Methods of the Pulse Wave Velocity Estimation based on Pneumatic Blood Pressure Sensor Data and Synchronous ECG Records

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Abstract: The article discusses a new method for diagnosing atherosclerosis with the help of a pneumatic blood pressure sensor recently developed by the authors. Since atherosclerosis is a progressive disease characterized by the deposition of cholesterol and certain fractions of lipoproteins on the walls of blood vessels, it is always accompanied by an increase in stiffness of the artery walls. One technique to assess arterial stiffness, is the measurement of arterial pulse wave velocity, that is the distance traveled by blood flow divided by the time it takes to travel that distance. So the direct method for estimating pulse wave velocity is to measure the transit time of a pulse wave between a pair of artery points by means, for example, of any tonometric sensors. In this connection the paper discusses the possibility of using a new type of sensors developed by the authors —– pneumatic sensors —- to measure the pulse wave transit time. However, given the existing features of these sensors and, accordingly, the special features of pressure measurements, it was necessary to significantly modify the direct method for estimating pulse wave velocity. The main modification characterizing the new, indirect method consists in evaluating the delay of the pulse wave at the points of the artery with respect to some characteristic moment of a synchronous ECG (e.g. the time moment of R–peak, that corresponds to heart ventricles contractions). The details of this method and its modification in the form of a simplified single–point method of estimating pulse wave velocity form the main content of the work.

1 INTRODUCTION

Today, cardiovascular disease is the main cause of the deterioration in the health of many people, including mortality, worldwide. In its turn, the most common cause of cardiovascular diseases is atherosclerosis, a progressive disorder leading to the build-up of cholesterol and other lipoprotein fractions on artery walls. Such a buildup is characterized by the formation of atherosclerotic plaques followed by wall calcification, which leads to artery deformation and narroing (up to occlusion). As this reduces the flow of oxygen-saturated blood to vital organs (e.g. heart and brain), it causes the myocardial and cerebral ischemia. As a result, the risk of such severe disorders as acute myocardial infarction or stroke (caused by thrombosis upon the occlusion) increases significantly (Laurent et al., 2006). For this reason now, the research and development of reliable methods for detecting atherosclerosis in early stages (subclinically) is an extremely important problem.

Atherosclerosis can be detected using damage markers of internal organs (e.g. heart, kidneys, arteries) during the invasive study. However, it is clear that non–invasive methods seem more appealing in terms of diagnosing atherosclerosis in the subclinical phase. Essentially, those methods are related to structural and functional assessment of the blood vessel state. In this context we must mention (A) Doppler ultrasonography used to evaluate the intima media thickness and analyze plaques, as well as the (B) ankle-brachial index evaluation method employed to identify peripheral artery disorders. Besides the aforementioned methods, today's medicine emphasizes a group of methods based on analyzing systolic blood pressure and, more generally, the shape of the blood pressure pulse wave. Largely, this trend can be explained by the discovery of the relationship between blood pressure parameters and arterial stiffness, with the latter depending on the calcification of walls.

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2 ASSESSMENT OF ARTERIAL WALL STIFFNESS BY PWV ESTIMATION

One of the most prominent parameters (the gold standard) for the assessment of arterial stiffness is the pulse wave velocity (PWV), i.e. the speed of the pressure pulse wave (PW) propagating along the walls of the artery caused by the release of blood flow, ejected by the heart during the systole (Evangelista, 2011). So, the direct PWV measurement method is underpinned by estimating the PW transit time $T_{pwtt} = T_2 - T_1$, i.e. the time for which the wave travels between two different points at the artery. In its turn, PWV will be the distance d travelled by wave divided by transit time: $V = d/T_{pwtt}$. Any pair of tonometric sensors can be used for the implementation of this method, provided that those sensors are located proximally above the surface arteries, distally against the heart (on the carotid, femoral, radial, and other arteries) (Kim and Kim, 2019), see Figure 1.

