Experimental Measurements of the Temperature Variation Along Artery-Vein Pairs from 200 to 1000 μm Diameter in Rat Hind Limb

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Theoretical studies have indicated that a significant fraction of all blood-tissue heat transfer occurs in artery-vein pairs whose arterial diameter varies between 200 and 1000 μm. In this study, we have developed a new in vivo technique in which it is possible to make the first direct measurements of the countercurrent thermal equilibration that occurs along thermally significant vessels of this size. Fine wire thermocouples were attached by superglue to the femoral arteries and veins and their subsequent branches in rats and the axial temperature variation in each vessel was measured under different physiological conditions. Unlike the blood vessels <200 μm in diameter, where the blood rapidly equilibrates with the surrounding tissue, we found that the thermal equilibration length of blood vessels between 200 μm and 1000 μm in diameter is longer than or at least equivalent to the vessel length. It is shown that the axial arterial temperature decays from 44% to 76% of the total core-skin temperature difference along blood vessels of this size, and this decay depends strongly on the local blood perfusion rate and the vascular geometry. Our experimental measurements also showed that the SAV venous blood recaptured up to 41% of the total heat released from its countercurrent artery under normal conditions. The contribution of countercurrent heat exchange is significantly reduced in these larger thermally significant vessels for hyperemic conditions as predicted by previous theoretical analyses. Results from this study, when combined with previous analyses of vessel pairs less than 200 μm diameter, enable one estimate the arterial supply temperature and the correction coefficient in the modified perfusion source term developed by the authors. [DOI: 10.1115/1.1517061]

Keywords: Bioheat Transfer, Countercurrent Heat Exchange, Microvasculature, Rat Hind Limb

Introduction

It is widely recognized that the blood flow distribution and detailed vascular geometry have a profound effect on the heat exchange between the blood and tissue and the heat exchange of the tissue near the surface of the body with the environment. Most investigations of countercurrent heat exchange in humans and other mammals have either examined the heat transfer between the major supply arteries and veins in the limbs [1] or the thermal equilibration in vessels less than 200 μm diameter in the microcirculation. The latter are not direct temperature measurements, but surface temperature measurements above small artery-vein pairs in thin two-dimensional tissue preparations [2–5]. No equivalent experiments have been previously performed for artery-vein pairs whose arterial diameter ranges from 200 to 1000 μm, although theoretical studies indicate more than half of all blood tissue heat transfer occurs in these vessels. Vessels of this size have been the most difficult to treat both theoretically and experimentally because they are both numerous and have a complicated three-dimensional architecture. Using a new experimental technique developed in this paper, we have been able to make the first direct measurements of the axial thermal equilibration in a branching three-dimensional network whose countercurrent arteries and veins are of this size. These studies have been performed on the femoral arteries and veins and their branches in the hind limbs of mature Sprague-Dawley rats.

The heat transfer function of the vascular system has been appreciated since the mid-19th century and has been quantitatively modeled by various investigators [6–9]. Various models have been introduced to simplify the tissue-vessel thermal interaction and provide a single effective bioheat transfer equation. One of the most widely-used continuum models was developed by Pennes [6], where the effect of the blood was modeled as a volumetric and isotropic source term. However, its fundamental assumptions as to where and how this thermal equilibration occurred were questioned by several investigators [7,10]. Theoretical models suggested that most blood-tissue thermal equilibration did not occur in capillaries, as assumed in Pennes, but in vessels between 50 and 500 μm and that there was little equilibration in vessels >1 mm diameter. Weinbaum et al. [10] proposed that the primary mechanism by which the microvascular blood flow alters the tissue heat transfer is incomplete countercurrent exchange in thermally significant microvessels of this size and introduced a new bioheat equation to describe this blood-tissue heat exchange [8].

The Pennes and Weinbaum-Jiji models represent two extreme situations of blood-vessel thermal interaction. In the original Pennes model, the arterial blood releases all of its heat to the

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surrounding tissue in the capillaries and there is no venous rewarming. As mention above, Pennes did not realize that thermal equilibration was achieved in vessels at least an order of magnitude larger than capillaries. In contrast, in the Weinbaum-Jiji model there is nearly complete countercurrent rewarming and this is assumed to be the main mechanism for blood-tissue heat transfer. Subsequent theoretical and experimental studies have shown this is a valid assumption only for vessels less than 200 μm diameter [2,11] where the both the artery and vein follow the local tissue gradient. Several theoretical studies have suggested that one way to overcome the shortcomings of both models was to introduce a ''correction coefficient'' in the Pennes perfusion term [9,12–15] which accounts for rewarming in the countercurrent vein.

