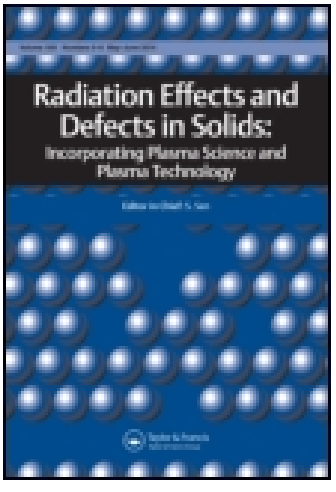




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# Characterization of ferric ions diffusion in Fricke gel dosimeters by using inverse problem techniques

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# Characterization of ferric ions diffusion in Fricke gel dosimeters by using inverse problem techniques

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Diffusion of ferric ions in ferrous sulfate (Fricke) gels represents one of the main drawbacks of some radiation detectors, such as Fricke gel dosimeters. In practice, this disadvantage can be overcome by prompt dosimeter analysis, and constraining strongly the time between irradiation and analysis, implementing special dedicated protocols aimed at minimizing signal blurring due to diffusion effects. This work presents a novel analytic modeling and numerical calculation approach of diffusion coefficients in Fricke gel radiation sensitive materials. Samples are optically analyzed by means of visible light transmission measurements by capturing images with a charge-coupled device camera provided with a monochromatic filter corresponding to the XO-infused Fricke solution absorbance peak. Dose distributions in Fricke gels are suitably delivered by assessing specific initial conditions further studied by periodical sample image acquisitions. Diffusion coefficient calculations were performed using a set of computational algorithms based on inverse problem formulation. Although 1D approaches to the diffusion equation might provide estimations of the diffusion coefficient, it should be calculated in the 2D framework due to the intrinsic bi-dimensional characteristics of Fricke gel layers here considered as radiation dosimeters. Thus a suitable 2D diffusion model capable of determining diffusion coefficients was developed by fitting the obtained algorithm numerical solutions with the corresponding experimental data. Comparisons were performed by introducing an appropriate functional in order to analyze both experimental and numerical values. Solutions to the second-order diffusion equation are calculated in the framework of a dedicated method that incorporates finite element method. Moreover, optimized solutions can be attained by gradient-type minimization algorithms. Knowledge about diffusion coefficient for a Fricke gel radiation detector is helpful in accounting for effects regarding elapsed time between dosimeter irradiation and further analysis. Hence, corrections might be included in standard dependence of optical density differences and actual, non-diffused, absorbed dose distributions. The obtained values for ferric ion diffusion coefficient are around $0.65\,\mathrm{mm^2\,h^{-1}}$, being in good agreement with previous works corresponding to similar Fricke gel dosimeter compositions. Therefore, more accurate 2D and 3D dose mapping might be attained, thus constituting valuable improvements in Fricke gel dosimetry, and parallely a high precision method of diffusion modeling and calculation has been developed.

**Keywords:** Fricke gel dosimetry; ferric ions diffusion; finite elements modeling; radiotherapy

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## 1. Introduction

Due to the introduction of modern radiotherapy techniques, such as conformal radiotherapy or Intensity Modulated Radiation Therapy (IMRT), there is an increasing need for accurate 3D dosimetry techniques for dose verification. In order to achieve precise 3D dose verification for modern radiotherapy treatments, the development and improvement of integrating dosimeters with enough precision and resolution in all dimensions are necessary. Traditional dosimeters such as ionization chamber, thermoluminescent dosimeter or film dosimeters do not satisfy the requirements for 3D tissue-equivalent dosimetry (*1*). On the other hand, gel dosimeters appear as a valuable and promising tool for 3D dose verification systems. There are two main types of gels used for dosimetric application: Fricke gels and polymer gels. The supposed advantage of polymer gels is that they do not diffuse significantly after irradiation, while this represents the main disadvantage of Fricke gel dosimeters. However, due to a more complicated elaboration process as well as greater costs, polymer gels might be less convenient than Fricke gels. Fricke gels can be analyzed either by nuclear magnetic resonance (NMR) (*2*) or by optical systems, which are economically largely more convenient. In order to optimize the optical analysis method, a novel technique employing thin Fricke gel dosimeter layers of suitable shapes was earlier proposed (*3*, *4*).

