Inclusion type radiochromic gel dosimeter for three-dimensional dose verification

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Abstract. For the verification of 3D dose distributions in modern radiation therapy, a new inclusion type radiochromic gel detector has been developed. In this gel, a hydrophobic leuco dye (leucomalachite green: LMG) was dissolved in water as an inclusion complex with highly branched cyclic dextrin. The radiation induced radical oxidation property of the LMG gel with various sensitizers was investigated. As a result, the optical dose responses were enhanced by the addition of bromoacetic acid and manganese (II) chloride. Unfavorable auto-oxidation of the gel was reduced when it was stored at 4°C.

1. Introduction
Radiochromic gel dosimeters are one of the promising tools for the verification of 3D dose distributions [1] in modern radiation therapy [2]. Among them, a micelle gel dosimeter has several advantages: water equivalency, no or low diffusion property, insensitivity to oxygen, lower toxicity, and suitability for optical CT read-out [3-7]. The micelle gel consists of leuco dye, surfactant, radical initiator, and gelling agent. In the gel, hydrophobic leuco dye is dissolved in water with a surfactant. However, formation of micelles is affected by surfactant concentration, ambient temperature, pH, and other chemicals [8].

To dissolve hydrophobic compound in water, it is also known to use inclusion compounds such as cyclic dextrins. Since it affords a prepared stable hydrophobic cavity, we focused on an inclusion type gel dosimeter. In this paper, we will describe the dose response of a newly developed radiochromic gel consisting of leucomalachite green (LMG) and highly branched cyclic dextrin (HBCD) [9, 10] as an inclusion host. The HBCD produced by the cyclization reaction of branching enzyme from amylopectin is highly soluble in water and has hydrophobic cavities.

2. Materials and Methods

2.1. Gel manufacturing
A typical LMG gel contains water, 4 wt% HBCD (Ezaki Glico Co), 2 wt% κ-carrageenan (Marine Science, KK-9), 4 mM bromoacetic acid (Tokyo Kasei Co), 0.3 mM LMG (Sigma Aldrich), 20 mM chloroform (Nacalai Tesque Inc), and 6 mM MnCl₂ (Katayama Chemical). After κ-carrageenan was dissolved in a two-third portion of water at 80°C, the solution was cooled to 55°C (solution A). In the remaining one-third portion of water HBCD was dissolved. Then 0.1 M-bromoacetic acid (BAA) and LMG-CHCl₃ were successively added and stirred for 30 min to create a clear solution. The solution was combined with 0.1 M-MnCl₂ and warmed to 55°C. Finally it was mixed with the above solution
A. The combined solution was poured into 1 × 1 × 4.5 cm³ of PMMA cuvettes for optical measurements and stored at 10°C before irradiations. A variety of LMG gels in this study were summarized in Table 1. Trichloroacetic acid (TCAA) or bromoacetic acid was chosen as a radical initiator. Several transition metal salts listed in Table 1 were chosen as a sensitizer.

| composition          | LMG-TCAA | LMG-BAA |
|----------------------|----------|---------|
| water                | MnCl₂     | MnCl₂   |
| k-Carrageenan [wt%]  | 2         | 2       |
| HBCD [wt%]           | 4         | 4       |
| TCAA [mM]            | 4         | -       |
| BAA [mM]             | -         | 4       |
| LMG [mM]             | 0.3       | 0.3     |
| CHCl₃ [mM]           | 5         | 5       |
| MnCl₂ [mM]           | 0, 6      | 0, 2, 4, 6, 8, 10 |
| MnSO₄ or Mn(NO₃)₂ [mM]| -        | 6       |
| CoCl₂, NiCl₂ or CuCl₂ [mM]| - | 6       |

HBCD: highly branched cyclic dextrin
TCAA: trichloroacetic acid, BAA: bromoacetic acid

2.2. Irradiation
The cuvette samples were irradiated with a medical linear accelerator (Clinac iX, Varian) using 6 MV photon beams. A source sample distance of 100 cm and a field size of 20 × 20 cm² at the isocenter was used to guarantee the beam flatness. The doses of 1, 2, 5, 10 and 20 Gy were delivered to each sample with a constant dose rate of 300 cGy/min at 20°C. The dose rate was changed from 100 to 600 cGy/min to examine the dose rate dependency.

