The impact of laser-induced thermocoagulation effects on the optical spectra of brain tissues

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Abstract. In this work, the results of spectral and optical studies of the grey matter tissues of the brain by a laser hyperthermia action are presented. The coefficients of optical absorption and transport scattering in the spectral range of 250-1500 nm are determined, and the features of the spatial distribution of the laser radiation intensity in the studied objects are identified. It is shown that the coagulation effects lead to compaction and an increase in the concentration of endogenous chromophores and structural elements, which is reflected in the optical properties of biological objects.

1. Introduction

One of the minimally invasive methods of laser medicine that is well-established in clinical practice is laser-induced thermal therapy for brain tumor to date (see, for example, [1-3]). At the same time, the main factors determining the success of laser thermotherapy are accurate dosimetry and model testing of procedures of the laser radiation effect, both on atypical and adjacent normal biological tissues, implying a detailed assessment of their physical and chemical state caused by the effect of photohyperthermia [4, 5].

Important information about structure parameters, biochemical composition, or physiological properties of biological objects is provided by spectral data of the optical absorption coefficient \( \mu_a \), scattering coefficient \( \mu_s \), and anisotropy factor \( g \). To date, many works have been devoted to study the optical properties of brain tissues and their pathologies. Using the spectrophotometric method of integrating spheres, such forms of pathological lesions as meningioma, astrocytoma or glioma were studied in detail, as well as the influence of various factors, including coagulation caused by the hydrothermal method (see, for example, [6-11]). At the same time, the specificity of the effect of coagulation effects on brain tissue induced by laser heating is still an urgent task of biophotonics and could be of interest for the development of both therapeutic and diagnostic methods in neurology.

The aim of this work is to study the dynamics of spectral optical properties of brain tissues as the effect of the thermal effect of laser radiation develops. The diffuse reflectance spectra were measured, and the absorption and transport scattering coefficients of intact and irradiated biological tissues in the spectral range of 250-1500 nm were determined. The features of the spatial distribution of the laser radiation intensity in the objects are identified by numerical simulation on the basis of the obtained results.
2. Materials and methods

The study of the spectral optical characteristics of the gray matter tissue of the human brain under the conditions of photothermal coagulation was carried. The biological tissues were obtained in the State Budgetary Institution of the Republic of Dagestan "Republican Clinical Hospital" and the samples were approximately 15.0×15.0×5.0 mm in size in the number of 15 pieces.

To perform laser hyperthermia, we used a solid-state Nd:YAG laser LQ529 (Solar Laser System, Belarus) with a radiation wavelength of 1064 nm, with a repetition rate of 100 Hz, and an average power of 2.0±0.1 W. The probe radiation was supplied to the biological tissue sample by means of a quartz fiber optic light guide, which formed a laser spot with a diameter of 10.0±1.0 mm on the surface of the object. Coagulation of biological tissues was achieved by laser heating to a temperature of 70.0±1.0 °C with 5 minutes exposure. Temperature control was carried out using two thermocouples located at a depth of 1 and 5 mm from the surface of the object.

The diffuse reflectance coefficient spectra \( R_d(\lambda) \) were measured on a spectrometric complex using a Y-shaped fiber-optic probe, consisting of two "sleeves" (transmitting and receiving) and a contact catheter, in which light-conducting channels were coaxially placed. The excitation of the photosignals was carried using an AvaLight-DH-S-BAL deuterium/halogen lamp (Avantes, the Netherlands), and registration was performed using an MS3504i spectrometer (SOL-Instruments, Belarus) in the wavelength range of 250-1500 nm.

The analysis of the diffuse reflectance coefficient spectra and the determination of the optical absorption \( \mu_a(\lambda) \) and transport scattering coefficients \( \mu'_s(\lambda) \) of biological tissues were carried out according to the method described in detail in [12]. Monte-Carlo method was used to model the spatial distribution of laser radiation intensity in biological tissues [13].

3. Results and discussion

Typical spectra of the diffuse reflection coefficient – \( R_d(\lambda) \), absorption coefficient – \( \mu_a(\lambda) \), and transport scattering – \( \mu'_s(\lambda) \) for gray matter tissues of brain in the intact and coagulated states are shown in Figure 1. As can be seen from the figure, against a background of backscattering, which determines the intensity of diffuse reflection, the absorption bands of blood are clearly visible (280±5, 418±5, 560±15 nm), as well as lipids and water (980±5, 1170±5, 1455±10 nm) near the wavelengths \( R_d(\lambda) \) of which it acquires deep minima [14]. Typical values of the reflection coefficient for intact biological tissues range from 0.025±0.01 in the UV and NIR regions to 0.4±0.01 in the transparency window. At the same time, the development of laser hyperthermia effects in biological tissues leads to an increase by a factor of 2 in the reflection intensity mainly in the area of blood and water absorption, but in the range of the transparency window, the increase does not exceed 20%.

