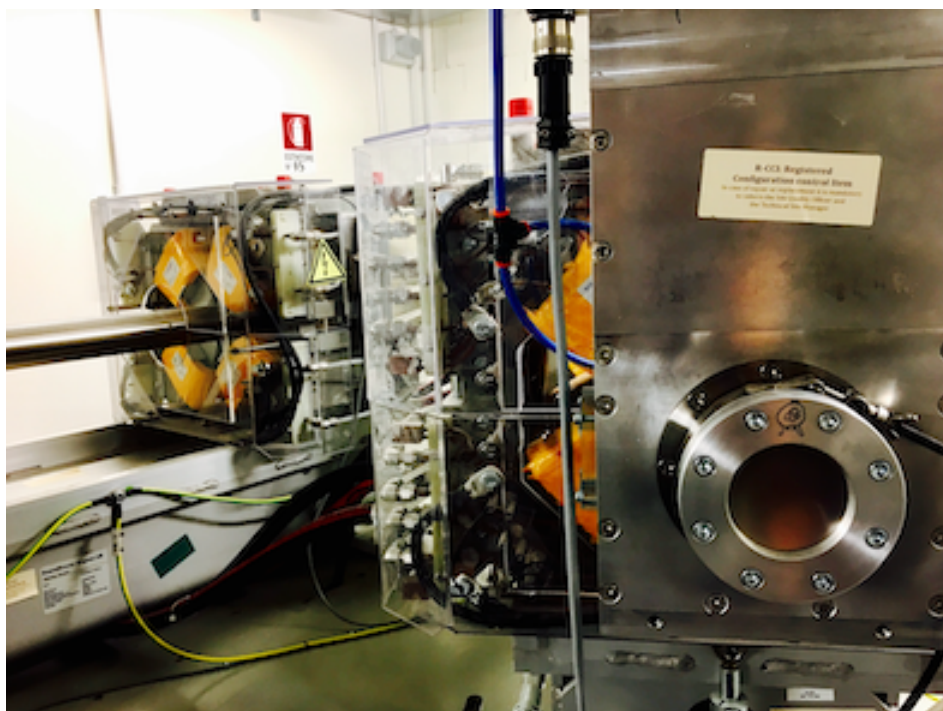


1st Workshop - Trento Proton Beam Line Facility

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Book of Abstracts

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Detectors - First Session / 6**Scintillator-based system for transversal dose profile reconstruction for clinical proton beams**

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A fast and reliable system to measure transversal charged particles relative dose profiles is desirable in any hadrontherapy facility, being the basis for an accurate treatment quality assessment procedure. For this purpose, a system for the lateral dose profile reconstruction was developed at the Laboratori Nazionali del Sud of Italian Institute for Nuclear Physics (INFN-LNS, Catania, Italy); it consists of a plastic scintillator screen (50×50 mm², 1 mm in thickness), mounted perpendicularly to the beam axis and coupled with a highly sensitive cooled CCD camera (resolution 1928×1452 pixels) in a light-tight box. The real-time data acquisition, the quantitative analysis of the beam profiles and the calculation of the dosimetric-relevant parameters along both horizontal and vertical directions, were entirely performed using specific in-house software libraries, developed on the LabView platform (National Instruments, Austin, TX, USA).

We report about the characterisation of the system in terms of short-term stability and linearity with the beam dose-rate. An inter-comparison with other common quality control devices, able to perform transversal beam profiles reconstruction (radiochromic films, Lynx detector and Timepix detector) has been also carried with a 100 MeV proton beam at the Trento Institute for Fundamental Physics and Applications (TIFPA, Trento, Italy) and the results will be reported and discussed as well.

Radiobiology & related applications / 7**Development of *C. elegans* as a model for studying neurodegeneration in space-related conditions**

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In light of future human exploration of deep space, a fundamental need is to understand how terrestrial organisms may be affected by the peculiar conditions that characterize this extreme environment. Moreover, it will be crucial to dissect how the individual genetic structure may jeopardize or facilitate the adaptation to deep space, with specific regards to normal functioning of the nervous system. In this project, we aim at establishing the nematode *C. elegans* as a convenient biological dosimeter, allowing to assess the effects of different space-relevant radiation beams on neurological function. We have already studied the response of selected groups of neurons to different doses of gamma-rays. We are currently in the process of assessing the qualitative and quantitative differences in neural disfunction and neurodegeneration induced by similar doses of protons, of the highest possible energy, in collaboration with TIFPA facility. This experiment will be a fundamental step in preparation of experiments with Galactic Cosmic Ray radiation, to be performed at reference facilities such as the GSI.

Radiobiology & related applications / 8**Preliminary results on biological effects and molecular alterations induced by combined proton-therapy and chemotherapy in high-grade glioma treatment**

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Although three decades of research have been trialled, the prognosis for patients with high-grade gliomas (HGGs) has not significantly changed.

The aim of our project is the development of a new combined treatment that could sensitize HGGs to therapies, reducing side effects and improving quality of life of the patients.

We will develop a new multidisciplinary protocol, combining the conventional used Doxorubicin (Dox) with proton therapy (PT), in order to elucidate the potential of this combined treatment as available approach for HGGs therapy.

First step experiments have been set up to investigate the effect of PT on cell growth. Two glioblastoma (GBM) cell lines (T98G and A172) were treated with scalar concentrations of PT (1Gy, 2Gy, 4Gy, 8Gy and 16Gy). After treatments, cells replication ability was evaluated by clonogenic assay.