The analyses in Weinbaum et al. [9] and Zhu et al. [15] have provided the theoretical framework for the present experiments. The combined model in [9] and [15], which is based on anatomical studies of Myrhage and Eriksson [16], suggests that thermal equilibration is achieved in two stages, first partial equilibration in supply arteries and veins (SAV vessels) as the arterial vessels decrease in size from 1000 to 200 μm diameter, and then final equilibration in the s vessel tissue cylinders where the vessels are all <200 μm. The new modified perfusion term in Weinbaum et al. [9] has the simplicity of the Pennes model, but also accounts for the venous rewarming by determining the net heat released from the countercurrent artery and vein to the surrounding tissue in the s vessel tissue cylinders. The model predicts that the venous rewarming accounts for typically 30 to 40% of the heat released by the countercurrent artery in s vessel tissue cylinders. The model for the SAV vessels in [15] predicts that the extent of the thermal equilibration in the SAV vessels depends greatly on the blood perfusion rate and the vascular geometry. However, the extent of venous rewarming is independent of the perfusion rate and approximately 40%. The principal objective of this paper is to demonstrate this equilibration experimentally in a branching vessel network whose vessels are of the same size as the SAV vessels in human limbs. We would also like to measure the size of the ''correction coefficient'' that appears in the modified Pennes source term in [9] and the extent of venous rewarming that occurs in these vessels.

There have been relatively few experimental investigations of local blood-tissue heat transfer because of the complicated 3-D vascular organization of most tissues and the difficulty in making measurements in blood vessels whose dimensions are comparable to the thermal probes themselves. The vascular casts in Weinbaum et al. [10] showed that nearly all microvessels in muscle tissue that were >50 μm dia, occurred as countercurrent artery-vein pairs. Subsequently, Lemons et al. [17] obtained detailed temperature profiles in the rabbit thigh which showed that if these vessel pairs were <200 μm dia. the temperature difference between the artery and vein would be 0.2°C or less. Crezee et al. [18] inserted a small plastic tube into the tissue of an excised bovine kidney and measured the disturbance in the temperature field in a plane perpendicular to the tube when heated water was circulated through it. The effect of forced perfusion in the tissue was shown to be equivalent to an enhancement in thermal conductivity k_{eff} as predicted by the Weinbaum-Jiji model. However, the macroscopic tissue temperature profiles measured by Roemer et al. [19] in canine thighs and by Xu et al. [20] in pig renal cortex were found to be in better qualitative agreement with the Pennes equation than the Weinbaum-Jiji equation. More recently, the authors have performed several experimental studies on different 2-D tissue preparations to evaluate the axial thermal equilibration in microvessels between 70 and 200 μm diameter [2–5]. These studies have demonstrated that the expression for k_{eff} is only valid for vessels less than 200 μm diameter. In these experiments the axial variation in vessel temperature is not measured directly, but deduced from high-resolution thermal images of the tissue surface in which one sees the combined effect of the artery-vein pair and not the axial variation of the temperature in each vessel.

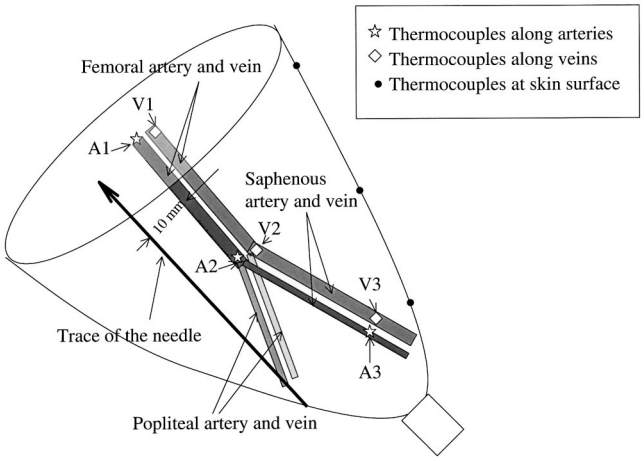

Fig. 1 Schematic diagram of the vasculature in rat hind leg and the locations of temperature sensors.

The present investigation is the first to directly measure the axial temperature profiles in both vessels of thermally significant artery-vein pairs that are <1 mm diameter with the smallest arterial vessels being just above 200 μm. These measurements are performed for a wide range of perfusion rates in which the vessels have been subjected to vasodilation, vasoconstriction and environmental cooling. The treatment of vessels of this size has proven to be the most difficult in bioheat transfer analysis. These vessels, which are usually referred to as *SAV* vessels in humans and large mammals, are too numerous to be treated individually and too large to fall within the framework of continuum models such as the Pennes or Weinbaum-Jiji bioheat equations. While the thermal equilibration in intermediate vessels of this size would be very difficult to measure in large animals, they are the main vessels supplying the limbs in small animals such as the rat. These experiments were performed using a new protocol in which fine wire thermocouples were directly attached after microsurgery to the femoral vessels and their subsequent branches in a rat hind limb.

