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Dunaev, Andrey

Andrey Dunaev, "Methodology of microcirculatory-tssue systems multimodal optical diagnostics," Proc. SPIE 12192, Optical Technologies for Biology and Medicine, 121920T (29 April 2022); doi: 10.1117/12.2626387

SPIE.

Event: XXV Annual Conference Saratov Fall Meeting 2021; and IX Symposium on Optics and Biophotonics, 2021, Saratov, Russian Federation

Methodology of Microcirculatory-Tissue Systems Multimodal Optical Diagnostics

Andrey Dunaev
Research and Development Center of Biomedical Photonics, Orel State University, Russia

ABSTRACT

A modern trend in the development of optical non-invasive diagnostics (OND), which makes it possible to reduce the number of disadvantages in individual applications of methods, is a multimodal approach when one diagnostic technology combines various optical and other physical research methods, which makes it possible to provide early diagnosis of functional changes before clinical manifestations of the disease based on the measurement results. In the last decade, there has been a steady increase in interest in the problems of non-invasive research of microcirculatory tissue systems (MTS) of the human body, which is due to their significant role in the pathogenesis of various diseases. For a wider introduction of OND technologies into clinical practice, it is necessary to further improve the methodology of the multimodal approach in the development of new methods and technical means for assessing the functional state of MTS in various fields of medicine.

Keywords: optical non-invasive diagnostics, multimodal diagnostics, biotechnical systems, methodology, microcirculatory-tissue systems

1. INTRODUCTION

Violations of the microcirculatory-tissue systems (MTS) of the human body play a key role in the pathogenesis of various diseases complications[1], for example, rheumatological[2], endocrinological[3], and otolaryngological[4] ones. Moreover, microcirculatory dysfunction plays a key role in the pathogenesis of gastrointestinal diseases, as well as ischemic organ damage in some acute abdominal surgical diseases. A modern trend in the development of optical non-invasive diagnostics[5] (OND) is a multimodal approach combining several optical (less often – additional non-optical) methods in one diagnostic technology[6]. This allows one to obtain highly efficient diagnostic tools for rheumatology[7], endocrinology[8,9], surgery[10], oncology[11], neurology[12], and other areas of medicine requiring determining the parameters of tissue perfusion-metabolic status. To ensure wider implementation of OND technologies into clinical practice, it is necessary to improve the multimodal approach methodology in the development of new methods and technical means for assessing the functional state of MTS in various fields of medicine[13]. It is also necessary to resolve physical and technical issues, including substantiating medical and technical requirements for improving OND devices[14], carefully working out the issues of monitoring the technical condition to check their performance[15,16], identifying hidden defects and failures, and comparing the results obtained on various devices.

This work aims to improve the quality of optical diagnostics of human body MTS and ensure the conditions for its widespread introduction into clinical practice through scientific substantiation and development of a general methodology of multimodal OND.

2. METHODOLOGY BASICS OF MULTIMODAL DIAGNOSTICS FOR MICROCIRCULATORY-TISSUE SYSTEMS STUDY

To solve the research problems, a systematic approach was used to develop an algorithm for the synthesis of multimodal OND for assessing the functional state of MTS in various diseases. According to the developed scheme of interrelations between the main parameters and states of the MTS in various diseases, depending on research purposes, it is proposed to jointly apply the appropriate methods of OND. The developed methodology of multimodal diagnostics is based on the synthesis of a biotechnical system (BTS). To synthesize the BTS of a multimodal OND to assess the functional state of the MTS, its main elements and the relationship between them were determined (Fig. 1).

* dunaev@bmecenter.ru; phone +7 4862 419806; http://www.bmecenter.ru/en

Optical Technologies for Biology and Medicine, edited by Elina A. Genina, Valery V. Tuchin,
Proc. of SPIE Vol. 12192, 121920T · © 2022 SPIE · 1605-7422 · doi: 10.1117/12.2626387

