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Absorbed dose to water standard for ^{192}Ir HDR sources using Fricke Dosimetry

Patrón de dosis absorbida en agua para fuentes de ^{192}Ir de alta tasa de dosis (HDR) usando dosimetría Fricke

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Abstract

The Fricke solution is a chemical dosimeter that is based on the oxidation of ferrous ions to ferric ions in the solution after interaction with ionizing radiation. It is composed of 96 % water (by weight), and its density is thus remarkably similar to that of water. In addition, studies show that the Fricke dosimeter can be used as a primary dosimeter in the determination of the absorbed dose to water for high dose rate (HDR) ^{192}Ir brachytherapy. The Radiological Sciences Laboratory of the University of Rio de Janeiro State (LCR/UERJ) has been investigating the use of the Fricke dosimeter in various applications for more than ten years, particularly in the area of radiotherapy. This review paper presents important improvements in recent years by the LCR/UERJ in the determination of the absorbed dose to water for ^{192}Ir sources. This includes a newly designed irradiation vessel, a new reading device, a description of the need for careful temperature control during irradiation and reading, a more accurate calculation of the correction factors and the results of an intercomparison with the National Calibration Laboratory of Canada. Careful preparation of the Fricke solution is one of the most critical steps in the process. Over the years, the LCR/UERJ has tested different methods of preparing the solution and the final procedure is presented. Regarding the irradiation vessel, a molded double-walled, spherical flask for the Fricke solution was first constructed and used to measure the absorbed dose to water. However, as it was difficult to manipulate the spherical flask, a second design also made with PMMA was molded as a cylinder, with a central tube where the source was centrally positioned. Different methodologies have been reported in the determination of the G-value, a key parameter in Fricke dosimetry, and herein, two different methodologies used by the LCR are reviewed.

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For the absorbed-dose-to-water determination for ^{192}Ir sources, the overall combined uncertainty associated with the measurements is estimated to be less than 1 % for $k = 1$. Thus, the obtained uncertainties for the determination of the absorbed dose to water using Fricke dosimetry are lower than those obtained using the standard protocols. With respect to clinical practice, this could improve the accuracy in the calculation of the dose delivered to the patients. Overall, the results show that Fricke dosimetry is a reliable system to measure absorbed dose to water as a standard for HDR ^{192}Ir.

Keywords: HDR, Fricke dosimetry, absorbed dose

Resumen

La solución de Fricke es un dosímetro químico basado en la oxidación de iones ferrosos a férricos en la solución después de la interacción con radiación ionizante. La solución está compuesta de 96 % de agua (en peso), así que su densidad es notablemente similar a la del agua. Adicionalmente, estudios muestran que el Fricke puede ser usado como un dosímetro primario en la determinación de la dosis absorbida en agua para braquiterapia de alta tasa de dosis (HDR), con ^{192}Ir.

Por más de diez años, el Laboratorio de Ciencias Radiológicas de la Universidad del Estado de Río de Janeiro (LCR/UERJ) ha investigado el uso de dosímetros Fricke en varias aplicaciones, particularmente en el área de radioterapia. Este artículo de revisión presenta importantes desarrollos del LCR/UERJ en años recientes para determinar la dosis absorbida en agua en haces de fuentes de ^{192}Ir. Esto incluye un nuevo diseño de un recipiente de irradiación, un nuevo dispositivo de lectura, la descripción de la necesidad de un control cuidadoso de la temperatura durante la irradiación y la lectura, un cálculo más preciso de los factores de corrección y los resultados de una intercomparación con el Laboratorio Nacional de Calibración de Canadá. La preparación cuidadosa de la solución Fricke es una de las etapas más críticas del proceso. A lo largo de los años, el LCR/UERJ ha probado diferentes métodos de preparación de la solución, y ahora se presenta un procedimiento final.

En relación con el recipiente de irradiación, un matraz esférico moldeado de doble pared para la solución Fricke inicialmente fue fabricado y usado para medir la dosis absorbida en agua. Sin embargo, como era difícil manipular el matraz esférico, un segundo diseño, realizado también con PMMA, fue moldeado como un cilindro, con un tubo central en cuyo centro es posicionada la fuente. Se han reportado diferentes metodologías para determinar el valor G, un parámetro clave en dosimetría Fricke, y aquí son revisadas dos metodologías usadas por el LCR.

Para determinar la dosis absorbida en agua en haces de fuentes de ^{192}Ir, la incertidumbre combinada total asociada con las medidas se estima por debajo de 1 % para $k = 1$. Así, las incertidumbres obtenidas para determinar la dosis absorbida en agua usando dosímetros Fricke son menores que las obtenidas usando los protocolos estándar.

Con relación a la práctica clínica, esto podría mejorar la exactitud del cálculo de la dosis entregada a los pacientes. En general, los resultados muestran que la dosimetría Fricke es un sistema confiable para medir la dosis absorbida en agua, como patrón para HDR con ^{192}Ir.

Palabras clave: HDR, dosimetría Fricke, dosis absorbida

1. Introduction

Fricke dosimetry, also called ferrous sulfate dosimetry, has been in use for several decades for different types of radiation beams [1]-[5]. The Fricke solution response depends on the oxidation, by ionizing radiation, of ferrous ions (Fe^{2+}) to ferric ions (Fe^{3+}). The solution contains 96% water (by weight), therefore, its density is close to the density of water. It is used in a dose range of 20-400 Gy and dose rates of up to 10^6 Gy/s [6], exhibiting a good linear response over the range of 5-70 Gy and an accuracy better than 2% for a 2 Gy/min dose rate [7]. The major disadvantages of Fricke dosimetry are its high sensitivity to impurities, and its sensitivity to the presence of oxygen in the solution [5], [8], [9]. For more than 10 years, the Radiological Science Laboratory of the Rio de Janeiro State University (LCR/UERJ) in Brazil has been investigating the use of Fricke dosimetry for different applications [7], [10]-[17]. The applications of Fricke dosimetry to ^{192}Ir HDR sources are one of the very most recent subjects of study [14], [18].

High-dose-rate brachytherapy (HDR) using ^{192}Ir is a widely used option for cancer treatment and requires an accurate dosimetry standard. However, a dosimetry standard for the direct measurement of absolute absorbed dose for ^{192}Ir HDR sources is not yet available. The AAPM TG-43 Report [19], and its update [20], constitute the accepted protocol for dose-to-water determination based on an air kerma strength (S_k) measurement. The dose-to-water conversion is done via the dose rate constant Λ, which converts the air-kerma strength to dose-to-water and uses different correction factors to account for scatter, attenuation, and anisotropy of the dose distribution [20]. Efforts are being made to establish a reliable method with reduced uncertainties for the measurement of the absorbed dose to water, thus improving the clinical treatment of patients.

Several authors have reported different methodologies to determine a standard for absorbed dose to water for ^{192}Ir sources. Sarfehnia et al. [21] developed the first methodology using a water-based calorimeter with uncertainties lower than 5% ($k=1$). Very recently [22] and [23] have reported a reduction in uncertainty to 1.9 % ($k=1$). The second was developed by Austerlitz et al. [8] using Fricke dosimetry, with an overall uncertainty of 3.4 % ($k=1$) and more recently de Almeida et al. [24], Salata et al. [14] and Malcolm et al. [18], [25] have reported consistent results using Fricke dosimetry as a standard.

