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Wearable wireless real-time cerebral oximeter for measuring regional cerebral oxygen saturation

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Abstract Monitoring regional cerebral oxygen saturation throughout the perioperative clinical process is important for successful patient outcomes. Cerebral oximeters based on near-infrared spectroscopy (NIRS) have already been used for monitoring brain oxygenation and hemodynamics to avoid intraoperative ischemic stroke and reduce postoperative cognitive dysfunction. The current devices are all designed to be used as a bedside monitor, limiting their use to situations that center around a hospital bed. There is a current lack of wearable, miniaturized, wireless equipment that can extend brain oxygenation monitoring to motion tasks or tight spaces. We design a head-mounted wearable wireless oxygen saturation monitoring on head (WORTH) band based on NIRS for monitoring regional cerebral oxygen saturation. The band is embedded with a highly integrated central block, which comprises an optical module, a microprocessor unit, a wireless communication module, and a power management module. The performance of the WORTH band is evaluated by a controlled hypoxia experiment and a squat-to-stand experiment. The results confirm that the WORTH band can record cerebral oxygen saturation with an accuracy comparable to that of a clinical monitor and demonstrate that it is also effective during motion tasks.

Keywords near-infrared spectroscopy, cerebral oxygen saturation, oximeter, rSO2, wearable

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1 Introduction

The human brain represents about 2% of the body's weight but accounts for 20% of the body's oxygen consumption [1]. Cerebral ischemia often results in neurologic, cognitive, or functional brain deficits. Detection and interventions for cerebral ischemia have long been significant issues in clinical applications, especially in surgeries affecting brain circulation. Researchers have sought reliable techniques for monitoring cerebral oxygen saturation. Near-infrared spectroscopy (NIRS) has emerged as a noninvasive optical neuroimaging technique that is safe, cost-effective, portable, wearable, and ecological and has been used for longitudinal monitoring [2–4]. NIRS is based on two principles [5]. The first is that

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superficial biological tissues of head are relatively transparent to light in the near-infrared spectrum (600–1000 nm). The second is that oxygenated-hemoglobin (HbO) and deoxygenated-hemoglobin (Hb) have different absorption characteristics. Cerebral oximeters based on NIRS have been approved by the US Food and Drug Administration for monitoring regional cerebral oxygen saturation (rSO2) of the brain continuously and noninvasively in clinical environments [6]. They provide noninvasive, continuous, and long-term measurement of rSO2. The rSO2 reflects information about the local balance between oxygen delivery and oxygen consumption in a tissue of interest. It may serve as an early warning of decreased oxygen delivery to the brain and provide a potential clinical benefit by alerting clinicians to perform timely interventions [7].

Pulse oximeters, which are based on the same near-infrared spectroscopy theory as rSO2, have been widely accepted in clinics for more than two decades, but they only measure peripheral arterial oxygen saturation (SpO2) and require pulsations to perform the measurement. Another important difference between them is that brain blood circulation is relatively independent of body blood circulation because they are in different blood supply circuits. Hence, SpO2 cannot accurately reflect the oxygen saturation status of the brain, e.g., cerebral hypoxia during cerebral ischemia. Cerebral oximeters, however, do not rely on pulsatile blood flow to capture signals [6, 8], enabling them to be used even under pulseless conditions. Owing to their unique advantages, cerebral oximeters have been used in a variety of clinical applications, such as carotid endarterectomy, neurosurgery, and intensive care [7, 9]. They have also been used for monitoring cerebral oxygen and assessing cerebral auto-regulation in patients during cardiac surgery with cardiopulmonary bypass [10, 11]. Previous publications have shown the significant role of cerebral oxygenation monitoring in predicting patient outcomes. Reduced rSO2 in perioperative and intraoperative periods has been related to postoperative morbidity and mortality as well as to a prolonged hospital stay in patients undergoing major cardiovascular surgeries [12]. Zheng et al. [13] reported an association between acute rSO2 desaturation during cardiac surgery and postoperative cognitive dysfunction. Parnia et al. [14] reported that higher rSO2 during cardiopulmonary resuscitation (CPR) may increase survival with favorable neurologic outcomes. Mailhot et al. [15] reported links between increased cerebral oxygen saturation and delirium resolution and proposed that cerebral oximeters can be used to assess oxygen levels as a biomarker for postoperative delirium in cardiac surgery patients.

In these previous studies, cerebral oxygen saturation was measured by cerebral oximeters as bedside monitors. Nevertheless, they all required that optodes with wires should be attached to the heads of subjects, which limits their applications to those centered around a hospital bed [16–18]. There is a lack of wearable, miniaturized, wireless equipment that could extend brain oxygenation monitoring to motion tasks or tight spaces. Actually, the principal challenges of designing a wearable, wireless oximeter for rSO2 measurement include: (1) designing a device that has a good performance but small and light-weight enough to allow it to be effectively and comfortably coupled to the scalp; (2) designing a miniaturized device that can highly integrate data acquisition and processing modules into a very small structure; (3) ensuring stable data transmission with wireless module and long-term continuous measurement with power supply; (4) considering power consumption, heating, and electrical safety.

