IL NUOVO CIMENTO **44 C** (2021) 135
DOI 10.1393/ncc/i2021-21135-1

Communications: SIF Congress 2020

Neutron activation and dosimetry studies for a clinical facility of Boron Neutron Capture Therapy

C. Magni(1)(2)(*), M. Ferrarini(3), I. Postuma(2), N. Protti(2), S. Fatemi(2), C. Gong(2), U. Anselmi-Tamburini(4), V. Vercesi(2), G. Battistoni(5) and S. Bortolussi(1)(2)

(1) *Department of Physics, University of Pavia - Pavia, Italy*
(2) *INFN, National Institute of Nuclear Physics, Unit of Pavia - Pavia, Italy*
(3) *CNAO, National Center of Oncological Hadrontherapy - Pavia, Italy*
(4) *Department of Chemistry, University of Pavia - Pavia, Italy*
(5) *INFN, National Institute of Nuclear Physics, Unit of Milan - Milan, Italy*

received 15 January 2021

Summary. — Boron Neutron Capture Therapy (BNCT) is a radiotherapy in which the patient is irradiated with low-energy neutrons after the administration of a borated drug targeting cancer cells. Neutron activation and dosimetry studies are presented, related to a facility for the BNCT treatment of deep-seated tumours. The clinical beam is obtained from a proton accelerator coupled to a beryllium target and a neutron moderator/collimator (BSA, Beam Shaping Assembly) mainly made of solid lithiated aluminum fluoride. This paper illustrates the neutron activation analysis study performed on different aluminum fluoride powders to evaluate their use to produce the BSA material, and an example of Monte Carlo calculation of the out-of-field dosimetry. This last aspect is crucial to evaluate the safety of a clinical neutron beam concerning the dose absorbed by peripheral organs.

1. – Introduction

Boron Neutron Capture Therapy (BNCT) is a non-invasive binary radiotherapy combining the low-energy neutron irradiation and a boron-enriched drug able to accumulate preferentially in cancer cells [1]. BNCT is based on the cross-section of ^{10}B for the capture of a thermal neutron, much higher compared to other interactions of neutrons with the elements present in biological tissues. The high-LET (Linear Energy Transfer) charged particles produced in ^{10}B(n,α)^{7}Li reaction have a range in biological tissue comparable with the average diameter of human cells. Thanks to suitable drugs, it is

(*) Corresponding author. E-mail: chiara.magni01@universitadipavia.it

possible to concentrate ^{10}B in the tumour more than in normal cells. The overall effect of the irradiation is thus the selective kill of the tumour, while sparing the surrounding healthy tissues.

The context of this work is the design of a clinical BNCT facility based on a 5 MeV, 30 mA radio frequency quadrupole proton accelerator. The interaction of protons with a beryllium target produces a high flux of neutrons, which are then filtered, moderated and collimated by a proper Beam Shaping Assembly (BSA) to ensure the desired clinical beam. A beam with the appropriate energy spectrum for the treatment of deep-seated tumours is obtained by means of a BSA having solid lithiated aluminum fluoride as the main constituent [2]. As the aluminum fluoride exists only in powder, a novel sintering process was set up to densify a mix of aluminum fluoride and lithium fluoride. A preparatory study through the Neutron Activation Analysis (NAA) method [3] was conducted on two kinds of aluminum fluoride powders to identify the best material for the BSA. After the elemental characterization, Monte Carlo simulations of clinical irradiation were performed to evaluate the dosimetric relevant quantities.

2. – Materials and methods

Lithiated aluminum fluoride has been proved to be the best material to tailor an epithermal beam for BNCT of deep-seated tumours from the neutrons produced by 5 MeV protons on a Be target. Since the BSA must be compact, have uniform density and good mechanical resistance, a sintering process on powders of lithium fluoride (LiF) and aluminum fluoride (AlF_3) has been set up in Pavia. A chemical-grade powder (origin VWR, supplier Alpha Aesar, with a declared purity higher than 99.99%in metals) and an industrial-grade powder (from Fluorsid, Cagliari) were investigated by NAA regarding their composition. In fact, trace elements may constitute a problem concerning their activation after exposure to high neutron fluence.

