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Ballistocardiogram as Proximal Timing Reference for Pulse Transit Time Measurement: Potential for Cuffless Blood Pressure Monitoring

Chang-Sei Kim, IEEE* [Member],

Department of Mechanical Engineering, University of Maryland, College Park, MD, USA

Andrew M. Carek*,

School of Electrical and Computer Engineering, Georgia Institute of Technology, Atlanta, GA, USA

Ramakrishna Mukkamala, IEEE [Member],

Department of Electrical and Computer Engineering, Michigan State University, East Lansing, MI, USA

Omer T. Inan, IEEE [Member], and

School of Electrical and Computer Engineering, Georgia Institute of Technology, Atlanta, GA, USA

Jin-Oh Hahn, IEEE [Member]**

Hahn is with the Department of Mechanical Engineering, University of Maryland, College Park, MD, USA

Abstract

Goal—We tested the hypothesis that the ballistocardiogram (BCG) waveform could yield a viable proximal timing reference for measuring pulse transit time (PTT).

Methods—From fifteen healthy volunteers, we measured PTT as the time interval between BCG and a non-invasively measured finger blood pressure (BP) waveform. To evaluate the efficacy of the BCG-based PTT in estimating BP, we likewise measured pulse arrival time (PAT) using the electrocardiogram (ECG) as proximal timing reference and compared their correlations to BP.

Results—BCG-based PTT was correlated with BP reasonably well: the mean correlation coefficient (r) was 0.62 for diastolic (DP), 0.65 for mean (MP) and 0.66 for systolic (SP) pressures when the intersecting tangent method was used as distal timing reference. Comparing four distal timing references (intersecting tangent, maximum second derivative, diastolic minimum and systolic maximum), PTT exhibited the best correlation with BP when the systolic maximum method was used (mean r value was 0.66 for DP, 0.67 for MP and 0.70 for SP). PTT was more strongly correlated with DP than PAT regardless of the distal timing reference: mean r value was 0.62 versus 0.51 ($p=0.07$) for intersecting tangent, 0.54 versus 0.49 ($p=0.17$) for maximum second derivative, 0.58 versus 0.52 ($p=0.37$) for diastolic minimum, and 0.66 versus 0.60 ($p=0.10$) for

**correspondence jhahn12@umd.edu.

*C. S. Kim and A. M. Carek are equally contributing first authors.

systolic maximum methods. The difference between PTT and PAT in estimating DP was significant ($p=0.01$) when the r values associated with all the distal timing references were compared altogether. However, PAT appeared to outperform PTT in estimating SP ($p=0.31$ when the r values associated with all the distal timing references were compared altogether).

Conclusion—We conclude that BCG is an adequate proximal timing reference in deriving PTT, and that BCG-based PTT may be superior to ECG-based PAT in estimating DP.

Significance—PTT with BCG as proximal timing reference has potential to enable convenient and ubiquitous cuffless BP monitoring.

Index Terms

Pulse Transit Time (PTT); Blood Pressure; Ballistocardiogram (BCG); Pulse Arrival Time (PAT); Electrocardiogram (ECG)

I. Introduction

Pulse transit time (PTT) is the time interval required for a pressure wave to travel between two sites (typically between a proximal site and a distal site) in the arterial tree. It has attracted a vast amount of interest due to its potential for convenient and ubiquitous blood pressure (BP) monitoring: in contrast to currently widespread BP measurement techniques such as auscultation [1] and oscillometry [2] which can only provide intermittent BP measurement due to requisite interventions (i.e., cuff inflation/deflation), PTT may enable cuffless beat-to-beat BP monitoring. In fact, there is a large volume of research effort that has been made in PTT-based BP monitoring (see, for example, recent reviews on this topic [3][4]).

The majority of PTT measurement techniques reported to date employ the electrocardiogram (ECG) as proximal timing reference by virtue of its convenience and robustness to motion artifacts (see, e.g., some recent work on BP monitoring based on ECG as proximal timing reference for measuring PTT [5][6][7][8][9]). In the literature, the time interval between ECG and a distal arterial waveform is referred to as pulse arrival time (PAT) rather than PTT: PAT consists of pre-ejection period (PEP: the time interval corresponding to the isovolumetric contraction of the heart) in addition to PTT. While PTT is closely related to BP via arterial compliance (i.e., if arterial BP increases, arterial wall tension increases, then PTT decreases due to a decrease in arterial compliance as dictated by the wave equation [10]), PEP is affected by several factors such as myocardial contractility and afterload (see, e.g., [11][12]). Therefore, the relation between BP and PAT is affected by PEP as well as PTT. Thus, the correlation between BP and PAT is likely to be deteriorated unless PEP and PTT consistently respond to a perturbation in BP. In the literature, PAT has been shown to correlate very well with BP (especially SP [13]). However, PAT has often shown poor correlation with DP when the “foot” of distal arterial waveform was used as distal timing reference [14][15][16], perhaps partly due to the adverse influence of PEP.

The ballistocardiogram (BCG) is a measurement of the reaction forces of the body to cardiac ejection of blood into the aorta. As such, it may represent a true proximal timing reference for PTT. The BCG signal has been studied for a long time: the BCG phenomenon was first

discovered in the late 1800s [17] then pioneered in the early 1900s [18] and studied heavily in the mid-1900s [19]. However, by the late 1960s, with the introduction of medical imaging technologies, BCG began to wane and has since been completely removed from clinical practice [20]. Recently, there has been a resurgence of BCG research internationally, mainly due to the convenience with which it can be measured outside of clinical settings. Researchers have demonstrated convenient and inexpensive options for BCG instrumentation such as a weighing scale [21], chair [22], bed [23], or with wearable sensors [24]. With these instruments, BCG has been shown to be capable of trending changes in cardiac output [25] and myocardial contractility [26]. On the contrary, it has not yet been rigorously explored for measuring PTT and, accordingly, estimating BP. Since BCG is a measurement of body movements associated with the mechanical ejection of blood from the heart, and since the time interval between ECG and BCG has been shown to be strongly correlated to PEP [27], we posit that BCG represents an opportunity to obtain a convenient and accurate proximal timing reference for measuring PTT.

