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Reflectance Photoplethysmography as Non-invasive Monitoring of Tissue Blood Perfusion

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Abstract— In the last decades Photoplethysmography (PPG) has been used as noninvasive technique for monitoring arterial oxygen saturation by Pulse Oximetry (PO), whereas Near Infrared Spectroscopy (NIRS) has been employed for monitoring tissue blood perfusion. While NIRS offers more parameters to evaluate oxygen delivery and consumption in deep tissues, PO only assesses the state of oxygen delivery. For a broader assessment of blood perfusion, this paper explores the utilization of dual-wavelength PPG by using the pulsatile (AC) and continuous (DC) PPG for the estimation of arterial oxygen saturation (SpO$_2$) by conventional PO. Additionally, the Beer-Lambert law is applied to the DC components only for the estimation of changes in deoxy-hemoglobin (HHb), oxy-hemoglobin (HbO$_2$) and total hemoglobin (tHb) as in NIRS. The system was evaluated on the forearm of 21 healthy volunteers during induction of venous occlusion (VO) and total occlusion (TO). A reflectance PPG probe and NIRS sensor were applied above the brachioradialis, PO sensors were applied on the fingers, and all the signals were acquired simultaneously. While NIRS and forearm SpO$_2$ indicated VO, SpO$_2$ from the finger did not exhibit any significant drop from baseline. During TO all the indexes indicated the change in blood perfusion. HHb, HbO2 and tHb changes estimated by PPG presented high correlation with the same parameters obtained by NIRS during VO (r^2=0.960, r^2=0.821 and r^2 =0.974 respectively) and during TO (r^2=0.988, r^2=0.940 and r^2=0.938 respectively). The system demonstrated the ability to extract valuable information from PPG signals for a broader assessment of tissue blood perfusion.

Index Terms— Beer-Lambert law, near infrared spectroscopy (NIRS), optical sensors, photoplethysmography, physiological monitoring, pulse oximetry.

I. INTRODUCTION

NON-INVASIVE optical technologies have contributed significantly in the continuous and noninvasive monitoring of tissue blood perfusion. Several modalities such as Photoplethysmography (PPG), Pulse Oximetry (PO), Laser Doppler Flowmetry, Near Infrared Spectroscopy, and Reflectance Spectrophotometry have been used in research and clinical settings for the quantitative and qualitative assessment of different tissue perfusion parameters [1]-[7].

Pulse oximetry (PO) is a noninvasive optical technique, which utilizes light at two different wavelengths for the estimation of arterial oxygen saturation. Light is applied to tissue and the light attenuations at Red (R) and Infrared (IR)

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wavelengths are filtered, processed and separated in pulsatile (*AC*) and continuous (*DC*) PPG [8]-[10]. The *AC* component reflects the changes in pulsatile arterial blood volume and it is synchronous with the cardiac cycle. The *DC* component depends on the nature of the tissue interrogated and represents the relatively constant absorption of skin, venous blood, non-pulsatile arterial blood and total blood volume in the light path [9]-[13]. Whereas *AC* components have a clinical importance for their synchrony with the cardiac cycle, *DC* components provide equally valuable information such as hyperemic or hypoaemic states, temperature changes, sympathetic outflow, venous volume fluctuations and other regulatory mechanisms [13]. *AC* and *DC* components, at the two different wavelengths, compose a physiological signal also known as Photoplethysmograph (PPG) [9]. The ratio between *AC* and *DC* components (i.e. Ratio of Ratios, see (1)) is directly correlated to arterial blood oxygen saturation (*SpO$_2$*) by empirical curves, permitting the continuous and noninvasive monitoring of arterial oxygen saturation by pulse oximetry [8]-[10], [12].

Pulse oximetry has found many applications in clinical and research settings. The most adopted use is the estimation of *SpO$_2$*. The technique provides continuous and noninvasive indication of *SpO$_2$*, presenting a valuable alternative to intermittent arterial blood sampling. Pulse oximetry is nowadays used in clinical settings for quick identification of possible hypoxic states such as respiratory failures, asthma and chronic obstructive pulmonary diseases [8], [12]. Pulse oximetry is regularly used in emergency medicine, surgery, neonatal care [8], [9] and it is mandatory during anesthesia [14].

The PPG trace however is not only used for the estimation of *SpO$_2$* by pulse oximetry. Several studies have been undertaken to prove the ability of the PPG waveform on providing additional information. The PPG has been used for heart rate analysis, Pulse Transit Time estimation, blood pressure estimation, respiration rate, vascular tone assessment, arterial and venous assessment, tissue viability, vasomotor function, thermoregulation and as a perfusion indicator [13]-[19].

Although pulse oximetry is a powerful clinical tool, it presents some limitations that have to be considered carefully by researchers and clinicians. Limitations such as anemia, skin pigmentation, nail polish, low perfusion, light interference, and venous pulsations might introduce errors [8]-[10], [20], [21]. Even though *SpO$_2$* and PPG waveform analysis provide a wide range of information, the majority of research in this field focuses in pulse oximetry which is a technique that does not indicate the correct blood perfusion status [12], [20].

Moreover, we did not find clear evidence in the literature on whether pulse oximetry (or the sole analysis of SpO_2 and AC PPG signals) could be considered as a reliable indicator of tissue blood perfusion when perturbations such as venous occlusion occur [12], [13], [22], [23].

