Investigation of Photoplethysmography, Laser Doppler Flowmetry and Near Infrared Spectroscopy during induced thermal stress

K Budidha, *Graduate Student Member, IEEE,* T Y Abay, *Graduate Student Member, IEEE,* and P A Kyriacou, *Senior Member, IEEE*

***Abstract*— Continuous assessment of blood flow, blood volume, and blood and tissue oxygenation are of vital importance in critically ill patients. Photoplethysmography (PPG), Pulse Oximetry (PO), Laser Doppler Flowmetry (LDF) and Near Infrared Spectroscopy (NIRS) are amongst the most widely used techniques to monitor such perfusion parameters. In this study, we investigated the feasibility of using dual-wavelength PPG signals on providing comparable information as LDF and NIRS, besides arterial oxygen saturation (SpO_2) as measured by pulse oximetry. All three techniques were investigated on six healthy volunteers during whole-body cold exposure. PPG and LDF sensors were attached on the finger and hand respectively, while NIRS was positioned above the left forearm. Measurements at room temperature (24°C) were followed and preceded by a cold exposure (10°C). The results showed that changes in pulsatile PPG amplitudes and hemoglobin concentration estimated from finger PPG signals indicate strong similarities with gold-standard LDF and NIRS measurements.**

I. INTRODUCTION

Continuous assessment of blood and tissue oxygenation in critically ill patients is of paramount importance, as that can prompt diagnosis of hypoperfusion and tissue hypoxia, and hence the effectiveness of any applied treatment is judged on the measurements. The non-invasive techniques commonly used to assess oxygen delivery to the tissue are Pulse oximetry, Near Infrared Spectroscopy (NIRS) and Laser Doppler Flowmetry (LDF). Although the indexes produced by all three techniques are different, the key information which they provide is similar, that is the adequacy of blood supply in the measurement area.

The most frequently used technique of the three is pulse oximetry. Pulse oximeters provide a robust measure of arterial oxygen saturation (SpO_2) by shining light at two different wavelengths into the vascular tissue, and measuring the changes in absorbed or reflected light occurring during the cardiac cycle [1]. The changes in light absorbances at both the wavelengths, during arterial pulsations are measured as a voltage signal known as photoplethysmograph (PPG). The PPG waveform is divided into two components. A pulsatile AC component synchronous with the cardiac cycle, representing the *blood flow* to the area, and a slowly varying DC component with a magnitude that is determined by the nature of the material through which the light passes (skin, cartilage, venous blood, etc,). Using the ratio of the PPGs acquires at both the wavelengths, SpO_2 is estimated [2].

LDF is a non-invasive technique used for monitoring *blood flow* in the micro-circulation. The technique uses low power light from a laser to measure blood flow in capillaries and underlying arterioles and venules close to the skin surface [3]. The attenuated light from the tissue is detected by a photodetector and the frequency shift in the emitted and detected light beams is thought to be proportional to the average speed of red blood cells. However, LDF provides a unitless index (Flux), which is difficult to interpret and it has been indicated to have reproducibility issues during repetitive measurements [3].

Near infrared spectroscopy (NIRS) is an optoelectronic technique widely used for regional quantification of tissue oxygenation (StO_2) in the body, and is predominantly used for quantifying the oxygenation status of brain tissue [4]. Again as with pulse oximetry, NIRS shines light at two or more wavelengths (from the near infrared region) into the vascular tissue and detects the attenuated light using a photodetector. The changes in light attenuation detected at both the wavelengths are then used to estimate chromophore concentrations by applying the modified Beer Lambert Law. Changes in *blood volume* to the tissue are then estimated by taking the sum of the calculated haemoglobin concentrations (i.e. total haemoglobin) [5].

The key difference between PPG/pulse oximetry, LDF and NIRS is the thickness of the tissue which is sampled. LDF measures blood flow variations typically across 1 mm of tissue, while PPG and NIRS measure blood volume variations across 1 cm and 2-3 cm of tissue respectively. Other key difference is that NIRS does not rely on the presence of arterial pulsations (AC signals), as in pulse oximetry, to estimate StO_2. Hence, NIRS will not fail in conditions of peripheral vasoconstriction. However, the device is very expensive compared to the other two techniques.

