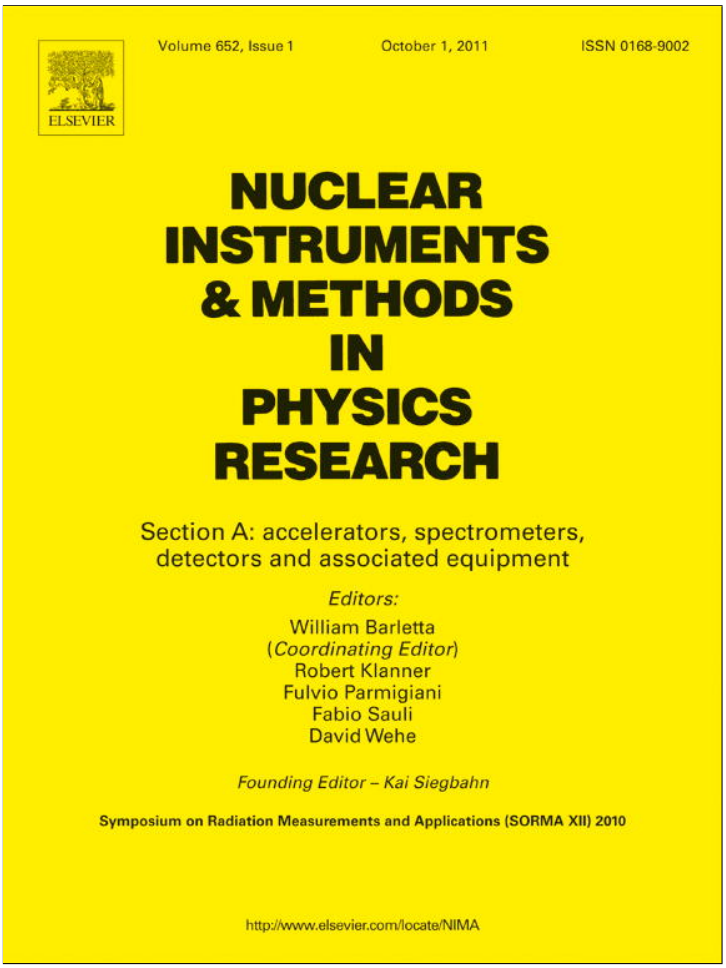

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Investigation of the dose characteristics of an n-NIPAM gel dosimeter with computed tomography

Kuan-Yu Chang [a], Tian-Yu Shih [b,c], Bor-Tsung Hsieh [c], Shu-Jun Chang [d], Yan-Lin Liu [c], Tung-Hsin Wu [e], Jay Wu [c,*]

[a] Department of Orthopedic Surgery, Mackay Memorial Hospital Taitung Branch, Taitung, Taiwan, ROC
[b] Department of Radiology, Cheng Ching Hospital at Chung Kang, Taichung, Taiwan, ROC
[c] Institute of Radiological Science, Central Taiwan University of Science and Technology, No. 11, Pu-Tzu Lane, Pei-tun District, 40601 Taichung, Taiwan, ROC.
[d] Health Physics Division, Institute of Nuclear Energy Research, Taoyuan, Taiwan, ROC
[e] Department of Biomedical Imaging and Radiological Sciences, National Yang-Ming University, Taipei, Taiwan, ROC

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ABSTRACT

Nowadays, radiotherapy attempts to deliver complex three-dimensional (3-D) dose distribution. The gel dosimeter, which can measure the 3-D dose output, is suitable for clinical use. This study developed an n-NIPAM gel dosimeter based on an *N*-isopropyl-acrylamide monomer, and used computed tomography (CT) to evaluate the characteristics of n-NIPAM gels. The n-NIPAM gel consisted of 6% gelatin, 5% monomer, and 2.5% cross-linker combined with 5 mM tetrakis (hydroxymethyl) phosphonium chloride (THPC) for deoxygenation. Dose responses of 2–15 Gy delivered by a linear accelerator were examined. Temporal instability, energy dependence, dose rate dependence, and spatial resolution were evaluated as well. Temporal instability appeared before 24 h post-irradiation. The maximum difference of sensitivity reached 33% for various dose rates from 100 to 500 cGy min^{-1}, while it was within 10% for X-ray energies from 6 to 15 MV. The average sensitivity of n-NIPAM under 6 MV and 400 cGy min^{-1} was 0.5689 HU Gy^{-1}, and the linearity (R^2=0.998) was comparable to that of the conventional NIPAM gels. For the spatial resolution, the edge spread distances were generally shorter than 6.5 mm for adjacent quadrants with different dose gradients of 5/10, 5/15, 10/20, and 15/20 Gy. We conclude that n-NIPAM has high linearity and high sensitivity. Although the energy dependence is minor, there is a slight dose rate dependence. The proposed dosimeter with CT readout is suitable in clinical radiotherapy to increase the accuracy of dose verification.

