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Normoxic polymer gel dosimetry using less toxic monomer of N-isopropyl acrylamide and X-ray computed tomography for radiation therapy applications

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ABSTRACT

Background: Polymer gel dosimetry has been used extensively in radiation therapy for its capability in depicting a three dimensional view of absorbed dose distribution. However, more studies are required to find less toxic and more efficient polymers for application in radiotherapy dosimetry.

Aim: The purpose of this work was to evaluate the N-isopropyl acrylamide (NIPAM) gel dosimetric characteristics and optimize the protocol for X-ray computed tomography (CT) imaging of gel dosimeters for radiation therapy application.

Material and methods: A polymer gel dosimeter based on NIPAM monomer was prepared and irradiated with ^{60}Co photons. The CT number changes following irradiation were extracted from CT images obtained with different sets of imaging parameters.

Results: The results showed the dose sensitivity of ΔN_{CT} (H) = 0.282 ± 0.018 (H Gy^{-1}) for NIPAM gel dosimeter. The optimized set of imaging exposure parameters was 120 kV$_p$ and 200 mA with the 10 mm slice thickness. Results of the depth dose measurement with gel dosimeter showed a great discrepancy with the actual depth dose data.

Conclusion: According to the current study, NIPAM-based gel dosimetry with X-ray CT imaging needs more technical development and formulation refinement to be used for radiation therapy application.

Aim

The main objective of the current study was to apply a less toxic polymer gel named as NIPAM for radiation dosimetry using x-ray computed tomography for data extraction from irradiated gels. Also, the effect of imaging techniques on dosimetry results including the kVp, mA and slice thickness was evaluated.

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1. Introduction

Application of X-ray computed tomography (CT) for the imaging of irradiated polymer gel was reported by Hilts et al. in 2000.[1] Several studies have been performed to reveal the potentials and advantages of the X-ray CT polymer gel dosimetry technique.[1–9] In recent years, application of different polymer gels to depict the dose distribution of radiation therapy beams has been a considerable area of research in radiation therapy dosimetry. However, the main aim of most studies has been focused on finding new monomers with lesser toxicity and higher sensitivity. Furthermore, different data acquisition methods such as X-ray computed tomography and ultrasound has been exploited by several research teams.[10,11] Application of a new polymer gel with lower toxicity named N-isopropyl acrylamide (NIPAM) has been reported by Senden et al.[12] They showed that the new polymer with less toxicity has good NMR and optical properties for polymer gel dosimetry application. The NMR response (R_2) of the dosimeters was analyzed for conditions of varying dose, dose rate, time post-irradiation, and temperature during irradiation and scanning. It was shown that the dose-response behavior of the NIPAM/bis gel dosimeter is comparable to that of normoxic polyacrylamide gel (PAGAT) in terms of high dose-sensitivity and low dependence on dose rate and irradiation temperature, within the ranges considered.[12] Apart from some recent studies performed using NIPAM gels searching the magnetic resonance and optical properties of the gel, there are a few studies on X-ray CT imaging of the new polymer following irradiation.[10,12,13] In the current study, the properties of the NIPAM-based gel dosimeter were evaluated using X-ray CT imaging. The purpose of this work was to evaluate the NIPAM based gel dosimetric characteristics and optimize the protocol for X-ray CT imaging of gel dosimeters for radiation therapy application.

