Original

Investigating the Sensitivity of New Formulation MAGAT and NIPAM Polymer Gels in the Radiation Therapy Dosimetry

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ABSTRACT

Background: Normoxic polymer gels have been used as a three dimensional (3D) dosimeter in radiation therapy, recently. The sensitivity of these gels is important in dosimetry and their improvement can be also useful.

Objective: In this study, different modalities of gel reading were used and the structure of gel changed due to the best improvement of sensitivity. The sensitivities of the new formulation of Methacrylic acid gel (MAGAT) and N-isopropyl acrylamide (NIPAM) polymer gel dosimeters were studied using two different reading methods of magnetic resonance imaging (MRI) and X-ray computed tomography (X-ray CT).

Material and Methods: In this experimental study, in addition to making the NIPAM polymer gel dosimeter, a new formulation of normoxic polymer gel dosimeter, which named MAGAT gel, was investigated. The gels were irradiated with 6 MV in low doses, including1, 1.5, 1.75, 2 and 2.5 Gy. MRI and X-ray CT did the reading of gel dosimeters a day after irradiation using an elevated protocol.

Results: The dose sensitivities of 0.92 HGy^{-1} and 0.47 HGy^{-1} were obtained for new MAGAT and NIPAM polymer gel dosimeters, respectively, based on the X-ray CT reading modality. The use of MRI reading modality and the dose sensitivities were 0.74 $S^{-1}Gy^{-1}$ and 0.27 $S^{-1}Gy^{-1}$ for new MAGAT and NIPAM polymer gel dosimeters, respectively.

Conclusion: The new formulation of MAGAT polymer gel with a suitable protocol of gel reading has a better response.

Keywords

Polymer Gel; Radiation Dosimeters; Radiation Therapy; Magnetic Resonance Imaging; X-Ray Computed Tomography; Methacrylic Acid

Introduction

One of the most effective techniques used for cancer treatment is radiation therapy. The most important aim of radiotherapy is to deliver enough doses to kill the tumor cells while supporting the adjacent healthy tissues. To achieve this purpose, the use of a reliable dosimetry method is essential. The dosimetry methods such as ionization chambers, silicon diode [1], radiographic and radiochromic films [2], thermoluminescent dosimeters (TLDs) [3] and polymer gels [4] are used. Polymer gel dosimetry is a three-dimensional (3D) dosimetry for radiation therapy and used to verify spatial dose distributions

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by medical physicists. Besides, polymer gel dosimeter containing tetrakis hydroxymethyl phosphonium chloride (THPC) is named a normoxic dosimeter because it can be prepared under normal atmospheric conditions. Because of adding the antioxidant to the gel, the main problems (their response to the presence of oxygen) are reduced. Polymer gels are sensitive to preparation conditions. The manufacture of normoxic gels requires less time and equipment. Fong introduced the normoxic polymer gel dosimeters, which have an antioxidant in structure [5]. Besides, several studies have investigated the accuracy of normoxic polymer gel dosimeters [6]. In addition, it was suggested that MAGAT could be the name of the construction of a normoxic polymer gel dosimeter [7, 8]. Polymer gel dosimeter was evaluated by various methods such as MRI [9], X-ray CT [10], Optical Computed Tomography (OCT) [11], Raman spectroscopy [12] and Ultrasound [13]. First, the technique of MRI of a gel dosimeter was proposed by Gore [14]. Moreover, Hilts [15] reported the application of X-ray CT for polymer gel dosimeter. In recent years, several studies have carried out to evaluate the potential of polymer gel for radiation therapy dosimetry using the X-ray CT reading method. To find a less toxic recipe, Senden [16] introduced the NIPAM polymer gel. In this study, the dose-response sensitivity of NIPAM polymer gel is investigated in low-dose radiation with the MRI and the X-ray CT. Additionally, the effect of adding maleic anhydride (MA) on the formulation of MAGAT polymer gel dosimeter is investigated for two reading methods of MRI and X-ray CT.

