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Studies of Fricke-PVA-GTA Xylenol Orange Hydrogels for 3D Measurements in Radiotherapy Dosimetry

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Abstract. The Fricke gels (FG) composition has been modified over the years in order to improve their dosimetric characteristic for spatial dose evaluation in radiotherapy. Some problems, in particular those related to the diffusion of ferric ions in the gel matrix, have limited the clinical use of FG and still represent significant challenges for the scientific community working in the field of gel dosimetry. In this work, FG based on poly-vinyl alcohol (PVA) as the gelling agent, glutaraldehyde (GTA) as a cross-linker and FG based on gelatine loaded with silicate nano-clay (laponite) were developed with the aim to overcome the diffusion drawbacks affecting the traditional FG. Neither the sensitivity to the radiation dose nor the diffusion coefficient were significantly altered by the addition of laponite into the Fricke xylenol orange gel formulation employed. By contrast, lower diffusion rates were obtained with PVA-GTA gels, suggesting that this matrix could have a promising use in the field of 3D dosimetry.

INTRODUCTION

The quality assurance of medical procedures that use ionizing radiation is a key element for patient safety and treatment outcome. In particular, the success of radiation therapy in treating cancer depends on the delivery of a lethal radiation dose to the tumor, with as little as possible harm to surrounding tissues [1]. A radiation-sensitive device able to map the distribution of the dose delivered in a clinical setting must combine suitable dosimetric features with the ability to capture and store the information on local variations induced by the delivered dose [1]. Dosimetric materials of different nature have been studied over the decades to assess their dosimetric performance for various radiation beams [2-13].

In 1984, *Gore et al.* [14] suggested that hydrogel containing a ferrous sulphate solution (Fricke gel - FG) could be employed in conjunction with magnetic resonance imaging (MRI) to determine 3D dose distributions [15-17]. FG dosimeters are good candidates for 3D dose assessment in biological materials because of their tissue equivalence. Moreover, in view of their chemical and morphological characteristics, FGs serve as dosimeters and as phantoms at the same time.

The literature includes numerous experiments on Fricke gel aimed at optimizing the composition to increase the sensitivity to dose and/or the local stability of the radiation-produced ferric ions and applications for clinical dosimetry. Various approaches are being developed with the aim to overcome this diffusion limitation [18]. Different research

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groups suggest a hydrogel system based on the use of poly-vinyl alcohol (PVA) cross-linked by adding glutaraldehyde (GTA) as a matrix for Fricke gel [19]. A further way to reduce the problem of ferric ions diffusion in FGs was recently proposed by the addition of laponite (silicate nano-sized clay particles) [20]. Other studies have been carried out both on PVA-GTA gel dosimeters [21-23] and laponite added ones [24]. In this work, further studies have been performed, using optical methods as analysis techniques, in order to get more data describing the behavior of these dosimeters.

MATERIALS AND METHODS

All types of Fricke gel were prepared using ultrapure water with the addition of 0.5 mM ferrous ammonium sulphate hexahydrate and 0.165 mM Xylenol Orange.

Gelatine Fricke gel (GFG) and gelatine Fricke gel loaded with laponite (LFG) were prepared using gelatine in the amount of 3.0% w/w and laponite in the amounts of 0.0%, 0.5%, and 1.0% w/w. Because of the basicity of the laponite, different quantities of sulphuric acid (from 25 mM to 97 mM) were added to obtain a 1.8 pH value in all the types of gel used in this study, independently of their laponite concentration.

PVA-GTA Fricke gels (PVA-GTA-FG) were prepared using commercially available PVA (Mowiol® 18-88) in the amount of 10% in weight of final volume and 26.5 mM GTA. Complete dissolution of Mowiol® in water can be easily obtained in approximately 40 minutes at 70°C, without the use of autoclave [19] or open vessel microwave digestion [20] that is required for other PVA compounds.

In order to measure optical absorbance (OA) spectra, gels were prepared in standard spectrophotometry cuvettes. Furthermore, for measuring the diffusion coefficients of the Fricke gel dosimeters, different samples were prepared within thin layers (FGLs). Details of the FGLs preparation can be found elsewhere [24].

Fricke gel dosimeters inside the cuvettes were uniformly irradiated with an irradiator based on a ^{137}Cs source. The dose range 0 Gy - 35 Gy was investigated. A Cary 100 UV-Vis spectrophotometer (Agilent Technologies, Santa Clara, CA, USA) was employed for OA measurements of the irradiated samples in the wavelength interval 350 nm -750 nm. OA spectra were acquired using as reference one un-irradiated sample for each batch.

FGLs prepared for diffusion measurements were irradiated to a dose of approximately 8 Gy with X-rays generated by an X-ray tube operating at 80 kV and 5 mA, details can be found elsewhere [24].

