To reference this paper:

Leung TS, Wittekind A, Binzoni T, Beneke R, Cooper CE, Elwell CE (2010), Muscle oxygen saturation measured using "cyclic NIR signals" during exercise, *Adv Exp Med Biol*. 662:183-9.

Errata:

Equation (1.1) should read:

$$A_\lambda = \{\varepsilon_{HHb,\lambda}[HHb] + \varepsilon_{HbO_2,\lambda}[HbO_2] + \varepsilon_{Mb,\lambda}[Mb] + \varepsilon_{MbO_2,\lambda}[MbO_2] + \mu_{a,\lambda}^{bk} + \mu'_{s,\lambda}\}l \tag{1.1}$$

Equation (1.2) should read:

$$\begin{aligned} A_{\lambda 1-\lambda 2} &= A_{\lambda 1} - A_{\lambda 2} \\ &= \{\varepsilon_{HHb,\lambda 1-\lambda 2}[HHb] + \varepsilon_{HbO_2,\lambda 1-\lambda 2}[HbO_2] \\ &\quad + \varepsilon_{Mb,\lambda 1-\lambda 2}[Mb] + \varepsilon_{MbO_2,\lambda 1-\lambda 2}[MbO_2] + \mu_{a,\lambda 1-\lambda 2}^{bk} + \mu'_{s,\lambda 1-\lambda 2}\}l \end{aligned} \tag{1.2}$$

Muscle Oxygen Saturation Measured Using "Cyclic NIR Signals" During Exercise

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Abstract A new approach to measure muscle oxygen saturation (SmO_2) using near infrared spectroscopy (NIRS) has been proposed in this paper. This approach exploits the cyclic NIRS signals seen during exercise which are often regarded as "movement artefacts". This new measure, which we term the "cyclic SmO_2", has the potential to be less affected by the myoglobin which is traditionally believed to be indistinguishable from haemoglobin using NIRS techniques. The cyclic SmO_2 also has fewer assumptions than the conventional SmO_2 measured using time, phase and spatially resolved spectroscopy methods. In a cycling exercise study, NIRS measurements were made over the Vastus lateralis muscle of 11 subjects. In a light exercise protocol, the group mean of the conventional SmO_2 was 51.7 ± 4.3% and that of the cyclic SmO_2 was 56.0 ± 3.9%. It was immediately followed by a hard exercise protocol and the group mean of the conventional SmO_2 was reduced to 42.6 ± 6.1% and that of the cyclic SmO_2 to 48.5 ± 5.6%. The reduction agrees with the general expectation. The cyclic SmO_2 is a promising new measure of muscle oxygenation.

1.1 Introduction

Near infrared spectroscopy (NIRS) has been widely used in measuring muscle oxygenation [1,2]. It is well known that NIRS signals are prone to movement artefacts which are especially prominent during exercise. They are often considered as noise and filtered out during data analysis. In this paper, we show that there is evidence to suggest that these movement artefacts or cyclic NIRS signals, as we prefer to call them, contain physiological information about the oxygenation of the muscle. Many commercial NIRS monitors today exploit the diffusion equation to derive muscle oxygen saturation (SmO_2), or more generally tissue oxygen saturation from optical measurements. In this approach, the diffusion equation is solved

based on a particular geometry, for example a homogenous semi-infinite half-space geometry, and a particular set of optical measurements. Examples of this type of monitors include Hamamatsu NIRO-200 (spatially resolved), ISS OxiplexTS (phase resolved) and Hamamatsu TRS-10 (time resolved) [2]. Based on the theoretical solution, an algorithm can be designed to calculate the absorption coefficients, μ_a from optical measurements. The μ_a measured at multiple wavelengths can eventually be converted into oxygen saturation via Beer Lambert law. However, these models assume a homogenous medium which is inevitably different from the reality and affects the accuracy. An obvious example in the muscle application is that a fat layer often exists between the surface mounted optical probe and muscle, making the medium an inhomogeneous one. As a result, reflected light is attenuated not only due to absorption in the muscle but also in the skin and the fat layer.

This paper introduces a new approach to measure SmO_2 during exercise which is not based on the diffusion equation but exploits the Beer Lambert law. The technique therefore does not require the assumption of a particular geometry or homogeneity of the medium. Instead, its principle is based on the assumption that the muscle is squeezed of blood during contraction, and refilled during relaxation. This newly defined measure is known as cyclic SmO_2. Unlike the conventional SmO_2, the cyclic SmO_2 is also expected to be less influenced by myoglobin.

