time and terminated. The system is allowed to return to baseline temperatures, and the process is repeated.

The "bioheat equation" is used in the development of the governing equations for the system. Different perfusion situations within the two media are simulated to assess the sensitivity of the technique to a variety of possibilities that might be found in actual surgery.

The method yields temperature field distributions along with a measurement of regional blood perfusion. Electrical energy is dissipated in the system, with the initiation of heating in the thermistor, and varied to maintain the temperature of the thermistor at a predetermined fixed value. The increase of heating above baseline temperature depends on the amount of heat lost to the surrounding media. The increase in thermistor heat dissipation is an indicator of perfusion rate. An increase in effective thermal conductivity (due to conduction and convection influences) will be related to the perfusion rate. The end result is an assessment of the effectiveness in monitoring blood perfusion with the thermistor approach. In essence, this is determined by the ability to discern kidney perfusion variations from the rate of heating required.

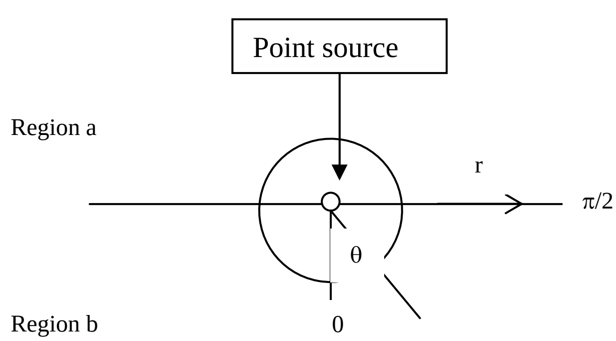

Figure 1. Diagram of Model

3.1 Model Formulation and Assumptions

3.1.1 Governing Equations and Model Geometry

The mathematical model is based on Pennes' bioheat equation [4], which was used to model the effect of perfusion on heat distribution and dissipation. Pennes' bioheat equation is described by

$$(\rho c)_t \frac{\partial T}{\partial t} = k_t \nabla^2 T_t + q_{perfusion} + q_{metabolic} \quad (1)$$

A finite difference model is developed based on Pennes' bioheat equation (1) to simulate the thermal aspects associated with the condition of perfuse and non-perfuse kidney in the model. In this study, the kidney and adjacent tissue are assumed to be homogeneous in nature with no internal heat generation.

The governing equation in the case of non-perfuse tissue in the spherical coordinate system becomes

$$\rho_t c_t \frac{\partial T_1}{\partial t} = k_t \left[\frac{1}{r^2 \sin\theta} \frac{\partial}{\partial \theta}\left(\sin\theta \frac{\partial T}{\partial \theta} \right) + \frac{1}{r^2} \frac{\partial}{\partial r}\left(r^2 \frac{\partial T}{\partial r} \right) \right] \quad (2)$$

$$+ q_{met}.$$

The heat input of the self-heating thermistor bead is modeled using the spherical measuring bead with pulse input method proposed by Chen [4]. This method employs applying a known quantity of heat to the tissue in question during a short time period. Chen notes advantages of this method are (1) the bead can be very small in nature; (2) fast measuring cycles; (3) high sensitivity; (4) and the results provide a clear distinction between a purely conductive non-perfused tissue and one with blood perfusion [4].

3.1.2 Model Parameters

3.1.2.1 Kidney and Tissue Properties

The thermal conductivity properties pertaining to the model for the human kidney and tissue are provided (Table 1). Baseline temperatures are assumed to be 33^{o}C.

3.1.2.2 Thermistor Heating

Thermistor heating is formulated as a point source at a constant temperature with varying energy output.

3.1.2.3 Assumptions

Assumptions used in the mathematical development of the model are summarized as follows:

a. The tissue transport is governed by the Pennes' bioheat transfer equation.
b. Thermistor modeled as a uniformly heated sphere of radius a.
c. Perfect thermal contact is assumed between the thermistor and the two adjacent media (kidney and tissue).
d. Properties of the kidney, tissue and thermistor are assumed constant.
e. The kidney and tissue are modeled as homogeneous medium.
f. Metabolic heating is assumed negligible.
g. Effects of perfusion are accounted for in an effective thermal conductivity.

	Thermal Conductivity (W/m ^{o}C)	Density (kg/m^3)	Specific Heat (J/kg ^{o}C)
Kidney (whole) perfuse (Region a)	0.543	1050	3787.76
Kidney (whole) non-perfuse lower bound (Region a)	0.49	1050	3787.76
Tissue (Region b) *remains constant	0.42	1050	3787.76

Table 1. Model Parameters [2,3]

3.1.2.4 Initial Conditions

At t=0 the kidney, tissue and thermistor probe are at the same temperature.

3.1.2.5 Boundary Conditions

As the radius of the system approaches infinity the temperature is that of the initial temperature. The temperature of the bead at $t=0^+$ is at a predetermined value above the baseline temperatures measured initially. The boundaries of the kidney and tissue that are in direct contact have the same temperature as that specified for the thermistor at that time.