Light transmittance images of the FGLs were acquired using a laboratory made equipment mounting a band-pass filter centered at 585 nm. Grey level light transmittance images of each FGL were acquired before irradiation and at consecutive times up to 6 hours post-irradiation. The differences of optical density Δ(OD) were calculated pixel by pixel. More details can be found elsewhere [24].

The mean profile of Δ(OD) along the length of each FGL was evaluated, as well as its temporal variation as effect of the diffusion phenomena. Data were fitted to an inverse square root function. Terms used are analogous to the equation defined previously [25].

OPTICAL ANALYSES

OA spectra of all the studied gel dosimeters (GFG, LFG and PVA-GTA-FG) were characterized by a broad absorption peak in the wavelength region between 500 nm and 600 nm.

Figure 1a and 1b show examples of OA spectra of Fricke gel dosimeters based on gelatine, with and without laponite, respectively. The shapes of the spectra exhibit a main absorption around 585 nm, with a shoulder extending in the lower wavelength region (500-560 nm). For a fixed dose, the relative intensity of the main peak at 585 nm with respect to the side shoulder changed with the gel composition.

In Figure 1c and 1d the differences between OA spectra of GFG and LFG irradiated at consecutive steps of about 3.5 Gy are shown. These differences are compared with the OA spectra of Fricke gel samples irradiated at 3.5 Gy. It is possible to state that the formation of the Fe^{3+}-Xylenol Orange complex returns a peak of absorption caused by the superposition of several peaks due to the different complexation. As the given dose increases, the growth of the main absorbance peak is due to the superposition of a peak around 510 nm and a peak around 585 nm. The growth of both peaks versus dose is regulated by different proportionality coefficients. This different trends are highlighted in panels c and d by arrows (continuous arrow for the peak at 510 nm and dashed arrow for the peak at 585 nm).

Similar trends were observed in PVA-GTA-FG dosimeters (Figure 1e and 1f) suggesting that the Fe^{3+}-Xylenol Orange complexation process is not greatly affected by the addition of laponite into the gel matrix or by the use of different gelling agents.

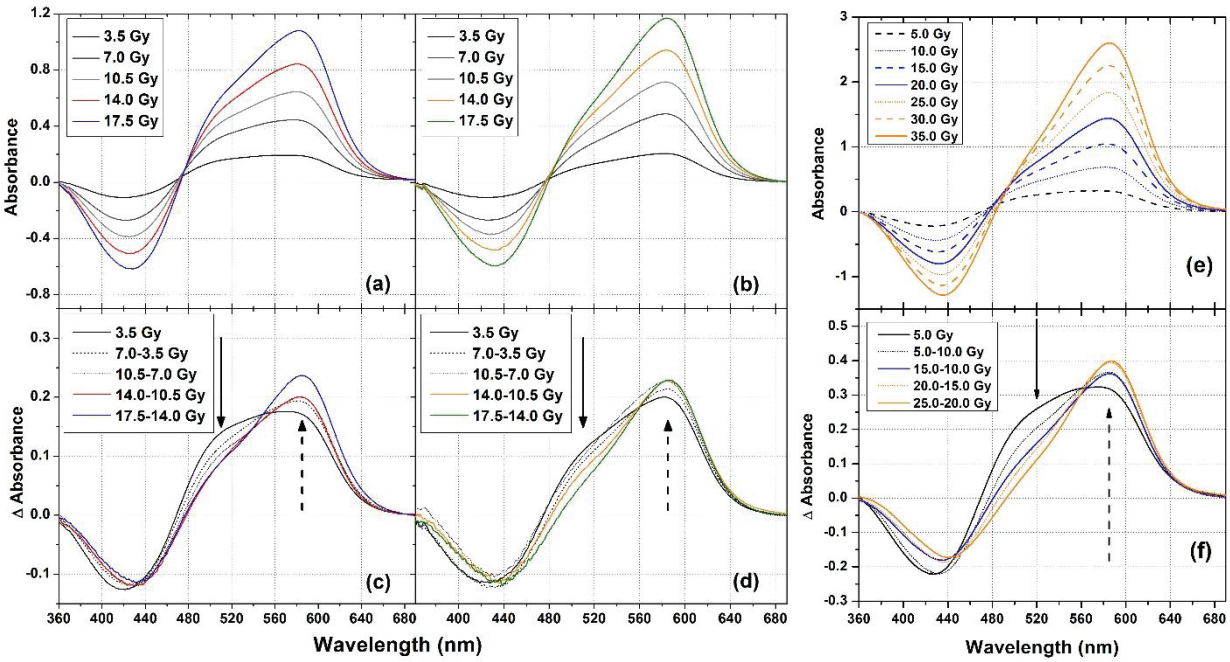

FIGURE 1. (Optical absorbance spectra of (a) of GFG dosimeters made with gelatine without laponite, (b) LFG with 1% laponite and (e) PVA-GTA-FG. Differences between OA spectra of FG dosimeters irradiated at consecutive steps: (c) GFG dosimeters made with gelatine without laponite, (d) LFG with 1% laponite and (f) PVA-GTA-FG.