After PT treatments, T98G cells showed an average colony count of: 0 Gy: 39 colonies; 1 Gy: 16.5 colonies; 2 Gy: 20.5 colonies; 4 Gy: 17.5 colonies; 8 Gy: 3 colonies and 16 Gy: 0.5 colony

Similarly, A172 showed an average colony count of: 0 Gy: 14 colonies; 1 Gy: 10.5 colonies; 2 Gy: 9.5 colonies; 4 Gy: 7 colonies; 8 Gy: 2 colonies; 16 Gy: 1.5 colonies.

These preliminary data, obtained from this pilot experiment, have indicated that GBM cells are sensitive to PT treatment. Moreover, growth and propagation ability of treated cells was inversely proportional to PT doses.

Ideed, the higher PT doses (8Gy and 16Gy) caused a drastic reduction in the number of colonies observed compared to the other experimental groups.

Subsequently, the cytotoxic effect of combined treatments Dox plus PT was evaluated in GBM cell lines (T98G and A172).

GBM cells were irradiated with several doses of PT (1Gy, 2Gy, 4Gy, 8Gy and 16Gy) and after 24 hours treated with increasing concentrations of Dox (0.05- 0.1- 0.2 and 0.5 µg/ml).

The cytotoxic effect of the treatments was assessed in terms of cell viability by MTT assay.

The optical density (OD) values (OD is directly proportional to the number of viable cells) detected in T98G (GBM cells resistant to Dox) were more or less constant in all irradiated groups compared to the control, except for 8Gy which showed a reduction in cell viability. Treatment with Dox, as expected and under all conditions, does not significantly change the OD values.

Finally, in A172 cells the OD value decreases from 0Gy to 16Gy proportionally to the intensity of the radiation, demonstrating the effectiveness of PT on this cell line.

Moreover, in this cell line, Dox treatments showed significant effects compared to controls.

The preliminary data obtained from MTT test demonstrated that the A172 cell line is sensitive to PT and to the combined treatment PT plus Dox (especially in the 16Gy plus Dox 0.5µg/ml group) with a significant reduction of cell viability.

Dox and PT novel combination may provide the rationale for a clinical application of this innovative multidisciplinary protocol in the treatment of GBM and other HGGs.

Further experiments have to be carried out to validate the preliminary data, increasing the statistics and the sample size.

Detectors - Second Session / 9**Calibration of the drift chamber detector within the FOOT experiment**

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The FOOT (FragmentatiOn Of Target) experiment aims to perform systematic measurements of nuclear fragmentation cross sections in the energy range useful for particle therapy and space radio-protection. The experiment is designed to measure both projectile fragmentation of different nuclei (C, O, He) on C and CH targets, and also to extract target fragmentation cross sections in p-C and p-O collision processes, by means of inverse kinematic reconstruction.

FOOT consists of two different setups for the detection of heavy ($Z \geq 3$) and light ($Z \leq 3$) fragments: the former are detected by a high precision tracking system in magnetic field, a time of flight measurement system and a calorimeter, while the latter are measured by a separated emulsion cloud chamber detector. Both the experimental setups include a drift chamber that is adopted to measure the direction and position of the incident primary particles. Extensive tests have been carried out at the experimental facility of Trento protontherapy in order to characterize the drift chamber. The space-time relations calibration and the performance have been assessed by means of the proton beam at the kinetic energy of 228 and 80 MeV. An external tracking system composed of different layers of microstrip silicon detectors was used as independent reference. The measured overall detection efficiency is 0.929 ± 0.008 . The detector spatial resolution has been evaluated to be $150 \pm 10 \mu\text{m}$ and $300 \pm 10 \mu\text{m}$ for the higher and lower beam energies, respectively. In addition, the upper limit on the drift chamber resolution has been found to be of $60 \div 100 \mu\text{m}$. These figures match the expectations required for the operation of FOOT. In this contribution we shall present the materials and the procedures adopted for the data taking, the detector performance assessment methods and the experimental results, together with an overview of the FOOT experiment.

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Radiation testing and space qualification of GAGG:Ce scintillator crystals for the HERMES project

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We discuss the experimental procedure and the results of an irradiation campaign on GAGG:Ce (Cerium-doped Gadolinium Aluminium Gallium Garnet) scintillator crystals, carried out in the framework of the HERMES-TP/SP (High Energy Rapid Modular Ensemble of Satellites – Technological and Scientific Pathfinder) mission at the Trento Proton Therapy Centre (TPTC) during January 2019. Samples from different manufacturers were irradiated with 70 MeV protons, at doses equivalent to

those expected over orbital periods representative of satellite lifetimes.

We report our findings on the degradation of light-output and on the modifications to the afterglow emission signature following proton irradiation. We briefly discuss a new model for GAGG:Ce afterglow emission resulting from relatively low-dose proton irradiations, such as those expected from repeated passages above trapped particle regions in low Earth orbit.

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Oxygen depletion measurements for different media with energetic proton beams.

