# The LARAMED project at the INFN-LNL: Direct cyclotron-based production of medical radionuclides *

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The cyclotron-based production of medical radionuclides is one of the research activities carried out in the framework of the SPES (Selective Production of Exotic Species) project at the Legnaro National Laboratories of the National Institute for Nuclear Physics (INFN-LNL). The heart of SPES is the 70 MeV proton-cyclotron with a dual-beam extraction that will enlarge the possibilities related not only to nuclear physics and astrophysics studies but also to applied research, including radionuclides production for medical applications [1]. The interdisciplinary LARAMED (LAboratory of RAdionuclides for MEDicine) project [2,3] is based on the direct-activation method to produce several innovative medical radionuclides. The LARAMED project's aim is to complete the entire production cycle, starting from the target manufacturing and nuclear cross section measurements to the radiopharmaceutical production. To achieve these goals the LARAMED facility is currently under completion and it includes:

- two different bunkers devoted to: (i) the production of limited amounts of novel radioisotopes for research purposes (i.e., support other research centers, as well as research studies at the preclinical level) by using high-current proton beam and (ii) experimental nuclear physics activities (i.e., mainly cross section measurements) by using a maximum current of 100 nA;
- two different laboratories respectively dedicated to target manufacturing and radiochemical separation and characterization of the obtained product.

At SPES both the target station and the target-holder have been designed and realized specifically for the cross section measurements. Waiting for the completion of the two LARAMED bunkers, we had the opportunity to use a different bunker temporarily. The use of the target station was therefore successfully tested and, in the future, it will be used for cross section measurements for the production of radioisotopes of medical interest. This work will present the results of these preliminary tests in view of the future research experiments.

**References**

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# Monte Carlo Simulations for Dosimetry and Microdosimetry for Biomedical Sample Irradiations with Thermal Neutron Beams *

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In the framework of the FRINGE project [1] investigating novel agents for Gd neutron capture therapy, neutron irradiations are performed at the Swiss Spallation Neutron Source (SINQ) at Paul Scherrer Institut (PSI), Switzerland and at the LVR-15 reactor at Research Centre Řež, Czech Republic. Cell cultures tagged with different Gd agents are irradiated with neutrons to study their cell killing effectiveness. The aim of the present study is to investigate the dosimetric characteristics of the two facilities for neutron irradiations of cell cultures. Monte Carlo simulations were performed using the MCNP6.1 code to evaluate the absorbed dose, the dose energy distribution, as well as to delineate microdosimetric spectra of protons, heavy particles and electrons for the two neutron beams examined. Such spectra allow for the prediction of the biological response of cells exposed in neutron fields based on response data obtained in gamma-fields. Microdosimetric data were combined with appropriate weighting functions, in order to determine the relative biological effectiveness (RBE) in each case. The present study supports the results of the *in vitro* cell culture irradiations performed in FRINGE, as well as implements a methodology allowing an estimation of the biological effectiveness of neutron fields with different characteristics.

**References**

[1] FRINGE Project Website: https://www.fringe-fetopen.eu/

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# Ortho-Positronium Emission Tomography (oPsET): a non-invasive technique for the in-situ measurement of tumour hypoxia using proton therapy

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Tumour hypoxia, a state of diminished oxygen tension compared with surrounding healthy tissue, is an established biological phenomenon which not only affects the response of the tumour to radiotherapy, surgery and chemotherapy, but can also indicate an increased risk towards metastasis [Muz2015]. Studies [Wal2014] have also reported a significant decrease in patient survival years for hypoxic tumours compared with their normoxic counterparts. A measurement of the hypoxic state of a tumour is, therefore, a valuable tool for clinicians to establish and monitor the staging of disease.

This project aims to show the potential for a measurement of tumour hypoxia, simultaneous to the delivery of a radiotherapy dose with proton therapy. The proposed technique takes advantage of the fact that the protons used to deliver the dose to the patient also induce nuclear reactions in the patient's body, creating radioactive oxygen and carbon atoms. During the radioactive decay of these atoms, positrons are emitted and can form the meta-stable positronium.

Previous studies [Shi2020, Mos2019] have shown that the lifetime of this positronium is dependent on the oxygenation level of the surrounding tissue. By combining technology routinely used to perform positron emission tomography (PET) imaging and experimental techniques used in fundamental nuclear physics experiments, this collaboration is proposing a non-invasive method for the measurement of tumour hypoxia without the need for additional imaging modalities. It is envisioned that this novel imaging modality will enable clinical staff to measure tumour hypoxia throughout a patient's fractionated dose delivery and enable the treatment plan to be modified and optimised according to the oxygenation state of the tumour. If employed, it is predicted that this technique could have benefits to patient outcomes and comfort in addition to financial benefits to healthcare providers.

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# Carbon ion treatment verification by means of Prompt Gamma Timing technique: first results at sub-clinical rate

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The Prompt Gamma Timing (PGT) method is a non-invasive and real-time approach to assess particle range by measuring the time of flight between the primary particle and PG detection. We report the first PGT results obtained with carbon ion beams at the sub-clinical rate at the CNAO (Pavia, IT).
An 8-strip silicon sensor beam monitor (1) and a Lanthanium Bromide LaBr3(Ce) detector for secondary prompt photons (fig.1.a) were used (2). The time resolution is about 30 ps for the beam monitor and 200 ps for the PG detector. A DT5742 digitizer sampled signals at 2.5 GHz, triggered by the PG detection. Experiments were conducted on a 30-cm homogeneous PMMA phantom and three inhomogeneous PMMA phantoms, irradiated with carbon ion beams at 398 MeV/u.
The preliminary results with sub-clinical rate beams are promising. The PGT distributions show different shapes allowing air cavities and bone insert identification (fig1.b). Ongoing analyses aim to evaluate PGT distribution uncertainty. Since the proposed PGT prototype can handle high-rate irradiations, further tests are foreseen to explore its applicability in a clinical environment.

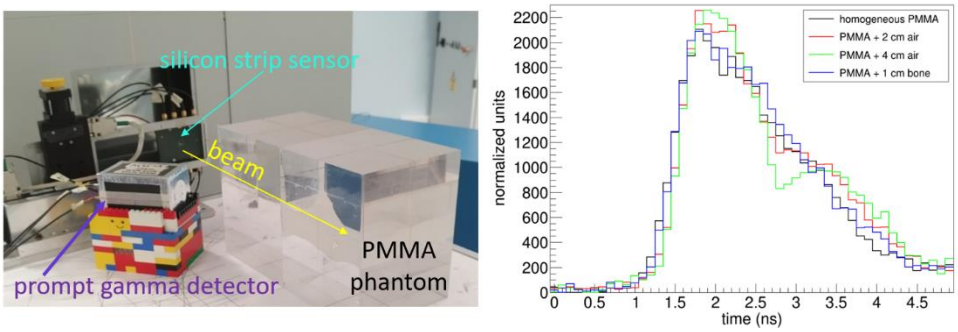


Fig.1 a) experimental setup b) PGT distributions with different phantoms

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