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A distributed system of wearable analyzers for the diagnosis of peripheral blood flow disorders in type 2 diabetes mellitus

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Abstract
This paper discusses a method for the diagnosis of peripheral blood flow disorders in type 2 diabetes mellitus (DM) using a distributed system of wearable blood microcirculation analyzers based on laser Doppler flowmetry. This method was tested in a clinical setting. The research resulted in the development of a classification model based on linear discriminant analysis and allowing the presence of peripheral blood flow disorders in patients with type 2 diabetes to be identified with sensitivity and specificity indicators of 0.88 and 0.90 respectively.

Introduction

Studies of the blood microcirculatory system (MCS) have remained the focus of attention of scientists for many decades due to its involvement in vital processes in the body, such that the MCS is one of the first links in the pathogenesis of a number of diseases [1, 2]. Systemic disorders of the MCS play a key role in the pathogenesis of complications of type 2 diabetes mellitus (DM). Research has shown that hyperglycemia persisting over prolonged periods of time can damage blood vessels and nerve endings and that microvascular abnormalities can appear as early as the in the preclinical stages of DM [3].

Visual examination, analysis of the medical history, Doppler ultrasound, rheovasography, etc. are used in clinical practice to identify disorders of the cerebral circulatory system in diabetes. However, these methods do not provide for assessment of the condition of the cerebral circulatory system in the early stages of pathology, so the probability of false negative diagnostic results remains quite high [1].

Laser Doppler flowmetry (LDF) provides a solution to this problem and is based on analysis of the Doppler frequency shift of optical probe radiation on reflection from red blood cells moving within tissues; it supports analysis of both the overall perfusion of tissues with blood and the mechanisms regulating microcirculatory blood flow. Despite the widespread use of LDF in investigations of peripheral blood flow disorders in clinical research addressing a variety of diseases [4, 5], it is still rarely used in clinical settings. Wider clinical implementation of this method is hampered by the fact that most studies involve the use of lengthy protocols using functional stress tests [6, 7], which are painful for the patient and inconvenient for medical personnel. Other serious obstacles are the use of bulky equipment and the employment of LDF devices using optical fibers, which creates additional inconvenience and increases sensitivity to motion artifacts.

The aim of the present work was to improve the quality of the diagnosis of peripheral blood flow disorders in type 2 diabetes by developing a diagnostic method based on a distributed system of wearable LDF analyzers to detect the presence of peripheral blood flow disorders with a lower probability of false negative results.

Materials and methods

This aim was addressed in experimental studies run at the Endocrinology Department of Orel Regional Clinical Hospital (Orel) involving 26 patients diagnosed with type 2 diabetes (12 men, 14 women, mean age 56 ± 13 years) and a control group consisting of 31 presumptively healthy volunteers (16 men, 15 women, mean age 51 ± 10 years) with no history of problems with the peripheral circulation.

A distributed system was developed and used in the current research; this consisted of four "LAZMA PF" wearable

