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METHODS FOR ASSESSING THE STATE OF MICROHEMOCIRCULATION OF BIOTISSUE BY SPECKLE-STRUCTURE OF MULTIPLE SCATTERED RADIATION

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Abstract. The characteristics of microcirculation of blood in human tissues were investigated by recording and analyzing a dynamic speckle pattern. Methodical approaches are proposed for evaluating the obtained data in order to verify speckle measurements using the widely used Doppler flowmetry technique.

Keywords: *blood, biotissue, Doppler flowmetry, microcirculation, specklemetry.*

Introduction

Currently, the speckle structure of scattered light is used in scientific and practical purposes to determine various characteristics of biotissues, for example, blood flow velocity. Microcirculation is an important prognostic factor for the diagnostics and treatment of a number of diseases, such as ischemia, atherosclerosis, arthritis, thrombosis, etc. The nature of microcirculation is mainly determined by blood flow parameters in arterioles, capillaries and venules. Microcirculation plays an important physiological role in ensuring the processes of oxygenation and metabolism in tissues, and also affects, for example, the optical properties of the skin. Theoretical modeling and experimental studies of the dynamics of blood flow are necessary for the diagnostics and deeper analysis of a number of diseases and humans pathologies in order to improve the quality of treatment.

However, the developed methods are built mainly empirically and are based on experimental data without a quantitative theoretical justification. This leads to an incomplete use of diagnostical and other possibilities, originally laid down in the speckle structure of ambient light.

The aim of this work is simulation of the speckle structure of multiple scattered light in multilayer biological tissues to assess microhemocirculation of biological tissue and to verify speckle measurements using the widely used Doppler flowmetry technique.

Method description

It is known that during irradiation of a scattering medium and, specifically, of biological tissue with coherent light, a speckle structure is formed in the medium, which

can be used to determine a number of characteristics of biotissues, for example, the size of its particles and the velocity of blood flow.

Analytical method of calculating the characteristics of the interference pattern formed by the repeatedly scattered light inside the multi-layer biological tissue as human skin kind at wavelengths of visible and near IR spectral ranges at laser irradiation is described in writings [1, 2]. It is based on a known relationship between light field coherence theory in the scattering medium and the radiative transfer theory.

The calculations assumed that the scattering particles are immobile. During the calculations, it was considered that it is a pulsed lighting of the medium surface when the pulse duration is much less than the characteristic travel time of the scattering centers. In the simulation, the well-known analytical solutions of the radiation transfer theory [4] were used in presenting of the scattering indicatrix as a sum of functions having substantially different angular scales [5] for dividing the total radiation into a coherent and incoherent background. The calculations assumed that the particles are immobile.

When modeling the movement of blood through the vessels, the following anomalous effects (rheological properties) of the blood flow were taken into account:

1) the Fareus effect - the dependence of the hematocrit on the diameter of the vessel, when erythrocytes are concentrated near the flow axis, as a result of which the average erythrocyte transport rate is greater than the average flow velocity in the vessel as a whole;

2) the existence of a non-erythrocyte parietal plasma layer near the vessel wall;

3) a blunt velocity profile compared to a Poiseuille flow profile;

4) the Fareus – Lindquist effect — the dependence of blood viscosity on the diameter of a blood vessel.

Based on a two-phase model of blood flow [6] and using the mechanics of multiphase media, blood for mathematical modeling is initially considered a two-phase viscous suspension consisting of two phases: the near-wall and paraxial plasma layers with erythrocytes. In the parietal layer, the concentration of erythrocytes is zero, and on the axis reaches its maximum. We use a single type of equations for the whole section of the vessel and set an arbitrary function of the distribution of red blood cells over the section of the vessel. The model does not take into account the effect of red blood cell deformation and their aggregation in small-diameter vessels on the local viscosity coefficient, red blood cell rotation, their transverse migration, as well as interaction with each other.

