Original Article

PROGRESS in MEDICAL PHYSICS 27(4), Dec. 2016
https://doi.org/10.14316/pmp.2016.27.4.175
pISSN 2508-4445, eISSN 2508-4453

Analysis of Physical Properties for Various Compositions of Reusable LMG and LCV Micelle Gel

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In this study, we evaluated the reusable leuco malachite green (LMG) micelle gel properties dependent on various components of chemical concentration and compared with leuco crystal violet (LCV). The gels were delivered to 10, 20, 30, 40 and 50 Gy at 6 MV photon beam from linear accelerator and analyzed using spectrophotometry. We confirmed that the reusable LMG and LVC absorbance wavelength peak were made up at 630 nm and 600 nm respectively. The transparency of reusable LMG decreased with higher amount of trichloroacetic acid (TCAA) and lower reusable LMG dyes. 1 mM reusable LMG was the lowest transparency. The sensitivity was increased depending on lower trichloroacetic acid (TCAA) concentrations and the amount of suitable surfactant (Triton X-100), which was found to be 7 mM. However, we were not able to investigate sensitivity effects factor from reusable LMG dyes. The gel dosimeter containing 16 mM TCAA, 7 mM Triton X-100 gel dosimeter showed the highest sensitivity at 0.0021±0.0001 cm^{-1}. Gy^{-1}. The sensitivity of LCV was found to be higher than reusable LMG at 0.0037±0.0005 cm^{-1}. Gy^{-1}. The reusable LMG and LCV dose responses were shown to be R^2=0.997, R^2=0.999 respectively, as stable measurement results. Future research is necessary to improve dose sensitivity, dose rate dependency and gel fading with extensive chemical formulations.

Key Words: Reusable LMG, LCV micell gel, Sensitivity, Dose response

Introduction

Recently, modern radiation therapy such as intensity-modulated radiation therapy (IMRT) and intensity-modulated arc therapy (IMAT) make it possible to eradicate cancerouse cell by delivering cytotoxic dose while minimizing the dose of normal cell.[1] Following extremely valuable modality doses of ionizing radiation for the treatment in a way is necessary for more accurate than ever before for delivering dosimetric quality assurance (QA).

One-two dimensional radiation dosimeter ionization chamber, thermal luminescence dosimetry (TLD), film and diode array have been used for conventional dosimeter.

However, dosimetric quality assurance for a new developed technique such as IMRT and IMAT are complex and time-consuming, so more sophisticated methods are needed including volumetric dosimeter.[2]

As the quality assurance tools, various gel dosimeters and readout systems have been studied extensively. They are integrating, volumetric, tissue-equivalent radiation gel dosimeter that can be quantify the delivered dose with high spatial resolution and accuracy represent.

The idea of using a gel to measure radiation originated in the early 1950s.[3] The gel dosimeter developed progressively

This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (No. 2015R1D1A1A01060463) and the Ministry of Science, ICT and Future planning (No. 2016M2B2A4911892), the National Research Foundation of Korea (NRF) Grant (2014K2A2A7060928).
Received 10 November 2016, Revised 24 November 2016, Accepted 25 November 2016

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from 1980 to 1990[4] as new polymer gel formulations were proposed. There are different types of gel-based dosimeter formulations available. The chemical changes which occur in the gels resulting from ionizing radiation are indirectly related to the radiolysis of water.[5] Through out this process, many kinds of molecules are dissociated into several highly reactive radicals and ions, such as hydrogen radical and hydroperoxy radicals.[6]

The polymer gel dosimeter has been studied for preclinical applications. The principle is that the free radical makes monomer change to polymerization. It is convenient to fabricate these gels economically but they tend to be effected by light-scattering, temperature and a sensitivity to oxygen.[7] Typically, polymer gel dosimetery have been used with different types of measurement tools such as magnetic resonance imaging (MRI) and computed tomography (CT). MRI has good spatial resolution, which is able to analyze using T2 relaxation time. But it takes a long time and needs complicated preparations.[8,9] Alternatively the optical CT scanning has been investigated. It can remain transparent after irradiation and reduce light scattering compared to polymer gel dosimetry. Recently, there have been investigations into various radiochromic dyes and materials that are leuco malachite green (LMG) and leuco crystal violet (LCV). For example, the PRESAGE^{TM} solid dosimeter consists of leuco malachite green (LMG) and halogenated hydrocarbon free radical initators dissolved in a transparent polyurethane plastic. Also new formualtions of PRESAGE^{REU} were investigated. It is reusable, Z_{eff}=8.1 and density of 1.07 g/cm^3, with CT number 130±20 HU when has been started colorless 24 hours and after 10 days, decreased the absorbance less than 99.96%.[10] In addition, PRESAGE^{TM}, PRESAGE^{REU} special 3D radiochromic dosimeter with various clinical applications for use with beta-emitting radionuclides,[11] and investigated for proton dosimeter.[12,13]

