Annex 5

PHYSICS OF EMERGENT BEAM

Three dimensional measurements of absorbed dose in BNCT by Fricke-gel imaging

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Abstract. A method has been studied for absorbed dose imaging and profiling in a phantom exposed to thermal or epithermal neutron fields, also discriminating between various contributions to the absorbed dose. The proposed technique is based on optical imaging of FriXy-gel phantoms, which are proper tissue-equivalent phantoms acting as continuous dosimeters. Convenient modifications in phantom composition allow, from differential measurements, the discrimination of various contributions to the absorbed dose. The dosimetry technique is based on a chemical dosimeter incorporated in a tissue-equivalent gel (Agarose). The chemical dosimeter is a ferrous sulphate solution (which is the main component of the standard Fricke dosimeter) added with a metal ion indicator (Xylenol Orange). The absorbed dose is measured by analysing the variation of gel optical absorption in the visible spectrum, imaged by means of a CCD camera provided with a suitable filter. The technique validity has been tested by irradiating and analysing phantoms in the thermal facility of the fast research reactor TAPIRO (ENEA, Casaccia, Italy). In a cylindrical phantom simulating a head, we have imaged the therapy dose from thermal neutron reactions with ^{10}B and the dose in healthy tissue not containing boron. In tissue without boron, we have discriminated between the two main contributions to the absorbed dose, which comes from the $^{1}H(n,\gamma)^{2}H$ and $^{14}N(n,p)^{14}C$ reactions. The comparison with the results of other experimental techniques and of simulations reveals that the technique is very promising. A method for the discrimination of fast neutron contribution to the absorbed dose, still in an experimental stage, is proposed too.

1. INTRODUCTION

As known, Boron Neutron Capture Therapy (BNCT) takes advantage of the high cross section of the nuclear reaction of thermal neutrons with ^{10}B:

$$^{10}B(n,\alpha)^{7}Li \qquad (\sigma = 3837\ b)$$

For treatment planning, besides the dose due to the presence of ^{10}B, it is necessary to determine the dose delivered by thermal neutrons in surrounding tissue without boron. In fact, the maximum admitted thermal neutron fluence during treatments is related to the dose in healthy tissue, which has to be within tolerance limits. Presently, the spatial distributions of absorbed dose in BNCT are commonly determined by means of computer simulations, with Monte Carlo or deterministic approach, but the necessary input parameters, which drastically determine the results, are not always satisfactorily determinable and the patient geometry is not easily simulated. Therefore, the experimental determination of the spatial distribution of absorbed doses is very important to support and validate the calculations.

Owing to the different Linear Energy Transfer (LET) of the different kinds of secondary radiation produced by neutron reactions in a medium, the determination of total dose is meaningless and the various contributions have to be separately identified. This result is commonly attained by means of elaborated simulation procedures. In practice, experimental dosimetry usually consists of fluence measurements, possibly complemented by some information about energy spectrum. On the other hand, both fluence and energy spectrum change from point to point in the medium, so that dose knowledge is very complex and difficult.

The here described technique for neutron dosimetry allows absorbed dose imaging and profiling in tissue-equivalent phantoms exposed to thermal or epithermal neutrons, discriminating between various contributions. The proposed technique is based on the imaging, after exposure, of phantoms made with a gel-dosimeter material of proper composition. From differential analysis of images detected in phantoms having convenient differences in the elemental composition, it is possible to separate the various contributions to the absorbed dose.

2. METHOD FOR ABSORBED DOSE IMAGING

As known, in ferrous sulphate solutions ionising radiation starts a chain of chemical reactions which results in the conversion of ferrous ions Fe^{2+} into ferric ions Fe^{3+}. The conversion yield has shown to be proportional, till saturation, to the absorbed dose. Therefore, after ionising radiation, from the variation of some detectable physical parameter depending on the ferrous and ferric ion amounts, the absorbed dose can be indirectly determined. In conventional Fricke dosimetry, the light absorption at about 300 nm is utilised, because such an absorption, negligible before ferrous ion oxidation, results to be proportional to the ferric ion concentration, that is to the absorbed dose. Spectrophotometric analysis has proved to be very reliable. Moreover, the different paramagnetism of ferrous and ferric ions gives an interesting technique for dose measuring: in fact, Nuclear Magnetic Resonance (NMR) analysis gives the possibility of spatial determination of paramagnetic species, because of their different influence on the spin relaxation times of the hydrogen nuclei of the solution. On account of this consideration, the feasibility of measuring 3-D distributions of absorbed dose in Fricke-infused gel-phantoms by NMR imaging has been suggested [1]. The sensitivity of such a technique is lower than that of spectophotometry, but this disadvantage is counterbalanced by the fact that, when ferrous sulphate solution is incorporated into a gel, the

ferrous ion oxidation yield has resulted to be considerably higher. In previous works, we have enquired the feasibility of dose imaging by means of NMR analysis [2] and the possibility of applying such a technique in thermal neutron fields for BNCT [3–6]. The main drawback consisted in the not negligible diffusion of Fe^{2+} and Fe^{3+} ions in the phantom. This effect causes a continuum loss of spatial resolution during the time between irradiation and analysis, so that a prompt phantom imaging after exposure is necessary to achieve good spatial resolution. Very often it is difficult to have such a possibility, in particular when exposures are performed in a nuclear reactor.

