

Research Article

A Unified Calibration Paradigm for a Better Cuffless Blood Pressure Estimation with Modes of Elastic Tube and Vascular Elasticity

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Although two modes of elastic tube (ET) and vascular elasticity (VE) have been well explored for cuffless continuous blood pressure (BP) monitoring estimation, the initial calibration with these two models could be derived from different mathematical mechanisms for BP estimation. The study is aimed at evaluating the performance of VE and ET models by means of an advanced point-to-point (aPTP) pairing calibration. The cuff BPs were only taken up while the signals of PPG and ECG were synchronously acquired from individual subjects. Two popular VE models together with one representative ET model were designated to study aPTP as a unified assessment criterion. The VE model has demonstrated the stronger correlation r of 0.89 and 0.86 of SBP and DBP, respectively, and the lower estimated BP error of -0.01 ± 5.90 (4.55) mmHg and 0.04 ± 4.40 (3.38) mmHg of SBP and DBP, respectively, than the ET model. With the ET model, there is a significant difference between the methods of conventional least-square (LS) calibration and aPTP calibration ($p < 0.05$). These results showed that the VE model surpasses the ET model under the same uniform calibration. The outcome has been unveiled that the selection of initial calibration methods was vital to work out diastolic BP with the ET model. The study revealed an evident fact about initial sensitivity between the modes of different BP estimation and initial calibration.

1. Introduction

Uncontrolled hypertension or high blood pressure (BP) was a major risk factor that links to potential development of serious diseases such as stroke, hypertensive heart disease, and coronary artery disease [1]. For early warning, diagnosis, and treatment of hypertension in time, continuous cuffless BP monitoring technology was imperative. Conventional standard cuff-based BP measurement (for example, auscultation and oscillometry) was able to provide instantaneous information about BP status [2]. However, these cuff-based approaches with recurrently inflating and deflating of the cuff stress the patient, caused periodic interruptions to blood

flow, affected the physiological state of the patient, and disturb the quality of sleep due to repeat inflating and deflating of the cuff that stress the patient [3]. Consequently, the cuffless solution caught the attention of many scholars since it overcomes disturbance issues existing in the traditional cuff-based method [4, 5].

As a noninvasive optical measurement technique, photoplethysmography (PPG) provided valuable information on physiological heart monitoring and cardiovascular system assessment of vascular parameters [4, 6]. The pulse arrival time (PAT), defined as the time interval between the R peak and the point with maximum gradient on the rising edge of PPG, showed a high correlation with BP, especially systolic

blood pressure (SBP) [4, 6, 7]. In recent years, the PAT-based BP estimated models capturing BP variations mainly fall into two categories: vascular elasticity (VE) model [5, 6] and elastic tube (ET) model [8]. Among these reports [5, 6, 8], both the ET model and the VE model had excellent performance for BP estimation. The ET model, originated from the elastic Windkessel model, was continuously improved with the requirements of the elastic pipeline and gradually applied to the estimation and prediction of arterial BP [9].

Recently, the ET model based on PAT showed a better BP estimation performance than the VE model [8, 10]. However, the VE model based on the M-K equation was also widely studied and developed in cuffless continuous BP measurement due to it described the pulse wave velocity (PWV) in an infinitely thin-walled elastic vessel [5, 7]. Here, PWV was a measure of arterial stiffness which was a key predictor of future cardiovascular risk, or the rate at which pressure waves move down the vessel [11]. It has been established as a highly reliable prognostic parameter for cardiovascular morbidity and mortality in a variety of adult populations including older adults, patients with end-stage renal disease, diabetes, and hypertension [12]. For long-term cuffless BP monitoring technology, especially in home, a kind of accurate and practical model was particularly important. Importantly, the calibration method determined the practicality or the convenience of the specific BP estimation model. However, under the same calibration method, the performance evaluation of different models was ignored by the researchers. Therefore, it was necessary to use a unified calibration method to optimize BP models that were derived from different modeling methodologies, i.e., elastic tube (ET) theory and vascular elasticity (VE) theory to verify their effectiveness and applicability in estimation.

According to our previous work [13], the least-square (LS) calibration method (abbreviated as LS method or LS) [8] was usually applied in the ET model to accomplish the calibration procedure. This method is used to determine unknown parameters for a specific BP model in the short-time monitoring due to requiring all data sets regarding PAT obtained from ECG and PPG signals and cuff BPs. Consequently, consecutive long-term monitoring could not be accurately completed and achieved. To our knowledge [13], the initial BP monitoring period should not be ignored in early warning, diagnosis, and treatment of unhealthy physical conditions. More importantly, the accuracy of BP estimation depends on the sample/point size for this LS method. Obviously, it was a great limitation to complete continuous BP monitoring using LS methods to obtain unknown coefficients or parameters in a specific BP estimation model for each subject.

By comparing with the LS method, one sample point-to-point (oPTP) pairing method (abbreviated as the oPTP method or oPTP) [5, 6] is a calibration technique that uses a one-to-one mapping relationship between model function and variable/sample to determine unknown parameters of the specific model, usually effectively adopted for calibration in the VE model, only needed one point to complete the whole calibration step. The oPTP method to some extent overcame the limitation of larger data samples in the LS method. However, the oPTP method demanded highly for one point/sample in the initial personalized calibration

procedure. It was important to highlight the fact that the selection of the initial point determined the quality of the BP estimation. The VE model required in a quiet state, however, the parameters, like PAT and BP, always fluctuated in a range of small variations at rest, as influenced by the accuracy of the VE model for BP estimation.

In this study, an advanced point-to-point (aPTP) pairing calibration method (abbreviated as the aPTP method or aPTP) was proposed to examine and access the effectiveness, the accuracy, and the robustness of BP estimation compared with the cumbersome LS method and sensitive oPTP method. The investigation in this study includes the following: (1) the correlation and overall performances between the cuff BP and the estimated BP were examined in a uniform calibration method, i.e., aPTP; (2) aPTP was studied to verify whether it could replace the LS method in personalized procedure; (3) for the ET model, the LS method and aPTP method were both studied to compare their effectiveness and the applicability for BP estimation; (4) for the VE model, BP estimation based on the aPTP method was investigated to verify whether possessing high accuracy and robustness compared with sensitive oPTP.

The purpose of the study is to evaluate the performance of VE and ET models by means of an aPTP pairing calibration method. With the study, a cost-effective cuffless BP monitoring approach could be emerged with an easy and durable personalized calibration. Such an approach could be anticipated to be a better choice when considering the practicality of long-term and continuous BP monitoring with both modes of elastic tube and vascular elasticity. Besides these, the study has proofed an evidence about the sensitivity of BP estimation along with these models and their initial calibration methods.

