From dark matter searches to proton therapy: Measuring target fragmentation with nanometric nuclear emulsions

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ABSTRACT

The DAMON (Direct meAsureMent of target fragmentatiON) project aims to explore the use of Nano Imaging Trackers (NITs) for the first direct measurement of target fragmentation caused by proton beams in cancer treatment. NITs are fine-grained nuclear emulsion films that offer a spatial resolution at the nanometric scale. DAMON's pilot test exposed a NIT-based detector to 211 MeV protons, paving the way for the first study of target fragmentation in direct kinematics. In this paper the preliminary results regarding the multiplicity of the fragments and their track lengths are reported.

1. Introduction

Proton therapy is a cancer treatment employed for deep solid tumors or those near organs at risk, that exploits the advantages of the protons depth-dose profile. At present, its efficacy is hindered by uncertainties in the Relative Biological Effectiveness (RBE) of proton beams [1]. It has been estimated that approximately 1% of the protons in a therapeutic beam undergo nuclear reactions in one centimeter of biological tissue [2]. These reactions lead to the fragmentation of target nuclei and the consequent production of short-ranged, highly ionizing particles. It has been shown that the contribution of these fragments to the RBE is not negligible, especially in the entrance channel [3]. The accurate evaluation of the RBE is crucial for efficient treatment planning but experimental measurements of target fragments are challenging due to their short range (≤ 100 μm in water for fragments produced by irradiation with protons up to 250 MeV). Data concerning target fragmentation is limited and so far it has only been collected using inverse kinematic approaches [4,5] which can introduce systematic errors. DAMON (Direct meAsureMent of target fragmentatiON) aims to achieve the first direct measurement of proton induced target fragmentation. To this aim, a novel kind of fine-grained nuclear emulsions known as "Nano-Imaging Trackers" (NITs) has been employed. The use of finer grains enables the detection of sub-micrometer tracks. The

detection of low energy ion tracks down to 50 nm with NITs has been demonstrated [6,7]. DAMON's measurements will enable to benchmark Monte Carlo (MC) transport codes and improve their accuracy for future treatment plans.

2. DAMON Pilot Test

2.1. Nano-imaging trackers

Despite decades of experimental applications, nuclear emulsions remain highly attractive because of their unmatched granularity and spatial resolution. Significant developments in the emulsion technology were achieved during the OPERA experiment [8]. An OPERA-like nuclear emulsion features AgBr crystals with an average diameter of 200 nm. The passage of ionizing radiation through the AgBr crystals induces atomic-scale perturbations that, through a chemical treatment, are developed into silver grains. OPERA-like grains have an average diameter of around 1 μm. Because a track can be detected only if the particle passes through at least two crystals, the spatial resolution is determined by the size of the silver halide crystals: smaller crystals are required to detect tracks a few hundred nm long. This is relevant for DAMON because it has been estimated, through a TOPAS MC
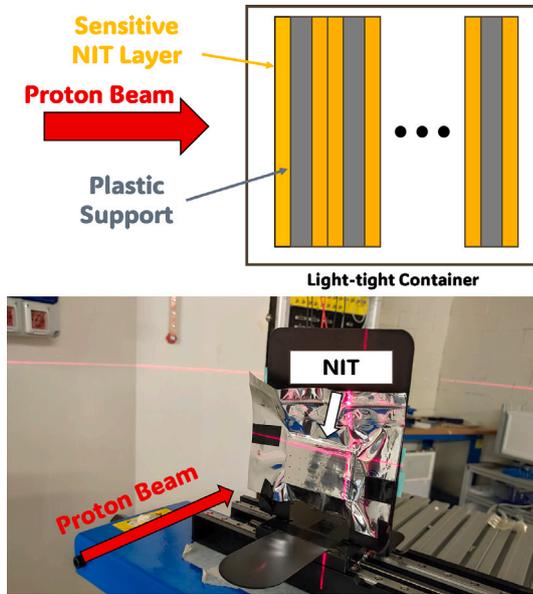

Fig. 1. Top: cross-sectional view of the detector. Bottom: pilot test detector in the experimental room of the Trento Proton Therapy Center. The laser system used for alignment is visible.

