Effects of Pulse Transit Time and Pulse Arrival Time on Cuff-less Blood Pressure Estimation: A Comparison Study with Multiple Experimental Interventions

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Abstract— **Pulse transit time (PTT) has been shown a correlation with blood pressure (BP), and it is considered as a potential marker for cuff-less BP estimation. However, pulse arrival time (PAT) including pre-ejection period (PEP) was utilized more widely because of its convenience to acquisition and calculation. In spite of this, whether PAT can surrogate PTT has been a controversial topic for many years. In this study, we designed an experiment on 55 subjects with multiple interventions, those could cause the changes in BP and PEP. We analyzed the linear and non-linear correlations between BP and PTT/PAT, and assessed the performances of PTT-based and PAT-based models on tracking the BP variation. Five typical BP estimation models were used for comparison. We found that PEP could change rapidly in response to the physical stress, and it was also related to sympathetic nervous system activity. Although PTT had a better linear correlation with BP, most of the PAT-based models showed more accuracy than PTT-based models in all of the interventions, especially for the calibrated model. It is suggested that PAT has the potential to predict BP, and the inclusion of PEP in the measurement of PAT is necessary.**

I. INTRODUCTION

Cuff-less blood pressure (BP) methodologies is playing an increasing role in cardiovascular health management due to its advantage of unobtrusive continuous monitoring. In previous studies, PTT has been proved as a marker of BP and used in the cuff-less blood pressure estimation model [1-2]. Since electrocardiograms (ECG) are more readily available, a great amount of researchers utilized PAT as a convenient surrogate of PTT [3-4]. In their studies, PAT corresponds to the duration that an arterial pressure wave from one artery takes to travel to another during left ventricular ejection, and is typically measured as the time delay between the R-Peak of the ECG and the peak of photoplethysmography (PPG). It is noteworthy that PAT is not equivalent to PTT, but it is equal to the summation of PTT and the PEP. PEP adds an additional variable to PAT-based BP estimation model, which changes the relationship between PTT and BP. On the other side, PEP can easily be influenced by stress and physical activities [5-6], those are closely related to BP variation. Therefore, the effects of PTT-based and PAT-based model has been a controversial topic for many years.

Some investigators have demonstrated that PTT with the PEP removed is a better marker of BP [7-9]. Zhang et al. compared the ability of PAT with PTT in predicting animals' BP by performing experiments on six dogs injected with drugs to extend their BP range [8]. The RMSE of PAT estimated diastolic blood pressure (DBP) and systolic blood pressure (SBP) were 9.8±5.2, 11.9±6.1 mmHg, compared to PTT of 5.3±1.2, 7.5±2.2 mmHg, respectively. The results suggest that PAT is significantly less effective than PTT in tracking blood pressure, but it is unclear how much of this effect translates to humans. While in experiments with phenylephrine interventions in humans, Finnegan et al. discussed the effect of PTT and PEP on changes in PAT in 30 volunteers injected with phenylephrine to alter blood pressure, the results showed a 5.49 mmHg RMSE in SBP estimation with interventions using PAT, while PTT resulted in a higher prediction accuracy with a 4.51 mmHg RMSE [9].

In contrast, other studies have suggested that PAT can be used as a surrogate of PTT [10-12]. For example, Wong et al. found a moderate correlation between BP and PEP [10]. PEP can be predicted BP in a linear regression with a standard deviation (SD) of 7.3mmHg in BP residue. These studies demonstrated that PTT did not change significantly during exercise while PAT decreased significantly, and the addition of PEP moderately increased the correlation between PAT and SBP [11]. The analysis revealed that, whether linear or nonlinear models were utilized, blood pressure predictions generated through PAT exhibited lower errors and higher correlation coefficients compared to those obtained through PTT [12]. PEP related to autonomic nervous system can easily be influenced by stress and physical activity, affecting BP variation. Thus, their studies demonstrated the impact of PEP on BP estimation remains could not be underestimated.

In this paper, we design an experiment with multiple interventions, which cause the BP variation. Then, we compare the effects of PTT and PAT on cuff-less BP estimation in different experimental interventions.

II. METHODS

A. Data Acquisition

In this study, we set up five experimental interventions that changed BP via different causes: 1) Lying on the bed for 5 min; 2) Upright sitting for 3 min; 3) Deep breathing at

This work was supported by the National Key Research and Development Program (2021YFF0703704); National Natural Science Foundation of China (62206269 and U1913210); Guangdong Basic and Applied Basic Research Foundation (2022A1515011217); Shenzhen Science and Technology Program (JSGG20211029095546003).