Therefore, we have considered an alternative technique for gel analysis, utilising spectrophotometry. The proposed method for gel-phantom imaging is based on transmittance measurements; we have designed and constructed a very simple portable instrument for image detection, which can be quickly assembled near the irradiation facility [7].

2.1. Gel dosimeter and portable imaging instrument

As before pointed to, in sulphuric acid solutions, ferric ions induce absorption peaks, in the UV region, at wavelengths near 300 nm. A considerable enhancement of the sensitivity of optical analysis is obtained by adding to the gel components a proper metal-ion indicator, which yields absorption in the visible spectrum. We have chosen Xylenol Orange ($C_{31}H_{27}N_2Na_5O_{13}S$, Fluka Chemie) which induces an absorption maximum at about 585 nm [8], as shown in Fig. 1. The difference in absorbency, at this wavelength, between irradiated and non-irradiated gels has shown to be linearly correlated to the absorbed dose. Visually, by increasing the absorbed dose, the colour of this Fricke-Xylenol-Orange infused gel (which for the sake of brevity we call FriXy-gel) changes from orange to violet.

The analysis technique is based on transmittance imaging performed by means of a CCD camera. In order to measure transmittance, the phantom to be inspected is composed of a set of piled up gel layers. Each layer consists of a stratum of gel within two transparent polyethylene or mylar films, held by a proper frame of the desired thickness and shape.

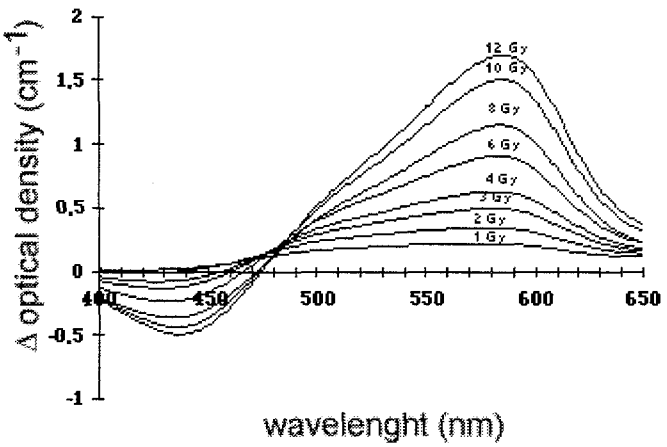

FIG.1. Difference in Optical Density between irradiated gel-samples and reference gel-sample.

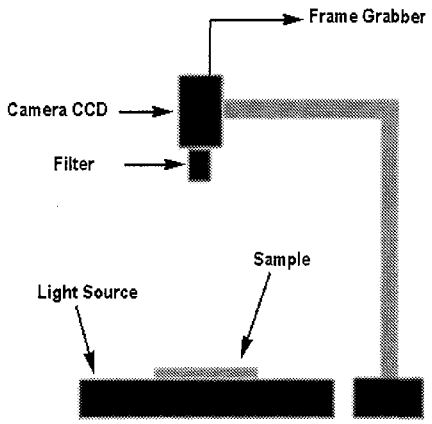

FIG.2. Instrument for imaging.

After exposure of the whole phantom to ionising radiation, each layer is promptly imaged and from the so obtained 2-D images, the 3-D distribution is reconstructed by means of convenient software.The instrument for transmittance image acquisition is composed of a CCD camera, an optical filter, a light diffuser and a PC. The interference filter (585 nm) is placed between the 50 mm camera lens and the CCD detector, to match the wavelength of the absorption maximum. A schematic view of the instrument is shown in Fig. 2.

2.2. Imaging technique

The absorbed dose can be correlated to the difference in Grey Levels (ΔGL) between irradiated and non-irradiated gels. These ΔGL values can be easily converted in differences of absorbency value, or Optical Density (ΔOD) with simple mathematics:

$$\Delta OD = \log_{10}\left(\frac{\Delta GL_{blank}}{\Delta GL_{trr}}\right)$$

The acquired transmittance images include a stripe of transmittance standards, with different optical densities. In a first step, the Grey Level values measured on the strip are utilised to test the stability of the light source and to evaluate possible correction factors. Moreover, with proper software for image elaboration, the Optical Density images can be obtained by means of direct dot elaboration of GL images. Finally, if some gels are exposed to known doses and analysed, then the γ-calibration curve is obtained and transmittance images can be converted into dose images.

