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In-room test results at CNAO of an innovative PT treatments online monitor (Dose Profiler)

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Summary. — The use of C, He and O ions as projectiles in Particle Therapy (PT) treatments is getting more and more widespread as a consequence of their enhanced relative biological effectiveness and oxygen enhancement ratio, when compared to the protons one. The advantages related to the incoming radiation improved efficacy are requiring an accurate online monitor of the dose release spatial distribution. Such monitor is necessary to prevent unwanted damage to the tissues surrounding the tumour that can arise, for example, due to morphological changes occurred in the patient during the treatment with respect to the initial CT scan. PT treatments with ions can be monitored by detecting the secondary radiation produced by the primary beam interactions with the patient body along the path towards the target volume. Charged fragments produced in the nuclear process of projectile fragmentation can be emitted at large angles with respect to the incoming beam direction and can be detected with high efficiency in a nearly background-free environment. The Dose Profiler (DP) detector, developed within the INSIDE project, is a scintillating fibre tracker that allows an online reconstruction and backtracking of such secondary charged fragments. The construction and preliminary in-room tests performed on the DP, carried out using the ^{12}C ions beam of the CNAO treatment centre using an anthropomorphic phantom as a target, will be reviewed in this contribution. The impact of the secondary fragments interactions with the patient body will be discussed in view of a clinical application. Furthermore, the results implications for a pre-clinical trial on CNAO patients, foreseen in 2019, will be discussed.

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1. – Introduction

Proton and carbon ion beams are currently used to treat deep-seated solid tumors resistant to the conventional radiotherapy, in particular when located close to Organs At Risk (OAR) [1]. When compared to standard radiotherapy treatments, the main advantage of this technique is the improved localization of the irradiated dose in the tumor region that helps in sparing the surrounding healthy tissues and organs. Charged particles lose most of their energy at the end of their path, in the region called "Bragg Peak (BP)", while the dose deposited by X-rays is exponentially decreasing as a function of the photons range inside the matter (fig. 1). Currently, the proton treatments are the most common, but the use of carbon beams has known an increase, at least in Europe in the last 10 years, with the beginning of the operation of several new facilities.

The intrinsic precision, due to the peculiar features of dose release in the BP region, is jeopardized by uncertainties in the knowledge of the actual primary particle range. Inhomogeneities, computed tomography artifacts, conversion to electronic density, intersession anatomical/physiological changes can lead to sensible range variations with a sensible change in the dose released in the target volume. New online dose monitoring devices have to be introduced into clinical use to avoid the risk to hit healthy organs and to take full advantage of the ability of particle therapy to deliver the dose to the Planned Treatment Volume (PTV) [2,3]. Currently, no technical solution is availble for the online monitoring of PT treatments that are involving "heavy ions" ($Z > 1$). Attempts to use PET scans immediately after the treatment, to validate the treatment quality, are reported in the literature (for a review see [4]).

Primary beam particles cannot be used for dose range monitoring, as they do not escape from the patient. A promising approach consists in the detection of the secondary particles (PET photons, prompt photons, neutrons and charged particles) produced by the nuclear interactions between the primary beam with the crossed tissues.

It has already been shown that the Bragg peak can be correlated with the emission pattern of secondary prompt photons in the energy range 1–10 MeV [5,6] and secondary

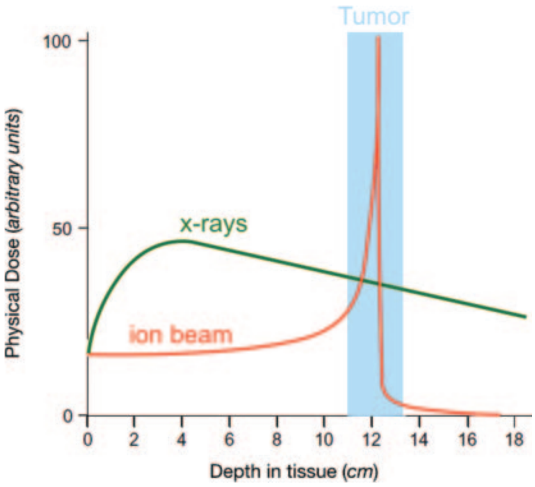

Fig. 1. – Physical dose release along the path traveled in matter for X-rays (green) and an ion beam (red). The tumor position is represented in light blue.