2. Materials and methods

2.1. Gel preparation

The polymer gel dosimeters were manufactured inside a fume hood and under normal atmospheric conditions. The gels consisting of NIPAM (Aldrich, 97%) and bis acrylamide and tetrakis hydroxymethyl phosphonium chloride (THPC) antioxidant were made using standardized procedures to maximize the reproducibility. The gel density was comparable to water and could be used for radiation dosimetry without any dosimetric correction factor and also the experimental procedures were based on the previous publications for normoxic polymer gel dosimeters.[12–14] for gel preparation, Gelatin (300 Bloom Type A) was allowed to swell in 80% of de-ionized water for 10 min at room temperature, then the solution was heated up to 50 °C. While stirring continuously, 3 wt% bis was gradually added to the solution at 50 °C, which took about 15 min, followed by the same amount of NIPAM monomer and then, by a gelatin–crosslinker mixture cooled to approximately 37 °C. Finally, a solution of the antioxidant THPC was prepared with the remaining 20% of water and added to the solution. The gels presented themselves as clear, transparent and slightly yellow liquid. The gel solutions were transferred into glass vials with of 20 mm^3 and then closed with rubber septa. The tubes were filled completely with gels and so the air inside the test tubes (above the gel) was completely evacuated to prevent excessive oxygen diffusion into the gel. The initial studies showed that with the air not removed from the test tube, the surface layer of the gel would not always polymerize upon irradiation, despite the presence of the antioxidant.[12] A similar observation was also made in the current study.

2.2. Irradiation

Irradiations were done approximately 3 h. post-manufacture using a Theratron-1000 ^{60}Co teletherapy unit (MDS Nordion, Canada). A phantom with the thickness of 10 cm and diameter of 20 cm was designed and machined to locate the gel vials (Fig. 1). The phantom was built from polyethylene with the density of 0.94 g cm^{-3}. The phantom was planned by a two-dimensional treatment planning system. The irradiation was performed using two parallel-opposed ^{60}Co beams with 30×30 cm^2 field size, delivering a uniform dose distribution to the depth of 1–2.5 cm. The inhomogeneity of dose distribution in target area, the location of gel container, was less than 1% overall. The dose rate was about 160 cGy/min at d_{max} with the source to surface distance of 100 cm.

To have different dose for each vial, the irradiation was interrupted each 0.8 min and vials were removed from phantom consecutively and replaced by a container filled with water. The irradiation was performed 2 h after gel formation. The doses of 4.5, 7.5, 10.5, 13.5 Gy were delivered to the four vials and one vial was left un-irradiated for background subtraction. The whole set of measurements was repeated three times for both calibration and other measurements. A computed tomography scan unit, Hi-speed Fxi (Siemens, Germany), was used for imaging of gel dosimeters as can be seen in Fig. 2.

For percent depth dose (PDD) measurement using the gel dosimetry, a glass container with the dimension of $3 \times 6 \times 20$ cm^3 was filled with NIPAM/bis gel and then fixed in a small water phantom with the dimension of $20 \times 20 \times 20$ cm^3.

Fig. 1 – The phantom designed for irradiation and X-ray CT imaging of gel filled vials.

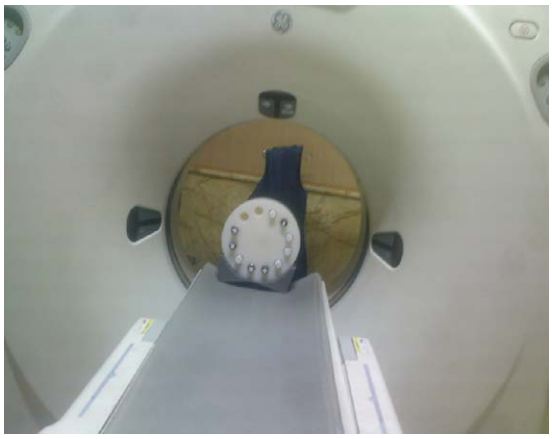

Fig. 2 – The imaging setup for X-ray CT imaging of vials exposed to different doses.

The gel was irradiated by 10 cm × 10 cm field size at the SSD of 100 cm to deliver the dose of 10 Gy to the depth of 5 mm.

2.3. *CT imaging technique*

After gel irradiation with the time interval of 8–12 h, the gel was imaged by the X-ray CT scanner. Different exposure techniques were applied for gel imaging. The effect of kV_p, mA and slice thickness on the noise of gel images were evaluated. Scan parameters were varied from set of parameters to access dependence of noise on each parameter. The slice thickness of 5 mm and 10 mm, 80, 120, 140 kV_p and 100, 150, 200 mA were used for imaging. From each set of scan parameters, two images were taken to remove artifacts by background subtraction for noise study. Standard deviation in CT number (σ_{NCT}) was measured from pixel region at the centre of final images.