In order to expand new experimental and clinical applications for subjects in a limited space or during a motion task, such as astronauts during training or spaceflight [19], we designed a NIRS-based cerebral oximeter, which we call the wearable wireless oxygen saturation monitoring band on head (WORTH band) because the band is designed to be wearable and wireless to measure the rSO2 of ambulatory subjects with self-monitoring. The WORTH band includes two light channels to take advantage of spatially resolved spectroscopy (SRS) technology. Bluetooth wireless technology is used to replace the optical fibers, and a minimized structural design is used to increase the device's comfort. Note that such a wearable wireless system will greatly expand the scope of possible applications for ambulatory monitoring of tissue oxygenation in brain research under natural, unrestrained circumstances, such as a hyperbaric oxygen chamber, human centrifuge training, and sports science.

2 Instrumentation

2.1 Overview

In this study, a miniaturized, modular, wearable and wireless cerebral oximeter WORTH band [20, 21] is designed to measure cerebral oxygen saturation. Figure 1 shows a schematic diagram of the wireless

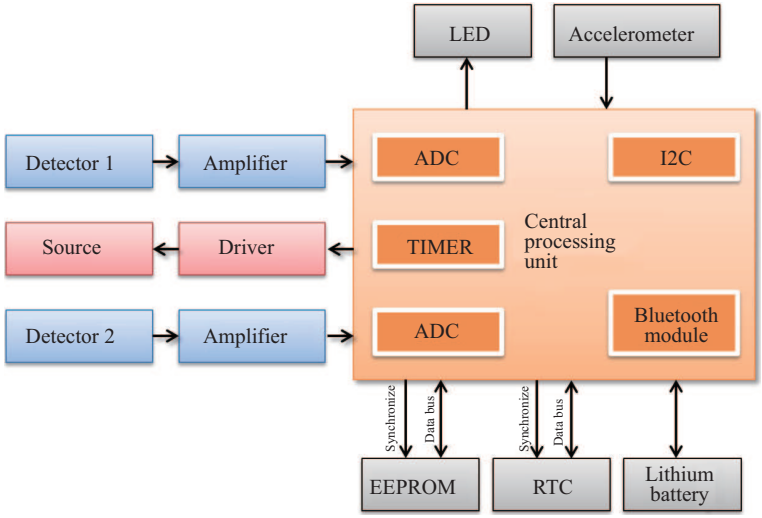

Figure 1 (Color online) Schematic diagram of the wireless cerebral oximeter (WORTH band). LED: light-emitting diode; ADC: analog to digital converter; EEPROM: electrically erasable programmable read only memory; RTC: real-time clock; I2C: inter-integrated circuit.

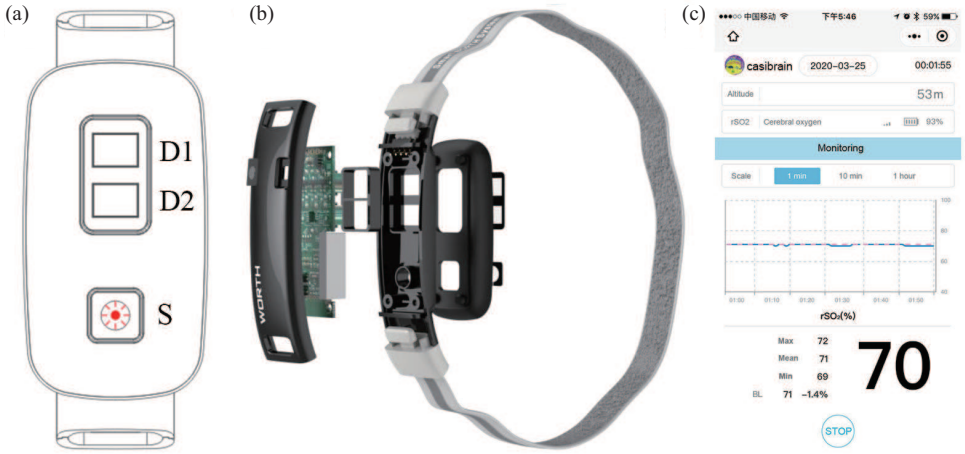

Figure 2 (Color online) The wearable wireless cerebral oximeter (WORTH band). (a) The arrangement of optical parts of the WORTH band; (b) the exploded view of the WORTH band; (c) the GUI interface on a smart phone.

cerebral oximeter, which is 90 mm ×18 mm ×8 mm and weighs 23 g. Figure 2 shows a picture of the wearable wireless cerebral oximeter (WORTH band).

