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BIOPHOTONICS

Modeling of Optimal Conditions for Oxyhemoglobin Photodissociation in Laser-Irradiated Biotissue

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Abstract—Based on the theory of radiation transfer and a model that describes the structure and optical properties of biotissues, we have found spectral conditions of irradiation of the skin surface that ensure efficient generation of molecular oxygen O_2 in the dermis due to the photodissociation of blood oxyhemoglobin. We show that, for maximal local O_2 formation at depths $z \le 0.2$ mm, 0.2 mm $< z \le 0.9$ mm, 0.9 mm $< z \le$ 2.5 mm, and $z > 2.5$ mm, it is more effective to use wavelengths in the intervals 418 ± 5, 575 ± 5, 585 ± 5, and 600 ± 5 nm, respectively. Physical reasons for the shift of optimal wavelengths toward the red range of the spectrum are described. We show that they are based on the selectivity of optical properties of the skin biotissue, which acts as of a kind of spectral filter the transmission curve of which depends on the depth. It is found that irradiation at a wavelength near 575 nm is optimal for the generation of a maximal amount of O_2 in the intire bulk of the dermis.

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INTRODUCTION

Oxygen is a key element in the metabolism of cells, and its concentration in tissues is important for many biochemical reactions to proceed efficiently. As is known, aerobic metabolism is primary in the mechanism by which cells are supplied with energy. Controlling this mechanism opens a unique possibility for its use in photo and laser therapy. In medicine, in many pathologies—such as, e.g., diabetes, burns, bedsores, malignant neoplasms, wounds, etc.—tissues are insufficiently supplied with oxygen. Lowering the oxygen supply to cells of biotissues by arterial blood considerably reduces the efficiency of drug therapy; increases the risk of infection and scar formation; and, in the limiting case, leads to necrosis of tissues.

It has been revealed experimentally [1] that light irradiation of a biotissue causes photodissociation of oxyhemoglobin HbO_2, which dissociates into deoxyhemoglobin Hb and molecular oxygen O_2. Later, photodissociation was studied in detail in vitro [2–7] and in vivo [8–11]. Its quantum yield q (the ratio of the number of formed O_2 molecules to the number of quanta absorbed by HbO_2) has been investigated in a series of works, e.g., by the method of laser kinetic spectroscopy [3, 5, 6]. In these works, it was shown that, upon excitation of photodissociation by light in the range of 350–650 nm, the values of q are almost constant (within the limits of experimental error), being 3–5% depending on temperature and other factors. From the analysis of experimental data, it was assumed that the photodissociation of oxyhemoglobin can be responsible for the biological action of light on tissues [12]. This mechanism is used to increase the level of O_2 in skin tissues in order to eliminate hypoxia (oxygen deficiency) [13], to stimulate aerobic (related to the oxygen consumption) metabolism in cells, and to achieve a therapeutic effect [14]. In measurements in the near-IR range of the spectrum, no photodissociation has been observed [3] and it was concluded that, up to the measurement error, the quantum yield is here at least 50 times lower, even though it is evident that the efficiency of photodissociation in vivo is proportional to the power of light absorbed by HbO_2 in the biotissue. In [15–17], an analytical method of calculation of characteristics of radiation fields under the human skin surface has been proposed. Using the theoretical results of these investigations, the absorption coefficients of different biotissue chromophores in homogeneous [18] and inhomogeneous [19] skin dermis were studied and the photodissociation efficiency of HbO_2 was quantitatively estimated [20]. The objective of this work is to optimize spectral conditions of biotissue irradiation through the skin surface in order to maximize generation of O_2.

