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Optical and NMR dose response of N-isopropylacrylamide normoxic polymer gel for radiation therapy dosimetry

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ABSTRACT

Background: Application of less toxic normoxic polymer gel of N-isopropyl acrylamide (NIPAM) for radiation therapy has been studied in recent years.
Aim: In the current study the optical and NMR properties of NIPAM were studied for radiation therapy dosimetry application.
Materials and methods: NIPAM normoxic polymer gel was prepared and irradiated by 9 MV photon beam of a medical linac. The optical absorbance was measured using a conventional laboratory spectrophotometer in different wavelengths ranging from 390 to 860 nm. R_2 measurements of NIPAM gels were performed using a 1.5 T scanner and R_2–dose curve was obtained.
Results: Our results showed R_2 dose sensitivity of $0.193 \pm 0.01\,s^{-1}\,Gy^{-1}$ for NIPAM gel. Both R_2 and optical absorbance showed a linear relationship with dose from 1.5 to 11 Gy for NIPAM gel dosimeter. Moreover, absorbance–dose response varied considerably with light wavelength and highest sensitivity was seen for the blue part of the spectrum.
Conclusion: Our results showed that both optical and NMR approaches have acceptable sensitivity and accuracy for dose determination with NIPAM gel. However, for optical reading of the gel, utilization of an optimum optical wavelength is recommended.

1. Background

Investigation on polymer gel dosimetry for radiation dosimetry has been the subject of a large number of studies in radiation dosimetry for two decades.[7,8,10,17,18,21] In spite of several exclusive advantages of this type of dosimetry, there have been also some factors to postpone its routine clinical application in many radiation therapy institutions.[20] Among the disadvantages, high toxicity of monomers used has been a considerable obstacle to overcome for many investigators.[3–5,18] In recent years a great amount of efforts has been made to facilitate their usage in clinic by finding new low toxic monomers as well as gel dosimeter fabrication in

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normal atmospheric conditions.[3,6,18] N-isopropyl acrylamide (NIPAM) polymer gel dosimeter was first studied by Senden et al. and its appropriate dosimetric properties for radiation therapy application were reported.[18] Dosimetric data acquisition by different methods, such as MRI, optical CT and X-ray CT were investigated separately by different groups.[1–3,18] In the study of Ghavami et al. the X-ray CT dose response of the NIPAM gel was investigated. The results showed that X-ray CT dose readout has potential for application in radiation therapy dosimetry, but further developments are required for its practical application in radiotherapy.[3]

Application of optical systems to extract dosimetric data from polymer gels has been the subject for research from ever since gel dosimetry was invented.[11,12,16] Using optical systems for polymer gel dose readout allows users to overcome dependency on magnetic resonance imaging systems in busy hospitals. Also, the long time and high price of R_2 measurements by MRI systems can be avoided using an affordable and easy to use optical system in a laboratory environment.[9,11–16,19,23] As far as we know, the optical dose sensitivity of NIPAM gel and its dependency on light wavelength have not been reported. So, it was the objective of the current study to address the unresolved issues in this regard. Additionally, in the current study the NIPAM polymer gel characteristics were studied by two data acquisition methods, including optical absorption measurements and magnetic resonance imaging and results were compared with previous studies.

2. Aim

The aim of the current study was to investigate the optical and magnetic resonance properties of NIPAM gel for application in radiotherapy dosimetry.

