Ph.D. in Information Technology
Thesis Defenses

February 24th, 2025
At 9:00 a.m.
Room Alpha – Building 24

Anita CARACCIOLO – XXXVII Cycle

DEVELOPMENT OF A GAMMA-RAY DETECTION UNIT FOR A SPECT SYSTEM FOR REAL-TIME DOSE MONITORING IN BNCT

Supervisor: Prof. Carlo Ettore Fiorini

Abstract:

This doctoral research focuses on the development of a gamma-ray detector designed for use in a Single Photon Emission Computed Tomography (SPECT) configuration, specifically for quantifying and localizing the dose delivered to patients during Boron Neutron Capture Therapy (BNCT). BNCT is a highly targeted form of hadron therapy that exploits the interaction between boron-10, selectively accumulated in tumor cells via specific binding compounds, and thermal neutrons used to irradiate the patient. This interaction produces two high linear energy transfer (LET) particles that release their energy within the targeted tumor cells. Due to its precise targeting capability, BNCT is particularly effective for treating infiltrative or diffuse tumors and tumors located near critical structures. Its clinical adoption has been limited by several challenges, including the generation of sufficient clinical neutron fluxes, the development of selective and non-toxic boron compounds, and the absence of real-time dose monitoring systems. Recent advancements in compact accelerator-based neutron sources have revitalized interest in BNCT, with several new facilities now operational or under construction worldwide. As a result, there is an urgent need to further develop BNCT-related technologies. The objective of this thesis was to develop a single unit of a BNCT-SPECT system, that aims to detect gamma rays at 478 keV emitted by boron neutron capture reactions to enable real-time dose monitoring. The development of this system is particularly challenging due to the unique requirements of BNCT, including the need to detect low concentrations of boron (tens of ppm) over a huge background of mixed radiation produced by the high-intensity neutron flux necessary for treatment. The development focused on an indirect conversion gamma-ray detector based on a LaBr3(Ce3++Sr2+) scintillator crystal, coupled with silicon photomultipliers (SiPMs) and read by custom electronics based on Application-Specific Integrated Circuit (ASIC) and Field-Programmable Gate Array (FPGA). The detector is combined with a pinhole collimator and an Artificial Neural Network (ANN) algorithm for two-dimensional position reconstruction of the gamma events. Over the course of this thesis, three successive versions of the detector were developed and are presented herein. A series of experimental measurements at the TRIGA Mark II research nuclear reactor of Pavia University validated the feasibility of the BNCT-SPECT unit developed. The system successfully detected 1 cm lateral displacements of a borated vial during neutron irradiation. These

results strongly suggest that the BNCT-SPECT system proposed and developed in this research holds significant promise for clinical applications.

Aicha Bourkadi IDRISSI – XXXVII Cycle

STUDY AND DEVELOPMENT OF A PROMPT GAMMA IMAGING DETECTOR FOR RANGE MONITORING IN CARBON ION RADIATION THERAPY

Supervisor: Prof. Carlo Ettore Fiorini

Abstract:

Particle Therapy (PT) is an advanced form of radiation therapy that utilizes protons, heavy ions (e.g., carbon ions), or neutrons to target tumors with high precision, minimizing toxicity to surrounding tissues compared to conventional radiotherapy. Unlike X-rays and electrons, which deposit dose exponentially with depth, heavy charged particles exhibit a Bragg peak, a sharp dose deposition at the end of their range, allowing precise targeting of tumor depths. However, PT's sensitivity to uncertainties, such as anatomical changes, physiological organ movement, and particle range calculations, can lead to dose mismatches, often necessitating larger safety margins and multiple fields, which increases radiation exposure to surrounding tissues.

In vivo particle range verification, particularly using prompt gamma imaging (PGI), has been identified as a promising solution for real-time dose profile monitoring, allowing for potential adjustments during treatment. PGI is based on prompt gamma photons emitted almost instantly by nuclear interactions within the patient's tissues.
This technique was already tested in clinical environment with a knife-edge-collimator camera for proton treatments achieving a range verification precision down to 1 mm, but remains relatively unexplored for Carbon Ion Radiation Therapy (CIRT).

C-ions offer several distinct advantages over protons in hadrontherapy due to their unique physical interaction properties, which result in a higher linear energy transfer (LET) and thus an increased relative biological effectiveness (RBE). This enhanced RBE allows C-ions to achieve a more effective therapeutic outcome, especially in treating hypoxic tumors, which are typically more resistant to conventional radiation therapies.