1. Introduction

Modern radiotherapy techniques, such as intensity modulated radiation therapy (IMRT) and stereotactic radiosurgery, allow the radiation dose to accurately conform to the target volume with complicated three-dimensional (3-D) shapes, while sparing the dose to surrounding tissues. Dosimeters with accuracy of 3–5% are necessary [1] to verify the absorbed radiation dose. Additionally, the ability to measure 3-D dose distributions with fine spatial resolution is required for treatment planning that contains steep dose gradients. Ion chambers, thermoluminescent dosimeters (TLDs), and X-ray films are common instruments for dose verification. However, they can only measure one- or two-dimensional dose distributions. The radiation-sensitive polymer gel, which has emerged in the last decade, is becoming one of the most promising 3-D dose verification tools.

Polymer gels consisting of a monomer in an aqueous gel matrix are polymerized after irradiation. The amount of polymerization is directly related to the radiation dose. Researchers have investigated several imaging modalities in an attempt to obtain the 3-D dose information from the gel. Previous approaches included magnetic resonance imaging (MRI) [2], optical computed tomography (OCT) [3], X-ray computed tomography (CT) [4], and ultrasound [5]. Among these modalities, X-ray CT is the most convenient due to its widespread availability in healthcare institutions. Recent studies showed its ability to distinguish the changes in CT numbers (CTNs) in the irradiated polyacrylamide gel (PAG) [6] and the *N*-isopropyl-acrylamide (NIPAM) [7] gel. However, the major limitation in the clinical use of X-ray CT is its low dose sensitivity. An ideal polymer gel dosimeter and readout system should have a highly sensitive dose response with good linearity and low energy and dose rate dependences.

In this study, we modified the formulation of the NIPAM polymer gel [8]. This new recipe, named n-NIPAM, possesses the advantages of the NIPAM monomer in terms of having lower

* Corresponding author. Tel.: +886 4 22391647x3004; fax: +886 4 22396762.
E-mail addresses: jwu@ctust.edu.tw, iamjaywu@gmail.com (J. Wu).

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toxicity than the acrylamide monomer and offering simpler inclusion in clinical dosimetry practices. We also assessed the dose characteristics of the n-NIPAM gel and evaluated the feasibility of using X-ray CT as a suitable 3-D dose verification tool for radiotherapy.

2. Materials and methods

2.1. Preparation and irradiation of the n-NIPAM gel

According to Senden et al. [8], the original NIPAM recipe consists of 5% gelatin, 3% *N*-isopropyl-acrylamide monomer, 3% *N,N′*-methylene-bis-acrylamide cross-linker, and 10 mM tetrakis (hydroxymethyl) phosphonium chloride (THPC) as an antioxidant. Herein, we modified the weight percentage of gelatin, monomer, and cross-linker to 6%, 5%, and 2.5%, respectively and added 5 mM THPC as an oxygen scavenger. This composition was determined by a preliminary study using the Taguchi analysis [9]. The n-NIPAM gel was prepared under normal atmosphere conditions and poured into 12 ml vials (Pyrex 9826, USA), 16 mm in diameter and 100 mm long, for CT experiments. The vials were covered with foil to protect the gel from ambient light. Finally, they were cooled in a 4 °C environment for 2 h for solidification before usage.

The n-NIPAM gel was placed at the center of a 4 cm-thick acrylic phantom with a 3 cm-thick solid water slab covered above and under the phantom. A medical linear accelerator (Clinac 21 IX, Varian, USA) with a 0° gantry angle and 10×10 cm^2 field size was used to irradiate the lower-half of the gel at 100 cm SSD. Radiation doses of 2, 5, 8, 10, and 15 Gy were delivered to the center of the vials at various energies and dose rates. One of the testing vials in each batch was spared for irradiation to serve as a 0 Gy reference. After dose delivery, the gels were stored in a refrigerator at 4 °C for subsequent CT scans.

