Radiation Induced Polymerization of N-isopropyl acrylamide Polymer Gel Characterized by Raman Laser

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Abstract. Radiation dosimeter is a device that can quantify the amount of a dose. One type of chemical dosimeter is known as a polymer gel dosimeter that is capable of measuring 3D dose distribution. Thus, this work aims to synthesize N-isopropyl acrylamide (NIPAM) polymer gel and study the effect of NIPAM monomer and N, N'-methylene-bis-acrylamide (BIS) crosslinker concentrations on the polymerization of NIPAM polymer, and NIPAM and BIS consumptions in gelatin matrix induced by gamma rays at dose between 0 to 21 Gy. The dose response of irradiated NIPAM polymer gel was determined using Raman spectroscopy. Raman peak intensities were identified in the samples at 815 cm\(^{-1}\) assigned bonding for C-C of NIPAM polymer gel, 1025 cm\(^{-1}\) assigned bonding for C=C of NIPAM and 2353 cm\(^{-1}\) bonding for C=C of BIS. The result shows that the intensity of carbon covalent bonds decreases, while the intensity of carbon single bonds increases after the irradiation process.

Keywords: Polymer gel, 3D dosimeter, Radiotherapy treatment, Raman laser

1. Introduction
There are several consequences that occur in the chemical dosimeter upon irradiation. Once the radiation energy is absorbed by the chemical dosimeter, it triggers bounded and free electrons to be ejected, and produces ions and free radicals, which may promote subsequent chemical reactions. Radiolysis of water results in the formation of hydrogen, (H\(^+\)) and hydroxyl (OH\(^-\)), as well as the chemically reactive uncharged free radicals of hydrogen, (H\(^•\)) and hydroxyl (OH\(^•\)). A series of events may take place that may end up with the subsequent chemical reactions of polymerization and crosslinking [1].

The first chemical dosimeter introduced is the Fricke dosimeter that contains ferrous sulphate solution, which is changed to ferric sulphate from the radiation-induced oxidation process of ferrous sulphate solution. Incorporated with gelatine, the Fricke dosimeter improved its capability to become tissue equivalent (TE) material and perform three-dimensional 3D dosimeter for the first time after being incorporated with the CT scanner or MRI scanner [2]. The Fricke dosimeter has been claimed to be a basic and standard dosimeter, since it fulfils most of the dosimeter standard features at the moment. An ideal dosimeter must be independent of dose rate, in which the dosimeter is not really sensitive with the different dose rate. Therefore, the measurement must be constant, when different dose rates are being applied, and the dosimeter only responds with different amounts of net absorbed doses [3].
There are many studies which emphasize on 3D polymer gel dosimeters of choice, due to their TE characteristic for clinical radiotherapy and radiation oncology. The main objective of radiotherapy is to irradiate the specific organ or tissue by destroying the cancerous cells but spare the normal healthy tissue within the surroundings [4]. The outcomes of the treatment are to either cure or just reduce the severity of the cancers. The radiation given is expected to change the target’s cancer cells chemically and biologically in tissues or organs.

In fact, many studies have stressed on the need of a dosimetric system which is able to quantify the absorbed dose in 3D since the development of complex radiotherapy treatment that applies a higher amount of dose and multi-direction of the beam. For instance, a procedure in IMRT must have complete verification of the 3D dose profile, due to the dynamic treatment that is applied a multi-direction of radiation beam [5]. Therefore, polymer gel dosimeter should fulfil the requirement of 3D dose verification by determining the high spatial resolution of 3D dose distribution prior to the actual radiotherapy procedure.

The new normoxic polymer gel dosimeter is based on N-isopropyl acrylamide (NIPAM) as the monomer and N, N’-methylene-bis-acrylamide as the crosslinker has been introduced [6], which reduces the toxicity of chemicals used and as easy preparation compared to normoxic polyacrylamide gels (nPAG). The introduction of NIPAM polymer gel dosimeter (Figure 1) is considered as an alternative to previously used polymer gel dosimeters because NIPAM monomer has lower toxicity and the dose sensitivity is comparable to the previous polymer gels [7]. Raman spectroscopy has been used to directly measure the covalent bonds present in the polymer gels, which is the correct method used in quantifying the amount of polymerization and the consumption of co-polymers of NIPAM polymer gel dosimeters.