2.2 Optical module

Near-infrared light of two wavelengths, 760 and 840 nm, penetrates through extracranial tissues such as the scalp and skull and eventually reaches the cerebral cortex via a time-multiplexed light emitting diode (LED) source (L760/840-05A) with an average optical output power of approximately 15 mW. As with previous spatially resolved spectroscopy systems [22, 23], the light detectors are two photodiodes positioned 3 and 4 cm from the source. A self-adhesive optode pad, which is made of a flexible medical material, is incorporated for stable and efficient optical contact and comfort.

2.3 System control and GUI

Because the electrical signals converted by photodiodes are low amplitude signals, analog amplifiers first magnify the signals and then transmit them to the ADC modules (12-bit resolution). The acquired data are down-sampled to enable more efficient storage, and the final acquired data rate is ten samples per second for each wavelength and photodiode. The central processing unit of the system is a microcontroller unit (MCU) (CC2540, Texas instruments) chip embedded with a Bluetooth wireless module, which

receives digital signals and processes them using on-chip algorithms. Then the signals are packaged with the time labels and transmitted wirelessly to a terminal such as a smart phone or pad via a Bluetooth module. A user-friendly graphical user interface (GUI) running on these terminals is used to conveniently manage the WORTH band and to display, save, and process the oxygen saturation data in real time. In addition, the oxygen saturation data stored in smart terminals can be uploaded to a cloud workstation so that the data can be shared with others in real time.

2.4 Power supply

The cerebral wireless oximeter WORTH band is powered by a 3.7 V lithium battery with a total capacity of 80 mAh. It is capable of working continuously for more than 24 h without recharging. The sampling rate can be decreased to increase the working time in applications that require long-term and dynamic recording.

2.5 Algorithm

The Beer-Lambert Law states that the transmission of light through a solution is a logarithmic function of the density or concentration (C) of the absorbing molecules in the solution. The intensity of the transmitted light is also a function of the pathlength (l) of light through the solution and the specific extinction coefficient (ε) for the material at the given wavelength (λ). Hence this law can be written as

$$I_{\text{out}} = I_{\text{in}} \cdot 10^{-\varepsilon \cdot C \cdot l} = I_{\text{in}} \cdot 10^{-\varepsilon \cdot C \cdot \text{DPF} \cdot d}, \tag{1}$$

where I_{in} and I_{out} denote the intensity of incident and transmitted light, respectively. DPF indicates the differential pathlength factor. d indicates the distance between source and detector. D_λ indicates the optical density for the wavelength λ. To take into account the scattering effect S_λ, a modified Beer-Lambert Law has been proposed. It calculates the optical density as

$$D_\lambda = -\log_{10} \frac{I_{\text{out}}}{I_{\text{in}}} = \varepsilon \cdot C \cdot \text{DPF} \cdot d + S_\lambda. \tag{2}$$

Eq. (2) describes the transmission of NIR photons into the brain. They undergo attenuation as a result of scattering and absorption by different chromophores. Optical densities are measured at several wavelengths selected for their proximity to the absorption peaks of the chromophores of interest. When investigating oxygenation, the dominant chromophores include HbO and Hb. Then the equation will be

$$D_\lambda = (\varepsilon_{\lambda 1,\text{HbO}} \cdot C_{\text{HbO}} + \varepsilon_{\lambda 1,\text{Hb}} \cdot C_{\text{Hb}}) \cdot \text{DPF} \cdot d + S_\lambda. \tag{3}$$

As typical spatially resolved spectroscopy (SRS) requires [22,24,25], two detectors located at d_1 and d_2 away from the source are used to collect light transmitted from the head. The subtraction of the optical density of the two detectors would remove the effect of scattering, S_λ. In other words, the combination of two detectors could enable the deduction of light attenuation from extracranial tissues, such as scalp and skull [23]. As for the noise, we consider two kinds of noise involved into the system, burst noise and physiological noise. We use a median filter to remove the burst noise. When there is a sample point captured, five continual points would have been measured. The median filter would be used on the five values to product a sample point. In order to remove physiological noise, we take advantage of low pass filter with the cutoff frequency at 0.5 Hz. Physiological noise can be thought as a kind of systematic noise, since the noise would contaminate light density of two detectors homogeneously. Therefore, the ratio of the light intensity of two detectors would also be helpful to suppress physiological noise. When two wavelengths of near infrared light are projected into the head, the subtraction of their optical densities by two detectors will be

$$D_{\lambda 1,d1} - D_{\lambda 1,d2} = (\varepsilon_{\lambda 1,\text{HbO}} \cdot C_{\text{HbO}} + \varepsilon_{\lambda 1,\text{Hb}} \cdot C_{\text{Hb}}) \cdot \text{DPF} \cdot (d1 - d2), \tag{4}$$

$$D_{\lambda 2,d1} - D_{\lambda 2,d2} = (\varepsilon_{\lambda 2,\text{HbO}} \cdot C_{\text{HbO}} + \varepsilon_{\lambda 2,\text{Hb}} \cdot C_{\text{Hb}}) \cdot \text{DPF} \cdot (d1 - d2). \tag{5}$$

