Dose response assessment of conventional Fricke: a relationship between UV-Visible and nuclear magnetic resonance techniques

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ABSTRACT

Conventional Fricke is an aqueous ferrous sulfate solution that has been widely studied in the field of chemical dosimetry. The feasibility of its use has become attractive for high dose measurements that are of clinical interest in the field of radiotherapy and for industrial purposes, in the irradiation of blood bags and the sterilization of surgical material. The derivation of the absorbed dose of Fricke depends on the radiation-induced oxidation of iron (II) ions (Fe\textsuperscript{2+}) present in the aqueous solution to iron (III) ions (Fe\textsuperscript{3+}), which occurs after exposure to ionising radiation. In this paper, it is proposed to evaluate the dose response of the Fricke dosimeter using two different analytical techniques, ultraviolet-visible spectrophotometry (UV-Vis) and nuclear magnetic resonance spectroscopy (NMR).

Twelve groups of samples were analysed in triplicate, irradiated with doses between 0 and 800 Gy, using a cobalt-60 source (\textsuperscript{60}Co). The dose rate of Fricke dosimeters was evaluated against the practical values obtained. The different methods allowed an analytical correlation of the species of oxidised iron (Fe\textsuperscript{3+}) using a linearity curve as a function of the applied radiation dose.

Keywords: Conventional Fricke, UV-Visible, nuclear magnetic resonance.
Fricke dosimetry, revealed to the scientific community almost a century ago, is still being presented as a safe and feasible system for determining the absorbed dose of ionising radiation. This system is considered an absolute standard in radiation chemistry, exhibiting high reliability in absorbed dose measurements by biological organs and tissues. A dosimeter is considered absolute when it can be assembled and used to measure the amount of energy deposited in its sensitive volume without the need for calibration in a radiation field [1,2,3]. The Fricke solution is regarded as a standard reference chemical dosimetry system under ISO/ASTM 51261 because of its reproducibility, linearity, and precision [4]. When irradiated, the ferrous ions (Fe$^{2+}$) present in the aqueous solution composition are oxidized to (Fe$^{3+}$). Quantitatively, the radio-induced oxidation of ferrous ions depends on the applied dose rate or exposure time of the ferrous ions. Since the Fricke dosimeter contains 96% water by weight, its dosimetry characteristics are remarkably comparable to those of water. Its valid reading range is 20 to 400 Gy [5,6,7].

The Fricke dosimeter has versatility in dose determining, which different techniques can be obtain. However, two most commonly used techniques are: optical and electromagnetic interaction methods such as the UV-Visible spectrophotometry (UV-Vis) [8,9] and nuclear magnetic resonance spectroscopy (NMR) [10-12]. The UV-Visible absorption spectrophotometry is applied to quantify the ferric ion Fe$^{3+}$ at the wavelengths of 225 and 304 nm in Fricke solutions. The Fricke dosimeter has different characteristics when it comes to its magnetic properties, although ions of Fe$^{2+}$ and Fe$^{3+}$ are paramagnetic species, they exhibit different magnetic moments that reflect different relaxation times [13]. These relaxation times can be correlated as the ion concentration by measuring the 1/T$_1$ and 1/T$_2$ relaxation rates in magnetic resonance imaging [10,14]. Gore et al., demonstrated by 3D dosimetry that ferric ions Fe$^{3+}$ have a greater influence on the proton relaxation time than ferrous ions Fe$^{2+}$, which allows Fricke dosimetry by magnetic resonance [10,15].

1.1. Reactive Species

There are substances and or materials that, when irradiated, can absorb ionising radiation energy and thereby change chemically. If this change can be measured and the intensity of the effect is proportional to the applied dose, this substance is a candidate for a radiation dosimeter [3]. An example
of this type of material is the Fricke dosimeter. As with all aqueous chemical dosimeters, the radiation interacts with water and producing free radicals (H and OH), which are highly reactive. Since the Fricke solution consists of 96% water, the most important reactive species are generated during the radiolysis of the water. In this process, electrons are ejected from the ionised water molecules and excited water molecules (H$_2$O*) are produced. This molecule is in an excited state (*) above the breaking threshold of the H-OH bond [2,3]. The radical OH can directly oxidise ferrous ion, for example, as described in chemical Equation 1. Furthermore, the Fricke solution has a high hydrogen concentration due to the acidity of the medium, thus in the presence of oxygen the chemical reactions occur more rapidly [3,4,6,14].

