Investigation of Photoplethysmography and Near Infrared Spectroscopy for the Assessment of Tissue Blood Perfusion

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***Abstract*— Pulse Oximetry (PO) and Near Infrared Spectroscopy (NIRS) are among the most widely adopted optical techniques for the assessment of tissue perfusion. PO estimates arterial oxygen saturation (SpO_2) by exploiting light attenuations due to pulsatile arterial blood (AC) and constant absorbers (DC) at two different wavelengths. NIRS processes the attenuations of at least two wavelengths to calculate concentrations of Deoxygenated ([HHb]), Oxygenated ($[HbO_2]$), Total Haemoglobin ([tHb]) and Tissue Oxygenation Index (TOI). In this work we present the development and evaluation of a reflectance PPG probe and processing system for the assessment of tissue perfusion. The system adopts both Pulse Oximetry and NIRS principles to calculate SpO_2, [HHb], and $[HbO_2]$ and [tHb]. The system has been evaluated on the forearm of 10 healthy volunteers during cuff-induced vascular occlusions. The presented system was able to estimate SpO_2, [HHb], $[HbO_2]$ and [tHb], showing good agreement with state-of-the-art NIRS and conventional PO.**

I. Introduction

Light has revolutionized medical technology in the last decades. Several optical techniques have been developed in order to measure blood oxygen content, haemoglobin concentrations, red blood cells velocity and other physiological parameters [1]. One of the main applications of in-vivo spectroscopic techniques is monitoring tissue blood perfusion [1]. Tissues in human body require the correct delivery of oxygen (O_2) and they should be able to discharge waste products such as Carbon Dioxide (CO_2). Thus monitoring perfusion status of tissues is fundamental in clinical practice [1]. Different non-invasive techniques and technologies have been applied for this purpose, but, with contrasting successes, some limitations still remain [1]. Among these techniques, Pulse Oximetry (or Photoplethysmography (PPG)) and Near Infrared Spectroscopy (NIRS) showed promising results [1].

In Pulse Oximetry (PO) red (R) and infrared (IR) light is applied to tissues. The backscattered and attenuated light intensities are detected by a photodetector and processed to calculate the arterial oxygen saturation (SpO_2). In this process, the signals are split into two components: pulsatile (AC) and non-pulsatile (DC). The AC component represents the light attenuation due to arterial blood pulsations, while the DC component refers to the constant attenuation due to tissue compartments and venous blood [2]. These two components of the signal, in both wavelengths, are then applied to calculate the Ratio of Ratios (RR) [2].

$$RR = \frac{\frac{AC_{RED}}{DC_{RED}}}{\frac{AC_{IRED}}{DC_{IRED}}} \quad (1)$$

An empirical calibration equation relates the RR to the SpO_2, expressed in percentage [3].

$$SpO_2(\%) = 110 - 25(RR) \quad (2)$$

Despite its potentiality, pulse oximetry presents some disadvantages such as dependency on pulsatile blood and motion artefacts [2]. Although Pulse Oximetry can detect arterial occlusion, it cannot assess venous ischemia [3].

Near Infrared Spectroscopy (NIRS) is a relatively new optical technique. In NIRS light is used to calculate the concentration of Oxygenated Haemoglobin ($[HbO_2]$) and Deoxygenated Haemoglobin ([HHb]) in deep tissues. Light attenuation is correlated to $[HbO_2]$ and [HHb] by the Modified Beer-Lambert Law;

$$A_\lambda = \ln(I_0/I) = \alpha_\lambda \cdot [c] \cdot d \cdot DPF + G \, . \quad (3)$$

Where A_λ is the light attenuation (in Optical Densities) at a specific light wavelength λ, I and I_0 are respectively the transmitted light intensities during and at the beginning of the measurement, α_λ is the attenuation coefficient of a substance at λ, [c] is the concentration of the substance (i.e. [HHb] and $[HbO_2]$), d is the distance between light source and detector, DPF is the Differential Pathlength Factor and G is a parameter of scattering [4].