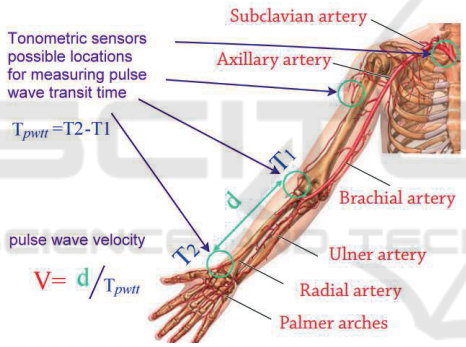

Figure 1: Tonometric sensors locations for PWV estimation. PWV V is calculated by dividing the distance d between the sensors by measured PW transit time T_{pwtt}.

To date, there are several types of tonometric sensors employed for estimating PWV under the above method. They may differ by the mode of action (from applanation tonometry, oscillometric approach, etc. to magnetic tomography) and by design. The detailed review of known direct PWV measurement methods employing various sensors and results derived here can be found in (Cavalcante and Lima, 2011), (Benetos et al., 2010). Typical reference values of PWV for people without significant cardiovascular problems that are currently used as guidelines for assessing the state of blood vessels can be found in (Benetos et al., 2010), see also Table 1.

Recently, the authors of this work also proposed to use a new type of sensors – pneumatic sensors for continuous arterial blood pressure monitoring in the problem of the pulse wave velocity estimation. However, in view of the existing features of these sensors and, accordingly, peculiarities in measurement methods, we had to significantly modify the direct method for estimating PWV. The main change characterizing the new, developed by us method consists in measuring indirectly the transfer time between a pair of points at the artery by measuring PW delays for both points in relation to the R–peaks of the ECG record (time moments of the heart ventricles contraction). The details of this method and the results obtained are presented below in the paper.

Table 1: PWV by age groups of patients in norm (1455 persons) – adapted from (Benetos et al., 2010).

Age (year)	Mean PWV (±2SD)	Median PWV (10-90 pc)
< 30	6.2 (4.7–-7.6)	6.1 (5.3–-7.1)
30—39	6.5 (3.8—9.2)	6.4 (5.2–-8.0)
40—49	7.2 (4.6–-9.8)	6.9 (5.9–-8.6)
50—59	8.3 (4.5—12.1)	8.1 (6.3–-10.0)
60—69	10.3 (5.5–-15.0)	9.7 (7.9–-13.1)
≥ 70	10.9 (5.5–-16.3)	10.6 (8.0–-14.6)
SD abbriviation is for standard deviation; 10 pc is upper limit (10%); 90 pc is lower limit (90%).		

3 USING PNEUMATIC BLOOD PRESSURE SENSORS IN PWV ESTIMATION

Some time ago the authors of this paper suggested a new method of non–invasive continuous arterial blood pressure measurement that employed the principle of local compensation and represented the advancement of applanation tonometry methods. In technical terms the principle is realized in the form of a pneumatic sensor (Antsiperov and Mansurov, 2019a), (Mansurov and Antsiperov, 2017), Figure 2.

From some perspective, the pneumatic sensor operates as a pressure relief valve (PRV). When the measuring unit's outlet is covered by soft tissues of the wrist, the continuous air flow from the receiver in pneumatic circuit coming into the chamber increases pressure P_{sen} in it. But, when P_{sen} slightly exceeds the artery wall pressure P_{art}, a part of the air leaks out due to elastic displacement of surface tissues, and that aligns P_{sen} to P_{art}, see Figure 2. However, it should be noted that there is one significant difference between the sensor and an ordinary PRV. While a pressure drop is a one–time event for a PRV during its normal operation, the sensor operates in conditions of perma-

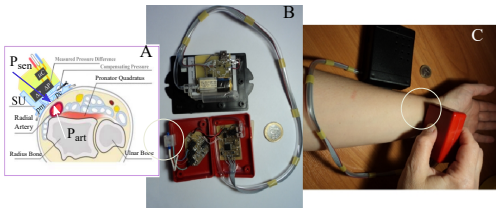

Figure 2: (A) the sketch of the pneumatic sensor's measuring unit (on the radial artery), (B) the sensor design including the electronic circuit with measuring unit (bottom) and pneumatic circuit (top), (C) location of the measuring unit on the patient's wrist during ABP monitoring.

nent air leakage, continuously tracking the changes of blood pressure: $P_{sen} \sim P_{art}$.

