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EFFECTS OF TISSUE OUTSIDE OF ARTERIAL BLOOD VESSELS IN PULSE OXIMETRY: A MODEL OF TWO-DIMENSIONAL PULSATION

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ABSTRACT. We describe a new model of pulse oximetry that addresses the disagreement between theoretical calibration curves based on Beer–Lambert's Law and test results based on human test subjects. Sources of this discrepancy include variability among human subjects, experimental conditions and the effect of optical radiation propagating in tissue surrounding arteries. Unlike the conventional model, our model considers the change in the relative proportion of light that does or does not pass through blood in pulsating vessels in addition to the change in the path length of optical radiation through the blood. Theoretical calibration curves based on this model agree with human test results and help to explain the variability between in vitro and in vivo test conditions.

KEY WORDS. pulse oximetry, pulse oximeters, blood oxygen, total hemoglobin.

INTRODUCTION

Pulse oximeters provide a noninvasive measurement of the concentration of hemoglobin with bonded oxygen in the arterial blood. They are now an indispensable measurement tool for patient monitoring, especially in operating rooms, emergency rooms, and intensive care units.

A pulse oximeter consists of two optical sources, operating at wavelengths λ_1 and λ_2, and an optical detector. The pulse oximeter response function is derived from Beer–Lambert's Law,

$$I = I_0 \exp(-\varepsilon_{h\lambda} c_h L), \tag{1}$$

where I is the probing light intensity received by the detector, I_0 the light intensity impinging on the artery, $\varepsilon_{h\lambda}$ the wavelength-dependent absorption coefficient, c_h the concentration (number of molecules or mol per unit volume) of the hemoglobin, and L the optical path length. The variation in transmitted optical radiation intensity I is a function of the path length change $\mathrm{d}L$ due to the pulsation of arterial thickness caused by the heartbeat,

$$\mathrm{d}I = I(-\varepsilon_{h\lambda} c_h \mathrm{d}L). \tag{2}$$

The hemoglobin of a normal patient is composed of hemoglobin with and without bonded oxygen, called oxyhemoglobin (O_2Hb), and nonbonded or reduced hemoglobin (RHb). The purpose of pulse oximetry is to measure the percentage content, s, of the O_2Hb in the arterial blood. The concentration of O_2Hb is then sc_h and

that of the RHb $(1-s)c_h$. O_2Hb and RHb each have absorption coefficients that vary with optical wavelength, $\varepsilon_{o\lambda}$ and $\varepsilon_{r\lambda}$, respectively. The combined absorption coefficient of the arterial blood can be expressed as

$$\varepsilon_{h\lambda} = [\varepsilon_{o\lambda}s + \varepsilon_{r\lambda}(1-s)]. \tag{3}$$

Because of the complex structure of human tissue at the probe site, it is impossible to know the input optical intensity I_0. However, the *relative* transmitted intensity change is expressed as

$$\mathrm{d}A_\lambda = \frac{\mathrm{d}I}{I} = -[\varepsilon_{o\lambda}s + \varepsilon_{r\lambda}(1-s)]c_h\mathrm{d}L. \tag{4}$$

The relative transmitted intensity change is directly proportional to the ratio of the AC and DC signals measured by the detector of the pulse oximeter. There are two unknowns in Equation (4), s and $\mathrm{d}L$, of which s is the quantity we want to know and $\mathrm{d}L$ varies continuously. Two separate measurements at probe wavelengths, λ_1 and λ_2 are required to solve for the two unknowns with the assumption that each wavelength undergoes the same pathlength change $\mathrm{d}L$ in passing through the blood. By calculating the ratio of $\mathrm{d}A_{\lambda_1}/\mathrm{d}A_{\lambda_2}$, the product $c_h\mathrm{d}L$ is cancelled yielding an expression relating s to R, the so-called *ratio of ratios*,

$$R = \frac{\mathrm{d}A_{\lambda_1}}{\mathrm{d}A_{\lambda_2}} = \frac{(\mathrm{AC}/\mathrm{DC})_{\lambda_1}}{(\mathrm{AC}/\mathrm{DC})_{\lambda_2}} = \frac{\varepsilon_{o\lambda_1}s + \varepsilon_{r\lambda_1}(1-s)}{\varepsilon_{o\lambda_2}s + \varepsilon_{r\lambda_2}(1-s)}, \tag{5}$$

