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Non-invasive determination of the irradiation dose in fingers using low-frequency EPR

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Abstract

Several reports in the literature have described the effects of radiation in workers who exposed their fingers to intense radioactive sources. The radiation injuries occurring after local exposure to a high dose (20 to 100 Gy) could lead to the need for amputation. Follow-up of victims needs to be more rational with a precise knowledge of the irradiated area that risks tissue degradation and necrosis. It has been described previously that X-band electron paramagnetic resonance (EPR) spectroscopy could be used to assess the dose in irradiated amputated fingers. Here, we propose the use of low-frequency EPR spectroscopy to evaluate non-invasively the absorbed dose. Low-frequency microwaves are indeed less absorbed by water and penetrate more deeply into living material (∼10 mm in tissues using 1 GHz spectrometers). This work presents preliminary results obtained with baboon and human fingers compared with human dry phalanxes placed inside a surface-coil resonator. The EPR signal increased linearly with the dose. The ratio of the slopes of the dry bone to whole finger linear regression lines was around 5. The detection limit achievable with the present spectrometer and resonator is around 60 Gy, which is well within the range of accidentally exposed fingers. It is likely that the detection limit could be improved in the future, thanks to further technical spectrometer and resonator developments as well as to appropriate spectrum deconvolution into native and dosimetric signals.

1. Introduction

Electron paramagnetic resonance (EPR) dosimetry of teeth is used to determine the dose absorbed by the victim in the absence of a dosimeter. EPR dosimetry is usually at X-band (∼10 GHz) (Wieser *et al* 2000) but it was recently suggested that L-band (∼1 GHz) EPR spectroscopy could also be used to measure the absorbed radiation dose in human whole teeth *in situ*, without removing the tooth from the mouth (Miyake *et al* 2000, Zdravkova *et al* 2002, 2003a, 2003b). Retrospective dosimetry is not limited to teeth. Other irradiated tissues, such as bones, although less radiosensitive, also exhibit analogous EPR signals (Breen and Battista 1995, and references therein). For example, beagle humerus cortical bone exposed to radiopharmaceuticals exhibited X-band EPR signals corresponding to absorbed doses of 10–20 Gy (Desrosiers *et al* 1993). Several human fingers that were overexposed in a radiation accident and amputated were also studied by EPR spectroscopy (Schauer *et al* 1993, 1996, Ikeya *et al* 1996, Kinoshita *et al* 2003) in order to estimate the dose of exposure.

Radiation injuries occurring after exposure to a local high dose (20 to 100 Gy) could lead to the need for amputation (Schauer *et al* 1993, 1996, Kinoshita *et al* 2003, Jalil and Molla 1992, Milanov *et al* 1993, Nakagawa *et al* 2001). Follow-up of victims should be more rational with a precise knowledge of the irradiated area that risks tissue deterioration and necrosis with respect to the local dose received. L-band EPR spectroscopy could be of great value to assess, non-invasively, the local dose to extremities. Low-frequency microwaves are less absorbed by water and penetrate more deeply into living material (∼10 mm in tissues with L-band compared with ∼1 mm with X-band). In this study, we demonstrate the feasibility of using L-band EPR to estimate the radiation dose in baboon and human fingers.

2. Materials and methods

^{137}Cs gamma-irradiated baboon fingers were supplied from the Unit of Dosimetry of Ionizing Radiation of IRSN (France). Four baboon fingers (mean diameter of 10.5 mm) were first stored in formalin and then irradiated once at 100, 300, 1000 or 3000 Gy respectively. After irradiation, all samples were kept in a freezer at −20 °C for about 10 months before the EPR measurements.

