Investigation of peripheral photoplethysmographic morphology changes induced during a hand-elevation study

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Abstract A hand-elevation study was carried out in the laboratory in order to alter peripheral blood flow with the aim of increasing understanding of factors affecting the morphology of peripheral photoplethysmographic signals. Photoplethysmographic (PPG) signals were recorded from twenty healthy volunteer subjects during a hand-elevation study in which the right hand was raised and lowered relative to heart level, while the left hand remained static. Red and infrared (IR) PPG signals were obtained from the right and left index fingers using a custom-made PPG processing system. PPG features were identified using a feature-detection algorithm based on the first derivative of the PPG signal. The systolic PPG amplitude, the reflection index, crest time, pulse width at half height, and delta T were calculated from 20 s IR PPG signals from three positions of the right hand with respect to heart level (−50, 0, +50 cm) in 19 volunteers. PPG features were found to change with hand elevation. On lowering the hand to 50 cm below heart level, ac systolic PPG amplitudes from the finger decreased by 68.32 %, while raising the arm increased the systolic amplitude by 69.99 %. These changes in amplitude were attributed to changes in hydrostatic pressure and the veno-arterial reflex. Other morphological variables, such as crest time, were found to be statistically significantly different across hand positions, indicating increased vascular resistance on arm elevation than on dependency. It was hypothesized that these morphological PPG changes were influenced by changes in downstream venous resistance, rather than arterial, or arteriolar, resistance. Changes in hand position relative to heart level can significantly affect the morphology of the peripheral ac PPG waveform. These alterations are due to a combination of physical effects and physiological responses to changes in hand position, which alter vascular resistance. Care should be taken when interpreting morphological data derived from PPG signals and methods should be standardized to take these effects into account.

Keywords Photoplethysmography · Hand elevation · Vasoconstriction · Vasodilation · PPG morphology · Reflection index · Vascular mechanics

1 Introduction

Photoplethysmography (PPG) is a non-invasive optical technique that exploits the variation in light absorption due to blood volume changes in the vessels close to the skin during the cardiac cycle [1]. It is widely used in pulse oximetry for calculation of heart rate and estimation of blood oxygen saturation using PPGs recorded at two wavelengths simultaneously [2]. However, current interest in cost-effective non-invasive sensor technology has seen a flourish of interest in furthering the application and utilization of the PPG waveform [4].

The PPG signal consists of a slowly varying (dc) baseline and a pulsatile (ac) component [1]. This cardiac-synchronous pulsatile component is assumed to depend solely on the arterial inflow of blood into a monitoring site such as the finger or earlobe [4]. As the ac PPG signal is similar in morphology to the arterial blood pressure waveform [5], it has been suggested that they are both influenced by similar vascular mechanisms [6]. Therefore, the PPG signal has been explored as a method to extract further circulatory and cardiovascular information from patients [1].

The PPG signal represents changes in volume (rather than pressure), so is dimensionally different to the blood pressure waveform. However, since arteriolar volume and pressure are positively correlated, the basic morphologies of both waveforms are similar and specific features common to both signals are observable. Both the blood pressure and ac PPG waveforms are described in terms of their systolic and diastolic phases. For example, in the systolic phase, the increase in arterial pressure is accompanied by an increase in arterial blood volume. Similarly to the blood pressure waveform, the ac PPG waveform also exhibits a dicrotic (or diastolic) peak in the diastolic phase of subjects with healthy compliant arteries [7].

Similarly to the blood pressure signal, the morphology of the PPG pulse changes with various vascular factors. Aging of the arteries or arteriosclerosis causes a diminution or disappearance of the dicrotic wave [8]. Furthermore, the peripheral PPG pulse has been described as becoming "damped, delayed and diminished" with increasing severity of vascular disease [1, 8]. In order to quantify these morphological changes, various features of the ac PPG pulse have been extracted and analysed [9, 10].

The most common morphological feature described in the literature is PPG pulse amplitude, or systolic amplitude. It has been shown that this variable is affected by many cardiovascular responses such as vasoconstriction due to a cold pressor test [11] or vasodilation due to reactive hyperemia [3], etc. However, it is difficult to compare systolic amplitudes between subjects or between measurement sites because absorption of light is dependent on local factors (such as skin pigmentation, sensor location etc.).

Much of the current work in the area of PPG morphology analysis, involves applying calculations commonly used on arterial blood pressure waveforms, such as Augmentation Index (AI) or Reflection Index (RI), to the ac PPG signal because of this relationship between pressure and volume [10, 12]. As the PPG wave propagates along the arterial tree, wave reflections are induced, with the most prominent reflection site being the bifurcation of the abdominal descending aorta [13]. However, the application of variables such as AI and RI also 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 [10]. This concept is taken from the arterial blood pressure signal, which has been shown to be a summation of forward and reflected pressure waves. Because of the relationship between pressure and volume, the ac PPG signal is also thought to be a summation of forward propagating and reflected blood volume waves [14] with the diastolic peak or point representing the reflected wave.

