The effect of vascular changes on the photoplethysmographic signal at different hand elevations

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Abstract

In order to further understand the contribution of venous and arterial effects to the photoplethysmographic (PPG) signal, recordings were made from twenty healthy volunteer subjects during an exercise in which the right hand was raised and lowered with reference to heart level. Red (R) and infrared (IR) PPG signals were obtained from the right index finger using a custom-made PPG processing system. Laser Doppler flowmetry (LDF) signals were also recorded from an adjacent fingertip. The signals were compared with simultaneous PPG signals obtained from the left index finger. On lowering the hand to 50 cm below heart level, both ac and dc PPG amplitudes from the finger decreased (e.g. 18.70% and 63.15% decrease in infrared dc and ac signals respectively). The decrease in dc amplitude most likely corresponded to increased venous volume, while the decrease in ac PPG amplitude was due to regulatory adjustments on the arterial side in response to venous distension. Conversely, ac and dc PPG amplitudes increased on raising the arm above heart level. Morphological changes in the ac PPG signal are thought to be due to vascular resistance changes, predominately venous, as the hand position is changed.

Keywords: photoplethysmography, oxygen saturation, venous pulsations, hand elevation, vasoconstriction, vasodilation

1. Introduction

Photoplethysmography (PPG) is a non-invasive, optical technique that measures relative blood volume changes in the blood vessels close to the skin [Allen 2007]. The PPG waveform comprises a pulsatile (ac) waveform superimposed on a slowly varying (dc) baseline. The ac component arises from the light absorbance variation due to pulsation of the elastic arteries and arterioles with each heartbeat [Phillips *et al* 2012]. The ac component has been described as having two phases: the upstroke is primarily associated with distension of the vessels during systole (referred to as the systolic phase), and the downstroke corresponds to the subsequent relaxation of the vessels during diastole and wave reflections from the periphery (referred to as the diastolic phase) [Allen 2007]. A dicrotic notch is usually seen in the downstroke of the PPG from subjects with healthy compliant arteries, while a ‘diminution or disappearance of the dicrotic wave’ occurs in patients with arteriosclerosis [Angius *et al* 2012, Millasseau *et al* 2006]. The dc component is generally associated with light absorption by non-pulsatile arterial blood, venous blood and tissue [Moyle 1998].

Photoplethysmographic signals are most commonly used in pulse oximeters for the estimation of arterial oxygen saturation and heart rate calculation [Kyriacou 2013]. More specifically, pulse oximeters utilise the ratio of absorbance of red and infrared light by the haemoglobin using the PPG signals to discriminate between arterial blood and the non-pulsatile absorbers. More recently, the PPG has been explored as a monitoring tool for other parameters, driven in part by its attractiveness as a simple, low-cost, non-invasive tool [Allen 2007].

Due to their morphological similarity, it has been suggested that the ac PPG signal has a direct relationship to arterial blood pressure waves [Reisner *et al* 2008], and as a result, the PPG signal has been explored as a method to extract circulatory and cardiovascular information from patients [Allen 2007]. The peripheral PPG pulse has been found to become "damped, delayed and diminished" with increasing severity of vascular disease and vascular aging [Allen 2007, Millasseau *et al* 2006]. Morphological analysis of the PPG in order to quantify vascular disease is performed by examining various features of the ac PPG pulse, including rise time, frequency characteristics, width/height ratio, amplitude and shape [Elgendi 2012, Alty *et al* 2007]. Other morphological work analyses the reflected wave component of the PPG [Yousef *et al* 2012]. This assumes that as the PPG wave moves from central arteries to the periphery, the more resistant vessels in the peripheral vasculature will induce reflection of the wave [Elgendi 2012], with the diastolic peak or notch representing the reflected wave. It has been found that in stiffer arteries with arteriosclerosis, the contribution of the reflected wave is more prominent in the systolic phase instead of the diastolic phase of the PPG due to earlier reflection [Angius *et al* 2012].

Although venous blood has generally been thought to be a static absorber of light, it has been shown that the venous blood volume does not in fact remain constant [Nilsson *et al* 2003]. In fact, the volume of the veins fluctuates in response to various physiological and physical effects, such as respiration [Phillips *et al* 2012]. It has been hypothesised that the response to respiratory pressure changes is much greater in veins than arteries [Shelley 2007] due to greater compliance of veins compared to arteries. Respiratory modulation of the PPG waveform [Natalini *et al* 2006] and observed peripheral venous pulsations [Wardhan and Shelley 2009] have been recorded and used in an attempt to estimate venous oxygen saturation [Shafqat *et al* 2012, Walton *et al* 2010].

While it is generally accepted that the PPG signal can provide valuable information about the cardiovascular system [Allen 2007], the origins of the PPG signal are still not fully understood. Furthermore, despite the similarities between them, the relationship between the pulsatile ac PPG signal and the arterial pressure waveform is complex [Chowienczyk *et al* 1999]. As a result, there remains a need for furthering understanding of the effect of various physical and physiological factors on the recorded PPG signals so that new clinical variables can be successfully extracted from this complex waveform [Shelley 2007].

While most work has focused on the arterial factors affecting the PPG signal, the aim of this current work is to investigate the contribution of the venous system to the morphology and modulations of both the ac and dc PPG components as measured from the finger. Alterations in venous blood volume, through pooling or drainage, will affect venous vascular resistance, and hence, assessment of vascular disease as described above. Furthermore, changes in venous volume and venous pressures, may result in the successful extraction of venous parameters, such as venous oxygen saturation. This investigation aims to provide increased understanding of the relationship between both venous and arterial components as

measured by the PPG, and allow for the possibility of augmenting photoplethysmographic algorithms to provide further analysis of the cardiovascular system. In particular, it is thought that this information may prove useful in various applications, for example monitoring non-invasive blood pressure, vascular resistance, non-invasive venous oxygenation or altered venous return.

