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Measurement of Blood Perfusion Using the Temperature Response to Constant Surface Flux Heating

H. J. Li,[1] X. X. Zhang,[1,2] and Y. F. Yi[1]

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A closed-form analytical solution of the Pennes bio-heat equation was developed for the temperature distribution in skin tissue subjected to a constant surface heat flux. Elevations in the surface temperature were revealed to be related to blood perfusion rates and heating fluxes based on which a new noninvasive approach has been developed to determine the blood perfusion rates. Sensitivities of the temperature elevation to blood perfusion and heating flux were investigated, as was the influence of thermal contact resistance on the perfusion estimate. It has been demonstrated that this influence is relatively small and can be effectively eliminated by application of highly conductive grease. An experimental system for this method was developed, and the blood perfusion rates in various human locations, including forearm, thigh, and calf, were measured using the system. The blood perfusion rate of skin tissue is in the range of 4 to 6 $kg \cdot s^{-1} \cdot m^{-3}$, which is in good agreement with those reported in the literature.

KEY WORDS: bio-heat; blood perfusion; constant surface flux heating; noninvasive estimation; thermal contact resistance.

1. INTRODUCTION

Microcirculation, blood flow in the capillary network and small arterioles and venules of less than 100 μm diameter, is usually referred to as perfusion, which is quantified as the blood flow rate per unit tissue volume. Perfusion plays a key role in the local transport of oxygen, nutrients, pharmaceuticals, and heat through the body. Measurements of tissue blood

[1] Department of Thermal Engineering, Tsinghua University, Beijing 100084, People's Republic of China.

[2] To whom correspondence should be addressed. E-mail: zhangxx@te.tsinghua.edu.cn

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flow are of great importance for the development of medical science, biomedical engineering and the technology for disease diagnostics, drug studies, and cancer treatment [1–3]. Despite its clinical significance, however, there is still no ideal way to measure perfusion.

Xu and Anderson [3] discussed various techniques [4–9] to estimate the perfusion rate, but their common shortcoming is that invasive probes are used to heat the tissue and measure the temperature. The probes inevitably lead to discomfort, especially for human beings. Therefore, noninvasive techniques for measuring blood perfusion have been under development for a long time and many interesting results have been reported [10–18]. Among them, Anderson et al. [10] applied sinusoidal heating to the biological tissue using ultrasound and then estimated the perfusion rate by applying numerical methods to solve the Pennes bio-heat transfer equation in the tissue. Another noninvasive approach based on the skin surface heat flux measurement [11–15] estimated the blood perfusion by comparing the heat flux predicted by the bio-heat equation to the measured value. Recently, Liu and Xu [1] proposed a noninvasive approach based on phase shifts between the skin surface temperature and the surface sinusoidal heating flux. However, accurate results are highly dependent on the accuracy of the phase shift estimate so the method is still in the process of development.

In this research, a closed-form analytical solution of the Pennes bioheat transfer equation was used for the temperature distribution in skin tissue subject to a constant surface heat flux. The elevation in the skin surface temperature is related to the blood perfusion rate, based on which a new noninvasive approach has been developed. The influence of the thermal contact resistance on the perfusion estimate was also investigated. The blood perfusion rate in various human locations, including the forearm, thigh, and calf, were measured experimentally. The accuracy of the results and the simple implementation of this method suggest that it can be successfully applied for medical applications.

2. THEORETICAL MODEL

Biological tissue can be analyzed as a semi-infinite medium with the well-known Pennes equation [19]

$$\rho C \frac{\partial T}{\partial t} = K \frac{\partial^2 T}{\partial x^2} + W_b C_b (T_a - T) + Q_m \tag{1}$$

where ρ, C, and K denote the density, specific heat, and thermal conductivity of the living tissue, respectively; C_b is the blood specific heat; W_b ($\mathrm{kg \cdot s^{-1} \cdot m^{-3}}$)

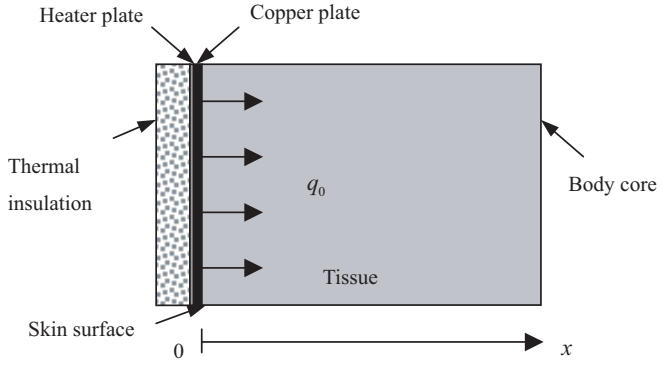

Fig. 1. Scheme for estimating blood perfusion rate using a constant surface heat flux.

is the blood perfusion rate; Q_m is the metabolic heat generation; T_a is the arterial blood supply temperature, and T is the tissue temperature. $x = 0$ is the skin surface (see Fig. 1).