Other common features that have been extracted from the PPG waveform include crest time, pulse width/height ratios and area under the pulse [15, 16]. These various analysis techniques have been applied to assess cardiovascular aging and systemic vascular resistance [9, 15], endothelial function and the response to vasoactive drugs [17, 18], in attempts to assess arterial blood pressure non-invasively [19], and even to assess systemic conditions such as chronic fatigue syndrome [20].

Although the use of these morphological variables have shown promising results, there remains a need for further systematic work and understanding in this area. Although it is generally accepted that the PPG signal can provide valuable information about the cardiovascular system, the origins of the PPG signal are still not fully understood [1]. Furthermore, despite the similarities between them, the relationship between the recorded pulsatile ac PPG signal and the arterial pressure waveform is complex [18]. As a result, there remains a need for furthering understanding of PPG signals so that new clinical variables can be successfully extracted from this easily acquired but complex waveform [21].

In order to increase understanding of factors affecting the PPG morphology, a hand-elevation study designed to alter blood flow to and from the finger was carried out in the laboratory. It is well known that the position of the limb relative to the heart has an effect on arterial flow and venous return [22], predominantly due to the hydrostatic effect [23, 24]. The effect of changing limb position on cardiovascular responses and tissue perfusion has been explored by different groups using various techniques including laser Doppler flowmetry and PPG [25–28]. The authors have shown in a previous study that right finger ac and dc PPG amplitudes change significantly as the right hand is placed above and below heart level in comparison with PPGs acquired simultaneously from the static left hand [29]. However, these studies have not explored further morphological variable changes in acquired signals. This paper outlines how changes in hand position can affect the morphology of the peripheral ac PPG waveform.

2 Methods and materials

2.1 Patients and measurements

Following approval by the Senate Research Ethics Committee at City University London, twenty consenting healthy volunteers [12 male, 8 female, mean age (±SD): 31.4 ± 7.2] with no known history of cardiovascular or cardiopulmonary disorders were recruited to the study. The study was carried out in the Biomedical Engineering Research Laboratory at City University London, in a room with an average temperature of 21.1 ± 1.2 °C. On arrival, blood pressure was measured from the subjects using an OMRON HEM-907 digital blood pressure monitor.

Figure 1 illustrates the experimental set-up for the hand-elevation study. All subjects were asked to sit comfortably in a height-adjustable chair. The left arm was placed on a static support, fixed at 'heart level', i.e. level with the vertical mid-point of the sternum. The right arm was placed on the adjustable hand rest, initially set at heart level. The adjustable hand rest allowed for the adjustment of the right hand height to predetermined levels at the relevant stages of the protocol. PPG signals from the index fingers of the right and left hands were measured using commercial transmission mode pulse oximeter probes and a custom-made PPG measurement system [29, 30]. All signals were simultaneously acquired by a data acquisition card (National Instruments PCIe-6321, National Instruments Inc., Austin, TX, USA) at a rate of 1000 Hz.

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 50 cm below heart level (−50 cm) and raising it to 50 cm above heart level (+50 cm). All signals were recorded for 2 min at each position.

2.2 Data analysis and statistics

The PPG signals from the right and left hands were processed and analysed retrospectively in Matlab (The Mathworks, Inc, USA). All PPG signals were filtered to remove noise and dc offsets. A bandpass FIR Equiripple filter (0.12–20 Hz) with 80 dB attenuation in the stop bands was designed, and the resulting filter coefficients were used with the *filtfilt* function in Matlab to perform zero-phase digital filtering of all signals.

From each volunteer, a 20 s sample of the ac infrared PPG signal was selected from the obtained PPG signals for three right arm elevations: heart level (0 cm), 50 cm below (−50 cm) heart level, and 50 cm above (+50 cm) heart level. To detect the systolic peak and foot points of each waveform, the first derivative of the PPG waveform was applied. The foot, or onset, of the PPG waveform can be related to a zero-crossing point before a maximal inflection, while the systolic peak is related to a zero-crossing point after that inflection (Fig. 2a). As clearly distinguishable diastolic peaks are not always observable, the diastolic point was defined as per Millasseau et al. [8], which states that the diastolic point is the point at which the first derivative is closest to zero. Therefore, if there was no clear diastolic peak, then the inflection point on the down slope of the waveform was used, which is a local maximum of the first derivative (Fig. 2b). The location of all points were detected automatically by a computer program but verified manually.

After successful identification of these points on all PPG waveforms, the following morphological variables were computed (refer to Fig. 2b):

Systolic Amplitude This is the change in the ac PPG from the foot of wave to the following maximum point on the PPG (x in Fig. 2b).

Crest Time Crest time, or rise time, is the time from the foot of the PPG waveform to its systolic peak [7]. To reduce the effect of inter-subject variability, this time difference was normalised to the PPG width (PW).

ΔT ΔT is the time difference between systolic and diastolic peaks [15]. It is thought to be related to the time taken for the pressure wave to propagate from the heart to the periphery and back [8]. To reduce the effect of inter-subject variability, this time difference was normalised to the PPG width.