2. Materials and Methods

2.1. Methods

2.1.1. Modeling Methodology for BP Estimation. The beating heart created BP and flow pulsations that propagate as waves through the arterial tree, and then, the waves were reflected at transitions in arterial geometry and elasticity [14]. As a hemodynamic parameter, arterial BP fluctuated on a beat-to-beat basis due to the dynamic interplay from vasomotion, neural regulation, and arterial mechanisms [6]. It was physiologically affected by four factors: arterial compliance, cardiac output, peripheral resistance, and blood volume [15]. Arterial compliance was evaluated by PAT since it was an index of arterial stiffness [16]. In regard to peripheral resistance and blood volume, one of the primary sources was the change in arterial diameter [17]. In recent years, the PAT-based BP estimated models mainly included two categories: elastic tube (ET) model and vascular elasticity (VE) model.

The ET model was developed from the theory of elastic tubes. It was based on two important assumptions and premises: (i) the blood vessel was equivalent to an elastic tube, and (ii) the compliance of the arterial system remained constant throughout the cardiac cycle [18]. Introducing the blood pulsation information and giving the arterial

compliance (C) into the transmission line of the pressure wave, the ET model was developed and proposed. Here, a novel BP estimation nonlinear model was derived by Esmaili et al. from the conservation of mass and momentum principle equation, called the M-M model [8], a representative ET mode. Arterial compliance as an important quantity with respect to these assumptions, used in physiology, was the degree to which a container experiences pressure or force without disruption [14]. It depended strongly on pressure. Considering the conservation of mass and momentum equations, it could be seen that C was a function of pressure on walls of blood vessels, i.e., BP.

The VE model was linked and established according to the Moens-Korteweg (M-K) equation [4]. In biomechanics, the M-K equation modeled a relationship between the wave speed or pulse wave velocity (PWV) and the incremental elastic modulus (a coefficient of elasticity) of the arterial wall or its distensibility [19]. It involved two assumptions: (i) the artery wall was thin and was modeled as a thin shell, and (ii) the thickness and radius of the artery still fixed as the blood pressure changes [20]. Additionally, PWV as an important quantity in the M-K equation was commonly used as a clinical marker of vascular elasticity [12]. Combining the M-K equation with an exponential arterial elasticity model [21, 22], the MK-EE model as a new BP-PAT model was obtained. It gave a logarithmic relationship between BP and the PAT. Moreover, a new BP-PAT model, i.e., MK-BH model [2], was introduced from the Bramwell-Hill (B-H) equation [5] to consider the nonlinear nature in the cardiovascular system. Based on the MK-BH model, Zheng et al. established a mathematical relationship between MBP and a factor that reflected the change in elasticity caused by pressure wave variations, which was called the dMK-BH model [5]. The modeling principle and mechanism about the above three representative models are expressed in Table 1.

2.1.2. A Unified Calibration Paradigm: Advanced Point-to-Point (aPTP) Calibration. As mentioned previously, the conventional LS method in the ET model required all data sets in the whole process of BP monitoring to accomplish the personalized procedure in the corresponding ET model that was derived from the theory of elastic tubes. Consequently, this could be extremely troublesome to implement this procedure. Remarkably, the popular oPTP calibration method only required one point/sample to obtain unknown parameters in the specific VE model that was derived from the theory of vascular elasticity. It is thus clear that one lone sample used to complete the initial calibration process is sensitive as such BP calibration may be accidental and inaccurate.

Here, a new aPTP method was proposed to overcome oPTP method's initial sensitivity and access BP estimation property under a unified paradigm for models that were derived from different modeling methodologies. The mapping relationship between dependent variable and independent variable was established through the available initial values. This technique was called the point-to-point pairing calibration method, i.e., one cuff BP value pairing with PAT_{mean} , a parameter with the average value of PAT. The advanced PTP (aPTP) calibration method (shown in Figure 1) was

developed from the traditional PTP calibration method in the present study.

Three steps of (1) the initial calibration processing, (2) the robust control strategy, and (3) the average treatment effect were established up as the aPTP method.

Step 1. Initial calibration processing.

Generally, the digital cuff-type BP monitor will obtain a set of SBP and DBP after each inflation and deflation. During this period, a series of PAT samples can be calculated according to the ECG and PPG signals detected by the sensors, that is, $PAT_1, PAT_2, \dots, PAT_l$. Here, l is the number of heartbeats during the inflation and deflation of the cuff sphygmomanometer. In this way, we can calculate the average value of this series of PAT samples as follows:

$$PAT_{\text{mean}} = \frac{1}{l} \sum_{i=1}^l PAT_i. \quad (1)$$

If there are N undetermined parameters ($N = 1$ and 3 for the VE and ET models in this study, respectively) among the BP estimation model, then N cuff BP (including SBP and DBP) and N mean PAT (i.e., PAT_{mean}) need to be paired one-to-one to obtain the values of the undetermined parameters. Here, it is defined as θ , that is, $SBP_0, DBP_0, PAT_0, a_i,$ and b_i . This pairing relationship can be understood as solving the inverse function of θ from the relationship $\mathbf{BP} = f(\theta; \mathbf{PAT})$ between BP and PAT, as follows:

$$\theta = f^{-1}(\mathbf{BP}, \mathbf{PAT}) \quad (2)$$

where θ , \mathbf{BP} , and \mathbf{PAT} are m -row and n -column matrices. The f denotes the one-to-one mapping relationship between BP and PAT. In addition, m and n denote the number of subjects and the undetermined parameters θ , respectively, in the BP estimation model. After this step, one determined parameter θ will be obtained.

Step 2. The robust control strategy.

Given the possibility that cuff BP values of subjects in a quiet state might be the same, in the present study, a robust control strategy is necessary to guarantee the validity and rigor of calibration for obtaining all parameter values in a specific BP model. In this regard, we propose two robust control strategies: function analytical solution definition and numerical floating control. The former is to determine whether each obtained model parameter θ_i is a real number, which ensures that this model parameter θ_i is valid in step 1. The latter is to determine whether each θ_i is different. This strategy will traverse whole θ_i obtained from step 1 in the resting state, which to some extent expands the limitation of the conventional oPTP pairing calibration method in the sample or point and the sensitivity of BP estimation. After this step, a set of determined parameters θ_i will be obtained.

TABLE 1: Summary of mathematical models to calculate BP from PAT.

Models	SBP	DBP	Category
M-M [8]	$a_1 + \sqrt{b_1 + c_1} * \frac{1}{PAT^2}$	$a'_1 + \sqrt{b'_1 + c'_1} * \frac{1}{PAT^2}$	ET model
MK-BH [2]	$SBP_0 - \frac{2}{\gamma * PAT_0} (PAT - PAT_0)$	$SBP - (SBP_0 - DBP_0) * \left(\frac{PAT_0}{PAT}\right)^2$	VE model
dMK-BH [5]	$DBP + (SBP_0 - DBP_0) * \left(\frac{PAT_0}{PAT}\right)^2$	$\frac{SBP_0}{3} + \frac{2DBP_0}{3} + \frac{2}{\gamma} \ln\left(\frac{PAT_0}{PAT}\right) - \frac{SBP_0 - DBP_0}{3} * \left(\frac{PAT_0}{PAT}\right)^2$	

Note 1: γ denoted a vascular information parameter. Note 2: SBP_0 , DBP_0 , and PAT_0 were the base value of SBP, DBP, and PAT, respectively, and could be determined at the beginning of monitoring by calibration using an additional cuff-type BP monitor device. Note 3: a_i , b_i , a'_i , b'_i ($i = 1, 2$); c_1 , c'_1 were the corresponding function coefficients.