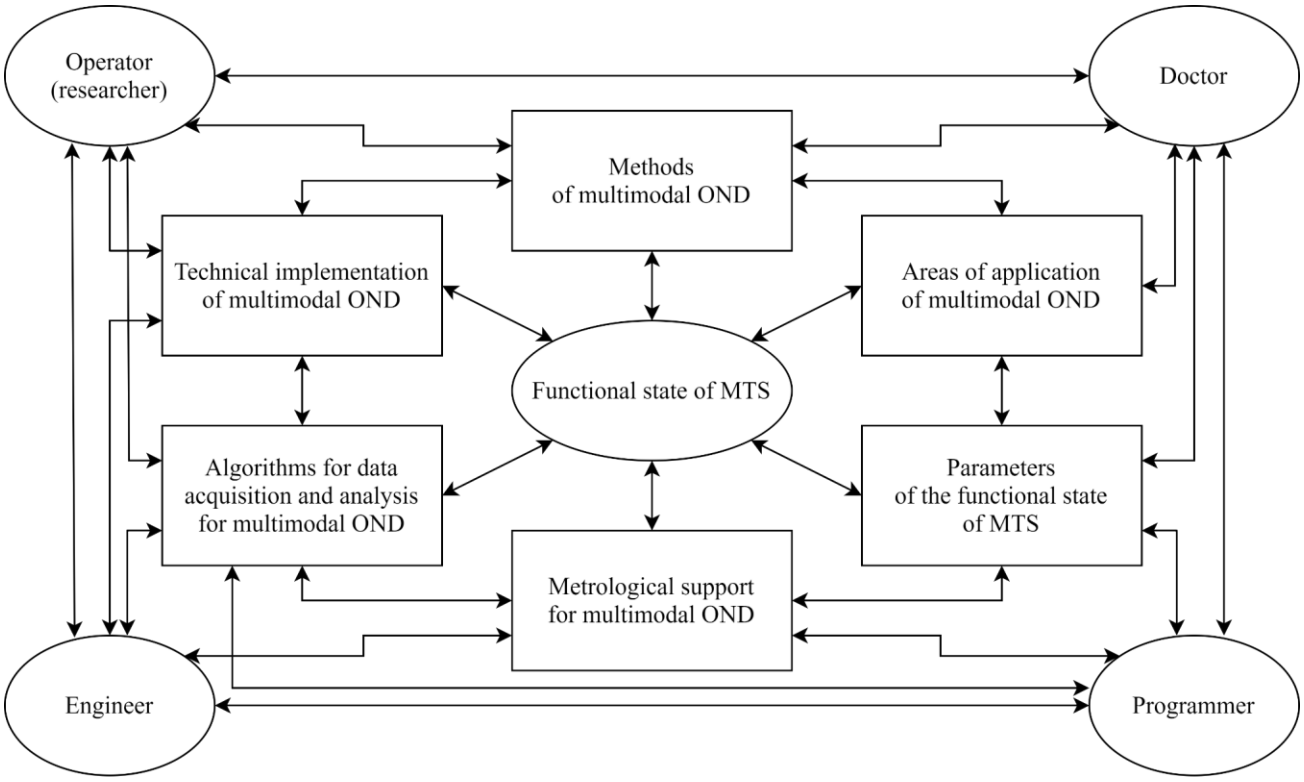

Figure 1. Elements included in the multimodal OND biotechnical systems for assessing the functional state of the MTS, and the relationships between them

When developing a method for synthesizing the BTS of a multimodal OND as a complex object, various concepts find their application:

1) a systematic approach, the tasks of which are to evaluate any object, regardless of its nature, as a certain single whole and to reveal the mechanisms that ensure the interconnected functioning of its simpler components;

2) an approach applied to bionic research, in which attention is focused on specific features of the functioning of body systems (in this case, human MTS), the study of which is necessary and sufficient to solve the problem of synthesizing a system with a given purpose (synthesis of a multimodal OND of the MTS functional state);

3) a multimodal approach to biomedical instrumentation, considering any biomedical device as an open BTS, that is, in the form of a set of biological (the object of research is a human MTS, the subject is an operator and/or a doctor) and technical elements (instrumental methods and a device multimodal OND)[17].

Considering the method for the synthesis of BTS multimodal OND, the following constituent elements of this process can be distinguished:

- determination of a set of specific areas of application of multimodal OND;

- selection of a set of multimodal OND methods and their combinations for each area;

- analysis of sources and ranges of values of parameters of the functional state of MTS for the development of multimodal OND in health and in case of pathological changes;

- determination of the most optimal technologies for the development of a multimodal OND;

- development of the technical implementation of the nodes of the multimodal OND device;

- development of algorithms for analyzing data recorded by the selected OND methods, and software that implements

these algorithms;

- development of metrological support for devices implementing multimodal OND;

- development of the organizational structure of the multimodal OND methodology.

