Characterization of the essential dosimetric properties of cosolvent-free polymer gel dosimeters: Recent progress in x-ray CT based normoxic polymer gel dosimetry

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Abstract. This work evaluates the temporal stability, spatial stability, batch reproducibility and dose rate dependence of a new cosolvent-free polymer gel dosimeter optimized for use with x-ray computed tomography readout. Temporal and spatial stability investigations reveal the new gel formulation should be imaged between 15-36 hours after irradiation. Intra- and inter-batch reproducibility were found to be excellent over the entire range of doses examined. A dose rate dependence was found for gels irradiated with machine dose rates between 100-600MU/min. An intensity-modulated radiation therapy treatment validation is also presented to illustrate an example clinical application using the new gel formulation.

1. Introduction

Until recently, x-ray computed tomography (CT) polymer gel dosimetry (PGD) has been hindered by low signal-to-noise CT images, largely resulting from gel formulations with low radiation sensitivity. Work to improve sensitivity has focused on identifying new dose-sensitive monomers [1, 2] and finding methods to increase the concentration of N, N’-methylenbisacrylamide (BIS) in the gel system [3-6]. A significant improvement was made using isopropanol as a cosolvent to increase the amount of BIS in the gel formulation [5]. It was further found that comparable sensitivity could be obtained by increasing BIS concentration using N-isopropylacrylamide (NIPAM) [6]. This new, cosolvent-free formulation, consisting of 15% NIPAM, 4.5% BIS, 5% gelatin, 75.5% deionized water and 5mM tetrakis hydroxymethyl phosphonium chloride (THPC), provides superior radiological tissue equivalence over the isopropanol recipe [7] and is the formulation of choice for this work. The aim of this study is to characterize the essential dosimetric properties of the new cosolvent-free polymer gel formulation. Temporal and spatial stability are investigated to evaluate the reliability of gel response. Intra-batch reproducibility is examined locally, within a single region of gel, and globally, throughout a gel volume. Inter-batch reproducibility is also examined using 3 independently fabricated gel batches. The dependence of gel response on machine dose rate is evaluated for irradiations delivered between 100-600MU/min. An example clinical application of the new gel formulation is also presented using a test intensity-modulated radiation therapy (IMRT) treatment validation.
2. Materials and Methods

2.1. Gel fabrication

All polymer gels were manufactured as described previously [6]. For the temporal stability study, the final gel solution was poured into 20mL scintillation vials (Wheaton Scientific, Millville, NJ) and sealed in acrylic phantoms [8]. For the remaining studies, completed gel solutions were transferred to 1L polyethylene terephthalate jars (Modus Medical Devices, London, ON). Blank gels for background subtraction were manufactured for the temporal and spatial stability studies as above using 5% gelatin, 0.5% NIPAM and 0.5% BIS. For the remaining studies, backgrounds were taken from central locations in each 1L gel that received less than 3% scattered dose from neighboring irradiations.

2.2. Gel irradiation

All gels were irradiated with 6MV photons using a Varian Clinac linear accelerator (Varian Medical Systems, Palo Alto, CA) at a machine dose rate of 400MU/min unless otherwise noted. Treatment planning for each experiment was performed using the Eclipse treatment planning system (Varian Medical Systems, Palo Alto, CA).

For the temporal stability study, gel vials were irradiated to a uniform dose of 10Gy as described previously [8]. For the remaining studies, a custom-built head and neck phantom, optimized for low CT image noise and reproducible localization [9], was used to position gels at CT simulation and radiation delivery.

The 1L gel used to investigate spatial stability was irradiated to 10Gy over half its volume using two parallel-opposed 20x8cm² wedged fields.

For the batch reproducibility and dose rate studies, a range of doses up to 28Gy were delivered using three intersecting 3x3cm² fields. The distribution was delivered to one end of a 1L gel to examine local intra-batch reproducibility and to both ends of a second 1L gel to examine global intra-batch reproducibility. Inter-batch reproducibility was examined by delivering the 3-field distribution to three independently fabricated gels at identical locations in each cylinder. For the dose rate study, the distribution was delivered to both ends of a 1L gel at 100 and 600 MU/min, respectively.

For the IMRT treatment validation, both calibration and test irradiations were delivered to the same 1L gel. The calibration irradiation consisted of the 3-field distribution described above. The IMRT treatment plan was designed to treat a concave target wrapped around an avoidance structure and consisted of 5 beams spread over anterior gantry angles, with a prescription dose of 22Gy.

2.3. Gel imaging

Imaging for all experiments was performed using a GE HiSpeed FX/i CT scanner (GE Medical Systems, Milwaukee, WI) operating at 120kVp and 200mAs [9].

Gel vials used to investigate temporal stability were imaged one at a time between 3-45 hours post-irradiation using a purpose-built phantom described previously [8]. Sixteen images were acquired through the centre of each vial using 10mm slice thickness.

