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PRINCIPAL SOURCES OF ERRORS IN NONINVASIVE MEDICAL SPECTROPHOTOMETRY. PART 1. PHYSICOTECHNICAL SOURCES AND FACTORS OF ERRORS

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Early results of complex experimental investigations on the study of instrumental and methodological errors of diagnostics in noninvasive medical spectrophotometry are described. Physical and technical sources and factors of errors are considered for measurements using nonbiological simulation measures. It is shown that the geometric and spectral characteristics of the optical elements and photodetectors, and also selected models and data-processing algorithms in the computer software of the instruments, have the greatest effect on the diagnostic errors.

Keywords: *noninvasive medical spectrophotometry, back-scattered radiation, soft biological tissues, laser Doppler flowmetry, optical tissue oximetry, laser fluorescence diagnostics, oxyhemoglobin saturation.*

A topic of investigation of modern noninvasive medical spectrophotometry (NMS) is the *in vivo* level of accumulation of various biomolecules and substances in a layer of biological tissue and also their dynamics over time [1]. Strictly speaking, diagnostic instruments that use this technology should be referred to by the term "means of measurements for medical purposes (MMMP)" [2]. Therefore, except for the study of the general engineering and theoretical foundations of the operation and design of such systems [3], in NMS it is necessary to create a complete system of metrological assurance – both for the instruments and also for the measurement methods overall. The standard [2], as part of the specialized medicotechnical requirements, represents sufficiently stringent metrological requirements for MMMP. Meanwhile, if we ignore the historically first diagnostic method of NMS (pulse oximetry [4]), then there is very little mention in the specialized literature of the other methods and instruments in this area of the metrological aspects of the measurements up to the present.

In one of the first publications of this kind [5], the scatter of the measurement results was investigated for a type of NMS – laser fluorescence diagnostics. Later, there began to appear experimental works from different countries, in which different particular questions concerning measurement errors were considered for other types of NMS, and also the creation of operating measures (in English terminology "optical phantoms of biotissues") for carrying out comparative measurements and estimates of the reproducibility of their results [6–8]. Only recently [9] has there been sufficiently systematic reporting of the basic theoretical principles of metrological assurance in this area, and detailed analysis has been provided for the most important and specific metrological terms concepts, and definitions in NMS. Also the measurement process has been classified, and certain key features of the metrology of *in vivo* measurements in NMS have been considered from the position of the so-called operational approach [10].

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The aim of the present article is the interpretation and analysis of the results of the initial pilot experimental investigations of the sources for development of the errors in the diagnostics of NMS, carried out on the basis of theoretical works [9]. The key problem was in the maximally wide search and analysis of all the basic physicotechnical and biomedical factors and effects, most strongly affecting the metrological characteristics of the methods and instruments of NMS. In the first stage, we considered physicotechnical factors and effects for model measurements on nonbiological simulation measures (SM). The second stage was devoted to search and analysis of the basic medicobiological and organizational-clinical factors and effects during natural measurements in a clinic.

One aim was the study of the following subject representation of the measurement problem. Diagnostic information on the biological object (BO) under investigation was obtained by the method of optical spectral probing [3, 11]. Such an active method of probing assumes illumination of the BO by an external low-power (milliwatt) light source of different spectral composition and the recording of the exiting secondary optical radiation that forms inside the object owing to the effect of light scattering. Since the BO contains a large quantity of light-absorbing chromophores (e.g., hemoglobin) and fluorophores (e.g., collagen), and formed elements of blood also are moving inside it, the exiting secondary radiation is weakened in power and contains additional spectral components due to the Doppler effect and fluorescence. Analysis of the spectral weakening, Doppler frequency shift, and fluorescence spectra enables us to draw a conclusion about the biochemical composition of the tissues of the BO, which also forms a physical basis for such diagnostic methods of NMS as laser fluorescence spectroscopy (LFS), optical tissue oximetry (OTO), laser Doppler flowmetry (LDF), etc. [1]. It is very important that such diagnostics be absolutely harmless to the organism and noninvasive. Therefore, they can be carried out daily an unlimited number of times, which is a significant advantage in clinical practice.