In the present method, a two step process is used to impose a constant heat flux at the skin surface ($x = 0$). The first step is to insulate the skin surface ($q|_{x=0} = 0$). Once the temperature field reaches steady state ($T_0(x, 0)$) for $q|_{x=0} = 0$, a constant surface heat flux can be applied so that

$$-K\frac{\partial T(0, t)}{\partial x} = q_0, \qquad x = 0. \tag{2}$$

where q_0 is the surface heat flux.

Assuming that Q_m is constant and subtracting the initial steady-state temperature field ($T_0(x, 0)$), one has

$$\rho C\frac{\partial \theta}{\partial t} = K\frac{\partial^2 \theta}{\partial x^2} - W_b C_b \theta \tag{3}$$

where $\theta(x, t) = T(x, t) - T_0(x, 0)$ is the temperature elevation due to the external heating. The initial condition for Eq. (3) is

$$\theta(x, 0) = 0 \tag{4}$$

The core temperature deep in the tissue can be approximated as a constant

$$\theta(x, t) = 0, \qquad x = L \tag{5}$$

where $x = L$ is the distance between the skin surface and the tissue core.

Once the temperature field reaches steady state ($\frac{\partial\theta}{\partial t}=0$), the particular solution $\theta_s(x)$ is [1]

$$\theta_s(x)=\frac{-\frac{q_0}{K}\sqrt{\frac{K}{W_bC_b}}\sinh\left[\sqrt{\frac{W_bC_b}{K}}(x-L)\right]}{\cosh\left(\sqrt{\frac{W_bC_b}{K}}L\right)} \tag{6}$$

Substituting $x=0$ into Eq. (6) gives

$$\theta_s(0)=\frac{q_0}{\sqrt{KW_bC_b}}\tanh\left(\sqrt{\frac{W_bC_b}{K}}L\right) \tag{7}$$

where $\theta_s(0)$ denotes the temperature elevation of the skin surface when the temperature field reaches a new steady state for q_0. Therefore, if the heating flux is specified and the biological properties (K, C_b) are known, the blood perfusion rate can be estimated by simply measuring the surface temperature to obtain $\theta_s(0)$.

3. NUMERICAL COMPUTATION

Typical values of the human tissue properties are: $\rho=\rho_b=1000\,\mathrm{kg\cdot m^{-3}}$, $K=0.5\,\mathrm{W\cdot m^{-1}\cdot K^{-1}}$, and $C=C_b=4000\,\mathrm{J\cdot kg^{-1}\cdot K^{-1}}$ [20]. For $W_b=5\,\mathrm{kg\cdot s^{-1}\cdot m^{-3}}$ (an average blood perfusion rate for the human skin), the predicted temperature response ($\theta(0,t)$) to the applied heat flux (q_0) is shown in Fig. 2. The distance between the skin surface and body core was chosen as $L=0.04$ m. For $q_0=400\,\mathrm{W\cdot m^{-2}}$, the predicted temperature response ($\theta(0,t)$) for various blood perfusion rates (W_b) shown in Fig. 3 shows a clear variation of the skin surface temperature elevation for various heat fluxes and blood perfusion rates. This temperature elevation can be easily recorded by a surface temperature sensor and used to estimate the perfusion rates. From Eq. (7), only when W_b approaches infinity, which does not occur in reality, will the elevation approach zero. Therefore, a surface temperature elevation will always occur. The results in Fig. 3 show that for a constant surface heat flux, less blood perfusion, results in a higher skin surface temperature elevation and a longer time for the temperature to reach steady state. However, for a constant blood perfusion rate, the heating time will not change even for different surface heat fluxes.

Typical temperature elevations in tissue during heating are shown in Fig. 4. The amplitude of the steady-state temperature elevation decays with depth below the skin surface (Fig. 5) with the temperature elevation decaying to essentially zero within a short distance of $x=3$ cm.

