ISSN 1392 – 124X INFORMATION TECHNOLOGY AND CONTROL, 2005, Vol. 34, No. 1

MATHEMATICAL METHODS FOR DETERMINING THE FOOT POINT OF THE ARTERIAL PULSE WAVE AND EVALUATION OF PROPOSED METHODS

Egidijus Kazanavicius, Rolandas Gircys, Arūnas Vrubliauskas

Department of Digital Signal Processing, Kaunas University of Technology
Studentu 50, LT-51368, Kaunas, Lithuania

Slava Lugin

Institute of Psychophysiology and Rehabilitation, Kaunas University of Medicine
Vyduno al. 4, LT- 00135, Palanga, Lithuania

Abstract. The evaluation of the arterial wall condition is most frequently based on such markers as arterial pulse wave velocity (PWV) and pulse transit time (PTT). To calculate these markers, it is necessary to determine the location of the foot of the arterial pulse wave (APW). This foot point is usually determined with the help of the second derivate maximum or tangent intersection foot-to-foot methods. This paper proposes two original methods for locating the APW foot point, namely: the bottom straight-line and forefront tangent intersection method and the APW foot polynomial approximation method. The main objective of this study is to compare the originally proposed methods with the tangent intersection and the second derivate maximum methods, with respect to error dispersion under different sound-to-noise ratios (SNR) and difference between the foot point of the APW without noise (APW reference value) and the foot point of the APW with a certain SNR.

The analysis of the APW signal with additive noise reveals that the second derivate maximum method results in the widest error dispersion, whereas the tangent intersection method results in the greatest difference between the APW reference value and the foot point of the APW with additive noise. The least difference between the APW reference value and the foot point of the APW with additive noise, as well as the least error dispersion is achieved in the APW foot polynomial approximation method.

1. Indroduction

Arterial wall distensibility is one of the most widely used characteristics to assess the state of a blood circulation system [10]. There are various reasons for diminished distensibility: natural aging [17, 16], smoking [15, 3], insufficient physical exercise [13, 14, 12], hypertension [2, 18], etc.

The aging process and hypertension are the main factors accounting for the diminution of arterial distensibility. The degree of change in the arterial wall depends on how long one has been suffering from the disease. Arterial pulse wave (APW) velocity and form also depend on the health of blood-vessels. Thus, the analysis of changes in the APW velocity [1] and form [6] provides additional markers (diagnostic indices), which allow judgments about the gravity and length of hypertension.

There are a number of non-invasive methods for evaluating arterial health. Such markers as the APW velocity (pulse wave velocity – PWV) and APW transit time (pulse transit time – PTT) are most frequently used to asses the health of the arterial wall [8, 9]. In order to calculate the APW velocity, it is necessary to measure the PTT between two distant points [19, 20, 11].

PTT can be calculated in two ways: 1) by simultaneously measuring two APWs at two points a known distance apart, and then calculating the foot-to-foot time delay between these two APWs; 2) by simultaneously measuring the electrocardiogram (ECG) and the APW at some point, and then calculating the time delay between the ECG R peak point and the APW foot point. Both cases involve locating the foot point of arterial pulse wave. The process is complicated by APW reflections, the triggering effect of the analog – digital converter (ADC), and interference in the sensor-receiver transmission line [7]. Sometimes, to avoid complications in determining the APW foot point, the maximum point of the first APW derivate is chosen as the characteristic point.

The objective of this study is to compare the proposed original methods for locating the foot point of the APW with the second derivate maximum method and the tangent intersection method, on the bases of error dispersion under different sound-to-noise ratios (SNR), and difference between the APW reference value (i.e. the foot point of the APW without noise) and the APW foot estimates (i.e. foot point values resulting from the analysis of the APW sequence with certain SNR).

2. Problem formulation

The APW foot is the minimal amplitude point between the rear front of the current wave and the forefront of the subsequent wave (Fig.1).

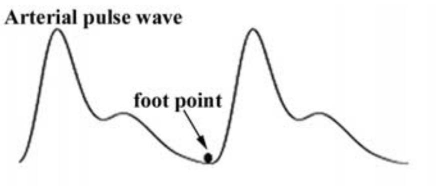

Figure 1. Arterial pulse wave and its foot point

Locating the foot point of the APW is not as a trivial task as it may look at first sight. It is known that, depending on a chosen measuring point, the APW reflections distort the APW foot to a certain degree (Fig.2).

