BIOMEDICAL
ENGINEERING

Photoplethysmographic signal rising front analysis for the discrimination of subjects with increased arterial ageing

Kristjan Pilt[*], Kalju Meigas, Kristina Kööts, and Margus Viigimaa

Department of Biomedical Engineering, Technomedicum, Tallinn University of Technology, Ehitajate tee 5, 19086 Tallinn, Estonia

Abstract. This study analyses the photoplethysmographic (PPG) signal waveform rising front in order to discriminate subjects with premature increase in arterial ageing. As a reference measure for the evaluation of the arterial system, the aortic augmentation index ($AIx@75$) was calculated using a SphygmoCor device. The study was carried out on 24 healthy subjects and 20 diabetes patients. Negative correlation relationships ($r = -0.68$ and $r = -0.77$) were found between the age and the slopes of the PPG signal. Significant differences were found between the healthy controls and diabetes patients. The highest difference between the two groups was found using the advanced signal processing algorithm for the slope calculation. The sensitivity, specificity, and accuracy of the method were 85%, 88%, and 86%, respectively. We conclude that the PPG technology with the advanced signal processing algorithm can be used for the discrimination of subjects with increased arterial ageing. This method gives the possibility to diagnose cardiovascular diseases in an early stadium.

Key words: photoplethysmography, waveform analysis, arterial stiffness, augmentation index.

1. INTRODUCTION

Increased arterial stiffness has been reported as one of the markers of cardiovascular damage [1]. Non-invasive methods and devices have been developed to evaluate the arterial system and to diagnose a cardiovascular disease in the early stage [2,3]. The SphygmoCor system can be used to estimate the aortic augmentation index (*AIx*) [4]. The *AIx* has been considered as an independent predictor of mortality and cardiovascular events [5,6]. In addition, *AIx* has been found to increase through ageing [7]. The values are higher on the patients with type I diabetes [8] and hypercholesterolemia [9], which can be explained by premature arterial ageing [10,11]. However, the SphygmoCor system is operator dependent and the measurements are often time consuming. A simple, inexpensive and operator independent method is needed to assess cardiovascular risk in the screenings of large populations.

The photoplethysmographic (PPG) technique has been considered as a simple and inexpensive technology for pulse wave recording. The analysis of the finger PPG waveform has been used as a non-invasive method to assess arterial stiffness [12,13]. PPG is a ubiquitous optical technique, based on the measurement of changes in blood circulation in the vascular bed of a tissue. PPG sensors are simple and inexpensive devices, consisting of a light emitting diode (LED) and a photodetector (PD) [14]. In the case of a finger clip sensor, light is emitted from the LED to the tissue and a small fraction of emitted photons is detected by the PD, placed on the opposite side of the finger. The AC component of the PPG signal is synchronous [15] with the heart rate and depends on the changes in the pulsatile pressure and blood volume.

The changes in the AC component waveform of the finger PPG signal, related to the arterial stiffness and cardiovascular ageing, have been investigated by different sophisticated methods in the time and frequency domain [12, 16–18]. In addition, the systolic

---

[*] Corresponding author, kristjan.pilt@cb.ttu.ee

and diastolic part of the PPG signal is successfully analysed through the waveform decomposition into Gaussian functions [19]. The slope of the PPG signal raising front has been analysed during the cold pressor test in order to monitor cardiovascular and nervous system reactivity [20]. In our pilot study we analysed the slope changes, caused by cold and warm stimulation [21]. In addition, it was found that the slope of the raising front of the PPG signal depends on the subject's age. It was found that slope of the raising front decreases in proportion to the increase of the subject's age. Similar results were found in the exhaustive study on population of healthy subjects, where the dependence of the slope of the PPG signal raising front on the age was investigated [22].

Focus here is on the analysis of the possibilities to use the slope of the PPG signal waveform for the discrimination of the subjects with accelerated arterial ageing, which is related to the premature increase in arterial stiffness. Compared to the study by Zahedi et al. [22] the signal processing algorithm for the raising front slope calculation is improved for better discrimination of the subjects. In addition, in this study the group of diabetes patients is included in order to test the methodology. The SphygmoCor system was used as a reference method for cardiovascular system age evaluation through aortic *AIx* calculation.