STRUCTURE AND OPTICAL CHARACTERISTICS OF SKIN

Our investigations are based on a model that describes the structure and optical properties of near-surface biotissue layers in the spectral range of 300–1000 nm, which was constructed from analysis and generalization of numerous experimental data [21–25]. Skin is represented as a three-layer medium,

which consists of a horny layer (stratum corneum), an epidermis, and a dermis. In the latter two layers, the volume concentration of two basic absorbing chromophores, melanin (f_m) and blood (C_v), respectively, can vary. The model makes it possible to specify [15, 26] optical dimensions and spectral characteristics of the medium from known structural (thicknesses of layers) and biophysical parameters of the tissue. The spectral characteristics are considered to mean the absorption and scattering coefficients and scattering indicatrices in each of the skin layers, while the biophysical parameters are concentrations f_m and C_v, capillary hematocrit H (the fraction of blood in capillaries occupied by erythrocytes), fraction C_h of the volume of erythrocytes that is occupied by hemoglobin, and degree of oxygenation of blood S (the ratio of the volume of HbO_2 to the volume occupied by the oxygenated and deoxygenated forms of hemoglobin). In what follows, we assume that the following parameters are fixed: $H = 0.4$ and $C_h = 0.25$ [27, 28]. In addition, since reliable quantitative data on photodissociation quantum yield q are unavailable, we will consider only the UV and visible spectral ranges, $\lambda = 300–650$ nm.

CHARACTERISTICS TO BE OPTIMIZED

Let us introduce the notion of differential photodissociation efficiency [29], which is defined as number of oxygen molecules $n(z, \lambda)$ that are formed per unit time and per unit volume at depth z when monochromatic light at wavelength λ and unit power density E_0 is incident on the surface,

$$n(z,\lambda) = \frac{\mu_a(\lambda) H C_h C_v(z) S \lambda q E(z,\lambda)}{hc}, \qquad (1)$$

where $\mu_a(\lambda)$ is the absorption coefficient of HbO_2, h is the Planck constant, c is the speed of light in the medium, and $E(z, \lambda)$ is the spectral radiation density or the spatial illuminance in the medium (in W/m^2) [30] (fluence rate). By definition, $E(\lambda, z) = \int_{4\pi} I(\lambda, z, \vartheta, \phi) d\Omega$, where $I(\lambda, z, \Omega)$ is the intensity of light as a function of the angular coordinates ϑ and ϕ, and $d\Omega = \sin\vartheta d\vartheta d\phi$ is the elementary solid angle. The differential photodissociation efficiency has the dimensionality of $cm^{-3}\ s^{-1}$. Integration of (1) over the thickness of the dermis yields the integral number of O_2 molecules (i.e., the integral photodissociation efficiency) formed in the entire bulk of the dermis with the area of 1 cm^2 per 1 s due to the photodissociation of oxyhemoglobin,

$$N(\lambda) = \frac{\mu_a(\lambda) H C_h S \lambda q}{hc} \int_{z_0}^{\infty} C_v(z) E(z,\lambda) dz, \qquad (2)$$

where $z_0 = d_1 + d_2$ is the coordinate of the upper boundary of the dermis (d_1 and d_2 are the thicknesses of the horny layer and epidermis, respectively). Quantity $N(\lambda)$ has a dimensionality of $cm^{-2}\ s^{-1}$. The upper limit of integration in (2) is set to be ∞, since the radiation density in deep layers of the dermis is negligibly small. In relations (1) and (2), it was taken into account that, in the general case, volume concentration of capillaries C_v can depend on depth z [27]. However, since it was shown in [17, 20] that, in the visible range of the spectrum, the layered structure of the dermis affects weakly the dependence of $E(z, \lambda)$ on depth z in the near-surface dermis, where the values of the radiation density are still significant, in calculations below, concentration C_v will be assumed to be constant.

It can be seen from (1) and (2) that the differential and integral quantities $n(z, \lambda)$ and $N(\lambda)$ are proportional to the products $\mu_a(\lambda)E(\lambda, z)$ and $\mu_a(\lambda)\int_{z_0}^{\infty} E(z,\lambda)dz$, respectively, which, up to the constant multiplier HC_hC_v, have the meaning of effective spectral absorption indices of oxyhemoglobin at a given depth and in the whole bulk of the dermis, respectively. Let us consider the problem of light transfer for the case in which the optical properties of the medium do not depend on E_0. It is evident that the spectral values of $n(z, \lambda)$ and $N(\lambda)$ can be increased at the expense of an increase in E_0. This approach is trivial, and it is related to the consumption of excess energy, which can lead to, e.g., additional and, frequently, undesirable heating of the tissue. In view of this, it is necessary to find wavelengths that would ensure maximal differential and integral photodissociation efficiencies for different structural and biophysical parameters of the tissue at a fixed power density of irradiation of the surface.

