The Impact of Myoglobin on the Efficiency of the Therapeutic Effect of Laser Radiation

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The results of numerical simulation of the interaction of laser optical radiation with myoglobin and oxymyoglobin in muscle tissue are presented. It is shown that the photodissociation of MbO_2 can adjust the concentration of oxygen in muscle tissue, directly in the irradiation zone. The criteria of the effectiveness of oxygenation combined effect on the biological tissue with laser radiation at two wavelengths are considered.

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1. Introduction

Study of the effect of light on the blood oxyhemoglobin (HbO_2) in blood vessels and capillaries is the aim of special interest in modern photomedicine and photobiology [1–4]. At present the efficiency of therapeutic effect is controlled with the help of an empirical unit based on average power density of laser radiation output. An experimental study on the therapeutic effect of He–Ne and argon laser radiation in open skin wound healing was carried out [5].

Due to the significant increase in collagen synthesis the optimal therapeutic effect was reached. Similar experimental study [6] with He–Ne laser radiation demonstrated the complete therapeutic healing of wound, but there are many papers that show big differences between obtained experimental results where therapeutic effect has been reached. The mechanism of the laser-tissue interaction is dependent on laser energy output. The effect of high-energy lasers is based on photothermal processes such as selective photothermolysis.

In Refs. [7, 8] we proposed the conception of the role of laser-induced photodissociation of blood HbO_2 in the biostimulation mechanism and the therapeutic effect of laser radiation. This approach is based on the study of laser radiation interaction with biological tissue on the molecular level with regard to the absorption of laser light by blood hemoglobin (Hb) and its derivatives (HbO_2 and HbCO). This optical technology of increasing local tissue oxygen (O_2) concentration due to the additional extraction of O_2 from blood HbO_2 is developed. It is shown that on the molecular level a key criterion in the mechanism of the therapeutic effect of laser radiation is based on restoring the O_2 concentration to the level required for normal cell metabolism. Laser-induced photodissociation of blood HbO_2 provides achievements of this criterion, enabling the control of local oxygen concentration in the irradiated region [9, 10].

In this paper the results of numerical simulation and analysis of complex effects of laser radiation on blood HbO_2 and muscle tissue oxymyoglobin MbO_2 are presented. The effective way of increasing tissue oxygenation efficiency depending on the rates of photodissociation of blood HbO_2 and muscle tissue MbO_2 are discussed.

2. Method of calculation

As shown in [10] photodissociation of blood HbO_2 *in vivo* provides the regulation of local O_2 concentration and, consequently, the degree of tissue oxygenation. The efficiency of this process depends on the wavelength and the output power of laser radiation, blood vessels density in the irradiation area, optical properties of the skin, and the depth of the blood vessels in tissue. To perform numerical calculation of laser radiation influence on the process of gas exchanges we consider a three-layer optical model of tissue, which consists of the corneal layer with the thickness 10–200 μm, epidermis (40–150 μm) and dermis (1.0–4.0 mm). This model allows to consider the process of laser radiation interaction with the major tissue chromophores and to calculate the real absorption (action spectra) of various forms of blood Hb *in vivo* in the blood vessels of skin taking into account the optical properties of the epidermis, which contains a chromophore melanin. Melanin has a broad absorption spectrum extending from the UV to near-IR spectral range.

In order to calculate the contribution of the muscle MbO_2 to tissue oxygenation there was developed an optical model of skin by adding two additional layers: subcutaneous fat and muscle layers. This model allows one to investigate the influence of laser radiation on the full cycle of gas exchange, which is well-known as a scheme of

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aerobic cell metabolism. According to this scheme, O_2 is transported from the lungs to the cells by the blood Hb. In the arterial blood Hb is predominantly presented in the form of HbO_2, and the venous blood contains both forms of hemoglobin. Muscle tissue contains Mb — a protein that is similar in structure and function to the accumulator and HbO_2. Skeletal and cardiac muscles are supplying molecular oxygen from MbO_2.