Methods

Twenty-two male Sprague-Dawley rats (weight$=$mean$\pm SD$, 467 ± 17 g) were used in this study. The rat was anesthetized with intraperitoneal injections of pentobarbital sodium (40 mg/kg) and put on a water-jacketed heating pad to keep it warm. Additional anesthetic (sodium pentobarbital, 15 mg/kg, I.P.) was administrated as needed. A tracheal tube was inserted to maintain a patent airway. The rectal temperature was monitored throughout the experiment with a thermocouple inserted into the rectum. The dissection began only after the rat was unresponsive to a toe pinch. The surgical procedure required approximately 30 minutes, and the subsequent experimental procedure required approximately one hour or less.

An L-shaped skin incision over the medial aspect of the groin and thigh region was made. The vasculature in the hind leg was viewed under a Nikon® SMZ800 dissection microscope stage (Image System Inc., Columbia, Maryland). The left femoral artery and vein and their subsequent branches were carefully exposed and separated from the surrounding fascia. The common femoral, superficial epigastric and saphenous vessels were identified. Once exposed, a continuous drip of the Kreb solution [3] suffused the thigh throughout surgery. Six high resolution thermocouples made with individual 50 μm copper and constantan wires were carefully attached with super glue to the femoral vessels and the saphenous branches (Figure 1). During the surgery, the field of view was

displayed on a closed circuit camera and videotaped for post experimental measurement of the vascular geometry. The blood flow rate in the left femoral artery was measured with a T106/T206 Animal Research Flowmeter (Transonic® System Inc., Ithaca, New York). The skin was then closed and the rat was placed in a box. The mean skin temperature was measured by three thermocouples placed along the axial direction of the hind limb, as shown in Fig. 1. The experiment was controlled and the data were acquired and recorded with LabView® software (National Instruments, Austin, Texas) running on a PC.

Two measurement protocols were used in the experiments. In the first protocol, temperature decay along the blood vessels was measured for two environmental conditions. After the femoral artery and vein were exposed and isolated, the average blood flow rate in the femoral artery was first measured by the flowmeter via a 0.7 mm V flow probe hooked around the vessel. The blood flow rate was measured before the placement of the thermocouples to ensure no interference between the temperature sensor and the ultrasound emitted by the flowmeter probe. The thermocouples were then attached to the blood vessels. After the skin and incision were closed, the rat was placed in the box at room temperature. The temperatures were then continuously measured at all sensor locations and recorded by the computer. After the steady state was established, a fine thermocouple embedded in a 26-gauge needle was inserted into the rat limb to measure the local tissue temperature. The needle was inserted to measure the steady state temperatures at different locations along the sensor path, as shown in Fig. 1. The trace of the needle was approximately parallel to the blood vessel pair and less than 10 mm from the axial path of the vessels. Next, a continuous flow of cold air was passed through the box to change the environmental temperature for the rat. The rat was then subject to a cold environment at 13°C. The same procedure was then repeated as at room temperature until a new steady state was established and the tissue temperature was measured by the needle probe. After the temperature measurement, while the rat was still exposed to the cold environment, the skin was reopened and the thermocouples were quickly removed from the blood vessel. Within 20 seconds, the flow rate in the femoral artery was measured by the flowmeter probe. Changes in temperature variation along the blood vessels and blood flow rate, therefore, could be recorded for each environmental condition.

The second protocol was used to measure the temperature decay under conditions of vasoconstriction and vasodilation. After the femoral artery and vein were exposed under the dissection microscope, the average blood flow rate in the femoral artery was measured first by the flowmeter. To induce an increase or decrease in the blood flow rate in the hind leg, 2 cc Na nitroprusside ($10^{-4.5}$ M) or NE (10^{-5} M) was injected intramuscularly at several locations in the leg muscle. Ten minutes after the injection, the blood flow rate in the femoral artery was measured for the vasoconstrictive or vasodilative conditions. The thermocouples were then attached to the blood vessels. The skin was closed. The rat was placed in the box at room temperature. The temperatures at all blood vessel and tissue locations were measured as described in the first protocol.

After the experiment, the rat was euthanized by a Na pentobarbital overdose I.P. (150 mg/kg). The hind leg was cut from the hip and weighed. The weight of the hind leg was measured (mean $\pm SD$, 32 ± 2.9 g). The blood vessel radius and the locations of the temperature probes were measured later from individual video images of the recorded videotape.

For each experiment, the steady state temperature variation and average blood perfusion rate were calculated. Statistical comparisons were performed using analyses of variance for repeated measures. Results were expressed as mean $\pm$ standard deviation (SD). Significance is evaluated at the 5% confidence level.

