

Minimum Detectable Change Estimates of Heart-to-Finger Arterial Pulse Wave Conduction  
Time in Cardiovascular-Healthy Young Adults

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## ABSTRACT

**Background:** Pulse wave velocity (PWV) measurements are the gold standard for assessing arterial stiffness and estimating time or treatment-related changes in cardiovascular status. What constitutes a statistically significant change is an important clinical consideration. This study aimed to describe the variability of heart-to-finger pulse wave conduction time (PWCT) to provide estimates of the minimum detectable change (MDC) dependent on the number of PWCT samples used.

**Materials and Methods:** Heart-to-finger PWCT was measured based on the time delay between the peak of the EKG R-wave and arterial pulse arrival at the left hand index finger as measured by a photoplethysmographic sensor. Measurements were done in 10 young adults ( $25.7 \pm 1.2$  years) while supine for 45 minutes. Depending on the subject's heart rate, these measurements yielded 2430 to 3750 contiguous PWCT for analysis. The variability in these PWCTs was used to determine the minimal detectable percentage change for specified p-values of 0.05, 0.01, and 0.001.

**Results:** Sample sizes of 10, 30, 50, or 300 contiguous PWCTs yield similar **MDC** estimates for a given targeted p-value. The MDC% depended on the chosen p-value, with values of MDC% for p-values of 0.05, 0.01, and 0.001 being 7.8%, 10.5%, and 13.6%..

**Conclusions:** **The estimates may help plan experiments when changes or differences in PWCT or PWV are of interest. Also, these MDC estimates may help assess the validity of clinical study outcomes if PWV changes are outcome measures. The main limitation of the estimates is that they are based on 10 healthy subjects.**

**Keywords:** pulse wave velocity, arterial stiffness, pulse conduction time, PWV, hfPWV

## INTRODUCTION

In the 2024 recommendations for the validation of noninvasive measurements of pulse wave velocity (PWV), it is stated that “Due to PWV beat-to-beat variability, at least 10 heartbeats must be recorded.” (Spronck, *et al.* 2024). This standard is based on the reference cited therein. (Svacinova, *et al.* 2020). In that study, PWV differences between a small group of 11 young adults were compared with 15 patients with diabetes mellitus based on the average of 300 consecutive pulses recorded over six minutes in a supine and head-up-tilt position. Although the primary findings of that paper clearly demonstrated an elevated PWV in the older diabetic patients, it did not appear to report anything that would indicate support for the “at least 10 heartbeats” that was put forward as a standard.

Furthermore, an extensive review of the duration of time used to estimate PWV ranged from five pulses to six minutes, with most a minute or less (van Velzen, *et al.* 2017). A central question that appears to be unanswered relates to estimating the expected variability in measured PWV as a function of the number of beats included in the estimate. Since PWV depends on the pulse wave conduction time, an alternate framing of this question might be as follows. To what extent does the average of  $n$  contiguous pulse wave conduction times (PWCT) vary as a function of  $n$ ? The potential importance of the answer to this query relates to its impact on an evidence-based guide for selecting a suitable sampling interval and estimating the minimum detectable change (MDC) in PWCT. **The present study aimed to measure the PWCT variability in 10 healthy supine-lying subjects during a 45-minute session and use these data to estimate the MDC for various sample sizes of included pulses.**

## METHODS

### Subjects

Ten volunteer subjects aged 24 to 28 years were recruited from 1<sup>st</sup> and 2nd-year medical students to participate in this research after signing a University Institutional Review Board (IRB) approved consent form (NSU-#2021-002). Entry requirements were (1) the ability and agreement to lie supine without significant movements for up to 60 minutes, (2) no history of cardiovascular or neurological conditions, (3) nonsmoker, and (4) willingness to forgo caffeinated beverages on the day of the experiment. Persons with diabetes mellitus were excluded from participation.