2.2. Gel responses to post-irradiation time, energy, and dose rate

To evaluate the temporal instability of the n-NIPAM gel with CT readout, the testing vials were stored for 1–120 h after dose delivery. The optimized post-irradiation time was evaluated and applied to other analyses in this study. Additionally, the energy dependence and dose rate dependence of the n-NIPAM gel were estimated using three different energies (6, 10, and 15 MV) and five different dose rates (from 100 to 500 cGy min^{-1}).

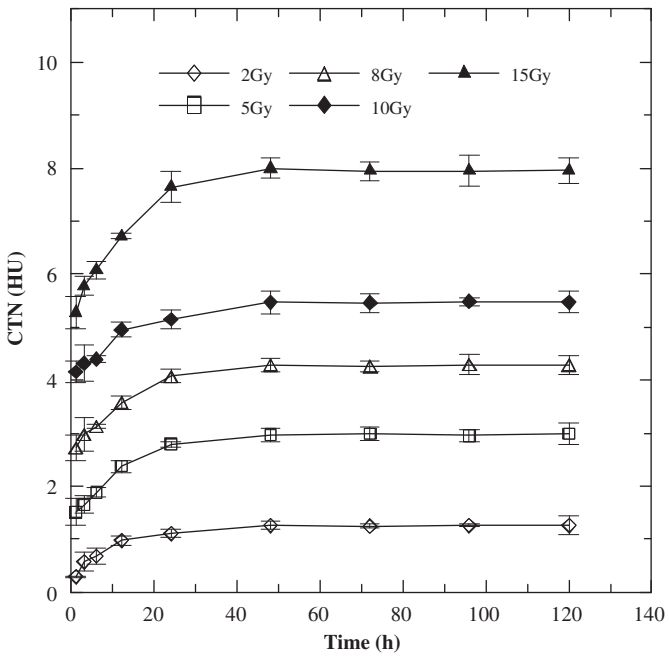

Fig. 1. Dose responses of varying post-irradiation times for 2–15 Gy. All the curves had a climb-up region and a saturation region.

2.3. Spatial resolution

To determine the spatial resolution with fractional doses, a culture dish with 50 mm diameter and 10 mm length was prepared to contain the gel for irradiation. The whole dish was first given a 5 Gy dose, and the upper half of the dish was blocked for another 5 Gy dose. The right-half of the dish was then

