Changes in the Spectral Characteristics of Plethysmographic Waveforms Due to PAOD

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Abstract: Peripheral arterial occlusive disease (PAOD) of increasing severity can lead progressively to disabling claudication, ischemic rest pain and gangrene. The blood supply of a limb with peripheral arterial disease is restored by surgical operations, which treats the critical limb ischemia (CLI) only in 30% of the cases. CLI occurs when the arterial lumen decreases significantly and the nutritive requirements of the tissues, supplied by microcirculation, cannot be met. In the present paper, a simple, non-invasive and low-cost technique is proposed for early screening diagnosis of PAOD. The approach is based on the investigation of the spectral characteristics of pulse waves measured by photoplethysmography. Painless, versatility and simplicity are significant merits of the proposed methodology.

1 INTRODUCTION

Atherosclerosis is the most common cause of the pathology of the major arteries of the lower extremities. The disease state is associated with the stenosis of vessels in extremities and the formation of a complex of clinical signs, designated as a chronic peripheral arterial obliterative disease. Progression of stenosis and (or) occlusion of major arteries results in the gradual decompensation of the blood flow in the extremity, increasing thus the rates of mortality and disability. In this stage of PAOD, critical limb ischemia takes place, and surgery is recommended. The purpose of vascular surgery is to restore a proper blood flow and to enlarge the lumen of a stenosed vessel. However, the postoperative mortality within the first year after surgery reaches 20%, and approximately half of the patients, who underwent surgery, need a second operation (Norgren et al., 2007).

Diagnosis of PAOD includes anamnesis description, physical examination, and medical tests, of which a Doppler ultrasound test of injured arteries and ankle brachial pressure index (ABPI) measurement are used most extensively. Doppler ultrasonography of lower extremities provides visualization of arterial injuries and the character of blood flow within the injured segments and a tentative estimation of the amount of damage and the degree of stenosis.

X-ray contrast aortoarteriography is a reliable imaging technique for optimal surgery planning. This method includes evaluation of the abdominal aorta with an intracardiac echocardiography probe, introduction of X-ray contrast agents and x-ray imaging of the vascular bed of the lower extremity. However, the x-ray technique can only be used in operating rooms, and is not suitable for fast preliminary diagnostic.

The optimal screening technique to examine PAOD meets several requirements: noninvasiveness, simplicity, reliability, reproducibility, and the possibility of obtaining rapid results. The most common method is based on the determination of the ankle brachial pressure index ABPI, which is the ratio of systolic leg blood pressure to systolic arm blood pressure. The value of ABPI<1 indicates the main blood flow disorders in lower extremities (Norgren et al., 2007). For PAOD, the value of ABPI is asymmetric, which is attributed to the various degrees of damage in the extremities. The above method is noninvasive and can be used for primary diagnosis of the disease. The disadvantage of this method is that it is prone to the subjectiveness of the practitioner. Besides, blood pressure drifting, since measurements on extremities are not performed simultaneously, limits the technique.

Pulse wave is a high blood pressure wave propagating through the aorta and arteries. It is caused

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by the ejection of blood from the left ventricle of the heart during contraction of its muscles (systole phase). The pressure wave propagates along the arterial segment of the vascular system, and a short-term expansion of the arterial wall can be palpated or registered as an arterial pulse. The velocity of pulse wave propagation in the vessels does not depend on the blood flow rate and is defined by the elasticity and diameter of the vessel, the thickness of vessel walls, and the density of blood.

The shape of the volume pulse wave is produced by the interaction between the left ventricle and the blood vessels of the systemic circulation. The first peak of the pulse wave is formed due to the systolic forward wave, and the second - due to the reflected wave, which arises from the reflection of the volume of blood circulating through the aorta and large arteries to the lower extremities and moving back to the ascending segment of the aorta. The available results (O'Rourke and Kelly, 1993) have indicated that the intensity of wave reflection is specified by the tone of small muscular arteries in the main areas of reflection. That is why, the pulse waveform analysis can adequately characterize the functional state and structural changes of a peripheral arterial bed.

There are different methods to register peripheral pulse waves: sphygmogram (Carter, 1968), PPG (Allen et al., 2008), (Erts et al., 2005), (Lin, 2011), impedance rheovasography (Schuhfried et al., 2003), (Sherebrin and Sherebrin, 1990), and Doppler sonography. It is known that the disorders of veins and vessels cause qualitative changes in the peripheral pulse waveform.