Equation (3) is the Modified Beer-Lambert law, in which the factor G is added to include light scattering. The term DPF is the Differential Pathlength Factor, and is multiplied to the optodes distance d to obtain the increased light pathlength caused by scattering [4].

In order to measure $[HbO_2]$ and [HHb] light at least two different wavelengths has to be applied to the tissue. These wavelengths are usually chosen in the near-infrared region of the spectrum (750-1000 nm) as, in this interval, the transparency of tissues is maximized [4]. Once $[HbO_2]$ and

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[HHb] have been estimated from (3), the Tissue Oxygenation Index (TOI) can be calculated;

$$TOI = {[HbO_2]}/{[HbO_2]+[HHb]} \quad (4)$$

Although PO and NIRS have some similarities, they are sometimes erroneously confounded. However, in the literature we have not found proof of a simultaneous investigation of PO and NIRS in the same tissue.

The first aim of this study is to demonstrate the inability of traditional PO, when compared to NIRS, on detecting venous ischemia. The second aim of this study is to evaluate the feasibility of a PPG reflectance probe and processing system on assessing tissue perfusion during venous ischemia. The system adopts both PO and NIRS principles in order to compensate limitations of traditional PO.

II. Material and Methods

A. Design and Development of a Reflectance PPG Probe

A reflectance PPG probe has been designed and developed (Fig. 1). Light Emitting Diodes (LED) were used as light sources. Two KP-2012 SRC and two KP-2012 SF4C (Kingbright, Taiwan) were used respectively as R (λ=660 nm) and IR (λ=880 nm) light sources. A silicon-photodiode with a large active area (7.5 mm^2) was used as photodetector (TEMD5010X01, Vishay Intertechnology Inc., USA). A probe PCB (Fig. 1(c)) was designed in order to solder the optical components in a reflectance configuration. The PCB routing and footprints were designed in an electronics design software platform (Altium Ltd, Australia). The PCB was then fabricated with Computer Numeric Control (CNC) technology. The LEDs and photodiode were soldered on the PCB at a source-detector separation distance of 5 mm. This distance allows the acquisition of PPG signals with high signal-to-noise-ratio (SNR) [5]. In order to avoid optical shunt, the photodiode was shielded with black rubber. A layer of clear epoxy medical adhesive was used to protect the optical components. To protect from ambient light, a black probe case has been designed on 3D CAD design software (Solidworks, USA) and fabricated in Polylactic Acid plastic (PLA) by 3D printing technology (Fig. 1(a) and 1(b)). The probe case has been also designed to facilitate the application of the probe on skin surface. Fig. 1(d) shows the final manufactured reflectance probe.

An identical PCB probe was developed and encapsulated into a pulse oximetry finger clip for acquisition of PPG signals from the finger. Both probes were used to acquire PPG signals and SpO_2.

B. PPG Processing System (ZEN PPG)

The probes were then connected to the *ZEN PPG*, a PPG processing system developed by the Biomedical Engineering Group at City University London [5]. The *ZEN PPG* is a portable, battery operated PPG processing system. Its modular design allows the simultaneous use of two independent channels [6]. The instrument provides currents for the light sources (LEDs) and acquires the raw analogue signals detected by the photodiode.

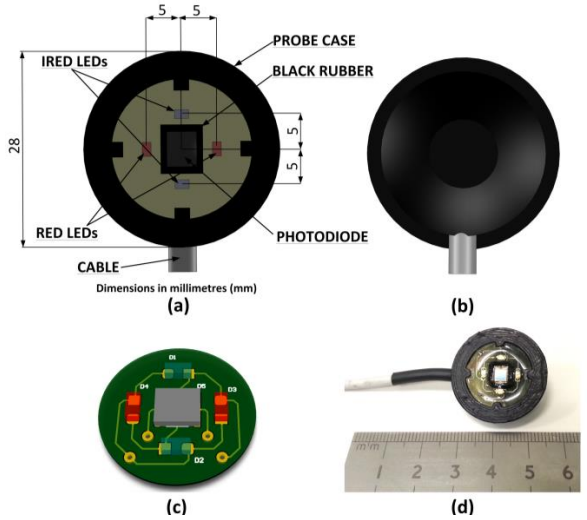

Figure 1. Reflectance PPG Probe. (a) Assembly 3D model of probe front, optical components and dimensions. (b) Assembly 3D model of probe backside. (c) Probe PCB model. (d) Final manufactured PPG reflectance probe.

