Initial performance evaluation of a 3D gel dosimeter based on modified tetrazolium compounds

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Abstract. Tetrazolium-based 3D gellan gum gel dosimeters have been reported previously and tested at several sites. They show no image diffusion and excellent stability; however, the dose sensitivity of the current commercial product, ClearView™, is relatively low for routine clinical applications. Here we report initial testing of a second generation product with increased sensitivity and retained non-diffusive properties. This formulation has a 25% increase in sensitivity relative to ClearView™. However, the sample has a higher initial attenuation and the background attenuation increases faster than ClearView™. The composition was tested in a 1-liter sealed container using a 2x2 cm, 6MV, x-ray beam, and show agreement between Monte Carlo simulation and measurements.

1. Introduction

Non-diffusing radiochromic hydrogels based on the reduction of colourless and water-soluble bisnitrotetrazolium chloride (BNC) to highly-coloured, water-insoluble formazan dye in a gellan gum matrix has been previously investigated as a potential robust hydrogel that can be shipped globally [1]. This material has been evaluated by several research groups and early formulations were found to have dose rate effects that limited quantitative 3D radiation dosimetry [2, 3]. Current formulations have higher concentrations of BNC (from 0.1 to 0.25 mM) and dose rate limitations appear to have been eliminated (in-house results, manuscript in preparation). While the current formulation is promising, higher dose sensitivity is preferred for many applications. Several new tetrazolium salts have been synthesized to achieve a more sensitive dosimeter (manuscript in preparation).

Two new tetrazolium compounds with increased dose sensitivity, based on 1 cm cuvette measurements, were selected for evaluation in one litre volumes for 3D dosimeter performance.
2. Methods

Gel samples were prepared to fill 10 cm diameter custom cylindrical PETE vessels. Optical cone beam computed tomography scans were performed with a Vista16 scanner provided by ModusQA with a 530 nm LED light source.

2.1. Gel preparation

Hydrogels formulations were similar to previously reported ClearView™ gels with the substitution of the dye precursor 0.25 mM of either 2-(benzothiazole-2-yl)-3-nitrophenyl-5-phenyl-2H-tetrazolium chloride (BtNP) or 2-(benzothiazole-2-yl)-3-(1-naphthyl)-5-phenyl-2H-tetrazolium chloride (BtNpP), synthesized in house. The gels contain 1.25% gellan gum and 10.2% propylene glycol by mass and have a mass density of ~1.02 g cm\(^{-3}\) and optical cone-beam computed tomography (CBCT) scans were performed in aqueous solutions containing 12% propylene glycol. Sample vessels were custom cylinders, constructed in house from 0.25 mm thick PETE film. The vessel fill port was sealed with aluminized tape to make an oxygen-impermeable vessel. Samples were stored at 21 °C in the dark.

2.1.1. Optical CT scanning

Samples were scanned with a Vista16 optical CBCT scanner, modified by placing a 1.5 cm diameter aperture at the diffuse source to reduce stray light. A 12% propylene glycol - 88% water solution was placed in the scanner aquarium to maximize FOV for optical CT scanning. After placing the sample in the scanner a 15-minute interval was used to let the aquarium liquid to relax to an optically uniform condition. Pre-irradiation and post-irradiation scans consisted of a 1000 projections acquired over 360 degree rotations and reconstructed at 0.05 cm\(^{-3}\) voxel size with OSC-TV iterative algorithm within the VistaScan software package.

2.1.2. Irradiation

A Varian 21iX series, medical, linear accelerator was used to irradiate samples. The AP beam was incident on the base of the upside-down gel. Beam conditions: 6 MV, dose rate 400 MU/minute, dose 2642 MU (~ 20 Gy), SSD = 90 cm, jaws set to 2x2 cm.

3. Results

The first gel, containing BtNP was formed yellow but turned brown within a day of preparation. It contained nonuniformities in refractive index that resulted in a low transmission, scattering material that produced noisy reconstructions. The second sample contained BtNpP and resulted in a clear, yellow gel that is the focus of this report. Immediately following irradiation, a purple image of the dose distribution was formed. The absorption spectrum maximum is at approximately 510 nm, and is included in the results presented in another paper at this conference, Penev et al. At the wavelength of interest (530 nm), dose sensitivity increase of 25% was recorded compared to current ClearView™ formulations from ModusQA. Figure 1 shows the normalized mean central depth dose for beam irradiations 2 and 4 days after gel preparation and corresponding Monte Carlo calculation. The attenuation coefficient plots versus depth were the same, indicating no change in dose sensitivity from top to base of gel over the 2 day period at 21 °C.

Figure 2 compares jaw-defined x profile at depth of maximum dose in gel versus Monte Carlo calculation at same depth in water. Both curves represent the average of 10 profiles from -0.25 to 0.25 cm in y direction. Each point can also be considered as a voxel size (x,y,z) = (0.05x0.5x0.05 cm). Each curve was normalized at beam centre and a constant background was subtracted from the gel reconstruction. Note the small under-response of gel at -2.5 cm is likely an artifact due to proximity of vessel wall.
Figure 1. Plot of normalized dose for BtNpP gel, 6 MV, 2x2 cm jaw defined, SSD= 90 cm, dose ~20 Gy. (solid line) irradiated 2 days post preparation, (dashed line) irradiated 4 days post preparation, (dotted line) Monte Carlo calculation.

Figure 2. Plot of x direction profiles at depth of 1.4 cm for 6 MV, SSD=90 cm, field size jaws=2x2 cm (at 100 cm). (circles) gel reconstruction, (solid line) Monte Carlo calculation, voxels size same.

4. Discussion
Agreement between Monte Carlo depth dose and gel reconstructions demonstrate uniform dose sensitivity for the bottom (beam entrance) to the top of the sample. Agreement between day 4 and day 2 indicate stability of the gel when stored in dark at 21 °C. Longer times were not evaluated due to observation of mould growth sites on day 4. It should be noted that the biological contamination issue can be addressed in large-scale manufacturing more easily than on the bench top by using clean manufacturing practices, and mould growth is not expected to occur in future samples. In contrast to the colourless ClearView™ gel based on BNC tetrazolium, the current formulation is yellow and the initial attenuation increases at a rate of 0.013 cm⁻¹ per day vs ~10⁻³ cm⁻¹ per day for ClearView™ gel. This initial background is likely related to the increased dose sensitivity. The gel and Monte Carlo beam
profiles are nearly the same providing a more stringent test of dose linearity, dose rate and energy independence of the gel formulation compared to central axis depth dose comparisons.

5. Summary
The BtNpP gel provides a 25% increased dose sensitivity compared to ClearView™ formulation and has an increasing background of 0.013 cm⁻¹ per day at 21 °C. Future work will include fine-tuning the compromise between sensitivity and background attenuation.

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7. References
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