This paper presents important improvements in the last years [12], [14], [24] by the LCR/UERJ in the determination of the absorbed dose to water for ^{192}Ir sources. This includes a newly designed irradiation vessel, a new reading device, a description of the need for careful temperature control during irradiation and reading, a more accurate calculation of the correction factors and the results of an intercomparison with the National Calibration Laboratory- NRC, Canada.

1.1. The Fricke system

Careful preparation of the Fricke solution is one of the most important parts of the process. Over the years, LCR/UERJ researchers have tested different methods of preparing the solution, and here the final result procedure is presented. The laboratory glassware is first cleaned with 5% diluted Extran (MERCK-KGaA, Darmstadt, Germany), rinsed at least 10 times, and then filled with sulfuric acid 96%, which remains in the glassware for at least 24 h. After this period, the glassware is rinsed at least 10 times and then dried in an oven. The Fricke solution is prepared using chemicals of high purity. The Fricke solution is prepared in a 1 L volumetric flask. First, 22 ml of sulfuric acid, 98% (MERCK-KGaA, Darmstadt, Germany), is diluted with 250 ml of high purity water (Millipore Milli-Q system). The water-acid mixture is preirradiated with 10 Gy, using a completely self-shielded X-ray irradiator for biological research (RS 2000X, Radsource, CA, USA). This preirradiation step is included in the preparation of the Fricke solution prepare to reduce the influence of trace impurities present in the sulfuric acid, as described by Palm and Mattson [26]. After 1 h, 0.06 g of sodium chloride [NaCl] (99.5%) (MERCK-KGaA, Darmstadt, Germany) and 0.392 g of ammonium iron (II) sulfate hexahydrate [$(NH4)_2Fe(SO_4)_2.6H_2O$] (99%) (MERCK-KGaA, Darmstadt, Germany) is added. Milli-Q water is added to the mark on the volumetric flask to achieve a final volume of 1 L. The flask containing the Fricke solution is then capped and stored away from light for 24 h before use.

The ammonium sulfate and sodium chloride were weighed using a calibrated analytical balance (Shimadzu. Japan) with an accuracy of 0.0005 g. A density of 1.0230 g.cm^{-3} at 25 °C was measured for the nonirradiated solution using a Densimeter Incoterm, calibrated at 22 °C with a resolution of 0.0001 g.cm^{-3}, which can be compared to the value of 1.0227

g.cm^{-3} at 25 °C reported by Olszansky et al. [16]. Daily readings of the optical density (*OD*) (absorbance), over a period of nine days using recently made solutions had no measurable differences compared to a month-old solution. Hence, a fading correction is not considered.

The *ODs* of the Fricke dosimeter solutions are measured at a wavelength of 304 nm using a Varian Cary 50 Bio spectrophotometer (Varian, Palo Alto/CA, USA) with a digital LCD display, a resolution of 1 nm and photometric accuracy of 0.010 AU. The repeatability of the wavelength is periodically verified by a set of standard absorbance filters traceable to the National Institute of Standards and Technology (NIST-USA). The cuvette holder has a compartment for a 1.0 cm thick cuvette. The nominal dimensions of the cuvette are 1.0 · 1.0 · 4.5 cm3, and the optical path length through it was measured to be 0.9991 ± 0.0005 cm. As defined in equation 2, the temperature of the Fricke solution during irradiation and readout influences the determination of the absorbed dose to water. One of the improvements of Fricke dosimetry at the LCR/UERJ was the acquisition of a thermal bath that stabilizes the temperature at 25 °C during the reading of the solutions.

1.2. Irradiation vessel design

Different vessels have been tested over the years by the LCR/UERJ to be used for the determination of the absorbed dose to water for HDR ^{192}Ir sources. The device used for the Fricke solution must have the following properties: the material should not react with the solution, or at least this reaction should stabilize over a short period of time; it must be possible to seal the vessel; it should be easy to transfer the solution from the vessel into the cuvette; and the volume of solution contained in the vessel must be sufficient to rinse and fill at least one cuvette. The first vessel developed by the LCR was a double-glass balloon, as shown in figure 1a The Fricke solution was kept between the two balloons and the source was conducted to the center of the vessel using a thin glass tube positioned in the center of the inside balloon. The disadvantages of this vessel were that glass is not water equivalent, it was impossible seal, and the solution was not homogeneously irradiated.

The second vessel designed by the LCR was a spherical PMMA vessel reported by de Almeida et al. [24]. A PMMA tube was fixed at the top of the flask to allow the center of the source inside the catheter to coincide with the geometrical center of the vessel, as shown in figure 1b. The irradiated solution volume was 8.0 cm^3, which was only sufficient to rinse and fill one cuvette and obtain one reading for each irradiation. The vessel is described in [24]. The main advantages of this vessel were that the density of PMMA is very close to that of water and the solution could be homogeneously irradiated, as the vessel is spherical. Only a ring in the center of this sphere was filled with Fricke solution, and the source was positioned in the center of this ring.

The effects due to possible chemical reactions between the $FeSO_4$ solution and the PMMA were tested over a long period of time, leaving the Fricke solution inside the holder and measuring it every day. It was observed that a nonirradiated Fricke solution reacted with the PMMA during the first 24 h to cause a significant increase in the optical density. Five flasks were tested five times with nonirradiated solutions, and this short-term effect was only observed in new flasks. The same reaction, which reaches equilibrium after 48 h, was described by Morrison and Boyd [27] for organic esters, possibly due to acid hydrolysis of the ester groups of the PMMA

This vessel had the advantage of spherical geometry, but its major disadvantage was the difficulty of inserting the solution into its ring-shape compartment without creating any bubbles, and it was very difficult to vert the solution from the vessel to the cuvette. Thus, an improved PMMA vessel was designed to reduce this disadvantage. It also allows the center of the source inside the catheter to coincide with the geometric center of the ring, which is filled with the Fricke solution, as shown in figure 1c. The irradiated solution volume is 18.4 cm^3, which is sufficient to rinse and fill at least two cuvettes and obtain two readings for each irradiation. The complete dimensions of this vessel can be seen at [14].

It is important to highlight that, in this cylindrical vessel, the distance from the center of the source to the center of the ring compartment where the Fricke solution is located during irradiation is 2.7 cm, so a Monte Carlo (MC) factor is required to convert the measurements to the standard reference position of 1 cm from the source in water, according to the TG-43 formalism [20]. This is the main disadvantage of this design. At present the LCR is testing a new vessel, which is a small version of the cylindrical one, but the distance from the source to the Fricke solution compartment is 1 cm. Pickler et al. studied this new vessel and analyze the effects of the interaction of Fricke solution and PMMA, as the surface/solution relationship of this small vessel changes from the larger cylinder [28].