Until now, no studies have been carried out to determine the effect of photodissociation of muscle MbO_2 on tissue oxygenation taking with regard to the diffusion rate of O_2. Practical interest is connected with determination of possible combinations of the oxygen diffusion rate into muscle tissue and the therapeutic efficacy of the combined effects of laser irradiation. In this paper we present a modification of three-layer optical model of skin by including subcutaneous fatty layer and muscle tissue. The optical model tissue is shown in Fig. 1.

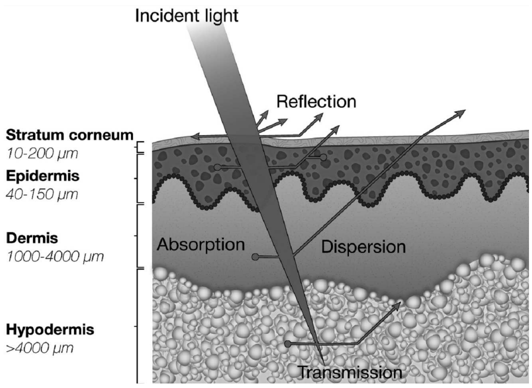

Fig. 1. Optical model of skin.

To perform numerical simulation, one should have *in vivo* data on the spectral characteristics of biological tissue, in particular, reliably measured absorption spectra of key chromophores, such as melanin, Hb, HbO_2, Mb, MbO_2, water and lipids.

In the literature a reliable information concerning spectral characteristic of lipid is very limited [11–14]. For the calculations we used the absorption spectrum of lipid — subcutaneous fat presented in [12]. Using this data we can calculate various rates of flow ratio of oxygen that releases from blood oxyhemoglobin due to laser-induced photodissociation of blood HbO_2 and muscle MbO_2.

The process of laser-induced tissue oxygenation involves the following steps: extraction of molecular oxygen from blood HbO_2 and increase in its concentration in blood plasma, the diffusion of oxygen into the skin tissue and muscle. The diffusion of O_2 depends on tissue individual density. Calculation of oxygen diffusion rate from blood plasma to biological tissue, on the basis of the model, is illustrated in Fig. 2.

In this model, we consider that tissue has a homogeneous structure with the same density throughout the whole volume and the blood vessels (arteries and veins)

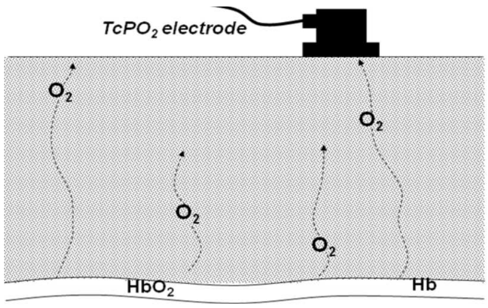

Fig. 2. Model of oxygen diffusion in tissue.

located deep. Oxygen is released into the plasma of arterial blood, diffuses through the skin tissue to the Clark electrode.

Experimental data obtained earlier in [15, 16] demonstrate that in all these cases we obtain approximately the same increase (about 4.3 times) in the rate of oxygen release from blood HbO_2 under the laser irradiation. In medical practice using laser therapy the phenomenon of laser-induced photodissociation of HbO_2 and changes in local concentration of oxygen at irradiation zone must be taken into account [17–21].

3. Results and discussions

Figure 3 shows a typical absorption spectrum of blood HbO_2 in the visible and infrared spectral range (A), and its action spectrum calculated by the Kubelka–Munk model [22]. As it can be seen in Fig. 3B, the blood HbO_2 *in vivo* effectively absorbs laser radiation in a relatively narrow spectral range. In the visible region the maximum of effective absorption band is at the wavelength $\lambda = 585$ nm, and there is a wide absorption band of blood HbO_2 in IR spectral range.

