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Andris Grabovskis
Zbignevs Marcinkevics
Uldis Rubins
Edgars Kviesis-Kipge

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Andris Grabovskis,[a] Zbignevs Marcinkevics,[b] Uldis Rubins,[a] and Edgars Kviesis-Kipge[a]
[a]University of Latvia, Institute of Atomic Physics and Spectroscopy, Raina Boulevard 19, Riga, LV-1586, Latvia
[b]University of Latvia, Department of Human and Animal Physiology, Raina Boulevard 19, Riga, LV-1586, Latvia

Abstract. Currently, photoplethysmography (PPG) is a frequently studied optical blood pulsation detection technique among biophotonic and biomedical researchers due to the fact that it shows high potential for estimating the arterial stiffness (AS). The extraction of diagnostically useful information requires standardized measurement procedure with good repeatability. However, the effects of a crucially important factor—the optimal contact pressure (CP) of the probe—are often ignored. Also, CP values are not reported to evaluate those effects. It is hypothesized that AS estimated from PPG pulse wave 2nd derivative parameter b/a is strongly inconsistent when recorded at nonoptimal probe CP. Our pilot study confirmed this during *in vivo* PPG recordings from conduit artery sites on five healthy subjects at variable probe CP (0 to 15 kPa) by using 880 nm reflectance type sensor, force transducer, and PPG alternating current (AC) signal pulse area derived optimal CP criterion. The b/a values, calculated from PPG with variable CP, showed variation >300 percent. In contrast, at the optimal CP, the b/a showed high repeatability (coefficient of variability <5 percent). The effect has been explained with exponential pulse pressure-volume relationship model which indicates the optimal CP range. [DOI: 10.1117/1.JBO.18.2.027004]

Keywords: arterial photoplethysmography; arterial stiffness; probe contact pressure; transmural pressure.

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1 Introduction

Inadequate alterations of arterial stiffness (AS) are known to be a timely, determinable indicator of endothelial dysfunction.[1] AS is a term widely used by clinicians to describe the elastic properties of the arterial wall and is directly proportional to the Peterson modulus.[1,2] Recent studies demonstrate that the stiffness of the conduit arteries is recognized as an important contributor to the development of cardiovascular disease as well as an independent predictor of cardiovascular morbidity and mortality, which includes hypertension and end-stage renal disease in general population.[3–5] The noninvasive assessment of AS consists of three main approaches, which include pulse wave velocity (PWV) measurement, pulse pressure or blood flow waveform analysis, and distensibility measurements of arterial pressure and diameter.[6] Photoplethysmography (PPG) is a simple, and promising, optical method for the stiffness evaluation using the signal pulse wave contour analysis and aforementioned PWV approaches even though the optical collection of reliable physiological information from the conduit arteries is still a challenging and controversial issue. There are a limited number of papers related to this technique.[7–10] The oldest, and most investigated, method for stiffness assessment is the PWV determination as it was suggested to be the gold standard.[11] However, this seemingly reliable method has many disadvantages such as the requirement of recording from two distant arterial sites, the lack of a precise definition to what constitutes the foot of the waveform and errors in the calculation of the path length between the optical probes. Moreover, PWV, itself, is sensitive to changes in heart rate (HR), blood pressure, and to the small changes in the arterial wall properties which may not be detected between individuals as the data generated can often show a considerable scatter for a given age range.[12–14] The other way to determine the optical measurement of AS is to use the pulse waveform derived parameters such as reflection and augmentation indexes. Still, many authors have a controversial opinion about the use of these indexes in the assessment of AS.[6,15] The promising, and comparatively new, AS characterizing index is the b/a ratio which is computed from the PPG AC pulse wave 2nd derivative peaks, a and b, as shown in Fig. 1. Proposed by Hashimoto et al., this index demonstrates a good correlation with AS changes altered by age, hypertension, and other vascular risk factors, and have been proven in many other studies.[16–19] However, there are reports of PWV and b/a indicating atherosclerotic alterations differently, yet providing valuable information concerning vascular modifications of aging.[20] Due to apparent simplicity of the measurement and commercially available equipment, the majority of published optical AS assessment studies shows the tendency to use the PPG by applying the probes on the fingertips and ear lobes, the diffuse and arterio-venous anastomoses rich vascular beds which are largely influenced by local temperature changes and sympathetic nervous system.[21–24] In contrary, few papers describe the procedure of AS assessment from superficial conduit arteries using PPG technique.[7,19] Hence, the lack of standardization in the PPG recording procedure and, particularly, in

