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A new method for noninvasive venous blood oxygen detection

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article

Abstract

Background: Blood oxygen saturation of vein (SvO₂) is an important clinical parameter for patient monitoring. However, the existing clinical methods are invasive, expensive, which are also painful for patients.

Methods: Based on light-absorption, this study describes a new noninvasive SvO₂ measurement method by using external stimulation signal to generate cyclical fluctuation signal in the vein, which overcomes the low signal-to-noise ratio problem in the measurement process. In this way, the value of SvO₂ can be obtained continuously in real time.

Results: The experimental results demonstrate that the method can successfully measure venous oxygen saturation by artificial addition of stimulation. Under hypoxic conditions, the system can reflect the overall decline of venous oxygen saturation better. When the results measured by the new method are compared with those measured by the invasive method, the root mean square error of the difference is 5.31 and the correlation coefficient of the difference is 0.72. The new method can be used to measure SvO₂ and evaluate body oxygen consumption, and its accuracy needs improvement.

Conclusions: Real-time and continuous monitoring can be achieved by replacing invasive method with noninvasive method, which provides more comprehensive clinical information in a timely manner and better meet the needs of clinical treatment. However, the accuracy of the new noninvasive SvO₂ measurement based on light-absorption has to be further improved.

Keywords: Noninvasive method, SvO₂, External stimulation signal

Background

SvO₂ and SaO₂ (blood oxygen saturation of artery) have been established as the basic parameters to evaluate oxygen delivery process and monitor patient's oxygen consumption. According to Fick Formula in Eq. (1)[1], the oxygen circulation in human body can be analyzed completely only by combining SvO₂ and SaO₂ together. Therefore, SvO₂ has a significant meaning in evaluating the health of patients.

$$\text{SvO}_2 = \text{SaO}_2 - \text{VO}_2 \div (1.34 \times \text{CO} \times \text{Hb}) \quad (1)$$

On the other hand, there is no existing noninvasive or continuous device for measuring SvO₂ in the market, even though light absorption method has already been widely

used to evaluate SaO₂. Besides the high price and inconvenient, invasive method also has more risk in clinical SvO₂ measurement.

Due to the lack of fluctuation signal in vein, SvO₂ can't be measured in the same way as SaO₂ is measured, for which light absorption method is valid because of the obvious impulse in artery. To overcome this problem a new noninvasive light-absorption method for SvO₂ measurement is proposed. In this method, we innovatively create vein impulse similar to artery impulse by artificially adding external stimulation signal during measurement, which enables the extraction of the stable venous signal from normal arterial pulse signal.

Methods

According to the Lambert–Beer's law, the intensity of light through the medium has different degrees of attenuation which depending on the thickness and concentration of the solution. Because the transmission light intensity will decrease with the increasing of the concentration and the thickness of the solution, the absorbance of a single solution can be calculated by Eq. (2)

$$A = \ln \left(\frac{I_i}{I_t} \right) = a \cdot C \cdot L \quad (2)$$

where A represents absorbance, the natural logarithm of the ratio of the incident light intensity to the transmitted light intensity; I_i represents the incident light intensity and I_t represents the intensity of the transmitted light, a represents the absorption coefficient, with different values for different solutions; C represents the solution concentration; L represents the optical path and is the distance that light travels through in the solution [2].

Be similar to mixed solution, the absorbance of blood can be calculated by optical absorption model for mixed solution as shown in Eq. (3), and there is no limit on the number of components in the solution. As we all know, the absorbance of the mixed solution satisfies the superposition theorem and is the superposition of all solution ingredients' absorbance at different concentrations and different absorption coefficients.

$$A = \ln \left(\frac{I_i}{I_t} \right) = \sum_{k=1}^{\infty} a_k \cdot C_k \cdot L \quad (3)$$

Equation (4) is the mixed absorbency at 660 and 940 nm with oxygen free hemoglobin and oxygenated hemoglobin under static condition, where λ is the wavelength of the original light.

$$A(\lambda) = \ln \left(\frac{I_i(\lambda)}{I_t(\lambda)} \right) = a_{Hb}(\lambda) \cdot C_{Hb}(\lambda) \cdot L + a_{HbO_2}(\lambda) \cdot C_{HbO_2}(\lambda) \cdot L \quad (4)$$

In dynamic state, the intensity change of the transmission light is induced by the change of optical path due to congestion artery, as shown in Eq. (5)

$$I(\lambda, t) = I_0(\lambda) \exp(-(s\beta_0(\lambda) + (1-s)\beta_r(\lambda))I(t)) \quad (5)$$

where I_0 and I represent the intensity of the incident light and the transmission intensity of the original light respectively. λ denotes the wavelength of the original light. t is the time. S is the oxygen saturation. β_0 and β_r are the absorption coefficients for the Hb and HbO₂ in the solution. $l(t)$ is the optical path from the light source to the photoelectric sensor [3].