The main reaction of Fricke gels caused by radiation is the oxidation of ferrous ($Fe2^+$) ions into ferric ($Fe3^+$) ions. In addition, the $Fe3^+$ yield is correlated with the absorbed dose. A gel matrix is used to fix spatially the ferrous sulfate solution, achieving better spatial resolution and slowing down the movement of produced $Fe3^+$ ions. However, Fricke gel dosimeters are susceptible to a non-negligible $Fe3^+$ ion diffusion effect after irradiation, which alters significantly the dose spatial distribution. Actually, diffusion is a well-known effect in Fricke gel dosimeters (*3*–*6*). Previous works have studied the diffusion effect mainly using magnetic nuclear resonance imaging methods (*5*, *7*, *8*).

Fricke gels infused with Xylenol Orange (XO) in the form of thin layers can be suitably optically analyzed (*3*, *4*, *6*, *9*, *10*). The analysis method consists basically of visible light transmission measurements through the thin dosimeter layers. The XO compound changes the radiochromic Fricke gel properties. The optical density difference, between before and after irradiation, can be proportionally correlated to the $Fe3^+$ yield, therefore it results proportional to the absorbed dose as well (*3*, *4*, *6*, *10*). Previous works have shown that dose distribution degradation, due to $Fe3^+$ diffusion, is significant beyond some tens of minutes after irradiation (*5*).

Diffusion is a convolution process. There is a correlation between the concentration distribution at a certain time $t$ and the initial distribution (at time $t = 0$). As a first approximation, this correlation can be considered as a Gaussian kernel convolution; therefore, the so obtained diffusion coefficient represents the average distance that ferric ions diffuse. A full description of the $Fe3^+$ diffusion effect should be obtained from a 3D solution of the diffusion equation taking into account, also, the steepness of the concentration distribution (*11*).

Modern radiotherapy techniques, such as IMRT and stereotactic modalities, usually involve high-gradient dose distributions; therefore, dose gradient dependency is of particular importance in employing Fricke gel dosimetry. Then, it becomes necessary to look for some strategy in order to avoid significant $Fe3^+$ diffusion effects; diffusion effect corrections may be performed by deconvolution techniques. Thereafter, it might be possible to achieve more accurate dose distributions by means of Fricke gel dosimeters; once diffusion coefficient $D$ is determined for further deconvolution by employing dedicated computer algorithms accounting for ferric ion diffusion within the elapsed time ($t$).

The impact of the concentrations of the different components on the diffusion coefficient and dose resolution in standard gelatine Fricke gels was previously studied (*12*). The effect of increasing the gelatine concentration showed no significant differences in the diffusion properties,

while increasing the $Fe2^{+}$ concentration from 0.5 to 1.0 mM did not change the diffusion effect, significantly and pH values between 1 and 2 did not seem to alter the diffusion of $Fe3^{+}$ ions in the gel.

The present study is dedicated to the determination of the diffusion coefficient $D$ of non-conventional Fricke gel dosimeters, which are suitably elaborated in the form of thin layers that are also XO-infused. The adopted Fricke gel layer dosimeter composition and elaboration procedure have been described in previous works (*3*, *4*, *6*, *9*). Fricke gel dosimeter layers of different shapes were prepared and irradiated with photon (18 MV) and electron (12 MeV) beams from a linear accelerator (Varian 2100C) employing adequate irradiation configurations in order to obtain convenient initial dose distributions within the dosimeters. The dosimeters were systematically analyzed, by means of visible light transmission images, several times after irradiation for the determination of the diffusion properties of this kind of dosimeters implementing novel mathematical framework of inverse problem based on finite elements approaches.



## 2. Material and methods

The Fricke gel layer dosimeters (3 mm thick) were manufactured following the preparation protocol described previously (*4*, *6*, *9*).

Hence, Fricke gel dosimeter layers are elaborated, essentially, having two different shapes: rectangular $120 \times 60\,mm^2$, and square, $120 \times 120\,mm^2$.

The samples were irradiated in different ways. The rectangular set of dosimeters was irradiated with an 18 MV photon beam from a linear accelerator (Varian 2100C, Varian®). The dosimeters were carefully shielded from the $50 \times 50\,mm^2$ photon beam by employing suitable 50-mm-thick cerrobend blocks. Therefore, one half of this group was irradiated in such a way to produce a rectangular ($30 \times 20\,mm^2$) initial dose distribution, while the other half was irradiated producing a circular (30 mm diameter) initial dose distribution. The corresponding initial dose distributions are shown in Figure 1.