RESULTS AND DISCUSSION

Let us consider optimal wavelengths that ensure maximal values of the differential photodissociation efficiency at particular depths (or in an interval of z). This information can be useful for laser therapy of a local pathological area of the tissue. An analysis of calculation results of the radiation density taking into account the optical properties of all chromophores of the tissue and its structure showed that there are only several irradiation wavelengths that lead to a maximal generation of O_2 at different depths in the dermis. These are 418, 575, 585, and 600 nm. Upon irradiation at other λ from the spectral range that is considered here, the differential photodissociation efficiency will always acquire smaller values. Figure 1 illustrates the depth structure of $n(z, \lambda)$ at these values of λ, as well as at a wavelength of 632.8 nm of a He–Ne laser, which is frequently used in experiments [10]. As can be seen from this figure, in the upper part of the dermis ($z \le 0.2$ mm), a maximum $n(z, \lambda)$ is yielded by irradiation with light at $\lambda = 418$ nm. With increasing z, the

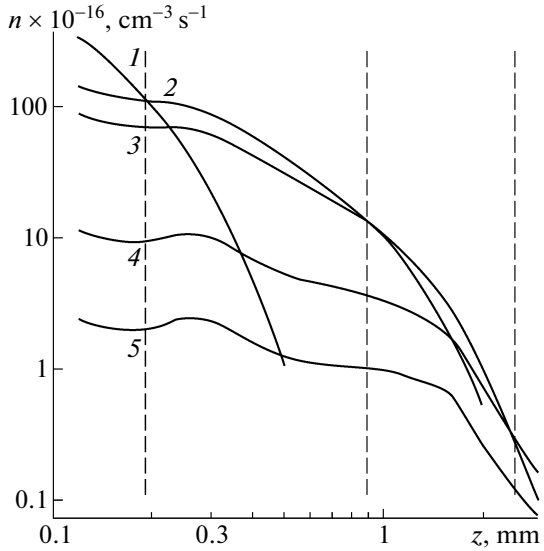

Fig. 1. Dependences of differential photodissociation efficiency on depth z in the dermis upon irradiation of the skin surface at wavelengths (*1*) 418, (*2*) 575, (*3*) 585, (*4*) 600, and (*5*) 632.8 nm; $f_m = 0.08$, $d_1 = 20$ μm, $d_2 = 100$ μm, $C_v = 0.04$, $S = 0.75$, $q = 0.05$, and $E_0 = 1$ W/cm^2.

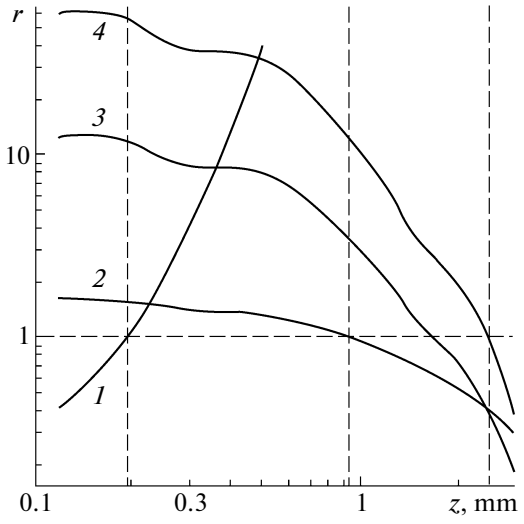

Fig. 2. Dependences of ratio r on depth z at $\lambda_1 = 575$ nm and $\lambda_2 =$ (*1*) 418, (*2*) 585, (*3*) 600, and (*4*) 632.8 nm; $f_m = 0.08$, $d_1 = 20$ μm, $d_2 = 100$ μm, $C_v = 0.04$, and $S = 0.75$.