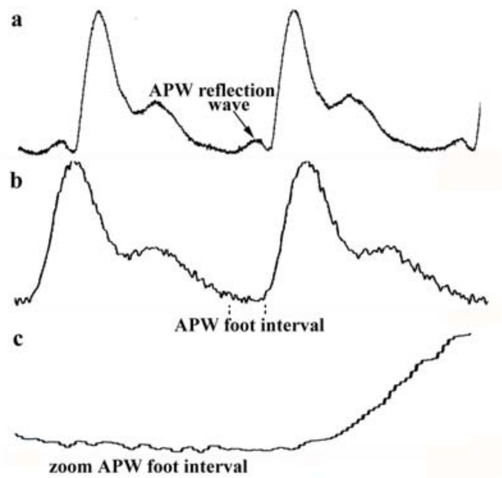

Figure 2. Arterial pulse wave with a reflection wave (a), arterial pulse wave without a reflection wave (b), zoomed interval of arterial pulse wave foot (c)

As Figures 2(b) and 2(c) show, the APW foot is long and flat, and the differences between nearby values are small. Consequently, even a slight noise caused by ADC triggering effect or interference in the sensor-receiver transmission line (Fig.2c) complicates the task of locating the APW foot point. The APW amplitude is normally thousands times as big as interference in the sensor-receiver transmission line; thus, the effect of interference on the whole system is insignificant. However, at the foot of the APW, where the signal is described as a slowly altering trend, this interference drowns the APW foot point completely.

3. Methods

The most widely used methods for determining the PWV are to measure the time delay between the characteristic, or 'timing', point on the two pressure waveforms that are a known distance apart. Most of the methods use the "foot of the wave" as the characteristic point, because this feature is sharply delineated and unaffected by differences in the shape of the pressure pulse waveform and the two recording sites. There are several mathematical methods (algorithms) for identifying the location of the "foot of the wave". SphygmoCor Vx offers a range of options for the algorithm to be used to locate the "foot of the wave".

The second derivate maximum method and the tangent intersection method are most often used to locate the APW foot point. This article offers two original methods – the APW foot polynomial approximation method and the method of bottom straight-line and forefront tangent intersection

In all the above-mentioned methods the ECG R peak point is used as the marker indicating the beginning of a cardio cycle.

3.1. The Second Derivate Maximum Method

An assumption is made, that the APW foot point corresponds to the maximum alter point in signal acceleration. The latter point corresponds to the maximum value of the second derivate of the signal.

At first, the APW sequence is passed through a low frequency filter characterized by a straight-line phase. Then the first and the second derivates are calculated. The second derivative is very sensitive to interference. If noise is yet not noticeable in the first derivative, in the signal of the second derivative it is obvious. Before locating the maximum point of the second derivative, the second derivative is smoothed by triangle moving average filter.

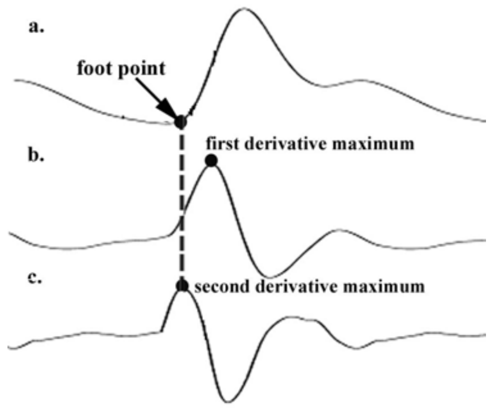

Figure 3. The APW and foot point (a), the first derivative of the APW (b), the second derivative of the APW (c)

The minimum of the second derivative corresponds to the maximal negative acceleration, i.e., to the maximal deceleration point at the forefront peak of the APW. The maximum of the second derivate corresponds to the maximal acceleration point at the foot of APW forefront (Fig.3).

3.2. Tangent Intersection Method

This method is based on the assumption that the APW foot point is located at the intersection of the straight-lines drawn through the rear and the forefronts of the APW (Fig. 4). The straight-lines are obtained by least mean squares method. Since the rear front of the APW ends at the ECG R peak, the APW rear front straight-line is drawn through the points just above the R peak, which occupy 2/5 of the whole RR. Forward front straight-line equation is calculated from the segment between the maximum point of the forefront first derivative and the five points below it.

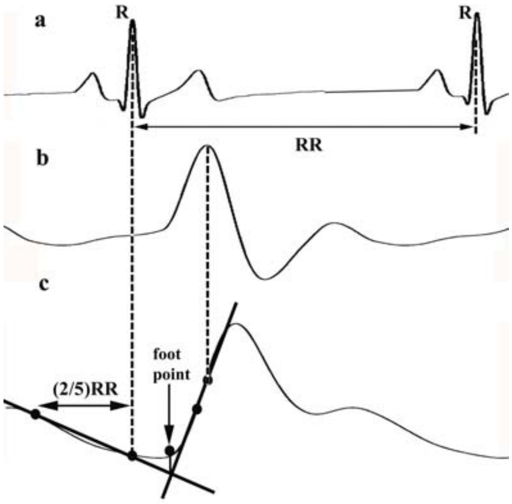

Figure 4. ECG (a), the first derivate of the APW (b), APW (c)

3.3. APW Foot Approximation Method

In this method, first it is necessary to determine a search interval, which begins at the ECG R peak and ends at the APW forefront point corresponding to the maximum of the first derivate. Then the search interval is divided into ten segments, straight-lines are drawn through the values of these segments following the least square method. Further analysis focuses on the start and the end points of the straight-lines.