### Measurements

A photoplethysmographic (PPG) pulse was recorded from the index finger of the left hand using a matched infrared emitter and photodiode sensor (TSD200, Biopac Systems, Goleta, CA, USA) that was gently but securely secured to the finger with Velcro. The system works with an infrared excitation of  $860 \pm 60$  nm with a detected wavelength of 800 nm. Blood pulses in the finger tissue modulate the infrared, causing changes in the sensor's resistance, producing a time-varying output voltage reflecting these pulsations. The PPG sensor output was coupled to a PPG amplifier (PPG100C, Biopac Systems, Goleta CA USA) set to a gain of 50, a low pass filter of 10 Hz, and a high pass filter of 0.05 Hz. EKG electrodes were connected to an EKG amplifier (EGC100C, Biopac Systems Inc., Goleta, CA, USA) to record EKG lead I. The PPG and EKG amplifier outputs were coupled to an analog/digital conversion device (DataQ Instruments, Akron OH, USA, model DI-720). Each channel was sampled at 1000 samples per second using Windaq recording and playback

software (DataQ Instruments, Akron, OH, USA), and the output channels were displayed and recorded on a laptop computer.

## **Procedures**

Subjects arrived at an experimental room at a time and day previously scheduled and took a supine position on a padded examination table. The EKG electrodes were placed to record a single lead EKG (Lead I), with one electrode placed on each forearm and one on the left ankle. After this, the PPG sensor was placed on the index finger of the left hand while the hand rested comfortably with the palm up. Five minutes after placing the PPG sensor, data recording was started for 45 minutes. During this time, the room lights were dimmed, talking was prohibited, and other disturbances were minimized. At the end of the recording interval, the subject's blood pressure was measured in their left arm with an automatic blood pressure system (HEM-711, Omron Healthcare, Sunrise FL, USA). An illustrative recording segment is shown in **Figure 1**, which displays an example of 30 contiguous PPG pulses.

## **Analysis**

The pulse wave conduction time (PWCT) was determined as the time delay between the peak of the EKG R-wave and the arrival of the PPG pulse at the finger site. The arrival time was determined using the peak of the second derivative of the PPG signal as a marker, as illustrated in **Figure 2**. This was done by detecting the recorded EKG's R-waves and determining the between peak duration using software (Advanced CODAS Analysis Software, DataQ Instruments, Akron, Ohio). The adequacy of the automated peak detection process was inspected visually for each pulse, and any missing or added

detections were manually corrected. This process resulted in a sequence of N contiguous PWCT in which N depended on each subject's average R-R interval over the 45-minute recording interval. A subject with an average heart rate of 60 beats/minute (R-R = 1 second) would yield  $45 \times 60 = 2700$  sequential contiguous PWCT. An example of a time series of contiguous PWCT so determined is illustrated in **Figure 3**. This subject had an R-R interval average  $\pm$  SD of  $0.798 \pm 0.058$  seconds with an average heart rate of 75.1 beats/minute, yielding 3400 contiguous PWCTs over the 45-minute measurement interval.

Based on each subject's PWCT time series, an MDC was calculated for different statistical significance threshold levels corresponding to p-values of 0.05, 0.01, and 0.001. The dependence of these MDCs on the number of pulse samples was determined by calculating the MDCs based on sample sizes of 10, 30, 50, 100, and 300 PWCT. The calculations to estimate the MDCs were based on the standard formula  $t\text{-value} \times \sqrt{2} \times \text{SD}$ , in which the t-value is the two-sided Students t-value corresponding to the sample size (number of PWCT used), and SD is its corresponding average standard deviation (Mayrovitz, *et al.* 2019; Spooner, *et al.* 2011). It is assumed that if MDC is being applied, there will be an equal number of samples before and after an intervention or condition change. Thus, in the example of a sample size of 10, the t-value is determined based on an N of 20 with 18 degrees of freedom.

## RESULTS

**Table 1** summarizes the details of each subject's parameters. The average age and body mass index (mean  $\pm$  SD) were  $25.7 \pm 1.2$  years and  $22.3 \pm 2.3$  Kg/m<sup>2</sup>. Systolic and diastolic blood pressures and heart rate, determined at the end of the 45-minute supine

lying interval, were  $119 \pm 6.8$  mmHg,  $74.7 \pm 4.2$  mmHg, and  $68.7 \pm 10.0$  bpm. Thus, the studied group represented a young adult panel with normal weight and blood pressure.

