Development and Initial Results with the First Specifically Built Clinical EPR Spectrometer

H. M. Swartz[1], T. M. Walczak[1], P. N. Lesniewski[1], I. K. Salikhov[1], O. Y. Grinberg[1], A. Iwasaki[1], P. A. Hein[1], R. J. Comi[1], J. C. Buckey[1], E. B. Hug[1], D. A. Schauer[2]

[1]Radiology, Dartmouth Medical School, Hanover, NH, United States, [2]Radiology & Radiological Sciences, Uniformed Svcs. University of the Health Sciences, Bethesda, MD, United States

Introduction

An increasing volume of literature confirms that *in vivo* EPR provides unique and useful information from animals, such as repeated measurements of oxygen in tissues, free radicals, and direct measurements of biophysical and physiological parameters. Now these capabilities are being extended to human subjects, using an *in vivo* EPR spectrometer specifically designed for clinical applications. The initial clinical applications are for repeated measurements of oxygen in: tissues at risk in peripheral vascular disease, wounds, and tumors. The instrument also is being used for retrospective dosimetry of potential exposures to high doses of ionizing radiation as could occur from the actions of terrorists or nuclear war.

Methods

The clinical *in vivo* EPR spectrometer operates at 1200 MHz, using the spectrometer designs that have been developed for use in animals. Our approach is to use spectroscopy, because of the higher signal/noise and the sensitivity of EPR spectra to many parameters that are of potential clinical value but cannot be measured with other techniques. EPR imaging, which is being developed by other laboratories and/or the use of lower frequencies, has the potential for providing additional clinically useful information. The magnet is a permanent magnet with 80 cm diameter pole pieces and a 50 cm gap, which is sufficient to accommodate a large adult in either a horizontal or a vertical orientation. Three different types of resonators have been adapted for use in the three types of initial clinical applications: oximetry of superficial sites, oximetry of deep-seated tumors, and post-exposure dosimetry of ionizing radiation. For measurements of oxygen in tissues within 10 mm of the surface, we use India ink as the oxygen sensitive material. It is injected into the areas of interest, and the surface resonator is placed over the sites for the measurements. Several sites can be measured simultaneously, using a magnet field gradient. This approach can be used to measure oxygen in critical regions of the legs of patients with peripheral vascular disease and in superficial malignant tumors. Oxygenation in wounds is measured using oxygen-sensing material that is placed within the wound in small oxygen permeable, biocompatible tubes. For deep-seated tumors, we use an implantable resonator with lithium phthalocyanine in the small (1-3 mm) loop. The loop, covered with an oxygen permeable biocompatible coating, is placed in the tumor at the time of biopsy. The small loop is connected by a thin cable to a larger loop (about 10 mm diameter) that is placed subcutaneously, which is then noninvasively magnetically coupled to a surface resonator. For measurements after a potential exposure to life-threatening levels of ionizing radiation, an intraoral resonator that fits closely around the teeth is used.

Results and Discussion

Protocols for several of the applications have been approved by the Committee on the Protection of Human Subjects. The initial configuration of the spectrometer has been implemented, and it is being used for studies in both humans and experimental animals. Studies of oxygenation in the skin of pigs have been carried out, using India ink as the oxygen sensitive material; this is the probably the largest animal that has been studied with *in vivo* EPR. The initial measurements of tissue oxygen in human subjects have been made in the foot at several different sites chosen for their clinical relevance, using 10 – 25 μl of oxygen-sensitive India ink injected in the feet of volunteers. The sites have reliably reported tissue oxygen levels from the same sites for more than 6 months and the measurements are continuing. A rapid response of the technique to changes in oxygenation in the tissues was demonstrated by making measurements while changing the amount of oxygen in the breathing mixture and during local compression of the blood supply to the sites of the India ink. The first measurements of irradiated teeth within the human mouth also have been made successfully. The sensitivity and applicability of the method makes it the method of choice to screen potentially exposed individuals (e.g. from terrorism, accident, or war) to determine if they have received clinically significant doses of radiation. It appears that quantification is more than sufficient for clinical decision making in the dose range of 100 cGy to super lethal doses.

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