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The radiosensitivity of biological systems is strongly affected by the system oxygenation. On the molecular level, this effect is considered to be related to the indirect damage and in particular to the effect of the OH• radicals. Several theories have been developed and among them the so called oxygen fixation hypothesis is so far the most accepted one. Recent studies open up another possible pathway which can also take part in the oxygen induced radio sensitivity. In oxygenated media, in particular, solvated electrons, eaq^- , and hydrogen atoms, H•, are generated in large quantities and react with dissolved molecular oxygen to form the superoxide anion, $O_2^{\bullet-}$, and its protonated form HO $_2^{\bullet}$. Both these species have been identified as possibly responsible of the oxygen driven radiosensitization effect. It has been observed that densely ionizing radiation can mitigate hypoxia induced radioresistance, motivating a growing interest in ion radiation therapy for the treatment of hypoxic tumors. On the microscopic scale, this effect can be explained as a track density effect. Monte Carlo track structure codes are particularly suitable for studying the microscopic processes involved in the radiation damage, including their spatiotemporal evolution. However, the majority of these codes are limited to pure water targets and in few cases in oxygenated water targets. Additionally, all these codes are subject to large uncertainties due to the very limited amount of experimental data for benchmarking, especially in oxygenated media. For low LET radiation an oxygen depletion rate of 0.33 $\mu\text{M}/\text{Gy}$ has been measured in PBS. Additionally, results of oxygen depletion in cell culture medium show an increased oxygen consumption (of a factor around 4/3) due to subsequent reaction with carbon centered radicals. First experiments with keV X-rays and clinical MeV photons from this group confirm these values. To our best knowledge however, no experimental data for protons and ion radiation in oxygenated targets is available.

These measurements result particularly relevant for the basic understanding of the chemical processes involved in the oxygen induced radio sensitivity on biological media, and allow to benchmark the chemical stage predictions of Monte Carlo track structure codes. The latter predictions are an essential step for building a mechanistic understanding basis for unraveling different processes, including the peculiar depletion features at high dose rate supposed as the driving force in the FLASH effect.

Within this context an experimental campaign to perform a series of oxygen depletion measurements in conventional dose rates for different proton beam energies in different oxygenated media has been approved at the Trento proton beamline and is planned for the next months. The experimental approach and preliminary results will be here presented.

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Dosimetry Experiments from GSI for Therapy and Space Radiation Research at the Trento Proton Therapy Facility

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In the last years, our group has performed different radiation physics experiments from the fields of particle therapy and space radiation protection. This contribution will summarize briefly the conducted experiments and present the obtained results.

One experiment investigated the entrance channel of proton Bragg curves. The shape of the first few centimetres of a proton depth dose profile is determined by the interplay of two different build-up effects: the build-up of delta electrons in the first few millimetres and the build-up of secondary protons and target fragments in the first few centimetres. Both could be characterized with high precision during an experiment at the Trento proton therapy center with a 220 MeV beam. A setup consisting of two large area parallel plate ionization chambers and polyethylene targets was used to measure the dose build-up and a permanent magnet was used to separate the two effects from each other [1].

In another experiment in Trento, we investigated a new alignment procedure for CMOS sensors. These first tests have proven the feasibility of the new software concept [2].

Also a scintillation detector setup that was later used in experiments at the Marburg Ion Therapy Center (MIT) to measure PET isotope production cross sections [3] was first tested at the experimental beamline in Trento.

Within the ROSSINI-2 project aiming on the characterization of shielding materials for cosmic radiation, we performed an experiment in Trento where the production of secondary neutrons in different shielding materials and their dose behind the shielding targets was assessed using TLD detectors at different angles [4].

[1] T. Pfhul, F. Horst, C. Schuy, U. Weber Dose build-up effects induced by delta electrons and target fragments in proton Bragg curves - measurements and simulations. *PMB* 63 (2018).

[2] C. -A. Reidel, C. Finck, C. Schuy, M. Rovituso, U. Weber. Alignment procedure of silicon pixel detectors for ion-beam therapy applications. *NIMA* 931 (2019).

[3] F. Horst, W. Adi, G. Aricò, K.-T. Brinkmann, M. Durante, C.-A. Reidel, M. Rovituso, U. Weber, H.-G. Zaunick, K. Zink, C. Schuy Measurement of PET isotope production cross sections for protons and carbon ions on carbon and oxygen targets for applications in particle therapy range verification. *PMB* 64 (2019).

[4] C. Schuy, C. La Tessa, F. Horst, M. Rovituso, M. Durante, M. Giraudo, L. Bocchini, M. Baricco, A. Castellero, G. Fioreh, U. Weber Experimental Assessment of Lithium Hydride's Space Radiation Shielding Performance and Monte Carlo Benchmarking. *Radiation Research* 191 (2018).

Detectors - First Session / 13

Direct Detection of MeV Protons by Flexible Organic Thin Film Devices

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The development of detectors for protons and heavy particles is a long-lasting research topic not only for fundamental applications, but, more recently, for monitoring energy and flow of particles in ion beam applications. However, the most demanding application of ion beams, for which accurate measurements are increasingly needed, is hadron therapy of cancer. For this application there is an increasing demand of systems apt for the accurate recording and mapping of the dose delivered during a treatment plan.

In proton therapy a detector has to satisfy two major requirements: i) the capability to detect dose rate and position of the beam in real time; ii) the monitoring of the dose on healthy tissues. In all these cases, detectors have to be in contact with the patient in order to record the dose in real time. A few types of detectors are able to reliably provide such information, such as silicon based MOSFET. The main drawbacks are the need of accurate calibration procedures and the fact that the detectors are intrinsically non-water equivalent with an energy-dependent response.

In this work we present the first study on responsivity of organic semiconductor detectors to proton beams. Organic semiconductors have already been demonstrated to be reliable detectors for ionizing radiation, and they offer also appealing properties for the proton beams monitoring. In fact, they can be processed and deposited at low temperature (<150 °C) by solution leading the possibility to realize multiple mm pixels of the order of mm² onto thin, flexible and large-area substrates. They do not require expensive fabrication processes and they are reusable and disposable, thus targeting a potential low-cost, industrially scalable sensing system. Finally, a crucial point for the dosimetry application is the fact that they are water tissue equivalent in terms of absorption and, consequently, the calibration of the sensor is not needed.

