The Regulation of Angiogenesis in Tumor Nodules by Oxygen with Laser Radiation

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Hypoxia in solid tumor is the major problem [1] that limits the efficiency of therapeutic methods, in particular, the method of photodynamic therapy (PDT). Hypoxia in cancer tissues occurs due to the fast growth of cancer cells and disordered angiogenesis. That why solid tumor is located in the regions with reduced oxygen concentration. Large hypoxic area within human solid tumor has been detected in measurements of oxygen tension directly inserting the oxygen electrode in tumor tissue.

In the method of PDT mechanism of tumor destruction is based on photochemically generation of singlet oxygen ($^1O_2$) and its toxicity for tissue cells. It makes oxygen a key component in the method of PDT. Generation of $^1O_2$ involves the following process:

$$[^1S_0] + h\nu \longrightarrow [^1S_1] + [^3S_1]$$
$$[^3S_1] + [^3O_2] \longrightarrow [^1S_0] + [^1O_2],$$

where $[^1S_0]$ - is the concentration of photosensitizer in solid tumor; $[^3O_2]$ and $[^1O_2]$ - are concentrations of molecular oxygen and its singlet form in tumor cell. The first stage of photochemical reactions involves excitation of the molecule of sensitizer by laser irradiation in its triplet state $^3S_1$. Second stage includes generation of singlet oxygen - $^1O_2$ due to interaction of triplet molecules of sensitizer $^3S_1$ with the oxygen molecules in ground state $^3O_2$. It makes oxygen a key component in the method of PDT. Rapid decrease of oxygen concentration in cancer tissue during the generation of $^1O_2$ in PDT is the main factor that induces a local tissue hypoxia. Improving the oxygenation of solid tumor masses to eliminate tissue hypoxia is remained as actual problem in modern Oncology.

In present two main methods of oxygenation are used. The oldest method is based on ventilation of lung with pure oxygen at normal pressure. This method is not selective in terms of local tissue oxygenation. An alternative the method of hyperbaric oxygenation (HBO) has been developed. The method of HBO based on inhalation of 100% oxygen greater than one atmosphere. This method is not selective andmay cause oxygen toxemia that limit its application.

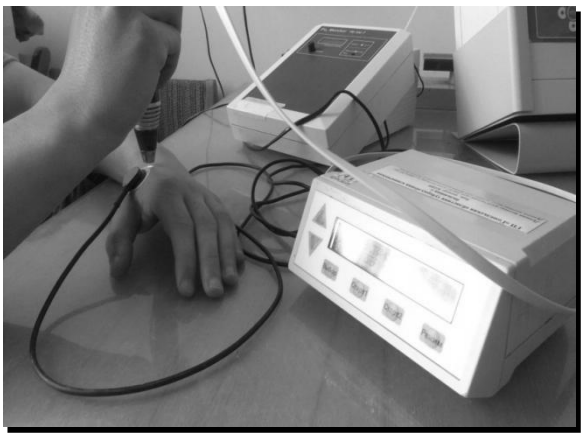
One of important abnormal characteristic found in most solid tumors is its location in the regions with reduced oxygen concentration. The role of hypoxia in developing of solid cancer remains unclear. The ability to vary local oxygen concentration by laser induced photodissociation of oxyhemoglobin opens unique possibility to investigate this problem.

In this paper the evaluation of our basic conception [2] and experimental study of laser-induced photodissociation of oxyhemoglobin for elimination of hypoxia in censer tissue is proposed.

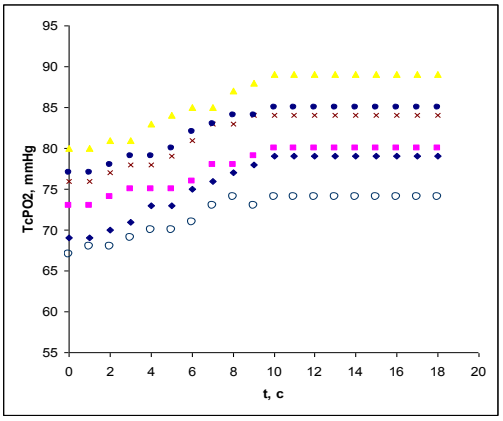
Laser-induced enrichment of tissue oxygenation allows use an effective optical method for therapy of pathologies where elimination of local tissue hypoxia is critical.

Basic principle of measuring the oxygen tension PO_2 in arterial blood is direct method of registration of gas that dissolved in blood plasma. For this usually is used Clark-type polarographic sensor ("TcPO_2 electrode"). When the sensor is exposed to oxygen, it creates an electrochemical reaction **(**$O_2 + 2H_2O + 4e^-$ R4OH^-**)** that causes current to flow through the cathode. The amount of current flowing in electrochemical cell is proportional to the value of oxygen tension PO_2 in blood

plasma or $TcPO_2$ that indicates oxygen tension in tissue. Transcutaneous oxygen monitor (TCOM) - "Radiometer" TCM-2 - is used for measuring the value of tissue oxygenation tension.



Experimental procedure



Kinetics of tissue oxygenation

In direct in vivo measurements of the tissue oxygen tension $TcPO_2$ electrode was placed on hand. First, initial oxygen tension was measured. Then He-Ne laser radiation at the power of 1,5 mW was applied. Kinetic of oxygen tension in tissue was investigated. Obtained results were normalized to initial oxygen tension value. Six set of measurement were carried out with the six voluntaries.

The value of oxygen tension during laser irradiation increases with the different rate and reaches saturation level approximately after 10 minutes of exposure. The value of $TcPO_2$ is increases about 1.6 times compare the initial one.

It should be noted that in order to reach experimentally observed the rise of $TcPO_2$ by 1, 6 times at the surface of tissue, the calculation indicates the increase of oxygen release rate from arterial HbO_2 into blood plasma should increase about 4,3 times.

It is exiting that the value of PO_2 in blood plasma reached by laser-induced photodissociation of HbO_2 is comparable to that one typically reaches by the method of HBO. The distribution of $TcPO_2$ in the volume at the irradiation zone is depended on the time of exposure and the properties of tissue.

Monitoring the kinetic of $TcPO_2$ gives unique possibility to control the process of laser-induced tissue oxygenation. Thus, a new method of optically elimination tissue hypoxia could be developed. This is an important in increasing the efficiency of solid tumor therapy by the method of PDT.

The obtained results give scientific background to develop new effective method of two colors Photodynamic Therapy of solid cancer.

References:

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