L BAND EPR TOOTH DOSIMETRY FOR HEAVY ION IRRADIATION

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Electron Paramagnetic Resonance (EPR) tooth dosimetry is being developed as a device to rapidly assess large populations that were potentially exposed to radiation during a major radiation accident or terrorist event. While most exposures are likely to be due to fallout and therefore involve low linear energy transfer (LET) radiation, there is also a potential for exposures to high LET radiation, for which the effect on teeth has been less well characterized by EPR. Therefore, the aim of this paper is to acquire fundamental response curves for high LET radiation in tooth dosimetry using L band EPR. For this purpose, we exposed human teeth to high energy carbon ions using the heavy ion medical accelerator in Chiba at the National Institute of Radiological Sciences. The primary findings were that EPR signals for carbon ion irradiation were about one-tenth the amplitude of the response to the same dose of 150 kVp X-rays.

INTRODUCTION

EPR biodosimetry

Ionizing radiation generates stable unpaired electron species in tooth enamel instantly upon irradiation, which persist for a very long time. The radiation-induced signal is proportional to the dose. Electron Paramagnetic Resonance (EPR) spectroscopy of teeth has been used to perform retrospective radiation biodosimetry, following radiation accidents and exposures (e.g. Chernobyl disaster, atomic bomb in Hiroshima, Nagasaki, critical accident in Tokai-mura) by conventional EPR dosimetry, which involves the isolation of tooth enamel for measurements made at the X-band (9.1–9.5 GHz)^(1–3). While this technique has been useful for retrospective studies of exposure based on exfoliated teeth, this approach is not applicable as a tool for performing screening after an event where a large number of people have potentially been exposed to clinically relevant doses of ionizing radiation because of the need to have an isolated tooth.

In vivo EPR tooth dosimetry

In vivo EPR tooth dosimetry using L-band (1.0–1.2 GHz) has been developed to allow measurements to be made with teeth in the mouth *in situ*^(4–6). This approach has several desirable characteristics to screen for significant radiation exposure following a

mass-exposure incident. It can be used in any individual with one or more intact central incisors, providing dose estimates at the level of an individual. The measurement is based on a physical phenomenon (radiation-induced free radicals in the enamel) that is unaffected by prior disease or concurrent stress or trauma. The method was initially developed for screening for triage for risk of acute radiation syndrome (with a screening threshold of two gray [Gy]). Such measurements can be made with acquisition times of <5 minutes. Equipment has been developed to enable the measurements to be made in the field with a transportable EPR tooth dosimeter. The specific characteristic utilized by EPR dosimetry is to measure stable free radicals.

However, the mechanisms on carbonate radical formation in hydroxyapatite by irradiation are not fully understood, especially for exposure to heavy ion radiation. There are some circumstances where this could be important. In the case of an improvised nuclear device, the exposure may include neutrons, particularly for survivors near to the center of a ground or airblast. If there are significant fluxes of neutrons, energy transfer by recoil protons would be in the form of higher LET radiation, but the extent of this exposure should be small in hydroxyapatite due to the low composition ratio of hydrogen in hydroxyapatite⁽⁷⁾. On the other hand, during space flights,

astronauts may be exposed to significant amounts of high linear energy transfer (LET) radiation.

Research purpose

We therefore initiated a study to determine the contributions of high LET radiation to the EPR signal. The primary goal is to acquire fundamental response curves for heavy ion irradiation in tooth dosimetry using L band EPR, to inform our basic understanding of EPR dosimetry.

MATERIALS AND METHODS

Carbon ion irradiation to human teeth

High-energy carbon ion field

The well-characterized high-energy carbon ion field of the heavy ion medical accelerator (HIMAC) located in Chiba at the National Institute of Radiological Sciences (NIRS) was used in this study. Natural human teeth were included in a polyethylene slab phantom and set at the Bragg peak region. We adjusted the spread-out Bragg peak (SOBP) as 60 mm to generate radicals uniformly in this region. Step-by-step irradiations from 10 to 30 Gy at the Bragg peak region were performed with 290 MeV/nucleon ^{12}C ions. This dose was specified as absorbed dose to water (Figure 1).