Near Infrared Spectroscopy (NIRS) is another optical technique, which estimates the concentrations of oxy-hemoglobin (HbO_2), deoxy-hemoglobin (HHb) and total hemoglobin (tHb) in deep tissues [24], [25]. Light in the near-infrared spectrum (700-1000 nm) is utilized in NIRS due to the relative transparency of human tissues in this spectrum, permitting a deeper penetration of light [25]. In NIRS, the Beer-Lambert law is used to derive the hemoglobin concentrations from the attenuation of light at two or more wavelengths [24]. An index representing the tissue hemoglobin saturation is then estimated from the ratio of HbO_2 and tHb [24]. In the last decades, NIRS has found a growing range of applications as tissue perfusion monitoring technique. The technique has been applied to measure cerebral and muscle perfusion, oxygen consumption, and blood flow in tissues. It also found applications in neonatal and foetal monitoring, somatic and splanchnic perfusion, peripheral vascular diseases, trauma medicine, sepsis, and plastic surgery [24]-[30].

NIRS and PO differ in the assessment of tissue blood perfusion. Even though conventional PO is a valuable technique adopted as standard of care in many clinical environments, it only permits the quantification of arterial oxygen saturation. This restricts its use as instrument for the assessment of global oxygen delivery to tissues. Therefore, PPG so far has been mainly utilized for the estimation of arterial oxygen saturation by pulse oximetry, with limited attempts in exploring the capability and potentials of the technique for a more complete assessment of tissue perfusion [31]. Alternatively, NIRS, by measuring changes in hemoglobin concentrations, provides a more inclusive representation of tissue blood perfusion. The tissue oxygenation index and hemoglobin concentration changes provide an indication of other possible alterations of tissue perfusion such as arterial blockage, venous congestion or oxygen delivery/consumption mismatches [28], [32].

This paper presents the implementation and application of a photoplethysmographic instrument that offers a more comprehensive assessment of tissue blood perfusion by PPG. The system comprises a processing system and a reflectance PPG probe and it uses AC and DC components for the estimation of arterial oxygen saturation (SpO_2) by conventional pulse oximetry. Furthermore, DC components are processed separately, as in NIRS, to estimate changes of concentrations in HbO_2, HHb and tHb using the Beer-Lambert law. The proposed system has been evaluated in healthy volunteers during induced vascular occlusions on the forearm. A commercial pulse oximeter and a NIRS system have been used simultaneously as references throughout the measurements.

II. METHODS

Fig. 1 shows the block diagram of the system proposed in this study and it comprises:
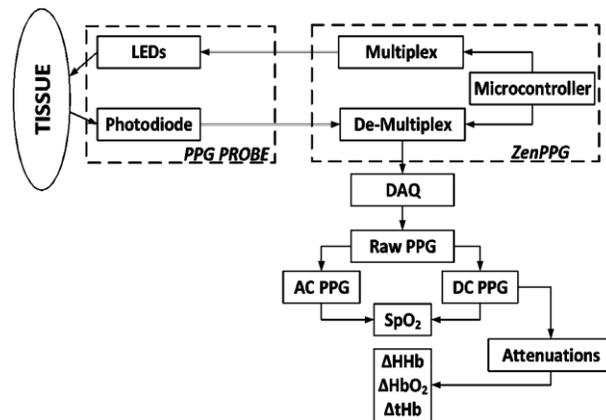

Fig.1. Block diagram of the proposed system.

- PPG processing system (*ZenPPG*);
- Reflectance PPG probe;
- Data Acquisition (DAQ).

The optical components (LEDs and photodiode) apply and detect light to and from the tissue. Red and Infrared light separation is achieved in the PPG processing system by multiplexer/de-multiplexer and controlled by microcontroller technology. Raw PPG signals are acquired by Data Acquisition system. Signals are further separated into AC and DC components and SpO_2 is estimated from their ratio. DC components are used to estimate changes in deoxy-hemoglobin (HHb), oxy-hemoglobin (HbO_2) and total hemoglobin (tHb). Each part of the system will be described in the following subsections.

A. PPG Processing System – ZenPPG

As commercial pulse oximeters present limitations on displaying and offering raw PPG signals, we opted for the use of the *ZenPPG*, a custom-made research PPG system. The *ZenPPG* is a flexible, dual channel, battery operated PPG processing system developed by the Biomedical Engineering Group at City University London [33], [34]. The instrument permits the acquisition of raw, dual-wavelength (red and infrared) and dual-channel photoplethysmographic signals [33].

The *ZenPPG* is composed of a modular architecture of exchangeable modules: system bus, power supply, core board, current-source, transimpedance amplifier, and probe module [33]. Customized PPG sensors can be connected to the system via DB9 connectors on the probe board. The current-source board is responsible of providing two separate currents to the light emitting diodes (LEDs). Currents in one channel are fully digitally controlled, whereas regulated by trimmers in the second channel [33]. The intermittent switching of light RED/IR is achieved by multiplexers, whereas the separation of the detected light in the two distinctive wavelengths is achieved by de-multiplexers [33]. The multiplexing/de-multiplexing process is controlled in the core board by microcontroller technology (Atmel ATtiny 2313-20SU, Atmel Corp., U.S.A). The ON/OFF switching of RED/IR light sources is carried at a frequency of 1 kHz. Once the light has

been emitted to the tissues, the detected light from the photodiodes (i.e. current) is converted to voltages by transimpedance amplifiers, before being de-multiplexed [33]. *ZenPPG* also comprises a 64-pin NI connector (National Instruments Corporation, Austin, Texas U.S.A) for the acquisition of the signals via *LabVIEW* and the digital control of the LEDs currents [33]. The system allows the full control of light emission and the simultaneous acquisition of raw PPG signals (*AC* and *DC*) from the two independent channels. *ZenPPG* has been recently used in PPG studies carried by the Biomedical Engineering Group at City University London [34]-[36].

