15

Compact sapphire fiber-optic probe for intraoperative analysis of microcirculation disorders

© A.A. Platonova[1¶], P.V. Aleksandrova[1], S.P. Kudryavtseva[2], A.K. Zotov[1,3], K.I. Zaytsev[1], K.B. Dolganov[1], V.N. Kurlov[3], I.N. Dolganova[3,4¶¶]

[1] Prokhorov General Physics Institute, Russian Academy of Sciences, Moscow, Russia
[2] Sechenov First Moscow State Medical University, N.V. Sklifosovskiy Institute of Clinical Medicine, Moscow, Russia
[3] Osipyan Solid State Physics Institute, Russian Academy of Sciences, Chernogolovka, Russia
[4] Saratov National Research State University, Saratov, Russia

[¶] e-mail: platlina.hibou2001@yandex.ru
[¶¶] e-mail: in.dolganova@gmail.com

Received December 09, 2024
Revised December 12, 2024
Accepted December 12, 2024

Microcirculation disorders and their consequences (hypoxia, ischemia, and subsequent tissue necrosis) are highly undesirable complications in clinical practice. Therefore, monitoring tissue conditions and detecting pathologies during surgical procedures is a crucial task in modern medicine. To address this challenge, this article presents a compact sapphire fiber probe based on the principle of spatially resolved diffuse reflectance analysis. This method enables the measurement of the effective attenuation coefficient of tissue and its temporal variations, thus allowing for intraoperative assessment of tissue state under conditions of impaired microcirculation. Due to the compact design of the probe, it can be used as an auxiliary tool for a wide range of surgical procedures and diagnostic applications. The feasibility of the proposed probe for detecting microcirculation disorders was analyzed experimentally, using two types of samples — a liquid phantom based on a lipid emulsion and hemoglobin and muscle tissue *ex vivo* — with the inserted enzyme. The effect of the enzyme on hemoglobin and muscle tissue, which mimics the effect of circulatory disturbance, qualitatively demonstrated the effectiveness of the sapphire probe.

Keywords: diffuse reflectance, effective attenuation coefficient, sapphire, intraoperative monitoring.

DOI: 10.61011/EOS.2025.05.61642.201-24

Introduction

Microcirculation is defined as the blood flow through the smallest vessels in the vasculature system (arterioles, venules, and capillaries), which supplies oxygen and nutrients to tissues and organs, while simultaneously removing metabolic products from them [1]. A change in such a vital process in the body can be caused by various pathological processes and/or surgical manipulations and lead to complications such as hypoxia, ischemia and subsequent tissue necrosis [2]. Evaluation of the tissue vascularization status is important in many types of surgical interventions, especially in such as plastic, abdominal, and traumatological operations, neuro- and oncological surgery [3], and in the diagnosis of diabetes mellitus [4,5]. Timely detection of disorders makes it possible to avoid occurring complications or eliminate them intraoperatively without additional surgical procedures. However, in modern medicine, microcirculation monitoring is still subjective and is analyzed by parameters such as tissue and blood color, vascular pulsation and tissue bleeding at the resection sites [6,7], which do not provide an accurate assessment of the condition.

An alternative approach to address this problem is to monitor the microcirculation status using optical methods and instruments. Various optical imaging and spectroscopy methods have been developed over the past decades to enchance the accuracy of tissue assessment, increase the number of successful operations, and facilitate the work of surgeons. Some of the most common techniques include: using indocyanine green (ICG) fluorescence spectroscopy [8,9], laser Doppler imaging [10,11], laser Doppler flowmetry [10], laser speckle contrast imaging [12,13], photoplethysmography [14,15], optical coherence tomography [16,17], spatially resolved diffuse reflectance (SRDR) analysis and and diffuse reflectance spectroscopy (DRS) [18–20]. All of these methods can be used to detect microcirculation disorders. Each of these methods has its own advantages and disadvantages. At the same time, diffuse reflectance analysis allows for the estimation of tissue optical parameters using relatively simple technical components within a compact instrument. Changes in these properties reflect the process of microcirculation disorders. Therefore, this technique formed the basis for the creation of a sapphire probe for the analysis of such a tissue condition.

