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Differential and Directional Effects of Perfusion on Electrical and Thermal Conductivities in Liver

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***Abstract*—Two different measurement probes - an electrical probe and a thermal conductivity probe - were designed, fabricated, calibrated, and used in experimental studies on a pig liver model that was designed to control perfusion rates. These probes were fabricated by photolithography and mounted in 1.5-mm diameter catheters. We measured the local impedance and thermal conductivity, respectively, of the artificially perfused liver at different flow rates and, by rotating the probes, in different directions. The results show that both the local electrical conductivity and the thermal conductivity varied location to location, that thermal conductivity increased with decreased distance to large blood vessels, and that significant directional differences exist in both electrical and thermal conductivities. Measurements at different perfusion rates demonstrated that both the local electrical and local thermal conductivities increased linearly with the square root of perfusion rate. These correlations may be of great value to many energy-based biomedical applications.**

I. Introduction

HYPERTHERMIC treatment and energy-based thermal ablative techniques are increasingly used on liver tumors when surgical resection is not an option. The transfer of radiofrequency (RF) energy into the target tissue and the subsequent spatial distribution of the induced heat are determined by tissue properties. Two salient tissue properties are electrical conductivity (σ) and thermal conductivity (K_{eff}). The extent to which these properties are related to tissue blood perfusion is not fully understood. However, they are generally thought to exert major influence on the size and shape of the ablated zone [1],[2]. Previous studies have focused on electrical and thermal properties of tissue on a macro scale (centimeter or larger) [3],[4]. However, an understanding of how local tissue conductivity properties are influenced by blood perfusion is needed. This study was undertaken to fill this need and to develop more accurate estimates of ablation zone dimensions and improved treatment planning.

To this end, we used an artificially perfused pig liver model to characterize the effect of perfusion on electrical and thermal conductivities of the tissue.

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II. Methods

A. Perfused Liver Model

Porcine livers were procured from a local slaughter house and placed in a Perfused Liver Model Workstation (Fig. 1)[5]. Liver preparation started within 2 hours after removal from the animal. The portal vein and hepatic artery were intubated (Tygon) and the vessels were ligated to the tubing. The liver was placed in the Workstation tank partially submersed in a bath of 0.9% saline. The tubing was connected to a perfusion circuit. The perfusate was circulated by a peristaltic pump that fed the portal vein and hepatic artery. The perfusate through the liver drained freely from the vena cava into the tank reservoir and was returned from the reservoir back to the pump.

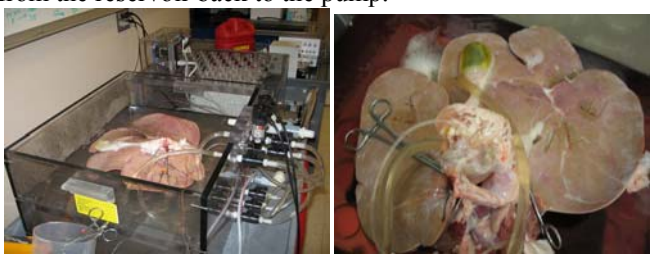

Fig. 1. Perfused Liver Model Workstation. Liver placed in a tank with 0.9% saline perfused through TYGON tubing (left) and shown with directional index markers on liver surface at sites of probe insertion (right).

The liver was subsequently flushed with iced heparin-saline solution (150000 units / 20L 0.9% saline) for 1-2 hours in the Workstation tank to remove blood clots prior to testing. Ice packs were placed in the saline reservoir to reduce tissue degradation.

The liver was perfused with 0.9% saline at 37°C after the flushing procedure was completed. The experimental data collection time was restricted to 2 hours to limit tissue degradation. The rotational speed of the peristaltic pump was controlled as dictated by the experiment. As an example, the pump rate could be adjusted to simulate human liver pressure or flow in the portal vein and hepatic artery. Human liver flow is 1500 ml/min [6] which corresponds to a pump rate of 280 RPM.

All perfusate flow through the pump must pass through the liver (assuming no leaks). To establish a relationship between the pumping rate and flow rate through the liver, the pump rate was set at different speeds and at each pump rate the circulated saline was collected from the vena cava in

a beaker during a prescribed time period. Hence the flow rate was measured at different pumping rates in perfused livers (Fig. 2). A linear relationship between the pump rate and the liver flow rate was observed. The average perfusion rate is simply the measured flow rate divided by the liver volume, a linear relationship between the averaged perfusion rate and pumping rate is implied. Our measurements of the effective thermal conductivity indicate that the local perfusion rate may vary considerably from the average perfusion rate. The absolute value at each location of the liver is unknown, but what can be reasonably assumed is that the local perfusion rate is also linearly related to the pump rate.

