The basic radiation properties of the N-isopropylacrylamide based polymer gel dosimeter

A.R. Farajollahi[1], F. Pak[2*], M. Horsfield[3], Z. Myabi[4]

[1]*Department of Medical Physics, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran*
[2]*Department of Medical Physics and Biomedical Engineering, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran*
[3]*Department of Cardiovascular Sciences, University of Leicester, Leicester Royal Infirmary, Leicester, UK*
[4]*Department of Radiology, Emam Reza teaching Hospital, Tabriz University of Medical Sciences, Tabriz, Iran*

► ***Original article***

**** Corresponding author:***
Dr. Farideh Pak,
Fax: *+98 21 66482654*
E-mail: *f-pak@razi.tums.ac.ir*

Revised: Aug. 2013
Accepted: Jan. 2014

Int. J. Radiat. Res., October 2014; 12(4): 347-354

ABSTRACT

Background: In this study the basic radiation properties of N-isopropylacrylamaide polymer gel dosimeter were determined together with verification of its soft tissue equivalency. ***Materials and Methods***: The NIPAM gel was prepared and irradiated approximately 2 h after manufacturing. The magnetic resonance (MR) images were made 24 h after irradiation. The nuclear magnetic resonance (NMR) response (R_2) of the dosimeters was analyzed for conditions of varying dose, batch, dose rate, time post-irradiation and energy. In order to verify tissue equivalence of NIPAM dosimeter, several parameters such as physical density, effective atomic number, relative electron density, CT (Computed Tomography) number and also elemental composition were determined and compared with those for soft tissue. ***Results***: The response of the gel was found to be stable 24 hours after irradiation. The results showed that the dose response of the NIPAM polymer gel is reproducible in same and different batches of chemical and the gel response was linear up to 26 Gy with r^2=0.995. In the measured range, the dose response of the NIPAM gel is independent of beam energy within less than ±0.02 and the dose rate had no effect on the gel response. This polymer gel has been found to be tissue equivalent. ***Conclusion***: NIPAM gel dosimeter appears to be a promising dosimeter in all aspects of dosimetric properties which were assessed in this study, in addition to the advantage of reduced toxicity which it has over other polymer gels.

Keywords: *NIPAM, MRI, R_2.*

INTRODUCTION

A gel dosimeter should meet a series of basic dosimetric properties such as stability, spatial integrity, dose rate and energy independence, reproducibility, linearity and tissue equivalence [1, 2]. Since the introduction of gel dosimeters in radiation therapy, great deal of research has been performed on gels' basic dosimetric properties to prove their clinical application [1].

First group of gel dosimeters was ferric based gel dosimeters[3] which had shown some unique features in dosimetry [4, 5]. Unfortunately diffusion of ferric ions through the gel matrix following irradiation degrades spatial dose integrity of this gel and limited its application in radiotherapy [6].

In order to preserve spatial dosimetric information on the gel after irradiation, Maryanski *et al.* in 1994 introduced polymer gel dosimeters based on the polymerization of acrylamide (AAm) and N,N'-methylen-bisacrylamide crosslinker infused in an aqueous agarose matrix upon irradiation [7]. As the concentration of polymerization is proportional

to the radiation dose, this can be lead to an increase in the transverse relation rate of water protons in magnetic resonance imaging (MRI). Polymer dosimeter did not have the diffusion limitation of Fricke gel, but there were other significant limitations that limited their clinical acceptance to some extent. Firstly due to inhibiting role of oxygen for polymerization process, the gel manufacturing must be done in a hypoxic environment [8-10] and secondly, neurotoxic and carcinogenic nature of monomers made manufacturing process inconvenient [11, 12].

Since introduction of polymer gel, there have been considerable number of researches carried out on the application of different polymer gels in radiotherapy most of which focused on improvement of composition in terms of oxygen contamination, solubility and toxicity while paying attention to its sensitivity and homogeneity. In 2001 Fong *et al.* introduced normoxic polymer gel dosimeters that could be manufactured in normal atmospheric condition by adding ascorbic acid as an antioxidant to the gel structure [13]. It was subsequently shown that other active anti oxidants such as gallic acid, trolox, N-acetyl-cysteine, and tetrakis (hydroxymethyl) phosphonium choloride (THPC) could also be used in manufacturing normoxic gels, but among these antioxidants, the most promising results were obtained by THPC [14, 15]. A number of studies were undertaken to investigate the accuracy of different formulation of normoxic polymer gel dosimeters with different monomers, crosslinkers and antioxidants [16-18].

