The response of PAG density to dose: a model and experimental investigations

M Hilts1,2, A Jirasek3 and C Duzenli1
1 Medical Physics, BC Cancer Agency – Vancouver Centre, Vancouver BC, Canada
2 Department of Physics and Astronomy, University of British Columbia, Vancouver, BC, Canada
3 Department of Chemistry, University of British Columbia, Vancouver, BC, Canada
E-mail: mhilts@bccancer.bc.ca

1. Introduction

X-ray computed tomography (CT) has emerged as a promising method of extracting three-dimensional (3D) dose information from polymer gel dosimeters [1,2]. CT gel dosimetry has many practical advantages: ease of use, relatively low cost and accessibility to cancer hospitals and has been shown to have clinical potential [3]. However, a primary disadvantage remains poor dose resolution due in part to the low sensitivity of CT contrast to dose. This CT contrast is the result of a small density change that occurs on polymerization [4] and advanced understanding of this density change is required in order to optimize gel sensitivity to CT. This work proposes a simple model that describes the radiation induced density change in polyacrylamide gel (PAG) as a function of polymer yield and an intrinsic density change that occurs, independent of polymer yield, on polymerization. Using this model in combination with experimental CT and Raman spectroscopy work, several fundamental properties of the PAG density response to dose are discovered. The result is a valuable framework on which to focus future developments of more sensitive CT polymer gel dosimetry systems.

2. A model of PAG density response to dose

For a given dose, the density change occurring in PAG (Δρ\text{gel}) can be expressed as a function of the weight fraction of polymer formed and an intrinsic density change (Δρ\text{polymer}) that occurs per weight fraction of monomer converted to polymer. Defining %P, analogous to %T, as the weight fraction of polymer formed in the gel, we can express the density change by

\[ \Delta \rho_{\text{gel}} = %P \cdot \Delta \rho_{\text{polymer}} \]  

(1)

For simplicity, %P will be referred to as polymer yield although this is not a true chemical yield.
At full polymerization nearly all the available monomer in a PAG system is consumed [5] and \( \%P = 0 \) for an unirradiated gel and \( \sim \%T \), as given in the initial gel composition \( (\%T_{0\text{Gy}}) \), for a fully polymerized gel. It follows that, for any dose, \( \%P \) can be expressed as a function of the fraction of polymer formed \( (f_p) \) and \( \%T_{0\text{Gy}} \):

\[
\%P = \%T_{0\text{Gy}} f_p
\]

where \( f_p \) is 0 for an unirradiated gel and 1 for a fully polymerized gel. \( f_p \) is related to the fraction of monomer remaining in the gel \( (f_m) \) by

\[
f_p = 1 - f_m
\]

where \( f_m \) is 1 for an unirradiated gel and 0 for a fully polymerized gel. Combining equations (1–3), the change in PAG density that occurs upon irradiation can be expressed as

\[
\Delta \rho_{gel} = \%T_{0\text{Gy}} (1 - f_m) \Delta \rho_{polymer}
\]

This equation indicates that for any dose the total PAG density change, \( \Delta \rho_{gel} \), depends on the amount of monomer in the initial PAG composition, \( \%T_{0\text{Gy}} \), the fraction of monomer consumed, \( f_m \), and an intrinsic density change that occurs per weight fraction conversion of monomer to polymer, \( \Delta \rho_{polymer} \). Using this model, the experimental investigations described below illuminate two important fundamental properties of the gel density dose response: (1) the dependence of \( \Delta \rho_{polymer} \) on PAG %C and (2) the linear relationship of \( \Delta \rho_{gel} \) with %T.

2. Experimental methods

All PAGs were manufactured using a standard procedure for which details are provided elsewhere [5]. Gels were made in 250 mL batches with varying %T and %C (all 5 % by weight gelatin) using electrophoresis grade acrylamide monomer, N,N’-methylene bisacrylamide (bis) crosslinker, gelatin (300 Bloom) (Sigma-Aldrich, St. Louis, USA) and deionized water. Gels were transferred, within an N\(_2\) environment, into 20 mL, high density polyethylene (HDPE) vials (Wheaton Science Products, Millville, USA), individually sealed in custom built 1” thick walled cylindrical acrylic phantoms, removed from the glovebox and set to gel in a refrigerator. The HDPE vials served to reduce CT scanning artifacts and provide rapid O\(_2\) diffusion into the gel post-polymerization and the acrylic phantoms provided an O\(_2\) barrier during polymerization and formed part of the irradiation phantom. Gels were irradiated ~3 hrs post-manufacture using 6 MV photons (CL21EX, Varian Medical Systems Inc., Palo Alto, USA) to uniform doses (2 to 20 Gy). One vial was left un-irradiated. All vials were exposed to oxygen ~ 15 hrs post-irradiation.