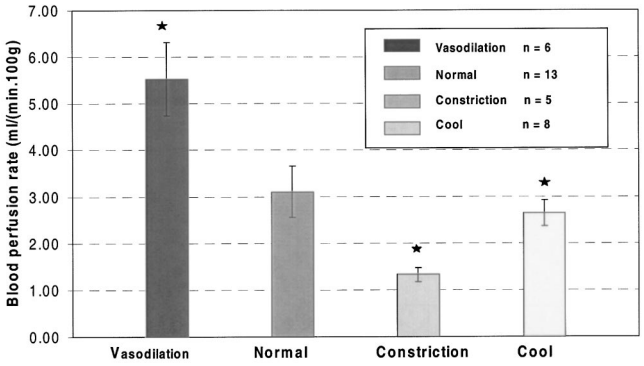

Fig. 2 Blood perfusion rates measured under different physiological conditions. Vertical bars denote mean$\pm SD$. n is the number of rats used. ⋆: blood perfusion rate that is significantly different ($p<0.05$) from that under normal conditions.

Results

It has been observed that most of the blood vessels in the rat hind leg occur as countercurrent vessel pairs. The femoral vessels are located deep in the hind leg and run parallel to the axial direction of the leg. The femoral artery usually branches into several blood vessels including the superficial epigastric, the popliteal artery, the saphenous artery and the muscular branch. The saphenous artery and vein pair runs obliquely toward the skin surface. In this experiment, temperatures are measured at three locations along the femoral artery and its subsequent branches. The first thermocouple, denoted as $A1$, is placed at the beginning of the femoral artery. The second thermocouple ($A2$) is placed at the beginning of the saphenous artery where the femoral artery takes a deeper course to the popliteal space approximately 12 mm from location $A1$. The third probe ($A3$) is attached to the saphenous artery approximately 15 mm downstream from $A2$, as shown in Fig. 1. Another three thermocouples are attached to the countercurrent vein at the same axial locations to measure the thermal equilibration in the vein.

The average blood perfusion rate ω [ml/(min·100g)] is estimated using the equation,

$$\omega = Q/(100 \cdot m) \tag{1}$$

where Q is the blood flow rate (ml/min) in the femoral artery and m is the weight (g) of the rat hind leg. The flow rates in the femoral artery for the cooling, vaso-constrictive, normal, and vaso-dilative conditions are 0.82 ± 0.07, 0.44 ± 0.05, 0.99 ± 0.18, and 1.73 ± 0.22 ml/min. This corresponded to volumetric perfusion rates of 2.6 ± 0.2, 1.3 ± 0.1, 3.1 ± 0.5, and 5.5 ± 0.7 ml/(min·100g). Figure 2 compares the measured blood perfusion rates under different physiological conditions. Compared to normal conditions, the decrease in the environmental temperature results in a 15% decrease in the blood perfusion rate. On the other hand, the constriction of the vascular bed in the hind leg induced by vasoactive agents results in a 56% decrease in the blood flow rate over the normal conditions, while vasodilation leads to a 75% increase. The sizes of the blood vessels at the measuring locations are estimated and are listed in Table 1. The mean diameter of the femoral artery under normal conditions is approximately 700 μm, and the femoral vein is more than twice that of the femoral artery. The artery tapers to 370 μm in diameter at $A3$. Under vasodilative conditions, the artery is dilated and a 24%–35% increase in its diameter is observed. On the contrary, during vasoconstriction the blood vessel size does not change significantly from that under normal conditions. The largest $A1$ arteries under normal and vasodilation conditions were 940 and 1120 μm and the smallest $A3$ arteries under normal and vasoconstriction conditions were 280

Table 1 Average Values of Vessel Diameters at Different Axial Locations and the Flow Rates

	conditions	*A*1	*V*1	*A*2	*V*2	*A*3	*V*3
	vasoconstriction (n=5)	686±120	1570±331	476±80	656±50	322±80	406±115
D (μm)	normal (n=12)	700±148	1620±283	450±90	580±183	370±70	450±117
	vasodilation (n=5)	950±145	1790±350	560±53	710±194	490±124	570±128

and 200 μm. The effective range of the arterial vessels in our experiments was thus from approximately 200 to 1120 μm.

Figure 3 illustrates the rectal temperature, the skin temperature and the temperatures at each axial vessel location. The femoral artery temperature is very close to the measured rectal temperature and the results show no significant difference between them. This result implies that the surface temperature of the vessel is a highly accurate approximation of the mean blood temperature in the vessel. Under the normal conditions the arterial temperature decays from 37.7°C ($A1$) to 35.9°C ($A2$), and 32.8°C ($A3$). A 4.9°C temperature difference between $A1$ and $A3$ is observed. The thermal equilibration in the arterial blood is only partially completed when the artery decreased to 370 μm in diameter since the temperature at $A3$ is still two degrees higher than the average skin temperature measured in the experiment. The drug-induced vessel dilation not only increases the blood flow rate in the vessel, but also results in a longer thermal equilibration length in the artery. Note that the increase in the blood flow rate significantly alters the skin temperature. Under vasodilative conditions, the arterial temperature decreases only 2.6°C as the vessel size changes from approximately 950 in $A1$ to 490 μm in diameter in $A3$ and the temperature at $A3$ is 3.3°C higher than the skin temperature. During cold environmental conditions, the skin temperature ($27.4\pm1.1°C$) is significantly lower than that in thermoneutral conditions ($29.9\pm1.9°C$).