3.2 Numerical Implementation

An axisymmetric finite difference code is developed to numerically implement the model. The time step is numerically determined according to stability criteria. Grid size within the kidney and tissue remain constant with varying radial and angular distance. The thermistor heating is implemented using a predetermined increase in baseline temperature. An output file was produced that gave temperature distribution throughout the kidney and adjacent tissue and energy dissipation values.

3.3 Analytical Solution Used for Comparison

To calibrate the accuracy of the numerical model, an analytical solution was sought. For this, a result given by Carslaw and Jaeger was used [5]. The solution adapted for comparison is a constant temperature sphere surrounded by a semi-infinite medium.

For this solution, two differences existed compared to the numerical model. One of these is that a uniform thermal conductivity is assumed. This can be easily handled in the numerical solution. The other is that the analytical solution is for a semi-infinite region while the numerical model is for a finite region. Since we are concerned with the heat transfer at the thermistor surface, this is not felt to be a significant problem.

4. REQUIREMENTS OF CLINICAL APPLICATION

The numerical model described in the previous section allows physicians to make quantitative assessments about the state of perfusion in post-operative patients from the output file will give temperature distribution throughout the kidney and adjacent tissue and energy dissipation values. By manually viewing the graphs generated from the model and comparing them to a baseline graph of the patient, the physicians can make qualitative assessments as well. The thermistor providing the temperature readings, however, generate data continuously which means that the physician would have to continuously review the output graphs. Ideally, then, the process of evaluating the results of the thermistor should be automated.

In order to automate the perfusion determination procedure, several open issues regarding the storage and retrieval of the data generated by the thermistor must be resolved. The most intuitive issue concerns the automation of the process of qualitatively assessing a newly generated set of thermistor readings. Specifically, given a set of thermistor temperature measurements taken from one cycle as input, the system needs to be able to compare them with a baseline set of thermistor temperature measurements from the patient. Since perfusion is considered to occur only if the baseline and real time measurements do not coincide, automating this process involves implementing a function that can compute the distance between two sets of measurements. Although several functions [6] exist for computing the distance between sets of measurements, the difficulty in implementing them comes in choosing a suitable threshold for the function to determine perfusion. Such a threshold value may be different for each patient. It may be necessary to correlate the distance between a thermistor cycle reading set and a baseline measurement set to perfuse and non-perfuse data.

Other issues related to developing a distance function to evaluate perfusion involve determining how efficiently such an evaluation can be made. The thermistor may be set to perform a varying number of readings in a heating cycle. An open question, then, is finding the minimum number of measurements that permit an accurate determination of perfusion. The reason why the number of readings should be minimized is that each set of readings will need to be stored in the system's underlying database for future reference. Again, identifying the minimum number of readings may involve correlating thermistor cycle readings to perfuse data. The difference here is that the system needs a correlation between perfuse and non-perfuse data and a subset of the readings from a single thermistor cycle.

Storing multiple sets of thermistor cycle readings for a single patient allows for the possibility of permitting physicians to pose other types of queries to the system. Specifically, a physician can pose a query such as "Given multiple sets of cycle readings over a period of time, how quickly did the reading change from indicating a perfuse state to a non-perfuse state?" This query would be helpful in allowing the physician to assess the viability of the organ and make timely therapeutic decisions. In addition, the physicians should be able to compare a set of multiple thermistor cycle readings to other sets. This would allow them to compare the amount of perfusion occurring in the transplanted organ. Implementing this requirement, however, means that the system would have to efficiently process queries of the type "Given a collection of thermistor readings over k cycles, find another set of k readings in the database that are similar." This involves the development and selection of a similarity function that permits comparing a collection of sets of cycle readings with another collection as well as identifying query processing methods that simultaneously search for matches for multiple sets of multidimensional data.

5. SUMMARY AND CONCLUSION

The comparison between the analytical results and numerical results proved to be quite good [7]. This gave some confidence in the numerical code. As another check, not shown here, the analytical results for steady-state heat conduction across a spherical shell is used. The numerical code is then run to steady-state conditions and the results compared to the analytical result. Again good comparisons were shown [7].

Once the validation of the code is achieved, the energy input is measured over a period of time over in the interface between the organ and the surrounding tissue. The energy values utilized in the numerical program are those anticipated to be used for in vivo inference of perfusion. Results from the data show that the typical difference between perfuse and non-perfuse situations may result in only a few (perhaps 3-4) percentages change [7].

A two-dimensional axisymmetric numerical model has been developed to assist in analyzing the potential of a heated thermistor probe to infer whether or not perfusion is occurring in a transplanted organ. The numerical model has been shown to compare well to a variety of benchmarking cases using analytical results.

In the model, effects of perfusion are handled using an effective thermal conductivity. Using the model we have shown typical variations of the parameter that would be measured (energy dissipation). It is clear from the results that the types of variations that might be manifested are quite small. Hence, very sensitive measurements of the energy dissipated will have to be used.

The successful implementation of the self-heated thermistor method to infer perfusion depends on automating the process of detecting changes in sets of thermistor readings. The system must be sensitive enough to detect changes of 3-4% in numerical values. In addition, samples of thermistor readings from wide variety of patients must be correlated against perfuse and non-perfuse states. Such a correlation is necessary for the development of a threshold value that can be used to map quantitative data to qualitative assessments of whether perfusion has occurred.

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