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Bilateral photoplethysmography studies of the leg arterial stenosis

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Abstract

A newly developed portable multi-channel photoplethysmography (PPG) device has been used for comparative studies of 20 healthy control subjects and 45 patients with diagnosed arterial stenosis in a leg. The peripheral blood pulsations were detected simultaneously at four body sites—the same fingers and toes of both arms and legs. The PPG pulses recorded at the periphery of the stenotic leg, if compared with those of the healthy leg, were much weaker, with delayed arrival as a consequence of increased pulse wave transit time (PWTT) due to higher vascular resistance. The specific PWTT delays for the occluded legs were in the range of 20–80 ms, while in the case of healthy subjects the leg PPG signals arrived without delays or with smaller time-shifts not exceeding 14 ms. The reference bilateral PPG signals detected at the fingertips did not show any notable PWTT delays in both groups. Parallel measurements of local blood pressures by means of the oscillometry method with subsequent calculation of the ankle–brachial index were performed. Convincing correlation between the bilateral differences in the local blood pressure (a routine tool for diagnostics of leg stenosis) and in the corresponding PWTT delay (Pearson's coefficient $r = 0.93$), as well as between the PWTT delay and the ankle–brachial index ($r = -0.96$) has been established. From the point of view of PWTT delay, the average value of leg stenosis diagnostic threshold was established to be in the range of 23 ± 9 ms, with full reliability above 32 ms. The obtained data may find further applications in alternative methodologies for detection and/or assessment of arterial occlusions in human extremities.

Keywords: photoplethysmography, non-invasive diagnostics, bio-signal processing, cardio-vascular assessment

1. Introduction

Reflection photoplethysmography (PPG) is a non-invasive method for studying peripheral blood volume pulsations by detection and temporal analysis of skin back-scattered optical radiation. Blood pumping and transport can be monitored at different body locations—fingertips, earlobes, forearms, forehead, etc—with relatively simple and convenient PPG contact probes. In addition to the classical single-probe technique (Hertzman 1937), several multi-channel PPG systems providing data flow from several body sites simultaneously have been developed and clinically tested over the recent years (Allen and Murray 2000, 2002, 2003, Nitzan *et al* 2002, Spigulis *et al* 2004, Spigulis 2005). The potential of the multi-channel PPG technique for clinical sensing and monitoring seems quite promising, especially regarding early detection and express-assessment of cardio-vascular pathologies (Spigulis *et al* 2004, Spigulis 2005). Direct measurements of the heartbeat pulse wave transit time (PWTT) offered by the multi-channel PPG technique (Nitzan *et al* 2002, Allen and Murray 2002, Spigulis *et al* 2004, Spigulis 2005) make it possible to estimate the arterial compliance, a physiologically significant parameter.

Bilateral photoplethysmography (Allen and Murray 2000) compares two PPG signal sequences recorded at anatomically symmetric sites of the human body (e.g. both earlobes or both index fingers), trying to extract physiologically important information from the observed differences. Allen and Murray (2002, 2003) studied large groups of healthy individuals and found their bilateral pulse wave characteristics at the ears, thumbs and toes from the points of view of PPG signal shapes and temporal characteristics (mean delays 0.9–1.5 ms).

Regarding the bilateral PPG studies in the cases of one-side vascular pathologies, there are only few qualitative observations of pulse shape deformations and temporal delays (Allen and Murray 2000, Spigulis *et al* 2004, Spigulis 2005). To the authors' knowledge, no systematic quantitative investigations of these features in larger patient groups have been reported so far. The present work is aimed at filling this gap with respect to patients having arterial stenosis in a leg. Using the originally developed four-channel PPG technology (Spigulis *et al* 2004), bilateral measurements were taken in representative groups of leg stenosis patients and healthy volunteers.

2. Technical details

2.1. Design of the device

2.1.1. Hardware. A schematic diagram of the device used in the study is shown in figure 1(a). It comprises four optical contact probes (applied simultaneously during the measurements) and a bio-signal acquisition/conversion circuit.

Each optoelectronic contact probe (figure 1(b)) emits cw-radiation into the skin tissues and detects the back-scattered radiation; the separated ac-component of the signals precisely reflects the skin blood pulsations at the probe-covered volume. All the four contact probes are geometrically identical; they comprise a GaAs emitting diode (diameter of the emitting area ∼2 mm, radiant power ∼10 mW, peak wavelength ∼940 nm, estimated mean penetration depth under the skin surface ∼2–3 mm) and a Si photodiode (square detection area 5×5 mm^2). Both diodes are fixed onto the measurement site by means of a finger-clip.

