Study on characteristic of Fricke xylenol gel dosimeter: application for dose evaluation in radiotherapy

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Abstract. Accurate assessment of the radiation absorbed dose delivered to a tumor and different organs is a potentially importance issue in clinical radiotherapy. The aim of this study is to evaluate the effectiveness of the Fricke Xylenol Gel dosimeter (FXG) to the gamma radiation from Co-60. With this aim, the dose response of FXG and its behavior have been investigated. The sensitivity and accuracy of FXG were validated by irradiating FXG with the gamma radiation at 1-200 Gy. To evaluate the long- and short-term consistency and reproducibility of FXG, the optical density was measured at 24, 48 and 120 h after irradiation. Light absorbance spectra were analyzed from 350-700 nm. Spectrophotometric measurement of FXG demonstrated the linearity up to 30 Gy, and then gradually reached a plateau. FXG showed a good stability over a period of 120 h after exposure to gamma radiation. FXG showed a high reproducibility which is in comparable to that of obtained from the ionization chamber. The FXG showed high accuracy, sensitivity and reproducibility, thus enabling determination of absorbed dose from the external beam radiotherapy.

1. Introduction

Recent advanced in radiotherapy techniques evolves from conventional irradiation towards highly conformal and precise radiotherapy, which aims to improve the outcome by escalating the dose to the target and minimizing the effect of radiation on normal tissue and critical organs. Accurate dosage evaluating tools are needed to assess the conformity of dose distribution for the radiation treatment planning system. Although absorbed dose can be evaluate using difference dosimeters such as diodes, ionization chamber, thermoluminescent dosimeter, radiochromic film dosimeter, gel dosimeter have more advantage to validate and verification of radiation dose distribution in the three dimensional (3D) system [1]. Among the current gel dosimeters, the Fricke gel dosimeter (FXG) is one of common chemical gel dosimeters that use in radiotherapy. FXG shows good characteristics that suitable for the measurement of dose spatial distribution in radiotherapy with a good resolution. FXG dosimeter can provide doses even in small irradiation fields and its results agree well with data of ionization chambers [2]. Moreover, FXG can be easily prepared with a high consistency reproducible, as well as spatial dose determination is possible very soon after irradiation [3]. Also, FXG is considered more relevant for absorbed dose determination in biological materials, since its effective atomic number and density are similar to those of water as well as soft tissues [4]. In addition, FXG dosimeter is able of recording the
dose distributions in 3D with formed into a different shapes by choosing a suitable mold, which is can be used to evaluate dose distributions under actual treatment conditions, as represented in the treatment planning system.

In this FXG system, the ferrous ions (Fe$^{2+}$) provides the chemical probe for the dosimeter while the gel provides some spatial localization of the radiation-induced changed. The presence of free radicals produced by water gamma radiolysis contributes to the oxidation of ferrous ions to ferric ions (Fe$^{3+}$). The addition of the xlenol orange (XO), a Fe$^{3+}$ complexing agent, the FXG dosimetric signal can be measured by means of optical absorbance in the visible range. Moreover, the absorbed dose by an irradiated FXG can be determined by measurement of the concentration change of Fe$^{3+}$. Furthermore, this Fe$^{3+}$ ions concentration presented in the FXG is linearly related to the absorbed dose of gamma radiation [3]. Therefore, it is very interesting to observe the response of the FXG dosimeter to doses of gamma irradiation which is corresponding to clinical radiology.

The purpose of this study is to evaluate the effectiveness of the Fricke xylenol gel dosimeter to the gamma radiation for a high-dose level as well as a low-dose level. With this aim, the dose response of FXG and its absorption spectra have been investigated. Moreover, the trend in time of the dose response was also studied.