The organic devices here presented act as a solid-state detector in which the energy released by the protons within the active layer of the sensor is converted into an electrical current. These sensors are able to quantitatively and reliably measure the dose of protons impinging on the sensor both in real-time and in integration mode. This study shows how to detect and exploit the energy absorbed both by the organic semiconducting layer and by the plastic substrate, allowing to extrapolate information on the present and the past irradiation of the detector. The measured sensitivity $S = (5.15 \pm 0.13)$ pC Gy⁻¹ and limit of detection $LOD = (30 \pm 6)$ cGy s⁻¹, of the here proposed detectors assess their efficacy and their potential as proton dosimeters in several fields of application, such as in medical proton-therapy.

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PROTON THERAPY X-RAY CT CALIBRATION BY PROTON TOMOGRAPHY

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PURPOSE

To present the GR5 project titled “XpCalib –Proton therapy X-ray CT calibration by proton tomography” recently financed by INFN.

BACKGROUND

In recent past, INFN research projects such as Prima, RDH and IRPT have studied the feasibility of proton Computed Tomography (pCT) as a tool to improve treatment accuracy in hadron therapy.

In this framework a pre-clinical prototype has been successfully built and tested under 210 MeV proton beam at the APSS Proton Therapy Centre in Trento.

Good quality proton tomographies of certified and anthropomorphic phantoms have been reconstructed using this apparatus. Our pCT system allowed directly measuring relative stopping power (RSP) 3D maps with an accuracy of about 1%, thus demonstrating the potential of this technique with respect to state-of-art methodologies based on the conversion of Hounsfield units (HU) from x-CT.

RATIONALE

Different x-CT calibration methods were investigated and applied to provide accurate RSP maps for patient treatment planning in proton therapy. Conventionally, single-energy x-CT calibration is obtained by scanning a number of tissue equivalent materials, which however have limitations in mimicking the radiological properties of real tissues, due to the degeneration of the relationship between relative electron density and CT numbers. To overcome this issue, a stoichiometric calibration has been introduced and, more recently, dual-energy x-CT methods have been investigated.

It is common practice in proton therapy to assume an uncertainty of about 3% in the estimated particle range, and to compensate for that in the planning phase, thus leading to an increased volume of healthy tissue being irradiated. By decreasing the uncertainty on the proton estimated range, a significant reduction of the irradiated healthy tissues surrounding the tumor with increased treatment conformity could be obtained.

OBJECTIVES

In this project the INFN pCT system will be used to extend its potential towards clinic applications in the field of proton therapy, to decrease the uncertainty on the proton estimated range.

In particular, by applying the pCT on biological test phantoms, we aim at improving the accuracy of the x-CT calibration in producing the RSP maps for proton therapy treatment planning to finally outperform most advanced dual energy x-CT techniques.

DESIGN OF THE STUDY

The x-CT system already in use for patient treatment planning in the Proton Therapy Centre of Trento APSS will be cross calibrated by means of the INFN pCT apparatus. The latter will be implemented in the experimental beam line room of the APSS centre. For cross-calibration, a set of dedicated biological phantoms will be designed and prepared.

RSP values of the biological phantoms directly measured by the pCT apparatus will be compared with the Hus obtained by x-CT measurements of the same phantoms in order to obtain a calibration map of this system.

Medical Physics Applications / 15**Results on proton Computed Tomography**

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In hadron therapy a highly conformed irradiation field is delivered to the target by moving the beam and modulating its energy. Treatment plans require precisely measured patients' Stopping Power (SP) maps, which are presently extracted from X-rays tomographies, so introducing unavoidable uncertainties. A direct measurement of the SP maps using protons (proton Computed Tomography - pCT), could mitigate this source of errors potentially enhancing the precision of the hadron therapy. The Prima-RDH-IRPT collaboration built a 5x20 cm² field of view pCT system, suitable for pre-clinical studies, using a microstrip silicon tracker and a YAG:Ce calorimeter.

In this talk a detailed description of the apparatus, together with the measurement methodology, will be given. Tomographies of electron density calibration and anthropomorphic phantoms taken using the experimental beam at the Trento Proton Therapy center will be shown. Very good correlation between measured and expected relative SP has been obtained from the density phantom tomography with discrepancies less than 1%. Anatomical structures of the order of one millimeter are visible in the anthropomorphic head phantom image as well as details of a titanium spinal bone prosthesis and a tungsten dental filling. Furthermore, pCT tomographies of the head phantom taken with our device, when compared with x-CT images of the same object, evidence a significant reduction of artifacts induced by the prostheses.

Radiobiology & related applications / 16

Development of a setup for small-animal proton imaging based on a miniaturized Timepix detector

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The SIRMIO (Small Animal Proton Irradiator for Research in Molecular Image-guided Radiation-Oncology) project [1] aims at developing a portable preclinical proton irradiator that can be installed at existing proton therapy centres. The clinical beam properties will be adapted to match requirements of small-animal irradiation using a dedicated energy degradation and focussing system [2]. Pre-treatment proton imaging will be performed for position verification and treatment planning. For compatibility of the imaging setup with synchrocyclotron-based facilities, where the high instantaneous particle flux exceeds detection capabilities of contemporary single particle tracking systems, we are developing a compact solution based on a miniaturized Timepix detector.

