Complex noninvasive spectrophotometry in examination of patients with vibration disease

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ABSTRACT

A lot of industry workers all over the world have dealings with a strong mechanical vibration as with daily technology processes. Very often such long-time professional vibration causes the so-called professional “vibration disease”, in English literature “white fingers syndrome”, caused by a local vibration of hands. Among different clinical features of the vibration disease a leader’s part of them consists of different cardiovascular and trophic disorders of tissues. The objects of the present study were the peripheral blood microcirculation, peripheral blood oxygenation and tissues hypoxia state in a finger skin under vibration disease. For this purpose we have used a combined noninvasive spectrophotometry diagnostic technique consisting of Laser-Doppler Flowmetry (**LDF**), Laser Fluorescent Diagnostics (**LFD**) and Tissues Reflectance Oximetry (**TRO**). The results show good possibilities of all mentioned above diagnostic methods in estimation of different vascular disorders. A good correlation between persistent microcirculation disorders and trophic disturbances revealed in tissues of distal ends of upper extremities of the patients with vibration disease was estimated. Additionally, in present study with the use of real and long-time TRO and LDF methods a good correlation between LDF and TRO data including correlation in detected rhythms of blood microcirculation was estimated as well.

Keywords: spectrophotometry, laser, diagnostics, fluorescence, oxygenation, saturation, blood flow, vibration disease, white fingers syndrome.

1. INTRODUCTION

A lot of industry workers all over the world have dealings with a strong mechanical vibration as with daily technology processes. Very often a long-time professional vibration causes the so-called professional “vibration disease” (**VD**), in English literature “*white fingers syndrome*”, caused by a local vibration of hands. Different vascular disorders such as angiodystonic or angiospastic syndrome, predominantly on fingers, along with the lesions of distal ends of peripheric nerves of upper extremities, play a leader’s part among clinical features of VD caused by the local vibration. It manifests as finger whitening, spontaneous or cold-induced, followed by a severe pain (angiospastic syndrome) or by hyperemia and hand edema with a sensation of “heat” (angiodystonic syndrome). Vascular disorders and disturbances of peripheric innervation including perivascular one lead to trophic alterations in the distal ends of upper extremities. Tissue trophic defects show as hyperkeratosis of palm and finger surfaces with multiple fissures and thickenings, dullness and deformations of nails. As the disease progresses, trophic disorders spread to the deep tissues of the hand, affecting bones of both palm and fingers (osteodystrophic syndrome). It is suggested that pathogenesis of trophic disturbances is, first of all, associated with persistent troubles of microcirculation.[1,2] Many authors consider VD caused by local vibration a peculiar “angio-trophoneurosis”, more expressed in distal ends of extremities, but it may also have a systemic character showing different types of visceropathy. [3-5]

In connection with the above mentioned, a necessity arises to early and objectively diagnose disorders of both tissue trophism and microcirculation to make a decision about the necessary treatment-and-prophylactic measures to prevent the disease progression. In recent years, the medical practice has been successfully enriched with new methods of noninvasive laser and spectrophotometric diagnostics, Laser-Doppler Flowmetry (**LDF**), noninvasive Laser Fluorescent Diagnostics (**LFD**) and Tissues Reflectance Oximetry (**TRO**), for example, to evaluate the clinical state of tissues, respiratory processes and blood microcirculation in it.[6-8] The noninvasive laser diagnostic methods are very promising in modern medicine and surpass many former ones for some indices and for significance of medical-and-biological information concerning tissue condition.[6-11] They allow a doctor, in instance, to apply a real-time monitoring and different functional tests (tests with a load) to diagnose in vivo different vascular disorders, functional activity of endogenous fluorophores in tissues, blood microcirculation specialties, oxygen utilization in tissues, etc., that is very important for all patients suffering from the VD.