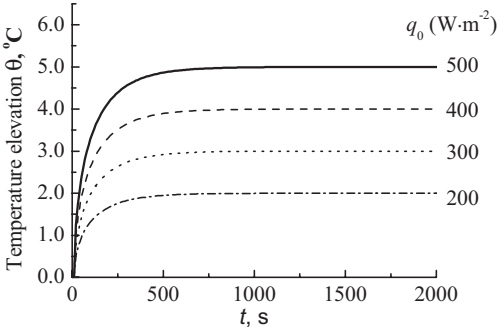

Fig. 2. Skin surface temperature elevation for different heat fluxes ($W_b = 5\ \mathrm{kg \cdot s^{-1} \cdot m^{-3}}$).

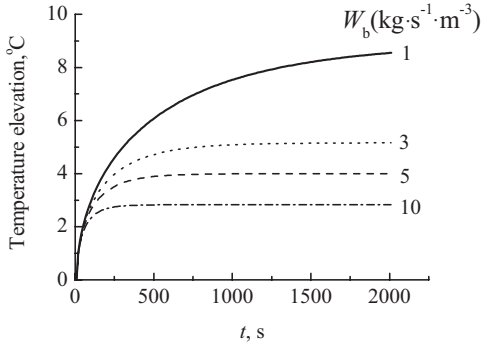

Fig. 3. Skin surface temperature elevation for different blood perfusion rates ($q_0 = 400\ \mathrm{W \cdot m^{-2}}$).

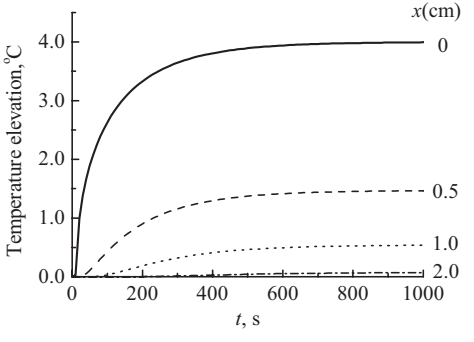

Fig. 4. Temperature elevations inside the tissue for constant surface flux heating ($q_0 = 400\ \mathrm{W \cdot m^{-2}}$, $W_b = 5\ \mathrm{kg \cdot s^{-1} \cdot m^{-3}}$).

3.1. Model Simplification

For $W_b = 1\ \mathrm{kg \cdot s^{-1} \cdot m^{-3}}$, $\tanh(\sqrt{\frac{W_b C_b}{K}}\, L) = 0.9984$ and continues to increase toward 1 as the blood perfusion increases. Experiment results show that the blood perfusion rate in human arms and legs is 2 to $6\ \mathrm{kg \cdot s^{-1} \cdot m^{-3}}$. Therefore, Eq. (7) can be simplified as

$$W_b = \frac{q_0^2}{K C_b \theta_s^2(0)} \tag{8}$$

This equation can be used to compute the blood perfusion rate in tissue by measuring the surface temperature elevation caused by a constant surface flux heating.

3.2. Sensitivity Analysis

For skeletal muscle tissues, the average blood perfusion rate can increase ten to twenty fold from the basal resting state to the exercise state [20, 21]. The calculated results shown in Fig. 2 indicate that higher heating fluxes cause larger skin surface temperature elevations. Therefore, high heating fluxes (i.e., $q_0 = 400\ \mathrm{W \cdot m^{-2}}$) are more preferable. The sensitivity of this technique to errors in the measured temperature elevation for a specified heating flux can be found from Eq. (8) as

$$\mathrm{d}W_b = -\frac{2q_0^2}{K C_b \theta_s^3(0)}\, \Delta\theta_s = -\frac{2W_b}{\theta_s(0)}\, \Delta\theta_s \tag{9}$$

This equation shows that the method becomes highly sensitive to measurement errors for low heating fluxes, again suggesting the importance of higher fluxes. However, living tissue should be protected by not using excessive heat fluxes.

3.3. Influence of Thermal Contact Resistance

The analysis has not included the effect of the thermal contact resistance between the temperature sensor and the skin surface, which is a major difficulty that has plagued noninvasive techniques using surface heating [11–15, 22, 23]. In an extreme situation when a uniform gap (δ) exists between the thermocouple and the skin, the contact resistance reaches a maximum value given by

$$R_t'' = \frac{\delta}{K_a} \tag{10}$$

where K_a is the thermal conductivity of air. At the skin surface,

$$q_0 = \frac{\theta_s^* - \theta_s}{R_t''} = K_a \frac{\theta_s^* - \theta_s}{\delta} \tag{11}$$

where θ_s^* is the temperature elevation measured by the thermocouple and θ_s is the actual skin surface temperature elevation obtained from Eq. (7).