As we can see all three techniques produce variable indexes based on similar principles. Hence in theory, by applying a Modified Beer Lambert Law as in NIRS to PPG signals acquired from a pulse oximeter, estimation of changes in oxygenated, deoxygenated, and total haemoglobin concentration is possible. It is also possible to correlate the flow measurements from LDF to the normalised AC PPG signal amplitude, to give an indication of the changes in blood flow. Hence we investigated the feasibility of obtaining the same parameters as NIRS and LDF from a finger PPG probe during induced hypothermia in healthy subjects.

Manuscript received 7th June 2015

K Budidha, T Y Abay and P A Kyriacou are with the Biomedical Engineering Research Centre, School of Mathematics, Computer Sciences & Engineering, City University London, London UK, EC1V 0HB. karthik.budidha.1@city.ac.uk, Tomas.Ysehak-Abay.1@city.ac.uk, p.kyriacou@city.ac.uk

II. METHODS AND MATERIALS

A measurement system was designed to acquire, display and store PPG, NIRS, and LDF signals during induced cold stress. The system consists of the following.

A. Finger PPG Probe and PPG Processing System

A custom-made, reflectance, finger PPG probe was developed for the acquisition of raw PPG signals from the finger. Two surface mount light emitting diodes (LED) were soldered on a printed circuit board (PCB) along with a silicon photodiode. The peak emission wavelength of the red *(KP2012SRC-PRV)* and infrared *(KP-2012SF4C, Kingbright, Taipei City, Taiwan)* LEDs was 660 and 880 nm, and the respective peak intensities of the LEDs were 2.4 mW/sr and 1.5 mW/sr (at 20 mA driving current). The photodiode used was a flattop photodiode with an active area of 0.65 mm^2 and peak sensitivity at 900 nm (SR 10 BP-BH, Excelitas technologies, Massachusetts, USA). The LEDs and photodiode were mounted at a center-to-center distance of 5 mm. The entire sensor was sealed using medical graded clear epoxy resin *(DYMAX 141-M, Dymax Corporation, Torrington, CT)* to avoid direct contact between the optical components and the skin.

A research processing system was used for the acquisition of raw PPG signals (AC + DC). ZenPPG is a custom-made research system developed by the Biomedical Engineering Centre at City University London [6]. It is able to acquire dual-wavelength, dual-channel, raw PPG signals.

B. NIRS Monitor and Laser Doppler

A commercial NIRS monitor *(NIRO 200NX, Hamamatsu Photonics, Shizuoka, Japan)* was adopted to record changes in haemoglobin concentrations. The NIRO 200NX adopts Spatially Resolved Spectroscopy and modified Beer-Lambert law to calculate Tissue Oxygenation Index and changes in haemoglobin concentrations. LEDs at specific emission wavelengths of 735, 810 and 850 nm are used as light sources, whereas two photodiodes, at a small separation distance between each other, detected the backscattered light. A separation distance of 4 cm between light emitter and detectors was used in this study in order to maximize the light penetration depth.

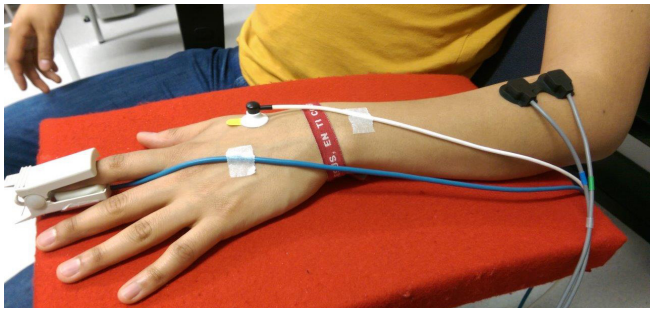

Fig. 1: Photograph of measurement setting showing finger PPG probe on index finger, NIRS sensor on the forearm and the LDF sensor on the back of the hand.