Most of the current polymer gel formulations, consist of Bis as a cross linker. The main concerns with Bis in these gel dosimeters are its limited water solubility and low crosslinking efficiency [19]. Several investigations have been done in order to improve Bis solubility or replace Bis with another more soluble efficient crosslinker. Normoxic methacrylic acid (MA), based polymer gels (MAc system) contain methacrylic acid, ascorbic acid, gelatin and copper, are crosslinker free dosimeter that were developed in 2001[13]. Due to higher sensitivities of MAc-based dosimeters to irradiation temperature and dose rate, especially when using THPC as an antioxidant, their dose response is less reproducible [17]. In 2008 Kovea et al. attempts in finding effective crosslinkers with increased solubility were unsuccessful (19). In the other experiment they could increased Bis solubility through adding some different co-solvent to the gel structure.

Acrylamide is also a dangerous neurotoxin and a suspected human carcinogen that can be readily absorbed through the skin, and as a result requires careful handling [20-22]. Although lack of acrylamide in MAc-type gels made them less toxic, they had some limitations which restricted their application [17].

The studies were ongoing using different monomers, with the objective of producing more accurate dosimeters that could reduce considerably the safety concerns, and thus would make handling of the dosimeter in clinical environments more convenient. Recently Senden et al., (2006) have investigated new dosimeter recipes by replacing acrylamide with three different monomers namely N-isopropyle acrylamide (NIPAM), diacetone acrylamide (DAAM) and N-vinyl formamide (NVF), among which NIPAM has shown a better dose response than the others [22, 23]. Even though these monomers are similar in their chemical structure to acrylamide, they are much less toxic and more soluble [24].

To date comprehensive studies on the dosimetric properties has only been performed for the few polymer gel compositions [17]. Therefore, the objective of this study is to explore the basic properties of NIPAM polymer gel including the effect of radiation beam energy, linearity of dose response together with verification of its tissue equivalency which are significant factors influencing radiation therapy applications.

MATERIALS AND METHODS

The NIPAM gel was prepared according to the method described by Senden *et al.* in 2006 [22]. In order to make the required amount of the polymer gel, first a concentration of 5% (by weight) gelatin (300 Bloom, type A, Sigma-Aldrich, USA)

was added to 80% of deionized water and left to swell for 10 minutes. It was then heated up to 50°c and stirred with a magnetic stirrer until the gelatin was fully dissolved. The solution was cooled down to 40 °C and while being stirred continuously 3% Bis (99%, Sigma–Aldrich, USA) was added. Once the Bis was dissolved, 3% NIPAM (Sigma –Aldrich USA) was added at 37 °C and stirred until complete dissolution was achieved. Finally a solution of antioxidant was prepared with 10 mM of THPC (MERCK-Schuchardt, Germany) and the remaining deionized water, which was added to the gel solution at 35°C. The resulting gel was then transferred to the vials and refrigerated for half an hour to solidify.

To avoid photopolymerisation, the samples were put in a cardboard box before irradiation. The gels were irradiated approximately 2 h after being manufactured, in a rectangular water bath made in-house from perspex, which was designed to simultaneously expose multiple test tubes to different doses. The samples were irradiated with 9MV X-rays from a Neptun 10 linear accelerator (Poland). The irradiation was directed perpendicular to the length of water bath (figure 1). To prevent a dose gradient in the gels, the vials were turned 180° halfway through the irradiation. The irradiated gels were kept at room temperature until the gels were imaged.

MR images of the gel were made 24 h after irradiation. The vials were imaged in a rectangular wooden box in which they had been placed in a fixed position 1 cm from each other. The box was placed in the head-coil of Philips Intra 1.5 T MRI scanner (General electric. USA). T_2 weighted images of 5 mm thick slice were taken parallel to the irradiated surface through middle of the gel using a multi slice spin-echo method, and transverse relaxation rates ($R_2=T_2^{-1}$) were then obtained from the signal decay data, using the image processing tool (Jim, verson 5.0). For all the measurements a repetition time (TR) of 4000 ms was used, with 15 echo time ranging from 700 to 1400 ms with increment of 50. Since the gel temperature at the time of MR imaging has great influence on the R2, all the images were taken on the same temperature (21°C).