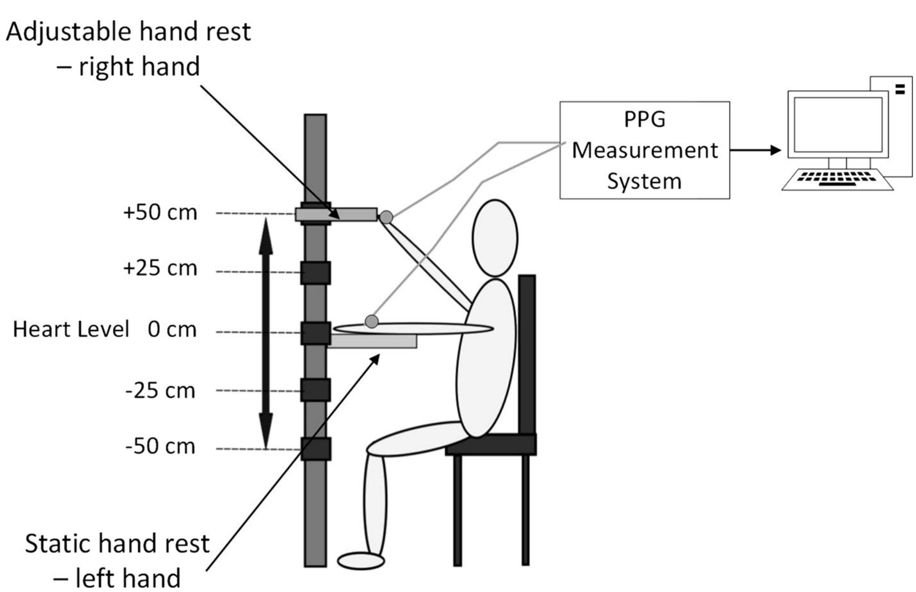


Fig. 1 Illustration of the investigational set-up for the hand-raising study

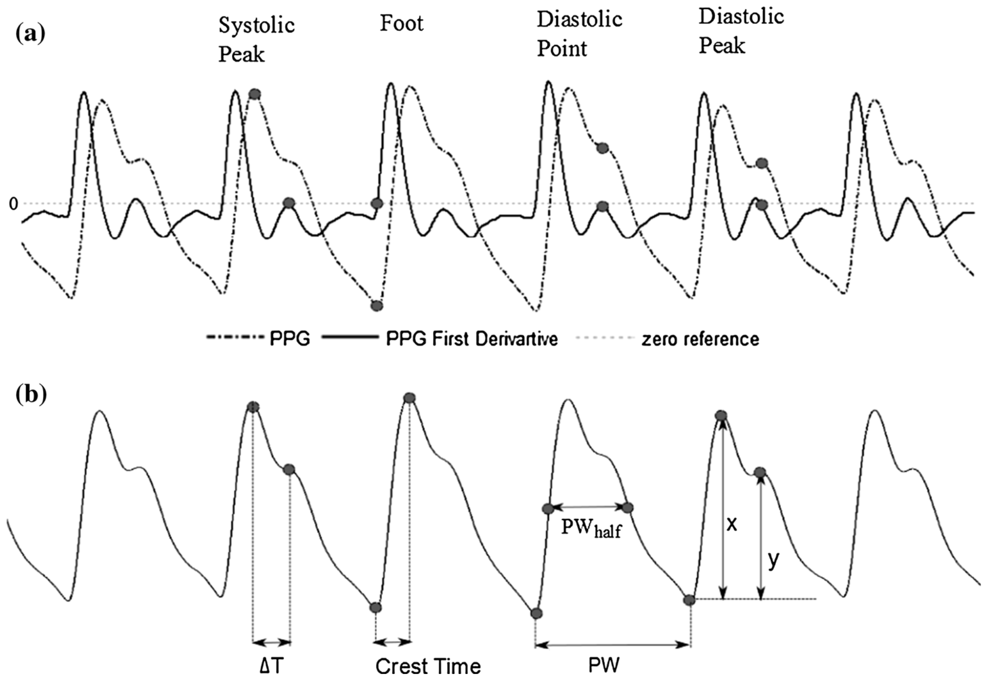


Fig. 2 **a** Determination of the systolic peak, foot and diastolic point or peak from the PPG waveform using the First Derivative of the PPG and **b** PPG morphological variables derived in this investigation (where *PW* pulse width, PW_{half} pulse width at half height, *x* systolic peak height, *y* diastolic peak height, and ΔT the time difference between systolic and diastolic peaks)

Pulse Width at Half Height (PW_{half}) This is the width of the pulse at the half height of the systolic peak amplitude. Awad et al. [16] suggested that this correlates with systemic vascular resistance better than the systolic amplitude. To reduce the effect of inter-subject variability, this variable was normalised to the PPG width (PW).