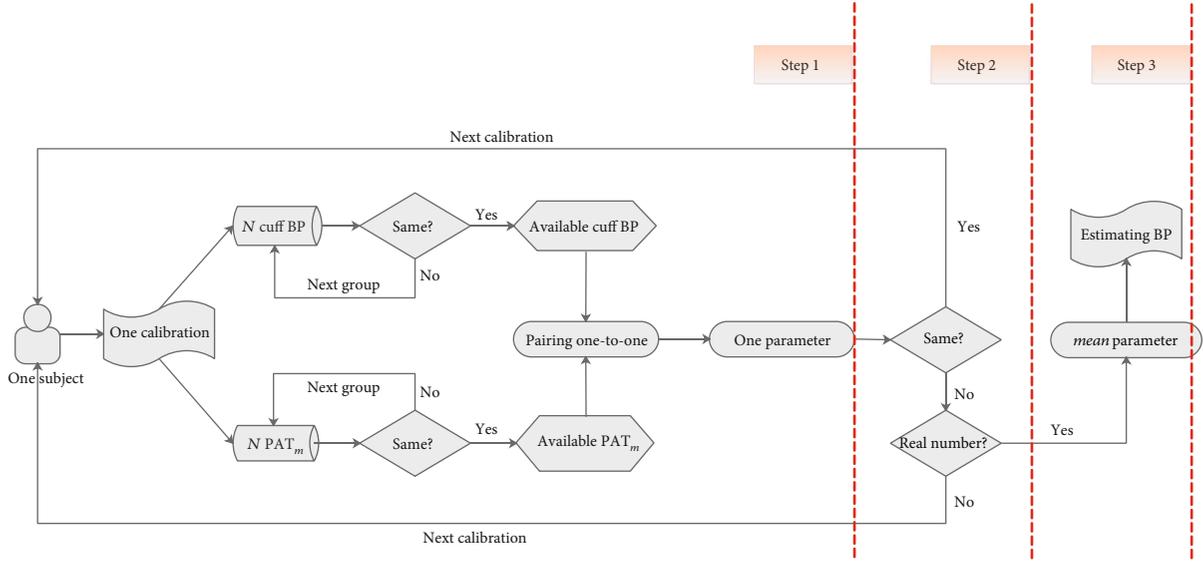


FIGURE 1: The aPTP calculation procedure for the BP monitoring system.

Step 3. The average treatment effect.

Finally, the average values of these parameters of their respective BP estimation models were taken as the final BP monitoring parameters, i.e., SBP_0 , DBP_0 , PAT_0 , a_i , and b_i , as follows:

$$\hat{\theta} = \frac{1}{M} \sum_{i=1}^M \theta_i, \quad (3)$$

where M denotes the number of available model parameter θ_i . The data collection of cuff BP and PAT from BP monitor and sensors, respectively, in the whole calibration process took about eight minutes, and the subjects were required to keep peace and quiet. This calibration process was done only one time per subject, and after deriving parameters in the BP estimator model, the BP could be estimated continuously. That is, using mentioned calibrated parameters $\hat{\theta}$ and their respective nonlinear models introduced in Subsection 2.1.1, SBP and DBP are estimated.

2.1.3. A Summary of Different Calibration Methods and BP Models in Terms of Mechanism.

The LS method and oPTP method were employed for the initial calibration of the ET model and VE model, respectively. The aPTP method could be directly applied to different BP models. And there was no need for extra requirements about distinguishing the modeling mechanism of the models for aPTP. More importantly, it only employed limited data sets at rest rather than all data sets throughout the process of BP monitoring to complete the personalized calibration procedure. The respective application of different initial calibration methods in two BP estimation modes is listed in Table 2. To go a step further, the relationship between the three calibration methods and respective performance is given in Figure 2 to elucidate them at a clear level.

2.2. Experimental Protocol.

This experimental protocol was performed in a study room with temperature $22.6 \pm 2.3^\circ\text{C}$ and relative humidity 60–70%. The PowerLab/16sp system (Castle Hill, ADInstruments, Australia, 2002) was employed to synchronously record and amplify the ECG and PPG signals. The ECG signal was filtered by a 1 Hz high-pass filter and a 40 Hz low-pass filter. Meanwhile, the PPG signal was filtered by a 0.5 Hz high-pass filter and a 20 Hz low-pass filter, and the sampling frequency was 1 kHz [8]. Since the PPG sensor was placed on the subject's left hand, the cuff-type

TABLE 2: Summary of initial calibration methods and mathematical models.

Measurements	oPTP	aPTP	LS	Category and mechanism	
M-M [8]	○	✓	✓	Nonlinear	Elastic tube (ET) model
MK-BH [2]	✓	✓	○	Linear, nonlinear	Vascular elasticity (VE)
dMK-BH [5]	✓	✓	○	Nonlinear	

Note 1: “✓”: applicable; “○”: not applicable. Note 2: a linear model for SBP estimation in the MK-BH model.

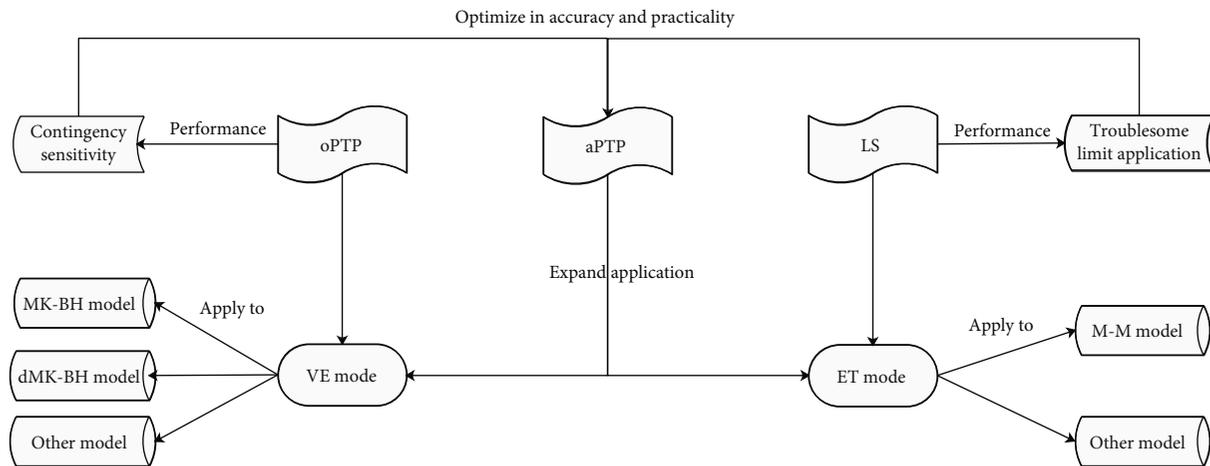


FIGURE 2: The relationship between the three calibration methods and respective performance.

