A reduction of diffusion in PVA Fricke hydrogels

S T Smith[1], K S Masters[1], K Hosokawa[1], J Blinco[1], S B Crowe[1], T Kairn[1,2] and J V Trapp[1]
[1]School of Chemistry, Physics and Mechanical Engineering,
Queensland University of Technology, Brisbane, Australia
[2]Genesis CancerCare Queensland, Brisbane, Australia

E-mail: s164.smith@qut.edu.au

Abstract. A modification to the PVA-FX hydrogel whereby the chelating agent, xylenol orange, was partially bonded to the gelling agent, poly-vinyl alcohol, resulted in an 8% reduction in the post irradiation Fe^{3+} diffusion, adding approximately 1 hour to the useful timespan between irradiation and readout. This xylenol orange functionalised poly-vinyl alcohol hydrogel had an OD dose sensitivity of 0.014 Gy^{-1} and a diffusion rate of 0.133 mm^2 h^{-1}. As this partial bond yields only incremental improvement, it is proposed that more efficient methods of bonding xylenol orange to poly-vinyl alcohol be investigated to further reduce the diffusion in Fricke gels.

1. Introduction

Fricke gels are based on adding gelling agents to the Fricke solution; an acidic oxygenated aqueous solution of ferrous ion (Fe^{2+}). Upon irradiation, a dose dependant transformation of ferrous (Fe^{2+}) to ferric ions (Fe^{3+}) occurs, which is detectable via MRI or optical CT scanning. Fricke gels are attractive for 3D dosimetry as they are easy to prepare and read out, are tissue equivalent over a very large photon energy range, and give reproducible results.

Unfortunately, the poor spatial stability of Fricke gels due to diffusion of Fe^{3+} ions constrains the permissible time between irradiation and read-out [1, 2]. This introduces an obvious practical inconvenience inhibiting the routine use of gels a clinical environment. Limited success in reducing Fe^{3+} diffusion rates is obtained using different gelling agents (gelatin, agarose, sephadex and poly-vinyl alcohol) and chelating agents such as xylenol orange [3, 4].

Chelators are organic chemicals that form two or more coordination bonds with a central metal ion. In xylenol orange Fricke gels, the oxidation of Fe^{2+} to Fe^{3+} induces an inherent increase in the electropositivity of the ion, allowing the co-ordination of the Fe^{3+} ion by the xylenol orange molecule. Upon this coordination, the Fe^{3+} ion bound to xylenol orange is no longer free to move throughout the gel matrix. As such, any subsequent diffusion of dose information is via movement of the much larger ferric-xylenol orange molecule.

To date, the best Fricke gel diffusion results have been obtained by the poly-vinyl alcohol (PVA) xylenol orange Fricke dosimeters proposed by Chu *et al* [5] Their work reports a diffusion coefficient of 0.14 mm^2 h^{-1}, about one order of magnitude less than that of conventional Fricke gels and about half of that of the agarose and gelatin gels with chelating agents [3, 4]. Here, we present a modification to the PVA xylenol orange Fricke gel that reduces diffusion by partially bonding xylenol orange to the PVA molecule.

2. Methodology

2.1 Gel preparation

All chemicals used for synthesis and gel mixing were purchased from Sigma Aldrich, Sydney. Prior to gel mixing, xylenol orange was chemically linked to PVA (XO-PVA). The final gel formulation was: 20% w/v XO-PVA, 50 mM sulfuric acid and 0.4 mM ferrous sulphate. A 24% w/v XO-PVA solution was made in a flask of 50 mM sulfuric acid while being stirred and heated on a hotplate to 65 °C. Once all XO-PVA was in the reaction vessel, the solution was raised to a temperature of 95 °C with a stopper used to minimize evaporation. Meanwhile, a solution containing 2.4 mM ferrous sulphate in 50 mM sulfuric acid was prepared. The XO-PVA was fully dissolved after 3 hours, indicated by a translucent solution, after which the temperature was dropped to 55 °C. Subsequently, five parts of the XO-PVA solution was mixed with one part of the ferrous sulphate solution to make a final 0.4 mM ferrous ion concentration in a 20% XO-PVA solution. Stirring of this mixture was continued for 30 min before the gel was poured into 1 cm plastic cuvettes and stored at 5 °C. For comparative measurements, the original PVA-FX hydrogel was also made using the method outlined in Chu *et al.* (with 20% PVA, 0.4 mM ferrous sulphate and 0.4 mM xylenol orange) [5].