where in practice, $(\mathrm{AC}/\mathrm{DC})_\lambda$ is determined from the measured AC and DC signals at each wavelength. This equation represents the fundamental working function of the conventional theory of pulse oximetry [1, 2]. Since the absorption coefficients $\varepsilon_{o\lambda}$ and $\varepsilon_{r\lambda}$ have been measured with sufficient precision from visible to near infrared wavelengths, a theoretical calibration curve of the relation between R and s can be generated according to Equation (5). Unfortunately, due to the complex structure of human tissue at the probe site, such as the fingertip or earlobe, this theoretical calibration curve disagrees with experimental results from human subjects. As a result, empirical calibration curves [3] are used to generate look up tables of *R(s)* to determine s from clinical pulse oximetry measurements. A large number of human subjects are tested to determine the empirical calibration curves. These tests are time consuming and costly, and more importantly, somewhat dangerous, as the subjects have to be de-saturated, that is, their oxyhemoglobin levels are reduced, to obtain data spanning a wide range of s. For the same reason, the empirical calibration curves are limited, with the lowest value for s being around 60%.

Results of pulse oximetry measurements are also affected by human variability [4]. Groups with varying demographic characteristics (for example, gender, age, weight, skin pigmentation) have yielded biases in the measurement results. This is believed to be at least partially due to the effect of other tissues outside the blood vessels. Studies have also revealed measurement biases at different laboratories [5], perhaps caused by different measurement conditions such as subject treatment, temperature, hematocrit, or factors associated with general physical fitness. However, very little is known about the real effect of other tissues that may impact the performance of pulse oximeters.

We have developed a new model of pulse oximetry that reveals specifically how other tissues outside the blood vessels impact pulse oximetry measurements. The key assumption of this model is a two-dimensional mode for blood vessel pulsation that considers that not all of the probing optical radiation passes through arterial blood. This is in contrast to the conventional pulse oximetry theory, which considers only one-dimensional pulsation (parallel to the light path) and assumes that all probe light passes through the arterial blood. We have created a theoretical calibration curve based on this model that agrees very well with the empirical calibration curve, which in turn helps to establish the validity of the model. Using this model, we may also be able to explain the variability of pulse oximetry measurements. This model has the potential to improve the process of the calibration of pulse oximeters and to reduce the uncertainty of pulse oximetry measurement.

NEW MODEL OF TWO-DIMENSIONAL PULSATION

Although Beer–Lambert's Law is the theoretical basis of pulse oximetry, relying exclusively on this model restricts the ability to explain the effects of other tissues. In this model, it is implicitly assumed that the tissue is uniform. However, the detector in a pulse oximeter, as any optical detector, receives and responds to the optical power P (units of W) instead of intensity I (units of $\mathrm{W/m^2}$). Optical radiation power P is the spatial integration of intensity I:

$$P = \int I\mathrm{d}a, \tag{6}$$

where a is the illuminated area. Transmitted intensity I is in general not uniform due to the complex structure of human tissue. Static effects of tissues outside of blood vessels, such as the absorption by the bones, have no effect on the pulse oximeter measurement. Only those effects that vary due to, and at the same rate as, blood vessel pulsation may impact the pulse oximeter measurement.

There might be numerous such effects, but many of them are trivial and may be ignored.