BP monitor (MB-300C, Jasun, China) was mounted on the right arms of a subject to provide a reference BP reading and reduce the effects of BP measurement on the PPG signal. Referring to the guidelines of the cuff-type BP monitor, the accuracy of the cuff-type BP monitor was ± 3 mmHg to be in compliance with the clinical golden standards of AAMI [23]. Specifically, the mean absolute error of less than 5 mmHg and the standard deviation (SD) of mean error of less than 8 mmHg (i.e., the difference should be within 5 ± 8 mmHg) were considered as an acceptable error rate referred to the AAMI guidelines [23].

It should be pointed that before starting the data collection process, we measured the BP of six subjects randomly using a cuff-type BP monitor (MB-300C, Jasun, China) and a conventional mercury sphygmomanometer with a rigorous experimental process. Obviously, the measured BPs were approximately the same for each subject (each person was at the rest or peace condition during BP measurement, so approximately the same values for BPs for each person were expected) [8]. Here, using these two devices, the mean absolute errors (MAEs) of SBP and DBP measurement values were 2.7 and 3.2 mmHg for six subjects, respectively.

2.3. Data Acquisition Procedure and Data Analysis. Twelve healthy subjects in the age range of 21-37 years (9 males and 3 females) without a history of cardiovascular or neurological disorders participated in this study. All participants gave written informed consent. The study was approved by the health center authorities at the University of Shanghai for Science and Technology.

Among these common BP interventions [4, 24, 25], a designated physical exercise is employed since it has been shown

to cause a sensible increase in both SBP and DBP up to 40 mmHg [7]. Currently, the same supervised physical exercise, which was climbing 12 floors at a constant rate for five minutes, was used for all the subjects to guarantee a greater change in BP to obtain a more accurate model estimation [26]. Just finishing the physical exercise, the cuff BP, the ECG, and the PPG signals were collected. Each subject with the cuff BP measurement was asked to sit upright on a chair 25 cm away from the table and breathe naturally to avoid the motion artifact interference. A total of data collection took around 15 minutes per subject after physical exercise.

Generally, the BP estimation based on PAT from a period of 30 s cuff BP, ECG, and PPG signals does not begin until the initial calibration procedure has been completed. In this study, a total of 365 pairs of cuff BP vs. PAT_{mean} , a parameter with the average value of PAT, data sets from at least 30,000 heartbeats were tested for twelve subjects. The estimated errors between the cuff BP and the estimated BP were evaluated as the mean error (mean) \pm standard deviations (SD) as well as the mean absolute difference (MAD). They were defined as follows:

$$\begin{aligned}
 \text{mean} &= \frac{1}{n} \sum_{i=1}^n (BP_{\text{est}_i} - BP_{\text{cuff}_i}), \\
 \text{SD} &= \sqrt{\frac{1}{n} \sum_{i=1}^n (BP_{\text{est}_i} - BP_{\text{cuff}_i})^2}, \\
 \text{MAD} &= \frac{1}{n} \sum_{i=1}^n |BP_{\text{est}_i} - BP_{\text{cuff}_i}|, \\
 \text{SSE} &= \sum_{i=1}^n (BP_{\text{est}_i} - BP_{\text{cuff}_i})^2, \\
 \text{RMSE} &= \sqrt{\frac{\text{SSE}}{n}}.
 \end{aligned} \tag{4}$$

where BP_{est_i} and BP_{cuff_i} denoted the i th BP measured through BP estimation models and by the reference cuff method, respectively, and n was the number of measured BP used for evaluation.

3. Results

Under a unified calibration paradigm, i.e., aPTP method, the ET model and VE model based on PAT were investigated from correlation and overall performance to assess their property for BP estimation. Further, we performed difference analysis to test whether the aPTP method showed better convenience than the cumbersome LS method for the ET model and higher robustness than the sensitive oPTP method for the VE model. More specially, we compared the estimated values of the model derived from each subject data with the corresponding reference values for the model derived from cuff BP for each subject through statistical analysis and regression analysis to ascertain whether there was any difference among the aPTP method and LS method for the ET model. Similarly, we also investigated the property of BP estimation under the conventional oPTP method and new proposed aPTP method for the VE model.

3.1. Assess the Performance under a Unified Paradigm for Different Modeling Methodology

3.1.1. Correlation. To compare the estimated BP results from the three most popular functions (M-M, MK-BH, and dMK-BH) quantitatively, we computed Pearson's correlation coefficient (r), the summed square of residuals (SSE), and root mean squared error (RMSE) between the cuff BP and the estimated BP for all subjects.

As shown in Table 3, a relatively high correlation with SBP was observed among the ET and VE models. The M-M model, as a nonlinear ET model, had the largest SSE and RMSE between both SBP and DBP compared to others. Moreover, the M-M model showed the weakest correlation coefficient with DBP ($r = 0.74$) compared with others. For the VE model, MK-BH and dMK-BH had higher correlation coefficients with BP than the ET model, i.e., M-M model. Remarkably, the dMK-BH had the highest correlation coefficient with BP ($r = 0.89$ for SBP and $r = 0.86$ for DBP) compared to others. More significantly, the dMK-BH model developed from the MK-BH model showed the smallest SEE and RMSE for estimated BP compared with the M-M model.

3.1.2. Overall Performances. The criteria for overall performance evaluation included mean errors of estimation, MAD of estimation, and SD of estimation. Moreover, the average value and 95% confidence intervals of BP estimated error were calculated to identify the influence of different models on the accuracy of estimated BP. A Kruskal-Wallis test with Dunn's multiple comparison test was executed to determine whether statistically significant differences were observed between the mean errors of the ET model and the VE model. These performances are shown in Figure 3.

According to Figure 3, the BP could not be properly estimated from the ET model compared to the VE model. This

M-M model had a mean \pm SD (MAD) of 1.11 ± 7.51 (5.57) mmHg for SBP and -0.23 ± 6.47 (5.13) mmHg for DBP estimated error, respectively, while the dMK-BH as a nonlinear model had a mean \pm SD (MAD) of -0.01 ± 5.90 (4.55) mmHg for SBP and 0.04 ± 4.40 (3.38) mmHg for DBP, respectively. For the VE model, the MAD of estimated errors in the dMK-BH model was decreased by 0.93 and 1.31 mmHg compared with MK-BH. Remarkably, the SD of the errors for all methods was within 8 mmHg for SBP and DBP. It was consistent with the AAMI requirements of 5 ± 8 mmHg/7 mmHg (mean \pm SD/MAD) for the BP estimated error rate [23]. Additionally, for SBP estimation using the aPTP method, a significant difference between the ET model and the VE model was not observed. In contrast with SBP estimation, there was a significant difference between the M-M model and the MK-BH model for DBP estimation ($p < 0.01$). Similarly, a significant difference between the MK-BH model and the dMK-BH model was also observed for DBP estimation ($p < 0.0001$).