The principle of this method is to analyze the intensity of diffusely reflected radiation from the studied sample. Radiation, as it propagates through a biological medium, undergoes multiple scattering and absorption by endogenous chromophores. The fraction of diffusely reflected light exiting the tissue can reach 30−40 % of the incident beam

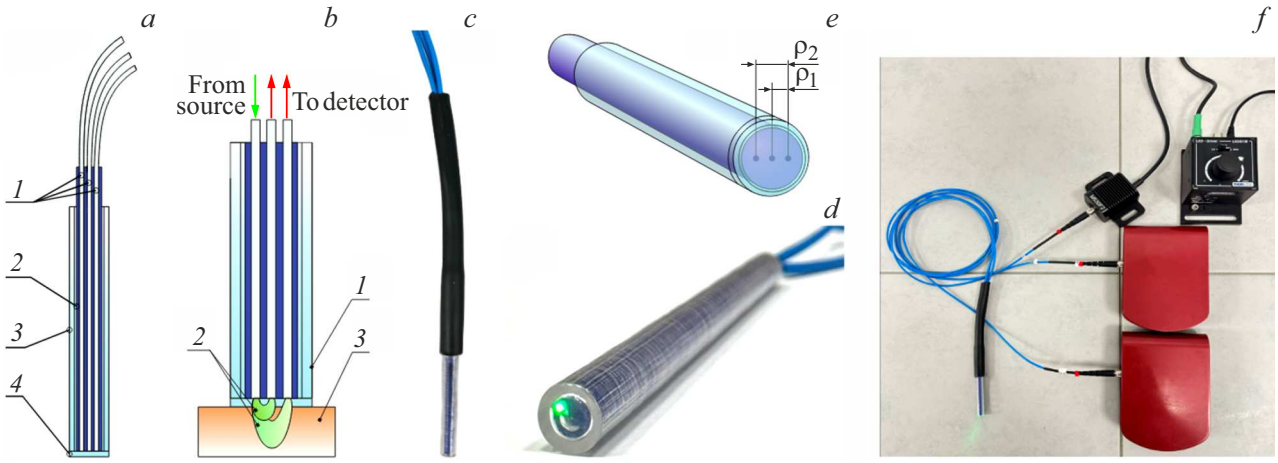

Figure 1. A sapphire probe for determining the optical properties of tissues in conditions of impaired microcirculation. (*a*) Sapphire probe circuit: *1* — optical fibers, *2* — plastic tube, *3* — sapphire tube, *4* — sapphire plate. (*b*) Optical scheme: *1* — probe, *2* — ray path, *3* — biological tissue. (*c*), (*d*) Photos of the sapphire probe. (*e*) Type of probe contact part, $\rho_1 = 1.3$ and $\rho_2 = 2.6$ mm. (*f*) Photo of the experimental setup.

energy. Alteration in the intensity of the reflected light from the illuminated tissue contains information about the level of the absorption coefficient and the transport scattering coefficient, reflecting such microcirculation parameters as the concentrations of oxy- and deoxyhemoglobin and the tissue saturation level [21–23]. This method of analysis provides fast and relatively simple quantitative determination of optical tissue parameters and their temporal changes, which is often used in various diagnostic applications [18,20,24–26]. For the task described in the present article, a multichannel optical fiber probe with one illuminating and several detecting channels located at radial distances in the range of 1−20 mm, can be used. The number of fibers may also vary. So, usually, 6−9 detection regions are used to evaluate the optical properties of the medium, determined by the reflective profiles [27].

This paper considers a sapphire fiber probe, which has only three fiber channels, which is characterized by its small size and simple design. The probe and its operating principle are described in detail in Ref. [28]. Its feasibility is studied in this paper using experimental studies. Two types of test objects, described below, were used for this purpose. The demonstration of the possibility of using such a probe for intraoperative monitoring of tissue conditions opens the way for its further integration into clinical practice as an auxiliary tool.

Compact sapphire probe

The primary challenge in constructing a fiber-optic probe based on diffuse scattering analysis is to secure the fibers in strictly defined positions within the probe. Furthermore, the design must ensure that these fibers are protected from chemical, mechanical, and other damaging impacts during operation, storage, disinfection, and sterilization. For this reason, the materials for the contact part and the external housing that protects the optical fibers must meet the following requirements: safety for use with biological tissues, compatibility with various disinfectants and sterilization methods, long service life, high optical transparency at the operating wavelength or in a given spectral range. Literature describes a variety of materials used for these purposes [27]. One of these materials is sapphire (Al_2O_3). Sapphire instruments have found their application in laser thermal and photodynamic therapy, in diagnostics based on optical methods [29,30], in surgical practice for conventional (sapphire scalpels [31]) and optical (sapphire tips and cones [29,32]) tissue resection, and also in cryosurgery (sapphire cryoapplicators [33,34]).

