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Radiation Dosimetry by Localized Magnetic Resonance Spectroscopy

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In 1984, Gore *et al.* demonstrated that magnetic resonance imaging (MRI) can be used to visualize dose distributions produced by ionizing radiation in phantoms of tissue-equivalent gels (*1, 2*). The technique uses the shortening of T_1 and T_2 relaxation times of hydrogen nuclei in aqueous solution of a ferrous salt, which is induced by the oxidation of ferrous to ferric ions during exposure with ionizing radiation. The purpose of the present study is to demonstrate the feasibility of a similar approach using localized magnetic resonance spectroscopy (MRS) for radiation dosimetry.

Since its discovery, a variety of works have been published using radiation dosimetry by MRI to demonstrate the feasibility of this technique for different types of irradiation, e.g., ^{60}Co (*3*), high energy photons (*4*), electrons (*5*), or protons (*6*). Others used the method for brachytherapy (*7–9*), stereotactic techniques (*10*), or the Gamma knife (*11*). Most results of these works are very inconsistent, since a variety of irradiated substances, energies, types of radiation, doses, phantoms, MR field strengths, coils, and pulse sequences have been used. Thus, a comparison of these data is very difficult and the method seems to be far from a reliable clinical use. A serious drawback of the method is its sensitivity to RF inhomogeneities. These can significantly affect the calculated doses using MRI, especially when ionic substances are used (*12, 13*). Another problem arises from the presence of rapid blurring of dose distributions within irradiated Fricke gels due to ion diffusion (*14*). Dose distributions can be stabilized by the use of polymer gels (*13, 15, 16*). However, these might be toxic and have a lower sensitivity, especially at higher doses. In any case, radiation dosimetry by NMR could be optimized by a fast measurement technique for dose evaluation. Since no phase-encoding steps as used in MRI are necessary for MRS, the minimum time necessary to assess relaxation time changes could be reduced by up to two orders of magnitude.

The gel phantoms used in the present study were prepared according to Olsson *et al.* (*17, 18*). Briefly, the gel used consisted of 1.5% by weight of agarose (agarose for electrophoresis, Fluka 05068, Fluka Chemie AG, Buchs, Switzerland), 50 m*M* sulfuric acid, 1.0 m*M* sodium chloride, and 0.5 m*M* ammonium ferrous sulfate hexahydrate. During mixing, the solution was bubbled with oxygen to increase dose sensitivity (*19*). Afterward 10 plastic vials were filled with the solution, 24 ml each. The vials were then placed within a tank containing approximately 20 liters of tap water. Irradiation was performed with 6 MV photons produced by a Philips SL 25 linear accelerator. Nine vials were given different doses between 1.1 and 33.0 Gy. One vial was taken as reference and not irradiated.

The MR measurements were started within about 10 minutes after irradiation with a Siemens Magnetom SP 4000 whole-body system and the standard circularly polarized knee coil at 1.5 T. All vials were placed together in a cardboard box with distances of about 1 cm between each vial. After image-guided localization using a Turbo-FLASH sequence, each of the vials was investigated by a localized STEAM sequence (*20–22*) with an echo time of 20 ms, a mixing time of 30 ms, and repetition times (TR) of 600, 1000, and 10,000 ms. The voxel size was $(1.5\ \text{cm})^3$. Six prescans followed by one acquisition were performed. The total investigation time for all vials including MRI was less than 25 min. Only the first point of each stimulated echo was recorded, no Fourier transformation or further post-processing of the MRS data was performed. The relaxation rate R_1 was determined from the slope in a two-point fit of the signal intensity differences between the shorter TR and the fully relaxed measurement (TR = 10,000 ms; i.e., $\geqslant 8 \times T_1$) against TR, representing the signal saturation. Figure 1 shows R_1 as a function of the given dose, the so-called dose response curve. The range from 7.7 to 33 Gy can be linearly fitted with a slope of 0.0375 $(\text{sGy})^{-1}$, $r^2 = 0.999$. Fitting the total dose range results in $r^2 = 0.988$.