A laser Doppler flowmeter *(moorVMS-LDF2, Moor Instruments, Devon, U.K.)* was used to measure skin blood flow. The device employs temperature-stabilized laser light with emission wavelength at 785 nm and optical fibers to shine light into tissue. The backscattered light intensity and Doppler shift are used to obtain red blood cells (RBC) movement. The RBC flow was expressed by an arbitrary-unit index (Flux). The flowmeter was also used to measure skin temperature.

C. Investigation Protocol

Six healthy volunteers (3 males and 3 females, mean age: 28 $\pm$ 3.2) were recruited for the study. Ethical approval was sought from the Senate Research Ethics Committee at City University London. Subjects with any history of cardiovascular diseases were excluded from the study. The subjects were also asked to wear just one layer of clothing during the experiment, to maximise the effect of cold temperatures on the cardiovascular system. The volunteers were seated in a comfortable wheel base chair. As shown in Fig. 1, the finger PPG probe was placed on the second digit of the left hand, while the NIRS sensor was placed above the brachioradialis of the same arm. The NIRS sensor was kept in place by means of a double-sided clear medical adhesive tape. The LDF sensor was placed on the dorsal surface of the left hand and it was attached to the skin by means of a ring-shape double-sided adhesive. After ten minutes of temperature acclimatization at 24 ± 2°C, the investigation protocol started by acquiring two minutes of baseline measurements. The volunteers were then moved to an adjacent temperature controlled room at a temperature of 10 ± 1°C. After ten minutes of measurements at a cold temperature, the volunteers were moved back to normal room temperatures (24°C).

D. Signal Acquisition and Data Analysis

The acquired signals were digitized by two PCIe-6321 NI DAQ Cards *(National Instruments Inc. TX, USA)*. LabVIEW was used for the signal acquisition. A Virtual Instrument (VI) was developed to acquire, display, and save the acquired signals in real time. Signals were digitized and acquired at a sampling frequency of 1 KHz. The VI simultaneously acquired the PPG, NIRS signals, LDF, and temperature measurements. Once the measurements were saved, post-acquisition analysis was performed in Matlab2013.

Changes in peak-to-peak amplitudes of pulsatile AC IR-PPGs were calculated in a two-seconds rolling window. In order to minimize inter-subjects variability, changes in AC infrared (IR) PPG amplitude and Flux were expressed as normalized values with respect to 10 seconds baseline measurement. Raw PPG signals acquired from the finger were used for the estimation of SpO_2 and relative changes in oxygenated haemoglobin (HbO_2), deoxygenated haemoglobin (HHb) and total haemoglobin (tHb) concentrations. The DC PPG components were obtained by applying a zero-phase low-pass filter with a cut-off frequency of 0.2 Hz while the