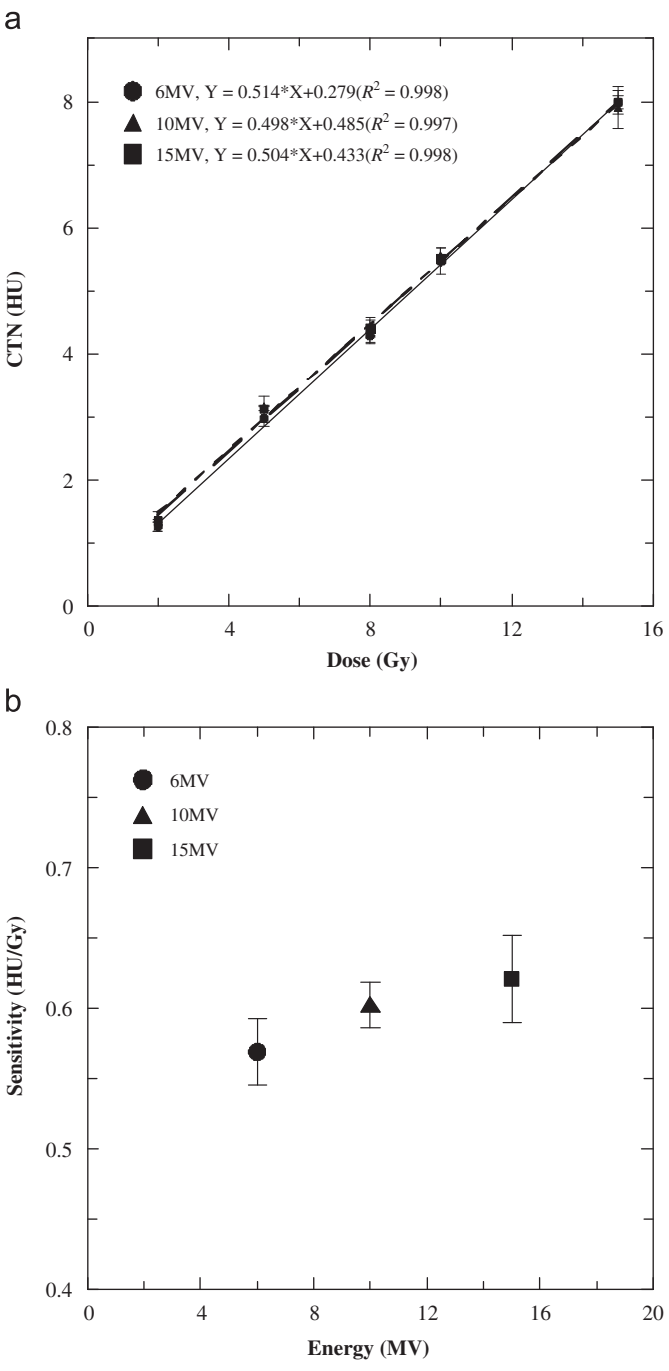

Fig. 2. (a) Dose response curves and (b) dose sensitivity for 6, 10, and 15 MV at 400 cGy min^{-1} dose rate. The linear regression of CTN was fitted to the doses from 2 to 15 Gy.

irradiated for 10 Gy by rotating the collimator to 90°. Consequently, the gel dish was subjected to doses of 5, 10, 20, and 15 Gy counterclockwise. The entire procedure was completed within 15 min. The edge spread effect was evaluated by analyzing the penumbra between two adjacent quadrants. The width of the penumbra was defined as the distance corresponding to 20–80% of the CTN, referred to as $D(20,80)$.

2.4. Image acquisition and analysis

The n-NIPAM gels were stored for 48 h post-irradiation to ensure complete polymerization. CT scanning was performed using a Toshiba Asteion 4 scanner (Toshiba, Tokyo, Japan) operating at 120 kVp, 150 mAs, and 20 °C. Gel images with a 512×512 matrix size and 6 mm slice thickness were acquired and analyzed by Matlab (Mathworks, USA) software. The dose response curves were formed by carefully drawing 2 mm-radius region of interest (ROI) at the center of the gel image and calculating the mean and the standard deviation of the ROI for different doses. The mean CTN of the 0 Gy testing vial was subtracted from the results as background. A linear regression model was then applied to evaluate the linearity and the sensitivity between the CTN and the given dose.

3. Results and discussion

Fig. 1 shows the CTN changes in the n-NIPAM gel as a function of post-irradiation time for radiation doses ranging from 2 to 15 Gy. All the curves had similar shapes, including a climb-up region and a saturation region. Temporal instability appeared roughly before 24 h in the climb-up region due to the prolonged polymerization reactions caused by long-lived free radicals. After 48 h, the linear attenuation coefficient of the irradiated gel became saturated and no significant difference in CTN appeared between various time points, indicating that polymerization was complete. This completion time is shorter than that in the original NIPAM gel [8] using MRI to measure R_2 dose response, which was beyond 72 h post-irradiation. A possible reason is the higher concentration of the gelatin in the n-NIPAM formulation.

Fig. 2 shows the dose response curves and dose sensitivity for different beam energies of 6, 10, and 15 MV at the 400 cGy min^{-1} dose rate. No significant changes of the dose responses from 2 to 15 Gy appeared in the n-NIPAM gel. The R^2 linearity results were all greater than 0.997. The linear regression of sensitivity was 0.5689 HU Gy^{-1} for 6 MV, 0.6026 HU Gy^{-1} for 10 MV, and 0.6208 HU Gy^{-1} for 15 MV. The differences were within 10%. The possible reason for the slight energy dependence is that high energy photons produce more secondary electrons when

