Investigation of Polymer BANG Gel Dosimetry Using X-Ray Computed Tomographic Imaging

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Abstract

The purpose of this work is to determine the optimal X-ray computed tomography (CT) imaging parameter settings for polymer BANG gel dosimetry. Several homemade polymer BANG gel samples were manufactured following the formulation demonstrated by Maryanski et al in 1994. The protocol for CT-based polymer BANG gel dosimetry was determined experimentally. Our preliminary results indicate that the optimal CT imaging parameter settings for polymer BANG gel dosimetry are: tube potential = 120 kVp, tube current exposure = 400 mAs, slice thickness = 5 mm, and images acquired per scan position = 20. The appropriate CT imaging time to be 2 days after irradiation observed form reproducibility analysis. A good linearity was performed between CT numbers with irradiation doses ranging from 2-14 Gy. The CT images of polymer BANG gel dosimetry acquired when following our protocol can accurately extract dose information in a clinical radiotherapy environment.

Keywords: Polymer BANG gel, Radiotherapy, Computed tomography

Introduction

A key goal of radiotherapy is to minimize radiation dosages in critical structures while accurately delivering appropriate dose distributions conforming to the clinical target volume (CTV). However, the complex geometry of tumor and organ structures renders this a difficult task. In recent years, three-dimensional (3D) conformal radiotherapy (CRT) and intensity modulated radiation therapy (IMRT) have permitted the exclusion of normal liver using beam's eye view (BEV) at various angles.   It is possible to deliver high radiation doses to the planning target volume (PTV) of the liver while sparing tumor-free regions of tissue.

There is a need in radiotherapy to measure the absorbed 3D dose distribution from 3D-CRT and IMRT irradiation techniques; however, making these measurements can be complex. First, accurate measuring requires a detector with the ability to integrate volumetric measurements. Second, the dose distribution of 3D-CRT and IMRT plans often contain sharp dose gradients, so a detector with good spatial resolution is essential. No dosimetric system currently in use - such as ion chambers, diodes, thermoluminescent dosimeters, or film - can fulfill all of the above requirements. The polymer gel dosimeter, which has emerged in recent years, may rise to meet these challenges [1,2].

In 1993, a polymer gel dosimeter was demonstrated that could store spatial dose information permanently [3]. A polymer gel dosimeter is a radiation-sensitive material that consists of a gel matrix infused with monomers that polymerize and cross-link in response to ionizing radiation [3]. An increasing number of reports [4-6] show that polymer gel dosimeters have the potential for making accurate volumetric measurements with sub-mm spatial resolution, are soft-tissue equivalent [1], and operate independently of incident radiation direction.

The radiation-induced polymerization of acrylic monomers takes place after the polymer gel dosimeters are irradiated. Physicists can obtain quantitative 3D dosimetry data from analyzing gel images [7]. There are 2 imaging modalities used to extract dose information from gel dosimetry: (1) magnetic resonance imaging (MRI) [8-10]; and, (2) optical computed tomography (optical CT) [11]. To date, however, physicists do not routinely employ gel dosimeters in clinical settings due to the lack of MRI scanners and optical CT scanners in the clinical radiotherapy setting.

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A recent feasibility study indicates that X-ray CT is a promising alternative imaging method for polyacrylamide gel (PAG) dosimeters based on changes in the linear attenuation coefficients after irradiation [12]. Previous investigations point toward X-ray CT as a simple, convenient, and relatively inexpensive way to implement polymer gel dosimetry into radiotherapy clinical practice because CT scanners and simulators already comprise integral components of treatment planning [13].

Since polymer gels liquefy at high temperatures, manufacturers suggest storing gel samples in the refrigerator [14,15], but it is difficult to keep polymer gel samples at such low temperatures during transport, especially when importing gels from the manufacture, MGS Research Inc. (U.S.A.). For this reason, the use of polymer gel dosimetry was limited in Taiwan. In order to overcome this limitation, we manufactured a 'BANG-type' polymer gel consisting of 5% gelatin, 3% acrylamide, 3% bis, and 83% water in-house in a previous study [16]. To our knowledge, this is the first successful fabrication of a polymer gel dosimeter in Taiwan.

The purpose of our current study was to investigate the feasibility of using X-ray CT for performing polymer BANG gel dosimetry. We investigated optimal CT imaging parameter settings for X-ray CT-based techniques for polymer BANG gel dosimetry via a series of characteristic experiments.