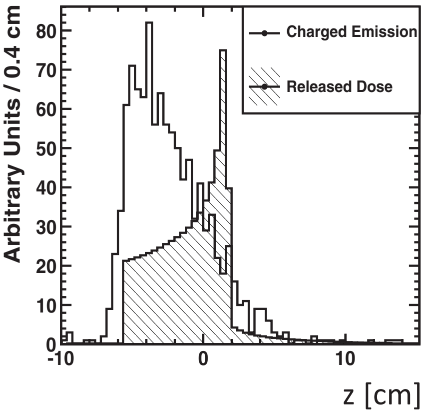

Fig. 2. – Longitudinal emission profile of charged secondary particles, detected at 90° with respect to the beam direction, produced by a $220\,\text{MeV}/u$ ^{12}C ion beam impinging on a PMMA target. The depth-dose distribution (hatched area) is superimposed [8].

charged particles with kinetic energies up to a few hundred MeV [7] (fig. 2). The carbon beam produces higher-energy, secondary charged particles with a larger flux when compared to the proton beam case. The detection of the neutral hadronic component (neutrons) is experimentally more demanding, but would allow to reach a significant statistics of detected particles, as they are abundantly produced even in proton treatments.

2. – Dose Profiler and INSIDE project

The Dose Profiler (DP) detector has been designed to detect the secondary charged particles (mostly protons) emitted as products of the nuclear fragmentation of the projectile (beam of ^{12}C). Those particles can be detected with a high efficiency and a small background achieving a high backtracking resolution. The largest fraction of the fragments is forward peaked, and it is mostly contained within a cone of few degrees with respect to the beam axis. However, the proton component shows a significant tail at large emission angles. These results have triggered several studies on the possibility to exploit charged fragments for monitoring purposes. In fact, large angles production is the most interesting for monitoring applications, because of the advantageous proton reconstruction resolution (the uncertainty on the emission point reconstruction is proportional to $(\sin\theta)^{-1}$, where θ is the proton emission angle), and for the difficulties related to the positioning in the treatment room of a detector along the incoming beam direction. It is expected that the charged particles yield at large angles remains relevant in the case of beams of particles heavier than protons [8]. Therefore, the potential use of charged particles detection for the PT treatments online monitoring can be especially appealing in ^{12}C therapy.

The DP has been developed in the framework of the INSIDE (Innovative Solution for monitoring in Hadrontherapy) project in order to work in a dual in-beam dose monitoring system able to detect at the same time secondary protons with the DP and, with a PET-γ detector, back-to-back photons from the annihilation of positrons emitted by β^+-decaying isotopes produced in the patient by the therapeutic proton or carbon ion beams. The whole system, shown in fig. 3, is planned to be integrated in the treatment room of

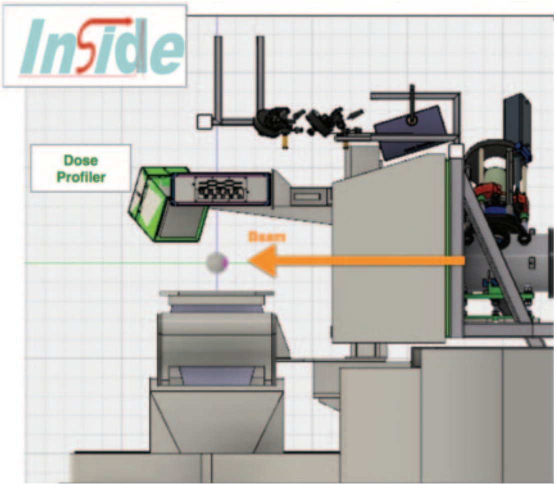

Fig. 3. – INSIDE: pictorial representation of the integration of the INSIDE simultaneous in-beam dose monitoring system developed for the online control of proton and carbon ions beams in the treatment room of CNAO.

CNAO (Centro Nazionale di Adroterapia Oncologia), in Pavia (Italy).