2. Materials and Methods

2.1 Gel dosimeters preparation
The Fricke gel dosimeter (FXG) consists of acid aqueous solution of ferrous sulphate and xylenol orange (XO), infused in a gelatinous matrix (i.e. FXG is containing of 3% w/v of gelatin from porcine skin (300 bloom, sigma-Aldrich), 1 mM ferrous ammonium sulphate (FAS), 25 mM sulphuric acid, 0.165 mM xlenol orange) [5]. Firstly, the Fricke solution was prepared by mixing sulfuric acid, FAS and XO, in this order, in the 50% of the distilled water. This solution was then kept in the dark at room temperature until use. Secondly, at the same time of the preparation of the Fricke solution, the gelatin powder was mixed with the remaining 50% of the distilled water. Thereafter, this gel solution was heated with constant stirring until it reaches 40 $^\circ$C. After 20 minutes at constant temperature, the gel solution was brought to cool in air, with continuous stirring. Once 30 $^\circ$C were reached, the prepared Fricke solution was infused into the gel solution, and then FXG was kept in the dark at room temperature for 6 h before being stored in a 4 $^\circ$C refrigerator.

2.2 Irradiation of Frick gel dosimeter
Fricke gel dosimeter was subjected to gamma radiation in a Co-60 Gamma Cell 220 Excel (MDS Nordion, Canada) which was calibrated using the Fricke reference standard and a transfer standard alanine dosimeter of the National Physic Laboratory, United Kingdom. The overall uncertainty of dose rate was 3.25% (95% confidence level). All samples were uniformly irradiated by placing FXG cuvettes in a specially designed an in-house of a polymethylmethacrylate phantom. Samples were exposed to gamma radiation in the central position of the un-rotated chamber of the cell. The dose rate at the central position was equal to 0.693 ± 0.23 Gy/sec at the time of the experimental prior.

2.3. Absorption spectra analysis of the Fricke Xylenol Gel dosimeter
The optical density (OD) of the FXG were carried out immediately after irradiation at the wavelength of 350 to 700 nm using the optical computer tomography scanners (Lamda 650, Perkin Elmer) with red light source. The response of the FXG sample was recorded as the absorbance at 585 nm as suggested by Gambanini et al [5].

2.4. Dose response and stability of the Fricke Xylenol Gel dosimeter
According to the report on the dose measurement with Frick dosimeter by Schereiner [3], the dose response of FXG can be correlated directly to the change in the optical density of the FXG before and after irradiation. The measurement of OD value was carried out before (non-irradiated FXG) and
immediately after irradiation at 585 nm. Therefore, the dose response of FXG can be defined as the net absorbance at 585 nm.

For spectrophotometric response stability determination the FXG were evaluated accordingly to previous study of Liosi et al. [6], with some modifications under two different conditions: 1) the stability of the FXG at the difference time points between the preparation and irradiation of the Fricke gel, and 2) the stability of the FXG at the difference successively scanned time of the Fricke gel after gamma irradiation. Firstly, the freshly prepared FXG were kept at the refrigerator of 4°C in the dark for 24 and 168 h before exposure to different doses of gamma radiation, then measured the OD value immediately after gamma irradiation. Secondly, irradiated FXG were subsequently evaluated for the post-irradiation stability by measured the OD value of the FXG at 60, 120 and 180 h after irradiation. The response of the FXG samples were recorded as the net absorbance at 585 nm.

3. Results and discussion

3.1 Absorption spectra analysis

Absorption spectra of FXG have been acquired by means of a spectrophotometric technique. The absorption spectra of the gamma irradiated Fricke gel dosimeter, with reference to a non-irradiated FXG sample, in the range of 1 up to 200 Gy are shown in the Figure 1. Our results of absorption spectra agree well with previous study by Liosi et al. [6], as clearly observed the isosbestic point. The absorption spectra consists of two peaks, one at a maximum OD value at about 585 nm that involved to the formation of strongly colored complexes of XO and Fe$^{3+}$ in the gel solution, and another one at a minimum OD value at about 439 nm which is displayed below the isosbestic point. The maximum net absorbance spectra of XO-Fe$^{3+}$ compound at 585 nm increases with the increasing of the exposure dose of gamma radiation from 1-200 Gy. This observed behavior has worth for further assessment concerning the correlation of the absorption spectra shape with the dose response variation.