To increase the efficiency of solving the above equations, near infrared light is chosen at the isobestic point near 800 nm where the absorptivity of Hb and HbO are equal [26]. Hence Eq.(5) will be

$$D_{\lambda 2,d1} - D_{\lambda 2,d2} = \varepsilon_{\lambda 2} \cdot (C_{\text{HbO}} + C_{\text{Hb}}) \cdot \text{DPF} \cdot (d1 - d2). \tag{6}$$

Combining (4) and (6), we can calculate a ratio as

$$\begin{aligned}\frac{C_{\mathrm{HbO}}}{C_{\mathrm{HbO}}+C_{\mathrm{Hb}}} &= \left(\frac{\varepsilon_{\lambda 1,\mathrm{Hb}}}{\varepsilon_{\lambda 1,\mathrm{Hb}}-\varepsilon_{\lambda 1,\mathrm{HbO}}}\right)\left[1-\left(\frac{\varepsilon_{\lambda 2}}{\varepsilon_{\lambda 1,\mathrm{Hb}}}\right)\left(\frac{D_{\lambda 1,d1}-D_{\lambda 1,d2}}{D_{\lambda 2,d1}-D_{\lambda 2,d2}}\right)\right] \\ &= -\left(\frac{\varepsilon_{\lambda 2}}{\varepsilon_{\lambda 1,\mathrm{Hb}}-\varepsilon_{\lambda 1,\mathrm{HbO}}}\right)\left(\frac{D_{\lambda 1,d1}-D_{\lambda 1,d2}}{D_{\lambda 2,d1}-D_{\lambda 2,d2}}\right)+\left(\frac{\varepsilon_{\lambda 1,\mathrm{Hb}}}{\varepsilon_{\lambda 1,\mathrm{Hb}}-\varepsilon_{\lambda 1,\mathrm{HbO}}}\right) \\ &= -\alpha\left(\frac{D_{\lambda 1,d1}-D_{\lambda 1,d2}}{D_{\lambda 2,d1}-D_{\lambda 2,d2}}\right)+\beta,\end{aligned} \tag{7}$$

where

$$\alpha=\frac{\varepsilon_{\lambda 2}}{\varepsilon_{\lambda 1,\mathrm{Hb}}-\varepsilon_{\lambda 1,\mathrm{HbO}}} \quad \text{and} \quad \beta=\frac{\varepsilon_{\lambda 1,\mathrm{Hb}}}{\varepsilon_{\lambda 1,\mathrm{Hb}}-\varepsilon_{\lambda 1,\mathrm{HbO}}}. \tag{8}$$

Because regional cerebrovascular oxygen saturation is a quantitative measure of hemoglobin saturation in the combined arterial, venous, and microcirculatory compartments of the brain, it can be measured by the ratio of the concentration of oxygenated hemoglobin (C_{HbO}) to the concentration of total hemoglobin ($C_{\mathrm{HbO}}+C_{\mathrm{Hb}}$) [27]. Then

$$\mathrm{rSO2}=C_{\mathrm{HbO}}/(C_{\mathrm{HbO}}+C_{\mathrm{Hb}})=-\alpha\left(\frac{D_{\lambda 1,d1}-D_{\lambda 1,d2}}{D_{\lambda 2,d1}-D_{\lambda 2,d2}}\right)+\beta. \tag{9}$$

In (9), parameters α and β will be known once we set the infrared light wavelengths to 760 and 840 nm because the absorption coefficients of HbO and Hb ($\varepsilon_{\lambda 1,\mathrm{HbO}}$, $\varepsilon_{\lambda 1,\mathrm{Hb}}$, and $\varepsilon_{\lambda 2}$) are in the near infrared spectrum. Since the wireless cerebral oximeter in this study is based on the same theory as other cerebral oximeters, the cerebral oxygen saturation can be considered to be a mixture of oxygen saturations, composed of 70% venous, 25% arterial blood, and 5% capillaries [28].