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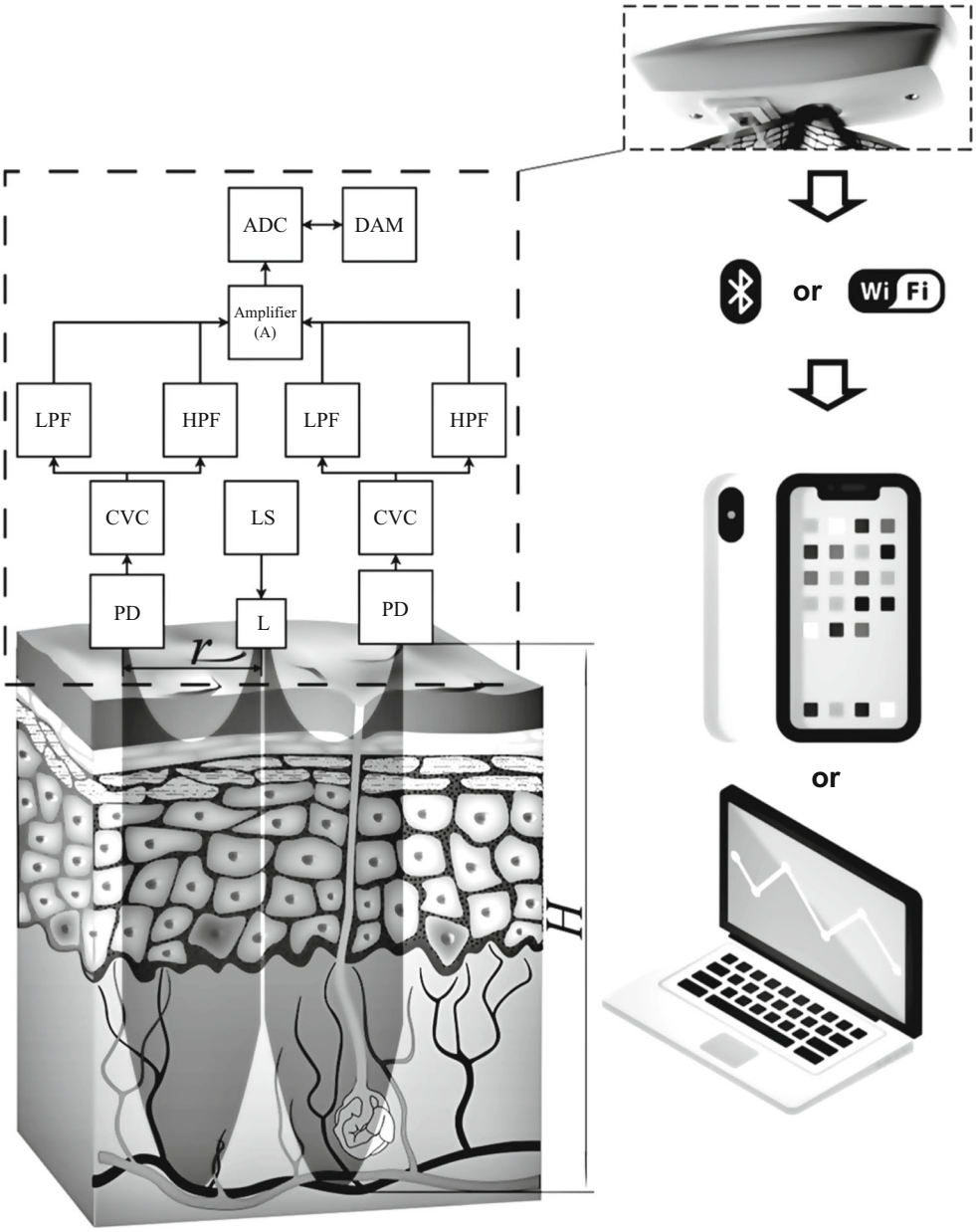

Fig. 1 Functional diagram of the wearable LDF analyzer

LDF analyzers (SPE LAZMA Ltd., Moscow). Each device contains an integral LDF channel built on the basis of a differential circuit [8], along with a wireless data acquisition module (DAM) using Bluetooth/Wi-Fi protocols (Fig. 1).

The analyzer operates as follows. The single-mode VCSEL laser (L) is supplied with current from the laser source driver (LS). In biological tissues, laser radiation is scattered and reflected from moving red blood cells, acquiring a Doppler frequency shift. The intensity of the light field on the skin surface is recorded by photodiodes (PD) positioned symmetrically in line with the laser source at the center. The photodiodes generate a photocurrent proportional to the incident radiation, which a current-voltage converter (CVC) converts into voltage. The signal is then transmitted to low-pass (LPF) and high-pass (HPF) filters. An analog-to-digital converter (ADC) converts the signal into digital form for subsequent transmission via Bluetooth or Wi-Fi to a personal computer (PC) or smartphone.

Theoretical numerical modeling the propagation of optical radiation in the skin using the Monte Carlo method generated specialized medical and technical requirements for wearable LDF analyzers, including a probe wavelength of 850 nm and measurement base value of $r = 1200\,\mu m$, which supports probing of biological tissue to a depth of more than 2 mm, thus allowing diagnostics of peripheral blood flow in layers up to the deep blood net dermis [9].

During the studies, wearable LDF analyzers were attached to the wrists 2 cm above the styloid process on the

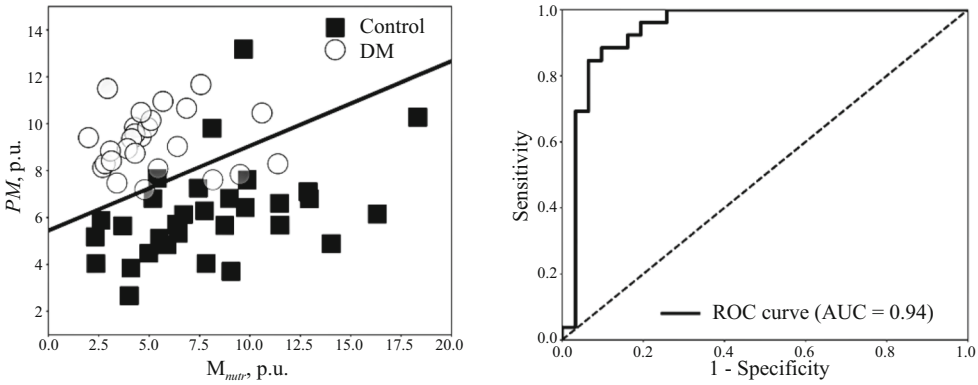

Fig. 2 Scatterplot of measured values with discriminant function plotted (**a**) and ROC curve to evaluate the performance of the classification model (**b**)

