Considerations for x-ray CT polymer gel dosimetry

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Abstract. This review paper addresses the basic considerations required when performing x-ray CT polymer gel dosimetry. The review focuses on recent developments pertaining to these basic considerations.

1. Introduction
X-ray CT remains an attractive modality for imaging irradiated polymer gel dosimeters (PGD). The system is robust, straightforward to implement, and x-ray CT scanners are readily available within radiotherapy clinics. While much of the research in the field is concentrated on MRI and optical CT imaging of irradiated PGD, x-ray CT imaging has been shown to be capable of providing images of irradiated PGD that are suitable for extracting useful dose information.

This overview is aimed primarily at highlighting developments within the field since the last review conducted in 2010 and earlier review work [1, 2]. As such, full details of early studies are not given here, but rather references are provided to these works. Some early results are provided for context.

2. General overview
The basic principle of x-ray CT PGD revolves around the fact that PGD undergo minute changes in density when irradiated with ionizing radiation. This was first demonstrated by Hilts et al in 2000 where they used an acrylamide based PGD irradiated with 6MV photons from a clinical linear accelerator [3]. The density change is attributed to a change in volume, as opposed to a change in mass, within the system. This volume change results from the radiation induced polymerization of monomer to crosslinker, along with a concomitant redistribution of water away from the formed polymer. The volume change has been estimated to be small (<1% for early acrylamide based systems) [1, 2]. While this is favourable in terms of maintaining the integrity of the dose distribution (i.e. radiation induced volume changes are not expected to lead to large material distortions), the small volume change has the negative effect of resulting in small changes in density and hence poor contrast in the CT images, as seen for example in Audet et al [4].

The images in the original work of Audet et al suffered from low contrast, and hence low dose resolution. A large effort since this first manuscript has been dedicated to improving the dose resolution of CT images acquired on irradiated PGD. However, this is not the only area of active research within the discipline. A large range of topics have been investigated and can be roughly categorized as outlined in table 1. Representative references are given to point the reader towards literature discussing the main topics outlined in the table. The remainder of the manuscript discusses recent work in some of these areas.
Table 1: Recent research areas in CT PGD. Representative references are given, with concentration focused on works within the last two years.

| Research Topic                                      | Reference          |
|-----------------------------------------------------|--------------------|
| Improving dose sensitivity (dose resolution)        | [5-9]              |
| Gel properties (stability, polymerization kinetics etc) | [5-8, 10, 11]      |
| CT imaging parameter optimization                   | [12-14]            |
| Post processing (filtering etc)                     | [15-19]            |
| CT dose considerations                              | [15, 20, 21]       |
| Clinical demonstrations                             | [4, 6]             |

3. Developments in x-ray CT PGD

3.1. Gel sensitivity
It is clear that the low dose resolution in images of irradiated PGD has been a key limiting factor in the technique gaining widespread usage. To address this issue a number of investigators have undertaken work with the aim of improving the sensitivity of PGD to radiation. Since the dose resolution of a system depends on both the slope of the dose response curve, as well as the uncertainty in the measurements, improving dose sensitivity should bring gains in dose resolution, if all other factors remain equal. Koeva et al undertook preliminary investigations in improving dose sensitivity of N-isopropyl-acrylamide (NIPAM) based PGD [7]. This initial study paved the path for later works, which included incorporating a cosolvent (isopropanol) into the formulation [22]. While isopropanol did significantly increase the dose sensitivity of NIPAM based PGDs due to the increased solubility limit of the crosslinker, the manufacturing technique and handling of the PGDs was complicated by the cosolvent. To overcome this, Chain et al proposed cosolvent-free NIPAM based PGD with increased sensitivity [5]. The increase in sensitivity was accomplished by recognizing that N-isopropyl-acrylamide is itself a cosolvent for the crosslinker, and hence by changing the relative fraction of monomer to crosslinker, an increased amount of crosslinker could be incorporated into the dosimeter and an increase in dose sensitivity could be realized. Figure 1 (left panel) illustrates the increase in dose sensitivity that is possible as the relative fractions of monomer and crosslinker are increased. Figure 1 (right panel) illustrates the resulting improvements in dose resolution with each formulation tested in figure 1 (left panel). It can be seen that PGD with high radiation dose sensitivity and high dose resolution can be manufactured for imaging with x-ray CT.

3.2. Gel properties
A number of researchers worked to establish the suitability of these new PGD formulations for robust x-ray CT PGD. Recently, Johnston et al undertook a comprehensive x-ray CT PGD analysis of Chain’s formulation. Within this study they established the post radiation temporal stability, intra and inter-batch reproducibility, calibration robustness, and dose rate dependence of the new gel formulation. As an example, figure 2 (left panel) illustrates that post irradiation polymerization can occur for up to ~20 hrs post radiation, and that this polymerization can be detected with x-ray CT. Figure 2 (right panel) illustrated that the high sensitivity NIPAM gel does exhibit a dose rate dependence.
Interestingly, an opposite trend in dose rate dependence was observed in [11], although the concentration of monomer and crosslinker in their PGDs are different from that of Johnston. Chang et al also illustrate a potentially mild energy dependence of NIPAM based PGD, as shown in figure 3.