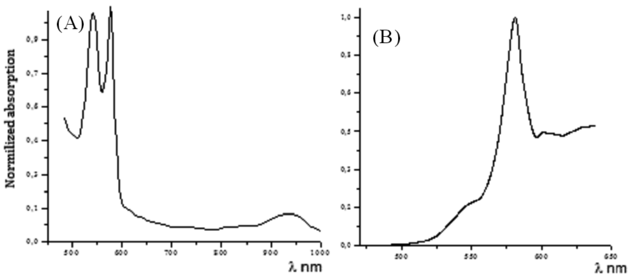

Fig. 3. The absorption spectrum of *in vitro* (A), and the action spectrum (B) of oxyhemoglobin in cutaneous blood vessels located at a depth of 1 mm in the skin tissue.

As it is shown [23–27] in irradiating area we observe laser-induced photodissociation of blood HbO_2. It means that we can optically, by light, extract additional amount of molecular oxygen. This phenomenon gives a novel technology in regulation of oxygen local concentration in tissue.

Thus, total concentration of tissue oxygen will be determined by the amount of oxygen delivered by blood microcirculation and extracted from the blood HbO_2

$$\sum[O_2] = [O_2] + [O_2{}^{h\nu}].$$

Therefore, the effectiveness of laser therapy may have a significant impact of MbO_2 photodissociation in muscle tissue. For investigation of this problem we carried out a numerical simulation of the interaction of laser radiation with MbO_2. In the same manner as in the one, described previously, calculating the action spectrum of blood HbO_2 we calculated the action spectra of Mb and MbO_2 at different depths in the muscle tissue (Fig. 4).

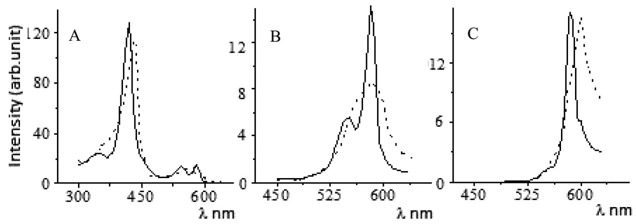

Fig. 4. The absorption spectrum of Mb (solid line) and MbO_2 (dotted line) *in vitro* (A) and its action spectra at a depth of 1 mm (B) and 2 mm (C).

As it can be seen in Fig. 4, the nature of the Mb and MbO_2 absorption spectra transformation is close to the spectra of the Hb and HbO_2. The calculated action spectrum allows one to determine the optimum wavelengths of the laser radiation for an effective photodissociation of MbO_2 and changing the local concentration of O_2 in muscle tissue. The action spectra for blood HbO_2 and muscle MbO_2 show that transcutaneous irradiation by laser light skin on blood vessels and muscle tissues demonstrates that there is a concurrent extraction of molecular oxygen.

Photodissociation of blood HbO_2 leads to release of oxygen into the blood plasma and its diffusion into the surrounding tissues. However, photodissociation of muscular MbO_2 causes the release of oxygen directly into muscle tissue. In this case, the rate of oxygen flow from the blood plasma into the muscle becomes significant in comparison with the rate of MbO_2 photodissociation. In laser therapy photodissociation of MbO_2 in the condition of low oxygen supply can cause deep hypoxia in the muscles and may cause negative result. This factor should be taken into account when the combined effects of laser therapy on two or more wavelengths using infrared radiation are considered.

4. Conclusions

Numerical simulations of the effect of laser radiation on gas exchange processes in biological tissues are presented.

It is shown that the photodissociation of oxyhemoglobin in the blood vessels and myoglobin in muscle tissue can later extract molecular oxygen, which allows it to regulate the local concentration of tissue in the immediate area of radiation exposure.

It is predicted that photodissociation of oxymyoglobin in the condition of low oxygen supply may cause deep hypoxia in muscles and have a negative result in application of the multi-wavelengths laser therapy. This factor should be taken into account when the combined effects of laser therapy on two or more wavelengths including IR radiation are considered.

Development of this optical method promises the improvement in the efficiency of laser therapy.

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