Human teeth

Japanese subjects donated 18 isolated human teeth; each tooth was whole, intact and without significant dental cavities or metal fillings. Six teeth were each exposed to one of three doses (10, 20 or 30 Gy), using a carbon ion beam.

Figure 1. A schema of the irradiation setup.

X-ray irradiation to human teeth

For a comparison of the EPR response of the enamel to X-rays and gamma ray, a human tooth was serially irradiated using X-rays to accumulated doses of 1, 5, 10 and 20 Gy and re-measured after each dose. Irradiation was performed using a X-ray apparatus (MBR-1505R2, Hitachi Power Solutions Co., Ltd, Tokyo, Japan) of 150 kVp and 4 mA, with 0.1-mm copper plus 0.3-mm aluminium filtering. During each exposure, air kerma was always monitored using the air chamber (N31003, Toyo medic, Japan). This air chamber was calibrated with the secondary standard dosimeter (Exradin A3 Ion Chamber, Standard Imaging Inc, USA) at Japan Quality Assurance Organization that is certified by Japan Calibration Service System. The expanded standard uncertainty of the air chamber ($k = 2$) was 5%. In this energy range, air kerma was similar with absorbed dose to water and the difference was within 5%. A standard tooth irradiated to 20 Gy by a ^{137}Cs source was provided by the EPR Center for the Study of Viable Systems at Dartmouth. This dose was also specified as absorbed dose to water.

EPR measurement

Irradiated teeth were measured for detecting the EPR signal by using the 1.2 GHz L band EPR at the National Institute of Public Health. Before irradiation, all teeth were measured using the EPR dosimeter to record their background signal amplitude.

Positioning of teeth

Teeth were precisely positioned using a custom-made bite block that located each tooth within the central homogeneous region of the magnet (Small Dipole Permanent Magnet for L-Band EPR, Model: BFMP-415/170-D, Resonance Research, Inc., MA, USA). Each tooth sample was placed in a dental putty mould (EXAFINE [putty type], GC Corporation, Tokyo, Japan) to ease both handling and positioning within the bite block; examination of the dental putty alone-confirmed it did not contribute significantly to the EPR signal.

EPR spectra acquisition

The EPR spectra were acquired using standard parameters of 20 scans; scan range of 2.5 mT, a scan time of 3 seconds and a modulation amplitude of 0.4 mT. This process was repeated for a total of three datasets at each dose, as well as at baseline. A plastic tube containing a solution of 4-oxo-2,2,6,6-tetramethylpiperidine-d16-1-15N-1-oxyl (also known as 15 N perdeuteratedtempone [PDT]), was fixed in a position in close proximity to the surface loop and used as a reference standard, as well as to monitor

EPR signal detection and the amplitude of magnetic field modulation through the whole period of measurements of all samples. The PDT EPR spectrum includes two resonance peaks that are offset from the peak of the irradiated tooth.

The spectra from each of the collected datasets were analysed using nonlinear least-squares fitting to estimate the peak-to-peak signal amplitudes of the radiation-induced signals, and of PDT. Radiation induced signals (RIS) and signals of PDT were then averaged to provide a mean amplitude for each tooth and at each dose (V_{RIS} and V_{PDT} , respectively). In order to account for variations in RIS amplitude that result from instrumental instability or external environmental factors, the ratio of V_{RIS} to V_{PDT} for each measurement was calculated and normalized to the same ratio in a standard tooth that was irradiated to 20 Gy. Accordingly, the dosimetric relative RIS amplitude value (Rel_{RIS}) associated with each tooth was calculated as the ratio to 20 Gy of these ratios of V_{RIS} to V_{PDT} .

Gamma ray spectroscopy

The gamma ray spectra of irradiated teeth were acquired using NaI detector (CANBERRA: CJ-NaI-3W).