Fig. 2. Comparison between DATA (green) and TOPAS (blue) of the width along the X axis of the proton beam at the Trento Proton Therapy Center. The red circle refers to the distance from the exit window during the exposure.

simulation, that at least 35% of target fragments, mainly originating from heavy nuclei, have ranges shorter than 10 µm. To overcome this limitations, NITs are used. NITs were originally developed to achieve a direct directional detection of WIMP (Weakly Interacting Massive Particle) induced nuclear recoils [9]. NITs feature silver bromide crystals with average diameter ranging from 20 nm to 80 nm. The size of the crystals can be tuned during the production process [9]. The sensitization of a NIT crystal employs an halogen acceptor (HA) [10] instead of the sulfur-plus-gold sensitization traditionally used for OPERA gel. A dedicated low temperature chemical development based on metol ascorbic acid (MAA) is used to minimize thermal noise. This leads to a much lower sensitivity to minimum ionizing particles (MIPs) with respect to OPERA-like nuclear emulsion films. DAMON uses NITs as both target and tracking devices. In terms of nuclear composition, NIT gel contains not only Ag and Br but also elements which are common in biological tissues such as H, C, O, N. Approximately, the mass fractions of these element are: Ag(39%), Br(28%), C(13%), O(12%), N(5%), H(2%). The plastic base, usually made out of polystyrene $(C_8H_8)_n$, contains carbon and hydrogen making the entire nuclear emulsion a suitable target for evaluating fragmentation events relevant to proton therapy. The fragmentation of Ag and Br nuclei with short-range tracks can be distinguished from that of lighter nuclei by measuring the range of the fragments.

2.2. Exposure at the trento proton therapy center

DAMON's pilot test was performed by using 211 MeV protons at the Trento Proton Therapy Center. The DAMON detector consisted of a bulk of NITs acting both as a target and tracking device. The detector used the Emulsion Cloud Chamber (ECC) configuration in which nuclear emulsion films are alternated with layers of passive materials. NITs with 70 nm AgBr crystals were produced at the underground Gran Sasso INFN Laboratory (LNGS), where a dark room for gel production and chemical development is present. Each NIT had two sensitive layers with a thickness of approximately 60 µm deposited on both sides of a non-sensitive polystyrene support (200 µm thick). The surface area was 6×4 cm². A total of 19 NITs were stacked. After production, the films were vacuum packed in a light tight bag and they were kept in a refrigerated box. A schematic representation of the exposure geometry
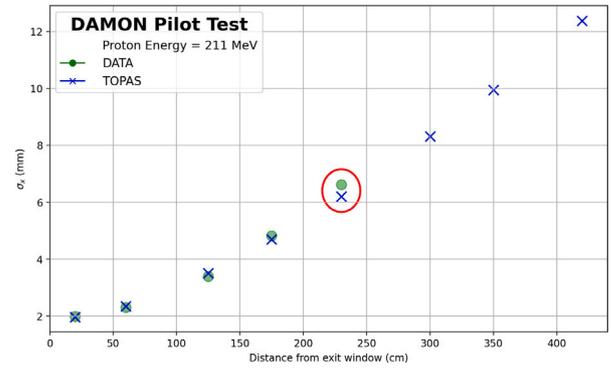
is shown in Fig. 1. As visible from the figure, the NIT detector was taped to a motorized translator, used for accurate positioning. For the exposure, the target proton density was set at 10^4 cm⁻². As previously mentioned, a simulation of the proton beam in the experimental room was performed with TOPAS MC in order to define the optimal exposure geometry and to estimate the properties of the secondary particles. The difference between the previously measured beam width [11] in the transverse plane and the simulated values was within 5% (Fig. 2). In order to achieve a uniform density on the surface of the emulsion film, a 5×5 spot grid and a motorized translator were used. The distance between the beam exit window and the detector was 230 cm. The nominal number of protons per spot was 11.000 except for the first spot where 85.000 protons were shot to test the reconstruction in higher density conditions. The incident beam flux was monitored by a thin plastic scintillator and the measured values agreed with the nominal ones within 3%.

3. Readout techniques

In order to fully exploit the nanometric size of NIT grains, the readout of these detectors is performed in two steps requiring two separate automated optical microscopes.