Fig. 1 shows the design of the sapphire probe. The length of the sapphire tube is 90 mm, the outer and inner diameters are 5.4 and 4.8 mm, respectively, and the thickness of the bottom at the end of the tube is 1.2 mm. To fabricate such a sapphire tube closed at one end, the edge-defined film-fed growth (EFG) technique for shaped crystals was used [35,36], as it allows obtaining crystals complex in profile without the use of labor-intensive additional mechanical processing. The diameter of the plastic shell inserted into the sapphire tube is 4.5 mm. It contains 3 thin through channels — one central and 2 lateral, distant from the central one by a distance of 1.3 mm (Fig. 1, *a*, *d*). Optical fibers are placed in these channels. The multimode fibers used in the probe have a numerical aperture of 0.22 and a core diameter of 200 μm. The first side fiber which delivers the radiation to the tissues is connected to an LED (M530F2, Thorlabs) with a maximum output power of 30 mW and a central wavelength of $\lambda = 530$ nm. An LED driver is used to adjust the output power. The choice of green light is due to the strong absorption of hemoglobin in the green region of the spectrum and the fact that the difference between the absorption spectra of oxygenated

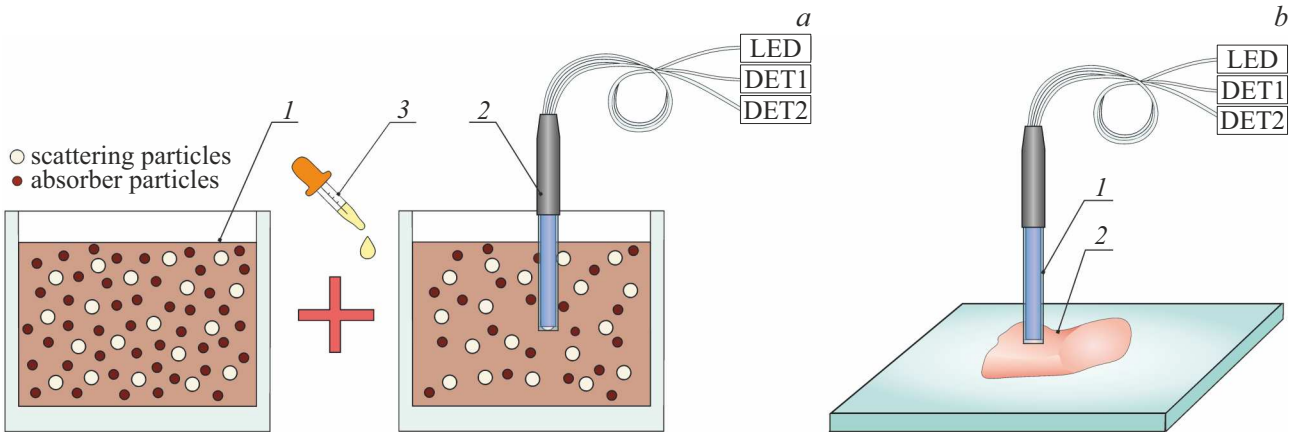

Figure 2. Illustration of experiments with tissue phantoms and muscle tissue samples. (*a*) Measurement of the parameters of a phantom consisting of a lipid emulsion with the addition of hemoglobin before and after the addition of rennet enzyme: *1* — phantom, *2* — sapphire probe, *3* — rennet enzyme. (*b*) Measurement of parameters of a muscle tissue sample: *1* — sapphire probe, *2* — tissue sample.

and deoxygenated hemoglobins is more distinguishable in this case [37]. However, this range imposes limitations on the depth of penetration into the tissue [38], and studies are possible only in the near-surface layers compared to superficial instruments.

The other two fibers, distributed from the source at distances of $\rho_1 = 1.3$ and $\rho_2 = 2.6$ mm, are used to detect diffusely reflected radiation from the sample; they are coupled to two compact spectrometers (CCS200, Thorlabs with a wavelength range of $\Delta\lambda = 200 - 1000$ nm). Original software is used to measure the signal at a specific time. The measurement period of the signals is 3 s. After that, the signal is smoothed and the intensities at a wavelength of 530 nm are analyzed. The optical part of the probe was calibrated, as indicated below to correct the signals. Background radiation that changes during the experiment can affect the results. For this reason, the method of background radiation suppression is employed by additional shielding from ambient light.

Tissue samples and phantoms used in the study

The feasibility of using a sapphire probe to determine changes in tissue optical properties during microcirculation disorders was studied in two experiments using rennet, an enzyme that alters the optical properties of tissues by coagulating proteins and destroying lipids [39]. In the first experiment, 3 liquid tissue phantoms with optical parameters similar to the biological medium were used, consisting of a 5% aqueous solution of a lipid emulsion (Lipoplus 20, B.Brown, Melsungen, Germany) (5 ml) and a different concentration of dried beef hemoglobin: 0.05, 0.10 and 0.15 g, to simulate tissues with different levels of absorption coefficient. 0.3 ml of rennet enzyme was added to all three samples for obtaining a gradual change in the optical properties of the phantoms. This led to a decrease in hemoglobin concentration and, consequently, a reduction in absorption (Fig. 2, *a*). The measurements were carried out within 5 min after the addition of the enzyme.

