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Modulation of finger photoplethysmographic traces during forced respiration: venous blood in motion?

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***Abstract*—Photoplethysmographic (PPG) signals were recorded from the fingers of 10 healthy volunteers during forced respiratory inspiration. The aim of this pilot study was to assess the effect of negative airway pressure on the blood volumes within the tissue bed of the finger, and the resultant modulation of PPG signals. The acquired signals were analysed and oxygen saturations estimated from the frequency spectra in the cardiac and respiratory frequency ranges. Assuming that respiratory modulation affects blood volumes in veins to a greater extent than in arteries, the local venous oxygen saturation was estimated. Estimated venous oxygen saturation was found to be 3.1% (±4.2%) lower than the estimated arterial saturation.**

I. Introduction

Photoplethysmographic (PPG) signals as detected by a pulse oximeter probe, and upon which pulse oximetry depends, may be described as periodic variation in absorbance of light by perfused tissue [1]. This absorbance variation is caused by the increase in the volume of the elastic arteries and arterioles, and hence an increase in optical path, in response to the systolic pressure pulse and subsequent relaxation of the vessels during diastole. Pulse oximetry algorithms estimate arterial oxygen saturation from the ratio of absorbance of red and infrared light by the hemoglobin using the acquired PPG signals to discriminate between arterial blood and the non-pulsatile absorbers in the tissue such as venous blood, skin, fat and pigments such as melanin [2].

Most interpretations of photoplethysmography, including conventional pulse oximetry algorithms, assume that the only time varying component of the absorbance signal (and hence the recorded PPG) is the systolic-diastolic variation in volume of the arterial 'compartment' of blood within the tissue. It has been shown that the venous blood volume does not in fact remain static, rather the volume of the veins vary in response to various physiological and physical effects [3]. Changes in intrathoracic pressure induced by the respiratory muscles (or mechanical ventilator) are transmitted from the large veins in the thorax (e.g. superior vena cava) to the peripheral veins. It may also be supposed that mechanical pressure waves may be transmitted from pulsating arteries to nearby veins, producing pulsatile pressures observed in veins under certain physiological conditions. Furthermore, the arterial blood volume is affected by respiration: the pulsus paradoxus effect, namely the reduction in cardiac output and resulting drop in blood pressure during inspiration [4].

By closely observing the PPG signal, artifacts produced by the all of the effects described above may sometimes be seen, despite heavy filtering and rescaling of the displayed PPG waveforms in commercial patient monitors. It has been suggested that inaccuracies in oxygen saturation may result from such artifacts, particularly in aggressively ventilated, under-filled patients [5]. It has also been suggested that various clinically useful variables may also be extracted from the raw PPG signals, using specialized algorithms to isolate and correctly interpret various signal components [6].

Canneson et al. noted that respiratory modulation of the PPG signal in ventilated patients reduces when intravenous fluids are given and suggest that the relative modulation of the PPG signal may be used as an indication of 'fluid responsiveness' (the increase in blood pressure after administration of a given volume of intravenous fluid) [7]. Gesquiere et al. demonstrated that the respiratory modulation increases when 450 mL of blood is removed from the patient [8]. It has also been suggested that suitable signal analysis of red and infrared PPG signals in the respiratory frequency range can produce estimations of local venous oxygen saturation and hence local arteriovenous difference [9–10]. This suggestion is based on the hypothesis that the response to respiratory pressure changes is much greater in veins than arteries. The compliance of partially-filled veins is very high compared to arteries, so it may be supposed that veins may distend considerably more than arteries in response to the modest ventilatory pressure changes.

The aim of this study was to investigate the effects of respiration on PPG signals measured from the finger in healthy volunteers performing periodic forced inspiratory maneuvers. In order to shed light on the mechanism of intrathoracic pressures to the venous system, airway pressure measured at the mouth during the maneuvers (as a surrogate for intrathoracic pressure) was compared with features appearing in the recorded PPG signals. Arterial and local venous oxygen saturation values were estimated by analyzing the PPG signals in the cardiac and respiratory frequency ranges respectively.