The DP design has been optimized targeting the measurement of the charged secondary particles tracks in the energy range 50–150 MeV. The aim is to assess the beam range from the reconstructed spatial emission shape, built extrapolating the detected tracks towards the beam direction. The detector is also capable of measuring the charged fragments kinetic energy, in order to refine, if needed, the data sample excluding the slowest fragments, that suffer from larger multiple scattering.

The tracking system is based on eight couples of orthogonal layers ($19.2 \times 19.2\,\mathrm{cm}^2$) composed by plastic scintillating fibres ($500 \times 500\,\mu\mathrm{m}^2$) as represented in fig. 4.

When a charged particle travels through a layer, it deposits energy in the scintillating fibres creating scintillation photons. A small fraction of the scintillation light is then guided by total internal reflection to the fibre ends, where it is detected by a Silicon PhotoMultiplier (SiPM) detector. The inter-plane distance is 2 cm, which corresponds to the minimum gap allowed by the front-end electronics, in order to maximise the detector angular acceptance and the compactness as well.

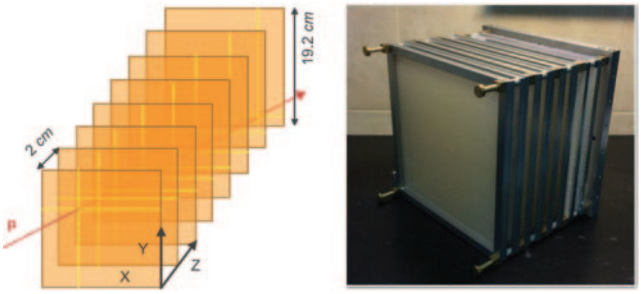

Fig. 4. – Left: schematic representation of the Dose Profiler. Right: view of the Dose Profiler layers during the assembly phase.

The DP was assembled in May 2017 in the mechanical workshop of the Scienze di Base Applicate per l'Ingegneria (SBAI) department (University of Rome, "*La* Sapienza").

3. – Benchmarking the detector performances using proton and carbon ions beams

In May 2017, the detector has undergone a performance characterization using the experimental room of the Trento proton therapy centre using protons beams at the energies of interest of PT. In July and November 2017 it was finally tested at CNAO to check the operation in "clinical-like conditions".

In the Trento facility, the DP has been tested using proton beams of $\sim 10^3$ p/s intensity with known monochromatic energy. The detector entrance face was 50 cm far away from the room isocentre to simulate a clinical condition. The distribution of the charge deposited in the fibers has been studied. The total amount of released charge Q_{fib} in the fibers is shown in fig. 5. The charge resolution has been evaluated using a normalized value:

$$Q^N_{fib} = \frac{Q_{fib}}{N_{lay}}, \tag{1}$$

where N_{lay} is the number of layers which have at least one cluster above threshold.

To evaluate the Dose Profiler efficiency, the detector has been irradiated with proton beams at 228 MeV, 159 MeV, 112 MeV, 70 MeV and 44 MeV, impinging the device center and with protons at 91 MeV, continuously moving the Dose Profiler position (using a remotely movable platform) with respect to the beam direction in order to test the full detector active volume. The layer detection efficiency $\epsilon_{i\nu}$ has been evaluated for each fibre layer i separately for the two views $\nu = x, y$ (each one corresponding to one of the layers of the orthogonal couple). The layer efficiencies resulting by the full volume scan at 91 MeV ($\sim 3 \times 10^6$ events) are reported in fig. 6. For the first 6 layers in each view the detection efficiency is of the order of 90%, which is an expected value considering

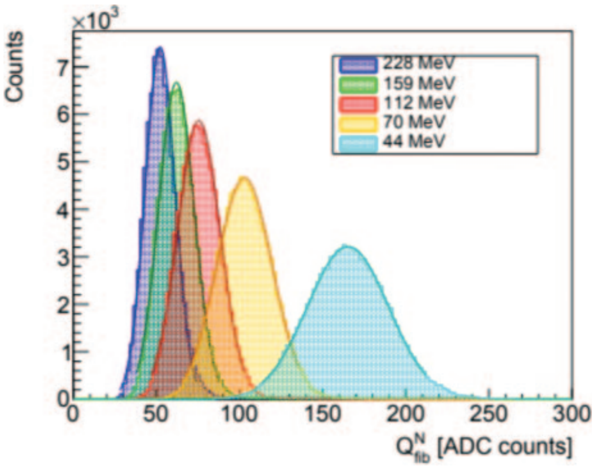

Fig. 5. – Distributions of the normalized deposited charge in the fibres for different energies. The normalization is done using eq. (1).

