Experimental properties of THPC based normoxic polyacrylamide gels for use in x-ray computed tomography gel dosimetry

A. Jirasek¹, M. Hilts², C. Shaw¹, and P. Baxter¹²

¹Dept. of Physics and Astronomy, University of Victoria and ²Dept. of Medical Physics, BC Cancer Agency - Vancouver Island Cancer Centre, Victoria, BC, Canada

1. Introduction
Of the antioxidants used to scavenge oxygen in polymer gel dosimeters, tetrakis(hydroxymethyl)phosphonium chloride (THPC) has been shown to hold great promise due to its rapid oxygen scavenging abilities [1]. However, there is evidence that the dose sensitivity of THPC based normoxic polyacrylamide gels (NPAG) is less than that of PAG manufactured under anoxic conditions [2]. The aim of the present study is to investigate the effects of THPC on the experimental properties of NPAG. Specifically we: (1) assess the use of THPC as an anti-oxidant for x-ray CT PAGAT dosimetry by investigating dose response reproducibility and stability, and optimal THPC concentration for maximum dose sensitivity while ensuring no O₂ inhibition; (2) investigate the reactions of THPC with gel constituents; (3) describe the reaction mechanisms of THPC in PAGAT polymer gels; (4) assess the effects of THPC on O₂ diffusion through the polymer gel.

2. Materials and Methods

2.1. Gel Manufacture
All gels were composed of 3% (by weight) acrylamide, 3% N, N’ methylene bis-acrylamide, 5% gelatin, 89% deionized water [3-4]. The quantity of hydroxymethyl phosphonium chloride (THPC) was varied as needed (2–100 mM). Gels were transferred to thin-walled pyrex NMR sample tubes for Raman spectroscopic analysis or plastic scintillation vials for x-ray CT imaging.

2.2. Gel Irradiation
Gels were irradiated to uniform doses between 0-20 Gy in purpose-built acrylic phantoms (described previously [3-4]) utilizing the 6 MV beam from a Varian 21X Clinac (Varian Assoc., Palo Alto, CA) linear accelerator.

2.3. CT Imaging
CT Imaging was performed using a GE HiSpeed X/i CT Scanner with scan parameters: 140 kVp, 200 mAs, 1 cm slice thickness, and 16 slices per image. A background image was subtracted from each dataset.
2.4. Raman Spectroscopy
Raman spectroscopy on irradiated polymer gels was performed utilizing a 785 nm laser, fibre-optic light collection, a 0.75 m monochromater for light dispersion, and a CCD camera cooled to -75 °C for light collection.

3. Results and Discussion

3.1. THPC as an anti-oxidant in CT PAGAT dosimetry
Figure 1a illustrates the slopes of the dose response curves (0 – 16Gy) for PAGAT gels manufactured, irradiated, and CT scanned under identical conditions but on different days. Results show that the reproducibility of the PAGAT gel response is typically within ± 0.01 H Gy\(^{-1}\) and is comparable to that of traditional PAG dosimeters. Note the large difference in absolute dose response (0.32 ± 0.01 H Gy\(^{-1}\) for PAGAT versus 0.83 ± 0.03 H Gy\(^{-1}\) for PAG). Possible reasons for this difference are described below.

Figure 1b illustrates the dose response of separate PAGAT gel batches irradiated 2 h, 6 h and 24 h post gel manufacture, all other experimental parameters being held constant. Results in figure 1b show that the reproducibility of PAGAT gels irradiated at moderate times post gel manufacture is excellent. Once the time of irradiation post gel manufacture becomes too long (e.g., 24 h), O\(_2\) penetration through the plastic scintillation vials impedes polymerization and contaminates the dose response.

Figure 2. Slopes of the dose response curves for gels with varying [THPC].
Figure 1c illustrates the CT dose response of the same PAGAT gel imaged 1 day and 5 days post gel irradiation. Results indicate that PAGAT gel stability for x-ray CT scanning is excellent, with no alterations to the dose response occurring over the tested time frames.

Figure 2 illustrates the slopes of the dose response curves for a range of [THPC]. The figure indicates that gel dose response slope achieves a maximum of \(0.8 \pm 0.3 \text{ H Gy}^{-1}\) at 4 mM [THPC] and then decreases to \(0.36 \pm 0.04 \text{ H Gy}^{-1}\) at 4.625 mM [THPC]. Beyond 4.625 mM the slope of the gel dose response curve decreases slightly as [THPC] increases, reaching a minimum of \(0.29 \pm 0.01 \text{ H Gy}^{-1}\) at 15 mM [THPC]. However, below 4.5 mM [THPC] gel dose responses are O\(_2\) inhibited at low doses.