The formal technical description of the given measurement problem is represented in Fig. 1. The optical sources of illumination of the BO within MMMP have a characteristic power of irradiation $P(\lambda)$ as a function of wavelength λ, produce in the illuminating aperture ω (for the instruments considered earlier with fiber-optic probes, ω is the aperture angle of the optical fiber) a potential material carrier of information about the object, which is the initial optical signal $S(x, y, \lambda, t)$, where x and y are the spatial coordinates of the surface of the BO, and t is the time. The BO being examined, through its opticophysical properties, is connected with features of the anatomic-morphological structure and biochemical composition of the tissues, encodes the initial probing signal of a certain dimensionless function of the coding $B(\lambda)$ in the general case of a nonstationary (i.e., continuous or rhythmically changing in time) function, transforming the initial signal into a secondary signal $S^*(x^*, y^*, \lambda^*, t^*)$ and changing its fundamental informational parameters: the spectral power density, the depth of the amplitude–frequency modulation, etc. The MMMP problem is to select a sufficiently powerful secondary coded signal in the collecting aperture ω^*, to purify it from external interference and noise and, taking into account information on the parameters $S(x, y, \lambda, t)$, to determine (calculate) all the important opticophysical and medicobiological properties of the BO, causing specific recorded coding of the signal [3].

Since in this area of medical diagnostics, no sample measurement means or measurement means certified at the state level exist at present, including standards for the quantities being measured, all the physicotechnical investigations developed for these aims were carried out for author works on SMs [11]. In all the experiments, the BOs were replaced by arbitrary "sample" nonbiological SMs [9], which hypothetically ideally simulated the opticophysical properties of the object and diagnostics for errors that do not enter into the natural instrumentation and methodologies. In order to carry out frequently repeated, statistical tests (measurements) on the same "sample" SMs with the same instruments of the same type, we needed to study, with various instruments of various manufacturers, the most important instrumental and methodological errors and differences of the measurement results, caused by imperfections or specifics of the structures of one or another instrument or its separate structural unit. For this, based on the results of statistical tests we estimated for each series of s identical (in the opinion of experimenters) measurements, the mean arithmetic value M_s of each of the parameters being recorded, the root-mean-square deviation (RMS) σ, and the scatter δ of the measurement results with respect to the level σ in percent of the quantity being measured (coefficient of variation $\delta = (\sigma/M_s)\cdot 100$). Then the results of all s of the series were compared with each other, and the differences in δ were analyzed for methodological and instrumental errors and their causes – both random and systematic.

Since all the instruments for NMS, from the point of view of theoretical metrology, in one form or another, realize the principle of indirect measurements [9], the method for carrying out the investigations included subsequent statistical anal-