For attaining good result reliability, the calibration procedure has to be performed with gel samples arranged in the same preparation, and moreover irradiation and analysis have to be carried out in an interval of time as short as reasonably possible, preferably in the same day. In fact, the stability in time of the gel dosimeter is not high. In a detailed study performed by analysing the dosimeter with NMR imaging [2], we have found good reproducibility of the

time dependence, whose knowledge allows to go up to reliable values. If this dependence has not been determined, by performing near-in-time calibration and analysis, reliable results are obtained.

3. DOSE IMAGING AND PROFILING IN PHANTOMS FOR BNCT PLANNING

3.1. Dosimetry of thermal and epithermal neutrons

The dosimetry of slow neutrons is difficult and particularly complex, because many kinds of energy release mechanisms are involved. In fact, neutrons do not directly produce ionisation in passing through matter: having no charge, they do not interact with atomic electrons, but with atomic nuclei. The deposition of dose by intermediate and fast neutrons in tissue is mainly due to hydrogen recoil nuclei, while thermal and epithermal neutrons release dose mostly through nuclear reactions. Thermal neutrons propagate in matter, till they are captured by an atomic nucleus, with a probability described by the isotope cross section. The cross-sections for such nuclear reactions highly depend upon neutron energy. The reactions are accompanied by the emission of energetic γ-rays or, like for ^{10}B, of ionising charged particles. If a deep tumour has to be treated, epithermal neutron beams are needed. In fact, to make up for the remarkable attenuation of thermal neutrons in tissue, intermediate neutrons are added in the beam, having a proper energy in order to produce a maximum in the thermal neutron fluence at the depth of the tumour. In this case, not only the energy release due to thermal neutrons has to be determined, but also the energy released in tissue by the recoil protons generated by the scattering of intermediate neutrons with hydrogen has to be considered, because its contribution may be significant.

For thermal neutrons, the main contributions to the absorbed dose in tissue come from hydrogen and nitrogen, through the nuclear reactions:

$$^{1}H(n,\gamma)^{2}H \quad (\sigma=0.33\ b) \quad \text{and} \quad ^{14}N(n,p)^{14}C \quad (\sigma=1.81\ b)\,.$$

The first reaction is responsible for dose depositions also far away from the site of interaction while the second one gives local dose deposition. In most common practical conditions, i.e. tissue-volumes with dimensions bigger than few centimetres, the first reaction is strongly dominant. Owing to the dissimilar linear energy transfer (LET) of the different radiation components, and to their different relative biological effectiveness (RBE), the total dose is meaningless, and it is necessary to determine the separate contributions to the absorbed dose of each field component. Possibly, this determination has to be made with 3-D resolution, because the relative contributions of the various dose components change with depth in tissue.

3.2. The FriXy-gel for BNCT

The first general condition for phantom dosimetry is that of achieving good tissue-equivalence of dose absorption in the substitute of which the phantom is composed. In thermal or epithermal neutron fields, this condition requires that the secondary radiation produced by the nuclear reactions is the same as that in tissue. The only possibility to obtain this equality is that of composing a tissue-substitute containing the same isotopes that give in tissue the main contributions to the absorbed dose, in the same percentage.

Since in our standard FriXy-gel the mass percentage of hydrogen is very near to that of most human tissues, in particular of brain tissue, a good tissue-equivalence is obtained for fast neutron energies. Moreover, if a proper amount of nitrogen is added to the gel's composition,

the dosimeter becomes equivalent to brain tissue for all neutron energies. With the purpose of determining the different contributions to the absorbed dose, we developed FriXy-gels with different elemental compositions. One gel was completely tissue-equivalent, and another one was nitrogen depleted. We also prepared a gel with the same composition of the standard one, but augmented with a concentration of ^{10}B typical for the therapy (30 μg/g). In Tab.1 the various compositions are shown and compared to that of adult brain tissue from ICRU-44 [9].

Table 1. Elemental composition of brain tissue and of developed gels.

	H	*N*	*C+O*	*Others*	
Brain (Adult)		10.7	2.2	85.7	1.4
FriXy-gel + N	10.9	2.2	86.8	0.1	
FriXy-gel standard		11.1	0	88.8	0.1

For various neutron energies, we have related the kerma factors for gel, evaluated utilising data of ICRU-26 [10], to the kerma factors for adult brain from ICRU-46 [11]. The resulted ratios, reported in Fig.3, show a good tissue-equivalence of the gel with nitrogen for all energies. As expected, the gel nitrogen-depleted departs from equivalence for thermal and epithermal neutrons, and this difference in kerma factors is a consequence of the absence of charged particles due to the reaction with nitrogen. Therefore, this gel can be utilised to measure the dose from the γ-rays emitted in the reactions with hydrogen.

