Improved dose sensitivity of normoxic polyacrylamide gelatin gel dosimeter with sucrose

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Abstract. To improve the dose sensitivity of normoxic polyacrylamide gelatin gel (nPAG) dosimeter, the effect of sucrose as an additive is investigated. The dose-transverse relaxation rate ($R_2$) characteristics of the samples of nPAG with different sucrose concentrations were examined, and temperature increases due to exothermic polymerization reaction in the irradiated gel were also measured. As the result, the dose-$R_2$ sensitivity increased (~3 times) with increasing sucrose concentrations (0-25%), while other characteristics of dose response, such as dose integral property, dose rate dependence and temporal stability, were consistent with those of typical nPAG dosimeter. And as the sucrose concentrations increased, a larger temperature increase was observed. These results clearly indicate that the polymerization rate is increased with increasing sucrose concentrations.

1. Introduction

Polymer gel dosimeter has been used for measuring the three-dimensional dose distribution delivered by recent radiation therapy techniques. It is a device utilizing the radiation-induced polymerization in the gel, and the results of the polymerization reaction increase the gel's solidity and opacity with the increase of irradiation dose. The three-dimensional dose distributions are imaged by MRI or Optical CT measurements [1, 2].

Many gel dosimeters having different vinyl monomers, gelling agents and deoxygenated techniques have been developed so far [3, 4]. Among them, the normoxic polyacrylamide gelatin (nPAG) gel is one of the promising dosimeters [5-7], which is composed of two monomers, acrylamide (Aam) and $N,N'$-methylenebisacrylamide (Bis), and gelatin. The nPAG dosimeter has advantages of the dose integral property and the less dose rate dependence, however the dose sensitivity for the transverse relaxation rate ($R_2$) is unsatisfactory (ca. 0.1 Gy$^{-1}$s$^{-1}$).

To improve this property, Koeva et al. have proposed the gels with co-solvents (glycerol or isopropanol) which dissolves more Bis (7%) in water [8, 9]. The dose sensitivity was improved to 2.7 times higher than that of typical nPAG gel. In their studies, co-solvents (carbohydrates) play an important role to enhance the dose sensitivity even in a case of 3% Bis concentration [9, 10], though
the mechanisms are not clear. It has been also reported that saccharide additive enhanced with the dose sensitivity of methacrylic acid-based gel [11] and Fricke type gel dosimeters [12]. According to these facts, we focused on sucrose as carbohydrate additive for nPAG gel dosimeter. In this paper, we report on the dose-\(R_2\) characteristics of nPAG with different sucrose concentrations and temperature increases due to exothermic polymerization reaction in the irradiated gel [13].

2. Materials and methods

2.1. Gel fabrication

In this study, the samples of nPAG with different sucrose concentrations were used (Table). The details of procedure of gel fabrication are as follows. Gelatin (300 bloom, Sigma Chemical co.) was added in water at room temperature and then it was heated at 60°C on a hot magnetic stirrer. After the solution got clear, it was cooled to 50°C and Bis (Wako Pure Chemical co.) was added. After Bis dissolved completely, sucrose was added. The solution was cooled to 40°C and Aam (Wako Pure Chemical co.) was then added. Finally, tetraakis(hydroxymethyl)phosphonium chloride (THPC 80%, Sigma Chemical co.) was added at 35°C. The solution was filled in 10 ml test tubes for MRI measurements or in 50 ml glass vials for temperature measurements. The samples were stored at 3-5°C in a refrigerator.

| Chemical                      | Concentration |
|-------------------------------|---------------|
| Water                         | 3 %           |
| Acrylamide                    | 3 %           |
| N,N'-methylenebisacrylamide   | 3 %           |
| Gelatin                       | 5 %           |
| Sucrose                       | 0 - 25 %      |
| THPC                          | 5 mM          |

2.2. Irradiation

The samples were irradiated between 10 and 16 hours after gel preparation with a medical linear accelerator (Clinac iX, Varian) using 6 MV photon beams at 5 cm depth in a water phantom. A source sample distance was 100 cm, a field size was \(10 \times 10\) cm\(^2\) and constant dose rate was 300 cGy/min at dose maximum depth. Firstly, the samples were irradiated to known dose up to 40 Gy to compare the dose-\(R_2\) response of each samples. Secondly, for examining the dependence on the dose integration in the dose response, the fractional irradiations up to 10 Gy of total dose were performed. The irradiation dose per fraction was 1 Gy and the time interval of each irradiation was one minute. And finally, various doses rate from 100 and 600 cGy/min at dose maximum depth were delivered. After irradiation, all samples were stored at 23°C in an incubator to obtain MR room-temperature equilibrium.