**Table 2** summarizes details of each subject's pulse wave and hemodynamic parameters. The overall group average (mean  $\pm$  SD) for PWCT was  $226.3 \pm 13.9$  ms with a calculated PWV of  $4.05 \pm 0.3$  m/sec. The PWV was calculated based on the measured distance from the right sternal border of the 2nd intercostal space to the tip of the left-hand index finger, which for this group was  $0.914 \pm 0.072$  m. In addition to the conduction speed determinations, the overall 45-minute EKG RR interval was  $0.891 \pm 0.143$  seconds. Each subject's MDC% for a target p-value  $\leq 0.05$  is shown in **Table 3** for sample sizes ranging from 10 to 300. There is considerable variation in MDC% among subjects for each sample size but only minor variations for each subject among sample sizes. The difference in MDC% calculated as the MDC% using 10 samples minus the MDC% using 300 samples was  $0.18 \pm 0.68$  % with a range of -0.62 to 1.87%.

#### **MDC% for p-value $\leq 0.01$**

Each subject's MDC% for a target p-value  $\leq 0.01$  is shown in **Table 4**. There is also considerable variation in MDC% among subjects for each sample size but only minor variations for each subject among sample sizes. The difference in MDC% calculated as the MDC% using 10 samples minus the MDC% using 300 samples was  $0.68 \pm 0.98$  % with a range of -0.52 to 3.2%. However, since the acceptable p-value is now increased, the absolute value of MDC% is also increased relative to those shown in table 3.

### **MDC% for p-value $\leq$ 0.001**

Each subject's MDC% for a target p-value  $\leq$  0.001 is shown in **Table 5**. There is also considerable variation in MDC% among subjects for each sample size but much less variation for each subject among sample sizes. The difference in MDC% calculated as the MDC% using 10 samples minus the MDC% using 300 samples was  $1.80 \pm 1.50$  % with a range of -0.03 to 5.6%. Since the acceptable p-value is increased further, the absolute value of MDC% is also increased relative to those shown in table 4.

### **Composite MDC% values**

The composite findings summarizing the overall MDC% for each p-value and sample size are shown in Table 6. The average MDC% among sample sizes for each p-value varies slightly, with the important change reflected in the variation among p-values for all sample sizes. The largest MDC% is observed for the smallest sample size for each target p-value. The difference between the smallest sample size (10) and the largest (300) increases slightly with increasing target p-values. The largest difference occurs for a p-value of 0.001 with an average MDC% difference of 1.8%.

## **DISCUSSION**

A major outcome of the present study is the characterization of the expected variability of arterial pulse wave conduction time (PWCT) in relation to the number of contiguous pulses included in the assessment. Considering a long observation time of 45 minutes, the analysis was based on many measured PWCT that, depending on the subject's heart rate, ranged from 2430 to 3735 PWCT. This quantification has allowed the



development of the minimum detectable change (MDC%) estimates representing a statistically significant change at p-values of 0.05, 0.01, and 0.001. Such estimates may be useful in planning experiments or procedures where changes or differences in PWCT or pulse wave velocity (PWV) are a parameter of interest. The principal findings are that there are only minor differences in MDC% among sample sizes from 10 to 300 contiguous PWCT with average MDC% values ranging from 8.00% to 7.76% at the p-value level of 0.05, 10.96% to 10.28% at the p-value level of 0.01 and 14.93% to 13.08% at the p-value of 0.001.

An important proviso is that these estimates are derived from a group of young, healthy adults whose sequential variations in PWCT may not be as large as in older individuals. (Marshall, *et al.* 2024) or people with specific cardiovascular conditions such as hypertension (McNally, *et al.* 2024) and heart failure (Esmaeili, *et al.* 2024). Considering this, the present MDC% values may conservatively be viewed as a lower bound on the expected MDC% values. Such differences may be evident when comparing the present PWV estimates to those obtained with measurements of PWV in 79 elderly ( $79.7 \pm 4.7$  years) and overweight patients ( $BMI 29.6 \pm 4.0 \text{ Kg/m}^2$ ) (Meyer, *et al.* 2016). In that study, MDC was calculated for three different PWV measurements made 40.3  $\pm$  9.5 days apart: carotid to femoral (cfPWV), brachial to the ankle (baPWV), and femoral to the ankle (faPWV). Their calculated MDCs were 4.11 m/s, 3.71 m/s, and 3.01 m/s respectively. Based on their data, the two-day average PWV was calculated as 11.99 m/s, 17.41 m/s and 10.63 m/s respectively. The corresponding PWV% for these values is estimated to be 34.28%, 21.3% and 28.32% respectively.

