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APPLIED RESEARCH

Evaluation of Pulse Transit Time for Different Sensing Methodologies of Arterial Waveforms

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ABSTRACT We perform a novel comparative analysis between optically and mechanically derived pulse transit time (PTT) that is universally employed technique for cuffless blood pressure (BP) estimation. For data collection two inline photoplethysmogram (PPG) sensors were mounted at the distal and proximal phalanxes of the index finger of each subject and top each PPG sensor fixture a finger ballistocardiogram (BPP) sensors were clamped. The clamped stacking of the BPP sensors over the PPG sensors provided vertical aligned acquisition of the blood flow waveform through the radial artery for both sensors. The analysis of variance (ANOVA) between PTT derived from the BPP and PPG sensors resulted in a statistically significant difference at $p < 0.05$. The PTT derived from the BPP sensors showed higher values,17.8 milliseconds on average, than the PTT derived from the PPG sensors. Higher accuracy PTT values will improve the estimation of cuffless BP and thus has the potential to revolutionize the technology.

INDEX TERMS Pulse transit time, photoplethysmogram, finger ballistocardiogram, pulse arrival time, cuffless blood pressure.

I. INTRODUCTION

Cardiovascular and hypertension-related mortalities and their associated complexities have increased significantly worldwide [1]. To address this situation, methods for continuous and non-invasive monitoring of hypertension are required for early detection patient prioritisation and early interventions. Arterial stiffness, which is estimated using non-invasive PTT methods, is known to be an indicator of hypertension [2]. PTT has proven to be a good estimator of blood pressure (BP) and it is reasonably well established that it is directly related to 1/PTT in a cardiac cycle [3], [4]. Systolic BP (SBP) estimation using a PTT technique shows higher accuracies than diastolic BP (DBP). Numerous studies have shown impressive results, but estimation accuracies still need to be improved which is ongoing research [5].

Pulse arrival time (PAT) and PTT are the most effective methods for the non-invasive assessment of arterial stiffness and cuffless BP estimation [3], [4], [5]. PAT is not a surrogate of a PTT, however, due to the electromechanical delay of the pre-ejection period (PEP) [6]. Research over the last decade has shown a higher correlation between PTT to BP than to PAT. According to the Moens-Korteweg equation, elasticity is inversely proportional to PTT which relates to stiffer arteries, resulting in higher wave speeds and smaller PTT value, and vice-versa. Comparisons between invasive and non-invasive assessment of PTT have validated that non-invasive assessment of PTT follows similar trends to the estimation of BP as an invasive PTT method [7]. PTT can be measured using various methodologies, for example,

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optical sensing of the arterial waveform using two inline photoplethysmogram (PPG) sensors for simultaneously acquiring the waveforms from two distal locations. BPP has higher precision and accuracy than PPG when validated against the SphygmoCor tonometer [8]. There are no reports, to our knowledge, of a comparison of PTT across modalities (PPG vs BPP) and intra-wavelength-based PPG PTT analysis [9], [10].

In this study, we have compared PTT derived from PPG waveforms against PTT derived from BPP waveforms. An agreement and ANOVA analysis have been used to compare PTT between the two sensing methodologies. The results show that PTT as measured by BPP has a larger value than PTT measured by PPG, which may help in reducing error in estimation accuracies.

II. BACKGROUND

A. PHOTOPLETHYSMOGRAM

PPG is a non-invasive photovoltaic-based measurement of change in volumetric blood flow through light absorption [11]. In transmission mode, the source of light is vertically aligned to the receiver; and in the reflection mode, the source of light is in line with receiver; and volumetric blood flow through tissues is acquire through absorption and reflection methods respectively. It provides blood oxygenation and heart rate measurement that is widely used in primary and intensive care settings [12].

PPG sensor works on the Beer-Lambert–Bouguer law [13] which is described as:

$$I\left(\lambda\right) = I_0 \exp\left[-\mu_a\left(\lambda\right) cd\right] \tag{1}$$

where $'I'$ is the intensity of light (lux), $'I_0'$ is the intensity of source light (lux), $'\lambda'$ is the light source wavelength (cm), $'\mu_a'$ is the absorptivity of substance/tissues (L/mmol*cm), 'c' is the concentration of the absorption of the substance/tissue which is constant in the medium (mmol/L), and 'd' is the optical path length of the medium (cm).

B. FINGER BALLISTOCARDIOGRAM

Finger ballistocardiogram (BPP) sensing is a non-invasive sensing technique which measures the distention waveform [14]. This arterial wall movement of the blood flow (BF) is due to the pressure waves when they are partially occluded against the bone. The polyvinylidene fluoride (PVDF) piezoelectric sensor is strapped around the index finger's distal phalanx. It works in a similar principle to that of the SphygmoCor tonometer.

