Hadron therapy range verification via Machine-Learning aided prompt-gamma imaging

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***Abstract*—The aim of this work is to demonstrate the capability of the i-TED Compton imager for range verification in quasi-real-time prompt gamma-ray (PG) monitoring. PG monitoring constitutes a promising technique for range verification in hadron therapy treatments. Hadron Therapy (HT) with protons introduces advantages with respect to the conventional radiotherapy because of the maximization of the energy deposition (dose) at the Bragg peak. i-TED is an advanced array of Compton cameras originally designed for neutron-capture nuclear experiments. However, due to its large detection efficiency, fast response, high time resolution, compactness, low sensitivity to neutron-induced backgroudns and image resolution, i-TED shows also an excellent performance for medical purposes such as PG monitoring. Furthermore, aiming at improved quality Compton images in the high-energy gamma-ray range characteristic of HT, a novel Machine Learning (ML) methodology has been developed and applied for identification of full-energy events. To that purpose, a detailed GEANT4 Monte Carlo (MC) study simulating a clinical irradiation has been performed. We conclude that due to the improvements obtained with ML and the use of GPUs, a system like i-TED can be used for quasi-real time PG monitoring. Finally, we will present first results from an experiment performed at the cyclotron of the CNA facility, Spain, where i-TED was simultaneously operated as in-beam PET and Compton imager.**

***Index Terms*—Nuclear imaging, Machine learning algorithms, Monte Carlo methods**

I. INTRODUCTION

Proton therapy presents advantages with respect to conventional radiotherapy maximizing the dose at the Bragg peak. Therefore, an improved targeting of the tumor region can be performed, minimizing the dose received by the neighboring tissues and reducing the long-term secondary effects of the radiotherapy on the patients [1]. As a drawback, the inherent range uncertainty of the protons associated to anatomical changes, patient setup errors and uncertainties from particle stopping power in different materials require to increase the safety margins in such type of treatments, strongly limiting its potential benefits [2].

In this context, several experimental methods to verify the proton beam range are being developed, mainly based on the Prompt Gamma (PG) rays and monitoring secondary particles [4]. However, PG monitoring offers the advantage of the high spatial correlation with the dose distribution [3]. Therefore, and because of the low probability of the nuclear reactions and the proton currents handled by the clinical accelerators, high efficiency imaging systems are required. However, there are still important challenges during the clinical irradiations [9]–[13]. Some of these aspects can be significantly improved by means of a system like i-TED. This imager was originally developed for neutron-capture time-of-flight nuclear experiments, where the radiative capture channel of interest is very weak, an excellent time-resolution is required and where high-energy gamma-ray energies have to be measured, immersed also in a very hostile neutron induced-background. A situation which does not differ much from the range-monitoring conditions during HT treatments. i-TED consists of an array of four two-plane Compton cameras. Each of them is based on five largest available monolithic $LaCl_3$ crystals, featuring a total sensitive volume of 1150 cm^3 with 3D position sensitive capabilities. For further details the reader is referred to [5]–[7].These neutron-capture experiments are characterized by a γ-ray emission matching well with the energies used for PG monitoring [8].

II. MATERIAL AND METHODS

One of the critical points for an accurate Compton image and ion-range reconstruction using a two plane Compton Camera is the correct identification of those events fulfilling that the γ-ray event deposits all its energy in the scatter and absorber planes (full-energy events). All other events with incomplete energy deposition lead to a deterioration of the final image and, therefore, of the ion-range assessment.

