TIFPA

Trento Institute for
Fundamental Physics
and Applications

User Proposal and Request for beam time at the Protontherapy Center

Via Al Desert 14, 38122 Trento, Italy

DATE 28/02/2025

PROPOSAL # ....

(To be filled in by TIFPA)

1. **Proposal type: (check one) Biology** ☐ **Physics** X **Other** ☐
   New (FRIDA enabling extension time)

2. **Proposal Type: A (Scientific)** X **Type B (Industrial)** ☐

3. **Title of Experiment** **FRIDA-WP3 QuADProBe**
   Funding Source INFN-CSN5
   Grant Title and Number FRIDA project
   Grant Start Date January 2022
   Grant End Date December 2025

4. **Principal Investigator** Raffaella Radogna
   Department Physics
   Institution INFN-Bari and University of Bari (UniBa)
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   70126 Bari
   Telephone 080 5442431
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4. **Beam time request:**
   A. Requested period
   B. Requested hours 7

5. **Signature**

   As Principal Investigator/Spokesperson for this proposal, I certify that everything in this proposal is accurate to the best of my knowledge and that my research team will abide by the rules and regulations at TIFPA. I also certify that the work described in the proposal is not proprietary and upon completion of research will be published in the open literature.

   PI/Spokesperson Signature Raffaella Radogna Date 28/02/2025

6. **Beam characteristics**

Energy* (MeV) MIN	MAX	Beam Time Requested (hr)**	Rate or Dose Rate or extractionCurrent Required*** (p/s or Gy/min or nA) MIN	MAX	Beam Diameter Required*** (cm)	Beam Uniformity Required*** (+/- %)	Dose Range
228		1h	1 nA		n.a.	n.a.	
228		1h	~ 300 nA		n.a.	n.a.	
74	228	75 min	1 nA		n.a.	n.a.	2cm steps
228		2h	1 nA	~ 300 nA	n.a.	n.a.	
154		20 min	1 nA		n.a.	n.a.	
220		20 min	1 nA				

*** For values available see Table in the User Guide**

**** For instruction on how to calculate the beam time hours see the User Guide**

***** Enter "n.a." if not an applicable requirement (i.e., any available can be used) or a range of values if a particular value is not required**

7. Personnel [PROVIDE INFORMATION FOR **ALL** PERSONNEL WHO WILL PARTICIPATE IN EXPERIMENTS AT TIFPA]

Role	Name	Affiliation	Phone	Email	Needs a dosimeter*
PI	**Raffaella Radogna**	**UniBa and INFN- Bari**	**393479541099**	**raffaella.radogna@uniba.it**	**Yes**
Coworker	**Simon Jolly**	**UCL**		**s.jolly@ucl.ac.uk**	**Yes**
Coworker	**Sonia Escribano**	**UCL**		**sonia.escribano@ucl.ac.uk**	**Yes**
Coworker	**Joseph Bateman**	**UCL**		**joe.bateman@ucl.ac.uk**	**Yes**
Coworker	**Annalisa Digennaro**	**UniBa**		**annalisadigennaro91@gmail.com**	**Yes**

*** Answer Yes or No. All dosimeters are provided by TIFPA**

8. Equipment and material*

a. List equipment and material to be provided by the beamline (items furnished by TIFPA)

• 50 mm PMMA absorber

b. List equipment and material to be provided by the user group (items **you** will bring to TIFPA)

• Portable enclosure
• 4 detector modules each made of 32 plastic scintillator sheets
• 4 Texas Instruments DDC232 custom circuit boards housing 32 Hamamatsu S12915-16R photodiodes
• FPGA development board for interfacing between DDC232 and pi
• Raspberry pi5 for control data acquisition and GUI
• Power strip to connect FPGA and daughter board
• DAQ laptop to back up option
• Control laptops
• D-LINK network hup to set in experimental room to connect pi5, DAQ laptop
• Router in the control room to take output from experimental room ethernet connection
• Ethernet cables and gloves

c. Indicate requirements for any special equipment or additional TIFPA facilities

None

d. Intentify/describe equipment/samples shipment methods

Equipment will not be shipped but carried by experiment participants.

***See User Guide for the list of materials that require the approval from TIFPA before the proposal can be submitted**

A. EXPERIMENTAL PROPOSAL (ALL APPLICATIONS)

a. Title of proposal (new)

FRIDA-WP3 QuADProBe test
(Integration of the "FRIDA-enabling" beam time request)

b. Overview of Project

Within the FRIDA collaboration, the INFN and UniBa team, in collaboration with the group led by Prof. Simon Jolly at University College London (UCL), is developing the Quality Assurance Detector for Proton Beam Therapy (QuADProBe) to make comprehensive measurements for proton beam Quality Assurance (QA). By combining measurements of proton beam transverse spot size, position and range into a single measurement, beam QA can be carried out more comprehensively with one beam delivery and in significantly shorter time. In addition, such a system would also enable fast Patient Specific Quality Assurance (PSQA) measurements to be made in real time without the need for manual intervention.