To alter venous blood volume and to achieve venous pooling and venous drainage in the hand, a hand-raising study was carried out in the laboratory. It is well known that the position of the limb relative to the heart has an effect on venous flow and return [Wilkins *et al* 1950], predominately due to the hydrostatic effect [Kammila *et al* 2002, Gavish and Gavish 2011]. In the dependent position (below heart level), venous return is impeded due to gravity–induced effects, while in the raised position venous return is enhanced. The effect of changing limb position on cardiovascular responses has long been explored [Wilkins *et al* 1950, Beaconsfield and Ginsberg 1955]. More recently, the effect of limb elevation on tissue perfusion has been explored using a micro-light guide spectrophotometer [Darmanin *et al* 2013]. It was found that the optimal superficial perfusion was when the arm was at heart level and the forearm at 45°. Almond *et al* evaluated dc PPG and laser Doppler flowmetry (LDF) signals from the finger using arterial occlusion at different arm positions [Almond *et al* 1988]. They concluded that under conditions of low venous filling and unimpeded venous return, changes in blood volume, as measured by the dc PPG, closely followed the changes in blood flow measured by the LDF. However, the use of a cuff to achieve arterial occlusion results in external disruptions to blood flow, and, hence, the correlations between LDF and the dc PPG cannot be due to postural effects alone. Xin *et al* (2007) examined the infrared PPG signal from the toe when the foot was raised above heart level, and found a corresponding change in ac amplitude. However, this work did not simultaneously monitor blood flow changes from the vascular bed under interrogation and was focused on the changes due to elevation rather than limb dependency. Furthermore, as their work was mainly on providing assessment of vascular diseases of the foot associated with diabetes, the PPG signals were obtained from the foot, which is not always an appropriate monitoring site for patients.

To overcome the limitations of these studies, and to provide a better indication of the effects of altering venous return on the PPG waveform, this work simultaneously measured ac and dc red and infrared PPG signals and laser Doppler flux from the left and right fingers while the right hand was placed at different positions relative to heart level. The purpose of the study was to further understand the contribution of venous blood to the photoplethysmographic signal in an attempt to identify possible features that can assist in the augmentation of PPG algorithms to provide more information about the cardiovascular system.

2. Materials and Methods

The experimental set-up used in this study is illustrated in figure 1. An adjustable hand rest was used to allow for the right hand to be placed at various heights above and below heart level, while the left hand remained static at heart level. PPG signals from the index fingers of the right and left hands were measured using a custom-made PPG measurement system (described in section 2.1). Commercial pulse oximeter, laser Doppler flowmetry and ECG devices were also used. All signals were simultaneously acquired by a data acquisition card.

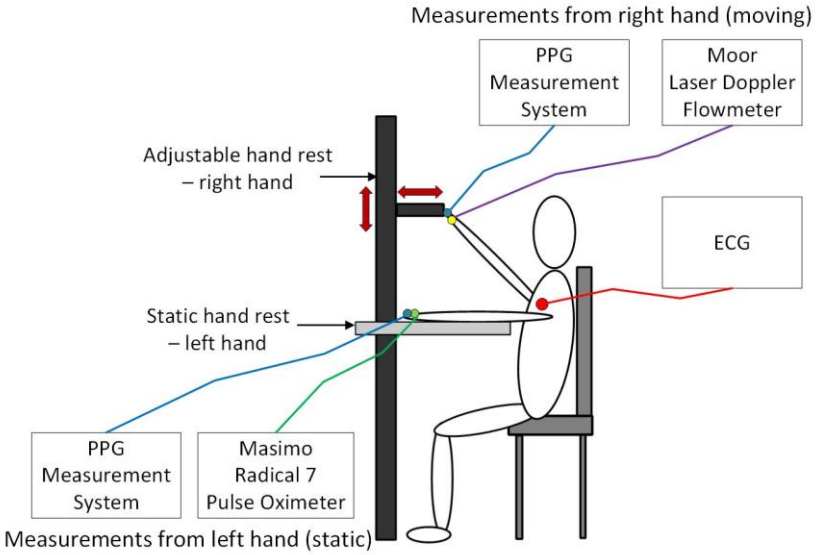

Figure 1. Illustration of the experimental set-up for the hand-raising study.

2.1 Photoplethysmographic measurement system

For the acquisition of photoplethysmographic signals, a custom-made two-channel dual wavelength PPG instrumentation system was developed [Rybynok *et al* 2013] capable of acquiring and displaying PPGs from the left and right hands simultaneously. The probes used with the system were standard commercial transmission mode finger pulse oximeter probes (Masimo Corporation, USA), utilising red and infrared light-emitting diodes (LEDS) at 660nm and 940nm respectively.

Figure 2 details the main functional components of the instrumentation system. Each channel included multiplexed current sources to drive the red and infrared light-emitting diodes (LEDs), allowing for them to be switched on alternatively in order to enable independent sampling of the red and infrared light by the photodetector. The microcontroller (ATtiny 2313-20SU) produced the clock signals to determine the multiplexing frequencies, which were set to 400Hz for each channel. The LED drive currents were all individually controllable through voltage reference circuits, adjustable by the user. In this case, the drive current for all LEDs was set to 25mA.

The output from the photodiode was passed into a transimpedance amplifier which converts the photodiode current into a voltage proportional to the detected light intensity. The output of the transimpedance amplifier was then fed into an eight channel analogue demultiplexer (MC1405BD) which uses the clock signals produced by the microcontroller to separate the signal into its red (R) and infrared (IR) components.

Both components were then passed to a low pass filter with pass band 0–40 Hz to remove switching artifact, coupled mains and other interference. These signals are subsequently referred to as *Rdc* and *IRdc*. The dc signals were then band pass filtered (passband: 0.4 – 17 Hz) and amplified in order to isolate the

ac PPG signal. These signals are subsequently referred to as *Rac* and *IRac*. All four signals from each PPG channel were digitized using a National Instruments PCIe-6321 16-bit data acquisition card (National Instruments Inc., Austin, TX, USA) using a sample rate of 1000 Hz.

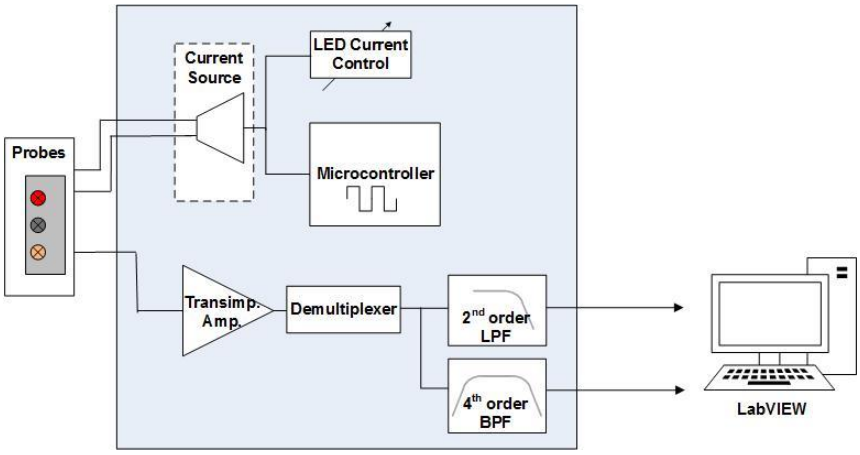

Figure 2. Basic block diagram of the PPG measurement system.