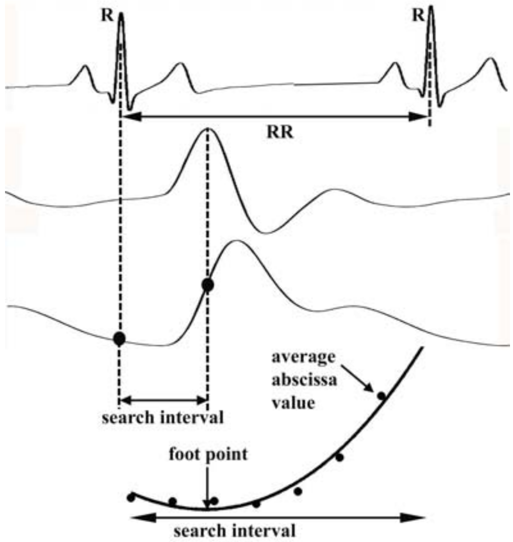

Figure 5. ECG (a), the first derivate of the APW (b), APW (c), zoomed search interval (d)

The abscissa value of the starting point of the current straight-line is summed up with the abscissa value of the end point of the previous straight-line, and the average abscissa value at a particular point is accumulated. The sequence of average abscissa values – the APW foot – is fit with the cubic polynomial. The point at which the APW foot gains the least value is considered to be the APW foot point (Fig. 5).

3.4. Bottom straight-line and Forefront Tangent Intersection Method

In this method, it is assumed that the APW foot point is at the intersection point of the straight-line drawn at the bottom of the APW sequence and the straight-line drawn through the forefront of the APW (Fig. 6).

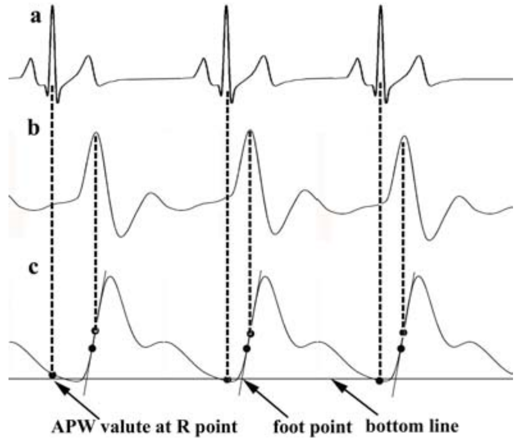

Figure 6. ECG (a), the first derivative of the APW (b), APW (c)

From all the APW values, only those values are selected which are at ECG R peaks. These value points are connected with a straight-line, according to the least square method. The straight-line is called the bottom line of the APW sequence. The APW forefront straight-line equation is calculated from the segment between the maximum point of the forefront first derivative and the five points below it. The point where the APW sequence bottom line and the current APW forefront tangent intersect is called the foot of the current APW.

4. Statistics

When two different methods are applied to measure the same variable, a question rises whether the results obtained from both methods will agree enough to allow substituting one method with another.

When the same method is used to analyze the same signal, but with different noise levels in the signal, a question rises whether the obtained results will be compatible enough to allow using the same method for analyzing signals with different noise levels.

In both cases, it is possible to use the same methodology to determine to what degree the obtained results agree.

If the same variable pertaining to one and the same object is measured a number of times using two different methods, it is hardly possible to expect that the average result values obtained from different methods will be the same.

The true value of the measured variable is usually unknown, thus the average of its values is considered to be its most accurate estimate. Using different analysis methods or having different noise levels, the limits of agreement are calculated by subtracting the results of one method from the results obtained through another method. The process of subtracting annuls the estimate values of variables under investigation, thus leaving only measurement errors, whose dispersion is determined by the Normal Law. (This can be validated by drawing a histogram.) Therefore, the average of measurement errors has to be close to zero. If the average $\bar{d}$ equals zero or is slightly different, it is claimed that the measure results agree and that one method can be substituted with another without losing measurement precision. By analogy, when the same method is used to analyze the same signal but with two different noise levels, the estimate values of variables under investigation are annulled by subtracting the results of the two measurements, thus leaving only estimation errors, 95% of which will be found in the interval between the average value and the value of the double standard deviation s : $\bar{d} - 2s$ and $\bar{d} + 2s$ [4].

Thus the question of precision of the results obtained through different measuring methods arises.

Precision is defined as a particular interval of agreement between measure values, obtained under certain conditions [21]. Since precision depends on the level of error dispersion, it is essential to define the conditions under which measurements are carried out, in order to accomplish a quantitative estimation of precision.