MatLab (The MathWorks Inc., USA) was used for all image processing and analysis. In both cases, including PDD measurement and studying the CT number variation with scan parameters, in order to reduce the noise, the irradiated gel was imaged 12 times and all images were averaged using MATLAB 10 software to produce final image for percent depth dose measurement.

The smallest available field of view (25 cm × 25 cm) was used for imaging and given the 512 × 512 matrix size in CT images; the scanned pixel dimension was 0.5 mm.

3. Results and discussion

The variation of CT number with dose is shown in Fig. 3 for two slice thicknesses and different kV_p and mA. These data were extracted from the image resulting from the averaging of 12 images. To quantify the noise content of original images (without averaging) we have calculated the image noise for all gel vials and the average noise was written against the kV_p and mA in Fig. 4. For 10 mm slice thickness, it can be seen that with increasing both exposure factors the image noise decreased and reached the level of about 6. The lowest noise is seen for 200 mA and 140 kV_p. But we should consider that the noise is not changed very significantly from 120 to 140 kV_p. We selected the 120 kV_p and 200 mA for gel tubes X-ray CT

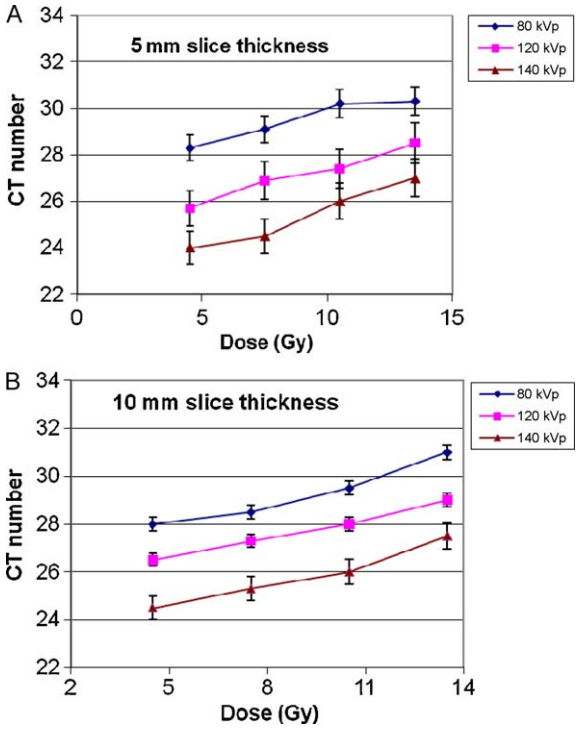

Fig. 3 – CT number variation with kV_p and mA for two slice thickness: (A) 5 mm, (B) 10 mm.

scanning in our experiment. Our results showed that using the 10 cm slice thickness make the images to show less noise in comparison to slice thickness of 5 mm. A slice thickness higher than 5 mm was not selected and studied due to significant loss of dose resolution of gel images.

The average ΔN_{CT}-dose response or dose sensitivity for NIPAM based gels in our study was ΔN_{CT} (H) = 0.282 ± 0.018 dose (Gy). The standard error indicates the uncertainty of the estimated slope in our study. The resulting dose sensitivity is in close agreement of recent study of Koeva et al.[10] They reported the average response of 0.291 ± 0.01 for their NIPAM

