Investigation of spatial resolution dependent variability in transcutaneous oxygen saturation using point spectroscopy system

Sheena P Philimon, Audrey K C Huong, Xavier T I Ngu

Faculty of Electrical and Electronic Engineering, Universiti Tun Hussein Onn Malaysia, Batu Pahat, Johor, Malaysia

Corresponding author: audrey@uthm.edu.my

Abstract. This paper aims to investigate the variation in one's percent mean transcutaneous oxygen saturation (StO2) with differences in spatial resolution of data. This work required the knowledge of extinction coefficient of hemoglobin derivatives in the wavelength range of 520 – 600 nm to solve for the StO2 value via an iterative fitting procedure. A pilot study was conducted on three healthy subjects with spectroscopic data collected from their right index finger at different arbitrarily selected distances. The StO2 value estimated by Extended Modified Lambert Beer (EMLB) model revealed a higher mean StO2 of 91.1 ± 1.3% at a proximity distance of 30 mm compared to 60.83 ± 2.8% at 200 mm. The results showed a high correlation between data spatial resolution and StO2 value, and revealed a decrease in StO2 value as the sampling distance increased. The preliminary findings from this study contribute to the knowledge of the appropriate distance range for consistent and high repeatability measurement of skin oxygenation.

1. Introduction

An accurate and reliable diagnosis tool for noninvasive measurement of tissue oxygenation is highly sought after in the biomedical field. Researches on optical investigation of skin oximetry has begun since 1980s [1], this topic has continued to gain extensive interest over the years with works evolving from point probe spectroscopy to highly advanced hyperspectral imaging system which allows in vivo visual assessment of oxygen saturation mapping [2-5]. This is owing to the noninvasive property of the system which allowed it to be employed on wounded or grafted skin. Furthermore, the application of this system is deemed more hygienic for clinical practice as compared to the conventional fingertip pulse oximeter wherein measurement of blood oxygen saturation using the latter technology required direct contact with the epidermal skin surface.

However, the main concern with the use of noninvasive spectroscopic system is the consistency and repeatability in the measurement of transcutaneous oxygen saturation (StO2) value. This value may vary due to several reasons such as changes in spatial and spectral resolution of the data. Previous studies [6] showed that inconsistency in the StO2 mapping obtained from the processing of spectroscopic images may be due to poor spatial resolution of data. Common technique used in the prediction of blood oxygen saturation is normally based on the wavelength dependent molar extinction coefficient of the medium absorbers, but the consistency of this value may be reduced with poor spatial resolution of the acquired data; this is largely caused by inconsistency in the angle of light.
reflected and scattered from the skin site before reaching the detection. Several initiatives were taken to solve this problem by statistical method of image reconstruction to reduce unwanted noise and improve spatial resolution. However, these methods involved complicated techniques such as additional analysis and algorithm to produce a uniform resolution [7]. Photoacoustic imaging had gained immense interest in clinical diagnosis and monitoring because of its high specificity of optical technique and high spatial resolution [8]. This research showed that spatial resolution is dependent on the penetration depth of the wave in the measurement of the absolute chromophore concentration.

Thus far, no work has yet been done to investigate variability and rate of changes in one's 
\[S\text{O}_2\] value with the differences in detector - skin sample separation. It is, therefore, the focus of this paper to investigate the variation in the mean 
\[S\text{O}_2\] value with differences in the detection range. This work assumed that data spatial resolution is linearly related to the sampling distance between the detector and targeted skin sample.