The analogue signals from PPG contact probes are digitized by an analogue-to-digital converter (16-bit accuracy, sampling rate 200 Hz) and transferred to the computer. All measurement channels are synchronized using the computer; amplification circuits of all the

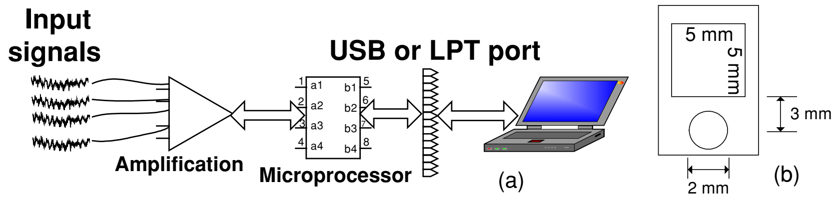

Figure 1. (a) Hardware of the device. (b) Design of the optical contact probe.

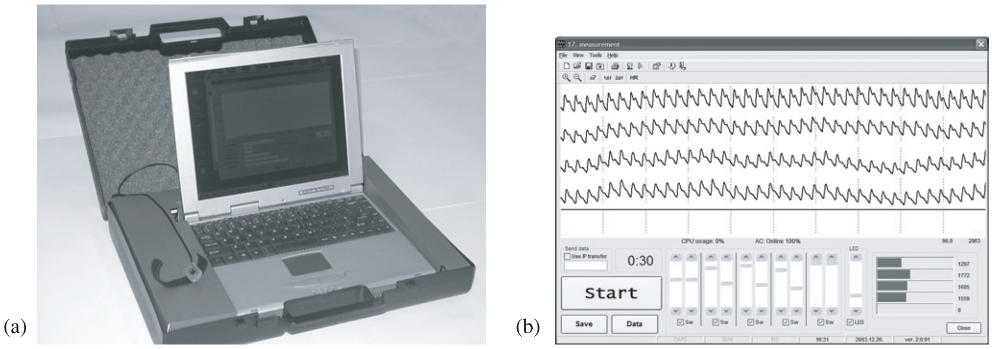

Figure 2. (a) The hand-held equipment case; (b) the PPG measurement software screenshot.

channels are identical and cause no time shift when amplification is changed. 6 ms time resolution (TR) of the system has been estimated, comprising 1 ms resolution of the PC timer and 5 ms duration between the subsequent readings.

The equipment is portable; it is placed in a hand-held case of size $44 \times 32 \times 9$ cm^3 and weight 4.1 kg (figure 2(a)); the PPG device is powered by the laptop battery and can operate up to 3 h without recharging.

2.1.2. Software. The software for multi-channel PPG measurements was developed at the University of Latvia. It was created using Microsoft Visual Studio 6.0 and consisted of three parts—for data acquisition, signal analysis and calculations. Hardware parameters such as signal amplification, LED intensity and PPG signal dc component offset were configurable through the software for each channel. The monitor screenshot in figure 2(b) demonstrates the four-channel PPG software, set in the data acquisition mode.

2.2. Subjects

A total of 45 patients (median age 65, range 55–80) and 20 healthy subjects (median age 45, range 27–70) were entered into the study. The height of the subjects was in the range of 170 ± 10 cm, and 80% of all the patients were men. As to the healthy subjects, both genders were represented in equal proportion (10/10). All the subjects were Caucasian and right-handed. A doctor checked the health condition of the 20 healthy volunteers, and none of them had any signs of cardio-vascular disease. The patients participating in the study had been diagnosed with unilateral stenosis in one leg, and many of the patients had obvious symptoms of it—pain, coldness or numbness. Skin temperature was also measured—typically 28–32 °C for healthy legs and 23–25 °C for stenotic legs. No vascular problems in the arms of all subjects were

