

# Opto-Acoustic Method of Tissue Oxygenation and Its Biomedical Application

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**Abstract.** Novel opto-acoustic method of tissue oxygenation and restoring normal cell metabolism is proposed. The results of in vivo investigation the phenomenon of laser-induced photodissociation of blood oxyhemoglobin and its biomedical applications are presented. Photodissociation of oxyhemoglobin, the main biological function of which is oxygen transportation gives a unique possibility of additional oxygen extraction for restoring normal cell metabolism. Optical method of determination the therapeutic “dose” based on the response of changes in tissue oxygen concentration in dependence on wavelength and intensity of laser radiation has been developed. It is shown that in order to make the methods of phototherapy as well as laser therapy really efficient one has to control the oxygen concentration in tissue keeping it at the necessary level.

## 1. Introduction

Therapeutic effect of low intensity laser radiation now is a well-established fact and in spite of that the mechanism of this phenomenon still remains topic of discussion this phenomenon is widely used in clinical practice. Considering the biological effect of “Laser-Tissue” interaction the phenomenon of in vivo blood oxyhemoglobin ( $\text{HbO}_2$ ) photodissociation should be taking into account.

The role of blood  $\text{HbO}_2$  photodissociation in the biological response and the mechanism of therapeutic effect of low intensity laser radiation were proposed in [1-3]. It was shown that the phenomenon of laser-induced photodissociation of blood  $\text{HbO}_2$  gives unique possibility controlling local concentration of molecular oxygen in tissue.

Molecular oxygen plays a key role in aerobic cell metabolism and energy production in biological tissue. Controlling this mechanism provides unique possibility of stimulation biological response on laser radiation and reaching desired therapeutic effect.

The problem of controlling the local tissue oxygen concentration and keeping it at the necessary for normal cell metabolism level is an actual problem in modern medicine [4].

The following criteria of tissue oxygen tension ( $\text{TcPO}_2$ ) in clinical practice now are accepted:

- $\text{TcPO}_2 \sim 40\text{--}100\text{mmHg}$  – normal cell metabolism;
- $20 > \text{TcPO}_2 < 40\text{mmHg}$  – tissue hypoxia;
- $\text{TcPO}_2 < 20\text{mmHg}$  – deep hypoxia and tissue necroses.

Different methods for elimination of tissue hypoxia in clinical practice are used. Hyperventilation of lung with pure oxygen at normal atmospheric pressure is the oldest method of oxygenation, but its low efficiency limits wide application.

More effective method is hyperbaric oxygenation (HBO) that is based on blood saturation with oxygen under high pressure. The method of HBO may cause oxygen toxemia that limits it routine application in clinical practice [5].

In this paper a new optical technology in local tissue oxygenation is presented. The results of the effect of laser radiation on blood  $\text{HbO}_2$  and its photodissociation are discussed.

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New method of determination of therapeutic "dose" during laser irradiation that based on the use of changes in oxygen concentration as a feedback signal is developed. It is shown that photodissociation of blood HbO<sub>2</sub> provides a unique possibility in additional oxygen extraction and restoring normal cell metabolism.

## 2. Laser-induced tissue oxygenation

As it well known amount of oxygen delivered by microcirculation for cell metabolism is the function of:

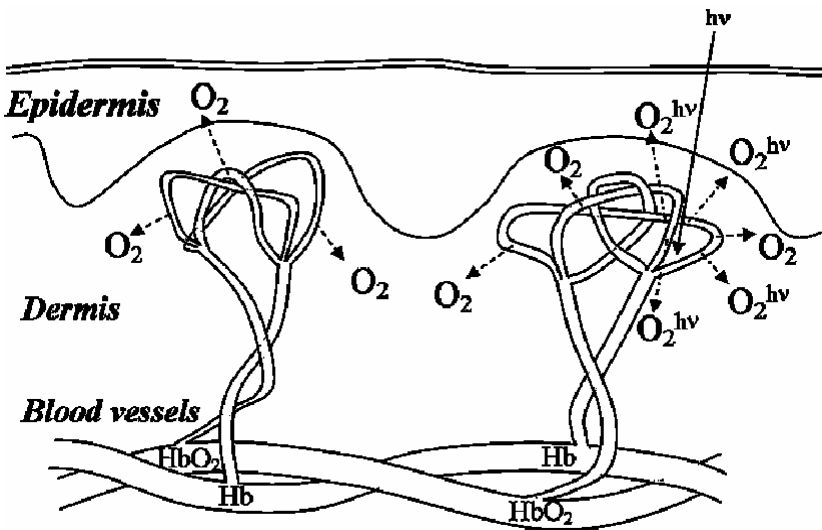
$$\Sigma O_2(TcPO_2) = f(F(HbO_2) * [O_2]) \quad (1)$$

Here HbO<sub>2</sub> is the value of arterial blood oxyhemoglobin and [O<sub>2</sub>] – is the concentration of oxygen in plasma. Deterioration of the blood microcirculation required extra oxygen supply to provide the demands of normal cell metabolism. This could be reached by in vivo laser-induced photodissociation of HbO<sub>2</sub> directly at the zone were it is necessary to increase the local concentration of free molecular oxygen.

As a result we obtain total concentration of oxygen delivering in conventional way and due to laser-induced photodissociation of blood HbO<sub>2</sub>:

$$\Sigma [O_2] = [O_2] + [O_2^{hv}] \quad (2)$$

This process clearly demonstrates that in vivo photodissociation of blood HbO<sub>2</sub> may be used for extraction of additional amount of molecular oxygen in tissue [6-8]. This process is illustrated in Fig. 1.

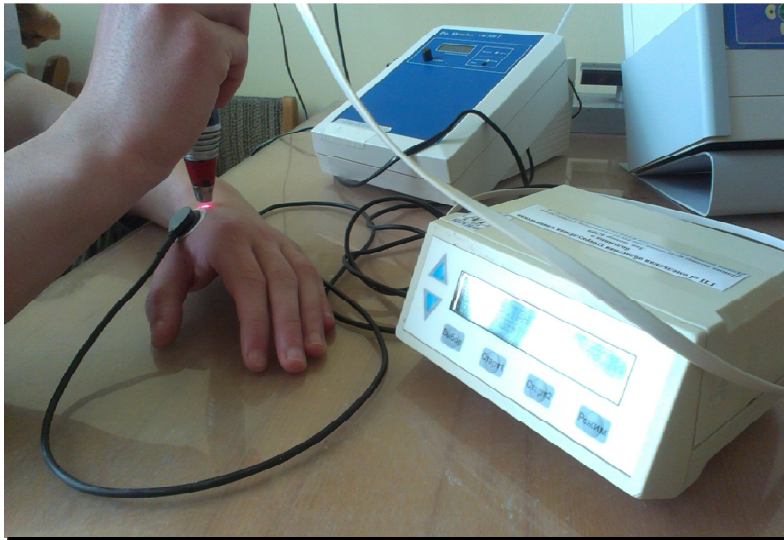


**Figure 1.** Optical method of additional oxygen extraction from HbO<sub>2</sub> and laser-induced tissue oxygenation.

Additional oxygen extraction allows develop novel optical technology in elimination of tissue hypoxia and restoring normal cell metabolism.

## 3. Experimental

Experimental investigation the phenomenon of laser-induced tissue oxygenation has been carried out using transcutaneous oxygen monitor (TCOM) – "Radiometer" TCM-4 (Fig. 2). Direct in vivo measurements of tissue oxygen tension TcPO<sub>2</sub> under irradiation by He-Ne laser at the power of 1mW has been taken. For this purpose usually uses Clark-type polarographic sensor ("TcPO<sub>2</sub> electrode", see Fig. 2) has been used.



**Figure 2.** Experimental setup for measuring local tissue oxygen concentration directly at the zone of laser irradiation.