B. Forearm Reflectance Probe

A reflectance PPG probe was developed and manufactured in order to be connected to *ZenPPG* and acquire raw PPG signals from the forearm. Fig. 2(a) shows the mechanical drawing of the reflectance PPG probe. It comprises of a printed circuit board (PCB), two red LEDs (KP-2012SRC-PRV, Kingbright, Taiwan) and two infrared LEDs (KP-2012 SF4C, Kingbright, Taiwan) with peak emission wavelengths at 660 and 880 nm respectively. These two wavelengths are opposite with respect to the isobestic point and they have different hemoglobin absorption coefficients, consenting the acquisition of R/IR signals for the estimation of SpO_2 [8]. The LEDs were driven to a corresponding radiant power between ~1.5 mW/sr and ~3.6 mW/sr. A silicon photodiode with a large active area of 7.5 mm^2 (TEMD5010X01, Vishay Intertechnology Inc., U.S.A) was selected for the acquisition of the backscattered light. The LEDs and photodiode were placed at a center-to-center distance of 5mm. This distance has been considered in the literature as satisfactory for the acquisition of PPG signals with adequate signal-to-noise-ratio (SNR) [37]-[39].

In order to guarantee mechanical stability and to protect the optical components from ambient light interference, the PCB was enclosed in a black case. The case was designed on 3D CAD design software and it was manufactured in Polylactic Acid plastic (PLA) by 3D printing technology. Black rubber was used to shield the photodiode from light shunting and a layer of clear epoxy medical adhesive (Dymax, 141-M) was used to cover the LEDs and the photodiode. Fig. 2(b) shows the final manufactured version of the reflectance PPG probe.

An identical PCB probe has been manufactured and enclosed in a pulse oximeter clip for the acquisition of raw reflectance PPG signals from the finger.

C. SpO_2, HHb, HbO$_2$ and tHb estimation

As mentioned above, *AC* and *DC* PPG signals are used to estimate arterial oxygen saturation. The ratio of the components (i.e. ratio of ratios, *R*), at the two wavelengths, is defined as:

$$R = \frac{AC_{RED}/DC_{RED}}{AC_{IRED}/DC_{IRED}} \tag{1}$$

Where AC_{RED} and AC_{IRED} are respectively the peak-to-peak amplitudes of the pulsating arterial signal at red and infrared
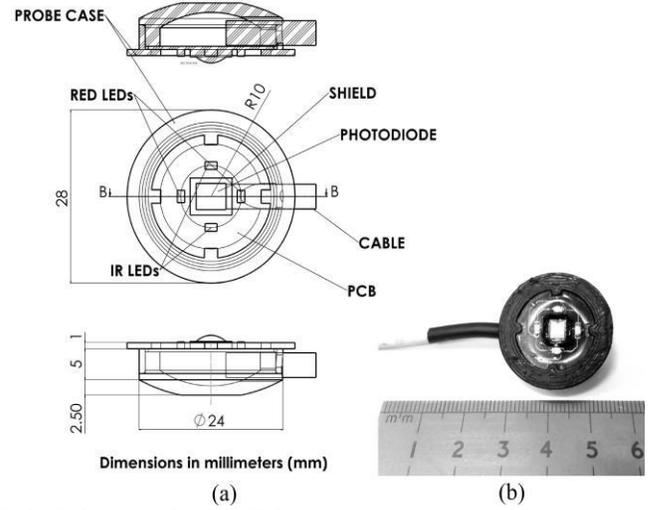

Fig.2. Reflectance forearm PPG probe. (a) Mechanical drawing, probe elements, and section. (b) Final manufactured reflectance PPG probe.

wavelengths and DC_{RED} and DC_{IRED} are the relatively constant values of light attenuation at the two respective wavelengths.

The following standard empirical equation correlates the ratio of ratios to arterial oxygen saturation, SpO_2.

$$SpO_2 = 110 - 25(R) \tag{2}$$

The formula has been extensively used in pulse oximetry and it correlates directly the ratio of ratios to arterial oxygen saturation [9]. Equations (1) and (2) were used in this study to estimate SpO_2 from PPG signals.

DC components represent the amount of light reaching the photodiode, thus directly relating to the amount of blood volume interrogated by the light beam. Optical Densities (*OD*), at the two light wavelengths employed, were used in this study to express changes in light attenuation due to variations in blood volumes. *OD*s (or light attenuation changes) were calculated from time changes of *DC* components as expressed in (3) and (4).

$$OD_{\lambda_1} = \Delta A_{\lambda_1} = \ln\left(\frac{DC(0)_{\lambda_1}}{DC_{\lambda_1}}\right) \tag{3}$$

$$OD_{\lambda_2} = \Delta A_{\lambda_2} = \ln\left(\frac{DC(0)_{\lambda_2}}{DC_{\lambda_2}}\right) \tag{4}$$

Where ΔA_{λ_1} and ΔA_{λ_2} are respectively the changes in light attenuation at the wavelengths λ_1 and λ_2, ln is the natural logarithm, $DC(0)_{\lambda_1}$ and $DC(0)_{\lambda_2}$ are the *DC* values at the beginning of the measurement for both wavelengths, and DC_{λ_1} and DC_{λ_2} are the *DC* values throughout the entire measurement.