We tested the feasibility of our setup at the experimental beamline of the Trento Proton Therapy facility with a 70 MeV proton beam. A miniaturized radiation camera MiniPIX [3], based on the single particle tracking ASIC detector Timepix, was placed 1 cm behind a μ CT calibration phantom consisting of a 10 mm thick solid water slab with 10 cylindrical tissue-equivalent inserts (16 mm length, 3.5 mm diameter). The reduced beam intensity (< 10,000 protons/second) assured the registration of individual protons for detailed event-by-event analysis despite the frame-based detector readout. The events were spatially binned and the median energy deposition within the 300 μ m thick silicon sensor chip was calculated for each bin. It was converted to water-equivalent thickness (WET) of the traversed material using a FLUKA [4,5] Monte Carlo based and experimentally validated conversion curve. The obtained WET values for all inserts were divided by their geometrical length and compared to relative (to water) stopping power from literature [6].

For all insert materials, the WET was in good agreement with literature (differences < 3%) at an estimated imaging dose of 5 mGy. The spatial resolution was 0.3 mm. Increasing the phantom-detector distance from 1 to 5 cm resulted in more blurring and hence worse spatial resolution. Yet, even at an air gap of 5 cm, spatial resolution was better than 0.7 mm. The acquisition time per radiography was 15–20 min.

While spatial and WET resolution at an acceptable dose show the feasibility of our compact setup, the acquisition time is too long to image living samples. This shortcoming can be solved by replacing the detector by its successor model (Timepix3-based), which features event-based readout and can hence sustain much higher particle rates. Imaging time can then be reduced by about two orders of magnitude, allowing faster radiographic, and ultimately tomographic imaging.

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Radiobiology & related applications / 17

The lack of p21 sensitizes colon cancer cells to radiation-induced apoptosis.

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Radiation therapy is the most-effective cytotoxic therapy available for the treatment of localized solid cancers. With the introduction of charged particle radiotherapy (proton therapy), the area of irradiated healthy tissue surrounding the tumor was further decreased. The aim of this study is to investigate the role of p53 in both X-rays and proton therapy treatments. p53 is a transcription factor with a key role in stress-dependent regulation of DNA repair, cell cycle arrest, cellular senescence, and apoptosis.

As a model, we used 3 isogenic derivatives of the colon cancer-derived cells HCT116: parental, TP53^{-/-}, and CDKN1A^{-/-} (coding for p21). To uncover treatment-specific biological effects, we analyzed cellular responses to irradiation, focusing on DNA damage, p53 targets activation, apoptosis induction, and 3D culture disaggregation.

As expected, X-rays caused DNA damage as early as 4 hours after treatment in all cells, detected by the formation of γ -H2AX foci. Interestingly, 24 hours post-treatment, parental cells repaired the radiation-induced damages more rapidly in comparison with p53 null cells. Moreover, the p53 null clone showed a higher apoptotic rate, indicating that p53^{-/-} cells could be more radiosensitive in respect to p53^{+/+} cells. To better mimic the shrinkage effect of radiation therapy on solid cancers, 3D spheroids were used. HCT116 parental, p53^{-/-}, and p21^{-/-} cells spontaneously formed spheroids in ultra-low attachment plates. Notably, while parental spheroids showed a reduction in diameter 13 days after the treatment, but still maintained a proper 3D organization, the p53^{-/-} and p21^{-/-} spheroids completely disaggregated. Moreover, the viability of p53^{-/-} and p21^{-/-} spheroids drastically dropped in response to X-rays, and analysis of PARP cleavage highlighted an increase in apoptosis particularly in p53 and p21 null cells.

These results suggest that the absence of p53-dependent responses through p21 enhances the sensitivity to irradiation.

Detectors - First Session / 18**Thermoluminescent dosimeters (TLD-100) performance in high-energy proton beam line**

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Three batches (A, B, C) of thermoluminescent dosimeters TLDs-100 (LiF:Mg, Ti), provided by the team of the Radioactivity Laboratory (LaRa) of Physics Department of Federico II University of Naples, were characterized to Trento Proton Beam Line. Afterwards, the TLDs have been used to obtain the dose profile in a series of radiobiological experimental activities implemented in the context of the MoVe IT CSNV project.

TLDs are well-established devices for clinical dosimetry [1, 2]: they are close tissue equivalent (effective atomic number 8.2, compared to 7.4 for tissue), low signal fading (5%-10% per year), wide linear response range (10 mGy-10 Gy), spatial resolution of 2 mm and high sensitivity [3]. The chips have density of 2.64 g/cm³ and nominal dimensions of 3.2 × 3.2 × 0.89 mm³, resulting easy to handle and peaceable in small inserts.

To enable the TLDs as dosimeters, an adequate calibration procedure in the range and beam of interest is necessary [4]. In order to characterize the TLDs, first they were exposed at TIFPA facility delivering a dose of 2 Gy. Therefore, the intrinsic sensitivity coefficient was calculated for each TLD and the calibration factor for each batch was carried out. Each TLDs batch was calibrated in the dose range 0-20 Gy obtaining the corresponding calibration curves. The calibration curves for each batch of TLD resulted to be linear in the dose range 0-10 Gy, whereas the quadratic model performs better than the linear model above 10 Gy dose level. The calibration factors in the range 0-10 Gy resulted equal to 4.6 ± 0.2 μC/Gy, 4.9 ± 0.1 μC/Gy and 5.4 ± 0.1 μC/Gy for the batch A, B and C respectively. Prior to each irradiation, TLDs were annealed in air at 400 °C for 1 hour, followed by a 2 hours annealing at 100 °C [5]. Several exposures of TLDs were performed, irradiating the dosimeters simultaneously to different cell lines: CHO-K1 cells, MDAMB-231 and U87. Both cells and TLDs were inserted in a biophantom designed by the biological dosimetry team on purpose. The monoenergetic proton beam of initial energy of 150 MeV, entered orthogonally to the biophantom. The planned dose ranged between 0.8-1.5 Gy in the Bragg peak. After each irradiation, the readout of TLDs was performed by a Harshaw model 3500 manual TLD reader. The TLDs have been read at 300 °C using a heating rate of 10 °C/s to optimize the TL signal-to-background ratio in the high temperature region. A continuous nitrogen flow was used to reduce chemiluminescence and spurious signals not related to the irradiation [6].

