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Continuous blood oxygen saturation detection with single-wavelength photoacoustics

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ABSTRACT

Blood oxygen saturation (SO₂) reflects the oxygenation level in blood transport and tissue. Previous studies have shown the capability of non-invasive quantitative measurements of SO₂ by multi-wavelength photoacoustic (PA) spectroscopy for diagnosis of brain, tumor hemodynamics and other pathophysiological phenomena. However, those multi-wavelength methods require a tunable laser or multiple lasers which are relatively expensive and bulky for field measurement environment and applications. Besides, the operation of multiple wavelengths, calibration procedures and data processing gets system complicated, which reduces the feasibility and flexibility for continuous real-time monitoring. Here we report a newly proposed method by combining PA and scattered light signals wherein imposing a hypothesis that scattering intensity is linear to the concentrations of oxygenated hemoglobin and deoxygenated hemoglobin weighed by blood scattering coefficients. A rigorous theoretical relationship between PA and scattering signals is thus established, making it possible that SO₂ can be measured with only one excitation wavelength. To verify the theory basis, both dual-ink phantoms and fresh porcine blood sample have been employed in the experiments. The phantom experiment is able to quantify the concentration of mixed red-green ink that is in precise agreement with pre-set values. The *ex vivo* experiment with fresh porcine blood was conducted and the results of the proposed single-wavelength method achieved high accuracy of 1% - 4% errors. These demonstrated that the proposed single-wavelength SO₂ detection is able to provide non-invasive, accurate measurement of blood oxygenation, and herein create potential for applying it to real clinical applications with low cost and high flexibility.

Keywords: Photoacoustics, scattering measurement, oxygen saturation, single wavelength

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1. INTRODUCTION

Blood oxygen saturation (SO₂) is defined as the ratio of the concentrations between oxygenated hemoglobin (HbO₂) to total hemoglobin (oxygenated hemoglobin plus deoxygenated hemoglobin, HbO₂+HbR), which is a very important physiological parameter in the medical and clinical fields. It shows the oxygen level of the lungs, blood transport and tissue oxygen consumption. It could provide a potential method for diagnosis and detection of brain, tumor hemodynamics, gene expression, and other pathophysiological phenomena [1-2] whose activities are highly sensitive to oxygen changes. Therefore, a simple, cheap, non-invasive and effective method is required for SO₂ monitoring. Pulse oximetry is a widely used and non-invasive method [3]. It is based on the light absorbing variations of the arterial blood following the heartbeat, while the absorption of the skin, muscle, bones and venous blood remain constant. The spectrophotometric method is used to calculate the arterial blood oxygen saturation using multi-wavelength light source [4-5]. However, this method has poor spatial resolution and suffers body movement. On the other hand, the photoacoustic (PA) effect is the mechanism referring to the generation of sound wave through the absorption of light and conversion to heat. Because the PA signal is proportional to the optical absorption and the local optical fluency, the photoacoustic microscopy (PAM) is able to calculate the blood oxygen saturation using multi-wavelength light source [6-8]. The PAM has high spatial resolution, but multi-wavelength PA measurement typically requires an expensive and bulky tunable high-power laser, which is undesirable in non-laboratory environment [9-11]. Besides, the spectral dependence of the local optical fluence, and hence the PA signal, combined with the unknown spectral properties of the surrounding tissues, present challenges to accurate

SO₂ measurements. Moreover, the operation of multiple wavelengths, calibration procedures and data processing gets system complicated, which reduces the feasibility and flexibility for continuous real-time monitoring. A recent study reports a single wavelength PA method based on the saturation of the optical absorption, but it may bring damage to organism due to the significantly high laser intensity [12]. In our study, both the optical absorption induced PA signal and diffusively scattered optical signal are collected [13-14]. Based on the PA signal equation and scattered optical equation, we can measure the SO₂ and the concentrations of the HbO₂ and HbR using single wavelength within the laser safety range.

2. METHODS AND RESULTS

2.1 Principle of Single-Wavelength Oxygen Saturation Estimation

The During laser-induced PA process, the acoustic signal is launched based on the principle of thermal expansion following the optical energy absorption by the sample. Here the blood vessel is the targeted object, we can acquire the PA signal.

$$P = A(\varepsilon_{HbO_2} C_{HbO_2} + \varepsilon_{HbR} C_{HbR}) \quad (1)$$

where A is related to ultrasonic parameter, system parameter, Gruneisen parameter and the local optical fluence which can be expressed as the multiplication of the local laser intensity and laser pulse width. These parameters are all constant for a fixed system setup and experimental environment. ε_{HbO_2} and ε_{HbR} are known molar extinction coefficients of oxygenated hemoglobin and deoxygenated hemoglobin. C_{HbO_2} and C_{HbR} are the unknown concentrations of oxygenated hemoglobin and deoxygenated hemoglobin. Therefore, the PA signal has linear relation with the concentrations of two main kinds of hemoglobin in the blood.

