

# STUDY OF CHANGES IN BLOOD MICROCIRCULATION IN NORMAL AND PATHOLOGICAL CONDITIONS USING WEARABLE PHOTONICS DEVICES

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**Abstract.** In this work, we applied a wearable distributed laser measuring system for the study of regional changes in blood microcirculation in healthy volunteers of different age and diabetic patients. It was found that age-related changes in blood microcirculation can be characterized by increased perfusion level in the fingers and decreased amplitudes of blood flow oscillations in the myogenic and endothelial ranges. The changes in the upper limbs blood microcirculation in patients with diabetes mellitus was also analyzed. A tendency to increased average values of skin blood perfusion in wrists and fingers was observed in patients group.

**Introduction.** The blood microcirculation system is an important, sophisticated part of the cardiovascular system. It plays a crucial role in the life support of all types of tissues in each part of the body. Changes in skin microcirculation can both precede clinical manifestations of pathological processes and be a consequence of various diseases and related complications [1-2]. For instance, persistently high blood sugar can damage blood vessels and nerves and microvascular abnormalities may both appear in the preclinical phases of diabetes and reveal itself as a vascular complication of the disease.

Laser Doppler flowmetry (LDF) is one of the modern methods of non-invasive optical diagnostics of the blood microcirculation system. The method is based on laser radiation sensing of biological tissues and further spectral and statistical analysis of radiation scattered and reflected from moving red blood cells [3]. LDF allows identifying complications of diseases associated with the blood circulatory system, assessing the blood perfusion at rest and in functional tests. Also, LDF allows for evaluation of the oscillatory processes in the microcirculatory system in the different frequency ranges characterizing the contribution of various factors to the signal: endothelial (0.0095-0.021 Hz), neurogenic (0.021-0.052 Hz), myogenic (0.052-0.145 Hz), respiratory (0.145-0.6 Hz) and cardiac (0.6-2 Hz) [4]. Multipoint LDF measuring systems allow for carrying out a simultaneous assessment of blood perfusion in several areas of the body and analyzing the asymmetry of microcirculation and synchronization of blood flow oscillations in symmetrical areas. The recent appearance of new ultra-compact single-mode energy-efficient VCSEL lasers has opened up fundamentally new opportunities for LDF measurements in wearable design [5].

The aim of this work was to study the field of use of a wearable distributed multipoint LDF system for the identification of age-related features in blood microflow and diagnosis of complications of diabetes mellitus.

**Materials and methods.** Experimental studies were carried out in frame of joint development activity and preliminary clinical trials of a novel wearable distributed multipoint LDF system «AMT-LAZMA 1» (Aston Medical Technologies Ltd., UK). This system can be used for skin blood microcirculation recordings with a wavelength of probing laser radiation of 850 nm. The studies involved healthy volunteers without identified health problems and patients with diabetes mellitus. All studies were conducted in the morning in a state of psychological and physical rest not earlier than 2 hours after a meal. The subject was sitting, his hands were located on the table at the heart's level. Laser analyzers were fixed on the body surface without pressure. Each study consisted of simultaneous registration of LDF signals from several symmetrical points on the human body for 10 minutes.

The studies were conducted in accordance with the principles set out in the Helsinki Declaration of 2013 by the World Medical Association and were approved by the Ethics committee of Orel State University.

**Results and discussion.** The first series of measurements involved 40 volunteers without identified health problems. The subjects were divided into two age groups: group 1 aged under 20 years (22 persons, mean age 19.4±0.6 years) and group 2 aged over 40 years old (18 persons, mean age 52.6±10.2 years). Blood perfusion was recorded on the palmar surface of the distal phalanges of the middle fingers of both hands.

Experimental data shows that the average level of perfusion increases significantly with age. The statistical difference was also observed in the amplitudes of myogenic and endothelial oscillations of microcirculation. Since both groups of volunteers included only healthy people with similar values of heart rate and blood pressure, it can be assumed that the result reflects the age-specific microcirculatory bed [6].

The second series of measurements involved 37 volunteers without identified health problems and 18 patients with diabetes mellitus. Healthy subjects were divided into two age groups: group 1 (16 persons, mean age 19.6±0.6

years) and group 2 (21 persons aged  $53.2 \pm 11.4$  years). Perfusion was recorded simultaneously on the dorsal surface of the wrists and on the palmar surface of the distal phalanges of the third fingers of both hands.

The highest level of blood perfusion in the fingers was observed in the older group of healthy volunteers, and the lowest values were recorded in the younger group. This result may be due to both changes in microhemodynamics and structural changes in the microcirculatory bed during aging, including an increase in the total parallel length of vessels [6]. In measurements on wrists, patients with diabetes had the highest perfusion level, and the first group of volunteers had the lowest. The increase in blood perfusion in patients with diabetes mellitus in basal conditions was described earlier in the works of other authors and is associated with the effect of diabetic neuropathy on blood flow [7].

**Conclusions.** The novel wearable sensor system for multipoint recordings of blood perfusion applied for measurements in healthy volunteers and patients with diabetes mellitus has demonstrated a good quality of recorded blood perfusion signals from areas of skin with different levels of microvascular bed density. The measurements in the groups of different age allowed for registration of age-specific changes in the blood perfusion as well as changes, which can be associated with the development of diabetes. The conducted experiments have shown that the implementation of the blood perfusion sensor as a fibre-free wireless wearable device is a very convenient solution to be applied as point-of-care testing. The obtained data can be considered further in the development of protocols for the studies of the blood microcirculation system in patients with different pathologies. The wearable implementation of LDF can become a truly new diagnostic interface to monitor cardiovascular parameters, which could be of interest for diagnostics of conditions associated with microvascular disorders.

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#### **References**

1. B.I. Levy, G. Ambrosio, A.R. Pries, and H.A. Struijker-Boudier, «Microcirculation in hypertension: a new target for treatment?», *Circulation*, 2001, **104**(6), 735–740.
2. S.B. Wheatcroft, I.L. Williams, A.M. Shah, and M.T. Kearney, «Pathophysiological implications of insulin resistance on vascular endothelial function», *Diabetic Medicine*, 2003, **20**(4), 255–268.
3. I. Fredriksson, M. Larsson, and T. Strömberg, «Model-based quantitative laser Doppler flowmetry in skin», *Journal of Biomedical Optics*, 2010, **15**(5), 057002.
4. G. Lancaster, A. Stefanovska, M. Pesce, G. Marco Vezzoni, B. Loggini, R. Pingitore, F. Ghiara, P. Barachini, G. Cervadoro, M. Romanelli, and M. Rossi, «Dynamic markers based on blood perfusion fluctuations for selecting skin melanocytic lesions for biopsy», *Scientific Reports*, 2015, **5**, 12825.
5. E.A. Zherebtsov, E.V. Zharkikh, I.O. Kozlov, A.I. Zherebtsova, Y.I. Loktionova, N.B. Chichkov, I.E. Rafailov, V.V. Sidorov, S.G. Sokolovski, A.V. Dunaev, and E.U. Rafailov, «Novel wearable VCSEL-based sensors for multipoint measurements of blood perfusion», *Proc. SPIE 10877*, 2019, 1087708.
6. L. Li, S. Mac-Mary, J.M. Sainthillier, S. Nouveau, O. de Lacharriere, and P. Humbert, «Age-related changes of the cutaneous microcirculation in vivo», *Gerontology*, 2006, **52**(3), 142–153.
7. J.C. Schramm, T. Dinh, and A. Veves, «Microvascular changes in the diabetic foot», *International Journal of Lower Extremity Wounds*, 2006, **5**(3), 149–159.