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# Wearable sensor system for multipoint measurements of blood perfusion: pilot studies in patients with diabetes mellitus

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## ABSTRACT

The growing interest in the development of new wearable electronic devices for mobile healthcare provides great opportunities for the development of methods for assessing blood perfusion in this direction. Laser Doppler flowmetry (LDF) is one of the promising methods. A fine analysis of capillary blood flow structure and rhythm in the time and frequency domains, coupled with a new possibility of round-the-clock monitoring can provide valuable diagnostic information about the state of microvascular blood flow. In this study, wearable implementation of laser Doppler flowmetry was utilised for microcirculatory function assessment in patients with diabetes and healthy controls of two distinct age groups. Four wearable laser Doppler flowmetry monitors were used for the analysis of blood microcirculation. Thirty seven healthy volunteers and 18 patients with type 2 diabetes mellitus participated in the study. The results of the studies have shown that the average perfusion differs between healthy volunteers of distinct age groups and between healthy volunteers of the younger age group and patients with diabetes mellitus. It was noted that the average level of perfusion measured on the wrist in the two groups of healthy volunteers has no statistically significant differences found in similar measurements on the fingertips. 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.

**Keywords:** laser Doppler flowmetry, blood flow, wearable blood perfusion sensor, diabetes mellitus, ageing

## 1. INTRODUCTION

Since the early 1990s, Dynamic Light Scattering (DLS) and Laser Doppler Flowmetry (LDF) measurements have become an object of wide research and industrial interest in the field of life sciences. That methods are based on optical non-invasive sensing of tissue using laser light and further analysis of the scattered radiation partially reflected by the moving red blood cells. A great advantage of the LDF technique is its ability to measure blood flow in a local area of tissue with an excellent temporal resolution.<sup>1</sup> At present, there is a surge of interest in wearable, electronic diagnostic devices. The main reason of such interest is due to the possibility of daily monitoring promising a new quality of diagnosis. Round-the-clock monitoring, even such a simple indicator like heart rate, allows for the acquisition of new information about the whole body state. Blood perfusion measurements promise a great improvement in such kind of diagnostics. The additional synergistic effect may be obtained by annotation of physiological data by location data as well as information about the current physical activity (accelerometer data).

In recent years, diagnosis, care and treatment of patients with diabetes mellitus (DM) have been the highest healthcare priorities. In 2017, over 425 million people worldwide were diagnosed with diabetes (estimates from

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the International Diabetes Federation).<sup>2</sup> This number is expected to increase to 629 million people by 2045. Clinical observations demonstrate that persistently high blood sugar can damage blood vessels and nerves and that microvascular abnormalities may already appear in the preclinical phases of diabetes.<sup>3,4</sup>

Microcirculation disorders manifest themselves in all parts of the body and affect the functioning of various organs, including kidneys, eyes, cardiovascular system and skin. This significantly reduces the life quality of patients and may lead to their full disability. Chronic hyperglycaemia and insulin resistance in DM cause increased vascular permeability, disruption of vascular tone, causing structural and functional changes in capillaries and arterioles.<sup>5,6,7</sup> The earliest, usually reversible, manifestation of these diseases is the development of microcirculatory dysfunction due to endothelial damage, excessive expression of certain adhesion molecules and other factors.

Assessment of the microcirculation may conveniently be performed in the skin because of its ease of accessibility. The cutaneous blood flow can be evaluated using various optical diagnostic methods,<sup>8</sup> of which laser speckle, videocapillaroscopy, optical coherence tomography, and laser Doppler flowmetry (LDF) are most frequently used.<sup>9,10,11</sup> On the theoretical basis of the LDF method, novel wearable VCSEL-based sensors for multipoint measurements of blood perfusion have recently been proposed.<sup>12</sup> The extensive tests of the system as part of pre-clinical studies are needed to justify the range of its applications for clinical practice. Thus, this work aimed to investigate changes in microcirculatory blood flow of healthy volunteers and patients with type 2 diabetes mellitus using the novel wearable blood perfusion sensor system.

## 2. THE METHOD OF RESEARCH

Experimental studies were conducted using wearable laser Doppler flowmetry monitors “AMT-LAZMA 1” (Aston Medical Technology Ltd., UK) for the analysis of blood microcirculation. The system comprises one or more wearable devices with an integrated LDF sensor and skin thermometer, and a wireless data acquisition module. Every wearable sensor in the system uses a VCSEL chip as a single mode laser source to implement fibre-free direct illumination of tissue. The devices implement identical channels for recording blood perfusion and allow simultaneous measurements at several points of the body. The fibre-free solution and direct illumination of tissue by the laser diode make it possible to avoid fibre coupling losses as well as to decrease the movement artefacts which are common in fibre-based LDF monitors (Figure 1).

