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Calibration System for Pulse Spectrophotometry Using a Double-Layer Pulsation Flow-Cell

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***Abstract*— We have studied noninvasive devices for measuring total hemoglobin and hemoglobin derivatives such as carboxyhemoglobin (COHb) and methemoglobin (MetHb). A calibration procedure needs to be developed to evaluate or calibrate these devices and pulse oximeters for clinical practice. However, people and animals are sometimes exposed to risk when they are used for calibration.**

In this paper, we propose a new in vitro calibration system for a pulse photometer. This system has a novel double-layer pulsation flow-cell that incorporates both venous and arterial blood flow. Using the calibration system, we are able to measure the in vitro pulsatile optical density ratio (Φ*vt*). The measured Φ*vt* agrees well with the in vivo pulsatile optical density ratio (Φ*vi*). This system simulates an in vivo environment with high accuracy and enables safe calibration. Consequently, the calibration system is able to standardize the performance and accuracy of pulse photometry.

I. Introduction

Pulse oximetry became indispensable as a clinical monitor for measuring blood oxygen saturation (SpO_2). We have used pulse spectrophotometry to develop noninvasive devices for measuring total hemoglobin and hemoglobin derivatives such as carboxyhemoglobin (COHb) and methemoglobin (MetHb) [1–6]. A calibration procedure is needed to evaluate or calibrate pulse oximeters and these devices. A pulse oximeter is calibrated by comparing the arterial blood oxygen saturation (SaO_2) measured using a CO-oximeter and the ratio of two pulsatile optical densities (Φ) measured at two different wavelengths using the pulse oximeter. When performing a calibration, SpO_2 is measured when the subject breathes at various oxygen partial pressures. Thus, calibrating a pulse oximeter requires a human or animal subject to breathe air with a low oxygen partial pressure, thereby exposing the subject to risk.

The motivation behind this study is to overcome this problem by developing an in vitro calibration system [7]. An extremely compact mock circulatory system and a single-layer pulsation flow-cell have been developed. Although we were able to measure the in vitro pulsatile optical density ratio (Φ*vt*) using this system, there was a discrepancy between Φ*vt* and the in vivo pulsatile optical density ratio (Φ*vi*) at the same oxygen saturations.

In this present paper, a new double-layer pulsation flow-cell is proposed and good agreement between Φ*vt* and Φ*vi* is obtained using this flow-cell.

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II. Calibration System

Figure 1 shows the calibration system. It consists of an arterial circulatory system, a venous circulatory system, and a double-layer pulsation flow-cell. The total blood volume of this circulatory system is approximately 400 ml and the dimensions of the system size are approximately 600 mm × 400 mm, allowing it to be easily installed in a small space.

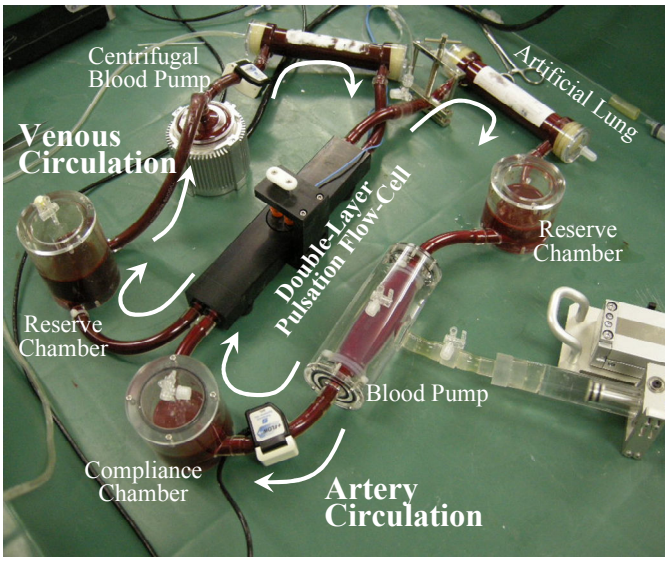

Fig. 1 Mock circulatory system

A. Arterial Circulation

The arterial circulatory system consists of several components: a compliance chamber, a reservoir chamber, a clamp, a blood pump unit, and an artificial lung. The compliance chamber, the clamp, and the reservoir chamber respectively simulate the elasticity of the aorta, the peripheral vessel resistance, and the blood in the veins. The arterial circulatory system can generate pulsatile waveforms that are similar to the aortic pressure and flow waveforms. The arterial blood pressure was set to 120/80 mmHg (Sys/Dia) and the

heart rate was set to 60 beats/min. The oxygen saturation of the circulating blood was controlled by the artificial lung.