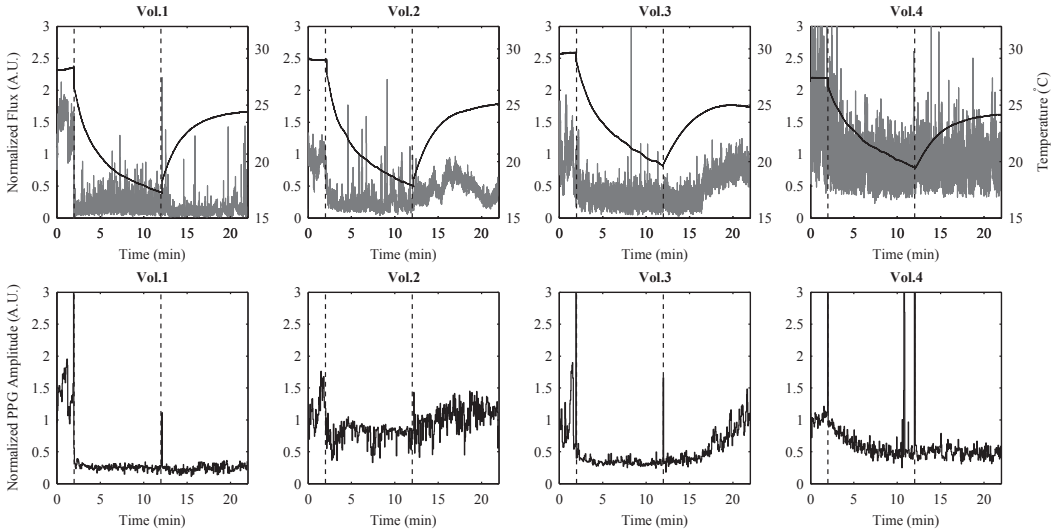

Fig. 2: Changes in normalized Flux (grey traces) and skin temperature (top black traces) and normalized AC IR-PPG amplitudes (bottom black traces). Vertical dotted lines represent the duration of the cold exposure.

AC PPG component was obtained with a zero-phase band-pass filter (cut-off frequency 0.5-7 Hz). SpO_2 was calculated in a three-seconds rolling window as in Eq. 1, [7].

$$SpO_2 = 110 - 25(R);\ where\ R = \frac{AC_R/DC_R}{AC_{IR}/DC_{IR}} \quad (1)$$

Where R is the Ratio of Ratios, AC_{IR} and AC_R are the peak-to-peak amplitudes of the infrared and red AC PPGs, and DC_{IR} and DC_R are the DC PPG components at both wavelengths.

The modified Beer-Lambert law was applied, as in NIRS, for the estimation of the haemoglobin concentrations. Eq. 2 shows the application of the modified Beer-Lambert law to single-wavelength PPG signals, assuming constant scattering [8].

$$\Delta A_\lambda = \ln\left(\frac{DC_{0\lambda}}{DC_\lambda}\right) = \left(\Delta[HbO_2]\varepsilon_{HbO_{2\lambda}} + \Delta[HHb]\varepsilon_{HHb_\lambda}\right) \times d \quad (2)$$

Where ΔA_λ is the light attenuation at one wavelength λ, $DC_{0\lambda}$ is the DC PPG component at the start of the measurement, DC_λ is the DC PPG component throughout the measurement, $\Delta[HbO_2]$ is the change in concentration of oxygenated haemoglobin, $\Delta[HHb]$ is the change in concentration of deoxygenated haemoglobin, $\varepsilon_{HbO_{2\lambda}}$ and $\varepsilon_{HHb_\lambda}$ are respectively the extinction coefficients of oxygenated and deoxygenated haemoglobin at wavelength λ, and d is the total optical path-length.

The solutions of the dual-wavelength (red and infrared) modified Beer-Lambert law are showed in Eq. 3 and Eq. 4. The derived hemoglobins concentration changes were calculated and expressed in mM.cm, assuming an unknown optical path-length. Total hemoglobin was calculated as sum of oxygenated and deoxygenated hemoglobins.

$$\Delta[HbO_2] = \frac{\Delta A_R.\varepsilon_{IR_{HHb}} - \Delta A_{IR}.\varepsilon_{R_{HHb}}}{(\varepsilon_{R_{HbO_2}}.\varepsilon_{IR_{HHb}} - \varepsilon_{IR_{HbO_2}}.\varepsilon_{R_{HHb}})} \quad (3)$$

$$\Delta[HHb] = \frac{\Delta A_{IR}.\varepsilon_{R_{HbO_2}} - \Delta A_R.\varepsilon_{IR_{HbO_2}}}{(\varepsilon_{R_{HbO_2}}.\varepsilon_{IR_{HHb}} - \varepsilon_{IR_{HbO_2}}.\varepsilon_{R_{HHb}})} \quad (4)$$

Relative changes in hemoglobin concentrations were estimated from the starting time of each step of the protocol (i.e. baseline, cold exposure, and recovery). An auto-zero set was performed on NIRS signals at the beginning of each protocol step.