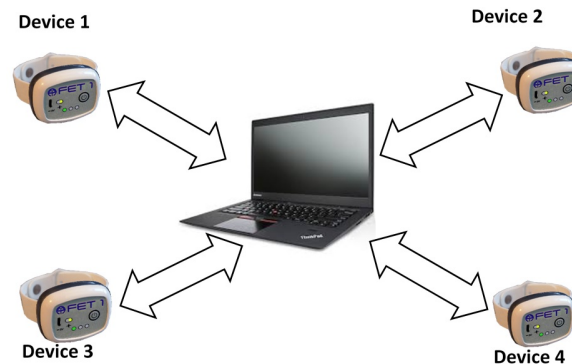


Figure 1. Wearable sensor system for multipoint measurements of blood perfusion

The accurate synchronisation of the time during recordings from different parts of the body makes possible the study of the synchronisation of the skin blood flow under different conditions. Figure 2 shows changes in the LDF signal, recorded in a test measurement on the fingertips and wrists, during the breath holding test. The black line on the graphs corresponds to the average value of perfusion in 2 symmetrical measurement areas, and the red area is the range of signal variations.

As can be seen from the graphs presented, blood tissue perfusion is higher and more synchronous when measured on fingertips compared to measurements performed on the wrists. The breath holding test causes a

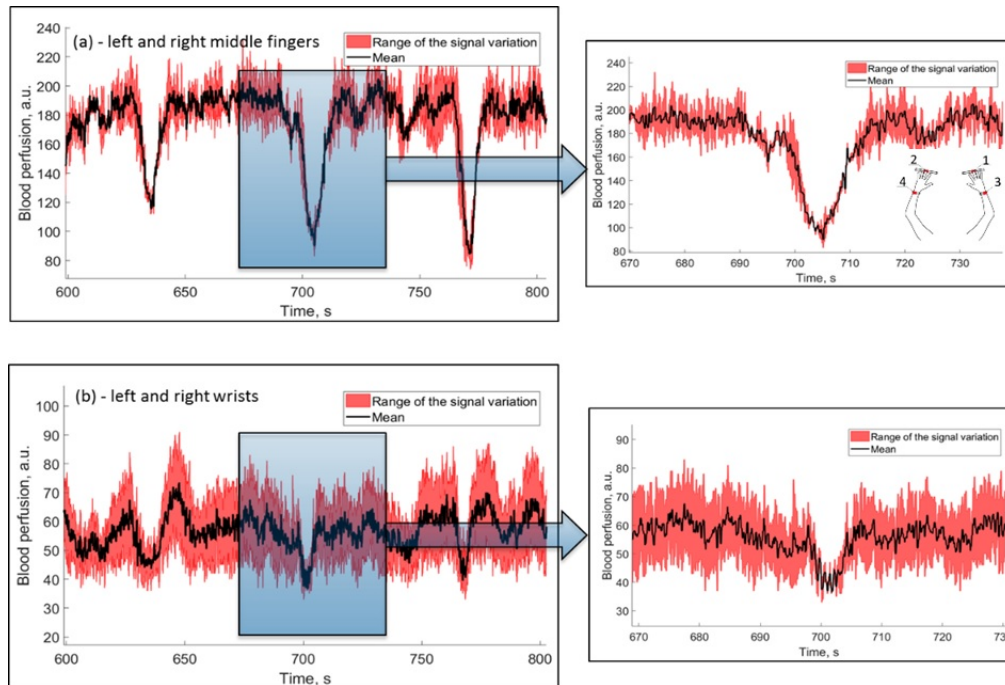


Figure 2. Test measurements with series of breath holding tests: (a) represents measurements from fingers, (b) represents measurements from wrists.

short-term vasoconstriction, which is observed as a drop in perfusion in both fingers and wrists. As could be observed from the graphs, despite the more extensive range of perfusion measurements in the wrists, under the provocative stimuli the microcirculatory blood flow in symmetrical areas of the body shows a rather synchronous response.