Address all correspondence to: Andris Grabovskis, University of Latvia, Institute of Atomic Physics and Spectroscopy, Raina Boulevard 19, Riga, LV-1586, Latvia. Tel: +371 28319090; Fax: +371 67228249; E-mail: andris.grabovskis@gmail.com

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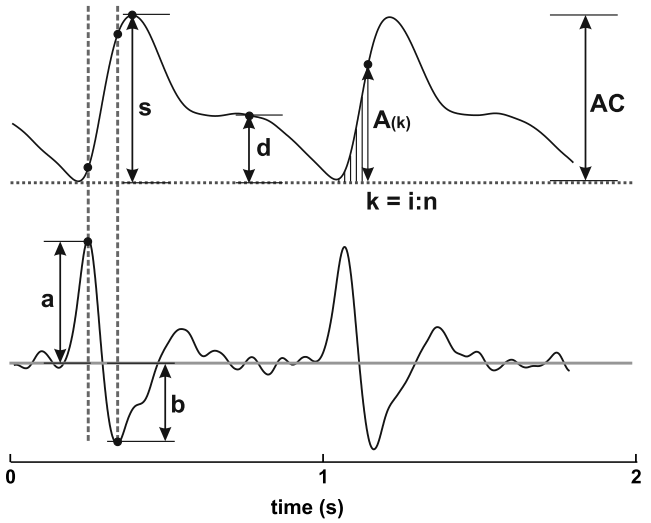

Fig. 1 PPG alternating current (AC) pulse waveform contour consisting of signal samples A_k; systolic peak amplitude s, diastolic peak amplitude d, 2nd derivative extremes a and b.

the unknown PPG probe CP conditions, may cause an inconsistency in the results when the pulse wave contour analysis derived parameters are computed.[25] In case of PWV, this has been explained by analyzing the tissue elastic properties beneath the PPG probe, similar to this study.[26] To the best of our knowledge, there were a few studies addressing the standardization issue and, currently, there are no papers suggesting any standardized criterion of the PPG probe CP except our previous pilot study results.[27,28] Current study focuses on development of methodology to achieve more reliable and valid PPG recordings. The aim of this study was to verify the effect of the PPG probe CP on the value of stiffness related parameter b/a and to clarify whether the previously developed optimal pressure parameter (OPP) can be used for a reliable recording of b/a.[28]

We hypothesized that the stiffness related PPG pulse wave parameter b/a is strongly inconsistent when recorded at nonoptimal probe CP.

2 Methodology

Five young and healthy subjects (3 male, 2 female, 23 ± 2 years old) were enrolled in this pilot study with their informed consent. This study was approved by the Scientific Research Ethics Committee of the University of Latvia, Institute of Experimental and Clinical Medicine. To perform measurement trials in resting conditions, subjects were held in a comfortable, supine position in a quiet and comfortable (23°C to 25°C) environment. The experimental setup and the design of PPG equipment were similar to those reported in our previous study revealing the OPP, as shown in Fig. 2.[28]

The PPG probe was placed on the skin over the three palpable pulse arterial sites (posterior tibial a., femoral a., popliteal a.), consecutively, in different recording trials, repeating the same procedure three times. The probe was fastened with the custom assembled micro-thread manipulator (UniSlide, Velmex Inc.) joined to film-type force transducer (FlexiForc A201, Tekscan) to provide variable CP recording.