Equation (5) can be easily reformulated as Eq. (6)

$$\frac{d(\ln I(\lambda, t))}{dt} = -(s\beta_0(\lambda) + (1-s)\beta_r(\lambda)) \frac{d(l(t))}{dt} \quad (6)$$

Then Eq. (7) can be derived from Eqs. (4), (5) and (6).

$$S = \frac{\frac{d\ln I(\lambda_R)}{dt} \beta_r(\lambda_R) - \frac{d\ln I(\lambda_{IR})}{dt} \beta_r(\lambda_{IR})}{\frac{d\ln I(\lambda_R)}{dt} (\beta_0(\lambda_{IR}) - \beta_r(\lambda_{IR})) - \frac{d\ln I(\lambda_{IR})}{dt} (\beta_0(\lambda_R) - \beta_r(\lambda_R))} \quad (7)$$

Assuming that Eq. (8) holds.

$$\frac{d(\ln I(\lambda, t))}{dt} \cong \ln \left(\frac{I(t_2, \lambda)}{I(t_1, \lambda)} \right) \quad (8)$$

We can rewrite Eq. (7) to Eq. (9) to calculate oxygen saturation

$$S = \frac{\beta_r(\lambda_R) - R\beta_r(\lambda_{IR})}{R(\beta_0(\lambda_{IR}) - \beta_r(\lambda_{IR}))(\beta_0(\lambda_R) - \beta_r(\lambda_R))} \quad (9)$$

where R (molar extinction coefficient) [4] is defined below and all the other variables are constant.

$$R = \frac{\ln(I(t_1, \lambda_R)/I(t_2, \lambda_R))}{\ln(I(t_1, \lambda_{IR})/I(t_2, \lambda_{IR}))} \cong \frac{\frac{d\ln I(\lambda_R)}{dt}}{\frac{d\ln I(\lambda_{IR})}{dt}} \quad (10)$$

According to Eqs. (7) and (9), the full parameters of the pulse oxygen saturation can be obtained by calculating the alternating current (AC) and direct current (DC) values of red light and infrared light of signals [5].

Usually, pulse fluctuation can lead venous oxygen signal overlap with the artery blood oxygen signal, which causes problem of low signal (SvO₂)-to-noise (SaO₂) ratio. Therefore, the extraction of the weak venous blood oxygen signal from artery blood oxygen signal is the key to non-invasive SvO₂ measurement. Based on clinical studies, a new method has been proposed. It measures the periodic fluctuation vein signal, whereas a new system has been designed to verify the method.

As Fig. 1 shows, the system consists of four main parts. Part.A is the monitor for data calculation and waveform display. Part.B is the system controller. This module can control the work of Part.A, Part.C and Part.D. Part.C is the photoplethysmography (PPG) signal sample module getting photoelectric volume pulse wave data. Part.D is the signal generation module. In this part, a ring-shaped inflatable air cuff (Part.D of Fig. 1) is used to produce stable signal as stimulate signal. By controlling Part.D, Part.C can gain the arterial PPG signal and the mixed PPG signal respectively, which is then displayed in Part.A.