3.1. Fast scanning

In the first step, the whole surface of each NIT is scanned to identify fragmentation events. The development of an optical microscope capable of rapidly scanning the irradiated samples has been an important part of the DAMON activities. This microscope (Fig. 3) features a blue 3×4 cm² LED ($\lambda = 450 - 470$ nm) as a light source and it is equipped with a EoSens 4CXP camera and a Nikon MRH01401 objective lens (40× magnification, $NA = 1.3$). Blue light is used because silver grains with average diameter of about 70 nm exhibit localized surface plasmon resonance at these wavelengths, making them easier to identify during scanning. The microscope is connected to a motorized stage featuring a vacuum pump that ensures good adherence of the NITs to the glass by removing any air pockets. The LASSO system is used to drive the instrument [12]. The working distance of the objective lens is longer than the thickness of a NIT. The bottom of the emulsion layer could be observed, however, a significant deterioration in image quality was present. This is due to the scattering of light in the plastic support before reaching the objective lens. At this time, R&D is ongoing to select a material with more suitable optical properties for the future samples. Because of this, the top and bottom sides of each emulsion have been scanned separately from each other. During the scan, the surface of the emulsion is divided into 400×300 µm² views and sequential images are acquired with along the vertical axis equal to 0.75 µm. The actual
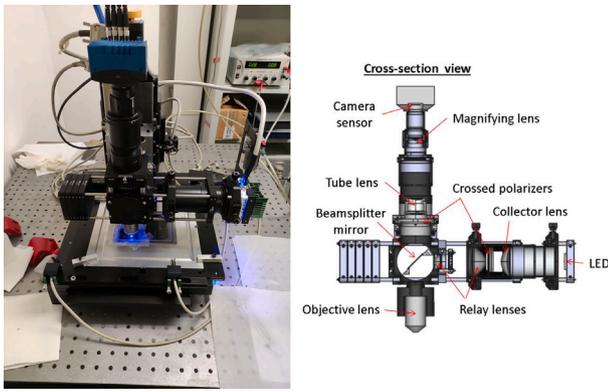
Fig. 3. Microscope used for fast scanning of DAMON NITs. On the right, the main components of the system are highlighted.
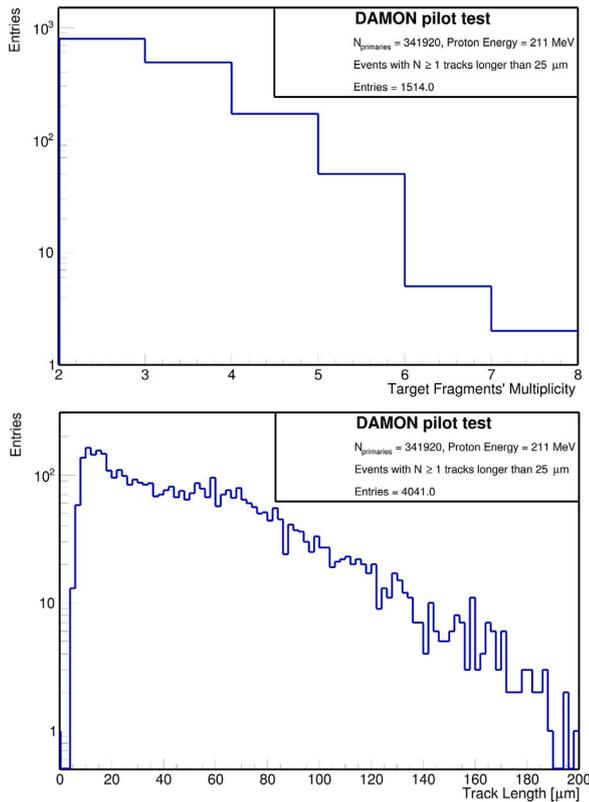

Fig. 4. Top: Multiplicity of target fragments reconstructed in the top side of 17 NIT films for the DAMON's pilot test. Bot: Track lengths of target fragments belonging to the same events.
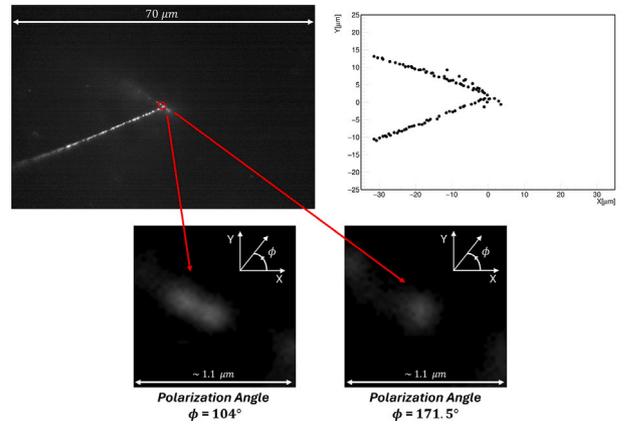

Fig. 5. Top Left: five secondary tracks move away from the interaction point, at a given position on the Z axis. Top Right: X-Y projection of reconstructed grains from the same interaction. Bottom: first grains of the top right track as seen by using light with different polarizations.

scanning speed was ≈ 3 cm^2/h which was sufficient for the amount of data acquired in the pilot run. Future developments will include the installation of a piezo drive to achieve even faster scanning speed.

