The study of N-isopropylacrylamide gel dosimeter doped iodinated contrast agents

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Abstract. Low toxicity of N-isopropylacrylamide (NIPAM) dosimeter was doped with clinical iodinated contrast medium agents (Iobitridol (Xenetix® 350) and organically bound iodine (Conray® 60) as radiation sensitizers; The suitable gel dosimeter preparation formula in this research was 5 w/w% gelatin, 5 w/w% N-isopropylacrylamide, 3 w/w% N,N-methylene-bis-acrylamide, and 5 mM Tetrakis phosphonium chloride. The spiral CT was irradiator, and 120 kVp was the operating tube voltage. The maximum radiation dose was 0.6 Gy, and optical CT was the gel measurement device used. The results showed SERs with the addition of radiosensitizers were 10.70 (Xenetix® 350) and 9.67 (Conray® 60), respectively. Thus, the polymerized gel dosimeter could be used in the efficacy evaluation of low-energy and low-radiation dose.

1. Introduction
Gel dosimeters were previously used for dose verification in radiotherapy. However, they have low sensitivity to low radiation dose. In 2005, Corde et al [1] boosted the radiation sensitivity of Fricke gel dosimeters by adding high-z number materials (iodine and barium) and giving 33.5 and 80 keV X-ray radiation using a single-energy synchronized accelerator. In the following year, Boudou et al [2] boosted the radiation sensitivity of polymeric gel dosimeters by adding iodine-containing developers and giving 50 keV single-energy X-ray radiation. In clinical practice, doctors usually add contrast agents into low-energy radiators to enhance regional image contrast ratio and obtain images with higher diagnostic value. This research aims to add iodinated contrast agents into a low toxicity gel dosimeter (NIPAM), use a low-energy X-ray machine, give low-dose radiation, and observe the CTDIw (up to 0.6 Gy) of the gel dosimeter.

2. Materials and method
2.1. NIPAM gel preparation
In this study, gel was prepared from gelatin, NIPAM, BIS, and THPC using two formulas: (1) 6 w/w%, 5 w/w%, 2.5 w/w%, and 5 mM, respectively, and (2) 5 w/w%, 5 w/w%, 3 w/w%, and 5 mM, respectively [3]. Linac (Varian) was used to radiate until 5 Gy linearity and sensitivity were achieved. Briefly, gelatin was dissolved in deionized water and heated to 45 °C. When the water was already transparent, NIPAM and BIS were added with continuous stirring for 25 min. Finally, THPC was added. After 2 min, the mixture was poured into a Pyrex spiral test tube. In this study, radiosensitizers
Iobitrindol (Xenetix® 350) and Iothalamate (Conray® 60) were added after dissolving NIPAM and BIS in water solution. As a result, two phase symmetries of the additives were produced: NIPAMXenetix® 350 and NIPAMConray® 60. For equal iodine equivalent, the addition doses are shown in Table 1.

![Table 1. Addition dosages of contrast agents to NIPAM dosimeter](image)

Table 1. Addition dosages of contrast agents to NIPAM dosimeter

| Contrast medium agents | Concentration in this product | Contrast agent doped amounts in 13mL NIPAM dosimeter |
|------------------------|-------------------------------|----------------------------------------------------|
| Xenetix® 350(NIPAMXenetix® 350) | 350mg/mL | 1.30mL |
| Conray® 60(NIPAMConray® 60) | 282mg/mL | 1.61mL |

2.2. Irradiation gel dosimeter
The doped NIPAM dosimeters were irradiated up to 0.6 Gy(CTDIw) by spiral computed tomography (Hi-speed, GE). The indoor temperature of the radiation chamber was 22 °C, the output tube voltage was 120 kVp, the tube current was 660 mAs, the CTDIw doses for the reference were 0.1, 0.2, 0.3, 0.4, and 0.6 Gy, and the radiation thickness was 10 mm. Polystyrene was used as a phantom in this process. Additionally, a medium-energy X-ray machine (Pantak HF 420C, National Standards Lab) was used. QRT filter disk assembly was used to simulate the quality of CT beam (error within 5% compared with IEC61267). CAFCHROMIC® XR CT2 and NIPAMXenetix® 350 were irradiated with 120 kV. The beam center distance was 150 cm. Doses of 0.1, 0.15, 0.2, 0.25, 0.05, 0.1, 0.15, 0.2, 0.25, and 0.3 Gy were given separately. Sensitivity comparisons were made regarding the radiation results against the gel dosimeter.