The set of square dosimeters were irradiated with a 12 MeV electron beam from the same linear accelerator but in this case dedicated shielding cerrobend blocks (30 mm thick) were used to produce a narrow beam by means of a 1 mm circular hole at the center of the block. This suitable shielding configuration would produce an almost punctual (1 mm diameter) initial dose distribution in order to mimic Dirac delta initial conditions, as shown in Figure 2.

As mentioned earlier, the optical analysis method has been already widely described in previous works (*3*, *4*, *6*, *9*). However, a brief description of the method is presented here. The method is based on visible light transmittance imaging through the dosimeters, which is detected just before and suitably after irradiation. The dosimetric gel is inserted in properly designed containers composed of two transparent Perspex sheets held by a frame. Dosimeters can be manufactured having different shapes depending on the convenience. In order to perform optical

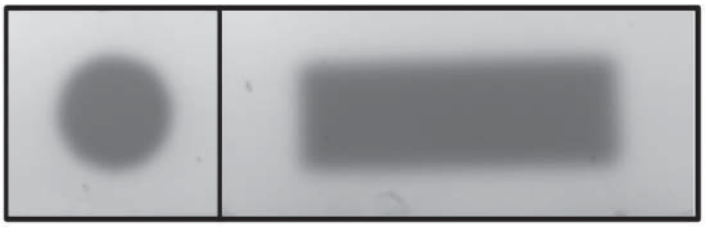

Figure 1. Transmittance (585 nm) images (30 min after irradiation) within the dosimeters. On the left: 30 mm diameter circular shape, and on the right a $30 \times 50\,mm^2$ rectangular shape.

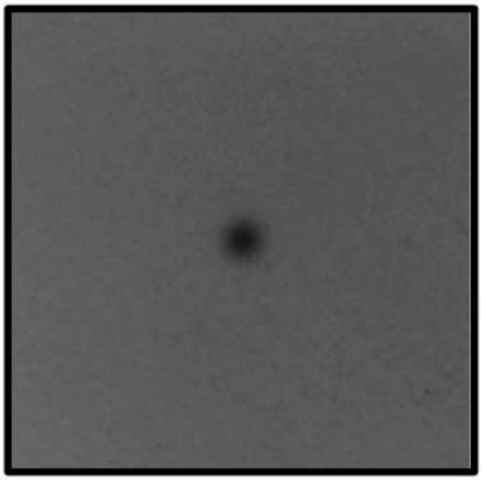

Figure 2. Transmittance (585 nm) images (45 min after irradiation) within the square dosimeter.



transmittance analysis, gel dosimeters are in the form of thin (3 mm) layers and they are placed on a plane and homogeneous illuminator. The images are detected by means of a high resolution charge-coupled device camera, which is supplied with a suitable optical filter (around 585 nm). The acquired images are processed and analyzed with a dedicated software *AQUILES v. 3.0* (MATLAB® supported; license MathWorks 3407-8985-4332-9223-7918). The images are first converted in Grey Level (GL) matrices and then analyzed in order to obtain the optical density difference ($\Delta$OD) distribution within the selected region of interest (ROI) defined by the user.

According to the Boltzmann main radiation equation, it is possible to demonstrate the suitability of approximating light fluence in this case by means of the Bouger–Lambert–Beer law (*6*, *13*). In this scenario, the employed optical analysis method can be mainly described by the following equation:

$$\Delta \mathrm{OD} = \mathrm{OD}^{\mathrm{After}} - \mathrm{OD}^{\mathrm{Before}} = \log_{10}\left(\frac{\mathrm{GL}^{\mathrm{Before}}}{\mathrm{GL}^{\mathrm{After}}}\right), \tag{1}$$

where 'Before' and 'After' stand for transmittance measurements carried out before and after irradiation, respectively.

The transmittance images are directly read and interpreted by the software and therefore the $\Delta$OD values are automatically calculated providing 1D (profiles), 2D (surfaces) and 3D (3D reconstructions from piled up single dosimeter layers) (*9*) information.