The modified Beer-Lambert law is extensively used in NIRS and it correlates the attenuation *A* of a monochromatic light beam to the absolute values of chromophore concentration, knowing the scattering contribution in the light path [24]. Equation (5) shows the generic form of the modified Beer-Lambert law.

$$A_\lambda = \ln\frac{I_0}{I} = \varepsilon_\lambda \cdot [C] \cdot d \cdot DPF + G \tag{5}$$

Where A_λ is the light attenuation at the wavelength λ, I is the light intensity detected, I_0 is the light emitted, *[C]* is the concentration of the chromophore C, ε_λ is the extinction coefficient of C at wavelength λ, d is the distance between light emitter and photodetector, *DPF* is the Differential Pathlength Factor, and G is a scattering factor. Continuous wave instruments are unable to determine the factor G [24], [25], thus limiting to the only estimation of relative changes in hemoglobins concentrations. As our system is a continuous wave instrument (i.e. PPG system), we opted for a differential approach, permitting only the calculation of relative changes in hemoglobin concentrations from the start of the measurement. This approach permits to assume that scattering in the tissue is constant during the measurement, thus eliminating G from (5) [24], [25]. Equation (6) and (7) show the system of linear equations for a dual-wavelength differential approach used in our PPG system.

$$\Delta A_{660}= (\varepsilon_{HHb_{660}}\Delta[HHb] + \varepsilon_{HbO_{2_{660}}}\Delta[HbO_2]) \cdot d \cdot DPF \quad (6)$$

$$\Delta A_{880}= (\varepsilon_{HHb_{880}}\Delta[HHb] + \varepsilon_{HbO_{2_{880}}}\Delta[HbO_2]) \cdot d \cdot DPF \quad (7)$$

Where ΔA_{660} and Δ_{880} are the attenuations at 660 and 880 nm, ε_{HHb} and ε_{HbO_2} are respectively the extinction coefficients of deoxy-hemoglobin and oxy-hemoglobin at the two wavelengths, *Δ[HHb]* and *Δ[HbO₂]* are the changes in concentration of the two hemoglobins, d is the distance between the light emitter and photodetector and *DPF* is the Differential Pathlength Factor.

The system of linear equations composed by (6) and (7) yields the solutions for the changes in hemoglobin concentrations:

$$\Delta[HHb] = \frac{\Delta A_{880}\varepsilon_{HbO_{2_{660}}} - \Delta A_{660}\varepsilon_{HbO_{2_{880}}}}{(\varepsilon_{HbO_{2_{660}}}\varepsilon_{HHb_{880}} - \varepsilon_{HbO_{2_{880}}}\varepsilon_{HHb_{660}}) \cdot d \cdot DPF} \quad (8)$$

$$\Delta[HbO_2] = \frac{\Delta A_{660}\varepsilon_{HHb_{880}} - \Delta A_{880}\varepsilon_{HHb_{660}}}{(\varepsilon_{HbO_{2_{660}}}\varepsilon_{HHb_{880}} - \varepsilon_{HbO_{2_{880}}}\varepsilon_{HHb_{660}}) \cdot d \cdot DPF} \quad (9)$$

$$\Delta[tHb]=\Delta[HHb]+\Delta[HbO_2]. \quad (10)$$

However, *DPF* values for the distance adopted in our PPG system (i.e. 5 mm) are not available in the literature. As a full estimation of the optical pathlength in the tissue was not feasible, we opted for representing the results as relative changes of hemoglobins concentrations in $mM \cdot cm$ ([absolute concentration] x [optical pathlength]).

D. NIRS System

A commercial NIRS system (*NIRO 200NX*, Hamamatsu Photonics K. K., Japan) was used as reference for the estimation of relative changes in concentration of deoxy-hemoglobin, oxy-hemoglobin and total hemoglobin. This NIRS device uses LEDs for the emission of light at three different wavelengths: 735, 810 and 850 nm [40]. Two silicon photodiodes, at a small spacing between each other, detect the backscattered light and Spatially Resolved Spectroscopy (SRS) is applied for the absolute estimation of hemoglobins

concentrations [41]. Tissue Oxygenation Index (*TOI*) is calculated as the ratio between oxy-hemoglobin and total hemoglobin as in (11).

$$TOI= \frac{HbO_2}{HbO_2+HHb} \quad (11)$$

An emitter-photodetector spacing of 4 cm has been adopted in this investigation, guaranteeing the deep penetration of the light beam in tissues [24], [25].

E. Experimental Set-Up and Protocol

The system was evaluated on healthy volunteers by inducing vascular occlusions on the forearm. Ethical approval was gained from the Senate Research Ethics Committee at City University London. Twenty-one (21) healthy volunteers (13 males and 8 females, mean age ± SD: 31.18 ± 7.55) were recruited for the investigation. Subjects with a history of cardiovascular disorders were excluded from the study. The physiological measurements were performed in the Biomedical Engineering Research Group laboratories at a room temperature of 22 ± 1 ºC. The volunteers were seated in a comfortable chair and their left arm was rested on a pillow to minimize vascular compression. The reflectance PPG probe was positioned on the volar side of the left brachioradialis, while the NIRS probe was placed above the same muscle, proximal to the PPG probe. The probes were kept in place on the skin by double-sided clear medical tape. In order to avoid eventual optical impediment, the clear medical tape was previously cut at the light emitters and photodiodes locations. Care was taken in not compressing the probes on the skin surface during placement of the sensors and during the entire protocol. The custom-made finger PPG probe was connected to the second digit of the left hand, while a commercial, transmittance pulse oximeter sensor (Radical 7, Masimo Corp., U.S.A) was placed on the third digit of the same hand. A cuff pressure was positioned on the left upper arm in order to induce vascular occlusions. The cuff was connected to a sphygmomanometer for the full control of the occlusions pressure. ECG was monitored and acquired throughout the measurements.

The volunteers' blood pressure was measured prior to the commencing of the measurements. After recording five minutes baseline measurements, the cuff was rapidly inflated to 60 mmHg (inflation time < 4-5 s) in order to induce venous occlusion and maintained at this pressure for two minutes. The occlusion pressure was then quickly released for two minutes (deflation time < 1-2 s) before re-inflating the cuff for further two minutes. Total occlusion was performed by inflating the cuff to 20 mmHg greater than the volunteer's systolic pressure. After two minutes of total occlusion, the cuff pressure was finally released and data acquisition was stopped as soon as all the signals returned to baseline values.