$$Fe^{+2} + OH \rightarrow Fe^{+3} + OH^-$$  \(1\)

An important property attributed to the Fricke dosimeter is related to the effective atomic number of the species present in the solution. The high water content and the low atomic number (Z) of the Fricke solution contribute to the fact that this dosimeter corresponds to human tissue and also responds well to low energy radiation fields [16].

1.2. Dose calculation for UV-Vis

To determine the absorbed dose with the Fricke dosimeter, it is necessary to know some important factors involved in the oxidation reaction. Among the factors studied, the chemical yield $G(Fe^{3+})$ has a great influence on the determination of the dose. This factor relates the production of a chemical species to the absorbed energy. According to Arango et al., the value of $G(Fe^{3+})$ decreases proportionally with decreasing photon energy or with increasing linear energy transfer (LET), while this factor is relatively independent of beam quality at higher energies [17]. The amount of Fe$^{3+}$ produced thus depends on the energy absorbed by the solution, as given in Equation 2, which is used to determine the absorbed dose when the UV-Vis technique is used [4].

$$D = \frac{A - A_0}{\rho G(Fe^{+3})I \bar{E}_m}$$  \(2\)
where \( A_0 \) and \( A \) are the absorbance values (optical density) of the pre-irradiated and irradiated solution, respectively, being considered a dimensionless quantity. The pre-irradiated solution is used as a control (background). The optical density value of these samples at 304 nm is subtracted from the irradiated samples, which helps to ensure that the Fe\(^{3+}\) naturally ions oxidised are not added to the Fe\(^{3+}\) species produced after irradiation. The term \( \rho \) corresponds to the density of the Fricke solution determined in the laboratory (1.027 g/cm\(^3\)), while \( G(\text{Fe}^{3+}) \) is the chemical yield of the solution and is related to the number of ferric ions released at 100 eV. The \( l \) in the equation is the optical path, i.e. the width of the cuvette used in the spectrophotometer, and this value is given at 1 cm. When the concentration is expressed in moles per litre and the optical path length in centimetres, the absorptivity is called the molar absorptivity and is represented by \( \varepsilon_m \), the molar absorption coefficient of the medium (2174 mol/l\(^{-1}\) cm\(^{-1}\)). The absorbed dose is obtained in the SI unit, Gy [3,4,14]. Another important quantity to be measured during the irradiation process and the measurement of the optical density (OD) of Fricke dosimeters is the temperature. It is known that the yield of ferric ion production \( G(\text{Fe}^{3+}) \) depends on the temperature of the medium during irradiation. Similarly, it is known that the molar extinction coefficient, which refers to the optical properties of the solution at a certain concentration of ferric ions, depends on the temperature during the spectrophotometric measurement [18]. It has been reported that at about 25 °C the \( G(\text{Fe}^{3+}) \) decreases by 0.12% when the irradiation temperature \( T_{\text{irrad}} \) decreases 1°C [19], while the ion \( (\text{Fe}^{3+}) \) decreases by 0.69% when the reading temperature \( T_{\text{read}} \) decreases by 1°C [20]. The reading temperature can be conventionally maintained at the reference level (25°C) controlling the temperature of the spectrophotometer sample chamber. In contrast, the temperature of the Fricke solution can vary considerably during irradiation, i.e. in a phantom, resulting in significant changes in the \( G(\text{Fe}^{3+}) \), which in turn leads to corrections of the readings in the order of 0.5% or more. Therefore, an accurate knowledge of the dependence of the \( G(\text{Fe}^{3+}) \) values with temperature is important to maintain the accuracy of the method under practical irradiation conditions. The term \( \Delta DO_{25,25} \) determines the optical density correction as a function of reference temperatures at 25 °C, both at irradiation and at reading, as a function of the difference in media temperatures at the time of irradiation and reading. This relationship is described in Equation 3, which was used to correct the irradiation temperatures at 25°C, which until then had been arbitrary [19-21].