Temperature variations along the femoral vein and its saphenous branches for different physiological conditions are shown in Fig. 4. One notes that the rewarming of the countercurrent vein is significant and obviously cannot be neglected. Under normal conditions, the arterial temperature decays 4.9°C to the location $A3$. Over the same axial distance the venous blood recaptures the heat released from the arterial blood leading to a 3.2°C increase in its temperature. The temperature difference between the countercurrent pair (Fig. 5) is as much as 2.1°C for the femoral vessels and it decreases to 0.4°C for vessels of 370 μm in diameter. Similar trends are observed during vasoconstriction and vasodilation.

The thermal equilibration in the countercurrent artery and vein is estimated by the ratio of the temperature decay over the distance between location $A1$ and $A3$ to the temperature difference between T_{core} and T_{skin}. Table 2 lists the thermal equilibration under the four physiological conditions. During vasodilatory conditions, the temperature decays only 44.4% and 36.1% for the artery and vein, respectively. The thermal equilibration lengths are shorter for the normal conditions where a 63.4% or 40.7% decay is observed for the artery or vein. Vasoconstriction of the vascular bed further shortens the thermal equilibration length. Since the vascular geometries are similar for these physiological conditions, the blood flow rate could be the main factor in determining the temperature decay in the countercurrent vessel pair. During the

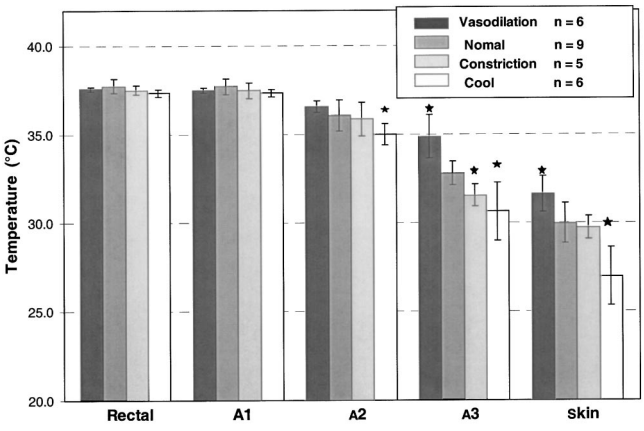

Fig. 3 Experimentally measured rectal temperature, skin temperature, and temperatures along the artery under different physiological conditions. *A*1, *A*2, and *A*3 represent different thermocouple locations along the arteries. *n* is the number of the measurements at each temperature sensor location. Vertical bars denote mean± *SD*. ⋆: temperature that is significantly different ($p<0.05$) from that under normal conditions at each measurement location.

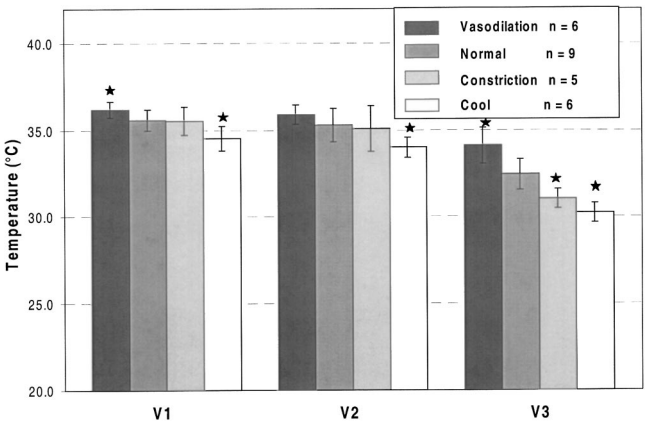

Fig. 4 Temperature variations along the femoral vein and its saphenous branches under different physiological conditions. *V*1, *V*2, and *V*3 represent different thermocouple locations along the veins. *n* is the number of measurements at each temperature sensor location. Vertical bars denote mean± *SD*. ⋆: temperature that is significantly different ($p<0.05$) from that under normal conditions at each measurement location.

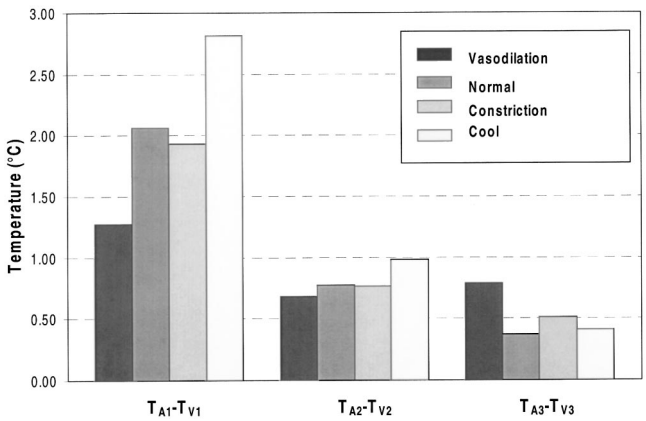

Fig. 5 Temperature differences between the countercurrent artery and vein along its axial direction under different physiological conditions.