3.2. Difference's Analysis Using Different Calibration Methods among the ET and VE Models

3.2.1. BP Estimation Using the Cumbersome LS Method and Convenient aPTP Method for the ET Model. Here, differences were tested with Kruskal-Wallis tests and with Dunn's multiple comparison tests to determine whether statistically significant differences between cuff BP and estimated BP obtained from the ET model using the LS method and aPTP method. More details are plotted in Figure 4.

According to Figure 4, there was a significant difference between the traditional LS method and the unified aPTP method for BP estimation using the ET model ($p < 0.05$). However, it was noteworthy that there were no significant changes on cuff BP and estimated BP based on the ET model. Particularly, there were no difference changes between the cuff BP and estimated BP based on the ET model by using the LS calibration method. Similarly, the difference changes were not found between the cuff BP and estimated BP based on the ET model by using the aPTP calibration method.

Moreover, for the ET model, we also investigated the correlation between the cuff BP and the estimated BP obtained by using LS and PTP calibration methods to test and verify whether using the LS method might reinforce the BP estimation performance. More details about regression plots are shown in Figure 5.

In Figure 5, based on the LS method that required all samples for BP estimation, r values obtained from all the subjects were 0.86 and 0.83 for SBP and DBP estimations, respectively. Regarding the aPTP method that only required small samples, r values for SBP and DBP estimations were 0.83 and 0.74, respectively. Consequently, under different calibration methods, the ET model showed larger differences in the performance of BP estimation, especially in DBP estimation.

3.2.2. BP Estimation Using the Sensitive oPTP Method and Robust aPTP Method for the VE Model. For the VE model, BP estimation using the unified aPTP method was investigated

TABLE 3: BP results using the BP models of ET and VE.

Models	SBP			DBP			Category
	r	SSE	RMSE	r	SSE	RMSE	
M-M [8]	0.83	14940	6.57	0.74	10690	5.56	Elastic tube (ET) model
MK-BH [2]	0.81	11610	5.79	0.77	8672	5.01	Vascular elasticity (VE) model
dMK-BH [5]	0.89	10180	5.42	0.86	5370	3.94	

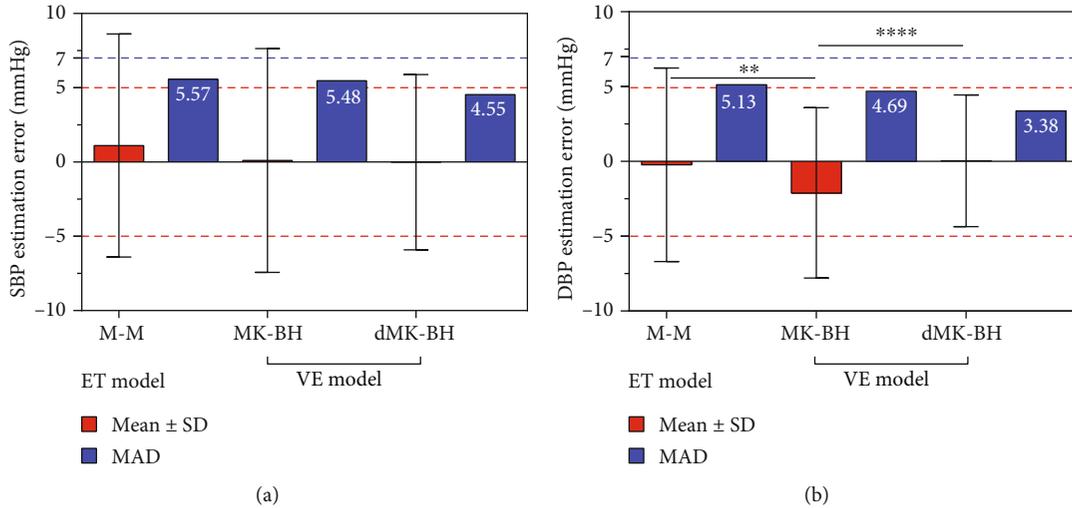


FIGURE 3: The overall comparison of different methods for (a) SBP and (b) DBP measurement. Note 1: the red and blue dotted lines denoted the largest boundary for mean error (5 mmHg) and MAD (7 mmHg). Note 2: significant differences: $*p < 0.05$, $**p < 0.01$, $***p < 0.001$, and $****p < 0.0001$.

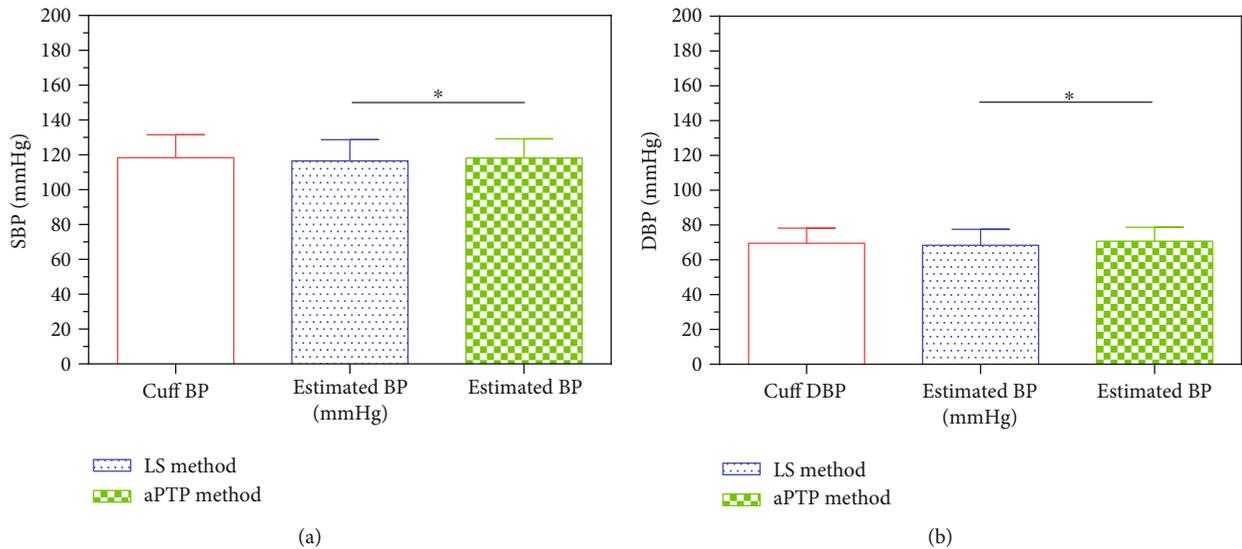


FIGURE 4: Difference comparisons between cuff BP and estimated BP based on the ET model by using LS and aPTP calibration methods. Significant differences: $*p < 0.05$, $**p < 0.01$, $***p < 0.001$, and $****p < 0.0001$.

to verify whether possessing high accuracy and robustness compared with sensitive oPTP. Here, we computed the r , SSE, and RMSE between cuff BP and estimated BP. Details of each estimated BP function are reported in Table 4 for the MK-BH model and Table 5 for the dMK-BH model.