\[
\Delta DO_{25,25} = \Delta DO_{T_{\text{irrad}},T_{\text{read}}} \left[ 1 + 0.0012(25 - T_{\text{irrad}}) \right] \left[ 1 + 0.0069(25 - T_{\text{read}}) \right]
\]
1.3. Dose calculation for NMR

The dose calculation of the samples submitted to the NMR technique depends on the relaxation time of the ferric and ferrous ions present in the Fricke [10]. In Equation 4, the values for the density $\rho$ and the chemical yield $G(\text{Fe}^{3+})$, are the same as mentioned above, since it is the same solution irradiated using the same source. $N_A$ corresponds to the Avogadro's constant, its value is calculated in the unit of the number of Joules per electron-volt. $R_2(D)$, $R_2(0)$ are equivalent to the relaxation rate of the dosimeter in time $T_2$, irradiated and pre-irradiated respectively. The values $(r_3^+, r_2^+)$ describe the relaxivities of the experimentally known ferric and ferrous ions for these species present in the Fricke solution, necessarily in that order [4, 22].

$$D = \frac{N_A \cdot e}{10\rho \cdot G(\text{Fe}^{3+})} \cdot \frac{R_2(D) - R_2(0)}{(r_{eff}^+ - r_2^+)}$$

Fricke dosimeters have many attractive features. The low operating costs, equivalence with human tissue, wide energy range and non-toxicity should be emphasised. These advantages, together with the advent of techniques such as NMR and UV-Vis make it easier to study the administered dose. It is noteworthy that the development of Fricke systems has played a continuing role in the field of chemical dosimetry. The aim of this work is to evaluate the response of the Fricke dosimeter as a function of the administered dose using the optical and electromagnetic interaction methods. The Fricke dosimeter presented here was developed within the Monte Carlo Modelling Expert Group (MCMEG) of the Federal University of Minas Gerais (MCMEG/UFMG).

2. MATERIALS AND METHODS

At first, a solution of sulphuric acid (H$_2$SO$_4$), 98% 0.4 mol/L was prepared, which in turn was previously irradiated with 10 Gy in a $^{60}$Co, of the Gamma Irradiation Laboratory of the Nuclear Technology Development Center (LIG/CDTN). To this solution, after one hour of irradiation, 0.392 g of ammoniacal ferrous sulphate hexahydrate, also known as Morh's salt (FeSO$_4$.(NH$_4$)$_2$ SO$_4$ + 6H$_2$O) and 0.06 g of sodium chloride (NaCl) were dissolved. The volume of the solution was made up to 1
liter with triple distilled water (Merck Millipore). All components used for the preparation of the Fricke solution are briefly described in Table 1. Before the solution was sent for irradiation, it was divided into 12 triplicate groups, each with a volume of 5 mL. They were stored protected from natural and artificial light for 24 hours before use. These groups of samples were irradiated with doses ranging from 0 and 800 Gy. The time between preparation and irradiation of the samples was between 26 and 30 hours. UV-Vis analyses were performed 2 hours after irradiation, while NMR measurements were performed two days after irradiation. A Hitachi U-2900 spectrophotometer and a Bruker Ascend-Neo 600 MHz nuclear magnetic resonance (NMR) spectrometer were used. Samples submitted for experimental analysis of NMR spectroscopy were dissolved in 100 ul of deuterated water(D₂O). The record of chemical changes taking place in the solution is based on the signal from this solvent. Transverse relaxation measurements were performed with CPMG sequence pulses [23]. The temperatures of the samples were permanently monitored throughout the irradiation and analysis process. The absorption doses of the samples were calculated using the values from the measurements of the UV-Vis and NMR techniques and Equations 2 and 4, respectively.