7 samples of chicken muscle tissue *ex vivo* with size of $20 \times 30 \times 10$ mm were used for the second experiment. A study area was selected in each case, and 0.3 mL of rennet was injected into the subsurface layer 10 minutes before the experiment. The diffuse reflected signal was measured continuously for 10 min (Fig. 2, *b*).

Rennet enzyme (pepsin) is a protease that catalyzes the cleavage of peptide bonds between amino acids in proteins. Pepsin is activated in the stomach from its inactive form — pepsinogen — under the influence of acid (hydrochloric acid) present in gastric juice. The enzyme acts by breaking peptide bonds, which leads to the formation of smaller peptides [40]. Muscle tissue, like any other, consists mainly of proteins such as actin, myosin, and other structural components. These proteins can be digested by the rennet enzyme. However, it is worth noting that its activity against muscle tissue proteins may differ from its activity against milk proteins (for example, casein), for which it was originally developed [41].

Determination of optical properties

To determine the optical characteristics, the theory of light diffusion in turbid media is applied [42,43]. According to this theory, the intensity value at the sample surface at a specific source-detector distance can be estimated as

$$I(\rho) = \left(\frac{C_1}{\rho^m}\right) e^{-C_2\rho}, \qquad (1)$$

where C_1 and C_2 are empirical parameters depending on the optical properties of the tissue, m depends on the distance ρ and is assumed to be 1 for the described probe. The parameter C_2 is related to the effective attenuation

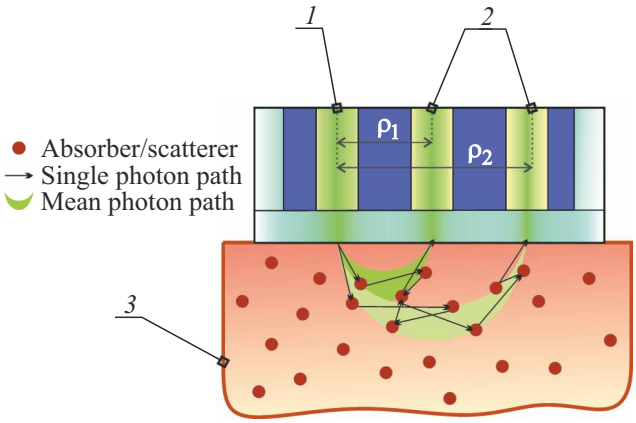

Figure 3. The path of the rays in the tissue sample recorded by the detector channels: *1* — illuminating fiber, *2* — detecting fibers, *3* — tissue sample.

coefficient $C_2 \simeq \mu_{\text{eff}}$, determined by the absorption μ_a and reduced scattering coefficients μ_s':

$$\mu_{\text{eff}} = \sqrt{3\mu_a(\mu_a + \mu_s')}, \tag{2}$$

where $\mu_s' = \mu_s(1-g)$, μ_s is the scattering coefficient, g is the anisotropy factor.

The sapphire probe has 2 detection channels. Therefore, $I(\rho_1)$ and $I(\rho_2)$ are measured during the experiment (Fig. 3). Using the formula (2) we easily obtain

$$\mu_{\text{eff}} \simeq \frac{\ln[I(\rho_1)\rho_1^m] - \ln[I(\rho_2)\rho_2^m]}{\rho_2 - \rho_1}, \tag{3}$$

Before measuring $I(\rho)$ and determining changes in μ_{eff}, the probe should be calibrated using a sample with known optical parameters. For this purpose, a 5% solution of Lipoplus 20 was used, the parameters of which are $\mu_a = 0.078\,\text{mm}^{-1}$, $g = 0.71$, $\mu_s = 5.07\,\text{mm}^{-1}$ [44], and measurements of diffuse reflected signals were carried out. Then, using the equation (1), the slope of the line $\ln[I(\rho)\rho^m]$, constructed from two signals $I(\rho_1)$ and $I(\rho_2)$, is compared with the slope of the line $\ln C_1 - C_2\rho$, where C_2 is determined by from the equation (2). Thus, the value for the correction of experimental data is determined. Calibration allows you to take into account measurement errors that occur mainly due to uneven sensitivity of the spectrometers, various losses in the fibers and reflections inside the sapphire probe.

Results

The time dependence of the effective attenuation coefficient of three liquid phantoms with different hemoglobin concentrations was obtained based on the expression (3) (Fig. 4, *a*). It can be observed that the change in μ_{eff} varies throughout the entire period for all samples. The reason for this phenomenon was the coagulation of hemoglobin and the breakdown of lipids induced by the enzyme. This result confirms the sensitivity of the sapphire probe to changes in the optical properties of samples with different levels of absorption coefficient.