Figure 1. Experimental set up of the NIAM gel irradiation.

RESULTS

Reproducibility of dose response

In order to investigate the absorbed dose response reproducibility, the polymer gel was manufactured as described and the gel vials were irradiated isocentrically to absorb doses of 1 to 10 Gy and one gel vial was kept unirradiated for background measurement. The experiment was repeated three times while keeping irradiation method and scanning parameters unchanged.

Figure 2 shows the results obtained from relaxation rate measurements (R_2) in three set of the samples, prepared on different days. The data in figure 2 shows that the dose response is highly reproducible over the range of the measured dose with difference of 3%; provided that the chemicals are taken from same batch.

As different batch of the chemical may have an effect on the gel's response, a set of the gel vials were prepared from different batches for the purpose of comparison. The results are shown in figure 3. It can be seen that there are no difference in the response of the gel within ± 2%.

Dose response sensitivity

The slope of the initial linear region of the R_2 versus dose plot, provides a measure called the R_2-dose sensitivity [17]. It is a useful quantity for comparing different gel formulations and MRI imaging techniques. Figure 4 shows the R_2 dose response of the NIPAM polymer gel dosimeter with slope=0.0889 (s^{-1} Gy^{-1}).

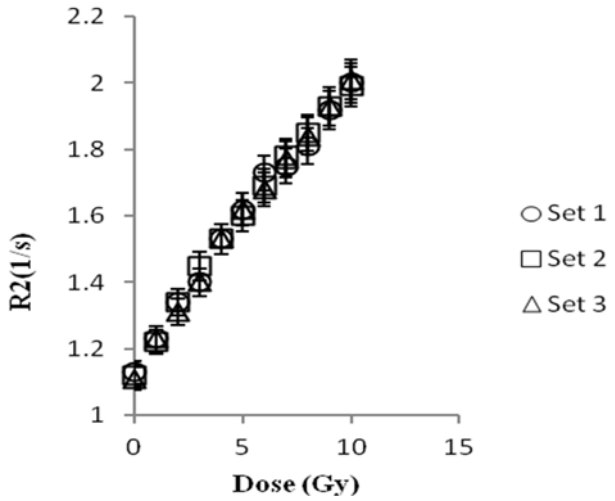

Figure 2. Reproducibility of three sets of NIPAM gel dose response with same preparation, irradiation and imaging method.

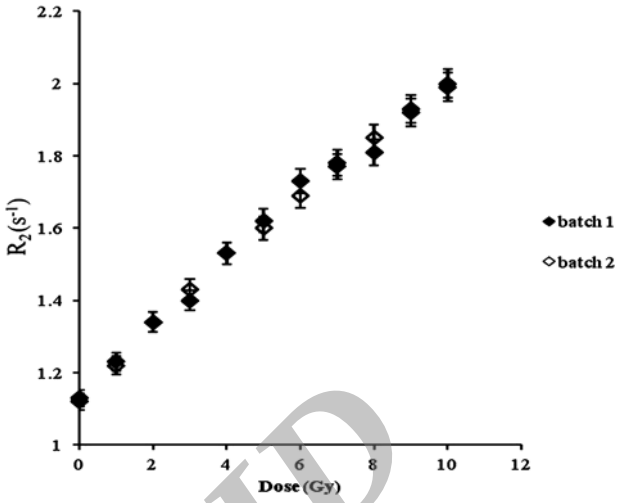

Figure 3. NIPAM gel dose response reproducibility of different batches of chemical.

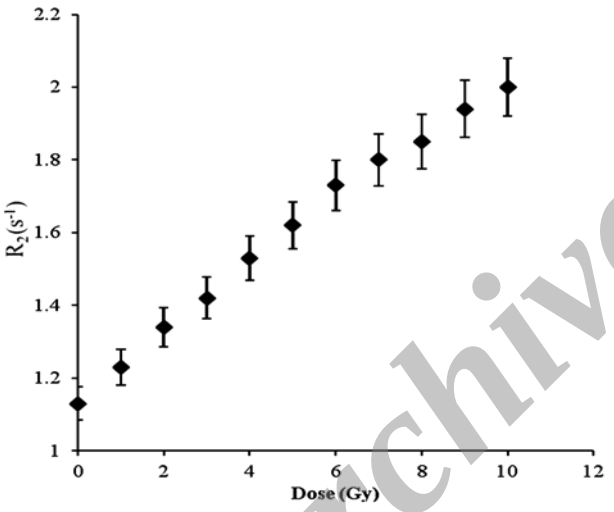

Figure 4. R_2 dose response of NIPAM polymer gel dosimeter.