![Chemical structures](image)

**Figure 1.** Chemical structures of (a) N-isopropyl acrylamide (NIPAM) (b) N,N’-methylene bis-acrylamide (BIS) (c) NIPAM polymer gel.
2. Method

2.1. Fabrication of Gel Samples

Fabrication of polymer gel under normal atmosphere took place in the laboratory without the use of a glove box based on a study done by Deene [8] and following the method proposed by Senden [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. Then, the gelatine solution was heated up to 45°C and continuously stirred by using a magnetic stirrer until the solution became clear and transparent. By turning off the heating element and the stirring pursued, 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 was approximately dissolved within fifteen minutes. Finally, the anti-oxidant, tetrakis hydroxymethyl phosphonium chloride (THPC) (5mM) was added to the solution and continuous stirred for about two minutes. The end product was filled into small ampoule tubes (2ml), which were sealed with parafilm and wrapped in an aluminium wrapper. Once completed, the samples of NIPAM polymer gels were stored in a refrigerator at a low temperature at approximately 4°C. Estimated within twenty-four hours, gels were taken out from refrigerator and equilibrated at room temperature prior to the irradiation process.

2.2. Irradiation of Gel Samples

The samples were equilibrated at room temperature which took less than 10 minutes. Afterwards, the samples were irradiated with gamma rays produced by a Cobalt-60 (Co60) source from Gamma Cell Instrument, model 220 Excel Irradiator (MDS Nordion, Ottawa, ON, Canada) (Faculty of Nuclear Science, National University of Malaysia). The radiation dose given was set at a control button of the chamber. One batch of samples was placed inside the refrigerator while the other samples were irradiated up to 21 Gy with a single dose per cycle. During the irradiation process, each sample was placed in a beaker filled with distilled water.

2.2. Raman Characterization

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

3. Results and Discussion

The main aim of Raman spectrometer analysis is to demonstrate that it is a laboratory characterization instrument that is able to characterize the polymer gel dosimeter in terms of polymer formation and co-monomers consumption. This instrument generally provides direct characterization which differs from other well versed imaging modalities such as MRI, ultrasound, CT scan and optical CT that provide indirect characterization [10]. This is because by using Raman instrument, the characterization of polymer gel will involve the molecular vibration which lies within the polymer gel.

A related study done by Jirasek [11], has stated that the dose sensitivity of BIS is smaller than monomer acrylamide (AA), indicating that more rapid consumption of BIS rather than AA following polymer acrylamide gel (PAG) irradiation which results from Raman characterization. These findings prove that Raman spectrometer provides direct measurement on sample constituents which have unique tools to explore the true nature of polymerization.

In this study, after the irradiation of NIPAM polymer gel dosimeter, the characterization process has been carried out by using Raman spectrometer. Therefore, the samples of gel dosimeters will absorb the energy difference between the incident and scattered radiation in the form of molecular vibrations, which are then evaluated by Raman spectrometer that is related to the process of inelastic
scattering. Each molecule has specific and unique sets of stretching and bending vibrational modes possessed by the covalent bonds within the molecules.

Every single of molecular bonding can represent a unique set of vibrational mode which differs from one molecule to the others. Thus, based on Raman theory, the specific molecular covalent bonds can be determined and quantified by analysing the intensity of scattered light as a function of the Raman shift from the scattered light energy. The characterization of NIPAM polymer gel by Raman spectrometer involves two activities which are polymer formation and co-monomer consumption.

3.1. Polymer formation of NIPAM polymer gel
The characterization of NIPAM polymer gel for polymer formation can be evaluated from the incoherent scattering photon energy of C-C stretching mode that increases in intensity. Based on the Raman spectrum analysis of the Raman peaks, the polymer formation has been monitored at 815 cm\(^{-1}\) following the intensity increment in C-C stretching mode of NIPAM polymer gel [12]. The Raman data were fitted to the monoexponential function, that takes all values from 0 to 21 Gy based on equation [11]:

\[
y = y_0 + A(1 - e^{-D/D_0})
\]

where, \(D_0\) is the sensitivity parameter, \(y_0\) is the Raman intensity at zero dose and \(A = \Delta y_{\text{max}} = y_{\text{max}} - y_0\) is the maximum differential dose response. \(y_{\text{max}}\) describes the maximum intensity over the dose range up to 21 Gy. Figure 2 (a) and (b) shows the positive monoexponential plots of the changes in intensities as a function of absorbed radiation dose at various concentrations of NIPAM and constant concentrations of BIS and vice versa.

![Figure 2](image-url)
The polymerization process of NIPAM polymer gel dosimeter will increase the intensity of carbon single bonds after the interaction of gel samples with gamma radiation. In particular, a lot of free radicals interact with both of the co-monomers in the NIPAM polymer gel composition and the huge amount of co-monomers will end up with greater increment in intensity, referring to the conversion of carbon double bonds to carbon single bonds, which indicates the existence of polymerization process.

Based on co-monomers concentration, it is seen that as the concentration of NIPAM and BIS increases, the rate of polymerization involving initiation and propagation phases also increases since there are more NIPAM and BIS being polymerized. It can be seen from the Raman spectra, in which the intensity of Raman spectra tends to be higher accordingly as the set of radiation dose from low to high being applied. It explains that the rate of initiation phase and propagation phase are higher due to the increased interaction of co-monomers in the formation of NIPAM polymer gel.