According to Table 4, for the MK-BH model, using the unified aPTP method that serves as an initial calibration method to estimate BP showed better performance than the traditional oPTP method. Compared with the oPTP method, a stronger correlation coefficient with SBP ($r = 0.81$) and SBP

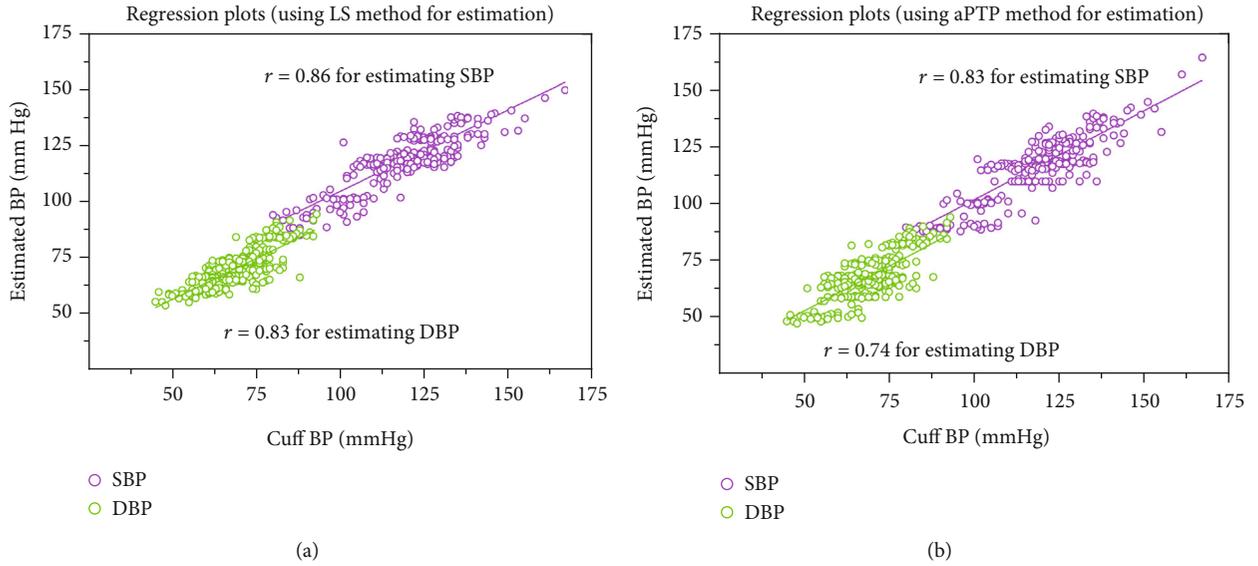


FIGURE 5: The correlation comparison of BP estimation based on the ET model by using the (a) LS method and (b) aPTP method.

($r = 0.77$) and the larger values of SEE and RMSE were observed. Similar performance also was found in the dMK-BH model according to Table 5.

Regarding AAMI [23], a BP device must comply with the constraints of mean error < 5 mmHg, the SD of the error < 8 mmHg, and the MAD of the error < 7 mmHg between the new technique and the reference. Hence, it was necessary to investigate the estimated errors of the VE model using the oPTP and aPTP methods to test whether the estimated BP based on a new proposed calibration method was acceptable under AAMI criteria. Here, differences were tested with Kruskal-Wallis tests and with Dunn's multiple comparison tests in Figure 6.

As observed from Figure 6, the estimated errors of the VE model, i.e., MK-BH and dMK-BH model, meet the AAMI requirements. More importantly, using the aPTP method for BP estimation showed high accuracy comparing with the oPTP method. For instance, the estimated error values of SD decreased by approximately 3 mmHg for the MK-BH model and dMK-BH model, respectively. For the MK-BH model, the estimated errors of MAD cut by 1.60 mmHg and 0.85 mmHg for SBP and DBP estimation when using the unified aPTP method. Similarly, for the dMK-BH model, the estimated errors between cuff BP and estimated BP had almost the same decline as the MK-BH model in the case of using the aPTP method. For DBP estimation, a statistically significant difference between the oPTP method and the aPTP method was observed for MK-BH ($p < 0.0001$) and dMK-BH ($p < 0.01$), respectively, and there was also a statistically significant difference between the MK-BH and dMK-BH models for oPTP ($p < 0.0001$) and aPTP ($p < 0.0001$), respectively. Note that difference changes were not found in SBP estimation.

3.3. Comparison with Prior Works. Our study achieved comparable results to the rest of the studies. Here, all results are presented in both mean \pm SD (MAD) and Pearson's correlation coefficient (i.e., r). Table 6 presents a comparison of the

results reported in this paper with the results reported in the literature.

Some comparisons regarding initial calibration methods could be made according to Table 6. Compared with the previous researches, the experimental samples in the present investigation were appropriately selected. Specifically, the experimental samples of 365 pairs of cuff BP vs. PAT_{mean} from at least 30,000 heartbeats in the present work were larger than investigations of Chen et al. [27], Esmaili et al. [8], Proença et al. [28], and Tang et al. [2], with the experimental samples of 200, 173, 166, and 169 pairs of cuff BP vs. PAT_{mean} , respectively. Also, the age range of 12 healthy subjects from 22 to 37 years old was appropriate according to Tang et al.'s work [2] and Huynh et al.'s investigation [29], with the age range of 12 healthy subjects from 20 to 31 years old and 15 healthy subjects from 24 to 34 years old, respectively.

In addition, Table 6 also provides more details on calibration methods, signal collection methods, and BP estimation errors. For instance, Huynh et al. [29] proposed a revised PTP calibration method by using three pairs of BP for BP estimation and achieved an accuracy of 0.31 ± 8.55 (6) mmHg and -0.5 ± 5.07 (5) mmHg for the estimated SBP and DBP, respectively. Similarly, Zheng et al. [30] selected oPTP as an initial calibration procedure and utilized ECG and PPG signals to estimate BP, reporting the error of 2.4 ± 5.7 (6) mmHg for the SBP estimation, and no errors regarding DBP were investigated. Baek et al. [31] further proposed a multiple regression of PAT, HR, and TDB (a kind of arterial stiffness index defined as the duration from the maximum derivative point to the dirotic peak in the PPG signal) [32] for BP estimation and achieved an accuracy of -0.02 ± 7.04 (5.50) and 0.00 ± 5.08 (3.86) mmHg for the estimated SBP and DBP, respectively. Recently, Simjanoska et al. [33] developed a probability distribution method to accomplish personalized procedure and reported the SD (MAD) of 10.22 (7.72) and 10.03 (9.45) for the estimated SBP and DBP, respectively.

TABLE 4: The performance of the MK-BH model using oPTP and aPTP calibration methods.

