



Istituto Nazionale di Fisica Nucleare

HDM

Hybrid Detector for Microdosimetry

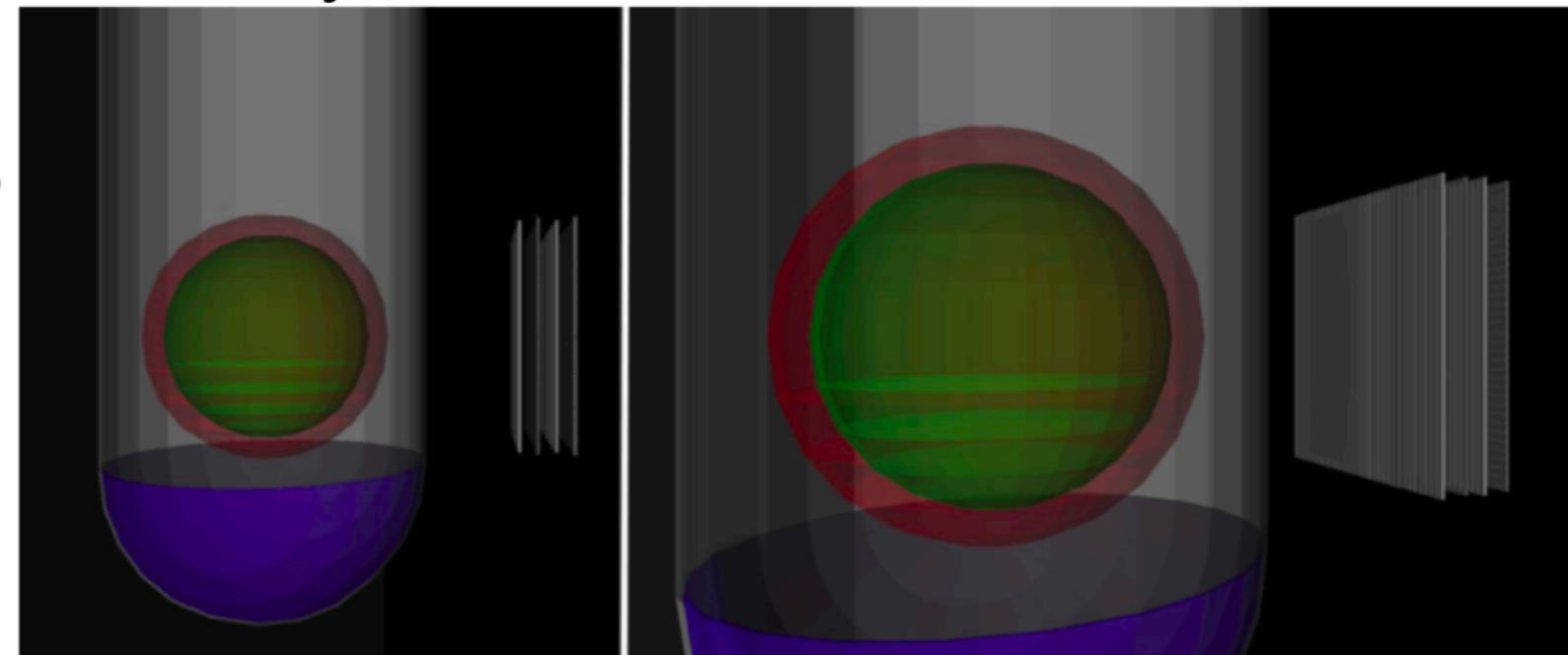
Principal Investigator: Chiara La Tessa (TIFPA)

INFN Project 2021-2023

To maintain the advantages of the TEPC and overcome the disadvantages, we propose the design for a new microdosimeter:

$$\text{HDM} = \text{TEPC} + 4 \text{ layers of LGADs}$$

LGAD (Low Gain Avalanche Detectors) are Silicon strip detectors recently developed. They can detect particles in a wide LET range with improved accuracy for timing and tracking measurements.



With 4 layers of LGAD, 2 oriented 2 in the X and 2 in the Y planes, we can reconstruct the track of the particle traversed in the TEPC with an accuracy of 300 μm . This feature improves the TECP spatial resolution and allow to calculate the actual length l of each particle without using the mean chord approximation.

Working Packages

3

WP Microdosimetry (Leader: G. Petringa)

Intercomparison

- Mini-TEPC (INFN-LNL)
- Nano-TEPC (INFN-LNL)
- Nano-TEPC (INFN-MI)
- Si-Telescope (INFN-MI)
- MicroPlus (INFN-LNS)
- TEPC (INFN-TIFPA)
- SiC (INFN-LNS)

New detector

- Preliminary with LGAD and TEPC
- Assembling

WP Simulations and radiobiology

- Radiobiological experimental tests adopting the same condition of detector irradiation
- Development of a new biological model based on the track length

Working Packages

LNS-FTE: 2.3

Giusi Forte

Luigi Minafra

Francesco Cammarata

Giorgio Russo

Giada Petringa

Richieste

Oscilloscopio programmabile con generatore di funzioni	15 k€
PCB preamplificatore e Alimentatore portatile	5k€