2.2 Volunteer Study

2.2.1 Subjects

The protocol was approved by the Senate Research Ethics Committee at City University London. Twenty healthy volunteers (12 male, 8 female, mean age (±SD): 31.4±7.2) with no history of cardiovascular or cardiopulmonary disorders were recruited to the study. Following a detailed explanation of the investigations objective, informed consent was obtained from all subjects.

2.2.2 Experimental Protocol

The study was carried out in the Biomedical Engineering Research Laboratory at City University London, in a room with an average temperature 21.1 ± 1.2 ˚C. Blood pressure was measured immediately prior to the measurement session. All subjects were asked to sit in a chair, whose height was adjusted if necessary to ensure that both arms were resting at 'heart level', i.e. level with the vertical mid-point of the sternum. Care was taken to ensure that the subject was in a comfortable position, in order to minimise any strain or stress on the arms. The left arm was placed on a static support, fixed at heart level. The right arm was placed on an adjustable hand rest, initially set at heart level. The adjustable hand rest allowed the researcher to adjust the right hand height to predetermined levels at the relevant stages of the protocol. Five right hand heights were selected: heart level (0cm), two heights below heart level (-25cm and -50cm), and two heights above heart level (+25cm and +50cm).

Once the subject was comfortable in the position, transmission mode probes were placed on the index fingers of the left and right hands and connected to the custom-made PPG measurement system (Section 2.1). This allowed for raw red and infrared PPGs signals from the stationary (left) and moving (right) hands to be obtained simultaneously and allow for the effect of hand height on the PPGs to be

investigated. A pulse oximeter probe was placed on the left middle finger and connected to a Masimo Radical 7 pulse oximeter (Masimo Corportation, USA) in order to provide reference SpO_2 signals. A laser Doppler flowmetry sensor (moorVMS-LDF2, Moor Instruments, UK) with skin temperature sensor was placed on the middle finger of the right hand to determine local changes in blood flow in the finger as the hand was moved to different heights above and below the heart level reference. The standard laser Doppler output, RBC flux, is the product of the number of moving RBCs in the microcirculatory vessels under the monitoring probe and their velocities. ECG electrodes were also attached to the subject and connected to a commercial ECG machine (Cardioline, San Diego, USA) to provide timing information. All signals from the commercial devices were digitized using a National Instruments PCIe-6321 16-bit data acquisition card (National Instruments Inc., Austin, TX, USA) using a sample rate of 1000 Hz. All signals were acquired, saved and displayed on a computer running LabVIEW (National Instruments Inc., Austin, TX, USA).

Before commencing the measurements, subjects were asked to practice timed breathing for one minute. To do this, they were asked to following a breathing rate timer implemented in LabVIEW and displayed on the screen in front of them. The breathing rate timer indicated when the subject should inhale and exhale and was set for equal inhalation and exhalation periods of 2.5 seconds each, giving 12 breaths per minute.

While maintaining a constant breathing rate, measurements were taken from all subjects at different positions of the right hand. Initial measurements were taken at heart level (0 cm), before lowering the hand rest to -50cm below heart level. The hand rest was then subsequently moved up to -25cm, 0 cm, +25cm, +50cm, and, finally, 0 cm. All signals were recorded for two minutes at each interval (seven intervals in total), with 30 seconds allowed for transition between different heights. The total measurement time was 17 minutes.

2.3 Data Analysis

All signals were processed and analysed retrospectively in Matlab (The Mathworks, Inc, USA). In order to remove high frequency noise, all ac and dc PPG signals and the flux signal were down-sampled to 100Hz. A lowpass FIR Equiripple filter with a cut-off frequency of 20Hz and with 80dB attenuation in the stop band was designed. The resulting filter coefficients were then used with the *filtfilt* function in Matlab in order to perform zero-phase digital filtering of all the signals. This is achieved by processing the input data in both the forward and reverse directions. To remove dc offset of the ac signals, a highpass FIR Equiripple filter with a cut-off frequency of 0.12Hz and with 80dB attenuation in the stopband was designed, and the ac signals were zero-phase filtered using the *filtfilt* function (as before).

PPG ac and dc amplitudes from both hands were calculated using a 2 second rolling window over the total measurement period (17 mins). From these amplitudes, SpO_2 values were estimated.

The mean amplitude of red and infrared ac and dc PPG signals acquired from left and right fingers were then calculated for each hand height (-50cm, -25cm, 0cm, 25cm, and 50cm) for all volunteers. Similarly, the mean SpO_2, mean commercial SpO_2, mean flux and temperature were also calculated for each height for all volunteers.

To facilitate comparison of general PPG amplitude change with hand height, the means of the means for red and infrared ac and dc PPG signals were calculated by averaging the mean PPG values across all subjects, along with the pooled variances (± Sp). Similarly, the mean of the means of flux, temperature and SpO_2 obtained from all volunteers were calculated for each interval.

As comparison of PPG signals in absolute numbers between subjects or between measurement sites (such as left and right hands) was not possible because absorption of light is dependent on local factors (such as skin pigmentation, sensor location), relative changes in PPG amplitudes were calculated. The percentage change of the ac and dc amplitudes with respect to baseline (0cm) was calculated for each hand for each volunteer. For example, $((Rac_{0cm}-Rac_{-50cm})/Rac_{0cm})*100$.

Statistical significance tests (Wilcoxon Rank Sum test) were then performed on the data to see the effect of changing the hand height has on the ac and dc PPG amplitudes. A P-value <0.05 was considered to be statistically significant.

3. Results

All blood pressure readings taken prior to the measurement session were within the accepted 'normal' range. The mean (±SD) systolic pressure across all volunteers was 122.8 ± 5.5 mmHg, while the mean (±SD) diastolic pressure was 81.9 ± 2.7 mmHg. The average heart rate for all subjects throughout the protocol was 72.1 ± 8.8 bpm. SpO_2 values from both the Masimo Radical 7 pulse oximeter and the PPG measurement system showed no significant change throughout the course of the protocol. The average SpO_2 value across all volunteers was 98.9 ± 2.4 from the commercial Masimo device and 98.2 ± 3.9 from the uncalibrated PPG measurement system.