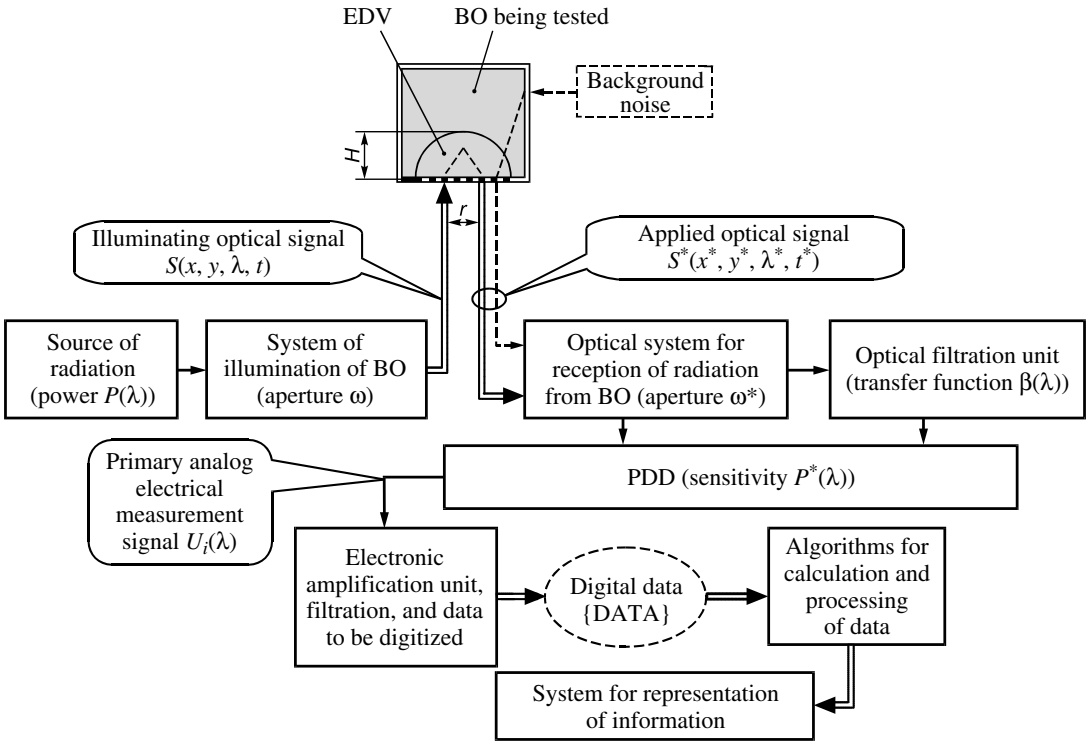

Fig. 1. Formal subject representation of the measurement problem in the area of NMS: BO – biological object ; EDV – effective diagnostic volume; PDD – photodetection device; r – base of measurements; H – maximum depth of probing.

ysis based on the scheme indicated above both for all the fundamental finite biomedical diagnostic data, calculated programmatically, and also for all the primary physical data measured directly by instruments having SM. The methodological errors connected with the ambiguity of the placement of the instrument probe on the object being investigated were studied by moving (tilting, rotating, etc.) the probe along the gage surface. The results obtained were compared with data from its fixed position. The systematic errors in each series of measurements were estimated by comparison of the averages of the measured instruments with SM of the values of all the fixed and medicobiological parameters with the nominal values of these parameters for each gage that were assigned to it at the construction stage, or by comparison of the averages of the measured values of the parameters being recorded by the test instrument (method) with the averages of the values of these parameters for each SM, averaged over all the instruments (methods) being tested in all the measurement series with this gage.

All the investigations were carried out with the use of three fundamental diagnostic technologies – OTO, LDF, and LFS. For the case of OTO, the physical parameters being analyzed were signals from a photoreceiver in millivolts in different spectral ranges of wavelength (green U_{G}, red U_{R}, and infrared U_{IR}) and relatively stationary functions of coding:

$$B_{\mathrm{rel}}(\lambda_i) = B_{\mathrm{st}}(\lambda_i)U(\lambda_i)/U_{\mathrm{st}}(\lambda_i),$$

where $B_{\mathrm{st}}(\lambda_i) = 1$ is a standard coding function of an ideal light-scattering gage (simulates bloodless tissue); and $U(\lambda_i)$ and $U_{\mathrm{st}}(\lambda_i)$ are voltages from the photoreceiver for channel λ_i for measurements with working SM and white scattered light from the gage.

The resulting biomedical data from analysis in this case were the calculated parameters of the tissue saturation of oxyhemoglobin of the peripheral blood S_tO_2 and the volume blood-filling of biological tissue V_b [1].

For the LFS method, the primary physical data being analyzed are the recorded amplitudes (spectral power densities) of the back-scattered radiation at the wavelength of the excitation source (laser) I_l and at the maximum of the fluorescence

spectra I_f for different excitation wavelengths and fluorescence recording. The final biomedical parameter is the modified coefficient of fluorescent contrast [5]:

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

where $\beta = 1000$ is the reduction coefficient of the optical filter (instrumental coefficient).

For LDF technology we estimated only the biomedical index of the perfusion of tissue by blood (index of microcirculation I_m) at probe wavelengths of 632 and 810 nm [12].

Equipment for the investigations included three samples of Spektrotest tissue oximeters, two laser Doppler instruments of the LAKK series, a multifunctional diagnostic LAKK-M unit, and an LESA-01 system of laser fluorescence diagnostics. In order to study the effect on instrumental errors of the construction features of the light guides used as optical probes in the LAKK-M and LESA-01 systems, we also made three interchangeable sets. Such a large assembly of diagnostic equipment is necessary for searching for regularities and sources for the origination of diagnostic errors inherent not in a single type of instrument (specific structure of instrument) or method, but in an entire class of given instruments realized by different methods and in different instrumental versions for different NMS methods.