2.2 Gel Irradiation

Gels were irradiated using a 6 MV photon beam from a Varian EX Clinac. All gel irradiations were performed in a water tank with 9 cm Solid Water and 1 cm Bolus backscatter layers to ensure dose homogeneity. All irradiations were performed with gel samples submersed at a depth of 1 cm with an SSD of 100 cm. For dose response measurements, gel cuvettes were irradiated with 0, 1, 5, 15, and 30 Gy. To perform diffusion measurements, half of each gel cuvette was irradiated with 30 Gy while the other half was shielded by shutting the lower jaw to the central axis and placing a 10 cm lead block 1mm over the light field edge; minimizing the half field penumbra.

2.3 Gel Read-out

To maximise signal to noise ratios and scanning resolution, the optical densities (ODs) of the gels were measured using the green channel of an Epson dual-layer flatbed film scanner. All OD values were obtained through the 1 cm path length defined by the cuvette dimensions with an imaging resolution of 266 dpi.

2.4 Diffusion Measurements

To quantify diffusion rates, the method outlined by Kron *et al.* was employed [3]. OD profiles were collected at varying time intervals between 1.5 and 112.5 hours after irradiation. These diffusion profiles were fit to equation (1):

$$\square = \square_0 + \frac{1}{2}(\square_1 - \square_0)\left[1 + \frac{(\square - \square_0)}{\sqrt{(\square - \square_0)^2 + \square}}\right] \quad (1)$$

Where Y is the measured OD at the position X, X_0 is the horizontal shift of the inflection point, Y_0 and Y_1 are the minimum and maximum values of Y, and n is the curvature parameter that characterises the slope of the inflection point. As demonstrated by Kron *et al*, a plot of n versus time after irradiation is linear and when the factor 0.212 is multiplied by its slope, the diffusion coefficient, D ($mm^2\ h^{-1}$) is obtained.

3. Results and Discussion

To highlight the reduction in diffusion of XO-PVA gel, figure 1 compares two OD profiles of each gel 72 hours apart. Formation of gel using XO-PVA resulted in increased scatter and consequently more noise was encountered in its OD profiles. Despite this, a clear reduction in the blurring effect across the profiles is present. The diffusion coefficient, measured for the PVA-FX hydrogel matched results

reported by Chu *et al.*, with D = 0.144 ± 0.002 mm^2 h^{-1}. The XO-PVA formulation yielded a diffusion rate of 0.133 ± 0.004 mm^2 h^{-1}, an 8% improvement on the existing PVA-FX gel, and the lowest reported thus far for any Fricke gel.