Table 2 Temperature decay along the artery and the vein

	artery: $[\mathrm{Ta}(0)-\mathrm{Ta}(\mathrm{L})]/[T_a(0)-T_{skin}]$	vein: $[T_v(0)-T_v(L)]/[T_a(0)-T_{skin}]$
cooling vasoconstriction	6.73/10.39=64.8%	4.32/10.39=41.6%
normal vasodilation	5.94/7.81=76.1%	4.46/7.81=57.1%
	4.92/7.75=63.4%	3.16/7.75=40.7%
	2.6/5.85=44.4%	2.1/5.85=36.1%

hyperemic condition, the blood vessel is dilated and a higher blood flow is induced, which results in a longer thermal equilibration length. Whereas, the blood flow rates for the cooling and normal condition do not differ significantly from each other, and the temperature decays by a similar percentage for both conditions.

Discussion

In this study, the flow rate in the femoral supply vessels was manipulated to simulate different physiological conditions. The volumetric blood flow rate increased approximately four fold in proceeding from vasoconstriction to vasodilation. Previous studies have shown that the blood perfusion rate in skeletal muscle under normal conditions varies from 1 to 3 ml/(min·100g) [21]. Results from our study were slightly larger than the upper limit of the previous measurements. This may be due to the anesthesia-induced vasodilation of the skeletal muscle and surgical trauma. Our experiment showed that intramuscular injection of the sodium nitroprusside induced an almost twofold increase in the blood perfusion. Our results suggest that this blood flow rate increase should be at least partially achieved by a decrease in vascular resistance since vasodilation was observed in some vessel generations. The blood perfusion rate achieved by nitroprusside is still much smaller than the previously reported value of 25 ml/(min·100g) during hyperthermia treatment [22]. An isolated hind limb may provide a better model if one wishes to better control the local blood perfusion rate. The isolated limb will permit a wider range of flow.

The heat exchange between countercurrent microvascular artery-vein pairs has attracted widespread attention since the combined theoretical and experimental studies by the authors [8,10] first suggested that this might be the dominant heat transfer mechanism in local blood tissue transfer. In this study the role of the heat exchange between the countercurrent artery and vein was examined in vessels that are the same size as the SAV vessels using an *in vivo* experimental model based on the rat hind limb. Thermal equilibration between arteries and veins with arterial diameter ranging from 200 to 1000 μm diameter was estimated from the measured axial temperature variation along the blood vessels. Previous studies [2,7,10] have estimated that most blood tissue heat transfer occurs in blood vessels between 70 and 500 μm diameter. No significant difference was observed between the rectal temperature and the temperature at location $A1$ suggesting that there was no significant heat loss from vessels larger than 700 μm diameter. In contrast, the arterial temperature decayed 4.9°C under normal conditions as the vessel size decreased from 700 μm to 370 μm diameter in passing from location $A1$ to $A3$. The present model indicates that a more realistic upper bound for the onset of significant thermal equilibration is probably closer to 700 μm diameter under normal conditions.

In our theoretical study of the arterial temperature distribution in *SAV* vessels ranging from 1000 to 300 μm in diameter [15], the arterial temperature decay was predicted for varying blood flow rates for two blood vessel branching patterns. The validation of the theoretical analysis can be qualitatively examined by comparing the experimentally measured temperature decay with the theoretically predicted temperature variation along the mid-sized blood vessels in rat hind limb. The blood flow rate in the femoral

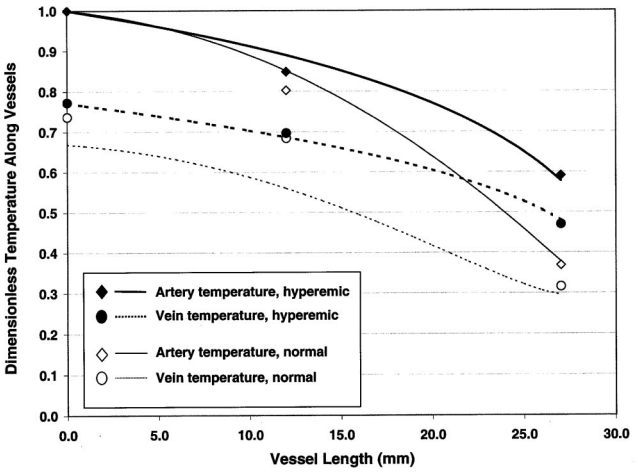

Fig. 6 Dimensionless temperatures along blood vessel surfaces in the rat hind limb under both normal and hyperemic conditions. Symbols represent experimentally measured dimensionless blood vessel surface temperature at different thermocouple locations. Lines denote the theoretically predicted blood vessel wall temperature in the axial direction.