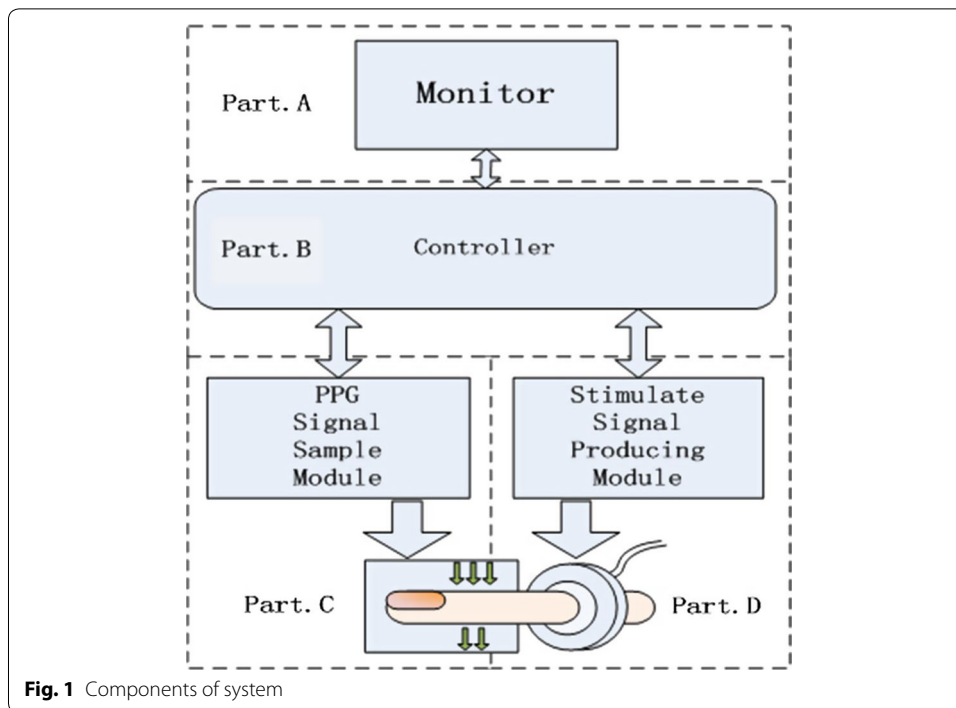


Fig. 1 Components of system

Periodic pressure can be added to finger by inflating and deflating the air cuff periodically. NIBP (non-invasive blood pressure) is used as a controllable parameter to set the threshold pressure for different people, while the frequency of inflation and deflation are controlled by a high-precision timer. Figure 2 is the control chart for the venous signal enhancement system. The stimulation control system is the module that controls the venous signal enhancement. The feedback adjustment is controlled by MCU. The detailed process is as follows: firstly, PPG of arteries and veins can be detected by dual-wavelength pulse oxygen measurement system; secondly, the signal frequency and strength of the two kinds of PPG are used as feedback to increase the signal of vein; thirdly, with feedback of the relationship between the signal-to-noise ratio of vein and arterial, the stimulation control system to stay in a stable and acceptable condition can be maintained (the signal frequency of the two kinds of PPG is different). Figure 3 briefly

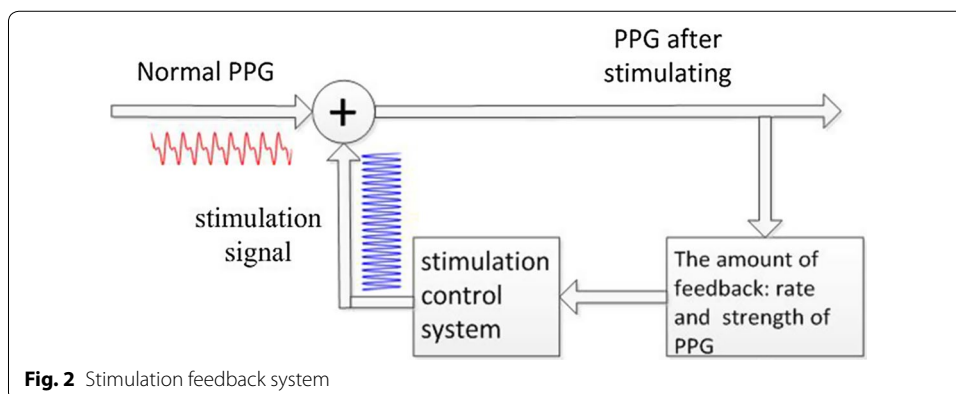
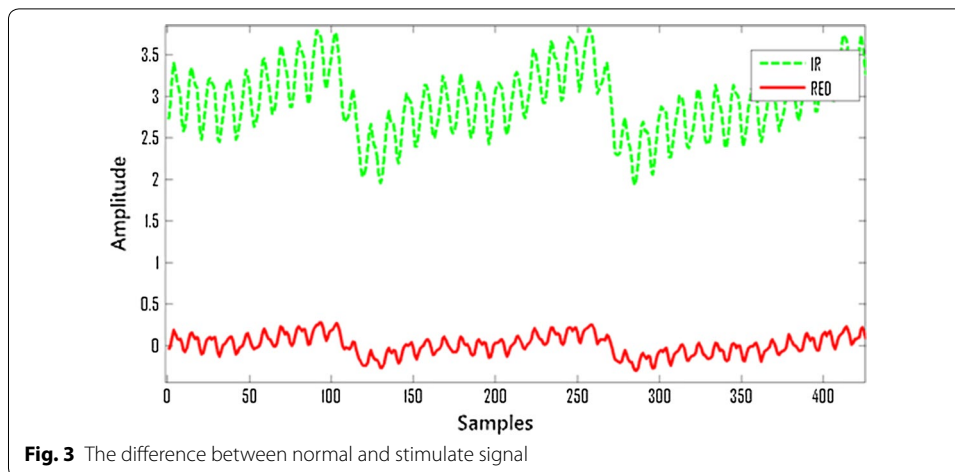