Material and Methods

Fabrication of new MAGAT polymer gel

In this experimental study, the preparation of a new MAGAT polymer gel dosimeter was done for gelatin (Bloom 300, type A), methacrylic acid (MAA), de-ionized water, maleic anhydride (MA) and THPC as an oxygen scavenger. The gel was formulated inside a fume hood under normal atmospheric conditions. Gelatin was added in 80% of the deionized water for 10 min to start gel preparation so that temperature reached 50°C; then maleic anhydride was added. At this time, a solution should reach 37°C. After that, the same amount of monomer was added. Finally, the solution of the antioxidant was prepared with the remaining 20% of water and mixed to the solution. Gelatin had the role of protecting the monomer in a 3D network, MAA played a monomer role and THPC was as an antioxidant. In addition, MA created a connection and formed a polymer network. The solution after washing the vials with de-ionized water and drying them was slowly poured until it was completely filled and covered with the Parafilm then wrapped in the aluminum foils. They were stored in a refrigerator at 4°C. The detail of the new MAGAT gel structure is shown in Table 1.

Fabrication of NIPAM polymer gel

The NIPAM polymer gel in the study was composed of gelatin, NIPAM (97%, Sigma-Aldrich), Bis (N, N´-methylene bis acrylamide), and THPC. The first, gelatin was kept for 10 min to swell in 80% of the de-ionized water and the solution was heated until 50°C. Then Bis and the same amount of NIPAM monomer were added and the solution was dissolved until a clear solution was obtained. The temperature decreased to 37°C. The antioxidant THPC was prepared with 20% of deionized water and added into the solution. The gel solutions were transferred into the vials, closed with the Parafilm, and finally wrapped in the aluminum foils to avoid any polymerization. Table 1 shows the detail of the NIPAM gel structure.

Irradiation of polymer gels

The new MAGAT and NIPAM polymer gels were irradiated with a 6MV photons beam us-

Table 1: Constituents and formulations of new MAGAT and NIPAM polymer gels

Gel / Materials	MAGAT	New MAGAT	NIPAM
De-ionized water	H_2O (%89)	H_2O (%89)	H_2O (%89)
Gelatin	Gelatin (%5)	Gelatin (%5)	Gelatin (%5)
Methacrylic acid	$C_4H_6O_2$ (%6)	$C_4H_6O_2$ (%3)	-
Maleic anhydride	-	$C_4H_2O_3$ (%3)	-
THPC	$C_4H_{12}CLO_4P$(10mM)	$C_4H_{12}CLO_4P$(10mM)	$C_4H_{12}CLO_4P$(10mM)
N-isopropyl acrylamide	-	-	$C_6H_{11}NO$ (%3)
Bis	-	-	$C_7H_{10}N_2O_2$(%3)

ing a linear accelerator (Elekta Cynergy Platform, UK), SSD of 100 cm and field size of 25 cm × 25 cm. This device has been calibrated to deliver 1 cGy/MU at the standard condition as the TRS-398 protocol. The vials were irradiated to deliver the low doses, including 1, 1.5, 1.75, 2 and 2.5 Gy at the depth of 5 cm. One of the vials was left without irradiation for background subtraction in the X-ray CT technique. The irradiation was implemented 24 h after making gels.

Reading of Polymer gels

MRI reading technique

The irradiated polymer gel vials were imaged using a 1.5 T clinical MRI scanner (Siemens Avanto, Germany) after 24 h as shown in Figure 1. These vials were moved to the MRI scanning room before imaging for equilibrating at room temperature (18°C). The MRI factors for the multiple spin-echo were as follows: echo time (TE) = 20–640 ms, inter-echo time = 20 ms, number of echoes = 32, repetition time (RT) = 6000 ms, slice thickness = 3 mm and field of view (FOV) = 250 ×250 mm^2. The signal intensities were measured in a circular region of interest (ROI) of each vial using the DICOM images in the MATLAB (Mathworks, R2017a, Version 9.2.0.538062) software. The signal changes were used to calculate the spin-spin relaxation, R_2 ($1/T_2$) by ($S = S_0 e^{-TE/T_2}$). The sensitivity was calculated as the slope of the curve [17, 18].