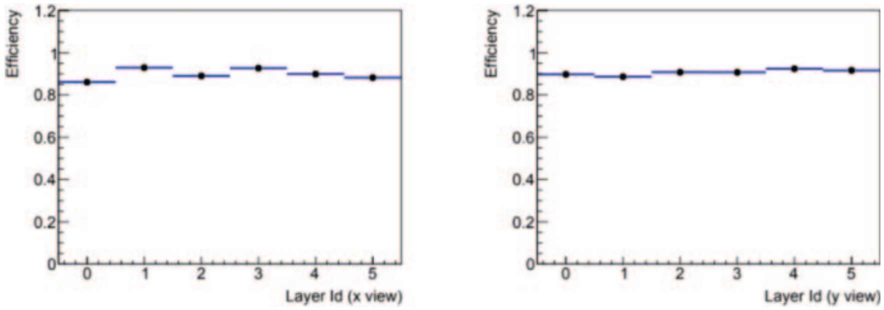

Fig. 6. – Detection efficiency for the first six fibre planes in each view: the layers oriented in the x-view and the y-view are shown in the left and right panels, respectively.

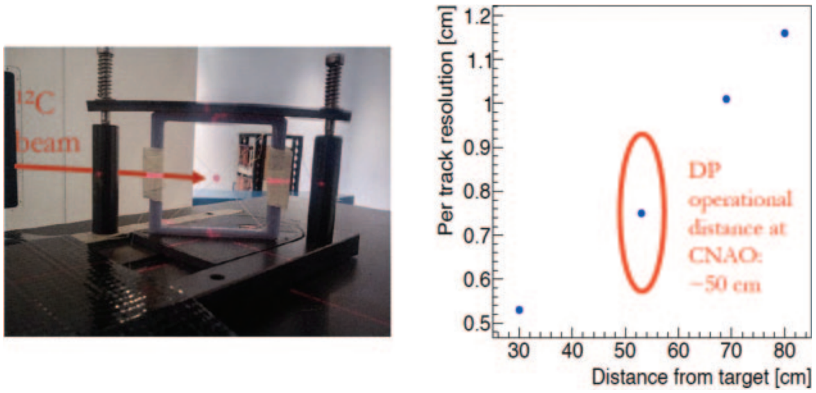

Fig. 7. – Left: setup of the test with a small plastic spherical target to simulate a point source of secondary fragments. The diameter of the sphere is 4 mm. Right: per-track resolution per distance from target. The operational distance at CNAO is ∼50 cm.

the dead space between the fibers, the fibre cladding and the possible light collection inefficiencies in the coupling with read-out electronics.

A per-track resolution (fig. 7) has been evaluated using a small plastic spherical target (diameter of 4 mm). The resolution at 50 cm (∼0.75 cm) was measured in the very same operational condition at CNAO and so it is the one that will be taken into account in the analysis.

During the test beam at CNAO, the interactions of pencil beams of different energies were studied using different targets and the RANDO® anthropomorphic phantom (fig. 8, left). After the calibration done in Trento, it was possible to correlate the charge deposited in the fibres with the energy of the secondary fragments. Using beams of ^{12}C with energy of 180, 220, 280 MeV/u, the distributions of energy represented in fig. 8 (right) was obtained. The detected fragments have average kinetic energies of ∼100–120 MeV. The cut at ∼50 MeV is caused by the trigger threshold.

The tests showed that the rate incurred by the DP reaches up to a value of 150 kHz. It is possible to detect charged particles at a high rate thanks to the fact that the dead time of the detector is ∼5 μs. In clinical applications, where one must be able to exploit all the available statistics delivered in small quantity and in a very rapid time, going to high rates is crucial.