3 Experiments and results

In this study, two experiments were conducted to validate the performance of the wireless cerebral oximeter. The first was a controlled hypoxia sequence at steady-state levels to measure cerebral oxygen saturation. The level of blood oxygen saturation was reduced in a controlled manner by altering the inspired oxygen concentration (FiO2) to achieve arterial oxygen saturation plateaus between 100% and 75% as measured by a finger pulse oximeter. The second one was a squat-to-stand task, the purpose of which was to verify the capability of the WORTH system to measure rapid hemodynamic changes when the body position changes dramatically. Twenty participants (18 males, age range in 22–43) were recruited for this study. Specifically, eleven subjects participated in the first experiment, and nine subjects participated in the second experiment. They were all healthy adult volunteers and had no neurological or psychiatric disorders. Written informed consent was obtained from each participant prior to the initiation of any pre-study examination. The experimental protocols were approved by the ethics committee of the Institute of Automation, Chinese Academy of Sciences. The analysis was conducted on MATLAB (The Mathworks Inc., Natick, Massachusetts, USA) 2013a platform. In this paper, all the experimental results are indicated as means ± standard error (SE), unless otherwise noted. The Pearson correlation coefficient was used to investigate the correlation between the different variables. The differences were accepted as significant when $p<0.05$.

3.1 Controlled hypoxia experiment

This experiment was performed to compare the performance of the WORTH band with a commercial cerebral oximeter FORE-SIGHT (CAS Medical Systems, Inc., Branford, CT, USA), which is approved for clinical use by the United States Food and Drug Administration (USFDA). The differences in performance between the two systems were compared quantitatively and statistically.

The protocol for this controlled hypoxia experiment was designed based on the work by Benni et al. [29]. As shown in Figure 3, the blood oxygen level was gradually reduced by adjusting the inspired oxygen concentration to achieve SpO2 (measured by a finger pulse oximeter YX301, Yuwell Medical Systems) between 100% and 75% during the experiment [29]. Baseline data were acquired for ten minutes

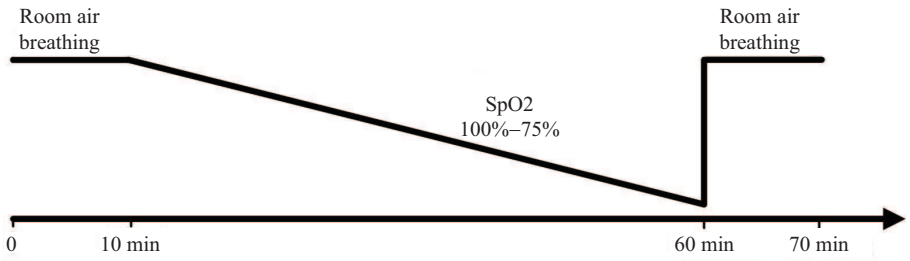

Figure 3 The experimental protocol of the controlled hypoxia experiment.

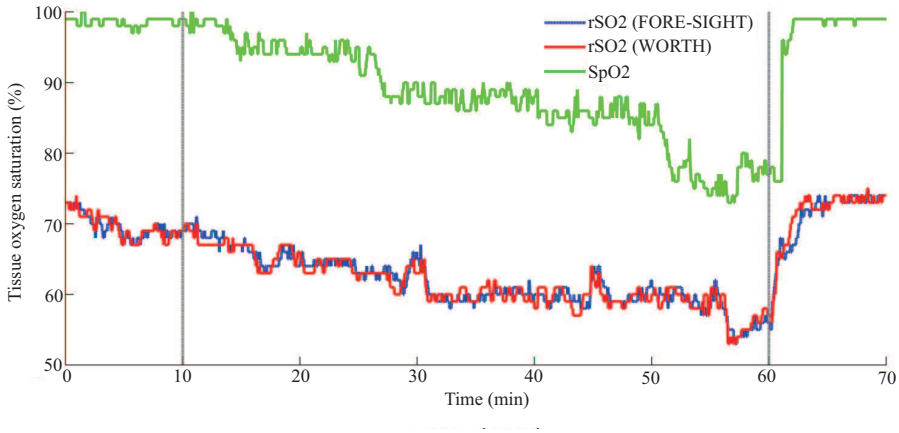

Figure 4 (Color online) Tissue oxygen saturation of a single participant during the controlled hypoxia experiment. The red, blue, and green curves indicate the rSO2 of the WORTH band, the rSO2 of the FORE-SIGHT oximeter, and the SpO2, respectively. The duration of the low concentration oxygen inhalation is indicated by the space between the two gray lines.

(normal room air breathing) before the hypoxia sequence. Five SpO2 platform levels were, in turn, 95% (11–20 min), 90% (21–30 min), 85% (31–40 min), 80% (41–50 min), and 75% (51–60 min). Finally, the cerebral oxygen saturation values were further recorded under normal room air breathing for ten minutes. Throughout the experiment, the wireless oximeter WORTH was placed on the forehead over the frontal cortex to record the rSO2. The participant's tolerance of the experimental protocol was assessed continually throughout the experiment and, if necessary, the study was prematurely terminated at the subject's request. Reliable data were obtained from five subjects. To further compare the performance between the WORTH band and the commercial cerebral oximeter FORE-SIGHT, six participants were required to wear the WORTH band and the FORE-SIGHT oximeter together and the data were recorded synchronously.