Four human little fingers and several dry phalanxes were supplied from an anonymous collection of the Human Anatomy Department of the Faculty of Medicine of UCL, where the samples were also prepared in the following way. The fingers, obtained at autopsy, were chemically processed, first with 3 l hot 40% $ZnCl_2$ aqueous solution containing 9 g l^{-1} NaCl, then with 10 l 40% $ZnCl_2$ aqueous solution with 500 ml glycerin and 250 ml Atrhryl (formalin-based stain). The bones were boiled for 3–4 days, scraped with bistouries, cleaned with grease-removing soap, dichloroethane, rinsed and dried. These samples (human fingers and bones) were irradiated in a Plexiglas cylinder with an x-ray beam (Philips 250 RT, 250 kV, 15 mA, 1 mm Cu filter) with a dose rate of 1.2 Gy min^{-1}. The EPR spectra were collected immediately after each irradiation and several days later. Of the four little fingers, one was irradiated for some preliminary experiments and another was used as a non-irradiated reference sample. The two others were successively irradiated by steps of 20–30 Gy up to 220 Gy and analysed by EPR after each irradiation. The same procedure was followed for dry bones: one phalanx was irradiated by steps of 10 Gy up to 90 Gy and one non-irradiated phalanx was used as a reference sample.

EPR measurements were carried out at room temperature using an L-band Magnettech EPR spectrometer (Berlin, Germany) equipped with a low-frequency microwave bridge operating at 1.23 GHz and an extended loop resonator (surface-coil of 12.5 mm inner diameter

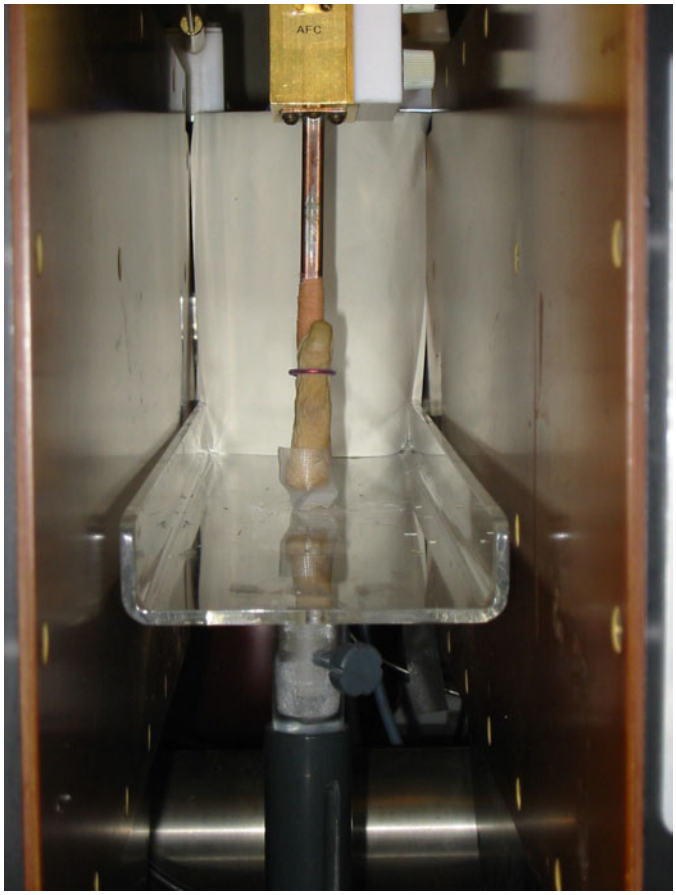

Figure 1. Picture of a human finger inserted into the surface-coil resonator in the gap between the electromagnet pole shoes of the L-band spectrometer.

(This figure is in colour only in the electronic version)

and 2 mm thickness) designed and built by Dr T Walczak (Dartmouth Medical School, Hanover, NH, USA) and whose characteristics have been described elsewhere (Zdravkova *et al* 2002). A frequency counter (CUB RF minicounter, Optoelectronics, USA) enabled the measurement of the microwave frequency. The spectrometer settings of the EPR parameters were 23 or 95 mW input microwave power, 3 mT sweep field, 1024 data points, 1 min scan time, 0.06 or 0.12 s time constant, 0.34 mT modulation amplitude, 40 or 60 scans.