2. Materials and methods

2.1. Point spectroscopy system and experimental procedure

Figure 1 shows the arrangement of optical system used in this work. The employed light source was a 9W white light emitting diode (LED) (from Lumiled Inc.) for illumination of skin surface. A commercial spectrometer (USB4000-UV-VIS-ES, Ocean Optics Inc., Florida) was used to detect the reflected light signals by means of a linear charge coupled detector (CCD) array and using the integration time of 100 ms. The former also has a built-in diffraction grating element to diffract the reflected light into a spectrum; this detection system is able to detect light intensity across spectral range of 200 – 850 nm with a sampling size of 0.2 nm. Signals detected were sent to a computer for further offline processing. In this system, the light source was placed at an angle of 10˚ from normal and at a distance of 80 mm from skin surface. Light reflected from skin surface was collected into an optical fiber with its tip positioned at an angle of approximately 30˚ from normal as shown in Figure 1. The arbitrarily selected distance between the fiber tip and the measurement sample were 30 mm, 50 mm, 100 mm, 150 mm and 200 mm while maintaining the same illumination and detection angle. The position of the light source remained consistent throughout these measurements. Three spectroscopic data were consecutively collected from each subject and the average of these data was taken to reduce the effects of signal noise.

Figure 1. Noncontact point spectroscopy system.

The estimation of percent 
\[S\text{O}_2\] value is based on the measured light attenuation. The white and dark reference data were taken for the calculation of the wavelength dependent light attenuation given by [9]
A(\lambda) = \log \frac{I_{\text{white}}(\lambda) - I_{\text{dark}}(\lambda)}{I_{\text{sample}}(\lambda) - I_{\text{dark}}(\lambda)}

(1)

where \( I_{\text{sample}}, I_{\text{white}} \), and \( I_{\text{dark}} \) represent reflectance data of the targeted skin sample, white and dark reference, respectively. The white reflectance data was given by the reflectance of a spectralon (from Labsphere, Inc.) with 99% reflectance whereas the dark reference was taken with optical fiber tip entrance blocked with a shutter.

A preliminary experiment was conducted on three nonsmoking healthy individuals, both male and female, aged between 26 and 27. Based on the report of the previous work [10] that showed high consistency in the predicted \( S_O^2 \) for fourteen Asian recruits using the similar optical system, it is reasonable to assume that this number of subject recruitment was adequate for this study. The work in [10] revealed a consistently low temporal fluctuation in \( S_O^2 \) around the value of 90% when subjects were in resting condition. This study conducted all the experiments in a dark room to reduce interference of stray light. Prior to the experiment, all subjects were required to provide their informed consent to declare no underlying illnesses such as heart and lung diseases, anemia, diabetes and asthma. Subjects were first acclimatized to a controlled room temperature set at 24 °C for a period of 15 minutes before noncontact reflectance spectroscopic data were measured from the right index finger at rest condition. Throughout the measurement, each subject was instructed to breathe normally and to sit in an upright position with their arm stretched and relaxed to allow unimpeded blood flow.

2.2. Extended Modified Lambert Beer model
This work employed Extended Modified Lambert Beer (EMLB) model proposed by Huong and Ngu [11] shown in Equation (2) in the estimation of percent \( S_O^2 \). This model is an extended version of the Modified Lambert Beer (MLB) model [12] by adding the third and fourth term into the equation. The derivation of the EMLB model has been extensively discussed by Huong and Ngu [11] but it is briefly discussed again in the following.

\[
A(\lambda) = G_0 + \mu_\lambda d_\lambda + G_\lambda \lambda + \lambda \exp(-\mu_\lambda d_\lambda)
\]

(2)

The third term in Equation (2), \( G_\lambda \lambda \), represents wavelength dependent light attenuation due to absorption and scattering processes in the epidermal layer. The fourth term is an exponential function included in the model to represent the effects of a nonlinear wavelength dependent scattering processes on the measured attenuation. The accuracy of the oxygen saturation value predicted using the EMLB model was validated using Monte Carlo method. The result showed that this model is able to predict the required oxygen saturation parameter value with a mean absolute error of approximately 0.4% as compared to 10% produced by MLB [11]. Light absorption, \( \mu_\lambda \), in Equation (2) is given from the extinction coefficient of oxyhemoglobin, \( \varepsilon_{\text{HbO}_2} \), and deoxyhemoglobin, \( \varepsilon_{\text{Hb}} \), as follows:

\[
\mu_\lambda (\lambda) = \left((\varepsilon_{\text{OxyHb}}(\lambda) - \varepsilon_{\text{Hb}}(\lambda))S_O^2 + \varepsilon_{\text{Hb}}(\lambda)\right)T
\]

