Optical Fiber Probe as a Source of Errors and Uncertainty in Measurements for Optical Noninvasive Diagnostic Devices and Techniques

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Keywords: Optics, Laser, Diagnostics, Results, Spectroscopy, Noninvasive, Medicine, Fiber, Measurements, Error, Uncertainty, Dispersion, Metrology.

Abstract: Over the last 10-15 years a large amount of methods and devices of noninvasive medical spectrophotometry including such techniques as *in vivo* Laser Fluorescent Diagnostics, Tissues Reflectance Oximetry, Laser Doppler Flowmetry, etc. has been developed and involved in a real clinical practice. In that number several problems of accuracy and reproducibility of clinical diagnostic results have been under discussion as well. But systematic metrological research in this field is still unknown. What dispersions and errors in diagnostic data can be estimated if measurements will be executed on the same object several times, by several doctors with different qualifications or using several devices from both the same and a different manufacturer? In this paper some results of the complex study of errors and uncertainties in diagnostic data caused by using an optical multi-fibers probe are presented. Dispersion and errors up to a level of +/-36,3% for the average registered values were discovered. It is shown that the interactive component of errors caused by interaction of the probe and a surveyed object gives the main contribution to the total uncertainty in diagnostic data.

1 INTRODUCTION

In recent 10-15 years a general medical practice has been successfully enriched with different new methods of noninvasive optical diagnostics such as a Laser-Doppler Flowmetry (LDF), Laser Fluorescent Spectroscopy (LFS), Tissues Reflectance Oximetry (TRO), etc., which all in totality are often referred to as *Medical Noninvasive Spectrophotometry* (MNS) (Rogatkin and Lapaeva, 2003). All these methods using optical spectral measurements allow a doctor to evaluate *in vivo* a biochemical compositions and a clinical functional state of soft tissues, especially to study the finenesses of metabolism and blood microcirculation processes in skin or mucosa (Tchernyi et al., 2006); (Kutai-Asis et al., 2008). As on the basis of these measurements attempts of estimation of quantitative differences in results for different groups of examinees are undertaken today, all these devices should have a reliable metrological providing (Rogatkin et al., 2010).

Several problems of accuracy and reproducibility of clinical diagnostic results in NMS, especially in TRO and LDF, already have been under discussion (Nishidate et al., 2007); (Jenny et al., 2011); (Pochivalik et al., 2011). But systematic metrological research in this field is still unknown. What dispersions and errors in the diagnostic data can be estimated if measurements will be carried out on the same object several times, by several doctors with different qualifications or using several devices from both the same and a different manufacturer? Which part of this or that device or of the method makes the main contribution to summary errors of measurements and to uncertainty of its final outputs? For example, the majority of modern *in vivo* spectrophotometric measurements both in medicine and biology are carried out today with use of an optical fiber probe. Figure 1 shows the examples. But general technical and metrological requirements to a multi-fiber diagnostic cord for the purpose of precise and reproducible clinical (biological) measurements are still unknown. Even more complex problem can arise, if the optical fiber probe is broken and its replacement is required. Will measurements after the replacement be equivalent to

Rogatkin D. and Smirnova O..
Optical Fiber Probe as a Source of Errors and Uncertainty in Measurements for Optical Noninvasive Diagnostic Devices and Techniques.
DOI: 10.5220/0004200002330238
In *Proceedings of the International Conference on Biomedical Electronics and Devices* (BIODEVICES-2013), pages 233-238
ISBN: 978-989-8565-34-1

previous ones or not? Up to now all these metrological problems were little discussed in special literature yet.

Figure 1: Diagnostic measurements with the use of a fiber optical probe on a patient (left) and on an animal (right).

One of the first papers on this problem was the paper in *Measurement Techniques* (Rogatkin et al., 1998). It has been shown that for LFS a total random error of *in vivo* measurements with the use of a fiber optical probe could reach a quite high level – around 40%. But all real reasons for that were not estimated by the authors at that time. This paper describes some of our results of the systematic study of sources of errors in NMS when using an optical fiber probe for different NMS methods and devices.

2 MATERIALS AND METHODS

We used experimental measurements on tissue-like non-living and self made phantoms as well as real measurements in clinics on 10 volunteers (patients). All volunteers provided informed consent prior to the measurements, in accordance with the guidelines of the Institutional Ethics Board. Three main NMS diagnostic techniques – LDF, LFS and TRO – were under our investigation. Used diagnostic equipment - a commercial laser based multifunctional noninvasive medical diagnostic system "LAKK-M" (see figure 2), which combines all three mentioned above diagnostic techniques in a single united hardware (Rogatkin et al., 2009).