3. Material and methods

3.1. Gel preparation and irradiation

According to previous studies,[3,18] gel dosimeters contained gelatin (5 wt%), monomer (3 wt%), N,N′-methylene-bis-acrylamide crosslinker (3 wt%) and tetrakis (hydroxymethyl) phosphonium chloride antioxidant (10 mM). The polymer gel dosimeters were manufactured inside a fume hood, and under normal atmospheric conditions. The gel consists of NIPAM (Aldrich, 97%) and Bis acrylamide and Tetrakis hydroxymethyl phosphonium chloride (THPC) antioxidant were made using standardized procedures to maximize the reproducibility of gel preparation. At first step, gelatin (300 Bloom Type A) was allowed to swell in 80% of the de-ionized water for 10 min at room temperature, then the solution was heated up to 50 °C. While being stirred continuously, 3 wt% Bis was added to the solution at 50 °C, which took about 15 min, followed by the same amount of NIPAM monomer. Then, the gelatin–crosslinker mixture was cooled to approximately 37 °C. Finally, a solution of the antioxidant THPC was prepared with the remaining 20% of water, and added to the solution. The gels showed itself as a clear, transparent and slightly yellow liquid. The gel solutions were transferred into cylindrical vials with a diameter of 1 cm and a volume of 10 mm^3, and then closed with rubber caps. One vial was not irradiated for background reading and the other vials were irradiated with 9 MV photon beam of Neptun linear accelerator. The vials were placed in the holes within a polyethylene block with the dimension of 30 cm × 15 cm × 10 cm. The dose distribution and dose homogeneity around vials were evaluated using the Alfard treatment planning system. The vials were irradiated with 1.5, 3, 5, 7, 9, and 11 Gy. The irradiation setup is shown in Fig. 1.

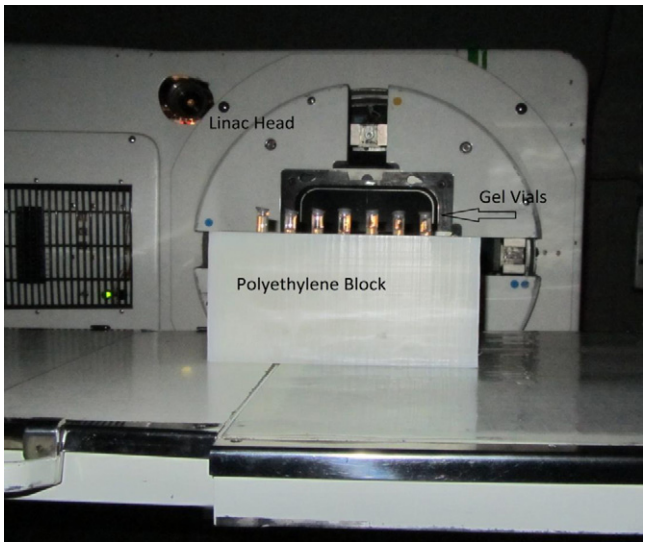

Fig. 1 – The experimental setup for gel irradiation. The white block shows the polyethylene block used for vials irradiation.

3.2. Optical absorbance of irradiated gels

A conventional laboratory spectrophotometer, Spectronic 20D (Milton Roy Company, Belgium) was utilized. A vial with distilled water was used for the zero absorbance calibration of the device. The optical absorbance of vials was measured at available wavelengths of visible light from 390 to 860 nm. For each vial, the absorbance measurements were repeated three times and the average value was used. Absorbance measurements were very reproducible with uncertainty less than 2% for all vials. For each set of measurement, the dose sensitivity of polymer gels in terms of absorbance per Gy was calculated.

3.3. Magnetic resonance imaging of irradiated gels

The irradiated vials were imaged using a 1.5 T magnetic resonance imager. To find R_2 of gels, 30 different protocols were used. Using Matlab software curve-fitting toolbox, the T_2 and therefore the R_2 values for all vials were obtained. For MR imaging, glass vials including non-irradiated and irradiated polymer gel samples were imaged using a 1.5 T clinical MRI scanner (Avento, Siemens, Erlangen, Germany). These samples were transferred to the MRI scanning room before imaging to equilibrate to room temperature (18 °C). All MR imaging was performed using a head coil. MRI

Table 1 – The optical dose sensitivity of NIPAM polymer gel for different wavelengths of the optical beam provided by a conventional spectrophotometer.