Depending on the belonging batch of the irradiated TLD, the proper calibration factor was used to obtain the dose absorbed to the cells along the proton beam in combination with the measure of the radiation-induced DNA damage, aiming to derive the value of Relative Biological Effectiveness (RBE).

The results of the experiments showed the feasibility of using TLDs-100 for dose verification in high energy proton beam.

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Space Applications / 19

Advanced solar particle event simulation at medical accelerators (CELESTIAL)

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Intense solar particle events (SPE) pose a significant risk to unsheltered astronauts and mission critical electronic systems. Over the duration of a typical SPE the whole-body dose in an unshielded scenario can reach more than 500 mGy and acute radiation effects like nausea and vomiting can occur. It is important to note that SPEs show large variations in dose depending on the specific energy distribution and fluences of a given SPE and the composition of the vehicle or habitat. In the EVA case, an astronaut is only offered minimal radiation protection by his/her space suit while during normal mission routine the astronauts are offered reasonable protection by their vehicle. Additionally, the high amount of radiation during an intense event can limit the lifetime of spacecrafts or satellite electronics and transient effects, like Single Event Upsets, can lead to irreversible system disruption.

To estimate the effects of SPEs on astronauts or electronics typically a series of serialized monoenergetic proton beams provided by a high-energy particle accelerator are used. Due to the serialized approach effects created by the complex interplay of e.g. different proton energies impinging on the e.g. biological sample within a short time period cannot be assessed. To mitigate the limitations of the current SPE simulation approach, a 3d-printed modulator was designed to instantaneously emulate the full energy and LET distribution of protons of a given SPE. The designed modulator consists of two parts, a porous material (e.g. LN300) to broaden the energy distribution of the primary protons and a complex, 3d-printed steel modulator. In short, particles impinging on the complex modulator pass through different thicknesses of the modulation structure. Depending on the traversed thickness, energy loss and multiple scattering are modulated differently. This results in a spatial homogeneous radiation field after all particles traversed a sufficiently large air gap (around 30 to 60 cm).

Within this context, an experimental campaign to benchmark and optimize this SPE simulation concept will be presented and submitted in the near future to the TiFPA PAC. The general design philosophy, Monte Carlo simulations on the expected performance as well as the proposed benchmarking experiments will be presented.

Detectors - Second Session / 20**Qualification of microstrip silicon sensors @ TIFPA proton beam.****Author:** Gianluigi Silvestre¹**Co-authors:** Benedetto Di Ruzza²; Keida Kanxheri¹; Maria Movileanu¹; Giovanni Ambrosi¹; Leonello Servoli¹¹ PG² TIFPA Trento**Corresponding Authors:** giovanni.ambrosi@pg.infn.it, keida.kanxheri@pg.infn.it, benedetto.diruzza@tifpa.infn.it, gianluigi.silvestre@pg.infn.it, leonello.servoli@pg.infn.it, maria.ionica@pg.infn.it

The proton beam available through TIFPA at Adrontherapy Center in Trento has been used in the past years to characterize the Silicon Microstrip prototypes for the FOOT experiment.

The FOOT (FragmentatiOn Of Target) experiment has a tracking subsystem, the MSD (Microstrip Silicon Detector), featuring three x-y coordinate measuring planes, each of which composed by two single sided silicon microstrip sensor, arranged orthogonally one respect to the other. In order to study if the pairing of the thin sensor (150 micrometer thick) and the front-end readout chip (VA1140) would fulfill the requirements, several test beam campaigns were carried out in the past three years. Several beam energies and setting were used to characterize the prototypes. The outcome validated the proposed technical solutions and will be presented .

A second series of test were also performed to validate a novel “grazing angle” approach for microstrip sensors, technique up to now tested only for pixel detector. In fact, using a proton beam impinging at different angles on the sensor surface, is possible to vary the actual energy deposited into the detector increasing the track length and also varying its fraction below a given strip. It is then possible to test the readout electronics saturation without actually having to use higher Z ions, as usually needed with the standard technique. Some preliminary results about these tests will be also presented.

Space Applications / 21**Lidal calibration at TIFPA proton beam line**

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LIDAL is a detector designed to study the radiation flux and energy spectra in Low Earth Orbit, it is onboard the International Space Station (ISS) since January 2020. It has been developed coupling a TOF system, based on fast plastic scintillators read by PMTs, with the ALTEA subsystem, a series of silicon detector telescopes which already operated on the ISS between 2006 and 2012 (Zaconte et al., 2010). This configuration adds Time of Flight measuring capabilities and sensitivity to Low Z ions to the energy loss measurements performed by the silicon strip detectors.

In this talk we will show results from LIDAL calibration and characterization, with protons at 220 MeV, 169 MeV and 91 MeV, that was conducted in June 2019 at TIFPA proton beam line. These results are going to be used to assess flight data that are continuously recorded on the ISS since January 2020.