Having identified the main components at the heart of the synthesis stage of a multimodal OND, it is possible to track their relationship with each other and with two sides of the biological component of the system - the biological object under study (human MTS) and researchers (doctor, operator, engineers, etc.).

Thus, the applicability of the basic concepts and principles of designing biotechnical diagnostic systems for the set goal was analyzed, and the main components of the method for the synthesis of multimodal OND biotechnical systems and their interrelations were highlighted.

3. BIOTECHNICAL SYSTEMS OF MULTIMODAL DIAGNOSTICS FOR ASSESSING THE FUNCTIONAL STATE OF THE MICROCIRCULATORY-TISSUE SYSTEMS

According to the biotechnical approach, a generalized BTS of multimodal OND was synthesized to assess the functional state of the MTS of the human body. In addition to the decision rule, the developed BTS consists of hardware and software, including 4 main blocks (Fig. 2): exposure unit; object of study, including, in addition to the biological tissue itself, test objects (optical phantoms); registration and data processing units.

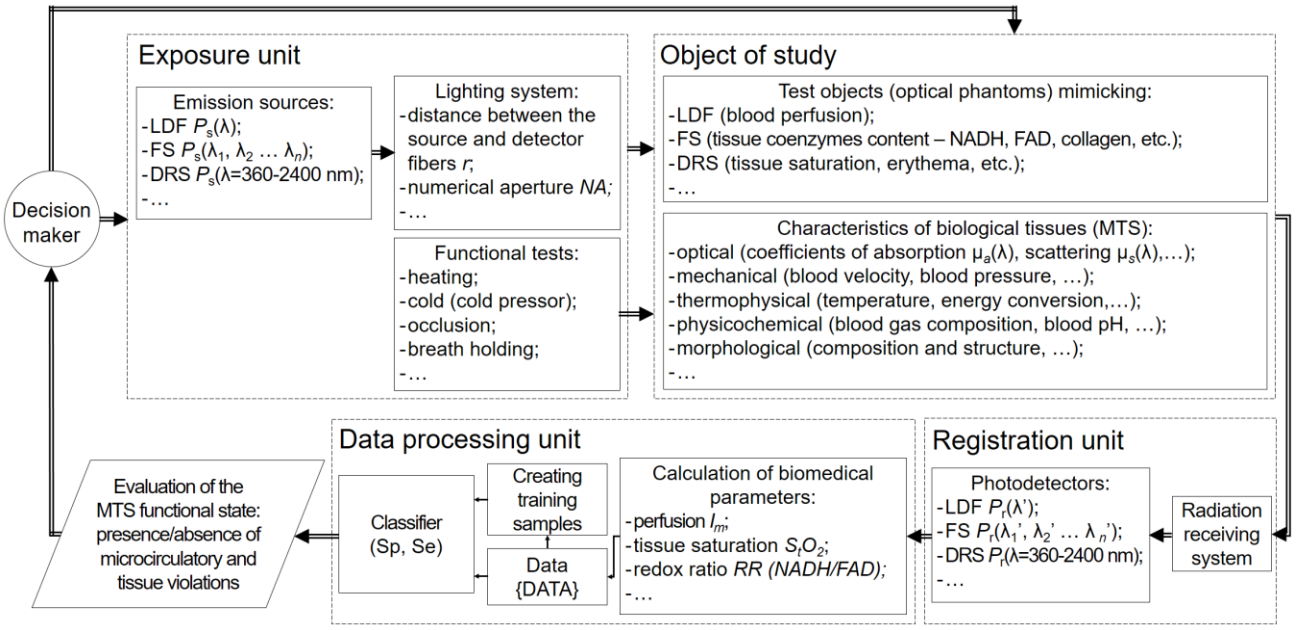

Figure 2. Scheme of generalized BTS of multimodal OND for assessing the functional state of the MTS

The exposure unit is represented by radiation sources for the applied OND methods, for example, laser Doppler flowmetry (LDF), fluorescence spectroscopy (FS), diffuse reflectance spectroscopy (DRS), etc., with the corresponding wavelengths and radiation powers $P_s(\lambda)$. The exposure unit also includes an illumination system, most often a fiber-optic probe, consisting of transmitting light fibers, characterized by the distance between the transmit-receive fibers (base of measurements - r), numerical aperture (NA), and other optical-physical parameters. The exposure unit also includes auxiliary devices and devices that allow performing various functional tests, for example, temperature (thermal, cold), occlusive, electrical stimulation, pharmacological, etc., to identify violations in the functional state of the MTS.