Conditions, when result values are obtained by the same operator, applying the same method to measure a number of similar objects, in the same laboratory, and using the same equipment, international standard [22] defines as repeatability conditions.

When the same variable is measured a number of times under the same repeatability conditions, the error dispersion interval does not change; however the error values vary. Under different repeatability conditions, both the error dispersion interval and the error values vary. This situation can be modeled. It is possible to model different repeatability conditions into sequences of random values, with different dispersions and zero average.

Precision obtained under repeatability conditions is called the coefficient of repeatability (*rc*). This coefficient defines error dispersion under discussed measurement conditions, when the average $\bar{d}$ of result differences (i.e. of errors) is equal to zero.

Having carried out a number of measures of the same variable of the same object, the average of result differences is calculated as follows:

$$d(i) = (x_2(i) - x_1(i)); \quad (1)$$

$$\bar{d} = \frac{1}{N}\sum_{i=0}^{N-1} d(i); \quad (2)$$

Here N is the number of measurement values; x_1 – the values of the first measuring; x_2 – the values of the second measuring; $d(i)$ – the value difference of the i[th] measurement; $\bar{d}$ – the average of measure differences. Thus the standard deviation s is calculated as follows:

$$s = \sqrt{\frac{1}{N}\sum_{i=0}^{N-1}\left(d(i) - \bar{d}\right)^2}; \quad (3)$$

Since all the measurements are carried out at the same time and under the same conditions, the average $\bar{d}$ of measurement values is equal to zero, and 95% of difference values are less than the $2s$ value. (When the average is not zero, it is not possible to calculate the repeatability coefficient. This happens when the results obtained during the first measuring affect the results of the second measuring, or the measuring method affects the variable under investigation.) Since $\bar{d}$ is required to equal zero, the repeatability coefficient is calculated by squaring all the difference values, summing them up, and then dividing the sum by the number of difference values and extracting the square root [4, 5]:

$$rc = \sqrt{\frac{1}{N}\sum_{i=0}^{N-1} d(i)^2}; \quad (4)$$

Here *rc* is the repeatability coefficient.

5. Methodology of Conducting the Experiment

At first, a time axis is modeled with the time period $T = 1 \cdot 10^{-3}$ s, and a quantization level of 12 bites is chosen; then the APW sequence with a constant period R=30 is modeled. The APW foot point is a time point when the APW gains the minimum value. In this sequence, there are R values of the APW foot point. When the APW foot point is located, its value is approximated to a whole millisecond number.

Before applying one or another method, the APW sequence is filtered through a 200[th] order low frequency FIR filter.

5.1. Estimating Measuring Method Precision on the Basis of Repeatability Coefficient

Different repeatability conditions are modeled into APW signal with different noise levels:

$$y_k = APWS + a_k t. \quad (5)$$

Here t is the noise signal, and its noise values are dispersed according to the Normal Law with a single dispersion and zero average; *APWS* is the signal of the pulse wave sequence; a_k is the multiplier which affects the dispersion of noise values; and k refers to the k^{th} repeatability conditions.

Under repeatability conditions k, the signal y_k noise ratio SNR_k remains the same (Table2). The sequence x_k of APW foot point values is obtained from the analysis the signal y_k.

To obtain more reliable results, twenty (n = 1 .. 20) realizations are generated, with a different noise t but with the same a_k. In this way one gets 20 different realizations of the signal y_k, with the same SNR_k.

$$y_{kn} = APWS + a_{kn}t \; . \tag{6}$$

Here n is the noise realization number under the k^{th} conditions.

The analysis of the signal y_{kn} provides us with the sequence x_{kn} of the *APW* foot point values. To estimate the repeatability coefficient, all N=20 sequences x_{kn} are grouped by two to form all the possible sequence x_{kn} pairs. The total number M of such pairs is equal to:

$$M = C_N^2 = \frac{N!}{2!(N-2)!}; \tag{7}$$

For each pair, differences are calculated:

$$d_{mk}(i) = (x_{1mk}(i) - x_{2mk}(i)); \tag{8}$$

Here x_{1mk} – the first sequence of the *APW* foot point values of the m^{th} pair, under repeatability conditions k; x_{2mk} – the second sequence of the *APW* foot point values of the m^{th} pair, under repeatability conditions k; m = 1 .. M; and I =1 . .R; R is the number of periods in the APW sequence;

The APW foot point values obtained using the same method and under the same conditions are calculated as follows:

$$\overline{d}_{mk} = \frac{1}{R}\sum_{i=0}^{R-1} d_{mk}(i) = 0\;; \tag{9}$$

Here R is the number of periods in the APW sequence.