X-ray CT reading technique

The X-ray CT was used to read irradiated polymer gel vials. Illustration of gel vials 24h after scanning with MRI was acquired using a 16-slice CT scanner (GE Medical Systems, Milwaukee, USA). The field of view 20 × 20 cm^2 and the 512 × 512 matrix size in the CT images were used. The angle of the gantry was 90° and the variation of CT numbers was calculated by the dose for 3.75mm slice thickness and 120 kVp. Moreover, the calibration curves were plotted for these conditions. Finally, the data was extracted using the MATLAB software [19].

Results

Figure 2 illustrates the dose-response of the new MAGAT polymer gel dosimeter for the MRI technique. The obtained sensitivity of this gel by the MRI technique was 0.74 $S^{-1}Gy^{-1}$, which was defined as a slope of dose-response. In addition, X-ray CT read the new MAGAT polymer gel with a slice thickness of 3.75 mm and 120 kVp. The variation of CT numbers of this gel with dose is shown in Figure 3. The results showed that the dose sensitivity was 0.92 HGy^{-1}. Figure 4 shows the

Figure 1: The scanning of irradiated polymer gel vials by 1.5T MRI.

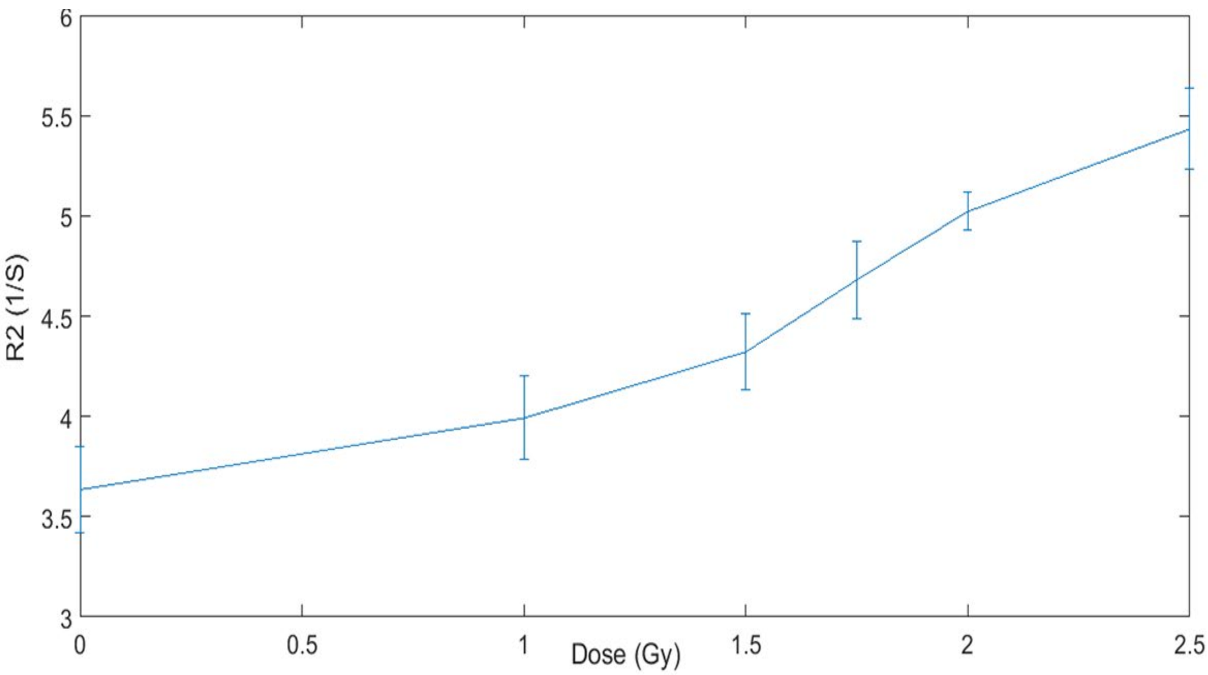

Figure 2: R_2 dose-response of new MAGAT polymer gel dosimeter.