Another consideration concerning the present study is that the calculated MDC% estimates apply to conduction times from heart to finger. The overall average PWCT for the present group (mean  $\pm$  SD) was  $226.3 \pm 13.9$  ms with a calculated pulse wave velocity (PWV) of  $4.05 \pm 0.3$  m/sec. This value is consistent with heart-to-finger PWVs measured in healthy subjects between ages 20-30 years (Allen & Murray 2002; Cho & Baek 2020; Tripathi, *et al.* 2017). It is noteworthy that because this conduction time is based on the time difference between the peak of the R-wave and the arrival of the finger PPG pulse, the PWCT will be underestimated because of the time difference between the R-wave peak and the opening of the aortic valve and the start of ventricular ejection. This pre-ejection period (PEP) has been measured in a group of 20 healthy subjects aged  $27 \pm 4$  years to be  $58.5 \pm 13$  ms (Kortekaas, *et al.* 2018). Subtracting this average PEP value from the measured average PWCT yields an adjusted PWCT of 168 msec. Using this adjusted conduction time, the adjusted PWV for the present group would be 5.46 m/sec. However, although the inclusion of the PEP alters the absolute value of the estimated PWCT, it does not affect the within-subject temporal variability (Kortekaas, van Velzen, Grune, Niehof, Stolker & Huygen 2018), which is the parameter of current interest.

A final consideration regarding the variability assessment is the potential variability in the detection of the pulse arrival time, which, as described, is based on using the peak of the second derivative of the PPG signal. However, this method is widely used and is reliable (Hashimoto, *et al.* 2002; Obeid, *et al.* 2021). Its theoretical limitation is that the second derivative signal may experience a minor phase delay that might extend the estimated

PWCT. However, this delay would be constant in each subject and not influence the within-subject variability.

## CONCLUSION

**The present study aimed to measure the PWCT variability in healthy supine-lying subjects during a 45-minute session and use these data to estimate the MDC for various sample sizes of included pulses.** Based on measurements of 2430 to 3750 contiguous heart-to-finger PWCT in 10 young adult healthy subjects, it is concluded that sample sizes ranging from 10 to 300 PWCT samples yield similar estimates for the minimum detectable change for a given targeted p-value. The average MDC% depended mainly on the chosen p-value, with mean values of MDC% for p-values of 0.05, 0.01, and .001 being 7.8%, 10.5%, and 13.6%, respectively. **These estimates may help in the planning of experiments or procedures when changes or differences in PWCT or pulse wave velocity (PWV) are a parameter of interest. Furthermore, these MDC estimates may help assess the validity of clinical study outcomes in which changes in PWV are used as an outcome measure. The principal limitation of the present estimates is that they are based on ten healthy subjects.**

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This research study was unfunded.

## Conflict of Interest

The author declares no conflict of interest.

## Data availability statement

The data supporting this study's findings are not publicly available because they were not included in the original consent forms. The anonymized data are available from the corresponding author upon request.

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## TABLES

Subject	Sex	Age (years)	Height (m)	Weight (Kg)	BMI (Kg/m <sup>2</sup> )	Systolic BP (mmHg)	Diastolic BP (mmHg)	Heart Rate (bpm)
1	F	26	1.73	59.09	19.76	116	72	82
2	F	28	1.78	78.18	24.68	117	76	54
3	M	27	1.83	81.82	24.41	134	82	66
4	M	26	1.73	72.73	24.33	120	70	57
5	F	24	1.65	54.55	19.97	107	68	83
6	M	26	1.63	67.27	25.40	122	78	73
7	M	25	1.73	68.18	22.80	116	72	67
8	F	23	1.65	54.55	19.97	117	76	68
9	M	26	1.70	61.36	21.14	119	75	76
10	F	28	1.63	53.64	20.25	122	78	60

Table 1. Participant demographics

Systolic and diastolic blood pressure (BP) and heart rate were measured with the subject supine at the end of the interval. Based on body mass index (BMI) values, only one subject (#6) would be classified as slightly overweight (BMI > 25.0).