Prior to the probe positioning, the arterial region (planned recording site) was insonated with an ultrasound system (Titan, Sonosite; L38 Linear array 10–5 MHz) by an experienced sonographer to reveal any abnormalities or peculiarities which might potentially interfere with a normal arterial site PPG recording as well as to measure the depth and diameter of artery. The stability of the systemic hemodynamic parameters, during the whole experiment, were confirmed by measuring the arterial blood pressure and heart rate by an oscillometric pressure monitor (UA-767Plus30, A&D Instruments) every 2 min. After the ultrasound examination and the determination of the location of the suitable arterial site by mechanical palpation, a single PPG probe was positioned on the skin over the conduit artery. During the recording, the probe CP was slowly increased to the maximum (which was determined by a complete disappearance of the PPG AC pulsations) or reduced until the probe lost contact with the skin. The data acquisitions, of both the PPG signal and force transducer signal, were performed simultaneously at a 4 kHz sample rate and analyzed offline with dedicated Matlab software "PPG Waveform Analysis" (Univ. of Latvia, IAPS, Rubins et al.). The stiffness related waveform parameter b/a was calculated from the 2nd derivative of PPG signal.

For indicating probe CP where PPG is being recorded in the conditions of unloaded arterial wall, OPP was calculated by Eq. (1) during signal processing in beat-per-beat manner:

$$\mathrm{OPP} = \frac{d}{s}\frac{1}{(n-1)}\sum_{k=1}^{n} A_k, \tag{1}$$

where d/s is the diastolic to systolic peak ratio of the PPG signal and $k = i{:}n$ are the samples of each PPG AC pulse; A_k is the amplitude of each sample of PPG AC signal, as shown in Fig. 1.

3 Results

All the subjects examined with the ultrasound imaging showed a normal geometry of the arterial tree at the PPG recording sites and systemic hemodynamic parameters were held constant during PPG measurement procedure (HR $= 68 \pm 5$ BPM; systolic pressure (P_{sys}) 118 ± 8 mmHg; diastolic pressure (P_{dia}) 78 ± 5 mmHg). The depths and diameters of the arteries differed among the subjects and the measurement sites. The smallest diameter and depth were observed for the posterior tibial artery (diameter: 2.1 to 3.2 mm; depth 3.2 to 5.2 mm), the medium values were for the femoral artery (diameter: 6.1 to 8.1 mm; depth 10.4 to 30.2 mm), and the highest values for the popliteal artery (diameter: 7.7 to 9.1 mm; depth 8.6 to 20.5 mm). The literature confirmed our results while

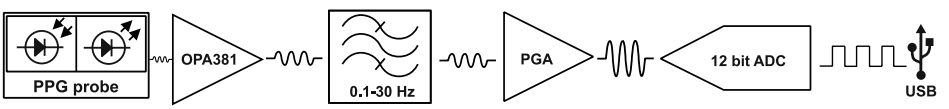

Fig. 2 Schematics of the PPG apparatus: a transimpedance amplifier (OPA381, Texas Instruments) based reflectance type PPG sensor with a photodiode (BPW34-FA, Osram, peak spectral response: 880 nm), an active 1st order feedback circuit 34 Hz low-pass filter, and the 875 nm LED (SIR91-21C/F7, Everlight, 400 mW, a transmission angle 20 deg, diameter 1.9 mm). The probe was connected to custom designed biosignal amplifier with an integrated band pass filter, consisting from 0.1 Hz 2nd order high-pass and 30 Hz 6th order low-pass filters.

indicating the difference in diameter between the genders and the difference of age.[29] The obtained PPG waveforms were typical for the particular arterial sites and were similar to those reported by Sapoznikov, Loukogeorgakis and our research group.[7,9,10] The optimal probe CP values significantly differ at each recording site ($p < 0.05$). Consequently, the highest optimal CP values were observed for the popliteal artery (15.2 ± 4.0 kPa), medium for the femoral artery (11.8 ± 2.9 kPa), and the lowest values for the posterior tibial artery (10.9 ± 3.1 kPa), mean $\pm$ sd. These results are in accordance with the ultrasound examination data in which they confirm the relationship of the arterial depth and the amount of underlying tissue.