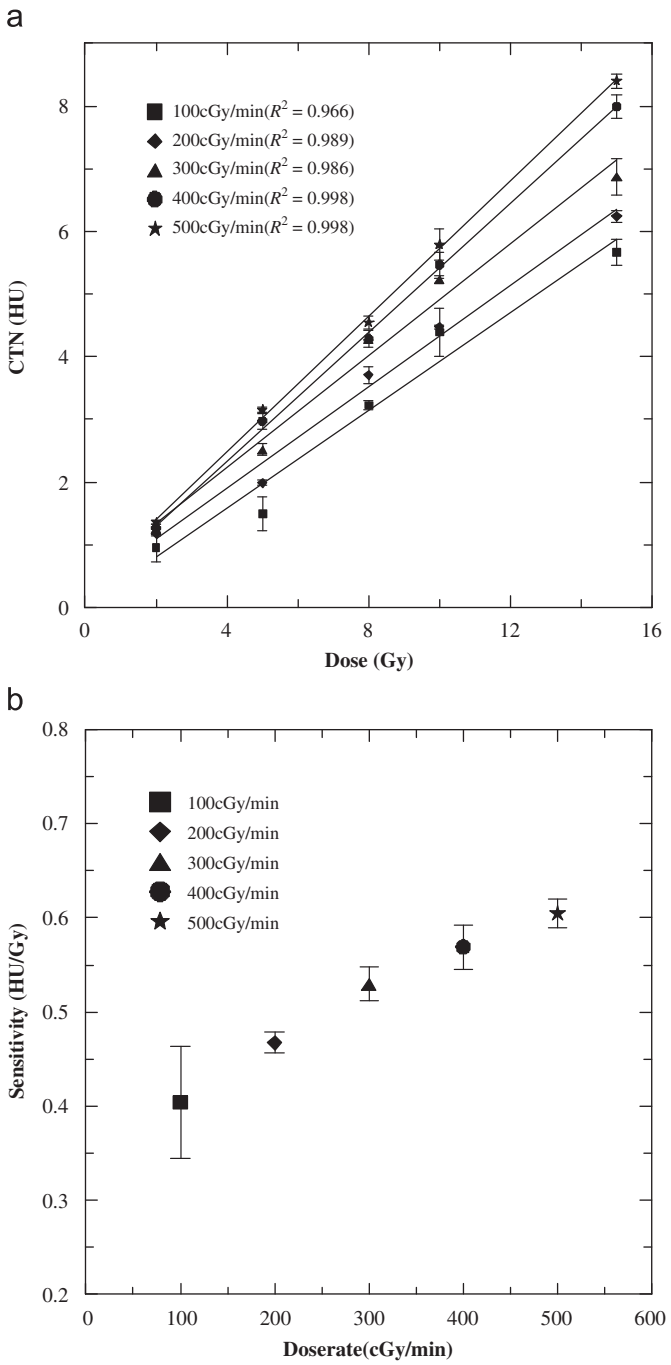

Fig. 3. (a) Dose response curves and (b) dose sensitivity for different dose rates ranging from 100 to 500 cGy min^{-1} under 6 MV. A linear relationship between dose rate and sensitivity can be found.

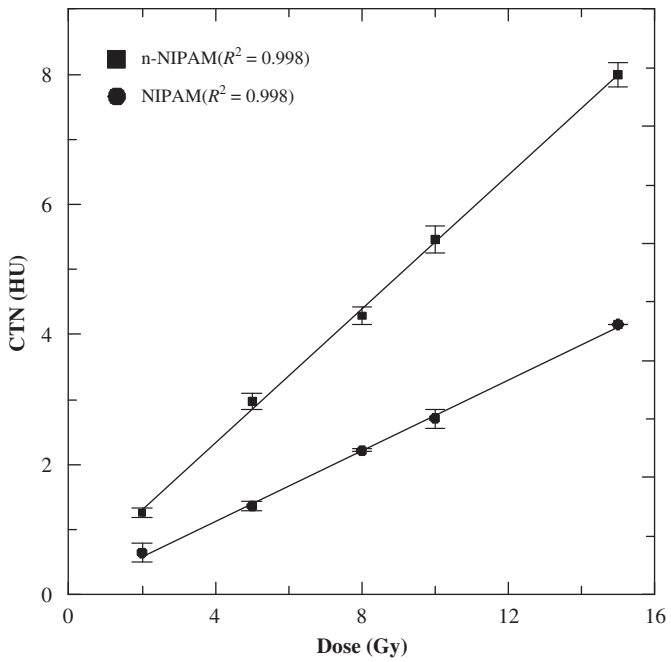

Fig. 4. Dose response curves of the original NIPAM and n-NIPAM recipes using beam parameters of 6 MV and 400 cGy min^{-1}. The sensitivity of NIPAM and n-NIPAM was 0.2537 and 0.5689 HU Gy^{-1}, respectively.