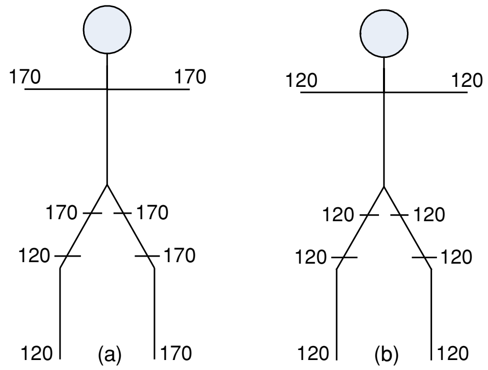

Figure 3. The local systolic blood pressure measurements: (a) patient with magistral artery stenosis in the right leg, (b) normal healthy subject.

found during the preliminary examination. None of the subjects had anatomical anomalies of the extremities (e.g., different length of the arms or legs). The subjects had not used any medications prior to the measurements.

All the patients and healthy subjects gave their informed consent to participate in the study.

2.3. *Clinical trial and protocol*

The trial was performed in hospital conditions. All the necessary measurements were taken at room temperature (23 ± 1 °C). The subjects were asked to relax for 5 min before the measurements to allow cardio-vascular stabilization. The subjects were lying in the supine position during the measurements; they were asked to breathe regularly and stay still for the measurement time. It was important to have a comfortable arm and leg position in order to keep the fingers relatively motionless for stable and repeatable recording.

During the first stage, a doctor evaluated the patients using local blood pressure measuring equipment based on arterial oscillometry (TASC Working Group 2000). Two cuffs were placed on both upper arms, on the upper and lower thighs and slightly above the ankles, and the corresponding local systolic blood pressure values were recorded. The example illustrating the results of this estimation for two subjects is shown in figure 3.

Next, the operator attached four PPG contact probes to the second fingertips and the second toes of the subject. To exclude any infection, the toe pads were cleaned with spirit. The ambient light in the room was turned off during the measurements. The PPG signals from all channels were recorded for 2 min, the time sufficient to collect reliable data and to avoid the influence of possible artefacts.

2.4. *PPG signal analysis*

Initially the pulses in all four channels were smoothed in order to reduce the random noise by moving average of three neighbouring points, and the pulses with visible artefacts were discarded. Time delay between the PPG pulse sequences (TD) was calculated in real time with 4 s period using the signal minima as references—see figures 4(a) and (b). The obtained data, typically about 100 readings per patient, were stored digitally for further analysis.

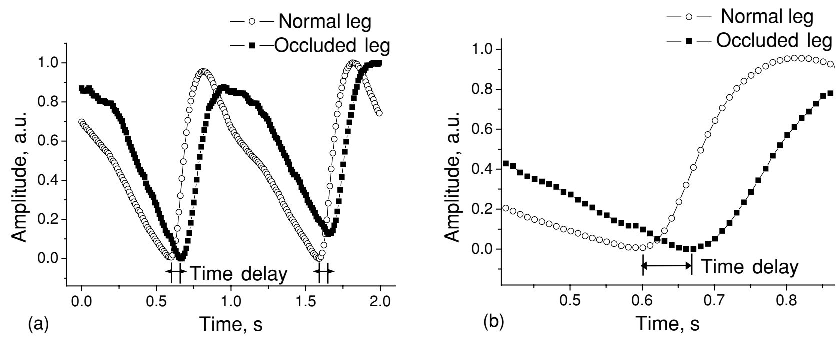

Figure 4. (a) Exploiting the minima of PPG signals for determination of the time delay. (b) The signal from the occluded leg is delayed for about 70 ms in this case.

The standard deviation SD of the time delay values for each subject was calculated as

$$\mathrm{SD} = \frac{1}{n-1}\left[\sum_{n}(\mathrm{TD}_i - \bar{\mathrm{T}}\bar{\mathrm{D}})^2\right]^{1/2}, \tag{1}$$

where n is the number of successful readings, TD_i the actual reading of the time delay and $\bar{\mathrm{T}}\bar{\mathrm{D}}$ is the average of the range. The total uncertainty of the PWTT delay values for a single subject was calculated as

$$\Delta = \sqrt{\mathrm{SD}^2 + \mathrm{TR}^2}, \tag{2}$$

where SD is the standard deviation and TR is the time resolution of the system. The uncertainty of the PWTT delay mean value for a group of subjects was calculated as

$$\Lambda = \frac{1}{n}\sum_{n}\Delta_n, \tag{3}$$

where n is the number of samples in the group and Δ_n is the total uncertainty for a single subject of the group.

