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Review

Multi-Site Photoplethysmography Technology for Blood Pressure Assessment: Challenges and Recommendations

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Abstract: Hypertension is one of the most prevalent diseases and is often called the "silent killer" because there are usually no early symptoms. Hypertension is also associated with multiple morbidities, including chronic kidney disease and cardiovascular disease. Early detection and intervention are therefore important. The current routine method for diagnosing hypertension is done using a sphygmomanometer, which can only provide intermittent blood pressure readings and can be confounded by various factors, such as white coat hypertension, time of day, exercise, or stress. Consequently, there is an increasing need for a non-invasive, cuff-less, and continuous blood pressure monitoring device. Multi-site photoplethysmography (PPG) is a promising new technology that can measure a range of features of the pulse, including the pulse transit time of the arterial pulse wave, which can be used to continuously estimate arterial blood pressure. This is achieved by detecting the pulse wave at one body site location and measuring the time it takes for it to reach a second, distal location. The purpose of this review is to analyze the current research in multi-site PPG for blood pressure assessment and provide recommendations to guide future research. In a systematic search of the literature from January 2010 to January 2019, we found 13 papers that proposed novel methods using various two-channel PPG systems and signal processing techniques to acquire blood pressure using multi-site PPG that offered promising results. However, we also found a general lack of validation in terms of sample size and diversity of populations.

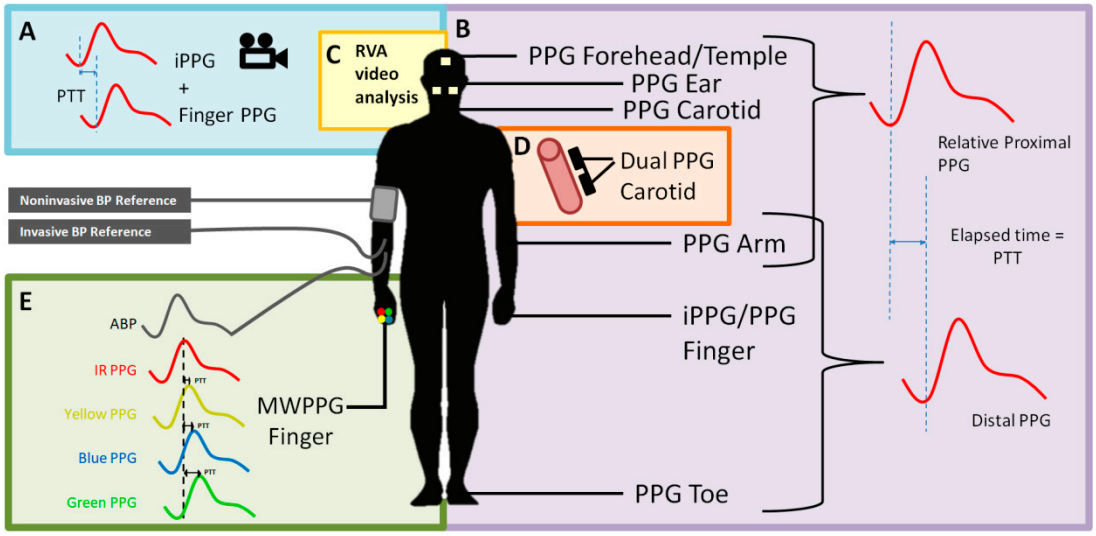

Figure 1. A visualization of the methods multi-site photoplethysmography (PPG) to measure the pulse transit time (PTT). Multisite PPG can make use of twos PPG probes, one proximal and one distal, to measure the time it takes for the pulse wave to travel a distance. (**A**,**B**) Two-location dual PPG/iPPG systems. (**C**) iPPG system. (**D**) Single artery dual PPG system. (**E**) Multiple wavelengths system. ECG—electrocardiography, IPG—impedance plethysmography, BCG—ballistocardiography, PCG—phonocardiography, PPG—photoplethysmography, iPPG—image-based PPG, and MWPPG—multi-wavelength PPG.