The temporal autocorrelation function (ACF) of diffusely reflected light was used to solve the radiation transfer equation in the diffusion approximation. The ACF is described by solving the stationary equation for the diffusion of photons [7, 8], under conditions of strong multiple scattering ($\lambda << l^* << L$, L is the characteristic sample size). For this, the ACF was presented in the form $G_1 = G_1^{(0)} + G_1^{(s)}$ where $G_1^{(s)}$ - the function that describes the effect of flow on the correlation function ("scattered" wave) $G_1^{(0)}$ - corresponds to the macroscopic case. The solution was found by formally solving the diffusion equation [9, 10] and coincides in form with the expression for an electromagnetic wave scattered on a dielectric cylinder [11]. The results were obtained earlier by other methods [12-14], and also confirmed experimentally [12, 13].We must note that the correlation function does not depend on the position of the detector (x,y) on the surface of the medium and on the value of the transport photon mean free path l^*.

According to the Wiener – Khinchin theorem, the power spectrum of temporal intensity fluctuations is obtained by Fourier transformation of its autocorrelation function. The normalized AFC fluctuations of the scattered field (that is diffused reflected light) $g_1(\tau)$ is associated with the energy spectrum of the signal $S(\omega)$ as a pair of Fourier transforms:

$$\boldsymbol{S(\omega) = \int_{-\infty}^{\infty} g_1(\tau) \cdot exp(-j\omega\tau) d\tau = \int_{-\infty}^{\infty} \frac{G(\tau)}{G(0)} exp(-j\omega\tau) d\tau} \quad (1)$$

Where $G(0)$ - the maximum of the time ACF of the scattered field fluctuations; $G(\tau)$ the magnitude of the time ACF fluctuations of the scattered field at the time τ.

To analyze the spectrum of intensity fluctuations, we used the statistics of the second kind. The variance, or zero moment, is equal to the average power of the process, the average value of which is zero. Dispersion is related to the average concentration <*C*> of moving particles in the sample volume. The average frequency of the spectrum [15], or the first moment M_1, is proportional to the root-mean-square velocity V_{rms} of the moving particles multiplied by their average concentration (perfusion) [16].

To estimate the volumetric flow rate, we use the normalized spectral momentum or root-mean-square velocity V_{rms} of moving particles [17]:

$$V_{rms} = M_1/M_0 = \frac{1}{2\pi}\int_{\omega_{min}}^{\omega_{max}} \omega \cdot S(\omega) d\omega \Big/ \frac{1}{2\pi}\int_{\omega_{min}}^{\omega_{max}} S(\omega) d\omega \quad (2)$$

It has been established that the following parameters can be used quite effectively to assess the state of cutaneous microhemodynamics: the average frequency of the spectrum; area covered by the spectrum.

Experimental part

The functional state of the skin microhemodynamics (MHD) was studied by a non-invasive speckle-optical method using the "Speckle-Scan" device. The device is designed and manufactured at the Belarusian State University of Informatics and Radioelectronics and is a laser speckle-optical system for monitoring blood microcirculation. With its help, the amplitude-frequency characteristics of the spectra of fluctuations of the speckle-field intensity, formed as a result of scattering laser radiation by biological objects, were calculated and carried out. The processing of the obtained results was carried out using a computer program in the frequency range of 40-1000 Hz with the determination of the spectrum power *S*, average frequency <*f*> of the spectrum, coefficient μ_s, band coefficient K_b, spectrum asymmetry coefficient A_s, ratios $<f>/A_s$.

At the same time, skin microhemodynamics was investigated by Doppler ultrasound (USDG) using the Minimax-Doppler-K device. When analyzing the USDG indices, the blood flow velocity was determined from the average velocity curve: V_{am} - average linear velocity (cm/s) and Q_{am} - average volumetric velocity (mL/min).

The data obtained by the USDG and the Speckle-Scan device were compared with each other and with a mathematical model of the propagation of laser radiation in the microcirculation channel. To compare the data obtained using both methods, we used a mathematical model [1] written in the MathCad program. The depth of the sensing light in the biological tissue at a wavelength of λ = 628 nm is 0.57 mm. The diameter of the investigated microvessels was about 200 microns.

