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Effects of the pre-irradiation storage procedure on the dose response of a Fricke xylenol orange gel dosimeter

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Abstract. The Fricke xylenol orange (FX) gel system is a chemical dosimeter characterized by good sensitivity, linear dose response, tissue equivalence, no toxicity, easy preparation, reproducibility and low cost. Thanks to the presence of the gelatinous matrix, the system is particularly suitable to perform reliable 3D mapping of the absorbed dose spatial distribution via magnetic resonance imaging (MRI) or optical techniques. The aim of this work is to study in a systematic way the influence of the pre-irradiation storage procedure upon sensitivity, dose response stability and lifetime of use of a FX gel system made with gelatin from porcine skin subjected to homogeneous irradiation. For this purpose, different pre-irradiation storage procedures, in terms of temperature and duration of each storage step, were investigated. In order to evaluate the dose response stability, the optical analyses of the samples were performed up to 6 hours after irradiation. Moreover, the samples were irradiated at time intervals of 24 hours for up to 7 days after preparation in order to evaluate the system lifetime of use. Regardless of their thermal and temporal life, the samples show linear dose responses in the investigated dose range (3–24 Gy) and an increase of sensitivity with the time elapsed between preparation and irradiation. Among the three pre-irradiation storage procedures considered here, a procedure that provides the best dose response stability and lifetime of use was identified and recommended for further use. The analyzed dosimetric system possesses good properties that make it promising for medical application, particularly concerning the evaluation of pre-treatment plan quality assurance within the conformational external beam radiotherapy.

Key words: radiation dosimetry • Fricke-gelatin-xylenol orange dosimeter • optical absorbance measurement

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Introduction

The Fricke dosimeter is an acidic oxygenated aqueous solution of ferrous ions [1–4]. Upon irradiation, the products of water radiolysis cause the oxidation of ferrous ions Fe(II) into ferric ions Fe(III), so that by the measurement of the Fe(III) ions concentration, the total absorbed dose can be evaluated [1, 2].

This dosimetric system has several advantages such as: good sensitivity, non-toxicity, linear response, easy preparation, reproducibility and low cost [1–4]. In contrast, the operative application of this aqueous system is limited by some disadvantages such as: (i) the Fe(II) ions auto-oxidation that can affect the measurement of the actual absorbed dose, and (ii) the Fe(III) ions fast diffusion in aqueous solution that does not allow 3D mapping of the absorbed dose [1, 2, 4, 5].

In order to perform the imaging of the dose distribution, the aqueous solution was incorporated into tissue equivalent gelatinous matrices of different origin: animal (gelatin from porcine skin or from bovine bones), vegetal (Agarose) and synthetic (PVA) [4, 5].

Both the aqueous and the gel dosimetric systems can be analyzed by optical or nuclear magnetic resonance (NMR) techniques.

In fact, the Fe(III) ions absorb light at 304 nm and therefore, through spectrophotometric analysis, the absorbed dose can be evaluated from the difference in absorbance measured before and after irradiation. The ultraviolet (UV) optical analysis of the gel dosimetric system is affected by the high absorption of the gel matrix in the UV range of wavelengths. For this reason, the dye xylenol orange (XO) was added to the system in order to shift the absorption wavelength in the visible range, in which the analysis is less affected by the presence of the gel matrix [2]. The XO chelates the Fe(III) ions, leading to the formation of the XO-Fe(III) complex that absorbs at 585 nm [2, 4–8]. Furthermore, the XO slows down the Fe(III) ions diffusion process, preserving the quality and the integrity of the dose data spatial distribution [9].

As regard to the NMR techniques, the absorbed dose is measured by the evaluation of the relaxation rates of the water protons [10, 11]. These parameters are dominated by the dipolar interaction between the spins of paramagnetic ions and the adjacent water protons. Fe(II) and Fe(III) ions possess different paramagnetic properties and, hence, affect the relaxation rates of the water protons in a different way. Consequently, the relaxation rate of the system is dependent on the Fe(II) and Fe(III) molar ratio and thus is related to the total absorbed dose [10, 11]. Although the addition of XO is not necessary to perform the NMR analysis, it is frequently added to the system to reduce the Fe(III) ions diffusion speed [9].