In this study, we tested the hypothesis that BCG waveform could be a viable proximal timing reference for measuring PTT (see Fig. 1). From fifteen healthy volunteers, we measured PTT as the time interval between BCG and a non-invasively measured finger BP waveform. To evaluate the efficacy of the BCG-based PTT in estimating BP, we likewise measured pulse arrival time (PAT) using the electrocardiogram (ECG) as proximal timing reference and compared their correlations to BP. To the best of our knowledge, this is the first intensive investigation to study the efficacy of BCG for the purpose of measuring PTT and estimating BP. We report our initial findings on how closely BCG-based PTT is correlated with BP, how the correlation between PTT and BP varies with respect to distal timing references, and how PTT compares with PAT in estimating BP.

II. Materials and Methods

A. Human Subject Study and Waveform Acquisition

Fifteen young, healthy volunteers without any history of hypertension or cardiovascular disease (age: 24 ± 3 years; gender: 10 males and 5 females; weight: 70 ± 12 kg; height: 175 ± 10 cm) were enrolled in our study, which was approved by the Georgia Institute of Technology Institutional Review Board. Upon providing written consent, standard gel electrodes (Ag/AgCl) were placed on each subject for modified Lead II ECG acquisition using a wireless amplifier (BN-EL50, Biopac Systems, Goleta, CA). For BCG acquisition, a customized weighing scale was built as described in a previous study [21]. For BP acquisition, a finger-cuff continuous non-invasive BP waveform sensor was placed on the middle finger of the subject (ccNexfin, Edwards Lifesciences, Irvine, CA). The sensors were interfaced to a computer via a data acquisition unit (MP150, Biopac Systems, Goleta, CA). The data were collected at 1 kHz sampling rate. The data acquisition schematic is presented in Fig. 2a. Each subject, while wearing all sensors, stood on the scale, and the experimental protocol was started (Fig. 2b). First, the subject stood still for 60 seconds for a baseline recording. Second, the subject was asked to breathe deeply and slowly. Third, the subject was asked to perform a sustained hand grip challenge in which the subject performed an isometric contraction against a fixed resistance with the contralateral hand to the one outfitted with the

sensors. In between the perturbations (deep breathing and hand grip), the subject stood at rest for 60 seconds.

B. Measurement of PTT and PAT

From the data thus collected, PTT and PAT were measured as follows. First, the BP waveform was smoothed by a Butterworth low-pass filter with 100 Hz cut-off frequency. Second, the R wave in each ECG beat was detected as the local maximum within each ECG beat. Third, individual BP and BCG beats were extracted guided by the ECG R waves. Fourth, BCG beats were smoothed with an exponential moving-average filtering technique as described in a previous study [27]. Fifth, the I wave of the BCG waveform was extracted from each BCG beat as the local minimum occurring right before the J wave (detected as the peak between the ECG R wave and the systolic maximum of BP waveform) within each BCG beat¹. Sixth, distal timing references were extracted from each BP beat using the intersecting tangent [28], maximum second derivative, diastolic minimum and systolic maximum methods. Finally, PTT associated with each individual beat was measured as the time interval between the BCG I wave and the distal timing references, while PAT associated with each individual beat was measured as the time interval between the ECG R wave and the distal timing references. Thus, a total of four PTT and four PAT values were determined for each beat (see Fig. 3).

C. Data Analysis

Before performing the correlation analysis, PTT and PAT sequences measured for each subject were smoothed with a Butterworth low-pass filter with 0.1 Hz cut-off frequency to prevent the degradation of PTT-BP correlation by inadequately measured PTT samples arising from the BCG beats corrupted by motion artifacts. Then, a logarithmic model (1), derived from the Moens-Korteweg equation [29] and an exponential arterial elasticity model proposed by Hughes et al. [30], was fitted to PTT-BP and PAT-BP data pairs associated with each subject to correlate PTT and PAT to BP:

$$P=K_1 \ln(T)+K_2 \quad (1)$$

where P denotes BP (DP, MP or SP), T is either PTT or PAT, and K_1 and K_2 are individual-specific parameters. For each subject, three sets of K_1 and K_2 values (each corresponding to DP, MP and SP, respectively) were derived via the least-squares method for PTT and PAT, respectively. Finally, using the same data pairs, PTT and PAT were transformed to BP by plugging them into the calibration equations.

In each subject, correlation coefficients (i.e., the r values) between true versus estimated DP, MP and SP were computed. Noting that four distal timing references were considered in measuring PTT and PAT, totally twelve r values were computed for each subject (3 BP \times 4 distal timing references). The statistical significance in differences between the r values associated with PTT versus their PAT counterparts was examined in two ways. First, the paired t-test was applied to the r values for PTT and PAT related to each distal timing

¹Though not shown in detail, we used the I wave in this study because the correlation between PTT and BP was consistently stronger with the I wave as proximal timing reference than J wave or H wave.

reference (i.e., 15 samples). Second, the paired t-test was then applied to the r values for PTT and PAT related to all the distal timing references (thus 60 samples). The second analysis was conducted to compare PTT and PAT independently of the choice of distal timing reference, due to the observation that the distal timing reference corresponding to the best r value was different in different subjects.

III. Results

The mean BP (DP, MP and SP) as well as HR and PTT values were largely different across subjects. DP, MP and SP varied up to $43.0 \pm 16.5\%$, $43.8 \pm 14.3\%$ and $46.2 \pm 15.5\%$ of the respective mean values, HR up to $62.3 \pm 21.1\%$, and PTT up to $90.3 \pm 47.9\%$, by the deep breathing and sustained hand grip maneuvers used in this study. Fig. 4 shows a representative time responses of BP, PTT and PAT to deep breathing and sustained hand grip maneuvers in a test subject.

Table II summarizes the r values evaluated for BP (DP, MP and SP, respectively) versus PTT as well as compares the r values evaluated for the relation between BP (DP, MP and SP) versus PTT and PAT. Fig. 5 shows a representative example of true versus PTT- and PAT-estimated BP in a test subject (the r values were 0.79 and 0.59 (DP), 0.83 and 0.69 (MP), and 0.84 and 0.75 (SP) for PTT and PAT, respectively). Fig. 6 shows the correlation plots for true versus PTT- and PAT-estimated BP associated with (a) the best, (b) a typical, and (c) the worst subject, in terms of the different in the r values between PTT-versus PAT-estimated BP. Fig. 7 shows the Bland-Altman statistics for BP associated with PTT (upper panel) and PAT (lower panel), respectively, computed across all subjects.