Effect of the time of imaging after irradiation

To investigate if the response of the gel going to be constant with the time after irradiation, the R_2 values of a series of the gels were measured for a period of one month, during which five measurements were made. Figure 5 shows the measured R_2 for doses of 0 to 10 Gy for five different occasions during a month. It is clear that there is no variation in gel's dose response with the time after irradiation in the stated measured time.

Effect of beam energy

Independence of dose response from radiation beam energy is one of the main concerns in radiation dosimetry [1, 17]. For assessing if the NIPAM gel response is independent of photon energies, two sets of NIPAM gel were prepared and irradiated to absorb doses of 1 to 10 Gy. Irradiations were made using two photon energies of 9 MV X-ray from a linear accelerator (Neptun 10, Poland) and 1.25 MV gamma ray of a ^{60}Co.

The results are shown in figure 6. It can be seen that the dose response of the NIPAM gel is independent of beam energy to within less than ±0.02 in the measured range.

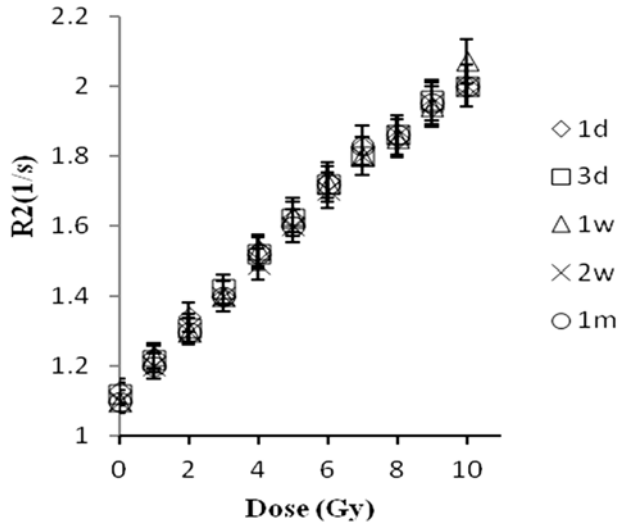

Figure 5. Stability of the NIPAM polymer gel response with time.

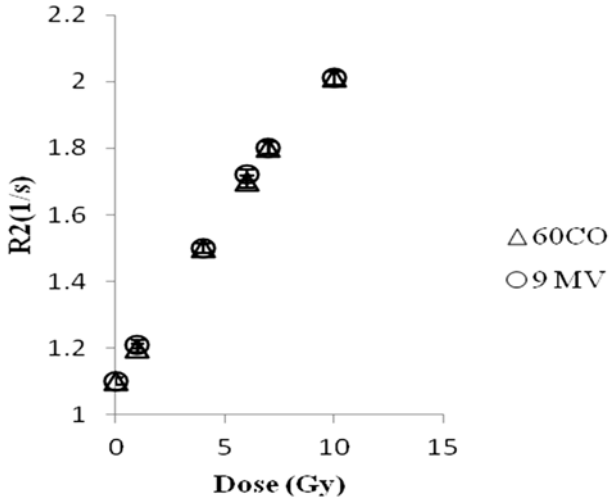

Figure 6. Effect of beam energy on NIPAM gel response.

Dose rate dependence

The dependence of the gel response on dose rate was also investigated. For this purpose the gels were irradiated with X-rays to the absorbed dose of 5Gy. In order to get different dose rates, varying SSD of 80, 90, 100, 110 and 120 were used and radiation beam were calibrated to give 5Gy in each SSD.

The results are shown in figure 7. The results indicate that the response of NIPAM gel is not affected by dose rate.