artery and vein and measured blood vessel dimensions in Table 1 have been used as input parameters in the model in Zhu et al. [15]. Figure 6 compares the theoretically predicted dimensionless temperature profiles (lines) with experimentally measured dimensionless temperatures (symbols) at those three axial locations. Note that the dimensionless temperature profiles in Fig. 6 are based on theoretical predictions for the average blood vessel wall surface. The theoretical model assumes that the countercurrent *SAV* vessel pair is embedded in a tapered tissue cylinder and that the *SAV* vessels run along the central axis of the tissue cylinder. The theoretical predictions for the decrease in artery and vein surface temperature agree favorably with the experimental measurements for both normal and hyperemic conditions. Both experimental and theoretical results show an approximately 30% (hyperemic conditions) or 65% (normal conditions) scaled temperature decay along the arteries from location $A1$ to $A3$, and approximately 70% venous rewarming. Significant differences between the theoretical predictions and experiment can be found at locations $A2$ and $V2$, although there is reasonable agreement for the total temperature decay. Since flood flow measurements were not obtained at locations $A2$ and $V2$ it is not possible to establish the origin of the differences between theory and experiment. To obtain a point to point comparison between model predictions and experimental data, one requires detailed vascular geometric information and blood flow rates in each individual blood vessel as input in the simulation. In fact, some research groups, such as Raaymakers et al. [23], have attempted to determine the detailed vasculature down to blood vessels of 500 μm diameter and have applied numerical methods to model individual blood vessels in three-dimensional tissue preparations. Obviously, numerical methods to model blood vessels individually can be very useful to study the blood flow effect on tissue-vessel thermal interaction provided the detailed 3-D vascular geometry can be ascertained. The main objective of the current experimental approach was not to map the detailed vasculature in rat hind limb but to develop a new experimental approach for measuring axial temperature variation in vessels where such measurements had not been previously possible. It should be possible in the near future to do 3-D numerical simulations for vessels in rat hind limb using an approach that combines the techniques in [23] and the present study.

The experimentally measured temperature difference between the countercurrent artery and vein varies from approximately 2°C

for the large femoral vessels for normal conditions to 0.4°C where the vessels taper to 370 μm diameter. These results indicate an increasingly larger departure from perfect countercurrent heat exchange as blood vessel diameter increases. The thermal equilibration length measured along blood vessels between 200 and 1000 μm arterial diameter is found to be comparable to or longer than the vessel length. For vessels of this size the Weinbaum-Jiji equation is no longer a reasonable approximation for describing the effects of thermal equilibration since the criterion for its validity is exceeded. The original Pennes perfusion source term is not accurate either, since the venous rewarming still accounts for a significant fraction of the total heat exchange. The ratio of the temperature variation in the vein to the maximum temperature gradient in the rat hind leg changed from 57.1% to 36.1% for the lowest and the highest measured blood flow rates, respectively. If one combines the venous rewarming contributed by the *SAV* vessels and smaller vessels, one obtains an approximately 70% rewarming in the rat hind limb. This suggests that the correction coefficient used in the modified Pennes source term in Weinbaum et al. [9] should be approximately 30% for the vasculature in rat hind limb. Since the range of blood perfusion in the present experiment is relatively narrow (fourfold), the effect of local blood perfusion on venous rewarming can not be fully assessed. Isolated organs in which a wider blood perfusion range can be achieved should be helpful in more adequately evaluating the limits of venous rewarming.

Conclusion

In conclusion, rat hind limb provides a very useful experimental model for studying thermal equilibration along countercurrent blood vessels comparable in size to SAV artery-vein pairs in 3-D tissue preparations. Temperature decay along the countercurrent blood vessels and temperature difference between the artery and vein at different vessel generations in rat limb can be measured directly by temperature sensors. The validity of the previously developed theoretical model [15] has been semi-quantitatively examined using the current experimental data. The temperature variations for different physiological conditions will help evaluate the arterial supply temperature variation and the correction coefficient in the modified Pennes perfusion source term in [9]. Results from this study, when combined with previous analyses of vessel pairs less than 200 μm diameter, enable one to describe the entire thermal interaction between blood and tissue. Furthermore, the rat hind limb model should be useful in the future in studying the effect of blood perfusion on vessel temperature distribution during hyperthermia as a treatment modality for various diseases.