Reflection Index (RI) The reflection index was calculated as the ratio of the height of the diastolic peak or point (y) to the height of the systolic peak (x) (Fig. 2b) [15]. RI has been used as a measure to infer the effect of peripheral vascular tone on pulse wave reflection (18).

For each variable, the mean value for each hand height (−50, 0, and 50) was calculated across volunteers. The mean of these variables across all the volunteers were calculated, along with the standard deviations (±SD) in order to facilitate comparisons of the changes in the variables with changes of the height of the hand.

Statistical significance tests (Wilcoxon Rank Sum test) were then performed on the data to see the effect changing the hand height has on these morphological variables. 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.

Figure 3 shows samples of the acquired infrared ac PPG signals from the left and right index fingers of Subject 3 for right hand elevations of 0, −50 and +50 cm with respect to heart level. It can be seen that the ac PPG signals from the right finger changed amplitude in accordance with the position of the hand, while the amplitude of the PPG signals from the left hand stayed relatively constant. This phenomenon was noted in 19 out of the 20 subjects for both red and infrared ac signals.

Using the feature-detection algorithm above, all peaks, foot points, and diastolic points of the waveforms were identified in 19 of the 20 volunteers (Fig. 4). In one volunteer, the obtained signals at 0 and +50 cm were extremely damped, and diastolic points could not be identified in the PPG waveforms when the hand was raised to 50 cm above heart level. Therefore, this data set was omitted from further analysis.

Figure 5 summarises the infrared ac PPG systolic amplitude changes across all volunteers. The mean of the means IR dc PPG amplitudes for the right and left hands from all volunteers (n = 19) for different right hand positions (±SD) are illustrated in Fig. 5a. For the lowest position (−50 cm), ac PPG signals from the right hand had the smallest amplitude. They then increased with corresponding increases in hand elevation. Although there is some variation in the ac PPG signals obtained from the non-moving left hand, it is on a much smaller magnitude than that observed on the right hand. This is further highlighted in Fig. 5b, which shows the mean percentage change in the IR ac PPG amplitudes for the right and left

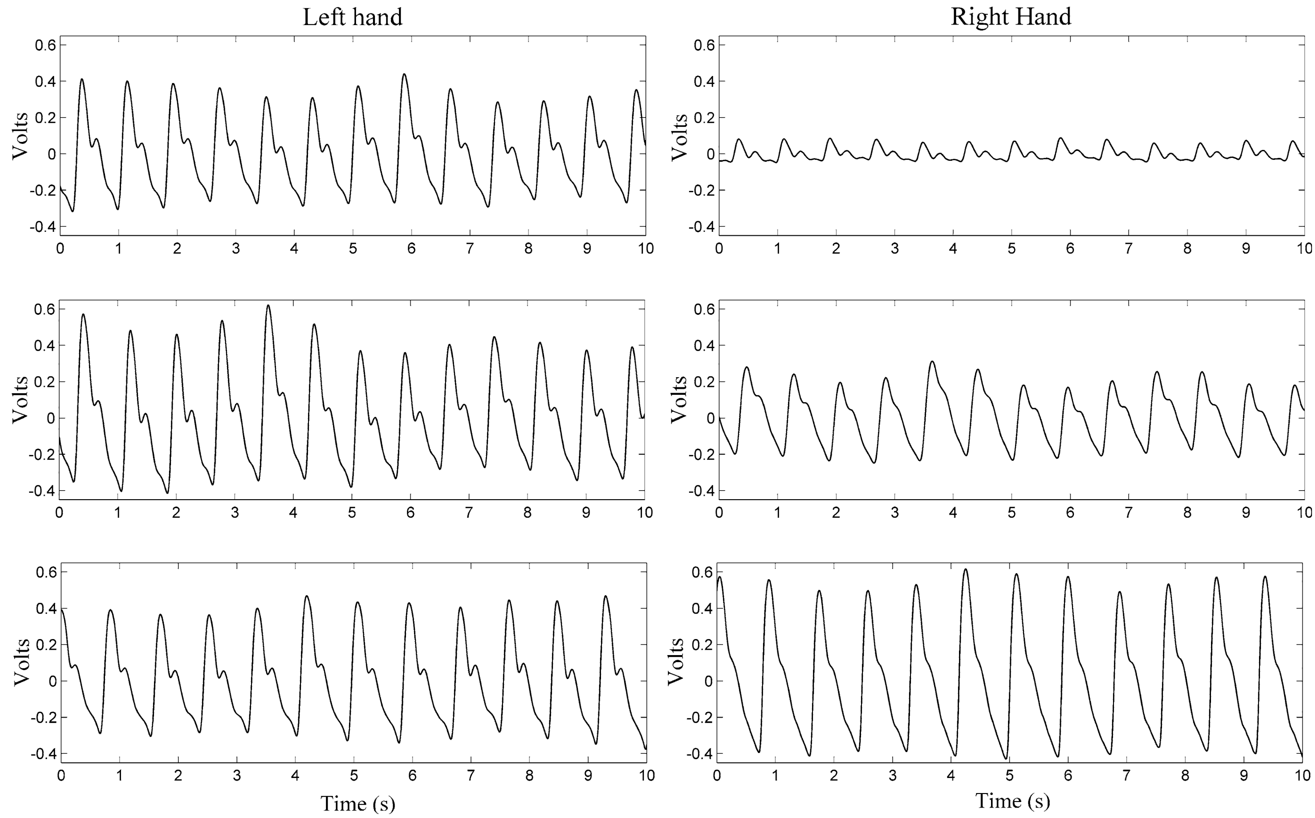


Fig. 3 Sample of infrared ac PPG signals from the left and right index fingers for intervals when the right hand was placed at −50 cm (*top*), 0 cm (*middle*) and 50 cm (*bottom*) relative to heart level