Calculation of radiation interaction and energy transfer

For comparison with experiments, simulations using Particle and Heavy Ion Transport code System (PHITS) Version 2.770⁽⁸⁾ and Electron Gamma Shower 5 (EGS5)⁽⁹⁾ were carried out to evaluate induced radioactive nuclides and energy transfer. In simulation, the carbon energy was set to be 290 MeV and the nuclide composition of hydroxyapatite was set to be ^{40}Ca : ^{31}P : ^{16}O : ^1H = 5.0: 3.0: 13.0: 1.0 setting the density as 2.0 g/cm^3 .

The cut off energy was 1(MeV) except for 10^{-3} (MeV) for photons, 10^{-1} (MeV) for electrons and positrons. The energy depositions in each region from the carbon ion exposure were calculated.

Statistical analysis

A regression analysis (using R Ver 3.2.2⁽¹⁰⁾) was used to test for significant relationships, using the formula: relative EPR signal = $\alpha + \beta \text{dose} + \epsilon$.

RESULTS

Experiments

Figure 2 shows a typical EPR spectra for a tooth irradiated by ^{12}C (30 Gy), together with the PDT standard lines. One tooth, measured at baseline, had an unusually high background signal and so was excluded from further analysis.

Figure 2. Typical EPR spectra of a tooth irradiated to 30 Gy by ^{12}C . Each dot shows measured EPR response at each magnetic field. The line shows the fitted curve.

Dose-response relationships of L band EPR

Statistically significant dose-response relationships are shown in Figure 3. The results from the linear regression were: relative EPR signal = $0.24 + (0.092 \times \text{dose})$; standard error for the slope was 0.013 ($p \leq .0001$). The mean response to 290 MeV carbon ions in the Bragg peak region was about one-tenth of that of 150 kVp X-rays. Meanwhile, the relative response for diagnostic X-ray was about four compared with gamma ray from ^{137}Cs source.

Induced radioactivity

The main activated nuclide was ^{11}C , confirmed by measuring the half-life of annihilation photons.

Simulation

Energy transfer of each radiation

According to calculations using PHITS and EGS5, 86% of the energy transfer to a tooth was from carbon, 7% from alpha particles and 5% from protons (Figure 4).

Energy deposition distribution of ^{12}C

Energy deposition per unit volume distribution by ^{12}C is shown in Figure 5.

Hydroxyapatite was located between 0 and 15 cm at the Z-axis; that means the Bragg peak was at a thin layer at ~15 cm distance from the entrance and -5 to 5 cm at the X- and Y-axis surrounded by 5 cm thickness rectangular polyethylene at the X-Y plane. For making a Bragg peak in the hydroxyapatite region, 15 cm thickness polyethylene slab was used with a width of -10 to 10 cm at the X- and Y-axis.

Induced radioactivity

Each type of induced radionuclide was calculated by using PHITS and D-chain. The top five dominant

Figure 3. EPR signal response for 290 MeV carbon ion irradiation. The EPR signal was standardized by 150 kVp X-ray irradiation.

Figure 4. Energy deposition ratio to hydroxyapatite located with 1 cm thickness at the surface of the phantom by each radiation type simulated by PHITS and EGSS, based on the average of tooth area from each radiation type resulted from ^{12}C irradiation.

Figure 5. Energy deposition distribution of ^{12}C irradiation.

nuclides with 1 hour cooling after a 20-minute irradiation of ^{12}C are ^{11}C (1.0), ^{31}Si (0.62), $^{34\text{m}}\text{Cl}$ (0.23), ^{13}N (0.22), ^{18}F (0.17), where the numbers inside the parentheses are the relative ratio standardized by the amount of radioactivity of ^{11}C , which was the most dominant nuclide.