Effects of temperature gradients on dose response were observed within the volume of Fricke xylenol orange (FX) gel phantom [12, 13]. In particular, a different response was observed between the bulk and the peripheral regions of cylindrical phantoms [12, 13]. This behavior is due to the temperature gradients experienced by the system within the volume during the pre-irradiation storage. This phenomenon can affect both the gelling process of the gelatinous matrix and the spatial distribution of the chemical compounds caused by the temperature-dependent solubility [12, 13].

The aim of this experimental work is to evaluate in a systematic way the dependence of the dose response of the FX gel dosimetric system made of gelatin (Fricke-gelatin-porcine skin, FGX) from the pre-irradiation storage in terms of temperature and duration of each storage step. The system has been studied in spectrophotometer cuvettes with an optical path of 1 cm and subjected to homogeneous irradiation. A systematic analysis has been carried out via spectrophotometric technique with the aim of identifying the particular pre-irradiation storage procedures that give rise to the best dose response stability up to 6 h and a lifetime of use up to 7 days after preparation.

Experimental

Materials and methods

The reagents used were ferrous ammonium sulfate (FAS) (Carlo Erba), sulfuric acid (Carlo Erba Reagent grade 96% pure), xylenol orange (Sigma-Aldrich, 33825) and gelatin from porcine skin of 300 bloom gel strength (Sigma-Aldrich, G2500). All glasswares were accurately rinsed with deionized water.

The dosimetric system was prepared by mixing the gel matrix with the Fricke solution. To prepare the Fricke solution, sulfuric acid (25 mM), FAS (0.5 mM) and Xylenol Orange (0.165 mM) were incorporated into 50% of water necessary for the preparation. In parallel, the gel matrix was prepared by mixing in a beaker the gelatin powder (3% w/w) with the remaining water and the resulting solution was heated in a water bath for 20 min at 45°C, with continuous stirring. Subsequently, the solution was kept at room temperature (20°C) until it reached 35°C. At this stage, the Fricke solution was slowly added to the gel matrix, making it carefully slide on the wall of the beaker in order to minimize air incorporation. The final solution, still in liquid phase, was poured into poly(methyl methacrylate) (PMMA) spectrophotometer cuvettes.

To optimize the gelling process, samples have to be stored in the dark at a temperature between 4 and 7°C until use [6, 7, 12, 13]. In order to analyze the dependence of the system response from the pre-irradiation storage modality, samples were stored following three different procedures. This was needed to examine the gelling process at different temperature rates. In particular, all the samples were prepared at room temperature (20°C) and were then stored as follows: (i) procedure No. 1: storage at 7°C immediately after preparation; (ii) procedure No. 2: initial storage at 20°C for 4 h after preparation and then at 7°C until irradiation; (iii) procedure No. 3: initial storage at 20°C for 8 h after preparation and then at 7°C until irradiation. Due to temperature dependence on the dose response, a greater uniformity of response between the samples can be expected by increasing the time interval before the cooling.

For each pre-irradiation storage procedure, the homogeneous irradiations were performed 24, 48, 96, and 168 h after preparation. The samples were subdivided into four irradiation groups, named a, b, c, and d. Table 1 shows the schema of the samples subdivision after the preparation and explains the classification of the 12 groups of samples thus created.

The homogeneous irradiations in the range 3–24 Gy were performed at room temperature by using a ^{137}Cs source. All the samples were stored at room temperature in the dark for at least 30 min for thermal equilibration prior to irradiation [14].

Table 1. Scheme of the samples subdivision according to the pre-irradiation storage procedure and the time elapsed before irradiation. The 12 different groups of samples thus created were named through the label: storage procedure number. Irradiation group

Classification of the group of samples				
Pre-irradiation storage procedure	Time elapsed before irradiation [h]			
	24	48	96	168
No. 1	1.a	1.b	1.c	1.d
No. 2	2.a	2.b	2.c	2.d
No. 3	3.a	3.b	3.c	3.d

The absorbance measurements at 585 nm were carried out at room temperature [14] using a dual-beam spectrophotometer (Lambda EZ210, PerkinElmer). From previous experiments, it was observed that the dose response of the system, with this particular receipt, does not change (within the experimental error) from 40 min after irradiation, and thus the system shows to have reached the chemical equilibrium within this time interval. Consequently, to study the dose response stability of the system, the analyses were performed after 1, 3 and 6 h after irradiation. Between absorbance measurements, the samples were kept in the dark at 7°C and then stored at room temperature for at least 30 min to reach the thermal equilibrium before each analysis. The blank samples of reference were subjected to the same thermal and temporal life as the irradiated ones.