Methods	SBP			DBP		
	r	SSE (mmHg)	RMSE (mmHg)	r	SSE (mmHg)	RMSE (mmHg)
oPTP	0.72	16220	6.848	0.73	10930	5.619
aPTP	0.81	11610	5.792	0.77	8672	5.006

TABLE 5: The performance of the dMK-BH model using oPTP and aPTP calibration methods.

Methods	SBP			DBP		
	r	SSE (mmHg)	RMSE (mmHg)	r	SSE (mmHg)	RMSE (mmHg)
oPTP	0.87	15790	6.755	0.75	8747	5.028
aPTP	0.89	10180	5.4.25	0.86	5386	3.945

4. Discussion

In this study, a called aPTP method was proposed to unify the paradigm of personalized procedure for BP estimation models (i.e., ET and VE models, see Subsection 2.1.1) deriving from different methodology mechanisms. Comparing with the cumbersome LS method and sensitive oPTP method, the effectiveness, the accuracy, and the robustness of BP estimation were further investigated to validate the property of using the aPTP method in the different ET model (M-M) and VE model (MK-BH and dMK-BH). According to our investigation, different personalized calibration methods showed large differences in both ET and VE models, respectively. Not only that, the performance of BP estimation was also quite different in the same BP model, i.e., ET or VE model. These findings were particularly evident in DBP estimation. Moreover, there is no significant difference for SBP estimation (see Figures 3, 4, and 6). By contrast, a significant difference for DBP estimation was observed (see Figures 3, 4, and 6) in both the BP model (M-M, MK-BH, and dMK-BH) and calibration methods (LS, oPTP, and aPTP). For instance, the correlation coefficients and the values of SSE and RMSE were different among ET and VE models using LS and aPTP methods (see Table 3), especially in estimating DBP for the ET model. These results warned us that more attention should be paid to the selection of initial calibration methods when estimating DBP for the ET model.

For the ET model, using the previous LS method significantly enhanced the correlation in the case of DBP compared with using the aPTP method (see Figure 5). A strong correlation in DBP was of great importance, since generally, in the literature [2, 5, 8, 21], correlation coefficients of DBP estimations were distinctly less than those of SBP estimations. Consequently, the LS method might be an effective method to achieve a strong correlation in DBP. At this point, we presented an evidence on using LS and aPTP methods would lead to different BP estimation performance for the ET model based on PAT obtained from ECG and PPG signals. However, the LS method could not meet the requirement of a small initial sample size, for example, some samples obtained

from 5-minute signals [21, 34] in personalized calibration procedure because it acquires all data sets for long-term BP monitoring. Although the aPTP method was slightly weaker than the LS method in the correlation between cuff BP and estimated BP, using aPTP to finish personalized calibration procedure for BP estimation still meets the AAMI criteria for the ET model and VE models, respectively (see Figure 3) due to better performance of BP estimation (see Figures 3 and 5; Tables 3, 4, and 5). Hence, using the same and uniform calibration method, for example, aPTP method, was confirmed to be necessary when comparing the property of BP estimation under BP models deriving from different modeling methodologies.

Key information to be observed is that the ET model (i.e., M-M) had larger estimated errors between cuff BP and estimated BP than the VE model under selecting the aPTP method as the initial calibration method (see Figures 3 and 5; Tables 3, 4, and 5). As mentioned previously, the ET model was developed from the theory of elastic tubes supposing the blood vessel was equivalent to an elastic tube [8]. In fact, the actual arterial system contained branches, which were elastically and geometrically taper and terminated within the microcirculation, rather than a simple tube [4]. Therefore, research on the influence of the vascular branches on the M-M model was interesting and necessary in the next study.

Regarding the VE model, i.e., MK-BH and dMK-BH, the performance of BP estimation has been investigated to assess the accuracy, the effectiveness, and the robustness using the conventional oPTP method and the proposed aPTP method. For the aPTP method, MK-BH and dMK-BH models showed greater property in terms of BP estimation than the oPTP method (see Subsection 3.2.2). The select aPTP using small samples (for example, data set obtained from 5-minute signals) [21, 34] is recommended as the initial unified calibration method by comparison with the LS method using all data sets as the consequence of convenience in personalized calibration procedure (see Figure 1). The outcome gained from the aPTP method has been expressed to be applied in the ET model and showed a good accuracy and effectiveness of BP estimation with meeting the AAMI requirement [23] (see Figures 3 and 4; Table 3).

Here, it was necessary to point out that no matter which calibration method was used, the dMK-BH model was superior to MK-BH in BP estimation (see Tables 3, 4, and 5; Figures 3 and 6). The basis of the modeling sources indicated the variability of BP estimation performance. As mentioned previously, the MK-BH model [2] was proposed based on the B-H equation and M-K equation to strengthen the correlation between the estimated DBP and cuff DBP. Furthermore, the dMK-BH model was developed from the MK-BH model through introducing MBP for better estimate BP. Hence, the introduction of MBP to the dMK-BH model might be a main reason of its more accuracy for BP estimation than the MK-BH model. This reveals that MBP was a key factor in the cuffless BP estimation model. However, as reported in some literature [5, 21, 27], the sensitive coefficient γ in the dMK-BH model limited its practicality to a great extent. Moreover, the vascular information parameter γ changed with aging and the development of cardiovascular

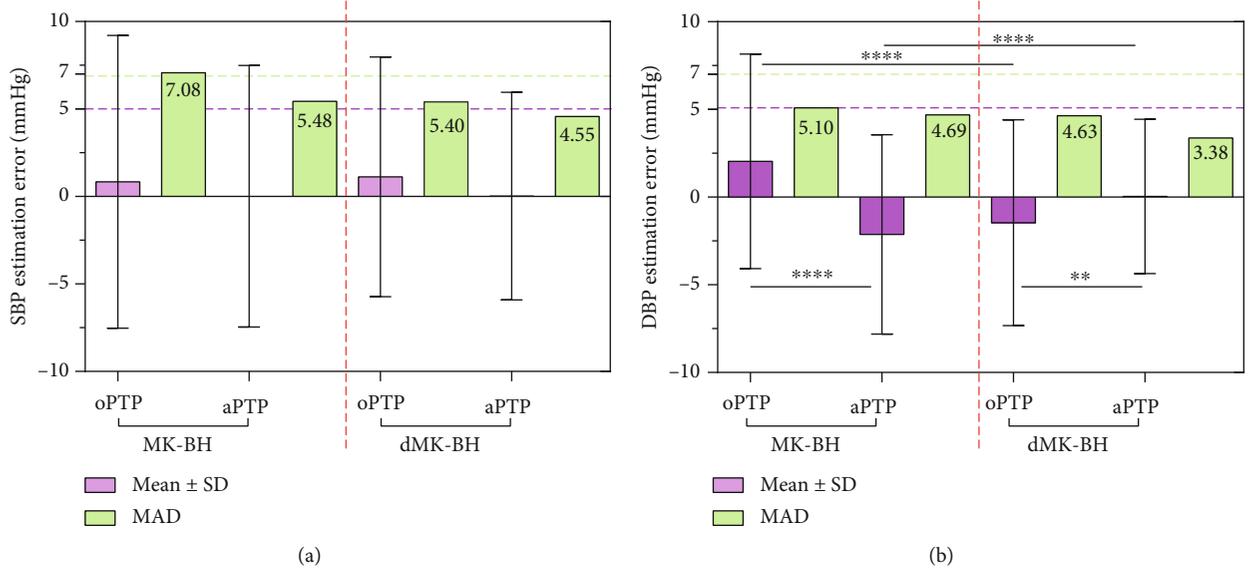


FIGURE 6: The overall performance comparison using oPTP and aPTP methods based on VE models to estimate (a) SBP and (b) DBP, respectively. Note: the purple and green dotted lines denoted the largest boundary for mean error (5 mmHg) and MAD (7 mmHg). Significant differences: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, and **** $p < 0.0001$.