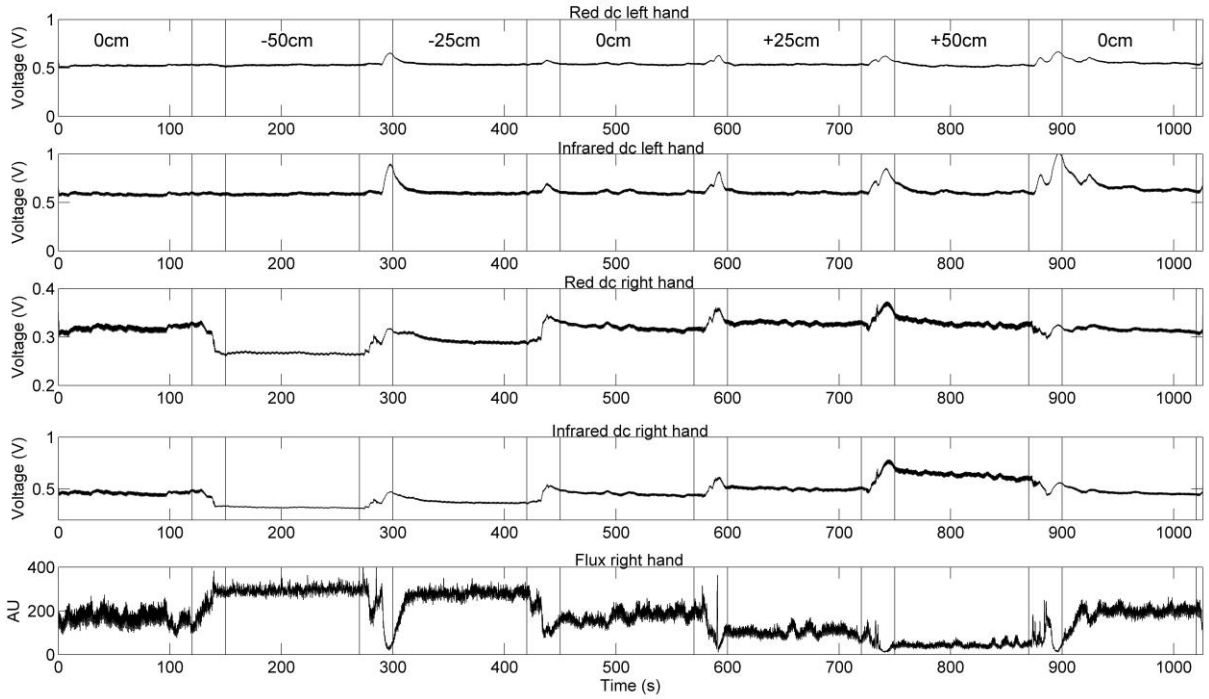

Figure 3. Red and infrared dc photoplethysmographic signals from the left and right hands for all positions of the right hand from Subject #15. Flux from the right hand is also given.

Figure 3 shows the acquired red and infrared dc PPG signals from the left and right index fingers and flux signal obtained from one subject (Subject #15) over the course of the protocol. In this example, which is typical, it can be seen that the red and infrared dc PPG signals from the right finger changed according to the position of the hand relative to the heart position. There were noticeable step changes, when compared to the corresponding left finger signals, most obvious in the initial change from heart level to -50cm below heart level. From -50cm, the dc signal gradually increased for each change in hand height up to +50cm, after which it decreased again following the hands return to baseline. For both the right and left hand, overshoots were observed as the right hand was moved from the dependent position into a higher position, for example at t=300s.

The LDF flux signal, acquired from the right hand, also changed in relation to hand position. In the majority of subjects, it showed an increase in flow on lowering the hand into a dependent position, and a reduction of flow as the hand was raised towards and above heart level (figure 3).

Figure 4 shows the acquired red and infrared ac PPG signals from the left and right index fingers and LDF signals obtained from the same subject (Subject #15) over the course of the protocol. It can be seen that the red and infrared ac PPG signals from the right finger changed amplitude in accordance with the position of the hand relative to heart position. For the lowest position (-50cm), ac PPG signals had the smallest amplitude. They then increased with corresponding increases in hand elevation. This phenomenon was noted in 19 out of the 20 subjects.

