An overview of polymer gel dosimetry using x-ray CT

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1. Introduction

The use of x-ray computed tomography (CT) for the imaging of irradiated polymer gels was first introduced at the 1st international conference on radiotherapy gel dosimetry, DOSGEL99, and in a subsequent paper [1,2]. These works showed dose dependent contrast in CT images of irradiated polyacrylamide (PAG) gel, quantified a CT dose response for PAG gel and thereby established the potential of CT as an alternative to MRI and optical CT for gel read-out. The advantages of CT read-out are practical ones: accessibility of CT to clinical radiation therapy environments, ease and speed of image acquisition, and a CT dose response that is stable and relatively insensitive to environmental factors. However, significant drawbacks include a very low sensitivity of CT number (H) to dose (~1%) and the fact that the act of imaging with CT will impart additional dose to the gel. Recent work has focused on means of understanding and minimizing these drawbacks.

The review paper presented at Dosgel 2006 [3] provided a thorough summary of the state of knowledge in the field at that time, and covered the following topics: the fundamental x-ray CT properties of polymer gel, dose response characteristics, CT imaging considerations, image filtering for noise reduction and CT gel dosimetry applications. This review serves as an “update” to the 2006 review paper and highlights new work that has been completed since this time. The material of the 2006 review will be repeated here only in very brief summary, and readers are referred to the 2006 review paper for details. The new work discussed includes: (a) normoxic polyacrylamide gel dosimetry; (b) x-ray CT dose in CT gel dosimetry and (c) image filtering for improved dose resolution.

2. A brief review of X-ray CT imaging of polymer gel dosimeter basics

2.1. Fundamentals

A small density change occurs in polymer gel upon irradiation which thereby changes the gel’s x-ray attenuation ($\mu$) and therefore the CT number ($N_{CT}$) and results in dose dependent contrast observed in CT images of irradiated gel. This change in density with dose has been measured experimentally for both PAG and MAGIC gels [4,5]. A typical CT dose response is mono-exponential with a region that can be approximated as linear at lower doses (the “quasi-linear” region, frequently used for relative...
dosimetry). An example (PAG gel, 6%T, 50%C) is shown below (Figure 1). This figure also illustrates the excellent reproducibility in CT dose response.

![Figure 1: A typical CT dose response for polymer gel (formulation shown is PAG gel, 6%T, 50%C). Note the excellent dose response reproducibility. From [3].](image)

Gel formulation can affect the shape and dose range of CT dose response, as well as the extent (and in some cases existence) of a quasi-linear region [6-13]. A model has been developed which provides an understanding of how composition might affect the density change [6]. For a given dose, the measured gel density change (or change in $N_{CT}$) is the result of two factors: 1) the amount of polymer formed and 2) an intrinsic density change that occurs on conversion of monomer to polymer. For PAG gel, the intrinsic density change was found to vary with the type of polymer formed and hence with the relative fraction of cross-linker in the system. The amount of polymer formed increased linearly with the total fraction of monomer (%T). Hence scope exists for optimizing gel formulation to CT imaging.

2.2. CT imaging optimization

Selection of CT technique (kV, mAs) does not affect the sensitivity of polymer gel dose response, however tube temperature does have an effect and a CT scanner should be fully warmed up prior to imaging [1]. Scan technique does have a tremendous effect on image noise and hence dose resolution [10,14 - 16]. Table 1, below, summarizes the effect selectable imaging parameters have on image noise. Increasing kV, mAs, slice thickness, number of averages and pixel dimension (post-processing) all serve to reduce image noise. However, these means of noise reduction all come at a price. In selecting a protocol for CT imaging polymer gel one must consider requirements for dose resolution (i.e. image noise), imaging time and spatial resolution. The difficulty lies in the conflict between achieving low noise (high CT scanning technique, large slice thickness and pixel size) and achieving both high spatial resolution (thin slices and small pixel size) and short imaging times (fewer slices imaged, low scan technique and therefore reduced load on the x-ray tube) [15]. Compromise will always be required and the “optimum” imaging protocol will depend on each application.
Table 1: Factors affecting CT image noise. From [3].

