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Polymer gel dosimeters for pretreatment radiotherapy verification using the three-dimensional gamma evaluation and pass rate maps

Ling-Ling Hsieh [a,b], Jiunn-I Shieh [c], Li-Ju Wei [d], Yi-Chun Wang [e,f], Kai-Yuan Cheng [a], Cheng-Ting Shih [d,*]

[a] Department of Medical Imaging and Radiological Sciences, Central Taiwan University of Science and Technology, No. 666, Buzih Road, Taichung 40601, Taiwan, ROC
[b] Graduate Institute of Biotechnology and Biomedical Engineering, Central Taiwan University of Science and Technology, No. 666, Buzih Road, Taichung 40601, Taiwan, ROC
[c] Department of M-Commerce and Multimedia Applications, Asia University, No. 500, Lioufeng Road, Taichung 41354, Taiwan, ROC
[d] 3D Printing Medical Research Center, China Medical University Hospital, China Medical University, No. 2, Yuh-Der Road, Taichung 40447, Taiwan, ROC
[e] Department of Biomedical Imaging and Radiological Sciences, National Yang-Ming University, No. 155, Sec. 2, Linong Street, Taipei 11221, Taiwan, ROC
[f] Department of Radiology, China Medical University Hospital, China Medical University, No. 2, Yuh-Der Road, Taichung 40447, Taiwan, ROC

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ABSTRACT

Polymer gel dosimeters (PGDs) have been widely studied for use in the pretreatment verification of clinical radiation therapy. However, the readability of PGDs in three-dimensional (3D) dosimetry remain unclear. In this study, the pretreatment verifications of clinical radiation therapy were performed using an *N*-isopropyl-acrylamide (NIPAM) PGD, and the results were used to evaluate the performance of the NIPAM PGD on 3D dose measurement. A gel phantom was used to measure the dose distribution of a clinical case of intensity-modulated radiation therapy. Magnetic resonance imaging scans were performed for dose readouts. The measured dose volumes were compared with the planned dose volume. The relative volume histograms showed that relative volumes with a negative percent dose difference decreased as time elapsed. Furthermore, the histograms revealed few changes after 24 h postirradiation. For the 3%/3 mm and 2%/2 mm criteria, the pass rates of the 12- and 24-h dose volumes were higher than 95%, respectively. This study thus concludes that the pass rate map can be used to evaluate the dose-temporal readability of PGDs and that the NIPAM PGD can be used for clinical pretreatment verifications.

1. Introduction

Clinical radiation therapy (RT) has rapidly developed in the past three decades. Intensity-modulated radiation therapy (IMRT) with advanced multileaf collimators [1–5] has replaced traditional three-dimensional (3D) conformal RT, and it is widely applied clinically to optimize the radiation dose coverage of tumor targets and to reduce the dose to surrounding organs at risk [6,7]. In addition, tomotherapy [8,9] and image-guided radiation therapy [10,11] have been used to provide fast and accurate dose delivery. These techniques have improved the therapeutic ratio and quality of clinical RT [12,13].

To maximize the absorbed dose difference between tumor targets and the surrounding normal tissue, a treatment planning system (TPS) is used to design a dose distribution containing high dose gradients, in which the dose changes rapidly within a short spatial distance [14,15]. Inaccurate dose delivery that reduces the dose difference between tumor targets and normal tissues can substantially decrease the therapeutic ratio, thereby degrading the treatment quality [16]. Therefore, pretreatment dose verification is crucial to ensure that the dose distribution delivered by a medical linear accelerator matches that planned originally [17–19]. In current clinical RT, several point and planar dosimeters have been used for dose verification including ionization chambers [20,21], thermoluminescent dosimeters [22], diode arrays [23,24], radiochromic films [25,26], and electronic portal imaging devices [27]. These dosimeters provide measurement results in the form of a point dose or dose map; however, a dose volume is required for verifying the 3D dose distribution in IMRT.

Polymer gel dosimeters (PGDs) were proposed to measure and record the entire dose volume; the PGD can overcome the ion diffusion effect observed in a Fricke gel dosimeter [28,29]. Moreover, the PGD exhibits tissue equivalence and high plasticity that are useful for medical dosimetry [30,31]. After irradiation, monomers in the PGD are polymerized and crosslinked. The degree of polymerization is a function of the absorbed dose. According to the physical and chemical changes observed in irradiated PGDs, the dose distribution recorded in the PGD can be read out using tomographic imaging modalities such as magnetic resonance imaging (MRI) [30,32], computed tomography (CT) [33,34], and optical CT [35,36]. Polymer

* Corresponding author.
E-mail address: songofdeath2121@gmail.com (C.-T. Shih).

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gel dosimeters formulated using different monomers or novel formulae were developed for achieving higher dose sensitivity and lower toxicity [37–39]. To evaluate the PGD performance, the dose distribution output from the TPS is commonly employed as a reference standard. However, most studies have evaluated the PGD by using a simple irradiation condition or dose distribution [40–43]. In addition, the measured dose distribution is typically evaluated using 2D methods or indices such as dose profiles, dose difference maps, and 2D gamma evaluation [44]. Consequently, the measurement quality and readable dose and time range of the PGD on 3D dosimetry remain unclear and warrant further study.

Several studies have reported on the performance of low-toxicity *N*-isopropyl-acrylamide (NIPAM) PGDs on 2D dosimetry [32,45–47]. In the current study, pretreatment verifications of a clinical IMRT case were performed using the NIPAM PGDs and a 3D gamma evaluation. The results were used to evaluation the performance of the NIPAM PGDs in 3D dosimetry. The measured dose volumes were compared with that derived using a TPS by calculating histograms of the dose difference volumes and performing 3D gamma evaluations.

