In-phantom dosimetry for BNCT with Fricke and normoxic-polymer gels

G Gambarini¹, ², S Agosteo³, M Carrara⁴, S Gay¹, ², M Mariani³, L Pirola⁴, E Vanossi¹
¹Department of Physics, University of Milan, Italy
²INFN Milan, Italy
³Department of nuclear engineering Polytechnic of Milan, Italy

Corresponding Author E-mail: Grazia.Gambarini@mi.infn.it

Abstract. Measurements of in-phantom dose distributions and images are important for Boron Neutron Capture Therapy treatment planning. The method for spatial determination of absorbed doses in thermal or epithermal neutron fields, based on Fricke-xylene-orange-infused gel dosimeters in form of layers, has revealed to be very reliable, as gel layer dosimeters give the possibility of obtaining spatial dose distributions and measurements of each dose contribution in neutron fields, by means of a properly studied procedure. Quite recently, BNCT has been applied to treat liver metastases; in this work the results of in-phantom dosimetry for explanted liver in BNCT treatments are described. Moreover, polyacrylamide gel (PAG) dosimeters in which a polymerization process appears as a consequence of absorbed dose, have been recently tested, because of their characteristic absence of diffusion. In fact, due to the diffusion of ferric ions, Fricke-gel dosimeters require prompt analysis after exposure to avoid spatial information loss. In this work the preliminary results of a study about the reliability of polymer gel in BNCT dosimetry are also discussed. Gel layers have been irradiated in a phantom exposed in the thermal column of the TRIGA MARK II reactor (Pavia). The results obtained with the two kinds of gel dosimeter have been compared.

1. Introduction

As known, Boron Neutron Capture Therapy (BNCT) is a promising treatment for different types of cancer based on the possibility of selective accumulation of the isotope $^{10}$B in tumour tissue and on the high cross section of such an isotope for thermal neutrons.

When a thermal neutron is captured by a $^{10}$B atom, alpha and lithium particles are produced which release their energy within a range comparable with cell diameter (10-20 μm). BNCT peculiarity with respect to conventional radiation therapies is that target is each tumor cell, discriminated by the presence of a higher $^{10}$B concentration with respect to healthy cells; this condition results in a higher dose in tumor then in healthy tissue.

In BNCT the absorbed dose results from four contributions: the therapeutic dose due to alpha and lithium particles released in the reaction of thermal neutrons with $^{10}$B ($^{10}$B (n,α) $^7$Li), the dose from protons due to the reaction of thermal neutrons with nitrogen ($^{14}$N (n,p) $^{14}$C), the gamma dose from the reaction of thermal neutrons with hydrogen ($^1$H (n,γ) $^2$H and background, if not negligible) and in the case of epithermal neutron beams, the fast neutron dose mainly due to recoil protons from elastic scattering with hydrogen nuclei.
Owing to the different relative biological effectiveness (RBE) of all the above mentioned dose components, it is necessary to determine the spatial distribution of each component both in tumor and in healthy tissue. The maximum admitted neutron fluence for a treatment is established from the dose in healthy tissue. Even if treatment planning will be finally established with computational simulations, experimental determinations are required to give necessary input parameters and usually to validate simulation results.

Therefore, the possibility of performing in-phantom dose imaging and profiling is of great importance for BNCT; the method for spatial determination of absorbed doses in thermal or epithermal neutron fields, based on gel dosimeters in form of layers, has shown to give the possibility to reach such a goal with good reliability 1,2].

Quite recently, BNCT has been applied to treat multiple and diffused liver metastases; this happened firstly in Italy, where the liver was explanted from the patient, irradiated in the thermal column of the TRIGA MARK II reactor of the University of Pavia and then re-implanted [3]. In this work the results of in-phantom dosimetry for liver in BNCT treatments are described.

