

## OXYGEN TENSION MEASUREMENTS IN TUMOR DURING HYPERTHERMIA

Butenin A.<sup>1</sup>, Kogan B.<sup>1</sup>, Treschalina E.<sup>2</sup>, Lukyanets E.<sup>1</sup>, Vorozhtsov G.<sup>1</sup>

<sup>1</sup>FGUP GNC NIOPIK, 123995 Moscow, Russia

<sup>2</sup>Blokhin Russian Cancer Research Center of RAMS, 115478 Moscow, Russia

### Introduction

Oxygen tension measurements in tissue are required in some fields of medicine particularly in oncology. Drawback of hard invasive oxygen sensors is their affecting on vasoconstriction and thus oxygen supply. Other mode is based on spectral measurement of ratio hemoglobin/oxyhemoglobin. But this allows supervising oxygenation in blood vessels rather than in cells of tumor where oxygen tension can be tens of times less. Phosphorescent oxygen-quenching sensors [1, 2] have been rapidly developed recently, due to their high sensitivity, selectivity and stability. Lifetime-based sensors possess some intrinsic advantages over intensity-based sensors:

- minimal interference by external noise-based sources;
- unaffected by light source intensity and photodetector sensitivity drift;
- independence on dye concentrations.

Here we consider application of lifetime-based phosphorescent liquid probe for oxygen tension measurements in mice tumors during sessions of laser induced hyperthermia.

### Materials and methods

Mice BDF with intramuscular inoculated melanoma were used as experimental models. Tumors heated by radiation of Nd:YAG laser (wave length of 1064 nm, power up to 10 W). Tumor temperature measured using thermocouple mounted into gilded medical needle (diameter of 0.35 mm). Palladium *meso*-tetra-(phenyl)-tetrabenzoporphin (Vinogradov and Wilson, 1995) was used as a phosphor. Dye was dissolved in medical liquid paraffin. Maximum absorption is at 629 nm. Phosphorescence emission is maximal at about 800 nm. Solution (3-10 mm<sup>3</sup>, concentration of 1.6 10<sup>-5</sup> M) was injected into tumor as oxygen tension probe. He-Ne laser (50 mW) was used for phosphorescence excitation. Rectangular excitation pulses (pulse duration of ~15 mcs, pulses repetition frequency of 50 Hz) are formed using mechanical chopper and irradiate injected probe. Phosphorescence is collected by lens to photomultiplier tube (Hamamatsu R3896). The photomultiplier output is amplified with amplifier (Hamamatsu C1053-51) and digitized. The digitization starts at the time of excitation pulse. The data for multiple pulses are collected by summing into 16-bit buffer. The single-exponential calculation was performed by fitting the natural logarithm of phosphorescence intensity as a function of time to a straight line.

### Results

Phosphorescence decay was near to exponential unlike water-soluble phosphorescent probe. It facilitates processing of measurement results. Oxygen tension kinetics during hyperthermia sessions is presented. Heating of a tumor is accompanied at first by vasodilatation, after that by vasoconstriction. Usually exposition during 15 min at temperature 45 °C led to irreversible damage of tumor blood vessels.

### References

1. S. A. Vinogradov and D. F. Wilson, Metallotetrabensoporphyrins. New phosphorescent probes for oxygen measurements. *J. Chem. and Application to Oxygen Sensing, Anal. Chem.*, 1995, **67**, 4112-4117.
2. A. V. Butenin, B. Ya. Kogan, S. N. Dashkevich, O. L. Kaliya, E. A. Lukyanets and G. N. Vorozhtsov, Oxygen phosphorescent probe, in “Fluorescence Microscopy and Fluorescent Probes”, Vol. 3, Espero Publishing, 1999, pp. 163-166.