Materials and methods

In the present work, we fabricated polymer BANG gel samples to investigate their characteristics in clinical radiotherapy settings. A protocol for CT-based polymer BANG gel dosimetry was established from optimizing CT imaging parameters and maximizing the image signal-to-noise ratio (SNR).

Gel preparation

We manufactured polymer BANG gel following the formulation developed by Maryanski *et al.* in 1994 [17]. The gel was composed of 3% N, N'-methylene-bis-acrylamide (BIS) (Sigma-Aldrich Pty., Ltd., Sydney, Australia), 3% acrylamide (AA) (Sigma-Aldrich Pty., Ltd., Sydney, Australia), 5% gelatin, nitrogen, and water. The polymer BANG gel dosimeters were produced in a nitrogen-filled glove box using the methods described below.

Gelatin powder was added to an Erlenmeyer flask containing the required volume of water at room temperature. This water was deoxygenated by bubbling humidified nitrogen through it at a flow rate of 1 Lmin^{-1} for at least 1 hour and continued to pass nitrogen gas over the mixture at the same flow rate from that point forward. Once the gelatin was saturated and swollen with water, the flask was placed in a 50℃ water bath. After the gelatin had completely melted, the flask was wrapped in aluminum foil, and added the acrylamide and BIS monomers. The mixture was then magnetically stirred until we obtained a clear solution. The glass vial was flushed with nitrogen in order to remove all oxygen. The polymer gel solution was poured into this glass vial and cooled to room temperature.

Gel irradiation

In order to provide sufficient buildup scatters during irradiation procedures, the gel samples were placed into the center of a water tank, keeping the central axis of the gel sample at a depth of 8 cm below the water surface. Three fiducial markers, visible with CT imaging, were adhered to the water tank using laser alignment in order to define a reference plane at approximately the center of the gel sample. This allowed for the subsequent comparison of the calculated dosages for both experimental and treatment planning.

Before irradiation, a set of 5-mm-thick CT images was acquired with a GE NXI CT scanner, and then the images of gel samples were transferred to the CadPlan Treatment Planning System (CadPlan-Helios, Version 6.2.7, Varian Medical Systems, Inc., Milpitas, CA, U.S.A.) for 3D dose calculations. The gel samples were irradiated 24 hours after preparation using a Varian Clinac 2100C linear accelerator (Varian Associates, Palo Alto, CA, U.S.A.) with an isocentric set-up. Several uniform dosages, which ranged from 2 to17 Gy, were delivered to each gel sample using 2 parallel, opposed 3× 3 cm^2 10-MV beams.

Gel imaging

After irradiation, the gel samples were removed from the water tank. The CT imaging procedures of the polymer BANG gel were carried out using a GE NXI CT scanner at room temperature (23 ℃). The CT scanner was fully warmed up before each scanning session.

We employed a fixed field of view (FOV = 25 × 25 cm^2) and pixel matrix size (512×512) to scan the gel samples. However, the CT image acquisition parameters were varied in this study to determine a protocol for CT imaging: tube voltage 80-120 kVp; tube current exposure 200-400 mAs; and slice thickness 2-5 mm.

The gel sample images were transferred to a personal computer and analyzed these using the image processing toolbox in MATLAB™/Simulink™ software (The MathWorks, Inc., Natick, MA, U.S.A.). The circular regions of interest (ROI) of 1-cm diameter were selected in the area of the coronal section at the central axis for the gel images. The doses delivered to ROI at the central axis were uniform for all gel samples. The mean values and standard deviations of CT number (CTN) were calculated for each ROI.

To investigate the dose sensitivity variations of polymer BANG gel dosimetry along with tube potentials and tube current exposures, the dose sensitivity (H/Gy) is defined as

$$Sensitivity = \frac{\Delta CTN}{D} \tag{1}$$

where ΔCTN is the CT number changed in ROI of gel sample due to irradiation, and D is the dose irradiated.