DISCUSSION

Dose-response for ^{12}C irradiation of L band EPR

Dose-response relationships of L band EPR for high LET radiation

The results confirmed that the EPR signal was observable for 10 Gy irradiation and that the intensity of the EPR signal increased linearly according to the added radiation dose. These results suggest that, in the case of the radiation dose to an astronaut typically consisting of relatively high LET, it would be possible to detect radicals in a tooth due to radiation exposure during a space flight, and it might also be possible to adapt this method for patients undergoing particle beam radiation therapy using high-energy carbon.

However, our results also suggest that the efficiency of total radical production by ^{12}C irradiation was relatively low, i.e. about one-tenth that of diagnostic X-ray and 0.4 that of gamma rays from ^{137}Cs . The main energy transfer was due to heavy ions and alpha particles due to fragment reaction of ^{12}C ⁽⁷⁾, which is consistent with previous knowledge about the specificity of radical production of these particles⁽¹¹⁾. Therefore, for detecting higher LET radiation exposure, EPR dosimetry has disadvantages regardless of its having a higher response to neutron exposure⁽¹²⁾.

Differences in dose-response relationships among different radiation types

EPR tooth dosimetry measures the amount of stable carbonate radical ions induced in the volume sampled by the resonator. The amount of radicals in the volume per radiation-absorbed dose [$\text{Gy} = \text{J/kg}$] indicates the efficiency of production by radiation exposure. Differences of efficiency of radical production between diagnostic X-ray, gamma ray of ^{137}Cs and Carbon ion indicate that the yield of radicals detected by EPR is less for the high LET radiation studied in these experiments.

The energy dependence of the yield of the product that is used to determine the dose is an important factor for radiation dosimetry and needs to be known for each method. In case of a thermoluminescence dosimeter for gamma ray dosimetry, we expected that the energy dependency would be reflected by mass energy-absorption coefficients for photons and mass stopping powers for charged particles; our results confirmed that calculated energy absorption considering element composition and measurements were in good agreement^(13–14). That means that the relationship between energy absorption, the number of trapped electrons due to energy transition and the glow intensity is well recognized, and it is possible to estimate glow intensity from energy absorption and to calculate a glow curve theoretically. Conversely, there is still a need to clarify the relationship between

radical generation and energy absorption for each irradiation and sample conditions for EPR dosimetry, especially for high LET radiation.

Our results have provided initial experimental data for a particular source, i.e. 290 MeV/nucleon ^{12}C ions. Further data are needed to confirm these results. They also highlight a need for further investigations, in part because this study limited its measurements of irradiated teeth to the Bragg peak region. Because of the relative dependency on radical production, in the event of actual irradiations with this or similar types of high LET radiation, the EPR signal response per unit absorbed dose is likely to increase at the outer region of Bragg peak and may therefore differ from what we reported. Furthermore even in a SOBP, physical radiation dose is not uniform.

Effect of induced radioactivity on L band EPR

Because the high energy radiation source that was studied (high energy carbon 12 ions) has the potential to induce radioactivity within the tooth enamel and thereby affect the total dose that was received by the tooth, we measured the induced radioactivity. The principal radioactivity was, as expected, from carbon-11. The total amount of radioactivity was quite small and should not affect the amount of the observed EPR signal. However, because of technical and safety considerations, we were not able to measure the induced radioactivity until 60 minutes after the irradiation with the carbon atoms was completed. Therefore, it would be desirable in the future to carry out radioactivity measurements starting immediately after the delivery of the carbon ions, to be able to fully evaluate contributions from very short lived radioactive products induced in the sample.

Finally, we should mention another limitation of this study. The dose measured with EPR was the dose to the tooth and therefore assumptions need to be made as to how representative this is in regard to the dose to the rest of the body⁽¹⁵⁾.

CONCLUSION

Using EPR of whole teeth as the dosimetry system, the high energy ^{12}C ions (290 MeV/nucleon) gave a lower response per unit dose compared to gamma from ^{137}Cs (40% of the gamma response) and to an X-ray from 150 kVp (10% of the X-ray response).

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