Substituting Eq. (11) into Eq. (8) leads to

$$\theta_s^* = \frac{q_0 \delta}{K_a} + \frac{q_0}{\sqrt{K W_b C_b}} \tag{12}$$

Equation (12) gives a modified relation to estimate the blood perfusion rate considering the thermal contact resistance

$$W_b^* = \frac{1}{K C_b \left(\frac{\theta_s^*}{q_0} - \frac{\delta}{K_a} \right)^2} \tag{13}$$

The error introduced by the contact resistance is the difference between perfusion rates from Eq. (13) and that from Eq. (8)

$$W_b: \quad \text{err}\% = \left| \frac{W_b - W_b^*}{W_b^*} \right| = \left| 1 - \frac{\left(\frac{\theta_s^*}{q_0} - \frac{\delta}{K_a} \right)^2}{\left(\frac{\theta_s^*}{q_0} \right)^2} \right| \tag{14}$$

The errors for various gap sizes δ are shown in Fig. 6 for two perfusion rates $W_b = 10\ \text{kg} \cdot \text{s}^{-1} \cdot \text{m}^{-3}$ and $W_b = 1\ \text{kg} \cdot \text{s}^{-1} \cdot \text{m}^{-3}$ when the skin surface is subjected to a heat flux of $q_0 = 400\ \text{W} \cdot \text{m}^{-2}$. The thermal conductivity of air was $0.0263\ \text{W} \cdot \text{m}^{-1} \cdot \text{K}^{-1}$. The tissue properties were the same as used previously. Curve 1 in Fig. 6 shows that, at $W_b = 10\ \text{kg} \cdot \text{s}^{-1} \cdot \text{m}^{-3}$, the error in the perfusion estimate introduced by the thermal contact resistance is less than 12%. When the perfusion rate decreases to $W_b = 1\ \text{kg} \cdot \text{s}^{-1} \cdot \text{m}^{-3}$, the influence decreases to less than 4% over the range of $\delta = 0$–$10\ \mu\text{m}$ (curve 2 in Fig. 6). This leads to the conclusion that compared with previous techniques that required absolute temperature data for the perfusion estimation, the present technique is substantially less sensitive to the thermal contact resistance. Furthermore, if the conductivity of the intermediate gap medium is increased to be much

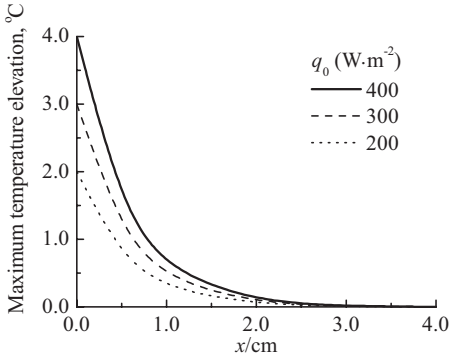

Fig. 5. Maximum temperature elevation in the tissue ($W_b = 5\ \mathrm{kg \cdot s^{-1} \cdot m^{-3}}$).

higher than that of the air, for example, $K_c = 1.0\ \mathrm{W \cdot m^{-1} \cdot K^{-1}}$ for a thermally conducting grease, the errors caused by the contact resistance can be dramatically reduced to less than 0.5% (curves 3 and 4 in Fig. 6).

4. EXPERIMENTAL

4.1. Experimental Setup

The general setup for estimating the perfusion rate using constant surface flux heating is shown in Fig. 7. The setup includes a dc electrical supply (0–5 V) to provide constant voltage to the heater, a digital multimeter (accuracy 0.1 mV) to detect the voltage, a data acquisition system (Keithley), and a computer with software for recording and processing the

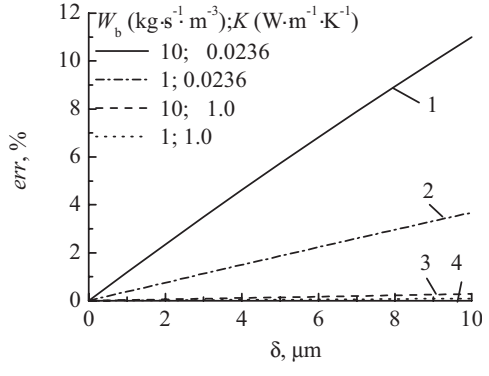

Fig. 6. Errors in perfusion rate estimates caused by the thermal contact resistance ($q_0 = 400\ \mathrm{W \cdot m^{-2}}$).