F. Signal Acquisition, Processing and Analysis

All the signals (raw PPGs, NIRS parameters, and pulse oximeter signals) were digitized by two NI-PCIe6321 Data Acquisition Cards (DAQ) and acquired on a LabVIEW Virtual Instrument (VI) (National Instruments, U.S.A). The analogue signals were acquired at a sampling frequency of 400 Hz. The
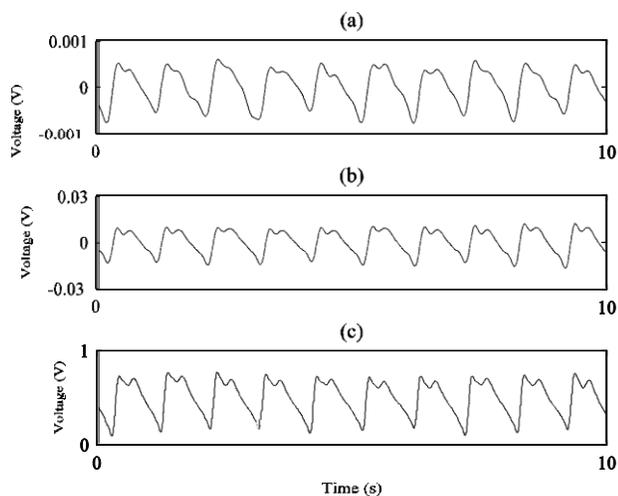
Fig.3. Infrared Photoplethysmographic traces from the forearm and fingers. (a) ZenPPG reflectance photoplethysmography from the forearm. (b) ZenPPG reflectance photoplethysmography from the finger. (c) Finger photoplethysmography from the commercial pulse oximeter.

VI was developed to acquire, filter, and display the measurements in real time, while raw signals were directly saved in a text file for further post-acquisition analysis. Algorithms were used for the real-time estimation and display of SpO_2 as in (1) and (2).

Off-line analysis of the signals was performed on MatlabR2013a (The Mathworks Inc., U.S.A). AC PPG signals were extracted by applying a Band-Pass digital filter (cut-off frequencies: $0.5 - 4$ Hz) to the raw PPG signals. DC components were obtained with a Low-Pass digital filter (cut-off frequency: 0.1 Hz). SpO_2 was calculated by applying (1) and (2) to a three seconds rolling window. Haemoglobin concentration changes and TOI, along with SpO_2 and single-wavelength PPG from the commercial pulse oximeter, were directly acquired from the devices' analogue outputs. Hemoglobin changes were estimated from DC PPG components by applying (6-11).

All the parameters were expressed as their mean (±SD). Mean SpO_2 and TOI values were calculated during 1-minute baseline segment, venous occlusion, and total occlusion. Spearman's correlation analysis was performed to determine correlation between changes in concentration of hemoglobins estimated from DC PPG components and NIRS during vascular occlusions. Mean increases (or drops) in hemoglobins concentrations were calculated as means of differences between hemoglobins values at the beginning and end of the occlusions. A Wilcoxon signed-rank test was also used to determine any statistical significant difference in the forearm SpO_2 from baseline to venous occlusion.

III. RESULTS

A. SpO_2 and TOI

Fig. 3 shows typical PPG traces acquired from the forearm and fingers of one volunteer during baseline measurements. AC PPGs from the forearm presented lower amplitudes compared with the fingers.

TABLE I
MEAN FOREARM AND FINGERS SpO₂ AND TOI VALUES DURING BASELINE, VENOUS OCCLUSION, AND TOTAL OCCLUSION

	Baseline		Venous Occlusion		Total Occlusion	
	Mean (%)	SD (%)	Mean (%)	SD (%)	Mean (%)	SD (%)
SpO2 Finger *ZenPPG*	98.3	2.0	98.9	2.6	78.3	1.8
SpO2 Finger Radical 7	98.5	0.8	98.1	1.1	39.2	32.0
SpO2 Arm *ZenPPG*	92.0	3.1	88.9	3.6	73.7	12.8
TOI (NIRO 200NX)	69.1	4.7	65.8	4.4	62.3	6.1

SpO_2 was calculated as in (1) and (2) from the PPG signals from both forearm reflectance probe and from the finger. Table I shows the mean SpO_2, TOI values and SD for the forearm and fingers during baseline, venous occlusion, and total occlusion.

SpO_2 estimated from the forearm during baseline measurements presented a lower mean value ($92.0 \pm 3.1\%$) when compared with SpO_2 values acquired from the custom-made finger probe and the commercial probe ($98.3 \pm 2.0\%$ and $98.5 \pm 0.8\%$ respectively). SpO_2 from the fingers did not exhibit any considerable mean desaturation from baseline during venous occlusion while, in contrast, SpO_2 from the forearm showed a statistically significant desaturation ($Z=-2.72$, $p=0.006$) with a mean drop of $3.1 \pm 3.6\%$. TOI exhibited a mean drop of $3.3 \pm 4.4\%$ throughout venous occlusion. During total occlusion, all the SpO_2 values have dropped as expected. These values are erroneous and not reliable readings originated from the absence of arterial pulsations and consequent increase in R. The disruption of oxygen delivery during total occlusion caused a decrease in HbO_2 concentration and a consequent drop in TOI value. Fig. 4 shows the means and SD of SpO_2 values and TOI during venous occlusion.