IV. Discussion

Despite its widespread use and demonstrated correlation with BP (especially SP), ECG-based PAT has often exhibited poor correlation with DP presumably due to its dependence on PEP. By virtue of its direct relation to the mechanical activity of the heart, BCG may potentially be used as proximal timing reference for PTT measurement. The central hypothesis of this study was that BCG could be a viable proximal timing reference in measuring PTT, and that BCG-based PTT may be superior to ECG-based PAT in estimating DP. To the best of our knowledge, this study is the first intensive investigation to examine the efficacy of BCG, compared with ECG, as a proximal timing reference for measuring PTT and estimating BP.

A. Subject Demographics and Physiologic States

The BP perturbation protocol designed in this study was able to widely vary BP and HR as well as PTT and PAT, which illustrates the adequacy of our BP perturbation protocol (see Table I).

B. Correlation between PTT and BP

PTT based on BCG as proximal timing reference was correlated with BP reasonably well (Table II, Fig. 5 and Fig. 6), and the corresponding confidence interval was also narrow (Fig. 7). The r values ranging between 0.54 and 0.66 between DP and PTT are much higher

than, while those ranging between 0.61 and 0.70 between SP and PTT are comparable to, those reported in the previous studies with ECG and non-invasive wrist/finger BP as proximal and distal arterial waveforms, respectively, such as 0.30 (DP) and 0.85 (SP) [31], 0.40 ± 0.35 (DP) and 0.70 ± 0.14 (SP) [32], 0.26–0.57 (DP) and 0.74–0.79 (SP) [33] and 0.41 (DP) and 0.26 (SP) [34].

Comparing the r values for PTT associated with each distal timing reference, the systolic maximum method resulted in the highest r values consistently for DP, MP and SP, followed by the intersecting tangent, diastolic minimum, and maximum second derivative methods. The differences in the r values between systolic maximum and intersecting tangent methods were not significant. In contrast, those between systolic maximum and maximum second derivative methods were significant ($p < 0.05$ for DP, MP and SP consistently). In general, systolic maximum is not considered as ideal timing reference due to its susceptibility to corruption due to the wave reflection phenomena [10]. In fact, studies have shown that intersecting tangent method is a preferred choice due to its robustness to morphological artifacts in the arterial waveforms (see, e.g., [35]). Regardless, we found two studies in which PTT determined using the systolic maximum as distal timing reference showed a strong correlation with SP despite a relatively weak correlation with DP (0.85 (SP) versus 0.30 (DP) [31] and 0.75 ± 0.10 (SP) versus 0.44 ± 0.34 (DP) [32]). Interestingly, subjects recruited in these studies, as well as ours, were healthy young adults. The efficacy of the systolic maximum method in these subjects may in part be attributed to relatively small wave reflection in these subjects, which may then resulted in negligible corruption of the systolic upstroke waveform (since early systolic augmentation of reflecting BP wave may be non-dominant in these subjects). Nonetheless, the statistical insignificance in the difference between systolic maximum versus intersecting tangent methods supports the recommendation that the latter is an adequate distal timing reference in measuring PTT [35].

C. Comparison with PAT

The r values associated with PAT were comparable to those we found in the previous studies in which ECG R wave and photoplethysmogram (PPG) were used as proximal and distal timing references (0.53 ± 0.10 for DP and 0.76 ± 0.05 for SP (mean \pm SD)) [36][13][37][15][38][39][16][40][41][42][43][7][44][5][14][9][6][45][8][46][47].

The most notable finding from the comparison between PTT versus PAT is that PTT was more strongly correlated with DP than PAT regardless of the distal timing reference: the mean r values associated with PTT for intersecting tangent, maximum second derivative, diastolic minimum, and systolic maximum methods were all higher than their PAT counterparts by 22% ($p=0.07$), 10% ($p=0.17$), 12% ($p=0.37$) and 10% ($p=0.10$), respectively (see Table II). As well, PTT-estimated BP resulted in modestly narrower confidence interval ($2\times$ SD) than its PAT counterpart: confidence interval associated with PTT was 8.8 %, 5.5% and 1.0% narrower for DP, MP and SP, respectively, when the intersecting tangent method was used as distal timing reference. Considering the relatively small number of subjects recruited in this study, the results for the intersecting tangent method look especially promising. In fact, the difference between PTT and PAT was statistically significant ($p=0.01$) when the r values associated with all the distal timing references (thus 60 r values)

were compared altogether. The BCG waveform is known to be more easily corrupted by motion artifacts (especially in the standing posture) compared with ECG. Nonetheless, PTT with BCG used as proximal timing reference exhibited stronger correlation to DP and MP than PAT. This supports the central hypothesis of this work, that BCG may be used as proximal timing reference for PTT, and that BCG-based PTT may be superior to ECG-based PAT in estimating DP. In contrast to DP (and MP as well), PAT modestly outperformed PTT in estimating SP, although statistical significance could not be established. This finding is actually consistent with the previous observations that PAT is strongly correlated with SP (though the underlying mechanism hasn't been clearly understood) [5][7][16][37][42]. Fig. 5 illustrates that (i) PTT- and PAT-estimated BP track true BP adequately and (ii) PTT is overall superior to PAT but is also more susceptible to motion artifacts (as exemplified by the fluctuations in PTT-estimated BP at $t=150$ s and $t=200$ s during the sustained hand grip maneuver), while Fig. 7 shows that PTT-estimated DP and MP are associated with smaller numbers of outliers compared with their PAT counterparts.

In sum, the results of our study indicated that PAT generally correlated well with SP and was noise robust, while PTT correlated with DP better than PAT. BCG was more susceptible to motion artifacts than ECG. However, it may be more convenient than ECG because its waveform can be measured without a sensor placed on the body.