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around 6 breaths/min lasting 2 min; 4) Playing online keyboard rhythm game for about 3 min; 5) Holding the gym ring with maximum handgrip stress for 1.5 min. There was a relaxation period before each intervention in order to stabilize the physiological signals. The physiological signals were recorded using a commercial data acquisition system BIOPAC MP150. ECG 100C, PPG 100C and EBI 100C were used for obtaining ECG, PPG and ICG waveforms. Reference BP were acquired by CNAP monitor. Signals from all channels are collected synchronously by BIOPAC MP150 at 1000 Hz sampling rate. Finally, 55 subjects across a wide age range were recruited in this experiment (age: 44±21 years; gender: 27 males). Among them, 5 hypertensions were included.

B. Data Pre-processing

Filtering methods were implemented to remove noise from acquired signals. For ECG signal, a bandpass filter was used. We set its low-pass cutoff frequency at 5 Hz and high-pass cutoff frequency at 30 Hz. For PPG signal, a low-pass filter was set with a cutoff frequency at 10 Hz. For ICG signal, which is the first-order derivative of the EBI signal, a low-pass filter was used with a cutoff frequency at 1 Hz. Next, we extracted the feature point of signals for each cardiac cycle. As shown in Figure 1, feature points of Q and R of ECG signal were detected by Pan-Tompkins method. The PPG peak denoted as Pk were extracted at the maximum of the PPG signal. For BP waveform in one cardiac cycle, detected maximum value of BP waveform was recorded as systolic blood pressure (SBP), and the minimum value of BP was diastolic blood pressure (DBP). ICG was analyzed by AcqKnowledge 4.2 software to obtain the B-point.

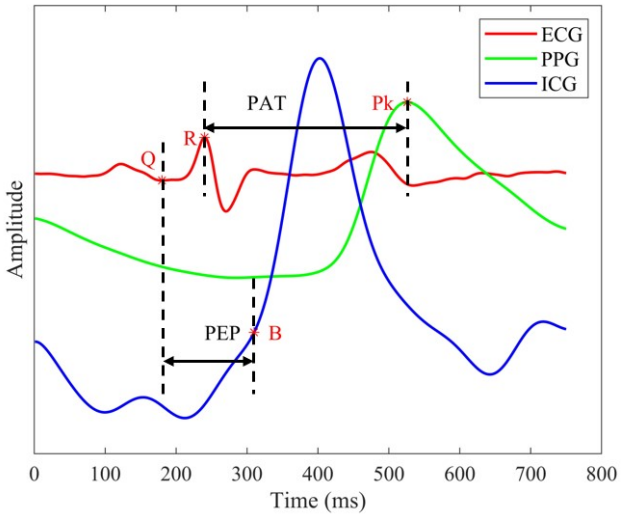

Figure 1. An illustration showed the PTT, PAT and PEP definition.

C. Feature Extraction

PTT and PAT were calculated based on the feature points detected above. The time delay between the R-peak of ECG signal and the peak of PPG signal Pk is defined as PAT; PEP is defined as the time difference between Q point of ECG signal and B point of ICG. PTT is obtained by subtracting PEP from PAT.

In addition to the above features, we also computed some other features for using in the machine learning model, including the mean, variance, absolute value integral, fuzzy entropy of the ECG, PPG and ICG. Thus, another 12 features obtained here.

D. Compared Models

The following calibrated and uncalibrated random forest models were used to assess the ability of PTT and PAT on blood pressure estimation.

(1) Model 1: A continuous BP estimation model with PTT as the independent variable was be used in our study [13]. The algorithm is given below:

$$SBP = SBP0 - \frac{2}{\gamma PTT0}(PTT - PTT0) \quad (1)$$

$$DBP = SBP - (SBP0 - DBP0)\left(\frac{PTT0}{PTT}\right)^2 \quad (2)$$

where SBP0, DBP0, PTT0 are parameters to be determined, we take the mean value of PTT at the first five sampling points of each subject. The value of γ is set as 0.031 mmHg according to the reference.