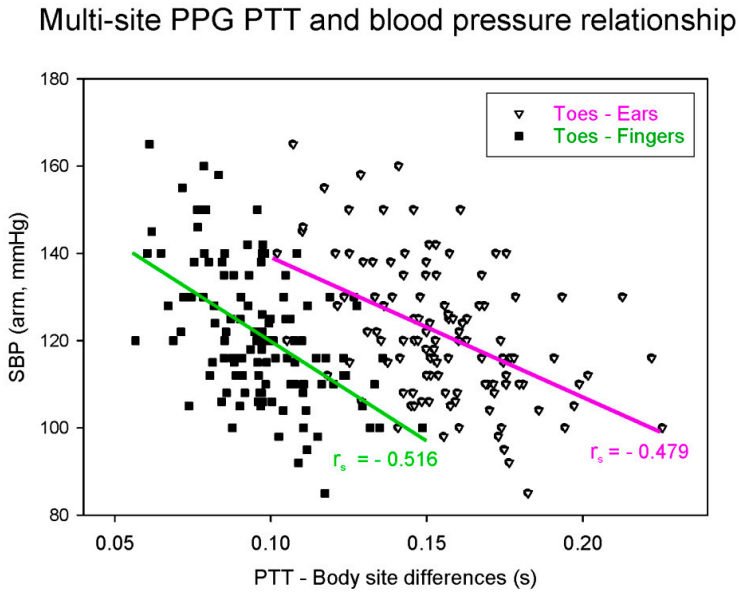

Figure 2. Dual probe multi-site PPG-derived pulse transit time (PTT) correlation with systolic blood pressure (SBP). The data used in this figure were adapted from Allen and Murray [19].

2. Methods

We conducted a thorough literature search using PubMed for articles exploring the use of multi-site PPG for BP measurement from 1/1/2010 to 1/1/2019. PubMed was used because it gave access to journal articles as well as conference proceedings. We decided to limit our search to the most recent decade, i.e., January 2010 to January 2019, because we were interested in the trend of the development of this technology in the recent decadal time frame. Note that the typical time frame is the most recent decade [20–22]. We used the following search terms, combined with "OR", using PubMed's

advanced search feature: ppg blood pressure determination, ppg blood pressure estimation, ppg hypertension estimation, ppg non-invasive blood pressure, ppg cuffless blood pressure, ppg cuff-less blood pressure, photoplethysmographic blood pressure determination, photoplethysmographic blood pressure estimation, photoplethysmographic hypertension determination, photoplethysmographic hypertension estimation, non-invasive hypertension classification, non invasive blood pressure monitoring, pulse transit time blood pressure estimation, multi-ppg blood pressure, multi-site ppg blood pressure, and multi-photoplethysmographic blood pressure. Our initial searches returned a significant number of studies regarding arterial stiffness and vascular disease; we therefore added the search term "NOT arterial stiffness." We are aware of the relatedness of vascular disease with hypertension [23]; however, including analysis of vascular disease via PPG would mean including many studies unrelated to BP. Therefore, we decided to limit the scope of our study to multi-site PPG for the analysis of BP in the hope that we could make more meaningful and BP focused recommendations.

We included any publication that examined multi-site PPG as a method for BP measurement. Our exclusion criteria included animal studies, review articles, articles that are not accessible in the English language (see the Appendix A), articles in which PPG was not used to estimate blood pressure, and articles that validated a trademarked PPG device with no discussion of the PPG technology or waveform itself. From January 2010 to January 2019, our search found 13 papers that fit the inclusion criteria (Figure 3).

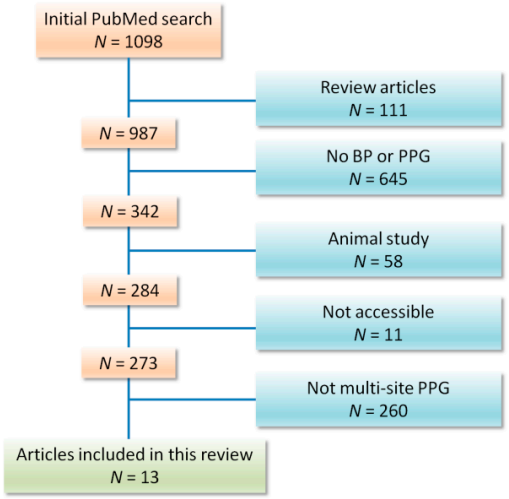

Figure 3. Flow chart of included studies. Thirteen studies could be included out of 1098 articles published between January 2010 and January 2019.

3. Results

Our PubMed search found 13 publications that studied multi-site PPG technology; all but one paper looked at using two measurement sites with a two-probe system [24]. The two probes are used to measure PTT (or its inverse PWV), which is correlated with BP. From January 2010 to January 2019, multi-site PPG publications followed a growing trend (Figure 4). In our analysis, we determined the sample sizes of each paper, the inclusion of any subjects with HTN or co-morbidities, and the method used as the gold standard to collect the reference BP measurements for comparison. Of these papers, only three had a sample size of more than 30 subjects: one each in 2011 [18], 2017 [16], and 2018 [25]. In addition, most of the papers either used healthy subjects with no HTN, co-morbidities, or pregnant women, or used health statuses that were undisclosed. One paper [26] compared hypertensive (N = 10) and normotensive (N = 10) subjects, as well as patients undergoing coronary angiography (N = 4). Another publication collected data from patients undergoing general anesthesia (N = 35) [18].