The results of determining the effective attenuation coefficient of muscle tissue weakening are shown in Fig. 4, *b*. The decrease in the average effective attenuation coefficient level was observed over the entire period for all samples. The following changes take place during the first 10 min in case of microcirculation disorders: edema, contracture changes, perivascular infiltration appear, and transverse striation disappears. These phenomena occur due to impaired blood flow and insufficient oxygen supply to the tissues, followed by activation of anaerobic glycolysis, which increases the concentration of lactate and develops lactate acidosis. During these processes, the production of adenosine triphosphate (ATP) decreases, which causes disruption of the function of transport of ions Na^+, K^+, Ca^{2+} and their intracellular accumulation and membrane depolarization. An excess concentration of calcium in cells activates enzymes such as lipase, endonuclease, and protease, and also uncouples the stages of oxidative phosphorylation Enzymes activated with the participation of calcium destroy the membranes of cellular organelles and plasma membranes, which leads to disruption of the structures of lysomes and the release of their enzymes into the cell and subsequent autolysis. The cells lose their ability to maintain homeostasis, water enters the cell and edema develops, the cells also lose their membrane structures, and plasmolysis occurs. The destruction of the membrane also leads to the accumulation of free fatty acids, which in turn causes reactive inflammation and tissue infiltration.

The rennet enzyme consists of the protease enzymes chymosin and pepsin, which are involved in the reaction of proteolysis and protein folding, which leads to the loss of the native conformation [39]. The effect of rennet enzyme on muscle tissue is similar to the changes in muscle tissue during microcirculation disorders, with the only exception that the enzyme causes changes in tissue and cellular structure, destroying the peptide bonds of muscle proteins. The type of changes in muscle fibers before and after the action of rennet enzyme are shown in Fig. 5.

Discussion

The purpose of this paper was to study the feasibility of using the proposed compact sapphire probe based on the analysis of spatially resolved diffuse reflected light intensity to determine the tissue optical parameters under microcirculation disorders. Optical characteristics can act as markers for the diagnosis of various pathological conditions, such as cancer, diabetes mellitus, and tissue ischemia. The effective attenuation coefficient can be one of such markers, which includes both scattering and absorption coefficients, and the experiments performed have confirmed the ability of

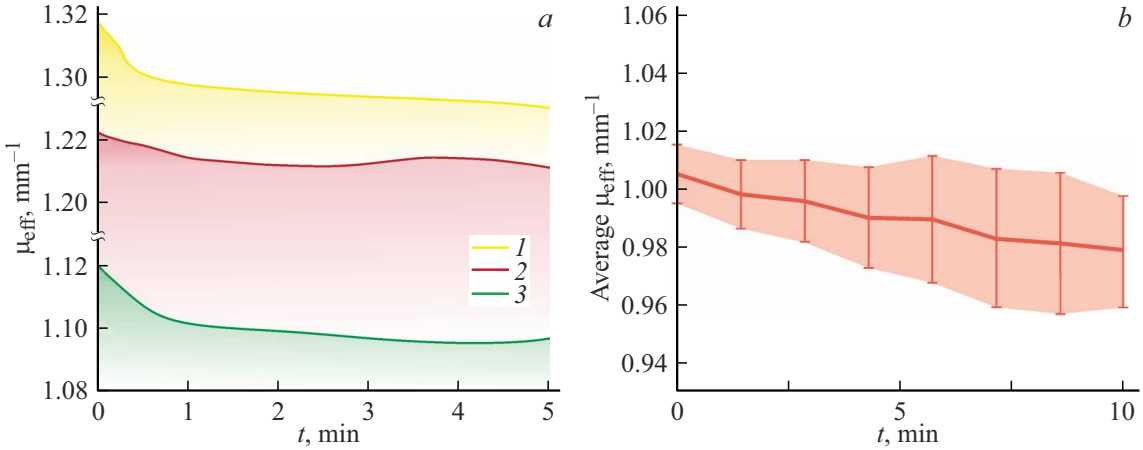

Figure 4. Measurement of the effective attenuation coefficient of samples using a sapphire probe. (*a*) Time change in the effective attenuation coefficient of the tissue phantom after the addition of rennet enzyme: *1* — for 0.05 g hemoglobin, *2* — for 0.10 g hemoglobin, *3* — for 0.15 g hemoglobin. (*b*) The average value of the effective attenuation coefficient of muscle tissue samples.

the proposed probe to detect changes μ_{eff} over time. Thus, it can find application in a wide range of diagnostic tasks.

The probe design used in this study is based on measurements of the intensity of diffusely reflected light from illuminated samples at a single wavelength of 530 nm, since, in particular, light at this wavelength was most strongly absorbed by hemoglobin, which is used in the experiment. However, the current LED may be replaced with other sources with various operating wavelengths to meet specific demands, or with a broadband light source to enable spectroscopic measurements. When using longer wavelengths, the depth of light penetration into tissue can be increased, but, on the other hand, it is important to consider the limitations imposed by the specific source-detector distance of the probe used, due to which the depth cannot exceed 1 mm. At the same time, the use of a broadband light source for measuring a spatially resolved diffuse reflected signal, for example, in near-infrared spectroscopy methods, provides a more precise characterization of tissue status by allowing independent determination of scattering and absorption coefficients and quantitative analysis of various chromophore concentrations. Such a methodology could potentially expand the future application scope of the described sapphire probe and facilitate the establishment of a threshold value for the effective attenuation coefficient that indicates the onset of pathological tissue conditions.