Figure 2: Multifunctional noninvasive diagnostic system "LAKK-M" with a multi-fibers optical probe.

Combined multi-fibers optical cord is used in it as an optical fiber probe to deliver light to the tested tissue and back to the diagnostic system, that makes it possible during one diagnostic procedure to collect all necessary diagnostic data from the same anatomic "point" of the examined tissue. Figure 3 represents the face-cut layout of the probe.

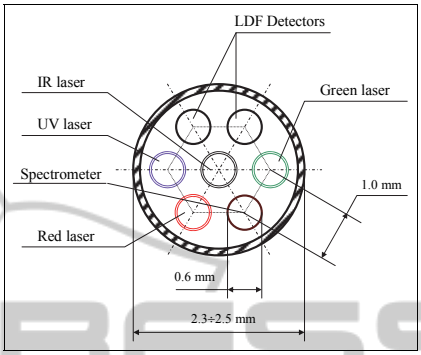

Figure 3: Layout of the multi-fibers optical probe.

Because of the absence today in the world of any international or national certified standards, gauges, reference materials or measurement instruments for NMS, indeed, any classic metrological research in the modern NMS is quite difficult. Therefore, in all our experiments we used a well-known statistical methodology of multiple-repeated measurements. It assumes carrying out s identical (according to the experimenter's point of view) series of tests (measurements) on the same object - on an imitational phantom or on a volunteer. In each series of measurements an experimental arithmetic mean value M_s of each registered diagnostic parameter as well as its experimental standard deviations σ were calculated. The relative deviation δ (factor of variation) in percentage of each parameter in the series was determined at next step of calculations:

$$\delta = (\sigma / M_s) \cdot 100\% \quad (1)$$

Finally, the results of all s series of experiments were compared among themselves, and distinctions in M_s and in δ were analyzed in terms of what methodical or instrumental (both random and systematic) reasons cause them.

For the purpose of having a reference material (tissue-like phantoms), a novel design of a set of solid imitational phantoms (measures) with tissue-like optical properties was made (figure 4). The measures are photostable and are made from standard materials with certified optical properties, so they are easily reproducible (see figure 5).

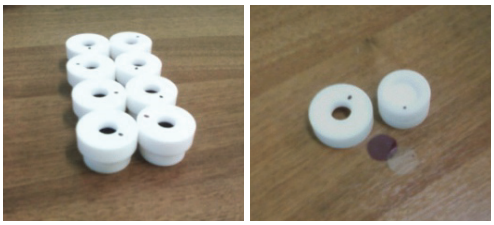

Figure 4: A set of self-made measures (left). Constructive specialties of the measure (right).

They consist of a light scattering solid foundation 1 and a number of spectral absorbing, scattering and fluorescent thin polymer films - layers 2. The frontal lid 3 with a window 4 for an optical fiber probe closes and rigidly holds all design.

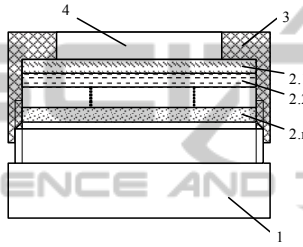

Figure 5: Some constructive specialties of the measures. 1- foundation, 2.1…2.n thin polymer films, 3 – lid, 4 – window for an optical fiber probe.

To avoid trembling of a fiber optical probe during measurements on the measures the optical cord was fixed in a stand (figure 6). Thus, all our measurements on phantoms were steady state.

Figure 6: Optical fiber probe is fixed in a stand.

Today for a number of NMS diagnostic methods there are already well-known medical or biological diagnostic parameters which are the output of the measurements and are expressed usually in absolute or in relative units. For example, in LDF technique a broad used diagnostic parameter is a blood flow (or an index of blood microcirculation - I_m) expressed in special perfusional units. TRO technique uses a tissue's saturation of haemoglobin S_tO_2 and total haemoglobin content (total blood volume – V_b) as the final medical output. We used all these parameters as final registered parameters for our statistical analysis as well.