| Factor affecting image noise (symbol) | Relationship to image noise ($\sigma_{CT}$) |
|---------------------------------------|-------------------------------------------|
| Phantom diameter ($d$)                | $\sigma_{CT} \propto d$                   |
| Tube voltage (kV)                     | $\sigma_{CT} \propto (kV)^{-1.4}$         |
| Tube current (mA)                     | $\sigma_{CT} \propto (mA)^{-0.5}$         |
| Slice scan time (s)                   | $\sigma_{CT} \propto s^{-0.5}$            |
| Number of averages (NAX)              | $\sigma_{CT} \propto (NAX)^{-0.5}$        |
| Pixel dimension ($\mu$)               | $\sigma_{CT} \propto e^{0.0} (or u^{-0.69})$ |
| Slice thickness ($h$)                 | $\sigma_{CT} \propto h^{-0.5}$            |

3. Normoxic polyacrylamide gel dosimetry

Traditionally, CT polymer gel dosimetry has been performed with anoxic polyacrylamide gel [1,7]. Recently, the technique has been extended to normoxic polyacrylamide gel (nPAG, [12]). Normoxic polyacrylamide x-ray CT gel dosimetry provides a reproducible, stable platform from which to undertake 3D dosimetry. Figure 2 illustrates the reproducibility in slope of a series of irradiated nPAG gels imaged with CT. Also shown are the comparable slopes for anoxic PAG. As can be seen, adding antioxidant, in this case tetrakis (hydroxymethyl) phosphonium chloride (THPC), reduces the overall dose sensitivity of the gel. nPAG CT gel sensitivity has been quoted at ~0.36 +/- 0.03 H/Gy [12, 9].

![Figure 2: Dose response reproducibility of nPAG with x-ray CT imaging. Also shown is the dose response reproducibility of anoxic PAG. From [12].](image)

Recently, efforts have been made to improve the overall dose sensitivity of polymer gels for readout with x-ray CT imaging. Koeva et al have investigated the use of bis-acrylamide co-solvents as a means of increasing the overall solubility limit of bis-acrylamide in the gel and hence increasing the dose sensitivity of the gel [17]. With no co-solvent, the solubility of bis-acrylamide in polymer gel is ~3% by weight. With bis-acrylamide co-solvent, the solubility limit can be increased to 10% (using isopropanol as co-solvent, [18]). Figure 3 illustrates the effects of adding increasing amounts of isopropanol to a N-isopropyl acrylamide gel containing 10% total monomer. Shown is the clear increase in dose sensitivity of polymer gel dosimetry using x-ray CT imaging. Bis-acrylamide co-solvent for increased dose response sensitivity has not, to date, been fully explored and offers excellent potential for improving the dose sensitivity performance of CT polymer gel dosimetry.
Figure 3: X-ray CT dose response for 10%, 50% C NIPAM/Bis dosimeters containing 0 (●), 10 (▲) and 30 (♦) wt% of isopropanol. An anoxic PAG dosimeter (6% T 50% C) (●) is included for comparison. From [17].

4. X-ray CT dose in imaged polymer gel dosimeters

A potential issue with utilising x-ray CT imaging with polymer gel dosimetry is the CT dose delivered to the gel during imaging, creating further polymerisation within the gel. CT dose inducing additional gel polymerisation can be particularly problematic in imaging protocols requiring a large number of image averages per slice. The effect of CT dose on gel polymerisation has been studied recently by [19]. Using a combination of CT dose measurements (with an ionisation chamber), CT imaging and Raman spectroscopic measurements, the CT-dose induced change in CT number for a range of imaging protocols and gel container sizes was reported. Table 2 shows the delivered CT dose and induced CT number ($\Delta N_{CT}$) in a range of imaging protocols. This study was performed for a polyacrylamide gel manufactured with tetrakis (hydroxymethyl) phosphonium chloride (THPC) as antioxidant, with a reported gel sensitivity of 0.36 ±/− 0.03 H/Gy.

As can be seen from table 2, induced $\Delta N_{CT}$ for all imaging protocols remains below the minimum detectable $\Delta N_{CT}$ of 0.2 H. For imaging protocols requiring large image averages (e.g. 64 averages) per slice, the $\Delta N_{CT}$ can exceed the minimum detectable limit (e.g. 0.5 H) and hence care must be taken to ensure that the gel is inactive prior to imaging. Of final note, the current literature contains results for only one type of gel (normoxic polyacrylamide gel). Recent efforts in the development of gels with increased sensitivity for CT imaging [17] will alter these results to some extent. Hence, future gel formulations will need to be tested for CT dose contamination.
5. Image filtering for signal enhancement in CT imaging or polymer gel dosimeters

A range of image filtering methods have been proposed for image enhancement in x-ray CT imaging of polymer gel dosimeters. We here review two of the most promising methods proposed to date, adaptive mean filtering and two point maximum entropy regularisation of CT images.

