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Time-frequency analysis and laser Doppler spectrum decomposition to reveal new feature space for diagnosis of diabetes mellitus vascular complications

Igor Kozlov[a], Evgeny Zherebtsov[a, b], Angelina Zherebtsova[a], Yulia Loktionova[a], Elena Zharkikh[a], and Andrey Dunaev[a]

[a]Orel State University named after I.S. Turgenev, Komsomolskaya St. 95, Orel, Russia
[b]Optoelectronics and Measurement Techniques, University of Oulu, Oulu, FI-90014, Finland

ABSTRACT

Early diagnostics of microcirculation complications is an important area for biomedical photonics application. The blood perfusion measurements are capable of identification of particular markers for diagnostics of many pathological conditions of blood microcirculation in the skin. In this work, we apply the laser Doppler flowmetry method with the ability to record and process the power spectra of registered photocurrent. This approach provides the estimation of signal amplitude distribution along with the frequencies of Doppler-broadened laser radiation and blood perfusion distribution. In this work, we investigate the blood flow in the skin by the time-frequency analysis of the recorded laser Doppler spectra. The conducted studies allowed us to propose new diagnostic criteria for the diagnosis of diabetes mellitus type 2 complications. The diagnostic parameters have been tested together with binary classifiers based on the linear discriminant analysis and demonstrated to be able to successfully distinguish the groups of volunteers of different age and patients with microvascular complications.

Keywords: laser Doppler flowmetry, type 2 diabetes mellitus, Doppler shift, time-frequency analysis

1. INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a disease which is projecting to affect about 17 per cent of the total number of people in the developed countries by the year 2030.[1] Micro- and macrovascular disorders in T2DM increase average medical expenses three times as much as without complications.[2] To date, a lot of instrument implementations have been developed to assess the severity of these complications using non-invasive control methods. A row of papers[3,4] show the possibility of evaluating the content of glycation products by fluorescence spectroscopy.[5] A large amount of research is devoted to evaluating the content of endogenous fluorophores NADH and FAD and evaluating the redox ratio.[6] The method of video capillaroscopy can make a direct assessment of capillaries, their shape, blood velocity, and other parameters.[7,8] Methods based on the registration of scattered coherent light are also widely used in the diagnosis of complications of diabetes mellitus. The following methods as speckle-contrast imaging,[9,10] laser Doppler flowmetry (LDF),[11,12] correlation spectroscopy, photoplethysmography has been validated to give diagnostically valuable information. The most commercially successful technique with practical applications is the method of laser Doppler flowmetry. This method has proven to be a powerful way to diagnose pathological conditions in the blood flow during the last 40 years of development. In this study, we suggest the approach for the analysis of the registered alterations in the broadening of the laser Doppler spectra during the heating test.

Further author information: (Send correspondence to Igor O. Kozlov)
Igor O. Kozlov: E-mail: i.kozlov@oreluniver.ru, Telephone: +7 920 814 04 58

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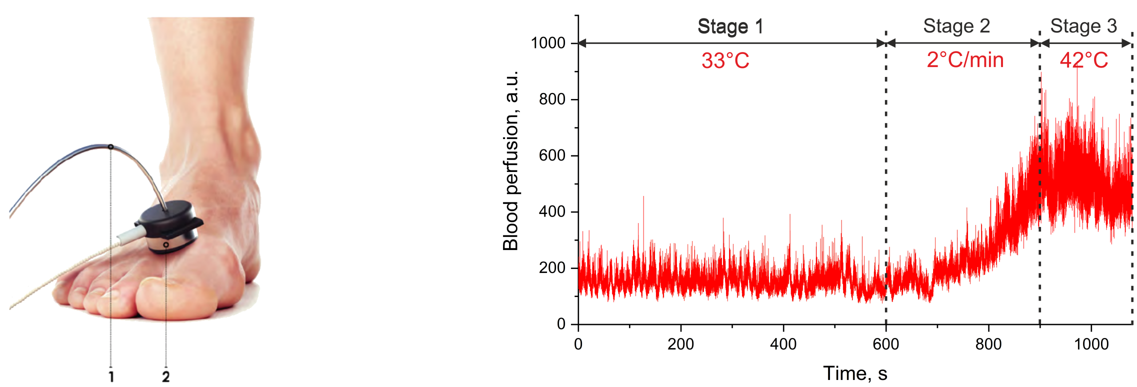
2. MATERIALS AND METHODS

The LDF method is based on the registration of scattered laser radiation from the skin that has undergone a Doppler frequency shift on moving red blood cells and represents the result in blood perfusion unit according to the following formula:

$$I_m = \int_{f1}^{f2} f \cdot S(f) df, \tag{1}$$

where $f-$ Doppler shift frequency; $S(f)$ – power spectrum on frequency f; $f1, f2$ – low and high frequencies of registered spectrum. The main direction of research in this method was the evaluation of oscillations in the blood flow. The measured signal in the laser Doppler flowmetry method is proportional to the blood perfusion, this method is able to register low-frequency flow oscillations.[13] In several publications, it is shown that the changing on oscillations of the microcirculation are manifested during various pathological conditions in T2DM concerning the blood supply.[14] The current development of the method is carried out both from the point of view of the instrument part and the recorded signal analysis. In this paper, it is proposed to modify the traditional technique for the blood perfusion calculation and associated with integrating the signal over a wide frequency range of the Doppler broadening. In our approach, we split the spectrum into 64 sub-bands from zero to 12800 Hz by 200 Hz per bandwidth and process the blood perfusion parameter from all sub-bands. Thus, we receive a blood perfusion distribution by a spectrum of Doppler-broadened laser radiation. To test our approach, we involved three groups of volunteers. Two groups of healthy volunteers were presented by 7 volunteers with ages 22 $\pm$0.5 (Group 1) and 7 volunteers with ages 51$\pm$6. The group with T2DM consisted of 6 volunteers (61$\pm$7 years old) with T2DM duration for more than 10 years. The study protocol was approved by the Ethics Committee at the Orel State University named after I.S. Turgenev. All volunteers signed the informed consent form. We chose the dorsal surface of the foot near the toes as the area of interest (AOI) and placed laser Doppler probe coaxially combined with Peltier element (Fig. 1). This AOI was chosen because the T2DM complications are frequently connected with the capillary net of foot skin. Lack of blood perfusion leads to loss of proprioception and sense of pain, as well as causes and necrosis.