In this study, the cerebral oxygen saturation values were calculated from the raw optical density data using the modified Beer-Lambert law and spatially resolved spectroscopy technology, which is illustrated in Subsection 2.5. The results of the tissue oxygen saturations during the low concentration oxygen inhalation experiment are shown in Figure 4.

As shown in Figure 4, during the baseline (room air breathing) period, the SpO2 was stable at $(98.7 \pm 0.2)\%$ while the rSO2 values of the WORTH band and the FORE-SIGHT oximeter remained at approximately $(73.4 \pm 1.6)\%$ and $(73.1 \pm 1.5)\%$, respectively. As the inspired oxygen concentration was slowly reduced, the SpO2 gradually dropped to $(70.3 \pm 1.2)\%$. At the same time, the cerebral oxygen saturation of the WORTH band and the FORE-SIGHT oximeter decreased respectively to $(57.7 \pm 0.9)\%$ and $(61.1 \pm 0.8)\%$. After the controlled hypoxia sequence, the participant was allowed to breathe room air, and the SpO2 increased steeply and returned to the baseline level immediately. Similarly, the rSO2 increased steeply and immediately for both the WORTH band and the FORE-SIGHT oximeter. Moreover, the rSO2 returned to baseline 2.4 ± 0.7 min before the SpO2. Note that the rSO2, as measured by both the systems, reached higher levels than the initial baseline.

The correlation between the readings for the different oxygen saturations in the controlled hypoxia experiment are calculated (Figure 5). Specifically, the changes in rSO2 between the WORTH band

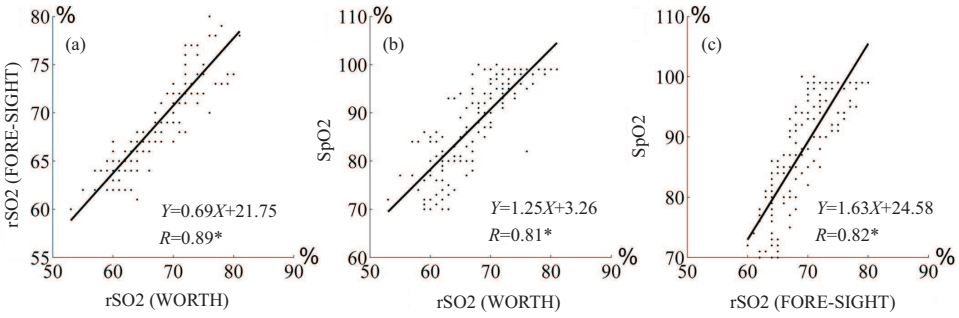

Figure 5 Correlation results of different oxygen saturations for the controlled hypoxia experiment. (a) Correlation of the rSO2 between the WORTH band and the FORE-SIGHT oximeter; (b) correlation between the rSO2 of the WORTH band and the pulse oxygen saturation SpO2; (c) correlation between the rSO2 of the FORE-SIGHT oximeter and SpO2.

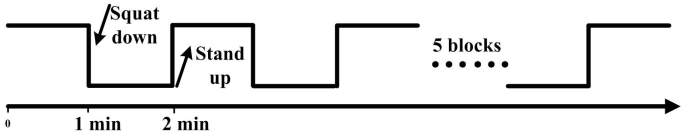

Figure 6 Experimental protocol of the squat-to-stand experiment.

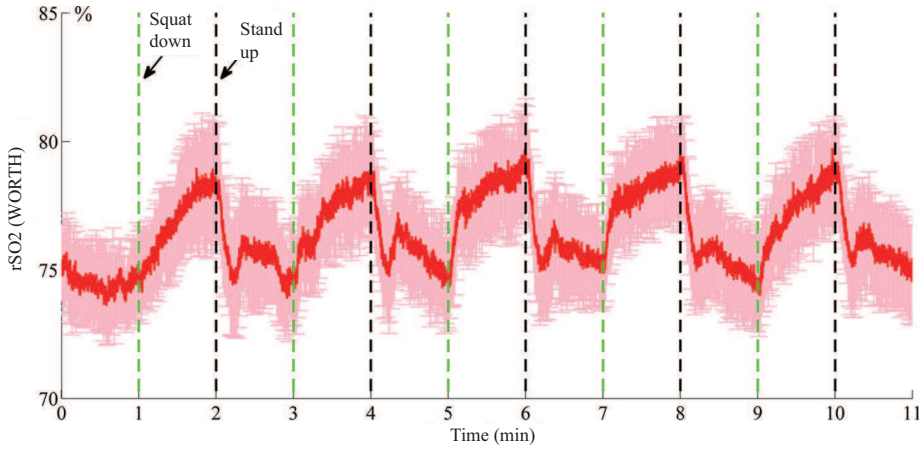

Figure 7 (Color online) The group-averaged results of the squat-to-stand experiment.