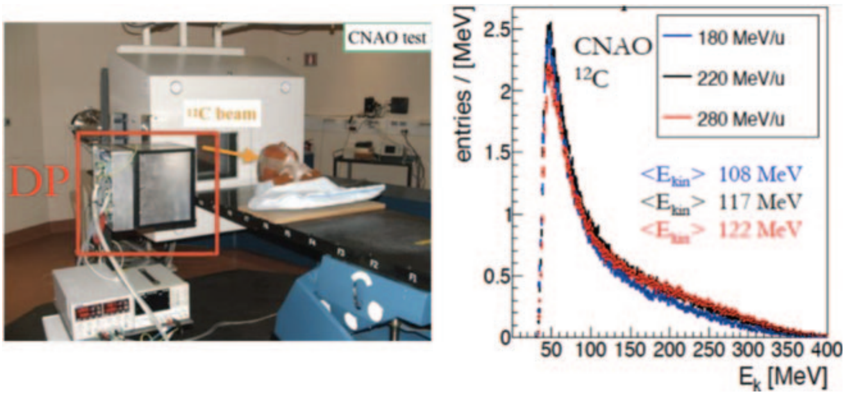

Fig. 8. – Left: setup of the CNAO test beam using RANDO® as target. Right: the distribution of the detected charged particles' energy for three different energies of the primary ^{12}C beams: 180 MeV/u (blue), 220 MeV/u (black) and 280 MeV/u (red).

4. – Accounting for secondary-particles interactions with matter

Charged particles suffer from absorption and multiple scattering interactions in matter which must be considered during the reconstruction.

The final precision achievable on the Bragg peak position depends on how much statistics can be collected and how well the interaction of the ions beams and of the emitted fragments with the patient body is handled.

A first approach of this matter effect has been to use a full MC to realize a weight that could consider the amount of absorbed particles (fig. 9). The simulation was based on the study of the interactions between fragments and a water target. This allows an experimental calibration.

Another approach under development is the "PET-like" Maximum Likelihood Expectation Maximization (MLEM) one. The idea is to use a fast GPU (Graphics Processing Unit)-based MC software to compute a correlation matrix, for each Pencil Beam, that

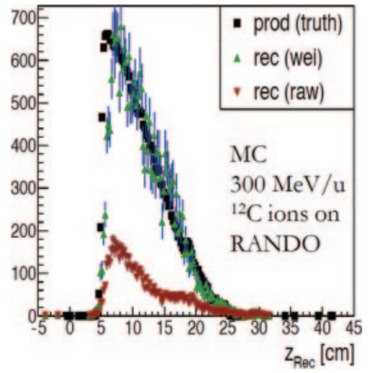

Fig. 9. – MC simulation of the production of secondary charged fragments in RANDO® using a ^{12}C beam of 300 MeV/u. The backtracking distribution of the detected particles is shown in red. The real distribution of production is represented in black and the unfolding using the weight is reported in green.

can be applied to realize an unfolding from the detected distribution to the production one. The advantage of using this method is that, thanks to the use of GPU, it can be used online.

5. – Conclusion

The Dose Profiler tracer has been extensively tested with protons and fragments with characteristics similar to those expected in a clinical treatment, confirming that the detector expectations of resolution and efficiency are met. A clinical trial at CNAO using the DP and PET detector is scheduled to start in 2019. Four pathologies were selected: Meningioma and Nasopharynx Cancer that are usually treated with proton beams; Adenoid Cystic Carcinoma (ACC) and Clival Chordoma treated with carbon ion beams. The first two pathologies, treated using protons, are going to be monitored with the PET detector, the others can be used with both devices. Those pathologies have been chosen as they represent two different operational situations: the ACC is usually subjected to a large morphological change, while in the Clival Chordoma the volume treated is expected to conserve its density. The data obtained during the treatment will be analyzed offline, completing the studies on the matter effects, and in this way it will be possible to finalize the accuracy on the monitoring of the BP achievable in clinical conditions.

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