dorsal side of the hands and to the plantar surface of the big toes. The study consisted of a ten-minute recordings of LDF-grams simultaneously in four areas of the body without any impact on the MCS system. During the study, the subject was positioned in a supine position, with the arms extended along the body.

Tissue perfusion was assessed on the basis of the LDF-grams recorded, in terms of the mean values of the MCS parameter (*PM*, p.u.). After data capture, LDF-grams were subjected to wavelet analysis to determine the amplitudes of blood flow oscillations in the endothelial (A_E), neurogenic (A_N), myogenic (A_M), respiratory (A_R), and cardiac (A_C) frequency ranges.

Nutritive blood flow (M_{nutr}, p.u.) was then calculated from the measured tissue perfusion and its spectral analysis:

$$M = A_M / (A_N + A_C) \quad (1)$$

Calculation of this parameter provides an assessment of the functioning of the nutritive bed and the distribution of blood flow along the capillary and shunt pathways [2].

Results

The experimental results demonstrated decreased values for *PM* and M_{nutr} in patients (13.97 ± 3.68 p.u. and 5.25 ± 2.45 p.u.) in the toes as compared with the control group (18.04 ± 6.42 p.u. and 8.07 ± 4.00 p.u.). Higher values of *PM* and M_{nutr} were also seen in the patients' upper limbs (9.23 ± 1.24 p.u. and 4.61 ± 2.06 p.u.) as compared with the control group (6.18 ± 2.08 p.u. and 2.50 ± 0.94 p.u.).

The results showing decreased levels of perfusion in the plantar surface of the toes in patients are consistent with results reported from most earlier studies [10–12] and point to the development of peripheral blood flow disorders in the lower limbs. Increased values of parameters in patients' wrists can be explained in terms of disorders being at an earlier stage of development in the upper limbs and an attempt by the body to compensate for developing disorders by activating nutritive pathways for blood flow.

To interpret the between-group differences and to classify novel objects in subsequent studies, a classification model was built using linear discriminant analysis, with the values of *PM* and M_{nutr} as diagnostic criteria. The discriminant variables in the classification model were the values of the microcirculation index of the upper limbs calculated from the LDF data and the values of the nutritive blood flow in the lower limbs calculated from spectral analysis of LDF grams. The classification model with the best sensitivity and specificity is:

$$f = -0.47M_{nutr} + 1.30PM - 7.09 \quad (2)$$

As can be seen from the scatterplot of the values of the study parameters (Fig. 2a), a displacement to the upper left region characterizes the transition to the presence of peripheral blood flow disorders. The area under the ROC curve (Fig. 2b) was 0.94, which indicates that the classification model has acceptable quality (sensitivity and specificity 0.88 and 0.90 respectively).

The resulting classification model provided the basis for development of a method for the diagnosis of peripheral blood flow disorders in patients with type 2 diabetes based on the use of a distributed system of wearable LDF analyzers and allowing diagnosis without functional tests. The algorithm of the method is presented in Fig. 3. The diagnostic method proposed here consists of a 10-min recording of the mean *PM* value in the patient's upper and lower limbs without using functional tests followed by calculation of the parameter M_{nutr} with further processing of the resulting values using a classification model to draw a conclusion that the type 2 DM patient does or does not have a peripheral blood flow disorder.

Based on the diagnostic method developed here and biotechnical systems (BTS) synthesis, a BTS for the diagnosis of peripheral blood flow disorders in type 2 diabetes was synthesized in the form of a distributed system of wearable LDF analyzers (Fig. 4).