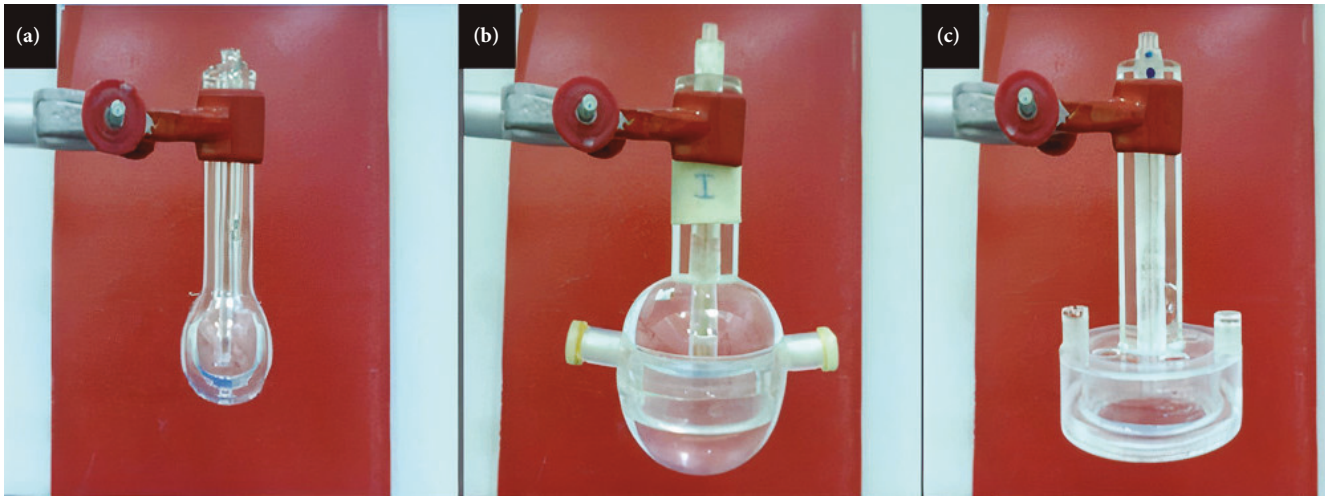

Figure 1. Irradiation vessels developed at the LCR
A. The double-balloon glass holder; B. The PMMA spherical holder; C. The PMMA cylindrical holder.

1.3. Irradiation and measurement procedures

The first irradiations with the ^{192}Ir source were performed with a spherical vessel. The center of the spherical vessel was filled with water, and the ring-shaped shell was filled with the Fricke solution. The whole flask was placed in the center of the 30 · 30 · 30 cm3 water phantom. The irradiated solutions were inserted and extracted using a small Pyrex graduated pipette and were subsequently transferred to a quartz cuvette. A Nucletron microSelectron irradiator was used with an alpha omega model 192Ir source through the catheter, allowing the source to be positioned in the center of the vessel. The irradiation time was calculated to deliver nominal doses ranging from 14 to 40 Gy. Due to temperature gradients during irradiation, a thermoprobe was used to monitor the temperature in the water phantom, and the irradiation started only after the temperature was stable.

Before each reading the cuvette was rinsed and filled with Milli-Q water and the absorbance was read to ensure that the cuvettes were clean. If the absorbance reading at 304 nm was as great as 0.0362 the cuvettes were considered clean, otherwise they were cleaned again, but using cotton swabs, with acetone and Milli-Q water, until the water reading was less than 0.0362. After that, the absorbances of the irradiated and control solutions were measured. The temperature measured during the irradiation is used to correct the dose-induced change in *OD* using a reference temperature of 25 °C. During the spectrophotometer reading the temperature was stabilized at 25 °C due to the use of the thermal probe. This relationship, initially described by Fregene [29] and modified by Olszanski et al. [9] is given in (2):

$$\Delta OD = (OD_i - OD_c)\cdot[1+0.0012\cdot(25-T_i)]\cdot[1+0.0069\cdot(25-T_r)] \quad (2)$$

where OD_i and OD_c are the optical densities of the irradiated and control solutions, respectively, T_i is the temperature in °C of the Fricke solution during irradiation, and T_r is the temperature in °C of the Fricke solution during the spectrophotometer reading. The control solutions were the Fricke solution that remained inside the vessel for the same amount of time as the irradiated solutions without being irradiated. A thermal bath inside the spectrophotometer was used to stabilize the temperature during the readings, at 25 °C [24].

After the measurements with the spherical vessel, the cylindrical vessel was used and the measurements with this vessel were done at the National Research Council Canada (NRC), to compare the standards of absorbed dose to water using Fricke dosimetry at both laboratories, the Radiology Science Laboratory (LCR) and the NRC. It was also possible to investigate any systematic effect in either methodology [14]. The irradiation methodology was almost the same, except that the microSelectron V2 ^{192}Ir source was used for irradiation and an NRC-modified Cary 400 Scan spectrophotometer was used for the readings. This system allows the reading of two cuvettes simultaneously, along with a standard absorbance filter and an empty optical path. The irradiation time was calculated to deliver nominal doses of approximately 14 Gy to the Fricke solution.

1.4. The determination of absorbed dose to water using Fricke solution

As discussed by Klassen et al. [5], the absorbed dose to the Fricke solution, D_F, was obtained from equation 3:

$$D_F = \frac{\Delta OD}{G(Fe^{3+}) \cdot L \cdot \rho \cdot \varepsilon} \quad (3)$$

where ΔOD is defined as the increase in OD at 304 nm taking into account the temperature effect as defined by (1), L is the optical path length of the cuvette, ρ is the density of the Fricke solution (1.023 g.cm^{-3}) at 25 °C, and ε is the molar extinction coefficient of the ferric ions (equal to 2174 M-1. cm^{-1} at 304 nm according to Cottens et al. [30]), $G(Fe^{3+})$ is the radiation chemical yield of ferric ions (equal to 1.555 ± 0.017 x10^{-6} mol.J^{-1}), which was obtained using the methods discussed in section f).

The quantity absorbed dose to water, D_w, is derived from the absorbed dose to the Fricke solution as proposed by Klassen et al. [5] and is defined in (4):

$$D_W = f \cdot p_{wall} \cdot D_F \cdot F_h \cdot k_{dd} = f \cdot p_{wall} \cdot \frac{\Delta OD}{G(Fe^{3+}) \cdot L \cdot \rho \cdot \varepsilon} \cdot F_h \cdot k_{dd} \quad (4)$$

where D_F is the absorbed dose in the Fricke solution, f is the dose conversion factor from Fricke solution to water, p_{wall} is the PMMA wall correction factor, F_h is the homogeneity correction due to the volume-averaging effect as described by Ochoa et al. [12] and k_{dd} is the correction factor due to the nonuniformity of the dose profile over the solution volume. In addition, in the case of irradiation with the cylindrical vessel, a K_{pos} factor was included in this equation to convert the dose from 2.7 cm to the dose at 1 cm. The correction factors were calculated using the MC method, as described in the next section.

1.5. Monte Carlo Simulations

The microSelectron HDR ^{192}Ir Alpha Omega source was used in the simulations and measurements for the spherical vessel, and the microSelectron V2 was used in the simulations and measurements for the cylindrical vessel. The specifications of the simulations are described at [14], [24].

The Monte Carlo particle-transport simulation code PENELOPE [31], was used to assess the data and the required corrections. In all cases, several simulations were conducted with at least three different random number generators, and the mean value was taken. The simulations were performed using a cluster with 192 processors taking the bare spectra, as reported by Borg and Rogers [32].

To validate our calculation results, these values were compared to the Borg and Rogers [32], Ma and Nahum [33] and Ma et al. [34] values, who used similar materials and geometry. In all three cases very comparable results were obtained. The Fricke solution data obtained from the PENELOPE database (identification number 160, with a density 1.024 g.cm^{-3}) was very close to the experimentally measured value of 1.023 g.cm^{-3} for the solution in our measurements.