Besides their main purpose (monitoring time–dependent blood pressure dynamics $P_{art}(t)$), the sensors described can be used as tonometers that register time parameters of PW (e.g. moments of systolic blood pressure values, pressure fronts, PW feet, etc.). Recently we have carried out corresponding experiments aimed at direct measurment of PWV with the help of blood pressure sensors as tonometers. A small group of volunteers (12 people) participated in these experiments, and a set of methods was used, that differed slightly in criteria (selection of characteristic points of the PW waveform) used to estimate the transit time. The results turned out to be consistent with the reference data given in Table 1.

However, the experiments also showed that the use of pneumatic sensors in the direct PWV measurment method is a scrupulous and complex procedure requiring fine and barely controllable measurements. The key reason for this is the problem of the proper positioning of pneumatic sensors – the issue we have already mentioned earlier (Antsiperov and Mansurov, 2019a), (Antsiperov and Mansurov, 2019b). In fact, to implement the local compensation method, the measuring unit's outlet has to be very small (less than 1 mm in diameter, while the preloaded radial artery is 3 mm in diameter). This said, to ensure proper measurements ($P_{sen} \sim P_{art}$), the outlet has to be positioned accurately above the artery's central axis (accurate to fractions of a millimetre). And as long as this artery is unobservable, the outlet is positioned recurrently, based on the signal waveform. As a result, the procedure of positioning the measuring unit turns out to be adaptive to the registered signal —– this means the blood pressure may change in unclear ways. If there are two sensors employed and they are located in different places on the artery (see Figure 1), the synchronous measurement with the concurrent monitoring of positions of both sensors becomes a hard–going task, accompanied by an abrupt decrease in the measurement stability on both channels.

4 INDIRECT METHOD FOR PWV ESTIMATION

The problem of measuring transit time with the help of pneumatic sensors was solved by virtue of applying an indirect method. Basically, this method implies carrying out measurements for two points at different time moments – in this case, only one sensor will be needed. This concept may be implemented the following reasons. Let us assume that the delay of PW is measured not between the selected points but in each of those points against another event (e.g. against time T_R of ventricular contraction, i.e. position of R–peak of the ECG). Denoting delays by δ_1 and δ_2 respectively, it would be true that $T_1 = T_R + \delta_1$ and $T_2 = T_R + \delta_2$. This said, the PW transit time between the selected points is $T_{pwtt} = T_2 - T_1 = \delta_2 - \delta_1$. Now, if delays δ_1 and δ_2 depend only on geometrical and physical properties of a respective artery and do not depend on dynamically changing environment, we do not have to assess them against the same T_R. To this end, δ_1 and δ_2 can be assessed against the events happening at different times, with the help of the same (the only) sensor.

To assess the possibility of realizing the aforementioned indirect PWV measurement method, our pneumatic sensor (Antsiperov and Mansurov, 2019a), (Mansurov and Antsiperov, 2017) was equipped with an additional channel for synchronous ECG signal processing. As the purpose of such a modification is relating time parameters of PW to the heart's rhythmic activity, ECG was implemented in the form of a very simplified single-channel amplifier based on the original dry electrode (without conductive gel) circuit without a neutral electrode.

Figure 3 shows the fragment of a 12–second synchronous dynamics of blood pressure signals $P_{sen}(t)$ measured with a modified pneumatic sensor on the patient's wrist (Figure 2 C) and ECG signal $V_{ecg}(t)$ from wrists of both hands. In Figure 3 on both signals the time markers (vertical lines) denote locations on time axis of R-peaks $T_R^{(i)}$, $i = 1, 2, \ldots$ and PW feet $T_f^{(i)}$, usually considered as beginnings of respective pulses. One can see with the naked eye that upon the explicit variability of R—-R intervals $(T_R^{(i+1)} - T_R^{(i)})$ and f–f intervals $(T_f^{(i+1)} - T_f^{(i)})$, the delay periods of PW against R–peak — pulse propagation times $T_{ppt}^{(i)} = T_f^{(i)} - T_R^{(i)}$ remain mostly the same.

The table 2 presents quantitative data on the variability of the R–R and f–f intervals, as well as the mean pulse propagation time and its standard deviation for 12 volunteers. As usual, variability can be estimated in any way by comparing the mean val-

Table 2: Temporal parameters of synchronously measured blood pressure (wrist) and ECG (leads on the wrists) signals.