5.1. Adaptive filtering

Adaptive mean filtering utilizes local image statistics, within a given filter window (or kernel size, K), to determine the power of the filter. The filter is expressed as

\[
f(x,y) = g(x,y) - \frac{\sigma_N^2}{\sigma_L^2} \left[ g(x,y) - m_L \right]
\]  

(1)

where \(f(x,y)\) is the filtered image, \(g(x,y)\) is the original unfiltered image, \(\sigma_N^2\) is the local variance (within the filter window), \(\sigma_L^2\) is the image noise, \(m_L\) is the local mean value of the image. 

Table 2: CT dose and induced \(\Delta N_{CT}\) for a range of imaging protocols. From [19].

| Imaging protocol | Phantom         | kVp | mA s | Slice (mm) | Dose/image (cGy) | # Image averages | \(\Delta N_{CT}\) |
|------------------|-----------------|-----|------|------------|------------------|-----------------|------------------|
| Volumetric (CTDI)| 16 cm diam. (Center) | 120 | 200  | 2          | 3.38±0.14        | 16              | 0.105±0.001      |
|                  |                 |     |      | 5          | 3.4±0.1          | 16              | 0.105±0.001      |
|                  |                 |     |      | 10         | 3.4±0.1          | 16              | 0.107±0.001      |
|                  | 16 cm diam. (Edge) | 120 | 200  | 2          | 3.5±0.1          | 16              | 0.109±0.001      |
|                  |                 |     |      | 5          | 3.5±0.1          | 16              | 0.110±0.001      |
|                  |                 |     |      | 10         | 3.6±0.1          | 16              | 0.111±0.001      |
|                  | 16 cm diam. (Center) | 140 | 200  | 2          | 4.4±0.2          | 16              | 0.136±0.002      |
|                  |                 |     |      | 5          | 4.4±0.2          | 16              | 0.136±0.002      |
|                  |                 |     |      | 10         | 4.5±0.2          | 16              | 0.138±0.002      |
|                  | 16 cm diam. (Edge) | 140 | 200  | 2          | 4.5±0.2          | 16              | 0.139±0.002      |
|                  |                 |     |      | 5          | 4.5±0.2          | 16              | 0.139±0.002      |
|                  |                 |     |      | 10         | 4.6±0.2          | 16              | 0.141±0.002      |
| Single slice (PD)| 16 cm diam. (Center) | 120 | 200  | 2          | 0.70±0.05        | 32              | 0.043±0.0002     |
|                  |                 |     |      | 5          | 0.91±0.06        | 32              | 0.056±0.0004     |
|                  |                 |     |      | 10         | 1.07±0.07        | 32              | 0.066±0.001      |
|                  | 16 cm diam. (Edge) | 120 | 200  | 2          | 1.6±0.1          | 32              | 0.099±0.001      |
|                  |                 |     |      | 5          | 1.7±0.1          | 32              | 0.107±0.001      |
|                  |                 |     |      | 10         | 2.1±0.2          | 32              | 0.133±0.002      |
|                  | 16 cm diam. (Center) | 140 | 200  | 2          | 0.83±0.06        | 32              | 0.051±0.0003     |
|                  |                 |     |      | 5          | 1.07±0.07        | 32              | 0.066±0.001      |
|                  |                 |     |      | 10         | 1.23±0.09        | 32              | 0.076±0.001      |
|                  | 16 cm diam. (Edge) | 140 | 200  | 2          | 1.5±0.1          | 32              | 0.095±0.001      |
|                  |                 |     |      | 5          | 2.0±0.1          | 32              | 0.125±0.002      |
|                  |                 |     |      | 10         | 2.1±0.2          | 32              | 0.130±0.002      |
| Calibration (PD) | Calibration Gel vials | 140 | 200  | 2          | 2.3±0.2          | 16              | 0.0720±0.0001    |
mean, sometimes called Weiner, filtering is typically performed using kernel sized between 3x3 and 11x11. Although larger kernels typically produce smoother images, these larger kernels also tend to compromise sharp gradients in the image. Hence, a tradeoff occurs between smoothness and image fidelity.