Wavelength (nm)	Fitted equation	R^2	Sensitivity (absorbance/Gy)
395	$y = 0.386x + 0.39$	0.99	0.386
400	$y = 0.374x + 0.37$	0.99	0.374
410	$y = 0.358x + 0.32$	0.99	0.358
420	$y = 0.340x + 0.27$	0.99	0.340
450	$y = 0.259x + 0.24$	0.99	0.260
480	$y = 0.209x + 0.21$	0.99	0.210
510	$y = 0.162x + 0.21$	0.99	0.162
540	$y = 0.122x + 0.21$	0.99	0.122
570	$y = 0.122x + 0.15$	0.99	0.120
600	$y = 0.082x + 0.18$	0.99	0.082
630	$y = 0.077x + 0.15$	0.99	0.077
660	$y = 0.060x + 0.24$	0.99	0.060
690	$y = 0.043x + 0.55$	0.98	0.043
720	$y = 0.087x + 0.79$	0.98	0.087
750	$y = 0.209x + 0.60$	0.90	0.210
780	$y = 0.260x + 0.64$	0.99	0.260
810	$y = 0.289x + 0.52$	0.99	0.290
840	$y = 0.310x + 0.31$	0.99	0.310
850	$y = 0.296x + 0.32$	0.99	0.300
860	$y = 0.296x + 0.28$	0.99	0.296

parameters for the multiple spin echo T_2-weighted protocol were: TE (echo time) = 22–676, inter-echo time = 22 ms, number of echoes = 32, TR (repetition time) = 5710 ms, BW (band width) = 130 Hz, slice thickness = 5 mm, FOV (field of view) = 105 mm × 120 mm and matrix size = 128 × 128. Imaging time was approximately 20 min. Then, the Dicom files of images were transferred to a personal computer. Signal intensities related to echo time series of each sample were measured in a circular region of interest in the middle of the tube. Regarding to the first two images, they were affected by stimulated echoes and deviated from the exponential decay curve,[22] they were removed from acquired images before fitting the T_2 curve. MATLAB curve-fitting toolbox was used for T_2 relaxation time measurement. The signal changes for various TE points of each vial were used to fit T_2 exponential curve, based on its corresponding signal model ($S = S_0\, e^{-TE/T_2}$), for T_2 relaxation time measurement. R_2 ($1/T_2$) relaxation rate values were calculated to plot a R_2–dose response curve. R_2–dose sensitivity was calculated as the slope of the R_2–dose response curve.

4. Results and discussion

Absorbance–dose response and their fitted equations of NIPAM gel for different wavelengths are shown in Table 1. Also, to better illustrate the line fitting on our data, absorbance–dose responses of polymer gel for three light wavelengths, including 450 nm (blue), 540 nm (green) and 630 nm (red), are shown in Fig. 2. The error bars show the standard deviation of measurements for each gel vials.

Fig. 3 shows the dose sensitivity variation of polymer gel with light wavelength. The aim was to find higher sensitivity for polymer gel dose reading. As is seen, the maximum sensitivity is near 400 nm in the blue region of the spectrum. However, it should be mentioned that it is not possible to read absorbance for doses higher than 10 Gy with the conventional

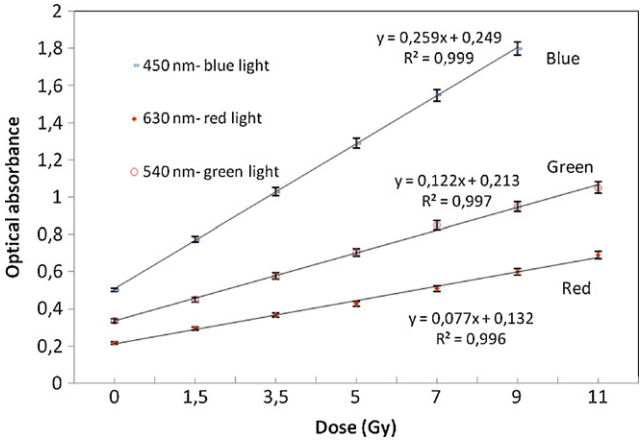

Fig. 2 – Dose–response curves for polymer gel analyzed by three different wavelengths of visible light.