Some other NMS diagnostic techniques don't have the standard output diagnostic parameters yet. LFS is one of the examples of that. Initially registered spectrum of autofluorescence of tissues with the use of "LAKK-M" system is presented in figure 7.

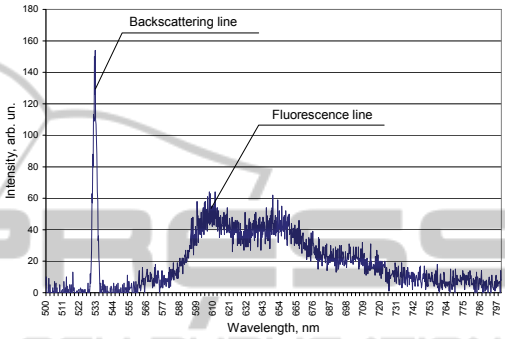

Figure 7: A typical autofluorescence spectrum of oral mucosa (excitation line 532 nm). Backscattered line 532 nm is reduced by $\beta \approx 1000$ times (instrumental coefficient).

There are two main regions in the spectrum – a region of excitation laser line (backscattered line) and the region of fluorescence, slightly shifted to the red waveband. To analyse that we used a previously approved approach of calculation of a modified fluorescent contrast coefficient K_f (Rogatkin *et al* 1998):

$$K_f = 1 + (I_f \cdot \beta - I_{bs}) / (I_f \cdot \beta + I_{bs}) \quad (2)$$

where K_f is the modified fluorescence contrast coefficient ($0 < K_f < 2$), I_f – registered light flux intensity in the maximum of fluorescence spectrum lines, I_{bs} - intensity of the registered backscattered laser radiation, β - instrumental reduction coefficient ($\beta \approx 1000$ to reduce I_{bs} to comparable level with the I_f magnitude).

3 RESULTS AND DISCUSSION

3.1 Results on the Problem of a Fiber Positioning Uncertainty

On the example of LFS technique first of all we have studied the problem of diagnostic errors due to variations of the positioning of a probe on a tested tissue surface. Like it was done in the basic paper

(Rogatkin et al., 1998) we studied the deviation δ of each registered and calculated parameter on volunteers in series of 10 measurements for each volunteer. But unlike sited paper in our study we have done that for the inner medical procedures with the use of endoscopic equipment. The endoscopy technique is one of the most difficult techniques to carry out in meaning of operating by the optical fiber probe. So, we expected to obtain a higher level of variations, in spite of the researcher had a high-level qualification both in NMS and endoscopic areas.

In this part of our research the excitation of the fluorescence was in the line of 532 nm, registration - in the region of lipopigments fluorescence (around 560 nm). From the medical point of view the lipopigments as well as porphyrins fluorescence in this region accompanies any destructive-inflammatory processes in tissues, so it is very important in clinics to assessment these fluorescence *in vivo* as accurately as possible. Results for 5 our volunteers are presented in Table 1.

Table 1: Results of endoscopic measurements.

Object	Statistic parameter	Registered signals, arb. un.		Medical K_f
		I_{bs}/β	I_f	
Patient 1, gastritis, gastroscopy	M_{10}	655,0	250,0	0,545
	σ	64,33	66,67	0,067
	δ (%)	**9,82**	**26,67**	**12,23**
Patient 2, gastritis, gastroscopy	M_{10}	420,0	190,0	0,627
	σ	63,25	31,62	0,121
	δ (%)	**15,06**	**16,64**	**19,36**
Patient 3, inflammation, colonoscopy	M_{10}	522,0	202,0	0,567
	σ	99,98	17,51	0,076
	δ (%)	**4,75**	**11,75**	**7,61**
Patient 4 ulcer colitis colonoscopy	M_{10}	743,0	206,0	0,436
	σ	69,77	13,50	0,035
	δ (%)	**9,39**	**6,55**	**8,11**
Patient 5 norm colonoscopy	M_{10}	448,0	245,0	0,706
	σ	70,05	62,41	0,150
	δ (%)	**15,64**	**25,47**	**21,17**

As one can see, variations in diagnostic data on a level up to ±20% around the mean value can be registered at endoscopic examination. One of the reasons for their emergence is the uncertainty of positioning of the optical fiber probe on the tissue. Figure 8 shows this phenomenon on the left. Another likely reason – penetration of external light from endoscopic source into the inspection area (into the so called diagnostic volume (DV) (Rogatkin *et al* 2010)). For exception of both reasons it was offered to use a steady tip on the probe as a support. Figure 8 shows the solution on the right.