Small amounts of the two powders were weighed with a precision of 0.01 mg and inserted into suitable plastic containers made of polyethylene. The samples were then activated through exposure to neutrons in the research reactor Triga Mark II at L.E.N.A. (*Laboratorio Energia Nucleare Applicata*) of University of Pavia. The irradiations were carried out in the Central Thimble and in the *Rabbit* facilities of the reactor, with total flux at the maximum power of 250 kW, respectively, equal to 1.91×10^{13} cm^{-2} s^{-1} and 8.37×10^{12} cm^{-2} s^{-1} [4]. The irradiation times were 2 hours in the Central Thimble and less than a minute in *Rabbit*, to detect long-lived and short-lived isotopes. Once the residual radioactivity allowed handling the powders, the emission spectra were acquired with a hyper-pure germanium detector. The analysis of the spectra with the GammaVision software led to the quantification of the trace elements present in the samples. Being the neutron spectrum in the reactor harder than the one to which the BSA will be subjected, only the isotopes with an activation threshold less than 3.5 MeV were considered important. The quantification of trace elements was obtained through the activation reaction rates obtained from spectrometry using the Høgdahl convention [5].

As explained in the next section, the outcomes of this Neutron Activation Analysis determined the selection of the industrial-grade aluminum powder as the best for the production of the solid material. The experimentally evaluated composition of such powder, including the quantified trace elements, was then implemented in a Monte Carlo simulation of the designed BSA. The transport code MCNP6 [6] was used, reproducing the neutron source distribution in the Be target, as described in [2]. The geometry of the treatment room was also created, and simulations of clinical irradiation were

TABLE I. – *Results of the NAA study on the samples of* AlF_3 *powders.*

Isotope	Industrial-grade [mass %]	Chemical-grade [mass %]	Product half-life
As-75	1.1×10^{-4}	1.2×10^{-7}	1.0778 d
Br-81	4.3×10^{-7}	6.5×10^{-7}	35.30 h
Cl-37	–	1.7×10^{-5}	37.24 min
Co-59	9.5×10^{-6}	1.18×10^{-5}	5.2714 y
Cr-50	–	9.8×10^{-8}	27.7025 d
Fe-58	4.3×10^{-7}	–	44.503 d
Ga-71	5.8×10^{-6}	–	14.10 h
La-139	–	3.0×10^{-7}	1.6781 d
Sb-121	1.1×10^{-7}	1.2×10^{-5}	2.7238 d
Sb-123	1.8×10^{-7}	2.7×10^{-5}	60.20 d
Sc-45	2.1×10^{-8}	3.2×10^{-7}	83.79 d
Se-74	–	2.9×10^{-8}	119.779 d
Zn-64	1.6×10^{-5}	–	244.26 d

performed to evaluate several quantities of interest for the design of the facility. The results of the calculations concerning the neutron activation of air, walls and patient, and the dosimetry distributions are reported in [7], proving that the best scenario from the radiation protection viewpoint is obtained with walls of borated concrete.

When designing a clinical facility, a very significant aspect is the beam safety for the out-of-field organs. In fact, dosimetry is important not only in the tumour and in the surrounding normal tissues, but also in the peripheral healthy organs. Radiation protection guidelines do not provide limits for the out-of-field dosimetry, being in radiotherapy the focus on the doses administrated to the tumour. However, the absorbed dose in healthy organs can be a useful tool to compare different beams or therapies in terms of patient safety. Due to recent evidences of radiation-induced cardiovascular diseases [8], this work focuses mainly on the dose absorbed by the heart as a representative example of safety evaluation.