By virtue of the presently important transitional and controversial situation concerning metrological terminology arising as a result of the introduction of international recommendations [13, 14] instead of [15–17], it makes sense in the framework of the description of the method for carrying out the experiment to improve both the position of the authors in connection with the use of the concepts of "error" and also "ambiguity of the measurement results." As was indicated in [9], if one adheres to the so-called operational approach to problems of metrology in NMS, more weight is given to the position of the authors [18]. It is sufficiently convincing to prove the necessity for using the concept of "measurement error" in the analysis and description of the causes for the inexactness of the result, hidden in the instrumental and methodological imperfections of the instrumental basis of measurement, and, parallel to this, the concept of the "ambiguity of the measurement results" if we refer to an analysis of the quantities and the confidence interval of the data measured in the experiment in one or another real measurement problem. Accordingly, for a description of the test results for evaluation of the metrological parameters of the measurement devices and systems, and also measurement methods in the large, we use the classical concept of errors, e.g., instrumental errors. The description of elementary diagnostic data for a specific patient in a clinic and the drawing of a final conclusion are related to the ambiguity of the measurement results. Here, the ambiguity of the clinical results cannot be less than a combination of the basic random and systematic errors of the diagnostics, the sources of which are the physical basis of the method, specific instrumental realization, and computational algorithms. In the general case, however, it can exceed them for the values of the additional instrumental and methodological errors produced by the features of the conditions (routes) of examination of the patient in the clinic, the different qualifications of the medical personnel, the development of an interactive component of the error [9] caused by the features of interaction of an MMMP probe with BO, etc.

The absence of certified and sample means of measurements in the area of NMS does not allow us to fully carry out all the classical requirements for conducting similar investigations, especially based on equally accurate and homogeneous measurements in different series. Therefore, where this was not considered possible, no estimation was made for homogeneity and equal-scattering of the measurement results from series to series, and it was assumed in the first approximation that they were equally accurate and homogeneous (equally scattered), so that all the data obtained can be compared internally and with the measurement results in other series, other instruments, and according to other methods of NMS. Thus, for the first stage of the investigations, attention is given mainly to sources that may introduce random and systematic errors and their approximation based on an analysis of the scatter of the measurement results by the different instruments and methods.

On a large scale, the averages of the statistical scatter of the measurement results of the primary physical signals for nonbiological working SMs for the majority of test methods and instruments of NMS are ±(2.5–3)%.[1] A typical fragment of the data obtained for OTO technology for individual (instantaneous) measurements by one of the Spektrotest oximeters for

[1] The scatter in the readings of one instrument for multiple measurements for an SM, neglecting the scatter of the comparative readings of different instruments for the same SM.

TABLE 1. Statistical Scatter of OTO Results for Individual (instantaneous) Measurements of a No. 0030 Spektrotest Oximeter for SM No. 1

Measure	Parameter	Photoreceiver signals, mV, for			$B_{rel}(\lambda_i)$ for			Values of medical parameters being calculated, rel. units	
		U_G	U_R	U_{IR}	λ_G	λ_R	λ_{IR}	S_tO_2	V_b
Sample, scattering light	M_{10}	3364	2994	3308	1.0	1.0	1.0	–	–
SM No. 1	M_{10}	437.9	1901	1746	0.131	0.639	0.525	0.914	0.231
	σ	7.818	19.61	13.95	0.004	0.007	0.006	0.032	0.007
	δ, %	**1.79**	**1.03**	**0.79**	**2.68**	**1.15**	**1.14**	**3.49**	**3.23**

TABLE 2. Scatter of Individual (instantaneous) Readings of Three Spektrotest Oximeters for SM No. 2

Instrument number	Parameter	Photoreceiver signals, mV, for			$B_{rel}(\lambda_i)$ for			Values of medical parameters being calculated, rel. units	
		U_G	U_R	U_{IR}	λ_G	λ_R	λ_{IR}	S_tO_2	V_b
0030	M_{10}	1863	2277	1865	0.554	0.761	0.564	0.601	0.027
0031	M_{10}	1807	2638	1965	0.523	0.731	0.557	0.587	0.031
0032	M_{10}	1841	2598	2196	0.570	0.747	0.566	0.511	0.023
Average over three instruments	***M***	**1837**	**2504**	**2009**	**0.549**	**0.746**	**0.562**	**0.566**	**0.027**
	σ	**28.17**	**197.9**	**169.8**	**0.024**	**0.015**	**0.005**	**0.049**	**0.004**
	δ, %	**1.53**	**7.91**	**8.45**	**4.32**	**1.99**	**0.83**	**14.62**	**8.64**

SM No. 1 is shown in Table 1. The nominal values for SM No. 1 are $S_tO_2 = 0.891$ and $V_b = 0.226$. The relative mean errors are $\delta_{M_{S_tO_2}} = 2.7\%$ and $\delta_{M_{V_b}} = 2.2\%$. The maximum scatter in a series of ten measurements was 1.8% for voltage U_G based on the green channel of the oximeter and correspondingly was 2.7% for $B_{rel}(\lambda_G)$. Subsequent analysis showed that this scatter has a random character connected with the noise in the opticoelectronic circuit of the instrument, the instability of the power, and the temperature drift of the dominant wavelength of the green radiator.