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II. MATERIALS AND METHODS

A. Measurement system

The measurement system consisted of a custom made finger pulse oximeter. The probe is a standard commercial finger pulse oximeter probe (GE Datex-Ohmeda, Helsinki, Finland). The instrumentation system comprises multiplexed emitter drivers, which produce 40 mA and 25 mA drive current in the red (660 nm) and infrared (940 nm) LEDs contained within the probe.

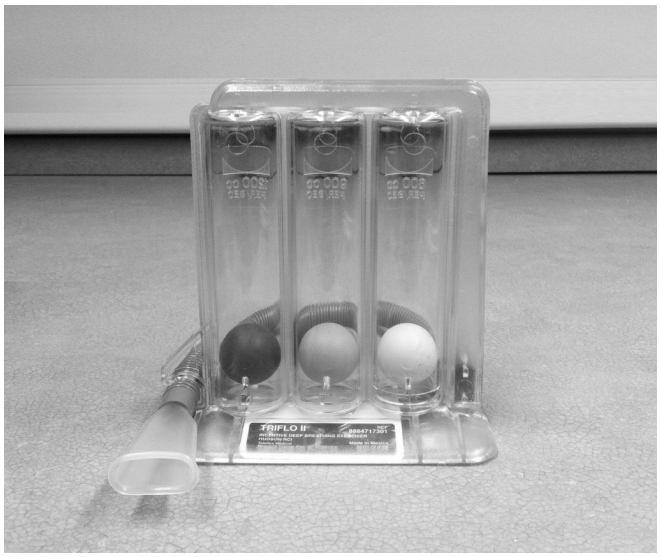

Figure 1. Photograph of incentive spirometer.

The output from the photodiode is passed to a transimpedance amplifier, then a demultiplexer to separate the signals into red and infrared channels. Each signal is then passed to a low pass filter with pass band 0–23.4 Hz to remove switching artifact, coupled mains and other interference. The signals are then digitized using two analog inputs of a National Instruments NI-6216 16-bit data acquisition card (National Instruments Inc., Austin, TX, USA) sampled at 100 Hz.

A mouthpiece consisting of a narrow tube 8 cm long and 8 mm internal diameter was used as a flow resistor to allow significant airway pressures to be generated during forced breathing. A port at the proximal (mouth) end was used to measure pressure at the mouth to give an estimation of large airway pressure. The port was connected to a signal conditioned 40PC001B1A pressure sensor (Honeywell Inc., Freeport IL, USA) via an airway gas sampling line of length 1.5 m and internal diameter approximately 2.4 mm. Indication of inspiratory flow was provided using a Triflo II incentive spirometer (Teleflex Medical, Research Triangle Park, NC, USA), whereby flow generated by the subject raises one to three plastic spheres placed in three parallel columns of air through which inspired air flows, the device working on a similar principle to an anesthetic Rotameter. Fig. 1 shows a photograph of the incentive spirometer. The red and infrared photoplethysmographic signals, together with airway pressure signals were recorded in a tab-delimited text file on a notebook computer running LabVIEW (National Instruments Inc.).

B. Experimental protocol

The protocol was approved by City University Senate Research Ethics Committee. Measurements were made on 10 healthy volunteers (5M, 5F, mean age 33.6 years). Subjects were asked to refrain from smoking and caffeinated drinks for three hours prior to the study and were seated in a chair with the right hand resting on a table in front of them. The pulse oximeter probe was placed on the index finger of the right hand and a commercial pulse oximeter probe (Masimo Corp. Irvine, CA, USA) was placed on the right middle finger. Subjects were asked to breathe through the flow mouthpiece while performing a series of timed forced inspirations followed by gentle expiration at a rate of 10 breaths per minute. During each inspiration the subjects were asked to raise all three spheres in the spirometer during each breath, with breaths prompted by an electronic metronome. Optical signals from the finger probe and airway pressure were recorded on the notebook computer, while oxygen saturation reading on the commercial pulse oximeter were noted at the end of each maneuver.