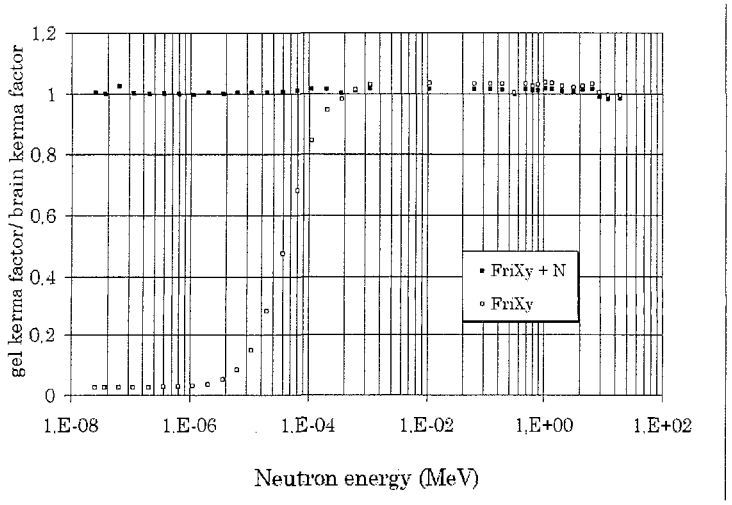

FIG. 2. Ratio between gel and brain kerma factors.

Preliminary calibrations were realised, exposing the three different types of gel to gamma radiation, in order to investigate the gamma sensitivity of the dosimeters with the different compositions. We have found that the sensitivity of the FriXy-gel with boron is slightly lower than that of the standard FriXy-gel, and also lower is the sensitivity of the gel with nitrogen.

3.3. Experimental results with thermal neutrons

In order to check the method for dose imaging and discriminating, some exposures have been made in the thermal column of the fast nuclear reactor TAPIRO, at the ENEA Casaccia Centre near Rome, where a proper thermal column was designed and constructed for BNCT experiments. This facility is a highly enriched ^{235}U research reactor. The nominal power is 5 kW (thermal) and the maximum neutron flux is 4×10^{12} $cm^{-2}s^{-1}$. In the thermal column, the moderating structure, designed by means of MCNP simulations, is composed of 40 cm thick graphite blocks. The structure, whose section is shown in Fig.4a, has a cubic shape. A 10 cm thick lead γ-shield was located inside the graphite, in order to have low gamma background in the irradiation volume, which is a cubic space with sides of about 18 cm. The thermal neutron flux in the thermal irradiation volume, at the maximum reactor power, was $3\cdot10^{8}$ cm^{-2} s^{-1}.

The phantom we have exposed to the neutron field was made up of a polyethylene cylinder (16 cm diameter, 14 cm height) with a coaxial cylindrical hole (6 cm diameter) as shown in Fig.4b. In the hole, four FriXy-gel rectangular layers (3 mm thick) were arranged in each exposure, by alternating gels having different compositions, in order to discriminate between the various contributions to the absorbed dose. We have chosen polyethylene as phantom material, because its hydrogen concentration makes the spatial distribution of the absorbed dose from the g rays emitted in the reaction with hydrogen to be very similar to that in tissue. Moreover, it was more practical than an entire phantom made of gel. In fact, the aim of the experiment was that of investigating the feasibility of such dose measurements and the reliability of the obtained results. When dose determinations in some specific situations will be needed, a convenient phantom will be designed.

In various thermal neutron exposures of the phantom, the FriXy-gel layers (standard, with nitrogen, with boron) were laid one upon another with horizontal orientation.

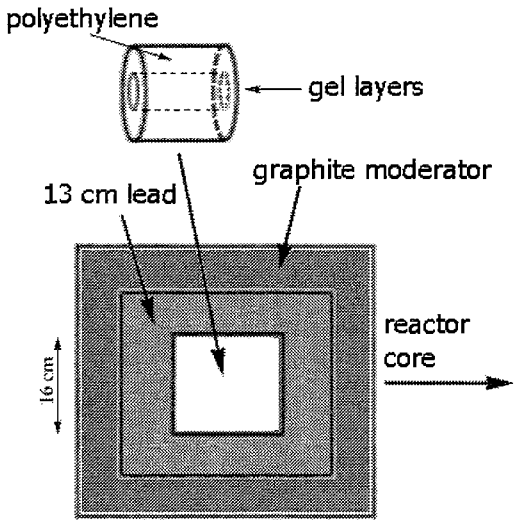

FIG. 3a. Moderator and irradiation set up.

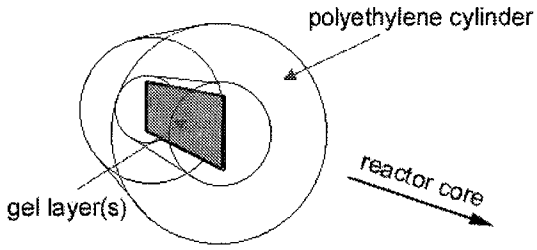

FIG. 3b. Polyethylene phantom.