The speciation mechanism of XO and Fe$^{3+}$ ions has been previously studied via complexation titration spectrophotometric analysis [7]. This systemic analysis of the absorbance spectra of FXG, providing information of the complexes mechanisms between XO and Fe$^{3+}$ ions (i.e. XO:Fe, XO:Fe, XO:Fe, and XO:Fe). The complexes of XO-Fe$^{3+}$ concentration depend strongly on the high concentration of Fe$^{3+}$ formed during the irradiation. However, other relevant complex mechanisms of XO and Fe$^{3+}$ interaction was also observed at low concentration of ferric ions, suggesting the deviation of absorbance spectra that observed at low absorbed doses from a linear response without threshold [8].

![Figure 1](image.png)

**Figure 1.** The absorption spectra attained after the gamma irradiation of FXG with different doses in the range from 1 up to 200 Gy.
3.2 Study of dose response

In order to investigate the observed variation in the dose response following gamma irradiation, the dose dependent conversion of ferrous ions into ferric ions has been investigated. As shown in the Figure 1, the XO-Fe$^{3+}$ complexes absorb visible light mainly around 585 nm. Thus, the net absorbance at 585 nm can be referred to the absorbed dose, which is directly correlated to the difference in optical density measured at 585 nm before and after irradiation [3]. The dose response curve of FXG to the gamma radiation in the range of 1 to 1000 Gy is shown in the Figure 2. For better understanding of the observed dose response at the low-dose level (0 – 30 Gy), the results in the Figure 2 were then reproduced as indicated in the Figure 3. The dose response curve shows an increase of net absorbance at 585 nm linearity as the absorbed dose increased with gradually reached a maximum response at higher dose at
200 Gy, and followed by gradually decreased from 200 to 1000 Gy. As shown in the Figure 3, it is obviously observed a linearity increase of dose response up to 30 Gy with a linear correlation coefficient of $R^2 = 0.99$, suggesting an absorbed dose sensitivity of FXG at a low-dose level, whereas this sensitivity diminish as the dose increased. Therefore, the FXG can be practically used as a promising tool for low-dose level dosimetry. In the case of the reduction of the dose response at higher level may due to the progressive depletion of XO that is no longer available for complexion with ferric ions, resulting in leveling out of the absorbance [9].

3.3 Stability of Fricke gel dosimeter
For a large range of energies of interest in radiation therapy, the FXG is an excellent water and tissue equivalence [10]. There are several studies that reported about the stability, reproducibility and dose response of gamma irradiated FXG [6-7, 11]. From this study, we also observed that the response of the FXG depends not only the radiation absorbed dose, but also other conditions such as the spontaneous oxidation of FXG and chemical interaction of FXG after the gamma irradiation.

For dose response of FXG has been reported to be strongly depend on the spontaneous oxidation of Fricke gel solutions, therefore, the time between the preparation and irradiation of the Fricke gel must be defined. As shown in the Figure 4, our FXG showed a very high stability of non-irradiated FXG over a period of 7 days. The spectrophotometric response of the FXG that was prepared and kept at 4°C in the dark for 24 and 168 h prior irradiation of 10-30 Gy, indicates a short- and long-term consistency and reproducibility of FXG.

Moreover, the scanned time after the irradiated the Fricke gel must be indicated in order to maximize the stabilization of chemical interaction of FXG after exposure to gamma radiation. The post-irradiation stability of FXG are shown in the Figure 5. The stability of dose response of irradiated FXG (10-30 Gy) was observed in the initial 3 h following irradiation. The spatial stability of a FXG has been previously reported as 6 h after irradiation [12].

![Figure 4](image-url) The linearity and stability of Fricke gel dosimeter prepared and stored at 4°C in the dark over a period of 24 h (■) and 168 h (♦) prior gamma irradiation.
Figure 5. Response stability of the irradiated Fricke gel dosimeter at 1-3 h post-irradiation with 1-30 Gy of gamma radiation.

4. Conclusion
According to the obtained results, Fricke gel dosimeter has many attractive features for absorbed dose evaluation for radiotherapy, as it is easy to prepare as well as high accuracy, sensitivity and reproducibility. FXG can be used to evaluate the absorbed dose for a very large photon energy range. The linearity of dose response of FXG at clinical radiation dose below 10 Gy, could bring some lights for a 3D dosimetric applications in radiotherapy.

Acknowledgement
This research was supported by Office of Atoms for Peace, Ministry of Science and Technology under the project of “Development and application of new materials for ionizing radiation dosimetry”.

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