### 3.3. Imaging parameter optimization

A complete investigation of image acquisition parameter optimization was undertaken by Hilts [13] using an acrylamide based PGD and, as these results are now well established, they will not be discussed here. More recently, Ghavami et al undertook similar investigations with a NIPAM based PGD and reported similar results to that of Hilts et al [14]. These results are consistent with CT theory and are not, typically, dependent on the PG formulation.

One additional area that has been investigated recently is that of CT reconstruction technique on image quality in CT PGD. Hindmarsh used raw data from the CT scanner and investigated the effects of differing reconstruction techniques on resultant image quality [12]. Notably, the group moved away from filtered backprojection algorithms and investigated iterative techniques. As shown in figure 4, Hindmarsh et al demonstrate that the modulation transfer function can be significantly altered depending on the reconstruction technique employed.
3.4. Post processing
Due to the low contrast in CT PGD images, image filtering has traditionally been a key component in post acquisition processing [17-19, 23]. Recently, Jirasek et al identified a structural noise component, in addition to standard stochastic noise, within CT PGD images [16]. This structural noise is due to inherent gel structure and is typically several pixels in extent. Hence, standard stochastic noise filtering techniques have proven ineffective in filtering this structured component. A new class of filter was implemented to address the structural noise within CT PGD images. The Remnant Artefact Removal (RAR) technique is based on a class of signal removal techniques [24]. In the present implementation, RAR strips “signal”, in this case considered to be the gel structure and unwanted remnant artefacts, from the image by utilizing fitting algorithms which discriminate between radiation induced large-scale dose structure (polymerization, ~>50 pixels in width) from inherent gel structure (~5 – 10 pixels in width). Figure 5 illustrates the efficacy of the Remnant Artefact Removal technique [16].
Figure 5: Top left panel: Synthetic wedge distribution with added stochastic and structural noise. Top right panel: Image of top left panel filtered with RAR. Bottom right panel: Difference map between top right panel and known wedge distribution. Bottom right panel: Representative profile through wedge distribution illustrating unfiltered, RAR, and adaptive mean filtered results. Lower traces are difference profiles between filtered and unfiltered profiles. Colourbars and y-axis (bottom right panel) are in Gy. From [16].

3.5. CT dose considerations
Traditionally, image averaging has been used to improve the signal to noise ratio in CT PGD images [3]. However, limiting factors in this approach include time, CT tube load, and CT dose imparted to the PGD which can initiate further polymerization and hence distort the desired dose distribution [20]. Recently Kakahel et al introduced a “zero-scan” method which aims to improve the image quality of CT PGD images while minimizing the CT dose registered in the final image [15]. In their method they acquire a large number of images (16 – 360) and, on a pixel-by-pixel basis, fit a function (linear, exponential, etc) to the CT number vs scan number data. This allows for an interpolation back to a “zero-scan” CT number which contains very little CT dose. Furthermore, since the fit function incorporates data from a large number of scans, image noise is reduced in the zero-scan interpolated image. Figure 6 illustrates representative results of the zero-scan technique.

3.6. Clinical demonstrations
In general, very few CT PGD studies to date have focused on clinical demonstrations. Audet et al did so in an early study where they focused on a stereotactic radiosurgery application [4]. Recently, Johnston et al used a NIPAM based polymer gel, full gel calibration and RAR filtering to demonstrate clinical utility of CT PGD. They used a head phantom irradiated with calibration, and IMRT test irradiations. Generally, excellent agreement between planned and measured doses was observed and the work clearly demonstrated the potential of CT PGD for clinical applications. Figure 7 illustrates representative results from the work.
Figure 6: Top left: initial image. Top centre: 360th image in series. Note increased signal from polymerization due to CT dose. Top right: averaged image (360 averages). Bottom left: zero-scan interpolated image, exponential fit. Bottom centre: zero-scan interpolated image, linear fit. Bottom right: zero-scan interpolated image, quadratic fit. From [15].

4. Summary
Recent work has made excellent progress in moving CT PGD towards clinical utility. Efforts in gel recipe development and optimization, advanced filtering and artifact removal, CT dose consideration, and demonstrations of clinical potential have all worked to advance CT PGD towards clinical viability.

5. References
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Figure 7: Top left panel: Calibration curve for a full gel calibration of NIPAM polymer gel. Top right panel: Gel colour map of binned isodose levels, compared with isodose lines from treatment planning calculations. Values shown are isodose percentages. Bottom left panel: Gamma map (3%, 3mm) between gel image and treatment plan (99.3% pass at isocentre slice, 93.4% pass through entire volume). Bottom right panel: Representative comparison between profile extracted from gel image and treatment plan. From [6].