1.2 Methods

1.2.1 Experiments

Eleven trained male subjects with (mean±std) age of 32±11 years, body mass of 77±9 kg, and height of 177±6 cm, participated in the study which was approved by the University of Essex research ethics committee. The peak aerobic power (PAP) was first determined using an incremental cycling protocol. A commercial NIR monitor (NIRO-200, Hamamatsu Photonics KK), which has a sampling frequency of 6 Hz and three wavelengths, i.e. 780, 813 and 853 nm, was used in the study. The optical source and detector were attached to the Vastus lateralis muscle of the subject. Subjects were asked to cycle a mechanically braked cycle ergometer fitted with power cranks at (i) 60 revolutions per minutes (rpm) at 40% of the PAP for 5 minutes (light exercise), and immediately afterwards at (ii) 80 rpm at 110% of the PAP for 1 minute (hard exercise). Three NIRS signals were measured with the NIRS monitor, namely, changes in oxy- and deoxy-haemoglobin concentrations ($\Delta[HbO_2]$ and $\Delta[HHb]$) and tissue oxygenation index (TOI, used as the conventional SmO_2 here).

1.2.2 Data analysis

The attenuation can be described by

$$A_\lambda = \{\varepsilon_{HHb,\lambda}[HHb] + \varepsilon_{HbO_2,\lambda}[HbO_2] + \varepsilon_{Mb,\lambda}[Mb] + \varepsilon_{MbO_2,\lambda}[MbO_2]\}l + \mu_{a,\lambda}^{bk} + \mu'_{s,\lambda} \quad (1.1)$$

where A_λ is the attenuation at wavelength λ, $\varepsilon_{HHb,\lambda}$, $\varepsilon_{HbO2,\lambda}$, $\varepsilon_{Mb,\lambda}$ and $\varepsilon_{MbO2,\lambda}$ are the specific extinction coefficients for deoxy- (HHb), oxy-haemoglobin (HbO_2), deoxy- (Mb) and oxy-myoglobin (MbO_2), [HHb], [HbO_2], [Mb] and [MbO_2] are their concentrations, l is the optical path length, $\mu_{a,\lambda}^{bk}$ is the absorption coefficient accounting for all background absorbers such as water and melanin, and $\mu'_{s,\lambda}$ is the reduced scattering coefficient. It should be noted that the correction factors for the wavelength dependence of path length are embedded within the specific extinction coefficients [3]. In order to reduce the effects of changes in $\mu'_{s,\lambda}$ which could be significant during exercise, the difference of A_λ between two wavelengths is calculated,

$$\begin{aligned} A_{\lambda1-\lambda2} &= A_{\lambda1} - A_{\lambda2} \\ &= \{\varepsilon_{HHb,\lambda1-\lambda2}[HHb] + \varepsilon_{HbO_2,\lambda1-\lambda2}[HbO_2] \\ &\quad + \varepsilon_{Mb,\lambda1-\lambda2}[Mb] + \varepsilon_{MbO_2,\lambda1-\lambda2}[MbO_2]\}l + \mu_{a,\lambda1-\lambda2}^{bk} + \mu'_{s,\lambda1-\lambda2} \end{aligned} \quad (1.2)$$

In the calf muscle, $\mu'_{s,\lambda}$ decreases steadily by 0.8% per 10 nm between 760 and 900 nm [4]. Therefore, $\mu'_{s,\lambda1-\lambda2}$ is expected to be small when λ_1 and λ_2 are reasonably close to each other. This approach has the same rationale as the dual wavelength photometry previously described in the literature [5]. Fig.1 depicts an example of the $A_{780-813}$ signals obtained from a subject during exercise. It can be seen that the cyclic signal resembles a sinusoid and the amplitude of the sinusoid can be considered as the difference between the peak (point X in the figure) and mean (point Y) values which can also be written as:

$$\Delta A_{\lambda1-\lambda2} \approx \{\varepsilon_{HHb,\lambda1-\lambda2}\Delta[HHb] + \varepsilon_{HbO_2,\lambda1-\lambda2}\Delta[HbO_2]\}l \quad (1.3)$$

It is assumed that both the background absorption and the amount of myoglobin do not change significantly during exercise. Therefore both terms are expected to be small and can be neglected from equation (1.3). To estimate the amplitude of the cyclic signal, the discrete Fourier transform (DFT) has been used. Both the fundamental and the first harmonic are often present in the amplitude spectrum. $\Delta A_{\lambda1-\lambda2}$ is then estimated as the total area (bandwidth=0.5 Hz) under the two spectral peaks. In this work, both $\Delta A_{780-813}$ and $\Delta A_{853-813}$ have been calculated,

