Comparison of the influence of inorganic salts on the NMR dose sensitivity of polyacrylamide-based gel dosimeter

S-I Hayashi\textsuperscript{1}, H Kawamura\textsuperscript{2}, S Usui\textsuperscript{1} and T Tominaga\textsuperscript{1}

\textsuperscript{1}Department of Clinical Radiology, Faculty of Health Sciences, Hiroshima International University, Higashi-Hiroshima, Hiroshima, 739-2695, Japan
\textsuperscript{2}Department of Radiological Sciences, Ibaraki Prefectural University of Health Sciences, 4669-2 Ami, Ibaraki, 300-0394, Japan

E-mail: rin@hs.hirokoku-u.ac.jp

Abstract. On the NMR dose sensitivities of polyacrylamide-based gel dosimeters irradiated by X-ray, the additive effect of various inorganic salts (electrolytes) is investigated. Among the various combination of cations (Li\textsuperscript{+}, Na\textsuperscript{+}, K\textsuperscript{+}, Mg\textsuperscript{2+}, Ca\textsuperscript{2+}, Sr\textsuperscript{2+}, Ba\textsuperscript{2+}, Zn\textsuperscript{2+} and Al\textsuperscript{3+}) and anions (Cl\textsuperscript{-}, NO\textsubscript{3}\textsuperscript{-} and SO\textsubscript{4}\textsuperscript{2-}), MgCl\textsubscript{2} is shown to be the most effective sensitizer. In the result, it is suggested that the extent of the increase of the dose sensitivity may correlate to the hydration power of cations rather than anions. Contrary to the dose sensitivity enhancement, the depression of melting point caused by the additives is also pointed out.

1. Introduction
Recently, several efforts have been made to improve the dose sensitivity of polyacrylamide-type gels [1] which contain \textit{N,N'}-methylene-bis-acrylamide (Bis) as a cross linker [1-3][2-4]. In the gels, crosslinking reactions lead the polymer created by irradiation to precipitation, which contributes to increase the dose response in the measurements of MRI [5, 6], X-ray CT [7], optical CT [8] and ultrasound [9]. However the low solubility of Bis in water (at most 3 wt\%) sets a limit on increasing the dose sensitivity. Koeva et al. [1][2] and Jirasek et al. [2][3] have increased the solubility of Bis in the \textit{N}-isopropylacrylamide (NIPAM) -based gel by adding a cosolvent (\textit{e.g.}, glycerol and isopropanol). Chain et al. [3][4] have reported that the increase of the concentration of monomer (NIPAM) leads the solubility of Bis to increase even in the gel without a cosolvent. Consequently, they caused the increase of dose sensitivity.

In our recent work, we have investigated the effect of some inorganic salts (electrolytes) on the NMR dose sensitivity of a methacrylic-acid-based gel (MAGAT) dosimeter [10]. In the results, it was found that the addition of inorganic salt, especially MgCl\textsubscript{2}, obviously increased the dose sensitivity. Moreover as the salt concentration increases, the increase of polymerization rate was also observed via the temperature measurements during irradiation. The results indicated that inorganic salts acted as an accelerator for radiation-induced free-radical polymerization in a methacrylic-acid-based gel. Increased dose sensitivity has been also observed in a polyacrylamide-based gel (PAGAT) and a NIPAM-based gel with MgCl\textsubscript{2} under the conventional Bis concentration [11]. Surprisingly, the dose sensitivity in a PAGAT gel with 1.0 M MgCl\textsubscript{2} was approximately one order higher than in a basic PAGAT gel.
To gain the deeper insight into the effects of inorganic salts on the NMR dose sensitivity in a PAGAT gel, in the present work, we will further examine the influence of various inorganic salts such as Li, Na, K, Mg, Ca, Sr, Ba, Zn and Al chlorides, nitrates and sulphates.

2. Materials and method

Basic PAGAT gels were prepared in the standard composition as shown in Table 1. Various inorganic salts (0.4 and 0.8 M) were added into the basic PAGAT gels, respectively. The resulting solution was subdivided by pouring into test tubes (1.5 cm diameter and 10 cm length). After allowed to room temperature, all samples were stored in a refrigerator at a fixed temperature (4 °C) for one day.

The irradiations were performed using the 10 MV photon beam of a medical linear accelerator (EXL-15SP, Mitsubishi Electric Co.). The test tubes were irradiated in a cubic water tank (30 x 30 x 40 cm³) at a depth of 10 cm at room temperature. The axis of the test tube was perpendicular to the beam. The SSD was 90 cm, and the field size of 10 x 10 cm² at the isocenter was used to guarantee the beam flatness. The doses of 2, 4, 6, 8 and 10 Gy were delivered to each sample with a constant dose rate of 1.69 Gy/min.