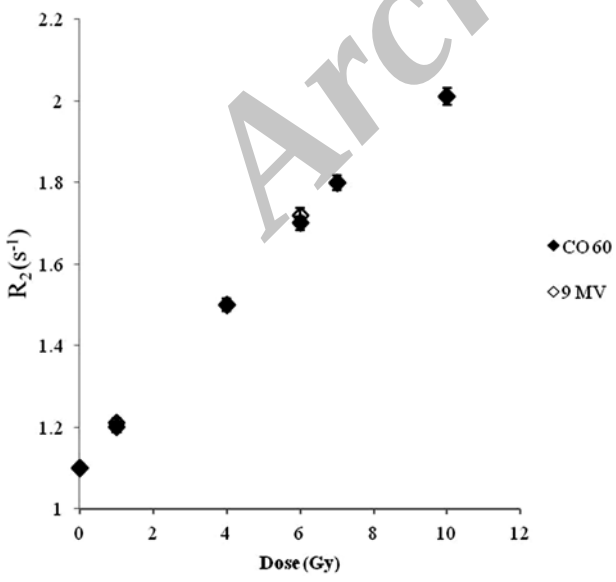

Figure 7. Variation of the NIPAM gel response with dose rate.

Linearity

Linearity of dose response is another concern in radiation dosimetry which affects the dynamic range of measurement. Therefore, the NIPAM polymer gel linearity was also investigated in this study. For this purpose, the gel vials were irradiated to absorbed doses ranging from 1 to 35 Gy. The results of R_2 measurements are shown in figures 8 and table 1. It can be seen that the NIPAM dose response is linear up to 26 Gy with r^2=0.995.

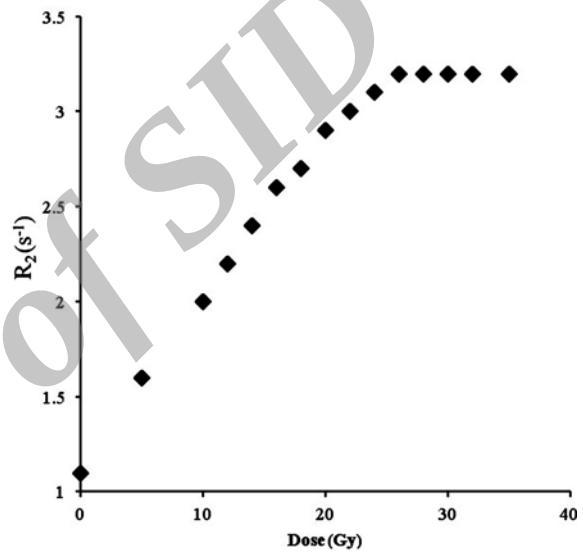

Figure 8. Linearity of the R_2 measurement to dose up to 35 Gy for NIPAM polymer gel.

Table 1. Correlations and slopes of the NIPAM gel for different doses of X-rays.

Dose (Gy)	r^2	Slope (s^{-1} Gy^{-1})
5	1	0.1
10	0.998	0.0886
12	0.999	0.0902
14	0.999	0.0911
16	0.999	0.0922
18	0.998	0.0901
20	0.998	0.0895
22	0.998	0.0875
24	0.996	0.0848
26	0.995	0.0819

Tissue equivalency

In order to verify tissue equivalence of NIPAM dosimeter, several parameters such as, physical density, effective atomic number, relative electron density, CT number and also elemental composition were determined and compared with tissue.

The density of the gel was measured several times and each time a vial of the gel was weighted and its volume was determined at room temperature. The gel density was found to be 1.007 g/ml. To calculate the effective atomic number McCullough and Holmes equation was used [25].

$$z_{eff} = \left[\frac{N_A \rho}{\rho_e^w}\right]^{1/a} \cdot \left\{\sum_j \frac{f_j}{(MWT)_j} \cdot \left[\sum_i n_{i,j} (z_{i,j})^{a+1}\right]\right\}^{1/a} \quad (1)$$

$$\rho_e^w = \frac{N_A \rho}{\rho_{ew}} \left[\sum_j f_j \left(\frac{\sum_i n_{i,j} z_{i,j}}{(MWT)_j}\right)\right] \quad (2)$$

Where $\rho_e{}^w$ is electron density relative to water, N_A is Avogadro number , ρ_{ew} the electron density of water, MWT molecular weight of the sample, f_j the some of mass fraction of the various molecular component of the gel, z_i is relative electron density and a=2.94 (atomic number dependence power for the interaction of interest).