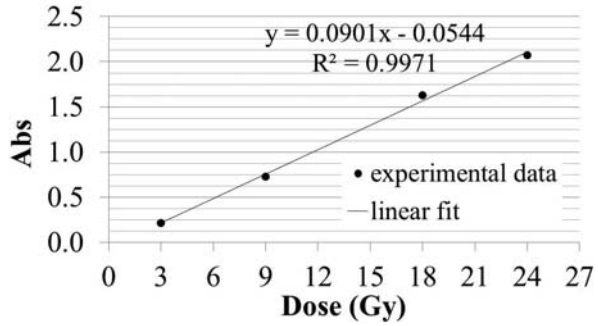

Fig. 1. Dose response of the group of samples 1.a. The sensitivity is 0.0901 Abs·Gy^{-1}. The errors are included in the size of the markers.

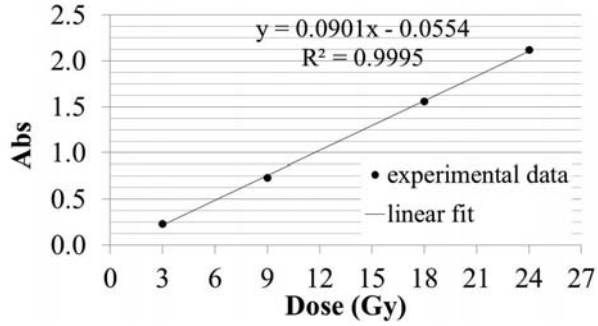

Fig. 2. Dose response of the group of samples 2.a. The sensitivity is 0.0901 Abs·Gy^{-1}. The errors are included in the size of the markers.

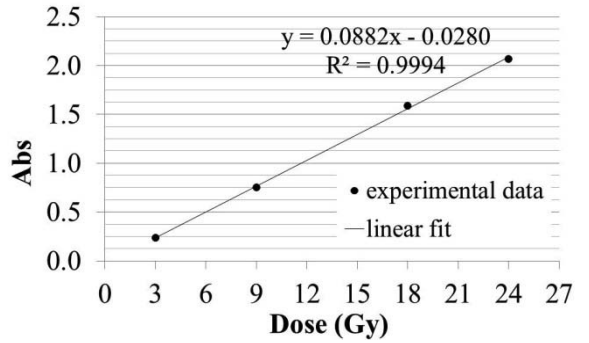

Fig. 3. Dose response of the group of samples 3.a. The sensitivity is 0.0882 Abs·Gy^{-1}. The errors are included in the size of the markers.

Results and discussion

Regardless of the pre-irradiation storage procedure adopted, the system dose response exhibited a linear behavior for the irradiations performed up to 7 days after preparation with sensitivity values in the range of 0.0882–0.1095 Abs·Gy^{-1}. As an example, the dose responses of the groups of samples 1.a, 2.a and 3.a are shown in Figs. 1–3. The sensitivities, that is the slopes of the fit lines, are 0.0901 Abs·Gy^{-1}, 0.0901 Abs·Gy^{-1} and 0.0882 Abs·Gy^{-1}, respectively. The figures concerning the remaining groups of samples are not reported here, but the data obtained are utilized for the results and the considerations reported below.

For each pre-irradiation storage procedure, the absorbance remains constant, within the experimental errors, up to 6 h after the homogeneous irradiation. In this way, the stability of the dosimetric system up to 6 h is verified. As an example, the Figs. 4–6 show the absorbance as a function of the time elapsed from irradiation for the groups of samples 1.a, 2.a and 3.a irradiated in the range 3–24 Gy. Similar results are obtained for the other groups of samples.