D. Limitations and Opportunities

This study has a number of limitations that must be examined in the follow-up investigations. First, the subjects recruited in this study were rather homogeneous: they were all young and healthy, and none was hypertensive. To rigorously assess the relevance and efficacy of BCG-based PTT, future work must evaluate how it can estimate BP in a large number of heterogeneous subjects from a wide range of populations. In particular, the efficacy of the systolic maximum as distal timing reference in older subjects should be examined. Second, this study did not explore diverse BP-varying perturbations. More specifically, we used only two perturbations in this study, both of which may have varied BP mainly by altering cardiac output. These perturbations also incurred body motion artifacts that may have distorted BCG measurement to an extent. In this regard, a wide range of BP perturbation protocols must be designed and employed to rigorously investigate the efficacy of BCG-based PTT. Third, with the goal of making initial grasp of strengths and weaknesses of BCG as proximal timing reference for PTT, this study employed only the basic foot detection methods that could be implemented very easily. However, the measurement of PTT and PAT may benefit from more sophisticated methods that are potentially more robust against artifacts and noise [48][49][50][51][52][53][54]. Future study must conduct comparative evaluation of PTT and PAT determined by such methods in estimating BP. Finally, this study did not examine the long-term validity of the calibration model (1) between BP versus PTT and PAT. The goal of this study was to examine the correlation between BP versus BCG-based PTT. So, long-term calibration capability of (1) was beyond the scope of this study. A related limitation is that we low-pass filtered PTT sequence (and PAT as well) before deriving (1). We employed low-pass filtering to automatically suppress the adverse impact of artifacts rather than manually removing the corrupted data for two reasons: identifying BCG beats corrupted by artifacts is very challenging; in addition, PTT

was perhaps continually influenced by artifact, especially during the sustained hand grip maneuver (Fig. 4). However, low-pass filtering may also have removed valuable information on high-frequency variability in BP from PTT sequence, thus limiting the validity of this study to the efficacy of PTT in tracking relatively slow variability in BP. Future work must examine the consistency and reliability of the calibration model (1) with respect to time over the course of a longitudinal study.

V. Conclusion and Future Work

We demonstrated that BCG may be used as proximal timing reference in measuring PTT, and BCG-based PTT may be superior to PAT in estimating DP. To the best of our knowledge, this is the first intensive study to examine the validity of BCG in measuring PTT, and ultimately, in estimating BP. The results from our study show promise. Yet, there are still open challenges before the efficacy of BCG in measuring PTT can be established. Follow-up studies are required to further elucidate the strengths and weaknesses of BCG as proximal timing reference in measuring PTT and estimating BP.

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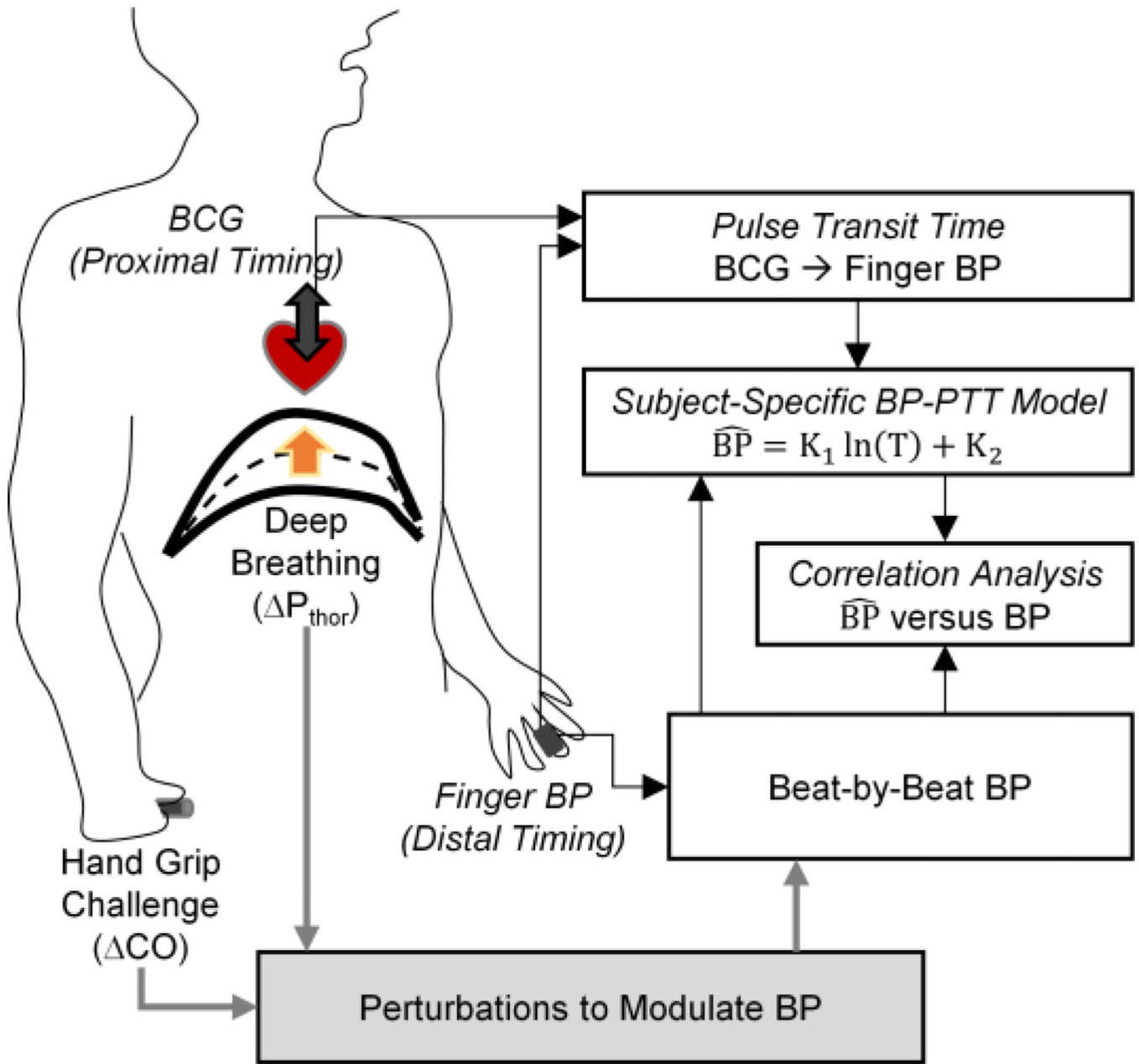


Fig. 1. Overview of the methodology used in this study to measure pulse transit time (PTT) using the ballistocardiogram (BCG) as a proximal timing reference, and to correlate PTT to blood pressure (BP) measured at the finger. Two perturbations were used to vary BP by modulating intra-thoracic pressure (P_{thor}) and cardiac output (CO) in order to assess the correlation between PTT and BP under varying physiologic states.