Previous researchers exposed PAG dosimeters to the atmosphere for a least 1 week before CT imaging in order to render the gels inactive and prevent further polymerization during CT scanning [12]. However, lengthy post-irradiation waits for gel dosimetry makes their use during dosimetric measurements time consuming. This disadvantage limits the radiotherapy applications.
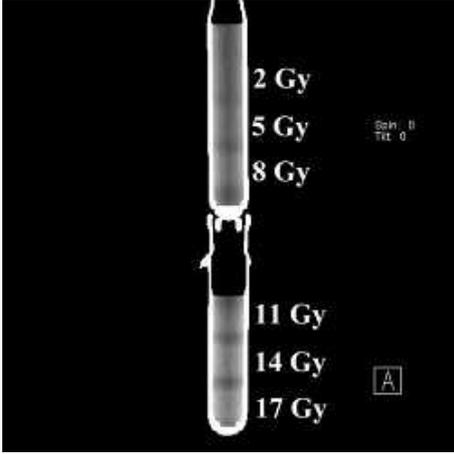
Figure 1. A polymer BANG gel sample following different irradiation doses (2-17 Gy).

Figure 2. Dose sensitivity of CT-based polymer BANG gel dosimetry at tube potentials of 80-120 kVp.

The post-irradiation wait time necessary for oxygen to diffuse through a polymer gel could potentially be shortened if the CT images could be acquired after polymerization was mostly complete. In this study, we did not expose BANG gel samples to oxygen; rather, the CT imaging procedures of gel samples were carried out at appropriate polymerization times following irradiation. The appropriate CT imaging time for polymer BANG gel samples were evaluated using CT images obtained over several imaging sessions on different days.

SNR improvement

Even when using optimized CT imaging parameters, low SNRs characterized the CT images of irradiated polymer gel dosimeters and obscured the dose information. To further increase image SNRs, we acquired 80 images and averaged these in the same position for one polymer gel sample to reduce CT image noise. The SNRs within the ROI were analyzed for a different number of averaged images. The SNR within the ROI is defined as [18]:

$$SNR = 10 \times \log(\frac{CTN_{mean}^{2}}{\sigma_{CTN}^{2}}) \qquad (2)$$

where σ_{CTN} is the standard deviation from the mean CT number (CTN_{mean}) of the irradiated polymer BANG gel.

Results and Discussions

The CT image pixel intensity was increased with increasing irradiation dose, as shown in Figure 1. Pixel intensity in CT images is typically expressed as a CT number, which is a measurement of the linear attenuation coefficient of the sample, μ, relative to the linear attenuation coefficient of water, μ_{w}. A CT number is defined as

$$CTN = 1000 \times \frac{\mu - \mu_{w}}{\mu_{w}} \qquad (3)$$

In CT-based polymer BANG gel dosimetry, the linear attenuation coefficient of polymer BANG gel varies with irradiation dose. The CT number changed (ΔCTN) between irradiated and non-irradiated gel is expressed as
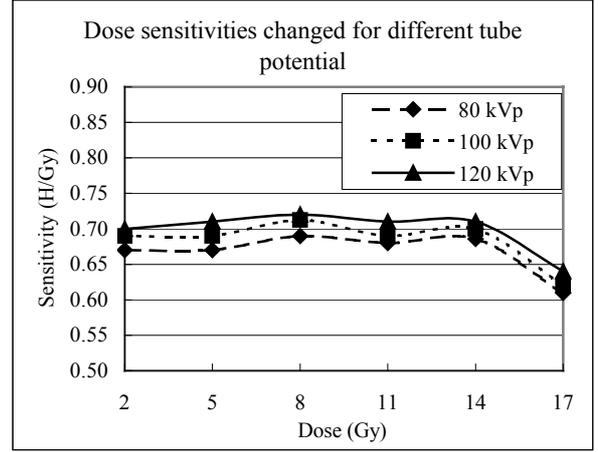
$$\Delta CTN = 1000 \times \frac{\Delta \mu_{gel}}{\mu_{w}} \qquad (4)$$

where the $\Delta \mu_{gel}$ is the change in the linear attenuation coefficient of the gel due to irradiation. The linear attenuation coefficient of a material is proportional to its physical density, ρ, which is expressed as

$$\mu = N_{e} \times \sigma_{e} \times \rho \qquad (5)$$

where N_{e} is the number of electrons per gram and σ_{e} is the electronic cross section. As a result, the relationship between the ΔCTN and the physical density changed ($\Delta\rho_{gel}$) for polymer BANG gel dosimetry can be expressed as

$$\Delta CTN \propto \Delta \rho_{gel} \qquad (6)$$

Possible mechanisms for the increased pixel intensity in polymer BANG gel CT images after irradiation must be related to increases in the physical density resulting from radiation-induced polymerization of acrylic monomers.