The ON/OFF switching of the LEDs is made possible with the use of a multiplexer, while the light detected by the photodiode is separated to its unique wavelengths using a demultiplexing circuit. Light sources are switched ON/OFF at a frequency of 1 kHz. The *ZEN PPG* has a 64-pin connector on the rear panel for connection to a National Instruments (NI) data acquisition system [5]. The system allows the digital control of light intensities on one of the channels. This is performed by digitally controlling the currents flowing through the LEDs [6]. Moreover the system allows the connection of different typologies of probes through a DB-9 connector on the front panel [6]. The PPG system has two independent transimpedance amplifiers (TA) in order to convert the currents from the photodiodes into voltages [6]. The gain of each TA can be changed by simply replacing the resistor gain on the amplifier. A detailed description of *ZEN PPG* can be found in [6].

The *ZEN PPG* has been chosen for its ability to use customized probes, its flexibility on controlling the intensities of emitted light, the presence of two independent PPG channels and, most importantly, for the acquisition of raw signals from the photodiode. In this study the gain of the TA for both channels was equal to 68000.

C. NIRS System

A commercial NIRS monitor (NIRO 200NX, Hamamatsu, Japan) was used to measure [HbO_2], [HHb], [tHb] and TOI. The monitor applies the Modified Beer-Lambert Law to estimate haemoglobin concentrations in tissue. NIRO 200NX employs Spatially Resolved Spectroscopy (SRS) to determine the scattering factor G in (3) [7]. LEDs are used

as light sources at wavelengths of 735, 810 and 850 nm [8]. Two photodiodes detect the backscattered light in a reflectance configuration and reconstruct the light propagation spatial profile for SRS [8]. The monitor provides analogue outputs for external data acquisition such as: [HbO_2], [HHb] and TOI [8]. An emitter-detector separation distance of 4 cm was adopted in this study in order to maximize light penetration depth in tissue [4]. A DPF of 3.59 for the forearm has been employed [9].

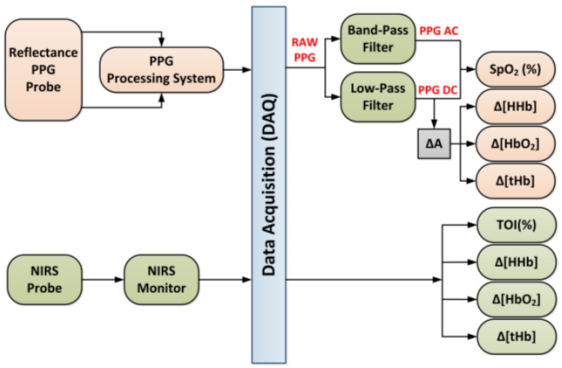

Figure 2. Block Diagram of the Data Acquisition and Processing System.

D. Data Acquisition System and Post-acquisition Data Analysis

The raw PPG signals from the *ZEN PPG* and the analogue outputs from the NIRS monitor were acquired by two NI-Pcle 6321 Data Acquisition (DAQ) Cards (National Instruments, USA). Each DAQ card can acquire 16 signals with a resolution of 16-bit and a sample rate of 250KS/s. Signals were acquired at a sample frequency of 400 Hz. A Virtual Instrument (VI) on LabVIEW was developed to acquire, filter, display and save the raw signals.
Once the signals were saved, post-acquisition data analysis was performed on Matlab.