Fig. 2 Stimulation feedback system



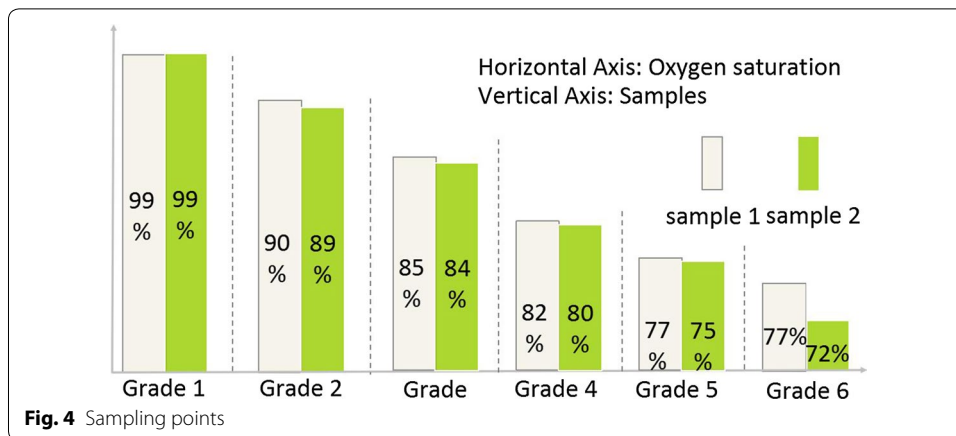
shows the difference between normal signal and stimulated signal. In the signals of IR and RED, every PPG contains multiple excitation signals. Besides, under the stimulation condition, both arterial signal and venous signal are affected.

The SvO₂ signal extraction process generally includes three steps. Firstly, the stimulated signal is wiped out and the normal SpO₂ signal is calculated. Secondly, the signal which is too far from our stimulation frequency is filtered and the peak of artificially stimulated signal is used as input data to calculate Mixed-SpO₂ in the normal way which is same to the calculation of SpO₂. Thirdly, SvO₂ is calculated. In this paper, venous PPG generated by the stimulation signal is used to calculate the venous oxygen saturation, which is the same as arterial oxygen saturation PPG used to calculate the arterial oxygen saturation. The PPG is recorded at 660, 940 nm for red and infrared transmission intensity changes. In theory, if PPG of the arterial blood signal can be used to calculate the arterial oxygen saturation, PPG of the venous blood signal can also be used to calculate the venous oxygen saturation. Because the features of the two signals are the same, SvO₂ can be calculated use the same method to calculate SpO₂. In fact, the signal the system acquired is the mixed signal. In the case of ideal signal to noise ratio, venous oxygen saturation can be calculated by formula (11) and formula (12).

$$\text{Mixed_SpO}_2 = (\text{SpO}_2 + \text{SvO}_2)/2 \quad (11)$$

$$R_{\text{SpO}_2} = R_{\text{SvO}_2} = \left(\frac{\Delta I_t^{660}}{I_t^{660}} \right) / \left(\frac{\Delta I_t^{940}}{I_t^{940}} \right) \quad (12)$$