So, the object of the present study was the investigation of blood microcirculation, peripheral vessels condition, average oxygen saturation in a peripheral blood and activity of a series of enzymes in tissues, especially porphyrins, participating in oxidation-reduction reactions of cellular respiration, in order to estimate trophic disorders in the hand's skin of patients with VD caused by local vibration with the use of combined LDF, LFD and TRO techniques.

2. MATERIALS AND METHODS

We observed 78 male in-patients aged 38-60 years (mean age 47.8±1.9) with the VD caused by the local vibration. The control group consisted of 12 men aged 35-60 years (mean age 42.1±2.6) without any cardiovascular disease.

The functional state of microcirculation was evaluated using LDF method. LDF method is based on the optic tissue probing with monochromatic laser light and analysis of a frequency shift of a signal reflected from the moving blood cells (predominantly the red cells - erythrocytes). The frequency shift of the backscattered light (Doppler's effect) is proportional to the speed of the cell motion in a tested tissue volume.[10] The advantage of the said method, in comparison with other ones (rheography, photo-plethysmography, fluorescent microangiography, etc.), consists of a quantitative definition of blood flow in tissue microcirculatory channels. Spectral analysis of the reflected signal in coordinates of signal magnitude and time allows a doctor to distinguish rhythmic fluctuations of blood flow which describe important processes taking place within microcirculatory bed – a condition of smooth muscular cells, neurogenic and myogenic components of blood flow regulation, and a functional activity of shunts.[11] To register microcirculatory indices **Im** (blood flow parameters) a computerized Laser-Doppler flowmeter "LAKK-01" (Lasma Co., RF) was used. Laser irradiation source, applied in our technique, the He-Ne laser (wavelength 632 nm) provides the laser light penetration into the skin to the depth of around 1.5-2 mm and estimation of blood flow in superficial vessels of the tissue volume of around 1.0-3 mm^3. Measurements were taken from the surface of 2-4 distal finger bulbs (the area of main contact with local vibration). Circulation was recorded during 3 minutes using sitting position of a patient, with a hand at the level of the heart. Processing of the registered data of the basal circulation (i.e. without functional tests) was conducted according to the software of LAKK-01 analyzer. In this case the following indices of blood flow were determined:

- **Arithmetic mean of microcirculation index Im** (***M***, *perfusion units (pf. un.)*) – the mean parameter of a blood flow proportional to both the average speed of erythrocyte motion and the number of erythrocytes in a tissue volume studied;
- **Root-mean-square deviation (σ,** *pf. un.***)**. This index describes variability of *M* with time.
- **Coefficient of microcirculation variation (*K*$_v$)** calculated by the formula as follows:

$$K_v = (\sigma / M) \cdot 100\%. \quad (1)$$

Calculated indices *M*, σ, and *Kv* represent a general estimation of the microcirculation state. More detailed analysis of microcirculation functioning was carried out at the second step of the data processing consisting of a computer calculation of blood perfusion fluctuations reflecting the mechanisms of blood flow regulation. Fluctuations were expressed through their frequency and amplitude (***A***).

To study microcirculation in the VD patients' tissues, the following blood flow fluctuations were estimated:

- **Low frequency (LF) fluctuations** with frequencies of 1-10 per minute (0.017-0.17Hz) – due to the rhythmic activity of the microcirculatory bed self-components. These fluctuations are subdivided in 2 groups. Fluctuations with frequencies of 1.2-3.6 per minute are characteristic for neurogenic tonus associated with an α-adrenoceptive (predominantly α1) activity in membranes of conjugated smooth muscle cells.[12] It is a contraction frequency of exclusively arterio-venule anastomoses depending on the sympathetic activity. Neurogenic tonus value, by its physiologic character, regulates both the total blood inflow to the microvessels and the state of anastomoses. Neurogenic tonus was expressed through an amplitude of neurogenic vasomotions – ***An***, *pf. un*. Fluctuations with frequencies 3.6-9.0 per minute are due to the internal myocytic self-activity according to pacemaker mechanism. They are characterized by an amplitude of myogenic vasomotions **–** ***Am***, *pf. un*. Myogenic vasomotions (or fluctuations of myogenic tonus) reflect the state of a resistant section and pre-capillary sphincters regulating the metabolic surface of nutritional vessels.
- **High frequency (HF) fluctuations** – 11-36 per minute – due to pressure differential in veins as a result of respiratory movements of the thorax. The said fluctuations were estimated by an amplitude of respiratory vasomotions **–** ***Ar,*** *pf. un.*
- **Pulse fluctuations (CF=constant frequency)**, due to alterations in erythrocyte motion rate at the expense of the differences between systolic and diastolic pressure. They reflect pulse fluctuations and are expressed through an amplitude of pulse vasomotions – ***Ap,*** *pf. un*.