No	Age (year)	Health status	Num of averag.	Mean R–R (sec)	SD R–R (sec)	Mean f–f (sec)	SD f–f (sec)	Mean R–f (sec)	SD R–f (sec)
1	60	infarct	35	0.8591	0.0077	0.8599	0.0101	0.1109	0.0038
2	25	healthy	34	0.9279	0.0357	0.9252	0.0343	0.1425	0.0039
3	27	healthy	43	1.0320	0.0236	1.0325	0.0240	0.1345	0.0023
4	50	healthy	50	0.9858	0.0384	0.9850	0.0407	0.1151	0.0045
5	62	tachyc.	48	0.8119	0.0065	0.8117	0.0061	0.1100	0.0020
6	56	hypert.	84	0.8575	0.0168	0.8572	0.0148	0.1103	0.0039
7	57	healthy	52	0.8222	0.0114	0.8215	0.0148	0.1174	0.0065
8	22	arrhyt.	22	1.0595	0.0435	1.0569	0.0434	0.1558	0.0026
9	22	arrhyt.	23	1.0506	0.0799	1.0532	0.0460	0.1374	0.0297
10	30	healthy	27	0.7250	0.0236	0.7259	0.0252	0.1311	0.0048
11	80	infarct	16	0.8648	0.0110	0.8633	0.0152	0.1100	0.0073
12	61	healthy	22	0.9125	0.0179	0.9067	0.0205	0.1060	0.0060

Mean and SD (standard deviation) were calculated after trimming 10 % of the lowest values and 10 % of the highest values (10-90 pc).

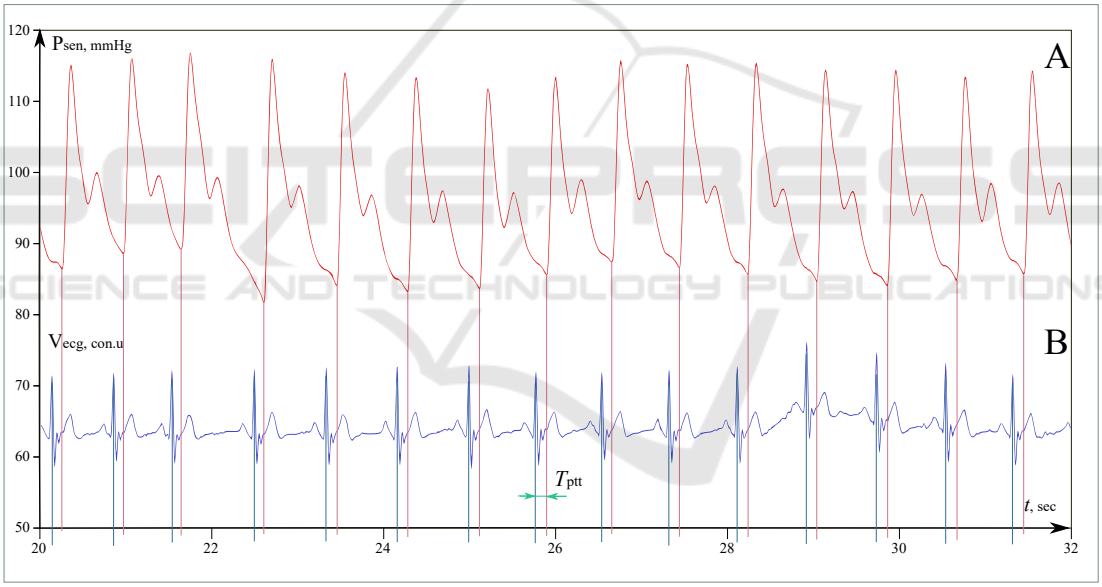

Figure 3: Synchronous measurement of (A) blood pressure and (B) ECG signals. Vertical lines denote moments of R–peaks and corresponding PW feet. The figure shows that even upon the variability of R—R and foot–foot intervals, pulse propagation time $T_{ppt} = T_f - T_R$ remains very stable.