(3)

where \( T \) is the total blood concentration and is given by the summation of the concentration of considered hemoglobin components. The \( S_O^2 \) shown in Equation (3) is defined as the fractional concentration of oxyhemoglobin with respect to \( T \). The values of \( \varepsilon_{\text{HbO}_2} \) and \( \varepsilon_{\text{Hb}} \) were from the report of Zijlstra et al. [13]. This work considered only their extinction spectrum in the wavelength range of 520 – 600 nm due to the distinctive differences of their absorption characteristics across this wavelength range (indicated by the red box) shown in Figure 2.
Figure 2. Wavelength dependent extinction coefficient of hemoglobin derivatives from the reports of Zijlstra et al. [13]. The recruited wavelength range is indicated by the red box.

2.3. Iterative fitting procedure
An iterative fitting routine was applied to seek for the optimum $S_{O_2}$ value using the *fminsearch* unconstrained nonlinear optimization function available in MATLAB. An initial value of '1' was assigned to the unknown parameters in Equation (2) before this fitting function iteratively sought the new value of fitting parameters based on the size of error between the value given from the EMLB and the real attenuation value, $\Delta E$. This fitting process was terminated when either the absolute mean $\Delta E$ is less than $1 \times 10^{-20}$ or the number of iteration has achieved 1000, whereby an optimum $S_{O_2}$ value was assumed to have attained.

3. Results and discussion
The percent $S_{O_2}$ was predicted for the right index fingers of three recruited subjects (identified as subject A, B and C) using the proposed method described in Section 2.1. Three measurements were consecutively taken from each subject at the considered five different detection distances; and the obtained mean $S_{O_2}$ reported for each distance is presented in Table 1. The calculated overall mean and standard deviation (SD) of $S_{O_2}$ at different detection-skin separation is also shown in Table 1 and plotted in Figure 3. The mean in the predicted $S_{O_2}$ for different detection system-skin site distance was evaluated and compared using a one way ANOVA in SPSS software (SPSS 22, Inc., Chicago, Illinois) with confidence level of 95%. The result revealed a statistically significant value of $\rho = 0.000$ in its correlation test. In the effort to investigate the performance of the employed system, the sum of detected photon flux for each detection distance was calculated and tabulated in Table 2.
Table 1. Comparison of average mean and standard deviation (SD) of \( \text{S}_2\text{O}_2 \) predicted for different subjects at varying detection system - skin site separation.

| Subject | Estimated percent \( \text{S}_2\text{O}_2 \) (mean ± SD) |
|---------|-------------------------------------------------------|
|         | 30 mm   | 50 mm   | 100 mm  | 150 mm  | 200 mm  |
| A       | 94.1±0.6% | 88.5±0.6% | 84.2±1.0% | 73.5±2.6% | 65.4±4.6% |
| B       | 90.5±1.9% | 79.6±1.0% | 77.4±2.7% | 73.1±1.5% | 57.9±2.5% |
| C       | 88.7±1.4% | 86.3±1.1% | 79.1±2.3% | 76.4±3.2% | 59.2±1.2% |
| Overall mean ± SD | 91.1±1.3% | 84.8±0.9% | 80.2±2.0% | 74.3±2.4% | 60.8±2.8% |

Table 2. Average photon flux detected at different detection distance.

| Detection distance (mm) | Average photon flux (pixel) |
|-------------------------|----------------------------|
| 30                      | 4312500                    |
| 50                      | 4475700                    |
| 100                     | 3118300                    |
| 150                     | 2197400                    |
| 200                     | 2278100                    |

Figure 3. The overall mean and standard deviation of \( \text{S}_2\text{O}_2 \) predicted for the recruited volunteers at different detection system - skin surface separation (in mm).