2. METHODS

2.1. Subjects

The study was performed in accordance with the Declaration of Helsinki and formally approved by the Tallinn Ethics Committee on Medical Research. The experiments were conducted in the North Estonia Medical Centre. The signals were recorded from 24 healthy subjects (mean age 41 ± 13 years) and 20 type II diabetes patients (mean age 44 ± 14 years). The subjects in the group of healthy controls were not on permanent medication and they were engaged in some physical activity at least once a week. The subjects were in supine position at least 10 min prior to and during the recording of the signals. During the experiments the room temperature was kept constant at around $23 \pm 1\,°C$.

2.2. Instrumentation

As a reference, the aortic *AIx* was estimated with the SphygmoCor (AtCor Medical, Australia) device. The pressure waves were recorded from the left hand radial artery by the sensitive wide band piezoelectric sensor [4]. On all the subjects, the operator index above 85 was achieved. The aortic pressure waveform was derived from the radial artery waveform using the validated generalized transfer function [23], illustrated in Fig. 1.
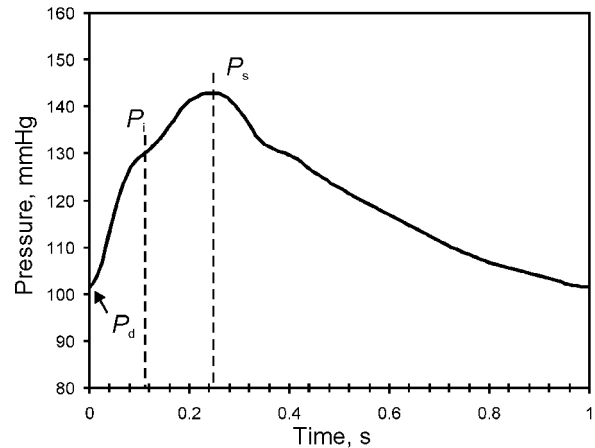

Fig. 1. Aortic pressure waveform with detected characteristic points P_d, P_i, and P_s for the *AIx* calculation.

The aortic *AIx* was estimated by SphygmoCor device and the augmentation pressure was divided with the pulse pressure [24], calculated as

$$AIx = \frac{P_s - P_i}{P_s - P_d},\qquad(1)$$

where P_s is systolic pressure, P_d is diastolic pressure, and P_i is the pressure value at the inflection point, which is detected from the fourth derivative of the pressure waveform [7]. According to Wilkinson et al. [25], the aortic *AIx* depends on the heart rate and the SphygmoCor normalizes the *AIx* to the heart rate of 75 bpm. The normalized *AIx* is denoted as *AIx@75*.

During the experiments, the pressure waveforms were recorded firstly with the SphygmoCor device. After that the physiological signals were recorded by the experimental measurement complex, described in [26]. The PPG signal was recorded from the index finger using the commercially available Envitec F-3222-12 finger clip sensor (Honeywell, Germany). The infrared LED of the sensor at a peak value of 880 nm was used. The sensor was connected to the lab-built PPG module, where the current of the LED was controlled and the photocurrent of the PD was converted to the voltage signal. The PPG module was connected to the PCI MIO-16-1 data acquisition card (National Instruments, USA) and the analogue PPG signal was digitized with a sampling frequency of 1 kHz. One minute long PPG signals were recorded from the left hand index finger of the subject.

2.3. Analysis of the signals

The recorded PPG signals were post-processed in MATLAB (Mathworks, USA). The PPG signals were filtered with high- and low-pass filters. The cut-off

frequencies were 0.5 Hz (order of the filter 4000) and 15 Hz (order of the filter 500), respectively. The filter was designed using the window method, with the Hamming window function.