Subject	Sex	PWCT (ms)	RR (sec)	L (m)	PWV (m/sec)
1	F	230.5 ± 11.1	0.725 ± 0.195	0.914	3.967
2	F	204.2 ± 10.8	1.111 ± 0.104	0.890	4.359
3	M	250.6 ± 5.6	0.853 ± 0.033	1.062	4.237
4	M	225.4 ± 5.8	1.089 ± 0.154	0.914	4.056
5	F	217.0 ± 6.9	0.730 ± 0.051	0.864	3.980
6	M	244.3 ± 8.3	0.800 ± 0.058	0.813	3.327
7	M	229.2 ± 5.7	0.898 ± 0.100	0.991	4.322
8	F	229.3 ± 8.1	0.915 ± 0.051	0.952	4.122
9	M	212.8 ± 5.9	0.761 ± 0.035	0.903	4.244
10	F	220.1 ± 8.9	1.023 ± 0.101	0.845	3.837

Table 2. Individual pulse wave features

PWCT is the pulse wave conduction time in ms. L is the distance measured from the right sternal border of the second intercostal space to the tip of the index finger of the left hand where the PPG sensor was placed. PWV is the calculated pulse wave speed in m/s based on the L value and the average PWCT. RR is the EKG RR interval averaged over the complete 45-minute measurement interval.



Subject / N	Number (N) of PWCT used to measure change or difference				
	10	30	50	100	300
1	13.28	12.04	11.63	11.48	11.41
2	14.54	14.73	14.74	14.91	15.00
3	5.94	5.79	5.77	5.84	5.98
4	5.55	5.57	5.56	5.54	5.59
5	6.43	6.11	6.01	5.98	5.98
6	8.98	8.69	8.59	8.61	8.62
7	5.38	5.34	5.32	5.35	5.36
8	5.34	5.73	5.80	5.88	5.96
9	5.74	5.49	5.42	5.46	5.47
10	8.81	8.82	8.72	8.82	8.83

Table 3. Individual minimum detectable percentage changes for a p-value of 0.05

Table entries are the minimum detectable percentage change (MDC%) calculated for each subject based on the number of PWCT used to estimate a change or difference for a target p-value of  $\leq 0.05$ .

Subject / N	Number (N) of PWCT used to measure change or difference				
	10	30	50	100	300
1	18.19	16.02	15.39	15.09	14.99
2	19.91	19.60	19.98	19.60	19.72
3	8.14	7.70	7.83	7.68	7.86
4	7.60	7.41	7.43	7.29	7.35
5	8.81	8.13	8.02	7.87	7.86
6	12.31	11.56	11.53	11.32	11.33
7	7.36	7.10	7.16	7.03	7.05
8	7.32	7.62	7.88	7.73	7.83
9	7.86	7.30	7.32	7.18	7.20
10	12.1	11.7	11.8	11.6	11.6

Table 4. Individual minimum detectable percentage changes for a p-value of 0.05

Table entries are the minimum detectable percentage change (MDC%) calculated for each subject based on the number of PWCTs used to estimate a change or difference for a target p-value of  $\leq 0.01$ .

Subject / N	Number (N) of PWCT used to measure change or difference				
	10	30	50	100	300
1	24.79	20.83	19.86	19.28	19.15
2	27.13	25.49	25.79	25.04	25.19
3	11.09	10.02	10.10	9.81	10.04
4	10.36	9.64	9.59	9.31	9.38
5	12.01	10.57	10.35	10.05	10.04
6	16.77	15.04	14.89	14.46	14.47
7	10.03	9.23	9.25	8.98	9.00
8	9.97	9.91	10.18	9.88	10.01
9	10.71	9.50	9.45	9.18	9.19
10	16.46	15.25	15.26	14.81	14.85

Table 5. Individual minimum detectable percentage changes for a p-value of 0.001

Table entries are the minimum detectable percentage change (MDC%) calculated for each subject based on the number of PWCTs used to estimate a change or difference for a target p-value of  $\leq 0.001$ .