These results were compared with those obtained by MRI. MR images were acquired using a double-echo turbo-spin-echo [or RARE (*23*)] sequence with echo times of 21 and 103 ms, a repetition time of 5000 ms, a slice thickness of 6 mm, a field of view of 135 × 180 mm, and a matrix size of 192 × 256. The slice was chosen in coronal direction in order to cut the center of all vials. The average signal intensities in MRI were determined within regions of interest (ROI). The ROIs had a radius of 10 pixels and were placed in the center of each vial. For both images with different echo

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times, identical ROIs were used. Under these conditions, the ratio of image intensities acquired with different echo times should vary linearly with spin–spin relaxation rate R_2 and thus linearly with dose (*13*). Figure 2 shows the image intensity ratio in MRI as a function of the given dose together with a linear fit. Here, the regression coefficient is 0.969.

The present study demonstrates the feasibility of a fast and reliable calibration and evaluation of the Fricke dosimeter by MR spectroscopy. The method is less sensitive to inhomogeneities of the B_1 field than MRI, since no refocusing 180° pulses are applied as in the case of spin echo, RARE, inversion recovery, or CPMG sequences, which have been frequently used for radiation dosimetry. Although in a recent study the RARE sequence turned out to be the best sequence for determination of T_2 (*24*), the dose response curve we determined by MRS was more linear. A spectroscopic technique for radiation dosimetry has been used previously by Olsson *et al.*, who used an NMR analyzer for determination of T_1 at a field strength of 0.25 T (*19*). However, no localized MRS nor MRI was possible using that small bore device. By the technique presented, volumes of interest of approximately 0.1–1000 ml can be easily investigated and given doses of radiation determined within a time on the order of one minute. The method could be extended by the use of multivolume techniques such as spectroscopic imaging or chemical-shift imaging (*25, 26*).

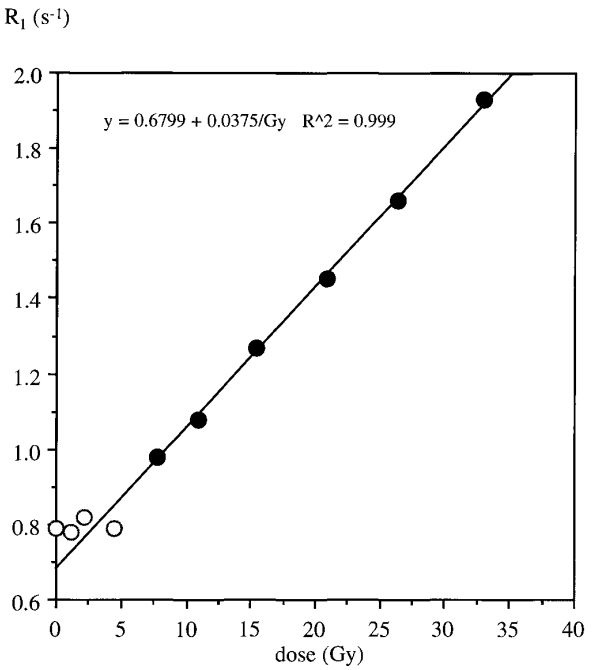

FIG. 1. Dose–response curve as determined with localized short echo time proton MRS. The range between 7.7 and 33 Gy (filled points) can be linearly fitted with $r^2 = 0.999$.

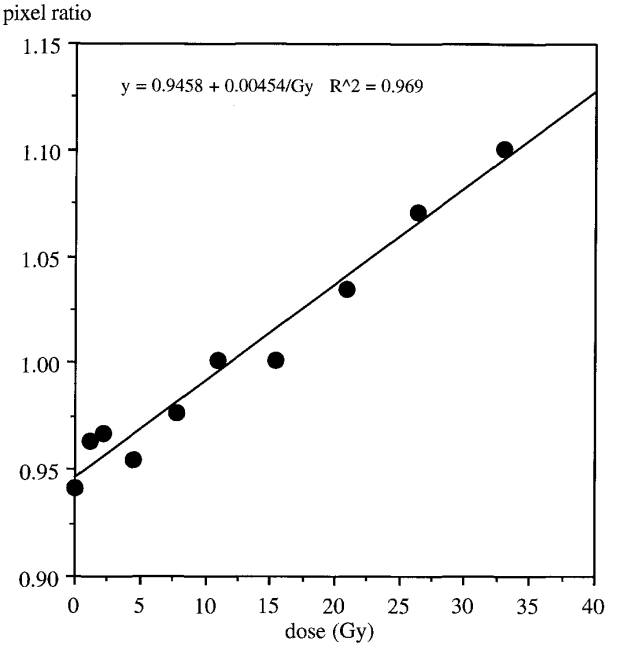

FIG. 2. Dose–response curve as determined with turbo spin-echo MRI.

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