On the other hand, the light will be scattered when it irradiates onto the sample. We hypothesize that the scattered light intensity is linearly related to concentrations of oxygenated hemoglobin and deoxygenated hemoglobin by scattering coefficients μ_{HbO_2} and μ_{HbR} at certain wavelength, shown as

$$I = B(\mu_{HbO_2} C_{HbO_2} + \mu_{HbR} C_{HbR}) \quad (2)$$

where H is related to system parameter and the local optical fluence. From the simultaneous linear equations (1) and (2), SO₂ value can be calculated as

$$\langle \text{SO}_2 \rangle = \frac{I \varepsilon_{HbR} \eta - P \mu_{HbR}}{I \eta (\varepsilon_{HbR} - \varepsilon_{HbO_2}) + P (\mu_{HbO_2} - \mu_{HbR})} \quad (3)$$

where $\eta = A/B$. The two parameters need to be calibrated since they are both related to specific system setup and experimental environment.

Figure 1. The system architecture with the single wavelength laser source, which is able to collect both PA and optical signals simultaneously. ConL: condenser lens; FC: fiber coupler; MMF: multi-mode fiber; ND: neutral density; PD: photon detector; US: ultrasound transducer.

2.2 Phantom study

To verify the hypothesis, phantom study was conducted by two kinds of dyes made from red and green inks to mimic HbO_2 and HbR , respectively. The experimental setup is shown in Fig. 1, where the optical absorption induced photoacoustic signal is captured by the ultrasound transducer (1MHz, V303-SU, Olympus), and the scattered light signal is captured by the photon detector (DET10A, Thorlabs). In the phantom experiment, two ink samples (green and red, Private Reserve Ink) were mixed in various concentration ratios to mimic different levels of SO_2 as pseudo- SO_2 , and $[\text{red}]$ and $[\text{green}]$ are used to mimic $[\text{HbO}_2]$ and $[\text{HbR}]$, respectively. Equation (1) and (2) can be simplified to:

$$P = A_1 C_{\text{red}} + A_2 C_{\text{green}} \quad (4)$$

$$I = B_1 C_{\text{red}} + B_2 C_{\text{green}} \quad (5)$$

So that the ratio of the red ink concentration in the total ink concentration $[\text{red}]/([\text{red}]+[\text{green}])$ which is used to represent pseudo- SO_2 can be expressed as

$$\frac{[\text{red}]}{[\text{red}]+[\text{green}]} = \frac{IA_2 - PB_2}{I(A_2 - A_1) + P(B_1 - B_2)} \quad (6)$$

By controlling the total concentration, the mixed samples have comparable optical absorption coefficients to that of blood. The OPO laser (Opolette 355, OPOTEK Inc.) outputs 532 nm wavelength light with 7 ns pulse width. During data collection, the mixed solution was injected into a silicone transparent tube with an inner diameter of 3 mm. The original red and green inks were diluted with water in four different ratios of 2:8, 4:6, 6:4 and 8:2, namely the fraction of $[\text{red}]/([\text{red}]+[\text{green}])$ changing from 20% to 80% with a constant interval of 20%. The parameters in two equations (4) and (5) are obtained through curve fitting. The fitting parameters were used in another set of mixed ink were made with the ratios of 1:9, 3:7, 5:5, 7:3 and 9:1 to verify the results.

Figure 2. The experimental results of phantom study. (a) Photoacoustic signal and (b) scattered optical signal along with pseudo-SO2 change. (c) The comparison between preset and measured pseudo-SO2.

Through curve fitting, the four parameters are obtained as $A_1 = 0.1936$, $A_2 = 0.1073$, $B_1 = 0.1205$, $B_2 = 0.1291$. Then the Pseudo-SO2 can be calculated from Eq. (6). The experimental results are shown in Fig. 2, where both photoacoustic signal and scattered optical signals are linearly related with SO2. A good accuracy of 4% ($R^2=0.96$) is achieved compared with state-of-art multi-wavelength approaches.

Figure 3. The experimental setup of ex vivo study.