We will show the time of flight distribution which yield to a time resolution ranging from 70 to 90 ps, and the comparison of the measured time of flight with the expected values.

For those particles which DE/Dx is above threshold in the silicon detector system we will present the measured energy loss spectra and its comparison with expected values.

Then we will demonstrate tracking capabilities of the device, from both the silicon detectors and the TOF subsystem.

Particle discrimination will be achieved by combining TOF and LET measurements. LIDAL is in this way the first detector in operation on-board the ISS capable of measuring all the characteristics of cosmic radiation relevant in the definition of biological risks for astronauts.

Detectors - First Session / 22

Responsivity and radiation hardness of siloxane-based scintillators as indirect sensors in the FIRE project under 37 MeV H⁺ irradiation @TIFPA centre

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The possibility to use polymer based scintillators for the detection of ionizing particles is of extreme interest in several fields, ranging from security purposes, where the revelation of neutrons and gammas is mandatory to hamper the traffic of nuclear weapons, workers radioprotection in sites as nuclear energy plants nuclear medicine laboratories and nuclear physics research facilities, design and built-up of original calorimeters to track muon. Polymeric materials present enormous advantages over inorganic scintillator: they are economic, they can be produced in several shapes and thickness, they are lightweight and display fast response time (ns). The light output is lower, but not dramatically, than most of inorganic crystals, but plastics are resistant to humidity and impacts,

whereas handling the precious, fragile crystals to couple it with the optics/electronics acquisition set-up might represent a challenging task.

In the last decades our research group developed new scintillators based on polysiloxane with added fluorophores to obtain flexible, transparent, tough, radiation responsive sensors with optimal performances as for light output, different particles sensitivity and recognition, and response repeatability. This flexible, lightweight and biocompatible material shows significant evidences of its possible and profitable use in the field of biomedical devices as in vivo radiation detector. In particular, the detection of protons during hadron therapy for specific cancer treatment is of paramount importance in order to precisely deliver the beam to the designated site with the maximum precision, thus preserving the surrounding normal tissue from damage. In this presentation, we show the response of selected series of siloxane scintillators to a H⁺ beam with energy of 37 MeV, available at the proton-therapy centre of the Provincia Autonoma di Trento (APSS). The samples, obtained as pellets with 1" diameter and two different thickness (1 mm and 20 mm), have been investigated in terms of ion beam induced luminescence (IBIL) and responsivity, evaluated with a power meter. In the case of IBIL technique, the scintillation light spectrum from 20 mm thick samples is recorded in real time during irradiation with a light collecting fiber and a "movie" of possible damaging events occurring to the polymer matrix and the dissolved dyes is recorded, observing the fate of their respective excited states. This experiment evidenced a stable emission signal, peaked at 430 nm, whose features remain unchanged up to high final fluence. In a contemporary experiment, using the back side of the same thick sample, the power of emitted light as A/W is measured directly, exploiting the full stopping of the beam into the 20 mm pellet (estimated range is 14 mm for 37 MeV). Once fixed the beam current, which has been selected in the range 1–300 nA, and in turn the proton flux, we varied the irradiation time between 1 s and 10 s and continuously measured the current in output of the power meter (Newport, sensor 818- SL). In this way, it is possible to estimate: i) the detection limit of the scintillator, ii) the linearity of the response versus proton flux, iii) the stability of the response for increasing ion fluence. The same experiment has been done using 1 mm thin scintillators coupled to an acrylic light guide to drive the signal to the power meter, with the aim of simulating the prototype of sensor proposed in the FIRE project: a fully flexible radiation monitor to preserve healthy tissues during prostate cancer treatment by hadron therapy.

Medical Physics Applications / 23

MoVeIT detectors characterization at Trento Proton Beam Line Facility

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Within the MoVeIT project of the National Institute for Nuclear Physics (INFN), the University of Torino and the INFN are investigating Ultra-Fast Silicon Detectors (UFSD) for proton beam monitoring in order to replace ionization chambers currently in use in Hadrontherapy.

Two devices are being developed based on UFSD: one for measuring the beam energy using Time-of-Flight (ToF) techniques, and the other aiming at counting single particles up to 100 MHz/cm². Strip sensors of two geometries {20 strips of 2.25 mm² (150 μm width x 15000 μm length, 216 μm pitch); 30 strips of 2.40 mm² (80 μm width x 30000 μm length, 146 μm pitch)} produced by FBK (Fondazione Bruno Kessler, Trento, Italy) were used for counting, while pads (80 μm active thickness, 3x3 mm² sensitive area) produced by HPK (Hamamatsu Photonics K.K., Japan), and strip sensors (600 μm pitch, 50 μm active thickness, 2.2 mm² sensitive area) produced by FBK were used for energy measurement. Tests for preliminary characterization were performed in the experimental room of the Trento Proton Therapy Center (Azienda Provinciale per i Servizi Sanitari, APSS), with 60-250 MeV clinical proton beams at 10⁶ – 10⁹ p/s fluxes. Varying the flux at different energies, the particle rate

was measured and compared with the one estimated by a pin-hole ionization chamber. The energy was obtained using ToF measurements from the telescope of two UFSDs sensors placed at a specific distance between each other and aligned along the beam direction.

The achieved efficiency of the counter prototype was greater than 98 % up to 10^8 p/s* cm^2 and few hundreds of keV deviations from nominal energies were achieved for all beam energies at 67 and 97 cm distance between the sensors corresponding to < 1 mm range.