To investigate dose sensitivity variations along with tube potentials, the gel samples were imaged with various the tube potentials (80-120 kVp). See Figure 2 for the dose sensitivities of polymer BANG gel for different tube potentials. The average dose sensitivities for the dose range of 2-17 Gy were 0.67±0.03, 0.68±0.03, and 0.70±0.03 (H/Gy) for tube potentials of 80, 100, and 120 kVp, respectively.

In general, the dose sensitivities of CT-based polymer BANG gel dosimetry were above 0.65 (H/Gy) for all tube potentials in this study, except for one data point, which received a 17 Gy irradiation. The dose sensitivities of polymer BANG gel samples at a dose of 17 Gy for each tube potential were relatively low compared to the other irradiation doses. Similar effects had been observed from other investigations with a PAG dosimeter at doses greater than 10 Gy [13]. The reduction in dose sensitivity may be due to the polymerization of acrylic monomers tends to saturate slightly at high dose regions. It is plausible that this effect might increase dosimetric measurement uncertainty because significant underestimations of dose responses in high-dose irradiation for CT-based polymer BANG gel dosimetry.
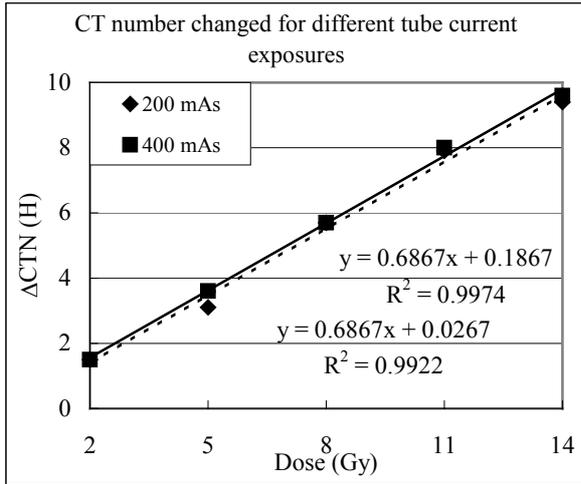
Figure 3. The CT number-dose response analysis of polymer BANG gel dosimetry for tube current exposures of 200 and 400 mAs.
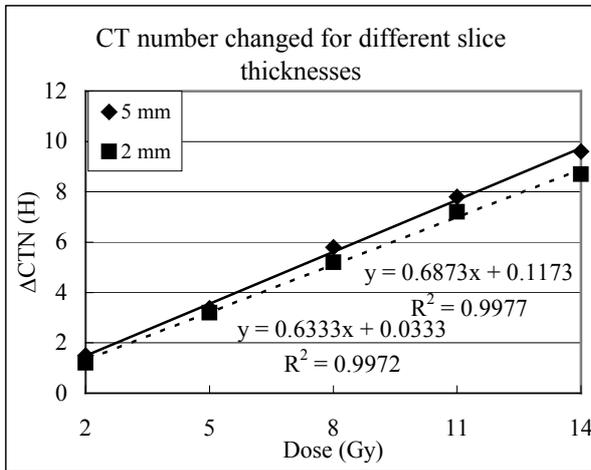

Figure 4. The CT number-dose response analysis of polymer BANG gel dosimetry for 2 and 5 mm slice thicknesses.

To minimize measurement variation, we further analyzed optimal CT imaging parameter settings for polymer BANG gel dosimetry in the 2-14 Gy dose range. The average dose sensitivities for dose range of 2-14 Gy were 0.68±0.01, 0.70± 0.01, and 0.71±0.01 (H/Gy), corresponding to tube potentials of 80, 100, and 120 kVp. It is therefore; the optimal tube voltage setting of 120 kVp was suggested from this work.

To investigate the ΔCTN of gel samples against scanning tube current exposure (mAs), the gel samples were imaged with tube current exposure of 200 mAs and 400 mAs. The CT number-dose response measured for tube current exposures showed in Figure 3. The same dose sensitivity (0.6867 H/Gy), indicated by the slope of the CT number-dose response curves, was observed for tube current exposures of 200 mAs and 400 mAs.