The repeatability coefficient of the mth pair is equal to:

$$rc_{mk} = \sqrt{\frac{1}{R}\sum_{i=0}^{R-1} d_{mk}(i)^2}\;; \tag{10}$$

The repeatability coefficient for all the m pairs under kth conditions is obtained by calculating the average:

$$RC_k = \frac{1}{M}\sum_{m=0}^{M-1} rc_{mk}; \tag{11}$$

Simultaneously analyzing the signal with different SNR_k and different repeatability conditions, different result dispersions are obtained. This situation is modeled by generating six *(K=6)* groups, each consisting of twenty *(N=20)* sequences of the signal y, calculated using equation (6). The signals of separate groups vary with respect to the value dispersion of the noise signal (Table 1).

Table 1

k	1	2	3	4	5	6
a_k	0	100	200	300	400	500

Different noise signal value dispersions lead to different signal-noise ratios (Table 2).

Table 2

k	0	1	2	3	4	5
SNR_k	∞	90.94	45.47	30.31	22.74	18,19

The comparison of RC_k coefficients allows drawing certain conclusions about the error dispersion in the method, when there are different noise levels. The smaller is the repeatability coefficient RC_k, the better the results of separate measurements agree when the signal contains the k^{th} noise level.

5.2. Calculating Agreement between APW foot point (reference value) and its estimate at Different Noise Levels

For every noise level SNR_k, *N=20* of APW sequences are generated. Then *n=1..N* of x estimates $\overline{x}_{kn}$ are calculated:

$$\overline{x}_{kn} = \frac{1}{R}\sum_{i=0}^{R-1} x_{kn}(i); \tag{12}$$

Here x_{kn} – the n^{th} APW foot point sequence, when the noise level in the signal equals SNR_k; R is the number of periods in the APW signal; *n=1..20*.

For each group k, the value $\overline{x}_k$ of the APW foot point estimate is calculated as follows:

$$\overline{x}_k = \frac{1}{N}\sum_{n=0}^{N-1} \overline{x}_{kn}\;; \tag{13}$$

To evaluate the accuracy of the method under different noise levels in the signal, it is necessary to compute the difference between the value x and its estimate $\overline{x}_k$:

$$d_k = x - \overline{x}_k\;; \tag{14}$$

If the difference d_k (14) equals zero or is close to zero, a conclusion can be drawn that noise does not affect the accuracy of the results at a given noise level in group k.

6. Results of the Experiment

When assessing the health of arterial blood-vessels, one frequently calculates pulse wave transit time PTT.

Method precision depends on several factors. The smaller is the method error dispersion under the same SNR_k (repeatability conditions), the more precise is the method. The less vary the method repeatability coefficient RC_k under different SNR_k, the more stable is the method, since the limits of error dispersion vary insignificantly under different *SNR*. If the limits of error dispersion in a particular method remain stable under different noise levels in the signal, the method can be applied for different *SNR* values without loosing its precision.

Since the time axis is modeled according to $T = 1 \cdot 10^{-3}$ s period, the results of the method are approximated to whole millisecond numbers.

6.1. Tangent Intersection Method

This method, in which the APW foot point is identified as the intersection point of two tangents drawn through the forefront and the rear front of the APW, results in the following error dispersion intervals $(\pm 1.96 \times RC_k)$ with different SNR_k (Fig.7).

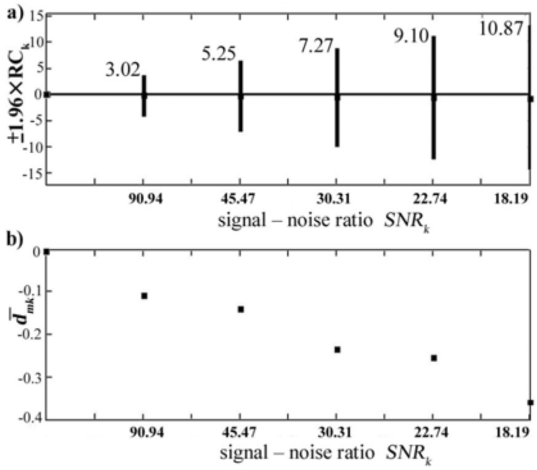

Figure 7. Error dispersion at different noise levels in the signal (a), the average of errors at different noise levels in the signal (b)

As we can see from Figure 7(a), under the maximal signal-noise ratio *SNR=18.19*, the error dispersion limits do not exceed $\pm$11ms, with 95% confidence interval. The probability of errors exceeding the $\pm$11ms boundary equals $p \le 0.05$.

The tangent intersection method meets the repeatability condition under all SNR_k $(k=1..5)$, i.e., the average difference values $\bar{d}_{mk}$ (9) are equal to zero (Fig.7(b)).

The difference between the reference value (i.e. the foot point of the APW obtained from the analysis of the APW sequence without noise) and its estimate (i.e. the foot estimate of the APW obtained from the analysis of the APW sequence with a certain SNR_k (14))is shown in Figure 8.