BPP sensor works the Kessel formula [15] which is described as:

$$\sigma = p_i \frac{r}{s} r \ll s \tag{2}$$

where $'\sigma'$ is circumferential tension of the artery (Pa), $'p_i'$ is the internal blood pressure (Pa), 'r' is the radius of the artery (m), and 's' is the wall thickness of artery (m). BPP dynamic pressure sensing can be described by Hooke's Law which is described as:

$$\sigma = E.\epsilon \tag{3}$$

where 'E' is the elastic modulus of the artery (N/m^2) and $'\epsilon'$ is the strain due pressure on the artery (dimensionless). Pulse transit time relationship to blood pressure

PTT is the time lag of pressure waveform between two measurement sites, in Eulerian frames of reference, on an artery. It is related to pulse wave velocity (PWV) which is mathematically expressed by Equation (4) as:

$$PWV = \frac{\Delta X}{PTT} \tag{4}$$

where 'ΔX' is the distance between the in-line sensors. The PWV relationship to artery elasticity is described by Moens-Korteweg (5):

$$PWV = \sqrt{\frac{Eh}{2r\rho}} \tag{5}$$

where 'E' is the Young's modulus of artery (kg/ms2), 'h' is the thickness of the arterial wall (m), 'r' is the inner radius of artery (m), and 'ρ' is blood density under controlled condition (kg/m^3). Young's modulus of a artery can be described as:

$$E = E_0 e^{\alpha P} \tag{6}$$

where 'E_0' is the Young's modulus of an artery at zero blood pressure (kg), 'P' is the arterial blood pressure (mmHg), and $'\alpha'$ is the curve fitting coefficient (1/mmHg). By analytical analysis of equation 1, 2 and 3, we obtain:

$$P = \frac{1}{\alpha} \ln\left(\frac{2r\rho\Delta X^2}{E_0 h}\right) - \frac{2}{\alpha} \ln\left(PTT\right) \tag{7}$$

We can observe that arterial pressure is directly related to the natural log of PTT; evidence for this has been provided by previous studies. Therefore, accurate assessment of PTT would result in better estimation of arterial pressure [10].

III. EXPERIMENTAL SETUP

The Biopac MP36R unit (Biopac System, USA) was used for subject's data collection, BPP and PPG sensor setting and interfacing was explained in Janjua et al. [8]. In this study two inline clamp-stacked PPG and BPP sensors were mounted at distal and proximal phalanxes, approximately 50mm apart, of the index finger of each subject. A block diagram of the acquisition system is shown in Figure 1.

A schematic diagram of the clamp-stacked mounting of the PPG and BPP sensors on figure is shown in Figure 2.

All the sensors were placed on the subject's non-dominant hand while seated in an armchair. The clinic room temperature was regulated at 22 ^{o}C and the acquisition were under a calm condition.

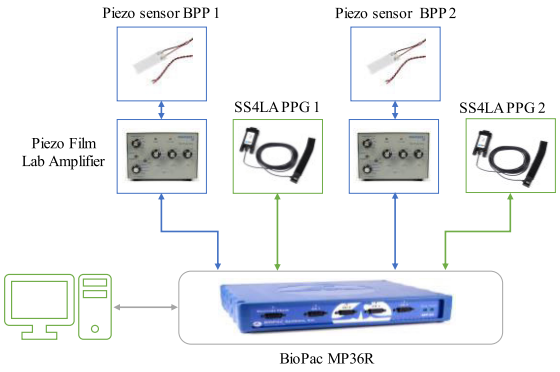

FIGURE 1. Block diagram of signal acquisition system used for the of subject's data collection.

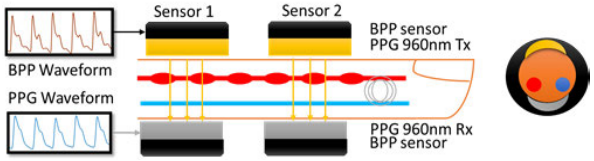

FIGURE 2. Schematic diagram showing the lateral (left side) and cross-sectional (right side) view of the inline placement of the sensors.

This study data was collated from seven healthy volunteers aged 30 ± 6 years from mixed or multiple ethnic background and average resting BP<=120/80. The 30 second window data was acquired after resting for 10 minutes. For this study, the ethical approval was obtained from hospital ethics committee, IRAS Project ID 166742. Subjects were asked to refrain from consuming alcohol for 36h and a meal/coffee for 2h before the collection of the data.