Table 1. Summary of findings of all papers included in this review.

Year	Authors	# Subjects	Age Range of Subjects (Years)	Gold Standard	Parameters Measured	Mean BP Absolute Difference	Absolute of Value of Correlation Coefficient between Estimated BP (or PTT Feature) and Referenced BP
2018	Liu et al. [26]	$N_1 = 10$ $N_2 = 10$	N/R	Finometer	PTT (ECG, ICG, $Finger_{PPG}$) PTT (MW $Finger_{PPG}$)	1.86 mmHg MAP	N/R
		$N_3 = 4$	N/R	IBP		2.72 mmHg MAP	N/R
2018	Wang et al. [25]	$N_1 = 30$	20–27	BP Cuff	PTT ($Wrist_{PPG}$ to Arm_{PPG} with MA)	N/R	$r = 0.75$ SBP $r = 0.78$ DBP
2018	Viejo et al. [24]	$N_1 = 15$	20–38	BP Cuff	PTT (2 $cheeks_{PPG}$, $forehead_{PPG}$)	N/R	$r = 0.85$ BP
2017	Nabeel et al. [16]	$N_1 = 35$	23–32	BP Cuff	PTT ($Carotid_{PPG}$ to $Carotid_{PPG}$) PTT ($Carotid_{PPG}$ to $Finger_{PPG}$) PTT (ECG to $Carotid_{PPG}$)	N/R	$r = 0.74$ SBP $r = 0.77$ DBP $r = 0.78$ MAP
2017	Nabeel et al. [29]	$N_1 = 5$	24–30	Tonometry	PTT ($Carotid_{PPG}$ to $Carotid_{PPG}$)	N/R	N/R
2017	Beckmann et al. [30]	$N_1 = 5$	25–36	N/R	PTT ($Wrist_{PPG}$ to Index $Finger_{PPG}$) PTT ($Wrist_{PPG}$ to Middle $Finger_{PPG}$) PTT ($Wrist_{PPG}$ to Ring $Finger_{PPG}$) PTT ($Wrist_{PPG}$ to Little $Finger_{PPG}$)	N/R	N/R
2017	Zhang et al. [33]	$N_1 = 29$	20–30	BP Cuff	PTT ($Face_{PPG}$ to $Finger_{PPG}$) PTT ($Temple_{PPG}$ to $Wrist_{PPG}$)	N/R	$r > 0.6$ SBP in 75.9% subjects
2016	Nabeel et al. [34]	$N_1 = 17$	21–34	BP Cuff	PTT ($Carotid_{PPG}$ to $Carotid_{PPG}$)	N/R	$r = 0.68$ SBP $r = 0.71$ DBP $r = 0.72$ MAP
2016	Liu et al. [35]	$N_1 = 10$	22–26	Finometer	PTT (ECG to $Finger_{PPG}$) PTT (MW $Finger_{PPG}$)	N/R	$r = 0.76$ SBP
2015	Nabeel et al. [36]	$N_1 = 13$	22–31	BP Cuff	PTT ($Carotid_{PPG}$ to $Carotid_{PPG}$)	N/R	$r = 0.5$ SBP $r = 0.66$ SBP $r = 0.63$ MAP
2015	Liu et al. [31]	$N_1 = 12$	24–35	ECG–PPG PAT	PTT ($Temple_{PPG}$ to Index $Finger_{PPG}$)	N/R	N/R
2011	Chen et al. [18]	$N_4 = 35$	17–21 and 58–62	IBP	PTT (Ear_{PPG} to Toe_{PPG})	2.16 mmHg SBP 1.49 mmHg DBP	N/R
2010	Proenca et al. [32]	$N_1 = 20$	20–37	Finometer	PTT (ECG, ICG, unspecified PPG) PTT (Ear_{PPG} to $Finger_{PPG}$)	N/R	$r = 0.22$ SBP

N_1 = normotensive subjects, N_2 = hypertensive subjects, N_3 = patients undergoing coronary angiography, N_4 = patients under general anesthesia, r = Pearson's correlation coefficient, Finometer = finger blood pressure, IBP = invasive BP, MW = multi-wavelength, MA = motion artifact, ECG = electrocardiogram, ICG = impedance cardiography, PTT = pulse transit time, N/R = not reported, SBP = systolic BP, DBP = diastolic BP, MAP = mean arterial pressure, $Finger_{PPG}$ = PPG collected from a finger.