(2) Model 2: Zheng et al. proposed a non-linear BP-PTT model [15]. All the parameters can be determined by a single calibration at the beginning of the BP measurement.

$$DBP = \frac{1}{3}SBP0 + \frac{2}{3}DBP0 + \frac{2}{\gamma}\ln\left(\frac{PTT0}{PTT}\right) - \left(\frac{SBP0-DBP0}{3}\right)\left(\frac{PTT0}{PTT}\right)^2 \quad (3)$$

$$SBP = DBP + (SBP0 - DBP0)\left(\frac{PTT0}{PTT}\right)^2 \quad (4)$$

(3) Model 3: Ding et al. proposed photoplethysmogram intensity ratio (PIR) as a potential indicator to improve the accuracy of blood pressure prediction, this paper uses a BP model based on PIR [].

$$\mathrm{DBP}=\mathrm{DBP0}\frac{\mathrm{PIR0}}{\mathrm{PIR}} \quad (5)$$

$$SBP = DBP0\frac{PIR0}{PIR} + (SBP0 - DBP0)(\frac{PTT0}{PTT})^2 \quad (6)$$

(4) Model 4: In this paper, we propose a machine learning model using random forest algorithm for comparison of the BP estimation. 12 features extracted above plus PTT or PAT are used as the input of the model. For model training, we used the first 80% of the data set as the training set and the last 20% as the test set. The data in the dataset is arranged by person to ensure that data from the same person does not appear in both the training and test sets. To compare the calibrated and uncalibrated models, the same test set is used for all the models.

III. RESULT

The correlation between PTT/PAT and blood pressure, the prediction results of the model based on PTT/PAT and the variability of PEP and heart rate with posture and exercise were investigated in this section.

A. Correlation of PAT and PTT to BP

Figure 2 shows the relationship between SBP and PTT /PAT for all subjects. The Pearson correlation coefficients and maximal information coefficient (MIC) were computed for PTT/PAT and SBP, respectively, where r was used to represent the Pearson correlation coefficient score.

PTT and PAT both showed positive correlation with SBP (r>0). The results indicate that the linear correlation between PTT and BP was better than that of PAT, as the r value for PTT was higher in all states. Conversely, the non-linear correlation between PAT and BP was stronger, as indicated by a higher MIC score for PAT.

B. Comparison of the performances between PTT and PAT

Table I shows the Mean Absolute Error (MAE), Standard Deviation (SD) values between reference BP and estimated BP calculated by four representative models. All models with calibration are obviously better than the random forest model, except for handgrip in model 2. It is suggested that the correlation between PTT and PAT and blood pressure varies among individuals, and calibration of individual models using accurate blood pressure values can reduce individual differences and improve the accuracy of the models.

For the calibrated models, the performances of PAT-based model in all experimental intervention are better than PTT-base models, which is consistent with the high nonlinear correlation between PAT and BP. It demonstrates that PAT is a more effective alternative to BP when using a calibrated model. In contrast, for the random forest model with multi-features, the differences of prediction accuracy are not significant between PTT-based and PAT-based models.

TABLE I. COMPARISON OF BLOOD PRESSURE PREDICTION PERFORMANCE BETWEEN PTT AND PAT FOR DIFFIRENT MODELS

Models	Parameter	Lying (mmHg)		Sitting (mmHg)		Deep breathing (mmHg)		Handgrip (mmHg)		Game (mmHg)	
		MAE	SD	MAE	SD	MAE	SD	MAE	SD	MAE	SD
Model 1 [13]	PTT	5.71	4.08	6.37	4.63	6.66	4.61	7.61	4.96	7.83	5.08
	PAT	**3.92**	**2.68**	**4.23**	**2.58**	**5.06**	**3.19**	**4.11**	**2.31**	**5.67**	**3.11**
Model 2 [14]	PTT	8.92	6.46	10.13	7.61	10.78	7.82	18.56	14.63	11.92	8.79
	PAT	**4.96**	**3.53**	**5.63**	**3.31**	**6.76**	**4.35**	**7.48**	**3.72**	**7.08**	**4.36**
Model 3 [15]	PTT	7.68	5.17	9.61	6.49	8.95	6.74	11.68	11.19	9.71	6.48
	PAT	**5.86**	**3.43**	**6.7**	**4.09**	**7.64**	**4.85**	**4.32**	**3.1**	**6.87**	**3.46**
Model 4	PTT	14.64	11.61	16.88	13.47	16.1	11.6	17.19	12.47	26.44	12.41
	PAT	14.07	11.16	15.37	14.45	16.17	11.74	24.41	18.78	28.77	18.88

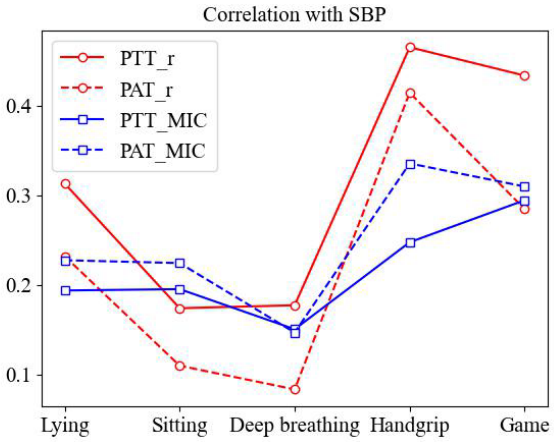

Figure 2. The correlation of PTT-BP and PAT-BP in different experimental interventions.