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References

[1] Bazett, H. C., and McGlone, B., 1927, ''Temperature Gradients in the Tissues in Man,'' Am. J. Physiol., **82**, pp. 415–451.
[2] Zhu, L., Lemons, D. E., and Weinbaum, S., 1995, ''A New Approach for Prediction the Enhancement in the Effective Conductivity of Perfused Muscle Tissue Due to Hyperthermia,'' Ann. Biomed. Eng., **23**, pp. 1–12.
[3] Zhu, L., Weinbaum, S., and Lemons, D. E., 1996, ''Microvascular Thermal Equilibration in Rat Cremaster Muscle,'' Ann. Biomed. Eng., **24**, pp. 109–123.
[4] Song, J., Xu, L. X., Weinbaum, S., and Lemons, D. E., 1997, ''Enhancement in the Effective Thermal Conductivity in Rat Spinotrapezius Due to Vasoregulation,'' ASME J. Biomech. Eng., **119**, pp. 461–468.
[5] Song, J., Xu, L. X., Weinbaum, S., and Lemons, D. E., 1999, ''Microvascular Thermal Equilibration in Rat Spinotrapezius Muscle,'' Ann. Biomed. Eng., **27**, pp. 56–66.
[6] Pennes, H. H., 1948, ''Analysis of Tissue and Arterial Blood Temperatures in the Resting Human Forearm,'' J. Appl. Physiol., **1**, pp. 93–122.
[7] Chen, M. M., and Holmes, K. K., 1980, ''Microvascular Contributions to Tissue Heat Transfer,'' Ann. N.Y. Acad. Sci., **335**, pp. 137–150.
[8] Weinbaum, S., and Jiji, L. M., 1985, ''A New Simplified Bioheat Equation for the Effect of Blood Flow on Local Average Tissue Temperature,'' ASME J. Biomech. Eng., **107**, pp. 131–139.
[9] Weinbaum, S., Xu, L. X., Zhu, L., and Ekpene, A., 1997, ''A New Fundamental Bioheat Equation for Muscle Tissue: Part I–Blood Perfusion Term,'' ASME J. Biomech. Eng., **119**, pp. 278–288.
[10] Weinbaum, S., Jiji, L. M., and Lemons, D. E., 1984, ''Theory and Experiment for the Effect of Vascular Microstructure on Surface Tissue Heat Transfer--Part I: Anatomical Foundation and Model Conceptualization,'' ASME J. Biomech. Eng., **106**, pp. 321–330.
[11] Charny, C. K., Weinbaum, S., and Levin, R. L., 1990, ''An Evaluation of the Weinbaum-jiji Bioheat Equation for Normal and Hyperthermic Conditions,'' ASME J. Biomech. Eng., **112**, pp. 80–87.
[12] Chato, J., 1980, ''Heat Transfer to Blood Vessels,'' ASME J. Biomech. Eng., **102**, pp. 110–118.
[13] Baish, J. W., 1984, ''Formulation of a Statistical Model of Heat Transfer in Perfused Tissue,'' ASME J. Biomech. Eng., **116**, pp. 521–527.
[14] Brinck, H., and Werner, J., 1994, ''Estimation of the Thermal Effect of Blood Flow in a Branching Countercurrent Network Using a Three-dimensional Vascular Model,'' ASME J. Biomech. Eng., **116**, pp. 324–330.
[15] Zhu, L., Xu, L. X., He, Q., and Weinbaum, S., 2002, ''A New Fundamental Bioheat Equation for Muscle Tissue: Part II–Temperature of SAV Vessels,'' ASME J. Biomech. Eng., **124**, pp. 121–132.
[16] Myrhage, R., and Eriksson, E., 1984, ''Arrangement of the vascular bed in different types of skeletal muscles,'' J. Photon Stud., **5**, 1-14.
[17] Lemons, D. E., Chien, S., Crawshaw, L. I., Weinbaum, S., and Jiji, L. M., 1987, ''The Significance of Vessel Size and Type in Vascular Heat Transfer,'' Am. J. Physiol., **253**, pp. R128–R135.
[18] Crezee, J., and Lagendijk, J. J. W., 1990, ''Experimental Verification of Bioheat Transfer Theories: Measurement of Temperature Profiles Around Large Artificial Vessels in Perfused Tissue,'' Phys. Med. Biol., **35**, pp. 905–923.
[19] Roemer, R. B., Moros, E. G., and Hynynen, K., 1989, ''A Comparison of Bioheat Transfer and Effective Conductivity Equation Predictions to Experimental Hyperthermia Data,'' Advances in Bioengineering, ASME Winter Annual Meeting, pp. 11–15.
[20] 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, **189**, pp. 15–22.
[21] Holmes, K. R., 1997, ''Biological Structures and Heat Transfer,'' in Report from the Allerton Workshop on The Future of Biothermal Engineering, pp. 14–45.
[22] Song, C. W., 1984, ''Effect of Local Hyperthermia on Blood Flow and Microenvironment: A Review,'' Cancer Res., **44**, pp. 4721s–4730s.
[23] Raaymakers, B. W., Creze, J., and Lagendijk, J. J. W., 2000, ''Modelling Individual Temperature Profiles from an Isolated Perfused Bovine Tongue,'' Phys. Med. Biol., **45**, pp. 765–780.