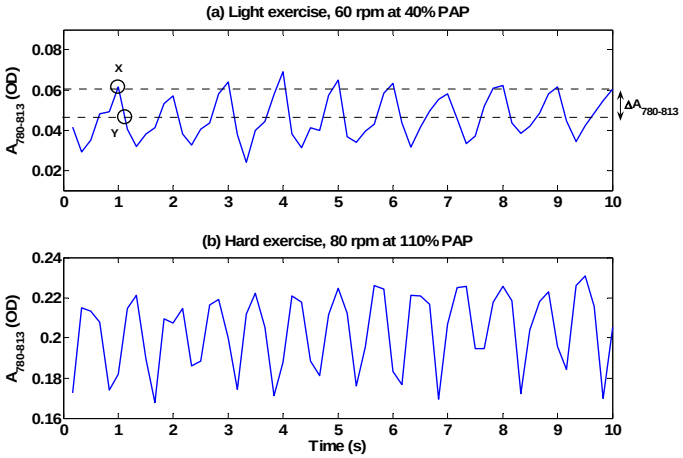

Fig. 1 An example of the cyclic optical signals $A_{780\text{-}813}$ in one subject during (a) light exercise, and (b) hard exercise. The scattering is greatly reduced in the $A_{780\text{-}813}$ signal and the signal's absolute amplitude contains mainly two parts, namely the constant (DC) and the varying (AC) parts. Absorption due to background absorbers and myoglobin are expected to be the same during exercise and are therefore regarded as the DC part. The AC part (the cyclic signal) predominantly accounts for the absorption changes caused by a portion of blood shifting in and out of the muscle during exercise. The amplitude of the AC part, i.e. $\Delta A_{780\text{-}813}$, is relatively free from the effects of scattering and other constant absorbers (the DC part).

and then converted into Δ[HHb] and $\Delta[HbO_2]$ by using multi-linear regression based on equation (1.3). Both Δ[HHb] and $\Delta[HbO_2]$ here can be considered as the amplitudes of the cyclic signals. The cyclic SmO_2 is defined as: cyclic SmO_2 = $\Delta[HbO_2]$ / ($\Delta[HbO_2]$+ Δ[HHb]).

Two sections of data were analysed for each subject, i.e. 30 s of data during the light (started from 3 mins into the exercise) and hard (started from 25 s into the exercise) exercises respectively. For each section of data, the mean conventional SmO_2 and one cyclic SmO_2 were calculated. To derive the cyclic SmO_2, the size of the DFT was 60 samples (=10 s) and a Hanning window of the same size was used with 50% (5 s) overlap. For 30 s of data, four amplitude spectra were obtained which were averaged to one smoothed spectrum from which the cyclic SmO_2 was calculated as described earlier.

A larger size for the DFT and the averaging of spectra would both ensure a more robust cyclic SmO_2 over time, but would also lead to a poorer time resolution. In using the parameters described above, only one value of cyclic SmO_2 can be calculated for 30 s worth of data. To illustrate how the cyclic SmO_2 compared with conventional SmO_2 in a finer time resolution, a different set of parameters were used to calculate the cyclic SmO_2 in one subject, i.e. the size of DFT = 12 samples (2 s) with 50% (1 s) overlap and no spectra averaging. Figure 2 shows both TOI and cyclic SmO_2 in transition from light to hard exercise.

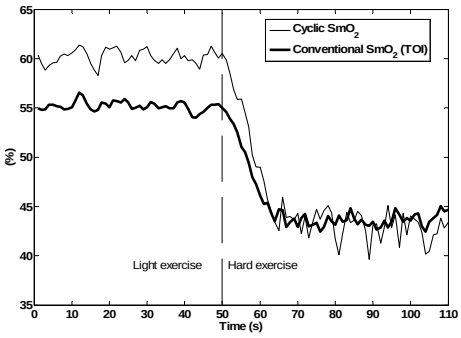

Fig. 2 Conventional (TOI) and cyclic SmO_2 in transition from light to hard exercise in one subject. DFT size = 12 samples: mean cyclic SmO_2 for the light exercise (time 0 – 30s) = 60.2% and that for the hard exercise (time 80 – 110s) = 43.0%. For comparison, DFT size = 30 samples: cyclic SmO_2 for the light exercise = 59.3% and that for the hard exercise = 42.3%.