The analysis of the spectral dependence of the optical coefficients (Figure 1B and 1C) allowed us to establish that the spectra of the absorption coefficient \( \mu_a(\lambda) \) largely inversely symmetric to the spectra of the reflection coefficient, but, in contrast to \( R_d(\lambda) \), are detect a number of additional components. Comparison of the obtained results with the known literature data (see, for example, [14, 15]) shows that in the visible region of the spectrum, the coefficient \( \mu_a(\lambda) \) is formed by a complex of endogenous chromophores, which should include oxy- and deoxyhemoglobin with absorption bands at wavelengths of 280±5, 350±5, 418±5, 545±5 and 577±5 nm. At the same time, the presence of spectral components in the IR range is caused by the presence of lipid complexes and water in biological tissues with absorption near the wavelengths of 760±5, 850±5, 970±5, 1170±5, 1220±5 and 1455±10.0nm. In this case, the maximum absorption values occur at the wavelengths of 418±5 nm (the Sore band) and 1455±10.0 nm, where \( \mu_a(\lambda) \) it reaches the values of 2.5 mm⁻¹. Closer to the area of the transparency window, the absorption coefficient decreases monotonically and decreases up to 100 times in the spectral region of 700-900 nm.

The effect of laser hyperthermia on biological tissues leads to an increase in both the absorption coefficient \( \mu_a(\lambda) \) and the transport scattering coefficient \( \mu'_s(\lambda) \). In particular, the absorption coefficient increases up to 1.5 times, mainly in the UV and visible regions, while near the water absorption bands (1170±5 and 1455±10.0 nm), the values decrease up to 40%. This fact shows the
changes in the ratio of endogenous chromophore concentrations due to cell dehydration and denaturation of hemoglobin molecules and structural tissue proteins. This leads to a decrease in the volume of biological tissues and, as a result, to an increase in the concentration of endogenous chromophores.

Figure 1. Spectra of diffuse reflection – $R_d(\lambda)$ (A), spectra of absorption coefficient – $\mu_a(\lambda)$ (B) and transport scattering – $\mu_s'(\lambda)$ (C) of gray matter tissue in the intact (curve 1) and coagulated states (curve 2). Circles – approximation of the transport scattering coefficient – $\mu_s'(\lambda)_{calc}$.

In comparison with the absorption coefficient, the spectral contour of the transport scattering coefficient $\mu_s'(\lambda)$ is a smooth curve that gradually transitions towards large wavelengths with spectral minima in the region of the intensive absorption bands of hemoglobin and water. This fact can be caused by an increase in the imaginary component of the complex refractive index of the medium near the strong absorption bands, when the number of multiple scattering photons decreases due to an increase in the number of interactions with endogenous chromophores along the free path [16, 17].

Analysis of the scattering anisotropy coefficient by approximating it with a power function of the form $\mu_s'(\lambda) = a\lambda^{-b}$ (where $\lambda$ is the wavelength in nm, $a$ is a function of the concentration of scattering particles, and the parameter $b$ determines their average size) [9-11], allows us to predict with good accuracy the function $\mu_s'(\lambda)$, which for intact biological tissues takes the form: $\mu_s'(\lambda)_{calc} = 68.508\lambda^{-0.72} + 3.92 \times 10^{10}\lambda^{-4}$.

It should be noted that the approximation of the coefficient of two power functions indicates the formation of the $\mu_s'(\lambda)$ spectrum by at least two types of particles. Moreover, the first term of this function with a wave exponent $b = 0.72$ is responsible for light scattering caused by sufficiently large particles (Mie scatterers), which can be cell nuclei and other large particles. The second term with the wave exponent $b = 4$ corresponds to Rayleigh’s particles, for example, mitochondria, lysosomes, and
other elements of the cytoplasm. In this case, for coagulated biotissues, the approximating function takes the form: 

\[ \mu'_{\text{calc}}(\lambda) = 162.42\lambda^{-0.78} + 1.35 \times 10^{11}\lambda^{-4} \]

A comparative analysis of the obtained expressions shows that with the thermocoagulation processes evolution, the effective size of the Mie scatterers decreases slightly, and their concentration of scattering particles increases significantly. The detected morphofunctional changes in the tissues of the grey matter of the brain may indicate the development of coagulation effects. Apparently, in the process of laser hyperthermia, there is a violation of the histostructure and architectonics of the brain tissue, expressed in the form of a decrease in the size of the structural elements of the cytoplasm, wrinkling and coagulation of the stroma. As a result, there is a compaction and an increase in the concentration of structural elements, leading to an increase by a factor of 3 in the transport scattering of coagulated media.

In addition, it is important to note that the obtained results of the spectral dependence of the coefficients \( \mu_a(\lambda) \) and \( \mu'_s(\lambda) \) for gray matter tissue of the brain not only agree well with the results of [8, 9], but also complement them due to a wide spectral range. At the same time, higher values of absorption coefficient observed in the spectral range of 250-600 nm, compared with the results of the works [7, 11], are most likely due to the difference in the sample preparation methods used. In [7, 11], bloodless histological sections with a thickness of no more than 0.5 mm were studied, while in our work, the samples of biological tissues were native semi-infinite medium with a thickness of 5.0±1.0 mm. In the meantime, the general dynamics of the optical properties of the studied biological objects during the development processes of photohyperthermia is identical and is in fully consistent with the results of the works [4, 5, 11].