C. Signal analysis

Amplitude spectra were obtained from discrete Fourier transforms (DFTs) of 24-second samples of each data set. The samples were taken after 30 seconds of recording in each case. The ratio of peak heights in the spectra of the red and infrared signals appearing at the cardiac frequency (1–2 Hz) was used to calculate the 'ratio of ratios' (R_{CARD}) as used in pulse oximetry algorithms for calculation of arterial oxygen saturation [2]. A similar method was used to estimate the ratio of ratios (R_{RESP}) this time using the peak heights of red and infrared at the respiratory frequency (approximately 0.167 Hz). Oxygen saturation values were calculated using the often-quoted equation used to calibrate Nellcor commercial pulse oximeters; a linear approximation of empirical data obtained from volunteer studies [11]:

$$ScO_2 = 110 - 25R_{CARD} \quad (1)$$

$$SrO_2 = 110 - 25R_{RESP} \quad (2)$$

where ScO_2 and SrO_2 are the oxygen saturations calculated at the cardiac and respiratory frequencies respectively. It was expected that ScO_2 should approximately equal the arterial oxygen saturation measured by the commercial pulse oximeter (SpO_2). The 'respiratory' saturation was expected to correlate more closely to local venous oxygen saturation. Although the venous saturation was not measured using a reference method, SrO_2 and ScO_2 values were compared to see if $SrO_2 < ScO_2$, and the differences tested for significance using a paired Student's t-test.

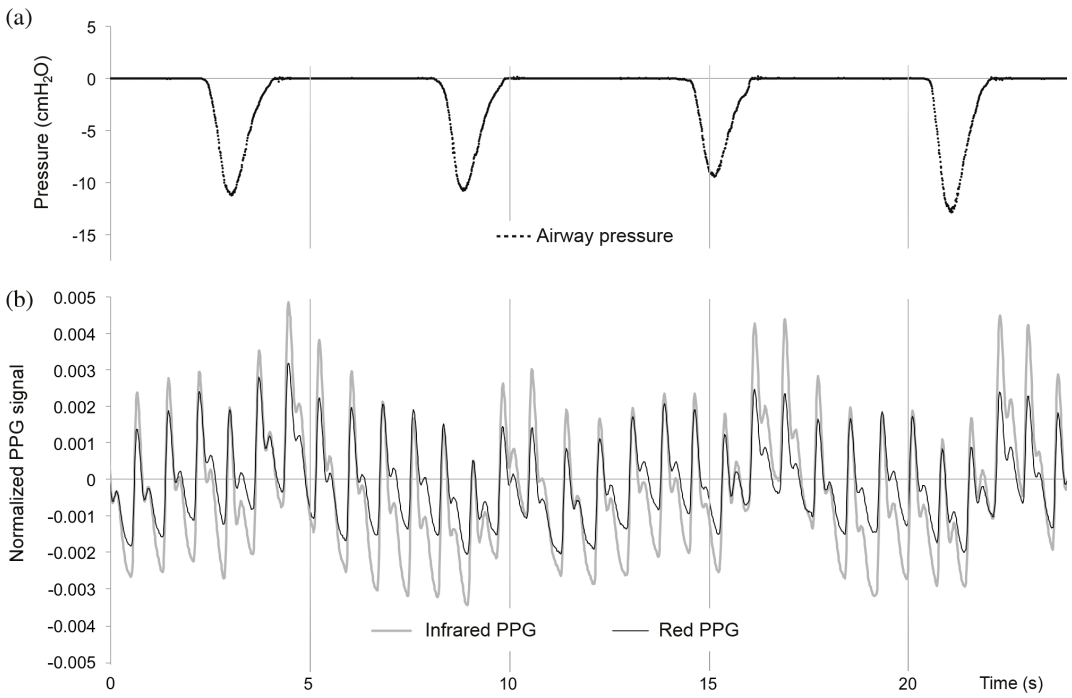

Figure 2 (a). 24-second sample of the airway pressure recorded in Subject #1. (b) Simultaneous red and infrared PPG signals recorded simultaneously from the finger.

