Photoplethysmographic Measurements on Clinical Patients (>65 y) and Healthy Cohorts Between Ages of 18–75 y

Matti Huotari, Juha Röning, Kari Määttä, and Pekka Ronsi

Abstract

The biomedical information on different indexes like arterial elasticity index (AEI), arterial age (AA) is used in many cases. However, their applicability for diseases earlier prediction like arteriosclerosis (AS) is seldom applied. Many illnesses are becoming common, especially cardiovascular disorders (CVD) among elderly people, and in females. It is predicted that the negative impacts of AS on young people can be greater than on the elderly people in the long run because of sedentary lifestyle. Degenerative changes in the arteries have many causes in addition to the lifestyle. Arterial elasticity (AE) would provide a direct indicator for cardiovascular healthiness and predict AS. AE can be challenging in the cases of elderly, but also in the case of the young persons whose endothelial functions have been earlier very good. The vessel properties would be important to know for characterization of both arterial diseases and the development of reliable devices. Photoplethysmography (PPG), and especially its response pulse wave decomposition, envelope analysis, and its second order derivative (SDPPG) open the new health information for clinics. PPG signals are correlated with the alterations in blood pressure, blood flow, arterial elasticity, and health indexes. Exposure of human to physical exercise has

been shown to improve endothelial function in patients with risk factors and heart failure. Exercise has been shown to be protective to cardiovascular disease. In addition according to this study, the exact mathematical solution for the pulse wave analysis has been replaced by numerical analysis method. In addition, a probability density function and a coherence function suits well to the inherent resting PPG process, and giving some intrinsic properties of the arterial pulsation phenomena.

Keywords

Photoplethysmography • Pulse waveform analysis
Arteriosclerosis • Probability density function
Decomposition • Pulse waveform decomposition
Envelope analysis • Arterial elasticity

1 Introduction

Photoplethysmographic (PPG) waveform represents peripheral blood flow. Electrocardiogram (ECG) produces information from the heart, but it does not provide any simple information on the arterial tree. PPG wave reflects both peripheral and central hemodynamic properties. PPG device uses infrared and red light emitting diodes which transmit light through the tissue to noninvasively measure hemodynamic parameters such as pulse wave form, and is thus a useful measure of vascular dysfunction and heart rate variability (HRV). HRV in subjects at rest, we can have the fingertip PPG, which is as accurate as ECG based HRV. On the other hand, the blood systolic and diastolic pressures exhibit short and long term pressure variabilities. However, PPG signals are sensitive to motion artefacts even in presence of small motion, both physical and psychological. Physiological and cardiovascular changes can be phasic related to the stimulus exposure but also tonic without close relation to exposures. The tonic response is related to the baseline.

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Many mathematical relations exist between blood pressure, blood flow, and arterial elasticity. However, in clinics blood pressures are measured on the periphery. If two PPG signals correspond to each other perfectly at a given frequency, the magnitude of coherence is 1, as in the case of finger IR and RED PPG. If they are totally unrelated coherence will be 0, as in the case of any PPG and phonocardiography (PCG). In PPG technology, the main difficulty is its quantitative analysis, namely calibration, and comparison of PPG wave measurement obtained from different patients and skin areas. Coherence is to explain cause and effect relations and their linearity. Coherence function is calculated as follows. The two parallel signals have their FFT transforms for coherence function. Coherence measures the degree of linear dependency of the two PPG signals for equal frequency components. In our measurements the light intensities and wavelengths (red 640 nm and infrared 920 nm) are fixed. In practice, the arterial pulse waveform is based on the propagating pulse wave from the left ventricle. It travels through the arterial circulatory system and arrives at the multiple peripheral, parallel capillary arteries. Capillaries can be identified visually by the naked eye, so we do not use any clearing material such as propylene glycol for the PPG measurements. The propagation velocity depends on heart generated pulse and arterial wall elasticity, which is not well understood. The composed pulse waveform can be decomposed with different mathematical analysis domains, such as time or frequency-based. A single PPG wave is the summation of forward and backward waves. It is likely that the PPG pulse waveform is composed of at least five components. The more elastic the arterial wall is, the slower the PPG pulse wave velocity is. Elasticity of the arterial wall changes as a function of aging, and blood pressure, as in the case of hypertension. This change can be measured by an inexpensive and operator independent PPG device. It has been worked with analysis of the arterial pulse wave and the second derivative of the PPG signal. The raw PPG signal reflects peripheral circulation, which is related both to arterial vasoconstriction and vasodilation controlled by the autonomic nervous system in the long term and modulated by the heart cycle beat intervals in the short term. However, the challenges with clinical subjects are the variability of the PPG signals from finger, toe, and nose, or even in the ear. Our need to analyse the signal on a case by case basis so long we don't have the proper electronic automation. For automated diagnosis also based on photoplethysmography would be important. The intensity of the PPG signal is a function of the blood volume in the tissue, and it fluctuates due to the cardiovascular cycle. The pulsation carries many

