Development of a radiochromic ferric oligomer hydrogel

Kevin Jordan and Masaya Sekimoto
London Regional Cancer Program, London Health Sciences Centre, University of Western Ontario, Dept. of Medical Biophysics
Kevin.jordan@lhsc.on.ca

Abstract. Ferrous gelatin hydrogels were prepared by using sulphuric acid concentrations lower than required to maintain radiation induced ferric ions fully hydrated. The ferric hydroxyl species that are produced following irradiation exhibit a radiochromic response that can be probed with blue light. The dose distribution shapes were stable in time, indicating no long term diffusion. An over response to dose gradients was observed both in one centimeter cuvette samples and litre volumes probed with optical cone beam CT. This ferrous hydrogel may represent a model system for studying iron radiochemistry in biological systems.

1. Introduction
The radiochromic conversion of acidic aqueous solutions of ferrous ions to ferric ions ([Fe(H$_2$O)$_6$]$^{3+}$) in the pH range 0.5 to 2 is known as the Fricke reaction. The extent of the reaction is measured by recording the absorbance change in the ultraviolet spectral region at 304 nm. By performing this reaction in hydrogels, convection mixing is eliminated and spatially resolution of the dose distribution is maintained. The corresponding 3D dose distributions were initially recorded in ferrous agarose gels with magnetic resonance imaging [1] because examination of ferrous agarose hydrogels at 304 nm is problematic. The agarose gels have sufficient scatter to make them appear translucent with visible light. The scatter is much great for shorter wavelength UV light. The ferrous gelatin gels appear transparent with visible light. However, the gelatin gels still absorb and scatter ultraviolet light and causes ferrous oxidation through photochemistry. The photochemistry becomes another variable for quantitative measurements. These effects make optical CT scanning of Fricke type gelatin hydrogel impractical at 304 nm for quantitative measurements over pathlengths greater than a few mm. However, dose responses in ferrous gels can and have been studied at 304 nm for 1 cm cuvettes [2].

In less acidic solutions ferrous ions are readily oxidized and the product ferric ions are hydrolyzed and form complexes that easily precipitate from water. Dinuclear and multinuclear species form resulting in red-brown colloidal gels. Hydroxospecies such as [Fe(OH)(H$_2$O)$_5$]$^{2+}$ are yellow due an ultraviolet charge transfer band which tails into the visible spectrum [3]. These species undergo photochemistry when illuminated and can result in the production of OH radicals. For this reason, aqueous iron photochemistry is under investigation as a potential mechanism for the inexpensive decomposition of pollutants in industrial effluent [4]. Iron chemistry is important in biological reactions and is considered to be base of several medical conditions. It is expected that basic iron chemistry may be effectively studied in gelatin hydrogels as model radiobiological systems. This preliminary study examines ferrous gelatin hydrogel radiochromic response at higher pHs where the anticipated distribution of species may have absorption spectra that can be optically probed with visible blue light. These multinuclear species are expected to have very low diffusion coefficients due...
to their higher molecular mass behaving like small polymers in hydrogel matrix. However, extrapolations from known pH dependence at higher acid concentrations predict these ferrous gels will have much lower radiation sensitivity and not useful as 3D dosimeters. This study is interested in the chemistry that is initiated by the radiation not the measurement of absorbed dose.

2. Methods
Ferrous gelatin hydrogels were prepared by adding ferrous ammonium sulphate (1 mM) to 4% gelatin solutions containing sulphuric acid at 30 C. The acid concentration was varied from 0.1 to 50 mM. Dose response and diffusion were studied with samples in 1 cm pathlength, disposable, poly(methyl methacrylate) cuvettes. One litre samples for optical CT scanning were poured into polyethylene terephthalate jars, supplied by Modus Medical Devices. Absorption measurements were performed with a Perkin and Elmer model 139, UV-VIS absorption spectrometer. Optical CT scanning was conducted with a commercial optical cone beam scanner, model Vista10 from Modus Medical Devices, modified for this experiment. The LED light box was removed and replaced with an actinic fluorescent lamp which was filtered with dark blue cobalt glass. The filtered emission spectrum was a narrow peak at 420 nm. The narrow bandpass filter at the CCD camera lens was also removed for this scan. The gel was optical CT scanned before and after axial, irradiation to 120 Gy at depth of maximum dose (d_{max}) with a 12 MeV electron beam, (field size 6 x 6 cm, SSD 100 cm, dose rate 400 cGy min^{-1} at d_{max}). The 512 image sets were reconstructed using software provided by with the Vista10 scanner. For the diffusion study, transmission images of half irradiated cuvettes (200 Gy) at 420 nm were recorded with an in-house optical cone beam scanner system at 12 pixels per mm resolution at several post irradiation times. The reference image was of air.