In this paper, we address photoplethysmography (PPG), which is a simple and low-cost optical technique for blood flow registration. The method is based on the determination of the blood volume in the tissue sample (see for the review (Allen, 2007)) placed between the receiver and the source of optical radiation. Radiation frequency is chosen so that it can be maximally absorbed by blood red cells. Strictly speaking, the signal is proportional to the number of red blood cells entering the region between the source and the receiver. Since the change in hematocrit (volume of blood red cells per unit volume of blood) during a single measurement is small, the intensity of the light recorded by the receiver is inversely proportional to the volume of blood in the lumen vessel area.

The registered signal, called a photoplethysmogram (PPG), is a superposition of the variable component (AC), associated with changes in the tissue blood volume synchronous with a heartbeat, and the slowly varying component (DC), associated with respiration, sympathetic nervous system activity, and thermoregulation (Allen, 2007), (Holohan, 1996). Also, the absorption of light by bones, skin, tissues, and the blood volume that remains unchanged in the venous and arterial segments of the microvascular bed add a constant level of PPG. Therefore, the absolute value of PPG has no physiological meaning, and only the pulsations of different frequency bands or the changes in the PPG level during the physiological tests can be used in practice.

When a PPG probe is attached distally to the artery stenosis, the waveform rises slowly, the peak becomes more rounded, and the second peak (dicrotic wave) is absent or attenuated. In (Allen et al., 2008), the authors derived a parameter set for describing pulse waveforms and performed the quantitative analysis of these parameters in healthy patients and patients with PAOD. Note that the spectral analysis of peripheral pulse waves in patients with PAOD has not been carried out previously, although the results presented in (F. Javed et al., 2010) have demonstrated the effectiveness of the Fourier analysis for the study of pulse waveforms in healthy volunteers.

Over the past two decades, the wavelet analysis has been used extensively to study the signals of various nature at different scales (Nesme-Ribes E. et al., 1995). The method has been developed significantly in the analysis of astrophysical data, and in the last decade introduced in the analysis of biophysical signals, in particular, to assess the status of central hemodynamics and peripheral circulation (Leondes, 2002), (Bernjak and Stefanovska, 2007). In the wavelet decomposition procedure, the effects of multiple harmonics, noise and motion artifacts are essentially weaker than in the case of Fourier decomposition (Nesme-Ribes E. et al., 1995).

Since the low-frequency fluctuations of the heart rate is mediated mainly by the sympathetic nervous system, it is also reasonable to attribute the low-frequency fluctuations in the baseline and amplitude of the PPG signal to the same nervous system. Furthermore, the fluctuations in the finger blood volume are due to the constriction and relaxation of the tissue blood vessels which are predominantly affected by the sympathetic nervous system (Nitzan et al., 1998).

The purpose of the paper is to investigate the spectral characteristics of PPG signal in LF and HF bands in the distal parts of lower extremities of patients with PAOD.

2 MATERIALS AND METHODS

The investigation were conducted for 59 male volunteers - 25 healthy (age 55 ± 9, ABPI 1.2 ± 0.6) and

34 (age 60 ± 11) with CLI, treated at the Department of Cardiovascular Surgery, Perm's Clinical Hospital No 4. In the investigation, we did not include patients with diabetes and autoimmune diseases of blood vessels. The main clinical manifestation, which occurred in patients selected for the study, was the presence of intermittent claudication. In this case, the diagnosis was made according to the recommendations of the TASC II in the presence of typical clinical symptoms for at least 2 weeks. The clinical examination, ABPI measurements and radionuclide aortoaretriography were used to verify the tentative diagnosis.

In the majority of cases critical limb ischemia produces different effects on the lower extremities of the person. In group B (34 records) we included PPG collected from the lower extremities seriously affected by arterial disease ($ABPI = 0.7 \pm 0.2$); the invasive methods supported the necessity of surgical revascularization. The contralateral extremities were less amenable to this disease, and PPG were included in group A (34 records). It should be noted that PAOD is a manifestation of generalized atherosclerosis, and so the measurements of the contralateral limb (group A, $ABPI = 1.0 \pm 0.2$) correspond to the atherosclerotic lesions of major arteries, which do not lead, at the time of the survey, to peripheral circulatory decompensation. Figure1 presents data corresponding to the control group and groups A and B.