ues (Mean) and standard deviations (SD) displayed in adjacent columns of the table for the corresponding intervals. To obtain the Mean and SD values the averaging was carried out by the number of cardiocycles (column Num of averag.) in each record made in a separate experiment (for a specific volunteer at a specific location on the artery of the measuring unit). These experiments were carried out using a single pneumatic sensor as a tonometer with its fixed locations on the radial and brachial arteries in 12 volunteers of different ages and health conditions. The measurement data obtained for one of two locations on the radial artery (on the patient's wrist) are given in Table 2 (Figure 3 shows the fragment of volunteer No 1's data). Eventually, the experiment results turned out to be consistent with the data obtained during the implementation of the direct method. To this end, they are consistent with the data given in Table 1. With that, the indirect method proved to be more convenient and less demanding than the direct method

(as expected). Also, the measurement of PWV with the help of the indirect method does not require any special training. Instead, the operator only needs to follow simple instructions. We think that after improving the method in compliance with existing medical requirements, the developed PWV measurement method can be used in clinical practice.

The experiments turned out to give an unexpected result – an opportunity to measure PWV with the help of one pneumatic sensor located at only one point. In essence, it impies that one imaginary sensor is located next to the aortic arch and the other – a real sensor – is located in the place, where the easiest measurement of blood pressure can be provided, e.g. above the radial artery, as illustrated in Figure 4 A. We should note that this concept is hardly innovative. There is already an accepted methodology for measuring PWV with the help of a combination of the ECG and a plethysmographic sensor mounted on the patient's finger. For details and references to similar methods, please refer (Bereksi-Reguig et al., 2017), (Castro et al., 2017), (Proenca et al., 2010), (Liu et al., 2011), (Oreggia et al., 2015). However, it is worth noting that although our method is similar to the well-known plethysmographic approaches, it interprets the measurement of the transit time T_{pwtt}, used to calculate PWV, somewhat differently (see Figure 4 B).

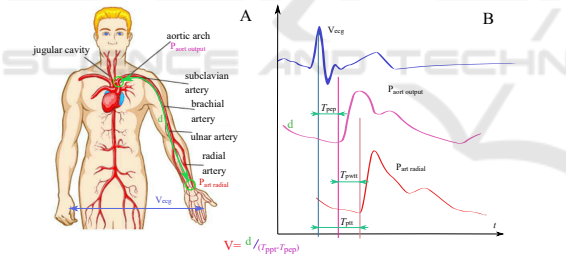

Figure 4: PWV estimation with only one sensor located at only one point. (A) imaginary sensor location above the aortic arch and real sensor location on the wrist. (B) illustration of relations between ECG $V_{ecg}(t)$, and blood PWs $P_{aortoutput}(t)$, $P_{artradial}(t)$ at locations shown in (A).

For exfmple, following their colleagues, the authors of (Bereksi-Reguig et al., 2017) are guided by the suggestion that the moment when R–peak appears in the ECG almost matches the moment when the pulse wave foot starts forming at the aorta output / at the beginning of the subclavian artery. With that, the pulse wave transition time T_{pwtt} can be taken as the delay period T_{ptt} – pulse transit time (see Figure 4 B). After that, by dividing d (distance from the jugular cavity to the finder tip) by the delay period, PWV will be measured as $V = d/T_{ptt}$. And though (Bereksi-Reguig et al., 2017) mentions that T_{pwtt} differs from T_{ptt} by the pre-ejection period T_{pep} (time between ventricular contraction and beginning of the formation of the pulse wave at the aorta output, see Figure 4), the authors consider that difference negligible ($T_{pep} \ll T_{ptt}$).