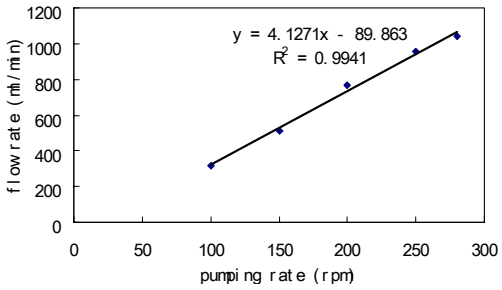

Fig. 2. Flow rates collected from the vena cava at different pump rates.

All conductance micro probe placements were guided by ultrasound imaging (Terason t3000 Ultrasound System) guidance to precisely locate the sensing surface of the probes relative to visible blood vessels in the liver. The direction that the probe faced was constantly monitored.

B. *Electrical Conductivity Probe*

The micro electrical probe was designed to measure σ in the liver at the lobule or millimeter scale. The design layout of the probe is shown in Fig. 3. A detailed description of the design and fabrication is given elsewhere [7]. Briefly, the probe was fabricated using standard photo lithography techniques and secured in a catheter with waterproof epoxy (Fig. 3).

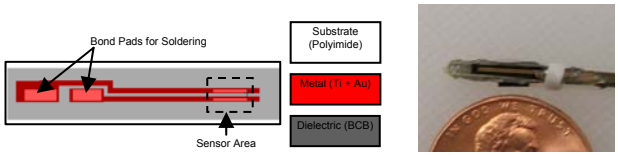

Fig. 3. The micro electrical probe mounted on a tube with an optical fiber temperature sensor attached

In use, the micro-electrical probe is inserted in the medium and the impedance across the two electrodes is measured using an impedance analyzer (HP 4294A) at 500 kHz, the working frequency of commercial RF applicators. To relate the measured impedance values to σ, a conversion factor is needed. To this end, we measured saline solutions with different salinities using both the two-electrode probe and a commercial four-ring probe (HI 9835, HANNA® Instruments). From these measurements, a cell constant defined as the product between σ and impedance was derived. Experimental measurements of different biological materials using the two-electrode probe using the calibration procedure described in [8] are in good agreement with those given in previous literature [9].

C. *Thermal Conductivity Probe*

A micro thermal probe was also designed to measure tissue thermal conductivity at the liver lobule scale and shown in Fig. 4. The design consists of two resistive inner thin film heating elements and two outer Resistance Temperature Detector (RTD) sensors on a glass substrate. A detailed description of the design and fabrication is given elsewhere [10]. The probe was fabricated using standard photo lithography techniques and mounted in a catheter with epoxy (Fig. 4).

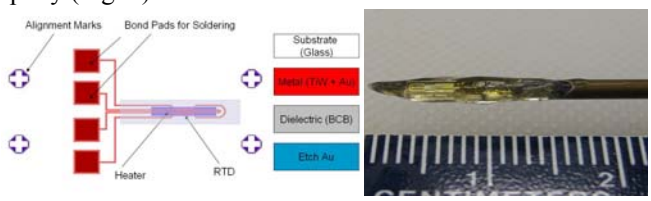

Fig. 4. The design layout of micro thermal conductivity probe (left) The picture of micro thermal conductivity probe assembled on a catheter (right).

The temperature response of the RTD sensor changes almost linearly with the logarithm of time under constant uniform heating by the inner heating elements. Thermal conductivity and thermal diffusivity can be determined by numerical fitting based on the temperature increase and slope. Following calibration of the thermal conductivity probe as described in [10], the thermal conductivity can be determined from the temperature and slope data [10].

III. Experiments and Results

A. *Electrical Conductivity Measurements in the Perfused Liver*

We did two sets of tests using the micro electrical probe in the perfused liver model. First, the relationship between electrical conductivity and perfusion rate was examined by measuring the σ at different perfusion rates. Second, directionality of electrical conductivity was examined by inserting the probe and turning it around the long axis of the probe to measure σ in each of the cardinal directions.