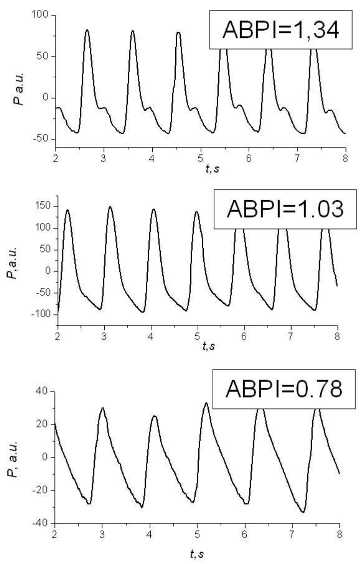

Figure 1: Characteristic form of pulse waves in the distal parts of the lower extremities measured in different groups: control group (top plot), group A (middle plot), and group B (bottom plot).

To investigate the influence of surgery on the low frequency pulsations we used in the study long-time (10 minutes) PPG records collected from 5 healthy subjects, 5 diseased persons before (B1 group) and 3 days after (the influence of operation anesthesia was excluded) the revascularization surgery (B2 group).

Registration of the PPG signal was carried out at controlled temperature ($24 \pm 1^{\circ}C$) after a fifteen-minute adaptation of the patient to the measurement system. Data were collected from the distal phalnax of second toe of the subject lying in the supine position. A standard patient monitor Microlux (Russia) designed to record the PPG signal in the transparent mode was used. The Nellcor PPG probe was held comfortably in place, and the interference from the external light sources was reduced.

The software was adapted for the purposes of the study, all signal pre-processing functions were disabled, sampling frequency was 50 Hz. Measurements were performed for 10 minutes in series with the two extremities. We did not consider the PPG, which could not be processed due to poor tissue perfusion or due to movement artifacts caused by the tremors of the extremities.

3 CALCULATION

Usually, by the spectral analysis the decomposition of the signal into a Fourier series of harmonic functions is meant. The harmonic functions are defined from $-\infty$ to $+\infty$, and in the analysis of real signals we are dealing with finite realizations. Choosing an analyzing function in the limited space, yields a generalization of the Fourier analysis - the wavelet analysis. This method gives better results in the analysis of short nonstationary data with a low signal to noise ratio. Since the PPG signal for extremities with CLI is rather weak and the signal to noise ratio is low, it seems reasonable to use wavelets. The discrete wavelet transform of the function $f(t)$ is

$$W(\nu,\tau) = \sqrt{\nu} \sum_{t=-\infty}^{\infty} f(t)\psi(t-\tau,\nu). \qquad (1)$$

In (1) t is the time, τ is the time shift, ν ($\sim 1/a$, where a - is time scale) is the frequency, and $\psi(t,\nu)$ is the function called an analyzing wavelet, the form of which depends on the signal of interest and the purpose of the study.

The wavelet transform (1) of one-dimensional signal gives a two-dimensional image on the time-frequency plane. This kind of presentation allows us to study the variation of the oscillation characteristics of different scales in time. Since we are dealing here with the stationary signal investigation, we consider a global power spectrum, which is obtained by integrating the power over time:

$$M(\nu) = \frac{1}{T}\sum_{t=0}^{T} |W(\nu,\tau)|^2. \qquad (2)$$

Normalization $\sqrt{\nu}$ in (1)allows us to compare the Fourier scalogram and wavelet global spectrum. We use the complex Morlet wavelet $\psi(t) = e^{2\pi i t} e^{-t^2/(2\sigma^2)}$ (Goupillaud et al., 1984) and the damping parameter $\sigma = 2$. This analyzing function has enough spectral resolution and is well localized in time.

The wavelet global spectrum (2) of each recording was performed in the frequency range 0.01-5 Hz by 100 harmonics with logarithmic frequency decomposition. Fig.2 shows a comparison of the Fourier scalogram and wavelet spectra for one PPG from the group of healthy patients. It is seen that the wavelet spectrum reproduces fairly well the main features of the Fourier spectrum.

Both, the power spectral density (called also the Fourier spectrum) and the wavelet spectrum demonstrate the presence of frequency pulsation. Although the spectra coincide in the frequency range under consideration, it is easier to analyze the wavelet spectrum. The limitation of the observation time leads to a very indented Fourier spectrum. The smooth power spectral density can be observed in the case when $T \to \infty$, but under real conditions the time interval is rather short. As we intend to create a time-saving method of screening diagnostics, which will last a few minutes, we cannot increase significantly the observation time.

We suggest to use the spectral characteristics of high frequency band for description of the pulse waveform, namely we use the energy, which is localized in the vicinity of $2\nu_{HR}$ frequency. In this frequency band the difference in the spectra of healthy and diseased people is very strong.

