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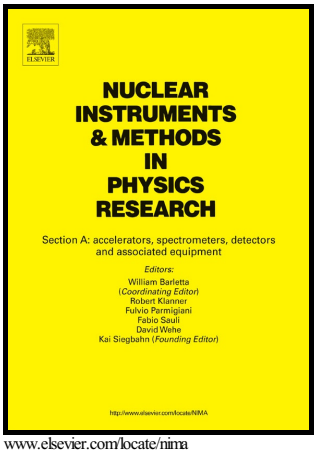

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Preliminary study for small animal preclinical hadrontherapy facility

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Abstract

Aim of this work is the study of the preliminary steps to perform a particle treatment of cancer cells inoculated in small animals and to realize a preclinical hadrontherapy facility. A well-defined dosimetric protocol was developed to explicate the steps needed in order to perform a precise proton irradiation in small animals and achieve a highly conformal dose into the target. A precise homemade positioning and holding system for small animals was designed and developed at INFN-LNS in Catania (Italy), where an accurate Monte Carlo simulation was developed, using Geant4 code to simulate the treatment in order to choose the best animal position and perform accurately all the necessary dosimetric evaluations. The Geant4 application can also be used to realize dosimetric studies and its peculiarity consists in the possibility to introduce the real target composition in the simulation using the DICOM micro-CT image. This application was fully validated comparing the results with the experimental measurements. The latter ones were performed at the CATANA (Centro di AdroTerapia e Applicazioni Nucleari Avanzate) facility at INFN-LNS by irradiating both PMMA and water solid phantom. Dosimetric measurements were performed using previously calibrated EBT3 Gafchromic films as a detector and the results were compared with the Geant4 simulation ones. In particular, two different types of dosimetric studies were performed: the first one involved irradiation of a phantom made up of water solid slabs where a layer of EBT3 was alternated with two different slabs in a sandwich configuration, in order to validate the dosimetric distribution. The second one involved irradiation of a PMMA phantom made up of a half hemisphere and some PMMA slabs in order to simulate a subcutaneous tumour configuration, normally used in preclinical studies. In order to evaluate the accordance between experimental and simulation results, two different statistical tests were made: Kolmogorov test and gamma index test. This work represents the first step towards the realization of a preclinical hadrontherapy facility at INFN-LNS in Catania for the future *in vivo* studies.

Keywords: preclinical studies, hadrontherapy, Geant4, dosimetry, small animal irradiation protocol

1. Introduction

Molecular and cellular processes involved in hadrontherapy response are very complex and still not fully understood at all. Further studies are required for a full understanding of biological processes in hadrontherapy field. In fact, *in vitro* studies highlighted the complexity of mechanism which regulate cell response to ionizing radiations (apoptosis, necrosis, senescence, survival). Moreover, cell response was found to be strongly cell-type and dose dependent [1–3]. It was observed that radiations induce release of local and systemic inflammatory molecules and signal molecules, which communicate the damage to non-treated cells and tissues (bystander effects) [4, 5]. Preclinical models represent the next step for the comprehension of biological processes and molecular mechanisms of response to radiation therapy, often used as a preliminary research for Phase 0 and Phase I human trials [6], with the aim of an application in clinical field [7]. The main purpose of this work is to lay down the foundation for the realization of a hadrontherapy preclinical facility in order to perform *in vivo* studies. Small animal irradiation systems must mimic the clinical application of radiation therapy as closely as possible. The irradiation technique has deeply evolved in the last years, producing new technologies such as the Intensity Modulated Radiation Therapy (IMRT) [8] that includes a highly conformal dose. The state of art is mainly focused on X-ray

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