2.3 In vitro study

To demonstrate the capability of imaging blood oxygen flux, *in vitro* experiments were performed using freshly collected porcine blood stored in a conical flask. The experiment is done in a modified system shown in Fig. 3. A transparent tube was used to export the blood to the water tank for PA and scattered light measurement. The conical flask was connected with an O₂ cylinder and a CO₂ cylinder to increase and decrease the SO₂ in the blood respectively. PA and scattered light signals at two different wavelengths are used to calibrate system parameters. For wavelength λ_1 ,

$$P(\lambda_1) = A(\epsilon_{HbO_2}(\lambda_1)C_{HbO_2} + \epsilon_{HbR}(\lambda_1)C_{HbR}) \quad (7)$$

$$I(\lambda_1) = B(\mu_{HbO_2}(\lambda_1)C_{HbO_2} + \mu_{HbR}(\lambda_1)C_{HbR}) \quad (8)$$

For wavelength λ_2 ,

$$P(\lambda_2) = A(\epsilon_{HbO_2}(\lambda_2)C_{HbO_2} + \epsilon_{HbR}(\lambda_2)C_{HbR}) \quad (9)$$

$$I(\lambda_2) = B(\mu_{HbO_2}(\lambda_2)C_{HbO_2} + \mu_{HbR}(\lambda_2)C_{HbR}) \quad (10)$$

Calibrated SO₂ can be calculated by dividing equation (7) with equation (9) as:

$$\langle \text{SO}_2 \rangle_{\text{Cal}} = \frac{P(\lambda_2)\epsilon_{HbR}(\lambda_1) - P(\lambda_1)\epsilon_{HbR}(\lambda_2)}{P(\lambda_2)(\epsilon_{HbR}(\lambda_1) - \epsilon_{HbO_2}(\lambda_1)) - P(\lambda_1)(\epsilon_{HbR}(\lambda_2) - \epsilon_{HbO_2}(\lambda_2))} \quad (11)$$

Taking wavelength λ_2 as reference wavelength, for example, the corresponding equations (9) and (10) have the same relation with equation (3). So from (3) and (11), we can obtain:

$$\eta = \frac{A}{B} = \frac{\langle \text{SO}_2 \rangle_{\text{Cal}} \cdot P(\lambda_2)(\mu_{HbO_2}(\lambda_2) - \mu_{HbR}(\lambda_2)) + P(\lambda_2)\mu_{HbR}(\lambda_2)}{I(\lambda_2)\epsilon_{HbR}(\lambda_2) - \langle \text{SO}_2 \rangle_{\text{Cal}} \cdot I(\lambda_2)(\epsilon_{HbR}(\lambda_2) - \epsilon_{HbO_2}(\lambda_2))} \quad (12)$$

Ultimately, wavelength λ_1 can be utilized as the single-wavelength laser illumination for SO₂ detection and continuous monitoring with calibrated value η :

$$\langle \text{SO}_2 \rangle_{\text{Mea}} = \frac{I(\lambda_1) \varepsilon_{\text{HbR}}(\lambda_1) \eta - P(\lambda_1) \mu_{\text{HbR}}(\lambda_1)}{I(\lambda_1) \eta (\varepsilon_{\text{HbR}}(\lambda_1) - \varepsilon_{\text{HbO}_2}(\lambda_1)) + P(\lambda_1) (\mu_{\text{HbO}_2}(\lambda_1) - \mu_{\text{HbR}}(\lambda_1))}. \quad (13)$$

Figure 4. The in vitro experimental results based on (a) conventional dual wavelength, and (b) proposed single wavelength approach.

To validate the measurement accuracy, conventional dual-wavelength method and a standard PO₂ electrode (DO-166MT-1, LAZAR Research Laboratories) was utilized to monitor SO₂ inside the tube as the preset values. Firstly, carbon dioxide (CO₂) is pumped into the blood to make the SO₂ close to 0%. Then oxygen (O₂) is continuously pumped into the blood to fine tune the SO₂ from 20% to 80% with 10% intervals. PA signals and scattering light signals were measured respectively. Meanwhile, to investigate the measurement accuracy, conventional dual-

wavelength (584 nm and 600 nm) method and a standard SO₂ meter were utilized to measure SO₂ accordingly. The experimental results are shown in Fig. 4 using both dual wavelength (Fig. 4(a)) and single wavelength (Fig. 4(b)). It demonstrates that both dual-wavelength and proposed single wavelength approaches could achieve good agreement with preset SO₂ value, where dual-wavelength approach gives higher accuracy ($R^2=0.95$) than single-wavelength approach ($R^2=0.92$).

3. SUMMARY

In conclusion, a novel approach fusing optical absorption and scattering for single wavelength SO₂ detection is proposed and proved experimentally on phantom and ex vivo blood. This proposed single wavelength approach may be highly integrated, inexpensive, and much simpler than multi-wavelength approaches for SO₂ monitoring, showing significant potential for portable and on-site diagnostics.

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