These 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. The study involved 37 healthy volunteers and 18 patients with type 2 diabetes. Volunteers with cardiovascular and other serious chronic diseases that affect the blood circulation system, alcohol or drug dependence were excluded from the studies. Before starting the measurements, each volunteer gave a voluntary informed written consent to participate in the experiment and passed a questionnaire to identify possible health problems. The healthy participants were divided into two groups according to their age: 16 volunteers with the age of  $19.6 \pm 0.6$  (group 1) and 21 volunteers with age  $53.2 \pm 11.4$  (group 2). The LDF signal was recorded using the blood perfusion measurement system on wrists and the fingertips of middle fingers of both hands.

Studies were conducted in a sitting position, in a state of physical and mental rest, not earlier than 2 hours after eating. The volunteer's hands were placed on the table at the heart's level. The blood perfusion was recorded for 10 minutes, while the sensors were attached to the palmar surface of the distal phalanx of 3rd fingers and both wrists.

### 3. RESULTS (AND DISCUSSION)

The figure 3 shows the scatterplots of parameters for the studied groups.

Studies have shown that the average perfusion differs between healthy volunteers of different age groups and between healthy volunteers of the younger age group and patients with diabetes mellitus. There was no statistically significant difference between parameters of the older aged control group and patients. On the fingertips, the highest level of perfusion is observed in the second group of healthy volunteers, and the lowest values are recorded for the first group. This result might be due to structural changes in microcirculation during

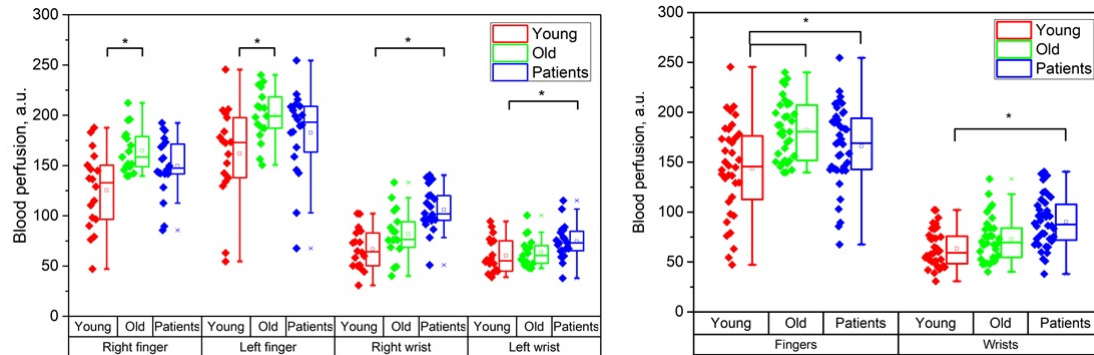


Figure 3. Measurements of mean blood perfusion in patients with type 2 diabetes: (a) - separate analysis for left and right sides of body and (b) data from symmetrical points combined together. Red young healthy volunteers (age of  $19.6 \pm 0.6$ ); green middle-age healthy volunteers (age of  $52.6 \pm 10.2$ ); blue middle-age patients with type 2 diabetes (age of  $53.2 \pm 11.4$ ).

ageing, including an increase in the total parallel vascular length.<sup>13</sup> When measuring on the wrists, patients with diabetes have the highest level of perfusion, and the smallest are the first group of volunteers. An increase in perfusion in patients with diabetes under basal conditions has been described in previous works by other authors in connection with the effect of diabetic neuropathy on the blood flow.<sup>14</sup> It is interesting to note that when measuring on the wrists, the average level of perfusion in the two distinct groups of healthy volunteers has no statistically significant differences found in similar measurements on the fingertips. This result may be due to the lower amplitude of the signal recorded on the wrists compared to records made on the fingers. It should be noted that when comparing the parameters of individual limbs, the difference between the level of perfusion in healthy volunteers of the younger age group and patients ceases to be statistically significant.