One factor that may significantly affect the distribution of transmitted light is that a portion of transmitted light does not pass through blood vessels at all and the amount of this portion varies with the pulsation of blood vessels. This effect was seen in a previous, unrelated study unpublished and carried out by one of the authors. In an in vivo experiment where a high level of methemoglobin, which has a very high absorption coefficient at the probing wavelength, was present in the arterial blood, the transmitted light received by the detector was far more than expected if one assumed that all light traveled through the blood. However, in the corresponding in vitro experiment where the blood contained the same amount of methemoglobin, the transmitted light was very close to the expected level. This discrepancy could be attributed only to that part of the transmitted light in the in vivo measurement that did not pass through blood and, as a result, was not attenuated as much. Figure 1 illustrates this effect. Because blood vessels are long tubes passing through the probing light beam, they have boundaries in only two dimensions for the beam, width and thickness. When the diameter of blood vessels change from diastole to systole, both the length and width of blood through which light must travel varies. In other words, the light path through the blood affected by pulsed blood varies along the axis from emitter to detector (parallel to the light path) as well as along the width of the light path (perpendicular to the light path). When the arterial blood vessels pulsate, the proportion of light that does and does not pass through arterial blood changes in addition to the pathlength change parallel to the light path. While the effect of the thickness of arteries is represented with the Beer–Lambert's Law, the effect of the varying width changes the proportion of light that does and does not pass through the arteries. Although the tissue structure at the probe site is a complex, inhomogeneous composition of blood vessels and other tissues, in order to simulate their net effects on pulse oximetry measurements, we may group together these two kinds of tissues into two parts, blood and soft tissue (hard tissue is excluded, as explained earlier). To further simplify the mathematics, we use a model of first order approximation as illustrated in Figure 2.

Assuming uniform light intensity from the source, the input optical power, P_0, may be expressed as

$$P_0 = \rho_0(W_a + W_T), \tag{7}$$

where W_a is the width of arterial blood and W_T is the width of other tissue. Because the third dimension along the tube of the arterial blood vessel undergoes no change during blood pulsation, its length is omitted and therefore linear density ρ_0 (W/m) instead of area density I (W/m^2) is used in Equation (7) and the following equations. The transmitted power, P, received by the detector is then composed of two parts, the first part, P_1, being light that

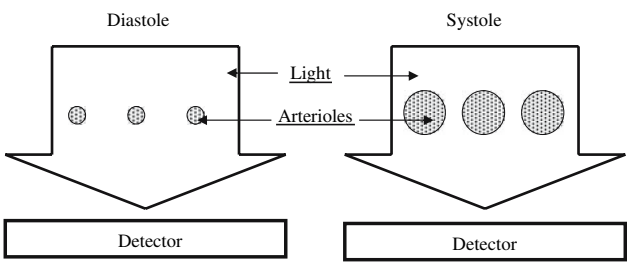

Fig. 1. An illustration of the concept of two-dimensional pulsation. At diastole, arterioles occupy less space, thus less light passes through arterial blood vessels but more light passes through other tissues. At systole, arterioles occupy more space (vertically and horizontally), thus more light passes through arterial blood vessels and less light passes through other tissues.

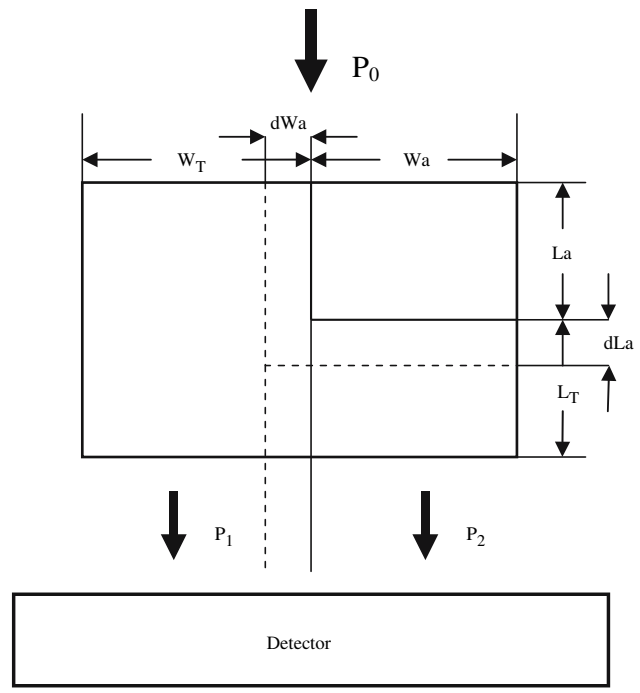

Fig. 2. An illustration of the two-dimensional pulsation model. All the arterial blood vessels are defined to be packed within one area with width W_a and depth L_a. Areas next to and beneath the arterial area are tissues outside the arteries illuminated by the probe light. The transmitted light received by the detector has two parts; one that passes through the arterial blood (P_2) and one that does not (P_1). When the blood vessels pulsate, the ratio of the two parts of light changes and influences the measurement results of pulse oximetry.