III. Results

Fig. 2(a) shows a 24-second sample of the airway pressure signal recorded from the Subject #1. Fig. 2(b) shows the infrared and red PPG signals from the custom-made pulse oximetry system recorded simultaneously and plotted on the same time axis. Note that for the purposes of the diagram signals were inverted and high-pass filtered to remove DC-offset. It can be seen that both infrared and red signals were modulated considerably at the respiratory frequency and the modulation is synchronous with each inspiration. Fig. 3 shows discrete Fourier transforms of the same infrared and red PPG signal. The 'respiratory' and 'cardiac' peaks can be clearly seen at the expected frequency ranges (approximately 0.167 Hz and 1–2 Hz respectively).

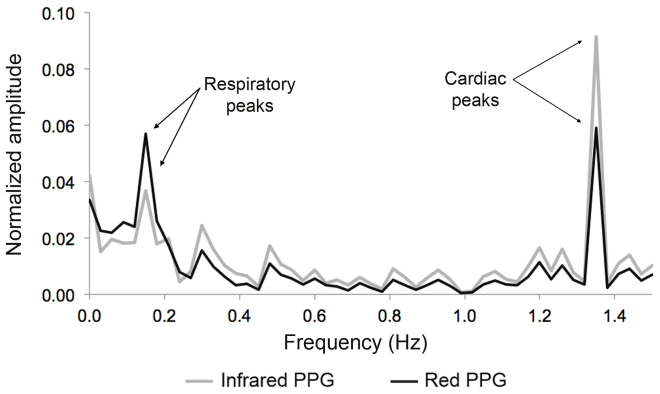

Figure 3. Discrete Fourier transforms of the infrared and red PPG signals from Subject #1

The ratio of ratios and oxygen saturations estimated from the DFTs at the cardiac and respiratory frequencies are shown in Table 1. It can be seen that in most (but not all) subjects $SrO_2 < ScO_2$. The mean difference ($SrO_2 - ScO_2$) is +3.11% (percentage saturation units), while the difference between pairs of measurements in each subject was significant (P=0.018). The difference ($ScO_2 - SpO_2$) was equal to –3.6% with significant difference between paired measurements (P<0.01).

TABLE I. OXYGEN SATURATION VALUES OBTAINED FROM COMMERCIAL PULSE OXIMETER (SPO2) AND CUSTOM MEASUREMENT SYSTEM (SCO2 AND SRO2)

Subject #	SpO_2	ScO_2	SrO_2	ScO_2–SrO_2
1	99.0	94.0	95.7	-1.7
2	99.0	96.5	95.0	1.5
3	100.0	99.3	88.1	11.2
4	99.0	94.6	95.1	-0.5
5	100.0	95.2	90.7	4.5
6	99.0	95.3	93.1	2.2
7	100.0	96.3	89.0	7.3
8	98.0	94.4	88.6	5.9
9	99.0	94.9	97.0	-2.1
10	99.0	93.6	90.9	2.7
Mean (±SD)	99.2(±0.7)	95.4(±1.7)	92.3(±3.3)	3.1(±4.2)

IV. Discussion

The aim of this study was to test the hypothesis that the venous blood volume in peripheral tissue changes in response to sharp negative intrathoracic pressure changes caused by forced inspiration. If this hypothesis is true, then modulation of the PPG signal caused by changes in venous blood volume could allow estimation of local venous oxygen saturation, assuming that a comparable modulation of arterial blood volume does not occur. The signals recorded from the custom pulse oximeter suggest that the overall (venous and arterial) blood volume in the finger certainly changes during inspiration, since respiratory-frequency modulation is observable in the time domain and frequency domain plots (Fig1b and Fig 2). The saturation values estimated from the cardiac pulsations are significantly lower than the values recorded from the commercial pulse oximeter. This is possibly due to the use of a generic algorithm designed for a specific commercial pulse oximeter probe of indeterminate geometry. The correlation between values could be improved if a dedicated algorithm could be implemented, especially if calibrated using DFT-derived ratio of ratios.