kinds of information about the function of the cardiovascular system, which is not yet known [1].

New bioengineering measurements and devices are needed to overcome the burden of the healthcare system. Notwithstanding its simplicity, PPG measurements and analysis have many challenges. Essential factors affect PPG pulse amplitude either increasing or decreasing. Especially decreased amplitude (smaller pulses) are caused by vasoconstriction pharmacologically, physiologically (by cold, surgical-induced stress, increased tissue congestion (venous)), hand or toe position lower than the heart (when measured at the finger or toe), or in Valsalva, low stroke volume (when critically reduced). Increased PPG amplitude (larger pulses) are caused by vasodilation pharmacologically, physiologically (by warming, sedation, sepsis), anesthesiologically (by regional blocks, decreased tissue congestion (venous)), and hand or toe position held above the heart (when measured at the finger or toe). We calculate numerically the second derivative of the finger, toe, and nose PPG pulse waveform. The closed form solution for the arterial pulse waveform can be obtained from the fluid dynamic equations, but due to the variability of parameters of the equations means that a closed form exact solution is impossible to derive or it would not have any closed form solution. The non-linear form of the equations prevents from deriving a closed form, analytic solution which could be used in studying the short-term control produced by the autonomous nervous system. Without accurate functional modelling of the PPG dynamics, we use its envelopes (upper and lower), in the application of normalization which provides very satisfactory results. Our envelope curve is the source data enveloped so that it is tangent to every peak in the raw or filtered PPG data. Origin software obtains the upper, lower, or both envelopes of the PPG data by applying a local maximum method combined with a cubic spline interpolation. Also arterial elasticity could be more exactly determined for the arterial stiffness indicator. For example, inter beat interval (IBI) plots are interesting measured from the subject finger versus toe. In this case it is calculated based on the second derivatives of PPG waveforms from the finger and toe. The nose and ear PPG signal could give more information on the head and neck arteries. The PPG signal is caused by the heart beat causing the percussion wave, followed by the tidal wave generated in the aorta. The other reflected waves are coming from the periphery as follows, dicrotic wave, reperfusion wave, and retidal wave. However, the origins of the waveforms of the PPG signal are not fully understood, it is generally accepted that PPG can provide valuable clinical knowledge on the cardiovascular

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system under study. The fluctuating flow of blood is measured as an alternating signal superimposed on a steady signal that makes a PPG waveform [1].