(a) (b)

Figure 1. Protocol description. (a) - area of interest. 1 — LDF optical fiber; 2 — Peltier element. (b) — Example of LDF recording with axon reflex manifestation during stage 3

Every experiment was conducted in three stages. At the first stage, the basal level of blood perfusion was recorded under 33°C temperature. Then, the temperature was gradually increased up to 42°C for 5 minutes by 2°C per minute. Finally, at the third stage, the perfusion was registered for 3 minutes. The temperature of 42 degrees was chosen because it provokes the “axon reflex”. This effect intensively increases the skin blood perfusion when that skin temperature is reached. For further data analysis, we calculate the cumulative sum for each registered power spectra. Every cumulative sum chart bin is calculated by a sum of that bin with the sum of all previous bins:

$$C_n = C_{n-1} + A_n, \tag{2}$$

where n — frequency bin, $n > 2$; A_n — power spectrum value on frequency bin n, C_n — cumulative sum of the sequence with size equals n. At the next step, we normalised every calculated cumulative sum chart on a sum of a corresponding power spectrum. Hereby, we receive a monotonically increasing chart.

3. RESULTS AND DISCUSSION

For cumulative sum chart to be calculated we chose recorded spectra during stage 1 and stage 3. After that, the averaged cumulative sum chart was calculated for sequences of power spectrum on stage 1 and stage 3. As the parameter describes the power spectrum broadening from stage 1 to stage 3, we introduce the concept called Area between Curves (ABC) (Fig.2). ABC-parameter represents the area between two cumulative sum charts

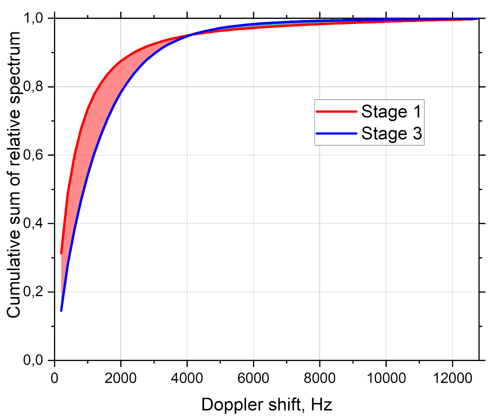


Figure 2. Example of cumulative sum charts for stages 1 and 3 and Area between Curves estimation

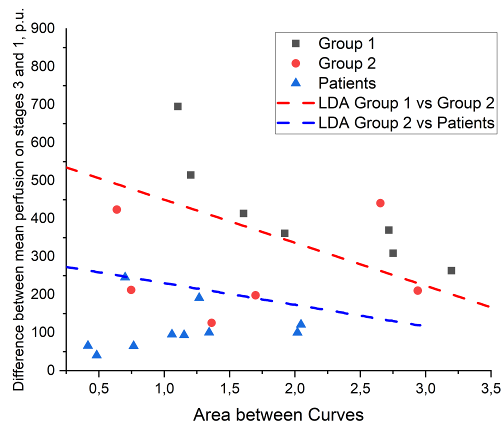


Figure 3. Linear discriminant analysis for groups of volunteers and patients

from first bin to intersection of charts coordinate. Thus, redistribution of signal amplitude along frequencies of Doppler broadening due to heating of skin surface can be evaluated by a simple parameter. Hence, the binary classifier can be obtained using calculated independent estimators. As a classification function, linear discriminant analysis (LDA) was chosen. For two comparison pairs between groups, LDA is shown on Fig.3: Group 1/Group 2 and Group 2/Patients. Area under Curve (AUC) as the metrics of classification accuracy is shown in Tab.1. In addition, we added AUC for both of chosen parameters separately. As for classifier for Group 1/Group 2, there is a higher AUC estimation than if chosen parameters were used separately. However, for Group 2/Patients the binary classifier does not show a better classification than single. This situation probably occurred due to a small number of involved volunteers and high variance in group 2.

Table 1. AUC for LDA and estimators for two comparison pairs of groups.

Estimators	**AUC**
Group 1/Group 2	
Difference between mean perfusion on stages 3 and 1	0.76
Area between Curves	0.64
LDA	0.86
Group 2/Patients	
Difference between mean perfusion on stages 3 and 1	0.92
Area between Curves	0.68
LDA	0.9

4. CONCLUSIONS

In this study, the new approach for laser Doppler flowmetry signal processing and data analysis is proposed. The utilisation of mean cumulative sum chart and mean blood perfusion increment between stages for binary classification of groups by ageing and patients with T2DM demonstrated a good result for heating test protocol. At the next step of our studies, we will involve more volunteers and patients. Further studies using cumulative sum charts will be aimed at identifying individual subgroups within a group of patients, based on the results of testing in accordance with the proposed protocol. That information is promising to allow the physicians to determine the functional state of the patient's blood microcirculation to a certain class and track changes using a relatively simple protocol and inexpensive devices.

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