	Number (N) of PWCT used to measure change or difference				
N	10	30	50	100	300
P ≤0.05	8.00 ± 3.40	7.83 ± 3.26	7.76 ± 3.21	7.79 ± 3.22	7.82 ± 3.21
P ≤0.01	10.96 ± 4.66	10.42 ± 4.33	10.44 ± 4.31	10.24 ± 4.23	10.28 ± 4.22
P ≤0.001	14.93 ± 6.35	13.55 ± 5.63	13.47 ± 5.57	13.08 ± 5.40	13.13 ± 5.40

Table 6. Composite average minimum detectable percentage changes

Table entries are the minimum detectable percentage change (MDC%) calculated for the entire group based on the number (N) of PWCT used to estimate a change or difference using target p-values of ≤0.05, ≤0.01, and ≤0.001. Entries are MDC% ± SD.

## FIGURE LEGENDS

Figure 1. Illustrative recording.

The electrocardiogram (EKG) and the finger photoplethysmographic (PPG) recordings are shown for a 30-pulse segment. The time base for this figure is 0.5 seconds/division.

Figure 2. Determining pulse wave conduction time (PWCT)

The PWCT is defined here as the delay between the peak of the EKG R-wave and the peak of the second derivative of the PPG pulse.

Figure 3. Example pulse wave conduction time sequence

This example pulse wave conduction time (PWCT) sequence is for the subject 6. The overall mean and SD of this sequence is  $244.3 \pm 8.3$  ms. The subject's average R-R interval was  $0.798 \pm 0.058$  s, with an average heart rate of 75.1 bpm.

## FIGURES

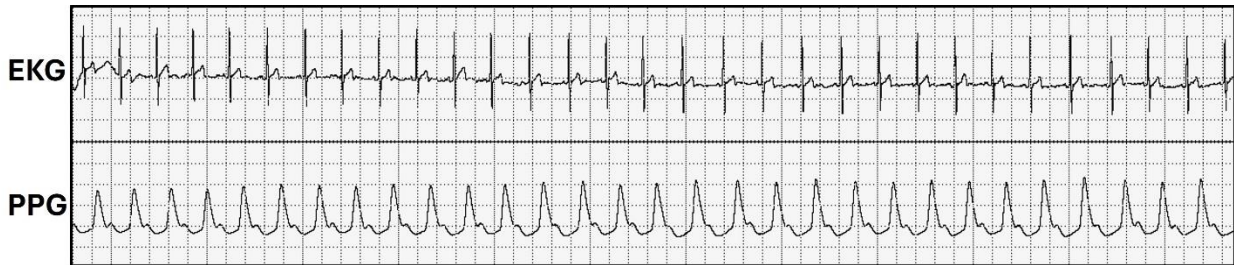


Figure 1. Illustrative recording.