The fingers were fixed on an expanded Polystyrene support and were inserted in the surface-coil resonator to a position between the first (distal) and second phalanx in order to be as close as possible to the bone. In this position, the baboon and human fingers completely fill the surface-coil resonator (figure 1). The top of the phalanx was positioned in the surface-coil plane (figure 2).

As already discussed previously (Zdravkova *et al* 2003b), an intrinsic resonator signal interferes with the radiation-induced signal. As the position, shape and intensity of this resonator signal vary with time, it is necessary to take the spectrum of the empty resonator before and after that of the finger, and to subtract it from the finger signal. This procedure was

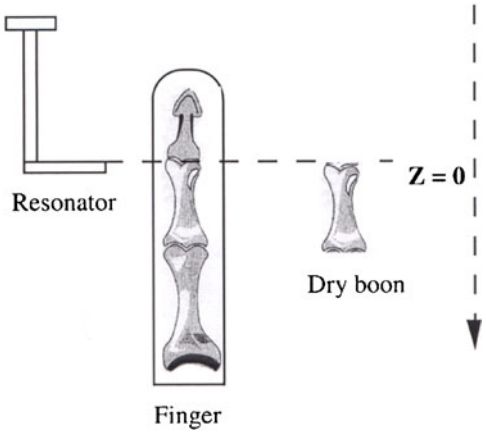

Figure 2. Vertical position of the finger and the bone inside the surface-coil resonator drawn separately for clarity.

followed for the baboon fingers which were irradiated at high doses and for which we did not have any non-irradiated finger at our disposal. For the less irradiated human fingers and bones, in order to have comparable resonator quality and sample filling factors for both spectra, we subtracted from the irradiated sample spectrum that of the non-irradiated reference finger or bone, recorded immediately before the irradiated finger or bone. In this way the intrinsic resonator signal should be more efficiently eliminated and the native signal strongly reduced. The spectra for the irradiated fingers were recorded five times for baboon and twice for human fingers. As the lineshape did not change in relation to the absorbed dose, the peak-to-peak first-derivative amplitude was taken as a measure of the relative radical concentration.

Small portions of the ends of the irradiated and non-irradiated human phalanxes were crushed and some powder EPR spectra were recorded at X-band with a Bruker EMX-8/2.7 spectrometer (100 kHz modulation frequency, 5 mW microwave power, 0.34 mT modulation amplitude, 5 mT field range, 1024 data points, 20.48 ms conversion time, 10.24 ms time constant, 50 scans). The magnetic field was measured by a Bruker ER 036 TM NMR teslameter and the microwave frequency by a Bruker EMX 040-1161.8A frequency meter.

3. Results and discussion

Figure 3 shows typical L-band EPR spectra of irradiated baboon and human fingers and human dry phalanx. It can be seen that the L-band spectrum is reduced to a single composite line. As in the case of irradiated whole tooth, this line originates principally from radiation generated CO_2^- (corresponding to the 'dosimetric signal' coming from the bone mineral—carbonated hydroxyapatite) and 'native' radicals due to the bone organic component (mainly collagen). It is known that the intensity of the native signal can vary greatly from sample to sample and is able to mask partly the dosimetric signal, especially in trabecular compared to cortical bone (Breen and Battista 1995).

The dose–response curve obtained with the peak-to-peak amplitudes of the composite line in the baboon fingers is presented in figure 4. The data are mean values and standard deviations (error bars) for five measurements. The relative standard deviations are in the range of 10–20%. The regression line intercept on the *y*-axis is significant. This result is probably related to the predominant contribution of the native species to the single composite L-band line. Indeed,