The detector design is reported in Fig. 1:

- a **scintillating fibre profile monitor** reconstructs the transverse dose beam profiles and measures the beam size and position;
- a plastic scintillator **range calorimeter** uses stacked layers of plastic scintillator to reconstruct the longitudinal dose profile and range.

Using scintillating material that is entirely water equivalent to intercept the beam, simultaneous measurements can be made of the proton beam parameters, reducing the QA time down to a few minutes.

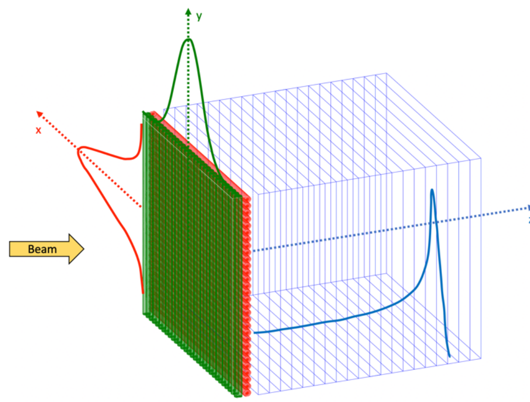

Figure 1: schematic diagram of the QuADProBe

Extensive development of the range calorimeter has already been realized in the past years at UCL showing that the detector is a promising candidate for fast, accurate range QA at conventional clinical dose-rate and, thanks to its dynamic range, also a viable solution at FLASH dose-rates. An overview of the achieved performance will be described in the next sections.

Pre-clinical systems of the scintillating-fibers profile monitor have already been realized and tested by colleagues at Heidelberg and CNAO. A prototype of such a beam profile monitor is currently under construction at INFN-Bari. As both portions of the detector have already demonstrated performance considerably exceeding the clinical requirement, the main challenge of the QuADProBe construction is one of system integration.

The purpose of the proposed experiment at TIFPA is to test the first integrated QuADProBe detector prototype using conventional and FLASH dose rates. In particular, we are interested in reconstructing pristine Bragg peaks performing an energy scan at conventional rates (from 70 to 228 MeV in 2 cm range steps) and a to test the linearity of the detector response as a function of the beam current using the TIFPA FLASH experimental line at 228 MeV (from the min to max operational current with 10% current steps). Finally, we would like to perform a spot scanning shifting the beam position of 0.5 cm around the central value.

c. Background and Significance

Comprehensive QA is necessary at every clinical proton beam therapy (PBT) centre: verification of the proton beam size, beam position and range in water is required daily in the hours immediately preceding the start of treatment, to ensure patients are treated safely. In addition, Patient Specific QA (PSQA) must be carried out to verify that the treatment plan for each patient is delivered accurately: this has traditionally required delivering the treatment plan to a water tank instrumented by a series of discrete dose monitors. An accurate measurement of the complete volumetric dose distribution requires repeated redelivery with incremental repositioning of the dose monitor array to completely cover the planned treatment volume: this must be repeated for each field and can take up to 2 hours per patient.

Since the first clinical PBT systems, there has been an awareness of the bottleneck that such time-consuming QA processes represent. This is particularly true for adaptive therapy, wherein a patient's treatment is replanned to account for anatomical changes based upon weekly reimaging at weekly intervals during treatment, rather than relying on a single diagnostic image prior to treatment. The improvements in treatment quality can be significant, especially where the tight dose conformity of PBT causes significant dose to be deposited in healthy tissue due to anatomical changes, but necessitate a subsequent PSQA measurement to confirm the updated plan accuracy. Accurate adaptive treatment also provides a route to hypofractionation, wherein the same overall dose is delivered to the tumor but in fewer, larger dose fractions.

One approach within the international community to speed up both daily beam QA and PSQA is through independent dose calculation based on log files, wherein the volumetric dose delivery is calculated after the fraction has been delivered based on the recorded machine parameters for each proton pencil beam spot. This however places more stringent constraints on beam QA measurements to validate the accuracy of the recorded log file parameters (spot position, range and dose) to ensure that the log file-based dose reconstruction is accurate; millisecond-timescale measurement resolution is also needed to resolve individual spots rather than simply measuring the integral dose delivery.

Internationally there is a growing need for faster and more comprehensive detector systems to allow both beam QA and PSQA to be carried out more rapidly, and also to provide the measurement resolution needed for machine log file QA. The ideal detector would allow measurements with the required sub-millimetre accuracy to be carried out in a matter of minutes. It would also be made of water-equivalent material meaning that range and scattering corrections would not have to be applied to the measurement, improving clinical accuracy.