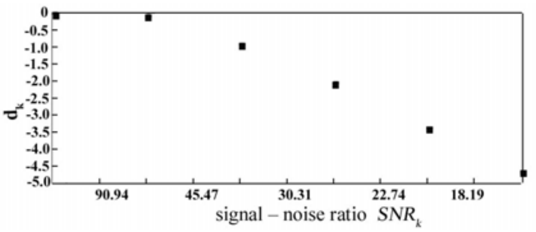

Figure 8. Difference between the standard foot point of the APW and the foot estimate obtained when analyzing the APW with certain SNR_k

The greater is the signal-noise ratio, the higher are the foot estimate values of the APW.

6.2. Second Derivate Maximum Method

The method, in which the APW foot point is identified as the maximum point of the second derivate of the APW, results in the following error dispersion intervals $(\pm 1.96 \times RC_k)$ with different SNR_k (Fig.9).

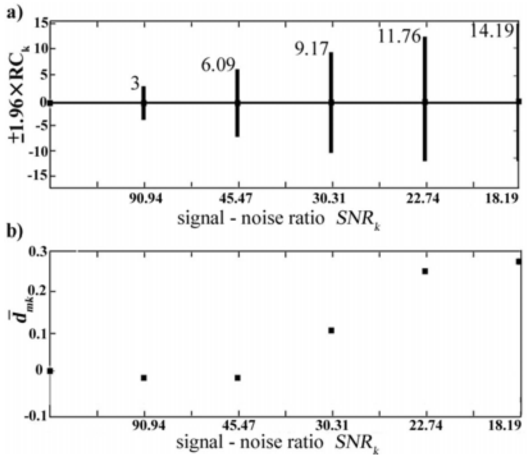

Figure 9. Error dispersion at different noise levels in the signal (a), the average of errors at different noise levels in the signal (b)

As Figure 9(a) shows, under the maximal signal-noise ratio SNR=18.19 the error dispersion limits do not exceed $\pm$14ms, with 95% confidence interval. The probability of errors exceeding the $\pm$14ms boundary equals $p \le 0.05$.

The method meets the repeatability condition under all SNR_k $(k=1..5)$, i.e., the average difference values $\bar{d}_{mk}$ (9) equal zero (Fig.9(b)).

The difference between the APW reference value and its estimate is shown in Figure 10.

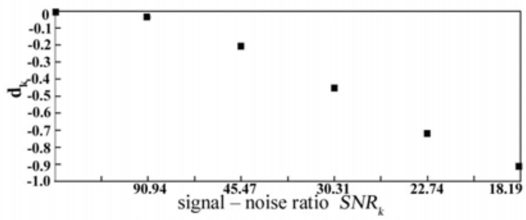

Figure 10. Difference between the standard foot point of APW and the foot estimate obtained when analyzing APW with certain SNR_k

The application of the second derivative maximum method to analyze the APW sequence reveals that the greater is the signal-noise ratio, the higher are the foot estimate values of the APW. The maximum difference is 1ms.

6.3. APW Foot Approximation Method

The method, in which locating the APW foot point involves finding the minimum point at the foot of the APW obtained with the help of the least square method and fit cubic polynomial, results in the following error dispersion intervals $(\pm 1.96 \times RC_k)$ with different SNR_k as shown in Figure 11.

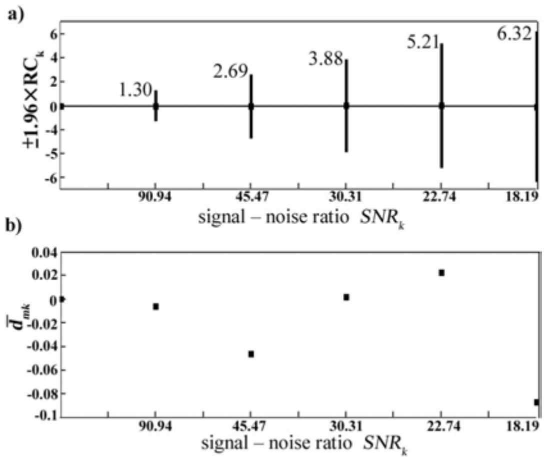

Figure 11. Error dispersion at different noise levels in the signal (a), the average of errors at different noise levels in the signal (b)

Figure 11(a) shows that, under the maximal signal-noise ratio *SNR=18.19*, the error dispersion limits do not exceed ±6ms, with 95% confidence interval. The probability of errors exceeding the ±6ms boundary equals p≤0.05.

The APW polynomial approximation method meets the repeatability condition under all SNR_k (k= 1 .. 5), i.e., the average difference values $\overline{d}_{mk}$ (9) equal zero(Fig.11(b)).

The difference between the APW reference value and the APW foot estimate is shown in Figure 12.