For the ^{192}Ir simulations, 200 million photons were used, using an absorption energy of 1 keV for photons and 100 keV for electrons with a maximum step size of 0.01 cm for the Fricke solution. Relevant PENELOPE parameters were set to C1 = C2 = 0.05 and Wcc = Wcr = 1.0 keV. The time for each simulation was approximately 25 h. The simulations of the experimental vessels were performed according to the measures described at [14], [24], using PMMA for all the walls. The source was positioned in the center of the vessels and the center of the vessel was placed at a depth of 10 cm in water phantom.

The correction factors are determined according to the literature [12], [24]. First, they were calculated for the spherical vessel, as defined in equation 4:

1) The correction for the volume-averaging effect, F_h:
   The center of the solution volume was considered the reference point for dose calculations. This volume was divided into five equal concentric spherical layers, and the absorbed dose was calculated for each layer and normalized to the dose of the central layer. The main components that influence the radial dose distribution are self-attenuation of the Fricke solution and nonuniformity of the photon fluence due to the beam divergence, which causes a small dose gradient. The obtained results showed that the average reading of all layers relative to the central one was 0.4% higher than the calculated value at the central layer.
2) The non water wall effect, p_{wall}:
   This factor considers the influence of the PMMA wall of the vessel on the dose deposited in the Fricke solution, compared to a vessel without walls.

3) The dose conversion factor from Fricke solution to water, *f*:
   This factor is due to the difference in dose deposited in the volume of Fricke solution compared with the dose that would be deposited in the same volume of water, a difference which arises from the difference in radiation absorption characteristics and density of Fricke solution and water.
4) The correction factor for the nonuniformity of the dose profiles over the solution volume, k_{dd}:
   This factor considers the magnitude of the anisotropy effect over 6 equally divided sectors around the source. The obtained value was:

The same factors were calculated for the cylindrical vessel, as published in [14], also using the PENELOPE code. The only different MC factor is K_{pos}, which converts the dose from 2.7 cm to 1 cm. Table 1 shows the calculated MC factors for both vessels.

Table 1. MC PENELOPE factors calculated for both vessels [14], [24]

MC Factors	Spherical Vessel	Cylindrical Vessel
F_h	0.996 ± 0.003	0.997 ± 0.002
p_{wall}	0.999 ± 0.004	0.999 ± 0.002
F	1.004 ± 0.003	1.001 ± 0.002
k_{dd}	1.000 ± 0.002	1.039 ± 0.002
k_{pos}	----	7.1932 ± 0.015

1.6. Determination of the *G-value*

Three different methodologies were used to determine the *G-value* [$G(Fe^{3+})$]. The first consisted of the estimation of the energy-weighted *G-value* from published values. A curve fitting was performed using the ionometric and calorimetric measurements reported by Fregene [29] and the calorimetric measurements reported by Klassen et al. [5]. It is important to highlight that the values obtained from Fregene [29] were reported in his paper without much experimental detail. A *G-value* was assigned for every 50 keV of energy in the energy interval from 1 to 900 keV. These values were weighted according to the photon fluence per MeV per 100 decays, as described in [24].

The *G-value* obtained from this methodology was 1.555 ± 0.017 x10^{-6} mol.J^{-1}, which was the value used for calculations of the absorbed dose to water using the spherical vessel. This value is comparable to the ionometric measurements data using dosimetry protocols reported by Franco et al. [11], 1.578 ± 0.016 x10^{-6} mol.J^{-1}. The selection of the mean energy was not a critical issue for the semilog plots used. The energy fluence for water was calculated using Monte Carlo methods by Borg and Rogers [32] and from this work. Figure 2 shows the plotted data from the literature used to calculate the *G-value*.

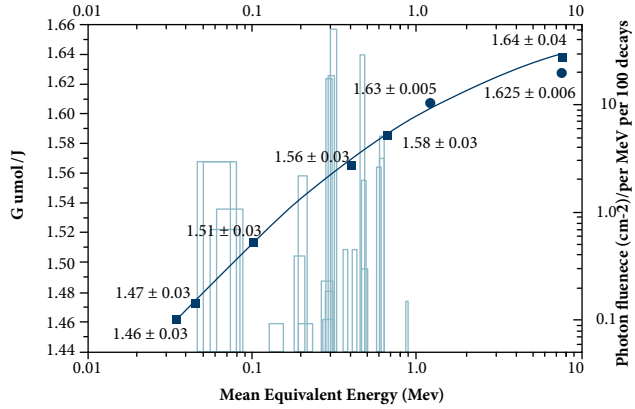

Figure 2. The *G-values* published in the literature
The full circles are the values reported by Klassen et al. [5], the full squares are those reported by Fregene [29], and the full line is all the data fitted in [24]. Source: modified from [24].

In the second method, the *G-value* was calculated based on the primary products, as described in [24]. The radiation yield of ferric ions in a Fricke solution can be expressed in terms of the radiation yields of the primary products due to radiolysis of the solution. Thus, the *G-values* were calculated using a fit of the *LET* values shown in figure 3 for 80 keV and ^{60}Co, both published by the ICRU 16 [35], and for ^{137}Cs, published by Meesungnoen et al. [36]. If the data are fitted using a first-order polynomial regression, the estimated *LET* value for ^{192}Ir is 1.28 keV. μm^{-1}, and if they are fitted with a second-order polynomial, the value is 1.237 keV. μm^{-1}. These values were used in the empirical formalism proposed by Meesungnoen et al. [36] in equation 5, to calculate the *G-value* in molecules per 100 eV for a given energy *x*:

$$G_x = \Sigma_{i=0}^{4} \alpha_i \times (Ln(LET))^i \qquad (5)$$

where the coefficients α_i (i = 0-4) are used to express the *LET* variations for radicals and for radiolysis of aqueous 0.4 M H_2SO_4 at room temperature. Table 2 presents the fitted coefficients for the aqueous 0.4 M H_2SO_4 at ambient temperature, as reported by Meesungnoen et al. [36].

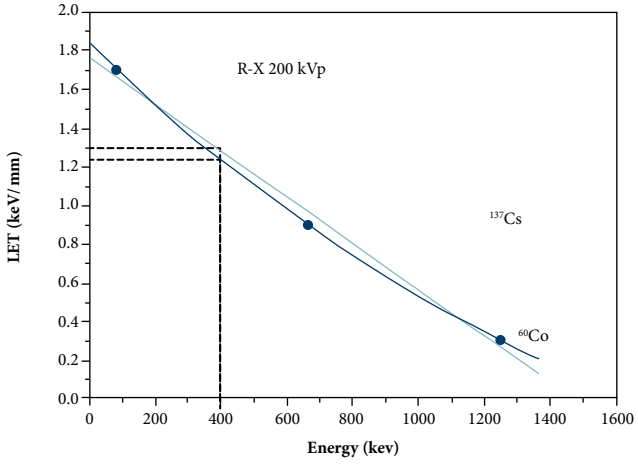

Figure 3. Interpolated LET value for the ^{192}Ir average energy using published data and two different curve fittings
Source: [24].