A smaller R^2 value (R^2 = 0.9922) was observed for tube current exposure of 200 mAs compared to that of 400 mAs (R^2 = 0.9974). The reason for this is that increasing the tube current
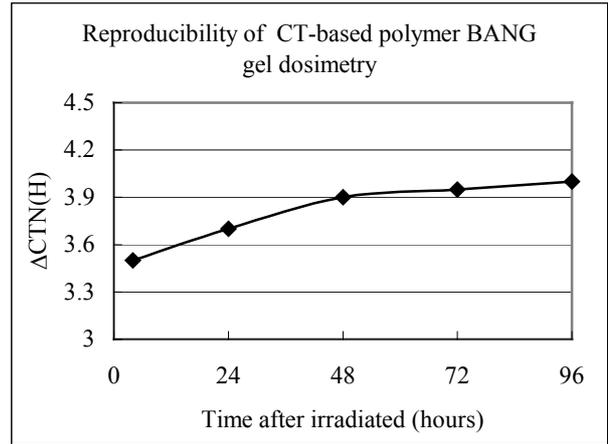

Figure 5. The CT number changed for polymer BANG gel dosimetry at different times after irradiation.

exposure increases the number of photons emitted from the X-ray tube, i.e., a greater number of photons reach the detectors, reducing statistical fluctuations in CT number [13]. Therefore, we suggest using a tube current exposure of 400 mAs for CT-based polymer BANG gel dosimetry to reduce counting fluctuations during CT imaging.

The ΔCTNs for slice thicknesses of 2 mm and 5 mm during CT imaging were evaluated, as shown in Figure 4. The dose sensitivities were 0.6333 and 0.6873 (H/Gy) corresponding to slice thicknesses of 2 mm and 5 mm, respectively. The dose sensitivity for the 5 mm slice thickness was higher than that of the 2 mm slice thickness. Similar effects had been reported for PAG dosimeters in other investigation [12].

Increasing the voxel size of a CT gel image increases the number of attenuation photons within the voxel, i.e., small density differences between voxels can be identified using a larger voxel size. The CT image of 5-mm-thick per slice is the most frequently used for 3D dose calculations in radiotherapy. In this work, we suggest using a slice thickness of 5 mm rather than the 10 mm recommended in previous investigations [12] due to increasing the voxel size results in the loss of spatial resolution of the CT gel image.

The reproducibility of a gel sample, which is indicated by the CT number-dose responses measured on different days, was evaluated at 5-Gy-irradaition region to determine appropriate CT imaging time of BANG gel after irradiation. The CT imaging times ranged from 1 hour to 4 days after irradiation, as shown in Figure 5. The ΔCTN was 0.2 H per 24 hours and 0.1 H per 48 hours before and after 2 days.

Radiation-induced polymerization of acrylic monomers continued after irradiation if the gel sample did not expose to oxygen; however, it did tend to slow down slightly after 2 days. Therefore, we propose that the appropriate CT imaging time is 2 days after irradiation for polymer BANG gel dosimetry. This improvement significantly shortens the CT imaging wait time noted previously, as a 1-week wait time was previously necessary for complete polymerization of the acrylic monomers.
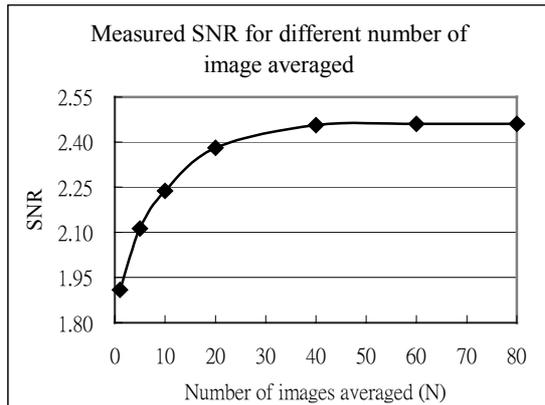
Figure 6. The signal-to-noise variations of CT images with a varied number of images averaged.
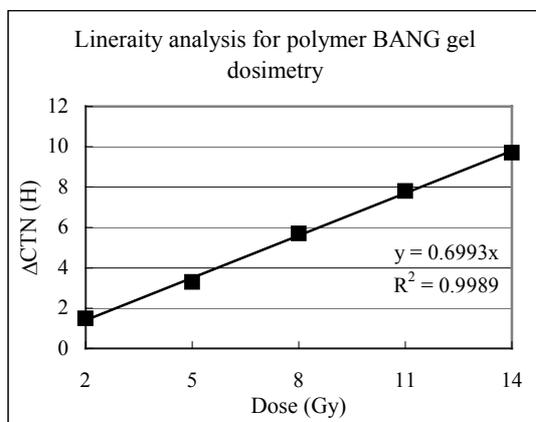

Figure 7. Linearity analysis for CT-based polymer BANG gel dosimetry in doses ranging from 2-14 Gy.