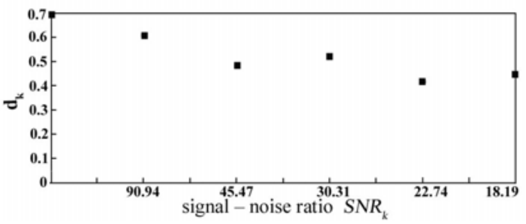

Figure 12. Difference between the standard foot point of APW and the foot estimate obtained when analyzing APW with certain SNR_k

The analysis of the APW sequence reveals that the greater is the signal-noise ratio, the higher are the foot estimate values of the APW. The maximum difference is 1ms.

6.4. Bottom straight-line and Forefront Tangent Intersection Method

The method, in which the APW foot point is identified as the intersection point of the bottom straight-line of the APW sequence and the straight-line drawn through the forefront of the APW, results in the following error dispersion intervals $\left(\pm 1.96 \times RC_k\right)$ with different SNR_k (Fig.13).

According to Figure 13(a), under the maximal signal-noise ratio *SNR=18.19*, the error dispersion limits do not exceed ±12ms, with 95% confidence interval. The probability of errors exceeding the ±12ms boundary equals p≤0.05.

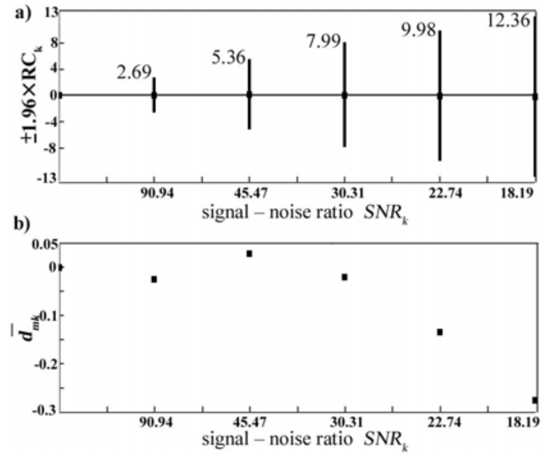

Figure 13. Error dispersion at different noise levels in the signal (a), the average of errors at different noise levels in the signal (b)

The method meets the repeatability condition under all SNR_k (k = 1 .. 5), i.e., the average difference values $\overline{d}_{mk}$ (9) equal zero (Fig.13(b)).

The greater is the signal-noise ratio, the higher are the foot estimate values of the APW. The maximum difference is 1ms, as shown in Figure 14.

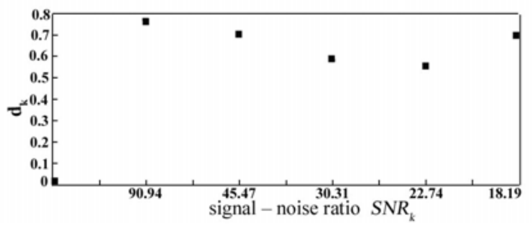

Figure 14. Difference between the standard foot point of APW and the foot estimate obtained when analyzing APW with certain SNR_k

7. Conclusions

The level of noise in the signal getting higher, one also obtains greater estimate values of the APW foot point. This could be explained by the fact that the forefront of the APW is the most quickly varying part of the signal, thus, it is least affected by noise.

The biggest error dispersion is obtained using the second derivate maximum method. Depending on what the noise level in the signal is, the error dispersion varies from ±0ms to ±14ms; whereas the difference between the reference value (i.e. the standard foot point of the APW) and its estimate does not exceed 1ms.

The biggest difference between the reference value of the APW foot point (signal without noise) and its estimate (signal with a particular noise) is estimated using the tangent intersection method. Here the difference between the standard foot point of the APW and its estimate reaches 5ms, and the error dispersion limits vary from ±0ms to ±11ms.

The bottom straight-line and forefront tangent intersection method reaches a ±12ms error dispersion limit; whereas the error dispersion limits of the APW polynomial approximation method do not exceed ±6ms. In both methods, the calculated difference between the reference value of the APW foot point and its estimate is less than or equals 1ms. In the bottom straight-line and forefront tangent intersection method, the error dispersion varies from ±0ms to ±12ms with respect to the noise level in the signal. However, when the APW cubic polynomial fit method is applied, the error dispersion varies from ±0ms to ±6ms.

Thus, when the analyzed signal contains noise, the APW cubic polynomial fit method is the most precise, as it results in the least error dispersion and the best agreement between the foot estimate values and the reference value of the APW.

As the results obtained in the experiment show, methods which are based on point-to-point (from the ECG R peak point to the APW foot point, or between the foot points of two PWs) estimation of PTT time are highly affected by noise and, thus, they do not permit reliable results. In order to obtain reliable results, it is necessary to apply methods according to which PTT time is calculated as a delay between two APW segments, least affected by noise and exposing the least value dispersion.