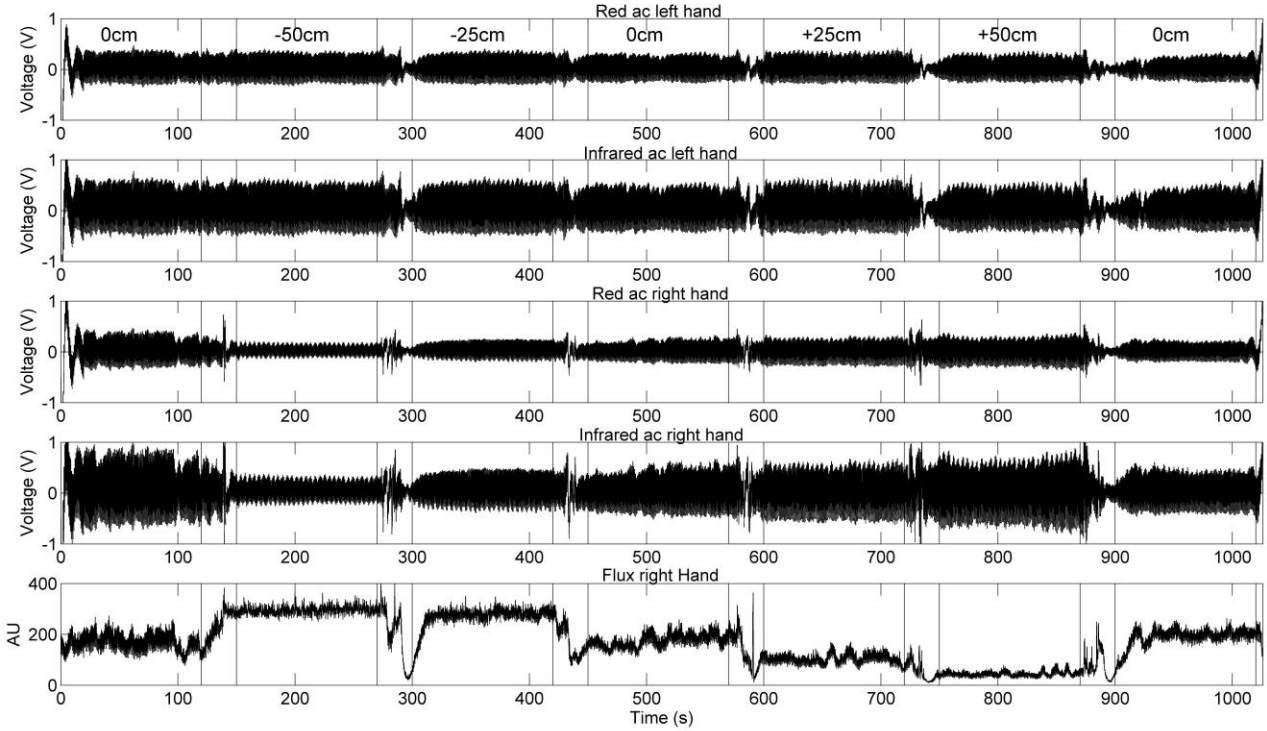

Figure 4. Red and infrared ac photoplethysmographic signals from the left and right hands for all positions of the right hand from Subject # 15. Flux from the right hand is also given.

Figure 5 summarises the infrared ac and dc PPG amplitude changes across all volunteers. The mean of the means IR dc PPG amplitudes for the right and left hands from all volunteers (n=20) for different right hand positions (± Sp) are illustrated in figure 5(a), while figure 5(b) shows the mean of the means IR ac PPG amplitudes for the right and left hands. The mean (n=20) right hand flux values for each position are also shown on each graph. It can be seen that the mean of the means ac and dc amplitudes from the right hand dropped when the hand is lowered and then gradually increased as the hand is raised further.

The mean ac and dc amplitudes from the left hand did not follow the same trend, with the mean dc amplitudes remaining relatively constant over the duration of measurement. The ac signals however demonstrated some variation, but on a much smaller magnitude than those for the right hand.

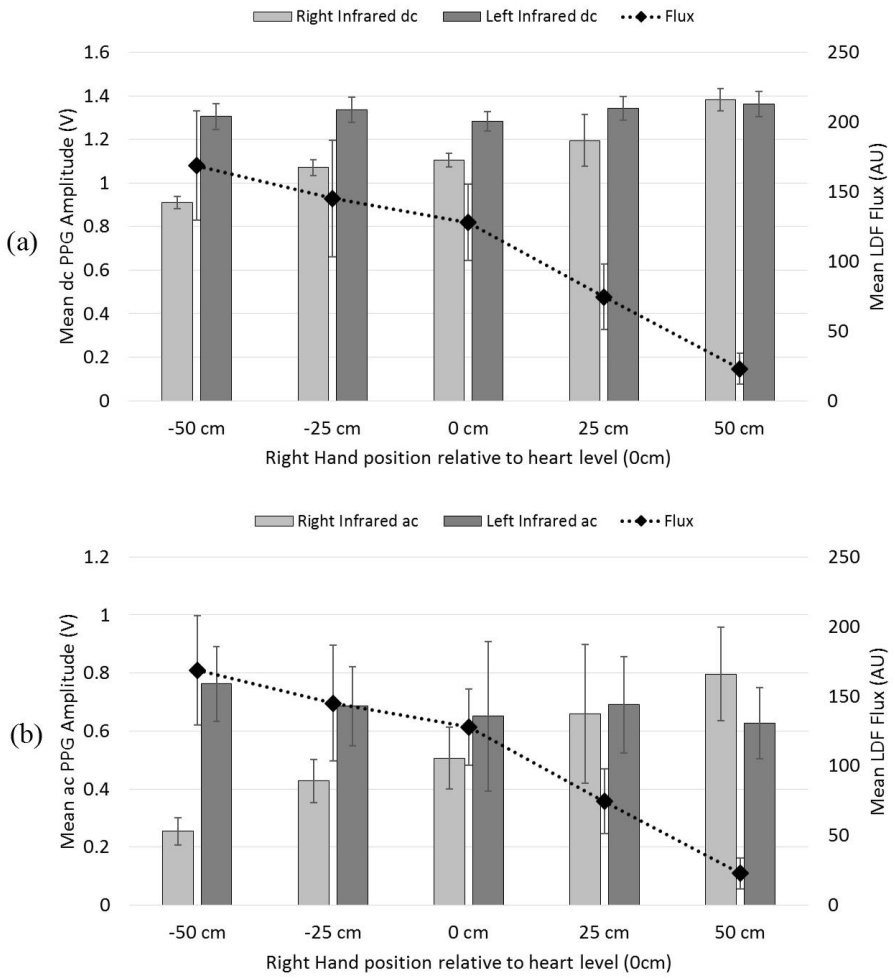

Figure 5 (a) Mean of the means infrared dc PPG amplitudes (± Sp) from all volunteers (n=20) for different right hand positions and **(b)** Mean of the means infrared ac PPG amplitudes (± Sp) from all volunteers (n=20) for different right hand positions. LDF flux is indicated in both plots.

As can be observed from figure 5, there was a difference in baseline (0cm) ac and dc PPG amplitudes from the left and right fingers due to local factors, and as a result it was necessary to compare PPG signals from each site in terms of their relative changes in amplitude as the right hand was moved to different levels. The baseline PPG signals taken when the right arm was at 0cm were taken as reference levels for each arm, and percentage changes relative to these were calculated for each volunteer for each right arm position. Table1 summarises the changes in the infrared signals for two hand positions (-50cm and +50cm). The red ac and dc PPG signals followed the same trend.

From Table 1 it can be observed that at a right hand position of 50cm below heart level, the relative changes of the IR ac and dc signals in all volunteers on the right hand underwent a larger percentage change than those observed from the left hand. The infrared dc signals from the right hand showed a mean decrease in amplitude of 18.7%, with nine volunteers showing an increase greater than 20%, while the infrared dc signals from the left hand only decreased on average by 4.95%, with no volunteer showing a decrease greater than 20%. The percentage decreases in ac PPG amplitude were much greater than those observed from the dc signals, but similarly showed larger average decreases in signal amplitude from the right hand than from the left.

Table 1. Summary of the percentage changes in infrared ac and dc PPG amplitudes from the right (RH) and left (LH) hands when the right hand was placed at 50cm below heart level and at 50cm above heart level for all volunteers (n=20).