To register an oxygen saturation (**SO2**) of peripheral blood into patients' fingers the noninvasive reflectance oximeter "Spectrotest"® ("Tciclon-Test" Co., RF) was used [12]. The "Spectrotest"® is intended to register a fractional content of oxyhaemoglobin per total haemoglobin as an average saturation between arterial and venous saturation in the tested tissue's volume (around 300 mm^2 under the tissue's surface). The temporal resolution to measure and calculate mentioned SO2 parameter is around 1 sec for presented new device, what allows a doctor to study a dynamics of SO2 in tested tissues during different functional tests (tests with a load). Two standard functional (loading) tests – the occlusion test (**OT**) and the respiratory test (**RT**) – were used to understand better the specialties of the patients' clinical state. The parameters of applied functional tests were as follows: the duration time of occlusion was 3-6 min and a duration time for the standard RT was 15 sec. Saturation parameters were registered during 1 min before each test and 5 min after that from the surface of 2-4 distal finger bulbs (the area of main contact with local vibration) as well as for the LDF examination.

To evaluate the functional state of vibration-affected tissues and cell enzyme activity, the endogenous tissue fluorescence induced by external He-Ne laser irradiation (wavelength 632 nm) was investigated. A spectral line of the fluorescence excitation and a spectral area of the registered fluorescence (650-800nm), used in our study, are specific for endogenous porphyrin,[13-20] which accumulates in tissues, as we proposed in our previous research[21], under the tissues chronic hypoxia condition. So the registration of increased fluorescence spectra from the tested finger's skin in comparison with normal skin must indicate a chronic hypoxia in a skin. To register the fluorescence spectra, LESA-01-spectroanalyser (Biospec Co., RF) was applied.[22] A 15 mW CW He-Ne laser was used as a source for fluorescence excitation. Tissue fluorescence was registered from the same bulb skin of 2-4 fingers of a patient using 2mm-wide diagnostic light-guide (fiber), assembling reception and irradiation fibers into united band, and a slight contact between the working end of the band and a patient's skin was achieved during the diagnostic procedures. In all our study a registered intensity of fluorescence was expressed through a **coefficient of fluorescence contrast** (K_f) calculated by the formula[8, 21]:

$$K_f = 1 + (\beta \cdot I_f - I_l)/(\beta \cdot I_f + I_l)\ , \qquad (2)$$

where: I_f - an amplitude of registered signal at the maximum of fluorescence spectrum (fluorescence line, see Fig. 1), I_l – an amplitude of the registered signal at the maximum of backscattered laser radiation from tissues (backscattering line), β - the instrumental coefficient ($\beta \approx 10^3$).[8] We have to special notice, as it was recently shown[8], that K_f (2) is proportional to fluorophores concentration in tissue and quantum efficiency of them.