PRAGUE

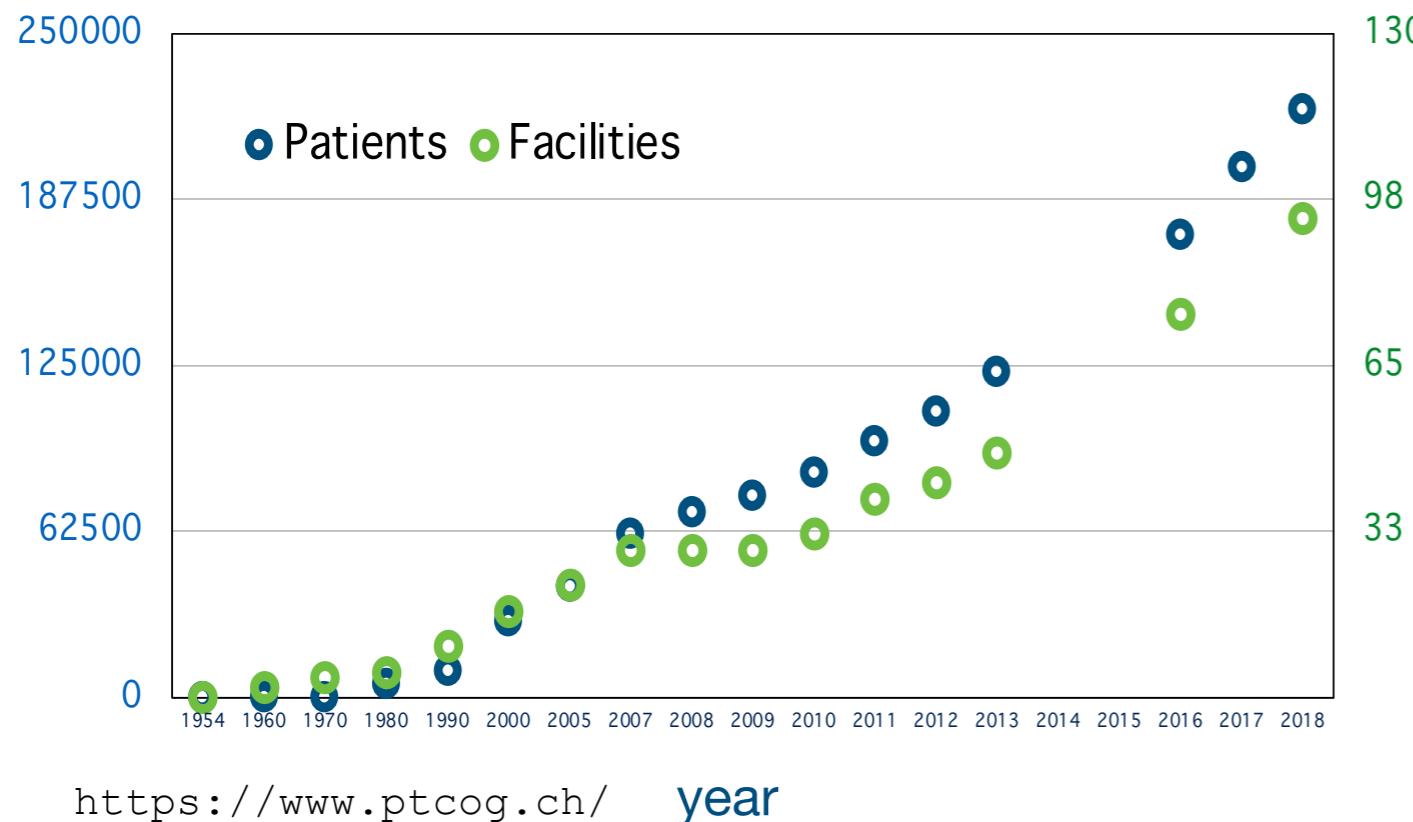
Proton RAnGe measure Using silicon carbide

Princial Investigator: Giada Petringa

Grant Giovani INFN 2020-2022

Protontherapy: proton range verification

Worldwide number of patients and protontherapy centers



Dose deposition highly sensitive to range variations. Strong request of accurate range verification

Daily quality accuracy:

- Fast and precise systems
- High spatial resolution
- High reproducibility
- Dose-rate and LET independent

Faster and safer? FLASH ultra-high dose rate in radiotherapy

¹MARCO DURANTE, PhD, ²ELKE BRÄUER-KRISCH, PhD and ³MARK HILL, PhD

¹National laboratories, Trento Institute for Fundamental Physics and Applications (TIFPA), National Institute of Nuclear Physics (INFN), University of Trento, Trento, Italy

²National laboratories, ESRF-The European Synchrotron, Grenoble, France

³Department of Oncology, CRUK/MRC Oxford Institute for Radiation Oncology, Gray Laboratories, University of Oxford, Oxford, UK

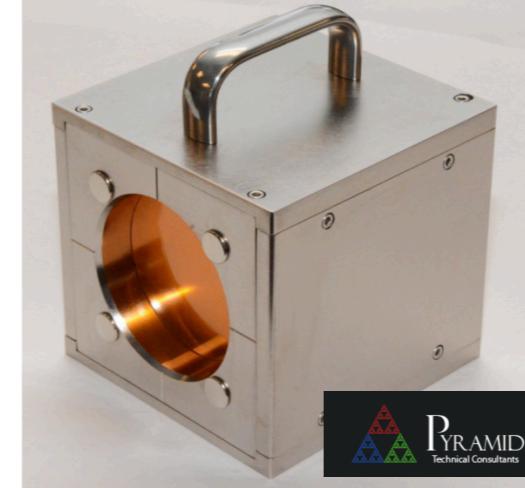
Protontherapy: proton range verification