does not pass through blood vessels and the second, P_2, that does:

$$P = P_1 + P_2 = \rho_0 W_T \exp[-g_T(L_a + L_T)] + \rho_0 W_a \exp[-(g_a L_a + g_T L_T)], \quad (8)$$

where g_a is the extinction of arterial blood and g_T the extinction of other tissues. We now use g instead of the multiplication product of absorption coefficient ε and concentration c because we will consider effects other than absorption in the blood and the concentration and absorption of other tissues are too complex to be modeled separately. The pulsation of arteries changes the relative proportion of these two optical power components as well as the path length of the blood vessels. We need to further discuss the portion of tissue in Figure 2 that lies beneath the blood portion with thickness of L_T. This portion of tissue is either pushed to move without changing its thickness and/or compressed with a change of the thickness due to the blood vessel pulsation. In the former case, the attenuation of optical power in this layer does not change because the pathlength in this area does not change. In the latter case, the density of the tissue, c_T, changes inversely proportionally to the change of path length L_T. As a result, the multiplication product of $c_T L_T$ is constant and does not change the transmitted power. We further assume that the relative width change is the same as the relative path length change of the blood vessel, that is,

$$\mathrm{d}L_a/L_a = \mathrm{d}W_a/W_a \quad (9)$$

(this assumption is reasonable if we consider that the area of blood is composed of numerous blood vessels that are circular and pulsate homogeneously in all directions). With these assumptions, we obtain

$$\mathrm{d}P = -\rho_0 W_a \exp(-g_T L_T)[\exp(-g_T L_a) - \exp(-g_a L_a) + \exp(-g_a L_a) g_a L_a] \frac{\mathrm{d}L_a}{L_a}. \quad (10)$$

As in Equation (4), we use $\mathrm{d}A$ to express the relative change of the transmitted optical power:

$$\mathrm{d}A = \frac{\mathrm{d}P}{P} = -\frac{\exp(-g_T L_a) - \exp(-g_a L_a)(1 - g_a L_a)}{W_r \exp(-g_T L_a) + \exp(-g_a L_a)} \frac{\mathrm{d}L_a}{L_a}, \quad (11)$$

where

$$W_r = W_T/W_a \quad (12)$$

is the ratio of the widths; however, it is also the ratio of input light that does not and does pass through the arterial blood. Similar to the conventional theory, we have the ratio of $\mathrm{d}A$ of the two wavelengths,

$$R = \frac{\mathrm{d}A_{\lambda 1}}{\mathrm{d}A_{\lambda 2}} = \frac{\exp(-g_{T\lambda 1} L_a) - \exp(-g_{a\lambda 1} L_a)(1 - g_{a\lambda 1} L_a)}{W_r \exp(-g_{T\lambda 1} L_a) + \exp(-g_{a\lambda 1} L_a)} \Bigg/ \frac{\exp(-g_{T\lambda 2} L_a) - \exp(-g_{a\lambda 2} L_a)(1 - g_{a\lambda 2} L_a)}{W_r \exp(-g_{T\lambda 2} L_a) + \exp(-g_{a\lambda 2} L_a)}, \quad (13)$$

where the relative path length change is cancelled. This equation represents our new calibration curve of the two-dimensional pulsation model. Compared to Equation (5) of the calibration curve of the conventional theory, the new equation contains three more parameters: L_a, W_r, and g_T. Two of these parameters, the path length L_a and the width ratio W_r, are variables of demographic characteristics and measurement conditions such as temperature, but are wavelength independent. The third parameter, the extinction of other tissue, g_T, is a complex contribution of other tissues and may be dependent on some of the demographic characteristics such as skin pigmentation. It is also wavelength-dependent. These parameters are dependent on properties of tissue of human subjects. Because of the existence of these three parameters, the new model makes it possible to explain the effects of other tissue in pulse oximetry, human variability, and effects of measurement conditions.