Subjects were requested not to make any movements and remain calm to reduce motion artefacts; they were also asked to restrict the trending of respiration rhythm. We assumed that there were no hydrostatic and gravitational variations in the artery under observation.

The maxima of the first derivative determines the steepest point on the blood flow waveform which is least affected by the reflected wave [16]. Physiologically, the first derivative represents the early systole of blood circulation during a cardiac cycle. In addition to the reflection wave effect, foot and peaks of blood flow are affected by other factors including skin colour, sensor skin contacts, and strapping pressure which have different responses depending on the sensing technology.

A. SIGNAL PROCESSING

The signals captured by the Acqknoweldge 5.0 software were exported in text format to MATLAB (R2018, MATLAB Inc.) software. The data of each subject was visually inspected to remove artefacts and crop the data for clean signals. The algorithm steps are as follows.

1) All the signals were normalised and detrended.
2) The first derivative of the signals was calculated.
3) The maxima of the first derivative (MoFD) were detected.
4) The difference was calculated between the MoFD for the inline sensor's waveform to find the PTT for PPG sensors (PTT-PPG) and PTT for BPP sensors (PTT-BPP).
5) If subjects' PTT-PPG waveform showed crossover, the PTT-BPP waveform data were discarded.
6) Bland Altman agreement analysis and ANOVA were used to find the agreement between PTT-BPP and PTT-PPG.
7) Regression analysis was used find the r^2-fit among the methodologies.
8) A histogram (HM) of the subjects was plotted.

IV. RESULTS

Cohort's PTT-BPP, PTT-PPG, and their trend curve, using a 9^{th} order polynomial, plots are shown in Figure 3. The cohort dataset showed higher PTT-BPP values by an average of 17.8 milliseconds compared to PTT-PPG values.

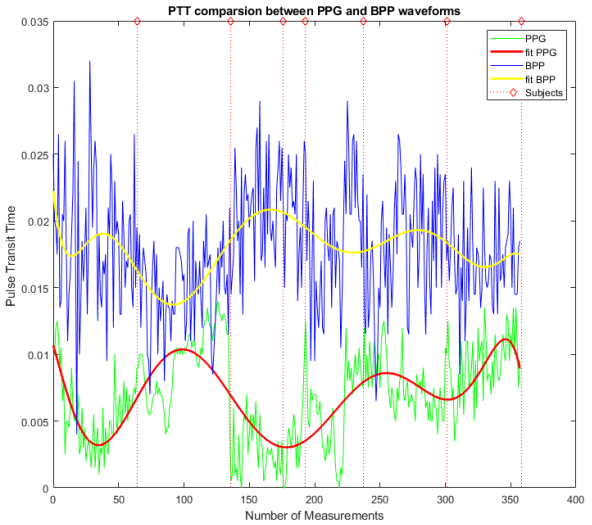

FIGURE 3. PTT-BPP, PTT-PPG data of the cohort and their trends.

The histogram for PTT-BPP and PTT-PPG plot is shown in Figure 4. Both waveform plots showed a normalised distribution. The datasets were tested for skewness, and none was found in any of the PTT-PPG or PTT-BPP datasets.

The PTT-BPP and PTT-PPG datasets were also tested using the repeated measure ANOVA which showed a significant difference with p-value ($p < 0.05$). Based on the p-value, it can be concluded that there is a significant difference between the groups. Interestingly, the PTT-BPP waveform showed consistent behaviour compared to PTT-PPG among the cohort datasets. This intermittent performance of PTT-PPG showed evading behaviour in tracking the blood flow waveform compared to PTT-BPP.

The Bland-Altman analysis was used to check agreement and its plot shown in Figure 4. The values of the limit of

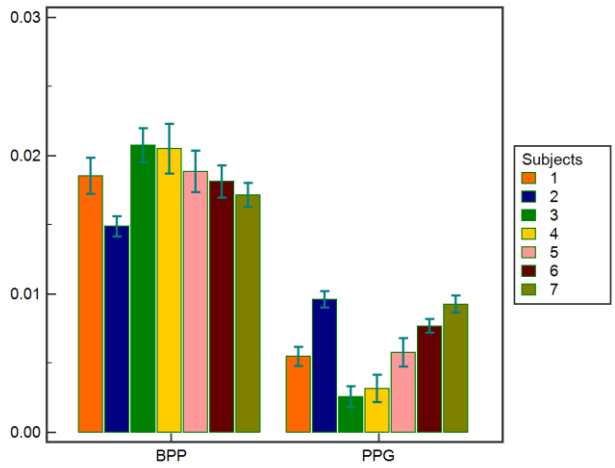

FIGURE 4. Histogram of PTT-PPG (PPG left) and PTT-BPP (BPP right) of the cohort with their variance.