A more important difference in the initial physical data for all the SMs used was detected during a comparison of the results of measurements by three different measurements from a single factory lot of instruments (Table 2). The nominal values for SM No. 2 were $S_tO_2 = 0.546$ and $V_b = 0.028$. The relative mean errors were $\delta_{M_{S_tO_2}} = 3.7\%$ and $\delta_{M_{V_b}} = 3.6\%$. Here the maximum voltage scatter was fixed at the level $\delta = \pm 8.5\%$ based on the red and infrared channels of the instruments. A reason for the increased scatter is the difference in the spectral characteristics (power density and sensitivity) of the radiators and photodetectors. However, this difference does not lead to a simultaneous increase in the scatter for $B_{st}(\lambda_i)$ since it is practically completely compensated by previous measurements for the standard light-scattering measure.

The maximum spread for all the methods and instruments had medicobiological indicators needing to be calculated even for comparatively small scatters in the measured physical signals. The computational algorithms presently used for the instruments in OTO have a very complex and multistep character, and when they are used, the scatter of the measurement results is two to three times greater than the measurement errors of the initial physical signals (see Tables 1 and 2). Thus, the major part (up to 50–80%) of the total measurement error in NMS is due to the computational algorithms.

A noticeable increase in the scatter of the indicators being recorded for SM is observed for a comparative analysis of the data obtained on one instrument but with different samples of optical-fiber probes. In Table 3, we present data from

TABLE 3. Scatter of Finite Biomedical Data for the OTO Method for an LAKK-M Unit for Three Optical Probes

Probe number	Parameter	Values of calculated medical parameters, rel. units	
		S_tO_2	V_b
001	M_{50}	0.575	0.107
011	M_{50}	0.815	0.117
021	M_{50}	0.572	0.099
Average over three instruments	***M***	**0.654**	**0.108**
	σ	**0.139**	**0.009**
	δ, %	**21.3**	**8.38**

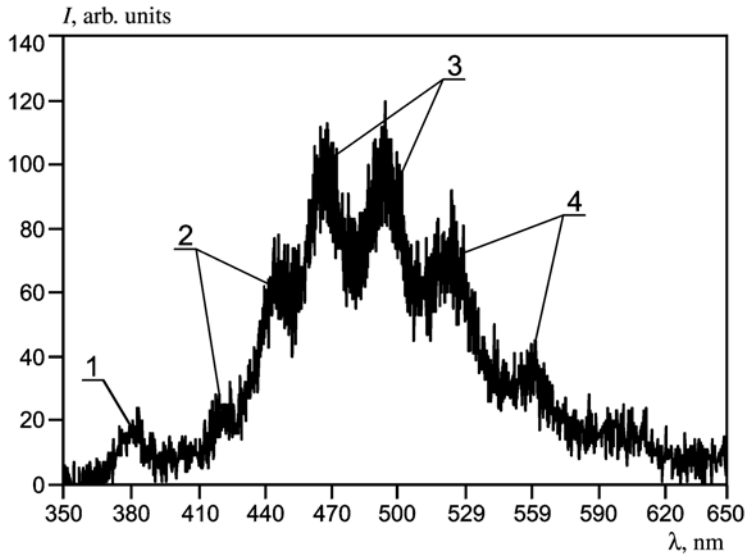

Fig. 2. Typical nonnormalized spectrum of fluorescence *I* recorded *in vivo* from the skin of a finger cushion for an LAKK-M unit during the excitation of fluorescence in the wavelength range λ = 370–380 nm with maxima: *1*) excitation lines; *2*, *3*, *4*) components of skin: collagen and elastin, nicotinamide, and flavin enzymes, respectively.

the LAKK-M unit for the OTO method with the use of three different probes from a single lot. We assume that the probes should be structurally identical but nevertheless contain certain technological scatters of the parameters of the apertures ω and ω^* and the bases *r* of the measurements (see Fig. 1) [9]. A cause of the resulting values for probe No. 011 is a small difference in the base of the collecting and illuminating fibers in comparison with the two other examples. Here it is necessary to note that it would be incorrect to treat the difference in the measurement results for an SM with the use of different types of instruments (see Table 2) or different examples of optical-fiber probes (see Table 3) having a spread in the values *r*, ω, and ω^* as a manifestation of the required diagnostic errors. The indicated structural features determine the effective diagnostic volume (EDV) of the examined object [9]. In the present case, not as many errors are observed as for the naturally different indicators of the instruments connected with different EDVs, from which we read the fundamental useful signal. For each such volume, the nominal values of all its physical and biomedical parameters should be normalized for each SM. Therefore, a direct comparison of the indications for different EDVs is not always methodologically correct.