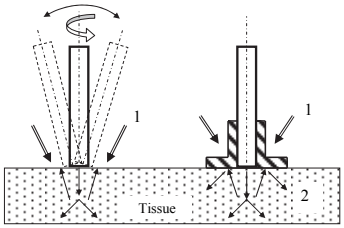

Figure 8: Uncertainties in the positioning of the used fiber probe (left) and the steady probe's tip (right). 1- External light; 2 – back reflected light.

To prove the efficacy of the solution and to avoid the factor of living tissues, a number of additional experiments were executed with the help of our lifeless measures. One part of the measurements was carried out without a tip; another part was carried out with a mirror tip and the third part - with the black tip absorbing light. Mirror and black options of the tip were necessary to assess the influence of additional illumination of the DV on results of measurements. Light getting into the tissue from the fiber optical probe due to backscattering leaves the tissue from the top boundary where the tip is placed. The leaving light can be absorbed by the tip (black option) or reflected back into the DV (mirror option). So, differences in M_s and δ can be evaluated in all these cases to establish the influence. Table 2 represents the results.

At the absence of the tip an uncertainty of probe positioning on the surface of measures leads to enhanced δ for K_f up to ±4,5% and to systematic increasing in average K_f due to the penetration of external light into the measure's DV. But absolute magnitudes of σ and δ are much less here than were observed in clinical study, that is a consequence of a steady state measurements on a phantom (see figure 6) as well as a lifeless character of it. Nevertheless, for a steady state phantom the magnitude of δ in 4,5% is quite big. The case with the lowest δ=0,9% is a case with a black tip. Thus, both positioning and external light penetration (apart from other reasons, biological reasons, for example) are the reasons for high-level variations in diagnostic data in LFS when a fiber optical probe is used.

3.2 Results on Replacing of the Probe

The considerable growth of the standard deviation σ for all parameters was observed at the comparative analysis of data received by the same diagnostic system when different copies of optical fiber probes from the same party of the probes were used.

Table 2: Experiments with a steady tip for the probe. Excitation line is 532 nm, registration line is 560 nm.

Steady probe's tip	I_{bs}/β , arb. un.			I_f , arb. un.			K_f^* , rel. un.		
	M_{25}	σ	**δ,%**	M_{25}	σ	**δ,%**	M_{25}	σ	**δ,%**
is absent	456,8	23,1	**5,1**	321,1	24,3	**7,6**	0,83	0,038	**4,5**
with a mirror bottom surface	465,7	10,3	**2,2**	313,8	7,2	**2,3**	0,81	0,009	**1,1**
with a black bottom surface	448,9	11,1	**2,5**	282,5	7,0	**2,5**	0,77	0,007	**0,9**

*Accepted nominal value for the phantom is K_f=0,78.

Table 3 presents such results for diagnostic TRO technique when using three similar copies of the probe. The measurements were made on the non-fluorescent measure No. 8. The reason for obviously dropping out values for the probe No. 011 was a small difference in the distance between receiving and illuminating fibers in the cord (see figure 3) in comparison with two other copies of the probe. This distance determines the effective DV in the surveyed object, therefore even a small variation of the distance leads to a slightly different DV and, as a consequence, to a little bit another registered physical as well as calculated medical parameters.

Table 3: Experiment with three copies of the probe.

Optical fiber probe	Statistic parameters	Calculated parameters, % *	
		S_tO_2	V_b
Probe № 001	M_{50}	57,5	10,7
Probe № 011	M_{50}	81,5	11,7
Probe № 021	M_{50}	57,2	9,9
On average	**M**	**65,4**	**10,8**
	σ	**13,9**	**0,9**
	δ	**21,3**	**8,38**

*Accepted nominal values for the measure No. 8 were S_tO_2=57,6 % , V_b=10,5 %.

Nevertheless, it is necessary to note, that the direct comparison of the diagnostic data when using different optical fiber probes with different distances between fibers in the cord or with different optical apertures of the fibers methodically isn't always correct. For each DV the constructive parameters of each fiber probe should be standardised and certified to have comparable results.