Table 2. Numerical values of the coefficients for the aqueous 0.4 M H2SO4

Radicals	Coefficients				
	α_0	α_1 (x10^{-2})	α_2 (x10^{-2})	α_3 (x10^{-2})	α_4 (x10^{-3})
$G_{H\cdot}$	3.601	-13.53	-5.974	-1.929	-4.979
$G_{OH\cdot}$	2.766	-18.80	-8.239	-2.127	-4.637
G_{H2O2}	0.8438	5.682	2.169	0.6284	1.988

Since the Fricke solution is 96% water by weight, the primary products produced by the radiation were mostly those of water. This process, though considered approximate, was extensively discussed by Klassen et al. [5], where it was assumed that the *G-values* for a Fricke solution behave in the same way as those for water.

The $G(Fe^{3+})$ obtained from the empirical formalism proposed by Meesungnoen et al. [36], based on primary products and *LET* values, were found to be 15.123 mol/100 eV (1.567 x10^{-6} mol.J^{-1}) and 15.144 mol/100 eV (1.569 x10^{-6} mol.J^{-1}) for the first and second-degree fits, respectively. This is rather close (within 1%) to the *G-value* determined using the published values from the literature.

In the third methodology the *G-value* determination was based on the NRC method, using polyethylene bags [25]. Briefly, this method consists of interpolating the G-values calculated for ^{60}Co and 250 kV X-rays for the average energy of ^{192}Ir (380 keV). In Salata et al. [13] the NRC methodology was used, but instead of the interpolating ^{60}Co and 250 kV to obtain the *G-value* for the ^{192}Ir energy, the *G-values* for 150 kV (effective energy of 68 keV), 250 kV (effective energy of 132 keV) and 300 kV (effective energy of 159 keV) were calculated using the air kerma measured using a calibrated ion chamber, and making it equivalent to the value absorbed to the Fricke solution, using a Monte Carlo calculated factor for this conversion. Instead of interpolations, as described by the NRC, the calculated $G(Fe^{3+})$ values were displayed in a graph. The line equation was used to determine the $G(Fe^{3+})$ for ^{192}Ir (380 keV). The measured *G-values* were 1.436 ± 0.002 µmol/J for 150 kV, 1.472 ± 0.002 µmol/J for 250 kV, and 1.497 ± 0.003 µmol/J for 300 kV. The used value of $G(Fe^{3+})$ for Co-60 (1.25 MeV) was 1,613 µmol/J, based on the literature [5].

The results for the $G(Fe^{3+})$ determination, based on the NRC method are shown in figure 4. The R-square of the fitted regression line between those *G-value* points was 0.991. Using the line equation, the calculate $G(Fe^{3+})$ for 380 KeV was 1.542 ± 0.015 µmol/J [13]. This value differs by 0.8% from $G(Fe^{3+})$ calculated using the energy-weighted published values, and 1.5% from $G(Fe^{3+})$ calculated using empirical formalism.

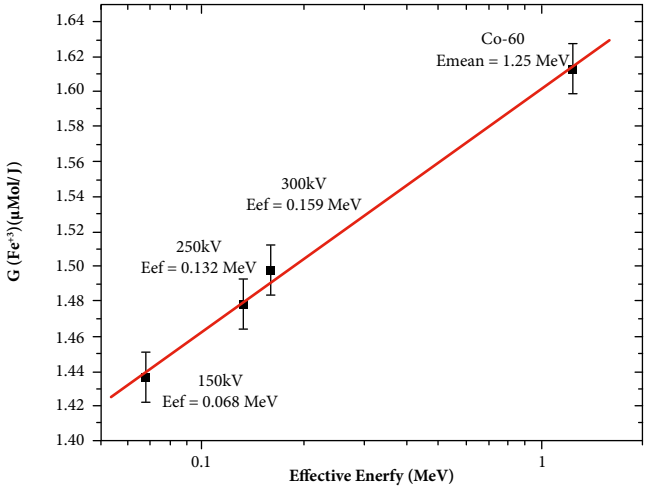

Figure 4. Values of $G(Fe^{3+})$ for different energies: 150 kV, 250 kV, 300 kV and ^{60}Co
Effective energy was used for all the X-ray qualities, but for Co-60, the mean energy was used. The error bars represent the Type A uncertainty

1.7. Measurements of absorbed dose to water

The results shown in figure 5 represent the average of three irradiations of Fricke solutions with two readings per irradiation per point and show the absorbed dose values ranging from 14.0 to 40.0 Gy, using the spherical vessel. The results from the cylindrical vessel are not shown, as they do not differ significantly from those presented in figure 5.

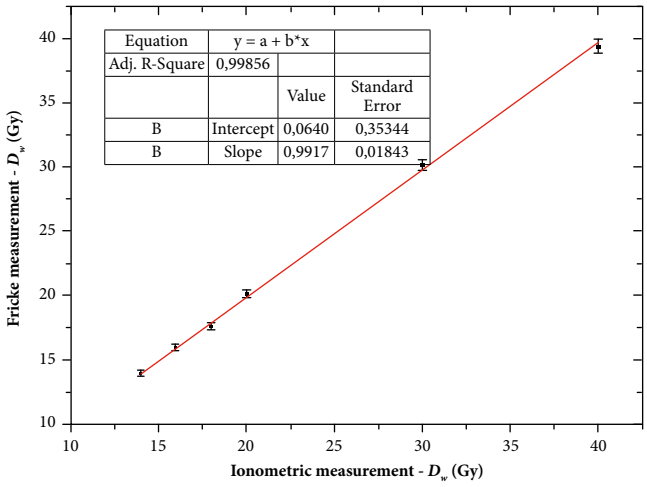

Figure 5. Absorbed dose to water values measured with Fricke dosimetry versus the nominal dose measured by a Farmer-type ionization chamber The X-axis represents the measured absorbed dose values with the ionization chamber and the Y-axis represents the measured absorbed dose values with the Fricke system with a total uncertainty of 1.4%, both for k = 1.

The results presented here are consequences of careful improvements in several aspects over 10 years, as follows:

Regarding the overall dimension of the irradiating vessel (by increasing the radial distance between the source and the solution, the uncertainty due to mechanical tolerances and the dose gradient across the solution were reduced);

» The use of a thermal bath and a calibrated thermistor in the spectrophotometer;

» The use of PMMA made the construction of the vessel easier and, as discussed earlier, has no measurable effect on the solutions;

» The cylindrical vessel is an improvement from the spherical vessel, making it easier to clean and fill with Fricke solution without creating bubbles. In addition, it allows two measurements for one irradiation, decreasing uncertainties as well.

1.8. Traceability to the international network of metrology validation

The results for both the *G-value* and the absorbed dose to water, using the Fricke dosimetry system of the two institutions, NRC and LCR, were comparable and published [14]. The two institutions have separately developed absorbed dose standards based on the Fricke dosimetry system. Both NRC and LCR developed different methodologies to determine the absorbed dose to Fricke solution. These differences include different ways of cleaning glassware and preparing the solution, and different vessel designs used for ^{192}Ir source irradiation. The main advantage of the NRC holder is that the D_w measurement is already measured at the recommended distance, 1 cm [20], while for the LCR vessel this distance is 2.7 cm, which requires an MC calculated factor to convert this measurement to 1 cm. This comparison was made at the NRC laboratory using an ^{192}Ir source. The NRC group has established a method to determine the $G(Fe^{3+})$ for ^{192}Ir based on an interpolation between *G-values* obtained at ^{60}Co and 250 kVp X-rays [18]. This measurement was repeated using the LCR Fricke solution to investigate possible systematic uncertainties. $G(Fe^{3+})$ for ^{60}Co and 250 kVp X-rays. Using the LCR Fricke system, an agreement was found with the NRC values within 0.5% and 1% for ^{60}Co and 250 kVp X-rays respectively. The standard uncertainty in the determination of $G(Fe^{3+})$ for ^{192}Ir was estimated to be 0.6%. For the comparison of absorbed dose measurements at the reference point for ^{192}Ir (1 cm depth in water, perpendicular to the seed long-axis), the ratio $D_w(NRC)/D_w(LCR)$ was found to be 1.011 with a combined standard uncertainty of 1.7%.