B. Hemoglobin Concentrations

Fig. 5, 6, and 7 show the mean changes of HHb, HbO_2 and tHb during venous and total occlusions. The hemoglobin concentrations changes estimated from DC PPG components followed the same trend with the signals produced by the NIRS system. HHb exhibited increases in its concentration in both occlusions. These were due to stagnation of venous blood caused by the blockage of its return in both occlusions. HHb concentrations estimated by NIRS and $ZenPPG$ presented a significant correlation during both venous occlusion ($r^2=0.960$, $p<0.05$) and total occlusion ($r^2=0.988$, $p<0.05$). At the end of both occlusions, the concentrations of HHb returned to baseline value.
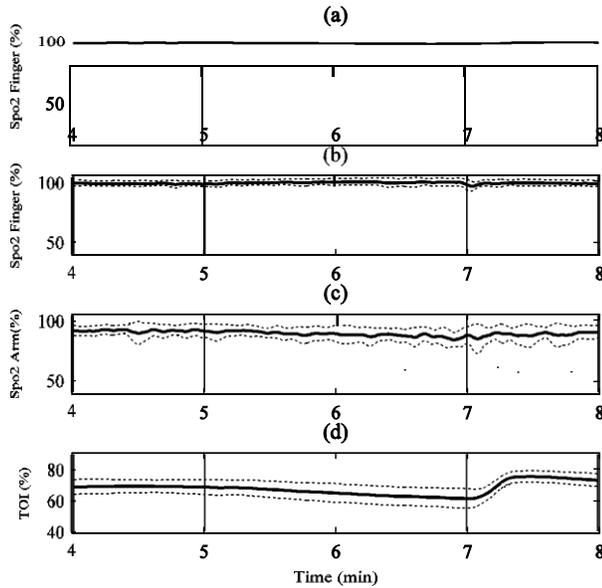
Fig.4. Mean and SD of SpO₂ and TOI for all the volunteers during venous occlusion. Vertical lines represent inflation and deflation of the cuff. (a) Finger SpO₂ from the commercial pulse oximeter; (b) Finger SpO₂ from ZenPPG; (c) Forearm SpO₂ from ZenPPG; (d) Forearm TOI from NIRS.

HbO₂ presented two different behaviors during the vascular occlusions. During venous occlusion the oxygen delivery to tissues was not compromised, hence an initial increase was observed, followed by a steady state. This increase is believed to be due to the impaired washout of blood caused by venous occlusion. During total occlusion, the oxygen delivery to tissues was impeded, causing a constant drop of *HbO₂* throughout the occlusion. *HbO₂* estimated by NIRS and *ZenPPG* presented high correlation during venous occlusion (r^2=0.821, p<0.05) and total occlusion (r^2=0.940, p<0.05). At the release of total occlusion, oxy-hemoglobin manifested an overshot caused by the post-ischemic hyperemic response of the tissue.

Fig.6. Mean and SD of *HbO₂* changes during venous and total occlusions from NIRS and ZenPPG. Left subplots: venous occlusion. Right subplots: total occlusion. (a) NIRS HbO₂ during venous occlusion (b) NIRS HbO₂ during total occlusion (c) ZenPPG HbO₂ during venous occlusion (d) ZenPPG HbO₂ during total occlusion. Vertical lines represent inflation and deflation of the cuff. Solid lines: mean; dashed lines: SD.

Total hemoglobin was estimated by summing *HHb* and *HbO₂* as in (10). Thus, its increase during venous occlusion is mainly due to the rise of *HHb* concentration. Total hemoglobin can be used as an estimate of total blood volume in tissues; hence, its increase during total occlusion represented the gradual accumulation of blood volume due to venous blood stagnation and steady arterial blood in-flow. During total occlusion, *tHb* showed an initial increase, followed by a relatively constant trend. Total hemoglobin estimated by NIRS and *ZenPPG* showed high correlation during both venous occlusion (r^2=0.974, p<0.05) and total occlusion (r^2=0.938, p<0.05). At the release of venous occlusion, *tHb* returned to its baseline values. An overshot of *tHb* was observed in all cases following the release of total occlusion, indicating the post-ischemic hyperemic response.
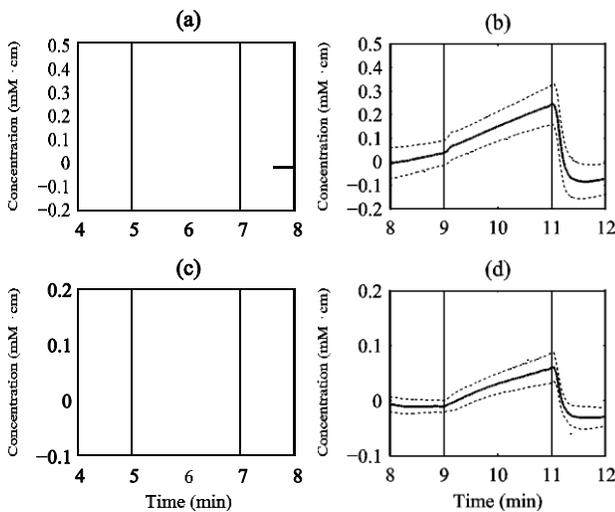