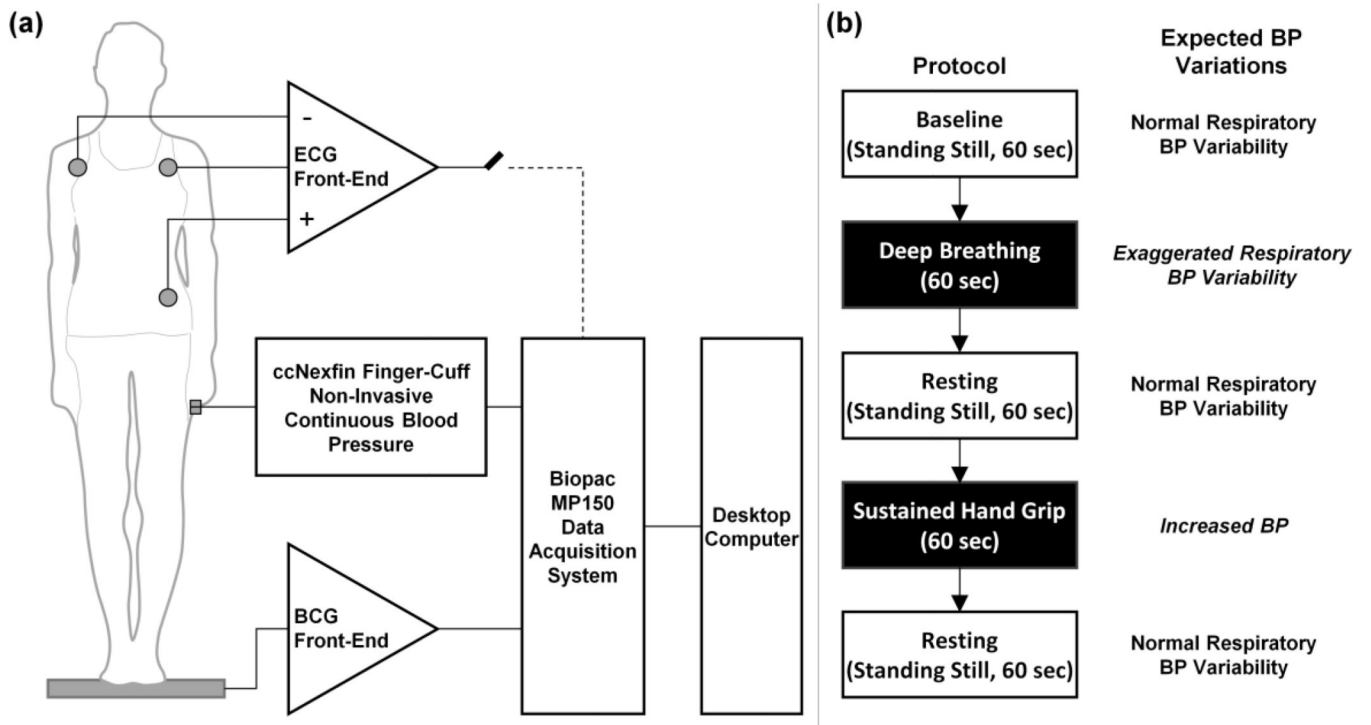


Fig. 2.

(a) Schematic measurement setup for ECG, BCG, and finger-cuff non-invasive BP waveform. (b) Overview of human subjects protocol (left) and associated BP variability anticipated with the various components of the protocol (right).