First a background tissue oxygen tension was measured. Then diode laser radiation at the power of 15mW was applied. The kinetics of tissue oxygenation in dependence of the time irradiation was experimentally investigated. For enhancing the phenomenon of laser induced tissue oxygenation acoustic ultrasound effect on blood microcirculation was used.

Obtained experimental results demonstrate that the process of oxygen extraction take place immediately at laser light absorption and remains constant during the irradiation.

#### **4. Results and discussion**

The results obtained were normalized to the initial oxygen tension value (Fig. 3). As it seen from Fig. 3 during laser irradiation the value of tissue oxygenation increases and exceeds its initial level by 1.6 times (curve 1) after ten minutes of illumination. In case of induced ischemia additional extraction of oxygen also is observed. This result clearly demonstrates that laser-induced tissue oxygenation could be applied in clinical practice for restoration of normal cell metabolism in tissue with damaged microcirculation. It should be noted that application of ultrasound waves significantly (about 25-30%) increases the value of tissue oxygen concentration. So, combination of optic with acoustic methods allows to increase the local tissue oxygen concentration.

The results of calculations demonstrate that in order to reach the experimentally observed rise of  $TcPO_2$  by  $\sim 1.6$  times on the tissue surface, the calculation indicating the increase of oxygen release rate from arterial  $HbO_2$  into blood plasma should increase by approximately 4.3 times.

Photodissociation of  $HbO_2$  induced by laser radiation and release rate of free molecular oxygen into blood plasma has been measured experimentally in vivo using highly sensitive pulse oximeter.

It is exciting that the value of  $PO_2$  in blood plasma reached by laser-induced photodissociation of  $HbO_2$  is comparable to that one typically reached by the method of HBO.

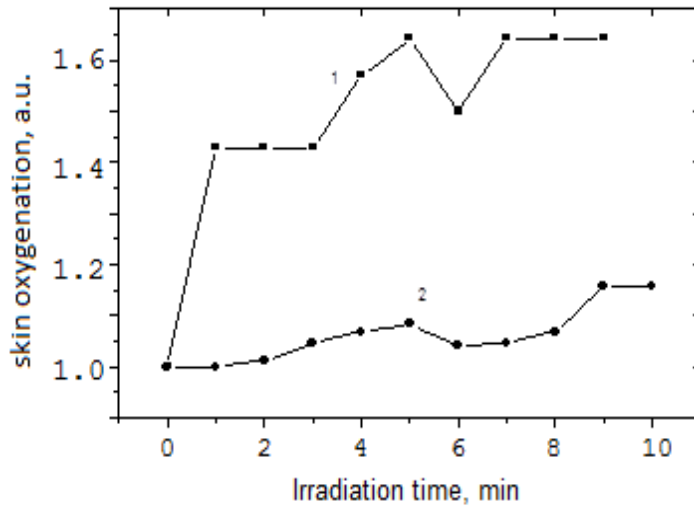
The distribution of  $TcPO_2$  in the volume at the irradiation zone depends on the time of exposure and the tissue properties.

The comparison of calculated results with experimental data demonstrates that kinetics of  $TcPO_2$  considered in relation to time of elimination by laser radiation gives possibility to determine  $O_2$  diffusion coefficient in tissue.

This means that one could calculate and determine how to reach desirable level of  $TcPO_2$  in zones with disturbed blood microcirculation such as solid tumour, burn or wounds. So it's possible to determine optimal parameters of irradiation taking into account the volume that has to be oxygenated and the time of elimination.

Thus suggested novel method can eliminate the deficit of oxygen until the new vascular net in

tissue is restored. This result could be applied for those pathologies where elimination of tissue hypoxia is critical.



**Figure 3.** The kinetics of laser-induced tissue oxygenation during laser irradiation in norm blood microcirculation – 1, and in artificially induced ischemia – 2.

Extra oxygen increases the rate of collagen deposition, epithelization and improve healing of split thickness grafts. Increased subcutaneous TcPO<sub>2</sub> has also improved bacterial defenses.