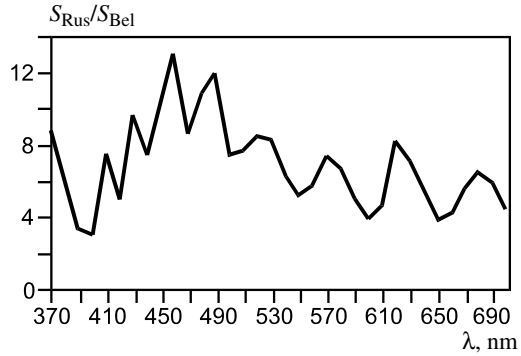

Fig. 3. Ratio of the spectral sensitivities S_{Rus}/S_{Bel} of the polychromators produced in Russia and Belarus.

On the other hand, it is necessary that we consider differences in measurement results that are not connected with the formation of an EDV but due to the spectral characteristics of the radiators and photodetection devices (PDDs) of different examples of single-type instruments to be instrumental errors. The most obvious example is the recording of the fluorescence of biological tissues in the LFS method. A typical, initially recorded spectrum of the skin of a finger using an LAKK-M unit for the excitation of fluorescence in the range 375–380 nm is shown in Fig. 2. The recording unit is based on a polychromator with standard linear TCD1304AP photodetectors [11]. The entire spectrum is recorded at the output of the polychromator at the same time. It is represented by the superposition of the fluorescence spectra of various natural components of biotissue, such as collagen, elastin, and nicotinamide [1], which have different intensities of fluorescence at different wavelengths. The existence in the spectrum of components of biotissue is indirectly confirmed by its nonmonotonic (notched) character, according to the separate maxima (based on their presence and amplitude). As a rule, we can form an opinion about the biochemical state of the tissue. In Fig. 2, we represent a possible interpretation of the separate maxima in the spectrum. However, this "notched" character of the spectrum can also be a consequence of the nonuniform spectral sensitivity of the linear PDD or other technical irregularities of the instrument. What is more, different manufacturers can use, in the construction of instruments, different PDDs, which leads to a distortion of the initial envelope of the spectrum and the corresponding methodological errors in the last interpretation of the biochemical composition of the biotissue.

To confirm these considerations, we present in Fig. 3 the measured ratio of the spectral sensitivities of the PDD of two single-type polychromators produced in the Republic of Belarus and Russia. On average, the sensitivity of the Russian instrument proves to be greater by a factor of 6.5. However, on the curve we note a "notched" nonuniformity of the ratio. It can also be one of the causes of the known disagreements in various publications based on the arrangement of the maxima of the fluorescence spectra of specific fluorochromes. Therefore, in NMS, a nonuniformity of the spectral sensitivity of a PDD becomes an important metrological characteristic, requiring normalization, checking, and standardization.

The effect of external background (noise) and subjective random errors connected with the ambiguity of the position operator of the working face of the light guide on the surface of the SM is graphically developed in experiments with different adapters (bearings) on the light guide, and also in comparison with the results of statistical tests with a bearing and without one. The bearing developed for instruments of the LAKK series, with a female connector on the optical fiber, serves both for decreasing the mechanical pressure of the fiber on the BO surface and also for screening the impact of the outside light in the EDV (Fig. 4). However, repeated reflection for backscattering of the radiation emerging from the object from the lower plane of the bearing in contact with it can introduce an additional error into the measurement result owing to the possible change in the illumination inside the EDV. An estimate of the action of this effect in LFS was carried out with the use of mirror-reflection and blackened adapters. Test results at a fluorescence excitation wavelength of 532 nm are represented in Table 4, from which the effect of the adapter is evident. When it is absent, the ambiguity of the positioning of the optical probe for SM leads to an increase of the relative scatter of the calculated coefficient K_f up to ±5% and its average