	50 cm below heart level % decrease				50cm above heart level % increase			
	dc PPG		ac PPG		dc PPG		ac PPG	
%	RH IR DC	LH IR DC	RH IR AC	LH IR AC	RH IR DC	LH IR DC	RH IR AC	LH IR AC
0 – 5%	2	15	0	4	3	9	1	2
6-10%	3	1	0	3	4	3	1	0
11-20%	6	4	0	7	2	3	0	7
21-30%	7	0	0	2	2	3	1	5
31-40%	2	0	2	3	2	2	5	2
41-50%	0	0	3	1	2	0	4	1
> 50%	0	0	15	0	5	0	8	3
Mean % change	-18.70	-4.95	-63.15	-17.00	+36.85	+12.30	+64.30	+25.45

For a hand position of 50cm above heart level, there was a similar difference in the relative changes of PPG amplitude (Table 1). For this hand position, all ac and dc signals from the right hand showed a greater average percentage increase than those acquired from the left hand.

To determine whether these changes in amplitude observed on the right hand with respect to baseline were significantly different from those on the left hand, a significance statistical test was performed. Data was first tested for normality using Shapiro-Wilk Normality test. As the data was found to not be normally distributed, a Wilcoxon Rank Sum test was used (Table 2). A p-value of <0.05 was considered

statistically significant. The changes in PPG amplitude were found to be significant in for the infrared and red dc signals and for the infrared ac signal. However, the red ac signal showed no significant difference.

Table 2. Results of Wilcoxon Rank Sum test between the relative amplitude PPG changes from baseline (0cm) for the right and left hands for -50cm and -25cm below heart level, and 25cm and 50cm above heart level. A p-value of <0.05 was considered statistically significant.

	P-values			
	IR DC	R DC	IR AC	R AC
-50cm	<0.001	<0.001	<0.001	0.24
-25cm	0.005	0.014	<0.001	0.255
+25cm	0.112	0.295	0.048	0.955
+50cm	0.003	0.156	0.003	0.167

Morphological differences were noted on the ac PPG signals obtained from the right hand for different positions. Figure 6 illustrates the ac PPG signals for different positions from subject 16. The shape of the ac PPG, in particular the diastolic slope, changed significantly for each position. With the hand at -50cm the diachrotic notch and associated diastolic peak were more pronounced than in the PPGs obtained from heart level (0cm). When the hand was elevated to 50cm above heart level, the PPG waveform became more damped and the diachrotic notch and diastolic peak were not distinguishable. This phenomenon was observed in all volunteers.

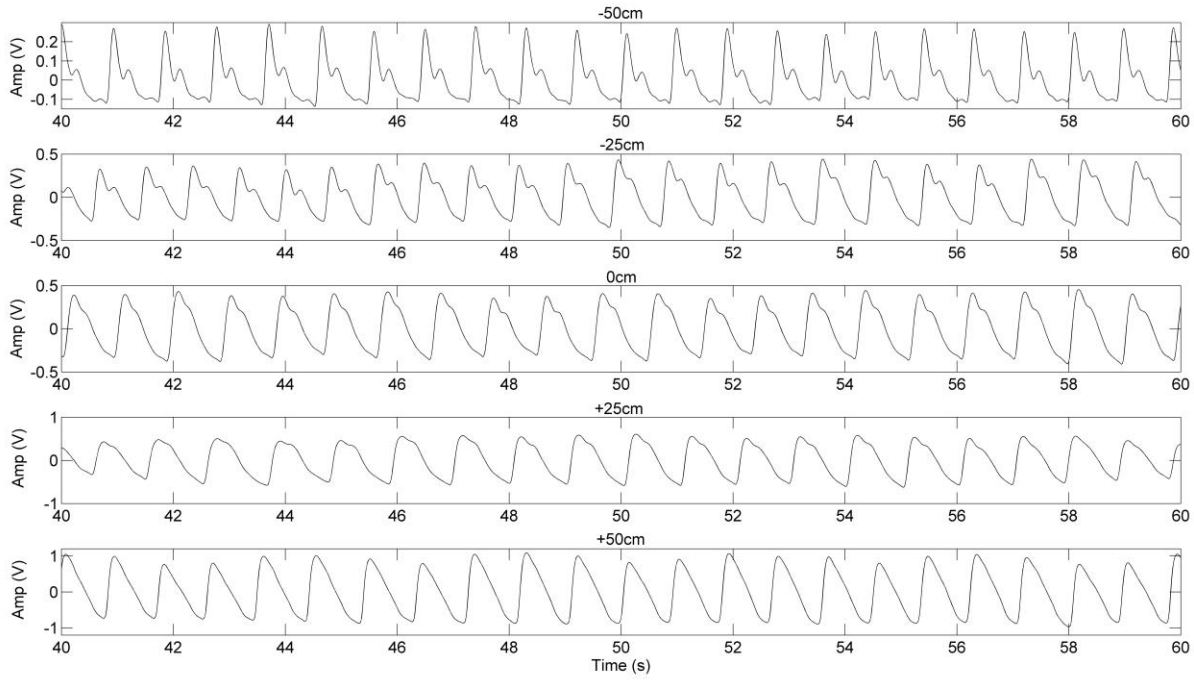

Figure 6. A 20 second segment of infrared ac PPG signals from the right hand of a volunteer (volunteer #16) for all positions of the right hand relative to heart level.

A clearer comparison of these morphological changes can be seen in figure 7(a), in which two PPG pulses acquired when the hand was at heart level are superimposed on the corresponding PPG pulses when the hand was lowered to 50cm below heart level, and raised to 50cm above heart level. All three pulses have been lined up so that the foot of the first pulse from each measurement site are aligned. There is a small difference in PPG pulse width due to the small variations in heart rate interval, and, hence, pulse width interval, throughout the course of the protocol. In this figure, we can see that all three waveforms have a sharp systolic upstrokes with sharp systolic peaks. However, the time from the foot of the wave to the systolic peak when the hand is at -50cm is shorter than when the hand was placed either at heart level or elevated by 50cm, even when the slight difference in pulse width is taken into consideration. The time to the systolic peaks of the 0cm and +50cm PPGs are similar.

