NONINVASIVE DIAGNOSTICS OF SKIN MICROPHYSICAL PARAMETERS BASED ON SPATIALLY RESOLVED DIFFUSE REFLECTANCE SPECTROSCOPY

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The ability to determine noninvasively microphysical parameters (MPPs) of skin characteristic of malignant melanoma was demonstrated. The MPPs were the melanin content in dermis, saturation of tissue with blood vessels, and concentration and effective size of tissue scatterers. The proposed method was based on spatially resolved spectral measurements of skin diffuse reflectance and multiple regressions between linearly independent measurement components and skin MPPs. The regressions were established by modeling radiation transfer in skin with a wide variation of its MPPs. Errors in the determination of skin MPPs were estimated using fiber-optic measurements of its diffuse reflectance at wavelengths of commercially available semiconductor diode lasers (578, 625, 660, 760, and 806 nm) at source–detector separations of 0.23–1.38 mm.

Keywords: skin, melanoma, microphysical parameters, diffuse reflectance, fiber-optic measurements, inverse problem, multiple regressions.

Introduction. Malignant melanoma is one of the most common and dangerous forms of skin cancer. The principal predisposing factor of developing it is UV radiation. Characteristic symptoms of malignant melanoma are an increase of the blood supply in the vicinity of the tumor and anomalously high reproduction of melanocytes, cells that produce the pigment melanin. The melanocyte aggregate acquires the ability to metastasize through lymphatic and blood vessels into any body part by overgrowing the epithelial basal lamina. This can lead to a lethal outcome without early and adequate intervention. It is extremely important to detect the pathological process in its early development stage, i.e., before breaching the boundary between the epidermis and dermis.

The traditional diagnosis of melanoma includes detection of suspicious pigmented skin neoplasms, removal of several square millimeters of surface tissue (biopsy), and subsequent histological investigation. It is well known that tumors have optical parameters that differ from those of normal tissue. Therefore, optical methods of detecting tumorous neoplasms [1–3] are capable in several instances of replacing or complementing the invasive biopsy used in oncology. Diffuse reflectance (DR) spectroscopy is one of the simplest and more effective methods [3]. The primary information in these methods consists of DR spectral coefficients of biological tissue that are measured using either a spectrophotometer with an integrating sphere [3–7] or fiber-optic systems with spatially separated optical radiation source and detector channels (spectroscopy with spatial resolution) [3, 8–12].

As a rule, results of DR measurements made using an integrating sphere or fiber-optic systems with a single spatial detector channel are interpreted by selecting the parameters of the direct problem for which its solution will be closest to the measurements. Thus, it is necessary for a consistent solution of the inverse problem that the number of spectral regions for detecting light reflected from tissue exceeds by several times the number of model parameters. This necessitates the use of expensive spectrometric equipment.

Spatially resolved spectroscopy methods based on DR measurements at several distances from the illumination point [3, 11, 12] enables information about the scattering and absorbing properties of biological tissue to be obtained separately. However, known methods for analyzing spectral-spatial characteristics of biological tissue DR either do not

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provide the required practical accuracy or require large computations and; therefore, make timely interpretation of the measurements impossible. Furthermore, all known methods are based on reproduction of tissue optical parameters (absorption coefficient and reduced scattering coefficient) from its DR spatial profiles and subsequent solution of the inverse problem from an interpretation of the reproduced optical parameters. Also, tissue optical parameters at various wavelengths are not independent but related to each other through tissue microphysical parameters (MPPs) that characterize its structure and component composition. In this respect it is obvious that tissue optical parameters can be determined with greater accuracy if not only the spatial but also the spectral component of information about DR of light from tissue are used.

A new method for timely interpretation together of the spectral and spatial characteristics of the light field reflected by tissue was proposed [13–15]. It consists essentially of finding the solution of the inverse problem using multiple regressions between independent components of spectral-spatial DR profiles and tissue MPPs. The method enables optical measurements to be interpreted in real time without solving a radiation-transfer equation and using complicated mathematical algorithms to solve inverse problems. An idea about the theoretically achievable accuracy for reproducing the desired parameters over the whole range of their possible changes can also be obtained. In addition, the effect of the number and accuracy of optical measurements on the consistency of the inverse-problem solution can be studied.

The present work focuses on noninvasive determination of skin MPPs that characterize malignant melanoma. Spatially resolved DR spectroscopy and regression dependences among the measured spectral-spatial DR characteristics of skin and its MPPs are used to solve this problem. The last include the concentration and effective size of skin scatterers, the melanin content in epidermis and dermis, and the hemoglobin concentration in dermis. According to numerous reports [4, 8, 9, 11, 12, 16, 17], these parameters have different values for normal and tumorous tissue. Therefore, they can be used to differentiate skin neoplasms and to detect cancerous tumors. Furthermore, as noted above, the very presence of melanin in the dermis can act as an indicator of melanoma.

**DR Measurement.** A device for measuring spectral-spatial DR profiles of biological tissues was described [15]. The device included a set of laser diodes, a fiber-optic probe equipped with source and detector fibers, a charge-coupled device (CCD), and an information processing unit. The fiber-optic probe contained two source fibers between which the detector fibers were closely placed. Radiation from the laser diodes was fed sequentially into the fiber-optic probe, through which it impinged on the tissue. Light scattered by the tissue was collected by the detector fibers and separated spatially using the CCD. Signals $P(L, \lambda)$ measured in this manner depended on the spectral-spatial profile of the skin DR coefficient $R(L, \lambda)$:

$$P(L, \lambda) = P_0(\lambda) R(L, \lambda) \tau(\lambda) S(\lambda),$$

where $L$ is the distance between the centers of the source and detector fibers; $\lambda$, the radiation wavelength; $P_0(\lambda)$, the laser-diode radiation power; $S(\lambda)$, the CCD spectral sensitivity; and $\tau(\lambda)$, the optical system transmission function. The skin parameters will be determined from the difference of the DR signal logarithms for spatially separated detector channels in order to obviate the need to calibrate the measurement device:

$$r(L, \lambda) = \ln(P(L, \lambda)/P(L_0, \lambda)),$$

where $L_0$ is the distance from the source fiber to the closest detector fiber. According to Eq. (1), the signals $r(L, \lambda)$ are independent of the apparatus constant and power of radiation sent to the tissue. They are determined only as the difference of the optical paths of the light fluxes corresponding to them. Moreover, the signals $r(L, \lambda)$, as shown below, were significantly less susceptible to the effect of epidermis parameters than the signals $P(L, \lambda)$. This enabled the interesting dermis parameters to be determined more accurately.

**Determination of Biological Tissue MPPs.** Let us consider that the detected signals $r(L, \lambda)$ are components of measurement vector $r$. The method for solving inverse problems of the optics of scattering media that was proposed before [13–15] consists essentially of the expansion of $r$ into the eigenvectors of its covariance matrix (forming an orthogonal basis) and obtaining the solution of the inverse problem based on the explicit analytical dependence between coefficients of the expansion $\xi_1, ..., \xi_N$ and parameters of the medium optic-microphysical model, in terms of which the measurements are interpreted. The expansion coefficients $\xi_n$ are equal to the scalar product of the difference between a realization of vector $\mathbf{r}$ and its average over the ensemble and eigenvector $v_n$ of covariance matrix $r$: 935