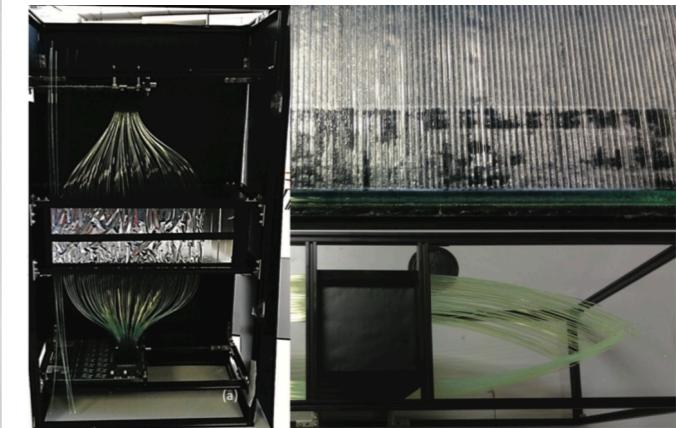
Water tank with a motorized system



Multi-layer Ionization Chambers



Multi Faraday Cups



Scintillator stack

Detector	Advantage	Disadvantage	Spatial resolution
Water Tank and ionization chamber	Linear response, LET and energy independent	dose rate dependent, high time consuming	~ 0.20 mm
MultiLayer Ionization Chamber	Linear response, LET and energy independent	dose rate dependent, low spatial resolution (order of mm)	~ 1 mm
Multi Layer Faradaycup	Linear response, LET and energy independent, dose rate independent	low spatial resolution (order of mm), high activation amount	~ 1 mm
Scintillator stack	High spatial resolution, linear response	LET and energy-dependent, low radiation hardness	~ 0.25 mm

PRAGUE objectives

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PRAGUE Proton RAnGe measure Using silicon Carbide

Realize the **first** on-line dosimeter for conventional and laser-driven ion beams based on a **new generation of Silicon Carbide**

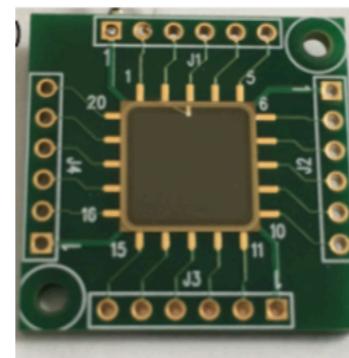
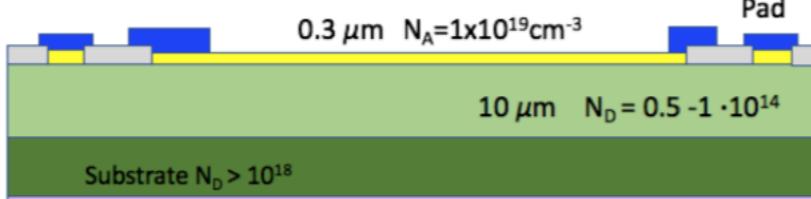
- dose rate independent**
- LET independent**
- linear response with absorbed dose**
- higher spatial resolution**
- saving time**

Adopted detectors

Call project funded by
CSNV (2016-2018)



Entrance and proximal position reconstruction

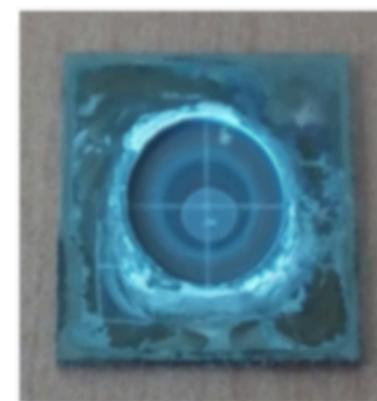
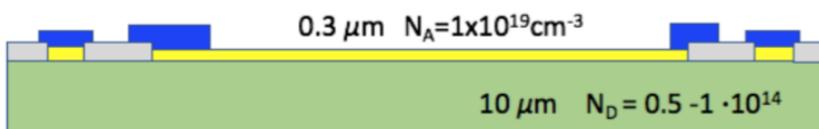