DIFFUSION MEASUREMENTS

Figure 2 shows the Δ(OD) profiles along the length of three different FGL samples partially screened with a lead layer during the irradiation, measured at 6 hour post-irradiation. A progressive flattering of the profile with the consequent blurring of the dose pattern was observed, as consequence of the gradual diffusion of ferric ions. This effect is significantly lower in PVA-GTA FG dosimeters than in gelatine FG, regardless of the presence of laponite.

Following the procedures described in [25] the diffusion coefficients of the different types of gel were calculated and the results are shown in figure 3.

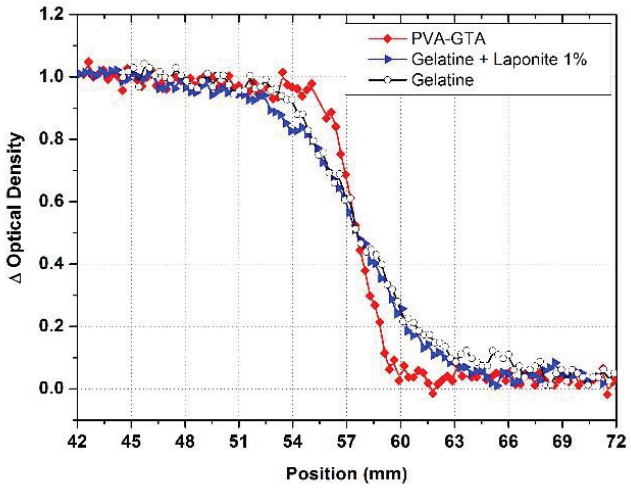

FIGURE 2. Examples of Δ(OD) profiles of different gel types measured at 6 hours post-irradiation times: red diamonds PVA-GTA-FGL; blue triangles gelatine-FGL with laponite 1.0% w/w; white dots gelatine-FGL without laponite.

No significant differences (*i.e.* within one standard deviation) among the diffusion coefficients of the investigated FG dosimeters based on gelatine were observed. Therefore, in the Fricke gel dosimeters studied here, the addition of laponite, in the amount of 0.5% or 1.0%, does not seem to affect the motion of radio-inducted ferric ions into the gel matrix. The obtained results are very similar to other values available in literature related to Fricke gel dosimeters prepared with gelatine [24]. By contrast, a significantly lower (*i.e.,* approx. 2.5 times) diffusion coefficient was obtained in PVA-GTA-FG dosimeters, confirming the higher stability of this synthetic gel matrix over the natural ones [19, 21].

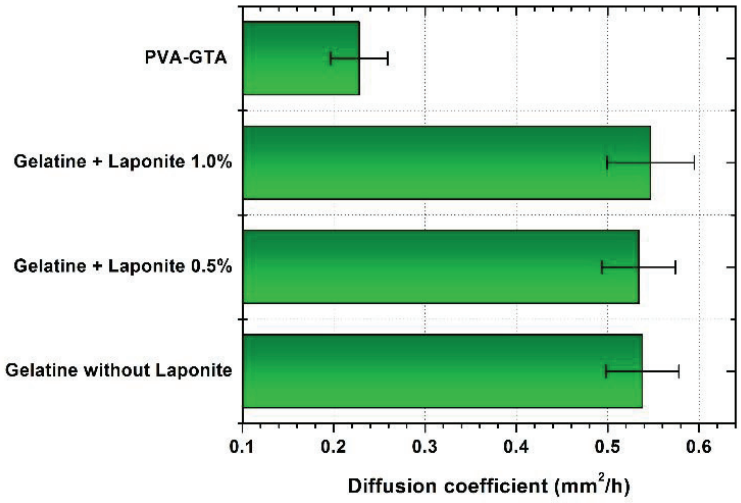

FIGURE 3. Diffusion coefficients for different types of Fricke gels.

CONCLUSIONS

Different types of Fricke gel dosimeters have been studied and compared to recent formulations. The analysis of the OA spectra has shown behaviors that associate all the different types of gels and are not affected by the type of matrix or by the presence of additives.

The presence of the laponite does not bring significant improvements in terms of diffusion of ferric ions within the matrix. The use of PVA chemically crosslinked greatly reduces the problem of diffusion. The use of Mowiol® leads to an improvement of the gel manufacturing procedures, guarantees greater gel purity, without altering the dosimetric properties. Additional studies are currently underway to test the dosimetric robustness of Mowiol®-GTA Fricke gel against parameters influencing gels preparation such as pH and gelation temperature. Measurements are also ongoing via magnetic resonance to be combined with optical analyses.

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