### 2.1. *Inverse problem technique*

In order to estimate the diffusion coefficient $D$, an inverse problem technique is proposed. Strictly, the probability distribution function $P$ represents the solution of the problem:

$$\nabla^2 P - \frac{1}{D}\frac{\partial P}{\partial t} = 0 \quad \text{in } \Omega \times (0, T), \tag{2}$$

$$\nu \cdot \nabla P = 0 \quad \text{in } \delta\Omega \times (0, T), \tag{3}$$

$$P(x, t = 0) = P^0(x) \quad \text{in } \Omega \tag{4}$$

for any choice of the parameter $D$. In this way, the diffusion coefficient is treated now as a fitting parameter which allows solutions optimization. Here, $\Omega$ represents the ROI, $\partial\Omega$ its boundary and $\nu$ the corresponding outward normal vector. The initial condition $P^0(x)$ is considered as the first optical transmittance acquired image.

Mathematically, the inverse problem can be established as: `find a parameter` $D$ `able to generate data P that best match the available (experimental) information over time` $0 \leq t \leq T$. For these purposes, objective function $J$ is constructed by

$$J(P;D) = \frac{1}{2}\int_0^T \int_\Omega (P(x,t) - \hat{P}(x,t))^2 \xi(t)\, \mathrm{d}x\, \mathrm{d}t, \tag{5}$$

which gives a notion of distance between the real data $\hat{P}(x,t)$ and the solution of the partial differential equation (PDE) $P(x,t)$ for any value of the parameter $D$. Experimental data (optical transmission images of Fricke gel samples) are available only for specific times $t_i$ in the interval $[0,T]$. Thus, the $\xi(t)$ function is defined as

$$\xi(t) = \sum_{i=1}^{n} M\, \mathrm{e}^{-M(t-t_i)^2}, \tag{6}$$

which is a characteristic function of $[0,T]$. With an adequate large value of $M$, $\xi(t_i + \mathrm{d}t) \approx 0$ and $\xi(t_i) = M$, allowing the calculation $J$ for the experimental data. For the mathematical formulation, an operator $E$ is defined such that

$$E(P,D) = \begin{bmatrix} \int_0^T \int_\Omega \left[\frac{\partial P}{\partial t}\lambda + D\nabla P \cdot \nabla\lambda\right]^2 \mathrm{d}x\, \mathrm{d}t \\ P(x,t=0) - P^0(x) \end{bmatrix}, \tag{7}$$

and the weak variational formulation of Equations (2)–(4): $E(P;D) = 0$.

The parameter that best matches the experimental information with the generated data provided by the direct problem can be computed by solving a PDE-constrained optimization problem, that is, by minimizing:

$$\text{minimize} \quad J(P;D), \tag{8}$$

$$\text{subjected to} \quad E(P,D) = 0, \tag{9}$$

$$D \in \mathcal{U}_{\text{ad}}, \tag{10}$$

where $\mathcal{U}_{\text{ad}}$ denotes the set of admissible values of $D$. In the ferric ion diffusion case, $\mathcal{U}_{\text{ad}}$ should be a subset of $(0,\infty)$. Notice that a solution $(P,D)$ must satisfy the constraint $E(P,D) = 0$, which constitutes the direct problem.

A dedicated MATLAB routine was developed and implemented to compute the weak solution of Equation (7) by using the finite elements method so that the optimization problem Equation (8) is solved by using a Trust Region Reflective method, by means of the built-in MATLAB function *fmincon*. For this purpose, the derivative of the function $J$ is computed using the adjoint method. This approach is much cheaper, computationally, than the sensitivity approach in which the direct problem is solved many times per iteration. More details may be found in specialized literatures (*14–16*).

Several inaccuracy sources are associated with diffusion coefficient calculation. Assuming that variables contributing to $D$ errors are independent, the overall uncertainty in $D$ can be determined by means of the usual propagation model as follows:

$$\sigma_D^2 = \sigma_{\text{Position}}^2 + \sigma_{\text{Noise}}^2 + \sigma_{\text{Num}}^2, \tag{11}$$

where $\sigma_{\text{Position}}$ is due to sample positioning in the optical transmission measurement instrument, $\sigma_{\text{Noise}}$ accounts for inherent noise in acquired images and $\sigma_{\text{Num}}$ represents the numerical calculation error.

The experimental data are used as the input of a high-level algorithm. Dedicated computational routines are implemented in order to allow automatic ROI's centering, minimizing possible discrepancy in sample position. Due to the high performance over all simulation processes, numerical errors can be considered negligible. Always, the obtained diffusion coefficient's overall uncertainties were less than 2% of the corresponding *D* value.