III. RESULTS

Fig. 2 shows the skin temperature, normalized Flux and normalized AC PPG amplitudes for four volunteers during all three stages of the experiment (22 min). During baseline, the mean skin temperature among all volunteers was 29.13 ± 1.44°C. During cold air exposure, skin temperature has dropped to 18.94 ± 0.97°C. This drop in temperature caused profound vasoconstriction of capillary vasculature leading to a significant drop in the amplitude of the AC PPG signals and the flux, in all the volunteers. The mean amplitude of the AC IR-PPG signals have dropped from 1.16 ± 0.27 to 0.51 ± 0.32 during the cold stimuli. Similarly, the normalized flux readings have reduced from 1.19 ± 0.32 to 0.36 ± 0.24. During recovery period, with an increase in temperature (mean: 24.94 ± 0.94°C), the amplitude of the AC PPG signals and the Flux have recovered. However, the degree of increase varied among all the volunteers. Nonetheless, the acquired results from both the techniques presented strong similarities during changes in cardiovascular response. Similar results were previously reported by Abdollahi et al. in a study comparing the difference between PPG and LDF during vascular occlusions. The authors found both techniques as sensitive indicators of ischemia [9].

Using the red and infrared PPG signals, the SpO_2s were estimated for the entire course of the study in all the volunteers. The estimated mean SpO_2 value among all the volunteers during baseline was $95.10 \pm 1.66\%$. During cold

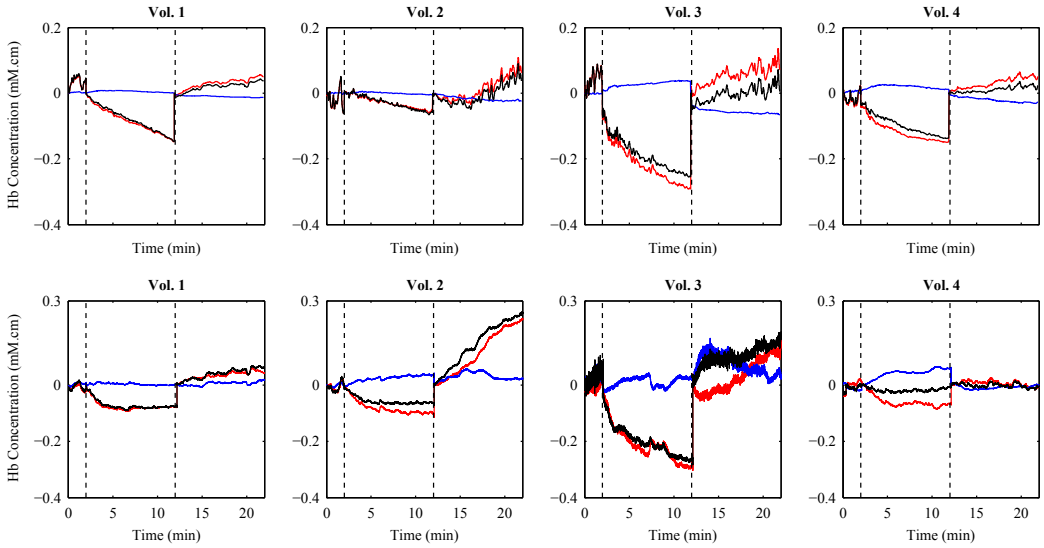

Fig. 3: Oxy (red traces), deoxy (blue traces) and total hemoglobin (black traces) changes estimated from finger PPG (top plots) and NIRS (bottom plots) in four volunteers. Vertical dotted lines represent the duration of the cold exposure.

stimuli, the mean SpO_2 among the volunteers has dropped to $88.21 \pm 2.16\%$. As SpO_2 is a global variable and does not vary significantly in healthy individuals, these drops have to be considered as erroneous values resulting from vasoconstriction. At the end of the recovery period, SpO_2 readings increased to $92.55 \pm 1.08\%$.