Pearson's coefficient (Freedman *et al* 1998) was used to correlate the obtained TD values with the local systolic blood pressure differences PD:

$$r = \frac{\sum_n \{(\mathrm{TD}_i - \overline{\mathrm{TD}})(\mathrm{PD}_i - \overline{\mathrm{PD}})\}}{\sum_n (\mathrm{TD}_i - \overline{\mathrm{TD}})^2}. \tag{4}$$

The r values in the range of 0–0.5 are related to weak positive relationships, the values 0.5–0.9 to moderate and the values 0.9–1 to strong correlation (Freedman *et al* 1998).

All the statistical calculations were done using the SigmaStat 3.1 software (SPSS Inc., Chicago, USA). A 95% confidence interval was chosen.

2.5. *Estimation of the ankle–brachial index*

The ankle–arm pressure index (also known as the ankle–brachial index or ABI) compares the systolic blood pressure of the ankle to that of the arm (brachial):

$$\mathrm{ABI} = \frac{P_{\mathrm{ankle}}}{P_{\mathrm{brachial}}}. \tag{5}$$

These measurements are useful in the assessment, follow-up and treatment of patients with peripheral vascular disease. A normal ankle–brachial index value is in the range of 1–1.1.

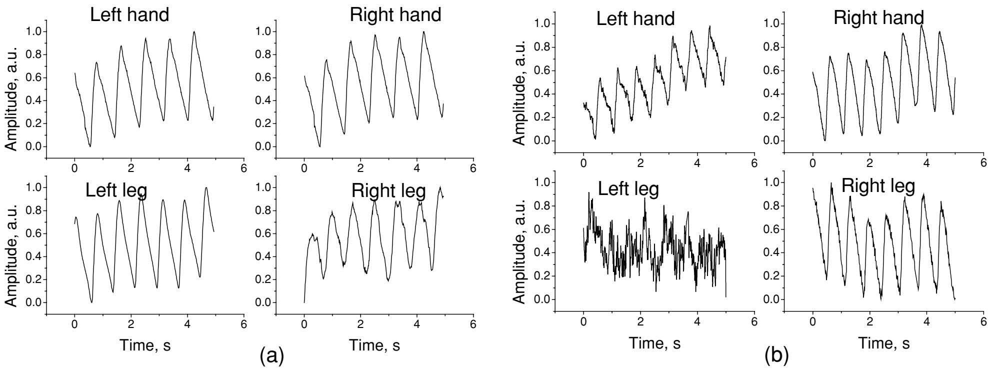

Figure 5. (a) An example of sufficient quality PPG signals with clear pulsations from a unilateral right leg stenosis patient. (b) The signals obtained from another patient with the same diagnosis. Pulsations from the left leg are hardly distinguishable.

This means that blood pressure at the ankle is the same or a little higher than that at the arm, and there are no signs of significant narrowing or blockage of blood flow. ABI values below 0.95 indicate narrowing of one or more blood vessels in the legs. If ABI < 0.8, pain in the foot, leg or buttock may occur during exercise. ABI values of 0.25 or below are related to severe limb-threatening peripheral vascular disease (Creager and Libby 2001).

3. Results

The quality of dual-channel PPG signals obtained from the toes was sufficient to determine TD for all the healthy volunteers (20 subjects) and in 88% of cases for the patients (40 subjects). The signals captured from the occluded leg of the remaining five patients were indistinguishable from noise, indicating that the blood flow pulsations in these cases had been practically blocked due to the arterial occlusions. Figure 5 gives examples of both sufficient (a) and insufficient (b) quality signals from the unilateral stenosis patients.

The shapes of PPG signals taken from healthy volunteers and from patients with unilateral leg stenosis were substantially different. For example, we compared the signals of right–left toes obtained from two subjects of similar age. The patient, a male of age 65, had arterial occlusion in his left leg, diagnosed by the local blood pressure examinations. A fragment of his two-channel peripheral PPG signal sequence is presented in figure 6(a). There is a clear difference in shapes of both toe-signals (figures 6(a) and (b)). To compare, in the case of a somewhat older healthy volunteer (figure 6(b)) the PPG signal shapes in two channels were much more similar (figures 6(a) and (b)).