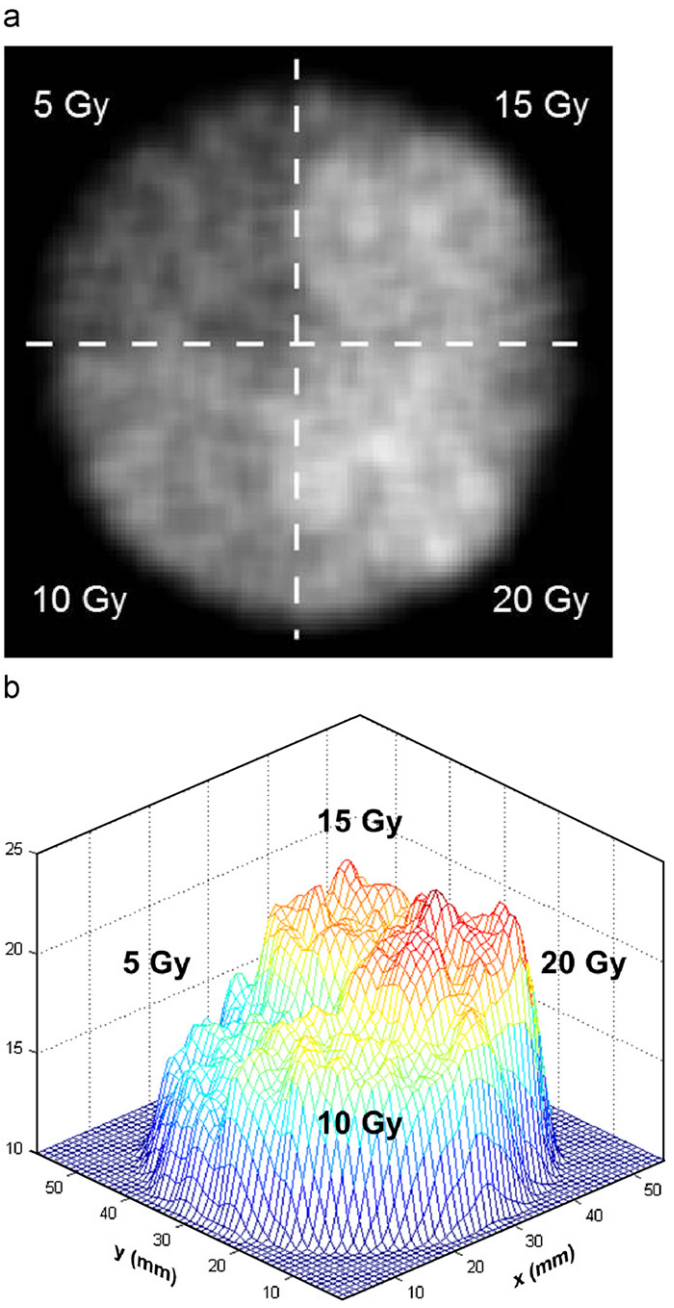

Fig. 5. (a) CT image and (b) corresponding mesh image of the culture dish with four quadrants subjected to doses of 5, 10, 20, and 15 Gy counterclockwise. The four regions of the dish can be well distinguished.

interacting with polymer gels. These electrons can initiate polymerization simultaneously in the local region.

Fig. 3 shows the dose response curves and dose sensitivity under 6 MV X-ray energy with different dose rates. A small dose rate dependence was found in the range of 100–500 cGy min^{-1}. When the dose rate increased, sensitivity increased linearly. The differences in sensitivity can be up to 33% over the whole dose-rate interval. This is because the amount of free radicals created from water is proportional to the dose rate. These radicals further induce the polymerization reaction. Fig. 4 illustrates the dose response curves of the original NIPAM and n-NIPAM recipes using beam parameters of 6 MV, 400 cGy min^{-1}, and 48 h post-irradiation. The n-NIPAM gel achieved a better dose sensitivity and comparable linearity over the quasi-linear dose range of 0–15 Gy.

Fig. 5 shows the CT image of the culture dish with four quadrants irradiated from 5 to 20 Gy doses. A 3×3 Gaussian filter was applied for noise reduction. The four regions of the dish were well differentiated, and the mean CTNs were 15.86 ± 0.54, 17.88 ± 0.42, 20.19 ± 0.72, and 22.46 ± 0.74. In addition, the edge spread distances, $D(20,80)$, were 2.38, 3.83, 6.23, and 4.07 mm for adjacent quadrants of 5/10, 5/15, 10/20, and 15/20 Gy dose gradients, respectively indicating that the CT readout can achieve good spatial resolution.

4. Conclusion

This study proposed a new composition of the NIPAM gel with 6% gelatin, 5% monomer, and 2.5% cross-linker. Several basic characteristics were evaluated by CT acquisition, including the dose response, temporal instability, energy dependence, dose rate dependence, and spatial resolution. Results showed that the n-NIPAM gel had less temporal evolution after 24 h, and obtained high dose sensitivity and linearity. Although the energy dependence was minor, there was a slight dose rate dependence. With the accessibility and stability of CT scanners, the n-NIPAM gel could be a promising 3-D dose verification tool in clinical radiotherapy practices.

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