5 PULSE TRANSIT TIME CORRECTION

However, our study showed that when the blood pressure sensor is installed on the wrist or higher on the arm, the suggestion $T_{pep} \ll T_{ptt}$ becomes very inaccurate or even incorrect. In fact, the authors of the recent study (Kortekaas and van Velzen, 2018) provided results of echocardiographic T_{pep} measurements for three groups, 20 persons in each, namely: focus groups with no cardiovascular disorders under 50 years (A), older than 50 years (B), and having cardiovascular risk factors (hypertension, dyslipidemia, kidney failure, and diabetes) (C). The results derived in (Kortekaas and van Velzen, 2018) can be summarized in the following way: T_{pep} for groups (A) and (B) lies in ranges 58.5 ± 13.0 msec and 52.4 ± 11.9 msec, respectively; for (C) within the range 57.6 ± 11.6 msec. By comparing these results with our data shown in Table 2, where T_{ptt} taken as "Mean R–f" for similar groups comes to 140.5 ± 10.1 msec for (A), 112.1 ± 4.8 msec for (B) and 110.4 ± 5.0 msec for (C), it is not too hard to figure up that T_{pep} represents a considerable part of T_{ptt} (up to half of the latter) in all groups. In this regard, it is interesting to note that the aim of the study (Kortekaas and van Velzen, 2018) was to substantiate the non–obvious assumption, as we show above, that $T_{pep} \ll T_{ptt}$.

For the foregoing reasons, PWV measurement should employ the correct formula $V = d/(T_{ptt} - T_{pep})$ that contains the pre-ejection period T_{pep}. Fortunately, it is not necessary to calculate T_{pep} in every case. The abovementioned study (Kortekaas and van Velzen, 2018) states that T_{pep} has weak individual variations, at least within specific groups (A, B, C) of patients. This said, having the reference values T_{pep} for the corresponding groups and determining the affiliation of each patient to one of these groups (for example, from his electronic health record – EHR), we can use the proposed method for measuring PWV only using the pulse transit time T_{ptt}, but adjusting it using the value T_{pep} for the corresponding group. The results of estimating PWV, using the data shown in Table2, are given in Table 3.

As seen from Table 3, the Pulse Wave Velocity obtained by us with the use of the modified pneumatic sensor following the simplified indirect PWV mea-

Table 3: PWV estimation based on synchronously measured blood pressure (wrist) and ECG Signals (wrist Leads).

No	Age (year)	Health status	Number of averag.	Mean T_{ptt} (sec)	Refer. T_{pep} (sec)	Distance d (m)	PW velocity V (m/sec)
1	60	infarct	35	0.1109	0.0576	0.70	13.1
2	25	healthy	34	0.1425	0.0585	0.68	8.1
3	27	healthy	43	0.1345	0.0585	0.66	8.7
4	50	healthy	50	0.1151	0.0524	0.65	10.4
5	62	tachyc.	48	0.1100	0.0524	0.68	11.8
6	56	hypert.	84	0.1103	0.0576	0.67	12.7
7	57	healthy	52	0.1174	0.0524	0.68	10.5
8	22	arrhyt.	22	0.1558	0.0585	0.66	6.8
9	22	arrhyt.	23	0.1374	0.0585	0.66	8.6
10	30	healthy	27	0.1311	0.0585	0.68	9.4
11	80	infarct	16	0.1100	0.0576	0.66	12.6
12	61	healthy	22	0.1060	0.0576	0.64	11.9

The pulse transition time values in the column "Refer. T_{pep}", used to calculate PW velocity V, were chosen as centres of T_{pep} ranges for groups A, B, C (see discussion above, based on (Kortekaas and van Velzen, 2018) data), while the groups were determined by the columns "Age" and "Health" for each volunteer.

surement method are consistent with reference values from Table 1. Moreover, they correctly reflect the age trends and known correlation between PWV and some disorders (infarct, arrhythmia). Guided by those first results, we can arrive at a general conclusion: despite the apparent simplicity of the measurement procedure, the suggested method delivers adequate PWV estimation results.

6 CONCLUSIONS

We can also make the following more specific and substantial conclusions. As the suggested method implies estimation of PWV in standard conditions of blood pressure monitoring with the help of a pneumatic sensor (Mansurov and Antsiperov, 2017), it can be cost–efficiently (by adding an ECG channel) modified and transformed into a versatile system that allows to estimate the stiffness of the artery walls. It suggests preliminary judgment about the state of the cardiovascular system, especially about the degree of atherosclerosis development. It goes without saying that additional costs include software augmentation (see (Bereksi-Reguig et al., 2017)) and examination methodology modification (blood pressure monitoring). However, we consider the cost increase negligible compared to the benefit delivered by the versatile system itself. Realizing that this theme has much room for studies and tests, we optimistically expect our efforts to pay off.

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