## 3. Results

Visible light transmittance measurements of XO-infused Fricke gel layer dosimeters were carried out just before and periodically after irradiation in order to obtain the dose distribution for several times after irradiation. Optical density difference profiles and surfaces were calculated by means of *AQUILES v. 3.0* as shown in Figures 3 and 4, respectively.

In order to traduce the input of the optical transmittance images of the Fricke gel samples, the developed software makes a special triangular grid of experimental data, as shown in Figure 5. The original meshing method is capable of automatically resizing triangles according to gradient changes along the image. Furthermore, this algorithm could be extended to volumetric information tetrahedron grids. A resume of the obtained *D* values is shown in Table 1.

In order to point out the diffusion effect in a clinical case, quality assessment measurements were carried out for a typical IMRT field. Figure 6 reports the transmittance images of the irradiated Fricke gel dosimeter layers. The images were taken at two different times: 45 min

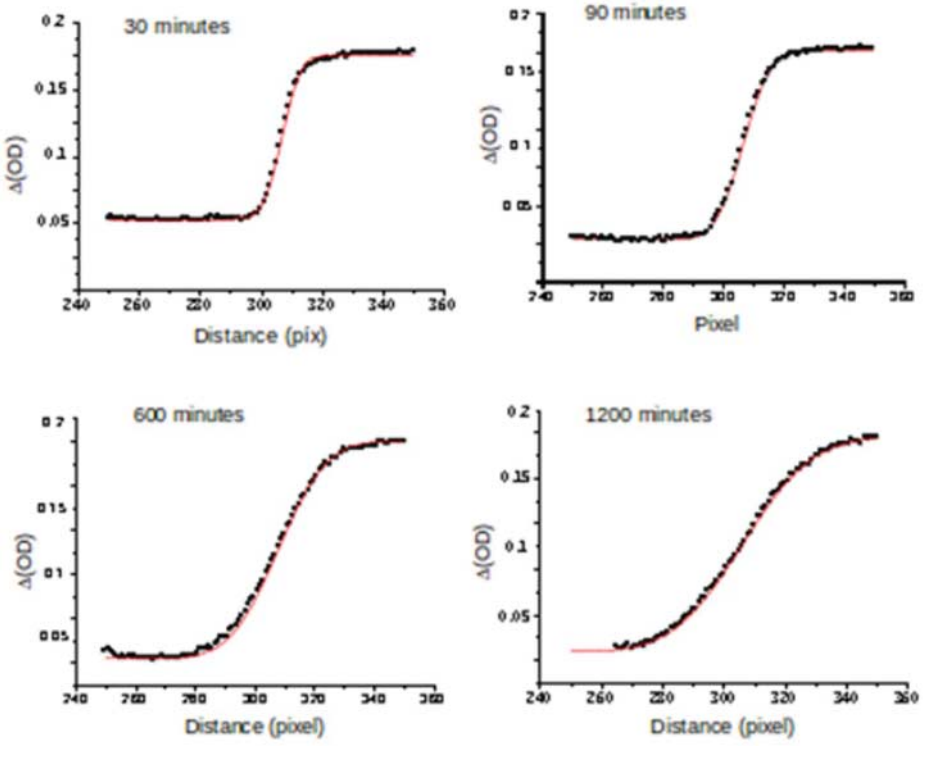


Figure 3. Sequence of some optical density differences ΔOD profiles and fittings (red solid lines) at several times after irradiation corresponding to the rectangular initial distribution. Top on the left: 30 min after, top on right: 90 min after, bottom on the left: 600 min after, bottom on the right: 1200 min after.