Along with the PRESAGE^{TM} and PRESAGE^{REU}, radio chromic micelle gel have been studied with LMG, LCV and surfactants. It is tissue-equivalent for a wide range of photons and less complicated to fabricate than PRESAGE^{TM}, which omits fabrication procedures involving pressure vessels and special containers.[14]

The purpose of this study was to investigate reusable LMG dye adjusting for micelle gel formulation and to determine the optical wavelength and evaluate optical properties with respect to modulate chemicals composition. The basic composition and properties of an LCV micelle gel were investigated as well.

Materials and Methods

1. Reusable LMG and LCV gel preparation

Various components of LMG gel have been proposed by researchers; a gelatin, a leuco malachite green, a trichloroacetic acid (CCl_3COOH), and a surfactant Triton X-100, all dissolved in high-purity distilled water. In this study we fabricated 9 kinds of groups (Table 1). Biodegradable collagen from pig skin gelatin (300 bloom, Sigma Aldrich, USA) was mixed with distilled water and heated to 43°C stirring with a magnetic bar until the gel melter and became cleared. The mixture was sealed air tight and cooled to around 30°C. During the process, a solution containing distilled water, trichloroacetic acid (Sigma Aldrich, USA) and Triton X-100 (Sigma Aldrich, USA) was stirred according to the chemical composition with blocked light. The temperature was checked for the final gel solutions. The resulting transparent process obtained a slightly colored pale green. Reusable LMG gel was immediately poured into cuvettes (1.25 cm×1.25 cm×4.5 cm) then stored in refrigerator with blocked light.

2. Irradiation procedure

The irradiation of micelle gels were performed under the same conditions using a linear accelator (Clinac IX, Varian

Table 1. Different gel groups for research reusable LMG and LCV composition.

	Gelatin (Wt.%)	LMG	LCV	CCl_3COOH (mM)	Triton X-100 (mM)
Group 1	4	0.5	-	16	7
Group 2	4	0.5	-	20	7
Group 3	4	0.5	-	30	7
Group 4	4	0.37	-	16	7
Group 5	4	0.6	-	16	7
Group 6	4	1	-	16	7
Group 7	4	0.5	-	16	4
Group 8	4	0.5	-	16	2
Group 9	4	-	1	30	8

Medical Systems, CA). As a reference, the irradiation temperature circumstance affects the absorbance of lueco dye. Therefore, prior to irradiation, a temperature equilibrium was achieved within a treatment room for 2 hours. The micelle gels were exposed to 6 MV energy, 400 MU dose rate, 15×15 cm^2 field, on a 5 cm solid water phantom. All gels were positioned 100 cm from the source to surface of solid phantom distance (SSD). To minimize the effect of second scatter, we avoided the edge of a 5 cm section and covered solid phantom with 1.5 cm water to set depth dose build up. The famer type ionization chamber (PTW3001) was used to obtain the depth dose for each energy with protocol TRS-398. Each gel sample was irradiated for 10 Gy, 20 Gy, 30 Gy, 40 Gy and 50 Gy. Remaining samples were irradiated to verify the dose linearity.

3. Optical measurement and analysis

All micelle gel dosimeters were stored for 1 day in refrigerator and taken 45 min prior to the experiment in order to equilibrate to room temperature. The spectrophotometry (Optizen Pop, mecasys, Korea) can measure a range of 160 nm～1000 nm and was used to analyze to 400 nm～830 nm. To evaluate the non-irradiation gels, base space in spectrometer was placed cuvette filled in distilled water as a reference. It made a subtraction gel dosimeter to distilled water so that we were able to obtain non-irradiation gel absorbance. Finally we obtained base gel absorbance difference subtraction between distilled water and base gel.