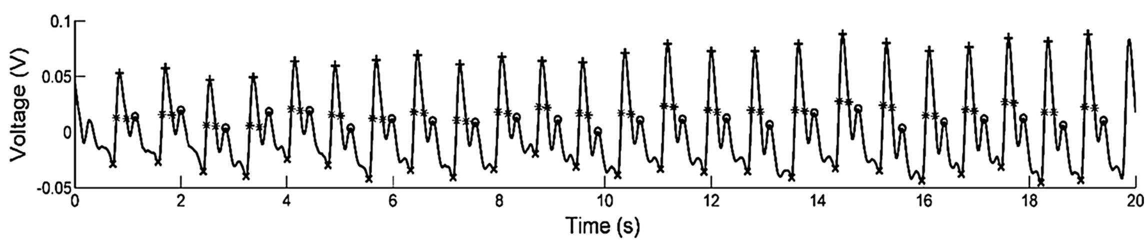


Fig. 4 Feature detection algorithm identifying PPG foot points (*times*), systolic peaks (*plus*), diastolic peaks or points (*circle*), and determining the half height position (*asterisk*) on IR PPG signals for all hand positions

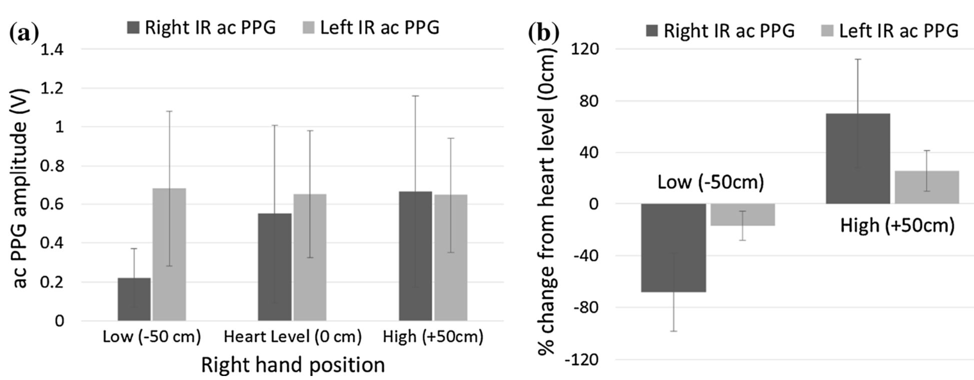


Fig. 5 **a** Mean (±SD) infrared ac PPG amplitude from the left and right hands for all volunteers (n = 19) for different right hand positions and **b** mean (±SD) percentage changes in the infrared ac amplitude relative to heart level when the right hand was placed at 50 cm below heart level and at 50 cm above heart level for all volunteers (n = 19)

hands with respect to heart level. The PPG signals from the right hand showed a mean decrease in amplitude of 68.3 % when the hand was lowered to −50 cm below heart level, while the PPG signals from the left hand only decreased on average by 17 %. Similar percentage changes are observed during hand elevation.

Figure 6 illustrates the changes in PPG morphology associated with changes in hand height for subjects 13, 14 and 18. In this figure, single PPG pulses from when the hand was at heart level are superimposed on PPG pulses when the hand was lowered to 50 cm below heart level, and raised to 50 cm 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. From this figure, we can see that all three waveforms have sharp systolic upstrokes with sharp systolic peaks, however features, such as crest time, appear to change in relation to hand position. Furthermore, as the hand is moved from low to high, the dicrotic notch and diastolic peak, become less pronounced, until they are hardly observable when the hand is elevated to 50 cm above heart level.

The barchart in Fig. 7 shows the means (±SD) of the calculated morphological variables for each hand height across all volunteers.

To determine whether the changes in the morphological variables observed on the right hand were significantly different for different hand heights, a significance statistical test was performed using the Wilcoxon Rank Sum test (Table 1). A p value of <0.05 was considered statistically significant.

The crest time and ΔT variables for all hand heights were found to be significantly different, although the p value for the ΔT variable between heart level (0 cm) and high (+50 cm) is larger (0.036) and may be interpreted cautiously. The difference in the RI and $PW_{halfheight}$ when the hand was in a dependent position compared to other positions was significant. However, the differences between these variables when the hand was at heart level or elevated showed no significant difference.