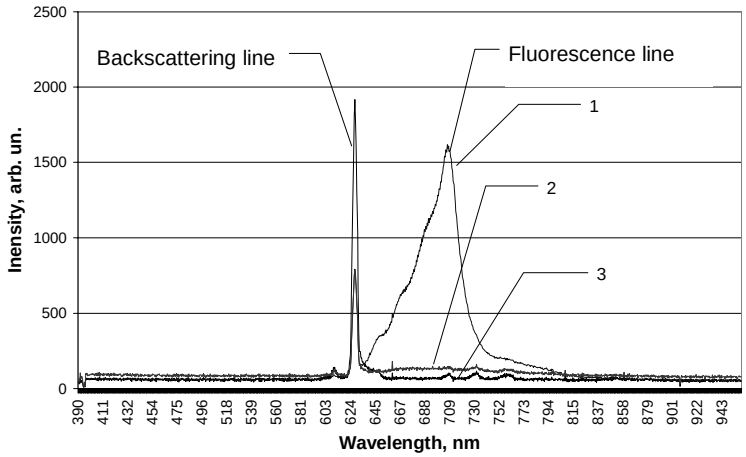

Fig.1. An example of registered fluorescence spectra. Excitation line 632 nm.
1 – tissue with strong hypoxia; 2 – intact (normal) skin; 3 – standard non-biological scatter.

3. RESULTS AND DISCUSSION

Table 1 demonstrates the incidence of the basic clinical syndromes manifesting vibration disease among 78 patients studied. The most frequent VD manifestations was the vascular disturbances as a peripheric angiodystonic or angiospastic syndrome in 73 (93.1%) patients, and in 92.3% of patients – as a hand's vegeto-sensory polyneuropathy. In 24 patients, a stage 1 of VD was diagnosed. As a rule, at the initial stage of VD, myodistrophic and osteodistrophic syndromes are absent. The stage 2 of VD with trophic tissue disorders was found in 54 patients.

Table 1. The incidence of basic clinical syndromes manifesting vibration disease.

Syndrome	Syndrome incidence: absolute value (%)
Peripheric angiodystonic syndrome	51 (65.3%)
Peripheric angiospastic syndrome	22 (27.8%)
Hand vegeto-sensory polyneuropathy	71 (92.3%)
Myodistrophic syndrome	31 (46.4%)
Osteodistrophic syndrome	21 (26.9%)

Results of LDF investigation without the use of any functional tests in patients' fingers with VD are shown in Table 2. In the stage 2 VD patients, an acute *M* fall was noted as well as an amplitude inhibition of all circulation rhythms, as compared with the control group (see examples of LDF-grams on Fig.2). The obtained values allow a doctor to estimate microcirculation according to V.I.Makolkin et al. classification[14] as a mixed pathologic type – a "spastic-and-stasic" one. The said type of microcirculation, in addition to angiospasm, demonstrates signs of intravascular alterations due to impairment of blood rheologic properties (blood cell aggregation, sludge-phenomenon, etc.). In the initial stage VD patients, there was no reliable *M* decrease, but a reliable inhibition of the low-frequency circulation waves was noted being associated with neurogenic and myogenic activity. In stage 2 VD patients, inhibition of the low-frequency fluctuations was more expressed. The results obtained are indicative of the affection of both perivascular innervation of microcirculatory bed and smooth muscular cells participating in modulating of vascular tonus. Microcirculation disorders were revealed in patients at rest, without any load-testing (functional testing), which suggested the persistence of vascular changes. This fact may explain the development of trophic disturbances in vibration-contact tissues.

Table 2. Laser-Doppler skin flowmetry of finger bulbs in VD patients and a control group.

Indices	Stage 1 VD (n=24)	Stage 2 VD (n=54)	Control (n=12)
M, pf. un.	14.2±0.32	9.5 ± 0.11*	16.7±1.5
δ, pf. un.	1.82±0.31*	0.66 ± 0.42*	3.90±1.58
Kv, %	7.10±0.12*	14.7 ± 0.16	13.0±2.0
Frequency amplitudes			
An, pf. un	1.86±0.10*	1.10±0.17*	4.09±0.27
Am, pf. un	1.42±0.06*	0.90±0.07*	3.79±0.52
Ar, pf. un	0.73±0.12	0.44±0.05*	1.21±0.15
Ap, pf. un	0.48±0.06	0.26±0.05*	0.53±0.08