2.3. Temperature measurement

The samples were left at the irradiation site for at least 1h before the irradiation to stabilize their temperature. The samples were wrapped in polyethylene sheet to avoid heat loss to air and were set in the beam axis center on Solid Water. The top surface of 50 ml vials was set at the same level at 100 cm source surface distance. A fields size was \(20 \times 20\) cm\(^2\). The samples were irradiated to dose up to 20 Gy. Temperature probe was inserted vertically into the center part of 50 ml glass vial. Temperature histories were recorded from the start to after irradiation with digital thermo-recorders (TR-52, T&D).

2.4. MR measurement

All images were acquired with 0.3 Tesla MRI system (AIRIS-II comfort, Hitachi) using multiple spin echo sequence with the following parameters, \(TE = 20\) and 250 ms, \(TR = 4000\) ms, thickness = 5 mm
(at a central beam axis of the irradiation), matrix size = 128 × 128, FOV = 140 × 140 mm², number of excitations = 3. All samples except for the study on temporal stability of dose response were measured at after three days post-irradiation. The $R_2$ values were calculated from two images ($TE = 20$ and 250 ms). The $R_2$ value of each sample was determined by averaging above 50 pixels of circular region of interest in images. The samples for the temporal stability study were measured successively at the time interval between one and five days after irradiation.

3. Results and discussion
The dose-$R_2$ response relations of the samples with different sucrose concentrations are shown in Fig. 1(a). The gradient of the dose-$R_2$ response (0-5 Gy) increases with increasing sucrose concentrations [Fig. 1(b)]. The sensitivity ($0.37$ Gy$^{-1}$s$^{-1}$) of nPAG with 25% sucrose was ca. 3 times higher than that ($0.12$ Gy$^{-1}$s$^{-1}$) of nPAG without sucrose.

Figure 1. The dose-$R_2$ relation of nPAG with different sucrose concentrations (a). The plot of the dose-$R_2$ sensitivity at the linear part (0-5 Gy) versus sucrose concentrations (b).

The temperature increase due to radiation-induced polymerization is shown in Fig. 2. It was observed just after the irradiation start. With increasing sucrose concentrations, the temperature increases proportionally due to the exothermic reaction.

Figure 2. The temperature histories of nPAG with different sucrose concentrations due to the exothermic radiation-induced polymerization reaction. The vertical broken line shows the time at the end of irradiation.

The result indicates that the polymerization rate increases with sucrose concentrations so that the dose-$R_2$ sensitivities increase. The reasons of the higher sensitivity due to the presence of sucrose are not clear at this stage, but some possibilities are considered. One is due to the decreasing of water content that causes the higher concentration of monomers in the gel. Another is due to chemical
interactions between carbohydrates and monomers/polymer molecules which are postulated in the previous studies [9-11]. It is interesting that the enhancement in sensitivity is observed in the gels with a variety of water-soluble carbohydrates (e.g. sucrose, alcohols [9, 10], glucose [11]) even though each gradient of an enhancement is not consistent. The change of the water environment (structure) due to the hydrates formed may promote the polymerization of monomers in the gel.

The maximum difference of $R_2$ between the fractional irradiation and the single shot irradiation was less than 2% below 10 Gy. The sample with above 20% sucrose showed slightly lower $R_2$ at higher dose rate (600 cGy/min). The temporal $R_2$ changes after irradiation were significant for less than one day and slightly increased after two days post irradiation. These characteristics are consistent with those reported for typical nPAG gels [6,7].

4. Conclusion
We have examined the characteristics of sucrose-containing nPAG system and found that the dose-$R_2$ sensitivity are significantly increased with increasing sucrose concentrations even in the case of 3% Bis concentration.

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