Preliminary study of a normoxic PAG gel dosimeter with tetrakis (hydroxymethyl) phosphonium chloride as an anti-oxidant

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1. Introduction

A study of the normoxic MAGIC polymer gel dosimeter and the role of the different component chemicals was previously published [1]. The concentration of the different chemicals was varied and, using MRI, the optimal formulation to give the maximum R2-dose response of the polymer gel upon irradiation was determined. The use of anti-oxidants such as tetrakis (hydroxymethyl) phosphonium chloride (THP) and N-acetyl-cysteine were found to be effective at scavenging oxygen and the rate of which was dependent upon the concentration. THP was found to have the highest reaction rate and also increased the dose sensitivity of the polymer gel. A new normoxic polymer gel formulation consisting of methacrylic acid, gelatin and THP, named MAGAT was investigated. The previously investigated hypoxic PAG [6] manufactured with the anti-oxidant ascorbic acid, named PAGAS was investigated. However, it was found that ascorbic acid was very slow at scavenging oxygen within the polymer gel system and further to this only a small response was observed over the large range of doses investigated.

A preliminary investigation is reported using both MRI and CT evaluation techniques of the hypoxic PAG formulation combined with the anti-oxidant THP in order to create a normoxic PAG polymer gel dosimeter. This formulation has been named PAGAT (polyacrylamide, gelatin and THP) polymer gel dosimeter.

2. Materials and methods

The PAGAT polymer gel formulation by % mass consisted of 3% N,N’-methylene-bisacrylamide (bis), 3% acrylamide (AA), 5% gelatin (300 bloom) and 89% ultra-pure water and 10 mM THP. All components were mixed on the bench top under a fume hood. The gelatin was left to soak in ultra-pure water for 10 minutes before heating commenced. The gel was heated to 48 °C and then bis was added and stirred until dissolved. The AA was added and then finally THP. When all ingredients were thoroughly mixed the polymer gel was poured into 15, 10 ml glass screw top calibration vials of
diameter 1.7 cm and length 4.3 cm and also poured into 30, 25 ml plastic screw top vials of diameter 2.4 cm and length 5.6 cm. The total manufacturing time was less than 1 hour.

Irradiation was conducted 3 hours post-manufacture using a Gammacell 200 60Co irradiation facility. The plastic vials were separated into two batches of 15 and then the glass and plastic vials were irradiated to a range of doses up to 40 Gy.

The polymer gel dosimeters in glass and one of the batches of plastic vials were imaged in a Siemens Symphony 1.5 Tesla clinical MRI scanner using a whole body coil and a receive only head coil. T2 weighted imaging was performed using a standard Siemens 32-echo pulse sequence with TE of 30 ms, TR of 3000 ms, slice thickness of 10 mm, FOV of 200 mm in both the frequency and phase encoding directions and with 1 acquisition. The vials of polymer gels were imaged on each of the first four days post-irradiation and again on the seventh and ninth days post-irradiation. The images were transferred to a personnel computer where T2 and R2 maps were computed using modified radiotherapy gel dosimetry image processing software [2] coded in MATLAB™ (The Math Works, Inc). The mean T2 value of each vial was plotted as a function of dose with the quasi-linear section being evaluated for R2-dose sensitivity.

The remaining 15 plastic vials of polymer gel dosimeter were imaged using a helical Toshiba Aquilion CT scanner 3 days post-irradiation. The vials were placed in a 25 cm external diameter water-filled phantom made from perspex and held in place by a thin perspex insert. The water phantom was imaged without the vials in place to acquire a background image which was subtracted from the imaged vials to remove artefacts. The vials were imaged with 135 kVp, 400 mA, 1000 ms and a slice thickness of 8 mm and a FOV diameter of 320 mm. To increase the signal-to-noise ratio 50 slices were acquired for each image set and averaged. These images were also processed using the modified radiotherapy gel dosimetry image processing software coded in MATLAB™. The mean CT number or Hounsfield unit (H) of each vial was plotted as a function of dose with the quasi-linear section being evaluated for H-dose sensitivity.

3. Results and discussion

Figures 1 and 2 show R2 as a function of dose up to 40 Gy for the PAGAT gel dosimeter measured in both glass and plastic vials respectively. The dose response curves were fitted with a bi-exponential curve. The quasi-linear region of the R2-dose response curve is observed up to approximately 6 Gy in both figures. This quasi-linear region is approximately 2 Gy less in range compared with results obtained in studies of hypoxic PAG gel compositions without the oxygen scavenger THP present [3–6].