The slope of the PPG signal rising front was calculated on the basis of the study by Zahedi et al. [22]. The first derivative signal $x'[n]$ (n is the number of the sample) was calculated from the PPG signal $x[n]$. For each recurrence, the maximal point m was detected from the first derivative signal. In addition, the amplitude of the PPG signal A_{PPG} was calculated for each recurrence (Fig. 2). The slope of the raising front of the PPG signal S_r was calculated for each recurrence as

$$S_r = \frac{x'[m]}{0.001} \cdot \frac{1}{A_{PPG}}. \qquad (2)$$

For each PPG signal, the average slope S_{rav} and the standard deviation were calculated.

The raising front of the PPG signal depends on the heart rate. With higher heart rate the waveform front tends to increase. The previously described and used algorithm [22] is not taking into account the changes in the heart rate. In this study we used the new PPG signal processing algorithm in order to compensate the effect of the heart rate on the slope calculation. The recorded PPG signals were postprocessed in MATLAB using the

algorithm described in [27]. The algorithm resamples the signal so that each recurrence in the signal contains an equal number of samples. This means that all the recurrences are normalized to the same length, i.e., to the same heart rate. All the recurrences were normalized to the length of 1 s, which corresponds to the heart rate of 60 bpm. Further, the signal was low-pass filtered using the Parks–McClellan low pass filter. According to our previous study [27], the following filter parameters were used: edge frequency 6 Hz, transition band 1 Hz, pass and stop band maximum allowable errors 0.001. As a result, all the recurrences of the PPG signal were limited equally with the same number of harmonic components. The slope of the raising front, denoted as S_n, was calculated for each recurrence using Eq. (1). Similarly, the average slope S_{norm} and the standard deviation were calculated to compare the results.

3. RESULTS

The average heart rates of healthy controls and diabetes patients are 66 ± 6 bpm and 78 ± 15 bpm, respectively. Figures 3a and c show the relationship between the age and the slopes of S_{rav} and S_{norm}. The data points are given with standard deviation bars. Similarly, Fig. 3e presents the relationship between the age and $AIx@75$. For each parameter, the regression lines and models are given. In addition, Pearson's correlation coefficient was calculated for each parameter using data points from healthy subjects.

For clarity, the Bland–Altman plots for each parameter are compared in Figs 3b, d, and f. A paired t-test was carried out in order to analyse the group differences between the healthy controls and diabetes patients. The t-test was carried out in MS Excel (Microsoft, USA) assuming unequal variances with $\alpha = 0.05$. A significant difference was found between the groups of healthy controls and diabetes patients ($P < 0.0001$) at $AIx@75$ and slope S_{norm}. The differences found between the two groups have a 1.4% probability of occurring by chance alone at slope S_{rav}. Based on the Bland–Altman plot, the sensitivity, specificity, and accuracy for each parameter were calculated and the results are presented in Table 1.
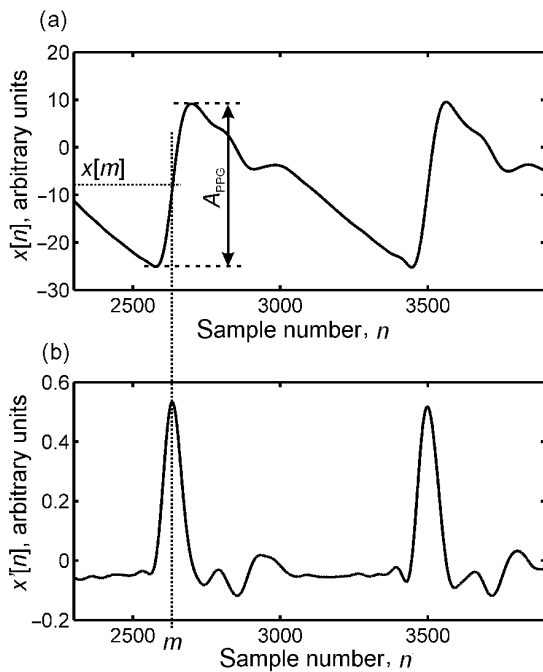

Fig. 2. The PPG signal $x[n]$ (a) and first derivative of the PPG signal $x'[n]$ (b) with detected sample number m, which marks the detected maximal point of the first derivative of the PPG signal.