A speckle-optical and USDG examination of skin MHD of a patient was performed in a sitting position, a manometer cuff was applied to the shoulder, the receiving-lighting sensor of the device was placed in the base of the dorsum of the first finger hand and the initial blood flow in the microcirculatory vessels of the skin in this area was measured by registration of the relevant parameters. Then the air pressure cuff was pumped to the pressure level exceeding the patient's systolic pressure by 30-40 mm Hg.

Compression of the brachial artery continued for 1 min, followed by rapid decompression of the vessel. The recording of speckle-optical and USDG curve was performed 1, 2, 3, 4, and 5 minutes after decompression of 10 patients 10 times each. Statistical processing of the obtained research results was carried out using the software package Statistica 10.0.

Results and discussion

Analysis of the obtained data shows that short-term exposure (compression) leads to deterioration of the blood microcirculation (Figures 1-4).

This is due to the fact that the blood flow increases as a result of the expansion of small arteries and arterioles, the vessels overflow with blood. At the same time, hydrodynamic resistance decreases, the volume Q_{am} and linear V_{am} velocity of blood flow increases in the tissue (Figures 2, .3), as well as the number of functioning capillaries.

In the microvasculature, the blood flow is represented mainly by the formed elements of blood. They move in layers relative to each other evenly, creating a laminar movement of the medium.

There is a division into axial flow (nucleus of blood cells) and erythrocyte parietal plasma layer. Reducing internal friction contributes to rapid blood circulation. Acceleration of the blood flow velocity reduces the time of blood contact with the tissue and reduces the diffusion time of oxygen in the tissue, which is compensated by an increase in the number of functioning capillaries per unit of tissue.

The volumetric rate of blood flow depends on the diameter of the vessels. The amount of blood flowing per unit of time through different parts of the vascular bed is the same.

Figure 1 shows the results of measurements of MHD using the speckle-metric method. Analysis of the measurement data showed that the averaged power of the fluctuation spectrum of the intensity of the scattered radiation $P(\omega)$ or the zero moment M_0 after decompression of the vessel increases by about 15% in comparison with the normal state (Figure 1 a, b).

With a decrease in the intensity of skin blood flow due to the onset of hyperemia, a decrease in the parameters $\langle f \rangle$ and Q occurs. Upon registration $\langle f \rangle$ and Q immediately after cessation of exposure, a sharp increase in these parameters to the values corresponding to normal blood flow was observed.

Due to the fact that the outflow of blood is not broken and there is no development of edema (rarely develops), the elasticity of the capillary wall does not change.

The expansion of the wall is not significant. However, the cross-sectional area of the microvasculature S_a as a whole increases due to an increase in the number of functioning capillaries. The intensity of the increase depends on the tonus (elasticity) of the vessels. The normalized moment (absolute blood flow velocity) after hyperemia decreases for some time, and then returns to its original value (Figure 1 e, f). The maximum relative error of

measurement of these parameters is no more than 10%. It is known that the linear velocity of blood flow is directly proportional to blood pressure [18]. Therefore, an increase in blood pressure leads to an increase in the linear velocity of blood flow, as can be seen from the figures (2 and 3 a, c). While comparing the experimental results with the data of mathematical modeling (Fig. 3), a positive correlation is observed, however, the changes amplitudes in microcirculation parameters in model calculations are little bit lower.