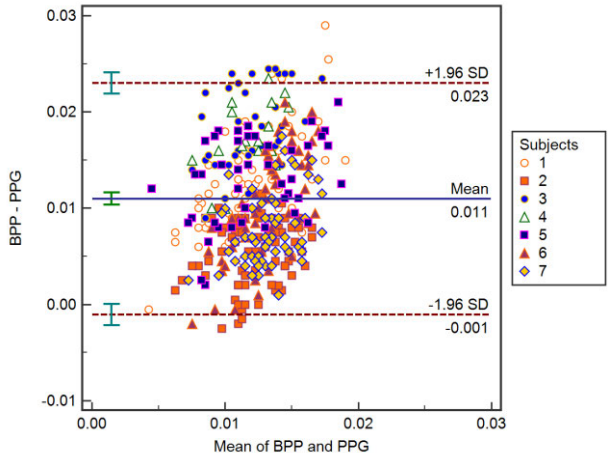

FIGURE 5. Bland-Altman analysis of PTT-BPP (BPP) and PTT-PPG (PPG) of the cohort dataset.

TABLE 1. PTT-BPP and PTT-PPG Bland-Altman parameters for agreement analysis of the cohort dataset.

Lower limit	95% CI	Upper limit	95% CI
-0.001050	-0.002140 to 0.00004064	0.02299	0.02190 to 0.02408

agreement and systematic differences is shown in Table 1 and Table 2. It can be concluded based on the analysis that almost all the dataset remained within 95% of the confidence interval with a few outliers. No biases were observed in the dataset and systematic mean difference was approximately zero (0.01097).

The regression analysis was performed to examine the proportion of variation between PTT-BPP and PTT-PPG cohort dataset and shown in Figure 6. The Spearmen's rank correlation was used to examine the biasness in regression analysis, and none was found.

TABLE 2. PTT-BPP and PTT-PPG Bland-Altman statistical difference of the cohort dataset.

Mean	SD	95% CI
0.01097	0.006132	0.01033-0.1161

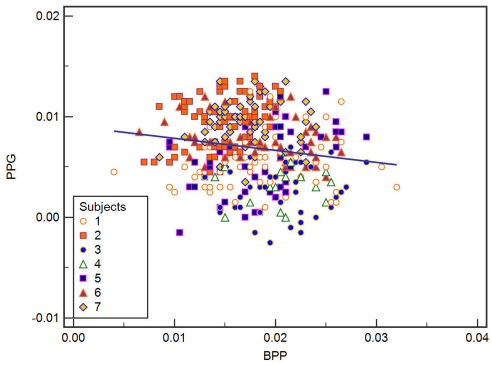

FIGURE 6. r^2-fit of PTT-BPP and PTT-PPG of the cohort dataset.

TABLE 3. r^2-fit correlation parameters for PTT-BPP and PTT-PPG of cohort dataset.

	regression	Spearmen's correlation	
Sample size	r^2	rho	Significance level
358	0.02405	-0.160	p=0.0024

V. DISCUSSION

A novel cross-comparison of PTT using different sensing methodologies is presented to evaluate the differences in PTT-PPG and PTT-BPP measurement precision and accuracies. The findings of this study are in line with finding of study from Janjua et al. [8] of BPP validation against the SphygmoCor tonometric waveform for haemodynamic indexes like the ageing index, stiffness index, augmentation index, etc.

According to Womersley's flow in the large artery, the rate of flow waveform is predicted to lags by 90^o to the pressure gradient [2], [8]. Similar analogy is observed here, where the BPP waveform, sensing of the distension waveform, directly relates to the pressure waveform [3] that may have resulted in improved assessments of PTT-BPP. It has been shown that PTT-BPP has quicker, and steadier responsiveness compared to conventional PTT-PPG measurements, hence it may help improve the accuracies pertaining to the estimation of BP using PTT [4], [5], [6], [17].

Healthy subjects' data was collated for controlled testing and evaluation of these techniques. Whereas, in three subject's PTT-PPG data plot showed a crossover to the PTT-BPP plot which highlights the inconsistency in tracking PTT by the PPG waveform due to changes in blood composition – their

data was discarded for this study. However, PTT-BPP showed a steady behaviour. It can be argued that in the absence of any interventions, for decreasing or increasing BP, the crossover poses a question for credibility regarding the use of PPG technology to measure PAT/PTT or similar parameters. Whereas PTT_BBP is found not to be affected by skin colour, blood composition, or sensitivity to oxygenation due to its very nature of pressure sensing methodology [7].

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