Table 1. The sensitivity, specificity, and accuracy of the parameters

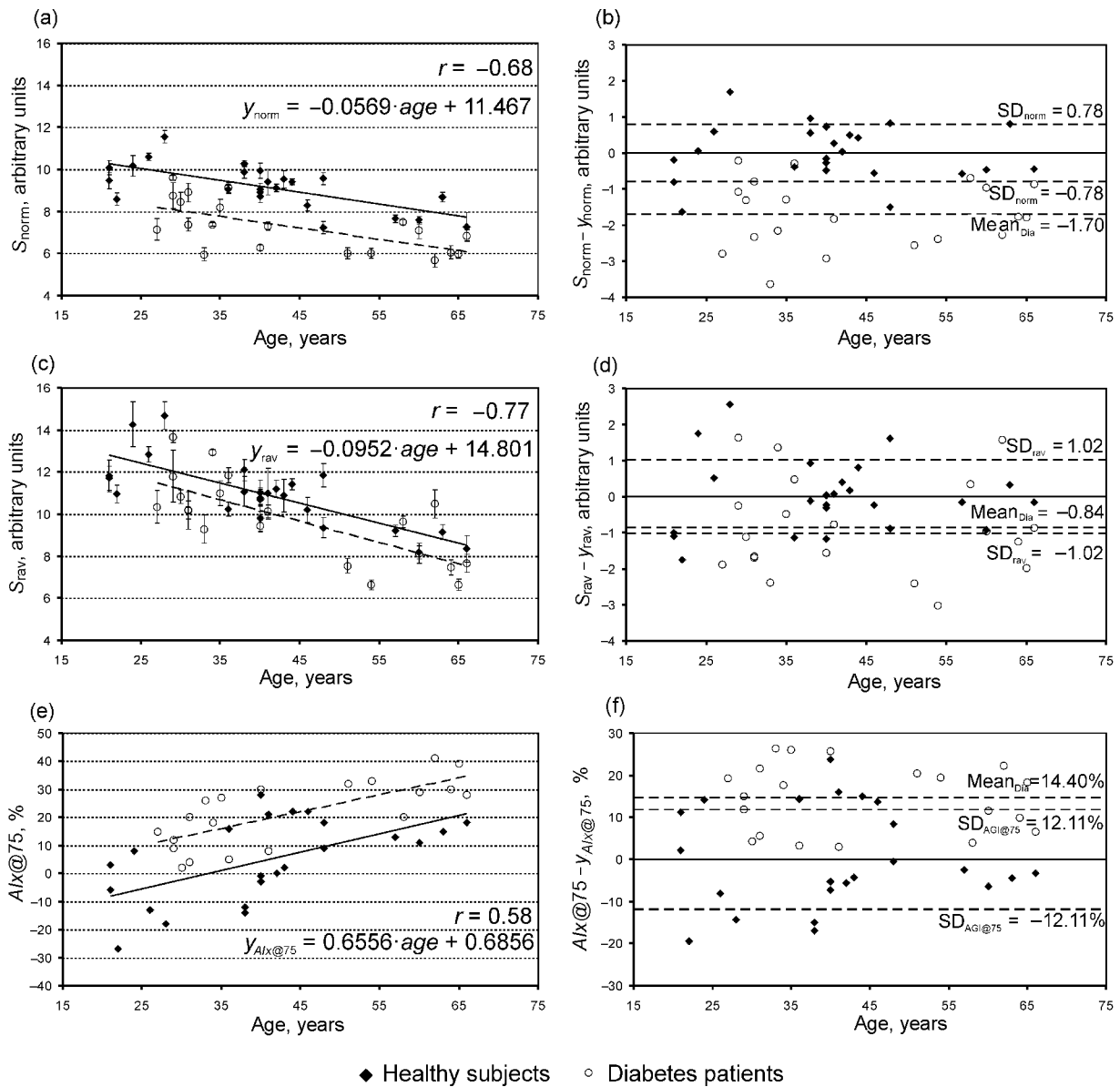|	S_{rav}, %	S_{norm}, %	$AIx@75$, %
Sensitivity	55.0	85.0	65.0
Specificity	70.8	87.5	79.2
Accuracy	63.6	86.4	72.7