A.1. Measurement of electrical conductivity at different perfusion rates

A liver was placed in the Prefused Liver Workstation and connected into the perfusion circuit. After perfusing at 270 rpm for 30 minutes, the electrical conductivity probe was inserted in the liver and the conductivity was measured at different pumping rates (0, 90, 180 and 270 rpm). The results are shown in Fig. 5 and indicate that σ increases with pump rate. Also a linear relationship exists between σ and the square root of the perfusion rate. This linear relationship

is indicated at all six locations. To the best knowledge of the authors, this relationship of increasing electrical conductivity with increased perfusion change has not been reported in previous literature.

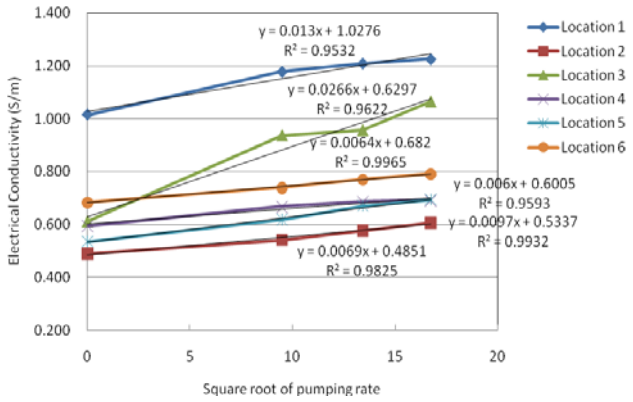

Fig. 5. The electrical conductivity versus the square root of pumping rate.

A.2. Measurement of directivity of electrical conductivity

Three livers were used for the directivity test. Four locations (Points A, B, C and D) of each liver were randomly chosen for the directional measurement. A transparent disk with a red arrow mark was used to indicate zero direction at each location (Fig. 1). The micro electrical probe was inserted into each location. The impedance value was measured at each of the cardinal directions; 0°, 90°, 180°, and 270° and was converted to σ as described earlier. The results are shown in Fig. 6 and values are listed in Table 1.

The average electrical conductivity is higher than *in vivo* data as shown in Table 1. This is expected since the perfusate we used had higher σ than blood. The average electrical conductivity (S/m) for Livers 1, 2, and 3 were 0.54, 0.66, and 0.53 and the standard deviations were 0.14, 0.17, and 0.10, respectively. These variations are higher than reported in previous literature [3],[8]. This is likely caused by the saline perfusate used in these tests which differs from blood. Therefore our perfused liver model has much higher non-homogeneity than *in vivo* data.

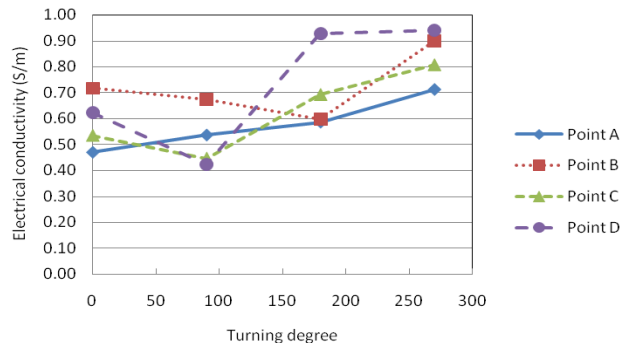

Fig. 6. Electrical conductivities measured rotational at the four cardinal directions in four different locations in Liver 2.

TABLE I
ELECTRICAL CONDUCTIVITY IN FOUR CARDINAL DIRECTIONS

	Facing direction	Liver 1	Liver 2	Liver 3
Electrical conductivity (σ) at Point A (S/m)	0	0.45	0.47	0.62
	90	0.62	0.54	0.63
	180	0.57	0.59	0.58
	270	0.59	0.71	0.67
Electrical conductivity (σ) at Point B (S/m)	0	0.39	0.72	0.47
	90	0.36	0.67	0.45
	180	0.45	0.60	0.48
	270	0.55	0.90	0.49
Electrical conductivity (σ) at Point C (S/m)	0	0.25	0.53	0.48
	90	0.43	0.45	0.47
	180	0.63	0.69	0.44
	270	0.75	0.81	0.58
Electrical conductivity (σ) at Point D (S/m)	0	0.65	0.62	0.31
	90	0.59	0.42	0.73
	180	0.58	0.93	0.50
	270	0.75	0.94	0.51

The electrical conductivities (σ) in different directions at the same location are quite different. When the probe faced different directions, the tissue between the two electrodes of the probe changed and σ varied. Low σ (Point C at Location 1) may be caused by contact with fatty tissue and high conductivities may be caused by neighboring blood vessels. This fact indicates there is a strong directivity of σ depending on local anatomical structure.