The results of the parameters for the NIPAM gel are shown in table 2 and are compared with those for water, muscle [26], bone [27], BANG [10], nMAG and nPAG [17].

DISCUSSION

The present work involved in the investigation of NIPAM polymer gel dosimeter, using MRI. The basic radiation properties of NIPAM were determined together with the verification of its soft tissue equivalency.

The response of NIPAM gel was found reproducible even for a different batch of chemicals. This result complies well with the work done by Senden *et al.* in 2006 [22] and also a work done by Hsieh *et al.* in 2011[29]. Even though all type of polymer gel exhibits good reproducibility using the same batch of chemical, some of them like BANG have been reported to have different responses to dose while using chemicals from a different batch [28].

The response of the gel was found to be stable 24 hours after irradiation. This is in contrast to the results that had been taken by Senden et al. in 2006 [22], Chang *et al.* in 2011 indicating stability of dose response after 72 hours [30] and Hsieh *et al.* 2011 by reporting termination of the polymerization process 5 hours after irradiation [29]. The differences in the results make further investigation necessary in this regard.

The study of dose response of NIPAM as a function of beam energy revealed no dependence on radiation energies of 1.25 MeV from ^{60}Co and 9 MV from linear accelerator. Unfortunately there is no data available to compare the result of this study. Looking at previous studies, De Deene *et al.* (2006) found dose response of PAG nPAG, and nMAG not

Table 2. Physical quantities of various substances and gel dosimeters.

Substance	$\rho_e{}^w$	ρ	N_{CT}	Z_{eff}
Water	1	1	0	7.42
Muscle [26]	0.94	1	-	7.61
Bone [27]	1.1	1.12	236	9.32
BANG [28]	0.994	0.991	17.7	7.33
nMAG [17]	1.046	1.0160	-	7.3149
nPAG [17]	1.035	1.0164	-	7.3250
NIPAM	1.03	1.007	32. 6	7.34

significantly affected by beam energy [17]. In a similar study by SellaKumar *et al.* in 2010 nPAG response was reported dependent on photon energy but this dependence was not considered dosimetrically significant [31]. They argued, this dependence can be clinically significant when using different energy for radiation of phantom and production of calibration curve.

One of the desirable features for a dosimeter in determining radiation dose distribution in 3D is its independence from dose rate [32]. In the present study it was found dose rate has no influence on the gel's dose response. This complies well with the works that have been done on BANG and BANG2 gels [28, 31, 33]. Other studies in this ground involving nPAG (PAGAT) nMAG and NIPAM have reported slight dose rate dependence of nPAG, NIPAM and higher dependence of nMAG [17, 22]. However, in spite of the reported low dependence of NIPAM, it is believed that dose response of this new formulation of polymer gel not significantly affected by dose rate in the ranges they studied. Therefore, it can be concluded that the result of this study can be comparable to that of Senden *et al.* [22].

It is advantageous for polymer gel dosimeters that exhibit higher linearity to insure its' application in a wider range of dose measurements in radiation therapy. The result showed that the absorbed dose response is linear up to 26 Gy. This is in contrast with the result that has been taken by Chain *et al.* in 2011 [34] and Jirasek in 2010 [35] by reporting linearity up to 19 and 20 Gy, respectively, using X-ray CT. Chang *et al.* (2011) also examined the linearity of the gel to radiation dose of 0-20 Gy, using optical computed tomography [30]. Their work resulted in linear gel response of up to 20 Gy with the linearity of 0.998 which in accordance with the result of this study in the same dose range.

The sensitivity of the gel which is defined as a slope of linear R_2 dose response curve was reported to vary as a function of gel components concentration [29]. The result of this study using 6% total monomer (50% C), 5% gelatin and 10 mM THPC exhibited much higher sensitivity (0.0889 S^{-1} Gy^{-1}) in comparison with the work that had been done by Hsieh *et al.* 2011[29] and Chang *et al.* 2011[30]. The discrepancy in the results may be due to the application of different imaging modalities as they scanned the gels using optical computed tomography, and possibly the way effects of external factors were controlled.