TABLE 6: Comparison results with prior work.

Calibration method	Acquired signals (measure location)	Subjects	Test samples (pairs of BP)	Accuracy w.r.t. cuff BP (mean \pm SD (MAD)/mmHg; r)
LS [27]	Only PPG: ear & toe	$N = 20$	200	SBP: 0 ± 8 (7) [†] ; / DBP: 0 ± 8 (7) [†] ; /
LS [8]	ECG: hands & leg; PPG: finger; PCG: chest	$N = 32$	173	SBP: 0.12 ± 6.15 (4.71); 0.95 DBP: 1.31 ± 5.36 (4.44); 0.84
LS [28]	ECG: thorax; EIT: thorax	$N = 24$	166	SPAP: $0.7 \pm 3.8^{\ddagger}$ (6 [†]); 0.87 [‡]
PTP, three pairs [29]	PPG: finger; IPG: wrist	$N = 15$	90	SBP: 0.31 ± 8.55 (6 [†]); 0.88 DBP: -0.5 ± 5.07 (5 [†]); 0.88
oPTP [2]	ECG: palms; PPG: finger	$N = 12$	169	SBP: 0.2 ± 5.8 (4.4); 0.89 DBP: 0.4 ± 5.7 (4.6); 0.83
oPTP [30]	ECG: arm; PPG: arm	$N = 10$	70	SBP: 2.4 ± 5.7 (6 [†]); 0.80 DBP: no estimation
Multiple regression [31]	ECG: back; PPG: thigh; BCG: thigh	$N = 5$	1147	SBP: -0.02 ± 7.04 (5.50); 0.86 DBP: 0.00 ± 5.08 (3.86); 0.81
Probability distributions [32]	Only ECG: chest	$N = 51$	3219	SBP: $/\pm 10.22$ (7.72); / DBP: $/\pm 10.03$ (9.45); /
aPTP, this work (MK-BH model)	ECG: wrist & foot PPG: finger	$N = 12$	365	SBP: -0.77 ± 7.79 (6.0); 0.83 DBP: 0.51 ± 5.70 (4.4); 0.74
aPTP, this work (dMK-BH model)	ECG: wrist & foot PPG: finger	$N = 12$	365	SBP: -0.54 ± 6.95 (5.3); 0.87 DBP: 0.24 ± 5.21 (4.0); 0.78

Note 1: “/” = not be estimated based on reported results or able to be reported in corresponding authors’ other work. Note 2: “†” = be approximately estimated from the corresponding Bland-Altman plots. Note 3: “‡” = the median value of the corresponding estimation accuracy index. Note 4: PCG = phonocardiogram; BCG = ballistocardiography; IPG = impedance plethysmography; EIT = electrical impedance tomography; SPAP = systolic pulmonary artery pressure.

diseases [22]. Therefore, it was not easy to obtain an optimal γ value in different ages and pathophysiologic conditions. Remarkably, pulse transmit time and photoplethysmogram intensity ratio (PIR) [6, 17] were recently suggested to apply in the establishment of the dMK-BH model for BP estimation to achieve better performance of BP estimation than before.

Referring to the preliminary outcome from this study, we are confident that the aPTP method as an effective calibration method could be used for ambulatory and home BP monitoring to some extent in the future. Furthermore, more in-depth measurements including ECG [4, 32], PPG [4, 6], BCG [31], IPG [29], PCG [8], and others [32] need to be involved in

future research to fully verify this aPTP calibration method. Considering that physiological functions such as vascular elasticity and vascular sizes of different individuals will change with time, periodic calibration should be considered to improve the reliability of BP measurement through recalibrating parameters in a specific BP estimation model. Recently, introducing some covariates including HR [34, 35], PWV [36], and PIR [6, 17] and extra relevant variables [37] into personalized calibration procedures was expected for achieving a better prediction of BPs.

Two limitations were also found to estimate BP. One limitation was that the practical application of the M-K equation using the VE model implied several assumptions [5, 6, 8, 14]. For example, one assumption was that the thickness to radius ratio [20, 36] was a constant, which led to the invalidity for complex behaviors and regulation of the involved arterial tree. Moreover, arterial segments involved in BP estimation were formed for both elastic and muscular arteries with different biomechanical properties. The influence of these factors on BP estimation was left for the further study. Similarly, for the ET model, the simple tube needs to be greatly improved to make this specific tube have more performance of actual arterial system contained branches for each subject. Another limitation was that the subjects were generally young and healthy. Hence, further studies with extensive validation that included a larger population of individuals recruited from different age groups were required to confirm and extend these conclusions. Meanwhile, some novel models including the description of the prejection period (PEP) were worth to be established due to the VE and ET models which were not well considered with the influence of PEP and vascular tone changes.

5. Conclusions

A called advanced point-to-point (aPTP) pairing calibration method was proposed to unify the paradigm of personalized procedure for two modes (VE and ET) of BP estimation models deriving from different methodology mechanisms. Comparing with the cumbersome LS method and the sensitive oPTP method, the outline of aPTP pairing calibration is with the following:

- (1) Characteristics: the aPTP method requiring small samples or points can improve the robustness and accuracy of the initial calibration technique in BP monitoring. At the same level, like using the aPTP method, the arterial VE model based on the M-K equation was superior to the ET model developed from the nonlinear theory of elastic tubes
- (2) Applicable scope: the aPTP method was made available for both VE and ET models. Its three-step calibration strategy provided a calibration paradigm for almost all BP estimation models. What is more, evidence was provided about sensitivity in both calibration methods and BP models
- (3) Further work: more in-depth measurements including ECG, PPG, ballistocardiography, and impedance

plethysmography are required to be involved in future research to fully verify and enhance this work

All in all, the aPTP method was expected to unify the initial calibration method under different BP models and achieve an easy and durable personalized calibration procedure for cost-effective cuffless BP monitoring technology.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare no conflict of interest.

Authors' Contributions

Jiang Shao and Ping Shi contributed equally to this work.

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