The significant variation and specific features of tissues across individual samples and subjects will affect the determined threshold value. This variability is explained by the complex structure of tissues and the different content of endogenous chromophores for each individual, which significantly affects the level of absorption and scattering coefficients of tissues [45]. To eliminate the influence of such a high variance in coefficient values on tissue state assessment, relative changes in the effective attenuation or absorption coefficient can be used for monitoring tissue

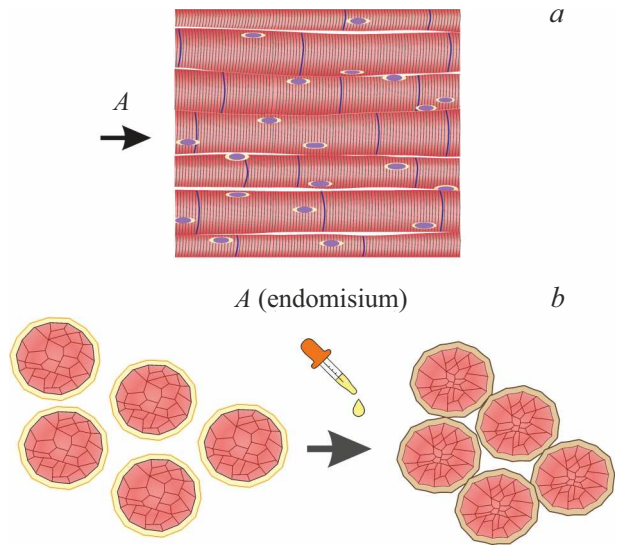

Figure 5. Schematic representation of the structure of muscle tissue. (*a*) Transversostriated skeletal muscle tissue. (*b*) View of the endomysium before and after the addition of rennet enzyme (protein denaturation process).

conditions. This approach requires that the baseline values of these parameters for healthy tissue are measured within the region of interest or in its immediate vicinity, whenever possible. Another way is to estimate the rate of change of μ_{eff} at a certain point in time. Nevertheless, this requires a preliminary determination of a clear relationship between the rate of change of this parameter and a violation of microcirculation. Establishing correlations between saturation level along with the concentrations of deoxyhemoglobin and oxyhemoglobin (markers of hypoxia, ischemia, and associated pathologies) and either absolute/relative intensity change μ_{eff} or even its rate of change, a separate study with a large number of in vivo samples is required. This

investigation would ideally encompass diverse tissue types, pathological conditions, injuries, or other factors that may modify baseline optical properties. Such correlations can be determined in subsequent studies.

The proposed sapphire probe features a compact design, making it highly suitable for clinical applications. It can be integrated into existing surgical processes as an auxiliary tool used both for continuous measurement of optical properties in a specific area of study during surgical procedures, and for periodic measurement of tissue parameters to determine its discrete changes. Moreover, the probe can be reused due to the properties of sapphire, allowing it to be disinfected and sterilized by various methods.

Conclusion

An experimental study was conducted in this paper for determining the feasibility of a sapphire compact probe for evaluating the tissue optical properties during microcirculation disorders. Based on the analysis of spatially resolved diffuse reflected light, it allows for a noninvasive determination of the tissue effective attenuation coefficient that changes during pathological processes. The feasibility of using a compact sapphire probe to detect changes in optical parameters was experimentally investigated using two types of objects: a tissue phantom with varying hemoglobin content and ex vivo muscle tissue, upon the addition of rennet enzyme. The results confirm the feasibility of using the developed instrument for intraoperative tissue monitoring, as they demonstrate the ability to observe the dynamics of the effective attenuation coefficient during changes in object parameters.

Compliance with ethical standards

This article does not contain any studies involving animals performed by any of the authors.

Funding

The study was supported by a grant from the Russian Science Foundation No.24-44-00082.

Conflict of interest

The authors declare that they have no conflict of interest.