◆ Healthy subjects ○ Diabetes patients

Fig. 3. The analysis of linear relationship between the calculated parameters and the subject's age. Linear relationships with Pearson's correlation coefficients between the age and the calculated parameters: (a) S_{norm}, (c) S_{rav}, and (d) $AIx@75$ with the regression models y_{norm}, y_{rav}, and $y_{AGI@75}$, respectively. Bland–Altman plots with standard deviation of models: (b) SD_{norm}, (d) SD_{rav}, and (f) $SD_{AIx@75}$ and the average difference of diabetes group $Mean_{Dia}$.

4. DISCUSSION

Figure 3a and c reveal negative linear relationship between the age and the slopes of the raising front of the PPG signal. This is in accordance with the results from our previous pilot study with a smaller number of subjects [21] and with earlier study by Zahedi et al. [22]. In addition, the positive correlation relationship was found between the age and the reference parameter $AIx@75$. Similar results were found in [7], and the

changes in the *AIx* due to the age are explained partially through the sclerotic processes in the arterial wall.

Figures 3a and c show that the absolute slope values of S_{rav} are higher than those of S_{norm}. According to the average heart rates, in most of the cases, to calculate S_{norm} the recurrences were stretched during the normalization process. This causes a decrease in the slope of the raising front. Partially, the difference in the absolute values of S_{rav} and S_{norm} can be caused by the differences in the bandwidth of the PPG signals. The bandwidth was wider at S_{rav}.

Figure 3b shows that the mean difference of the diabetes patients group, who have probable premature increase in arterial stiffness, has noticeably lower S_{norm} values than the group of healthy controls. According to Table 1, the slope of S_{norm} has higher sensitivity, specificity and accuracy compared to the slope S_{rav}. This shows that to improve the discrimination between healthy subjects and subjects with increased arterial stiffness, the advanced signal processing can be used in the calculation of the raising front slope. Furthermore, the sensitivity, specificity and accuracy of S_{norm} are even higher at the reference methodology calculated parameter *AIx@75* (Table 1).

5. CONCLUSIONS

The possibilities to use the slope of the PPG signal waveform for the discrimination of the subjects with accelerated arterial ageing were investigated. As a reference measure for the evaluation of the arterial system age, the aortic augmentation index was calculated using a SphygmoCor device. It was found that slope of the PPG signal raising front correlates negatively with subject's age. In addition, it was found that the slope is lower in case of diabetes patients, which is related to the accelerated arterial ageing. Two groups in this study are relatively small. However, the results show a possibility to use the inexpensive PPG technology with the advanced signal processing algorithm for the discrimination of subjects with increased arterial ageing.

ACKNOWLEDGEMENTS

REFERENCES

1. Amar, J., Ruidavets, J. B., Chamontin, B., Drouet, L., and Ferrières, J. Arterial stiffness and cardiovascular risk factors in a population-based study. *J. Hypertens.*, 2001, **19**, 381–387.

2. Rajzer, M. W., Wojciechowska, W., Klocek, W., Palka, I., Brzozowska-Kiszka, M., and Kawecka-Jaszcz, K. Comparison of aortic pulse wave velocity measured by three techniques: Complior, SphygmoCor and Arteriograph. *J. Hypertens.*, 2008, **26**, 2001–2007.

3. Skilton, M. R., Boussel, L., Bonnet, F., Bernard, S., Douek, P. C., Moulin, P., and Serusclat, A. Carotid intima-media and adventitial thickening: comparison of new and established ultrasound and magnetic resonance imaging techniques. *Atherosclerosis*, 2011, **215**, 405–410.