dose-response of NIPAM for the reading technique of MRI. The obtained dose sensitivity of NIPAM polymer gel by the MRI technique was 0.27 $S^{-1}Gy^{-1}$. The variation of CT numbers with the dose for NIPAM polymer gel dosimeter is depicted in Figure 5 in which the dose sensitivity of NIPAM was 0.47 HGy^{-1} obtained by the X-ray CT technique. Increasing absorbed dose in both new MAGAT and NIPAM gels in the studied range of doses leads to an increase in the spin-spin relaxation, R_2 and CT numbers. The error bars reveal the uncertainty of the measurements by the MRI and X-ray CT techniques for new MAGAT and

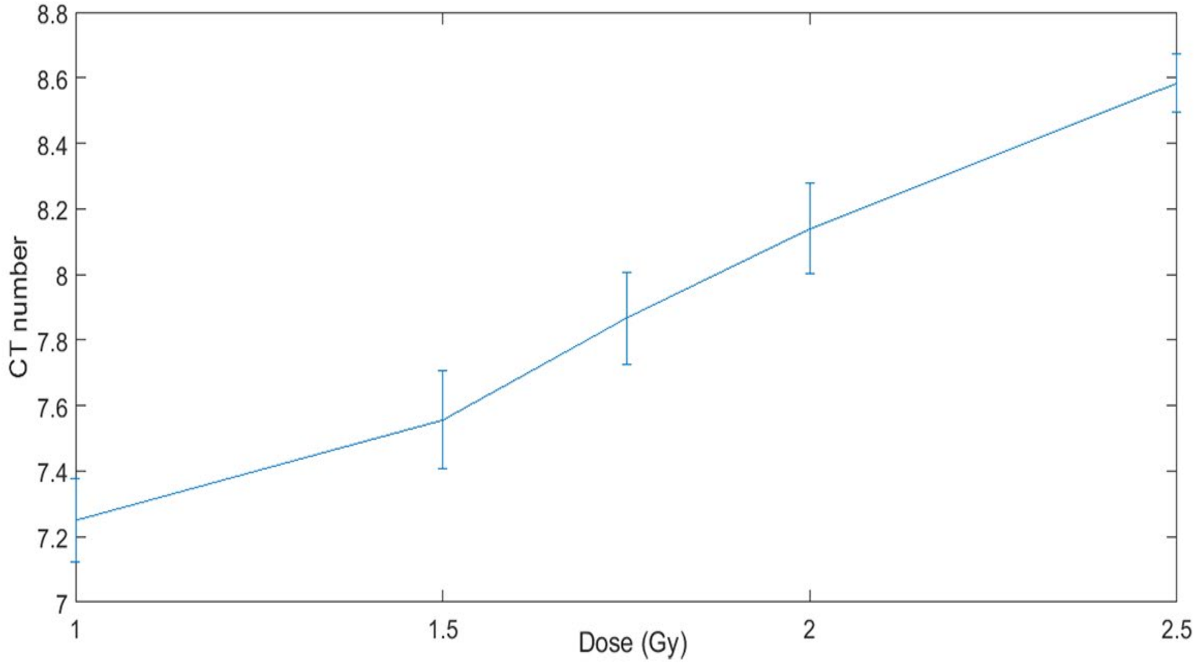

Figure 3: The CT numbers with the dose for the new MAGAT polymer gel dosimeter.