An interesting characteristic of the Adaptive filter is that it is well suited to multiple passes over the same image. Hence, not only can the kernel size be adjusted to a specific need, the number of iterations over the image can also be tuned. The effects of kernel size and number of iterations was studied recently for a range of image SNR [20]. As an example, figure 4 illustrates the results of Weiner filtering a noisy “U”-shaped synthetic CT image with varying kernel sizes and a range of total number of iterations. As can be seen from figure 4, increasing kernel size and/or the number of iterations has a positive effect on noise reduction in filtered images. At some point, moving to excessively high kernel size or number of iterations becomes counterproductive, as image distortion (blurring) becomes unacceptably high. Hence, care must be taken in choosing the kernel and iteration number.

![Figure 4](image_url)

**Figure 4:** (a) Profiles through a “U” shaped image using kernel sizes if K=3, 7, and 11 and between 1 and 3 filter iterations. (b) Error histograms between filtered and unfiltered images. From [20].

A second example utilizes a more realistic, although still synthetic, “CT gel image” of a prostate conformal therapy dose distribution. Figure 5 illustrates the effects of Weiner filtering on a noise filled conformal prostate dose distribution. Most impressive perhaps is the large improvement in dose-area histograms afforded by Adaptive mean filtering. In this case a relatively large kernel (K=11) and moderate iterations (n=2) was used. This combination of parameters was made due to the reasonably low dose gradients in the image, hence allowing for a large kernel.
Figure 5: Adaptive mean filtering (K=11, n=2) for a conformal prostate “gel” image. (a) noise free image with filtered image contour overlay, (b) profiles through noise-free, filtered and unfiltered images, and (c) dose area histograms of noise-free, filtered and unfiltered images. From [20].

5.2. Two point maximum entropy

A second method for noise reduction in CT gel images has been investigated recently [21]. Two point maximum entropy method (TPMEM) regularisation is a powerful technique that, although more complex than Adaptive filtering, works particularly well on low SNR data and also allows for a large amount of flexibility in the amount of smoothing undertaken on the image. The aim of TPMEM is to minimise the function

\[ T = -S + \lambda \chi^2 \]  

(2)

where \( S \) is the entropy function, \( \chi^2 \) is the chi square function, and \( \lambda \) is a Lagrange multiplier which mediates the relative contributions of smoothness (\( S \)) and fidelity (\( \chi^2 \)) in the resultant image. The entropy function is given by

\[ S = \sum -p \ln p + q \ln q \]  

(3)

where \( NP \) is the number of points in the input data and \( p \) and \( q \) are fractional probabilities in any two adjacent data points,

\[ p = \frac{x_i}{x_i + x_{i+1}} \quad q = \frac{x_{i+1}}{x_i + x_{i+1}} \]  

(4)

The \( \chi^2 \) function is calculated over all point and between the recovered (smoothed) and initial dataset (image). In general, the routine is run until a stopping criterion of \( \chi^2 = NP \) is reached. However, this stopping criterion is to some extent flexible and hence can be written as

\[ \chi^2 = X \cdot NP \]  

(5)

where \( X \) is a tuneable parameter, typically between \( X = 0.6 - 1.4 \). This offers a very unique capability to tune the resultant image to either greater smoothness or greater fidelity, depending on the desired outcome. Furthermore, this is not attained via a typical windowing method where greater smoothness is attained through a larger filter window and, hence, at the potential expense of image gradient degradation.
The algorithm for implementation of TPMEM for 1D (vector) data can be written as:

i. Initiate initial recovered spectrum to uniform values (e.g. choose each $x_i$ as mean value of all $d_i$). Choose minimum and maximum limits for $\lambda$ (e.g. $10^{-9} < \lambda < 10$).

ii. Set $\lambda = \lambda_{\text{low}}$. Set initial vector to flat estimate (i.e. use (i)). Minimise equation (1) using a conjugate gradient decent method. Record resulting $\chi^2$.

iii. Set $\lambda = \lambda_{\text{high}}$. Set initial vector to flat estimate (i.e. use (i)). Minimise equation (1) using a conjugate gradient decent method. Record resulting $\chi^2$.

iv. Bisect $\lambda$. ($\lambda = (\lambda_{\text{low}} + \lambda_{\text{high}})/2$) using a root bisection method. Set input vector to output of (ii) or (iii), depending on which has lower $\chi^2$. Minimise equation (1) using a conjugate gradient decent method. Record resulting $\chi^2$.

v. Is $\chi^2 = X \cdot \text{NP}$ within tolerance (e.g. 5% of NP)?
   a) If no and if $\chi^2 > \text{NP}$, set $\lambda_{\text{high}} = \lambda$. Go to (iv).
   b) If no and if $\chi^2 < \text{NP}$ set $\lambda_{\text{low}} = \lambda$. Go to (iv).
   c) If yes, exit and record data.