***** The difference between groups of VD patients and a control group is reliable ($p<0.01$)

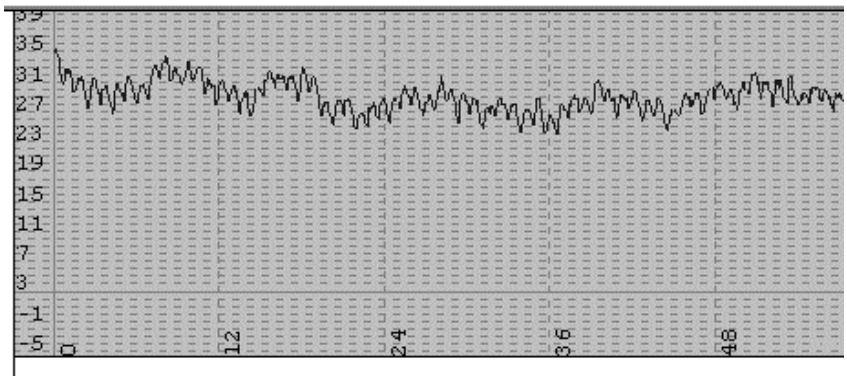

Fig. 2. An example of LDF-gram (*Im* versus time, sec.).
All LF, HF and CF fluctuations of circulation are clearly seen. M=26.14 pf. un., σ = 1.99.

The studying of endogenous fluorescence of affected hand tissues showed a long-term rise in the fluorescence contrast coefficient K_f . In stage 2 VD patients with expressed trophic disorders of finger tissues the mean K_f value was 0.23 ± 0.08. In the initial stage VD patients K_f also increased but less significantly. In the control group the same index didn't exceed 0.08 ± 0.05. All this data are collected in Table 3. But what is important to mark: in spite of obtained data of increased fluorescence from all the affected tissues under the VD, increased intensity of tissue fluorescence in our present trial didn't reach such great values, which we have usually observed in malignant tissues.[15]

Table 3. Mean $\mathbf{K_f}$ values of porphyrin compounds in VD patients' fingers and in a control group.

Indices	Stage 1 VD (n=24)	Stage 2 VD (n=54)	Control group (n=12)
$\mathbf{K_f}$, rel. un.	0.17± 0.08	0.23±0.08	0.08±0.05

It is interesting as well, that what is the bottom of the increased fluorescence of porphyrin compounds in pathologically altered tissues isn't completely investigated yet and is under discussion in special scientific medical literature. [7, 8, 15-21] In majority of publications on oncologic problems, for example, the said type of fluorescent activity is associated with growth of malignant tumors. So, it is frequently suggested that endogenous porphyrins are accumulated in tumors in larger concentrations (if compared with normal tissues) as a result of intensive cells' proliferative activity. However, it is known that alterations in benign tissues, for example, the erosive-and-ulcerated defects of the stomach and duodenum, can also show an increased endogenous fluorescence (though less expressed).[6-8, 21] In this connection, the results here obtained are rather indicative. Our previous studies on the changes of fluorescent activity in the erosive-and-ulcerated defects of the stomach and duodenum allowed us to suggest that increased accumulation of endogenous porphyrins was due to the chronic local tissue hypoxia.[21] In present cases, an increased cells' proliferation in the hand

skin of VD patients is out of the question at all, and, therefore, porphyrin accumulation here is most likely due to the tissue hypoxia. Theoretically, endogenous porphyrins are cytochrome components of mitochondria taking large part in oxidation-reduction reactions of the respiratory chain of electron transfer. And, therefore, their accumulation in tissues may be a compensation-and-adaptation reaction in response to chronic hypoxia induced by circulation troubles caused, in their turn, by the long-term vibration effect. Some authors, it's true, think that such a fluorescence spectrum (Fig. 1) is characteristic not only of endogenous porphyrins, but of lipofuscin as well. However, this fact changes little the above considerations. Lipofuscin is a complex of enzymes also participating in the system of cell oxidation during respiration. Lipofuscin accumulation, according to opinion of many researchers, is associated with cell "aging", and in pathologic processes – with oxygen deficiency in tissues and dystrophic processes developing in them.[16] So, lipofuscin accumulation may be indicative of a chronic tissue hypoxia as well.