15 × 15 mm²

Design



Distal position reconstruction



15 × 15 mm²

Realization



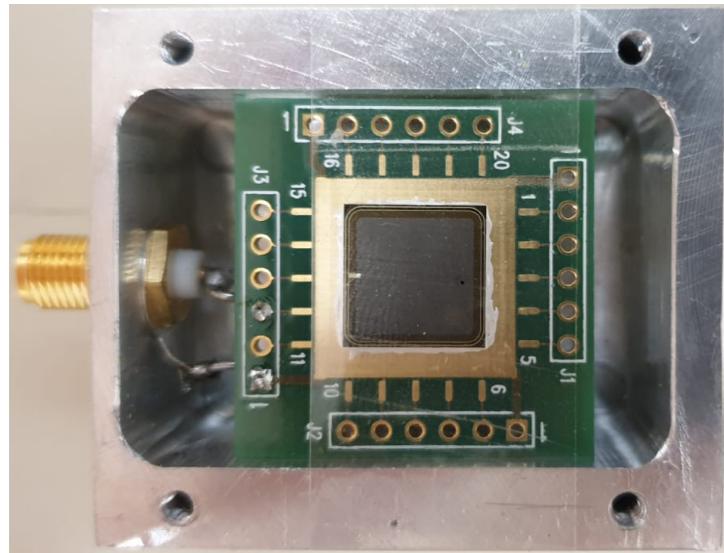
STMicroelectronics

Assembling and Test

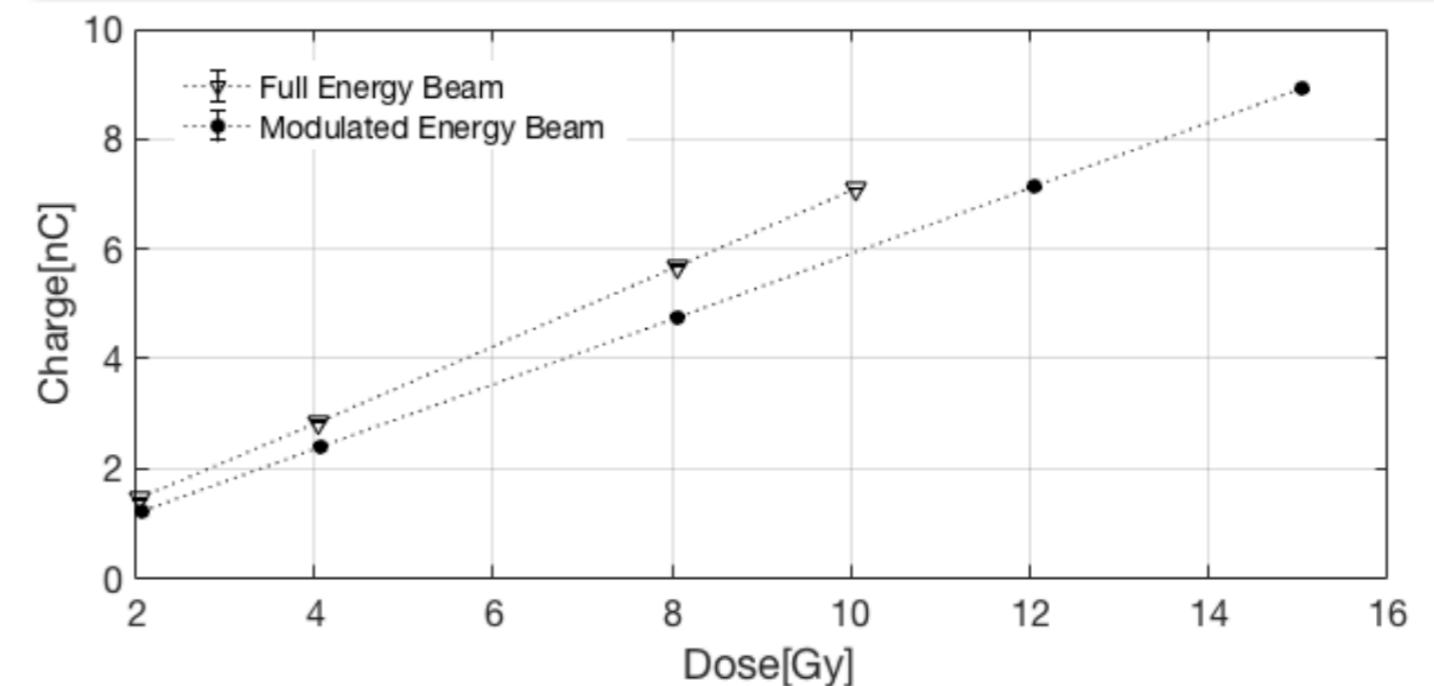
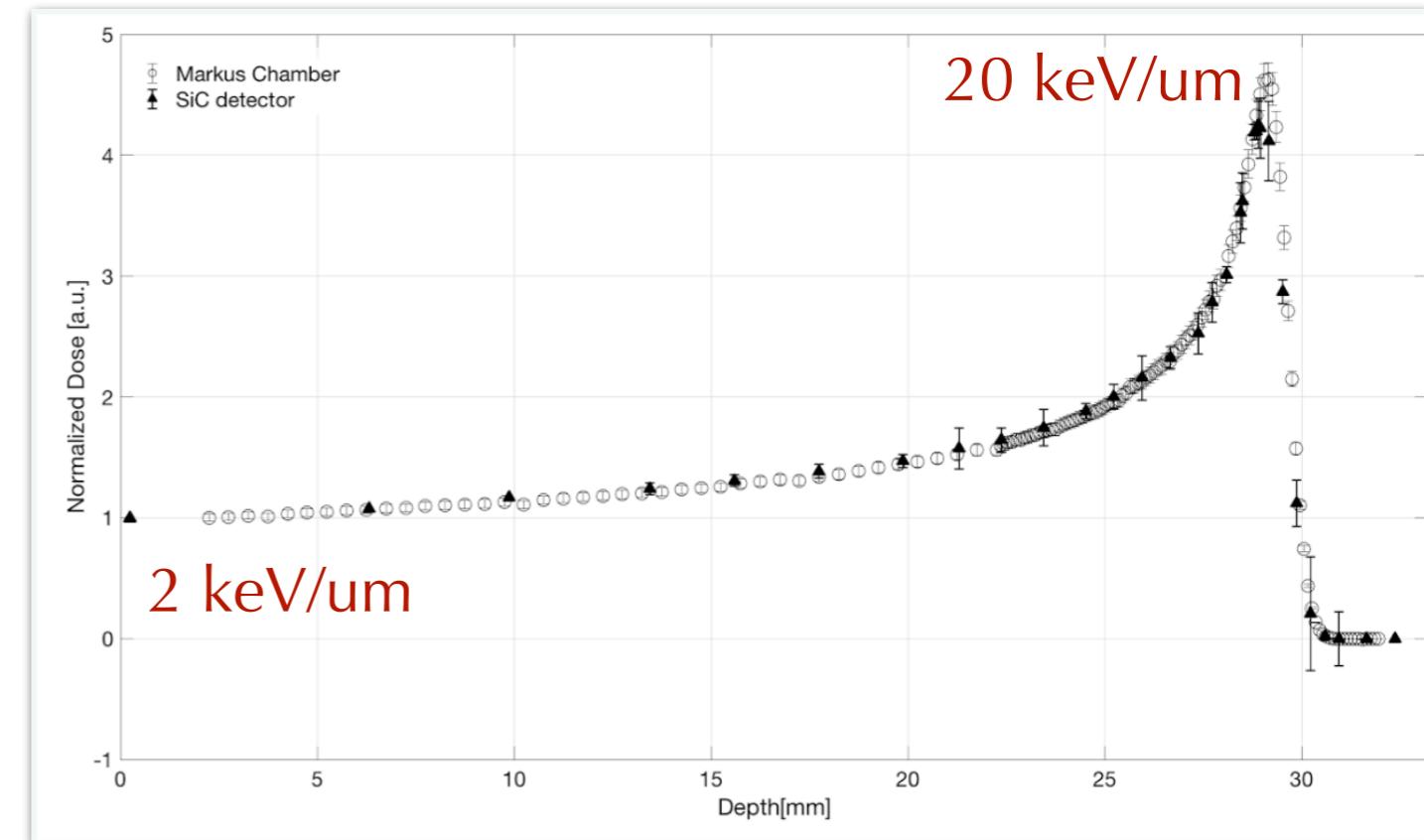
Preliminary Dosimetric Characterization