TABLE 4. Scatter of the Results of Measurements of I_l/β, I_f, and K_f for SM No. 10 with Fluorescence at $\lambda = 532$ nm

Bearing	I_l/β			I_f			K_f		
	M_{25}	σ	δ, %	M_{25}	σ	δ, %	M_{25}	σ	δ, %
Absent	456.8	23.09	5.05	321.1	24.27	7.56	0.83	0.0367	4.45
Mirror	465.7	10.33	2.22	313.8	7.23	2.30	0.81	0.0085	1.06
Black	448.9	11.04	2.46	282.5	7.00	2.48	0.77	0.0072	0.93

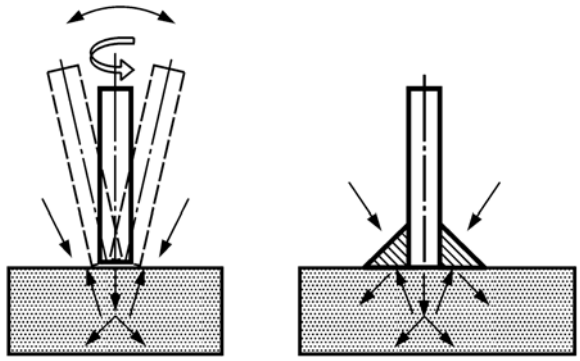

Fig. 4. Ambiguity of positioning of optical probe (*a*) and optical probe with screening bearing (*b*).

value owing to the impact of the background irradiation in the EDV. The minimum scatter and error in the determination of K_f are observed for the case of the black, absorbing light from the adapter. The mirror adapter owing to the repeated reflection of the radiation on the planes that are in contact with it has a systematic error with SM as a result of the measurement of K_f but this does not considerably increase the random errors of its determination. The assumed nominal value for SM No. 10 is $K_f = 0.78$.

For carrying out measurements by the LFS method, the transfer function of the clipping filter $\beta(\lambda)$ of the optical-filtering unit of the device has a large effect on K_f (see Fig. 1). An estimate was made by comparing the results obtained from one SM for the two similar diagnostic systems LESA-01 and LAKK-M with different clipping filters and, accordingly, different $\beta(\lambda)$. A sufficiently important difference in the measured values of K_f was revealed. For certain wavelengths and an SM, it proved to be at the level ±(30–40), which is very substantial. For series production and a widespread introduction into medical practice of similar MMMP of different manufacturers, the function $\beta(\lambda)$ together with the parameters $P(\lambda)$, r, ω, and ω^* should be one of the sharply normalized and regulated metrological characteristics of the instruments.

An analysis of the set of results of investigations of physicotechnical sources of formation of diagnostic errors in the area of NMS enabled us to draw some basic conclusions.

The most important physicotechnical sources of differences in the readings of the instruments are the nominal (acting) values of the spectral power density of the sources of the radiation $P(\lambda)$ and sensitivity of the PDD of a diagnostic instrument, apertures ω and ω^*, and base r of the systems of illumination and reception of radiation, the transfer function $\beta(\lambda)$ of the optical filtering unit of the instrument, and also the selected computational algorithm for the medical readings.

The sources for generation of the basic random and systematic instrumental errors due to the lack of ideality of the apparatus part of the MMMP are as follows:

1) the random technological scatter, nonuniformity over the spectrum and time instability (e.g., temperature) of the nominal spectral sensitivity of the PDD;

2) the random technological scatter and short-time instability (for the time segment of a single diagnostic procedure) of the nominal power density of the sources $P(\lambda)$; and

3) the random technological scatter of the parameters r, $\beta(\lambda)$, ω, and ω^* from instrument to instrument.

The principal sources of additional random and systematic instrumental errors are:

1) the external optical noise (light) and parasitic scattered radiation from a diagnostic instrument incident on its measurement channel and the EDV of the examined object, changing the operating conditions of the measurements according to the illumination regime for the object; and

2) the instability over time of the parameters r, $\beta(\lambda)$, ω, and ω^*, e.g., owing to impurities or wear of the optical elements of the instrument structure, especially the working surfaces of data units and probes in contact with the diagnostic object.

The most important sources of basic methodological errors in NMS are the selected model and algorithms for programmed processing of the data; and the subjective, arbitrary positioning of a data unit on the object.

The effect of other errors and physical disturbances, e.g., electromagnetic aiming or errors of digitalization and voltage measurements with a PDD inside the diagnostic instrument, was negligibly small (±1% of the total measurement error).

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