Fabrication of NIPAM polymer gel dosimeter and characterization using Raman spectroscopy

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Abstract. Gel dosimeter is a kind of radiation dosimetry medium that has been extensively applied in radiotherapy treatment. In this study, the samples of NIPAM-based polymer gel that possessed a good potential as 3D radiation dosimetry were fabricated. The samples of polymer gel were irradiated up to 18 Gy by using gamma irradiator with 60Co sources at a constant dose rate. Upon irradiation, the chemical changes in polymer gel were measured and evaluated by using a Raman spectrometer. Polymerization refers to an increment in Raman intensity at 815 cm\(^{-1}\), assigned for C-C stretching mode of NIPAM polymer gel, as the dose was increased. Consumptions of the co-monomers refers to a decrement in Raman intensities at 1025 cm\(^{-1}\) and 2353 cm\(^{-1}\) assigned for C=C stretching modes of NIPAM and BIS respectively, as the dose was increased. Result showed that following irradiation, the amount of carbon single bonds increases while the amount of carbon covalent bonds decreases.

1. Introduction

\(N\)-isopropyl acrylamide (NIPAM) monomer in polymer gel composition together with \(N, N'\)–methylene-bis-acrylamide (BIS) as the cross linker was first introduced by Senden [1], which had relatively less toxicity than the other monomers applied in previous literature such as normoxic polyacrylamide gels (nPAG) [2]. According to Mesbahi [3], the dose response of NIPAM polymer gel was proven to be comparable to normoxic polyacrylamide gel (PAGAT), which was established by Senden [1] to have high dose sensitivity and less dependent on dose rate and irradiation temperature. Study done by Cheng [4] also found that NIPAM polymer gel could be beneficial and effective in dose verification of clinical Intensity Modulated Radiation Therapy (IMRT).

Moreover, Mesbahi [3] observed that NIPAM polymer gel was better than PAGAT gel in linearity since the dose response of NIPAM was significantly linear within a larger dose range. Thus, this kind of polymer gel was very important to act as dosimeter for particular medical procedures which requires the need of accurate radiation dose determination [5]. In this study, NIPAM polymer gel that was characterized by Raman spectroscopy was chosen to evaluate and probe the changes in molecular structure of the polymer gels upon irradiation. Our aim is to further investigate the potential of NIPAM polymer gel which had unique qualities by using Raman spectroscopy instrument to monitor the characteristic set of covalent bond on each molecule within the gel dosimeter. The analysis through Raman spectra may reflect the activity of polymer formation and monomer consumption that depicts the activities occurring at the molecular level [6].

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2. Materials and Methods

2.1. Gel Manufacture

Fabrication of polymer gel under a normal setting took place in the laboratory without using a glove box based on the study by Fong [7,9] and following the method proposed by Senden [1,9]. Initially, gelatine (6 wt%) (bovine skin, Type B, Sigma Chemical Co) was added to the deionized water and stirred for five minutes at room temperature. Next, the gelatine solution was heated up to 45°C and continuously stirred by using magnetic stirrer until the solution became clear and transparent. By turning off the heating element while stirring was continued, the monomer and co-monomer, BIS (2-4 wt%) (Sigma Chemical Co) and NIPAM (2-4 wt%) (Sigma Aldrich) were poured into the gelatine in the beaker and approximately dissolved within 15 minutes. Finally, the anti-oxidant, tetrakis hydroxymethyl phosphonium chloride (THPC) (5mM) was added to the solution as it was continuously stirred for about two minutes. The end product was poured into small ampoule tubes (2ml), which were then sealed with parafilm and wrapped with aluminium wrapper. Once completed, the samples of NIPAM polymer gels were stored in a refrigerator at low temperature of approximately 4°C. In about 24 hours, the gels were taken out from the refrigerator and equilibrated at room temperature prior to undergoing the process of irradiation.

2.2. Gel Irradiation

In ensuring that the temperature was at an equilibrium, the samples were equilibrated at room temperature which took less than 10 minutes, since the sample size was considerably small. Afterwards, the samples were irradiated with gamma rays produced by Cobalt-60 (Co$^{60}$) source from Gamma Cell Instrument, model 220 Excel Irradiator (MDS Nordion, Ottawa, ON, Canada) (Faculty of Nuclear Science, National University of Malaysia) (Figure 1). The radiation dose applied was set via a control button in the chamber.

One sample was left to remain inside the refrigerator while the other samples were irradiated up to 18 Gy with a single dose per cycle. During the irradiation process, each sample was placed in a beaker filled with distilled water.

![Figure 1. Gamma cell instrument, $^{60}$Co model 220 Excel Irradiator](image-url)
2.3. Raman Spectroscopy of NIPAM

All samples were characterized by using Raman spectrometer (RSI 2001, Raman system, INC) (Figure 2) that is equipped with 532 nm solid-state diode green laser and a thermoelectrically cooled CCD array seven days following irradiation. After a while, the manipulation and analysis of data were measured by using Grams/32 software, version 6. Through the analysis process, all spectra were corrected to the set base line, smoothened and further evaluated via Fourier Transform (FT). From the data collection, a constant correction factor of 80% of the smoothing parameter was used.