Dose readout from the samples was performed using a 1.5 T scanner (EXCELART Vantage, Toshiba Medical Systems Co.) with a quadrature torso SPEEDER coil. A multiple spin-echo sequence was applied using the following parameters, (TR / TE's / FOV / Slice Thickness / Matrix Size) = (4 s / 30, 250 ms / 128 x 224 mm² / 5 mm / 128 x 224) with a resulting voxel size of 1.0 x 1.0 x 5.0 mm³. The transverse relaxation rate $R_2$ is determined by $R_2 = \frac{1}{T_2} = \ln\left(\frac{S_1}{S_2}\right)/(TE_2 - TE_1)$, where $T_2$ is the transverse relaxation time, and $S_1$ and $S_2$ are the signal intensities at echo times, $TE_1$ and $TE_2$, respectively.

Table 1: The composition of basic PAGAT gel and the additives of various inorganic salts. For convenience, the molarity of inorganic salts and THPC per 1000 g of water is represented by M in this article.

| Chemical                                         | Concentration |
|-------------------------------------------------|---------------|
| Water                                           | 89 wt%        |
| Gelatin                                         | 5 wt%         |
| Acrylamide                                      | 3 wt%         |
| $N,N'$-methylene-bis-acrylamide                  | 3 wt%         |
| Tetrakis(hydroxymethyl)phosphonium chloride (THPC) | 10 mM         |
| Inorganic salt (electrolyte) (Li, Na, K, Mg, Ca, Sr, Ba, Zn and Al chloride (without Al), nitrate and sulfate) | 0.4, 0.8 M |

3. Results and Discussion

Figures 1 shows the NMR dose responses of the PAGAT gel dosimeters containing various inorganic salts. Some salts not shown in the figures were insoluble in a basic PAGAT gel or inhibited the gelation at room temperature.

Figures 1(a) and 1(b) show the dose responses of the PAGAT containing 0.8 M and 0.4 M of various chlorides, respectively. The results indicate that the enhancement of the sensitivity and the concentration dependence are observed more or less in all gels and MgCl₂ is the most effective sensitizer among them. In the previous work, it has been suggested that the enhancement of the dose sensitivity is caused by “gel effect” and correlate with the power of hydration of the metal cation added [10]. The hydration is more effective for cations having a smaller radius and larger charge. In the present results also, the enhancement of the sensitivity is larger for bivalent elements than for univalent ones, and is larger for Mg than for Ca. These results may also support our hypothesis.

In comparison with the sensitivities in PAGAT/MgCl₂ (0.4M) and in PAGAT/LiCl (or NaCl, KCl) (0.8M), the former shows larger enhancement of the sensitivity than the latter. The power of hydration
of Cl$^-$ is generally smaller than that of cation having smaller radius. (For example, the ratio of the hydrated ion radius and the crystal ion radius of Mg$^{2+}$ and Cl$^-$ are 4.8 and 1.4, respectively [12].) Therefore the influence of cations should be dominant rather than anions.

Figure 1(c) shows the dose responses in the PAGAT containing 0.4 M of various nitrates. Similar tendency on the sensitivity to the gel containing chlorides (figure 1(b)) is observed while no appreciable increase in the sensitivity was observed in univalent salts. In the gel containing nitrates, magnesium salt was again the most effective additive.

Figure 1(d) shows the dose responses of the PAGAT containing 0.4 M of various sulfates. The change in the sensitivity is small but still the enhancement is observed in all gels with each additive. In addition, the $R_2$ values in un-irradiated gels are a little higher than those in the gels containing chlorides or nitrates. It may be due to the insolubility of the sulfates itself.

Figure 1: Dose-$R_2$ responses of PAGAT containing different inorganic salt. (a) : 0.8 M of chlorides, (b) : 0.4 M of chlorides, (c) : 0.4 M of nitrates and (d) : 0.4 M of sulfates. The error bars show the standard deviation in $R_2$ calculated in a ROI. The data point of PAGAT in all figures comes from same basic PAGAT sample.
The ratio of the hydrated ion radius and the crystal ion radius of NO$_3^-$ and SO$_4^{2-}$ are 1.2 and 1.6, respectively and they are nearly same as Cl$^-$ [12]. Therefore it was expected that the effect is also nearly same as chloride. However, from the above results, they seem to depress the increase of the dose sensitivities except Mg(NO$_3$)$_2$ while chloride may be the most harmless as a counter ion.

4. Conclusion
In this work, we investigated the influence of various inorganic salts on the NMR dose sensitivities in a polyacrylamide-based gel. In the results, MgCl$_2$ was indicated the most promising sensitizer among the inorganic salts examined in this work. From the viewpoint of the tissue equivalency also, MgCl$_2$ may be more desirable rather than other heavy atoms. However the influence of the depression of melting point was observed in the gel with higher concentration of inorganic salts. In order to apply the gel dosimeter with inorganic salt to clinical use, the optimization of the composition and the use of a cross-linker for gelatin-matrix such as formaldehyde [13] are required. On the other hand, polymer gel dosimeters containing inorganic salt may be also beneficial for use with other imaging modalities such as X-ray and optical CT. The studies on other characteristics of polymer gel containing inorganic salt, such as dependency on dose rate and dose integral, spatial and temporal stability, and water and tissue equivalency, are under way.

5. References
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