The object of study, which includes, in addition to the biological tissue itself, test objects (optical phantoms, imitation measures), which allow calibration and control of the technical condition of the measuring channels used in multimodal OND. So, for example, for the LDF-channel, a test object is needed that simulates blood perfusion, for the FS-channel, a test object that simulates a different composition of biological tissue coenzymes (NADH, FAD, collagen, etc.), and for

the DRS-channel, a test object is required simulating different levels of tissue saturation, erythema index, melanin index, and other biomedical parameters.

The registration unit includes both a radiation receiving system, which also consists of receiving optical fibers, most often located in the middle of a fiber-optic probe, and of photodetectors of the measuring channels used, for example, LDF, FS, and DRS. It should be emphasized that this fiber-optic probe with transmit-receive light guides combines the illumination system of the exposure unit and the radiation reception system of the registration unit. The proposed design of the combined fiber-optic probe makes it possible to record the power of the secondary (emerging from biological tissue) radiation $P_r(\lambda')$ with a different wavelength from the probed wavelength (for example, for LDF and FS), and in the case of DRS, registration occurs in the entire range from UV to NIR wavelengths (most often, 360-2400 nm), and actually from one diagnostic volume of the biological tissue under study (about 1-2 mm^3).

The final one - data processing unit - is based on computing algorithms of a personal computer (PC) and includes directly the calculation of the main biomedical parameters based on the data recorded by the used OND methods, for example, the microcirculation index (I_m) in LDF, tissue saturation (S_tO_2) in DRS, redox ratios (RR) in FS, etc. Based on the developed research protocols, including the use of various functional tests to increase the information content and accuracy, a data array (DATA) is formed, and a training sample is created. Further, these data are fed into a classifier developed for a specific diagnostic task (for example, the detection of microcirculatory or perfusion-metabolic disorders in patients with rheumatological or endocrinological profiles, etc.) with acceptable statistical indicators (sensitivity Se, specificity Sp) exceeding their current level in clinical practice. According to the proposed approach, the use of the decision rule (classifier) allows one to provide a diagnostic result to the doctor in the form of the presence/absence of microcirculatory-tissue disorders, as well as to determine the causes of the identified disorders and, thereby, brings the OND technology closer to the level of standard diagnostic methods.

Based on the BTS of multimodal OND a method for assessing angiospastic and microcirculatory disorders in rheumatic diseases, and a method for assessing microcirculatory-metabolic disorders in MTS of lower limbs in diabetes mellitus were developed. Also in this work, algorithms were developed for assessing the state of the MTS of the human body under various conditions, such as sports and physiological stresses, during physiotherapeutic treatment and minimally invasive surgical procedures. The developed methods are based on the combined application of several widely used methods of OND, such as LDF, DRS, FS, etc. It is important to emphasize that in these cases the results of multimodal diagnostics are not just a set of registered biomedical parameters, which are difficult to interpret by doctors due to both their complexity and high variability, but the information about the presence/absence of specific disorders in the MTS with the possibility of analyzing their causes.

In addition to considering the general issues of multimodal OND devices construction, the substantiation of specialized medical and technical requirements was carried out. It allowed one to take into account the effect of blood circulation in biological tissue and the pressure of the optical probe on the measurement results. To improve the metrological and technical support of multimodal OND, it is also necessary to develop new approaches and devices for monitoring their technical condition. Improved test objects (optical phantoms) for the most common optical methods in medical practice (LDF and FS) have been proposed since they are the basic ones in modern multimodal OND.

4. CONCLUSION

The developed methodology of multimodal OND can be used to build medical decision support systems for the widest areas of medicine. The results of the work can be extended to other areas of medicine, for example, to improve optical biopsy methods in minimally invasive surgery, rheumatology, endocrinology, otolaryngology, dermatology, neurology, etc. The introduction of multimodal diagnostics into wearable devices (fitness bracelets, smartwatches) for long-term in vivo monitoring (daily or during sleep, tracking of circadian biorhythms; during treatment in a hospital or at home) also has great diagnostic potential.

ACKNOWLEDGEMENTS

The study was supported by the Russian Science Foundation under the project №21-15-00325.

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