and the FORE-SIGHT oximeter were highly correlated with each other throughout the experiment; the correlation coefficient (R) was 0.90 ($p < 0.01$). The difference in the rSO2 between the two systems was $(1.6 \pm 0.2)\%$. The correlation coefficient between the rSO2 (WORTH) and pulse SpO2 was 0.81 ($p < 0.01$). The correlation coefficient between the rSO2 (FORE-SIGHT) and SpO2 was 0.82 ($p < 0.01$).

3.2 Squat-to-stand experiment

This experiment was conducted to test the wearability and reliability of the wireless cerebral oximeter for monitoring cerebral hemodynamics using a squat-to-stand experiment. A block paradigm was employed in this experiment. The entire experimental protocol consisted of an initial baseline period (1 min) followed by five blocks in which each block included squatting for one minute and then quickly standing for one minute. The experimental protocol is shown in Figure 6. The WORTH band oximeter was placed on the forehead of the participants. During the experiment, the participants were instructed to maintain a high level of attention and listen to the commands clearly spoken by a smart phone. The smart phone was also used to configure, display, and save the oxygen saturation data via Bluetooth. We provided a "training" mode before the task. Auditory commands ("squat down" and "stand up") were used to indicate the onset of different actions. The participants were requested to respond as quickly as possible when they heard the commands.

As shown in Figure 7, the rSO2 remained relatively stable during the baseline at $(75.5 \pm 1.3)\%$. In

the squatting period, the rSO2 increased steadily throughout the one minute to $(80.1 \pm 1.5)\%$. Once the standing command was heard and the participants stood up immediately, the rSO2 fell dramatically to $(74.8 \pm 1.8)\%$ within 12.2 ± 0.7 s. Moreover, the rSO2 undershot the baseline before finally settling down after approximately 28 ± 1.2 s. This pattern was repeated consistently for all participants in five runs.

4 Discussion

Cerebral oximeters based on near-infrared spectroscopy have increasingly been used during the perioperative period of cardiovascular operations. They may improve the outcomes of patients in a variety of clinical situations. Evidence for its use beyond cardiac surgery is continuously emerging, but the existing cerebral oximeters are all monitors designed for clinical applications. To further widen the application fields for cerebral oximeters, we designed a wireless cerebral oximeter and validated its performance in two experiments.

4.1 Unique advantages of the wireless oximeter

Cerebral rSO2 can be measured by NIRS because the human brain is translucent to near-infrared light. Pulse oximeters based on NIRS have been utilized in clinical situations for more than two decades. However, they merely measure peripheral arterial SpO2. In contrast to pulse oximeters, cerebral oximeters are independent of pulsatile blood flow [7]. They can provide a non-invasive, objective assessment of cerebral oxygenation saturation even in pulseless conditions and can serve as a warning sign of interoperative hemodynamic or metabolic compromise or as a predictor of postoperative cognitive dysfunction. They can also help clinicians detect and manage regional oxygenation issues under various circumstances, such as during surgeries and anesthesia.

In recent years, clinicians have employed different brands of cerebral oximeters to monitor regional oxygen saturation in a variety of clinical situations [7]. For example, Kussman et al. [30] used a FORE-SIGHT$^{\text{TM}}$ (CAS Medical Systems, Branford, CN, USA) system in children with heart disease and chronic hypoxemia. Vretzakis et al. [31] used an INVOS$^{\text{TM}}$ (Covidien, Inc., Boulder, CO, USA) system to direct blood transfusions during cardiac surgery and reported that INVOS is useful for assisting clinicians in making clinical decisions. The NIRO-200NX (Hamamatsu Photonics, Hamamatsu City, Japan) system has also been used to quantify the impact of extra-cerebral oxygenation. Everdell et al. [18] designed a portable wireless NIRS system in which a multicore cable was used to connect the two parts. The CerOx$^{\text{TM}}$ (Ornim Medical, Lod, Israel) system is based on ultrasound-tagged NIRS, uses three wavelengths between 780 and 830 nm, and measures cerebral and somatic saturation and blood flow. All of the above monitors consist of a control unit and a pair of optodes. The two parts are connected by either fibers or wires. This kind of industrial design limits applications to those around a hospital bed. Moreover, the cables used for light or data transmission could introduce motion artifacts into the measurements. Thus, there is a lack of a wearable and miniaturized detection system for monitoring cerebral oxygen saturation in situations such as sports science, hyperbaric chambers, and pre-hospital settings.