Overall, we observed a 300 percent to 400 percent variation of the stiffness related parameter b/a during the incremental and decremental change of probe CP (states A, B, and C), as depicted in Figs. 3 and 4.

As expected, the b/a values obtained at the optimal probe CP showed a negligible measurement site dependency (CV < 6%), popliteal artery (0.66 ± 0.08), femoral artery (0.69 ± 0.09), and posterior tibial artery (0.73 ± 0.09), mean $\pm$ SD as shown in Fig. 5. Such data represents the b/a values corresponding to the conduit AS of young and healthy subjects that can be explained by a similar compliance of the muscular type arteries. Similar results are illustrated in another prominent study.[16] That can be explained by a similar compliance of the muscular type arteries.

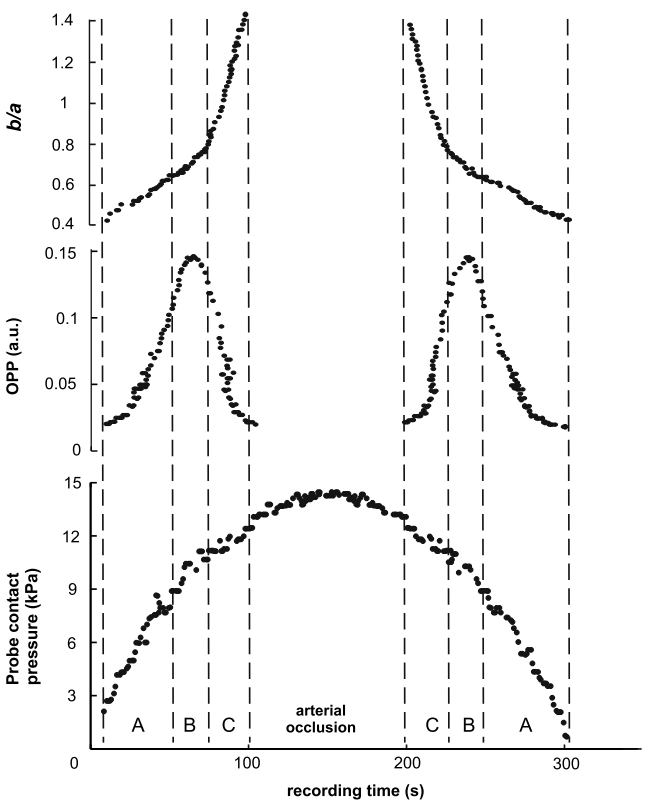

Fig. 3 Representative example of one subject: PPG recorded from the femoral site. The variable probe contact pressure (CP) (bottom curve) induced changes of the PPG AC waveform parameters: optimal pressure parameter (OPP) and 2nd derivative amplitude ratio b/a, which is related to arterial stiffness. The probe CP is partly conducted to the arterial wall. The OPP maximum indicates zero transmural pressure where the external pressure affecting the arterial wall P_{effect} is equal to the mean arterial pressure (MAP), state B, providing repeatable, standardized measurement conditions. It also indicates the conditions of the unloaded artery wall and optimal CP value. At state A probe CP is insufficient, intra-arterial pressure exceeds the external pressure and the transmural pressure is positive, while in state C transmural pressure is negative and the P_{effect} is between MAP and systolic pressure. The PPG pulse wave contours, corresponding to each measurement state (A, B and C), are illustrated in Fig. 4.

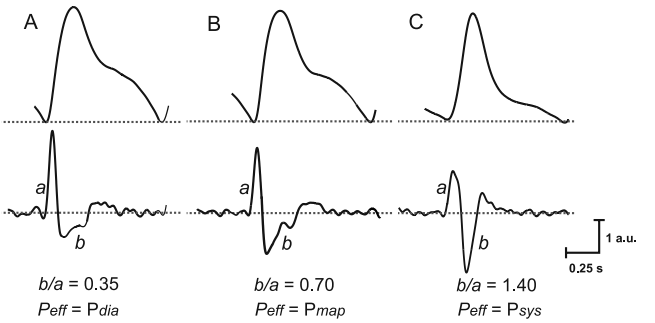

Fig. 4 PPG AC pulse wave and the corresponding 2nd derivative parameter b/a, recorded from one subject. States A, B, and C are in accordance with probe contact pressure condition states in Fig. 3, and P–V relationship in Fig. 6.

