Characterization of a commercially-produced chemically stable Fricke gel dosimeter

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Abstract. The successful manufacturing of a modified Fricke gel with increased shelf life in a pilot scale (20-liter) commercial production facility is reported. The gels remained chemically stable and usable for over 30 days. Linear dose dependence was observed for cumulative doses up to 30 Gy. Dose-depth studies showed a good correlation between the experimental data and theoretical expectations, but the dose response appeared to be energy-dependent.

1. Introduction
The ferrous sulfate–gelatin dosimeter (Fricke gel) has been extensively studied over the past two and a half decades, but its applications remain mostly limited to academic research. Whereas this dosimeter is relatively easy and inexpensive to prepare, it has never been produced on a large scale or as a commercial product because of the perceived fast image deterioration due to fast iron diffusion post-irradiation [1, 2] and the short shelf-life of the Fricke gel [3]. Regarding the diffusion, a non-diffusing nanocomposite Fricke gel for ion dosimetry at high doses has recently been reported [4]. Furthermore, even when a diffusing Fricke gel is used, fast gel scanning modes such as cone beam optical computed tomography (CT) have been shown to yield reasonable dose distribution profiles [5]. Regarding the shelf-life, we have previously demonstrated that the ferrous iron auto-oxidation can be drastically reduced with appropriate additives [1]. This modified Fricke gel composition was licensed to Modus Medical Devices, Inc. (London, ON, Canada) in October 2013. Modus Medical has since assembled a pilot-scale, commercial gel manufacturing facility with a capacity of 20 liters per batch. Here, we report on the characterization of the dose response, stability and reusability of two of the first batches produced at the new facility.

2. Experimental

2.1. Gel manufacturing
A 20-litre jacketed process reactor was supplied by Chemglass Life Sciences (Vineland, NJ, USA), with built-in controlled stirring, aeration, temperature, and pH measurement. External peripherals, supplied by Cole-Parmer (Canada) and McMaster-Carr (USA), include: a high capacity heating/cooling circulating bath, liquid transfer peristaltic and gear pumps, tubing and miscellanea. In order to avoid contamination of the gels, all internal surfaces of the reactor and all other wetted parts were selected from acid- and oxidation-resistant medical- or food-grade materials: glass and
polytetrafluoroethylene (Teflon®) for gel processing; polypropylene and polyethylene terephthalate (PET) for liquid/gel storage; flexible polyvinyl chloride, Noreprene® and polyvinylidene fluoride (Kynar®) for tubing and miscellanea; and stainless steel (grade 316L) in the pump head of the gear pump. The stainless steel had minimal contact with the gel solution with a liquid residence time less than two seconds. The gear pump was pre-conditioned in order to remove easily leachable surface materials by circulating warm dilute sulfuric acid (10 wt.%) for a period of two hours.

The gel manufacturing procedure is a multistep process which was optimized for high efficiency and batch-to-batch consistency. The final manufacturing step, before the dispensing of the product into PET jars, was filtration of the gel solution through a 0.45 µm membrane capsule filter (AcroPak™ 500, Pall Corp., USA) for improved optical clarity. The jars were placed into a custom built 100-liter water bath, cooled gradually to gelation, and then refrigerated at 4-6 °C until further use.

2.2. Gel compositions and testing

Two batches of the modified Fricke gel [1] were prepared using 300 Bloom bovine bone gelatin (Rousselot International, Peabody, MA, USA), identical with the Eastman gelatin used in [5]. Deionized water, sulfuric acid (SA), glyoxal (Gx) and ferrous ammonium sulfate hexahydrate (FAS) were supplied by Caledon Labs (Georgetown, ON, Canada), xylenol orange (XO) was purchased from TCI America (Portland, OR, USA), and 4-nitro-1,10-phenanthroline (Nn) from Alfa Aesar (Ward Hill, MA, USA). All chemicals were of analytical or higher grade and used without further purification. The first batch (lot no.: H09) contained in mmol/L: SA:FAS:XO:Nn:Gx = 30:0.10:0.1:0.07:2. The second batch (lot no: H10) contained in mmol/L: SA:FAS:XO:Nn:Gx = 30:0.12:0.1:0.07:2. The higher iron concentration in H10 was used to increase the sensitivity of the gel. Both batches had 4 wt.% gelatin and were filled into 1-liter PET jars.

All irradiations were performed at the London Regional Cancer Program (LRCP) in London, ON, Canada. The H09 gels were used in a longitudinal study of the dose sensitivity and gel stability over 32 days using a cobalt-60 source (Eldorado 6, Atomic Energy of Canada Ltd.), that had an initial dose rate of 136 cGy.min

For each irradiation, a jar of gel was positioned vertically over the source, partially shielded with a 40 mm thick lead block and exposed to a 5 Gy dose. The jar was then rotated by 90° and exposed to a new 5 Gy dose (figure 1). On day 35 after preparation, five previously unused gels were exposed to uniform doses in the range from 1.25 to 20 Gy to confirm the linearity of the dose response.