Another interesting feature of signals taken in the cases of unilateral stenosis is the considerably drifting PWTT delay time. As an example, the TD variations for the 65 year-old patient with a diagnosis of one-side arterial occlusion and a local systolic blood pressure difference 50 mmHg, ranged during 2 min between 40 and 80 ms (average time delay 58 ms), as illustrated in figure 7(a). In the case of a 69 year-old healthy volunteer the delay time varied around zero with amplitude less than 5 ms (figure 7(b)). Consequently, the absolute TD drift values in the case of the patient were considerably higher.

The main clinical data of this study are collected in table 1.

Figure 8 illustrates the obtained relationship between PD and TD. The corresponding value 0.93 of Pearson's coefficient (4) shows a good correlation between the TD and PD

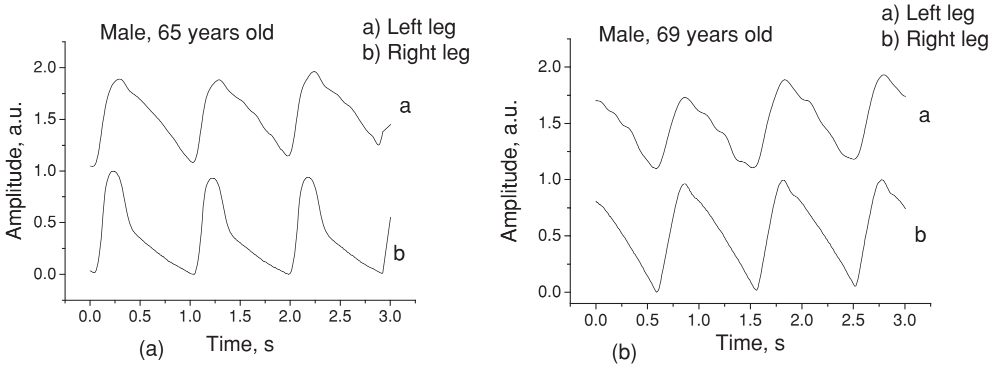

Figure 6. Comparison of the four-channel 3 s PPG recordings taken from a patient with signs of left leg occlusion (a) and from a healthy volunteer (b). Both subjects are of similar age.

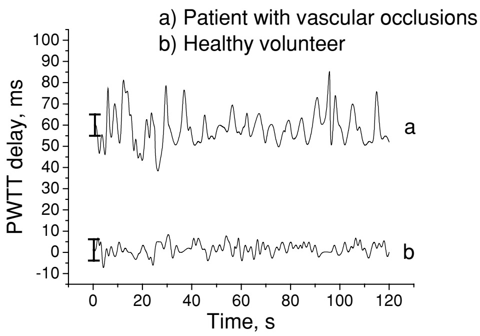

Figure 7. Drift of the TD values detected from the toes of both legs for (a) patient and (b) healthy subject. In the case of the patient the drift clearly exceeds the measurement error.

Table 1. Bilateral pressure differences (PD), PWTT delays (TD) and ankle–brachial index (ABI) for the investigated subject groups.

Extremities	PD (mmHg)	Number of subjects	TD (SD) (ms)	ABI
Healthy subjects' arms	<10	20	7(4)	
Patient arms	<10	45	8(3)	
Healthy subjects' legs	<10	20	8(4)	1.0–1.1
Patients legs	20	3	23(7)	0.85–0.95
	30	5	31(6)	0.7–0.8
	40	10	41(10)	0.65–0.75
	50	12	53(6)	0.5–0.6
	60	6	63(9)	0.4–0.55
	70	4	78(13)	0.25–0.45

values in both groups of subjects. The approximated linear dependence can be expressed as TD (ms) = $-2.98 + 1.15 \times$ PD (mmHg).

The relationship between the ABI and TD values in the patient group is illustrated at figure 9. The corresponding value of Pearson's coefficient is -0.96, confirming a strong correlation. The approximated linear dependence can be expressed as TD (ms) = $129 - 124 \times$ ABI. One can note that the approximation line crosses the ABI axis at the value about 1.05 that corresponds to the healthy state.

