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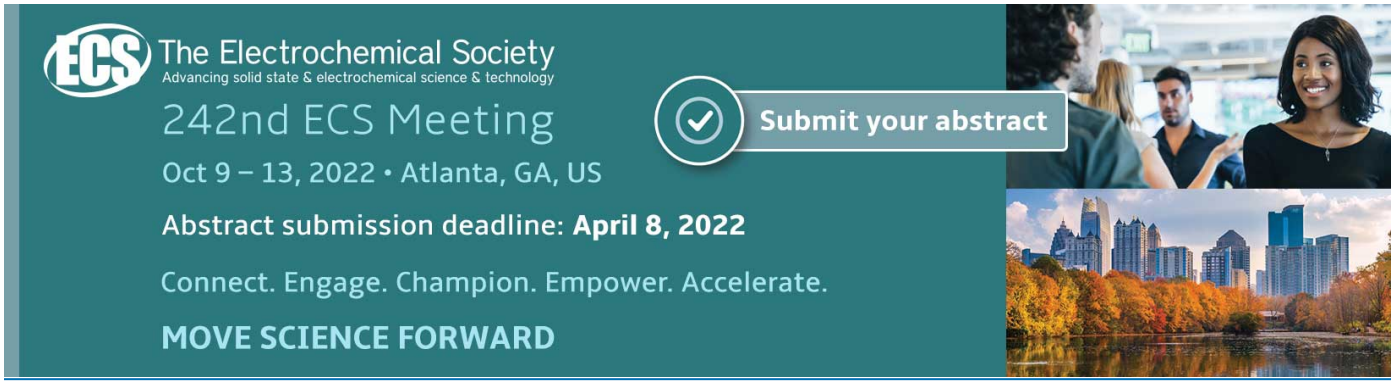

Flexible radiochromic dosimeters development for complex irradiation beams

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Abstract. In vivo dosimetry for patient radioprotection is a real challenge concerning new radiotherapy treatments. In this study we aim to develop a dosimeter based on tissue equivalent material, flexible and adaptable to the patient morphology in order to perform in vivo dosimetry for complex irradiation beams. Here, we report the evaluation in standard beams of highly flexible dosimeter composed of a silicone elastomer and containing leucomalachite green as radiochromic dye and give a first estimation of LMG-micelle hydrogel response. All results are compared to a commercially available PRESAGE® dosimeter.

1. Introduction

Despite the emergence of several technological innovations in the field of external radiotherapy, patient radioprotection is still a real challenge, particularly in complex beams. Indeed, radiotherapy has gained more and more complexity making failure possible at different steps of the treatment. Dosimetry and mostly *in vivo* dosimetry is taking a central and crucial role in quality insurance.

The use of radiation sensitive matrix for dosimetry purposes was proposed as early as the 1950s [1]. Since then, new formulations [2-4] have been developed such as PRESAGE® [5-7] which contains leucomalachite green (LMG) as leucodye in a polyurethane matrix. Despite some advantages PRESAGE® presents the main drawback for our application of being a hard matrix.

Research on dosimeter has focused on gaining more and more sensitivity as well as lower the dose detected. A way to enhance sensitivity, is to incorporate high-Z compounds in the dosimeter matrix to increase the dose response of the material.

Here we present the results of a highly flexible LMG-based dosimeter contained in a silicone elastomer matrix and of a polymer gel made of Pluronic®, these could be mould to exactly fit the patient to obtain accurate *in vivo* dosimeter. Dosimetric parameters were evaluated as dose, dose rate and energy dependency in standard beam. An evaluation of the dosimeter in flattening filter-free (FFF) mode was

performed. Our results were compared to a new version of commercially available PRESAGE® dosimeter.

2. Experimental Part

2.1. Materials

Reagents were used as received without further purification. SYLGARD® 184 Silicone Elastomer Kit was purchased from Dow Corning. Leucomalachite Green (LMG) (4,4′-Benzylidenebis(N,N-dimethylaniline), Pluronic® F127, Tween 80 (polysorbate 80) were purchased from Sigma Aldrich (Merck). Chloroform was purchased from VWR. PRESAGE® dosimeter were purchased from John Adamovics. PRESAGE® formulation: 2-methyl-LMG-DEA, trimethylbenzene, carbon tetrabromide and polyurethane

2.2. Fabrication

2.2.1. LMG elastomer. SYLGARD® 184 Silicone Elastomer Kit was used. The polymer base and the curing agent were used in a 10:1 weight ratio. The dosimeter contained 0.24 wt% of LMG and 1.9 wt% of chloroform. A planetary centrifugal mixer (Thinky, ARE-250) was used to mix all the components together.