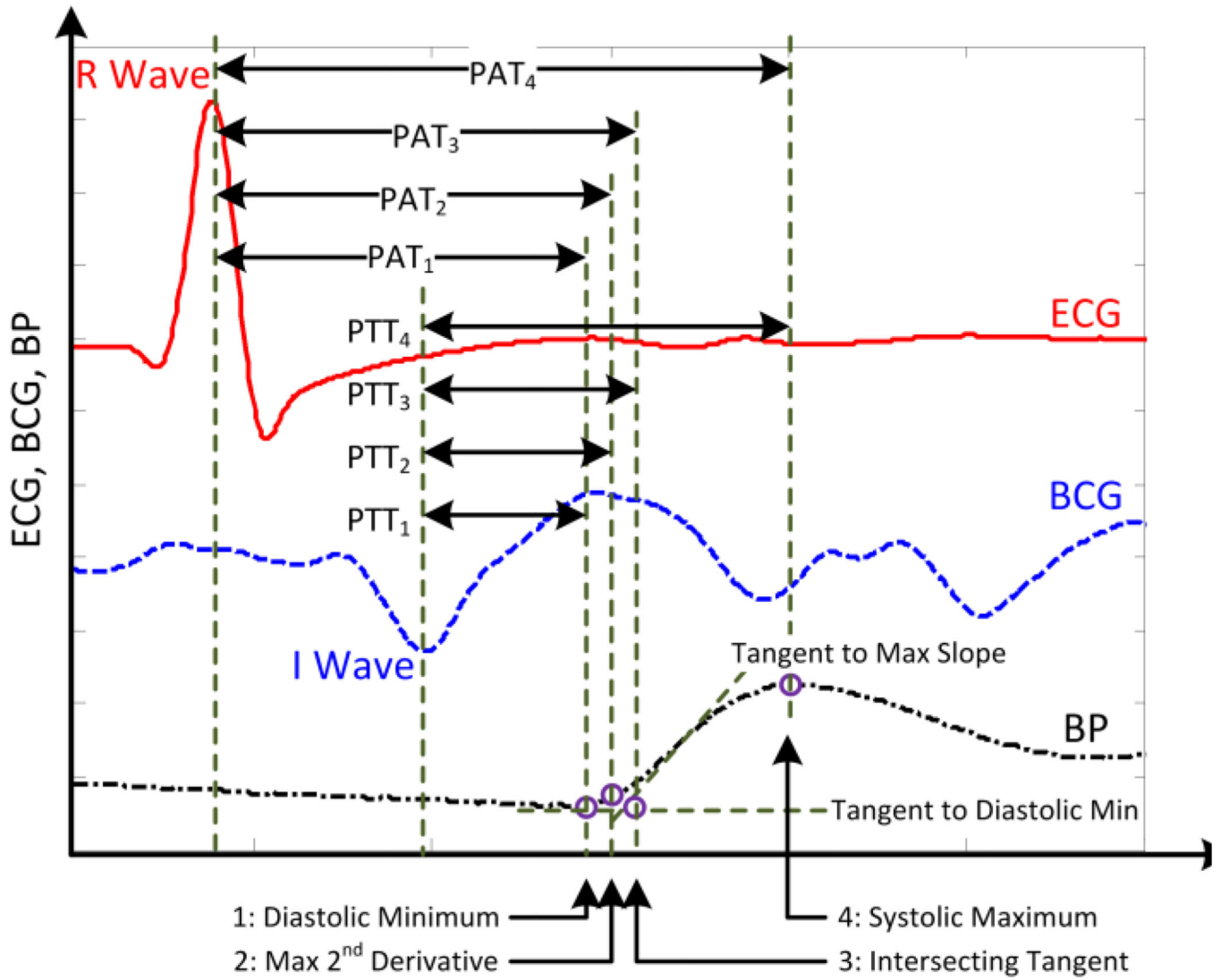


Fig. 3. Measurement of PTT and PAT using four distal timing references. The BCG I wave and ECG R wave were used as proximal timing references for PTT and PAT, respectively. The subscripts 1–4 in PTT and PAT denote distal timing reference (1: diastolic minimum, 2: maximum 2nd derivative, 3: intersecting tangent, 4: systolic maximum).

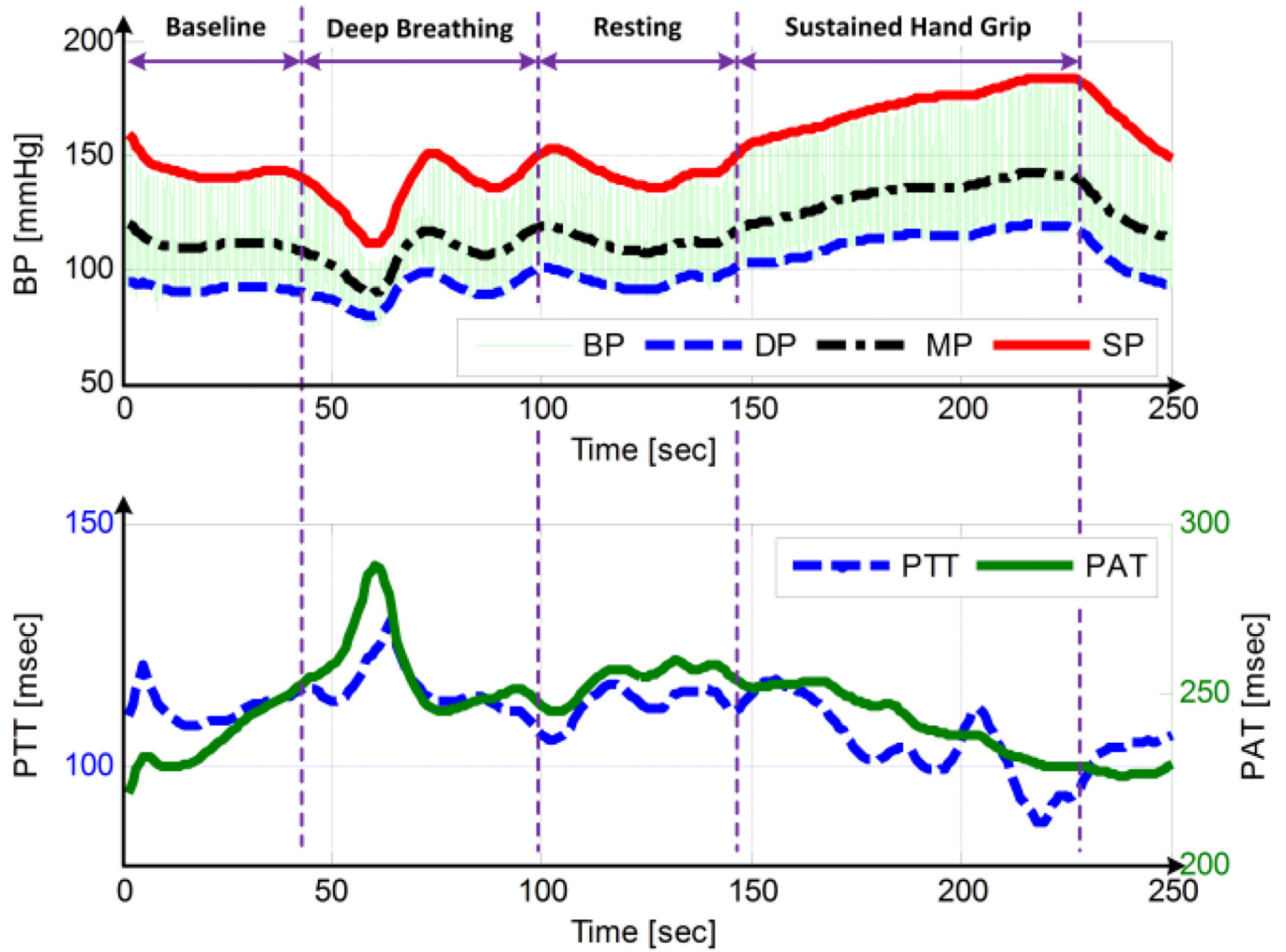


Fig. 4. BP, PTT and PAT responses to deep breathing and sustained hand grip maneuvers in a test subject (Subject #3).

