Fricke dosimetry of irradiated sugar by $^1$H NMR relaxation

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Abstract. Linear dose response in the range 0-30 Gy was observed in spin-lattice and spin-spin relaxation rates of water protons in 10 wt% sugar Fricke solutions at 300 MHz and 25 MHz. Spin-lattice dose sensitivities were higher at 300 MHz (0.058 s$^{-1}$ Gy$^{-1}$ with xylenol orange, 0.024 s$^{-1}$ Gy$^{-1}$ without) than at 25 MHz (0.047 s$^{-1}$ Gy$^{-1}$ with xylenol orange, 0.026 s$^{-1}$ Gy$^{-1}$ without), despite slightly less linearity. Spin-spin dose sensitivities at 25 MHz (0.029 s$^{-1}$ Gy$^{-1}$ with xylenol orange, 0.033 s$^{-1}$ Gy$^{-1}$ without) were slightly higher than corresponding spin-lattice dose sensitivities. Unirradiated sugar was found to accelerate background oxidation in Fricke solution, following a logistic time development curve.

1. Introduction
Electron paramagnetic resonance spectroscopy of γ-irradiated table sugar suggests the presence of at least three long-lived species of radiation-induced free radicals [1]. When dissolved in Fricke solution, these free radicals can oxidize Fe$^{2+}$ to Fe$^{3+}$. Davidson and Jordan [2] demonstrated a linear relationship between optical absorbance and delivered dose in the range 1-20 Gy, using the chelating organic dye xylenol orange as an indicator for the oxidation state of iron. NMR should also be sensitive to the dose-dependent oxidation of iron since Fe$^{2+}$ and Fe$^{3+}$ are paramagnetic ions that have different spin relaxation enhancement effects. Dosimetry of irradiated Fricke solution [3] and gelatin matrix [4] by spin-lattice relaxation measurement of water protons has been well characterized and successfully modeled by multiple site fast exchange in the Fe$^{2+}$ and Fe$^{3+}$ solvation shells. The present study explores the possibilities for using $^1$H NMR spin-lattice and spin-spin relaxation measurements in Fricke-sugar dosimetry.

2. Experiment
Food-grade granulated table sugar was purchased from a local grocery store and used without further processing. Thin plastic bags containing 3 g of sugar crystals were positioned at 100 cm source-to-axis between a 2 cm layer of solid water phantom placed on top for maximal build-up of Compton electrons and a 10 cm layer of solid water placed below for backscattering. The sugar was irradiated to doses of up to 30 Gy with 6 MV X-rays at a dose rate of 400 cGy min$^{-1}$ in a 10×10 cm$^2$ field from a Varian C-Series Clinac (Varian Medical, Palo Alto, CA).

An aqueous Fricke xylenol orange (FX) solution containing 0.3 mM ferrous ammonium sulfate (Sigma-Aldrich Ltd., Oakville, Ontario, Canada), 0.05 mM xylenol orange (Sigma-Aldrich Ltd.) and 50 mM sulfuric acid (Sigma-Aldrich Ltd.) was prepared following the formulation of Davidson and...
Jordan. As NMR analysis did not require the optical properties afforded by xylenol orange, an analogous Fricke solution without xylenol orange was prepared to study the dosimetric behaviour in the absence of chelating agents. Both solutions were stored at 4°C to minimize background development due to auto-oxidation. Sugar solutions (10 wt%, 0.32 M) were allowed to develop at room temperature for a total of 3 hours before storage at 4°C. Each sample was taken out 30 minutes before measurement to return to room temperature.

High-field NMR experiments were performed on a Bruker Avance-300 spectrometer (7.04 T). Spin-lattice relaxation times (T₁) were measured with a saturation recovery pulse sequence. A soft pulse at the water resonance frequency was applied for 4 seconds to destroy the initial magnetization, followed by 16 variable recovery delays ranging from 0 to 30 seconds. The recovered magnetization was read with a 90° pulse. Manual shimming was performed in the absence of deuterium locking. Two scans were taken following one dummy scan for each measurement. It is worth mentioning that T₁ measurement of water by inversion recovery was found to be unreliable at high field due to radiation damping, a positive feedback coupling between a strong precessing magnetization and induced currents in the coils of the probe (see Mao and Ye, 1997 [5]).

Low-field NMR experiments were performed on a MARAN 25 MHz bench-top spectrometer (Resonance Instruments Ltd., Witney, Oxon, UK). An inversion recovery pulse sequence with 16 variable recovery delays between 0 and 30 seconds was used to measure T₁. Spin-spin relaxation times (T₂) were measured using a Carr-Purcell-Meiboom-Gill echo train pulse sequence [6] with 8000 echoes at 1 ms intervals.

3. Results & Discussion

Dose sensitivity is defined as the change in relaxation rate per Gy of delivered dose, as determined by linear regression. Figures 1 and 2 compare the effect of the chelating agent xylenol orange on the dose sensitivity of the spin-lattice relaxation rate (T₁⁻¹). Sensitivities obtained at 300 MHz were higher than those at 25 MHz. Measurements at 25 MHz appear more consistent with linearity than those at 300 MHz, possibly due to residual radiation damping effects during the readout period at the higher field. The greater field-dependence of the relaxation rate in the absence of xylenol orange may partly reflect a longer correlation time (τ_c) of the bulkier chelated iron complexes.

At 25 MHz, the spin-spin dose sensitivity, figure 3, appears to be slightly higher than the spin-lattice dose sensitivity. The lower dose sensitivity observed in the presence of xylenol orange may be

![Figure 1](image1.png)  
**Figure 1.** Dose dependence of spin-lattice relaxation rate in Fricke-xylenol-sugar system. Dose sensitivities are 0.058 s⁻¹ Gy⁻¹ at 300 MHz and 0.024 s⁻¹ Gy⁻¹ at 25 MHz.

![Figure 2](image2.png)  
**Figure 2.** Dose dependence of spin-lattice relaxation rate in Fricke-sugar system. Dose sensitivities are 0.047 s⁻¹ Gy⁻¹ at 300 MHz and 0.026 s⁻¹ Gy⁻¹ at 25 MHz.
attributed to competition between water and the chelating agent for coordination sites on the paramagnetic centres.

The delay between solution preparation and measurement can influence the dose sensitivity, due to the gradual signal development characteristic of Fricke dosimeters. Figure 4 shows preliminary data from our investigation of development time optimization. A logistic function modelled well the acceleration in background oxidation due to unirradiated sugar. After subtraction of this effect from a decaying exponential fit to the 30 Gy data, preliminary estimates suggest that maximum signal-to-background occurs between 16 to 48 hours of development at room temperature. Analogous experiments show a similar behaviour for the spin-lattice relaxation with and without xylenol orange.

4. Conclusions
Based on the results of this study, $^1$H NMR relaxation can be a viable alternative to optical techniques in probing dose-dependent oxidation of Fe$^{2+}$ in sugar-Fricke solutions. Higher dose sensitivities than those reported above may be achievable once the measurement technique is optimized. Further work is currently underway to explore the reaction kinetics in order to understand the chemical pathways connecting the free radicals from irradiated sugar with Fe$^{2+}$ oxidation.

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