The WORTH band in this study was assembled based on modular architecture and took advantage of wireless communication to transmit and receive signals. It is small (90 mm $\times$18 mm $\times$8 mm in size and 23 g in weight), wireless, and wearable. The rSO2 data was transmitted via Bluetooth to a smart terminator so that the system could be used in various applications without any restriction of wires. A user-friendly interface on a smart phone could both configurate the system and conduct data transformation in real time and conveniently. The oxygen saturation data could be uploaded to a cloud workstation at any time for either backup or sharing with others in real time. Our wireless oximeter was powered by a lithium battery and can work for more than 24 hours continuously without recharging. This allows for longitudinal monitoring even during sleep. Therefore, the wireless oximeter is a highly miniaturized and integrated system that could greatly expand the scope of possible applications such as resuscitation in a pre-hospital setting or brain monitoring under natural, unrestrained circumstances.

4.2 Performance of the WORTH band

To validate the WORTH band oximeter, two experiments were conducted to quantify and assess its performance. In the first experiment, the wireless oximeter was compared statistically with a commercial

brand of equipment using a controlled hypoxia experiment. The second experiment tested the portability of the wireless cerebral oximeter during a moving task using a squat-to-stand experiment.

In the controlled hypoxia experiment, arterial oxygen saturation was gradually decreased from $(98.7 \pm 0.2)\%$ to $(70.3 \pm 1.2)\%$ by turning down the inspired oxygen concentration. Correspondingly, the rSO2 (cerebral oxygen saturation) of both the WORTH band and the FORE-SIGHT oximeter decreased from $(73.4 \pm 1.6)\%$ and $(73.1 \pm 1.5)\%$ to $(57.7 \pm 0.9)\%$ and $(61.1 \pm 0.8)\%$, respectively. Note that the reduction in the SpO2 was greater than that of the rSO2. The reason might be due to the preferential supply of oxygen to the brain in situations where there is an insufficient oxygen supply. After the controlled hypoxia sequence, the participant was requested to breathe room air for ten more minutes; the SpO2 immediately returned to the baseline level. Note that the rSO2 of the two oximeters also increased rapidly but reached higher levels than the initial baseline. Moreover, the slopes of the increases in rSO2 and SpO2 differed during the immediate transition. The rSO2 reached a plateau faster than the SpO2. Throughout the experiment, the trends of the changes in rSO2 as measured by the two systems were highly consistent. The results confirmed that the WORTH band can record cerebral oxygen saturation with an accuracy comparable to that of a commercial clinical monitor. Moreover, the rSO2 (WORTH) was also correlated to the pulse SpO2.

During the squat-to-stand experiment, the rSO2 rose steadily during the squatting period, but once the standing period started, the rSO2 dropped dramatically at first and then increased to undershoot the baseline by a small amount. After that, the rSO2 gradually returned to the baseline. This pattern of cerebral oxygen saturation changes was repeated consistently for all participants in all five runs. The underlying mechanism appears to be that when the participant was squatting for a while, their waists and legs were tortuous and the height of the body was low so that the blood could not flow up and down readily. Therefore, the rSO2 measured over the frontal cortex was higher in the squatting position. When the participant stood up suddenly, the blood pressure in the lower extremities was relieved immediately [29]. When the body posture rapidly changes from a squatting position to a standing position, the stress of gravity on the various organs of the body was different. These changes increased the circulating blood volume of the lower extremities and allowed the cerebral perfusion pressure and cerebral oxygen saturation to drop to a low level, causing head ischemia or temporary insufficiency of cerebral blood supply. Hence the rSO2 decreased steeply when the standing period began. When the blood circulation to the head was restored, the rSO2 could gradually return to the initial baseline. This is why standing up quickly after squatting can cause dizziness. Our results showed that the difference in cerebral oxygen saturation between squatting and standing was around $(5.3 \pm 1.6)\%$. The results also demonstrated that the WORTH band could be used for monitoring cerebral oxygen saturation during physical training, such as motion tasks.

4.3 Limitations

There are some aspects of the design that could potentially be changed to further improve the performance of the wearable wireless oximeter. One of the limitations of the WORTH band is that only two optical channels were used. Future studies using more channels would be helpful for assessing the brain circulation at a higher spatial resolution. A second limitation is that the wireless system could only be used on the forehead. Future modifications of the WORTH band could employ an advanced optode array design that could cover more areas of the brain. Although these issues currently limit the widespread use of the WORTH system, its development and its application in this study are a meaningful step in the development of a portable cerebral oximeter system that will be usable in a variety of situations.

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