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Neutron flux and gamma dose measurement in the BNCT irradiation facility at the TRIGA reactor of the University of Pavia

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ABSTRACT

University of Pavia is equipped with a TRIGA Mark II research nuclear reactor, operating at a maximum steady state power of 250 kW. It has been used for many years to support Boron Neutron Capture Therapy (BNCT) research. An irradiation facility was constructed inside the thermal column of the reactor to produce a sufficient thermal neutron flux with low epithermal and fast neutron components, and low gamma dose. In this irradiation position, the liver of two patients affected by hepatic metastases from colon carcinoma were irradiated after borated drug administration. The facility is currently used for cell cultures and small animal irradiation.

Measurements campaigns have been carried out, aimed at characterizing the neutron spectrum and the gamma dose component. The neutron spectrum has been measured by means of multifoil neutron activation spectrometry and a least squares unfolding algorithm; gamma dose was measured using alanine dosimeters.

Results show that in a reference position the thermal neutron flux is $(1.20 \pm 0.03) \times 10^{10}\,cm^{-2}\,s^{-1}$ when the reactor is working at the maximum power of 250 kW, with the epithermal and fast components, respectively, 2 and 3 orders of magnitude lower than the thermal component. The ratio of the gamma dose with respect to the thermal neutron fluence is 1.2×10^{-13} Gy/(n/cm^2).

1. Introduction

Boron Neutron Capture Therapy (BNCT) is an experimental radiotherapy based on the administration of a drug able to concentrate ^{10}B in tumour cells, followed by low energy neutron irradiation. Thermal neutron capture in ^{10}B generates two high LET particles (α and ^{7}Li ion) that lose all their energy in a range comparable to the cell diameter. In this short path, the charged particles cause irreparable damage to the cell where the reaction takes place, without directly affecting the surrounding healthy cells. Provided a sufficient boron concentration ratio between tumour and normal tissue, and a suitable neutron beam, the effect of the irradiation is selective at a cell level, delivering a lethal dose to the tumour while sparing the healthy tissues. Because of this characteristic, BNCT is a promising option to treat disseminated and infiltrated tumours that cannot be surgically removed nor treated with photon or hadron therapy [1].

In Pavia, BNCT has been tested as a therapy for whole organs (liver and lung) invaded by multiple metastases, and as an adjuvant treatment for tumours difficult to eradicate like osteosarcoma. The research started on liver, and led to a clinical application in two patients,

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following the challenging protocol of ex-situ organ irradiation [2]. This application required the building of a proper irradiation position and its characterization in terms of neutron and photon dose components by experimental measurements and Monte Carlo simulations. The facility consists in an air channel ($40 \times 20 \times 100\ cm^3$) surrounded by graphite that ensures a good level of neutron thermalization. It is shielded with two bismuth walls that absorb the gamma radiation coming from the reactor core. The photon component is in fact a source of unwanted background dose in BNCT because it affects all the tissues in a non-selective way. A model of the whole reactor was produced using MCNP (version 4c2) [3] and the simulation results were validated with experimental measurements [4].

The facility is presently used to test the toxicity and the effectiveness of BNCT via *in vitro* and *in vivo* experiments. Moreover, a position in the thermal column is used to measure boron concentration in cell samples or tissues taken from animal models treated with new boronated formulations. In particular, the possibility to treat large portions of lung with external epithermal neutron beams has been explored, requiring the demonstration of the selective absorption of ^{10}B by lung tumour [5], and of BNCT effectiveness in an animal model. Monte Carlo calculations have been performed to design special shields for small animals (rats and mice) with windows for the tumour irradiation [6,7]. Animals are inserted in an air channel in the thermal column, at the same position where the liver had been irradiated, in order to keep the irradiation time as short as possible. In this second phase of BNCT research at the TRIGA reactor, new measurements and simulations have been carried out, with the goal of refining the dosimetry and producing proper treatment planning for animals.

This paper describes the measurements and the simulations performed in the recent years to characterize the dosimetry in the TRIGA thermal column, following an integrated approach based on neutron activation measurements, Monte Carlo simulation and alanine irradiation. Fig. 1 shows the MCNP5 geometry of the TRIGA reactor with the Thermal Column and the positions where the measurements were carried out.

The activation measurements performed were part of an international inter-comparison of thermal neutron facilities for samples and animal irradiations, comprising the MURR reactor in Missouri and the RA-3 reactor in Argentina [8]. The experiments and calculations were performed in collaboration with Idaho National Laboratory, where a protocol based on multi-foil neutron activation spectrometry and a least squares unfolding algorithm was developed for this specific purpose [9]. As the neutron field inside the thermal column has a broad energy spectrum, detectors with different behaviours of the cross section were used, in particular: “1/v materials” for the thermal range, resonance detectors for the epithermal range and a threshold detector for the fast component. Combining the information of the activation of each detector enabled the reconstruction of the neutron spectrum over the whole energy range, basing on a priori knowledge of the flux obtained by Monte Carlo simulation.