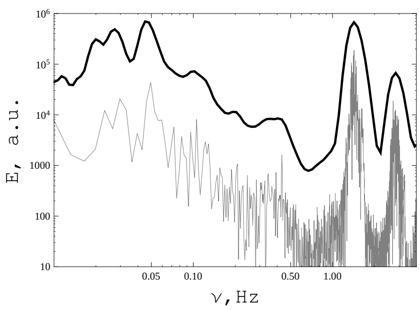

Figure 2: Fourier (black thick line) and wavelet (gray thin line) spectra of PPG signal.

To compare the energy of pulsation at cardiac frequency ν_{HR} and at $2\nu_{HR}$, we define the dimensionless frequency $(\tilde{\nu})$ and energy $\tilde{E}(\tilde{\nu})$, which is maximum in the range from 0.3 to 5 Hz.

$$\tilde{E}(\tilde{\nu}) = E(\nu)/Max[E(\nu)] \tilde{\nu} = \nu/\nu|_{Max[E(\nu)]} \qquad (3)$$

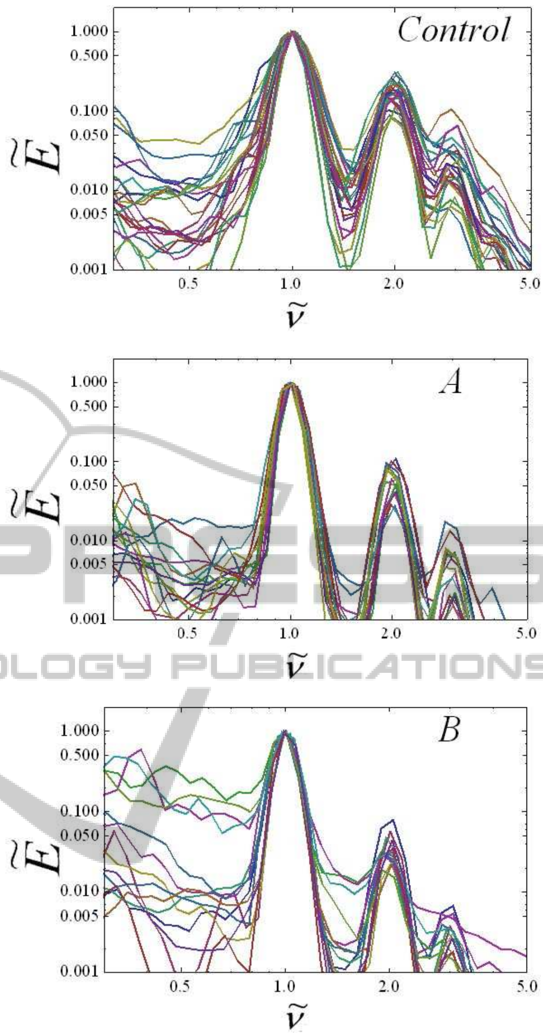

Figure 3: Normalized wavelets in the control group (top panel), subgroup A (middle panel), and subgroup B (bottom planel).

The observed spectra, which were normalized using $\tilde{E}$ and $\tilde{\nu}$, are shown in Fig.3. In the spectra of signals obtained in the control group (top panel in Fig.3), the secondary peak is observed in the frequency range 1.7-2.2 Hz. In the group A (middle panel in Fig. 3) the energy of oscillations within this frequency range is smaller, which is shown by the peak that is less pronounced at these frequencies. In group B the reflected wave due to the so called "early reflection" coincides with the main peak producing no visible dicrotic wave (Nichols et al., 2011) (bottom panel in Fig.1). It is accompanied by a decrease in the energy spectra, as shown in the bottom panel of Fig.3.

We did not examine the spectra, within which we could not identify accurately the first harmonic because of severe arrhythmias and/or poor perfusion of tissues with blood. So we excluded 5 persons from

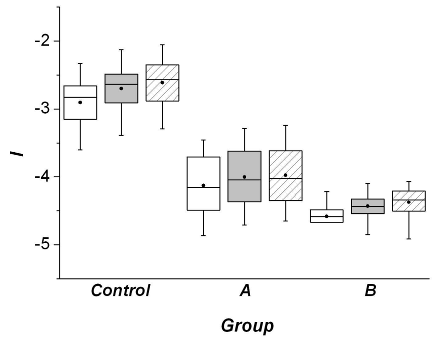

Figure 4: Distribution of I for different groups: dots denote mean values, straight line - medians, and upper and lower boundaries of boxes correspond to distribution percentiles (25% - lower, 75% - upper). Hatching indicates different limits of integration (open rectangles $\nu_1 = 1.8$, $\nu_2 = 2.2$; gray rectangles $\nu_1 = 1.7$, $\nu_1 = 2.3$; hatched rectangles $\nu_1 = 1.6$, $\nu_1 = 2.4$.