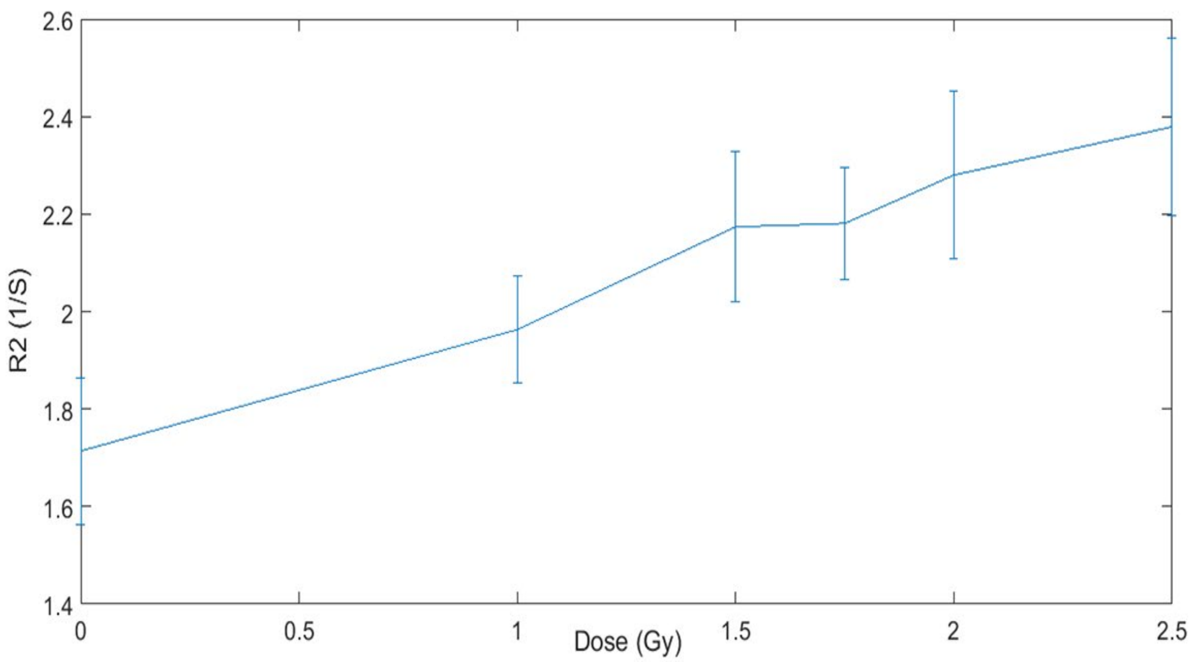

Figure 4: R_2 dose-response of NIPAM polymer gel dosimeter.