most efficient wavelengths are successively shifted toward the red range of the spectrum: in the interval 0.2 mm $< z \le 0.9$ mm, this is $\lambda = 575$ nm; at 0.9 mm $< z \le 2.5$ mm, this is $\lambda = 585$ nm; and at $z > 2.5$ mm, this is $\lambda = 600$ nm. The boundary values of these depths are indicated in Fig. 1 by vertical dashed lines. The data were obtained at $f_m = 0.08$, $d_1 = 20$ μm, $d_2 = 100$ μm, $C_v = 0.04$, and $S = 0.75$. Results of calculations at other structural and biophysical parameters of the tissue (not shown) typical for human skin, which vary in the ranges 15 μm $\le d_1 \le 25$ μm, $0.02 \le f_m \le 0.08$, $60 \le d_2 \le 120$ μm, $0.02 \le C_v \le 0.06$, and $0.5 \le S \le 0.97$, showed that the positions of the boundaries within which a particular wavelength is most efficient are rather stable with respect to changes in d_1, f_m, d_2, C_v, and S. Thus, the presented coordinates can vary in depth in narrow limits $z \pm \Delta z$, i.e., approximately 0.2 ± 0.03, 0.9 ± 0.05, and 2.5 ± 0.1 mm. This allows one to use these wavelengths—418, 575, 585, and 600 nm—for generation of a maximal number of molecular oxygen in the corresponding depth intervals in the dermis [29]. Attention should be paid to the fact that the relative width of the interval of depths $\Delta z/z \cong 0.15$ is the greatest in the case of irradiation at the wavelength of 418 nm, which is related to a quite strong dependence of the radiation density on the tissue parameters, which will be explained below. It follows from Fig. 1 that the radiation of, e.g., a helium–neon laser at a wavelength of 632.8 nm, which was used in [10], is less efficient at any depths from the point of view of increasing the level of O_2 in the dermis compared to the level achieved with irradiation at 575, 585, or 600 nm. In other words, upon irradiation of the skin surface at a wavelength of 632.8 nm, the amount of molecular oxygen formed in the dermis is approximately 5–50 times smaller than that in the case of irradiation at the above-indicated wavelengths of 418, 575, 585, and 600 nm in the corresponding intervals or depth z.

In order to quantitatively compare the values of $n(z, \lambda)$ and $N(z)$ upon irradiation of the surface at different wavelengths, we introduce the ratios

$$r(z, \lambda, \lambda_2) = n(z, \lambda_1)/n(z, \lambda_2) \quad (3)$$

and

$$R(\lambda, \lambda_2) = N(\lambda_1)/N(\lambda_2), \quad (4)$$

which show by how many times the differential photodissociation efficiency at given depth z and the integral photodissociation efficiency upon irradiation of the skin surface at wavelength λ_1 are greater (or smaller) than the corresponding quantities upon irradiation with the same power density at wavelength λ_2.

Figure 2 shows dependences of ratio r on the depth that were calculated with the wavelength of 575 nm taken as λ_1 and the wavelengths 418, 585, 600, and 632 nm used as λ_2. Here, the boundary values of the depths indicated above are also shown by vertical dashed lines. The data presented in Fig. 2 make it possible to estimate how much the use of the wavelengths 418, 575, 585, and 600 nm is more efficient for the excitation of the photodissociation of oxyhemoglobin and for the increase in the level of molecular oxygen in the biotissue at the corresponding depths in the dermis. For example, by determining the ratio of the numerical data that correspond to curves *3* and *2*, we can find by how much the amount of O_2 molecules

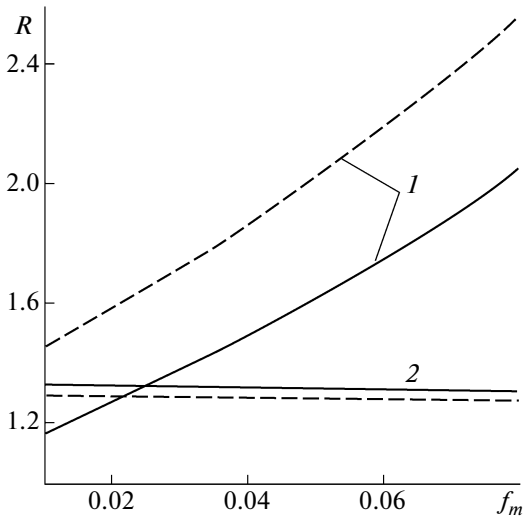

Fig. 3. Dependences of ratio R on the volume concentration of melanin at $\lambda_1 = 575$ nm and $\lambda_2 = (1)$ 418 and (*2*) 585 nm for $C_v =$ (solid curves) 0.04 and (dashed curves) 0.08; $d_1 = 20$ μm, $d_2 = 100$ μm, and $S = 0.75$.

obtained upon irradiation of the surface at the wavelength of 585 nm is greater or smaller than that obtained upon irradiation at 600 nm.