Fig. 3 shows changes in oxygenated, deoxygenated and total hemoglobin measured by PPG and NIRS during the course of the study. During cold exposure, the oxy- and total hemoglobin measured by PPG on the finger decreased significantly in all the volunteers. The decrease in both hemoglobins indicates the onset of vasoconstriction. Oxy- and total hemoglobins measured from NIRS indicate strong similarities with PPG-derived measurements during baseline and cold stimuli. The concentration of the deoxyhemoglobin measured from NIRS showed an increase in all the volunteers during the cold stimulus. This increase is most likely due to shivering activity produced by the skeletal muscle (i.e. brachioradialis). However the degree of deoxygenation varied from one volunteer to another. This may suggest that skeletal muscle shivering was triggered by subject-dependent responses to cold exposure. Similarly the concentration of deoxyhemoglobin estimated from finger PPG signals increased in all the volunteers. However the relative changes in deoxygenation as estimated from PPG signals were lower compared to the measurements from NIRS. The quantitative differences in the estimated concentration between both the systems is due to the deeper penetration depth of the NIRS and anatomical differences in the measurement locations (i.e., NIRS interrogating skeletal muscle and PPG on finger).

IV. CONCLUSIONS

The results in this study suggest that PPG presents strong similarities with the other two techniques. The AC PPG amplitudes provided information about the microcirculation, similarly to laser Doppler flowmetry. Moreover, the DC PPG signals have proved to estimate hemoglobin concentrations changes as NIRS. Thus, the AC and DC components of PPG signals can give additional information in conditions of compromised peripheral perfusion, where pulse oximeter reading become unreliable. However, extended investigations in a larger group of volunteers is required to validate this further.

REFERENCES

[1] K. Budidha and P. Kyriacou, "The human ear canal: investigation of its suitability for monitoring photoplethysmographs and arterial oxygen saturation," *Physiological measurement*, vol. 35, no. 2, p. 111, 2014.

[2] Y. Mendelson and B. D. Ochs, "Noninvasive pulse oximetry utilizing skin reflectance photoplethysmography," *Biomedical Engineering, IEEE Transactions on*, vol. 35, no. 10, pp. 798–805, 1988.

[3] M. Leahy, F. De Mul, G. Nilsson, and R. Maniewski, "Principles and practice of the laser-doppler perfusion technique," *Technology and Health Care*, vol. 7, no. 2, pp. 143–162, 1999.

[4] D. A. Hampton and M. A. Schreiber, "Near infrared spectroscopy: clinical and research uses," *Transfusion*, vol. 53, no. S1, pp. 52S–58S, 2013.

[5] A. Pellicer and M. del Carmen Bravo, "Near-infrared spectroscopy: a methodology-focused review," in *Seminars in Fetal and Neonatal Medicine*, vol. 16, no. 1. Elsevier, 2011, pp. 42–49.

[6] V. Rybynok, J. M. May, K. Budidha, and P. A. Kyriacou, "Design and development of a novel multi-channel photoplethysmographic research system," in *2013 IEEE Point-of-Care Healthcare Technologies (PHT)*, Jan. 2013, pp. 267 –270.

[7] J. P. Phillips, R. M. Langford, S. H. Chang, P. A. Kyriacou, and D. P. Jones, "Photoplethysmographic measurements from the esophagus using a new fiber-optic reflectance sensor," *Journal of biomedical optics*, vol. 16, no. 7, pp. 077 005–077 005, 2011.

[8] T. Abay and P. Kyriacou, "Reflectance photoplethysmography as non-invasive monitoring of tissue blood perfusion," *IEEE Transactions on Biomedical Engineering*, vol. PP, no. 99, pp. 1–1, 2015.

[9] Z. Abdollahi, J. Phillips, and P. Kyriacou, "Evaluation of a combined reflectance photoplethysmography and laser doppler flowmetry surface probe," in *Engineering in Medicine and Biology Society (EMBC), 2013 35th Annual International Conference of the IEEE*. IEEE, 2013, pp. 1728–1731.