A batch of 14 cuvettes were prepared as follows. In an adapted Thinky mixer container, 50 g of SYLGARD® 184 Silicone Elastomer Base and 5 g of SYLGARD® 184 Silicone Elastomer Curing Agent were poured. The silicone mixture was mixed for 1 min at 900 rpm using the planetary mixer. Meanwhile, in a small vial 137.5 mg of LMG was dissolved in 370 µL (548 mg) of chloroform. The organic solution was poured in the matrix mix and the container was mixed for 6 min at 900 rpm. Finally, 370 µL (548 mg) of chloroform was put in the container. The mixture was stirred for an additional 1 min at 900 rpm. The mixture was poured into disposable PMMA cuvettes (1x1x4.5 cm^3), closed with caps and let allowed to cure in the dark at room temperature for 48 hours.

2.2.2. LMG micelles in Pluronic. First, the micelles were synthesized by the nanoprecipitation technique [8] and Tween 80 was used as surfactant. Then, a solution of Pluronic® F127 was poured onto the micelles to form the gel. The gel contained 0.22 wt% LMG and 1.47 wt% of chloroform. A viscous solution of Pluronic® F127 30 wt% was prepared prior to the preparation of the radiochromic hydrogel and kept in the fridge. Magnetic stirring was used to prepare the gel.

A batch of 12 cuvettes were prepared as follows. In a beaker with a magnetic bar, 1.5 g of viscous Tween 80 was solubilized in 25 g of distilled water. Meanwhile, in a small vial 140 mg of LMG was dissolved in 625 µL (925 mg) of chloroform. This organic solution was poured drop by drop onto the Tween 80 solution under magnetic stirring, leading to the formation of micelles that have a size of about 40 nm (size given by dynamic light scattering (DLS)). Working in an ice bath to avoid quick gel formation, 35 g of Pluronic® F127 30 wt% solution was added to the micelles solution under magnetic stirring. The mixture was then poured into disposable PMMA cuvettes (1x1x4.5 cm^3), closed with caps and allowed to reach room temperature for gelification.

2.3. Irradiation

Irradiations were performed on a Versa-HD System (ELEKTA) at DOSEO Platform (CEA Saclay). The cuvettes were irradiated in a 10 x 10 cm^2 field whether with an energy of 6 MV or 18 MV. 0.7, 1.3, 2.6 and 5.3.$Gy.min^{-1}$ using the flattening filter and 13.7 $Gy.min^{-1}$ in the flattening filter-free (FFF) mode The cuvettes were placed between two PMMA sheets in order to have a Source-Surface Distance (SSD) at 97.5 cm and a Source-Detector Distance at 100 cm.

2.4. Dose read-out and data analysis

The absorbance of the cuvettes was measured with a spectrophotometer (Cintra 4040, GBC Scientific Equipment Pty Ltd) between 350 and 800 nm. The spectra before irradiation were measured maximum

within an hour before irradiation and after irradiation within a half-hour. Data were analysed using GraphPad Prism, all spectra were baseline corrected using the average between 750 and 800 nm.The optical change caused by the irradiation was determined, for each formulation, by measuring pre- and post-irradiation absorbance at the maximum of absorption (*i.e.* 627 nm for LMG-based material and 635 nm for PRESAGE®).

3. Results & Discussion

LMG elastomer, LMG micelles and PRESAGE® were irradiated using a Versa-HD System at 6 MV with a dose-rate of 5.3 Gy.min^{-1}. The materials' dose response was taken as the slope of the curve fit of the difference of absorbance after and before irradiation (Δabs) against the dose (Figure 1). The dose response of LMG elastomer is 2.2 x 10^{-2} Gy^{-1}.cm^{-1} which is slightly higher than the value we obtained for PRESAGE® (1.6 x 10^{-2} Gy^{-1}.cm^{-1}). Yet, this value is 4-fold higher than the one reported for a previous formulation of PRESAGE® [9]. Note that the dose response of LMG elastomer could change depending of the LMG batch. The lowest detectable dose was 0.3 Gy for LMG elastomer whereas 0.6 Gy for PRESAGE®.

LMG micelles present the lowest dose response of the study (5.7 x 10^{-3} Gy^{-1}.cm^{-1}) even though the amount of LMG and chloroform in the hydrogel is quite comparable to the quantities in the LMG elastomer. While, dose response is low in comparison to LMG elastomer, LMG micelles hydrogel is transparent and water-based, making it easier to incorporate aqueous gold or silver-based metallic nanoparticles in order to increase the sensitivity. Indeed, incorporation of high-Z compounds in the matrix could increase the number of secondary electrons generated by physical interactions between photons and the material, thus increase the dose response.