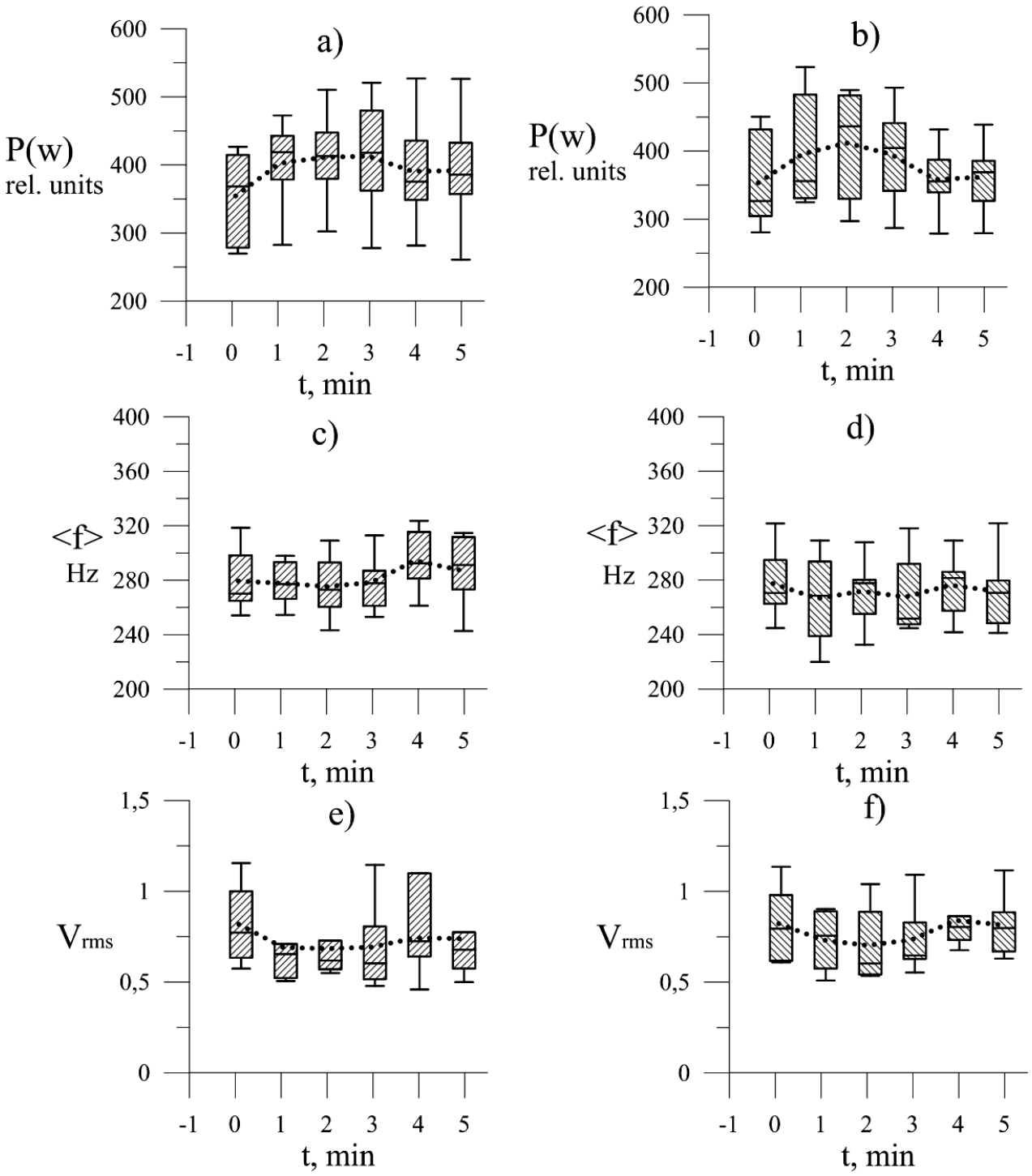

Figure 1. The values of the spectrum power (*a, b*), average frequency (*c, d*) and blood flow velocity (*e, f*) measured by the Speckle-Scan device: *a, c, e* - left hand; *b, d, f*- right hand.