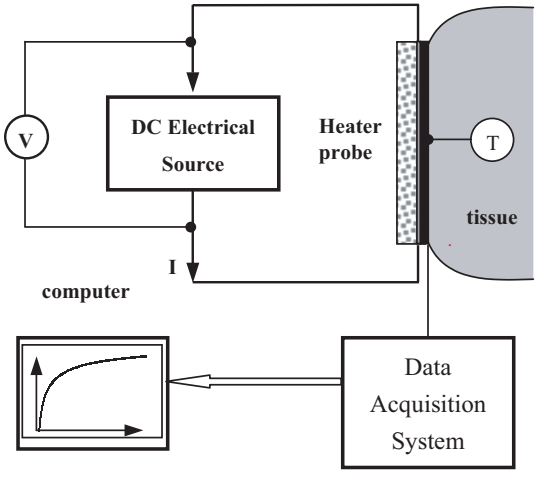

Fig. 7. Experimental setup for estimating blood perfusion rate using a constant surface heat flux.

signals. The heater, shown in Fig. 8, was 3.0 cm in diameter and had a resistance of 16.38 Ω. Previous heating probe designs, especially those incorporating simultaneous heating and temperature recording [7–14], provide very useful references for practical applications of the present method. The cylindrical heater had 5 layers: the thermal insulation on the outside (Φ 3.5 cm), an air layer, another thermal insulation layer (Φ 3 cm), the heater plate (Φ 3 cm), and a copper plate (Φ 3 cm) which provided a uniform heat flux at the applicator surface. A thermocouple (type-T) was attached to the center of the applicator surface.

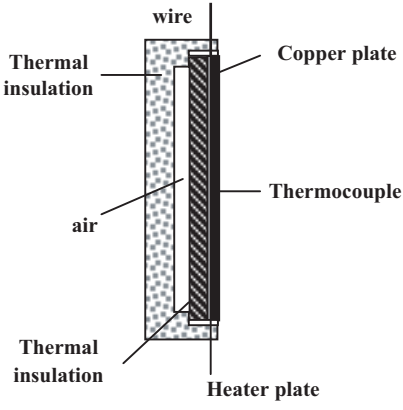

Fig. 8. Heater design.

The size of the probe certainly induces two-dimensional effects over the test times. Temperature elevation of the skin surface is less than what is predicted by the one-dimensional assumption. Consequently, the perfusion estimate is somewhat higher than the real value. Numerical calculations show that the error in the perfusion estimate introduced by the probe size is less than 12% when the diameter of the probe is 3.0 cm and 6.5% when the diameter is 4.0 cm.

4.2. Method

The experimental procedure also used two steps to impose a constant heat flux at the skin surface. The first step was to use the heater assembly with the power off to the skin surface until the temperature reached steady state. Then, the electricity was turned on to provide the heat flux until a new steady-state temperature was reached. Considering the well-insulated design, the heat flux can be estimated as

$$q_0 = \frac{U^2}{RA} = \frac{4U^2}{R\pi d^2} \tag{15}$$

where U is the voltage, R is the heater resistance, and d is the heater diameter. A highly conductive grease was applied to the contact area between the heater and the skin to eliminate the influence of thermal contact resistance on the blood perfusion rate estimate.

5. RESULTS

The blood perfusion rate at various locations in humans was measured repeatedly for different conditions using the experimental system. A typical measured temperature variation during the heating is shown in Fig. 9. Temperature elevations of the forearm skin surface (measured by the thermocouple attached to the center of the applicator surface) are shown in Fig. 10 for different heating fluxes. The blood perfusion rates can be estimated from these temperature elevations. The different perfusion rates for various locations are given in Table I and Fig. 11. The results in Fig. 11 show that the perfusion rate in the forearm is larger than in the other two locations. Furthermore, as expected, larger heating fluxes cause larger perfusions rates as the human body tries to reduce the tissue temperature by increasing the blood flow.