The raw PPG signals from the *ZEN PPG* were split into AC and DC components. The PPG AC components were derived by applying a 4th order band-pass digital filter (cut-off frequencies 0.5-4 Hz) while PPG DCs were obtained by a 2nd order low-pass digital filter (cut-off frequency of 0.1 Hz). The two components (AC and DC) were then used to estimate the SpO_2 as in (1) and (2).
The raw PPG signals were not only used for calculating SpO_2, but changes of [HbO_2] and [HHb] were also estimated from the PPG DC components (R and IR). In order to solve the two equations system (5) and (6), without the knowledge of G, a differential approach was adopted [4]. The changes in attenuation ΔA from the start of the measurement were used to estimate changes in [HbO_2], [HHb] and [tHb] throughout the measurement (Δ[HbO_2], Δ[HHb] and Δ[tHb]). The following set of Beer-Lambert Law equations was applied:

$$\Delta A_R = \ln\left(\frac{DC_R(0)}{DC_R}\right) = (\alpha_{R\_HbO_2}\Delta[HbO_2] + \alpha_{R\_HHb}\Delta[HHb])d' \quad (5)$$

$$\Delta A_{IR} = \ln\left(\frac{DC_{IR}(0)}{DC_{IR}}\right) = (\alpha_{IR\_HbO_2}\Delta[HbO_2] + \alpha_{IR\_HHb}\Delta[HHb])d'. \quad (6)$$

Where $\Delta A_{R/IR}$ are the changes in light attenuation at R and IR wavelengths, $DC_R(0)$ and $DC_{IR}(0)$ are respectively the DC components (in voltage, V) for red and infrared wavelength at the beginning of the measurement, DC_R and DC_{IR} are the DCs changes during the measurement, α_R and α_{IR} are respectively the extinction coefficients at red (R) and infrared (IR) wavelength of HbO_2 or HHb, adapted from [10], d is the product of the emitter-detector distance (0.5 cm) and the DPF (3.59). Fig. 2 shows the block diagram of data acquisition and processing system.

E. Investigation Set-up and Protocol

The entire system was evaluated in 10 healthy volunteers (7 males and 3 females). Ethical approval was gained from the Senate Research Ethics Committee at City University London. The volunteers were seated in a comfortable chair in the Biomedical Engineering Group laboratory and their left arm was placed on a pillow. The NIRS probe was placed on the external side of the left brachioradialis muscle by means of a double sided clear adhesive tape. The reflectance PPG probe was placed on the volar side of the same muscle and attached by medical tape. Positioning of the PPG probe was preceded by brachial artery location by handheld Doppler Ultrasound. The developed finger PPG probe was connected to the second digit of the left hand. A commercial Pulse Oximetry finger probe (Radical 7, Masimo Corp., USA) was placed on the third digit of the same hand. Volunteers' blood pressure (BP) was acquired prior to the commencing of the investigation. A blood pressure cuff connected to a sphygmomanometer was placed on the upper arm in order to induce vascular occlusions.

The investigation protocol consisted of two minutes of venous occlusion (VO), two minutes of "no-occlusion" and two minutes of total (arterial and venous) occlusion (TO). The latter was applied at 20 mmHg over the volunteer's systolic pressure, while VO was performed at 60 mmHg. Baseline measurements preceded and followed every occlusion step.

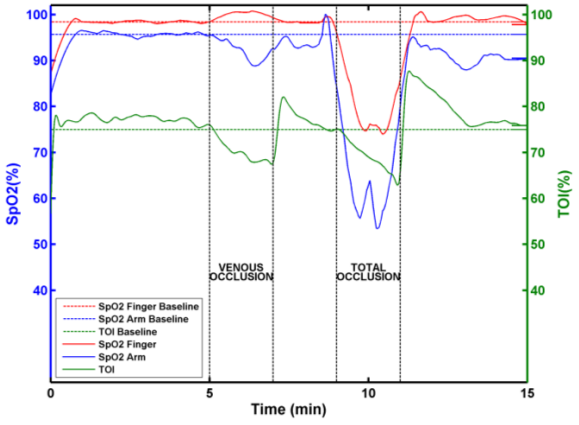

Figure 3. Changes in SpO_2 and TOI during venous and total occlusion in one volunteer. A significant drop in SpO_2 can be observed only during total occlusion. TOI drops during both occlusions.

