

Comprehensive benchmarking strategies for BNCT beams based on predicted clinical outcome.

Lucas Provenzano
Comisión Nacional de Energía Atómica (CNEA), Argentina
Email: lucasprovenzano@hotmail.com

Hanna Koivunoro
Neutron Therapeutics, Finland

Ian Postuma
Istituto Nazionale di Fisica Nucleare (INFN), Pavia, Italy

Juan M. Longhino
Comisión Nacional de Energía Atómica (CNEA), Argentina

Esteban F. Boggio
Comisión Nacional de Energía Atómica (CNEA), Argentina

Ruben O. Farias
Universidad Favaloro, Argentina

Silva Bortolussi
Istituto Nazionale di Fisica Nucleare (INFN), Department of Physics, University of Pavia, Italy

Sara J. González
Comisión Nacional de Energía Atómica (CNEA), Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina

Introduction: Boron Neutron Capture Therapy (BNCT) is a treatment modality that combines high and low LET radiations to inactivate tumor cells [1]. Since these radiations produce different levels of biological damage, the assessment of the clinical performance of a BNCT beam requires the evaluation of radiobiological figures of merit (FOM) capable of estimating the expected success of a radiation treatment. Primary free-beam in-air physical quantities describing the incident beam intensity and quality proved suitable to guarantee adequate and safe BNCT beams [2]. However, their usefulness to assess the therapeutic potential of a beam (i.e., the ability of the beam to control a tumor without unacceptable complications) and the versatility (i.e., the variety of scenarios for which the therapeutic potential is acceptable), is limited. This work presents the development and innovative use of probability models to evaluate and compare the aforementioned characteristics referred to as the beam performance.

Materials and Methods: A model of uncomplicated tumor control (UTCP) that describes the probability for controlling a HN tumor without severe complications in the mucosal membrane was introduced for the first time in BNCT. The proposed UTCP combines the expression of the tumor control probability (TCP) for non-uniform doses, and a normal tissue complication probability (NTCP) model able to predict mucositis grade 3 or higher after a BNCT treatment [3]. A systematic study comprising a simplified HN cancer model is presented as a practical application of the introduced FOMs for assessing and comparing the performance of different beams. The UTCP was calculated for the clinical beams RA-6 B2 and FiR1 of the Argentine and Finnish reactors, respectively, and for two the realistic epithermal beam designs, the RA-6 B3 and RFQ, based on modifications of the actual BNCT facility in Argentina, and on the proton Radiofrequency Quadrupole accelerator manufactured by INFN in Italy. Different applications of the introduced

FOMs considering real HN cancer patients treated in Finland were analysed. Results were discussed in the light of physical characteristics of the studied beams and treatment outcomes.

Results: The maximum value of the UTCP proved to be a suitable and a sensitive FOM to assess the performance of a beam revealing particularities of the studied sources that the standard FOMs do not reveal. The systematic study showed to be an adequate procedure to evaluate and compare the performances of different BNCT beams regardless the energy spectra.

Conclusions: Current developments of probability models for other targets guarantee the applicability of the proposed procedures to other treatments of interest in BNCT. The UTCP evaluated for real cases of patients showed to be useful tools both for retrospective analysis of the BNCT treatments carried out with existing facilities, and for prospective studies of feasibility and beam optimization. Clinical trials of HN cancer treatments with accelerator-based BNCT in Japan, Taiwan and Finland are ongoing or about to start. The presented developments along with the proposed applications would be a practical and useful aid to guide treatment decisions.

References:

1. G. Locher. Biological effects and therapeutical possibilities of neutrons, *Am J Roent Radium Ther*, 36, 1–13 (1963).
2. TECDOC Series 1223. Current Status of Neutron Capture Therapy (International Atomic Energy Agency (IAEA). (2001).
3. S. J. González, E. C. C. Pozzi, A. M. Hughes, L. Provenzano, H. Koivunoro, D. G. Carando, S. I. Thorp, M. R. Casal, S. Bortolussi, V. A. Trivillin, M. A. Garabalino, P. Curotto, E. M. Heber, G. A. S. Cruz, L. Kankaanranta, H. Joensuu and A. E. Schwint. Photon iso-effective dose for cancer treatment with mixed field radiation based on dose–response assessment from human and an animal model: clinical application to boron neutron capture therapy for head and neck cancer *Phys. Med. Biol.* 62 7938–7958 (2017).