As was noted above, the positions of the boundary depths at which a particular wavelength is most efficient are rather stable with respect to changes in the structural and biophysical parameters of the tissue. Clearly, the values of r and R are varied in this case at the expense $E(z, \lambda)$. The radiation density at the wavelength of 418 nm, which strongly depends on f_m and C_v, is the most sensitive to changes in the tissue parameters. This is explained by the fact that, in the blue range of the spectrum, the absorption of light both by melanin and by blood is maximal [21–25], appreciably exceeding the absorption at other wavelengths in the range of 575–600 nm. Below, we will illustrate the influence of concentrations f_m and C_v on the generation of O_2 using the integral photodissociation efficiency as an example.

Let us now determine optimal wavelength λ_1 for generation of O_2 in the entire bulk of the dermis. The calculations showed that, if the parameters of the tissue are varied in the limits indicated above, the integral photodissociation efficiency acquires maximal values upon irradiation of the surface at only one wavelength of 575 nm [31]. Figure 3 compares the values of R for $\lambda_1 = 575$ nm, $\lambda_2 = 418$ nm (curves *1*), and $\lambda_2 = 585$ nm (curves *2*) in relation to the concentration of melanin f_m at two values of C_v. The wavelength of 418 nm corresponds to maximal absorption of oxyhemoglobin $\mu_a(\lambda)$ [21, 24] in the considered spectral range of 300–650 nm, and $\lambda_2 = 585$ nm was recommended in [7] for the wavelength that ensures a maximal effective absorption index of HbO_2 in the entire bulk of the dermis. From Fig. 3, we can conclude that, upon irradiation at the wavelength of 575 nm, the integral photodissociation efficiency is approximately 1.2–2.5 and 1.2–1.3 times greater compared to the values of this parameter obtained upon irradiation at $\lambda_2 = 418$ and 585 nm, respectively. It is seen that the values of R at $\lambda = 418$ nm depend much more strongly on f_m and C_v compared to 585 nm. Obviously, as f_m and C_v are increased, the light fields at any wavelength decrease because of increased absorption of the medium, but, in the blue range of the spectrum, this effect is more pronounced, while the irradiation at $\lambda_1 = 575$ nm becomes more favorable from the viewpoint of generation of O_2. A sufficiently strong sensitivity of the radiation density at $\lambda_2 = 418$ nm accounts for a wide relative interval of depths z, in which the blue light initiates the photodissociation mechanism more efficiently. We note that small values of $R(\lambda)$ (about 1.2 or lower) at $\lambda_2 = 418$ nm take place at low concentrations of melanin, $f_m \le 0.02$, which are characteristic of such a skin pathology as vitiligo [16]; therefore, they are not very typical.

Relations (1)–(4) correspond to monochromatic illumination of the skin surface at wavelength λ_1 or λ_2. If the mechanism of photodissociation and generation of oxygen is initiated by a light beam in spectral interval $\Delta\lambda_{1,2}$ near wavelength $\lambda_{1,2}$, expressions (3) and (4) take the form

$$r^*(z, \lambda_1, \lambda_2) = \int_{\lambda_1-\Delta\lambda_1}^{\lambda_1+\Delta\lambda_1} n(z, \lambda)d\lambda \Big/ \int_{\lambda_2-\Delta\lambda_2}^{\lambda_2+\Delta\lambda_2} n(z, \lambda)d\lambda, \quad (5)$$

$$R^*(\lambda_1, \lambda_2) = \int_{\lambda_1-\Delta\lambda_1}^{\lambda_1+\Delta\lambda_1} N(\lambda)d\lambda \Big/ \int_{\lambda_2-\Delta\lambda_2}^{\lambda_2+\Delta\lambda_2} N(\lambda)d\lambda. \quad (6)$$