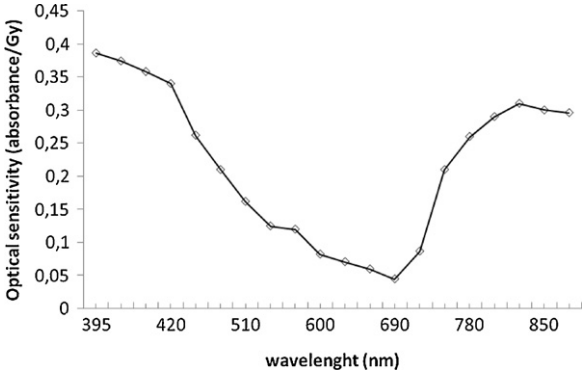

Fig. 3 – The optical dose sensitivity of NIPAM polymer gel for different wavelengths of visible light.

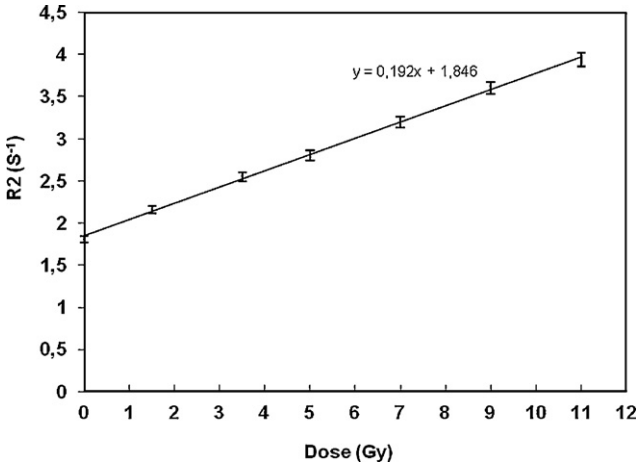

Fig. 4 – R_2–dose response curve of the NIPAM polymer gel. The error bars show the uncertainty of measurements.

spectrophotometer at 400 nm, because the absorbance will reach 2, the maximum value. So, a reading system based on laser and photodiode should be designed and used for higher doses at that wavelength. However, the study showed that it is possible to quantize the absorbed dose in radiation therapy using NIPAM gel and an ordinary spectrophotometer with acceptable accuracy. In a similar study, the absorbance–dose response of NIPAM gel was determined using a home-built He–Ne laser at 630 nm and a photo-absorbance detector.[18] The optical response of NIPAM gel was linear up to 20 Gy and it showed the highest dose sensitivity among the studied polymer gels. Our results were in complete agreement with those results. Also, the absorbance–dose responses for other light wavelengths were provided in the current study. Our results showed that to have higher dose sensitivity for NIPAM polymer gel in optical systems, the blue part of the light spectrum is preferred. However, as can be seen in Fig. 3, the longer wavelengths of the light spectrum (>690 nm) could provide other potentials for better dose sensitivity of gels. But, it is really hard to find cheap and available red lasers for this part of light spectrum.

The results of R_2–dose response of NIPAM gel are shown in Fig. 4. The error bars show the uncertainty of R_2 measurements. It can be seen that there is a linear relationship between R_2 and absorbed dose for all vials. The dose sensitivity for our gel was calculated to be 0.193 R_2/Gy for dose range of 0–11 Gy. It was in close agreement with the results of Senden et al. In their study, it was found that the R_2–dose response of NIPAM/Bis gel dosimeter was comparable to that of normoxic polyacrylamide gel (PAGAT) in terms of high dose-sensitivity and low dependence on dose rate and irradiation temperature. Also, the dose–response (R_2) of NIPAM/Bis was linear over a greater dose range than the PAGAT gel dosimeter.[18]

5. Conclusion

In the current study the NIPAM polymer gel optical and NMR characteristics were studied using a conventional spectrophotometer and a clinical magnetic resonance imager. Our R_2–dose response was comparable to the previous study.[18] The absorbance–dose responses for different light wavelengths were investigated and our results found higher dose sensitivity for blue light, while this had not been reported in former studies. Our study recommended optical absorbance–dose investigations for other polymer gels to provide more information for optimum design of optical systems for gel dosimetry.

Conflict of interest

None declared.

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