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Experiential test @CATANA
facility of LNS-INFN



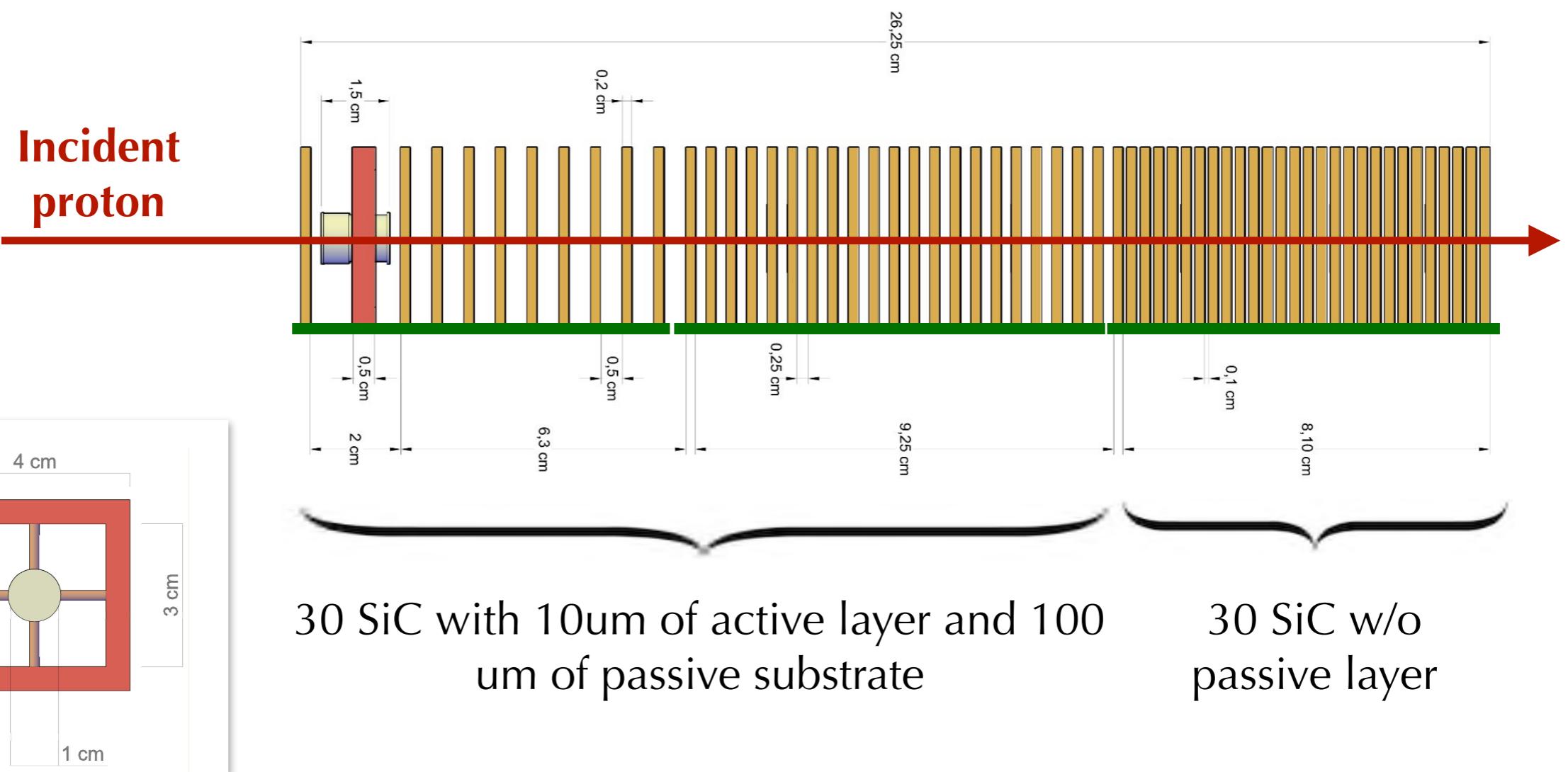
Irradiation field: 5mm in diameter
Energy: 62 MeV proton beam
Modulated and Pristine beam
Beam Current: $10^6\text{-}10^8 \text{ p/cm}^2$