The empty spaces between the gel and the cylinder were filled up with properly shaped polyethylene pieces, in order to avoid vacuum spaces and to have a good global tissue-equivalence. So, in each position of all the gel layers, the absorbed dose due to the γ rays generated by neutrons in the reactions with hydrogen is the same that would be absorbed, in the same position, in tissue. Moreover, in the gel containing nitrogen, the dose due to the particles generated in the reactions with such nuclei, which is locally released, is absorbed in addition to the previous one, and its value is equal to the corresponding absorbed dose in tissue. Therefore, from differential analysis of images, all contributions to the absorbed dose can be obtained.

In Fig.5, images and Grey-Level profiles of irradiated gels (with boron, standard and with nitrogen) are shown. The visible transversal gradient, showing a lack of symmetry in the thermal neutron field, was found with conventional dosimeters, too. Properly elaborating the images of different gel layers (standard, with nitrogen, with boron) each one normalised with respect to its own calibration, it is possible to image the dose contributions due to gamma radiation and to protons in healthy tissue and the therapy dose from boron. To translate images into dose values, the γ-calibration of each dosimeter gel was utilised; in such a way, the dose due to γ-radiation is directly obtained from standard FriXy-gel, and by means of properly made subtraction operations the γ-equivalent dose of the other secondary radiation can be derived. To obtain the correct values of all doses, the sensitivity of the dosimeter to the various radiation has to be considered. For the standard Fricke dosimeter, it is known that the dosimeter response to high LET protons is lower than that to γ rays, because there is dependence upon LET of the production of OH and H radicals, which determine the radiation-induced oxidation of ferrous ions. The possible LET dependence of the dosimeter with the chemical composition we have prepared deserves to be determined. We have not yet started studying the gel response to protons, because previously we aim to search how to prepare a dosimeter-gel containing the desired amount of nitrogen which presents best characteristics, i.e. best sensitivity and, principally, more reliability and stability in time. So, for the gel with nitrogen we have utilised the γ-calibration with no correction factor. The dose due to ^{10}B (that comes from the energy released both from α particles and ^{7}Li ions) seems to be not well described by the γ-equivalent dose. In a previous experiment [3], where Fricke-infused gels were analysed by means of NMR imaging, we have found that the apparent sensitivity of the gel dosimeter to the secondary radiation from ^{10}B was about one half of that to γ-radiation. So, we have considered that this effect could be present in the case of the FriXy-gel also. We have related the γ-equivalent dose measured in a certain position of the dosimeter to the theoretical

absorbed dose [12] (originating from the α and ^{7}Li particles) evaluated, in the same position, on the basis of the fluence value measured with an activation foil. Then we have brought a correction factor of 0.588 to the γ-equivalent dose to obtain the dose due to ^{10}B. A good determination of the sensitivity of the dosimeter gel to the secondary particles of the ^{10}B reaction is necessary and its study is in program. In Fig.6 the dose profiles are reported.

As mentioned before, in the analysis of images, we have found noticeable trouble coming from the fact that the gel with nitrogen has resulted to have lower higher variation in time, and also if we try to take into account this effect, the reliability of results is lower. It will be convenient to find a best technique to prepare the gel-dosimeter containing nitrogen, in order to achieve unfailing behaviour.