The more visual results of TRO investigation are presented in fig.3-4. As it was estimated the different changes and rhythms in SO2 dynamics can be observed by TRO technique as well as different blood perfusion rhythms by LDF one. Moreover, it was shown that the "Spectrotest" ® can indicate the changes in SO2 parameter during both OT and RT. Under occlusion, for example, it allows a doctor to observe an SO2 decreasing in a tissue, while the LDF index **Im** shows for a doctor nothing except the so-called "*biological zero level*" (Fig.4). After occlusion procedure both parameters show the post-occlusion hyperemia in a finger skin.

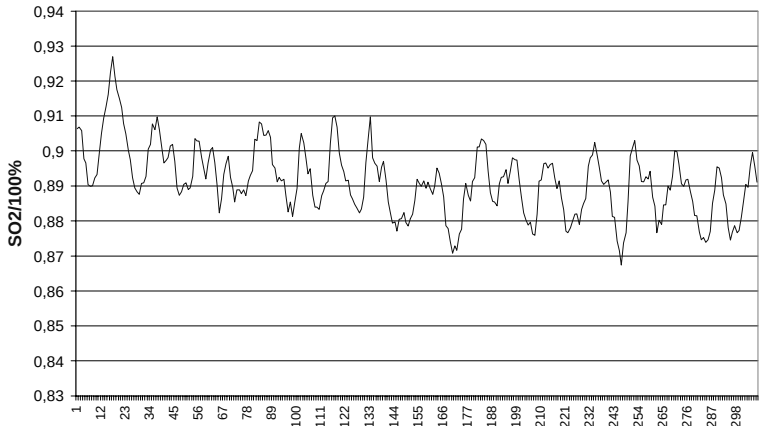

Fig. 3. An example of SO2-gram (**SO2/100%** versus time, sec.)

From one hand, it shows the good work of oximeter "Spectrotest" ® and a reality of calculated SO2 parameter. From the other hand, one can ask: what a parameter is registered by the "Doppler" device if the simple absorption spectroscopy technique can register the same rhythms without the use of any complex Doppler frequency shifts? We can assume that in common cases the LDF apparatus indicate a complex process in a capillary blood flow. Not only a Doppler signal, but also a number of processes accompanying a tissue blood circulation. It is sensitive to the total light attenuation by the haemoglobin and by the oxy-haemoglobin of a blood as well, especially in a case of the use of He-Ne laser as a light source when the spectral absorption by different fractions of haemoglobin is differ for the wavelength 632 nm.

The studying of blood oxygen saturation in affected patients' finger tissues showed that in a general case the vessels dysfunction leads to chronic hypoxia condition into finger skin for VD patients. Table 4 illustrates initial obtained results before different functional tests application. More intensive oxygen utilization in skin lead to decreasing of registered SO2 mean parameter, because the arterial saturation is usually around 97-98% and not changes more than 1-2% for people without any bronchial disorders.

Table 4. Mean SO2/100% values in VD patients' fingers and in a control group.

Indices	**Stage 1 VD (n=24)**	**Stage 2 VD (n=54)**	**Control group (n=12)**
SO2/100%.	0.83± 0.06	0.89±0.05	0.81±0.08

We don't present here any numerical results, except fig. 4 as an example, for SO2 investigation during RT and OT. For the functional tests in application to TRO parameters, SO2 in instance, there are no special developed and scientific-based algorithms for such data processing. So, for the present, we can mark only that it is necessary to develop them in a future.