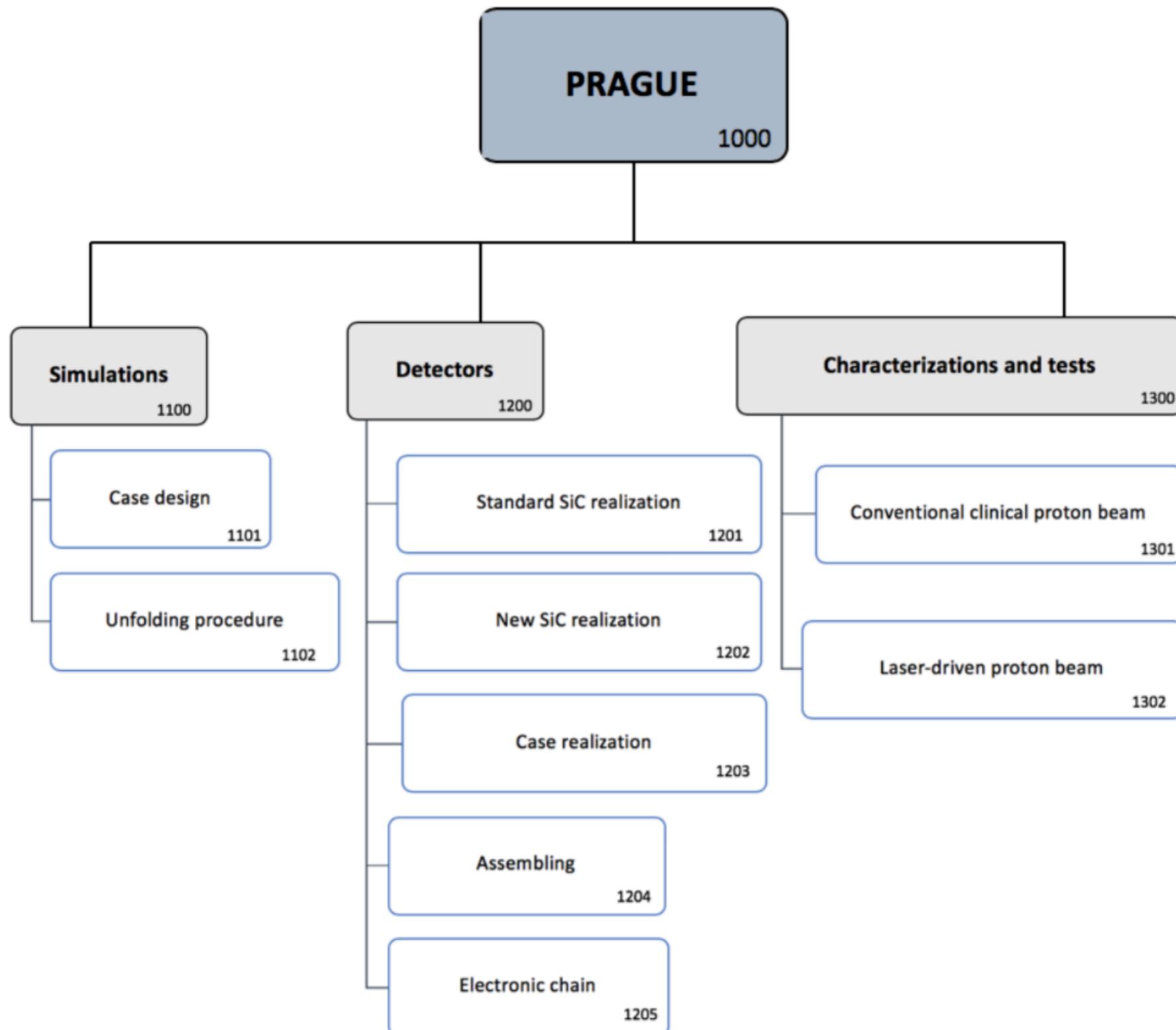
PRAGUE detector

II

PRAGUE Proton RAnGe measure Using silicon Carbide



Activity Description



Milestones 2020

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Deadline	Descrizione	Status
30 Giugno 2020	Design delle maschere	6 mesi di ritardo
30 Settembre 2020	Definizione dell'elettronica	3 mesi di ritardo
31 Ottobre 2020	Test su fascio di prototipi già disponibili	Completata all'80%
31 Dicembre 2020	Caratterizzazione di prototipi su fetta	1 anno di ritardo