2 Subjects and Methodology

The clinical patient measurements were conducted in Oulu University Hospital (Oulu, Finland) as a clinical device test (test II), where we studied 17 patients of who 10 subjects exhibited normal arterials and 7 patients with peripheral arterial disease according to the ankle brachial index (ABI). The data were acquired by means of USB-NI 6012 (16 bit) measurement card connected to the SignalExpress software (NI) having a sampling frequency of 1 kHz. The studies was approved by the ethical review boards of the Oulu University and University Hospital and the Finnish National Supervisory Authority of Health and Welfare (VALVIRA). Informed consents were obtained from the test subjects, who abstained from alcohol, caffeine, and strenuous exercise in the 24 h up to the day of the tests. The age causes changes in the PPG pulse shape and also on the second derivative of the PPG (SDPPG) wave forms on which the calculated ratio B/A (the first minimum, the first maximum, respectively, Fig. 2). Also an asynchronous PPG pulse appears as a time delay between the left forefinger PPG and left second toe PPG. The delays are the longer, the more elastic the person's arteries are. We see that automation is needed on the PPG analysis.

Theoretically in PPG measurements, the transmission (T) of light through a series of N attenuators (e.g. haemoglobin molecule) can be written as the product or summation of the transmission through each of the individual attenuator, since each one attenuates the light that is incident upon it:

$$T_{\text{overall}} = I_{\text{out}}/I_{\text{in}} = T_1 T_2 T_3 \dots T_N \quad (1a)$$

or in otherwise

$$\log[T_{\text{overall}}] = \log[I_{\text{out}}/I_{\text{in}}] = \log[T_1] + \log[T_2] + \log[T_3] + \dots + \log[T_N] \quad (1b)$$

where T_i are any attenuator, I_{in} and I_{out} are the incident and transmitted light intensities, respectively. Unity transmission indicates that all of the incident light I_{in} passes through the attenuators without loss and $I_{\text{out}} = I_{\text{in}}$ while transmission $I_{\text{out}} = 0$ is complete extinction, and $T_{\text{overall}} = 0$ by Eq. 1a and 1b.

When an absorbance term is inject in the similar case, we get for N attenuators being some biological components

$$A_{\text{total}} = E_1 C_1 L_1 E_2 C_2 L_2 \dots E_N C_N L_N \quad (2)$$

Transmittance (T), reflectance (R), and absorbance (A) added together as giving 1, accordingly

$$1 = T + R + A = 1 \quad (3)$$

PPG signal is originating by the very small change in blood volume caused by each heartbeat. As the volume of blood in tissue changes, the absorption of light by red cells also changes because of their orientation. In decomposition analysis of the pulse waves produces five components: percussion wave, tidal wave, dicrotic wave, reprecussion wave, and retidal wave. SDPPG waveform envelopes produce the distinction of five sequential waves called the initial positive wave, the early negative wave, the late upsloping wave, the late down sloping wave, and the diastolic positive wave.

3 Results and Discussion

As an example, Fig. 1 shows PPGs for red (620 nm) and infrared (920 nm) measured from the index finger, and second toe of a 31, and 51 years male, respectively. The data sets behaves differently compared with each other.

It is worth noting that the discussed system for arterial elasticity diagnosing is based on analysis of set of arterial finger, toe, and nose PPG pulses that are uncovered from the PPG envelopes. Figure 2 shows B/A ratio as a function of time for from the left index finger for infrared (black) and red (red), and from the left second toe for infrared (blue) and

Fig. 1 PPGs measured from left index finger, left second toe by infrared led (black lines), by red led (red), from left second toe by infrared led (blue), by red led (violet) from a 31 and 51 years male healthy cohort. Inset for a 5 s PPG records (Color figure online)

Fig. 2 On the left side, PPG measured from left index finger by infrared led (black line), by red led (red), from left second toe by infrared led (blue), by red led (violet) (normalized 0,...,1), and by PCG

(green) from a 22 years male healthy cohort. On the right side, raw PPG recording of finger infrared PPG for over 500 s from a 33 years male healthy cohort (Color figure online)

Fig. 3 SDPPG for 5 s from the left index finger by infrared led from a 32 years male healthy cohort, where A is marked by triangle pointing down (red) and B by triangle pointing up (blue) from Fig. 1 right side PPG (Color figure online)

red (magenta) from a 32 years male healthy cohort. We can see that the functions are dynamic changing much after about the first minute. The coherence is a statistic function that examines the relation between two signals, in this case two biomedical signals to estimate the power transfer between input and output of a linear system. If the signals are ergodic, and the system function is linear. Here it is used to estimate the causality between the finger and toe PPG. Values of coherence will always satisfy $0 \leq \text{coherence} \leq 1$ as a function of frequency (Fig. 3). Figure 4 shows the coherence as a function of frequency for each PPG pairs.