A human phantom was simulated in the room, testing three representative positions for a clinical treatment, with the beam irradiating the head and neck region, the thorax or the lower limb. The MIRD phantom was used, a geometrical human model with 22 internal organs and more than 100 sub-regions [6]. The doses were calculated as explained in [7], by the nuclear reactions occurring in biological tissue irradiated with neutrons in a BNCT treatment. A conservative irradiation time of 2 hours was assumed and the boron concentration in the healthy organs was set to 15 parts per million. The doses were evaluated changing the composition of the walls of the treatment room as in [7]. Ordinary concrete, concrete with 5% of natural abundance boron, ordinary polyethylene and polyethylene with 7% of natural abundance lithium were tested.

3. – Results and future studies

The results of the NAA study are summarized in table I, which shows the mass percentages of the impurities detected in the industrial-grade and chemical-grade AlF_3 powders. The half-lives of the isotopes that can be produced by neutron activation in the BSA are also listed. The chemical-grade powder was found to contain a greater amount

Table II. – *Calculated absorbed doses in the heart in a* 2 h *treatment.*

Beam position	Concrete [Gy]	Concrete+B [Gy]	Polyethylene [Gy]	Polyethylene+Li [Gy]
Head	0.96	0.79	0.83	0.78
Thorax	2.04	1.87	1.92	1.86
Lower limb	0.97	0.25	0.77	0.21

of impurities leading to long-lived activation products. With a view to the future facility, this result, coupled with the fact that the chemical-grade powder gives worse results in terms of sintering, indicated the industrial-grade powder as the best candidate for the BSA core.

The calculated absorbed doses in the heart are shown in table II, with their dependence on the irradiation position and on the tested composition of the walls in the treatment room. In every position and for each of the walls configurations the absorbed dose is less than or comparable to 2 Gy. As expected, concerning heart dosimetry, the best wall configurations are borated concrete and lithiated polyethylene. Studies as [9] suggest a linear dose-response relationship between the dose absorbed in the heart and the rate of myocardial infarction in patients treated with radiotherapy. Converting the doses reported in the cited work in single-fraction using BED formalism [10], the mean dose received by evaluated patients is 4 Gy and the risk of myocardial infarction increases considerably over 6.8 Gy. Even expressing the values of table II in photon-equivalent units, by means of the commonly used RBE factors for the dose components in BNCT [1], the absorbed dose by heart in a BNCT treatment is lower than 3.3 Gy (RBE-weighted). From these values, calculated in conservative assumptions, BNCT with the designed beam remains below the dose above which the risk of myocardial infarction increases considerably according to [9]. Further research should be conducted, however such findings suggest that BNCT with these settings is a viable treatment modality from the point of view of radiation-induced cardiovascular diseases.

Future work will investigate the distribution of absorbed dose in the heart volume, being one of the factors taken into account in [9]. Also, similar studies regarding out-of-field dosimetry will be conducted in other organs at risk, to characterize in detail the beam regarding patient safety.

REFERENCES

[1] Coderre J. A. and Morris G. M., *Radiat. Res.*, **151** (1999) 1.
[2] Postuma I., *Clinical Application of Accelerator-Based Boron Neutron Capture Therapy: Optimization of Procedures, Tailoring of a Neutron Beam and Evaluation of its Dosimetric Performance*, PhD Thesis, University of Pavia, 2015.
[3] Greenberg R. R. *et al.*, *Spectrochim. Acta Part B*, **66** (2011) 193.
[4] Alloni D. and Prata M., *Irradiation Channels and neutron fluxes at the Pavia TRIGA Mark II Research Reactor*, LENA Technical Report, 2014.
[5] Verheijke M. L., *J. Radioanal. Nucl. Chem.*, **183** (1994) 293.
[6] *MCNP - A General Monte Carlo N-Particle Transport Code*, LA Report, 2003.
[7] Magni C. *et al.*, *Appl. Radiat. Isot.*, **165** (2020) 109314.
[8] Adams M. J. *et al.*, *Crit. Rev. Oncol. Hematol.*, **45** (2003) 55.
[9] Jacobse J. N. *et al.*, *Int. J. Radiat. Oncol. Biol. Phys.*, **103** (2019) 595.
[10] Fowler J. F., *Brit. J. Radiol.*, **62** (1989) 679.