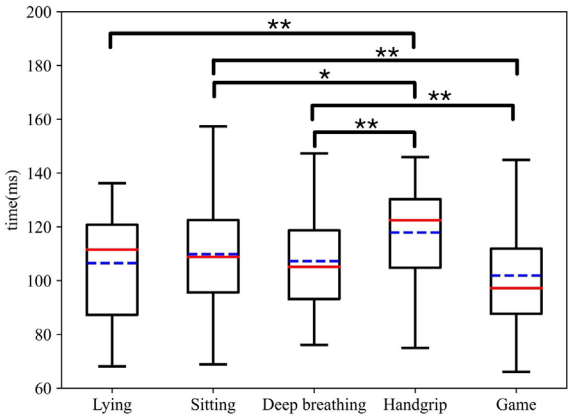

Figure 3. Box plot of pep in multiple interventions.

C. The results of PEP analysis

Figure 3 shows the box plot of PEP in five experiment interventions, where the blue dashed line represents the mean value of PEP and the red solid line represents the median value of PEP. In this paper, we performed a t-test between the PEPs of the five types of interventions with each other. For the calm state (lying or sitting), PEP changed slightly during the posture change. However, PEP values in the handgrip and game test changed significantly compared to the calm state. According to the results of the t-test, the PEP of the calm state and the grip state are significantly different, which indicates that PEP shows some correlation with physical stress.

In Figures 4, the error bar depicts the variation of mean and SD of PEP between SBP and DBP with all interventions, where the dots indicate the mean of the data and the line segments indicate the SD of the signal. It can be seen from the graph that PEP has the same trend with both SBP and DBP, especially for deep breathing, handgrip and game.

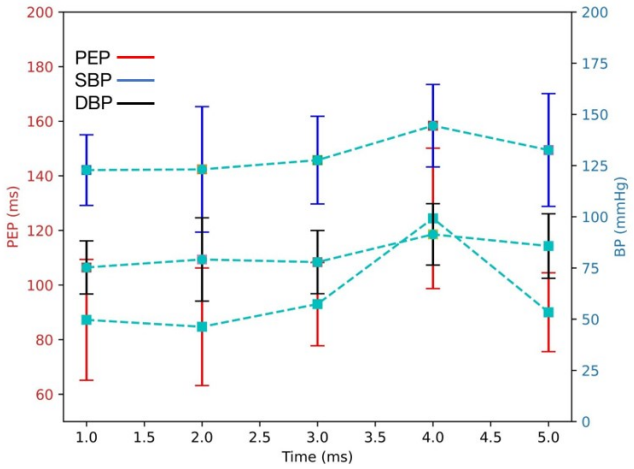

Figure 4. Error bar of SBP, DBP and PEP

III. Discussion

In the previous studies, it has been proved that PEP is an indicator, which is associated with stress and sympathetic nerves system activity []. Our study calculated HRV responds to sympathetic nerves. In deep breathing, handgrip and game state, HRV have some fluctuations compared to the calm state, which confirmed that alterations in sympathetic nerves are induced in our intervention experiments. Moreover, the PEP of handgrip and game states were significantly different from other states, demonstrating that PEP is associated with autonomic and stress. For both PAT-based and PTT-based models, the PAT-based model outperformed the PTT-based mode in the model with calibration, indicating that PEP played a positive role in blood pressure prediction. Our study computed results on a heterogeneous dataset that included volunteers with blood pressure abnormalities, which may explain the large prediction error of the uncalibrated random forest model.

IV. Conclusion

In conclusion, PAT was a better predictor of blood pressure than PTT for calibrated models in multiple interventions, which leads to PEP' changes. Meanwhile, due to the ease of PAT measurement, this finding will be helpful for cuffless continuous BP measurement. Because the data in this paper contain a complex population with a wide age range and the inclusion of a small number of patients with hypertension. Therefore, BP cannot be estimated well using a population-based uncalibrated model. In future studies, the dataset would be expended as much as possible to use as many samples as possible for fitting the uncalibrated model.

Acknowledgment

The authors thank Xiangdong Zhang and Minghui Gao for their kind help with the data collection, and also the subjects who participated in the study.

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