B. *Venous Circulation*

The venous circulatory system consists of a centrifugal blood pump, a reservoir chamber, and an artificial lung. The venous circulatory system generates a steady flow. The venous blood pressure was set to 0 mmHg. The oxygen saturation of the circulating blood was controlled by the artificial lung as for the arterial circulation.

C. *Double-Layer Pulsation Flow-Cell*

Figures 2 and 3 show the developed double-layer pulsation flow-cell. The flow-cell has both venous and arterial flow. The pulsation of the arterial flow displaces the arterial diaphragm. It also displaces the venous diaphragm in the opposite direction to that of the arterial diaphragm. This changes the thickness of the venous flow. Thus, Φ is affected not only by the arterial pulsation but also by the venous pulsation. Water was used to fill the space between the photodiode and the diaphragm to prevent refraction of the diaphragm.

Equation (1) gives the in vitro pulsatile optical density ratio (Φvt) of the double-layer flow-cell.

$$\Phi vt = \frac{E'a_{660} - E'v_{660}\cdot(\Delta Dv/\Delta Da)}{E'a_{940} - E'v_{940}\cdot(\Delta Dv/\Delta Da)} = \frac{\sqrt{Ea_{660}\cdot(Ea_{660}+F)}+Zs_{660}-\sqrt{Ev_{660}\cdot(Ev_{660}+F)}\cdot(\Delta Dv/\Delta Da)}{\sqrt{Ea_{940}\cdot(Ea_{940}+F)}+Zs_{940}-\sqrt{Ev_{940}\cdot(Ev_{940}+F)}\cdot(\Delta Dv/\Delta Da)} \quad (1)$$

$E'a_{660}$ and $E'a_{940}$ are the absorbances caused by the arterial pulsation, while $E'v_{660}\cdot(\Delta Dv/\Delta Da)$ and $E'v_{940}\cdot(\Delta Dv/\Delta Da)$ are the absorbances caused by the venous pulsation. F is the scattering coefficient of blood. Zs_{660} and Zs_{940} are the components of the scattering coefficients that depend on wavelength. ΔDa and ΔDv are the displacements of the artery and vein thicknesses, respectively. Ea_{660} (Ea_{940}) and Ev_{660} (Ev_{940}) are the arterial and venous absorbances at 660 nm (940 nm) and are given by equations (2) and (3), respectively.

$$Ea_{660,940} = Eo_{660,940}\cdot Sa/100 + E_{660,940}(1 - Sa/100) \quad (2)$$

$$Ev_{660,940} = Eo_{660,940}\cdot Sv/100 + E_{660,940}(1 - Sv/100) \quad (3)$$

$Eo_{660,940}$ are the absorbances of oxyhemoglobin (O_2Hb) at 660 nm and 940 nm, respectively. $E_{660,940}$ are the absorbances of reduced hemoglobin (RHb) at 660 nm and 940 nm, respectively. Sa is the arterial oxygen saturation (SaO_2) and Sv is the venous oxygen saturation (SvO_2). Since Eo_{660}, Eo_{940}, E_{660}, E_{940}, F, Zs_{660}, and Zs_{940} are constants, Sv and $\Delta Dv/\Delta Da$ are determined by fitting equation (1) to Φvi. According to the equation (1), when Sv increases, the position of the curve shifts in the positive direction.

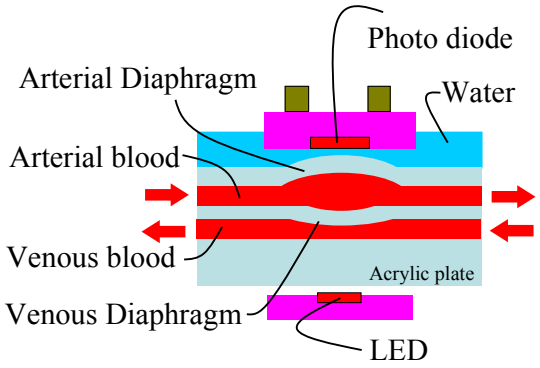

Fig. 2 Double-layer flow-cell model.