The algorithm terminates when either $\chi^2 = X \cdot \text{NP}$ within a specified tolerance, or when the root-bisection accuracy has been exceeded. To extend the algorithm to 2D (image) data, The algorithm is extended to:

(i) Initiate initial recovered image to uniform values (e.g. choose each $x_i$ as mean value of all $d_i$). Choose minimum and maximum limits for $\lambda$ (e.g. $10^{-9} < \lambda < 10$).

(ii) Set $\lambda = \lambda_{\text{low}}$.

(iii) Set input vector to row 1 of image. Minimise equation (1).

(iv) Set input vector to column 1 of image. Minimise equation (1).

(v) Set input vector to row 2 of image. Minimise equation (1).

(vi) Set input vector to column 2 of image. Minimise equation (1). ...

(vii) Set input vector to row N of image. Minimise equation (1).

(viii) Set input vector to column N of image. Minimise equation (1).

(ix) Calculate and record $\chi^2$ for entire image.

(x) Set $\lambda = \lambda_{\text{high}}$. Repeat (iii)–(ix).

(xi) Bisect $\lambda$. ($\lambda = (\lambda_{\text{low}} + \lambda_{\text{high}})/2$). Set input image to output of $\lambda_{\text{low}}$ or $\lambda_{\text{high}}$ minimisation, depending on which has lower $\chi^2$. Minimise image, (iii)–(ix).

(xii) Is $\chi^2 = X \cdot \text{NP}$ within tolerance (e.g. 5% of NP)?
a) If no and if $\chi^2 > X \cdot NP$, set $\lambda_{\text{high}} = \lambda$. Go to (iii).

b) If no and if $\chi^2 < X \cdot NP$ set $\lambda_{\text{low}} = \lambda$. Go to (iii).

c) If yes, exit and record data.

Note that this implementation of the algorithm is designed for square (NxN) images. NxM images can easily be accommodated through padding to NxN.

From equation 2 and the algorithms presented above, it can be seen that TPMEM does not rely on a window, pre se, to achieve smoothing and that, hence, window size does not determine the amount of smoothing to be undertaken. Rather, the technique relies on an interplay between two functions, one dedicated to smoothing the data (the entropy function) and the other dedicated to maintaining image fidelity (the $\chi^2$ function). Furthermore, this interplay can be finely tuned through the X parameter in the stopping criterion, hence a user defined balance can be obtained for smoothness vs fidelity in any given image.

Figure 6 illustrates the TPMEM method applied to the same U-shaped pattern as in figure 4. Different amounts of smoothing were generated through the application of a range of X values in the stopping criterion. As can be seen from figure 6, larger X values lead to larger amounts of smoothing. Although not as dramatic as in the Adaptive mean filtering case, some sharp contrast definition can be lost in this method if too large an X parameter is chosen in the routine.

It should be noted that TPMEM comes with a larger “overhead” than Adaptive filtering. That is, whereas Adaptive filtering can be executed in Matlab in very few lines of code (the Weiner filter is built into Matlab), TPMEM requires some user generated code to enable the algorithm to run effectively. However, the tradeoff for the added complexity is that TPMEM works exceedingly well on very low SNR data, which can be beneficial for some x-ray CT imaging protocols. Hence, choosing between Adaptive filtering and TPMEM should be based on the quality of the given data.

Figure 6: TPMEM filtering of a U-shaped pattern. (a) profiles through unfiltered, noise-free, and TPMEM filtered images. X values range between X=0.6 to X=1.4; (b) error histograms showing improvement in image fidelity for filtered images. From [21].
6. Conclusions

Recent work in x-ray CT polymer gel dosimetry has concentrated on (i) moving to normoxic gel formulations, (ii) understanding the effects of CT dose on polymer gel dose distribution integrity, (iii) image filtering for dose resolution improvement and, recently, (iv) new gel formulations for improved x-ray CT dose response sensitivity. Results indicate that CT imaging remains an attractive possibility for polymer gel dosimetry. Further work on improved formulations for CT polymer gel dosimetry is currently underway and stands to offer increased dose response sensitivity, hence bringing the technique closer to MRI and optical CT in its clinical utility.

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