These promising results demonstrate that UFSD could be a viable option to improve the conventional monitors and further improvements are therefore being developed. Among them, a new detector geometry is being produced by FBK to cover a sensitive area of 2.74×2.74 cm^2 and will be tested in the coming months, it features 146 strips of 114 μm width x 26214 μm length, 180 μm pitch.

Detectors - Second Session / 24

Qualification of microstrip silicon sensors @ TIFPA proton beam.

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The FOOT (FragmentatiOn Of Target) experiment has a tracking subsystem, the MSD (Microstrip Silicon Detector), featuring three x-y coordinate measuring planes, each of which composed by two single-sided silicon microstrip sensor, arranged orthogonally one respect to the other. In order to study if the pairing of the thin sensor (150 micrometers thick) and the front-end readout chip (VA1140) would fulfil the requirements, several test beam campaigns were carried out in the past three years. Several beam energies and settings were used to characterize the prototypes. The outcome validated the proposed technical solutions and will be presented.

A second series of tests were also performed to validate a novel “grazing angle” approach for microstrip sensors, technique up to now tested only for pixel detector. In fact, using a proton beam impinging at different angles on the sensor surface it is possible to vary the actual energy deposited into the detector increasing the track length and also varying its fraction below a given strip. It is then possible to test the readout electronics saturation without actually having to use higher Z ions, as usually needed with the standard technique. Some preliminary results about these tests will be also presented.

Detectors - Second Session / 25

TOPS: Time Of flight Plastic Scintillators

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Organic scintillators are largely exploited in a wide range of detectors due to their capability to obtain very good time resolutions. Plastic scintillators are also relatively cheap, easy to manipulate and light (low density) with respect to conventional crystal scintillators. Traditionally they are exploited to perform very precise measurements of particle Time of Flight (TOF) and more in general fast detectors. The research and development on organic scintillators is always active and in this framework a collaboration between the physics, engineering and chemistry groups of University "Sapienza" of Rome and Centro Studi e Ricerche Enrico Fermi started the TOPS project (Time Of flight Plastic Scintillators) focused on the development of a new class of plastic scintillators. TOPS scintillators have been realised in liquid and solid samples and their intrinsic characteristics have been studied. The samples show very promising light output with respect to anthracene and commercial scintillators and extremely good timing properties. In order to improve the matching between the emission/absorption spectra of the scintillators, doping material have been added as wave-shifter. The use of MDCD as doping improved the performances of a fraction of the scintillator samples. Based on the comparison of the light output values obtained in measurements with cosmic rays, a selection of the most promising scintillators has been investigated also from the timing point of view. The scintillation time characteristics of the TOPS plastic samples at different concentration that have been analysed so far with minimum ionizing particles and carbon at 700 MeV will be shown. A commercial plastic scintillator has been used as a reference in all the setup. The samples response in terms of light output and timing properties with proton beams and a dedicated measurements campaigns would be of large interest for this project.

Detectors - Second Session / 26

Dose Profiler and MONDO characterisation with proton beams at the Trento proton beam line facility

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In Particle Therapy (PT) the nuclear interactions between the beam projectiles and the nuclei of the volume under treatment produce a large amount of secondary particles which can escape from the patient body and/or interact with the patient itself. In carbon ion therapy, the detection of the secondary protons resulting from the ion beam fragmentation can be exploited to spot possible range variations, as the fragments production yield is correlated to the density of the tissues crossed by the beam. Besides the charged fragments, an important secondary neutron component is also present, contributing to an undesired and not negligible dose deposition far away from the tumor region, enhancing the risk of secondary malignant neoplasias development after the treatment. An accurate neutron production characterisation (flux, energy and emission profile) is hence needed to significantly improve the evaluation of possible long-term complications.

The Dose Profiler (DP) and MONDO detectors are plastic scintillating fiber-based devices designed to detect and track respectively the secondary protons and neutrons produced in PT treatments. The DP is composed by 8 planes ($20 \times 20 \text{ cm}^2$) of scintillating fibers read-out by Silicon Photomultipliers. It is currently operating at CNAO (Centro Nazionale di Adroterapia Oncologica, Pavia, Italy) as a monitoring device for carbon ion treatments, in the framework of the INSIDE project. The DP sensitivity to range variation is under evaluation within a clinical trial (ClinicalTrials.gov Identifier: NCT03662373) started in July 2019. The MONDO detector consists in a matrix of scintillating fibres, arranged in x-y oriented layers (total active volume $16 \times 16 \times 20 \text{ cm}^3$) that are read-out by a dedicated SPAD sensor designed and produced in collaboration with FBK (Fondazione Bruno Kessler). The neutrons kinetic energy and direction are reconstructed tracking of the recoil protons produced in double-elastic scattering neutron interactions. The detector is currently under development at CREF, FBK and Sapienza "University of Rome".

In 2017 the DP underwent to an intensive characterization campaign at the experimental cave of the Trento proton-therapy center. Proton beams at different energies have been used to measure the DP detection efficiency, the spatial and energy resolution. In the same campaign, a MONDO prototype consisting of a reduced-size fiber matrix read-out by a preliminary version of the SPAD-based sensor has been tested to evaluate the light response of the fibers using proton beams in the energy range of interest. In this contribution all the activities carried on at the Trento beam line facility will be summarised and the obtained results will be reviewed.

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A novel Hybrid Detector design for Microdosimetry applications: HDM

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Medical Physics Applications / 28

Enhancing prompt gammas production for online dose verification in proton therapy

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Experimental route to QEye, an innovative device for high-resolution range verification in ocular tumour treatments

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