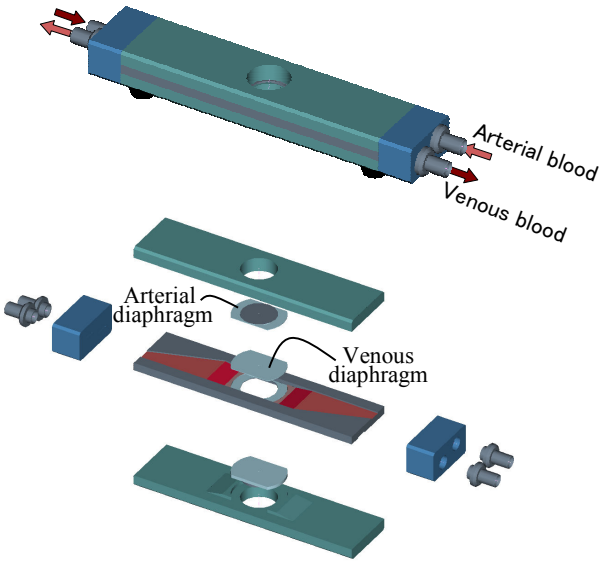

Fig. 3 Schematic diagram of the double-layer flow-cell.

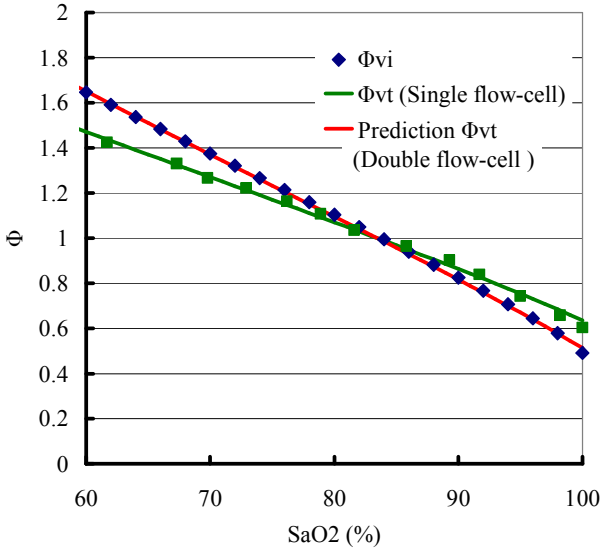

Fig. 4 Pulsatile optical density ratio (Φ) versus oxygen saturation (SaO_2). According to equation (1), when Sv lies between approximately 70% and 85% and $\Delta Dv/\Delta Da$ lies between 0.2 and 0.3, the predicted Φvt is in good agreement with Φvi.

When $\Delta Dv / \Delta Da$ increases, the slope of the curve becomes steeper. When *Sv* is between approximately 70% and 85% and $\Delta Dv / \Delta Da$ is between 0.2 and 0.3, the predicted Φ*vt* is in good agreement with the characteristics of Φ*vi* (as shown in Fig. 4). Figure 4 also shows Φ*vt*, which was measured using the single-layer flow-cell [7]. There is a discrepancy between Φ*vt* measured using the single flow-cell and Φ*vi*.

III. Results

To evaluate the double-layer model, we fabricated three different double-layer flow-cells ($\Delta Dv / \Delta Da$: 0.6, 0.1, and 0.3). Figure 5 shows a photograph of these flow-cells. We measured the relationship between the oxygen saturation (SaO_2) and Φ*vt*. SaO_2 was measured using a CO-oximeter (OSM3, Radiometer) and Φ*vt* was measured using a pulse oximeter (modified OLV-3100, Nihon Kohden Corporation).

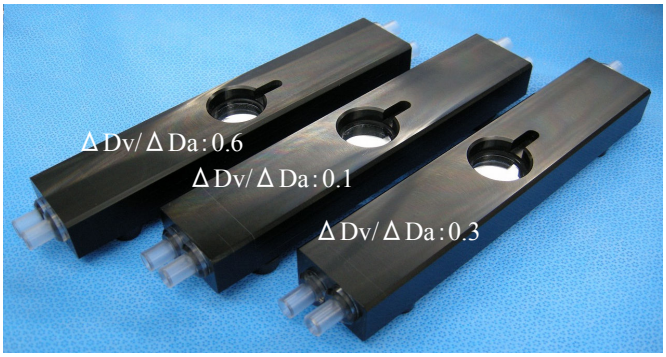

Fig. 5 Fabricated double-layer flow-cells.