We investigated the dose sensitivity factor from various chemical formulations. Groups 1, 2, 3 varied the composition ratio of trichloroacetic acid (CCl_3COOH), groups 4, 5, 6 adjusted the reusable LMG analysis to basic gel transparency. Groups 7, 8 changed the amount of Triton X-100 and group 9 was fabricated a LCV to compare with reusable LMG (Table 1). There have been many studies stating that gelatin creates background noise.[9] Therefore, the gelatin weight was fixed at 4 wt.% to reduce effective gel dosimeter. All data were recorded in Microsoft Eexcel and converted Origin (Originlab, USA,MA) format files to analyze results and statistics.

Results and Discussion

1. Optical spectrum

Fig. 1 shows the absorbance spectrum 400～830 nm for reusable LMG composition doses at 0, 10, 20, 30, 40 and 50 Gy. The base gelatin had no high peak and slowly decreased absorbance. Jordan K et al.[15] the LMG wavelength peak was represent 633 nm. The absorbance peak of reusable LMG gel dosimeter was measured at 630～635 nm and differed with the LCV gel dosimeter peak at 600 nm.[16] Based on wavelength peak data, every group was selected standard wavelength to measure in certain absorbance.

2. The effect of various formulations

We controlled the amount of reusable LMG, trichloroacetic acid (CCl_3COOH) and surfactant. Many studies have reported that higher concentration of trichloroacetic acid results in less sensitivity.[1,15,17] In gel dosimeter groups 1, 2, 3 the concentration of trichloroacetic acid were found to affect dose sensitivity. The optimal gradient of sensitivity was 16 mM trichloroacetic acid group 1 at 0.0021±0.00014 cm^{-1}. Gy^{-1}.

The dependency of reusable LMG concentration on sensitivity was not different. However, gel absorbance of non-irradiated gel dosimeter group 4 and 6 were 0.067±0.004 cm^{-1}. Gy^{-1} and 0.246±0.02 cm^{-1}. Gy^{-1} respectively. The effects of reusable LMG to sensitivity have been proven throughout many

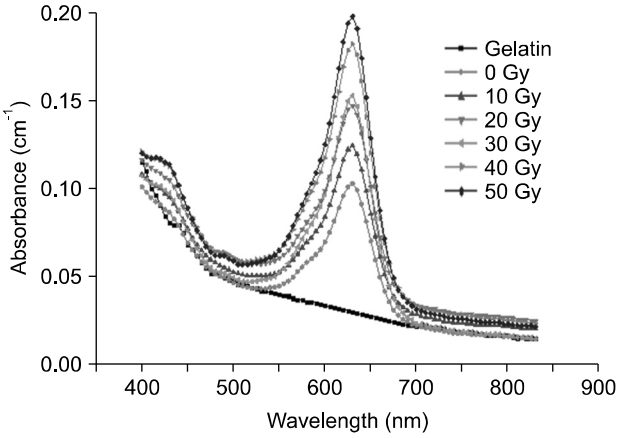

Fig. 1. The wavelength spectra of reusable LMG micelle gel for various doses. Peak sensitivity was marked at the wavelength of 630~635 nm.

reports, but in this study, we were not able to find the effect of reusable LMG to sensitivity. Because reusable LMG has heavy molecular weight which means it is necessary to increase the other chemical relative weight compositions. Future studies comparing LMG sensitivity to formulation change is necessary. Triton X-100 concentration, group 1 was marked the best sensitivity (Fig. 2). The highest non-irradiated gel absorbance was also group 1. The surfactant does not affect the dose sensitivity and the 7 mM concentration of triton X-100 was suitable. On the other hand, Triton X-100 maintains sufficient transparency for reusable LMG. Previous reports suggest that LCV has more radiation sensitivity than LMG.[15,17] In this study, gel dosimeter group 9's radiation sensitivity was 0.0037± 0.0005 cm^{-1}. Gy^{-1}, which is higher than reusable LMG gel dosimeter (0.001～0.0021 cm^{-1}. Gy^{-1}). In previous study, the LCV dose sensitivity gradient was rapidly increased up to 10 Gy, and showed even dose sensitivity.[16] Compared to LCV gel dosimeter, reusable LMG gel dosimeters showed a similar dose sensitivity pattern (Fig. 3). The maximum dose sensitivity of LMG gel was 0.0021±0.0004 cm^{-1}. Gy^{-1} and is a similar sensitivity to reported by Jordan K et al.[15] (0.0028～0.046 cm^{-1}. Gy^{-1}). We found that 0.5 mM reusable LMG, 16 mM trichloroacetic acid and 7 mM triton x-100 concentration was optimal for transparency, dose sensitivity and characterized dose gradient up to 50 Gy. The highest linearity curve showed LCV gel dosimeter group 9 as the same as reference R_2=0.999.[16] Reusable LMG group 4 linearity was R_2=0.9972 (Fig. 4) and also displayed a stable dose response.