In the diastolic phase (the time from the first peak to the foot of the next PPG waveform) there are sharp differences. The diastolic slope in the -50cm PPG signal declines rapidly from the systolic peak in comparison to that obtained from the heat level position. The diachrotic notch is clearly visible in this position, as is the diastolic peak. At heart level, an inflection point, associated with the diachrotic notch and peak, is visible, while in the elevated position the appearance of the diachrotic notch has diminished and is not distinguishable from the systolic peak. The ratio of the diastolic peak or inflection to the systolic peak of the baseline PPG is much higher at heart level than for the -50cm PPG (figure 7(b)).

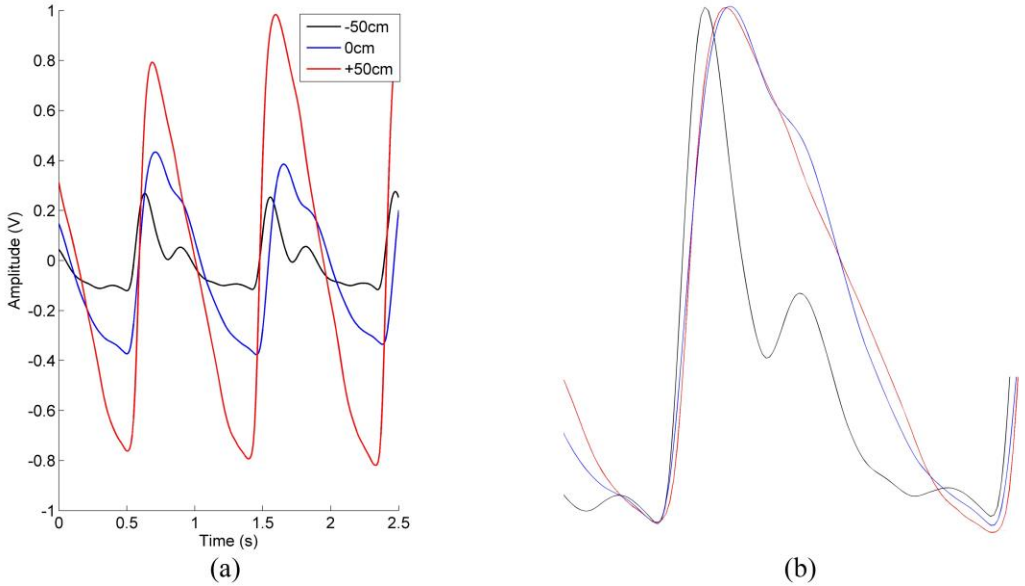

Figure 7. Comparison of infrared PPG pulse morphology from heart level (blue), 50cm below heart level (black) and 50cm above heart level (red) with (a) the unaltered PPG signals and (b) the PPG signals scaled to be of approximately the same amplitude

A further peak on the diastolic part of the PPG waveform was observed in the -50cm position (figures 6 and 7). In 11 volunteers, this peak was prominent, in 6 volunteers, it was observed intermittently, while in 3 it was not evident. This pulse occurs regularly at towards the foot of the PPG and may be due to pulsations of venous blood, as the blood volume in the veins of the hand increases.

4. Discussion

In this study, arterial and venous effects on acquired ac and dc photoplethysmographic signals from the finger were investigated during a hand-raising exercise. The purpose was to further understand the contribution of venous blood to the plethysmographic signal in an attempt to identify possible features that can assist in the augmentation of PPG algorithms to provide more information about the cardiovascular system.

In order to disrupt venous distribution in the finger, a hand-raising exercise was carried out on twenty volunteers. However, in a system as complex as the cardiovascular system the venous flow cannot be altered independently of any effects on arterial flow, and, as such, changes in ac and dc PPG morphology due to both arterial and venous changes were observed.

As observed in figure 3, by changing the hand position relative to heart level, blood flow in the hand was altered, as the LDF flux signal changed for different hand heights. Moving the hand to a dependent position, 50cm below heart level, increased the measured flux signal. The flux then decreased for each elevation step of 25cm up to the maximum height of 50cm above heart level. These flow changes are possibly due to hydrostatic pressure changes induced in the tissue bed of the hand. Elevating the arm reduces the local arterial pressure by approximately 0.77mmHg/cm of vertical displacement from the heart [Gavish and Gavish 2011], while lowering the hand increases the local arterial pressure by the same factor. Therefore, the pressure changes due to moving the hand to -50, -25, +25 and +50 cm with reference to heart level can be considered to be -38.5mmHg, -19.25mmHg, +19.25mmHg and +38.5mmHg respectively.

The effect of venous pooling and venous drainage in the hand was clearly observed in the dc PPG signals. In all subjects, both the red and infrared dc amplitudes reduced when the hand was lowered from 0 cm to 50 cm below heart level. As the dc PPG signal largely reflects the non-pulsatile absorbers in the finger tissue bed, it can be deduced that the decrease in dc PPG amplitude due to increased light absorption at both wavelengths is due to increased venous blood, as its return to the heart is opposed by gravity. Raising the arm in steps of 25cm to the maximum height of 50 cm above heart level, showed increasing steps in the magnitude of the dc PPG signal, and, hence, increasing venous return.

The reduction in arterial pulsatile blood volume when the arm was placed below heart level, as evident in the smaller ac PPG amplitudes (figure 4), suggested local vasoconstriction of the arteries in the finger. The induced disruptions to blood flow and perfusion pressures in the finger were probably counteracted through autoregulatory adjustments on the arterial side rather than the venous side. When the hand is in a dependent position, venous return is impeded and as blood pools the venous walls distend. This triggers an associated constriction of the arteries, referred to as the venoarterial reflex (VAR) [Bahadir *et al* 2007]. Another mechanism that could be contributing to this local vasoconstriction is the myogenic response, or Bayliss effect. Blood vessels, particularly arteries and arterioles, exhibit a strong myogenic response, resulting in smooth muscle contraction as transmural pressure rises [Lott *et al* 2009].

Conversely, on arm elevation above heart level, the amplitude of the ac PPG signals increased compared to the baseline (0cm) signals, suggesting vasodilation of the arteries. Some researchers suggest that a reduction of the venous pressure on arm elevation may result in the withdrawal of the venoarterial reflex and contribute to greater arterial vasodilation [Bahadir *et al* 2007]. Similarly, the myogenic response would cause a relaxation of the artery walls as transmural pressure falls [Lott *et al* 2009].