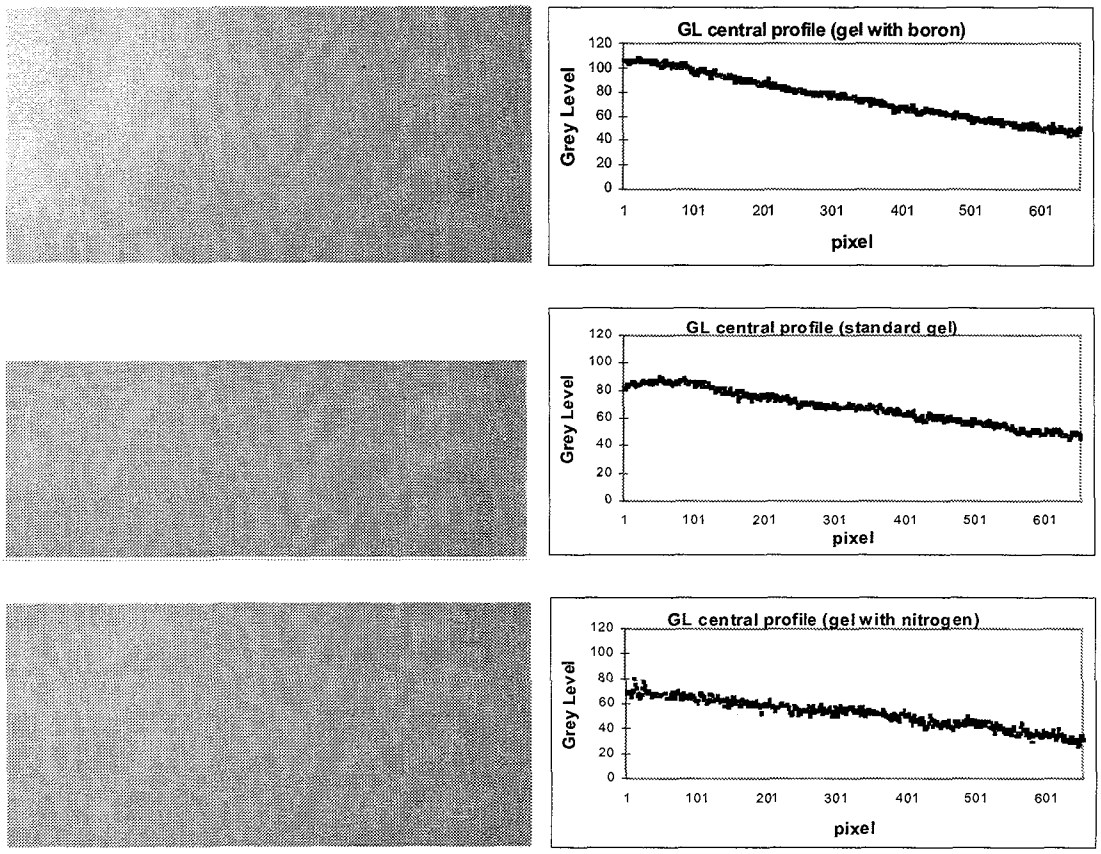

Fig. 5. Transmittance images and Grey Level profiles of gels with the various compositions.

4. INTERCOMPARISON WITH OTHER EXPERIMENTAL RESULTS

To check the validity of the method, some measurements with standard techniques were performed, and the results were inter-compared. In particular, activation techniques and thermoluminescent dosimeters (TLD) were employed. In such measurements, the cylindrical cavity of the phantom was filled with polyethylene, and the dosimeters were located in small hollows, in positions corresponding to gel layers.

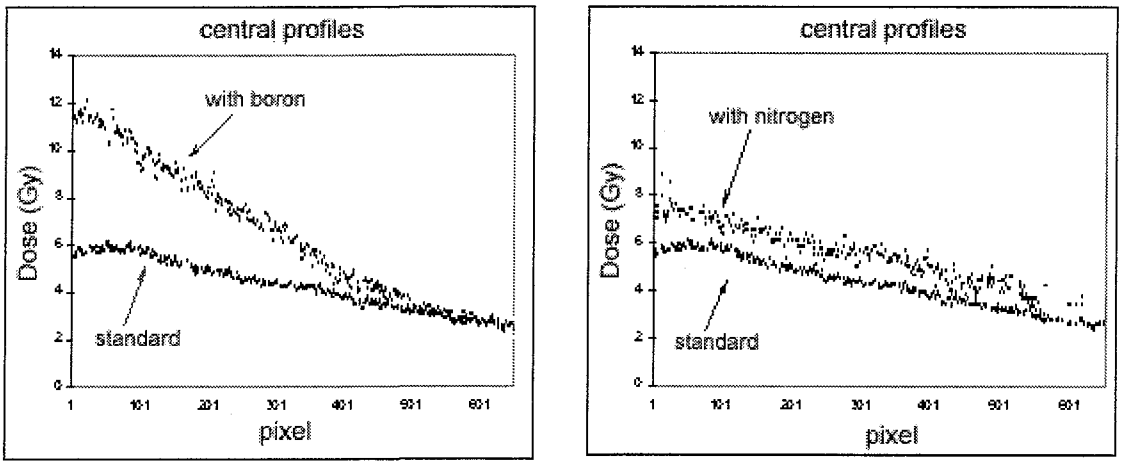

FIG.6. Dose profiles in the various gel dosimeters.

By means of activation technique, thermal neutron fluence values in some positions in the phantom were measured. By means of TLDs, both γ ray dose values and thermal neutron fluences were measured. The activation foils used were made of gold or indium in form of thin disks (1 cm diameter). Foils were located in polyethylene supports, in the same positions of TLD dosimeters (but in separate exposures). In order to determine thermal neutron fluences, two exposures were performed, with foils, in the same positions, naked or screened with Cadmium. The foils were properly oriented in order to avoid mutual shielding. For γ ray dose determinations, TLD-300 chips (CaF_2:Tm) were utilised, whose sensitivity to thermal neutrons is very low, so that up to fluences of the order of 10^{12} cm^{-2} they have a response not affected by thermal neutron contributions. Thermal neutron fluxes in discrete position were measured with TLD-100 chips (LiF:Mg,Ti). The fluence values measured with TLD-100 and with activation foils were very close to each other. Such data were utilised to test the consistency of the various profiles obtained by elaborating gel images.