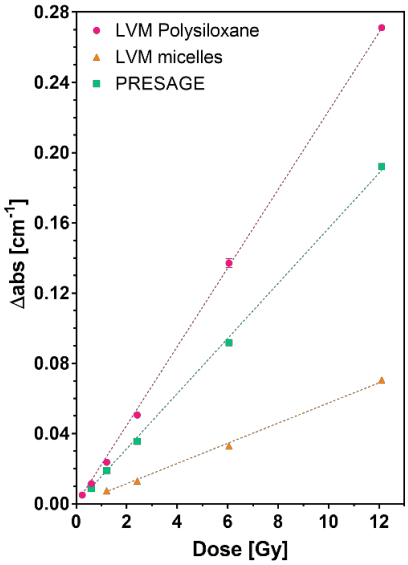

Figure 1. Difference of absorbance after and before irradiation as a function of dose for three different dosimeters. Materials were irradiated at 6 MV with a dose-rate of 5.3 Gy.min^{-1}. LMG elastomer (circles), LMG micelles (triangles) and PRESAGE® (squares).

LMG elastomer and PRESAGE® were also evaluated at another energy, *i.e.* 18 MV (Figure 2). A small difference in dose response was observed for the LMG elastomer samples that were irradiated with a 6 MV photon beam than those irradiated with an 18 MV photon beam, whereas a bigger difference was observed for PRESAGE® samples. Small energy dependency is definitively an advantage towards LMG elastomer.

Both materials were also tested at different dose-rate at an energy of 6 MV and an irradiation dose of 1.2 Gy (Figure 3). For PRESAGE® samples, it is difficult to discern a trend, indeed the experimental points are dispersed quite hectically (data point for the dose-rate 2.6 Gy.min^{-1} is hidden by the LMG elastomer point). On the contrary, LMG elastomer showed a decrease of sensitivity with the increase of dose-rate. With the flattening filter (*i.e.* for the following dose rate: 0.7, 1.3, 2.6 and 5.3.Gy.min^{-1}) a decrease of about 10% was observed relative to 0.7 Gy.min^{-1}, in flattening filter-free (FFF) mode (*i.e.* 13.7 Gy.min^{-1}) a decrease of about 25% was observed still relative to 0.7 Gy.min^{-1}. The decrease is

relatively small and maybe by increasing the number of samples, we would see no dependency with the dose-rate.

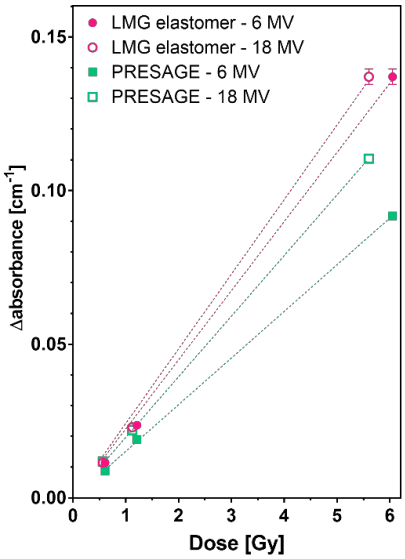

Figure 2. Difference of absorbance after and before irradiation against dose. Materials were irradiated whether at 6 MV (full symbols) or at 18 MV (unfilled symbols), with a dose rate of 5.3 Gy.min^{-1}. LMG elastomer (circles) and PRESAGE® (squares).

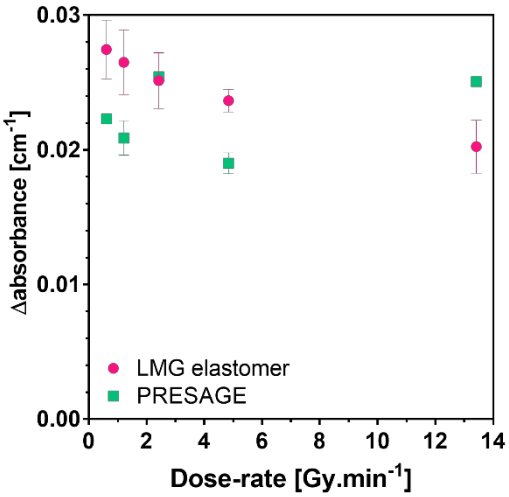

Figure 3. Difference of absorbance after and before irradiation against dose-rate. Materials were irradiated at 6 MV with a dose of 1.2 Gy. LMG elastomer (circles) and PRESAGE® (squares).

4. Conclusion

This silicone-based elastomer is highly potent for *in vivo* dosimetry. The aim of the project is to have a flexible dosimeter able to fit patient body and the highest sensitivity as possible. It presents a comparable sensitivity to PRESAGE® but above all, no energy dependence and relatively low dose-rate dependency. LMG micelle dosimeter was evaluated in this study due to the possibility to incorporate quite easily nanoparticles, relatively low dose sensitivity was found for this material. Further investigations will be carried out related to nanoparticles preparation in solvent to directly incorporate in LMG elastomer in order to combine good elastomer properties and increase in sensitivity.

5. Acknowledgment

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