#### 4. CONCLUSIONS

The novel wearable sensor system for multipoint recordings of blood perfusion applied for measurements in healthy volunteers and patients with type 2 diabetes has demonstrated a good quality of recorded blood perfusion signals from areas of skin with different levels of microvascular bed density. The conducted experiments have showed that the implementation of the blood perfusion sensor as a fibre-free wireless wearable device is a very convenient solution to be applied as a point-of-care testing. 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 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] Johnson, J. M., Minson, C. T., and Kellogg Jr., D. L., "Cutaneous vasodilator and vasoconstrictor mechanisms in temperature regulation," *Comprehensive Physiology* **4**, 33–89 (2014).
- [2] IDF, "Diabetes atlas. 8th edition." <http://www.diabetesatlas.org> (2017).
- [3] Caballero, A. E., Arora, S., Saouaf, R., Lim, S. C., Smakowski, P., Park, J. Y., King, G. L., LoGerfo, F. W., Horton, E. S., and Veves, A., "Microvascular and macrovascular reactivity is reduced in subjects at risk for type 2 diabetes," *Diabetes* **48**(9), 1856–1862 (1999).

- [4] Smirnova, E., Podtaev, S., Mizeva, I., and Loran, E., "Assessment of endothelial dysfunction in patients with impaired glucose tolerance during a cold pressor test," *Diabetes and Vascular Disease Research* **10**(6), 489–497 (2013).
- [5] Dremin, V. V., Sidorov, V. V., Krupatkin, A. I., Galstyan, G. R., Novikova, I. N., Zherebtsova, A. I., Zherebtsov, E. A., Dunaev, A. V., Abdulvapova, Z. N., Litvinova, K. S., Rafailov, I. E., Sokolovski, S. G., and Rafailov, E. U., "The blood perfusion and nadh/fad content combined analysis in patients with diabetes foot," *Proc. SPIE* **9698**, 969810 (2016).
- [6] Filina, M. A., Potapova, E. V., Makovik, I. N., Zharkih, E. V., Dremin, V. V., Zherebtsov, E. A., Dunaev, A. V., Sidorov, V. V., Krupatkin, A. I., Alimicheva, E. A., Masalygina, G. I., and Muradyan, V. F., "Functional changes in blood microcirculation in the skin of the foot during heating tests in patients with diabetes mellitus," *Human Physiology* **43**(6), 693–699 (2017).
- [7] Mizeva, I., Zharkikh, E., Dremin, V., Zherebtsov, E., Makovik, I., Potapova, E., and Dunaev, A., "Spectral analysis of the blood flow in the foot microvascular bed during thermal testing in patients with diabetes mellitus," *Microvascular Research* **120**, 13–20 (2018).
- [8] Daly, S. M. and Leahy, M. J., "Go with the flow: A review of methods and advancements in blood flow imaging," *Journal of Biophotonics* **6**(3), 217–255 (2013).
- [9] Volkov, M. V., Kostrova, D. A., Margaryants, N. B., Gurov, I. P., Erofeev, N. P., Dremin, V. V., Zharkikh, E. V., Zherebtsov, E. A., Kozlov, I. O., and Dunaev, A. V., "Evaluation of blood microcirculation parameters by combined use of laser doppler flowmetry and videocapillaroscopy methods," *Proc. SPIE* **10336**, 1033607 (2017).
- [10] Dremin, V. V., Zherebtsov, E. A., Makovik, I. N., Kozlov, I. O., Sidorov, V. V., Krupatkin, A. I., Dunaev, A. V., Rafailov, I. E., Litvinova, K. S., Sokolovski, S. G., and Rafailov, E. U., "Laser doppler flowmetry in blood and lymph monitoring, technical aspects and analysis," *Proc. SPIE* **10063**, 1006303 (2017).
- [11] Potapova, E. V., Dremin, V. V., Zherebtsov, E. A., Makovik, I. N., Zharkikh, E. V., Dunaev, A. V., Pilipenko, O. V., Sidorov, V. V., and Krupatkin, A. I., "A complex approach to noninvasive estimation of microcirculatory tissue impairments in feet of patients with diabetes mellitus using spectroscopy," *Optics and Spectroscopy* **123**(6), 955–964 (2017).
- [12] Zherebtsov, E., Sokolovski, S., Sidorov, V., Rafailov, I., Dunaev, A., and Rafailov, E., "Novel wearable vcsel-based blood perfusion sensor," *2018 International Conference Laser Optics (ICLO)*, 564–564 (2018).
- [13] Li, L., Mac-Mary, S., Sainthillier, J.-M., Nouveau, S., de Lacharriere, O., and Humbert, P., "Age-related changes of the cutaneous microcirculation in vivo," *Gerontology* **52**, 142–153 (2006).
- [14] Schramm, J., Dinh, T., and Veves, A., "Microvascular changes in the diabetic foot," *International Journal of Lower Extremity Wounds* **5**(3), 149–159 (2006).