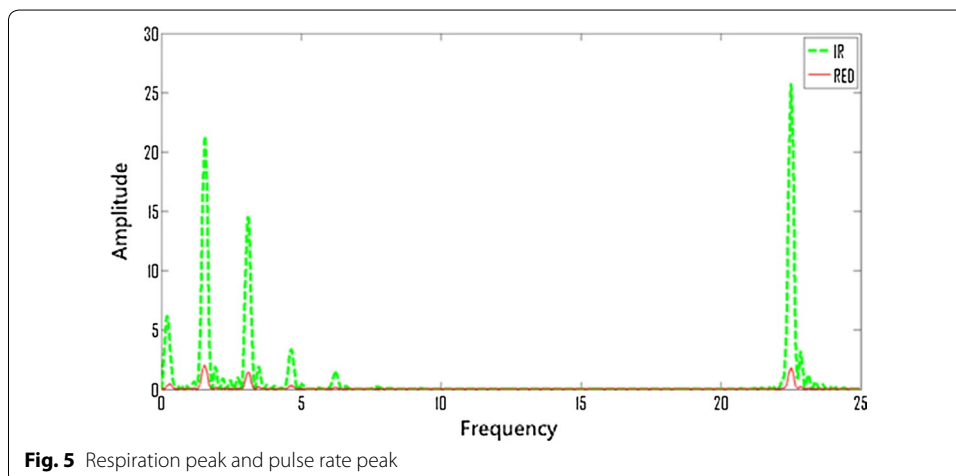
At last, the invasive blood gas analysis is utilized as the golden criterion to calibrate the data measured by our system, referring to the calibration process of SpO₂. The blood gas analysis platform of the laboratory can control the oxygen concentrations by adjusting the intake of oxygen. The system records the values of SaO₂ and SvO₂ in noninvasive method, at the same time the blood samples of artery and vein are sampled in 100–70 % hypoxic state. 24 samples of venous blood were sampled near from our finger in consistent with the process showed in Fig. 4. The sampling was conducted at six oxygen



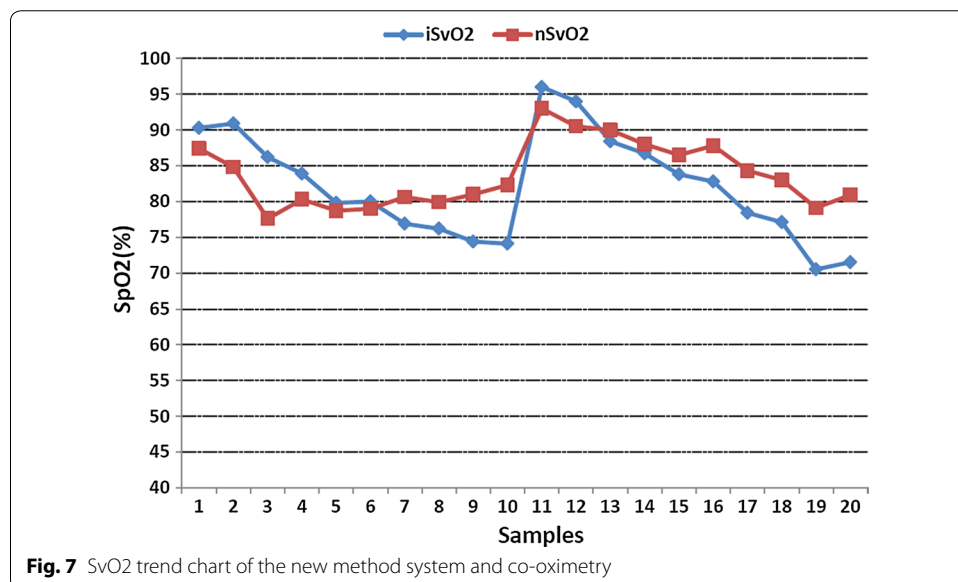
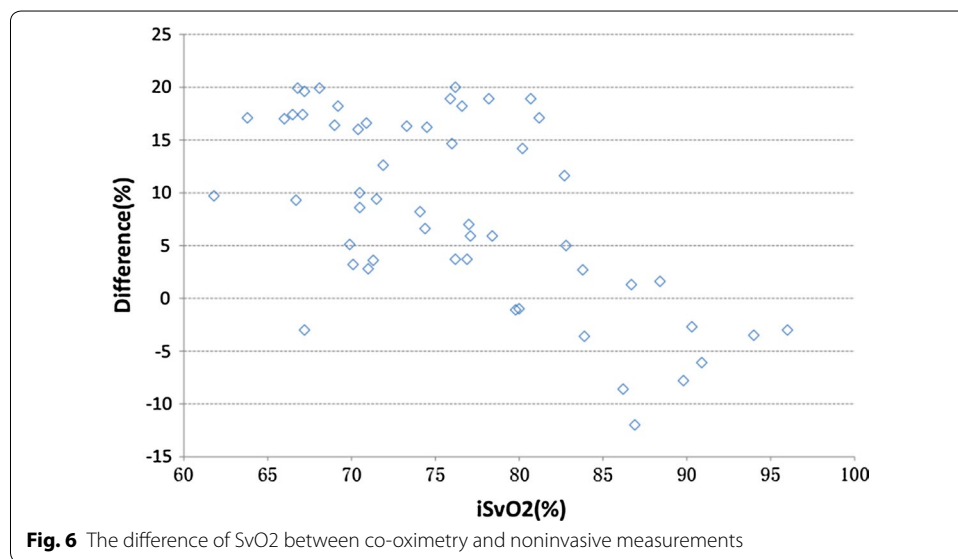
saturation levels, with two samples collected at each level. This was repeated twice to acquire the 24 samples.