3. Results
The radiation sensitivities of the gel formulations were a strong function of pH. At wavelengths less than 350 nm, the response increased with lower pH. In contrast, at 420 nm, the sensitivity increased as the sulphuric acid concentration decreased from 50 to 0.1 mM. The absorption spectrum of irradiated gels peaked at less than 340 nm and tailed past 450 nm. In figure 1, transmission profiles of a cuvette that had been half irradiated to 200 Gy is shown. The profiles at 0.5 and 3.5 hours post irradiation are shown. Note the later profile was offset in order to demonstrate the stability of the profile shape. The offset was necessary due to baseline drifts due to auto oxidation and changing lamp output. Transmissions were referenced to air. Note the over response to absorbed dose in the vicinity of the dose gradient. Specifically, the sharp dip in transmission near 17 mm position. Since the profiles are identical all radiochromic reactions are complete in less than 0.5 hours and there is no diffusion of the radiochromic products.

A transverse slice from the 3D reconstruction corresponding to the depth of maximum dose is shown in figure 2. The post irradiation scan required 8 minutes and was initiated 10 minutes post irradiation. Note the enhancement in radiochromic response at the edges of the electron beam. This effect is consistent with the x-ray half sample irradiation of figure 1.
Figure 1. Transmission profiles for “ferric polymer” hydrogel with air reference recorded at 0.5(-) and 3.5(■) hours. Right half of gel cuvette (~17 to 35 mm) irradiated to 200 Gray. Note over response at dose gradient.

Figure 2. Transverse slice from 3D optical CT reconstruction of ferrous gel at depth of maximum dose, 12 MeV, 120 Gy, 6 x 6 cm field size. Note radiochromic over response at edge of beam.
4. Summary
Ferrous hydrogels prepared with lower concentrations of sulphuric acid than required to maintain ferric oxidation species as single iron molecules do exhibit a small radiochromic response that can be optically probed with blue light. The reaction is rapid and complete in less than 10 minutes. The shape of the radiochromic 3D distribution is fixed, demonstrating that diffusion the species absorbing blue light is not measurable on the time scale of three hours. A marked over response to dose gradients was observed for both x-ray and electron beams. The nature of the over response requires further investigation but it appears that ferrous ions in the low dose region, diffuse to multinuclear species growing in the gradient regions. The results demonstrate that this material is inappropriate for conventional radiation dosimetry but may be a model system for chemical dosimetry within biological systems.

Acknowledgements: Funding was from Ontario Research and Development Challenge Fund: Ontario Consortium for Image-guided Therapy and Surgery and London Regional Cancer Program Small Grants fund.

References
[1] Gore JC, Kang YS and Schulz RJ, 1984 Measurement of radiation dose distributions by nuclear magnetic resonance (NMR) imaging, Phys Med Biol 29, 1189-97
[2] Hill B, Bäck S, Lepage M, Simpson J, Healy B and Baldock C, 2002 Investigation and analysis of ferrous sulfate polyvinyl alcohol(PVA) gel dosimeter, Phys Med Biol 47:4233-46
[3] Cotton FA and Wilkinson G, 1980 Advanced inorganic chemistry: A comprehensive text 4th ed, Wiley Interscience
[4] Horvath CO and Huszank R, 2003 Degradation of surfactants by hydroxyl radicals photogenerated from hydroxioiron (III) complexes, Photochem. Photobiol. Sci., 2, 960-966