The results presented in Table 1 showed the variability of the mean \( \text{S}_2\text{O}_2 \) depending on the separation between the detection system and targeted skin sample, while Table 2 revealed a decrease
in the signal level of the collected data with an increase detection distance. The reduce in the average photon flux resulted in the lowering signal to noise performance, this is then propagated through analysis and given rise to the increase uncertainty in the predicted \( S_2 \). It must also be mentioned that the large separation between the detection system and skin sample yields large field of view of imaging. This renders a reduce data spatial resolution and imaging specificity, and the detection of signals reflected from region other than the examined skin sample, which is then lead to a reduce \( S_2 \). These are confirmed with the decrease in the mean value and an increase in the variation of \( S_2 \) shown in Table 1.

Meanwhile, the analysis of data using a one way ANOVA test showed significant differences \( (\rho = 0.000) \) in the predicted mean \( S_2 \) between groups (different separation of detection system - skin site). It is found in this work that at a distance of 30 mm, the \( S_2 \) estimated by the EMLB is significantly high with a mean value of 91.1 ± 1.13\% . This is followed by mean \( S_2 \) of 84.8 ± 0.9\% for detection distance of 50 mm. These values are comparable to that observed in the works of previous researchers who used different analytical model namely Kubelka Munk [14] and Cumulant based forward model (CM) [15, 16]. The results in Table 1 and Figure 3 also revealed small standard deviation among these subjects, indicating good repeatability of the analytical technique and the proposed experimental method when the imaged skin site is of close proximity to the detection system (<50 mm). It must also be mentioned that a decrease in the \( S_2 \) value to 60.8 ± 2.8\% at the 200 mm separation between skin site - detection system was of similar range to that observed in the previous related work in [17] that used multispectral imaging system. Based on the small differences in the predicted mean \( S_2 \) for the considered distance of 30 mm and 50 mm shown in Table 1, it is reasonable to assume that at a distance of less than 30 mm, no significant differences in \( S_2 \) would be observed.

Figure 3 shows that the variability in the predicted \( S_2 \) increases with the distance. In addition to the reduce signal to noise performance, this observed variation was probably due to differences in one’s skin thickness, skin tone and health status. These observations were also reported in [17] whose work focused on central forehead, posterior forearm, thenar region of palm and proximal ankle of the recruited subjects. Although the present system may be used on other skin sites, index finger was selected here largely due to the fact that a higher \( S_2 \) is likely expected in acral skin (non-hairy skin sites i.e. palm, sole, face), as compared to the nonacral skin sites (i.e. posterior forearm, leg). This is contributed by the presence of arteriovenous anastomoses (AVAs) which can be found in abundance in the acral skin site [14]. The AVAs provide circulatory connection between the artery and veins and also produce shunting of oxygenated arterial blood into the venous compartment during muscle relaxation.

4. Conclusion

This work concluded that \( S_2 \) varies with differences in data spatial resolution, and a high, consistent and good repeatable \( S_2 \) value would be expected with the use of a small separation between skin site and the detection system of approximately 50 mm or less. This study observed an inversely proportional relationship between detection distance and the predicted \( S_2 \), wherein the mean \( S_2 \) decreased from 91.1 ± 1.3\% to 60.83 ± 2.8\% as the measurement distance increased from 30 mm to 200 mm. The variability in the predicted value was also related to the detected signal levels. The highlight of this study is the feasibility of adopting point spectroscopy system for noninvasive measurement of \( S_2 \) value. Future work includes determining differences in \( S_2 \) on wounded and unwounded skin samples. Nevertheless, the primary interest of this work is to determine a suitable distance range that would give an appropriate and accurate \( S_2 \) value using the EMLB model and proposed fitting algorithm.
Acknowledgement
The authors would like to thank all volunteers who participated in this study. This work was financially supported by the Ministry of Education Malaysia under FRGS grant no. 1581. This paper was partly sponsored by the Centre for Graduate Studies UTMH.

