Development of a reusable PVA-GTA-I gel dosimeter for 3D radiation dose assessments

J Taño1,4, S Hayashi2, S Hirota1, CA Gonzales1,3,4 and H Yasuda1
1Department of Radiation Biophysics, Graduate School of Biomedical and Health Sciences, Research Institute for Radiation Biology and Medicine, Hiroshima University, 1 Kasumi 2-3, Minami-ku, Hiroshima 734-8553, Japan
2Department of Clinical Radiology, Faculty of Health Sciences, Hiroshima International University, Higashi-Hiroshima, Hiroshima 739-2695, Japan
3Department of Radiation Oncology, Graduate School of Biomedical and Health Sciences, Hiroshima University, Kasumi 1-2-3 Minami-ku, Hiroshima 734-8551, Japan
4Phoenix Leader Education Program (Hiroshima Initiative) for Rennaissance from Radiation Disaster, Hiroshima University, Japan

E-mail: hyasuda@hiroshima-u.ac.jp

Abstract. A novel formula of crosslinked polyvinyl alcohol (PVA) with glutaraldehyde (GTA), a tri-iodide complex, and glucono-δ-lactone (GDL) acid for gel dosimetry was investigated in the present study. The objectives of this study were to evaluate the formula’s dose response properties through spectrophotometry and possible reusability by reannealing. After production, the gel samples were irradiated from 1 to 70 Gy of gamma-rays from a Cs-137 source with a constant dose rate of 0.857 Gy/min. Spectrum data were obtained using a UV-Vis spectrophotometer and analyses were done for dose linearity, dose sensitivity versus GTA concentration, and absorbance profile versus time. The resulting unirradiated gel samples were colorless and transparent, while the irradiated samples turned to a reddish-brown hue with a peak absorbance response at 490 nm. Dose linearity results indicated R² values of 0.9, 0.986 and 0.8 for GTA concentrations of 7 mM, 15 mM and 30 mM, respectively. Moreover, dose sensitivity is higher for lower concentrations of GTA. Time progression results indicated that the absorbance decreases within one day after irradiation and increases subsequently. Through reannealing for 24 hours at 45°C in an oven, a colorless material with an absorbance value identical to the unirradiated samples was finally made for samples irradiated from 1 to 20 Gy, while the 70 Gy irradiated sample had a significant decrease in color and absorbance peak. This radiochromic gel dosimeter is promising and should be useful for 3D radiation dose assessments. Further investigation of the formula and preparation techniques are suggested for future experiments.

1. Introduction

In the recent years, various advancements in gel dosimetry have been made in line with the continuous progress of radiotherapy technologies and complication of the treatment plans that need precise dose distributions in the bodies of patients [1-8].

There have been notable developments of Fricke-gel dosimeters containing polyvinyl alcohol (PVA) crosslinked with glutaraldehyde (GTA) as base matrix. The crosslinking of PVA and GTA allows the
construction of transparent gels at room temperature and the reduction of diffusion in the gel matrix due to the ease of reactions between PVA hydroxyl groups and GTA. The diffusion coefficient of the gel is defined by the concentration of the GTA [4, 9].

Some gel dosimeters have also been investigated. Kozicki et al [5] reported that radiochromic gels based from a Pluronic co-polymer matrix and leuco malachite green was effective for measuring 3D distribution of doses from both radiotherapy beams. Zhang et al [10] developed a gel dosimetry system for radiation that was composed of 2-hydroxyl acrylate (HEA) monomer and PVA-GTA matrix combined with a photoinitiator; this material showed good stability, dose response and linearity.

And recently, Sunagawa et al [11] reported a radiochromic gel indicator with a PVA base matrix doped with potassium iodide. This gel indicator has high sensitivity and changes from colorless to red after exposure to radiation. Based on their result, Hayashi et al. have applied this system to a novel three-dimensional (3D) radiochromic gel dosimeter using gellan gum as a gelling agent [12]. However, the improvement in terms of temporal and spatial stabilities and transparency has still required.

Motivated by the aforementioned studies, in the present study, we examine the feasibility of a novel gel dosimeter composed of polyvinyl alcohol (PVA) crosslinked with glutaraldehyde (GTA) as base matrix and combined with an iodide such as potassium iodide (KI), and additives such as fructose and a mild acid such as glucono-δ-lactone (GDL).