References

[1] R. **Asmar, A. Benetos, J. Topouchian, P. Laurent, B. Pannier, A. Brisac, R. Target, B.I. Levy.** Assesment of arterial distendibiliy by automatic pulse-wave velocity measurement: validation and clinical application studies. 1995, *Hypertension Dallas* 26, 485-490.

[2] **A.P. Avolio, S.G. Chen, R.P. Wang, C.L. Zhang, M.F. Li, M.F. O'Rourke.** Effects of aging on changing arterial compliance and left ventricular load in a northern Chinese urban community. *Circulation* 1983, 68, 50-58.

[3] **A.D. Blann, U. Kirkpatrick, C. Devine, S. Naser, C.N. McCollum.** The influence of acute smoking on leucocytes, platelets and the endothelium. *Atherosclerosis* 1998, 141, 133-139.

[4] **J.M. Bland, D.G. Altman.** Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* (1986); 1, 307-310.

[5] British Standards Institution. *Precision of Test Methods, 1: Guide for the Determination of Reproducibility for a Standard Test Method. London, England: British Standards Institution;* 1979, *BS* 5497, *part* 1.

[6] **J.N. Cohn, S. Finkelstein, G. McVeigh, D. Morgan, L. LeMay, J. Robinson, Mock.** Noninvasive pulse-wave analysis for the early detection of vascular disease. *Hypertension Dallas* 26, 1995, 503-508.

[7] **F.M. Gary, M.A. Pfeffer, P.V. Finn, J.M. Pfeffer.** Comparison of techniques for measuring pulse-wave velocity in the rat. *J.Appl Physiol* 1997, 82(1), 203-210.

[8] **X. Girerd, S. Laurent, B. Pannier, R. Asmar, M. Safar.** Arterial distensibility and left ventricular hypertrophy in patients with sustained essential hypertension. *Am. Heart J.* 1991, 122, 1210-1214.

[9] **R.N. Isnard, B.M. Pannier, S. Laurent, G.M. London, B.Diebold, M.E. Safar.** Pulsatile diameter and elastic modulus of the aortic arch in essential hypertension: noninvasive study. *J. Am. Coll. Cardiol*, 1989, 13, 399-405.

[10] **T. Kanda, E. Nakamura, T. Moritani, Y. Yamori.** Arterial pulse wave velocity and risk factors for peripheral vascular disease. *Eur. J App Physiol* 2000, 82, 1-7.

[11] **D.A. McDonald.** Regional pulse-wave velocity in the arterial tree. *J.Appl Physiol*, 1976, 24, 73-78.

[12] E. **Nakamura, T. Moritani, A. Kanetaka.** Further evaluation of physical fitness age versus physiological age in women. *Eur J.Appl Physiol* 1998, 78, 195-200.

[13] **E. Nakamura, T. Moritani, A. Kanetaka.** Biological age versus physical fitness age in women. *Eur.J.Appl Physiol* 1990, 61, 202-208.

[14] **E. Nakamura, T. Moritani, A. Kanetaka.** Effects of habitual physical exercise on physiological age in men aged 20±85 years as estimated using principal component analysis. *Eur.J.Appl Physiol* 1996, 73, 410-418.

[15] **J. Nilsson**. Growth factors and the pathogenesis of atherosclerosis. *Atherosclerosis* 1986, 62, 185-199.

[16] **M.F. O'Rourke, G. Mancia.** Arterial stiffness (editorial). *J.Hypertens* 1999, 17, 1-4.

[17] **K.G. Reddy, R. Nair, H.M. Sheehan, J.M. Hodgson.** Evidence that selective endothelial dysfunction may occur in the absence of angiographic or ultrasound atherosclerosis in patients with risk factors for atherosclerosis. *JACC* 1994, 23, 833-843.

[18] **A.C. Simon, J. Levenson, J.D. Boutheir, M.E. Safar, A.O. Avolio.** Evidence of early degenerative changes in large arteries in human essential hypertension. *Hypertension* 1985, 7, 675.

[19] **S. Yoshimura, J. Sugai, J. Hashimoto.** An estimation of arteriosclerosis by the measurement of pulse wave velocity and an analysis of the clinical effect of therapeutic agents on atherosclerosis. *Cor Vasa* 1968, 10, 173-182.

[20] **S. Yoshimura, M. Hasegawa, Y. Yabe.** Correlation between aortic pulse wave velocity and arteriosclerosis. *Jpn.J.Clin Pathol* 1973, 21, 79-86.

[21] ISO 3534-1, "Statistics - Vocabulary and symbols – Part 1: Probability and general statistical terms".

[22] International Organization for Standardization. Accuracy (trueness and precision) of measurement methods and results. *Part* 1: *general principles and definitions* (ISO 5725-1). *Geneva, Switzerland*: ISO, 1994.