Table 1: Composition of the Fricke solution

<table>
<thead>
<tr>
<th>Components</th>
<th>Concentration Mol.L⁻¹</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulphuric acid</td>
<td>0.4</td>
<td>Analytical reagent grade from Merck-KgaA-Darmstat, Germany.</td>
</tr>
<tr>
<td>Mohr’s salt</td>
<td>0.001</td>
<td>Analytical reagent grade from Merck-KgaA-Darmstat, Germany.</td>
</tr>
<tr>
<td>Sodium chloride</td>
<td>0.001</td>
<td>Analytical reagent grade from Fmaia-PA-ACS-Cotia, Brazil.</td>
</tr>
<tr>
<td>Water Mili-Q</td>
<td>-</td>
<td>Merck- M-Millipore- Direct-Q®3- Molsheim, France</td>
</tr>
</tbody>
</table>
3. RESULTS AND DISCUSSION

3.1. UV-VIS and NMR

Readings of irradiated Fricke solution samples were obtained using UV-Vis and NMR analysis techniques. The presence of ferric ions (Fe$^{3+}$), formed after irradiation, present two optical absorption bands in the ultraviolet range. One at 224 nm and the other at 304 nm [20]. According to Figure 1, it is possible to visualize these absorption bands that were identified through the optical absorption scanning spectra as a function of the analyzed wavelength range. The increase in absorbance values in these bands is clearly visible. This fact is due to the proportional increase in the concentration of Fe$^{3+}$ ions in the solution in relation to the applied radiation dose, known as the Lambert-Beer effect [2]. For the dose calculation, using the UV-Vis technique, the range of 302 nm was considered, as it is repeatable for the different radiation doses employee. Figure 2 shows the response of the Fricke dosimeters as a function of the applied doses in the range of 10 to 200 Gy. These dosimeters showed linearity for absorbed doses close to 200 Gy. However, doses higher than this value indicated saturation in the spectrophotometric response.

**Figure 1:** Optical absorption spectra of aqueous Fricke, samples irradiated and non-irradiated with gamma radiation ($^{60}$Co).

**Figure 2:** Spectrophotometric response for the samples irradiated with gamma irradiation ($^{60}$Co).
Changes in the concentration of ferric ions can be detected by the NMR technique. The conversion of ferrous ions to ferric ions in the solution after irradiating the samples causes a change in the relaxation times of the aqueous solution. As shown in Figure 3, the results obtained were based on studies already described by Gore et al. [10], where the signals determined from the ion-proton interaction were analyzed and plotted, demonstrating a linear correlation of the relaxation rate ($R_2$) in relation to the absolute dose. It is understood that the relaxation times of these samples decrease with the increase in the concentration of ferric ions produced after irradiation. Remembering that the relaxation rate ($R_2$) is related to the exponential decay of the transverse magnetization. This proves that, for longer relaxation times obtained in the reading, lower is the energy absorbed by the dosimeter. Consequently, the variation in the spin relaxation time ($T_2$) of the hydrogen nuclei is substantially reduced due to the dynamics of the paramagnetic species present in the Fricke solution [24]. Figure 4 shows a representation of the relaxation rate as a function of the different concentrations of Fe$^{3+}$ produced in non-irradiated samples. These samples were produced from an iron III standard solution in order to know the relaxation rate for different concentrations ferric ion. From these data it is possible to mathematically determine the relaxation time ($T_2$) in unknown samples of Fricke solutions. Another alternative is to estimate the absorbed dose by Fricke dosimeters using the straight equation that can be mathematically obtained with the data expressed in Figure 3.

**Figure 3:** Linear correlation analysis of ($R_2$) as a function of absolute dose.

**Figure 4:** Linear correlation of the relaxation rate ($R_2$) as a function of the concentration of (Fe$^{3+}$).
Table 2: Average absorbed doses for the Fricke dosimeter, obtained by UV-Vis and NMR techniques.