2.3. Optical density measurement
The optical densities of the gel samples were measured with a spectrophotometer (Shimadzu UV-1200) at 630 nm before and after irradiation. The optical dose responses of the LMG gels were evaluated by subtraction of the optical density of before and after irradiated samples.

3. Results and Discussion
By using HBCD as the host compound, hydrophobic leucomalachite green was easily dissolved in water with chloroform. Auto-oxidation of leuco dye is an unfavorable property of radiochromic gels because it lowers the dose sensitivity [7]. While dissolving LMG in water, a significant coloring was observed above 60°C. Therefore, the solution was kept at room temperature (20°C) before it was combined with a gelling agent solution. We used k-carrageenan as a gelling agent, because both gelatin and agarose yielded a somewhat cloudy gel in the presence of 4 wt% of HBCD.

The initial optical densities of the gels were different between batches because the temperature histories during the preparations were not exactly the same for each of the samples, however, their optical dose responses were almost the same when the initial value was subtracted from the irradiated one.

In contrast to LMG micelle gel dosimeters, our inclusion type LMG gel showed no optical dose responses up to 20 Gy without transition metal salts. When adding manganese (II) chloride in the gel, dose responses were observed. The dose sensitivity increased with increasing MnCl₂ concentration (2-8 mM). The gels having other manganese (II) salts, sulfate or nitrate, also showed the same dose responses as was found in the gel with manganese (II) chloride. On the other hand, addition of cobalt (II), nickel (II), or copper (II) chloride was ineffective in the dose response. Although the exact
mechanism is not known at this stage, we speculate that manganese (II) ion is quite stable and once it is oxidized to a higher oxidation state, it acts as a strong oxidizing agent.

The effect of halocarbon radical initiator was then examined and it was found that the gel with BAA showed a nearly 2 times higher sensitivity ($8.5 \times 10^{-3}$ cm$^{-1}$ Gy$^{-1}$) than that of TCAA ($4.0 \times 10^{-3}$ cm$^{-1}$ Gy$^{-1}$) (figure 1) or those of the reported radiochromic micelle gels [3, 6]. Since bond dissociation energy of C-Br is lower than that of C-Cl, BAA effectively generates a bromine radical which abstracts hydrogen atom from leuco dye.

The optical densities were increased by increasing the post-irradiation time due to the auto oxidation of leuco dye. When samples were stored at room temperature (ca. 20°C), the dose sensitivities also increased (figure 2). This auto oxidation can be reduced by storage of the samples in a refrigerator (4°C). The time-dependences of the optical density were $3.0 \times 10^{-3}$ cm$^{-1}$ h$^{-1}$ at 20°C and $0.49 \times 10^{-3}$ cm$^{-1}$ h$^{-1}$ at 4°C, respectively.

Dose rate dependency was observed in our inclusion type gel (figure 3), as was previously reported on radiochromic micelle gels [6, 7]. Using 100 cGy/min dose rate resulted ca. 17% (at 4 Gy) and 21% (at 8 Gy) higher optical dose responses than those of 600 cGy/min.

![Figure 1](image1.png)

**Figure 1.** Effect of initiators on the dose sensitivity of LMG-MnCl$_2$ (6 mM) gels. The dose sensitivities (TCAA: $4.0 \times 10^{-3}$ cm$^{-1}$ Gy$^{-1}$, BAA: $8.5 \times 10^{-3}$ cm$^{-1}$ Gy$^{-1}$) were calculated at the linear part (<5 Gy).

![Figure 2](image2.png)

**Figure 2.** Dose response change of LMG-BAA-MnCl$_2$ (4 mM) gel by post-irradiation times.
4. Conclusion
We have newly developed an inclusion type radiochromic gel detector consisting of LMG-HMBC, BAA, and MnCl₂. It can be easily prepared and has relatively high dose sensitivity. The auto oxidation property was reduced by storage in a refrigerator (4°C). However, the unfavorable dose rate dependency remains to be overcome for clinical applications.

5. References
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Figure 3. Dose rate dependence of LMG-BAA-MnCl₂ (6 mM) gel.