1.9. Uncertainty budget

For the nominal dose of 20 Gy, Table 3 [24] lists all the sources of uncertainties involved in the experimental procedure using Fricke dosimetry to measure absorbed dose to water. In general, the uncertainties are conservative, corresponding to the upper limits. The uncertainties in all quantities and correction factors in (4) are indicated. As a result, the overall combined uncertainty, as described in detail in Table 3, were significantly reduced to 1.4% for k = 1 compared to those reported earlier by Austerlitz et al. [8]

The type B uncertainties for the MC calculations were the most difficult cases to estimate and they are still unclear in several papers [36]-[44]. In a recent work Wulff et al. [42] have specifically treated this issue, taking into account the various contributions related to the systematic uncertainties that also exist in the present work, such as stopping powers, spectrum, photon cross sections and transport parameters. For this case the geometry sensitivity was also evaluated, and the differences were negligible. Although we have not performed a specific analysis for our geometry, the final value of 0.2% reported by Wulff et al. [42] was adopted here.

Table 3. Uncertainty budget in the determination of D_w using the Fricke solution [24].

Source of Uncertainty	Type A (%)	Type B (%)	Reference
Irradiation Procedure			
Dummy/real source position		0.1	
Transit time		0.016	
Solution Specification			
Molar extinction coefficient		0.35	[5]
Density	0.100	0.100	Manufacturer
Source-solution distance	0.01	0.02	Manufacturer
Reading Process			
Dose determination	0.48		Manufacturer
Cuvette-light path	0.05	0.06	Manufacturer
Instrument stability		0.10	
Instrument repeatability		0.10	
Wavelength bandwidth		0.01	[45]
Solution temperature	0.010	0.15	Manufacturer
Correction Factors			
G(Fe^{3+}) value		1.12	[28], [34], [46]
p_{wall}	0.3	0.2	
Volume averaging	0.2	0.2	[42]
k_{dd}	0.1	0.2	[42]
Dose conversion factor for Fricke to water f	0.2	0.2	[42]
Combined Standard Uncertainty (%)	1.42		
Expanded Uncertainty for k = 2.0 (%)	2.84		

The values shown in table 3 for the correction factors were based on the measurements for the spherical vessel, but as shown in table 2, those values are not significantly different from the values calculated for the cylindrical vessel.

2. Conclusion

Chemical dosimetry using a standard $FeSO_4$ solution is an interesting and reliable option as a standard for the quantity absorbed dose to water generated by HDR ^{192}Ir sources. The overall uncertainties involving the vessel dimensions, wall thicknesses, dose calculation, wall attenuation, UV light band, source anisotropy, *G-value* and source transit time were estimated to be less than 1.4% for $k = 1$.

Some characteristics of the device used for the Fricke solution must be considered: the wall material should be water equivalent and should not chemically react with the solution; it must be sealed, but easy to vert the solution from the vessel into a cuvette to be read by the spectrophotometer. LCR has been working on an adequate vessel during the past 10 years. The first vessel developed was water equivalent and the solution volume was irradiated only at the central ring resulting in a homogeneously irradiated solution. However, it was very difficult to fill with the solution without creating bubbles and to vert the solution into the cuvette. The current device is a cylindrical ring, in which the solution is disposed and has corrected those problems. However, one setback is the fact that the measurement reference point is 2.7 cm from the source. It was then necessary to calculate an MC correction factor to give the absorbed dose to water at the reference point $D_{w\,(r0,\theta0)}$ in the TG-43 formalism [20]). Now LCR is working on a very similar device of a cylindrical shape but is using a distance of 1 cm as the reference point from the source. These ongoing improvements, such as the source position being now calculated at the center of the ring, an easier way to fill the vessel with the Fricke solution, and an easier way to vert the solution into the cuvette of the device are very important in reducing the uncertainties of the Fricke dosimetry as an option for ^{192}Ir source calibration.

One of the key parameters used to determine the absorbed dose of the Fricke solution is the *G-value*. This parameter is crucial and can be defined as the number of molecules of Fe^{+3} produced per joule of energy absorbed in the solution. Different authors, using different methods, have determined this value but those data are either rather old or specifically have energies below that of ^{60}Co. The LCR group has used three methods to calculate this coefficient: ionometric, estimation of the energy-weighted G value from published values, and interpolations based on the NRC method. The values are consistent when compared with each other and differ by 1.5% at most. The NRC method is simple to use, requiring a PMMA support for the polyethylene bags, and the associated uncertainties are usually lower. The LCR group is performing more measurements for different energies using this method.

The outcomes of the LCR and NRC comparison demonstrate that the results obtained for absorbed dose to water using LCR and NRC methodologies are very similar, even considering the reported differences in their methodologies. These results are extremely important to reaffirm the use of Fricke solution as an actual primary standard for HDR brachytherapy ^{192}Ir source dosimetry. The use of an absorbed-dose-to-water standard for Ir-192 dosimetry will reduce the associated uncertainty on $D_{w\,(r0,\theta0)}$ and avoid the use of a calculation-based dose rate constant.

The obtained uncertainties for the determination of the absorbed dose to water using the Fricke dosimetry are lower

than those obtained using the standard protocols, the AAPM TG-43 Report [19], and its update [20]. This can be reflected in clinical practice, as the calculation of the dose delivered to the patients can be more accurate.

Beside the application of Fricke dosimetry for ^{192}Ir sources dosimetry, there are other studies using Fricke solution that have been developed by the LCR. One is the use of Fricke dosimetry for ^{137}Cs blood irradiator dosimetry using a specific phantom that was constructed and patented by the authors to perform these measurements [47], [48]. The other study tests the Fricke dosimeter properties as a potential system to be used in a postal dosimetry project for research irradiators [49]. In addition, the application of Fricke dosimetry for the determination of the absorbed dose to water for medium-energy X-ray beams was also studied and compared to the standard protocol TG 61 [50]. A new study also in progress concerns the use of Fricke dosimetry for the determination of the absorbed dose to water at linear accelerators. This work compares two different methods to determine the absorbed dose to water using Fricke dosimetry, opening up the possibility of using one of them as postal dosimetry [51].

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References

[1] O. Moussous, S. Khoudri, and M. Benguerba, "Characterization of a Fricke dosimeter at high energy photon and electron beams used in radiotherapy", *Australasian Physical and Engineering Sciences in Medicine*, vol. 34, no. 4, pp. 523-528, 2011, https://www.doi.org/10.1007/s13246-011-0093-1.

[2] J. Law and A. T. Redpath, "Measurement of ferric ion concentration in the Fricke dosemeter", *Physics in Medicine & Biology*, vol. 16, no. 3, pp. 531-532, 1971, https://www.doi.org/10.1088/0031-9155/16/3/419.