The difference between b/a values at states A and B is not significant ($p < 0.05$). A significant b/a error, compared to optimal CP conditions, arises only if the PPG signal is being recorded at conditions where P_{effect} is higher than the MAP, state C ($p < 0.001$; one way repeated measures analysis of variance). This is consistent with our own previous observations during measurements of arterial bed PPG (unpublished data).

4 Discussion

More detailed explanation of our results can be made by using the arterial P–V relationship model. According to the Marey's criterion, the OPP maximum indicates, on the PPG measurement conditions, where the arterial wall is unloaded (the P_{effect} equals to MAP and PPG AC pulse area reaches maximum value).[30] Instead of the mean PPG AC pulse area, we used area derived parameters, OPP, which additionally reflects the relationship between the systolic and diastolic wave of the PPG signal and is uncoupled from the DC component fluctuations. The probe CP influence, on b/a, could be explained by

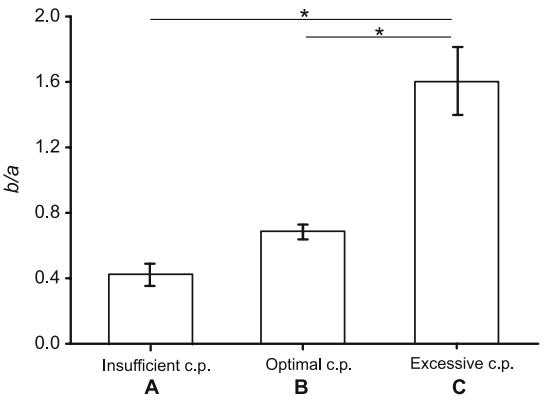

Fig. 5 Representative example of b/a values calculated from PPG signal from one subject, three measurement sites, at all three contact pressure (CP) states (A—insufficient CP; B—optimal CP, refers to maximum OPP; C—excessive CP, Fig. 3) expressed as mean $\pm$ sd. Significant difference is marked by asterisks ($*P < 0.05$).

the exponential model proposed by Raamat and Baker.[31,32] The model describes the arterial volume (V) dependence on the transmural pressure, P_{transm}, by the system of equations:

$$V = \begin{cases} V_{\text{bal}} e^{\frac{C_{\text{bal}}}{V_{\text{bal}}} P_{\text{transm}}} & for\ P_{\text{transm}} \le 0 \\ V_{\text{sys}} - (V_{\text{sys}} - V_{\text{bal}}) e^{\frac{C_{\text{bal}}}{V_{\text{sys}} - V_{\text{bal}}} P_{\text{transm}}} & for\ P_{\text{transm}} \le 0 \end{cases}, \tag{2}$$

where V_{bal} and C_{bal} are the arterial volume and compliance at the zero transmural pressure, while V_{sys} is the arterial volume at systolic pressure.

Numerous studies show the direct relationship between the oscillating arterial volume and the PPG signal AC waveform[33,34] and, therefore, from this, we associate the arterial P–V relationship with PPG pulse wave.

To explain the b/a dynamics near its peak values in Fig. 3, the PPG AC waveform should be examined by realizing the zero transmural pressure, $P_{\text{transm}} = 0$, at the upper limit state, systolic pressure, which is the highest pressure value within the pulse cycle. Then, the arterial wall is unloaded only at the peak of the pressure wave while, at all other times, it will be constricted by the excess pressure imposed by the state C in Figs. 3 and 6.