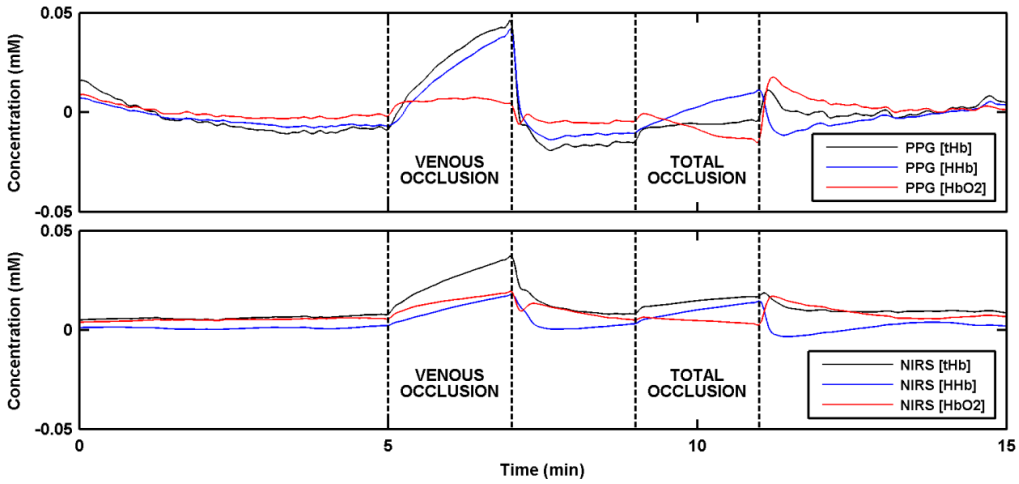

Figure 4. Changes of Haemoglobin concentrations during venous and total occlusion in one volunteer. The upper graph shows the changes of [tHb], [HHb] and [HbO2] derived by PPG DC components. The bottom graph shows the same parameters derived by NIRS.

III. Results

Fig. 3 and 4 show the traces for SpO_2, TOI and haemoglobin concentrations. The developed PPG probes (arm and finger) were able to acquire good quality PPG signals. SpO_2 and TOI values during baseline measurements were found in the normal physiological ranges. However, the probe on the arm slightly under-estimated SpO_2 when compared to the finger probe. [HbO_2], [HHb] and [tHb] did not exhibit significant physiological changes during baseline period. Venous occlusion should not cause any variation in SpO_2 values as AC components of the PPG signal are not affected. However, small drops in SpO_2 values estimated with the arm probe have been observed during VO. These might most probably caused by movement artefacts. Nevertheless the presence of pulsations might still mislead to a normal blood perfusion status. Moreover SpO_2 from the finger probe did not exhibit any drop during VO. The Tissue Oxygenation Index derived by NIRS exhibited the correct drop in oxygenation due to increase of [HHb] during VO. During total occlusion, pulse oximetry readings were erroneous and unreliable, causing a drop in SpO_2. However NIRS continued to provide information on tissue perfusion by the drop in TOI due to the decrease in [HbO_2].

The values of [HbO_2], [HHb] and [tHb] derived from PPG DC signals calculated in (5) and (6) demonstrated a fair representation of NIRS derived parameters as showed in Fig. 4. Although the PPG system was unable to detect VO by the conventional SpO_2, the estimation of haemoglobin concentrations from DCs attenuations provides an additional parameter to assess tissue perfusion. The combined use of both modalities (PPG and NIRS) would give a more holistic monitoring of arterial and tissue perfusion. However the differences in haemoglobin concentrations estimation between PPG and NIRS might be due to the different light wavelengths adopted, optodes separation distance (i.e. different light penetration in tissues) or the superior algorithm used by the NIRS device (SRS).

IV. Conclusions

This pilot study wanted to evaluate the possibility of combing Pulse Oximetry and NIRS for the assessment of changes in tissue blood perfusion. The combination of the two modalities provided a complete mapping of arterial and tissue perfusion simultaneously. More regular in-vivo studies will be pursued in order to investigate the utilization of the two modalities in more detail.

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