[3] J. Law and A. T. Redpath, "The measurement of low energy x-rays III: Ferrous sulphate G-values", *Physics in Medicine & Biology*, vol. 13, no. 3, pp. 371-382, 1968, https://www.doi.org/10.1088/0031-9155/13/3/304.

[4] R. K. Broszkiewicz and Z. Bulhak, "Errors in ferrous sulphate dosimetry", *Physics in Medicine & Biology*, vol. 15, no. 3, pp. 549-556, 1970, https://www.doi.org/10.1088/0031-9155/15/3/315.

[5] N. V. Klassen, K. R. Shortt, J. Seuntjens, and C. K. Ross, "Fricke dosimetry: The difference between G(Fe3+) for 60Co γ-rays and high-energy x-rays", *Physics in Medicine & Biology*, vol. 44, no. 7, pp. 1609-1624, 1999, https://www.doi.org/10.1088/0031-9155/44/7/303.

[6] "ISO/ASTM 51026: Practice for using the Fricke dosimetry system", 2015.

[7] E. M. Arango, A. Pickler, A. Mantuano, C. Salata, and C. E. de Almeida, "Feasibility study of the Fricke chemical dosimeter as an independent dosimetric system for the small animal radiation research platform (SARRP)", *Physica Medica: European Journal of Medical Physics*, vol. 71, no. March, pp. 168-175, 2020, https://www.doi.org/10.1016/j.ejmp.2020.03.006.

[8] C. Austerlitz *et al.*, "Determination of absorbed dose in water at the reference point D (r 0, θ0) for an ^{192}Ir HDR brachytherapy source using a Fricke system", *Medical Physics*, vol. 35, no. 12, pp. 5360-5365, Dec. 2008, https://www.doi.org/10.1118/1.2996178.

[9] A. Olszanski, N. V Klassen, C. K. Ross, and K. R. Shortt, "The IRS Fricke Dosimetry System", Ottawa, 2002.

[10] C. E. de Almeida *et al.*, "Standard absorbed dose to water for HDR brachytherapy sources with Fricke dosimetry", *IFMBE Proceedings*, vol. 25, no. 1, pp. 1055-1056, 2009, https://www.doi.org/10.1007/978-3-642-03474-9-296.

[11] L. Franco, S. Gavazzi, M. Coelho, and C. E. de Almeida, "Determination of the Fricke G Value for HDR ^{192}Ir Sources Using Ionometric Measurements", in Standards, applications and quality assurance in medical radiation dosimetry (IDOS), International Atomic Energy Agency, 2011.

[12] R. Ochoa, F. Gómez, I. H. Ferreira, F. Gutt, and C. E. de Almeida, "Design of a phantom for the quality control of high dose rate ^{192}Ir source used in brachytherapy", *Radiotherapy and Oncology*, vol. 82, no. 2, pp. 222-228, 2007, https://www.doi.org/10.1016/j.radonc.2007.01.005.

[13] C. Salata, M. David, P. Rosado, and C. de Almeida, "SU-F-BRA-10: Fricke Dosimetry: Determination of the G-Value for Ir-192 Energy Based On the NRC Metho-

dology", *Medical Physics*, vol. 42, no. 6Part26, pp. 3535-3535, 2015, https://www.doi.org/10.1118/1.4925221.

[14] C. Salata *et al.*, "Validating Fricke dosimetry for the measurement of absorbed dose to water for HDR ^{192}Ir brachytherapy: A comparison between primary standards of the LCR, Brazil, and the NRC, Canada", *Physics in Medicine & Biology*, vol. 63, no. 8, 2018, https://www.doi.org/10.1088/1361-6560/aab2b8.

[15] C. Salata *et al.*, "SU-F-19A-02: Comparison of Absorbed Dose to Water Standards for HDR Ir-192 Brachytherapy Between the LCR, Brazil and NRC, Canada", *Medical Physics*, vol. 41, no. 6Part22, pp. 388-388, 2014, https://www.doi.org/10.1118/1.4889028.

[16] C. B. V. Andrade *et al.*, "Evaluation of radiotherapy and chemotherapy effects in bone matrix using X-ray microfluorescence", *Radiation Physics and Chemistry*, vol. 95, 2014, https://www.doi.org/10.1016/j.radphyschem.2013.04.031.

[17] P. H. Rosado et al., "Determination of the absorbed dose to water for medium-energy x-ray beams using Fricke dosimetry," *Medical Physics*, 2020, https://doi.org/10.1002/mp.14473.

[18] I. El Gamal, C. Cojocaru, E. Mainegra-Hing, and M. McEwen, "The Fricke dosimeter as an absorbed dose to water primary standard for Ir-192 brachytherapy", *Physics in Medicine & Biology*, vol. 60, no. 11, pp. 4481-95, 2015, https://www.doi.org/10.1088/0031-9155/60/11/4481.

[19] R. Nath, L. L. Anderson, G. Luxton, K. A. Weaver, J. F. Williamson, and A. S. Meigooni, "Dosimetry of interstitial brachytherapy sources: Recommendations of the AAPM Radiation Therapy Committee Task Group No. 43", *Medical Physics*, vol. 22, no. 2, pp. 209-234, 1995, https://www.doi.org/10.1118/1.597458.

[20] M. J. Rivard *et al.*, "Update of AAPM Task Group No. 43 Report: A revised AAPM protocol for brachytherapy dose calculations", *Medical Physics*, vol. 31, no. 3, pp. 633-674, 2004, https://www.doi.org/10.1118/1.1646040.

[21] A. Sarfehnia, K. Stewart, and J. Seuntjens, "An absorbed dose to water standard for HDR ^{192}Ir brachytherapy sources based on water calorimetry: numerical and experimental proof-of-principle", *Medical Physics*, vol. 34, no. 12. United States, pp. 4957-4961, Dec. 2007, https://www.doi.org/10.1118/1.2815941.

[22] A. Sarfehnia and J. Seuntjens, "Development of a water calorimetry-based standard for absorbed dose to water in HDR ^{192}Ir brachytherapy", *Medical Physics*, vol. 37, no. 4, pp. 1914-1923, 2010, https://www.doi.org/10.1118/1.3366254.

[23] A. Sarfehnia, I. Kawrakow, and J. Seuntjens, "Direct measurement of absorbed dose to water in HDR ^{192}Ir brachytherapy: Water calorimetry, ionization chamber, Gafchromic film, and TG-43", *Medical Physics*, vol. 37, no. 4, pp. 1924-1932, 2010, https://www.doi.org/10.1118/1.3352685.

[24] C. E. de Almeida *et al.*, "A Feasibility Study of Fricke Dosimetry as an Absorbed Dose to Water Standard for ^{192}Ir HDR Sources", *PLoS One*, vol. 9, no. 12, p. e115155, 2014, https://www.doi.org/10.1371/journal.pone.0115155.

[25] M. McEwen, I. El Gamal, E. Mainegra-Hing, and C. Cojocaru, "Determination of the radiation chemical yield (G) for the Fricke chemical dosimetry system in photon and electron beams", National Research Council of Canada, 2014. https://www.doi.org/10.4224/23002718.

[26] A. Palm and O. Mattsson, "Influence of sulphuric acid contaminants on Fricke dosimetry", *Physics in Medicine & Biology*, vol. 45, no. 9, 2000, https://www.doi.org/10.1088/0031-9155/45/9/403.