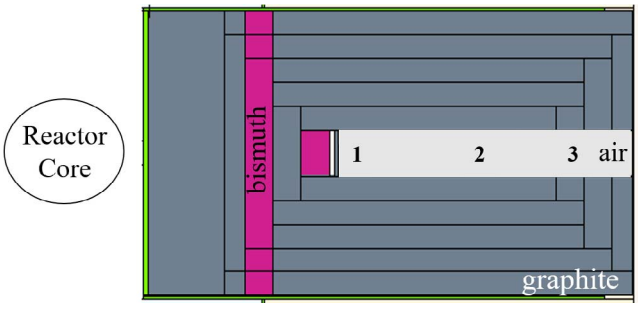

Fig. 1. Thermal column (longitudinal view) with the measurements positions. The neutron spectrum was measured in position 1 (130.95 cm from the centre of the core) while gamma doses were measured in positions 1, 2 (174.95 cm from the centre of the core) and 3 (208.95 cm from the centre of the core). Grey: graphite, magenta: bismuth, green: Boral (borated aluminium), white: air.

The alanine dosimetric system was mainly employed for gamma dose determination because of its valuable dosimetric features as passive radiation detector. In fact, ionizing radiations induce stable free radicals in the crystalline structure of the amino-acid L-α-alanine, quantitatively detectable via Electron Spin Resonance (ESR) technique [10]. These free radicals remain trapped in the matrix of alanine, with a very low fading (less than 1% per year in proper environmental conditions) [11]. Since the number of radicals generated is proportional to the delivered dose in a very wide range of energy, the amino-acid is widely employed as a passive solid-state dosimeter [12,13]. Photon tissue-equivalent composition, linear response in a very wide dose range (from around 1 to over 10^5 Gy), low dependence on the radiation quality, signal stability after irradiation, low dose-rate dependency, low cost and non-destructive readout (differently from thermoluminescence technique) are key advantages of alanine as dosimeter for photon and electron beams and for these properties alanine system was chosen for gamma dose determination [14–16].

Furthermore, ESR detectors response to different kinds of radiation was widely studied and recently an increasing interest has aroused toward neutrons and high LET charged particles [14,17–22,16,23, 15,24–37]. To compare the response of alanine to different radiation qualities and energies, the figure of merit considered is the Relative Effectiveness (RE) of an incident radiation with respect to ^{60}Co rays (with energies 1.173 and 1.333 MeV) in producing stable radicals. The RE is defined as the ratio of signals (S_{rad} and S_{Co}) after equal doses (D_{rad},D_{Co}) of reference radiation and radiation under investigation:

$$RE = \frac{S_{rad}}{S_{Co}} \quad \text{when} \quad D_{rad} = D_{Co}.$$

The energy dependence of RE for photon beams of different spectra, is experimentally demonstrated to be very low, while RE strongly depends on LET if the dose is deposited by charged particles. When energy is delivered by high-LET particles, the generated radicals are spatially more concentrated and can undergo recombination. The concentration of stable free radicals produced per ion generally decreases with decreasing of energy. Consequently, a decrease of RE is demonstrated to occur in correspondence of a LET increase over around 50 MeV/cm (5 keV/μm in water). Palmans [22] summarized the experimental RE measured in different experiments in the last 40 years for protons of energy between 1.2 and 60 MeV, fitting the curve of RE as a function of the effective energy of the proton beam (considering the effect of saturation) with a sigmoid. The sigmoid shows that for protons of energies between 0.6 MeV (protons generated from thermal neutron capture in nitrogen $^{14}N(n,p)^{14}C$ and 3.5 MeV (protons produced by elastic scattering of fast neutrons in hydrogen), RE is about 0.6. Schmitz et al. calculated that – for nitrogen protons – the RE value is 0.56 ± 0.01 [23] In the same paper, calculated RE values for the epithermal part of the spectrum are reported between 0.58 and 0.71 depending on the facility. The goal of this part of the work was to determine gamma dose in the thermal column, coupling alanine measurements to MC simulations. Alanine was shielded from thermal neutrons and an accurate MC model evaluated the neutron component still contributing to the dose absorbed by alanine. As a byproduct, the RE of all the dose components were evaluated by irradiating these dosimeters without any shielding in the thermal column at the TRIGA reactor in Pavia.

2. Materials and methods

2.1. The neutron spectrum measurements

First, a comprehensive analysis of the neutron spectrum was carried out. Three different set-ups were irradiated at the maximum reactor power of 250 kW: a set of bare foils, a set of foils under 1 mm thick Cd covers, and a foil under a thick ^{10}B shield. In particular: Au and Mn bare foils were irradiated for 10 min to measure the thermal component, In,