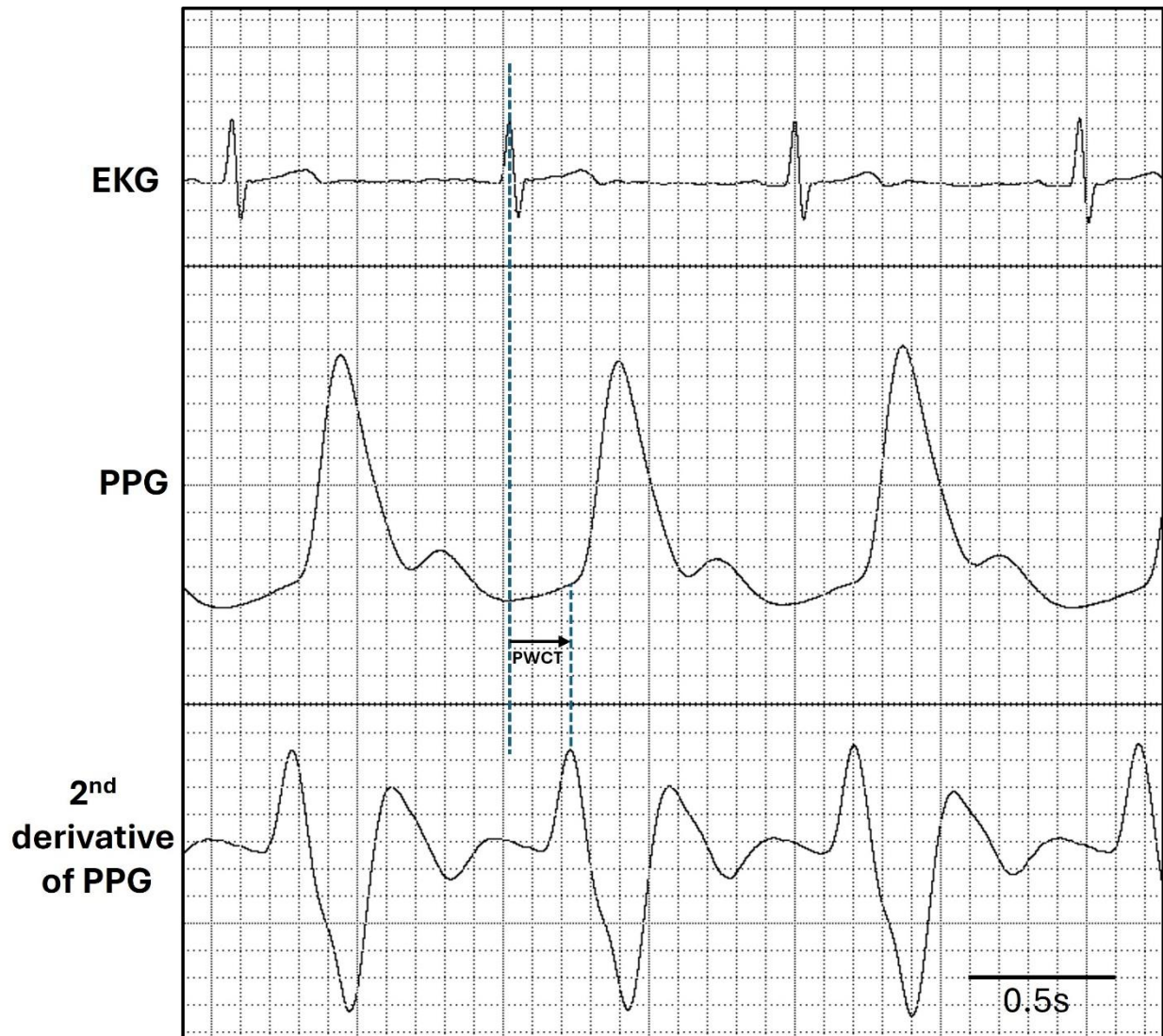


Figure 2 Determining pulse wave conduction time (PWCT)

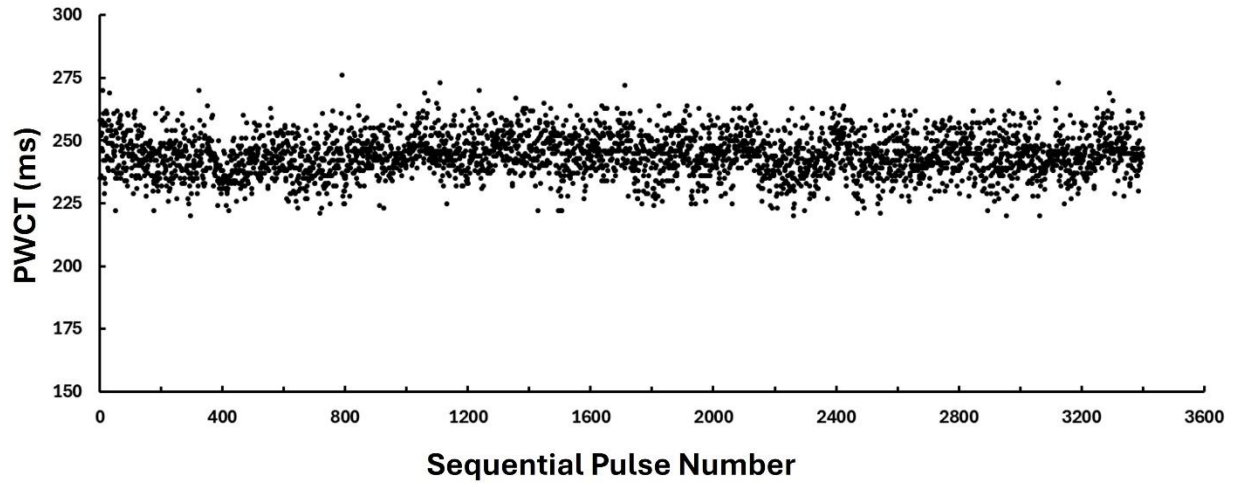


Figure 3. Example pulse wave conduction time sequence