References

[1] P.F. Do Amaral Tafner, F.K. Chen, R.R. Filho, T.D. Corrêa, R.C. De Freitas Chaves, A.S. Neto. Rev. Bras. Ter. Intensiva., **29** (2), 238–247 (2017). DOI: 10.5935/0103-507X.20170033

[2] C.A. den Uil, E. Klijn, W.K. Lagrand, J.J. Brugts, C. Ince, P.E. Spronk, M.L. Simoons. Prog. Cardiovasc. Dis., **51** (2), 161–170 (2008). DOI: 10.1016/j.pcad.2008.07.002

[3] N. Nakayama, S. Kuroda, K. Houkin, S. Takikawa, H. Abe. Acta. Neurochir., **143** (1), 17–24 (2001). DOI: 10.1007/s007010170133

[4] V.V. Tuchin, J. Popp, V. Zakharov. *Multimodal Optical Diagnostics of Cancer* (Springer Nature, Cham, 2020). DOI: 10.1007/978-3-030-44594-2

[5] D.K. Tuchina, V.V. Tuchin. J. Biomed. Photonics. & Eng., **4** (2), 020201 (2018). DOI: 10.18287/jbpe18.04.020201

[6] R. Fitridge, M. Thompson. *Mechanisms of Vascular Disease: A Reference Book for Vascular Specialists* (The University of Adelaide Press, Adelaide, 2011). DOI: 10.1017/UPO9781922064004

[7] G.H. Pratt, E. Krahl. The American J. Surgery, **87** (5), 722–729 (1954). DOI: 10.1016/0002-9610(54)90171-3

[8] A. Raabe, J. Beck, R. Gerlach, M. Zimmermann, V. Seifert. Neurosurgery, **52** (1), 132–139 (2003). DOI: 10.1097/00006123-200301000-00017

[9] M. Mokrý, P. Gál, M. Harakalová, Z. Hutnanová, J. Kusnír, S. Mozes, J. Sabo. Photochem. Photobiol., **83** (5), 1193–1196 (2007). DOI: 10.1111/j.1751-1097.2007.00132.x

[10] V.L. Fredrickson, J.J. Russin, B.A. Strickland, J. Bakhsheshian, A.P. Amar. Neurosurgy Clin. N. Am., **28** (4), 603–613 (2017). DOI: 10.1016/j.nec.2017.05.011

[11] A.I. Krupatkin. Hum. Physiol., **44**, 581–591 (2018). DOI: 10.1134/S0362119718050079

[12] N. Hecht, J. Woitzik, J.P. Dreier, P. Vajkoczy. Neurosurg. Focus, **27** (4), E11 (2009). DOI: 10.3171/2009.8. FOCUS09148

[13] S.M.S. Kazmi, E. Faraji, M.A. Davis, Y.-Y. Huang, X.J. Zhang, A.K. Dunn. Biomed. Opt. Express, 6 (7), 2258–2608 (2015). DOI: 10.1364/boe.6.002588

[14] A.A. Kamshilin, V.V. Zaytsev, A.V. Lodygin, V.A. Kashchenko. Sci. Rep., **12** (1), 1143 (2022). DOI: 10.1038/s41598-022-05080-7

[15] O.V. Mamontov, A.V. Shcherbinin, R.V. Romashko, A.A. Kamshilin. Appl. Sci., **10** (18), 6192 (2020). DOI: 10.3390/APP10186192

[16] L. Wang, Z. Chen, Y. Li, J. Yang, Y. Li. Sci. Rep., **9** (1), 5980 (2019). DOI: 10.1038/s41598-019-42520-3

[17] E. Kiseleva, M. Ryabkov, M. Baleev, E. Bederina, P. Shilyagin, A. Moiseev, V. Beschastnov, I. Romanov, G. Gelikonov, N. Gladkova. Diagnostics, **11** (4), 705 (2021). DOI: 10.3390/diagnostics11040705

[18] M.G. Nichols, E.L. Hull, T.H. Foster. Appl. Opt., **36** (1), 93–104 (1997). DOI: 10.1364/AO.36.000093

[19] M. Larsson, H. Nilsson, T. Strömberg. Appl. Opt., **42** (1), 124–134 (2003). DOI: 10.1364/ao.42.000124

[20] Z. Shi, Y. Fan, H. Zhao, K. Xu. J. Biomed. Opt., **17** (6), 067004 (2012). DOI: 10.1117/1.jbo.17.6.06700

[21] C. Zhu, S. Chen, C.H.-K. Chui, B.-K. Tan, Q. Liu. Biomed. Opt. Express, **7** (2), 570–580 (2016). DOI: 10.1364/boe.7.000570

[22] R.C. Mesquita, N. Skuli, M.N. Kim, J. Liang, S. Schenkel, A.J. Majmundar, M.C. Simon, A.G. Yodh. Biomed. Opt. Express, **1** (4), 1173–1187 (2010). DOI: 10.1364/boe.1.001173

[23] S. Fantini, M.-A. Franceschini, J.S. Maier, S.A. Walker, B.B. Barbieri, E. Gratton. Opt. Eng., **34** (1), (1995). DOI: 10.1117/12.183988