Since non tissue equivalent dosimeters cause a perturbation in radiation field, and it affects the accuracy of absorbed dose measurements, one of the main advantages of gel dosimeters could therefore be their tissue-equivalency. Substituting N-isopropyl acrylamaide for acrylamaide and utilizing THPC in NIPAM necessitate the verification of new gel in term of tissue equivalency. The result of this investigation indicated that. Although NIPAM composition differs from the earlier formulation of polymer gel, its' effective atomic number, electron density and mass density are still close to water, therefore, NIPAM polymer gel can also be consider tissue equivalent.

CONCLSION

NIPAM gel dosimeter appears to be a promising dosimeter in all aspects of dosimetric properties evaluated in this study. This polymer gel can be considered as tissue equivalent dosimeter. In addition, its lower toxicity, together with its higher linearity makes it a suitable dosimeter in a wider range of absorbed dose measurements in radiotherapy.

Conflict of interest: *Declared none.*

REFERENCES

1. Baldock C, De Deene Y, Doran S, Ibbott G, Jirasek A, Lepage M, Mc Auley KB, Oldham M, Schreiner LJ (2010) . Polymer gel dosimetry. *Phys Med Biol,* ***55:****R1-63.*
2. Hurley CA (2006) The development of normoxic polymer gel dosimetry using high resolution MRI. Ph.D. thesis, Queensland University of Technology, Brisbane
3. Gore JC, Kang YS, Schulz RJ (1984) Measurement of radiation dose distributions by nuclear magnetic resonance (NMR) imaging. *Phys Med Biol,* ***29:****1189-97.*
4. Chan MF and Ayyangar KM(1995) Confirmation of target localization and dosimetry for 3D conformal radiotherapy treatment planning by MR imaging of a ferrous sulfate gel