In order to reduce the CT image noise in irradiated polymer gel dosimetry, 80 images were acquired and averaged from the same scan position. The SNR analysis (equation 2) was applied to quantify the SNR improvement of the averaged images. Figure 6 shows the relationship between measured SNR and the number of images averaged (N) for the sample with 14-Gy-irradiation. As expected, we observed significant SNR improvements for averaged CT gel images, which ranged from 1.91 for unprocessed images to 2.46 for 80 averaged images.

The number of images that can be averaged is limited by X-ray tube heat loading and the resulting increases in imaging time. Imaging time using this method is within 10 min. Thus, when many images are required, averaging 20 images per scan position was recommended to reduce heat loading and imaging time without much loss in the SNR. When only a small number of images are required to span a gel volume or if acquiring thinner noisier images (2 mm), averaging at least 40 images were suggested. Because the dose delivered from the CT scan was within mGy degree per scan, which could be neglected compared to the irradiation doses (2-14 Gy), the CT number would not be altered significantly due to an increase in CT imaging.

In order to assess our CT imaging protocol, we imaged the polymer BANG gel samples using the optimal parameter settings described above. Figure 7 shows the CT number-dose response. In previous investigations, a linear region was observed for doses up to 10 Gy followed by a slight decrease in the response for PAG dosimeters. The CT-dose response of the PAG dosimeter was fitted with a mono-exponential function for doses up to 50 Gy; however, a linear regression fit was employed in this work because our experimental data consisted of relatively low doses (2-14 Gy) compared to other works.

Good linearity was observed between CT numbers and irradiation doses in this work. The dose sensitivity of polymer BANG gel was about 0.70 ±0.02 H/Gy, which was comparable to 0.85 ± 0.03 H/Gy [12] and 0.71 ± 0.02 H/Gy [13] for PAG dosimeters.

Conclusions

In this work, we developed a protocol for CT imaging polymer BANG gel dosimetry in order to produce quality CT images with useful dose information in a clinical environment. Our protocol includes optimal CT imaging parameter settings, image averaging to improve SNR, and an appropriate imaging time after irradiation. The CT number-dose response of the polymer BANG gel showed good linearity up to 14 Gy before showing signs of slight saturation.

The appropriate CT imaging time was 2 days after irradiation for polymer BANG gel dosimetry without exposure to oxygen. This is a significantly shorter waiting time for CT imaging compared to that of previous works in which the PAGs were exposed to oxygen. However, this scheme requires keeping all the gel samples in the same condition before imaging, as slight radiation-induced polymerization of the acrylic monomers continues after irradiation.

Oxygen inhibits the polymerization of a polymer BANG gel; therefore, we frequently employed glass containers to ensure that the gel samples were maintained in an oxygen-free atmosphere. Because of the high density of glass (2.3 g×cm^{-3}), the container walls produced beam-hardening artifacts in the CT images. Although the use of glass material to simulate bone materials has been reported [9], a soft-tissue equivalent medium is desirable for most clinical dose verification procedures.

In order to minimize beam-hardening artifacts from the glass containers, we will use Barex® containers — which are composed of a material that has high-oxygen barrier properties — in future studies. The density of Barex® material is 1.15 g/cm^{-3}, which is nearly a soft-tissue equivalent [5]; therefore, beam-hardening artifacts will be minimized. Using Barex® containers could potentially improve the SNR of CT-based polymer BANG gel dosimetry.

Physics can accurately extract dose information using CT imaging from gel dosimetry, which can serve as a relatively inexpensive and accessible means of analyzing polymer BANG gel dosimetry in a clinical radiotherapy environment. Our future work will focus on dosimetric verifications in radiotherapy using CT-based polymer BANG gel dosimetry.

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