4 Discussion

Good quality PPG signals were obtained from all volunteers at all positions of the right hand. The feature detection algorithm, based on the first-derivative of the PPG waveform, successfully identified all systolic and diastolic points in the PPG signals of nineteen subjects.

Changes in right hand PPG systolic amplitudes were observed from all volunteers as the hand changed position relative to heart level (Figs. 3, 4). The amplitude of the right hand PPG waveform decreased on lowering the hand to 50 cm below heart level, and then increased as the hand was elevated back to heart level and finally up to 50 cm above heart level. It is believed that this change in PPG amplitude was due to the venoarterial reflex (VAR) [29]. When the hand is in a dependent position, venous return is impeded and the blood pools, causing the venous walls to distend. The venoarterial reflex responds to this distension of the venous wall by triggering arterial vasoconstriction [31]. Conversely, on limb elevation, the venoarterial reflex is removed and the arteries distend.

Further changes in PPG morphology were observed from all subjects at different hand positions (Fig. 5). The most obvious change was the dicrotic peak, which diminished in all subjects on hand elevation and only a dicrotic point could be observed and detected. Interestingly, these morphological trends are similar to examples of photoplethysmographic waveforms from patients with different

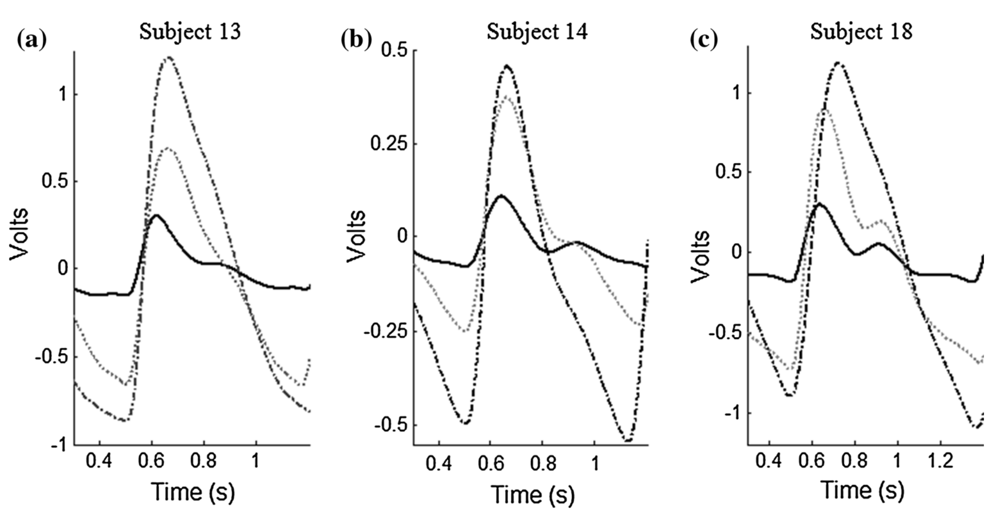


Fig. 6 Comparison of infrared PPG pulse morphology from heart level (*dot*), 50 cm below heart level (*solid*) and 50 cm above heart level (*dot–dash*) from **a** subject 13, **b** subject 14 and **c** subject 18

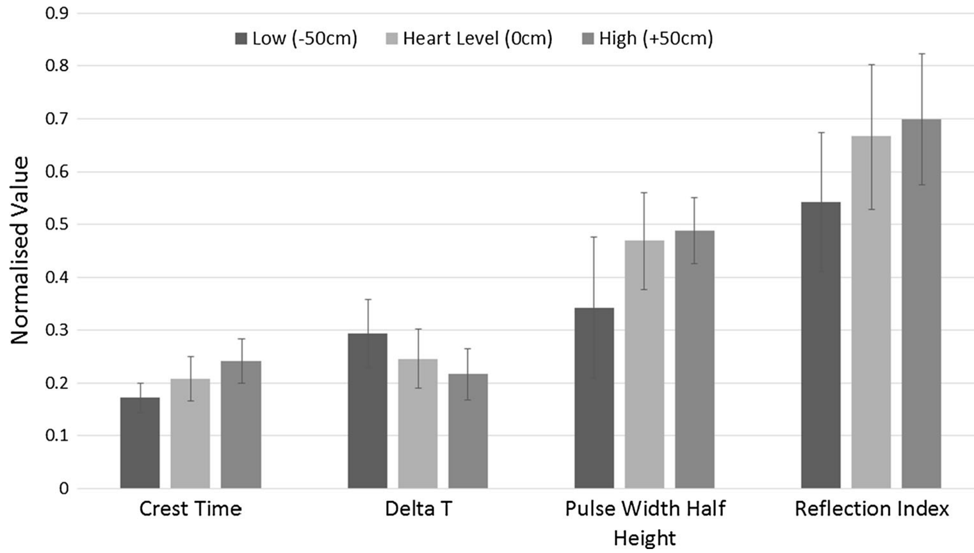


Fig. 7 Mean infrared ac PPG morphological variables (±SD) across all subjects (n = 19) for different right hand positions