2. Materials and methods

2.1. Gel production

All PVA-GTA-based gels were prepared using ultrapure water and analytical grade chemicals. After the water was heated to 80 °C, the PVA (1000 of polymerization degree, partially hydrolyzed, 86–90 mol% saponification, Wako Pure Chemical Co., Japan) was added and completely dissolved for approximately 30 minutes using a magnetic stirrer at 80 °C. The mixture was then allowed to cool down to 25°C, after which, the KI (Wako Pure Chemical Co.) and fructose (Wako Pure Chemical Co., Japan) were added until fully dissolved. Then, the GDL (Wako Pure Chemical Co., Japan) and GTA (25% aqueous, Nacalai Tesque, Inc., Japan) were put into the solution for final incorporation. The solution was stirred constantly throughout the mixing process. In order to test the dependence of sensitivity with respect to GTA concentration, three sets of samples were prepared with various GTA molarities. The summary of the reagent concentrations is shown in Table 1. The final mixture was poured into 10 x 10 x 45 mm PMMA cuvettes with a parafilm cover for contamination from air and evaporation to air be prevented. All cuvette samples were placed inside an oven with the temperature at 45°C for 12 hours to allow gelation.

| Solution | potassium iodide (M) | fructose (M) | GDL (mM) | GTA (mM) |
|----------|----------------------|--------------|----------|----------|
| A        | 0.1                  | 0.1          | 25       | 7        |
| B        | 0.1                  | 0.1          | 25       | 15       |
| C        | 0.1                  | 0.1          | 25       | 30       |

2.2. Cs-137 irradiation

A Gamacell410 Exactor Low Dose Rate Research Irradiator (Best Theratronics Ltd., Canada) was used to irradiate the samples. This equipment is located in the Radiation Isotope Facility at the Kasumi campus of the Hiroshima University; it has dual Cs-137 radiation sources with total activity of 178 TBq. This equipment has been regularly checked for its dose rate and has dose uniformity of ±7% in the whole area of a sample container with 260 mm in diameter and 100 mm in height. As of June 2018, the dose rate was 0.857 Gy/min. The samples were irradiated with 1, 2, 4, 6, 8, 10, 15, 20 and 70 Gy (for water) and one sample was kept unirradiated as control.
2.3. UV-Vis Spectrophotometry
The absorbance data of the samples were obtained through a NanoDrop™ 2000c UV-Vis Spectrophotometer (Thermo Fisher Scientific Inc., USA). This device is located in the same campus as the Cs-137 irradiation equipment. All samples were examined 0.125 days (4 hours) after irradiation. Spectrum data were analysed for dose response linearity, dose sensitivity versus GTA concentration, absorbance profile versus time and post-annealing absorbance value.

3. Results and Discussion
The resulting gel dosimeters were transparent if unirradiated and turns to a reddish-brown hue after exposing to gamma-rays, with UV-Vis absorbance peak at 490 nm. Figure 1 shows the increasing gradient corresponding to the doses from 0 Gy (left) to 70 Gy (right).

![Figure 1. Photograph of the PVA-GTA-I samples (GTA=7mM). The dose levels from left to right were: 0 (Control), 1, 2, 4, 6, 8, 10, 15, 20 and 70 Gy.](image)

3.1. Dose response
The dose response plots and linear regression curves of the different samples at 490 nm are shown in Figure 2. These plotted points were generated as the means of the measured data for each sample set during the first measurement or 4-hours post-irradiation. It was seen that the solution having lower GTA concentration (Solution A) exhibited a good linearity in the dose response up to 70 Gy ($R^2 = 0.999$). While, both Samples B and C showed lower $R^2$ values; it is attributable to the absorbance values of the samples exposed to the two lowest doses (i.e. 1 and 2 Gy) in both Solutions B and C, wherein the measured data are approximately the same with those of the control sample’s value.

3.2. Sensitivity and Minimum Detectable Dose
The data obtained above were evaluated using the method developed by Marini, *et al* [4]. The sensitivity of the gel dosimeter was obtained from the slope of the linear regression lines. As shown Figure 2, the sensitivity of the gel dosimeter significantly increased as the GTA concentration decreased; the sensitivities of Samples A, B and C in a 10 mm optical path were $2.5 \times 10^{-2} \pm 0.001$ (1 s.d.), $1.7 \times 10^{-2} \pm 0.001$ (1 s.d.) and $1.5 \times 10^{-2} \pm 0.001$ (1 s.d.) Gy$^{-1}$, respectively. Table 2 shows a comparative summary of the sensitivity changes with previously reported gel dosimeters. According to the results on our samples, it is hoped that the sensitivity of the PVA-GTA-I gel dosimeter will be improved through further optimization.

| Matrix              | Reference | Sensitivity (Gy$^{-1}$)$^a$ | Uncertainty |
|---------------------|-----------|----------------------------|-------------|
| PVA-GTA-I (A)       | $b$       | 0.025                      | $\pm 0.001$ |
| PVA-GTA-I (B)       | $b$       | 0.017                      | $\pm 0.001$ |
| PVA-GTA-I (C)       | $b$       | 0.015                      | $\pm 0.001$ |
| PVA-GTA-Fricke      | [4, 9]    | 0.073                      | $\pm 0.001$ (1 s.d.) |
| 20% XO-PVA          | [13]      | 0.014                      | Not reported |
| 20% PVA hydrogel    | [3]       | 0.046                      | Not reported |

$^a$Sensitivity through 10 mm optical path; $^b$Authors from this study.
The minimum detectable dose (MDD) was obtained through the following equation:

\[ MDD = \frac{3\sigma}{s} \]  
(1)

where \( \sigma \) represents the standard deviation of the absorbance values of the unirradiated (control) samples and \( s \) is the linear regression slope of each sample in the dose response curve. Using the equation above, the computed values of MDD were derived as 5.5x10^{-2} ± 0.001, 7.8x10^{-2} ± 0.001 and 9.3x10^{-2} ± 0.001 Gy for samples A, B and C, respectively.