Thus a unique possibility in selective and local increase of the concentration of free molecular oxygen in tissue which enhances metabolism of cells has been developed.

Laser-induced enrichment the tissue oxygenation stimulates cell metabolism and allows developing new effective methods of therapy as well as laser therapy of pathologies where elimination of local tissue hypoxia is critical.

Laser-induced photodissociation of HbO<sub>2</sub> may serve as a unique method in laser therapy for optical increase of free molecular oxygen local concentration in tissue which significantly enhances cell metabolism.

It is valuable that even in the case of ischemia it is possible to extract additional oxygen from arterial blood and restore normal cell metabolism. Thus laser-induced tissue oxygenation allows using optical method eliminate the deficit of oxygen until the new vascular net in tissue is restored.

The obtained results provide experimental argumentation for considering the primary mechanism of biostimulation and therapeutic effect of low energy laser radiation that could be based on increasing tissue local oxygen concentration directly in the zone of irradiation.

This phenomenon allows developing an objective method of controlling the efficiency of treatment by laser phototherapy. Now in clinical application the parameters of laser radiation can be tuned to optimal wavelength, power and exposition time taking into account optical characteristics of the patient skin.

The obtained results also show the way of increasing the efficiency of biostimulation and the therapeutic effect of low energy laser radiation based on its combination with the method of oxygen hyperventilation therapy.

An important conclusion can also be drawn from the obtained results. In interpretation of the biostimulation and therapeutic effects of laser radiation the phenomenon of induced photodissociation of blood HbO<sub>2</sub> should be taken into account. Control the value of tissue oxygenation becomes important in reaching maximal therapeutic effect.

## 5. Conclusion

New opto-acoustic method of local tissue oxygenation has been developed. The value of tissue oxygen concentration increases significantly during the laser irradiation in combination with the effect of

ultrasound wave on improving blood microcirculation.

It is shown that establishing the therapeutic “dose” of laser radiation could be based on controlling the local concentration of free oxygen in tissue.

To make the phototherapy as well as laser therapy methods really efficient one has to control the local oxygen concentration in tissue keeping it at the necessary level. This goal could be reached by the use of laser-induced oxyhemoglobin photodissociation in combination with the ultrasound methods of blood microcirculation improvement.

The efficiency of developing method is comparable to the method of HBO gaining advantages in local action.

Novel method of determination of optical “dose” based on using the changes in tissue oxygen concentration as a feedback signal for the optimization of low intensity laser radiation therapeutic effect has been developed.

Photodissociation of oxyhemoglobin, the main biological function of which is molecular oxygen transport gives a unique possibility of additional oxygen supply and allows develop laser-optical method of tissue hypoxia elimination that restores normal cell metabolism.

### References

- [1] Takas S and Stojanovich S 1998 Diagnostic and biostimulating lasers *Med. Pregl.* **51**
- [2] Baxter G 1994 *Therapeutic lasers: Theory and Practice* (Edinburgh New-York)
- [3] Tuner J and Hode L 2002 *Laser Therapy: Clinical practice and scientific background* (Prima Books AB)
- [4] Asimov M et al. 1998 Action spectra of laser radiation on hemoglobin of skin blood vessels *Journal of Applied Spectroscopy* **65**
- [5] Asimov M et al. 2007 Investigation of the kinetics of tissue oxygenation under the effect of low intensity laser radiation *J of Appl. Spectr.* **74**
- [6] McGrath, et al. 2003 Compositions and method of tissue superoxygenation (U.S. Pat. No. 6,649,145)
- [7] Asimov M et al. 1998 Investigation of the efficiency of laser action on hemoglobin and oxyhemoglobin in the skin blood vessels *Proc. SPIE.* **3254**
- [8] Abergel R et al. 1987 Biostimulation of wound healing by lasers: Experimental approaches in animal models and in fibroblast cultures *J. Dermatol. Surg. Oncol.* **3**