3.2. Reactions of THPC with gel constituents
Even for THPC concentrations of <5 mM, after all O\(_2\) has been scavenged from the gel, there may be unreacted THPC remaining in the solution. Hence, it is possible that THPC may react with other constituents of the polymer gels, thereby affecting the temporal stability and dose response of the dosimeters. Possible reactions are described below.

3.3. Acrylamide and Bis-Acrylamide
Figure 3(a) illustrates the intensities of the Raman vinyl CH bending mode of acrylamide in an unirradiated solution of 6% acrylamide, deionized water, and with differing concentrations of THPC. As can be seen from the figure, there is negligible change in the acrylamide peak intensity as more THPC is added to the solution. Hence, no, or absolutely minimal, reactions of THPC with acrylamide are occurring in unirradiated PAGAT gels. Similar results are found for bis-acrylamide (figure 3b).

3.4. Gelatin
Figure 3c illustrates Raman spectra acquired on solutions of 5% gelatin, water, and either 0 mM or 100 mM THPC. Figure 3c illustrates a clear decrease in gelatin band intensity upon the addition of THPC to the solution, suggesting a definitive chemical change within the gelatin solution. This is further highlighted below.

3.5. Reaction mechanisms of THPC

\[ (\text{HOCH}_2)_4 \text{PCl} \cdot (\text{HOCH}_2)_4 \text{POH} + \text{HCl} \]
\[ \text{HOCH}_2)_4 \text{POH} \cdot (\text{HOCH}_2)_4 \text{P} + \text{HCHO} + \text{H}_2\text{O} \]

It is the THP which can scavenge O\(_2\) through

\[ (\text{HOCH}_2)_4 \text{P} + 0.5\text{O}_2 \cdot (\text{HOCH}_2)_4 \text{P} = \text{O} \]

*Gelatin.* Gelatin is a single or multistranded polypeptide chain containing groups of amino acids. These amino acids are typically linked together in several hundred units and in helical form to give the gelatin strands. Reeves and Guthrie (1956) have shown that THPC can react with and polymerize both primary and secondary amines. They report that reactions of monomeric amines and THPC at room temperature are exothermic and take place readily [6]. For example, in the case of arginine, THPC+Arg would yield structures as in scheme 1. Hence, the reduction of THPC can then allow THPC to react with moieties on the gelatin chains to further increase the coagulation and cross-linking of the gelatin.
3.6. Oxygen Diffusion
The increased crosslinking due to the inclusion of THPC affects the rate of \( O_2 \) diffusion through polymer gel. Figure 4 illustrates the differential rates of \( O_2 \) diffusion for gels manufactured with varying [THPC]. This effect has implications for the timescales required to render gels inactive through exposure to oxygen.

4. Conclusion
PAGAT gels exhibit reproducible and stable dose response characteristics when imaged with x-ray CT, however CT dose response sensitivity is lower than for anoxic PAG. THPC reactions with gelatin are possible and increase the crosslinking of the gelatin matrix. This affects the rate of oxygen diffusion through the polymer gels.

5. References
[1] De Deene Y, Hurley C, Venning A, Vergote K, Mather M, Healy B J and Baldock C 2002 A basic study of some normoxic polymer gel dosimeters Phys. Med. Biol. 47 3441-3463
[2] Brindha S, Venning A, Hill B and Baldock C 2004 Experimental study of attenuation properties of normoxic polymer gel dosimeters Phys. Med. Biol. 49 N363-N361
[3] Hilts M, Jirasek A and Duzenli C 2004 Effects of gel composition on the radiation induced density change in PAG polymer gel dosimeters: a model and experimental investigations
[4] Jirasek A and Duzenli C 2001 Phys. Med. Biol. 46 1949-1961

[5] Vullo, W J 1968 Studies concerning neutralization of tetrakis(hydroxymethyl)phosphonium chloride and reaction of tris(hydroxymethyl)phosphine with formaldehyde J. Org. Chem. 33 3665-3667

[6] Reeves W and Guthrie J D 1956 Intermediate for flame resistant polymers: reaction of tetrakis(hydroxymethyl) phosphonium chloride Indust. Eng. Chem. 48 64-67