References
[1] M. Van Gemert, S. L. Jacques, H. Sterenborg, and W. Star, "Skin optics," IEEE Transactions on biomedical engineering, vol. 36, pp. 1146-1154, 1989.
[2] T. Chen, "Hyperspectral imaging for the remote sensing of blood oxygenation and emotions," 2012.
[3] A. Huong and X. Ngu, "Noninvasive diagnosis of carbon monoxide poisoning using Extended Modified Lambert Beer Model," in 2nd International Conference on Electronic Design (ICED), 2014, 2014, pp. 265-269.
[4] A. Vogel, V. V. Chernomordik, S. G. Demos, R. Pursley, R. F. Little, Y. Tao, et al., "Using noninvasive multispectral imaging to quantitatively assess tissue vasculature," Journal of Biomedical Optics, vol. 12, pp. 051604-051604-13, 2007.
[5] A. Huong, S. Philimon, and X. Ngu, "Multispectral imaging of acute wound tissue oxygenation," Journal of Innovative Optical Health Sciences, p. 1750004, 2017.
[6] R. Zhang, W. Verkruysse, B. Choi, J. A. Viator, B. Jung, L. O. Svaasand, et al., "Determination of human skin optical properties from spectrophotometric measurements based on optimization by genetic algorithms," Journal of Biomedical Optics, vol. 10, p. 024030, 2005.
[7] J. A. Fessler and W. L. Rogers, "Spatial resolution properties of penalized-likelihood image reconstruction: space-invariant tomographs," IEEE Transactions on Image processing, vol. 5, pp. 1346-1358, 1996.
[8] J. Laufer, D. Delpy, C. Elwell, and P. Beard, "Quantitative spatially resolved measurement of tissue chromophore concentrations using photoacoustic spectroscopy: application to the measurement of blood oxygenation and haemoglobin concentration," Physics in medicine and biology, vol. 52, p. 141, 2006.
[9] M. C. Phillips and N. Hô, "Infrared hyperspectral imaging using a broadly tunable external cavity quantum cascade laser and microbolometer focal plane array," Optics express, vol. 16, pp. 1836-1845, 2008.
[10] A. Huong, S. Philimon, and X. Ngu, "Noninvasive Monitoring of Temporal Variation in Transcutaneous Oxygen Saturation for Clinical Assessment of Skin Microcirculatory Activity," in International Conference for Innovation in Biomedical Engineering and Life Sciences, 2016, pp. 248-251.
[11] A. Huong and X. Ngu, "The application of extended modified Lambert Beer model for measurement of blood carboxyhemoglobin and oxyhemoglobin saturation," Journal of Innovative Optical Health Sciences, vol. 7, 2014.
[12] R. N. Pittman and B. R. Duling, "A new method for the measurement of percent oxyhemoglobin," Journal of applied physiology, vol. 38, pp. 315-320, 1975.
[13] W. G. Zijlstra, A. Buursma, and O. W. van Assendelft, Visible and near infrared absorption spectra of human and animal haemoglobin: determination and application: VSP, 2000.
[14] L. Caspary, J. Thum, A. Creutzig, D. Lubbers, and K. Alexander, "Quantitative reflection spectrophotometry: spatial and temporal variation of Hb oxygenation in human skin," International Journal of Microcirculation, vol. 15, pp. 131-136, 1995.
[15] A. K. C. Huong, "Spectroscopic analysis of scattering media via different quantification techniques," Thesis, University of Nottingham, 2012.
[16] A. K. C. Huong, S. P. Philimon, and X. T. I. Ngu, "Non-invasive estimation of blood oxyhemoglobin and carboxyhemoglobin saturations using Cumulant based forward model," ARPN Journal of Engineering and Applied Sciences, vol. 10, pp. 8421-8426, 2015.
[17] S. P. Philimon, A. K. Huong, W. Hafizah, P. Ong, and X. T. Ngu, "Optical investigation of variability in body region dependent transcutaneous oxygen saturation," in *IOP Conference Series: Materials Science and Engineering*, 2016, p. 012089.