![Figure 1. R2 versus dose for glass vials.](image1)

![Figure 2. R2 versus dose for plastic vials.](image2)
Table 1 lists the change in the R2-dose sensitivity and the R2(0) intercept with post-irradiation time for the quasi-linear regions for the glass and plastic vials shown in figures 1 and 2. Over the quasi-linear range, the change in R2 is approximately 1.2 s\(^{-1}\) for both vial types with both the R2-dose sensitivity and R2\(_0\) continuing to increase up to 202 hours post-irradiation. The R2-dose sensitivity of the PAGAT polymer gel was (0.197 ± 0.004) s\(^{-1}\)Gy\(^{-1}\) in glass vials and (0.192 ± 0.004) s\(^{-1}\)Gy\(^{-1}\) in plastic vials at 202 hours post-irradiation compared with (0.331 ± 0.012) s\(^{-1}\)Gy\(^{-1}\) for previous studies of hypoxic PAG formulations [5]. Both figures indicate the PAGAT dosimeter had not reached steadystate by 202 hours post-irradiation. For the hypoxic PAG dosimeter, the post-irradiation polymerisation tended to steady state after a period of approximately 12 hours post-irradiation [5]. Further studies are required to investigate the nature of the observed temporal changes in the PAGAT dosimeter.

| Imaging time post-irradiation [hours] | Glass vials | Plastic vials |
|--------------------------------------|-------------|---------------|
|                                      | R2-dose sensitivity [s^{-1}.Gy^{-1}] | R2\(_0\) [s^{-1}] | R2-dose sensitivity [s^{-1}.Gy^{-1}] | R2\(_0\) [s^{-1}] |
| 10                                   | 0.177 ± 0.003 | 0.888 ± 0.009 | 0.167 ± 0.003 | 0.848 ± 0.012 |
| 34                                   | 0.195 ± 0.003 | 0.980 ± 0.010 | 0.189 ± 0.003 | 0.978 ± 0.012 |
| 58                                   | 0.194 ± 0.003 | 1.045 ± 0.010 | 0.191 ± 0.004 | 1.060 ± 0.013 |
| 82                                   | 0.195 ± 0.003 | 1.078 ± 0.010 | 0.190 ± 0.003 | 1.099 ± 0.011 |
| 154                                  | 0.205 ± 0.004 | 1.169 ± 0.010 | 0.200 ± 0.004 | 1.202 ± 0.013 |
| 202                                  | 0.197 ± 0.004 | 1.185 ± 0.011 | 0.192 ± 0.004 | 1.219 ± 0.013 |

Figure 3 shows the X-ray CT H-dose response of the PAGAT polymer gel up to 40 Gy. The dose response curve was fitted with a bi-exponential curve. The H-dose sensitivity in the quasi-linear region was (0.70 ± 0.03) H Gy\(^{-1}\) compared with previous results of (0.86 ± 0.04) H Gy\(^{-1}\) [7] and (0.71 ± 0.02) H Gy\(^{-1}\) [8] obtained in studies of hypoxic PAG gel compositions without the oxygen scavenger THP.

![Figure 3. H versus dose for plastic vials.](image-url)
4. Conclusion

In this preliminary study the PAG polymer gel dosimeter has been combined with the anti-oxidant tetrakis (hydroxymethyl) phosphonium chloride. The polymer gel was manufactured upon the bench top in less than one hour and irradiated on the same day. PAGAT had a linear dose response up to 6 Gy using MRI evaluation and a R2-dose sensitivity comparable with other studies of hypoxic PAG. PAGAT had a linear dose response up to 10 Gy using CT evaluation and a H-dose sensitivity which compared favourably with previous studies of the hypoxic PAG.

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 3441–63
[2] Murry P and Baldock C 2000 Research software for MRI radiotherapy gel dosimetry Australas. Phys. Eng. Sci. Med. 23 44–51
[3] Baldock C, Lepage M, Bäck S Å J, Murry P, Jayasekera P M, Porter D and Kron T 2001 Dose resolution in radiotherapy polymer gel dosimetry: effect of echo spacing in MRI pulse sequence Phys. Med. Biol. 46 449–60
[4] Maryanski M J, Schulz R J, Ibott G S, Gatenby J C, Xie J, Horton D and Gore J C 1994 Magnetic resonance imaging of radiation dose distributions using a polymer-gel dosimeter Phys. Med. Biol. 39 1437–55
[5] Lepage M, Jayasekera P M, Bäck S Å J and Baldock C 2001 Dose resolution optimization of polymer gel dosimeters using different monomers Phys. Med. Biol. 46 2665–80
[6] Baldock C, Burford R P, Billingham N, Wagner G S, Patval S, Badawi R D and Keevil SF 1998 Experimental procedure for the manufacture and calibration of polyacrylamide gel (PAG) for magnetic resonance imaging (MRI) radiation dosimetry Phys. Med. Biol. 43 695–702
[7] Hilts M, Audet C, Duzenli C and Jirasek A 2000 Polymer gel dosimetry using x-ray computer tomography: a feasibility study Phys. Med. Biol. 45 2559–71
[8] Trapp J V, Bäck S Å J, Lepage M, Michael G and Baldock C 2001 An experimental study of the dose response of polymer gel dosimeters imaged with x-ray computed tomography Phys. Med. Biol. 46 2939–51