Both the venoarterial reflex and myogenic response mechanisms have been explored in the literature during limb dependency, particularly in the foot [Rathbun *et al* 2008]. Okazaki *et al* (2005) calculated that in healthy men the VAR and the myogenic response contribute 55% and 45%, respectively, to local postural skin vasoconstriction.

Interestingly, this observed vasoconstriction of the arteries when the hand is dependent doesn't impede skin blood flow in the finger as measured by LDF flux. It is hypothesised that arteriovenous anastomoses (AVAs) may also play a role in these observed changes in skin blood flow. In skin sites, such as the pulp of the finger, there are numerous AVAs that are richly innervated by sympathetic vasoconstrictor nerves and play a large role in thermoregulation [Midttun and Sejrsen 1996]. It has been estimated that 80–90% of total skin blood flow passes through thermoregulatory AVAs and does not enter the capillary bed [Forst *et al* 1998]. The LDF signal is thought to be largely indicative of thermoregulatory and subpapillary blood flow [Forst *et al* 1998].

The increase in microvascular flow on hand dependency may be due to increased flow through the AVAs in the finger pulp. When the capillary pressure is raised on limb dependency and the diameter of the pre-capillary arterioles decreases, the blood will be re-routed directly into post-capillary venules via arteriovenous anastomoses and capillary pressure will be reduced [Zuther 2013]. Conversely, on limb elevation, the capillary pressure decreases, blood does not flow through the A-V anastomoses as it is directed straight to the capillaries to an effort to increase capillary pressure [Zuther 2013]. Midttun and Sejrsen (1996) reported that when the pulp of the thumb or the toe was elevated above heart level, blood flow rate in the AVAs decreased, corresponding to the falling pressure head. They suggested that the AVAs are passive vessels at orthostatic movements and do not exhibit autoregulation.

Examples of photoplethysmographic waveforms from patients with different levels of systemic vascular resistance given in the literature [Lee *et al* 2011, Angius *et al* 2012] exhibit the same morphological trends as illustrated in figures 6 and 7. Awad *et al* (2007) showed that the pulse width at half height increased with increasing systemic vascular resistance. This is also observed in the signals obtained in this study (figure 7).With increased vascular resistance, it has been reported that the reflected wave arrives earlier, appearing during systole in cases of high systemic vascular resistance so that it becomes difficult to distinguish between the forward travelling and reflected waves [Millasseau *et al* 2006]. Similarly, in figure 6, as the hand is moved from low to high, the dicrotic notch and diastolic peak, become less pronounced, until they are not observable when the hand is elevated to 50cm above heart level. In comparison with these findings, the morphological features of the PPG pulse obtained at -50cm can therefore be associated with low systemic vascular resistance, while those at +50cm are similar to those associated with high systemic vascular resistance.

These results, however, suggest that venous resistance influences the PPG morphology to a greater degree that the arterial resistance. On arm elevation the veins collapse as the atmospheric pressure is greater than the venous transmural pressure. This collapse increases the systemic vascular resistance, by increasing

postcapillary resistance, and, hence, reduces flow [Hildebrandt *et al* 1994]. However, the pre-capillary resistance has decreased, due to vasodilation of the arteries (observed through the obtained PPG signals of higher amplitude). As a result, the ratio of post to pre capillary resistance (Rv/Ra) has increased. While in the dependent position, the arteries constrict increasing the pre-capillary resistance. The veins, however, extend, decreasing the post-capillary resistance and decreasing the post- to pre- capillary resistance. Furthermore, the role of the A-V shunts will also affect vascular resistance. Increased flow through the A-V anastomoses effectively results in a short circuit with associated low resistance, as is the case when the hand is dependent. However, more work needs to be conducted in this area to quantify the factors that affect ac PPG morphology. Nevertheless, it should be noted that changes in arm position cause notable changes to the PPG morphology, hence, any study assessing features of the PPG signal in assessing vascular resistance should control the height of the measurement area relative to heart level.

It is hypothesised that the appearance of prominent pulsations at the base of the diastolic phase of the PPG signal in 11 volunteers when the hand was lowered to -50cm is due to venous pulsations (figure 7). Such pulsations have been identified in the diastolic phase of the PPG waveform and correlate with venous pressure [Shelley *et al* 1993]. At 50cm below heart level, an increase in venous pooling was observed by a decrease in the dc PPG signal in all volunteers. Also, the systolic and diastolic phases of the ac PPG signal have changed, with steeper slopes observed for both these phases as the movement of blood through the capillary bed increases. These faster transition times of both the systolic and diastolic phases may aid to "unmask" the venous pulsations. When the hand is down, the fully distended veins may also act as a low resistant conduit for pressure waves generated by the right atrium contraction, allowing for increased venous pulsations. Conversely, when the hand is up, collapsed veins block these pressure waves, resulting in no observed venous pulsations. Furthermore, there may be a transfer of arterial pulsations to the venous blood due to the increased flow through the A-V anastomoses [Schramm *et al* 1997]. Hence, it is suggested that attempts at estimating venous oxygen saturation may be more successful by placing the hand in a dependent position enabling greater accuracy of the calculated venous saturation values.

This investigation has some acknowledged limitations. Firstly, there may be a possible "order effect" on the acquired data and future work should investigate whether moving the hand from an elevated to a dependent position alters the data. Secondly, some important physiological parameters were not measured that could aid in better quantifying the obtained data. A non-invasive continuous blood pressure signal, would allow for alterations in arterial or venous pressures in the finger to be considered. Also, an additional blood flow sensor to monitor the arterial flow into the hand, rather than only the flow in the capillary bed, would allow for better assessment of the cardiovascular responses in the finger.

In conclusion, the alteration of venous return in the finger through a hand-raising study has many effects on both the ac and dc PPG signals. The change in the dc PPG signal may reflect the venous blood volume as the volume is reduced on elevation and increased on dependency. The alterations in the ac PPG signal are due to a combination of arterial and venous effects. The myogenic response and the venoarterial reflex cause the arteries to constrict and relax in relation to increased venous and arterial pressures. These effects can be clearly observed in the amplitude of the ac PPG, which alters with hand positon relative to heart level. It is hypothesised that venous resistance has a larger effect on the PPG morphology than arterial resistance, and that hand position should be carefully considered when morphological analysis of arterial stiffness is being applied to the PPG waveform. Finally, it is suggested that when the hand is in a

dependent position 50 cm below heart level, the effects of venous pulsations are more clearly observed in the PPG. Measurements from this position may provide useful in extracting important venous parameters, such as venous oxygenation.

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