2. Materials and methods

2.1. NIPAM gel preparation

The formula of the NIPAM PGD used in this study was modified from that proposed by Senden et al. [37]. The NIPAM PGD was fabricated using gelatin (300 Bloom Tape A, Sigma-Aldrich, St. Louis, MO), an NIPAM monomer (97%, Sigma-Aldrich, St. Louis, MO), the crosslinking agent *N*,*N*'-methylene-bis-acrylamide (BIS, Merck, Darmstadt, Germany), the antioxidant agent tetrakis (hydroxymethyl) phosphonium chloride (THPC) (80%, Sigma-Aldrich, St. Louis, MO), and deionized water, and the weight fractions are listed in Table 1. Briefly, the NIPAM PGD was prepared as follows: the gelatin and deionized water were mixed by stirring for 10 min at approximately 22 °C. The gelatin-water solution was then heated to 45 °C by using a hot-plate magnetic stirrer until it became transparent. The NIPAM monomers and BIS were poured into the solution under stirring for approximately 15 min. Finally, THPC was added under stirring for another 15 min. The prepared PGD was poured into Pyrex tubes for calibration, and a gel phantom was used for measuring the dose distribution. The tubes and phantom were subsequently placed in a customized cylindrical polymethylmethacrylate holder with a diameter and height of 130 mm and wall thickness of 5 mm. The entire holder was then covered with aluminum foil and stored in a refrigerator at 4 °C for 6 h to prevent light-induced polymerization before the complete solidification of the PGD. In addition, the holder was placed in a magnetic resonance (MR) scanning room at 22 ± 1 °C after irradiation and between MR scans to avoid the influence of temperature on the polymerization of the PGD [48].

2.2. Dose delivery of calibration tubes and gel phantom

The tubes and phantom were irradiated using a 6-MV medical linear accelerator (Clinac 21EX LINAC, Varian Medical Systems, USA). The output of the accelerator was validated daily to have an error lower than 3%. The calibration tubes were irradiated by absorbed doses of 0, 1, 2, 5, and 8 Gy to obtain a dose-response curve (DRC) for dose conversions. The dose delivery of the tubes was performed using the following parameters: a beam angle of 0°, dose rate of 400 cGy/min, and field size of 10×10 cm^2. During irradiation, the tubes were placed in an acrylic phantom (length: 30 cm; width: 30 cm; thickness: 4 cm) that was sandwiched between 3-cm-thick solid water slabs. The gel phantom was applied to measure the dose distribution of a clinical IMRT case of intracranial meningioma. In this case, dose delivery was performed using a 6-MV photon beam with the following parameters: a dose rate = 400 cGy/min; number of fields = 5; and source-to-axis distance = 100 cm. The prescribed dose (D_p) at the center of the phantom was 5.6 Gy. The dose distribution in the gel phantom under irradiation in the IMRT case was calculated using the Eclipse TPS with the analytical anisotropic algorithm (Varian Medical Systems, Palo Alto, CA), and the results were used as a reference standard for evaluations. To prevent the radiation dose to the gel phantom in CT scans, CT images for calculating the dose distribution were acquired using a cylindrical phantom having the same geometry as the gel phantom. The cylindrical phantom was filled with gelatin to mimic the photon attenuation characteristics of the gels. The CT images of the cylindrical phantom were acquired using a CT simulator (Marconi AcQsim, Philips Medical Systems Ltd., Stevenage, UK) with the following scanning parameters: tube voltage of 120 kVp, tube current of 200 mA, and slice thickness of 1 mm. After irradiation, dose readout of the calibration tubes and gel phantom were performed using an MRI with a head coil. Due to the limited size of the coil, the tubes and phantom cannot be imaged simultaneously. Dose readout of tubes and phantom separately could cause the readout results were from different postirradiation time, if the tubes and phantom were irradiated at the same time. Therefore, a 40-min time interval between the dose delivery of the tubes and phantom was used to ensure the same postirradiation readout time for the tubes and phantom.

Table 1
Formula of the NIPAM polymer gel dosimeter used in this study.

Composition	Weight fraction (%)
Deionized water	89
Gelatin	5
NIPAM (monomer)	5
BIS (crosslinking agent)	3
THPC (mM)	10

2.3. Dose readout using magnetic resonance imaging

A clinical 1.5 T MR scanner (Magnetom Symphony, Siemens AG, Erlangen, Germany) with a head coil was used for the dose readouts of the NIPAM PGD. The T2-weighted images of the tubes and phantoms were acquired using a multiple-spin echo sequence with a repetition time of 3000 ms, echo spacing of 22 ms, and number of echoes of 16. The field of view, slice thickness, and matrix size of the acquired images were 240×240 mm^2, 5 mm, and 512×512, respectively. After MR imaging, the T2-weighted images acquired at different echo times were converted into R2 values as follows [49]: The measured T2-weighted signals and their echo time were used to determine the T2 value pixel-by-pixel using least-square fittings with a T2 relaxation model. The R2 values were calculated using 1/T2 values. DRCs were obtained through the linear fitting of the mean R2 values and the absorbed doses of the tubes with the function $R2 = a \times D + b$. The R2 maps of the gel phantom could then be converted into dose maps using the DRCs. Additionally, the temporal stability of the NIPAM PGD was investigated through the MR imaging of the tubes and phantom at 2, 6, 12, 24, 168, 360, 720, and 1440 h postirradiation. For each measurement time point, the R2 maps were converted into dose maps by using the DRCs at the same time points.

2.4. Evaluation of 3D dose distributions measured using NIPAM PGD

The readability and temporal stability of the NIPAM PGD in measuring 3D dose distributions were evaluated using percent dose difference histograms and 3D gamma evaluations. For the his-