2. Materials and Methods

Gel dosimeters in form of layer give the possibility of obtaining continuous dose distributions of each dose component in phantoms exposed to thermal or epithermal neutron, by means of a properly studied and developed procedure [2]. The dosimeter analysis is performed through imaging of visible light transmittance detected by means of a CCD camera; dose images are finally obtained by means of proper algorithms [1].

Gel dosimeters are aqueous systems (gel matrices infused with a chemical dosimeter in millimolar concentration) and their isotopic composition can be conveniently adjusted so that in neutron fields the absorbed dose due to each secondary radiation is really almost the same as the one absorbed by tissue.

To separate the dose components, a couple of gels layers (thickness 1-3 mm) is used, one with a standard composition not containing isotopes that react with thermal neutrons producing charged particles and the other with the same composition added with an isotope giving such kind of reaction. The thin layer-geometry doesn’t alter sensibly neutron transport, even if the isotopic gel composition is changed. The two gel layers are irradiated in the same position of the exposed phantom and the separation of two dose contributions is obtained by means of a proper computational elaboration of the two dose images.

The technique above described has been developed utilizing Fricke-xylene-orange-infused gel dosimeters, in which the radiation induces oxidation of ferrous ions. The composition of Fricke-xylene-orange-infused gel has been described in previous works [2]. However, due to the so produced diffusion of ferric ions, Fricke-gel dosimeters require prompt analysis of samples after exposure in order to avoid distortion or even spatial information loss. Since neutron irradiation is performed far away from the laboratory where these gels are produced and analyzed, unsafe transport of sophisticated and huge instruments - CCD camera, source of light for transmittance imaging, optical filter - is necessary.

This is the reason why polyacrylamide gel (PAG) dosimeters (here after named as polymer gel) have been recently tested [3] and are currently in early research, in which a polymerization process appears as a consequence of absorbed dose [4] and no diffusion phenomena are present. The composition of PAG gel is: 3% acrylamide, 3% N,N'-methylene-bisacrylamide, 4% gelatin, ultra-pure water as residual.

In figure 1 a spectrophotometer analysis of the response relative to bored and not bored polymer gel is reported: this figure shows adding boron doesn’t alter the dosimeter: in fact, the two curves coincide. In these measurements and in all the experiments involving polymer gel, the analysis has been performed after 24 hours from its preparation.
In this work the preliminary results of a study about the reliability of polymer gel in BNCT dosimetry are also discussed.

A phantom, whose photo is reported in figure 2, has been made of two cylindrical polyethylene shells (empty hemicylindrical halves) totally filled with non dosimetric, tissue-equivalent gel (4% of Agar in H₂O): dosimetric gel layers can be then inserted in the phantom’s central plane and all the structure can be properly closed avoiding empty volumes. Phantom’s shape results to be a cylindrical structure 10.5 cm in diameter and 12 cm high with a volume hence chosen as similar as possible to the human liver’s (ICRP Publication 89).

In this experiment ¹⁰⁹B isotope hasn’t been added to the phantom filling gel as done in previous experiments finalized to brain dosimetry for BNCT [2] since the quantity of ¹⁰⁹B added to the dosimeters composition was settled at 40 ppm, meaning a very low ¹⁰⁹B concentration in healthy tissue in the case of explanted liver: in fact, the ¹⁰⁹B concentration ratio among tumor and healthy tissue is much higher in explanted liver than in brain treatment [5]. So, although neutron transport is determined mainly to ¹⁰⁹B concentration in healthy tissue surrounding the tumoural sites and the concentration in tumour and in dosimeters doesn’t alter it sensibly, the phantom filling gel has not been added with any ppm of ¹⁰⁹B being very low in the case of 40 ppm in tumour.