The head and neck phantom used for CT simulation and radiation delivery was used to position gels at CT readout for all remaining investigations. For the spatial stability study, the 1L gel was imaged at 4 locations along the length of the cylinder between 15-47 hours after irradiation. Scans acquired at different times were separated by 3.0cm to avoid CT dose between neighboring acquisitions [10]. Thirty-two images were acquired for each scan using 5mm slice thickness.

For the batch reproducibility, dose rate and IMRT validation studies, 25 images were acquired using 3mm slice thickness. The local intra-batch gel was scanned at 3 locations within the irradiated region. For the remaining studies, images were acquired through the centre of each distribution.

2.4. Data processing

Data processing was completed using Matlab (The Mathworks, Natick, MA). Image averaging and background subtraction were performed for all data sets followed by image filtering using an adaptive mean filter (3x3, n=1) [11] and remnant artefact removal (parameters optimized for each study) [12].
Processed images for the temporal stability study were analyzed by extracting the mean and standard deviation of CT numbers ($N_{CT}$) within a circular region-of-interest for the irradiated gel vial and an unirradiated blank gel. The radiation-induced change in $N_{CT}$ above an unirradiated gel ($\Delta N_{CT}$) was then computed for each vial and plotted as a function of time between irradiation and imaging.

For the spatial stability study, 7 adjacent $\Delta N_{CT}$ profiles through the diameter of the 1L cylinder were extracted for each scan. The mean and standard deviation of $\Delta N_{CT}$ were then computed over 7 pixels in a direction perpendicular to the profiles and plotted as a function of distance in the image.

Processed images for the batch reproducibility and dose rate gels were used to generate dose-response curves using a new pixel-by-pixel calibration technique outlined previously [13]. A dose-response curve was also generated for the IMRT distribution and used to convert $\Delta N_{CT}$ to dose for the test irradiation image. Measured and planned IMRT doses were then compared using an isodose plot, 2D gamma map [14] and dose profiles.

3. Results and Discussion

3.1. Gel Characterization

Figure 1a illustrates the time-course of post-irradiation polymerization for the cosolvent-free gel. An initial increase in $\Delta N_{CT}$ is observed between 0-15 hours after irradiation. Beyond 15 hours, the polymerization reaction stabilizes. It is therefore recommended that at least 15 hours is allowed between irradiation and imaging for this gel formulation.

Figure 1b shows profiles of $\Delta N_{CT}$ extracted along the diameter of a 1L gel irradiated to 100 Gy and half its volume. Profiles agree within experimental uncertainty for scans acquired 15-36 hours after irradiation, indicating spatial stability is excellent within this time frame. Beyond 36 hours, a small overshoot in response is observed. Further investigation is required to determine the exact mechanism causing the observed overshoot. Nevertheless, an upper limit on the time between irradiation and imaging of 36 hours is recommended for the new gel recipe.

Figure 1c shows dose-response curves for the local intra-batch (slices 1-3), global intra-batch (regions 1-2) and inter-batch (batches 1-3) reproducibility studies plotted with the average fit function as a reference. Excellent dose-response reproducibility is achieved over the entire dose range studied. The intra-batch reproducibility achievable within a single region of gel and throughout a 1L volume prove calibration and test irradiations can be delivered to the same gel dosimeter. Similarly, the inter-batch reproducibility shown indicates the new gel is insensitive to small variations in the PGD process.

Dose-response curves for gels irradiated using machine dose rates between 100 -600 MU/min are illustrated in figure 1d. The shape of the dose-response curve changes as a function of dose rate, indicating a machine dose rate dependence for the new gel formulation. As dosimetric error could occur in a clinical application if machine dose rate was not consistent between calibration and test irradiations, caution must be exercised when using the new gel for clinical applications. The
implication for variations in dose rate beyond machine dose rate (i.e. variations in deposited dose rate, mean dose rate over treatment delivery, intensity modulation, etc.) are the subject of current study.

3.2. Clinical application

Figure 2a compares gel measured doses to the corresponding planned isodose levels for the IMRT treatment validation. It is readily seen that agreement between gel and planned doses is excellent. Similarly, the gamma distribution shown in figure 2b gives a nearly complete pass rate (99.3%). Excellent agreement between planned and measured doses is again observed in the row and column profiles through the middle of the distribution, shown in figures 2c and 2d, respectively. By all parameters, the test treatment validation shown here illustrates a remarkable improvement over previous CT PGD clinical applications [15-16].

Figure 2: Comparison of planned and measured doses for the IMRT treatment validation using (a) an isodose plot, (b) 2D gamma map and (c) row and (d) column profiles.

4. Conclusions

The results of this work illustrate that the new cosolvent-free polymer gel formulation has promising dosimetric characteristics for CT PGD. Temporal and spatial stability investigations reveal the response of the gel is reliable between 15-36 hours post-irradiation and excellent batch reproducibility is achieved for doses between 0-28 Gy. The implication of the observed machine dose rate dependence remains to be determined and is the focus of current study.

5. References

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