The question arises of how the dependence of the photodissociation efficiency on $\Delta\lambda_{1,2}$ will change. To compare the values of the differential and integral photodissociation efficiencies at different λ, we will take $\Delta\lambda = \Delta\lambda_1 = \Delta\lambda_2$, which will ensure identical values of the spectral power density of irradiation for the considered wavelengths. Figure 4 presents the dependences of (a) r^* at fixed depths z and (b) R^* on $\Delta\lambda$. As above, we took for λ_1 the wavelength of 575 nm. It is seen that, upon an increase in $\Delta\lambda$, in general, the photodissociation efficiency for the used wavelengths decreases, which is related to the fact that peculiarities of spectral dependences of the optical characteristics of the biotissue are smoothed and are averaged over a broader interval $\Delta\lambda$. Therefore, to initiate the photodissociation mechanism, it is more favorable to use laser radiation instead of conventional radiation sources, since this makes it possible to ensure a fairly high spectral power density on the skin surface and a noticeable increase in the amount of O_2 in a narrow range $\Delta\lambda$. This decrease is especially important for

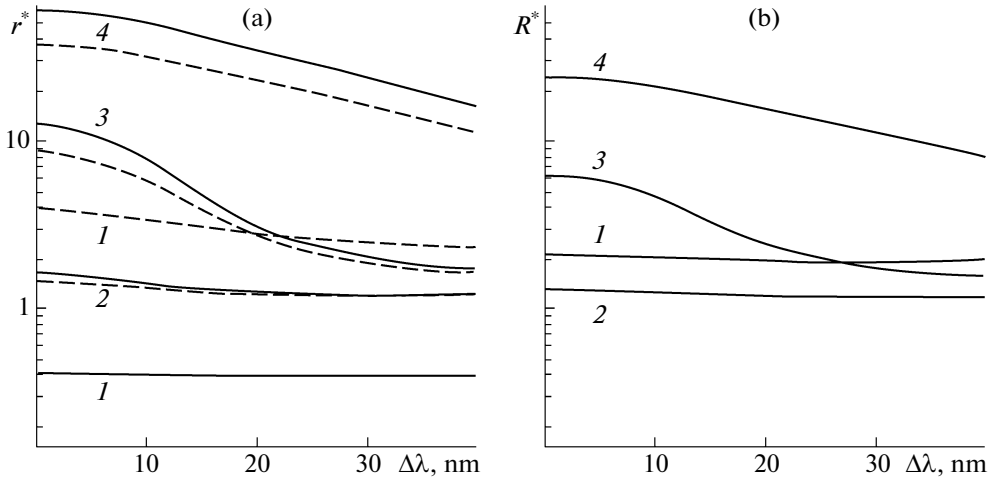

Fig. 4. Dependences (a) of r^* at $z = 0.12$ (solid curves) and 0.3 mm (dashed curves) and (b) of R^* on halfwidth $\Delta\lambda$ of the irradiation spectrum for $\lambda_1 = 575$ nm and $\lambda_2 = 418$ (curves *1*), 585 (*2*), 600 (*3*), and 632.8 nm (*4*); $f_m = 0.08$, $d_1 = 20$ μm, $d_2 = 100$ μm, $C_V = 0.04$, and $S = 0.75$.

$\lambda_2 = 600$ and 632 nm, whereas, at $\lambda_2 = 418$ nm, it is less pronounced. For the other pair, $\lambda_1 = 575$ nm and $\lambda_2 = 585$ nm, broadening of $\Delta\lambda$ also not very significantly affects the values of r^* and R^*, since these wavelengths are close to each.