Exp. Run - Flash Condition

14

proton 62 MeV - Full Energy

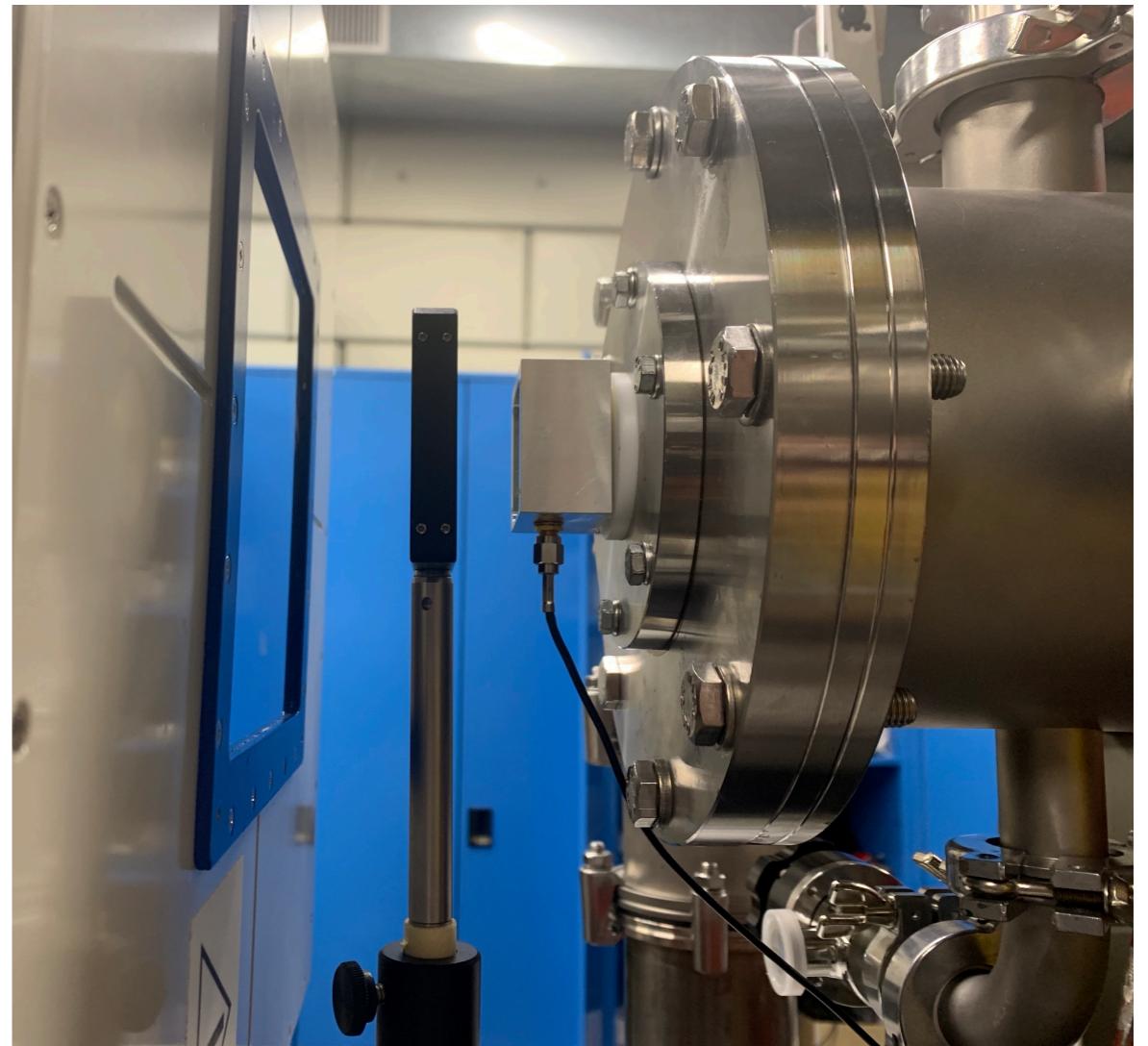
Beam current: 1 - 50 nA

Shot time: 10ms - 200ms

Beam Collimator: 1x1cm²

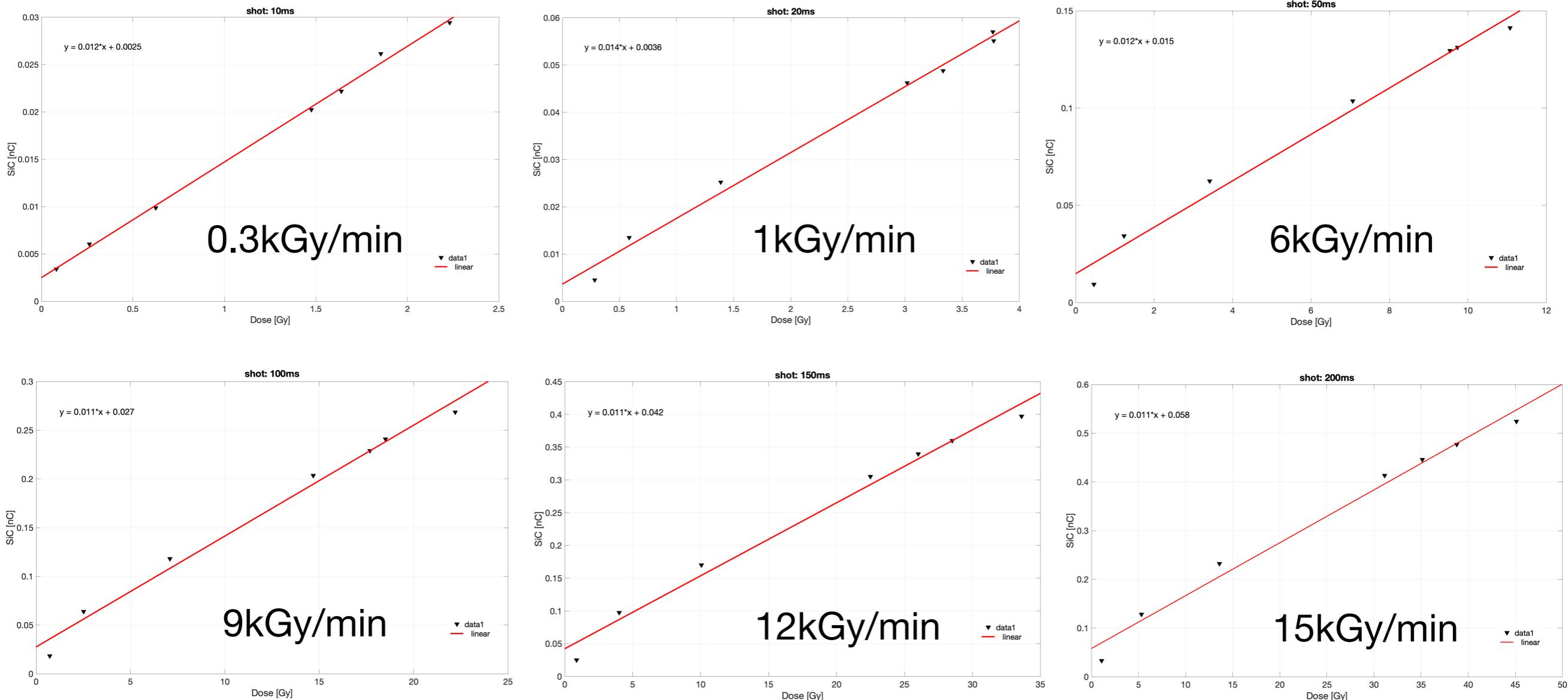
Detector Collimator: 5x5 mm²

Detector (ST): 10um - 1x1cm²



Dose Linearity - Flash Condition

15



Dose rate dependence ~ 7%



NIRVANA

NuovI RiVelAtori per NAnodosimetria

Princial Investigator: Valeria Conte (LNL)

INFN Project 2019-2021

Linear Energy Transfer

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LET-dose