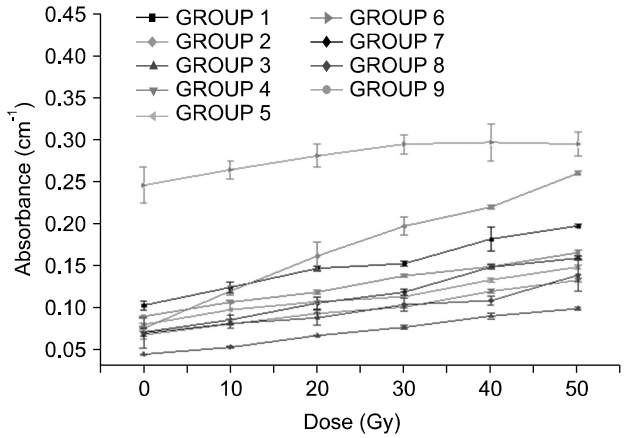

Fig. 2. The dose absorbance curves of various reusable LMG and LCV compounds.

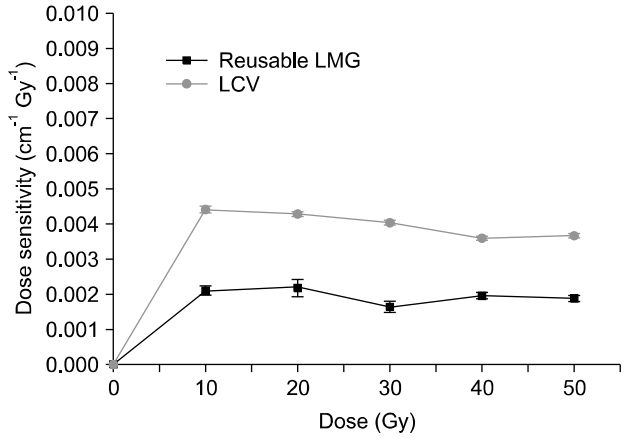

Fig. 3. Comparisions of the dose sensitivity of reusable LMG with that of LCV.

Conclusion

The transparency of reusable LMG gel depended on mixing temperature and formulations. The melting point of reusable LMG was around 33°C. The optimized transparency was shown in the final mixing temperature to be 28～30°C. J Vandecasteel et al.[1] and Jordan K et al.[15] had many formulations and used various chemicals to increase dose sensitivity, linearity and reproducibility. Throughout this study we confirmed that dose sensitivity depends on the amounts of tri-

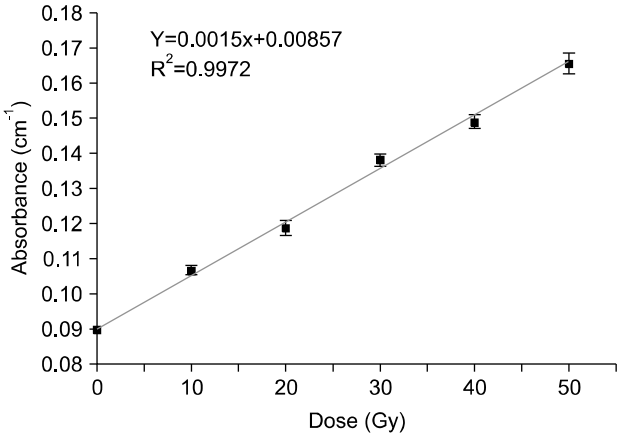

Fig. 4. The dose response curve of reusable LMG measured as their absorbances (It containes 0.37 mM Reusable LMG, 16 mM TCAA, 7 mM Triton x-100 and 4% w/w gelatin).

chloroacetic acid and surfactant. The LCV gel had been reported to have high dose sensitivity, good stability and lower dose rate dependency than the LMG. However, various reusable LMG dye chemical formulations have not been investigated yet. In order to find the optimal ratio, it is necessary to do additional experiments. Throughout this experiment, we realized that reusable LMG gel's properties varied.

The most important thing is that we need to reduce the variation of gel processing and implement the multiple experiments with various chemical formulations. The accumulated dose properties date will be helpful to fabricate multiple micelle gel dosimeter easily. Furthermore we expect to be a foundation to develop micelle and solid 3D gel dosimeter instead of commercialized PRESAGE solid gel.

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