head phantom. Med Phys, **22:**1171-5.
5. Schulz RJ, deGuzman AF, Nguyen DB, Gore JC (1990) Dose-response curves for Fricke-infused agarose gels as obtained by nuclear magnetic resonance. *Phys Med Biol, **35:**1611-22.*
6. Baldock C, Harris PJ, Piercy AR, Healy B (2001) Experimental determination of the diffusion coefficient in two-dimensions in ferrous sulphate gels using the finite element method. *Australas Phys Eng Sci Med, **24:**19-30.*
7. Maryanski MJ, Schulz RJ, Ibbott GS, Gatenby JC, Xie J, Horton D, Gore JC (1994) Magnetic resonance imaging of radiation dose distributions using a polymer-gel dosimeter. *Phys Med Biol, **39:**1437-55.*
8. Baldock C, Burford RP, Billingham N, Wagner GS, Patval S, Badawi Rd, Keevil SF (1998) Experimental procedure for the manufacture and calibration of polyacrylamide gel (PAG) for magnetic resonance imaging (MRI) radiation dosimetry. *Phys Med Biol, **43:**695-702.*
9. De Deene Y, De WC, Van DB, Derycke S, De NW, Achten E (1998) Three-dimensional dosimetry using polymer gel and magnetic resonance imaging applied to the verification of conformal radiation therapy in head-and-neck cancer. *Radiother Oncol, **48:**283-91.*
10. Farajollahi AR, Bonnett DE, Ratcliffe AJ, Aukett RJ, Mills JA (1999) An investigation into the use of polymer gel dosimetry in low dose rate brachytherapy. *Br J Radiol, **72:**1085-92.*
11. Hepworth SJ, Leach MO, Doran SJ (1999) Dynamics of polymerization in polyacrylamide gel (PAG) dosimeters: (II) modeling oxygen diffusion. *Phys Med Biol, **44:** 1875-84.*
12. Papagiannis P, Pantelis E, Georgiou E, Karaiscos P, Angelopoulos A, Sakelliou L, Stiliaris S, Baltas D, Seimenis I (2006) Polymer gel dosimetry for the TG-43 dosimetric characterization of a new 125I interstitial brachytherapy seed. *Phys Med Biol, 5**1:** 2101-11.*
13. Fong PM, Keil DC, Does MD, Gore JC (2001) Polymer gels for magnetic resonance imaging of radiation dose distributions at normal room atmosphere. *Phys Med Biol, **46:** 3105-13.*
14. De Deene Y, Hurley C, Venning A, Veergote K, Mather M, Healy BJ, Baldock C (2002) A basic study of some normoxic polymer gel dosimeters. *Phys Med Biol, **47:** 3441-63.*
15. Clive B (2006)Historical overview of the development of gel dosimetry: a personal perspective. *Journal of Physics: Conference Series, **56:**14.*
16. Bayreder C, Georg D, Moser E, Berg A (2006) Basic investigations on the performance of a normoxic polymer gel with tetrakis-hydroxy-methyl-phosphonium chloride as an oxygen scavenger: reproducibility, accuracy, stability, and dose rate dependence. *Med Phys, **33:** 2506-18.*
17. De Deene Y, Vergote K, Claeys C, De WC (2006) The fundamental radiation properties of normoxic polymer gel dosimeters: a comparison between a methacrylic acid based gel and acrylamide based gels. *Phys Med Biol, **51:**653-73.*
18. Karlsson A, Gustavsson H, Mansson S, McAuley KB, Back SA (2007) Dose integration characteristics in normoxic polymer gel dosimetry investigated using sequential beam irradiation. *Phys Med Biol, **52:**4697-706.*
19. Koeva VI, Csaszar ES, Senden RJ, McAuley KB, Schreiner LJ (2008) Polymer Gel Dosimeters with Increased Solubility: A Preliminary Investigation of the NMR and Optical Dose-Response Using Different Crosslinkers and Co-Solvents. *Macromol Symp, **261:**157-66.*
20. Geoffrey S Ibbott (2004) Applications of gel dosimetry. *Journal of Physics: Conference Series, **3:**58.*
21. MSDS (2006) Material safety sheet acrylamaide. *Sigma Aldrich, USA.*
22. Senden RJ, De JP, McAuley KB, Schreiner LJ (2006) Polymer gel dosimeters with reduced toxicity: a preliminary investigation of the NMR and optical dose-response using different monomers. *Phys Med Biol, **51:**3301-14.*
23. Pak F, Farajollahi AR, Movafaghi A, Naseri AR (2013) Influncing factors on reproducibility and stability of MRI NIPAM polymer gel dosimetry. *BioImpacts, BI, **3:** 163.*
24. Kim BM (2006) Fundamentals of Polymer Gel Dosimeters. *Journal of Physics: Conference Series, **56:**35.*
25. McCullough EC and Holmes TW (1985) Acceptance testing computerized radiation therapy treatment planning systems: direct utilization of CT scan data. *Med Phys, **12:**237-42.*
26. Parker RP, Hobday PA, Cassell KJ (1979) The direct use of CT numbers in radiotherapy dosage calculations for inhomogeneous media. *Phys Med Biol, **24:**802-9.*
27. Kron T, Metcalfe P, Pope JM (1993) Investigation of the tissue equivalence of gels used for NMR dosimetry. *Phys Med Biol, **38:**139-50.*
28. Farajollahi AR (1999) An investigation into the application of polymer gel dosimetry in radiotherapy. *Medical Physics, **26:** 493-493.*
29. Hsieh B, Chang Y, Han R, Wu J, Hsieh L, Chang C (2011) A study on dose response of NIPAM-based dosimeter used in radiotherapy. *Journal of Radioanalytical and Nuclear Chemistry **290:**141-8.*
30. Chang YJ, Hsieh BT, Liang JA (2011) A systematic approach to determine optimal composition of gel used in radiation therapy. *Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment, **652:**783-5.*
31. Sellakumar P, James Jebaseelan Samuel E (2010) Study on energy dependence of PAGAT polymer gel dosimeter evaluated using X-Ray CT. *Radiation Measurements, **45:**92-7.*
32. Low DA and Mutic S (1997)Abutment region dosimetry for sequential arc IMRT delivery. Phys Med Biol **42:**1465-70.
33. Novotny J, Jr., Spevacek V, Dvorak P, Novotny J, Cechak T (2001) Energy and dose rate dependence of BANG-2 polymer-gel dosimeter. *Med Phys, **28:**2379-86.*
34. Chain JN, Jirasek A, Schreiner LJ, McAuley KB (2011) Cosolvent-free polymer gel dosimeters with improved dose sensitivity and resolution for X-ray CT dose response. *Phys Med Biol, **56:**2091-102.*
35. Jirasek A, Hilts M, McAuley KB (2010) Polymer gel dosimeters with enhanced sensitivity for use in X-ray CT polymer gel dosimetry. *Phys Med Biol, **55:**5269-81.*