Based on the data of the optical coefficient spectra \( \mu_a(\lambda) \) and \( \mu'_s(\lambda) \) using Monte Carlo simulation method, the spatial distribution of light intensity was calculated \( h(z) = I(z)/I_0 \), where \( I_0 \) is the intensity of the incident light, \( I(z) \) is the intensity of light in the medium at depth \( z \). The results of these calculations in the form of 3-dimensional spectra \( h(z) \) for gray matter tissues of brain in the intact state (A) and during laser coagulation (B) are shown in Figure 2.

![Figure 2. 3-D spectra of light intensity spatial distribution of gray matter tissue in the intact (1) and coagulated states (2). A – Spectra of light intensity spatial distribution in tissues in the wavelength range of 250-1500 nm. B – Spectral profile of intensity \( h(z) \) at wavelengths of 300, 1064 and 1460 nm. C – Spectral profile of intensity \( h(z) \) at tissue depth \( z \) – 0.01, 0.2, and 0.7 mm.](image-url)
object at a certain distance \( z_{\text{max}} \left( \mu_a(\lambda) + \mu_s'(\lambda) \right)^{-1} \), where \( I(z) \) it can be up to 1.5 times higher \( I_0 \).

At the same time, in the region of strong absorption at wavelengths of 250-400 nm and 1450, the maximum luminous flux falls on the surface, where \( h(z) \to 1 \), and \( z_{\text{max}} \to 0 \).

For comparative analysis, Table 1 shows the value of the parameter \( h(z) \) for the studied biological tissues at depth \( z \) for the following wavelengths of 300, 1064 and 1460 nm. As can be seen from the table, for intact tissues, the grey matter tissue of brain \( h(z) \) exceeds \( h(z) \) and \( h(z) \), respectively, by 10-12\% and 25\%, and the parameter \( z_{\text{max}} \) exceeds \( z_{\text{max}} \) and \( z_{\text{max}} \), up to about 1.5 times, respectively.

Table 1. The parameters of illumination \( h(z) \) and characteristic distance \( z_{\text{max}} \) for the gray matter tissues of brain in normal and by the evolution of laser thermocoagulation processes at wavelengths of 300, 1064, 1460 nm.

| The state of biological tissues | \( h(z) \) \( z_{\text{max}} \) (mm) | \( h(z) \) \( z_{\text{max}} \) (mm) | \( h(z) \) \( z_{\text{max}} \) (mm) |
|-------------------------------|---------------------------------|---------------------------------|---------------------------------|
| Intact tissues                | 1.0±0.1/0.01                    | 1.22±0.3/0.22±0.03              | 1.15±0.2/0.17±0.02              |
| Coagulated tissues            | 1.0±0.1/0.01                    | 1.12±0.2/0.13±0.02              | 1.07±0.2/0.12±0.02              |

The effect of heat-induced processes relative to the intact group leads, mainly, to a reduction of the characteristic distance \( z_{\text{max}} \) up to 1.5 times, while \( h(z) \) it varies within 10\%. The detected dependence of the parameters \( z_{\text{max}} \) and \( h(z) \), apparently, is associated with a significant increase in the values of the optical coefficients for violation of the histomorphological structure of biological tissues.

Due to the above, it can be concluded that for the purpose of conducting photothermal or photodynamic exposure procedures, using a near-infrared laser is more preferable. Ultraviolet light sources can be used for laser ablation of surface formations in comparison with the near-infrared lasers, since the depth of light penetration in the short-wave region does not exceed several cell layers.

4. Summary

Thus, summarizing and synthesizing the results obtained leads to the following conclusions:

1. The spectral contour of the diffuse reflection coefficient of brain tissues is formed by the spectral absorption bands of hemoglobin, lipid complexes and water, at the wavelengths of which, the absorption coefficient \( \mu_a(\lambda) \) acquires characteristic maxima.

2. The laser hyperthermia leads to an increase in the diffuse reflection coefficient by up to 2 times, which is caused by an increase in the absorption coefficients by 1.5 and transport scattering by up to 3 times.

3. The approximation of the coefficients \( \mu_s'(\lambda) \) by two power function indicates a decrease in the size of cellular organelles, a shrinking of the stroma, and, as a result, a compaction of biological tissues with an increase in the concentration of endogenous chromophores and structural elements.

4. The spatial distribution of light intensity in biological tissues significantly depends on the magnitude and ratio of the optical coefficients. In the area of the therapeutic window, where \( \mu_a \ll \mu_s' \), the maximum light intensity is located at a distance of 0.25±0.3 mm from the surface of the medium and can be up to 1.5 times higher than the incident intensity.

5. The development of laser-induced thermocoagulation processes leads to decreasing in both the illumination amplitude and the characteristic distance an average of 30\%.

The results obtained in this work can be used in modeling the nature of the propagation of laser radiation during the processes of planning of laser thermotherapy procedure of malignant brain tumors and adjacent normal tissues.
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