For high energy γ-rays such as those used for PG monitoring, only a low fraction of the events will produce full-energy events. Therefore, a large background is expected in the image. Aiming at improving this situation, a novel ML algorithm has been developed and applied in this work for the reliable identification of full energy events. More specifically, it consists

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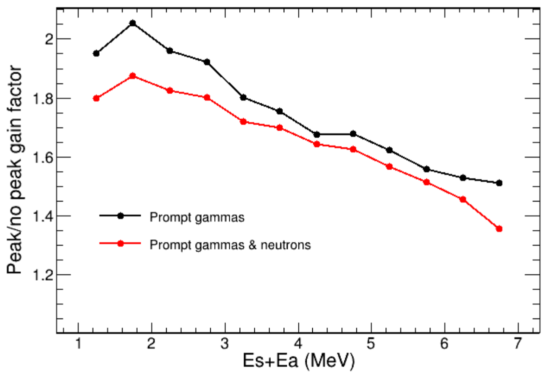

Fig. 1. Gain factor ratio as a function of the add-back deposited energy. The black and red lines represent, respectively, the results with only γ-ray events and including neutron events.

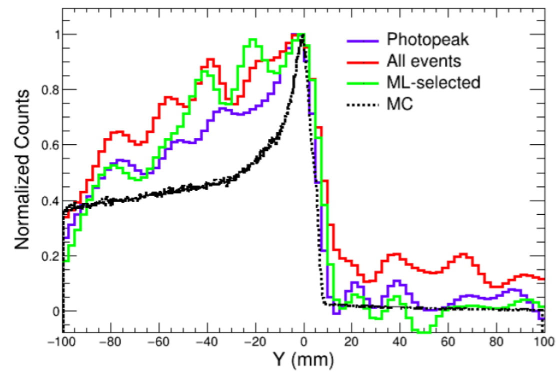

Fig. 2. Compton images 1D projections along the proton beam axis combining the four main transitions in PG. See text for details.

of a neural network classifier implemented in Tensorflow [14]. The architecture and activation functions were chosen based on the best performance in terms of accuracy.

GEANT4 [15] MC simulations were used for the training and evaluation of the ML algorithms. In the training, dedicated simulations of the response of i-TED to γ-rays of energies homogeneously distributed between 200 keV and 7 MeV and spatially originated in a random position within a $20\times20\times20$ cm^3 air cube, replicating the expected field of view of the detector. Each MC event contains the same features that can be obtained experimentally, namely, 3D interaction position and deposited energy in each detection plane conveniently convoluted with experimental resolutions [6]. Additionally, the probability for a Compton interaction with energy equal to the add-back energy was calculated using the Klein-Nishina formula. The MC output was split into 14 energy intervals of add-back deposited energy between 200 keV and 7 MeV and the same number of either kind of events were selected from the MC output for each energy interval. For each energy range we trained an independent classifier.The evaluation of the ML was performed using a simulation of a 180 MeV proton beam impinging on a PMMA phantom that lately will be used to demonstrate the imaging improvement.

The gain factor with respect to the situation where the ML algorithms are not applied is significantly, as it is shown in Fig. 1, both with and without including the impact of neutrons in the study. The gain spans from almost a factor of 2 at 2 MeV down to 1.4 for 7 MeV gamma-rays (in add-back energies). **This result indicates, that a two-plane Compton camera in combination with this sort of algorithm, can provide a better performance than the widely used three-layer approach, where detection efficiency is severly compromised.**

III. Preliminary results and outlook

The final results obtained from the MC study are summarized in Fig. 2, which shows the Compton images projection along the proton beam axis. The reconstruction algorithm used is based on an analytical inversion [16] implemented in GPU to provide the best accuracy and time performance. The three solid curves shown in Fig. 2 correspond to the image with only full-energy γ-ray events, the image with no selection including neutron events and the corrected result after the ML-classifier is applied. The true depth distribution (MC) is shown as the black dashed line.

These algorithms have been tested on data taken at Centro Nacional de Aceleradores (CNA) of Spain. In these measurements 18 MeV protons impinged on a 5-layers stack of thin Nylon foils, separated by 1.6 cm and surrounded by two i-TED modules. The latter could be therefore simultaneously operated as a positron-emission tomograph (PET) for in-beam image reconstruction from 511 keV positron annihilation gamma-rays, and also as high-energy prompt-gamma Compton imagers. A comparison between both approaches will be presented, together with a short outlook on the next steps of this work in this field.

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