Fig.5. Mean and SD of HHb changes during venous and total occlusions from NIRS and ZenPPG. Left subplots: venous occlusion. Right subplots: total occlusion. (a) NIRS HHb during venous occlusion (b) NIRS HHb during total occlusion (c) ZenPPG HHb during venous occlusion (d) ZenPPG HHb during total occlusion. Vertical lines represent inflation and deflation of the cuff. Solid lines: mean; dashed lines: SD.
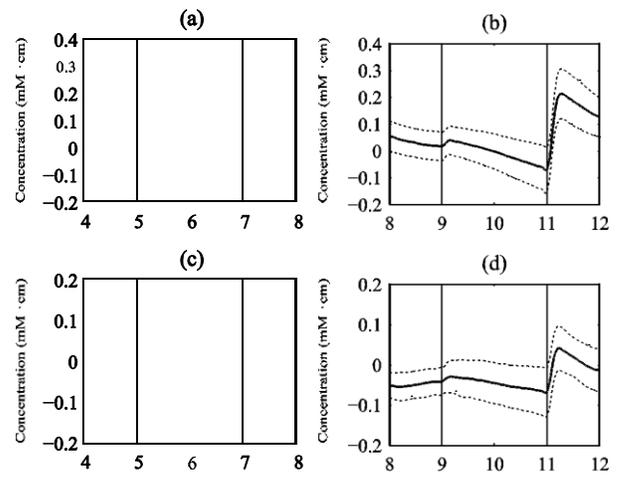

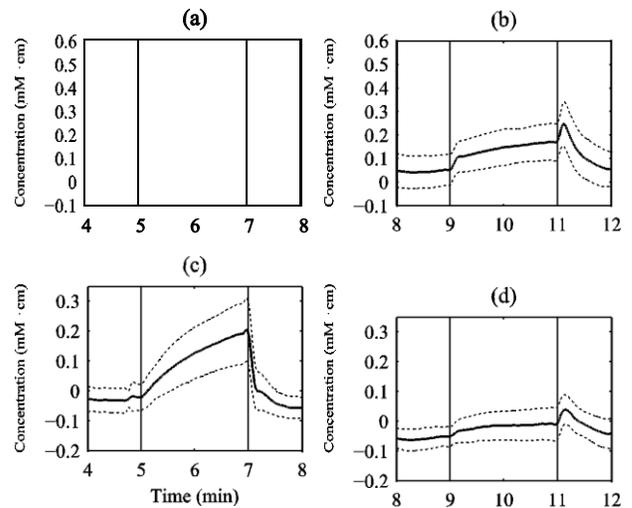Fig.7. Mean and SD of tHb changes during venous and total occlusions from NIRS and ZenPPG. Left subplots: venous occlusion. Right subplots: total occlusion. (a) NIRS tHb during venous occlusion (b) NIRS tHb during total occlusion (c) ZenPPG tHb during venous occlusion (d) ZenPPG tHb during total occlusion. Vertical lines represent inflation and deflation of the cuff. Solid lines: mean; dashed lines: SD.

Table II shows the mean increments and decreases of *HHb*, *HbO₂* and *tHb* estimated by NIRS and *ZenPPG* during both occlusions. The values were calculated as the means of the differences in amplitude at the beginning and end of the occlusion periods.

TABLE II
MEAN CHANGES (±SD) IN HHB, HBO₂ AND THB CONCENTRATIONS (in mM · cm) DURING VENOUS AND TOTAL OCCLUSION

	Venous Occlusion		Total Occlusion	
	NIRS	ZenPPG	NIRS	ZenPPG
HHb	0.257 (±0.072)	0.102 (±0.042)	0.209 (±0.055)	0.071 (±0.027)
HbO₂	0.128 (±0.080)	0.115 (±0.063)	-0.086 (±0.058)	-0.026 (±0.044)
tHb	0.385 (±0.139)	0.2179 (±0.088)	0.122 (±0.046)	0.044 (±0.043)

IV. DISCUSSION

Mean SpO_2 and *TOI* values during baseline measurements were in their physiological ranges and they were in good agreement with previous studies [23], [29], [42]. However, baseline SpO_2, which was estimated by the reflectance probe on the forearm, presented lower values compared with SpO_2 calculated from the fingertips. This has not to be considered a physiological difference in arterial blood saturation as both sensors estimated SpO_2 from the same arterial branch. Nevertheless, these lower values for the forearm are in agreement with the trends showed in an earlier similar study by Mendelson and McGinn in which a reflectance PPG sensor was developed for the estimation of SpO_2 from the forearm and calf of healthy adults. Regression analysis revealed lower SpO_2 values estimated from the forearm and the calf when compared to a transmission finger probe [43]. These differences were attributed to the difficulty to extract high amplitude PPG from locations with a low capillary density such as the forearm and calf [43]. In order to facilitate the acquisition of PPG signals from the two locations, Mendelson and McGinn incorporated a heating element into the reflectance sensor to increase the skin temperature [43]. However, in this study we decided not to use the same approach as heating the skin might affect the blood perfusion, thus conflicting with vascular occlusions adopted in this study. We also observed from our experience that low values of SpO_2 on the forearm might be due to higher *R*-values caused by a higher absorption of red light in the forearm when compared with fingers. Moreover, the presence of large superficial veins on the forearm may affect the accuracy of the SpO_2 values calculated [44].

Except the forearm, all the estimated SpO_2 values did not significantly vary during venous occlusion. In contrast, and as it was expected, they dropped during total occlusion. The absence of any relevant drop during venous occlusion should be considered a serious limitation of pulse oximetry on monitoring tissue blood perfusion. Shafique et al. observed that significant drops in *AC* PPG amplitude were seen only for occlusion pressures exceeding the diastolic pressure (e.g. 75 mmHg). We think this inability of pulse oximetry may introduce risks in situations when a more complete perfusion monitoring is required. As pulse oximetry relies on pulsating arterial blood for the estimation of SpO_2, the absence of pulsations in total occlusion causes the pulse oximeter to fail in the calculation of SpO_2 [23]. Even though a desaturation during venous occlusion was detected, the presence of arterial pulsations (i.e. *AC* PPG), and an unaffected SpO_2 on the fingers, might still be misjudged as an adequate blood perfusion [13].