Results and discussion

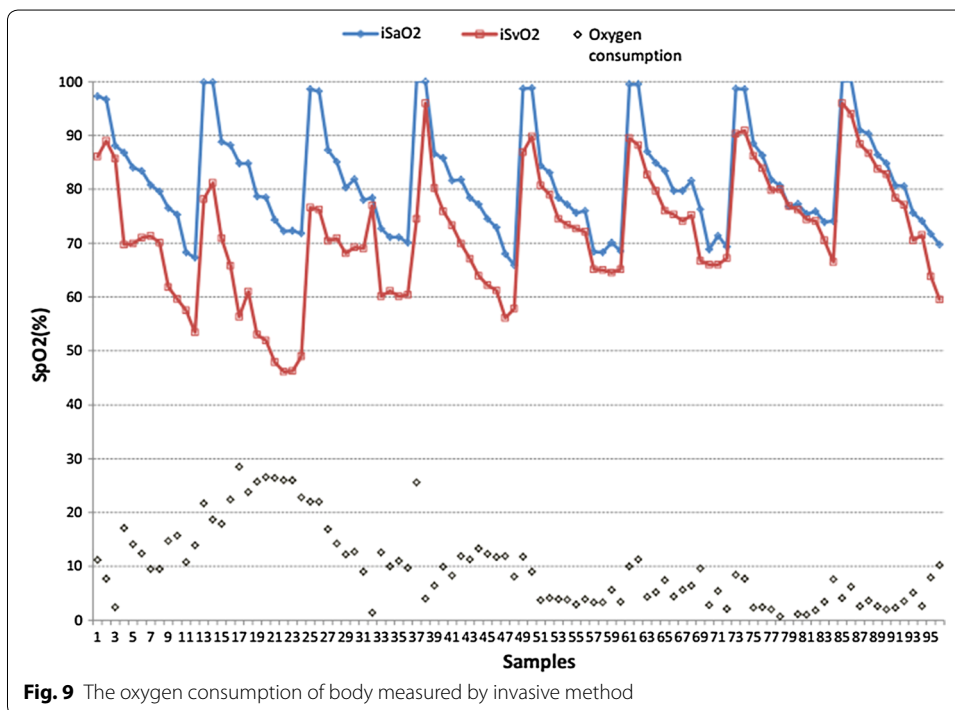
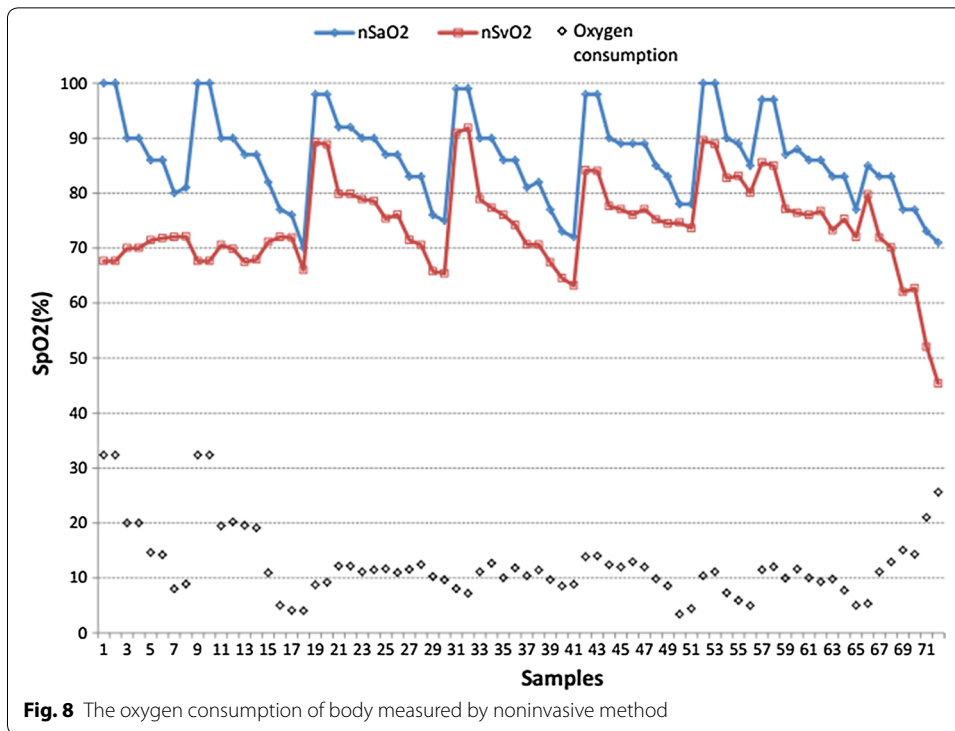
In this manuscript, we introduced a system for the continuous and noninvasive measurement of SvO₂. Our system utilizes a control system to modulate the adjustable stimulation signal that is essential to the measurement process, in which the stimulation signal rate shouldn't be the same as patients' pulse rate. The power spectrum of PPG in Fig. 3 can be found in Fig. 5, which can be divided into low frequency spectrum for pulse and high frequency spectrum for stimulation signal. The peaks of the power spectrum of the two kinds of signal are separated in frequency domain. In this way the ordinary FIR filter can be used to extract the pulse spectrum for the calculation of arterial oxygen saturation easily, and the stimulation signal for the calculation of the venous oxygen saturation. The experimental results indicate that the method of addition artificial stimulation can successfully transform the vein interference signal of pulse oxygen saturation measurement into useful signal to venous oxygen saturation measurements without compromising the pulse oxygen measurement. In addition, under hypoxic conditions, the system can reflect the overall decline of venous oxygen saturation better.