B. Thermal Conductivity Measurements in the Perfused Liver

B.1. Measurement of thermal conductivity at different perfusion rates

The thermal conductivity probe was inserted in the perfused liver and the pump rates were varied as before (Fig. 7).

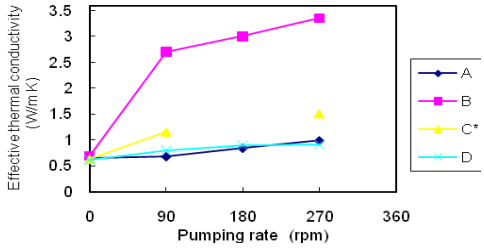

Fig. 7. Effective thermal conductivities (K_{eff}) change at different pumping rates in four locations (A, B, C, D).

Location B in Fig. 7 is in a major blood vessel. C is next to a vessel, A and D are 1 cm from a major vessel. The high effective thermal conductivity (K_{eff}) at location B was expected because the probe was subjected to the direct

conductive heat loss in a blood vessel. Probe placements away from major blood vessels, such as locations A and D, measured the lowest K_{eff} values. The conductivity was 50% higher at location C than at A and D.

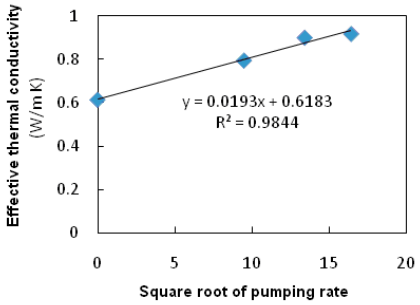

Fig. 8. Effective thermal conductivity (K_{eff}) versus square root of pumping rate at location D.

Re-plotting the data we found that the increase in K_{eff} is in a linear relationship with the square root of the pump rate [10], hence the square root of perfusion.

B.2. Measurement of directivity of thermal conductivity

The thermal probe was inserted into each location of the perfused liver and K_{eff} values were taken at each of the cardinal directions (similar to *Section A.2*)(Fig. 9).

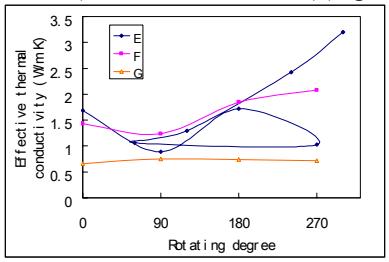

Fig. 9. The effective thermal conductivity (K_{eff}) change at different rotation degrees at location E, F, and G.

Locations E and F were 1 cm from a vessel. Location G was far away from large vessels. A significant difference in K_{eff} was measured in different directions when rotating the probe. The measured values trend toward sinusoidal as the probe is rotated (E and F) but accumulated damage to the tissue may occur (240° and 300°) as the probe is rotated several times. Location G demonstrates that directional variation may be small when K_{eff} values are low. These results indicate a significant directional difference of K_{eff} in perfused liver is observed when the probe is close to a blood vessel and the local perfusion rate is high.

IV. Discussion

Both electrical and thermal conductivity micro probes demonstrate that perfusion rate affects these properties and that both σ and K_{eff} are directional.

Nonhomogenity of liver tissue is well known. Our measurement of σ at the lobule scale provided larger variation than previously reported. We used saline as our perfusate which has higher σ than blood, and could cause larger variation. Also the impact of scale reduction from centimeter to millimeter must be further investigated. These studies are the first to measure and describe directivity of σ in liver. We defined this as a directional change caused by the local tissue composition variation at the lobule scale. Further correlating this directivity of both σ and K_{eff} with the local anatomical structure will be helpful to understand this unique phenomenon in the liver. The vascular structure of the liver, both marco- and micro-vessels are contributors.

Our experimental tests indicated an important correlation between both σ and K_{eff} and the perfusion rate. This correlation has profound implications for many biomedical applications. The relationship between perfusion and tissue conductivities has a significant impact on energy-based biomedical devices.

V. Conclusion

The experimental data presented in this study demonstrated that both electrical and thermal conductivities are significantly affected by the rate of perfusion. Both electrical and thermal conductivities have directionality and may be characterized as vector fields in perfused tissue.

Acknowledgment

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