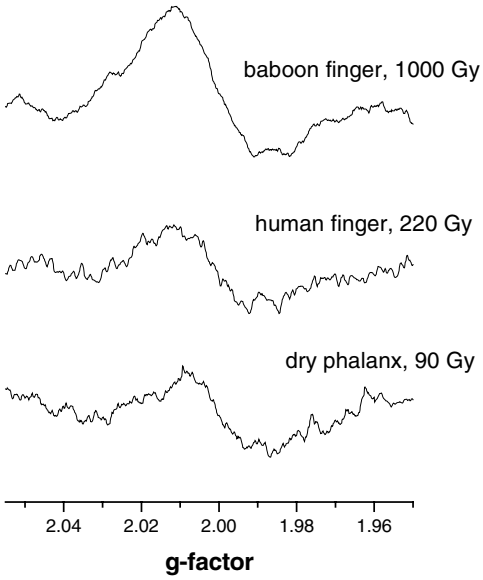

Figure 3. L-band EPR spectrum of a 1000 Gy irradiated baboon finger after subtraction of the empty resonator spectrum, and L-band spectra of a 220 Gy irradiated human little finger and a 90 Gy irradiated human dry phalanx after subtraction of the non-irradiated reference finger or bone spectrum.

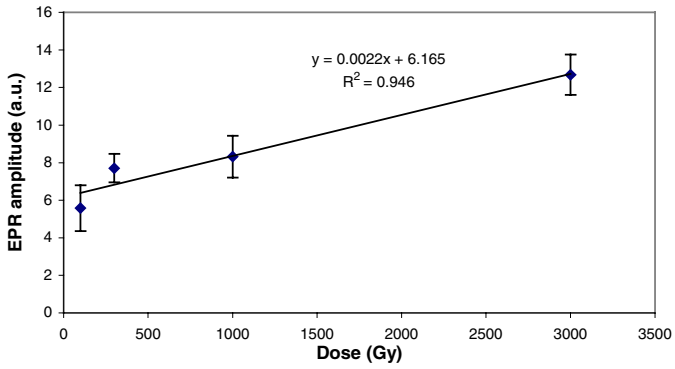

Figure 4. Dose–response curves obtained with peak-to-peak amplitudes of the composite line of baboon fingers. Each result corresponds to a different finger, which received a single dose. The error bars are standard deviations from five spectra.

only the empty resonator signal spectrum was subtracted from the finger spectrum. Actually, both organic and inorganic components are radiosensitive, but the native species is known to be much less radiosensitive than the carbonated hydroxyapatite. In teeth enamel the native component is 10 to 20 times less radiosensitive than the inorganic component. Moreover, the organic radicals are also less stable than CO_2^-.

Figure 5 shows X-band spectra of non-irradiated and irradiated crushed human phalanxes. The non-irradiated powder spectrum already exhibits a small CO_2^- component, which is strongly enhanced by the irradiation. Consequently the L-band spectrum can be considered as being due principally to the CO_2^- signal. The dose–response curves for the two human little

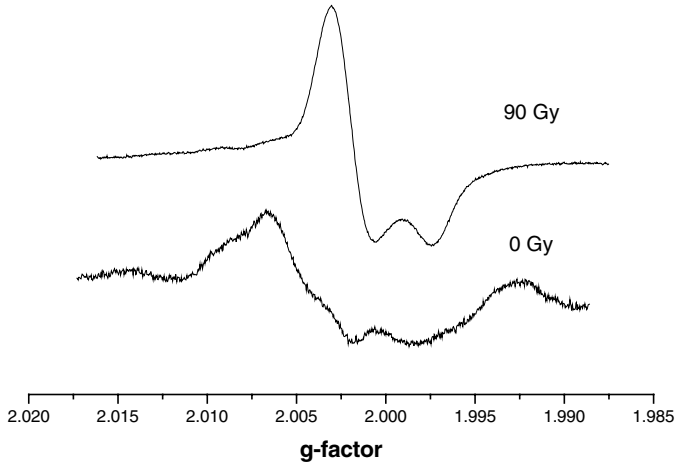

Figure 5. X-band spectra of non-irradiated and 90 Gy irradiated crushed human phalanx. The spectrum of the non-irradiated sample is ∼18 amplified compared with that of the irradiated one.