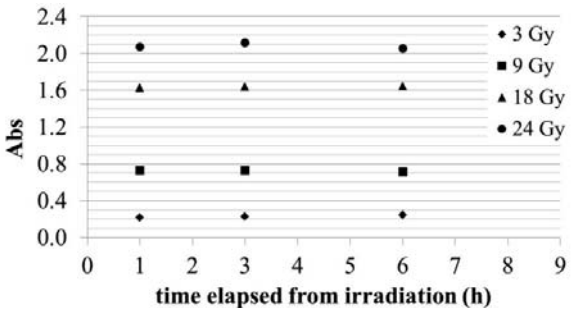

Fig. 4. Group 1.a: absorbance as a function of the absorbed dose and the time elapsed before the analysis. The errors are included in the size of the markers.

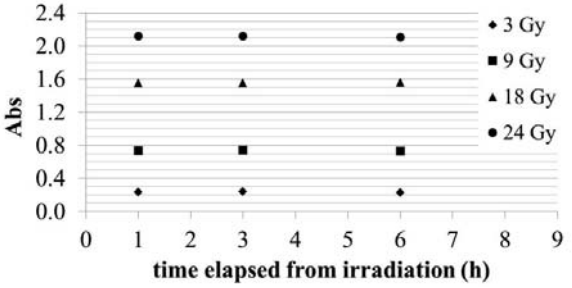

Fig. 5. Group 2.a: absorbance as a function of the absorbed dose and the time elapsed before the analysis. The errors are included in the size of the markers.

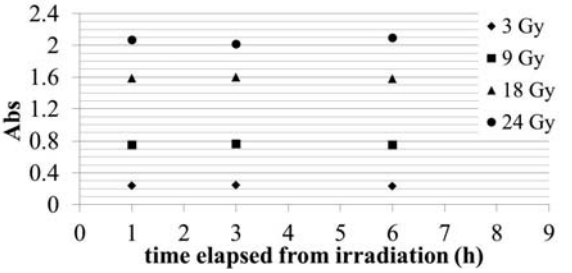

Fig. 6. Group 3.a: absorbance as a function of the absorbed dose and the time elapsed before the analysis. The errors are included in the size of the markers.

The sensitivity analysis was performed exploring the groups of samples stored in accordance with each pre-irradiation storage procedure. The results are reported in Figs. 7–9 as a function of the time elapsed before irradiation for each analysis at 1, 3 and 6 h after irradiation.

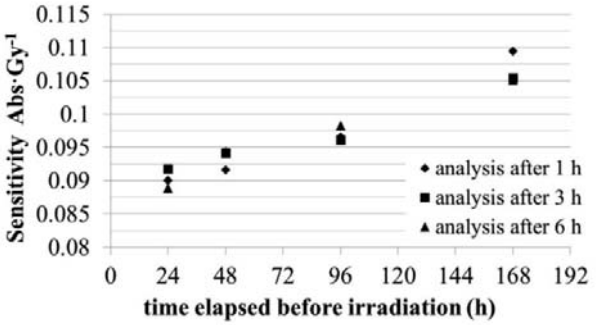

Fig. 7. Pre-irradiation storage procedure No. 1: the sensitivity is represented as a function of the time elapsed before irradiation for each analysis. The errors are included in the size of the markers.

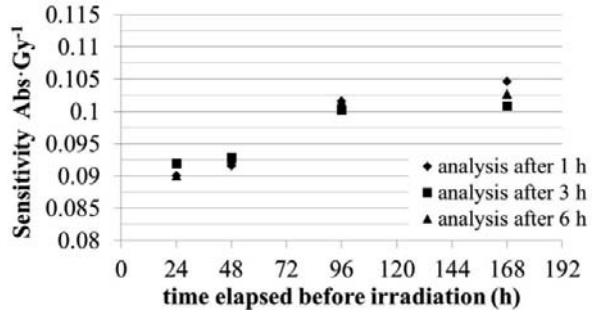

Fig. 8. Pre-irradiation storage procedure No. 2: the sensitivity is represented as a function of the time elapsed before irradiation for each analysis. The errors are included in the size of the markers.