Figure 6 shows the relationship between Φ*vt* and SaO_2 obtained using the flow-cell for which $\Delta Dv / \Delta Da$ is 0.6. SvO_2 was set to 88%, 77%, and 70%.

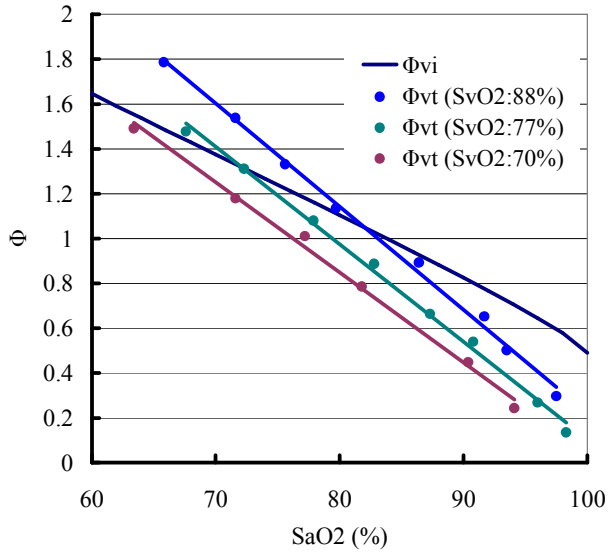

Fig. 6 The relationship between Φ*vt* and SaO_2 obtained using the flow-cell for which $\Delta Dv / \Delta Da$ is 0.6. SvO2 was set to 88%, 77%, and 70%.

Figure 7 shows the relationship Φvt and Sao_2, using the flow-cell which $\Delta Dv / \Delta Da$ is 0.1. SvO_2 was set to 90%, 80% and 70%.

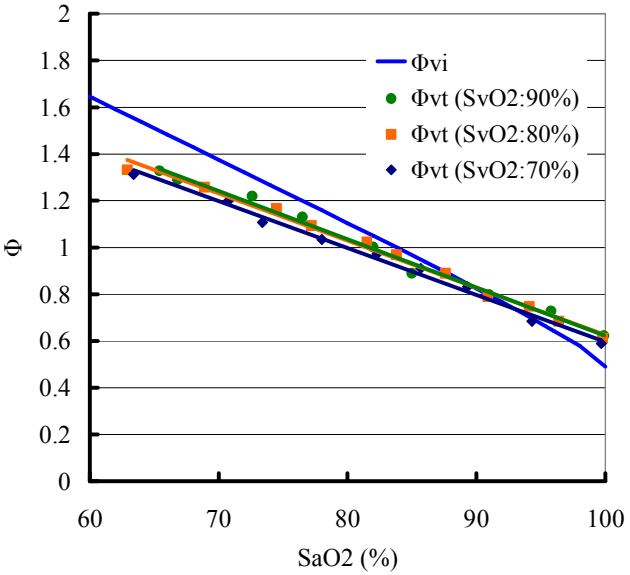

Fig. 7 The relationship between Φ*vt* and SaO_2 obtained using the flow-cell for which $\Delta Dv / \Delta Da$ is 0.1. SvO2 was set to 90%, 80%, and 70%.

Figure 8 shows the relationship between Φ*vt* and SaO_2 obtained using the flow-cell for which $\Delta Dv / \Delta Da$ is 0.3. SvO_2 was set to 88%, 87%, and 86%.