To compare the results obtained with such dosimeters with the results obtained by elaborating FriXy-gel images, from the dose profiles of gel with boron the profiles (in corresponding positions) of gel without boron were subtracted, after normalisation for gel sensitivity. In such a way, the contribution of γ-rays emitted in the reactions with hydrogen is removed, and the resulting profile is the dose due to reactions with ^{10}B only. The so obtained values are quickly converted into fluence values. The flux profiles are in such a way evaluated. The comparison of the obtained fluxes with flux values measured by means of activation foils and TLDs, as shown in Fig. 7, confirm the reliability of the technique.

5. FINAL CONSIDERATIONS

The described results show that the technique is very promising and induce us to make improvements, in order to achieve higher precision and to get more knowledge.

With regards to the instrument for gel imaging, a refinement is in progress for what concerns image detection and transfer. Moreover, the proper software still in development will give the possibility of compensating for the lack of uniformity in the illuminator and for its instability in the time. The gel behaviour needs to be studied more widely.In fact, exposures in the thermal column of the reactor take long times, of the order of five hours.

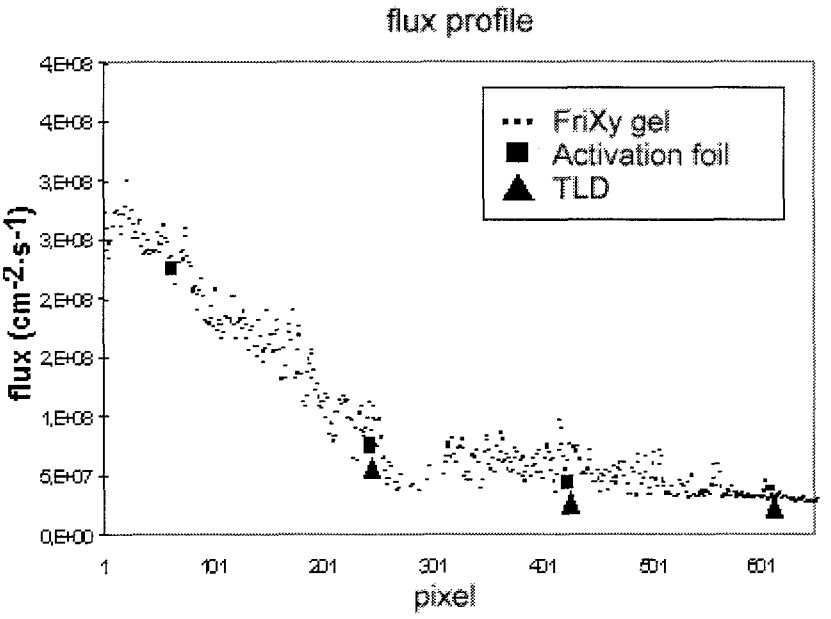

FIG.7. Inter-comparison of flux profile obtained with FriXy-gel and fluxes measured with activation foils and with TLDs.

So, it is necessary to understand how sensitively the gel can undergo modifications in the irradiation time, and how such effect can be taken into account in order to achieve good reproducibility and reliability of results. For achieving the desired amount of nitrogen, we have added the chemical compound Urea to the gel components, but the resulting gel-dosimeter, in addition to a lower sensitivity, has shown higher instability in time. It should be therefore very important to find a better method of preparation of the gel with nitrogen.

Another very important argument, presently in study in our laboratory, is the measurement of the contribution of fast neutrons to the absorbed dose. As said before, in epithermal neutron fields this contribution will be not negligible with respect to the dose from thermal neutrons in tissue without boron. This contribution is mainly due to the recoil protons resulting from inelastic scattering of neutrons with hydrogen nuclei, and its radiobiological effectiveness is different from that of γ-radiation emitted in the reaction, with hydrogen too, of thermal or epithermal neutrons. Therefore the 'total dose' is meaningless, and discrimination is necessary in all situations in which neither contribution is negligible with respect to the other. We aim to face the problem by means of differential analysis of images of absorbed dose in FriXy-gels made with light and with heavy water [13]. The method we are considering and testing is based on the consideration that in heavy-water Fricke solution the ferrous ion oxidation yield is higher than in light-water Fricke solution in a γ ray radiation field, but the opposite situation was found in neutron fields [14,15]. We are investigating the response of a heavy-water FriXy-gel dosimeter, to enquire the possibility of separating the dose from fast neutrons by differential analysis of images obtained by heavy/light-water made gels. The heavy-water gel layer will be made with the maximum thinness compatible with the reliability of images, so to minimise the perturbation of the tissue-equivalence of the phantom. The proper orientation of the gel layer with respect to the neutron beam direction

will be estimated too in order to minimise the perturbation of fast neutron slowing due to the heavy water. This experiment is recently started.