In the state of zero transmural pressure, arterial volume is always equal to V_0. During the state A, over one pulse period, oscillating volume of artery is above the level $V_0 = V_{\text{sys}}$ at C, thus, it is smaller than oscillating volume of artery during the state B which is in accordance to Marey's criterion of maximum oscillations at the MAP.

At the state C, the arterial compliance C_{bal} reaches its maximum value only at systole which produces the steeply rising PPG waveform and maximum b/a value, state C, at the Figs. 4 and 6.

During the optimal state B, the oscillating arterial volume, Fig. 6 crosswise, and the mean PPG AC area (and the OPP) reaches maximum, as shown in Fig. 3(b), which produces a more rounded and smooth waveform related to the zero transmural pressure at the MAP, as shown in Fig. 4(b).

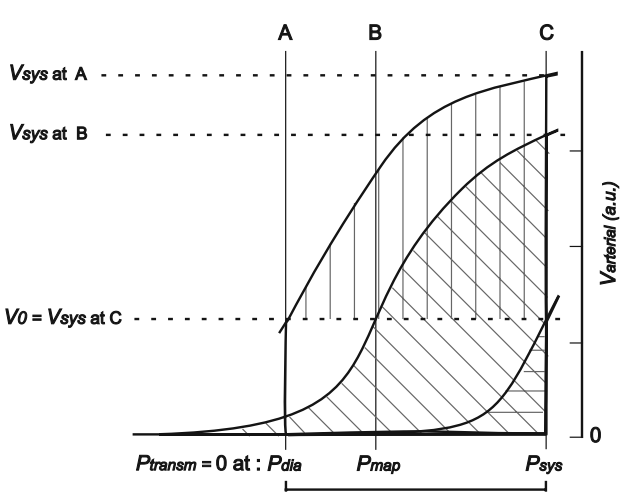

Fig. 6 P–V relationship at the different zero transmural pressure ($P_{\text{transm}} = P_{\text{arterial}} - P_{\text{effect}} = 0$) conditions. P_{transm} is zero at: P_{dia} (state A), MAP (state B) and P_{sys} (state C). Each state corresponds to its specific oscillating arterial volume (vertically, crosswise and horizontally hatched areas, respectively) producing PPG AC signal.

Hereby, the reliability of the OPP criterion was elegantly shown in our experiment during the incremental and decremental change of the probe CP, whereas, the b/a value returned within 5 percent tolerance between both cases. The same was observed for the optimal probe CP value. Being dependent on the measurement site, it returned within the same tolerance both incremental and decremental CP cases.

Overall, it indicates that our measurement is repeatable. Our suggestion to use the PPG waveform parameter, such as the OPP, is based mainly on the evidence of the close tolerance of repeated maximum values (usually CV < 5%) every time when CP is optimal. Our observations show that even if the OPP amplitude maximum values vary more, the AS parameter b/a and probe CP values, returned from the analysis, are only slightly different (CV < 8 percent). This suggests that decreasing the probe CP from the maximum to the optimal is correct when the OPP reaches the next maximum instead of the value of the previous one. The variable probe CP induced notable changes to the PPG parameters OPP and b/a. Parameters display similar values during increment and decrement of probe CP within the measurement trial, thus, confirming the consistency of measurement conditions. This should be considered as the most important reason why the noninvasive contact-manner PPG measurements should be performed in the controlled probe CP conditions. Currently, this factor is still not properly acknowledged and often disregarded while designing the experimental protocol.

So far, OPP range is being calculated offline after the measurement trial, which allows only a fraction of PPG pulses that corresponds to its maximum value to be selected (selection criteria). By improving the data acquisition software with real-time OPP computation, initial OPP range assessment could be added to the experimental protocol prior to performing physiological measurements, thus, ensuring that signal is recorded in standardized conditions.

5 Conclusions

We conclude that, in the case of an uncontrolled probe contact pressure, PPG waveform derived parameters, particularly b/a, are inconsistent. Therefore, the results obtained in such measurement trials should be interpreted with precaution. Our present findings can be considered a step toward standardization of probe contact pressure and more reliable recording of contact-manner PPG signal.

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