4. Wilkinson, I. B., Fuchs, S. A., Jansen, I. M., Spratt, J. C., Murray, G. D., Cockcroft, J. R., and Webb, D. J. Reproducibility of pulse wave velocity and augmentation index measured by pulse wave analysis. *J. Hypertens.*, 1998, **16**, 2079–2084.

5. Laurent, S., Cockcroft, J., van Bortel, L., Boutouyrie, P., Giannattasio, C., Hayoz, D. et al. Expert consensus document on arterial stiffness: methodological issues and clinical applications. *Eur. Heart J.*, 2006, **27**, 2588–2605.

6. London, G. M., Blacher, J., Pannier, B., Guerin, A. P., Marchais, S. J., and Safar, M. E. Arterial wave reflections and survival in end-stage renal failure. *Hypertension*, 2001, **38**, 434–438.

7. Kelly, R., Hayward, C., Avolio, A., and O'Rourke, M. Noninvasive determination of age-related changes in the human arterial pulse. *Circulation*, 1989, **80**, 1652–1659.

8. Wilkinson, I. B., MacCallum, H., Rooijmans, D. F., Murray, G. D., Cockcroft, J. R., McKnight, J. A., and Webb, D. J. Increased augmentation index and systolic stress in type 1 diabetes mellitus. *QJM*, 2000, **93**, 441–448.

9. Wilkinson, I. B., Prasad, K., Hall, I. R., Thomas, A., MacCallum, H., Webb, D. J. et al. Increased central pulse pressure and augmentation index in subjects with hypercholesterolemia. *J. Am. Coll. Cardiol.*, 2002, **39**, 1005–1011.

10. Ravikumar, R., Deepa, R., Shanthirani, C., and Mohan, V. Comparison of carotid intima-media thickness, arterial stiffness, and brachial artery flow mediated dilatation in diabetic and nondiabetic subjects (The Chennai Urban Population Study [CUPS-9]). *Am. J. Cardiol.*, 2002, **90**, 702–707.

11. Cockcroft, J. R. and Wilkinson, I. B. Arterial stiffness and pulse contour analysis: an age old concept revisited. *Clin. Sci. (London)*, 2002, **103**, 379–380.

12. Brillante, D. G., O'Sullivan, A. J., and Howes, L. G. Arterial stiffness indices in healthy volunteers using non-invasive digital photoplethysmography. *Blood Press.*, 2008, **17**, 116–123.

13. Clarenbach, C. F., Stoewhas, A. C., van Gestel, A. J., Latshang, T. D., Lo Cascio, C. M., Bloch, K. E., and Kohler, M. Comparison of photoplethysmographic and arterial tonometry-derived indices of arterial stiffness. *Hypertens. Res.*, 2012, **35**, 228–233.

14. Allen, J. Photoplethysmography and its applications in clinical physiological measurement. *Physiol. Meas.*, 2007, **28**, R1–R39.

15. Selvaraj, N., Jaryal, A., Santhosh, J., Deepak, K. K., and Anand, S. Assessment of heart rate variability derived from finger-tip photoplethysmography as compared to electrocardiography. *J. Med. Eng. Technol.*, 2008, **32**, 479–484.

16. Korpas, D., Hálek, J., and Dolezal, L. Parameters describing the pulse wave. *Physiol. Res.*, 2009, **58**, 473–479.

17. Millasseau, S. C., Ritter, J. M., Takazawa, K., and Chowienczyk, P. J. Contour analysis of the photo-plethysmographic pulse measured at the finger. *J. Hypertens.*, 2006, **24**, 1449–1456.

18. Sherebrin, M. H. and Sherebrin, R. Z. Frequency analysis of the Peripheral Pulse Wave detected in the finger with a photoplethysmograph. *IEEE Trans. Biomed. Eng.*, 1990, **37**, 313–317.

19. Rubins, U. Finger and ear photoplethysmogram waveform analysis by fitting with Gaussians. *Med. Biol. Eng. Comput.*, 2008, **46**, 1271–1276.