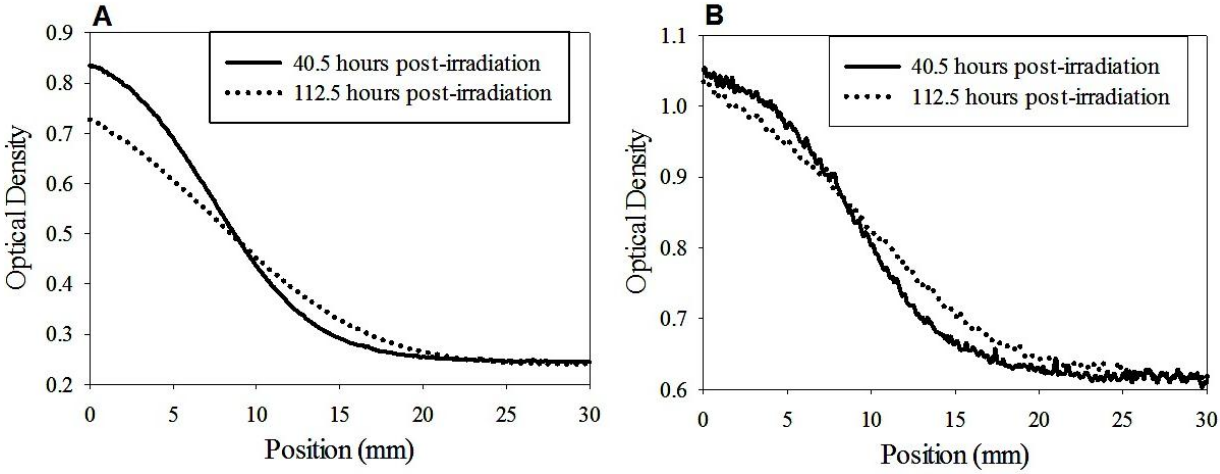

Figure 1. Optical density profiles in half-irradiated cuvettes 40.5 and 112.5 hours post irradiation with air reference for (a) PVA-FX gel and (b) XO-PVA gel.

The mechanism governing the decreased diffusion rate in XO-PVA gel is partial bonding of xylenol orange to PVA. Ferric-xylenol orange molecules bound to the PVA gel matrix are unable to diffuse. Therefore the diffusion measured in this gel can be attributed to the fraction of xylenol orange molecules, which did not successfully bond to PVA during the preparation of XO-PVA. To further improve this result, more efficient methods of bonding xylenol orange to PVA must be explored.

In figure 2, the dose response of both gels is presented. Both show a linear dose response for doses ranging from 0 to 30 Gy. It must be noted that the initial OD of the XO-PVA is almost three times that of the original PVA-FX gel. Our measurements showed a 30% reduction in the dose response of the XO-PVA gel with an OD dose sensitivity of 0.014 Gy^{-1} and a corresponding optical attenuation coefficient of 0.032 cm^{-1} Gy^{-1}. The uncertainties displayed in figure 2 were calculated by propagating standard deviations of pre- and post-scan pixel values through OD calculations. Referring to this data, it is apparent that these gel dosimeters are capable of resolving single Gy doses, within uncertainty.

4. Conclusions

Preparing gels from xylenol orange functionalised PVA yields a dosimeter with an OD dose sensitivity of 0.014 Gy^{-1} and a diffusion rate of 0.133 mm^2 h^{-1}; an 8% reduction from PVA-FX gels with the same PVA and ferrous ion concentration. Adding approximately 1 hour to the practical time between irradiation and readout, this improvement, although incremental is an important first step in the exploration of functionalised polymers in 3D hydrogel dosimeters. To improve on these results, more efficient methods of synthesising XO-PVA are to be investigated. More broadly, the bonding of reporter molecules to gelling agents may be a general chemical approach to elimination of diffusion in Fricke gels.

5. Acknowledgments

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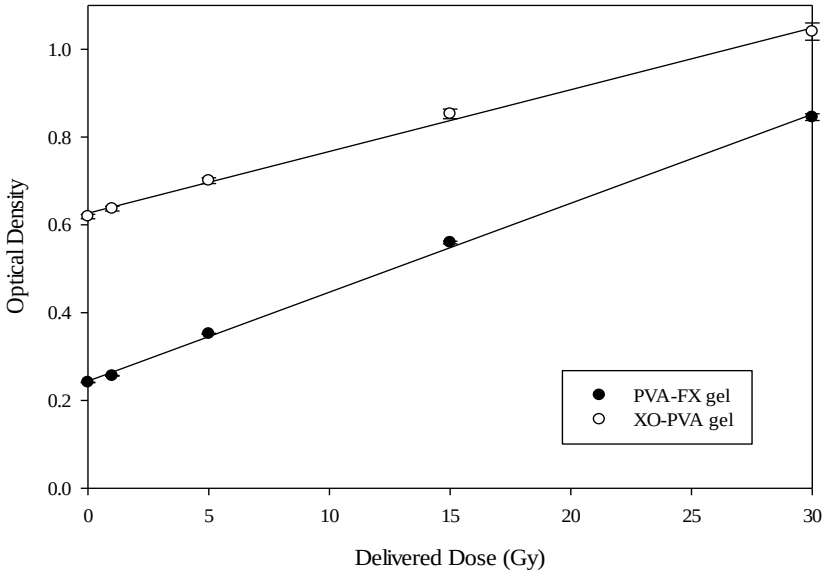

Figure 2. Radiochromic dose response of PVA-FX gel and XO-PVA gel.

6. References

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