Physically, the reason for the considered spectral peculiarities of the photodissociation efficiency is clear. This is the wavelength selectivity of the optical properties of the basic absorbing chromophores of the tissue, in particular, melanin and blood. In this case, the biotissue behaves as a spectral filter, the relative transmission curve of which depends on depth z. The above-noted red shift of irradiation wavelengths optimal for a local increase in the concentration of O_2 can be explained easily. In upper layers of the dermis, where the incident light is not very strongly attenuated, maximal values of the differential photodissociation efficiency are ensured by irradiation with the violet light, because of the absorption peak of HbO_2 in the Soret band at $\lambda = 418$ nm [21, 24]. With increasing z, the radiation in the blue–violet interval of the spectrum is attenuated almost completely and the photodissociation of HbO_2 is most efficient near the local light absorption maximum of oxyhemoglobin at $\lambda = 575$ nm. We note that, in the intermediate range of wavelengths, there is another local absorption maximum of HbO_2 at $\lambda \cong 540$ nm, the intensity of which is roughly the same as of the peak near $\lambda = 575$ nm. However, in the short-wavelength range of the spectrum, the absorption of melanin is stronger and, as calculations showed, irradiation of the tissue with the light at $\lambda \cong 540$ nm is less efficient at all depths compared to $\lambda = 575$ nm. Upon further increase in z, the maximum of the differential photodissociation efficiency falls on the long-wavelength wing of the absorption band of HbO_2, rather than on its peak. This is related to competition between two factors that oppositely affect the differential photodissociation efficiency. Namely, as the irradiation wavelength is shifted toward the red range, radiation density $E(\lambda, z)$ increases, whereas $\mu_a(\lambda)$ decreases.

The fact that wavelength $\lambda = 575$ nm is optimal for generation of molecular oxygen in the entire bulk of the dermis is a consequence of the integral character of spectrum $N(\lambda)$. Indeed, as was shown above, the effective absorption index of HbO_2 (or the product $\mu_a(\lambda)E(\lambda, z)$, which, in fact, is the integrand function in expression (2)) is maximal in a rather wide interval of depths, roughly, from 0.2 to 0.9 mm. At these values of z, the radiation density is still rather high compared to that at $z \geq 1$ mm and its contribution to the integral photodissociation efficiency upon irradiation of the tissue at $\lambda = 575$ nm is maximal. Irradiation at other wavelengths is less efficient from the point of view of generation of O_2 because of a small interval of depths in which $\mu_a(\lambda)E(\lambda, z)$ has a maximum (e.g., for $\lambda = 418$ nm) or because of significantly weakened radiation density $E(\lambda, z)$ at large z ($\lambda = 600$ nm).

We also note that the calculations for a dermis that is inhomogeneous in depth [17], which are similar to those presented above, showed that the considered regular features of optimal spectral conditions for the irradiation of the skin surface remain almost unchanged. There are only insignificant quantitative differences (within 10%) between these two cases.

CONCLUSIONS

We have developed a technique for investigation of light absorption by oxyhemoglobin of blood and its subsequent photodissociation with the formation of molecular oxygen. The technique is analytic and takes into account the influence of optically significant

chromophores of the tissue on light fields. It makes it possible to select optimal wavelengths for the irradiation of the skin surface, which ensure a local increase in the number of O_2 molecules at different depths in the dermis that is at least ten times greater than that obtained at other λ from the examined spectral range of 300–650 nm, for which experimental data on the photodissociation quantum yield are available. With increasing z, optimal wavelengths are shifted toward the red range of the spectrum from approximately 418 to 600 nm because of a change in the transmission coefficient of the biotissue. We have determined the boundaries of depths z in the dermis at which the mechanism of oxyhemoglobin photodissociation is initiated more efficiently by radiation at different λ. We have suggested four optimal wavelengths: 418, 575, 585, and 600 nm. It has been found that the positions of these boundaries are stable with respect to changes in the structural and biophysical parameters of the tissue, which were varied in the ranges typical for human skin. For generation of oxygen in the entire bulk of the dermis, the wavelength in the range around 575 nm is the most efficient. In this case, the number of O_2 molecules that were formed as a result of photodissociation of oxyhemoglobin can be increased by a factor of 2.5 or greater compared to that obtained with the use of other λ. The obtained results may be useful for researchers in the area of biomedical optics, as well as for medical practitioners dealing with different aspects of phototherapy, including laser therapy.