20. Selvaraj, N., Jaryal, A., Santhosh, J., Deepak, K. K., and Anand, S. Monitoring of cardiovascular reactivity during cold pressor test using photoplethysmography. In *IEEE Proc. International Conference on Signal Processing*. Chennai, 2008, 363–367.

21. Pilt, K., Meigas, K., Temitski, K., and Viigimaa, M. The effect of local cold and warm exposure on index finger photoplethysmographic signal waveform. In *Proc. 35th Annual International Conference of the IEEE EMBS*. Osaka, 2013, 2300–2303.

22. Zahedi, E., Chellappan, K., Ali, M. A., and Singh, H. Analysis of the effect of ageing on rising edge characteristics of the photoplethysmogram using a modified Windkessel model. *Cardiovasc. Eng.*, 2007, **7**, 172–181.

23. Chen, C. H., Nevo, E., Fetics, B., Pak, P. H., Yin, F. C., Maughan, W. L., and Kass, D. A. Estimation of central aortic pressure waveform by mathematical transformation of radial tonometry pressure: validation of generalized transfer function. *Circulation*, 1997, **95**, 1827–1836.

24. Murgo, J. P., Westerhof, N., Giolma, J. P., and Altobelli, S. A. Aortic input impedance in normal man: relationship to pressure wave forms. *Circulation*, 1980, **62**, 105–116.

25. Wilkinson, I. B., MacCallum, H., Flint, L., Cockcroft, J. R., Newby, D. E., and Webb, D. J. The influence of heart rate on augmentation index and central arterial pressure in humans. *J. Physiol.*, 2000, **525**, 263–270.

26. Pilt, K., Meigas, K., Viigimaa, M., Temitski, K., and Kaik, J. An experimental measurement complex for probable estimation of arterial stiffness. In *Proc. 32nd International Conference of the IEEE Engineering in Medicine and Biology Society*. Buenos Aires, 2010, 194–197.

27. Pilt, K., Ferenets, R., Meigas, K., Lindberg, L.-G., Temitski, K., and Viigimaa, M. New photoplethysmographic signal analysis algorithm for arterial stiffness estimation. *The Scientific World Journal*, 2013, **2013**(2013), 9 pp.

Fotopletüsmograafilise signaali analüüs kiirenenud arterite vananemisega uuritavate eristamiseks

Kristjan Pilt, Kalju Meigas, Kristina Kööts ja Margus Viigimaa

Uurimistöö eesmärgiks oli analüüsida fotopletüsmograafilise (PPG) signaali lainekuju tõusvat fronti, eristamaks kiirenenud arterite vananemisega uuritavaid tervetest. Arteriaalse süsteemi seisundi ja bioloogilise vanuse hindamiseks kasutati võrdlusena aordi augmentatsiooniindeksit (*AIx*), mis määrati SphygmoCor-i seadmega. Uuring viidi läbi 24 tervel ja 20 diabeeti põdeval patsiendil. Omavahel korreleerusid negatiivselt ($r = -0{,}68$ ja $r = -0{,}77$) vanus ning kahe erineva meetodiga arvutatud PPG-signaali tõusva frondi tõusud. Statistiliselt olulised erinevused leiti kahe uuritavate grupi vahel kõikide parameetrite korral. Suurim erinevus kahe grupi vahel leiti PPG-signaali frondi tõusus, mille arvutamiseks kasutati edasiarendatud PPG signaalitöötlusalgoritmi. Meetodi tundlikkus, spetsiifilisus ja täpsus olid vastavalt 85%, 88% ning 86%. Kokkuvõtteks võib järeldada, et PPG-signaali registreerimise meetodit koos edasiarendatud signaalitöötlusalgoritmiga saab kasutada kiirenenud arterite vananemisega uuritavate eristamiseks tervetest. Seega võimaldaks kirjeldatud meetod diagnoosida kardiovaskulaarseid haigusi varajases staadiumis.