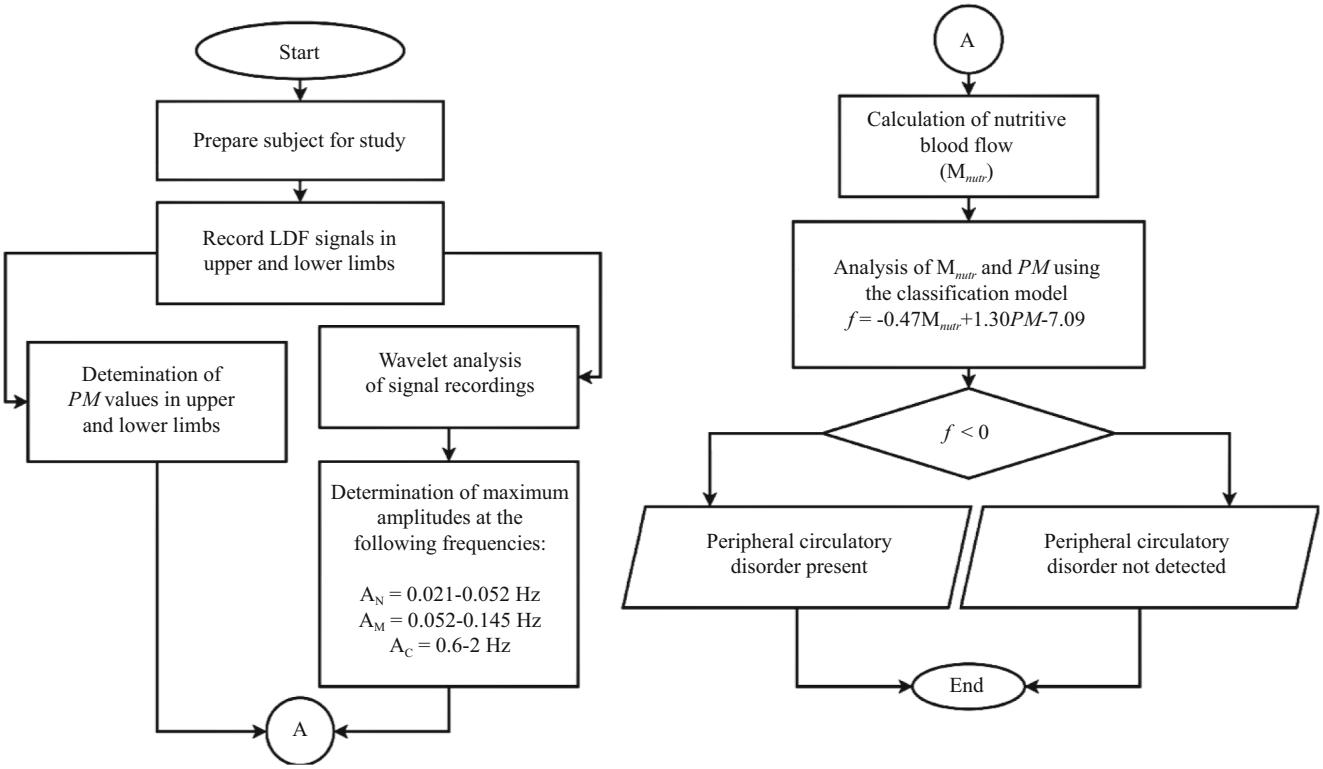

Fig. 3 Algorithm for the diagnosis of peripheral blood flow disorders for patients with type 2 diabetes

The BTS works as follows: the doctor attaches the wearable LDF devices and then starts the diagnostic process using a PC. The devices transmit data to the PC via Bluetooth or Wi-Fi, and, after data recording on the PC is complete, the *PM* and M_{nutr} parameters are calculated. The classification model is then used to form a conclusion as to whether the patient has or does not have a peripheral blood flow disorder.