3.3. Time progression
Absorbance profiles measured after 0.125, 1, 2, 4, and 7 days post-irradiation are shown in Figure 3. It was seen that the absorbance decreased within one day after irradiation and then gradually increased afterwards. The decrease during the initial period may be caused by the reduction of the polyiodide ion to mono-iodide ion due to the excess GTA or fructose. On the other hand, the increase of absorbance is attributable to the oxidation of the iodide ion or reaction with the light. These hypotheses should be investigated in future experiments.

3.4. Reannealing
The feasibility on the reuse of the gel was initially examined by using the cuvette samples that were irradiated using Gammacell40 (Figure 1) and then reannealed for 24 hours at 45°C in the oven. As result, the samples irradiated from 1 to 20 Gy became colourless, while the 70 Gy irradiated sample converted to a lighter hue, as shown in Figure 4. This colour change was confirmed with the absorbance spectra also, as shown in Figure 5. The absorbance values of the samples irradiated from 1 to 20 Gy were comparable to that of the control sample. On the other hand, the 70 Gy sample demonstrated a lower absorbance peak at 490 nm compared to its previous value in Figure 2. These results suggest the possibility of reusing the gel dosimeter through annealing. Further examination on the reproducibility, sensitivity and stability of the gel dosimeter is recommended for future studies.
4. Conclusions

A novel gel dosimeter based on a formula of crosslinked PVA-GTA mixed with KI and GDL was produced. Its characteristics after exposure to Cs-137 gamma-rays were examined with the spectrophotometry techniques. The utilization of the of PVA-GTA as a base matrix resulted to highly transparent gels. Exposure to gamma-rays converts the colour of the gel dosimeter to a reddish-brown hue which allows dose relationship evaluation through spectrophotometry or other optical techniques. The results of the investigation on linearity in dose response and sensitivity indicated that the formula with the lowest concentration of GTA performed the best with $R^2=0.999$, sensitivity $= 0.025 \pm 0.001$ Gy$^{-1}$ and MDD$=0.545 \pm 0.001$ Gy. Time progression results show that the trend of the absorbance curve in time starts to fade in the first day post-irradiation and then increases subsequently. The formulas with the higher concentrations of GTA were less sensitive and had higher absorbance fading compared to the 7mM GTA samples. Annealing could make the gel transparent with absorbance values approximately similar to that of an unirradiated sample. Finally, the data acquired from this study suggest a promising future of the radiochromic gel dosimeter for radiation dose assessments. Further investigation of the formula’s properties and preparation techniques are recommended for future experiments such as: increasing the annealing temperature and utilizing other cross-linkers other than aldehydes.

5. Acknowledgements

The authors would like to thank Prof. Francesco d’Errico, PhD for his insights and guidance in the utilization of crosslinked PVA and GTA in gel dosimetry. This work is supported by JSPS KAKENHI (Grant Number 17K09072).

6. References

[1] Hayashi S et al 2012 Radiat. Phys. Chem. 81 884-8
[2] Fernandes J P et al 2009 J. Phys.: Conf. Ser. 164 53-8
[3] Chu K C et al 2000 Phys. Med. Biol. 45 955-69
[4] Marini A et al 2017 Radiat. Meas. 106 618-21
[5] Kozicki M et al 2018 J. Photochem. Photobiol. A Chem. 351 197-207
[6] Oldham M et al 2017 in Clinical 3D Dosimetry in Modern Radiation Therapy (Ed. Mijnheer B) (ISBN: 9781315118826)
[7] Mather M L et al 2003 Phys. Med. Biol. 48 N269-75
[8] Baldock C 2009 J. Phys.: Conf. Ser. 164 012002
[9] D’Errico F et al 2017 Radiat. Meas. 106 612-7
[10] Zhang W et al 2016 J. Photochem. Photobiol. B Biol. 163 100-4
[11] Sunagawa T et al 2017 Mem Fukui Univ Technol (in Japanese) 47 105-10
[12] Hayashi S et al 2017 Proc 114th Sci Meet Japan Soc Med Phys (8th Japan-Korea Jt Meet Med
[13] Smith S T et al 2015 J. Phys.: Conf. Ser. 573 6-10