DETAILS OF THE PARAMETERS AND OTHER CONSIDERATIONS

Water content

Other effects that may significantly affect pulse oximetry measurements may have been neglected in the conventional theory. Let us first consider the water content in the blood. Whole blood is composed mainly of red blood cells (RBC) and water. The percentage volume concentration of RBC in the blood is called hematocrit, H, which is normally about 37–43% for females and 43–49% for males. Inside the RBC there are hemoglobin and more water. One RBC contains about 280 million hemoglobin molecules, which constitute about one third of the weight of a RBC. The remaining two thirds is water. With these facts, we derived (see Appendix) the concentrations of hemoglobin and water in whole blood with hematocrit H as $c_h H$ and $c_w(1-0.304H)$ mol/l, where c_h is the concentration of hemoglobin (number of molecules or mol per unit volume). The value of c_h is 5.2 mmol/l when $H = 100\%$ and c_w, the concentration of pure water, is 55.6 mol/l. The concentration of water in whole blood is about four orders of magnitude higher than that of

hemoglobin. Although the absorption coefficient of water is more than five orders of magnitude less than that of the hemoglobin at 900 nm, the effect of water on absorption is about 6% of that of hemoglobin (at 940 nm, this number is about 16%) and is by no means negligible.

Blood cell scattering

The volume of a RBC is about 90 μm^3, so its linear dimensions are on the scale of only a few micrometers. This dimension is larger than the wavelengths (0.6–1 μm) used in pulse oximetry. Thus when light is incident on the RBC, Mie scattering will occur. This scattering will be proportional to the concentration, H, of RBC. However, when H is 100%, the medium is uniform and there is no Mie scattering. The Mie scattering should be proportional to $g_{Ms}H(1-H)$,[1] where g_{Ms} is the Mie scattering coefficient determined empirically and almost independent of wavelength [6, 7]. Light that enters a RBC will have a chance to scatter again when it hits the hemoglobin molecules. Because the size of a hemoglobin molecule is much smaller than the working wavelengths, this scattering is Rayleigh scattering, which is proportional to the reciprocal of the fourth order of wavelength. The Rayleigh scattering should be proportional to the total amount of hemoglobin present in the blood, which is in turn proportional to H because the amount of hemoglobin inside RBC is more or less constant. Rayleigh scattering by hemoglobin can be expressed as $g_{Rs}H(\lambda_0/\lambda)^4$, where g_{Rs} is the scattering coefficient at λ_0 and determined empirically.

Combining the two effects of water content and blood scattering, the extinction of the light passing through arterial blood is

$$g_a = [\varepsilon_o s + \varepsilon_r(1-s)]c_h H + \varepsilon_w c_w(1 - 0.304H) + g_{Ms}H(1-H) + g_{Rs}H(\lambda_0/\lambda)^4. \quad (14)$$

The values of g_{Ms} and g_{Rs} can be determined empirically by best fitting data of in vitro experiments with blood in a pulsating cuvette. The blood in the cuvette is a one-dimensional sample that obeys Beer–Lambert's Law with g_a in the form of Equation (14).

Values of blood path length L_a, ratio W_r, and extinction of other tissue g_T

Values of blood path length L_a, ratio W_r, and extinction g_T due to other tissue vary in human subjects. Because of the complex nature of tissue composition at the probe site, it is difficult to assign an exact value to each of these parameters. Because of the complex optical-tissue effect, these values are not the direct physical measures, but rather apparent values. They should be considered as effective path length, effective width ratio, and effective tissue extinction. Further, because of human variability, the values used in computer simulation should be the average or median of all possible human subjects. Because the physical thickness of a human finger is about 15 mm, we may assume that L_a is in the range of millimeters. The estimate of width ratio W_r is less obvious. With the assumption that the percentage of blood in tissue is 5% [8] and considering the two-dimensional cross section of the blood vessels, W_r is about 4.5. Taking into account that blood vessels are mainly located in horizontal layers, this ratio may be lower. Considering also human and probe site variability, W_r is likely between 1 and 5. The major contribution for g_T is probably from muscle (soft tissue). It comprises two functions: absorption and scattering. There have been many studies [9] on the optical properties of human tissues. Since the effect of the tissue is so complex, it is difficult to derive exact values of g_T at the wavelengths of interest. We may only estimate the range the values may fall in. Based on the data in the literature, in the computer generation of the calibration curve, we adjusted the value of g_T to best fit the experimental data.