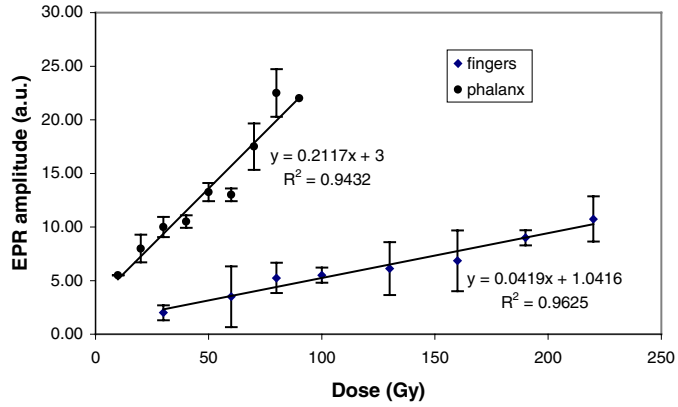

Figure 6. Dose–response curves obtained with peak-to-peak amplitudes of two human little fingers and a human dry phalanx successively irradiated up to 220 Gy (fingers) or 90 Gy (phalanx). The error bars are standard deviations from four spectra (two fingers recorded twice) or two spectra (phalanx recorded twice).

fingers and the human dry phalanx are presented in figure 6. The data are mean values and standard deviations (error bars) for four (fingers) or two (phalanx) measurements. Most relative standard deviations are similar to those of the baboon fingers, but some reach 30%. Linear dose–response curves up to 100–200 Gy are frequently encountered after photon irradiation of bones (Breen and Battista 1995, Desrosiers *et al* 1993, Schauer *et al* 1996, Kinoshita *et al* 2001, 2003).

It is clearly seen that the human dry bone is more sensitive than the human whole finger. The ratio of the slopes equals ∼5 with the geometrical conditions used in this study. This value actually is somewhat underestimated due to the position of the isolated second dry phalanx, which is not topped by the first phalanx (figure 2). This difference is not surprising because of the attenuation effect of the tissue between the surface-coil resonator and the bone in the whole finger (absorption of the wave by the water).

The ratio of the intercept on the *y*-axis to the slope of the line yields the dose equivalent to the signal amplitude of unexposed samples. This dose equivalent can be considered as the bias of measurements and is equal to 14 ± 16 Gy for the dry bone and 25 ± 32 Gy for the fingers. Defining the detection limit as two standard deviations of the bias (Zdravkova *et al* 2003b) yields around 30 Gy for bones and 60 Gy for fingers. This detection limit is well in the range of fingers accidentally exposed to intense radiation sources (20 to more than 100 Gy). However, there is a need to further improve the detection limit as reports on the need for amputation have been described for doses as low as 25 Gy. The present limitations are related to the presence of the native component which overlaps the dosimetric CO_2^- signal (in X-band EPR dosimetry measurements a chemical separation of collagen and bone mineral is sometimes performed) and the spectrometer instabilities (intrinsic fluctuating resonator signal, noise, etc). Higher microwave powers should improve the detection of the dosimetric signal CO_2^- and saturate the native signal. Improvements in sensitivity could also be achieved by designing coils designed to better fit the shape of the fingers.

4. Conclusions

This work presents preliminary results indicating the feasibility of correlating the L-band EPR signal in human fingers with the received radiation dose. The ratio of dry bone to whole finger radiosensitivities was estimated to be around 5. The detection limit achievable with the present spectrometer and resonator is around 60 Gy. This value is within the range of doses reported in fingers in accidents. This detection limit could be reduced by using higher microwave powers, by technical improvements in spectrometer and resonator allowing reductions in noise and parasitic intrinsic signals, and by appropriate spectrum deconvolution into native and CO_2^- signals.

Acknowledgments

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