Figure 2. Raman spectrometer (RSI 2001, Raman system, INC)

3. Results and Discussion

3.1. Raman Spectroscopy Analysis

Raman spectra is actually a vibrational Raman effect that directly describes the monomer consumption and polymer formation following irradiation process. Through the Raman spectrometer, the relative intensity is represented by the energy difference of scattered radiation that can be gained and is shown on a chart as a function of difference in wavelength. The well-defined peak on the chart may represent unique and characteristic molecular bond of certain vibrational energy in the gel samples. The characteristic frequencies of every single functional group were characterized based on the previous literature as documented by Jirasek [6,10].

The consumption of cross linker BIS and monomer NIPAM were characterized at wave number 1025 cm\(^{-1}\) and 2353 cm\(^{-1}\) assigned to carbon covalent bond (C=C) stretching mode of NIPAM and BIS respectively. Following the monomers consumption, the significant peak was also characterized at wave number 815 cm\(^{-1}\), assigned to NIPAM polymer formation. All of these peaks were selected as the main signatures of the polymerization process since the peaks were well defined, relatively intense and not covered by other peaks within a similar frequency range.

Figure 3 (a) and (b) show that, as the NIPAM polymer gel was irradiated, NIPAM monomer and BIS cross linker were consumed, as reflected by the intensity reduction of significant peak from unirradiated gel (0 Gy) to irradiated gel (18 Gy). A decreasing peak intensity was exhibited at these two peaks as the amount of radiation dose was increased. The reduction in the amount of C=C bonds with increasing radiation dose was due to the consumption of NIPAM and BIS monomers to form NIPAM polymer gel.

Meanwhile, with increasing radiation dose, the amount of C-C bonds increased, indicating that the intensity increment was due to the formation of NIPAM polymer following irradiation. As shown in Figure 3 (c), the intensity increment was at a significant peak from 0 Gy gel to irradiated 18 Gy gel.
Figure 3. Raman peaks of NIPAM polymer gel assigned the stretching of (a) C=C (1025 cm\(^{-1}\)) of NIPAM, (b) C=C (2353 cm\(^{-1}\)) of BIS, (c) C-C (815 cm\(^{-1}\)) of NIPAM polymer gel

3.2. Polymerization Process

Depicting the mechanism of the polymerization process of NIPAM polymer gel is straightforward. Figure 4 shows the chemical structures of NIPAM and BIS and the initial NIPAM polymer gel that was formed following irradiation by gamma instrument. The double bonds in Figure 4 (a) and 4 (b)
tend to be broken and affected because after the irradiation process, the stretching double bonds of co-monomers had turned into stretching single bonds. The polymerization process was initiated and completed until the polymer becomes inactive, since the supply of monomer and cross linker had been exhausted.

Irradiation triggered the production of free radicals (R\textsuperscript{•}), which were unstable and reactive, and could subsequently react with the co-monomers (NIPAM and BIS) to open up the double bonds (C=C). These free radicals of co-monomers then interacted with the new co-monomers and propagated a chain reaction in the formation of NIPAM polymer gel. Later, the crosslinking between copolymers of NIPAM and BIS were also triggered by the free radical species that shared electrons to develop a crosslink between two copolymers chain as depicted in Figure 4 (c).

![Figure 4](image-url)

**Figure 4.** Initiation phase of chemical structure (a) N-isopropyl acrylamide (NIPAM) (b) N,N’-methylene bis-acrylamide (BIS) (c) propagation of NIPAM polymer gel

The process of propagation continued until the supply of both monomer and cross linker were finished, or the polymer active sides were ended at all. It was shown that as polymer being formed from the initiation phase, that would involve a lot of monomer units being used up that finally terminated the polymerization reaction [11,6].

The characterization process had established based on the principle of radiation-induced changes which would include polymerization reaction as well as cross linking reaction, hence resulted towards
rigidity changes of polymer gel structure [12]. Those changes could denote different information based on absorbed dose characterization of Raman intensity. Obviously, once the radiation dose irradiated the polymer gel samples in small ampoule tubes, those samples had color changes from transparent solution to become whitish solution. The whitish color was varied from lower to higher dose, in which the appearance of solutions would be from less whitish to more whitish.

4. Conclusion
The fabrication of NIPAM polymer gel was evaluated using Raman spectroscopy to compare between unirradiated and irradiated gel by analysing the Raman intensities based on the effect of initial composition of monomer and cross linker in the polymerization process of NIPAM gel dosimeters. There were changes in the Raman intensities as a function of absorbed dose, in which it was proven that the radiation may induce the gel samples to be polymerized. The increment and decrement in Raman intensities as the radiation dose increases indicate that there is an occurrence of a polymerization process and the monomers consumption process respectively. The rate of polymerization increased as the amount of carbon single bonds increased and the rate of monomers consumption increased as the amount of carbon covalent bonds decreased after irradiation.

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