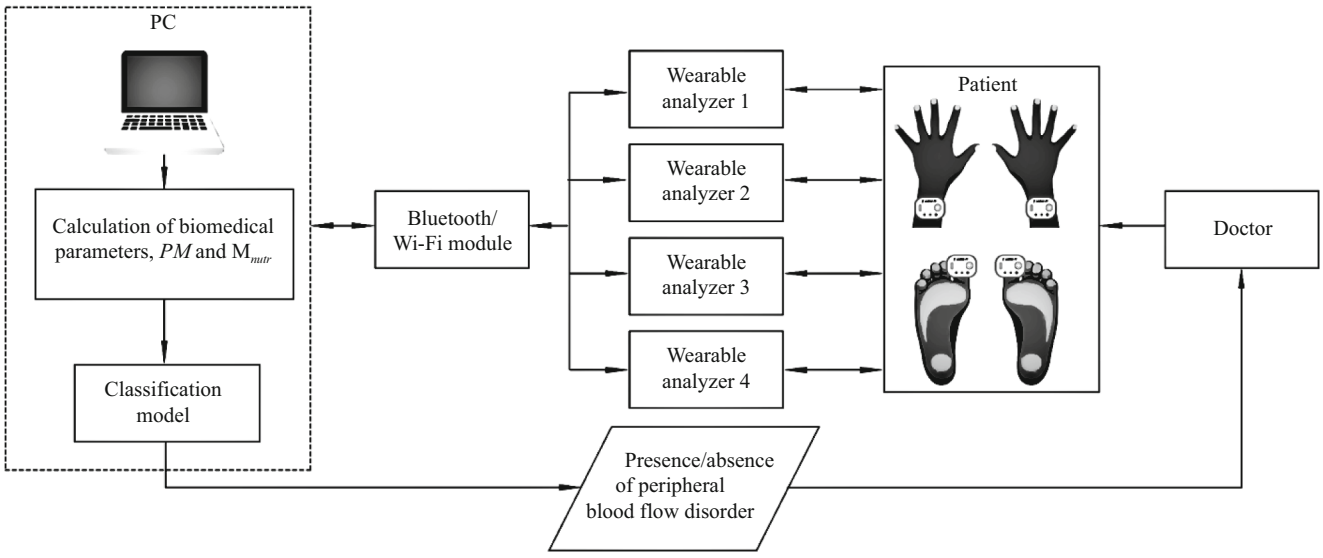

Fig. 4 BTS for the diagnosis of peripheral blood flow disorders in type 2 diabetes

Conclusions

Thus, this study proposes a principle for constructing a distributed system of wearable analyzers supporting simultaneous recording of LDF signals in patients' upper and lower limbs. This method for the diagnosis of peripheral blood flow disorders in type 2 diabetes supports the detection of the presence of pathology with sensitivity and specificity indicators of 0.88 and 0.90 respectively, which reduces the likelihood of false negative diagnostic results.

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References

1. Dunaev AV (2022) Multimodal optical diagnostics of the microcirculatory tissue systems of the human body. TNT, Staryi Oskol
2. Krupatkin AI, Sidorov VV (2013) Functional diagnostics of the state of microcirculatory tissue systems: fluctuations, information, nonlinearity. Guidelines for doctors. Librokom, Moscow
3. Caballero AE, Arora S, Saouaf R, Lim SC, Smakowski P, Park JY, King GL, LoGerfo FW, Horton ES, Veves A (1999) Microvascular and macrovascular reactivity is reduced in subjects at risk for type 2 diabetes. Diabetes 48(9):1856–1862
4. Martini R, Bagno A (2018) The wavelet analysis for the assessment of microvascular function with the laser doppler fluxmetry over the last 20 years. Looking for hidden informations. Clin Hemorheol Microcirc 70(2):213–229
5. Kralj L, Lenasi H (2023) Wavelet analysis of laser doppler microcirculatory signals: current applications and limitations. Front Physiol 13(1):1076445
6. Kulikov DA, Glazkov AA, Kovaleva YA, Balashova NV, Kulikov AV (2017) Prospects of Laser Doppler flowmetry application in assessment of skin microcirculation in diabetes. *Diabetes mellitus* 20(4):279–285
7. Fuchs D, Dupon PP, Schaap LA, Draijer R (2017) The association between diabetes and dermal microvascular dysfunction noninvasively assessed by laser doppler with local thermal hyperemia: a systematic review with meta-analysis. Cardiovasc Diabetol 16(1):11
8. Sidorov VV, Rybakov YL, Gusakov VM, Evtushenko GS (2021) A system of local analyzers for non-invasive diagnostics of the general state of the compartments of the microcirculatory tissue system of human skin. Meditsinsk Tekhn 330(6):4–6
9. Zharkikh EV (2023) Modeling of the diagnostic volume for a portable laser Doppler flowmetry device. Fundam Priklad Prob Tekhn Tekhnol 357(1):140–147
10. Jörneskog G, Brismar K, Fagrell B (1995) Skin capillary circulation severely impaired in toes of patients with IDDM, with and without late diabetic complications. Diabetologia 38(4):474–480
11. Urbancic-Rovan V, Stefanovska A, Bernjak A, Ažman-Juvan K, Kocijančič A (2004) Skin blood flow in the upper and lower extremities of diabetic patients with and without autonomic neuropathy. J Vasc Res 41(6):535–545
12. Jonasson H, Bergstrand S, Nystrom FH, Länne T, Östgren CJ, Bjarnegård N, Fredriksson I, Larsson M, Strömberg T (2017) Skin microvascular endothelial dysfunction is associated with type 2 diabetes independently of microalbuminuria and arterial stiffness. Diab Vasc Dis Res 14(4):363–371