[24] V.V. Tuchin. *Tissue Optics: Light Scattering Methods and Instruments for Medical Diagnosis*, 3rd ed. (SPIE, California, 2015). DOI: 10.1117/3.1003040

[25] A.M.K. Nilsson, R. Berg, S. Andersson-Engels. Appl. Opt., **34** (21), 4609–4619 (1995). DOI: 10.1364/ao.34.004609
[26] B. Hallacoglu, A. Sassaroli, S. Fantini. PLoS One, **8** (5), e64095 (2013). DOI: 10.1371/journal.pone.0064095
[27] U. Utzinger, R.R. Richards-Kortum. J. Biomed. Opt., **8** (1), 121–147 (2003). DOI: 10.1117/1.1528207
[28] A.A. Platonova, P.V. Aleksandrova, A.I. Alekseeva, S.P. Kudryavtseva, A.K. Zotov, K.I. Zaytsev, K.B. Dolganov, I.V. Reshetov, V.N. Kurlov, I.N. Dolganova. J. Biophotonics, **17** (11), e202400368 (2024). DOI: 10.1002/jbio.202400368
[29] K. Stock, T. Stegmayer, R. Graser, W. Förster, R. Hibst. Lasers Surg. Med., **44** (10), 815–823 (2012). DOI: 10.1002/lsm.22091
[30] I.N. Dolganova, I.A. Shikunova, A.K. Zotov, M.A. Shchedrina, I.V. Reshetov, K.I. Zaytsev, V.V. Tuchin, V.N. Kurlov. J. Biophotonics, **13** (10), e202000164 (2020). DOI: 10.1002/jbio.202000164
[31] M. Ahmad, M. Ismail. J. Cosmet. Dermatol., **20** (11), 3610–3615 (2021). DOI: 10.1111/jocd.14006
[32] T.J. Polletto, A.K. Ngo, A. Tchapyjnikov, K. Levin, D. Tran, N.M. Fried. Lasers Surg. Med., **38** (8), 787–791 (2006). DOI: 10.1002/lsm.20382
[33] A.V. Pushkarev, S.S. Ryabikin, D.I. Tsiganov, A.K. Zotov, V.N. Kurlov, I.N. Dolganova. J. Biomed. Photonics & Eng., **8** (4), 040501 (2022). DOI: 10.18287/JBPE22.08.040501
[34] I.N. Dolganova, A.K. Zotov, L.P. Safonova, P.V. Aleksandrova, I.V. Reshetov, K.I. Zaytsev, V.V. Tuchin, V.N. Kurlov. J. Biophotonics, **16** (3), e202200288 (2023). DOI: 10.1002/jbio.202200288
[35] H.E. LaBelle. J. Cryst. Growth, **50** (1), 8–17 (1980). DOI: 10.1016/0022-0248(80)90226-2
[36] V.N. Kurlov, S.N. Rossolenko, N.V. Abrosimov, K. Lebbou. *Crystal Growth Processes Based on Capillarity: Czochralski, Floating Zone, Shaping and Crucible Techniques* (John Wiley and Sons, Capstone, 2010). DOI: 10.1002/9781444320237.ch5
[37] W.G. Zijlstra, A. Buursma, O.W. van Assendelft. *Visible and Near Infrared Absorption Spectra of Human and Animal Haemoglobin* (Taylor and Francis Group, London, 2021). DOI: 10.1201/9780429071096
[38] A.N. Bashkatov, E.A. Genina, V.I. Kochubey, V.V. Tuchin. J. Phys. D. Appl. Phys., **38** (15), 2543 (2005). DOI: 10.1088/0022-3727/38/15/004
[39] D.S. Myagkonosov, D.V. Abramov, I.N. Delitskaya, E.G. Ovchinnikova. Pisevye Sistemy/Food Systems, **5** (1), 47–54 (2022). DOI: 10.21323/2618-9771-2022-5-1-47-54
[40] B.M. Dunn. Chem. Rev., **102** (12), 4431–4458 (2002). DOI: 10.1021/cr010167q
[41] J. Mótyán, F. Tóth, J. Tózsér. Biomolecules, **3** (4), 923–942 (2013). DOI: 10.3390/biom3040923
[42] A. Ishimaru. Appl. Opt., **28** (12), 2210–2215 (1989). DOI: 10.1364/ao.28.002210
[43] T.J. Farrell, M.S. Patterson, B. Wilson. Med. Phys., **19** (4), 879–888 (1992). DOI: 10.1118/1.596777
[44] H. Assadi, R. Karshafian, A. Douplik. Int. J. Photoenergy, **2014** (1), 471764 (2014). DOI: 10.1155/2014/471764
[45] N. Kollias, I.S. Seo, P.R. Bargo. J. Biophotonics, **3** (1–2), 15–24 (2010). DOI: 10.1002/jbio.200900066

Translated by A.Akhtyamov