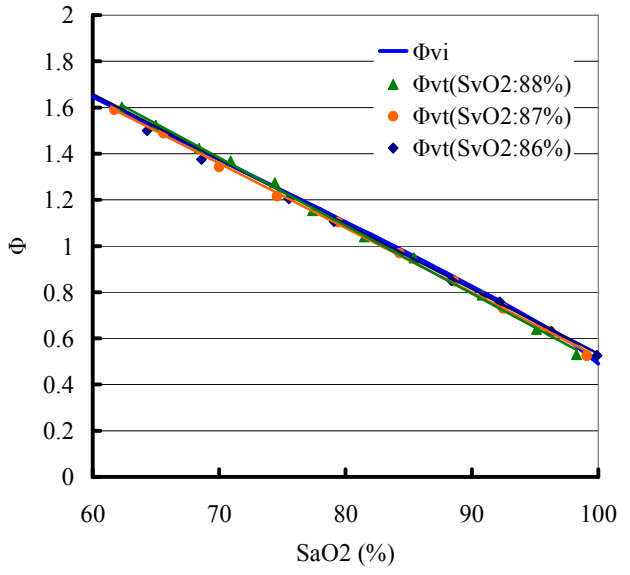

Fig. 8 The relationship between Φ*vt* and SaO2 obtained using the flow-cell for which $\Delta Dv / \Delta Da$ is 0.3. SvO2 was set to 88%, 77%, and 86%.

IV. Discussion

When $\Delta Dv / \Delta Da$ was 0.6, the slope of the Φ*vt* curve was steeper than that of Φ*vi*, whereas when $\Delta Dv / \Delta Da$ was

0.1, the slope of the Φ*vt* curve was gentler than that of Φ*vi*. Therefore, Φ*vt* measured using these flow-cells were not in agreement with Φ*vi*. However, when $\Delta Dv / \Delta Da$ was 0.3, Φvt accorded well with Φ*vi*. This result agrees with equation (1). In every case, when SvO_2 increased, the position of the curve shifted in the positive direction. This result is also in agreement with equation (1).

Aoyagi conjectured that the tissues are pulsated by the arterial pulsation and that the difference between Φ*vi* and Φ*vt* is due to the tissue's pulsation [8]. However, using our double-layer pulsation flow-cell, which included venous pulsation caused by arterial pulsation, we were able to obtain a good agreement with the characteristics of Φ*vi* in an in vitro environment. Therefore, the developed system can be used for simulating and calibrating a pulse spectrophotometer.

Previously, people or animals were used for calibrating pulse oximeters. They sometimes were exposed to risk, because calibration necessitated breathing air having a low oxygen partial pressure. The developed circulatory system and the double-layer pulsation flow-cell can simulate in vivo absorption characteristics with a high accuracy. Thus, the system can be used to perform safe in vitro calibration of a pulse photometer.

V. Conclusion

In the past, people were used for calibration for pulse spectrophotometry. However, using people or animals is potentially dangerous and should be avoided. To this end, we developed a new in vitro calibration system as a substitute for in vivo calibration. Safe calibration can be performed using this system.

This system consists of an arterial circulatory system, a venous circulatory system, and a double-layer pulsation flow-cell. The arterial circulatory system was able to generate pulsatile waveforms that were similar to the aortic pressure and flow waveforms. The venous circulatory system generated a steady flow. Arterial and venous blood flowed through the developed double-layer pulsation flow-cell. The pulsation of the arterial flow displaced the arterial diaphragm. It also displaced the venous diaphragm in the opposite direction to the displacement of the arterial diaphragm. This changed the artery thickness as well as the vein thickness. Thus, the pulsatile optical density ratio (Φ) was affected not only by the arterial pulsation but also by the venous pulsation.

To evaluate the double-layer model, we fabricated three different double-layer flow-cells. The ratios of the displacement of the artery thickness and that of the vein thickness ($\Delta Dv / \Delta Da$) were 0.6, 0.1, and 0.3. When $\Delta Dv / \Delta Da$ was 0.6, the slope of the Φ*vt* curve was steeper than that of Φ*vi*. When $\Delta Dv / \Delta Da$ was 0.1, the slope of the Φ*vt* curve was gentler than that of Φ*vi*. And when $\Delta Dv / \Delta Da$ was 0.3, Φ*vt* was in good agreement with Φ*vi*. These results concur with the prediction formula.

The developed circulatory system and the new double-layer flow-cell that incorporates arterial blood flow as well as venous blood flow can simulate the characteristics of in vivo absorption. Therefore, the system can be used to safely calibrate a pulse photometer in vitro. Additionally, the calibration system will be useful for standardizing pulse photometry performance and accuracy.

This system can simulate in vivo environments with high accuracy so it can be applied to various studies of pulse spectrophotometry such as noninvasive measurement of total hemoglobin, hemoglobin derivatives, and blood glucose levels.

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