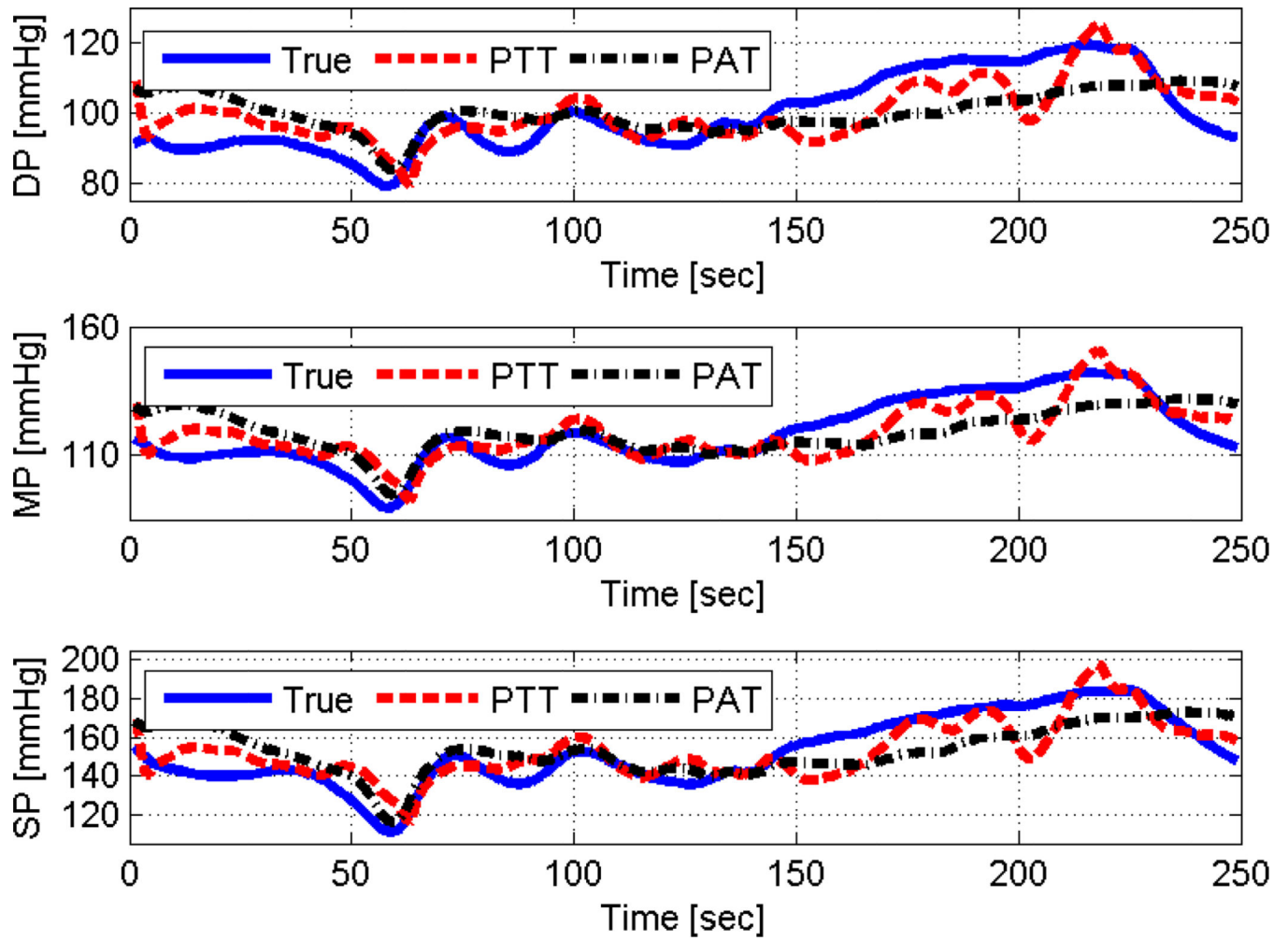


Fig. 5.
True versus PTT- and PAT-estimated BP in a test subject (Subject #3).

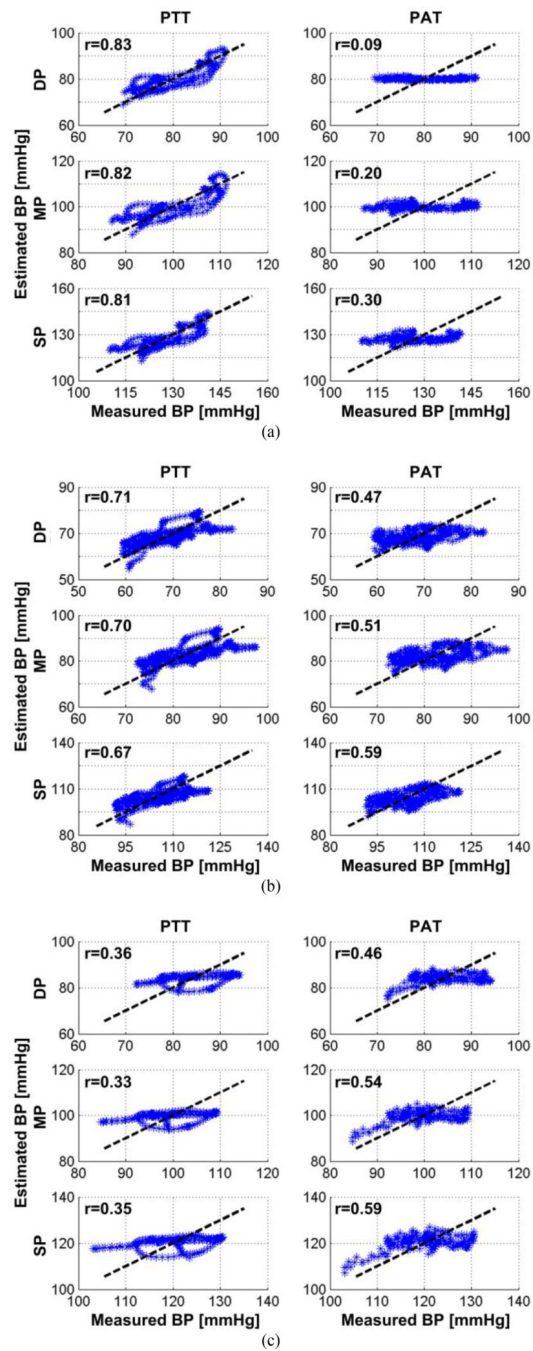


Fig. 6. Correlations between true versus PTT- and PAT-estimated BP. (a) Best case (Subject #7). (b) Typical case (Subject #4). (c) Worst case (Subject #12).