The QuADProBe would provide the following advantages for PBT.

- Beam QA can be performed far more efficiently: total daily QA, including detector setup and removal, would take around 10 minutes.
- The technology choice allows a cheaper, more robust and lighter detector that is easy to set up. This allows the detector to be mounted to the treatment nozzle, simplifying setup and enabling measurements at multiple gantry angles without manual adjustment.
- PSQA measurements can be performed measuring spot-by-spot rather than just integral dose. The measured volumetric dose is reconstructed in software, allowing direct comparison with the treatment plan whilst reducing the amount of time a treatment room is occupied for PSQA.

Moreover, there are significant challenges with respect to dosimetry for FLASH proton therapy. The gold-standard ionization chamber-based detectors used for the measurement of proton depth-dose curves have been found not to scale up to FLASH dose-rates, largely due to the ion-recombination effect. Scintillators are of particular interest for FLASH PBT thanks to their fast response times on the order of nanoseconds and dose-rate independence in the scintillation light output.

d. Progress Report (renewal proposals) or Preliminary Results (new proposals).

Extensive development of the range calorimeter has already been realized in the past years at UCL. Exceptional results have been achieved, with a range resolution significantly exceeding the sub-millimetre requirement [1], including world-first measurements of mixed Helium-Carbon beams [2]. A compact detector prototype made of a series of 14 optically-isolated 100 × 100 × 2.85 mm polystyrene scintillator sheets, each directly coupled to a photodiode, has been used for the measurement of pristine and spread-out Bragg peaks at Clatterbridge cancer centre (CCC) in Wirral, with a range reconstruction accuracy up to 0.2 mm with 60 MeV beam and measurement times of few seconds [3].

The latest detector prototype is realized with a modular design: 128 scintillator sheets of size 100 × 100 × 3 mm are arranged into 4 modules of 32 sheets, where each sheet is directly coupled to a photodiode (see Fig. 2). Fast analogue-to-digital conversion facilitated measurement of scintillator sheet light output to 20-bit precision at 6 kHz, with a dynamic range of up to 350 pC. Due to the nanosecond decay time of the plastic scintillator and the large dynamic range of the detector, range measurements are also possible at FLASH dose rates.

Proton range measurements with the full-size detector were performed at The Christie proton beam therapy facility at clinical (approx. 1 nA nozzle current) and at FLASH dose-rate (approx. 50 nA nozzle current and 245 MeV). The detector was also tested at UMCG PARTREC in Groningen, Netherlands at beam intensities up to 50 nA. The range reconstruction accuracy was found to be within 0.4 mm of facility reference across the full clinical energy range (results presented at PTCOG61 by S. Escribano). Preliminary results showed an issue with the linearity of the scintillator light output with beam current that requires further with the proposed experiment.

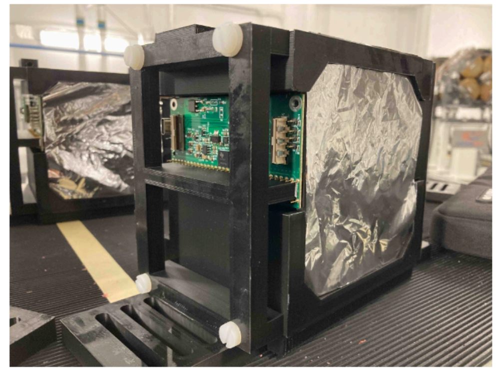
Figure 2: Range calorimeter module made of 32 sheets pf plastic scintillator.

The feasibility of making all beam QA measurements simultaneously has been explored operating the range calorimeter in combination with a transmission calorimeter developed at NPL, which offers dose measurements with consistent repeatability with less than 2% (k=1), and a Monolithic Active Pixel Sensor (MAPS) developed at the University of Birmingham, which is able to measures beam spot size and position with sub-millimetre accuracy. The system was tested at the UCLH PBT centre covering the measurements of both single energy pristine Bragg curves at a range of energies and positions, and a series of box fields, including treatment plans with multiple gantry angles (results presented at PTCOG62 by S. Jolly). Limitations in the acquisition rate of the MAPS suggest that a scintillating-based solution for the transverse dose profiles is suggested at FLASH regimes.

The scintillating fiber profile monitor developed by the group in Heidelberg was tested with clinical ion therapy beams and showed resolutions in position below 30 µm with commercially available fibers and photodiode arrays [4]. The prototype under constructions within the FRIDA collaboration has only undergo an exploration beam test with the experimental linear proton beam at the LinearBeam facility in Ruvo di Puglia. The proposed experiment aims at testing the QuADProBe integrated system with clinical conditions.