APPLICATIONS

We generated a theoretical calibration curve based on the new model that agrees very well with experimental data (Figure 3). The experimental data were collected on thirteen male and female adult subjects. The wavelengths of the pulse oximeter used in the experiment were 638 and 939 nm. The absorption coefficients of O_2Hb and RHb at these wavelengths were obtained from standard spectrum absorption curves of hemoglobin. The total hemoglobin tHb is 15 g/ml, which corresponds to hematocrit, H, of about 43%, roughly the average of the general population. The scattering coefficients of blood g_{Ms} and g_{Rs} were determined from a previous in vitro experiment as 0.6 and 0.3. Path length L_a is 5 mm, and W_r is 4.0. For the best fit, the extinction of other tissue g_T at 638 and 939 nm are 0.5 and 0.9 cm^{-1}, respectively. In Figure 3, we also plotted the conventional theoretical calibration curve based purely on Beer–Lambert's Law (Equation 1) and the curve of the one-dimensional model but with g_a including the effect of scattering and taking the form of Equation (14).

Figure 4 shows calibration curves for different total hemoglobin, illustrating how the amount of hemoglobin

[1] A scale factor of $H(1-H)(1.4-H)$ was derived in Ref. [6]. Since H in humans is around 0.4, the factor of $(1.4-H)$ is roughly 1. Therefore we adopted the simple form without the factor of $(1.4-H)$.

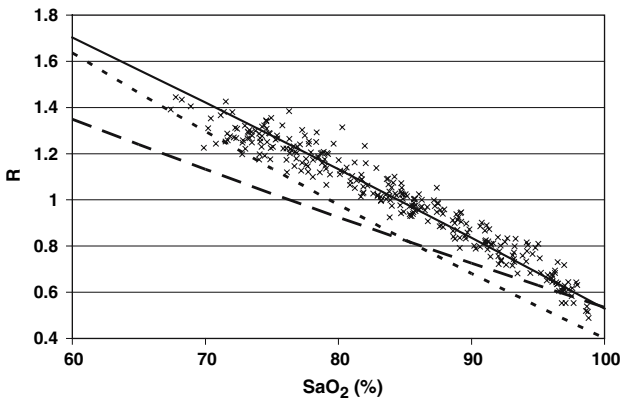

Fig. 3. Simulation results based on the two-dimensional pulsation model. Data points (×) are human test results. The wavelengths of the pulse oximeter are 658 and 939 nm. The solid curve is computer generated with the same wavelengths, and tHb = 15 g/dl, blood path length L_a = 0.5 cm, width ratio W_r = 4.0. The dotted curve (- - -) is the conventional theoretical calibration curve based on Beer–Lambert's Law. The dashed curve (— — —) is one-dimensional pulsation but with g_a including the effect of scattering and water absorption. SaO2 is the true arterial oxygen saturation measured by CO-Oximetry (IL-682).

will affect the measurement results. Figure 5 shows the effect of the parameter W_r, the ratio of portions of blood that do not and do pass through the blood. Empirical calibration curves of pulse oximeters were generated assuming implicitly the average values of the general population of parameters that may influence the measurement results. When individual subjects with parameter values different from the average are tested, errors will occur. However, with the new theory, if some of the parameter values of the test subject are known, it is possible to make corrections accordingly and thus reduce the measurement error. Further studies are needed to link

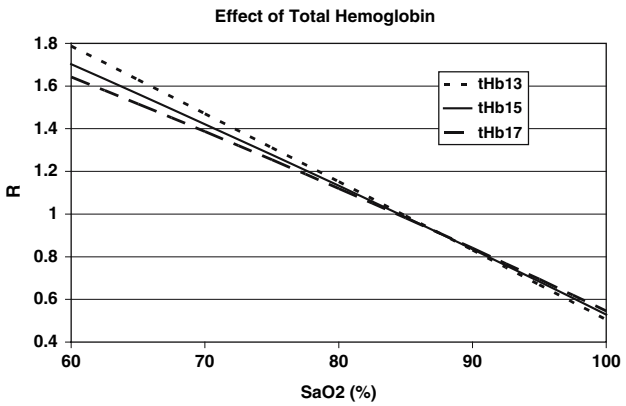

Fig. 4. Calibration curves with tHb = 13, 15, and 17 g/dl. Other parameters are the same as in Figure 3.