2.3. Radiated gel measurement using Optical Computed Tomography
After post-irradiated 24hrs, NIPAM gels were measured by optical computed tomography (a single 632nm He-Ne laser beam). It was evaluated of gel at different optical densities was detected before/after irradiation.

\[
\text{Optical density(OD)} = \log \frac{I_{\text{in}}}{I_{\text{out}}} \tag{1}
\]

\(I_{\text{in}}\): Decrease of 632nm laser light intensity in NIPAM gel.
\(I_{\text{out}}\): Decrease of 632nm laser light intensity in irradiated NIPAM gel

2.4. Quantification of radiation sensitivity
This study is mainly targeted at low-energy and low-dose gel dosimeter reactions. Therefore, quantifying the reaction results is helpful for verifying the test results. The radiation sensitizer of sensitivity enhancement ratio (SER) is defined as the ratio between the slope of doped radiation sensitizer to NIPAM gel and without doped radiation sensitizer to NIPAM gels:

\[
\text{SER} = \frac{\text{slope}^{\text{doped}}}{\text{slope}^{\text{non-doped}}} \tag{2}
\]

3. Results and discussion

3.1. Optimal gel formulation
Different gel formulas also generate different reaction results. Studies show that the appropriate BIS content is 2.5 w/w% to 3 w/w% [3]. The gelatin content in this study was decreased from 6 w/w% to 5 w/w% [3]. As shown in Figure 1, the linearity (R²) and sensitivity (slope) were 0.9954 (0.1293 Gy⁻¹) and 0.9843 (0.0693 Gy⁻¹), respectively. The results showed that the polymerization reaction increased with decreasing gelatin content. Because gelatin consumes long-lived radicals, higher gelatin concentrations were relatively lower polymerization rates [3, 4]. The formula 5 w/w% gelatin, 5 w/w% NIPAM, 3 w/w% BIS, and 5 mM THPC was adopted because it enables the gel dosimeter to have higher linearity and sensitivity.
3.2. Measurement results using Optical Computed Tomography

Figure 2(a) showed when the samples were irradiated with X-ray photons whose most probable energy is close to the K-edge absorption of iodine (~33 keV) [5]. Comparing of different energy to irradiate NIPAMXenetix® 350 and NIPAM Conray® 60, has great linearity of 0.995 and highest sensitivity of 0.428 Gy-1. Figure 2 (b) showed NIPAMXenetix® 350 had highest slice width response profile than NIPAM Conray® 60 even non-doped to NIPAM gel (purple). According to literature, polymer gel can be used as an alternative dosimeter to TLD for the determination of Slice width dose profile (SWDP) [6]. However, there are also some problems in application of gel dosimeter for CTDI measurements such as their low sensitivity [7]. In this study, NIPAM gel doped Iodine to sensitivity enhancement that can be more easier to determination of SWDP.

3.3. Sensitivity enhancement ratio (SER)

Table 2 showed the SER of NIPAMXenetix® 350 was higher than NIPAM Conray® 60. For kilovoltage energy X-rays, increase is produced by photoelectrons and Auger electrons after photoelectric effect on the heavy atoms [8]. This effect can be produced more free radical to increase polymerization for NIPAM gel. However this enhancement effect of the probability relative reduction with increasing energy of X-ray.

3.4. Comparison sensitivity of radiated radiochromic film and NIPAM gel

Chemical film radiation is used in alignments such as verifications of beam evenness, photon flatness, beam width, and so on. Changes in the ash medium of chemical films are used to determine the radiation reaction. The enhancement results for NIPAMXenetix® 350 with radiochromic film of the maximum difference to 3.54 at the dose is 0.3 Gy (Figure 3). In this study, the optimal formulation
only doped to 1.30 mL in 13 mL NIPAM gels. To increase doped concentration of radiation sensitizers to polymer gel dosimeter can be more enhanced sensitivity of radiation doses [5]. In this study, the content of Xenetix® 350 added is 1.30 mL. The gap could be narrowed down when the volume of the radiosensitizer added is increased.

Table 2. SER values of different radiosensitizers in NIPAM gels.

| Irradiated gels | Gel response of sensitivity | Correlation coefficient | SER  |
|-----------------|----------------------------|-------------------------|------|
| NIPAM non-doped | 0.04                       | 0.91                    | 1.00 |
| NIPAM Xenetix® 350 | 0.43                     | 0.99                    | 10.70|
| NIPAM Conray® 60 | 0.39                      | 0.99                    | 9.67 |

Figure 3. OD reactions of v CAFCHROMIC® XR CT2 and NIPAM after being radiated with 120 kV a medium-energy X-ray machine (Pantak HF 420C, National Standards Lab)

4. Conclusion
In the past, polymeric gel dosimeters are used for dose verification in high-energy radiation therapy plans. Our results suggested that radiosensitizers are helpful in the feasibility of low-energy and low-dose radiation verifications using NIPAM gel dosimeter.

5. References
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