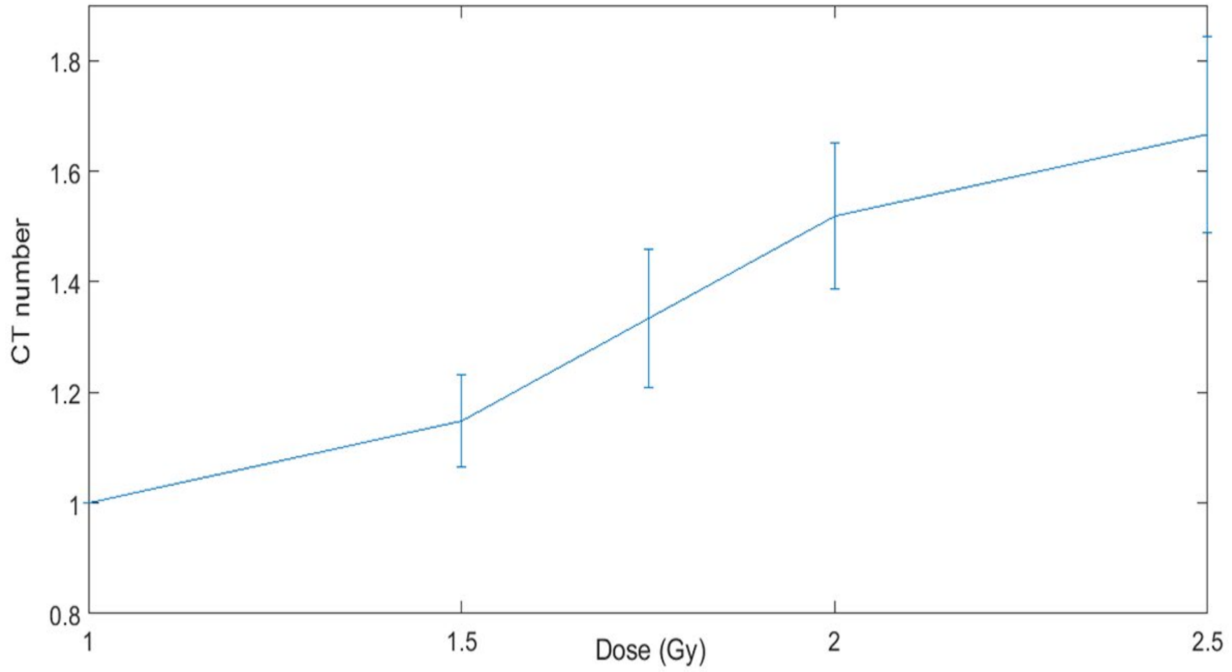

Figure 5: The CT numbers with the dose for the NIPAM polymer gel dosimeter.

NIPAM gels.

Discussion

This study aims to increase the sensitivity of MAGAT polymer gel by adding new materials for the reading techniques of MRI and the X-ray CT and compare it with the NIPAM polymer gel that has low toxicity. The correlation between Hounsfield units (HU) and absorbed dose has been analyzed by investigating the X-ray CT images. The X-ray CT has potential as a device for normoxic polymer gel dosimeters. The best protocol was recorded to find R_2 of gels and used for the MATLAB software to obtain the values R_2 for all vials. In this study, MA and NIPAM are as monomer and Gelatin is as the solvent-forming factor used in the dosimeter; in addition, this gelatin prevents diffusion by preserving spatial information. The monomers were polymerized by the amount of radiation. The THPC considers as the appropriate antioxidant for polymer gel dosimeter that THPC had the highest reaction rate and increased the dose sensitivity of polymer gels. In a study carried out on the X-ray CT imaging of MAGAT normoxic polymer gel, the dose-response of $\Delta N_{CT}(H)=0.85\pm0.08$ dose (Gy) was reported [20]; the dose sensitivity of the new MAGAT polymer gel is almost better than the MAGAT polymer gel dosimeter for the X-ray CT at the present work. Furthermore, some of the advantages of the X-ray CT technique are as follows: the speed of image achievement, insensitive to environmental influences and benefit clinical implementation. Reconstruction of an image by X-ray CT is a process dividing into small voxels and generating CT numbers, which are related to the attenuation coefficient. Compton could relate this correlation to beam attenuation versus photoelectric interactions. Image filtering using MATLAB software considerably decreases imparting additional dose and enhances images of X-ray CT to obtain the best sensitivity of polymer gel dosimeter. Choosing some factors such as kVp and slice thickness in the protocol of X-ray CT is required to reduce the image noise. The results showed that the performance potential of the NIPAM polymer gel dosimeter was reliable at the low dose. In this study, increasing sensitivity for application in clinical use could improve with modifying formalism [21]; thus, it has been seen that the reduction in percentage of monomer and addition in new material (MA) causes sensitivity of gel to increase by focusing on the modified gel formalism that Figures 2 and 3 are in good agreement with this result.

Conclusion

Polymer gel dosimetry is a useful method for treatment in radiation therapy and an important technique for verification of 3D dose distribution. The new formulation of MAGAT polymer gel makes it a suitable dosimeter for the measurement of dose distribution. The results indicated that the read-out of X-ray CT dose has the potential for radiation therapy. A suitable protocol for X-ray CT imaging polymer gel must be considered to reduce noise. In conclusion, the new MAGAT polymer gel dosimetry is suitable for the clinical implementation of dosimetry. To analyze the better response of the dose using in the dosimetry, it is to utilize the different structures of normoxic polymer gel.

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Conflict of Interest

None

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