Table 1 Results of Wilcoxon Rank Sum test between the calculated morphological variables from the right hand IR PPG for different hand heights: heart level (0 cm), low (−50 cm) and high (+50 cm)

	p values			
	Crest time	Delta T	$PW_{halfheight}$	Reflection index (RI)
Heart level (0 cm)–low (−50 cm)	<0.001	0.004	0.001	<0.001
Heart level (0 cm)–high (+50 cm)	0.001	0.036	0.355	0.314
Low (−50 cm)–high (+50 cm)	<0.001	0.001	0.001	<0.001

A *p* value of <0.05 was considered statistically significant

levels of systemic vascular resistance given in the literature [7, 15]. In order to quantify these observations, morphological variables frequently cited in the literature were calculated.

Morphological features seen in the PPG wave should be interpreted with some caution as mechanisms explaining arterial pressure wave morphology may not be fully applicable to PPG, since the latter refers to volume changes rather than pressure. However the arteriolar diameter (Δd) responds to changes in transmural pressure (Δp) according to the following relation [32]:

$$\Delta d = \frac{\Delta p}{E} \times \frac{D}{h}$$

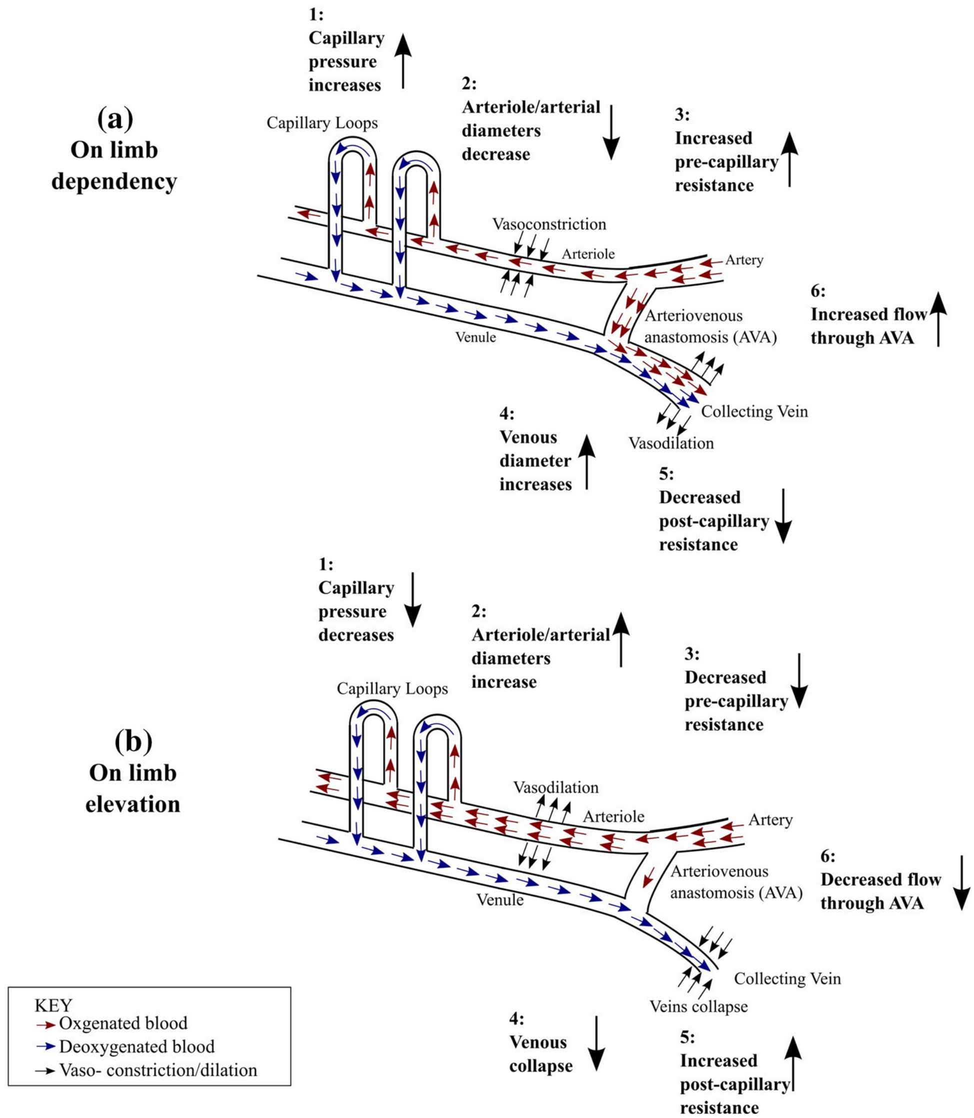
where E is the Young's modulus of the artery wall, D is the diameter of the vessel and h is the wall thickness. Changes in D and h over the cardiac cycle are small [33] so to a first approximation the relationship between diameter (and optical path) and pressure is linear. It may be reasonably assumed that PPG features closely approximate, both in amplitude and timing, their arterial pressure wave counterparts.