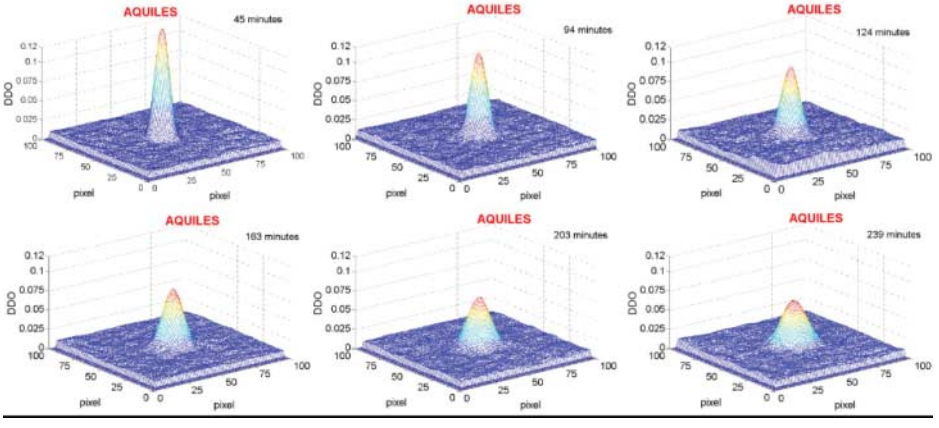


Figure 4. Sequence of optical density differences (ΔOD) surfaces for several times after irradiation. Starting from up-left (45 min after) to bottom-right (239 min after).

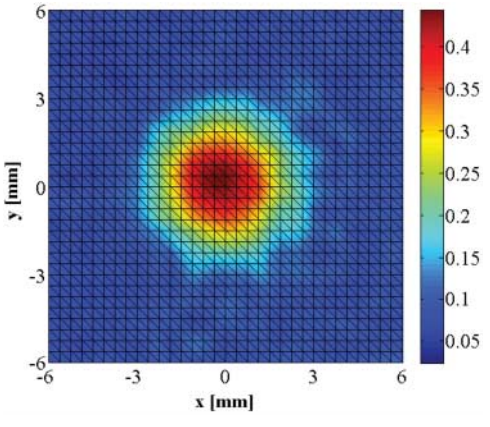


Figure 5. Triangular grid trace over corresponding ROI of optical transmission signal (in arbitrary units).

Table 1. Obtained *D* values for each initial dose distribution.

| Set of dosimeters | Initial dose distribution shape | *D* value [$mm^2\ h^{-1}$] |
|---|---|---|
| Rectangular | Circular | $0.68 \pm 0.02$ |
| Rectangular | Rectangular | $0.65 \pm 0.02$ |
| Square | Point-like | $0.65 \pm 0.01$ |

after irradiation and 150 min after irradiation. In Figure 7 profiles are presented, together with ionization chamber reference measurements.

## 4. Discussion

Although the linear approach presented in previous works is a simpler implementation, it takes into account only a single profile of information. As is known, diffusion phenomenon depends on the concentration of ferric ions in the surroundings, as remarked in the preceding sections.

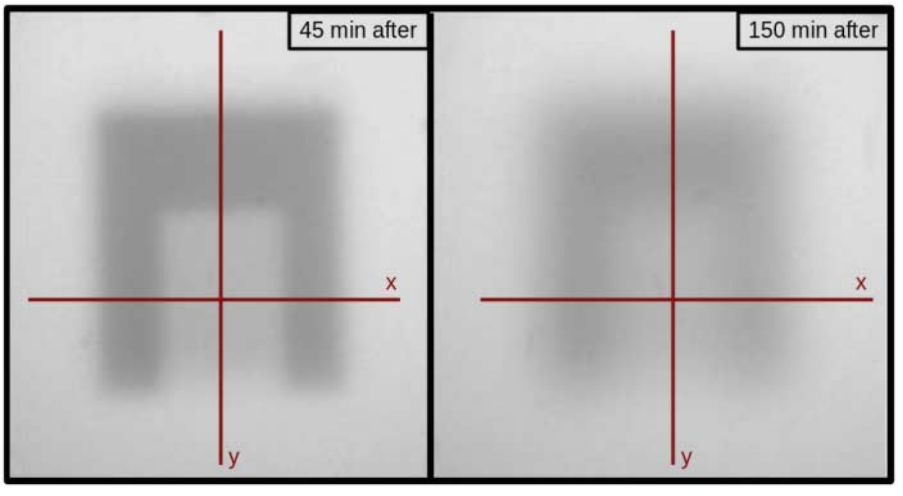


Figure 6. Transmittance (585 nm) images for the intensity modulated test field.