3. Experiments and results
Phantom has been exposed in the thermal column of the TRIGA MARK II reactor in Pavia (Italy) where two extra corporeal treatment of human liver metastases with BNCT were performed some years ago [5].
Two couples of Fricke and polymer gels in according to the experimental protocol previously described have been irradiated in phantom with the aim to value the dose contributions from charged particles \(^{10}\text{B}(\text{n},\alpha)^{7}\text{Li}\) and gamma rays (mostly from the reaction with phantom’s hydrogen nuclei) in the same situation of human liver irradiation.

To validate the gel results, bare and cadmium shielded gold activation foils have been used to deduce thermal and epithermal fluxes and termoluminescent dosimeters Ca\(_2\)F:Tm (TLD 300) have been used to measure gamma dose because their poor sensitivity to neutrons. TLD 300 have a very high sensitivity to reactor background low energy photons, nevertheless they have shown to give a reliable response for in-phantom measurements: in fact in this conditions gamma background dose is negligible respect to dose from \(^1\text{H}(\text{n},\gamma)^2\text{H}\) reaction [6].

The irradiation conditions have been settled to 30 minutes for all the techniques as far as irradiation time concerns and 250, 160, 2, 1.5 kW for polymer gel, Fricke gel, TLD and activation foils respectively as far as reactor power concerns.

In figure 2 in-phantom dose distributions obtained with Fricke gel are reported, validated by the results from activation foils and TLD 300 which have been normalized to the irradiation conditions (i.e. time and power) of this experiment. In this figure, therapeutic dose and gamma dose are shown; the therapeutic dose has been valued considering the gel sensitivity to charged particles (high LET) is less than the sensitivity to gamma rays by a factor of 0.42 ± 0.03 as resulted from former experiments [2].

![Figure3](image)

**Figure3.** Dose distributions in phantom. 1:total Dose, 2: boron dose (40 ppm), 3: gamma dose

An alternative visualization of boron dose is given in figure 3, where dose distribution in the whole dosimeter’s plane is shown. This image is one of the possible outputs of a software properly developed to elaborate dose images revealed with gel layer dosimeters and usable also in other radiation fields.
Figure 3. 2-dimensional boron dose distribution in phantom. Top: different colors mean the dose gradient. Down: Grey level image relative to difference of optical density. The rectangular shape correspond to dosimeter zone drown in the upper graph.

Since the liver irradiated at the TRIGA MARK II reactor in Pavia had been rotated of 180 °C [5], after an half of the total treatment time, also the dose distribution in this situation is reported: the results are shown figure 4.

Figure 4. Dose distributions in the case of phantom rotation.
1: total Dose, 2: boron dose (40 ppm), 3: gamma dose

Charged particles and gamma dose have been weighted for Relative Biological Effectiveness (RBE) factors in order to make evident the effects of their different cell killing efficacy. RBE factors used in this work are listed are: 0.5 for gamma rays and 4.3 for $^{10}$B at 40 ppm. RBE doses are reported in figure 5.
Finally, in figure 7 the dose distribution results relative to preliminary polymer gel applications to BNCT dosimetry are reported. Comparing the dose images relative to the dosimeter without boron and the bored one, it can be verified that bored polymer gel is sensitive to neutrons. Nevertheless, although the linearity range of response has been respected in these measurements, it can be verified that dose distributions don’t coincide with those relative to Fricke dosimetry; this circumstance is present also in photon beams where this distortion of shape is actually more visible. This distortion is probably due to not optimized layer procedure preparation that should be improved.

4. Conclusions
The experiment described in this work was aimed to evaluate dose distributions in a liver simulating phantom with gel layer dosimetry for BNCT treatments. The results obtained especially with Fricke gel have shown good likelihood if compared with activation foils and TLD results which are standard and more consolidated techniques. The goodness of these results stimulates to keep on new
measurements with phantoms of more realistic shape and dimensions, to explore the effects of different $^10\text{B}$ amounts accumulated in phantom and to improve today’s dosimetry to an extended and volumetric dosimetry technique.

5. Acknowledgements
This work was partially supported by Istituto Nazionale di Fisica Nucleare (Italy).

6. References
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