Radioprotective Action of Low-Intensity Light into the Red Absorption Band of Endogenous Molecular Oxygen

A V Ivanov¹, A A Mashalov¹ and S D Zakharov²,³

¹ Blokhin Russian Cancer Research Center, 115478, Moscow, Russia
² Division of Quantum Radiophysics, Lebedev Physical Institute, Russian Academy of Sciences, 119991, Moscow, Russia
³ National Research Nuclear University MEPhI, 115409, Moscow, Russia

E-mail: ivavi@yandex.ru, imhaemo_6june@ronc.ru, stzakhar@sci.lebedev.ru

Abstract. Application of ionizing radiation in oncology (radiation therapy) is a widespread way to eliminate malignant tumors. Normal tissues are inevitable included in any radiation field, and their reliable protection is actual till now. All attempts to solve the problem are based on search of effective radioprotectors, i.e. chemical compounds of various classes, which should be entered into the patient. To date about 50,000 compounds with some radioprotection properties had been tested, but the most effective of them have been simultaneously the most toxic. Here the preliminary results of researches devoted to development of an optical technique on basis of the light-oxygen effect for the protection of women with breast cancer from side effects of the radiation therapy are presented. A low intensity emission of the semiconductor laser in a red spectral interval was used to excite a very small quantity of endogenous molecular oxygen in $O_2(\Delta g)$ state. It is shown, that application of the method at occurrence of earliest signs of radiation injury allows notably reducing dangerous breaks in radiation therapy course.

1. Introduction

Basic tendency in oncology is reduction of radiotherapy course duration by means of increasing the ionizing radiation intensity. However side effects, i.e. radiation induced injuries of normal tissues, forces sometimes to interrupt the standard course to give to patient a time for their restoration. Such interrupts are extremely undesirable as they allow to some malignant cells is adapted and increase their radioresistance [1].

This global problem is not completely solved till now. A well-known strategy consists in search of antioxidants with low toxicity which would be capable to neutralize effectively radicals induced by the ionizing radiation [2]. Other ways, such as hyperbaric oxygenation, hyperthermia, hyperglycemia, have been offered also, however those have not found wide clinical application.

Here we report on possibility to increase resistance of women with breast cancer to post-radiation damages by help of a spectral-selective light. A fundamental basis of the technique is the light-oxygen effect (LOE), universal phenomenon found out at all levels of the biological organization - from pure water and protein solution up to human [3-5].

The primary photophysical act of the light-oxygen activation (LOT) is direct, i.e. without any photosensitizers, excitation of blood-dissolved oxygen molecules by photons into a metastabil singlet energetic state [6]. At small doses of the singlet oxygen an activation of patient’s aerobic metabolism
occurs, whereas large doses of this agent, on the contrary, have caused cell damages. Wavelength of light source, its power and exposition dose are interdependent and must be selected carefully as molecular oxygen absorbs light only in narrow spectral intervals including a “red” band. Semiconductors lasers are convenient instruments for such purposes [7].

2. Materials and Methods
Light induced radioprotection effect was studied for women with breast cancer. Two group of 26 women (non-randomized research) and 37 women (randomized research) with a control (without light activation) of 30 women only for second group were formed. All patients have been subjected breast therapy with total dose up to 62 Gy after surgical intervention and/or 2-4 courses of polychemotherapy. Patients received also the standard pharmacological preparations warning skin’s radiation injuries.

The 635 nm wavelength semiconductor laser was used for the LOT. The mammary gland and axillary’s area were subjected light irradiation. A LOT course has consisted of 12-15 daily procedures 1 hour before of each radiation impact. The light power density on patient’s skin and total exposition dose were 12-15 mW/cm$^2$ and about 3 J/cm$^2$ for one procedure correspondently.

3. Results
In first group the LOT procedures have been begun with delay when total dose of 28 - 44 Gy has been supplied and most of patients had a skin’s radiation pathology of II - III degrees. Nevertheless, at 21 from 26 women a medical effect has been received. The effect was expressed in the form of reduction or disappearance of pain, itch, a hypostasis and hyperemia in an irradiated zone of skin. It has allowed avoiding undesirable breaks in treatment. The others five patients have been forced to interrupt the course on 8 - 10 days for treatment of excessive skin injuries; note that the LOT did not stop during those breaks.

In other group of 37 patients the LOT has been applied at once after occurrence of first signs of radiation injury (erythemas, radioepithelites). The LOT has proceeded up to the termination of the radiotherapy course. Results are summarized in the Table.

| Table. Light induced reduction of skin’s radiation injuries at radiotherapy of breast cancer |
|---------------------------------|---------------------|----------------------|---------------------|---------------------|---------------------|---------------------|
| Operation                        | Total number of patients | Number of patients with different grade of radiotoxicity | Breaks in treatment (from 8 to 12 days) |
|                                 |                      | O | I | II | III |                      |
| Belated light therapy            | 26                    | - | 4 | 16 | 6   | 5 (19%)              |
| Timely light therapy             | 37                    | 2 | 25| 8  | 2   | 0                    |
| Control (without light)          | 30                    | - | 12| 14 | 4   | 8 (27%)              |

4. Discussion
It has long been known that the oxygen molecules in electron excited state, named the singlet oxygen, can damage cells. In oncology, singlet oxygen is produced by means of dyes (photosensitizers) and is used in the photodynamic therapy of cancer. However, we have showed earlier that the cell response to photodynamic action depends on the singlet oxygen dose and formation rate and varies from cell stimulation up to cell destruction. Moreover, both cellular activation and cellular destruction can be realized without photosensitizers using direct photoexcitation of endogenous oxygen. Surprisingly, but from the lasers used for this purpose, large light fluxes are not required. This phenomenon is the light oxygen effect.
Here we show other surprising property of the LOE. Using it, it is possible to increase a protection of healthy cells against damaging action of an ionizing radiation, not reducing its injuring potential in relation to malignant cells. This way of increase of efficiency of radiotherapy seems to us promising. Its advantage over other methods is that it does not require entry into a patient's blood of any exogenous drugs: oxygen is abundant in tissues. Also, the technique is non-toxic.

Feature of singlet oxygen in small doses have activating effect on organism and damaging effects in large doses is apparently the manifestation of a general phenomenon called hormesis. Many medicals exhibit the hormesis effect, e.g. curare, poison in large doses and drug in low ones. The difficulty is to find a dose boundary separating opposing responses. In our context, the optimal photon dose is critically dependent on the wavelength. More details on this issue will be presented elsewhere.

5. Conclusion
Protection of normal tissues from ionizing radiation is the most serious problem in radiation oncology. The light-oxygen effect confirmed earlier at all levels of the biological organization - from pure water and protein solution up to human can be used for such purposes. The molecular oxygen dissolved in blood is a primary target for light photons whereas singlet oxygen, the product of this interaction, is an activating agent. Optimum results are reached when the light protection procedures is followed earliest signs of tissue damage induced by ionizing radiation.

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