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REFERENCES

1. Q. H. Gibson and S. Ainsworth, Nature **180** (4599), 1416 (1957).
2. B. M. Dzhagarov, P. N. Dyl'ko, and G. P. Gurinovich, Dokl. Akad. Nauk SSSR **275** (3), 765 (1984).
3. B. M. Dzhagarov, V. S. Chirvonyi, and G. P. Gurinovich, in *Laser Picosecond Spectroscopy and Photochemistry of Biomolecules*, Ed. by V. S. Letokhov (Nauka, Moscow, 1987) [in Russian].
4. B. M. Dzhagarov, V. A. Galievskii, N. N. Kruk, and M. D. Yakutovich, Dokl. Akad. Nauk **366** (1), 121 (1984).
5. S. V. Lepeshkevich, N. V. Konovalova, and B. M. Dzhagarov, Biokhimiya **68** (5), 676 (2003).
6. S. V. Lepeshkevich, J. Karpiuk, I. V. Sazanovich, and B. M. Dzhagarov, Biochemistry **43** (6), 1675 (2004).
7. V. I. Bukatyi, E. V. Semdyankina, and P. I. Nesteryuk, Izv. AltGU, No. 1, 111 (2009).
8. B. M. Dzhagarov, E. A. Zhavrid, Yu. P. Istomin, and V. N. Chalov, Zh. Prikl. Spektrosk. **68** (2), 151 (2001).
9. M. M. Asimov, R. M. Asimov, A. N. Rubinov, et al., Zh. Prikl. Spektrosk. **73** (1), 90 (2006).
10. M. M. Asimov, A. N. Korolevich, and E. E. Konstantinova, Zh. Prikl. Spektrosk. **74** (1), 120 (2007).
11. G. A. Zalessskaya, N. V. Akulich, A. V. Marochkov, et al., Zh. Prikl. Spektrosk. **77** (3), 451 (2010).
12. G. A. Zalessskaya and V. S. Ulashchik, Zh. Prikl. Spektrosk. **76** (1), 51 (2009).
13. M. M. Asimov, R. M. Asimov, and A. N. Rubinov, Zh. Prikl. Spektrosk. **72** (3), 422 (2005).
14. M. M. Asimov, R. M. Asimov, A. N. Rubinov, et al., Preprint (In-t Fiziki Belarus, Minsk, 2008).
15. V. V. Barun and A. P. Ivanov, Opt. Spektrosk. **100** (1), 149 (2006).
16. V. V. Barun, A. P. Ivanov, A. V. Volotovskaya, and V. S. Ulashchik, Zh. Prikl. Spektrosk. **74** (3), 387 (2007).
17. V. V. Barun and A. P. Ivanov, Kvantovaya Elektron. **40** (4), 371 (2010).
18. V. V. Barun and A. P. Ivanov, Opt. Spektrosk. **106** (1), 89 (2009).
19. V. V. Barun and A. P. Ivanov, Zh. Prikl. Spektrosk. **77** (1), 82 (2010).
20. V. V. Barun and A. P. Ivanov, Zh. Prikl. Spektrosk. **78** (4), 610 (2011).
21. S. A. Prahl, http://omlc.ogi.edu/spectra/hemoglobin/index.html.
22. S. L. Jacques, http://omlc.ogi.edu/news/jan98/skinoptics.html.
23. W.-F. Cheong, S. A. Prahl, and A. J. Welch, IEEE J. Quantum Electron. **26** (12), 2166 (1990).
24. V. V. Tuchin, *Lasers and Fiber Optics in Biomedical Investigations* (Fizmatlit, Moscow, 2010) [in Russian].
25. A. N. Bashkanov, E. A. Genina, and V. V. Tuchin, J. Innov. Opt. Health Sci. **4** (1), 9 (2011).
26. V. V. Barun and A. P. Ivanov, Biofizika **49** (6), 1125 (2004).
27. I. V. Meglinskii and S. D. Matcher, Opt. Spektrosk. **91** (4), 692 (2001).
28. M. J. C. Van Gemert, S. L. Jacques, H. J. C. M. Sterenborg, and W. M. Star, IEEE Trans. Biomed. Engin. **36** (12), 1146 (1989).
29. V. V. Barun, A. P. Ivanov, V. V. Tuchin, et al., Patent Appl. No. 131602 (2011).
30. A. P. Ivanov, *Optics of Scattering Media* (Nauka i Tekhnika, Minsk, 1969) [in Russian].
31. V. V. Barun, A. P. Ivanov, V. V. Tuchin, et al., Patent Appl. No. 131640 (2011).

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