MULTI-PARAMETER ANALYSIS IN BLOOD CIRCULATIONAND PERFUSION BASED DIAGNOSTICS

Stewart* N.A. [1], Dunaev A.V. [1], Sokolovski S.G. [1], Sidorov V.V.[2], Rafailov E.U. [1]

[1]*University of Dundee, Dundee, UK*
[2]*SPE "LAZMA" Ltd, Moscow, Russia*
[*]*Corresponding author's email: N.Z.Stewart@dundee.ac.uk*

Multi-functional non-invasive laser-based diagnostic systems, single devices integrating various optical diagnostics techniques, represent a promising and progressing area in biomedical spectrophotometry. These systems typically combine a number of approaches: laser fluorescence diagnostics (LFD), absorption spectroscopy (tissue reflectance oximetry – TRO), laser Doppler flowmetry (LDF) and pulse oximetry. This allows medics and clinicians not only to receive the collective results of the biochemical and physiological parameters which would normally be collected by each individual technique but also to perform multi-parameter patient examination to identify more subtle individual characteristics of blood flow and tissue metabolism based on the simultaneous use of different diagnostic techniques[1]and comprehensive data analysis. This possibility is realized in the LAKK-M system which allows the following blood microcirculation parameters to be obtained: index of blood microcirculation (I_m), tissue oxygen saturation (S_tO_2), relative blood volume (V_b), arterial blood saturation (S_aO_2). Together with collection and analysis of fluorescence spectra of tissue endogenous biomarkers this device is a unique and comprehensive system for research and diagnostics in various fields of biomedicine (cardiovascular diseases, diabetes, cancer, cosmetic surgery, etc.).
However, numerous experiments have identified unacceptably high variations in LDF and TRO readings (up to 30%of standard deviation from the average value for each parameter)[2]. This presents a serious problem for the correct interpretation of data acquired by doctors and seriously limits the prospects for use of this approach in general medical practice. This work aims to overcome this high level of parameter variation and via the use of complex relative parameters which reduce to variations and ease the analysis and interpretation of blood flow parameters, tissue oxygen utilization and biomarkers levels. Furthermore, improved interpretation at a quantitative level of flow velocity based on LDF is targeted by correlation with representative cardiovascular flow phantoms. It is important that this approach can be used for all four LAKK-M channels resulting in increased and readily interpretable information content.
One of these parameters is index of oxygen rate of use in tissue, defined as[3]:

$$U = (S_aO_2 - S_tO_2)/V_b. \qquad (1)$$

This parameter characterizes the specific oxygen consumption per unit of blood volume in the selected region of biological tissue.
Oxygen transport in microvasculature and its respiration in the tissue is estimated by characteristics – oxygen metabolism efficiency (OME):

$$OME = M \cdot U \cdot FRR, \qquad (2)$$

where M – average of perfusion unit (I_m); FRR – fluorescence redox ratio. One of the approaches to calculate FRR is:

$$FRR = I_{NADH} / I_{flavins} \qquad (3)$$

where I_{NADH} – amplitude of fluorescence of reduced coenzyme nicotinamide-adenine dinucleotide (NADH), $I_{flavins}$– amplitude of fluorescence of flavin adenine dinucleotide (FAD). Another approach to figure out this parameter could be :

$$FRR = (I_{NADH} + I_{flavins}) / I_{flavins} \qquad (4)$$

Selection of the preferred option for the calculation of *FRR,* in our opinion, requires further research. To estimate the ranges of variation of the parameters represented, full range of measurements were carried out on 3 apparently healthy volunteers 3times a day for 2 weeks. The middle finger tip of right hand was optical probed with LDF, and TRO for 3 min, and then with LFD. The parameter U was in a range of 1.5 to 6.3, the parameter *OME* was between 78.7 and 147.4 (according to (3). In addition, each volunteer is clearly peculiar to a more narrow range of values. Typically, for a healthy volunteer (measurement taken in middle finger) the typical values of the complex parameter *OME* are in the range of 70-120.
Thus, the parameter *OME* is a more informative characteristic of cutaneous blood microcirculation condition in comparison with individual diagnostics measurements, i.e. microcirculation is much more variable and adapts for specific physiological needs of the tissue. The complex approach of tissue investigation *in vivo* allows physicians to receive complementary data about microhemodynamics, oxygen consumption and condition of metabolic processes for their interpretation and decision making concerning disease diagnosis. Moreover *OME* could be chosen as a general parameter which in the future would serve as a general yea/no marker for diagnostics.
This work was supported by FP7 EU IAPP project (MEDILASE, #806026).

References:
1. Rogatkin D.A., Sokolovski S.G., Fedorova K.A., Stewart N.A., Sidorov V.V., Rafailov E.U. Basic principles of design and functioning of multifunctional laser diagnostic system for non-invasive medical spectrophotometry // SPIE Proc., Vol. 7890, 2011. – 78901H.
2. Makarov D.S., Rogatkin D.A. Physiological deviation of individual blood microcirculation parameters as a source of errors in noninvasive medical spectrophotometry // Proceedings the 9-th International conference «Physics and radioelectronics in medicine and ecology PREME'2010». – RF: Vladimir, 2010. – p.82-86.
3. Krupatkin A.I., Rogatkin D.A., Sidorov V.V. Clinical-diagnostic parameters for complex investigation of microhaemodynamics and oxygen transport in the system of microcirculation / Abstr. book of the VI-th. International Conference "Hemorheology and microcirculation" – RF, Yaroslavl, 2007.– p.106.