The total and gamma profiles obtained from the images have been compared with calculated profiles found in literature, and the agreement has revealed satisfactory.

APPENDIX

Standard FriXy-gel composition:

ferrous sulphate solution [1 mM $Fe(NH_4)_2(SO_4)_2 \cdot 6H_2O$], sulphuric acid [50 mM H_2SO_4] and Xylenol Orange [0.11 mM $C_{31}H_{27}N_2Na_5O_{13}S$, Fluka Chemie]in the amount of 50% of the final weight Agarose SeaPlaque [$C_{12}H_{14}O_5(OH)_4$, Fluka Chemie] in the amount of 1% of the final weighthighly purified water [H_2O] in the amount of 49% of the final weight

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REFERENCES

[1] R.J.SCHULZ, A.F.DEGUZMAN, D.B.NGUYEN, J.C.GORE, Dose-response curves for Fricke-infused gels as obtained by nuclear magnetic resonance. Phys. Med. Biol. **35**, 1611–1622 (1990).

[2] G.GAMBARINI, S.ARRIGONI, M.C.CANTONE, N.MOLHO, L.FACCHIELLI, A.E.SICHIROLLO, Dose-response curve slope improvement and result reproducibility of ferrous-sulphate-doped gels analysed by NMR imaging., Phys. Med. Biol. **39,** 703–717 (1994).

[3] G.GAMBARINI, S.ARRIGONI, M.BONARDI, M.C.CANTONE, D.DEBARTOLO, S.DESIATI, L.FACCHIELLI, A.E.SICHIROLLO, A system for 3-D absorbed dose measurements with tissue-equivalence for thermal neutrons. Nucl. Instr. And Meth. **A 353,** 406–410 (1994).

[4] G.GAMBARINI, C.BIRATTARI D.MONTI, M.L.FUMAGALLI, A.VAI, P.SALVADORI, L. FACCHIELLI, A.E.SICHIROLLO, Fricke-infused Agarose gel phantoms for NMR dosimetry in Boron Neutron Capture Therapy and Proton Therapy. Radiat. Prot. Dosim. **70**, 571–575 (1997).

[5] G.GAMBARINI, D.MONTI, M.L.FUMAGALLI, C.BIRATTARI, P.SALVADORI, Phantom dosimeters examined by NMR analysis: a promising technique for 3-D determination of absorbed dose. Appl. Radiat. Isot. **48**, 1477–1484 (1997).

[6] G.GAMBARINI, Three dimensional determination of absorbed dose by NMR analysis of a tissue-equivalent phantom-dosimeter. In: B. Larsson, J.Crawford, R.Weinreich (eds) Advances in Neutron Capture Therapy, Volume I, Medicine and Physics. Amsterdam: Elsevier Science (1997) 208–211.

[7] G.GAMBARINI, G.GOMARASCA, R.MARCHESINI, A.PECCI, L.PIROLA, S.TOMATIS, Three dimensional determination of absorbed dose by spectrophotometric analysis of Ferrous-Sulphate Agarose gel. Nucl. Instrum. and Meth. **A 422**, 643–648 (1999).

[8] A.APPLEBY AND A LEGHROUZ, Imaging of radiation dose by visible colour development in ferrous- agarose-xylenol orange gels. Med. Phys. **18**, 309–312, 1991.
[9] ICRU REPORT 44, Tissue Substitutes in Radiation Dosimetry and Measurement (1989).
[10] ICRU REPORT 26, Neutron Dosimetry for Biology and Medicine (1977).
[11] ICRU REPORT 46, Photon, Electron, Proton and Neutron Interaction Data for Body Tissues (1992).
[12] T.MATSUMOTO, O.AIZAWA, Depth-dose evaluation and optimisation of the irradiation facility for boron neutron capture therapy of brain tumours. Phys. Med. Biol. **30**, 897–907 (1985).
[13] G.GAMBARINI, U.DANESI, P.MARCHESI, P.PALAZZI, A.PECCI, Imaging and profiling of absorbed doses in thermal neutron fields for Boron Neutron Capture Therapy (BNCT, Report INFN/TC-99/10, 1–18 (1999).
[14] K.NAKAMURA, Dosimetry of fission neutrons and gamma rays from nuclear-reactors by paired Fricke solutions. Journ. Nucl. Sci. and Technol. **29**, 269–275 (1992).
[15] M.HIMIT, T.ITOH, S.ENDO, K.FUJIAWA, M.HOSHI, Dosimetry of mixed neutron and gamma radiation with paired Fricke solutions in light and heavy water. Journ. Radiat. Res. **37**, 97–106 (1996).