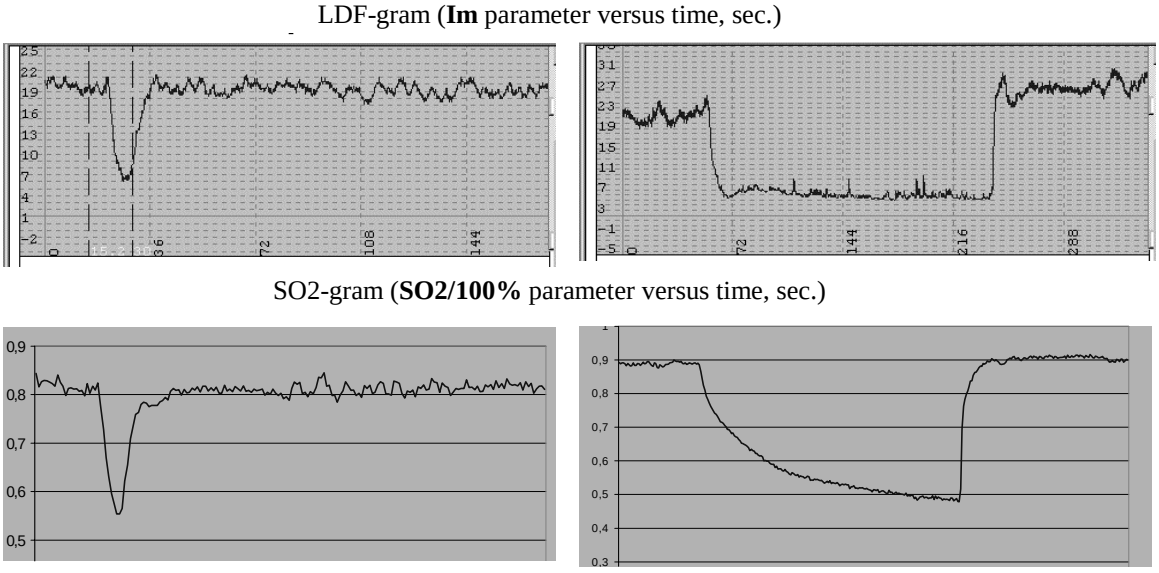

Fig. 4. An example of results of different functional tests.

4. CONCLUSION

Thus, in the present study, we were first to objectively reveal with the use of complex noninvasive optical methods of LFD, LFD and TRO an association of persistent microcirculation disturbances with both the changes in oxidation-reduction reactions of cell respiration and development of trophic lesions in distal ends of upper extremities in patients with VD. Now we can formulate our main results as follows:

1. Microcirculation disorders (according to LDF data) were revealed in the majority of patients with VD even at rest, without any load (functional) testing, which was indicative of the long-term vascular alterations and could explain the trophic defects in the vibration-contact tissues.
2. Microcirculation disorders (according to LDF data in patients with an expressed disease stage) may be classified as a spastic-and-stasic type of microhemodynamics. In addition to angiospasm, this type of circulation demonstrates intravascular troubles due to impaired rheologic properties of the blood.
3. In VD patients with initial and expressed disease stages, specific signs of LDF-gram are revealed manifesting inhibition of the low-frequency circulation waves (characteristic of myogenic and neurogenic vascular tonus) which is indicative of the lesions of both perivascular nerves and smooth muscular cells of the blood vessels.
4. Rise in intensity of endogenous fluorescence of enzymes participating in respiratory cell oxidation (endogenous porphyrins, lipofuscin) in vibration-affected tissues is indicative of a degree of chronic hypoxia due to microcirculation disorders.
5. TRO technique confirms well the chronic hypoxia condition in tissues of VD patient hand's fingers. As it was estimated the different changes and rhythms in SO2 dynamics can be observed by TRO technique as well as different blood perfusion rhythms by LDF one. So, the special algorithms for dynamic data processing must be developed in a TRO technique, especially for the processing of functional tests results.
6. Summarizing, the methods of noninvasive LDF, LFD and TRO are very effective and informative techniques in revealing angiotrophic disturbances in patients with VD including its early stages. Moreover, it can be

proposed, that the complex use of them makes it easier to choose both an adequate therapy and dynamic express-verification of the treatment result.

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