However, the use of prompt gamma imaging (PGI) technique in C-ion therapy introduces specific challenges. Notably, C-ions produce a higher neutron yield per ion and require fewer incident particles to deliver the same physical dose as protons. These characteristics significantly impact the signal-to-background ratio, presenting a critical challenge for accurate PGI measurements. Consequently, the optimization of detection efficiency and the ability to discriminate between gamma and neutron emissions are paramount in adapting PGI for Carbon Ion Radiation Therapy (CIRT).

In this Ph.D. thesis, the potential of PGI for range verification in CIRT environment has been explored using a prototype knife-edge slit-camera system.

First, Monte Carlo simulations were conducted using FLUKA, a versatile Monte Carlo code for particle transport. In those simulations, a knife-edge slit camera was employed to detect secondary particles emitted in the 3-7 MeV energy range from an ICRP (International Commission on Radiological Protection) soft tissue phantom, simulating a patient irradiated with a mono-energetic pencil beam of carbon ions (C-ions) at 150 MeV/u. This energy was chosen to align with the therapeutic energy range used in CIRT.

The simulation results indicated that a layer-by-layer range verification could be achieved with a 4 mm precision using a 10 cm x 10 cm detection module, provided that an average of approximately 5 x 10^7 primary particles are delivered.

To validate these findings, a first 64-ch prototype was developed and tested at the Centro Nazionale di Adronterapia Oncologica (CNAO) in Pavia, Italy. This experiment employed a knife-edge-collimator camera prototype, utilizing a 8×8 pixelated LYSO scintillator (5 x 5 cm^2) coupled with a 64-SiPM array, four GAMMA (Gain Amplitude Modulated Multichannel ASIC) ASICs and a FPGA-based DAQ system. Prompt gamma (PG) profiles were measured by irradiating a plastic phantom with a C-ion pencil beam at clinical energies and intensities. Additionally, the detector was translated in different positions to expand the field of view (FOV) to 13 x 5 cm^2.

The prototype successfully detected Bragg-peak shifts with a precision of approximately 4 mm for a sample statistic of roughly 4 x 10^8 C-ions (3 x 10^8 for the extended FOV), which was larger than initially anticipated. Despite this, the detector demonstrated significant potential for accurately verifying dose delivery precision after a treatment fraction, which is essential in clinical practice. To our knowledge, this experiment marks the first instance where range verification based on PGI was applied to a carbon ion beam at clinical energy and intensities, highlighting the viability of PGI for real-time range verification in C-ion therapy.

A second 32-ch prototype featuring a 8×4 pixelated LYSO scintillator (5 x 2.5 cm^2) coupled with a 32-SiPM array, two SITH (Spectroscopy Imaging Timing Hadrontherapy) ASICs and a FPGA-based DAQ system. This system has better count-rate capabilities, up to 700 kHz per channel and timing capabilities (less than 1 ns).
Recently, also this system has been tested at CNAO both with carbon ion and proton beams and the preliminary results indicated the possibility to detect the PG shifts at high statistics for both the particle beams.

Moreover, for the particularly challenging extraction of the prompt gamma profile—correlated to the Bragg peak fall-off position—from the neutron background, Pulse Shape Discrimination (PSD) was investigated using crystals with selective responses to neutrons and gammas. A first prototype was developed based on a 1"x1" CLYC-6 (Cesium Lithium Yttrium Chlorid) scintillator coupled with 4x4 array of SiPMs and read out by a SITH ASIC. This prototype was tested at CNAO during the experimental campaign using the 64-ch PGI detector prototype, using the same irradiation setup.

The Figure of Merit (FOM) obtained was 1.29 at t_1 = 120 ns and t_2 = 1500 ns, which is adequate to effectively perform PSD. This result provides a further option for future research on PGI, based on

the CLYC scintillator, particularly when paired with the SITH ASIC, to mitigate neutron background interference in prompt gamma-ray (PG) measurements during hadrontherapy.

Keywords: Particle Range monitoring, Prompt Gamma Imaging, Hadrontherapy, Carbon ion Radiation Therapy

PhD Committee

Prof. Giacomo Borghi, **Politecnico di Milano**

Prof. Kazuki Tsuchida, **Nagoya University**

Prof. Etienne Testa, **Université Lyon1**