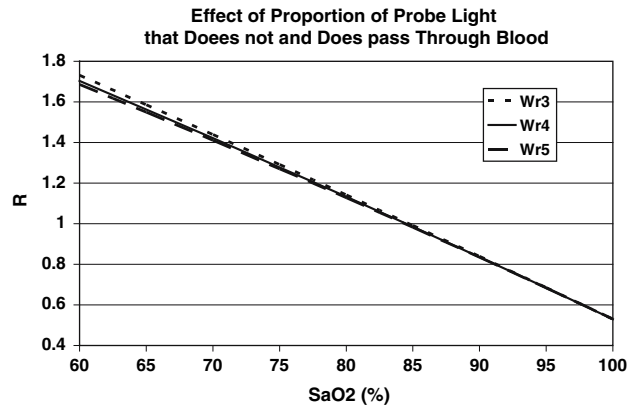

Fig. 5. Calibration curves with different other tissue to blood ratios, W_r = 3, 4, and 5.

demographic characteristics and measurement conditions with the parameters in the new model.

CONCLUSIONS

The transmitted light in its path from the light source to the detector of a pulse oximeter undergoes absorption and scattering on tissue outside the arterial blood vessels as well as attenuation from the arterial blood. When the blood vessels pulsate during the measurement, the relative portions of light that do and do not pass through the arterial blood change. As a result, the impact of tissues outside the blood vessels varies at the same rate as the blood vessel pulsation. This is the basic assumption of our two-dimensional model of pulse oximetry. Based on this model, we developed a new expression of the R–SaO_2, from which we generated a calibration curve with reasonable values of model parameters that agrees with human test data. We generated curves that showed the impact of the amount of hemoglobin and the ratio of blood and other tissue the probe light encounters.

With further study, this new model of pulse oximetry has the potential of improving the process and reducing the uncertainty of the calibration of pulse oximeters. We expect that the model will reduce measurement bias and error by taking into account environmental conditions and the demographic characteristics of the test subjects.

APPENDIX: CALCULATIONS OF WATER CONTENT IN WHOLE BLOOD

Whole blood is composed of red blood cells (RBC) and water. The percentage volume concentration of RBC in

the blood is hematocrit, H. Inside the RBC there is hemoglobin and more water. The volume of a single RBC is about 90 μm^3, so the concentration (number of molecules or mol per unit volume) of RBC in the whole blood with hematocrit of H is about $1.1 \times 10^{13} H$/l. One RBC contains about 280×10^6 of hemoglobin molecules. The concentration (number of molecules or mol per unit volume) of hemoglobin is $1.1 \times 10^{13} H \times 280 \times 10^6 / (6.023 \times 10^{23}) = 5.2H$ mmol/l. We denote $c_h = 5.2$ mmol/l, the concentration of hemoglobin when $H = 100\%$. The molecular weight of hemoglobin is 67,000 g/mol. This gives the density (weight per unit volume) of hemoglobin of $348H$ g/l in the whole blood. Hemoglobin constitutes about one third of the weight of a RBC and the remaining two thirds is water. The density of water in the whole blood inside RBC is therefore $696H$ g/l. Water outside the RBC constitutes $(1 - H)$ percentage in volume of whole blood. The density of this portion of water is $1{,}000(1 - H)$ g/l because the density of pure water is 1,000 g/l. The total water density in whole blood is the sum of those inside and outside the RBC, which is $1{,}000(1-0.304H)$ g/l. With the molecule weight of water being 18 g/mol, the concentration of water in the whole blood is $1{,}000(1 - 0.304H)/18$ mol/l. 1,000 g/l is the density and $c_w = 1{,}000/18 = 55.6$ mol/l the concentration of pure water. The concentration of water in whole blood is then $c_w(1-0.304H)$ mol/l.

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