A HiSpeedCT/i CT scanner (GE Medical Systems, Milwaukee, USA) operating at 120 kV, 200 mAs, 25x25 cm\(^2\) field of view, 1 cm slice thickness and Standard reconstruction, was used for all gel imaging. The 10 vials for each batch of gel (0 to 20 Gy) were imaged simultaneously using a styrofoam phantom designed to improve the signal to noise ratio (SNR) from previous vial CT imaging techniques [2]. In addition, 16 images were averaged to increase SNR and a set of 10 unirradiated background gel vials were imaged and used to remove artifacts by background subtraction [1,2]. An example of a final image is shown in figure 1. Using MatLab (The Math Works Inc., Natick, USA), mean CT numbers \( (N_{CT}) \) were extracted from the centre of each vial (21x21 pixels) and, by subtracting \( N_{CT} \) for the 0 Gy vial, \( \Delta N_{CT} \) was calculated. From these results, changes in PAG density \( (\Delta \rho_{gel}) \) were calculated and dose responses
constructed for each gel formulation. Raman spectroscopic data used in this study is from previous work and details are provided elsewhere [5].

3. Results and discussion

3.1. ∆ρ\text{polymer} dependence on %C

The density dose response for PAGs of varying %C are shown in figure 2a. The 0 and 100 %C PAGs are 3 %T and the remaining gels are 6 %T. Qualitatively, the sensitivity and shape of the response depend strongly on PAG formulation. This is as expected since, as described by the model (equation (4)) these curves are dependent on both polymer yield and the intrinsic density change. The %P component of ∆ρ\text{gel} for these same gel formulations can determined from Raman data measuring $f_m$ (studies performed previously by this group), using equations (2) and (3). The result, shown in figure 2b, is as expected: higher yield for intermediate %C PAGs (30 and 50 %C) than for low or high %C PAGs. This result derives from $f_m$ and is explained qualitatively by considering the type of polymer formed [5].

![Figure 1. CT image of irradiated PAG vials.](image)

The effect of %C on ∆ρ\text{polymer} is isolated from the overall PAG density change (figure 2a) by applying the model (equation (1)) and using the polymer yield data in figure 2b. The results, shown in figure 2c, indicate that ∆ρ\text{polymer} is ~1.5 times greater for PAGs of low or high rather than intermediate %C.

Structurally this infers that ∆ρ\text{polymer} is larger on polymerization of linear or highly cross-linked polymer than on formation of a more web like polymer structure. This trend is opposite to that seen for polymer yield (figure 2b). It is possible that the increased density contributes to the low yield observed for the low and highly cross-linked PAGs. The implication of this result is that %P and ∆ρ\text{polymer} (equation 4) cannot be maximized simultaneously. However, intermediate %C PAGs show the greatest ∆ρ\text{gel} dose responses, indicating that %P dominates in determining overall PAG density change. As such, future efforts to increase the sensitivity of polymer gel to CT imaging should focus on increasing polymer yield rather than on maximizing the intrinsic density change.
Figure 2. The total density change ($\Delta \rho_{\text{gel}}$) (a), polymer yield (%P) (b) and intrinsic density change ($\Delta \rho_{\text{polymer}}$) (c) for PAGs of varying %C.

3.2. Linearity of $\Delta \rho_{\text{gel}}$ with %T

The $\Delta \rho_{\text{gel}}$ dose responses for 0 %C PAGs with 3 and 6 %T are shown in figure 3. The response of the 6 %T PAG is, within uncertainty, twice that of the 3 %T PAG, indicating that $\Delta \rho_{\text{gel}}$ is linear with %T.

Figure 3. Linearity of $\Delta \rho_{\text{gel}}$ with %T for a 0 %C PAG.

On examination of CT sensitivity data in a work by Trapp et al [2], this linearity with %T is also observed for 50 %C PAGs. This confirms our model and indicates that $f_m$ and $\Delta \rho_{\text{polymer}}$ (equation (4)) are governed by %C alone. In terms of increasing the sensitivity of polymer gel to CT scanning, %T should be maximized.
4. Conclusions

A model is developed that describes the density change occurring in irradiated PAG as a function of polymer yield ($\%P$) and an intrinsic density change that occurs on polymerization ($\Delta\rho_{\text{polymer}}$). Applied to experimental data, this model proved useful illuminating fundamental properties of PAG density dose response. These results provide a framework on which to focus future efforts to improve the sensitivity of CT polymer gel dosimetry.

References

[1]  Hilts M, Audet C, Duzenli C and Jirasek A 2000 Polymer gel dosimetry using x-ray computed tomography: a feasibility study **Phys. Med. Biol.** 45 2559–71
[2]  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
[3]  Audet C, Hilts M, Jirasek A and Duzenli C 2002 CT gel dosimetry technique: comparison of a planned and measured 3D stereotactic dose volume **J. Appl. Clin. Med. Phys.** 3 110–8
[4]  Trapp J V, Michael G, De Deene Y and Baldock C 2002 Attenuation of diagnostic energy photons by polymer gel dosimeters **Phys. Med. Biol.** 47 4247–58
[5]  Jirasek A I, Duzenli C, Audet C and Eldridge J 2001 Characterization of monomer/crosslinker consumption and polymer formation observed in FT-Raman spectra of irradiated polyacrylamide gels **Phys. Med. Biol.** 46 151–65