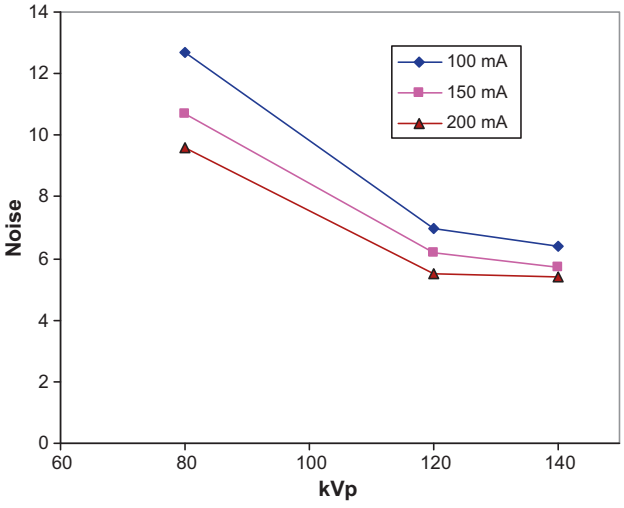

Fig. 4 – The effect of different kV_p and mA setting on noise content of NIPAM polymer gel image with 10 mm slice thickness.

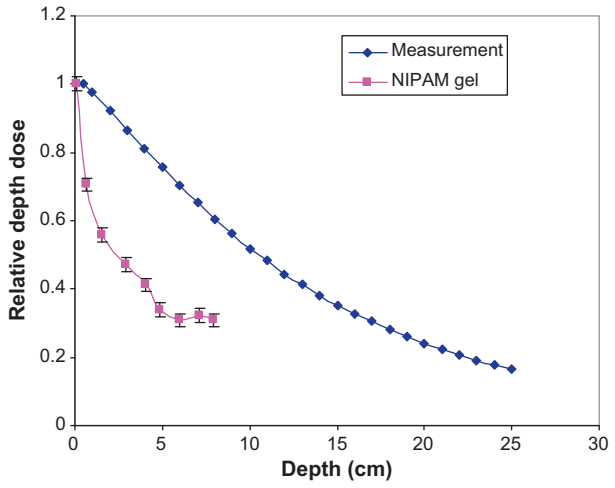

Fig. 5 – Relative depth dose comparison between NIPAM/bis gel and water phantom measurements.

based gels with the same formulation. The differences lie in the experimental uncertainties of both studies.

The relative depth doses for cobalt photons were measured using our polymer gels and compared with data measured by water phantom. The results are shown in Fig. 5. As can be seen, the dose measured by a gel dosimeter shows abrupt drop-off of depth dose which is not consistent with the actual depth dose values. It could be the result of gel insensitivity to gradual decrease of dose with depth and so it fails to follow the real depth dose fall-off for the ^{60}Co photon beam. In other words, it can be said that the dose resolution of the current gel is not sufficient to image the actual variation of dose with depth for radiotherapy application.

In a study on X-ray CT imaging of PAGAT Normoxic gel, a ΔN_{CT}-dose response of ΔN_{CT} (H) = 0.685 ± 0.11 dose (Gy) was reported.[15] In spite of lower toxicity of NIPAM gel, it shows that the dose sensitivity of the NIPAM dosimeter is almost three times lower than the PAGAT gel dosimeter. On the other hand, our results on the effect of different CT imaging parameters on the image noise were very similar to the results of the above mentioned study. Our results are consistent with the results of Kovea et al. and the differences could be attributed to the small differences in CT imaging exposure parameters and gel preparations. However, the depth dose measurement using polymer gel and X-ray CT needs more investigation to improve the gel sensitivity to radiation. Although our experiment showed the dosimetric properties of NIPAM based polymer gel using X-ray CT, its application for clinical use needs more formulation refinements.

4. Conclusions

In the current study the dosimetric properties of newly developed polymer gel with reduced toxicity were evaluated for radiation therapy dosimetry. The results showed that although the gel is sensitive to radiations used in radiation therapy and the CT number of irradiated gel changes after irradiation, due to higher image noise and lower sensitivity of the NIPAM polymer to the radiation, the NIPAM gel dosimeter is not yet able to fulfill the requirements of dosimetry in radiation therapy. However, further studies on newer polymer gel formulation and recipe in order to increase the sensitivity of gel dosimeters are suggested.

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