Tissue Oxygenation Indexes measured from the forearm exhibited the expected drops in agreement with previous studies when NIRS was used in conjunction with vascular occlusions [29], [30]. During both occlusions, *TOI* showed

desaturations, providing a fair indication of changes in tissue blood perfusion. Throughout venous occlusion the continuous increase in *HHb* concentration, and relative steady state of *HbO₂*, caused a constant fall in *TOI* in all volunteers. The increase in *HHb* and the simultaneous decrease of *HbO₂* during total occlusion caused a more severe *TOI* desaturation.

SpO_2 and *TOI* are extensively used in clinical and research settings [8]-[10], [12], [20]-[23], [28]-[30]. The SpO_2 only provides oxygen delivery information (i.e. arterial blood oxygen saturation) and it cannot be used as sole indicator of tissue blood perfusion. Its dependence on pulsatile arterial PPG components restricts its use in situations where changes in perfusion are not directly reflected in arterial blood. On the other side, *TOI* (also called in the literature as StO_2 or rSO_2) is not dependent on arterial pulsations and its lower values, compared to SpO_2, are more representative of mixed blood oxygen saturation (arteries, capillaries and veins) [25]. Moreover, the index is directly calculated from the ratio of *HbO₂* and *tHb* (*HbO₂*+*HHb*) and its changes indicate perfusion variations directly affecting this ratio. Thus, we believe the estimation of Δ*HHb*, Δ*HbO₂,* and Δ*tHb*, along with SpO_2, from PPG signals could improve the ability of the technique in following changes in blood perfusion.

The changes in *HHb*, *HbO₂* and *tHb* obtained from *DC* PPG components were in agreement with the same parameters measured by NIRS as can be seen in Fig. 5, 6 and 7. The three hemoglobins measured by NIRS followed the same trends described previously in the literature when venous or total occlusion occur [29], [32], [45], [46]. The hemoglobins changes allowed the distinction of venous occlusion where it was unnoticed by conventional pulse oximetry. At the release of occlusion, all the hemoglobins returned to their baseline. In particular, *HbO₂* and *tHb* exhibited correctly the post-ischemic hyperemic response of the tissue after release of total occlusion. The initial increase of *tHb* in total occlusion was due to the non-instantaneous inflation of the cuff over systolic pressure and the consequent initial build-up of venous blood. These results suggest that haemoglobin concentration changes can be extracted from PPG signals. Very recently, Akl et al. reported results from an animal study in which PPG signals were used for monitoring liver tissue. In their work, a PPG probe was placed on the parenchymal tissue of two swine and NIRS principles and multi-linear regression analysis were performed to track changes in perfusion and oxygenation [47]. The quantitative differences observed in our study between the PPG-derived and NIRS-derived hemoglobins have to be

related to the different light penetration depths. While the large LEDs-photodiode spacing in NIRS allows the deep penetration of light in tissues (approximately up to 2 cm) [25], [26], the small separation distance in our reflectance PPG probe (i.e. 5 mm) limits the penetration depth to only few millimeters in the skin layers. The spacing employed in our reflectance PPG probe has been chosen for the best acquisition of PPG signals and as a trade-off between light intensities and photo-detection system. Another parameter affecting the light penetration depth is the specific light wavelengths adopted to illuminate the tissues; the NIRS monitor adopted in this study employs LEDs at nominal wavelengths of 735, 810 and 850 nm, in contrast with the 660/880 nm pair used in our PPG reflectance probe. Thus, the shallower light penetration of our reflectance PPG probe could be considered the cause for lower SpO_2 values estimated from the forearm. The PPG signal detected by our probe is likely to originate from capillaries structures within the skin. As capillaries contain a mixture of arterial and venous blood, the calculated SpO_2 values have lower values compared to fingers. Furthermore, the decrease of SpO_2 from the forearm during venous occlusion may be caused by the shifting of arterial/venous blood ratio in capillaries due to venous congestion. However, superficial layers (skin) and deep tissue (brachioradialis) share the same major arteries and veins; hence, occlusions of these vessels produce changes in blood perfusion in both compartments. Furthermore, monitoring skin circulation, which serves as a blood reservoir and has a weaker autoregulation, can be used as an early indicator of changes in blood perfusion in more internal organs [2], [48]. Although myoglobin and hemoglobin in muscles cannot be distinguished when measured by NIRS [26], we decided to express the NIRS parameters as 'only-hemoglobin' changes.

The rate of increase in HHb, or the decrease rate of HbO_2, measured by NIRS during venous or total occlusions have been used as indicators of oxygen consumption [27], [28], [49]. Therefore, the values in Table II may be used as comparative indicators of oxygen consumption. In particular, the part of tissue interrogated by our PPG probe (i.e. skin) appears to have a lower consumption rate when compared with tissues measured by NIRS (i.e. muscle). These differences in metabolic rate are in agreement with physiology tables on oxygen consumption of various human body tissues [50].

Future work will focus on the improvement of the PPG reflectance probe, for instance the placement of the LEDs, in order to achieve a more homogeneous interrogation of volume of tissue. In addition, the probe could be further miniaturized.

V. CONCLUSION

In this work, we explored the capabilities of a photoplethysmographic system in providing additional information, when compared to conventional photoplethysmography, on changes in blood perfusion during vascular occlusions. The system estimated arterial blood oxygen saturation as a conventional pulse oximeter and it applied the Beer-Lambert law for the estimation of changes of concentration of deoxy-hemoglobin, oxy-hemoglobin, and total hemoglobin. The evaluation of the system in healthy volunteers demonstrated that hemoglobins concentration changes estimated from PPG could be a valuable additional tool for the assessment of blood perfusion. The promising comparative results with the NIRS system showed that the photoplethysmography boundaries might be effectively extended to NIRS.

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