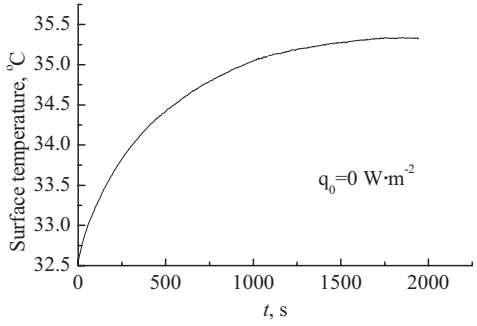

Fig. 9. Skin surface temperature variation after covering with unheated heater.

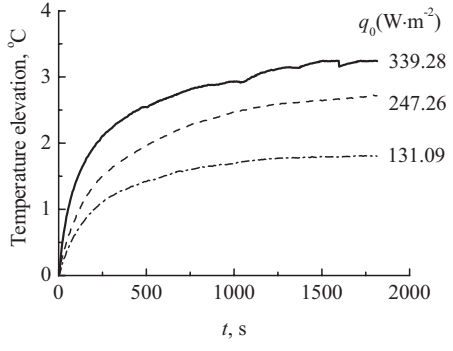

Fig. 10. Forearm skin surface temperature elevation for different heat fluxes.

Table I. Perfusion Rates W_b ($kg \cdot s^{-1} \cdot m^{-3}$) in Human Forearm, Calf, and Thigh at Rest for Different Heating Fluxes

q_0 ($W \cdot m^{-2}$)	Forearm $n = 5$	Calf $n = 5$	Thigh $n = 5$
131.09	4.83±0.67	4.75±0.26	4.65±0.14
189.95	5.46±0.81	5.07±0.12	4.88±0.28
247.26	5.79±0.61	5.44±0.45	5.14±0.17
339.28	6.13±0.44	5.45±0.64	5.21±0.28

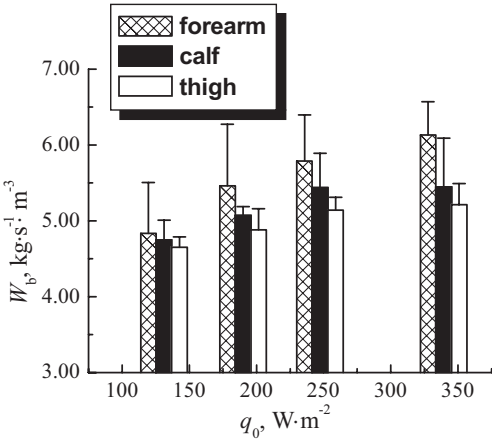

Fig. 11. Blood perfusion rates in human forearm, calf, and thigh at rest when subjected to different heating fluxes.

6. CONCLUSION AND DISCUSSION

The present paper uses the analytical solution of the Pennes equation for the constant heat flux boundary condition [1]. The solution is used for a new noninvasive method to estimate the blood perfusion rate by monitoring the temperature elevation between two steady states. A modulated heat flux ($q_0 = 300$ to $400\ \mathrm{W \cdot m^{-2}}$) is preferable to balance the danger of thermal damage from high heat fluxes with the need for a high heat flux to reduce errors in the measured temperature elevation. Numerical computations show that applying highly conductive grease to the interface between the heater temperature sensor and the skin can effectively eliminate errors caused by the thermal contact resistance.

The present perfusion estimation method has two steps. The first step is to insulate the skin surface until the tissue temperature reaches steady state. Constant surface heating is then initiated. The steady-state surface temperatures are recorded for each step. Higher blood perfusion rates will result in shorter times to reach steady state. Therefore, the present method appears to be more suitable for perfusion measurements in highly perfused tissues.

Perfusion rates in the human forearm were measured for different conditions, from the basal resting state to exercising state. The perfusion rate while exercising was 1.5 to 2 times that of the resting rate. Substituting

Eq. (15) into Eq. (8), the sensitivity of this technique to errors in the measured voltage and temperature elevation can be obtained as

$$d\omega_b = \frac{16}{(R\pi d^2)^2 K\rho_b C_b} \sqrt{\left(\frac{4U^3}{\theta^2} dU\right)^2 + \left(\frac{2U^4}{\theta^3} d\theta\right)^2} \tag{16}$$

From this equation, the measurement error can be estimated as about 2%. Considering the measurement error and two-dimensional effects of the probe, the total error of this technique was about 13%. Therefore, this method can be successfully applied to medical inspection applications.

Since the measurement of blood perfusion depends on the thermal properties (K, ρ_b, C_b) of specific tissue in this method, practical applications should acquire these values to properly estimate the blood perfusion rates.

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