B group and 8 from A group. To quantify the energy fluctuations in some frequency band, we introduce an index I defined by

$$I = \log \int_{\nu_1}^{\nu_2} \tilde{E}(\tilde{\nu} d\tilde{\nu}), \qquad (4)$$

where ν_1 and ν_2 are the boundary frequencies for the chosen interval. To compare the reflected wave energy, we take the integral with the limits in the vicinity of $\nu = 2$. Fig.4 illustrates the distribution I for different combinations of the boundary frequencies ν_1 and ν_2. The variation of the frequencies within certain limits does not cause changes in the statistically significant properties of the quantities of interest, namely, the differences between the group data remain reliable even though the integration interval becomes twice as much.

Table 1 summarizes the mean values of the index I and ABPI measured in the examined groups. The obtained results are presented as a M$\pm$SD (M - mean values, SD - standard deviation). The mean values for different groups were compared in the analysis of reliability by applying the Mann-Whitney test. The reliability $p < 0.05$ is considered statistically significant. From Table 1 it follows that in the examined groups the values of index I differ significantly, and the difference is more reliable for index I than for ABPI.

4 LOW FREQUENCY PULSATIONS

Fig.5 presents the averaged spectra of long PPG records. The subjects with PAOD have the higher low-frequency energy, which can be attributed to the fact that compensatory mechanisms increase the blood flow supply. After the revascularization surgery, the low-frequency pulsations associated with the sympathetic nervous system are depressed. Since the PPG were collected 3 day after surgery, the effect of anesthesia should be negligible.

Table 1: Comparison of the ankle-brachial index (*ABPI*) with the index (I) for different groups.

groups	A	B	Control
ABPI	1.0 ± 0.2	0.7 ± 0.2	1.2 ± 0.6
		p_{AB}=0.005	$p_{AC} = 0.04$
			$p_{BC} = 0.04$
I	-4.1 ± 0.5	-4.6 ± 0.4	-2.9 ± 0.4
		p_{AB}=0.02	$p_{AC} < 0.00$
			$p_{BC} < 0.001$

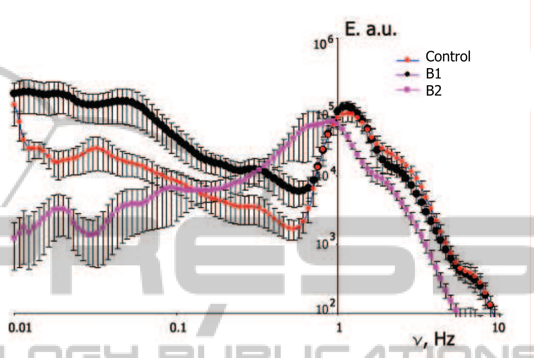

Figure 5: Averaged spectra of control group, PAOD with CLI subjects (B1 group) and the same PAOD subjects 3 days after revascularization surgery (B2 group).

5 SUMMARY

In this study, the spectral method has been applied for a quantitative description of the characteristics of pulse waves in the lower extremities of patients with PAOD.

It is shown that index I determined as the ratio of energy of the heart beat frequency νHR and on the $2\nu HR$, obtained by integrating the normalized spectra in a defined frequency band is significantly different in the examined subgroups. The experiments have indicated that the proposed technique has high sensitivity and can be used as the traditional tool (ABPI determing) in screening diagnostics. It has been found that the ratio of secondary and primary waves in the limb with CLI is several times smaller than the same ratio in the healthy limb.

Obtained results may favor further development of research in this area. The merits of the proposed methodology such as painless, versatility and simplicity, as well as an ever increasing use photoplethysmographic monitors in clinical practice create conditions that promote implementation of the proposed method for screening diagnosis of PAOD.

Restrictions imposed in connection with the use of PPG are associated with weak signals generated by motion artifacts or with the limited peripheral blood flow (F. Javed et al., 2010). The numerical analysis of the PPG signals proposed in this paper can be applied to pulse waveforms obtained by other registration techniques.

The results obtained in the study of LF waves associated with sympathetic nervous system are also presented. The spectral analysis of the PPG signal shows, that LF pulsations of blood flow of subjects with PAOD are higher then of healthy ones. The cause of it can be microcirculation adaptation to the decreased blood flow in the limb. The amplitude of LF oscillations becomes smaller after surgery. This can be explained by suppressing active mechanisms, induced by peripheral nervous fibers trauma.

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