To identify the stability and reliability of the system, we studied nine healthy adults. Five volunteers took part in the invasive experiment and others took part in the noninvasive experiment. Invasive blood gas analysis (co-oximetry, golden criterion) was used to benchmark the accuracy and stability of the system. Referring to the standard calibration process of SpO₂, samples of venous blood near from subjects' fingers were collected. The sampling point is approximately set in 6 levels of oxygen saturation, and recorded twice for each subject (Fig. 4). The difference between the values which measured by the system and co-oximetry is almost within -10 to 10, as shown in Fig. 6, which includes all the data points without excluding any outliers. Figure 7 displays changes in nSvO₂ (noninvasive SvO₂) and iSvO₂ (invasive SvO₂) through different oxygen saturation levels from one subject. The root mean square error (the difference of SvO₂-iSvO₂) is 5.31



and the correlation coefficient (the difference of SvO2-iSvO2) is 0.72. In general, the system is stable but the accuracy should be further improved. Oxygen consumption is equal to SaO2 minus SvO2. Figure 8 shows is the oxygen consumption estimated by the noninvasive method, and Fig. 9 is the oxygen consumption estimated by the invasive method.



The oxygen consumptions in the two figures are very close. Therefore, the new method can be used to assess the body oxygen consumption.

Conclusions

The experimental results indicate that the noninvasive method can be a feasible approach for SvO₂ measurement. Adding the external stimulation signal to vein solved the problems of the lack of fluctuation signal and improved signal-to-noise ratio in the measuring process. This new method of SvO₂ measurement can potentially meet the unmet clinical needs, reducing the time and cost involved.

Additional file

Additional file 1: Raw Data.

Abbreviations

SvO₂: blood oxygen saturation of vein; SaO₂: blood oxygen saturation of artery; PPG: photoplethysmography; nSvO₂: noninvasive SvO₂; iSvO₂: invasive SvO₂.

Authors' contributions

MMZ, SKZ and LQW carried out the measurement, analysis and drafted the manuscript. XZ and JLY conceived and designed the experiment and revised the manuscript critically. All authors read and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

Availability of data and materials

The dataset supporting the conclusions of this article is included within Additional file 1.

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