The H10 gels were irradiated from above with square beams of photons (3×3 cm at 90 cm source-to-surface distance (SSD)) or electrons (4×4 cm at 100 cm SSD) on a Varian 21iX linear accelerator at the following energies: 6 and 10 MV (photons), 9, 12, 16 and 20 MeV (electrons). The centers of the beams were off-set from the center of the gel by 1 cm. The 6 MV dose depth curves were compared against the preliminary results from Monte-Carlo simulations of small field photon beams, courtesy of Kevin Jordan and Matt Mulligan at the LRCP. All scans were performed with a Vista15 cone beam optical scanner (Modus Medical Devices), with an amber LED source at 590 ±5 nm. Image processing was done using ImageJ 1.44 (National Institutes of Health, USA) and Matlab 7.9.0 (The Mathworks Inc.).

3. Results and discussions

Figure 1 shows the dose response behavior of the H09 gels over the course of 32 days, plotted as the change of attenuation (Δμ) versus the height of the gel. The left panel presents a typical example, where zone A received 10.0 Gy, zone D received the dose transmitted through the lead shield (approximately 0.8 Gy), while zones B and C received 5.0 Gy plus half of dose D. Note that at the bottom and top of the gels there are zones where the jar geometry and the scanner capabilities prevent exact attenuation measurements. Those zones are excluded from further analysis. Assuming linear dose dependence, the signals at A plus D should be equal to that of B plus C. The absolute error of linearity was generally less than 2×10⁻³ cm⁻¹, which is close to the noise level, measured as standard deviation at (1-2)×10⁻³ cm⁻¹. Over the course of two weeks, the same gel was re-irradiated the same
way three more times, maintaining linearity close to the noise level up to the third irradiation at day 11 (central panel). Six additional gels were irradiated at various time intervals up to 32 days after the batch was prepared (right panel). The error of linearity was close to the noise in all cases. The dose responses in the different gels were remarkably similar over the full course of the experiment, with the exception of Day 7. In that particular case, the temperature of the gel during irradiation may have played a role, as it had not been properly conditioned and cold Frick gel is known to be less sensitive [5]. In addition, the re-irradiation of the first gel on the same day did not yield an increased sensitivity (central panel) as expected based on previous experience. Four of the gels were irradiated multiple times (only one is shown here) and generally, in the follow-up irradiations, the gels exhibited higher sensitivity but the linearity of the dose response was maintained up to a cumulative dose of 30 Gy (central panel).

Figure 1. Dose responses of gels H09 over the course of a month. Left - single irradiation, center - multiple irradiations (10 Gy) of the same gel, right - first irradiations (10 Gy) of multiple gels.

On day 35 after the batch preparation, five gels were irradiated uniformly at increasing doses from 1.25 to 20 Gy. The light attenuation was in a linear dependence with the dose for all gel heights ($R^2 > 0.999$, data not shown). The dose sensitivity at 18 mm gel height was calculated to be $11.6 \times 10^{-3}$ Gy$^{-1}$ cm$^{-1}$ ($R^2 = 0.9999$). However, the absolute dose sensitivity was impossible to determine, as the surface at the bottom of the jar is concave and prevents accurate dose calculation when the gel is irradiated from below.

Dose response calibration and dose-depth curves were obtained from the H10 gels. Photon beams with known doses at 30 mm below the gel surface were used for calibration of the dose response (figure 2, left), obtaining a sensitivity of $19.5 \times 10^{-3}$ Gy$^{-1}$ cm$^{-1}$ with an excellent linearity ($R^2 > 0.9995$). Compared to H09 the sensitivity was higher, as expected due to the higher iron concentration. The experimental dose-depth distributions for the 6 MV photon beams correlated with the Monte Carlo simulations well with $R^2 > 0.99$ for all but the lowest dose (figure 2, center). It should be noted that the noise in the scans played a significant role, especially at the extreme top and bottom sections of the jars. Figure 2 (right) shows the dose-depth curves for the 10 MV photon beams and electrons beams at four energies. Unfortunately, by the time of the submission of this manuscript, we do not have complete modeling of the 10 MV dose depth curves, and the 10 MV data has not been correlated to modeling predictions. The calculated doses (calibrated with the 6 MV and 10 MV photon beams) fit...
well with the 9 and 12 MeV electron beams, the 16 and 20 MeV beams showed higher than expected responses, which may indicate an energy-dependent dose response. Further examination of that effect is required before we can arrive at any definitive conclusions.

![Graph showing dose response and depth curves in H10 gels]

**Figure 2.** Dose response (left) and dose-depth curves in the H10 gels (center and right); \(d_{\text{max}}\) refers the depth of maximum dose.

### 4. Conclusions
Considering the prolonged stability and sensitivity of the reported product, we believe that the commercial production facility at Modus Medical has had a successful start of operation. The gels showed excellent dose linearity (relative dose response) and consistent sensitivity for over 30 days. However, the absolute dose response was less stable and is possibly energy-dependent. Future product development will focus on examining these effects, as well as minimizing the noise in the gel scans.

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### 6. References
[1] Harris P J et al 1996 *Phys. Med. Biol.* 41 1745
[2] Baldock C et al 2001 *Australas. Phys. Eng. Sci.* 24 19
[3] Penev K I et al 2013 *Phys. Med. Biol.* 58 1823
[4] Maeyamaa T et al 2014 *Rad. Phys. Chem.* 96 92
[5] Olding T et al 2010 *J. Phys.: Conf. Ser.* 250 012028