3.2. Offline reconstruction

The offline reconstruction software used in this work relies on the FEDRA framework [13]. During scanning, clusters of white pixels are identified by LASSO. The FEDRA software merges close clusters to form grains, and later links sequences of aligned clusters to form *micro-tracks* in each of the emulsion layers. Linking was performed in two steps. First, a cut on the maximum distance between grains equal to 5 μm was applied in order to avoid linking grains belonging to different tracks. Secondly, aligned micro-tracks were merged together to compensate

for the possible presence of gaps longer than 5 μm due to the failed reconstruction of a few grains. The identification of fragmentation events from the reconstructed micro-tracks is described in Section 4.

3.3. Super resolution scanning

The detection of micro-tracks with lengths $\lesssim 220$ nm originating from target fragmentation is made possible by the use of an optical super resolution (SR) microscope. This microscope achieves super resolution by exploiting the Localized Surface Plasmon Resonance (LSPR) phenomenon which is linked to the excitation of conduction electrons on the surface of metallic nanoparticles immersed in dielectric media. Silver grains inside the sensitive layers of NIT exhibit LSPR at near blue wavelengths. LSPR depends on the size and shape of the nanoparticle. Silver grains can be approximated as ellipsoids and a maximum in the reflected light can be recorded when the polarization direction of the incident light matches the direction of the ellipse's major axis. Because the orientation of close grains is random, this feature enables the resolution of structures closer than the optical diffraction limit. More details about this instrument can be found in [6,7]. In the context of DAMON, the reconstructed target fragmentation events will be analyzed with 8 different polarizations with the SR microscope in order to fully characterize these events. This step is crucial for the rejection of fragmentation events on Ag and Br, as their fragments are expected to have the lowest ranges.

4. Results

The NIT sample used for the pilot test had a low sensitivity because of the HA sensitization and low temperature development. Most of the proton tracks could not be reconstructed in this conditions because of their relatively low ionization. Alternative sensitization and development approaches are currently under test. Present low sensitivity reduces the background from MIP tracks. The essential background is a few MeV alpha tracks emitted from radioactive isotopes, such as environmental Radon and the Uranium and Thorium decay series, naturally present in the emulsion gel. The majority of these tracks have a known track length of $\simeq 20$ μm. Because of this, a cut requiring at least one micro-track longer than 25 μm has been applied to identify a target fragmentation event. A more detailed assessment of background events from alpha tracks will be conducted in the future. Linear fits were performed to reject micro-tracks due to the random association of close grains. Moreover, a maximum impact parameter to the vertex equal to 5 μm was accepted. This approach was used to analyze the

top side of 17 NIT films and it yielded 1514 fragmentation interactions. Approximately 70% of those interactions originated inside the emulsion gel layers. The multiplicity and track length of secondary particles emerging from these interactions are shown in Fig. 4. As expected, events with higher multiplicity are more rare. A significant fraction of fragments has track lengths $\leq 20\,\mu m$, while approximately 10% of them travels more than $100\,\mu m$ (secondary helium and protons). It should be noted that very short tracks ($\lesssim 200\,nm$) are not included in the figures and that the reconstruction efficiency for tracks with lengths of a few μm will be improved substantially by the second step of the readout. A preliminary test of the SR approach was performed on one of the fragmentation events reconstructed after fast scanning (Fig. 5). The image shows how two close grains, which would appear to be a single structure because of the diffraction limits, can be resolved as separate objects using light with different polarizations.

5. Conclusions

DAMON aims at measuring for the first time proton induced target fragmentation in direct kinematics. To achieve the needed spatial resolution, the experiment employs NITs, which are fine grained nuclear emulsion films. The first exposure to a proton beam was performed at the Trento Proton Therapy Center. The readout process consists of a fast scan to identify fragmentation interactions and a super resolution scan to completely characterize these events. The analysis of the top side of 17 NITs has revealed 1514 fragmentation events. The following step will be the application of the SR technique to these events in order to detect tracks shorter than the optical diffraction limit.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

Data availability

The raw data supporting the conclusion of this work will be made available by the authors on request, without undue reservation.

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