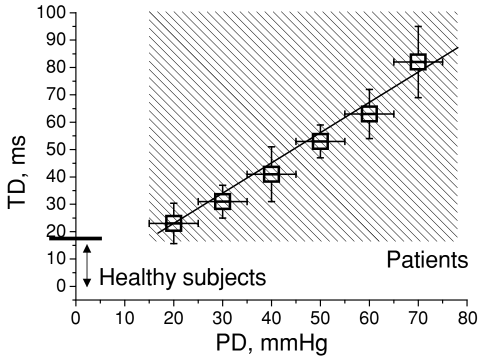

Figure 8. The correlation of PD and TD values in the unilateral leg stenosis patient group.

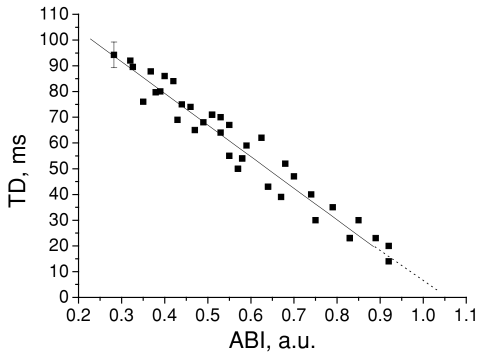

Figure 9. The correlation of ABI and TD values for the patient group.

A certain TD is inherent also to those supposed as healthy subjects. This may be caused by certain bilateral discrepancies in the PD between the extremities (below 10 mmHg, the accuracy limit of the local BP measurements) and possible individual anatomic peculiarities. The mean values of the TD differences between the right and left sides in the healthy subject group were determined as 2.0 ms for the arms and 0.2 ms for the toes; they generally agreed with the data of other authors (Allen and Murray 2002). However, the calculated values of standard deviation (1) were much higher—7.1 ms for arms and 8.4 ms for legs, with the maximum deviation 12 ms and 13 ms, respectively.

4. Discussion and summary

The results obtained in this study show a convincing correlation between the local blood pressure differences (used as a routine tool for unilateral stenosis diagnostics) and the PWTT delay values measured by means of the multi-channel PPG technique. The data obtained from the PPG estimation demonstrated a linear correlation with the bilateral local blood pressure differences in the range of 10–70 mmHg. The maximum observed TD value for the healthy volunteers did not exceed the minimum value obtained from patients with unilateral stenosis of a leg. The correlation between TD and ABI (figure 9) has also been established. A quantitave threshold of the TD values that are characteristic for the leg stenosis patients can be evaluated from the presented data; if analysing the results accordingly to formula (3), the threshold is

23 ± 9 ms (figure 8). Taking into account possible uncertainties and statistical distributions, we could estimate also the 'confidence threshold'—the TD value that most probably relates to the unilateral leg stenosis. This value was determined to be 32 ms.

The PPG parameters that additionally might be used for assessment of unilateral stenosis are the signal pulse shape deformation (figure 6) and the characteristic drift of the TD values in real time (figure 7).

The newly developed multi-channel PPG system showed good potential for clinical measurements; it could also be useful for GPs and convenient for home care. This refers particularly to older subjects, especially if they start to feel numbness and/or pain in one extremity. Regular PPG measurements would help us to assess the disease at an early stage and convince the patient to consult a doctor in order to avoid serious complications. As to the clinical applications of the described methodology, in the future it might be an alternative to more time-consuming methods used today for detecting vascular diseases.

No patients of bilateral stenosis were entered in our study. The discussion is open as to whether it is possible to detect PWTT delays and assess this disease by using the multi-channel PPG technique. In our opinion, the main course of future action should be focused to analyse the shape differences of the PPG pulses, frequency analysis of the signals and PWTT delays.

The results of this study indicate that the PPG technique may have the potential of being used as a tool for estimation of the extent to which the disease has affected the vessel. Similarly as the PD approximately indicates the degree of narrowing in the blood passage, the TD also varies depending on the degree of occlusion in the vessel. In general, the approach as described here could be extended for assessment of unilateral stenosis in arms as well; however, this requires further studies.

5. Conclusion

The PWTT delay obtained from analysis of bilateral PPG signals seems to be a useful parameter for assessment of unilateral arterial stenosis. To determine more precise values of the diagnostic threshold and the PD–TD and the ABI–TD correlation coefficients, better accuracy of local blood pressure measurements (e.g. by means of the Doppler technique) and higher time resolution of the PPG system would be needed. The originally developed measurement system has proved reliable for data capture and estimates of the PWTT delay values in real time.

Acknowledgments

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