[27] M. Mosher, "Organic Chemistry. Sixth edition (Morrison, Robert Thornton; Boyd, Robert Neilson)", *Journal of Chemical Education*, vol. 69, no. 11, p. A305, Nov. 1992, https://www.doi.org/10.1021/ed069pa305.2.

[28] A. Pickler *et al.*, "Effects of chemical reactions between Fricke solution and PMMA vessel", *Submiss. Process.*

[29] A. O. Fregene, "Calibration of the ferrous sulfate dosimeter by ionometric and calorimetric methods for radiations of a wide range of energy", *Radiation Research*, vol. 31, no. 2, pp. 256-72, 1967, [Online]. Available: http://www.ncbi.nlm.nih.gov/pubmed/6025862.

[30] E. Cottens, A. Janssens, G. Eggermont, and R. Jacobs, *Absorbed dose calorimetry with a graphite calorimeter, and G-value determinations for the Fricke dose meter in high-energy electron beams.* Viena, International Atomic Energy Agency, 1981.

[31] OECD Nuclear Energy Agency., *Penelope : a code system for Monte Carlo simulation of electron and photon transport.* Nuclear Energy Agency, 2001.

[32] J. Borg and D. W. Rogers, "Spectra and air-kerma strength for encapsulated ^{192}Ir sources", *Medical Physics*, vol. 26, no. 11, pp. 2441-4, Nov. 1999, https://www.doi.org/10.1118/1.598763.

[33] C.-M. Ma and A. E. Nahum, "Dose conversion and wall correction factors for Fricke dosimetry in high-energy photon beams: analytical model and Monte Carlo calculations", *Physics in Medicine & Biology*, vol. 38, no. 1, pp. 93-114, Jan. 1993, https://www.doi.org/10.1088/0031-9155/38/1/007.

[34] C. Ma, D. W. O. Rogers, K. R. Shortt, C. K. Ross, A. E. Nahum, and A. F. Bielajew, "Wall-correction and absorbed-dose conversion factors for Fricke dosimetry: Monte Carlo calculations and measurements", *Medical Physics*, vol. 20, no. 2, pp. 283-292, Mar. 1993, https://www.doi.org/10.1118/1.597128.

[35] "Report 16", *Journal of the International Commission on Radiation Units and Measurements*, vol. os9, no. 1, p. NP. 1970, https://www.doi.org/10.1093/jicru/os9.1.report16.

[36] J. Meesungnoen, M. Benrahmoune, A. Filali-Mouhim, S. Mankhetkorn, and J.-P. Jay-Gerin, " Monte Carlo Calculation of the Primary Radical and Molecular Yields of Liquid Water Radiolysis in the Linear Energy Transfer Range 0.3-6.5 keV/μm: Application to 137 Cs Gamma Rays 1", *Radiation Research*, vol. 155, no. 2, pp. 269-278, Feb. 2001, https://www.doi.org/10.1667/0033-7587(2001)155[0269:mccotp]2.0.co;2.

[37] T. H. Kirby, W. F. Hanson, and D. A. Johnston, "Uncertainty analysis of absorbed dose calculations from thermoluminescence dosimeters", *Medical Physics*, vol. 19, no. 6, pp. 1427-1433, Nov. 1992, https://www.doi.org/10.1118/1.596797.

[38] G. M. Mahmoud and R. S. Hegazy, "Comparison of GUM and Monte Carlo methods for the uncertainty estimation in hardness measurements", *International Journal of Metrology and Quality Engineering*, vol. 8, p. 14, May 2017, https://www.doi.org/10.1051/ijmqe/2017014.

[39] I. Farrance and R. Frenkel, "Uncertainty in measurement: a review of monte carlo simulation using microsoft excel for the calculation of uncertainties through functional relationships, including uncertainties in empirically derived constants", *The Clinical Biochemist Reviews*, vol. 35, no. 1, pp. 37-61, Feb. 2014, [Online]. Available: http://www.ncbi.nlm.nih.gov/pubmed/24659835.

[40] C.-M. Ma *et al.*, "Effect of statistical uncertainties on Monte Carlo treatment planning", *Physics in Medicine & Biology*, vol. 50, no. 5, pp. 891-907, Mar. 2005, https://www.doi.org/10.1088/0031-9155/50/5/013.

41] B. Thomadsen *et al.*, "93 TG-138 REPORT: UNCERTAINTIES IN PHOTON EMITTING BRACHYTHERAPY SOURCE DOSIMETRY", *Radiotherapy and Oncology*, vol. 103, p. S38, May 2012, https://www.doi.org/10.1016/S0167-8140(12)72060-1.

[42] J. Wulff, J. T. Heverhagen, K. Zink, and I. Kawrakow, "Investigation of systematic uncertainties in Monte Carlo-calculated beam quality correction factors", *Physics in Medicine & Biology*, vol. 55, no. 16, pp. 4481-4493, Jul. 2010, https://www.doi.org/10.1088/0031-9155/55/16/s04.

[43] P. Castro *et al.*, "Study of the uncertainty in the determination of the absorbed dose to water during external beam radiotherapy calibration", *Journal of Applied Clinical Medical Physics*, vol. 9, no. 1, pp. 70-86, Dec. 2008, https://www.doi.org/10.1120/jacmp.v9i1.2676.

[44] "Joint Committee for Guides in Metrology (JCGM) 2008 Report 100: Evaluation of Measurement Data-Guide to the Expression of Uncertainty in Measurement" [Online]. Available: https://www.bipm.org/utils/common/documents/jcgm/JCGM_100_2008_E.pdf.

[45] R. J. Shalek and C. E. Smith, "CHEMICAL DOSIMETRY FOR THE MEASUREMENT OF HIGH-ENERGY PHOTONS AND ELECTRONS", *Annals of the New York Academy of Sciences*, vol. 161, no. 1, pp. 44-62, 1969, https://www.doi.org/10.1111/j.1749-6632.1969.tb34040.x.

[46] K. E. Stump, L. A. DeWerd, J. A. Micka, and D. R. Anderson, "Calibration of new high dose rate ^{192}Ir sources", *Medical Physics*, vol. 29, no. 7, pp. 1483-1488, 2002, https://www.doi.org/10.1118/1.1487860.

[47] A. Mantuano *et al.*, "Technical Note: Fricke dosimetry for blood irradiators," Medical Physics, 2020, https://doi.org/10.1002/mp.14487

[48] A. Mantuano, C. Salata, M. G. David, C. L. Mota, G. J. De Amorim, and L. A. G. Magalhães, "Fantoma para Irradiadores de Sangue", BR 10 2018 073239 0, 2018.

[49] A. Mantuano, C. L. Mota, C. Salata, A. Pickler, L. A. G. Magalhães, and C. E. de Almeida, "A pilot study of a postal dosimetry system using Fricke dosimeter for research irradiators purpose", *Submiss. Process*.

[50] C. M. Ma *et al.*, "AAPM protocol for 40-300 kV x-ray beam dosimetry in radiotherapy and radiobiology", John Wiley and Sons Ltd, 2001. https://www.doi.org/10.1118/1.1374247.

[51] C. Salata *et al.*, "Determination of Absorbed Dose to Water Using Fricke Dosimetry for (6) MV Photons Beams", *Medical Physics*, vol. 47, no. 6, pp. e255-e880, 2020, https://doi.org/10.1002/mp.14316.