Threshold dose effect in FXG gels: real or apparent?

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1. Introduction
An earlier study with radiochromic ferrous xylenol orange gelatin (FXG) gels, reported that the dose response of gels irradiated with a 12 MeV electron beam (6 x 6 cm² field size, 100 SSD) changed with storage time (at 4°C) and revealed inconsistency with calibrated ion chamber data [1]. The varying dose response with storage time was believed to be caused by the auto-oxidation of Fe(II) to Fe(III) ions. Hence, it was hypothesized that a reproducible FXG gel dose response could be attained by pre-exposing the gels to a ‘priming’ dose as a substitute to natural auto-oxidation. To this end, dose fractionation experiments were conducted whereby the change in optical attenuation per unit dose interval was measured for two dose fractions [2]. In the first fraction, the change in attenuation coefficient ($\Delta \mu$) was measured with respect to the non-irradiated sample and for the second fraction, $\Delta \mu'$ was measured with respect to the first fraction irradiation (Figure 1a). The results showed a threshold dose in the first fraction while the second fraction irradiation demonstrated a linear response.

Figure 1. (a) Illustration of the dose fractionation experiment with 1 cm PMMA cuvettes. All $\mu$ values were referenced to water. (b) The dose response (at 589 nm) for the 1st and 2nd fraction irradiation of an FXG gel. A threshold dose of up to 0.5 Gy is observed in the 1st fraction irradiation of an FXG gel. The uncertainty in the measured values are within the size of the data points (also true for all remaining figures).
without an intercept (Figure 1b). Furthermore, it was found that the threshold dose could be removed by pre-irradiating the FXG gel dosimeter with a uniform ‘priming’ dose or by allowing natural auto-oxidation of Fe(II) to Fe(III) ions to occur over a period of weeks. If not accounted for, the threshold dose can lead to lost low dose information, inconsistencies in dose calibration and poor reproducibility if the intercept value is not a constant. The purpose of this present study was to identify the chemical and or physical mechanism responsible for the threshold dose and to control it in order to achieve better reproducibility and reliable calibration across the entire linear dose range.

2. Methods
A systemic investigation of the chemical causes of the threshold dose was performed. Specifically, two potential chemical sources were investigated: (1) impurities which could compete with Fe(II) ions and prevent the radioproduction of Fe(III) ions [3,4] and or (2) different chemical species produced at various dose levels, each having their characteristic absorption spectrum [5]. The procedure used for the manufacture, irradiation and absorbance spectroscopy of the FXG gels has been previously described [2]. Gel samples were prepared using three different supplies of xylene orange (XO): reagent grade Sigma, Aldrich and Sigma-Aldrich. Concentrations of ferrous ammonium sulfate, XO and sulfuric acid were varied to identify the source of impurities. Gelatin-free aqueous FX solutions and gel samples with varying concentrations of ferric ammonium sulphate (Sigma) were also prepared to determine how these affected the threshold dose value.

3. Results and Discussion
Within FXG gels made with XO supplied by Aldrich and Sigma-Aldrich, respectively, a threshold dose value of 0.5 ± 0.1 Gy was measured. The threshold dose value was lowered to 0.20 ± 0.05 Gy when a reagent grade supply of XO from Sigma was used. Gelatin-free FX solutions also exhibited a threshold dose (Figure 2a). There was no correlation between threshold dose and varying concentrations of ferrous ammonium sulfate and sulfuric acid. These results suggest that the chemical constituents per se are not responsible for the threshold dose. Reducing the concentration of XO from 0.05 to 0.025 mM lowered the threshold dose value to 0.11 ± 0.02 Gy. The threshold dose was also decreased by increasing the concentration of ferric ammonium sulphate. Using a ferric ammonium sulphate concentration of 7.5 μM reduced the threshold dose value to 0.04 +/- 0.03 Gy, effectively removing this troublesome effect. The decrease

![Figure 2](image-url)

**Figure 2.** (a) Gelatin-free aqueous FX solution dose response (1st fraction) for three different supplies of XO. (b) The apparent threshold dose effect is removed when measurements are taken at the shorter wavelength of 543 nm.
in threshold dose by either lowering the XO concentration or increasing the Fe(III) ion concentration can be explained by the creation of different Fe(III)$_i$:XO$_j$ complexes formed [5], depending on the dose level. At lower doses where the Fe(III) ion concentration produced is small, the probability of forming a single Fe(III)$_i$:XO$_j$ complex is high. At higher doses, more Fe(III) ions are produced and the probability of forming a double Fe(III)$_i$:XO$_j$ complex increases. Each complex produces its characteristic optical absorption and at wavelengths of 589 nm the sensitivity is biased to the Fe(III)$_i$:XO$_j$ complex whereas at shorter wavelengths (eg. 543 nm) the sensitivity is biased to the Fe(III)$_i$:XO$_j$ complex. By increasing the Fe(III) ion concentration either at the time of making the gels, through accelerated (by pre-irradiation) or natural auto-oxidation (by time) of Fe(II) to Fe(III) ions, the probability of forming the double complex at smaller doses increases and the threshold dose is negated. The apparent threshold dose effect at 589 nm can be removed by reducing the concentration of XO and shifting the equilibrium concentrations to favour the production of Fe(III)$_i$:XO$_j$. At lower doses the concentration of Fe(III) ions becomes much higher compared to that of XO. Thus, the probability of forming the Fe(III)$_i$:XO$_j$ complex increases and can be detected with good sensitivity at 589 nm.

The threshold dose effect can also be avoided by using wavelengths below 589 nm in order to only detect the single Fe(III)$_i$:XO$_j$ complex. Figure 2b shows the results of measuring the FXG gel dose response at 543 nm and as expected there is no threshold dose since Fe(III)$_i$:XO$_j$ is produced before Fe(III)$_i$:XO$_j$. This confirms that the threshold dose stems from the duality of chemical species formed in FXG gels and the sensitivity to detecting these species using spectroscopy at suboptimal wavelength. In order to achieve the most accurate dose calibration, a multi-component spectral analysis of FXG gels should be performed at varying dose levels and the optimal wavelength selected for quantitative and reproducible optical CT scanning of these radiochromic gel dosimeters.

4. Conclusion
The results from this present study show that chemical impurities are not responsible for the threshold dose effect. The threshold dose is an apparent effect, that is, an artifact of the spectroscopic measurement of multiple Fe(III)$_i$:XO$_j$ species formed at varying dose levels and it can be avoided by selecting an optimal wavelength that is sensitive to detecting only the species of interest. By resolving the threshold dose issue, it will be possible to precisely and accurately verify doses in 3D over a wide range of dose gradients produced by modern radiotherapy machines (i.e. IMRT).

5. References
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