3.3 Results on the Problem of Different Qualification of Researcher

Also, in our study we investigated errors caused by absence of a sufficient qualification of a doctor to manage the optical fiber probe. With each examinee 3 series of mutual-repeated tests (on 5 measurements in each series) were carried out. With first volunteer a young postgraduate student worked to whom the necessary technique - most precisely positioning of the probe in the same place at each measurement and without visible pressure weren't told. With second volunteer another, more skilled postgraduate student worked and after his attention was specially turned on the need of careful control of pressure and of installation place for the probe on the body of the patient. The third volunteer was under control of the most skilled researcher. Obvious reduction of σ and δ from test to test was registered (see Table 4). I.e. a professional qualification of researchers as well as a precisely formulated diagnostic algorithm (a route of the inspection and needed conditions) are important components for reduction of errors in NMS.

Table 4: Influence of qualification of the diagnostician on the results in TRO.

Calculated medical parameters, %						
	Volunteer 1		Volunteer 2		Volunteer 3	
	V_b	S_tO_2	V_b	S_tO_2	V_b	S_tO_2
Series 1 M_5	11,9	87,6	20,9	73,0	28,0	84,0
Series 2 M_5	8,5	97,3	16,6	85,2	27,5	82,6
Series 3 M_5	17,7	77,6	16,6	85,5	27,4	82,7
M_3	**12,7**	**87,5**	**18,0**	**81,2**	**27,6**	**83,1**
σ_3	4,6	9,9	2,5	7,1	0,3	0,8
δ_3	**36,3**	**11,3**	**13,8**	**8,7**	**1,1**	**0,9**

3.4 Results on the Problem of Different Probe Pressures

In previous section a problem of probable influence of the probe pressure on final diagnostic results was mentioned. All measurements are often performed in contact with the tissue, so the contact pressure can affect the local optical properties of the tissue that, in turn, can lead to an emergence of the so-called *interactive component of errors* (Rogatkin et al., 2010), caused by interaction of the surveyed object and the measurement tool. The contact pressure is one of the reasons for that. Though the influence of the contact pressure are described quite well today (Reif et al., 2008); (Lim et al., 2011), nevertheless we decided to add such research in our study. We

used LDF diagnostic technique and calibrated cargoes which were put on a tip of the probe. An example of continuous recording of the blood microcirculation index I_m in the finger pulp skin at different probe pressure levels is presented in figure 9.

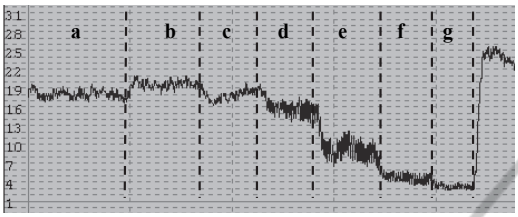

Figure 9: Registered blood flow at different pressure: (a) without pressure, (b) 0.6 G/mm^2; (c) 1.2 G/mm^2; (d) 2.3 G/mm^2; (e) 8.6 G/mm^2; (f) 10.2 G/mm^2; (g) 14.9 G/mm^2.

The diagram shows that the pressure of around 10 G/mm^2 almost completely blocks the blood flow in the finger skin. The more pressure is increased the more different fluctuations in I_m arise within the pressure interval 2-10 G/mm^2. In a similar way the pressure impacts both on TRO and LFS data, because under pressure the blood is squeezed out of the microvasculature, and light absorption by blood is decreased in the DV. The changes in absorption determine a maximum of registered I_m in the *b* interval of the pressure. Thus, the interaction of a surveyed biological object and an optical fiber probe can lead to dramatic instrumental errors without appropriate pressure control. More than 50% of the total error according to our data can be accounted by the interactive component of the error.

4 CONCLUSIONS

In the present study we have investigated some main sources of errors and uncertainties in diagnostic data caused by using an optical multi-fibers probe in NMS. With the use of well-known statistical methodology of multiple-repeated measurements both on lifeless imitational tissue-like phantoms and on real clinical patients (volunteers) the dispersion and errors up to a level of +/-36,3% of the average registered quantities were discovered in NMS. It is shown that the interactive component of errors caused by interaction of the optical fiber probe and surveyed object gives the main contribution to the total uncertainty of the measurement results.

The direct comparison of the diagnostic data when using different probes with different distances between fibers in the cord shows that for each DV the constructive parameters of each optical fiber probe should be standardised to have comparable results. Also, a professional qualification of doctors as well as a precisely formulated diagnostic route of the inspection of patients are important components of actions to reduce errors in NMS.

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