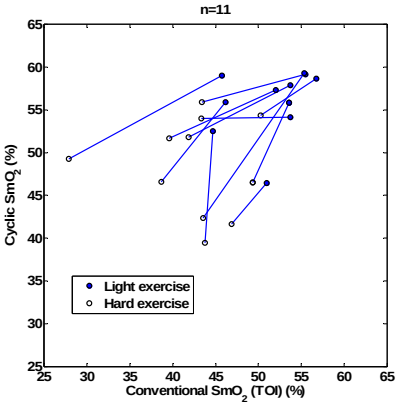

Fig. 3 Conventional (TOI) and cyclic SmO_2 for all 11 subjects during light and hard exercise

Figure 3 depicts the conventional and cyclic SmO_2 during light and hard exercise in 11 subjects. In all subjects, both the conventional and cyclic SmO_2 are higher during light exercise than during hard exercise. This is indeed expected from a physiological point of view because in muscle undergoing a more intense exercise regime the oxygen consumption increase is greater than any compensatory change in muscle blood flow. As less oxygen remains in the muscle, a lower SmO_2 is expected. Table 1.1 shows the group mean and standard deviation of the conventional and cyclic SmO_2 during light and hard exercise. The cyclic SmO_2 has higher means and smaller standard deviations in both light and hard exercise.

Table 1. Group mean and standard deviation of the conventional (TOI) and cyclic SmO_2 during light and hard exercise in 11 subjects

	Light exercise	Hard exercise
Conventional SmO_2 / TOI (%)	51.7 ± 4.3	42.6 ± 6.1
Cyclic SmO_2 (%)	56.0 ± 3.9	48.5 ± 5.6

1.3 Discussion

The measurement of cyclic SmO_2 requires the generation of cyclic NIRS signals from the exercising muscle. Previous research showed that muscle blood flow in

both the artery and vein is decreased during muscle contraction, and increased during muscle relaxation due to changes in intramuscular pressure, a mechanism known as the "skeletal muscle pump" [6-7]. The main assumption in our technique is that the cyclic NIRS signal $\Delta A_{\lambda 1-\lambda 2}$ is predominantly caused by absorption changes due to a portion of blood shifting in and out of the muscle during exercise. This portion of shifting blood can be considered as the net change of blood volume caused by contraction and relaxation during muscle exercise. It is expected that the venous blood accounts for a larger proportion of the shifting blood because the venous compartment has a lower pressure therefore allowing a larger blood volume change. As a result, the cyclic SmO_2 should be more biased towards venous oxygen saturation. We also assume that the thickness of the fat layer does not change significantly during exercise and that the blood vessels inside the fat are not "squeezed" or redistributed. Exercising muscle would undergo both anatomical and blood flow changes, both of which cause scattering changes. To reduce the effect of scattering changes during exercise, the dual wavelength photometry algorithm was introduced in this work. Myoglobin and haemoglobin have very similar absorption spectra and they are often considered indistinguishable using NIRS [1-2]. The cyclic SmO_2 is able to minimize the effect of myoglobin because the amount of myoglobin in the probed muscle is expected to remain constant during the exercise and the algorithm of the cyclic SmO_2 is capable of subtracting off the effect of any constant absorbers. However, the accuracy of the cyclic SmO_2 is still to be affected by the wavelength dependency of path lengths which is a factor applicable to all NIRS problems in general [4].

Acknowledgments The authors would like to thank Hamamatsu Photonics KK. and the EPSRC (EP/F006551/1) for their financial support of this work.

References

1. Quaresima V, Lepanto R, Ferrari M (2003) The use of near infrared spectroscopy in sports medicine. J. Sports Med Phys Fitness **43**: 1-13
2. Wolf M, Ferrari M, Quaresima V (2007) Progress of near-infrared spectroscopy and topography for brain and muscle clinical applications. J. Biomed. Opt. **12**(6): 062104
3. Essenpreis M, Elwell CE, Cope M, et al (1993) Spectral dependence of temporal point spread functions in human tissues. Appl. Opt. **32**(4), 418-425
4. Matcher SJ, Cope M, Delpy DT (1997) In vivo measurements of the wavelength dependence of tissue-scattering coefficients between 760 and 900 nm measured with time-resolved spectroscopy. Appl. Opt. **36**(1), 386-396
5. Hoshi Y, Hazeki O, Kakihana Y, Tamura M (1997) Redox behaviour of cytochrome oxidase in the rat brain measured by NIRS. J. Appli. Physiol. **83**(6) 1842-1848
6. Lutjemeier BJ, Miura A, Scheuermann BW, et al (2005) Muscle contraction-blood flow interactions during upright knee extension exercise in humans. J. Appl. Physiol. **98** 1575-1583
7. Dobson JL, Gladden LB (2003) Effect of thythmic titanic skeletal muscle contractions on peak muscle perfusion. J. Appl. Physiol. **94** 11-19.