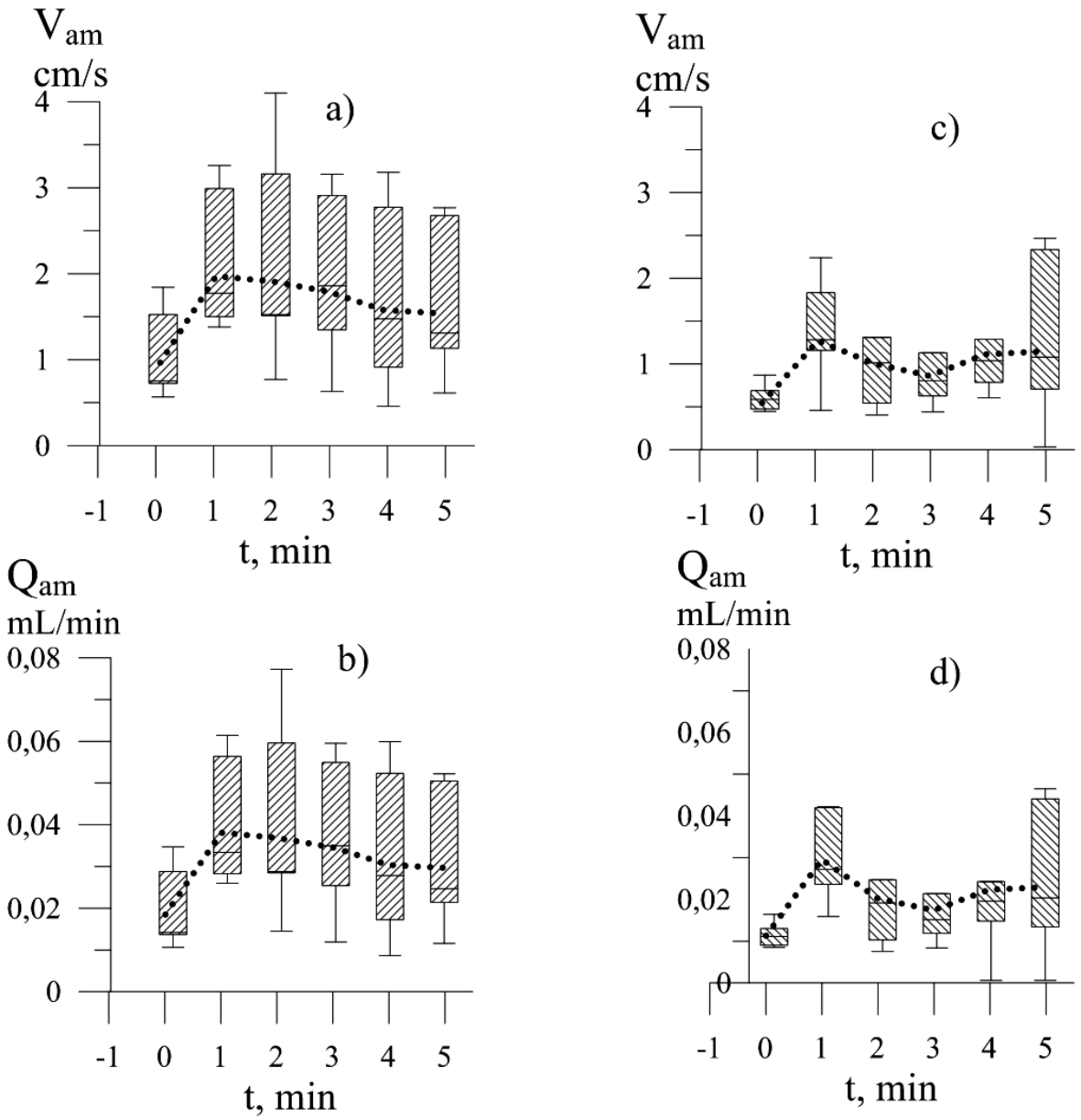

Figure 2. Values of linear (*b, d*) and volumetric (*a, c*) blood flow rates, measured USDG device: *a, c* - left hand*; b, d* - right hand.

The observed differences may be related to the fact that when measuring the USDG velocity of the blood flow, not only capillary blood flow is taken into account, but also blood flow in arterioles and venules, which is not fully taken into account in this mathematical model. Also, when a vessel is clamped as a result of hyperemia, along with the expansion and overflow of blood vessels in the local area, red blood cell deformation and aggregation occur, which is not taken into account in the mathematical model. After hyperemia, the blood flow rate over time is restored to its original values.

The size of the capillary filtration area, that is, the amount of transcapillary exchange and the volumetric rate of capillary blood flow, to a large extent depend on the functional capacity of the capillary bed, determined by the number of open capillaries. Therefore, by determining the volumetric rate of capillary blood flow or counting the number of open capillaries, it is possible to judge the amount of transcapillary exchange in the tissues.