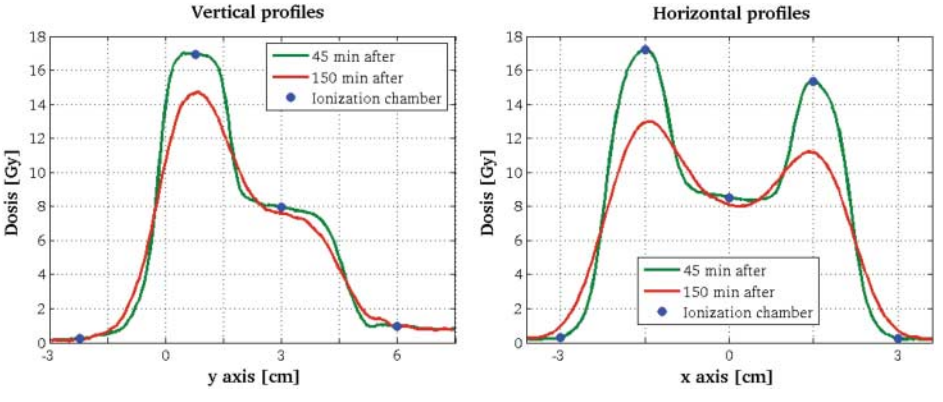


Figure 7. Absorbed dose distribution profiles for the intensity modulated test field. Corresponding uncertainties are around 2%.

Moreover, due to the inherent geometry of the thin layers technique of Fricke gel dosimetry, it should be natural to compute the diffusion coefficient by means of a bi-dimensional approach.

In this sense, the proposed approach based on inverse problem techniques proved to be a more reliable and appropriate strategy for attaining accurate values of the diffusion coefficient *D*. Besides, the inverse problem technique has a robust theoretical background.

After performing several tests with IMRT fields, analogous to the example reported in Figures 6 and 7, a range was established for selecting the optimal time elapsed between irradiation and optical analysis of Fricke gel dosimeter layers. Actually, durations within the range of 30–50 min after sample irradiation seem to be a good balance, compromising good enough performance and allowing to implement feasible procedures in practice.

As reported in Figure 7, it is highlighted that the choice of 45 min for the time elapsed between the irradiation and imaging of Fricke gel dosimeter layers appears suitable, in accordance with the reference values obtained from ionization chamber measurements at different positions within the IMRT field. Even considering the inherent complexity of IMRT fields, it is noticeable that excellent agreements were found between Fricke gel and ionization chamber measurements for all positions where comparisons were performed. On the other hand as shown

in Figure 7, it is clear that spatial resolution of dose distribution suffers significant degradation when samples are imaged at a longer time after irradiation.

It might be pointed out that once a protocol for the imaging procedure is implemented, it should be considered that for practical features the starting point would be conveniently established as the moment of sample imaging unlike the irradiation time. In fact, properties of invariance of diffusion equation allow the possibility of determining the diffusion coefficient by translation of time origin, which is actually not relevant from a mathematical point of view if external conditions remain unchanged.

Finally, Monte Carlo simulations performed to check tissue-equivalence of a sensitive material ensure that minor changes in Fricke gel composition might not affect drastically the radiosensitive properties (*17*). However, more exhaustive studies of diffusion effects in Fricke gel solutions might be performed in order to account for differences in chemical compositions of the sensitive material of the dosimeter (*3*, *6*). Moreover, it has been pointed out that Fricke gel dosimetry by means of optical analysis of thin layers might present minor, but possibly not negligible, variations due to the storage temperature of irradiated samples (*6*, *18*).



## 5. Conclusions

This paper has presented a novel method for achieving a bi-dimensional approach to the diffusion coefficient calculation by means of finite elements techniques. The method has been suitably and successfully adapted and applied to Fricke gel dosimetry by means of optically analyzed dosimeter layers.

A specific framework was proposed and developed for calculation algorithms implementation based on the finite elements theory. The goal of assessing diffusion properties has been satisfactorily accomplished by modeling and solving the bi-dimensional approach to the diffusion master equation. Therefore, the diffusion coefficient for the standard composition of Friche gel dosimeter layers has been determined by means of calculation methods that include experimental data. Moreover, the obtained results agree, within the experimental uncertainties, with previous works (*3*, *5*–*7*). In particular, it is worth remarking that the agreement exists even when calculations in previous works were carried out by means of NMR analysis.

In summary, the present work provides a bi-dimensional approach to the diffusion coefficient calculation, thus improving the available calculation modalities for this feature. Finally, the methods described here may also be applied to the problem of compensating for the effects of diffusion in clinical applications of the Fricke gel dosimetry, which could be possible by specifying the deconvolution process characterized by the determined diffusion coefficient *D*.

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