It is worth noting that arterial elasticity diagnosing is based on analysis of set of arterial finger, toe, and nose PPG pulses that are uncovered from the PPG envelopes. However, SDPPG can be used for evaluation of vascular aging. Figure 4 shows SDPPG based ratio B/A for red as a function of corresponding ratio for infrared measured from the index finger for (a) a 34 years male, for (b) a 65 years

Fig. 4 The PPG signals (left) from the finger infrared led (black), red led (red), and toe infrared led (blue). On the right coherence functions of PPGs measured between the left index finger by infrared and red, and finger with the infrared led between the left second toe by infrared led. On the bandwidth the coherence is about 1 for finger-finger (black)

and finger-toe (red), and about 1 on the measurement band for the finger and toe, respectively. On the right side the decomposed single pulse waveform (0.999 correlation coefficient between the measured and model). Probability function is shown on the bottom of the Figure (Color figure online)

Fig. 5 SDPPG based b/a ratio from the left index finger for infrared (black) and red (red), and from the left second toe for infrared (blue) and red (magenta) from a 32 years male healthy cohort from Fig. 1 the whole right PPG (black) (Color figure online)

Fig. 6 The six patient data based decomposed functions, coherence and probability functions as examples

male patient, for (c) a 65 years female healthy cohort, and (d) a 22 years male healthy cohort. b/a ratio might reflect the large arterial elastic properties, or even AS. In Fig. 5 the case (b) is an AS patient and (c) is a healthy cohort. The arterial elasticity indexes are nowadays based on a single value. Figure shows, however, the elasticity is a variable parameter based on b/a ratio as a function of time. Figure 6 shows the six patient data based decomposed functions, coherence and

probability functions as examples. They all have the different analysed functions, coherence, and also probability density functions (Fig. 7).

Figure 8 shows the male persons' data based on the physical exercise effect. The physical exercise exposure could be good input for testing purposes. Further test would be needed to make clear the different causes of response patterns before and after exercise. Figure 9 shows the

Fig. 7 SDPPG based ratio B/A for red as a function of corresponding ratio for infrared measured from the index finger for **a** a 34 years male, for **b** a 65 years male patient, for **c** a 65 years female healthy cohort, and **d** a 22 years male healthy cohort

Fig. 8 PPGs measured from left index finger, left second toe by infrared led (black lines), by red led (red), from left second toe by infrared led (blue), by red led (violet) from a 33 years subject before physical exercise **(a)** and after physical exercise **(b)**, respectively, for a 5 s record shown (Color figure online)

Fig. 9 IBI-plots of SDPPG based IBI for two patients (>65 y) measured from left index finger, left second toe by infrared led. The correlation coefficient for **a** 0,850, and **b** 0,998, respectively

Fig. 10 Phase-space-plots of PPG from the index finger of a young male (36 y) (A), two patients (>65 y) (B), and (C). The pattern of the phase-space plots are different for the elderly. Inside the graph there is

the corresponding PPG for 5–10 s in time (black the normalized PPG and red the phase delayed PPG, respectively) (Color figure online)

correlation between the finger and toe IBI functions for two persons. In the case 8(a) the correlation coefficient is 0.850 and 8(b) it is 0.998. AA and AEI of the human arteries can be easily determined by PPG signal waveform. Patterns of the PPG waveforms are originating from the very small change in blood vessel walls caused by human ageing, Fig. 10.

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