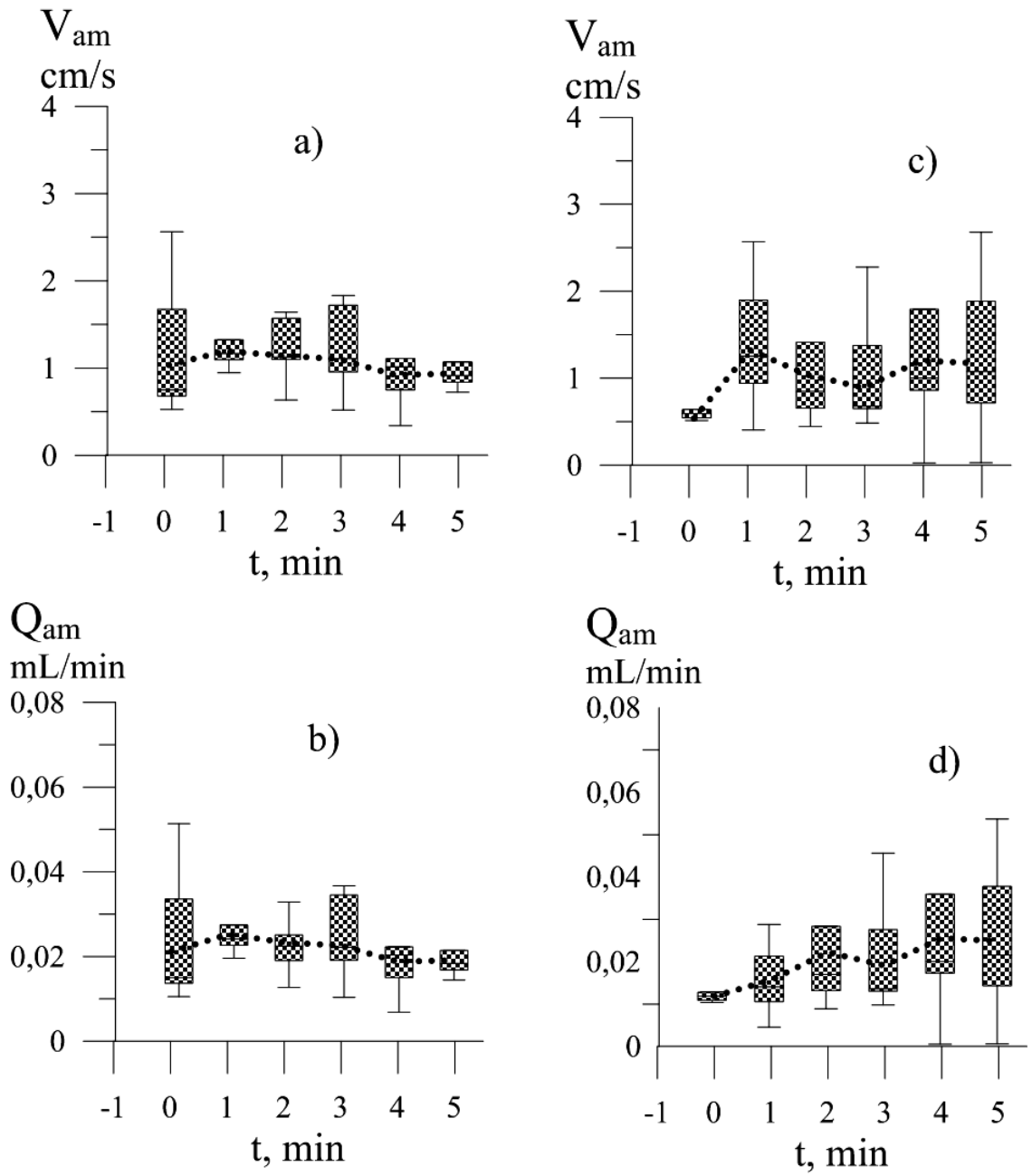

Figure 3. The values of linear *(b, d*) and volumetric (*a, c*) blood flow velocities in the simulation in the MathCad program: *a, c* - the left hand; *b, d* - right hand.