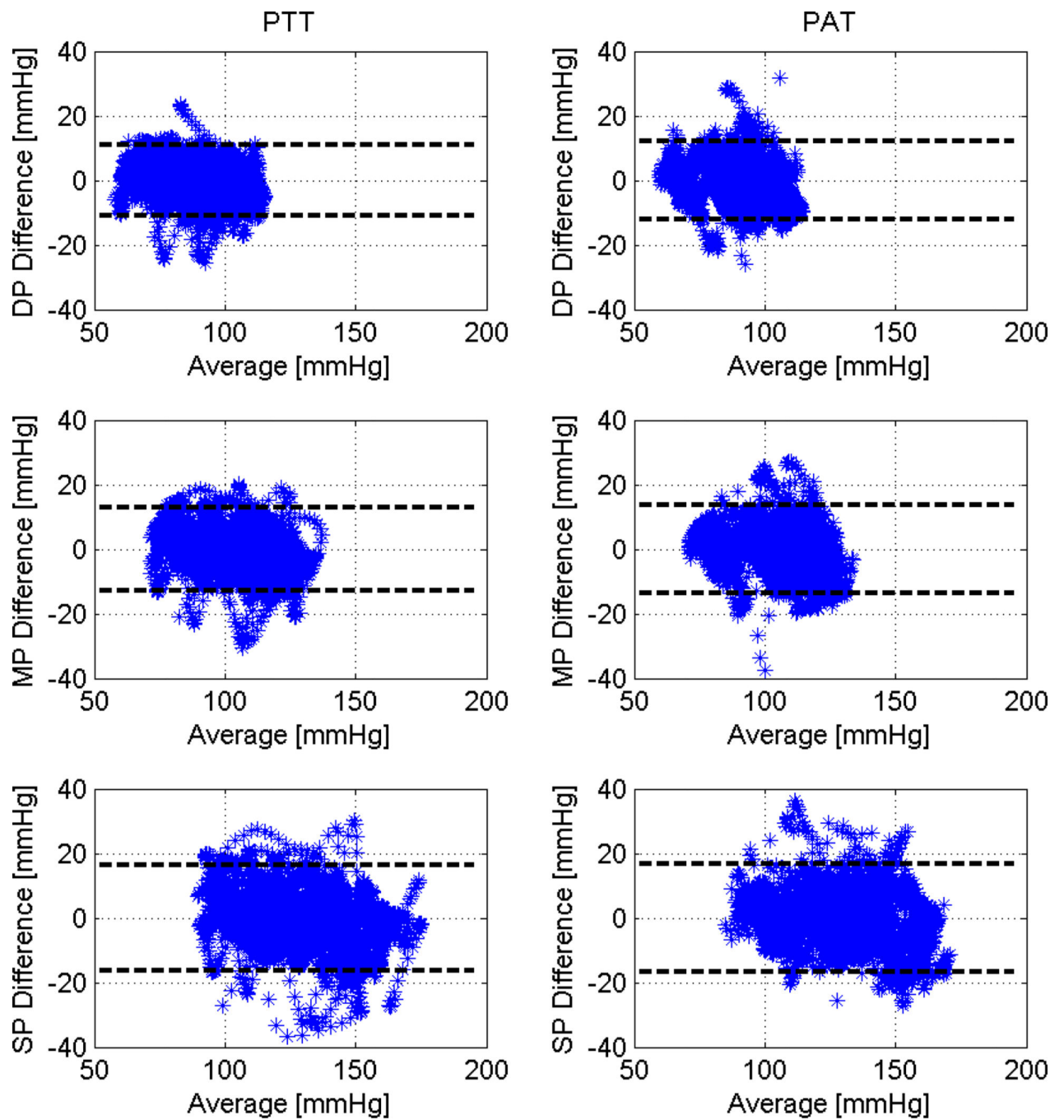


Fig. 7. Bland-Altman statistics associated with true versus PTT- and PAT-estimated BP (all subjects).

Subject physiologic states: BP varied up to ± 24 (DP), ± 27 (MP) and ± 42 (SP) mmHg by the BP perturbation protocol designed in this study. PTT and PAT estimated by the intersecting tangent method is reported.

TABLE I

	DP [mmHg]	MP [mmHg]	SP [mmHg]	HR [mmHg]	PTT [msec]	PAT [msec]
Mean	89.5 \pm 11.1	105.1 \pm 11.8	130.2 \pm 16.0	91.1 \pm 21.3	87.5 \pm 13.1	205.8 \pm 25.4
Range	37.8 \pm 12.1	45.6 \pm 13.6	60.0 \pm 21.0	56.4 \pm 21.4	78.5 \pm 41.2	52.7 \pm 24.2

TABLE II

Correlation of PTT and PAT to BP (mean±SD). Difference was measured in terms of average improvement in PTT-based correlation relative to PAT-based correlation.

		DP	MP	SP
Intersecting Tangent	PTT	0.62±0.16	0.65±0.14	0.66±0.14
	PAT	0.51±0.19	0.59±0.17	0.66±0.16
	Difference (p-value)	22 % (p=0.07)	10 % (p=0.35)	0 % (p=0.99)
Max 2 nd Deriv	PTT	0.54±0.16	0.58±0.14	0.61±0.13
	PAT	0.49±0.18	0.56±0.16	0.63±0.15
	Difference (p-value)	10 % (p=0.17)	4 % (p=0.62)	-3 % (p=0.60)
Diastolic Min	PTT	0.58±0.20	0.60±0.18	0.61±0.18
	PAT	0.52±0.25	0.60±0.23	0.66±0.22
	Difference (p-value)	12 % (p=0.37)	0 % (p=0.98)	-8 % (p=0.36)
Systolic Max	PTT	0.66±0.15	0.67±0.14	0.70±0.12
	PAT	0.60±0.14	0.66±0.13	0.72±0.11
	Difference (p-value)	10 % (p=0.10)	2 % (p=0.61)	-3 % (p=0.56)
All	PTT	0.60±0.17	0.63±0.15	0.65±0.15
	PAT	0.53±0.20	0.60±0.17	0.67±0.17
	Difference (p-value)	13 % (p=0.01)	5 % (p=0.34)	-3 % (p=0.31)