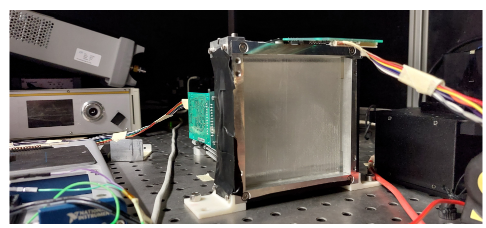
Figure 3: Scintillating fiber beam profile.

References
[1] L. Kelleter et al (2020), "A scintillator-based range telescope for particle therapy", Phys. Med. Biol. 65 165001, doi:10.1088/1361-6560/ab9415.
[2] L. Volz et al (2020), "Experimental exploration of a mixed helium/carbon beam for online treatment monitoring in carbon ion beam therapy", Phys. Med. Biol. **65** 055002, doi:10.1088/1361-6560/ab6e52.
[3] Saad Shaikh et al (2024), "Spread-out Bragg peak measurements using a compact quality assurance range calorimeter at the Clatterbridge cancer centre", Phys. Med. Biol. **69** 115015, doi: 10.1088/1361-6560/ad42fd.
[4] B.D. Leverington et al (2018) "A prototype scintillating fibre beam profile monitor for Ion Therapy beams" JINST 13 P05030

e. List three (3) of your publications that will assist the PAC in evaluating your work.

References [1,2,3].

f. Previous accelerator experience (1 paragraph maximum)

The previous accelerator experience as been described in the previous sections. Overall, through the years, the different prototypes of the range module have been tested with the following accelerators:

Birmingham 28 MeV beam (2017), MedAustron (2017, 2018), Heidelberg (2018, 2019), UCLH (2021, 2022, 2024), The Christie (2022), PARTREC (2022), Clatterbridge (2023).
The beam tracker module has been tested in an exploration test at the LinearBeam facility under development at Ruvo di Puglia, Bari, Italy (2024).

B. BEAM TIME REQUEST Provide enough details to justify your beam time request.

a. DETAILED PLAN for the experiments to be carried out

The experimental plan is articulated as follow:

- Set up mains cabling and networking in treatment and control rooms.
- Install detector enclosure and detector modules in the experimental room (60 min).
- Background measurements (no beam requested) (5 min).
- Detector calibration requires “shoot-through” measurements which accounts for differences in individual scintillator sheet light output, photodiode response and scintillator-photodiode coupling. This process is performed by making use of the plateau region in the Bragg curve at the highest energy available and by shooting the high-energy proton beam through the centre of the front and back of each detector module individually. Calibration shoot-through measurements of each of the 4 stack modules is performed either rotating case or module for back shoot-through:
    - 8 beam deliveries are needed at 228 MeV conventional current (2 beam deliveries, back and forth, per each module) (45 min);
    - additional 2 or 3 beam deliveries at 228 MeV conventional current might be needed to find the minimum custom DDC232 circuit board full scale range that does not saturate the signal (15 min);
    - 8 beam deliveries at 228 MeV FLASH current (2 beam deliveries, back and forth, per each module at max tolerated current) (45 min);
    - additional 2 or 3 beam deliveries at 228 MeV FLASH current might be needed to find the minimum DDC232 full scale range that does not saturate the signal (15 min).
- Installation of full size detector made of 4 stack modules (10 min).
- Pristine Bragg peak measurements at clinical current for full clinical range:
    - 15 beam deliveries from 228 MeV (32.5 cm range) to 74 MeV (4.5 cm range) in steps of 2 cm range. This corresponds to energies: 74, 91, 106, 119, 131, 143, 154, 164, 174, 184, 193, 202, 211, 220, 228 MeV (75 min).
- Beam current scan from minimum to maximum operating current in steps to 10% in current intensity at 228 MeV:
    - 50nA beam used to assess the max operating current for the detector dynamic range of 350 pC (5 min)
    - 10 beam deliveries with currents from 50nA to max operating current in steps of 10% (100 min)
- Spot scanning:
    - pristine Bragg Peak measurements at fixed energy (154 MeV and 220 MeV) and clinical current shifting the beam up, down, left and right wrt central position by 5mm. 4 beam deliveries per energy for a total of 8 beam deliveries. If the scan can’t be performed with the accelerator, the enclosure will be moved in the experimental room (40 min).

For each beam delivery, our acquisition time is 5 seconds. This gives us an optimal number of events. For FLASH beam time restrictions, we could consider reducing the acquisition time, if necessary.
More details are available at the following link: https://www.hep.ucl.ac.uk/pbt/wiki/Proton_Calorimetry/Experimental_Runs/2025/Trento_2025-03

b. Name of the liaison scientist
Dr. Emanuele Scifoni

c. Other information that will be helpful in justifying your beam time assignment (optional)

None.