The main problem of speckle-metry and Doppler diagnostics is that the exact value of the scattering characteristics (-factor, etc.) used in the proposed optical microscopic models is not a priori known [17].

Figure 4 shows the autocorrelation functions of field fluctuations when particles are scattered back at different pressures after decompression of the brachial artery in the different time periods of changes registering.

As it can be seen from Figure 4, the autocorrelation function $g_1(\tau)$ *i*s sensitive to changes in pressure in the vessel, and hence in the volumetric blood flow, which results in a change in the steepness of the characteristic and coincides with the dynamics of changes in the blood flow in Figures 1-3.

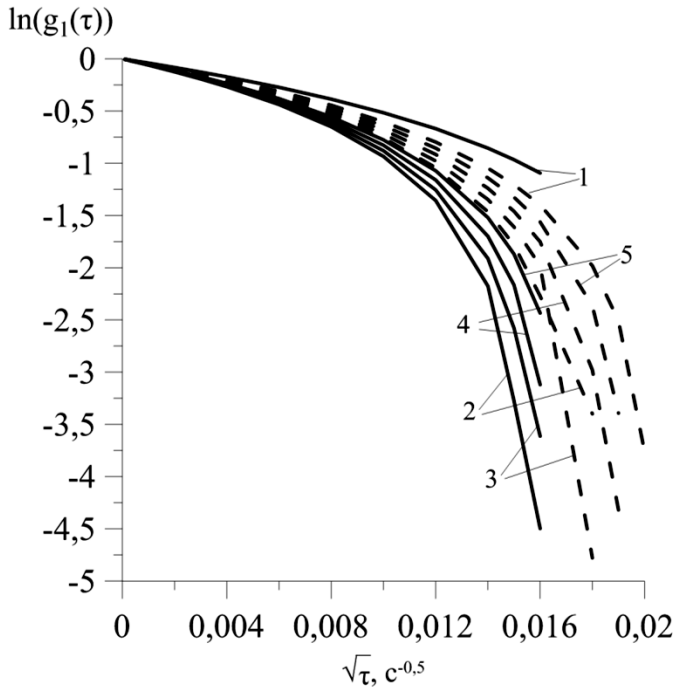

Figure 4. Typical autocorrelation functions $g_1(\tau)$ of field fluctuations under conditions of different dynamics of blood flow in the experiment with compression of the brachial artery calculated in the MathCad system, 200 μm - *solid curves*, 100 μm - *dashed curves 1 - before compression; 2 - after 1 min. 3 - after 2 minutes; 4 - in 3 minutes; 5 - after 4 minutes*

At the time of decompression, the excess pressure formed due to an increase flow of blood increased blood flow, the rate became higher than normal, as it can be seen in Figure 4 (curve 2), the autocorrelation function of the intensity fluctuations of backscattered back radiation sharply changed its slope. Gradually, after 4 minutes, vascular tone and blood flow velocity returned to a normal value, the slope of the autocorrelation function began to return to its former form (Figure 4, curves 3-5).

It needs to be noted that when the ordered movement of particles prevails over the Brownian movement, the semi-log graph $g_1(\tau)$ has the form of a straight line, the slope of which is proportional to the flow rate of the scattering particles

Conclusion

The speckle structure of multiply scattered light in multilayer biotissues was simulated to evaluate microhemocirculation of a biotissue. Verification of the speckle-metric method of monitoring the MHD (device “Speckle-scan”) was carried out using the methods of ultrasonic Doppler flowmetry and mathematical modeling of the propagation of laser radiation in the microhemocirculatory bed. It was found out that the parameter “average frequency of the spectrum” largely reflects the perfusion, while the area under the spectral curve reflects the capacity of the capillary bed. The slope of the autocorrelation function, which directly depends on pressure, can be used to diagnose vascular tone (elasticity). Further research of the model, associated with the introduction into consideration of additional factors affecting MHD, will improve the quality of results interpretation obtained in the control of microcirculation by the method of speckle-metry.

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