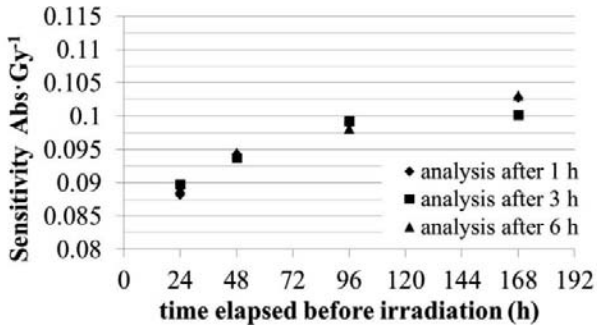

Fig. 9. Pre-irradiation storage procedure No. 3: the sensitivity is represented as a function of the time elapsed before irradiation for each analysis. The errors are included in the size of the markers.

From Figs. 7–9, it can be inferred that, regardless of the undergone pre-irradiation storage procedure, the system sensitivities increase monotonically as a function of the time elapsed before irradiation. This sensitivity trend has not been shown to be reproducible. Therefore, this dosimetric system requires calibration every time.

A lower variability of the sensitivities between the absorbance data was observed for samples cooled at 7°C after an initial storage at room temperature (i.e. pre-irradiation storage procedures No. 2 and No. 3), as shown in Figs. 7–9.

In order to quantify the sensitivity variability underlined, for each pre-irradiation storage procedure, the averages and the corresponding percentage relative standard deviations (%RSD) of the obtained sensitivities have been calculated and reported in Table 2. For each time elapsed before irradiation, the groups of samples stored according to the pre-irradiation storage procedure No. 2 and No. 3 lead to smaller %RSDs values, that is, smaller variation of the sensitivity over time, with respect to the pre-irradiation storage procedure No. 1, as shown in Figs. 7–9 and quantified in Table 2. Therefore, samples that have been initially stored at room temperature for a time interval between 4 and 8 h before cooling to 7°C (i.e. pre-irradiation storage procedures No. 2 and No. 3) show a homogeneous and stable dose response over time.

Moreover, regardless of the pre-irradiation storage procedure adopted, the groups of samples irradiated 168 h after the preparation show higher sensitivities in comparison to the samples irradiated after 24, 48 and 96 h, but, on the other hand, are characterized by greater %RSDs (Table 2). This behavior makes the samples irradiated after 168 h not sufficiently reliable and therefore, the lifetime of use should be shorter than 96 h from preparation (about 4 days).

Conclusion

Three pre-irradiation storage procedures, different in terms of temperature and duration of each storage step, were investigated in order to evaluate their effect upon sensitivity, dose response stability and lifetime of use of a Fricke-gelatin-xylenol orange (FGX) dosimetric system subjected to homogeneous irradiation.

The experimental results show a homogeneous and stable dose response for samples stored at room

Table 2. Average sensitivities and %RSDs for the three measurements (1, 3 and 6 hours after irradiation) and for each pre-irradiation storage procedure

	Mean sensitivity	Time elapsed before irradiation [h]			
		24	48	96	168
No. 1	[Abs·Gy^{-1}]	0.0902	0.0933	0.0970	0.1066
	[%RSD]	1.61	1.64	1.19	2.30
No. 2	[Abs·Gy^{-1}]	0.0907	0.0924	0.1011	0.1066
	[%RSD]	1.15	0.76	0.80	1.85
No. 3	[Abs·Gy^{-1}]	0.0890	0.0941	0.0988	0.1020
	[%RSD]	0.90	0.44	0.56	1.56

temperature (20°C) for a time interval between 4 and 8 h after preparation and then cooled at 7°C until irradiation.

Regardless of the pre-irradiation storage procedure, the system lifetime of use is estimated to be about 4 days after preparation.

Further studies will be carried out on the pre--irradiation storage procedure of a FGX larger phantom in order to optimize the sensitivity, dose response stability over time and lifetime of use of this dosimetric system in view of a medical application for the routine evaluation of the pre-treatment plan Quality Assurance (QA).

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