3.2. Co-monomers consumption of NIPAM polymer gel

The characterization of NIPAM polymer gels can be analyzed from the incoherent scattering photon energy of C=C stretching mode of both co-monomers. From the Raman spectrum analysis of the Raman peaks, the consumptions of NIPAM and BIS have been monitored at 1025 cm\(^{-1}\) and 2353 cm\(^{-1}\) respectively based on the intensity decrement of C=C stretching mode of NIPAM polymer gel (Baldock et al., 1998). The Raman data were fitted to the monoexponential function, that takes all values from 0 to 21 Gy based on equation [11]:

\[
y = y_0 - A(1 - e^{-D/D_0})
\]

Figure 3 (a) and (b) shows the negative monoexponential plots of the changes in intensities as a function of absorbed radiation dose at various concentrations of NIPAM and constant concentrations of BIS and vice versa.

According to Gustavsson [13], the consumption of a monomer and a crosslinker occurs once the polymer gel dosimeters were irradiated with ionizing radiation. The consumption of co-monomers and crosslinking activities reduces the intensity of carbon double bonds in the molecules. The Raman spectra obtained at the specific wavelength contains information of specific energy of molecular vibration in which particularly the consumption of NIPAM monomer and BIS cross linker can be monitored at wavelength 1025 cm\(^{-1}\) and 2353 cm\(^{-1}\) of the entire Raman spectra that shows consistently decrement in intensity as the radiation dose increases. The intensity decreases following the initial concentration of BIS and different concentration of NIPAM and also following the initial concentration of NIPAM and different concentration of BIS. The polymerization takes place with the consumption of NIPAM monomer and BIS crosslinker. In this phase, a lot of free radicals interact with both of the co-monomers in the NIPAM polymer gel composition and the big amount of co-monomers tends to end up with a greater decrement in Raman intensity, referring to the conversion of carbon covalent bonds to carbon single bonds that indicates the occurrence of polymerization process.

The Raman intensity represents the amount of C=C stretching bonds in the molecules, in which in the monomer consumption, the intensity tends to decrease as the radiation dose and the co-monomers concentration increase generally.

The decrement in Raman intensity due to the consumption of NIPAM monomer and BIS cross linker is referred to the high amount of C=C bonds in the gel compositions which have been cut off to become C-C single bonds by the process of radiation scission. Thus, from the result, it shows the reduction in Raman intensity, which refers to the reduction in the amount of C=C bonds in the molecules. At higher radiation dose, there is a fewer amount of co-monomers in the composition as a result of further polymerization; thus the amount of co-monomers is no longer sufficient to enable the process of monomer consumption to be at the higher rate like the one at the lower radiation dose. Moreover, presumably, at higher radiation dose, both co-monomers have been consumed more rapidly which ends up with less significant decrement of C=C bonds, due to the decreased C=C bonds in the
composition. It can be seen in the trend of Raman spectra, in which the intensity of Raman spectra tends to be reduced accordingly as the set of radiation dose from the lowest to the highest being applied. It explains the rate of initiation phase and propagation phase are higher due to more interaction of co-monomers in the consumption of monomer towards the formation of NIPAM polymer gel.

In terms of co-monomers concentration, as the concentration of NIPAM and BIS increases, the rate of co-monomers consumption involving initiation and propagation phases also increases since there are more NIPAM and BIS being consumed and converted to polymer. The existence of BIS cross linker in the gel composition obviously leads to the increment of NIPAM consumption that varies from 2% to 4% of the BIS concentration. Thus, pertaining to the role of BIS cross linker instead of NIPAM monomer itself, it is seen to be very effective in the process of monomer consumption, in which as the BIS concentration increases, the intensity decreases significantly, and that indicates that the NIPAM monomer has been consumed very efficiently.

**Figure 3.** Relative changes in Raman intensities of C=C stretching of NIPAM showing the consumption of NIPAM as a function of absorbed radiation dose, (a) various concentrations of NIPAM and constant concentrations of BIS and (b) various concentrations of BIS and constant concentrations of NIPAM.

4. **Conclusion**

The polymerization of NIPAM and BIS to the NIPAM polymer gel, results to the breaking of carbon double bonds to single bonds and crosslinking between NIPAM and BIS of NIPAM polymer gel. Thus, as the radiation dose increases, the rate of co-monomer consumption increases, shown by the intensity of carbon covalent bond decreasing. Also, as the radiation dose increases, the consumptions
of co-monomers are higher, which leads to the decrement of the C=C bonds intensity. In contrast, the breaking of C=C bonds to C-C bonds during the higher radiation dose, can directly increase the intensity of C-C bonds.

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