<table>
<thead>
<tr>
<th>Samples Fricke</th>
<th>UV-Vis</th>
<th>NMR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nominal dose (Gy)</td>
<td>Experimental dose (Gy)</td>
</tr>
<tr>
<td>A2</td>
<td>10</td>
<td>10.29</td>
</tr>
<tr>
<td>A3</td>
<td>30</td>
<td>29.31</td>
</tr>
<tr>
<td>A4</td>
<td>50</td>
<td>49.99</td>
</tr>
<tr>
<td>A5</td>
<td>70</td>
<td>71.08</td>
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<tr>
<td>A6</td>
<td>90</td>
<td>89.70</td>
</tr>
<tr>
<td>A7</td>
<td>100</td>
<td>97.97</td>
</tr>
<tr>
<td>A8</td>
<td>200</td>
<td>192.92</td>
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<tr>
<td>A9</td>
<td>300</td>
<td>246.20</td>
</tr>
<tr>
<td>A10</td>
<td>400</td>
<td>303.07</td>
</tr>
<tr>
<td>A11</td>
<td>600</td>
<td>379.97</td>
</tr>
<tr>
<td>A12</td>
<td>800</td>
<td>537.56</td>
</tr>
</tbody>
</table>

The experimental results of the dose calculations (Table 2) in the range of 10 and 200 Gy confirmed that the two analytical methods applied to the Fricke dosimeter are linear as it also shown in Figures 2 and 3. The results obtained in the practical evaluation of conventional Fricke showed that both UV-Vis and NMR techniques were efficient in reading experimental doses below 100 Gy. Showing an uncertainty of approximately 3 Gy. It was experimentally demonstrated that the conventional Fricke works satisfactorily for high energy dosimetry ($^{60}$Co) in the range of 25 to 400 Gy. Another point worth mentioning is the NMR technique. The results calculated mathematically for doses above 200 Gy had their experimental values close to the nominal value, even with uncertainties greater than 10.7 Gy when comparing the same dose intervals that were determined by the UV-vis technique. The uncertainty calculations presented in Table 2 were determined from the expanded uncertainty calculations. These uncertainties are related to the dosimeter response, the source dosimetry for irradiated distances and the sample temperature during reading and irradiation.
Although the UV-Vis technique does not respond properly for doses above 200 Gy, this does not mean that this method should be ignored. It is possible to see the conventional Fricke applicability for industrial purposes such as irradiation of blood bags and also for the field of high-dose radiotherapy. It is debatable whether chemical dosimetry using Fe$^{3+}$ ions induced by radiation is a sensitive method for UV-Vis technique, but it is demonstrated that the conventional Fricke is a useful and safe system for dose investigations, when compared to other same systems that works the form indirect in determining absorbed dose [25]. The research characterizing the Fricke dosimeters is quite detailed and requires a high degree of analytical rigor in developing tests that can be better represented in future work and will serve as an incentive for low dose clinical applications.

4. CONCLUSIONS

The aim of this work was to evaluate the response of the Fricke dosimeter as a function of the administered dose using the optical and electromagnetic interaction methods. It has been experimentally demonstrated that the conventional Fricke works satisfactorily for dosimetry of high energies ($^{60}$Co) in the range of 25 to 400 Gy. The two analysis techniques investigated have thus proven to be efficient and can be integrated into the dosimetry system. However, when the operating costs of the individual analytical methods are considered, it can be seen that the NMR technique although more efficient at high doses, requires high costs demand. In contrast, the UV-Vis technique, even though it is an older analytical tool, continues to work perfectly for scientific purposes. Conventional Fricke are already a reality in reference dosimetry. But the choice of technique used for their reading requires even more research and adaptation to maintain the reliability of the dose response. We therefore assume that the conventional Fricke dosimeters produced by the MCMEG/UFMG group showed a good response as a function of the applied dose for the range from 10 to 100 Gy.

ACKNOWLEDGMENT

The authors thank the partner laboratories for their support and dedication in carrying out this work: LIG/CDTN for providing materials and irradiating the samples, LAREMAR-DQ/UFMG for performing the NMR analyses, and LCR/UERJ for donating the Fricke reference dosimeters. The
following Brazilian institutions support this research project: Research Support Foundation of the State of Minas Gerais (Fapemig), Brazilian Council for Scientific and Technological Development (CNPq) and Coordination for the Capacitation of Graduated Personnel (Capes). Prof. T. C. F. Fonseca is grateful for the financial support provided by CNPq (Nº 302990/2021-6 PQ – 4/2021 and 424734/2018-4 APQ) and Fapemig (Project APQ-01388-21, APQ-00083-18 and BPD-00963-22).

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