The crest time, or time from the foot of the PPG waveform to the systolic peak, was found to increase in all volunteers as the hand was raised (Fig. 6). The crest time variable details the early systolic phase, which is due to the rapid injection of blood during systole. Crest time has been shown to increase with increasing severity of vascular flow resistance [7, 34]. It is speculated that the increase in crest time could also be partly due to the arterioles being emptier during diastole in the elevated hand compared to baseline, so their capacity for systolic filling, and hence the filling time, is increased.

Conversely, ΔT decreased as the hand was elevated from −50 cm below heart level. Rubins et al. [13] reported that this variable decreases due to increasing vascular tone and higher pulse wave velocity in the arteries associated with vascular aging. It is thought that the decrease seen in this study may, as with the increased crest time, also be partly attributable to extended arteriolar filling time with increasing hand elevation.

Both RI and PW_{half} increased with hand elevation, although a statistically significant difference was only observed between the values for when the hand was lowered in comparison with the other two positions. With increased vascular resistance, it has been reported that the reflected wave arrives earlier, appearing during systole in cases of high systemic vascular resistance (SVR) so that it becomes difficult to distinguish between the forward travelling and reflected waves [8]. According to Awad et al.

Fig. 8 Illustration of the physiological effects that may occur on **a** limb dependency and **b** on limb elevation



[16] the increase in PW_{half} reflects increases in SVR, while other studies have shown that increases in RI reflect increased resistance [35].

These results suggest that changing the position of the hand temporarily alters the effective vascular flow resistance. In comparison with the literature, these morphological variables (CT, RI, ΔT, and PW_{half}) calculated for the PPG pulses obtained at −50 cm can therefore be associated with low vascular flow resistance, while those at +50 cm are similar to those associated with high resistance.

In general, discussions of systemic vascular resistance focus on the resistance of arteries and arterioles. Studies have shown that the vasoconstriction induced by a cold pressor test increases resistance as measured by RI [35], while arterial vasodilation, after systemic administration of glyceryl trinitrate reduces the RI and the SVR [35]. Contradictorily, in this study, hand dependency to −50 cm below heart level is associated with both vasoconstriction, as evident in the reduction in ac PPG amplitudes, and decreased resistance. Therefore, the resistance of the arteries and arterioles must not be the major influence on the morphology of the PPG signal during the hand-elevation study.

It is hypothesized that it is venous resistance that influences the PPG morphology to a greater degree than the arterial resistance. On arm elevation, the veins collapse as the atmospheric pressure is now greater than the local venous pressure. This collapse increases the systemic vascular resistance by increasing postcapillary resistance [36]. In the dependent position, the arteries constrict increasing the pre-capillary resistance. The veins, however, extend, decreasing the post-capillary resistance. This hypothesis is illustrated in Fig. 8.

Furthermore, in the pulp of the finger, there are numerous arteriovenous anastomoses that generally play a large role in thermoregulation [37]. 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 [38]. 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 [38]. Midttun and Sejrsen [37] 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. 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. This hypothesised role of the AVAs is also illustrated in Fig. 8.

Therefore, it seems that for the peripheral PPG pulse, it is the downstream resistance that has the greatest effect on shape variables, such as reflection index, while arterial resistance affects the change in systolic amplitude. 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 significant 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. Furthermore, the extent of the contribution of arterial and venous resistance to these morphological changes and variables would be particularly useful.

Limitations associated with this study include the fact that there may be a possible "order effect" on the acquired data. Future work should investigate whether moving the hand from an elevated to a dependent position alters the PPG morphology and calculated variables in a similar way. Secondly, the identification of the dicrotic point or peak from certain PPG recordings is not straightforward, suggesting the need for an improved detection method. In signals that appear very damped and rounded, and where the dicrotic peak is not visible to the eye, detection of the appropriate point becomes challenging. Furthermore, many of the detailed morphological variables interchangeably use the diastolic peak or inflection point, depending on which can be identified, which may cause errors when comparing PPG waveforms of different morphologies.

In conclusion, changes in hand position relative to heart level can significantly affect the morphology of the peripheral ac PPG waveform, due to a combination of physical and physiological effects. Hydrostatic changes cause variation in intravascular pressure in the arteries and veins of the limb, certainly affecting arteriolar filling and emptying. In addition, the systolic amplitude of the PPG is altered by the venoarterial reflex, which causes the arteries to constrict and relax in relation to changes in venous and arterial pressures. Common morphological variables, such as crest time and reflection index, all changed with hand position, suggesting that raising the arm temporarily increases systemic vascular resistance, while lowering the arm decreases it. It is hypothesized that the morphological changes of the peripheral PPG waveform are more sensitive to changes in downstream venous resistance, rather than arterial/arteriolar resistance. Further work is required to fully understand and further quantify morphological analysis of the PPG waveform.

Compliance with ethical standards

Conflict of interest Dr. M Hickey, Dr. JP Phillips and Prof PA Kyriacou have have no conflicts of interest or financial ties to disclose.

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