Development of micro-pellets holding EPR oxygen sensors

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Introduction

The evolution of the oxygen pressure in tissues is a crucial information in physiology, pathophysiology and therapy such as radiation oncology. EPR oximetry is based on the introduction of an oxygen sensor in tissues. By measuring the EPR line width which is very sensitive to the oxygen environment, it is possible to measure oxygen from the same site over long periods of time.

Objectives

The present study deals with the development of biocompatible and retrievable inserts that may be used in EPR oximetry. Here, we developed and evaluated cylindrical micro-pellets made of Teflon holding lithium phthalocyanine (LiPc) as oxygen sensors. This configuration should enable to protect the tissues from direct interactions with the sensor. Moreover, the design was chosen to allow an easy implantation in tissues, to avoid a spreading of the sensors inside the tissues, and to allow the removal of the sensor after use. Two types of applications are sought: 1) use in animal in very precise areas (such as brain studies in animals); 2) first use in clinical EPR oximetry.

Materials and Methods

Cylindrical micro-pellets were made by injection into a Teflon® AF2400 tubing (ID: 0.034") of a suspension of LiPc in a solution of Teflon® AF2400 in FC-75 solvent (3% p/v). The pellets were then dried for 24 h in an oven at 70°C. X Band EPR was used to build calibration curves and to determine the kinetics of response of the sensor (EPR line width as a function of pO2). Micro-pellets were sterilized by dry heating (120°C for 24 hours). Micro-pellets were surgically implanted in the leg muscle of rats. A L-Band EPR spectrometer was used to determine the oxygen pressure *in vivo*.

Results

Using the described procedure, it was possible to develop micro-pellets with different sizes (Figure 1). LiPc crystals were homogenously distributed in the cylinder. Optical verification of micro-implants allow to select micro-pellets without bubbles or cracks. The kinetics response of the sensor was very rapid when changing the oxygen environment of the sensor (Figure 2). *In vivo* studies in rat muscles gave pO_2 values that are consistent other values obtained with other techniques. When interrupting the blood flow, the EPR line width decreased to hypoxia values (Figure 3).

Conclusions

Micro-retrievable inserts holding EPR oxygen sensors have been developed. The new design allows the preservation of the favorable characteristics of LiPc, while allowing easy implantation inside the tissues and removal from the tissues after studies. This design could be valuable for first clinical EPR oximetry studies in patients.

Figure 1 :
Picture of micro-pellets holding LiPc

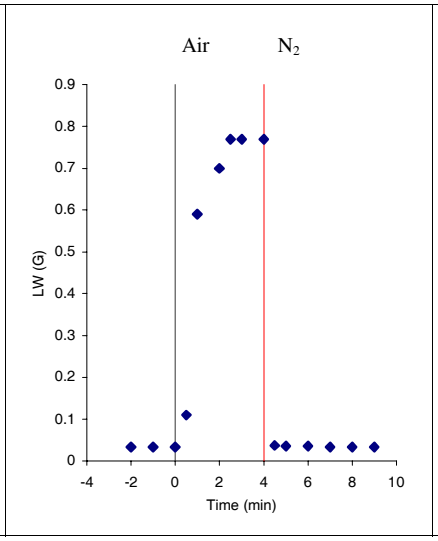

Figure 2 :
Response of the LiPc inserted in the micro-pellets to changes in oxygenation in the environment

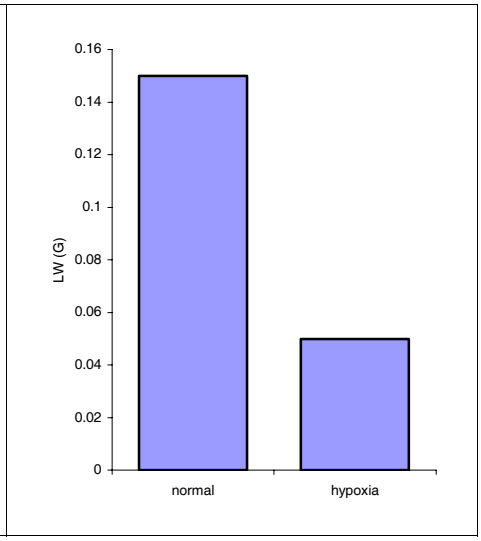

Figure 3:
Typical *In vivo* EPR measurements carried out in the leg of a rat before and after interruption of the blood flow