The average 'respiratory' saturation (SrO_2) was lower then the 'cardiac' saturation (ScO_2) as would be expected if SrO_2 truly represents local venous oxygen saturation. The fingers do not contain large masses of skeletal muscle or other highly metabolic tissue, so the oxygen uptake in the finger is almost certainly quite small. The expected oxygen saturation of venous blood in the hand would therefore not be as low as say mixed venous oxygen saturation as measured using a pulmonary artery catheter. It is not possible to conclude whether the venous saturation estimated using this non-invasive method is 'contaminated' by respiratory-frequency modulation of arterial blood without further research. A study whereby PPG signals recorded using the custom measurement system from anesthetized mechanically ventilated patients is planned. The oxygen saturation of venous blood sampled from the dorsal vein in the hand will be measured using a hemoximeter and the results used to validate non-invasive venous saturation values derived from the PPG signals. Although recording venous oxygen saturation in the finger is not in itself clinically useful, these studies will hopefully demonstrate that accurate non-invasive estimation of arterio-venous saturation in other sites, perhaps using internal reflectance mode PPG probes could give invaluable insight into the metabolism and oxygen consumption in specific vital organs.

References

[1] J. Allen, "Photoplethysmography and its application in clinical physiological measurement," *Phys meas*, vol. 28, pp. R1–R39, 2007.

[2] J. Moyle, *Pulse Oximetry (Principles and Practice)*, 2nd ed. London: BMJ Books, 2002.

[3] L. Nilsson, A. Johansson, S. Kalman, "Respiratory variations in the reflection mode photoplethysmographic signal. Relationships to peripheral venous pressure," *Med Biol Eng Comp*, vol. 41, pp. 249-254, May 2003.

[4] Michard F., "Changes in arterial pressure during mechanical ventilation," *Anesthesiology,* vol. 103**,** pp. 419-28, 2005.

[5] P. D. Mannheimer, M. P. O'Neil, Ewald Konecny, "The influence of larger subcutaneous blood vessels on pulse oximetry", *J Clin Mon Comp*, vol.18, pp.179–188, April 2004.

[6] Kirk H. Shelley. "Photoplethysmography: Beyond the calculation of arterial oxygen saturation and heart rate," *Anesth & Analg*, vol. 105, pp. S31-S36, Aug 2007.

[7] M. Cannesson, Y. Attof, P. Rosamel et al., "Respiratory variations in pulse oximetry plethysmographic waveform amplitude to predict fluid responsiveness in the operating room, " *Anesthesiology,* vol. 106**,** pp. 1105–11, 2007.

[8] M. J. Gesquiere, A. A. Awad, D. G. Silvermen et al., "Impact of withdrawal of 450 ml of blood on respiration-induced oscillations of the ear plethysmographic waveform." *J Clin Mon Comp,* vol. 21**,** pp. 277-82, 2007.

[9] Z. D. Walton, "Measuring venous oxygenation using the photoplethysmograph waveform," M.D. thesis, Dept. Anesth., Yale Univ., New Haven, CT, USA, 2010.

[10] J. P. Phillips, P. A. Kyriacou, D. P. Jones et al. "Pulse oximetry and photoplethysmographic waveform analysis of the esophagus and bowel," *Curr Op Anesth,* vol. 21, pp.779–783, 2008.

[11] T. L. Rusch, R. Sankar, J. E. Scharf, "Signal processing methods for pulse oximetry," *Comput Biol Med*, vol. 26, pp. 143-59, 1996.