$$\bar{L}_D = \frac{\sum_{i=1}^N L_i \varepsilon_i}{\sum_{i=1}^N \varepsilon_i}$$

$$\bar{L}_D^{Total} = \frac{\sum_{j=1}^n [\sum_{i=1}^N L_i \varepsilon_i]_j}{\sum_{j=1}^n [\sum_{i=1}^N \varepsilon_i]_j}$$

LET-track

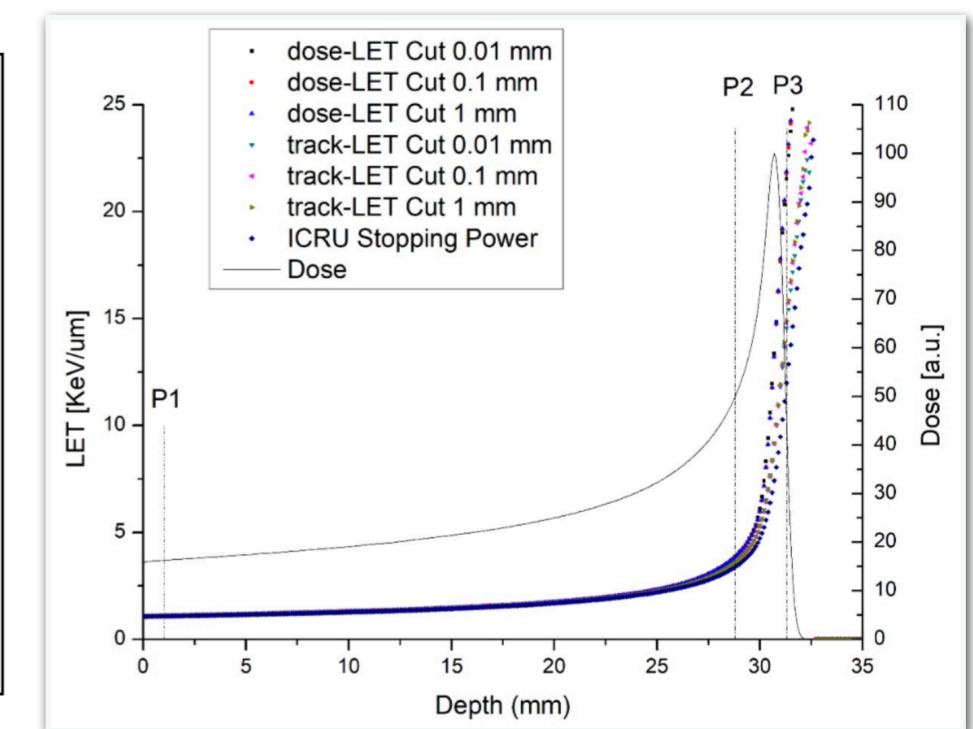
$$\bar{L}_T = \frac{\sum_{i=1}^N L_i l_i}{\sum_{i=1}^N l_i}$$

$$\bar{L}_T^{Total} = \frac{\sum_{j=1}^n [\sum_{i=1}^N L_i l_i]_j}{\sum_{j=1}^n [\sum_{i=1}^N l_i]_j}$$

good stability level

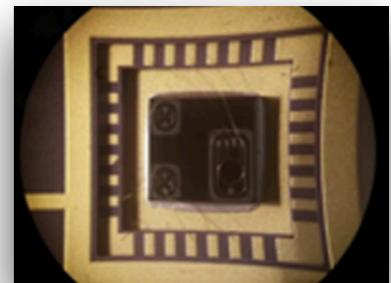
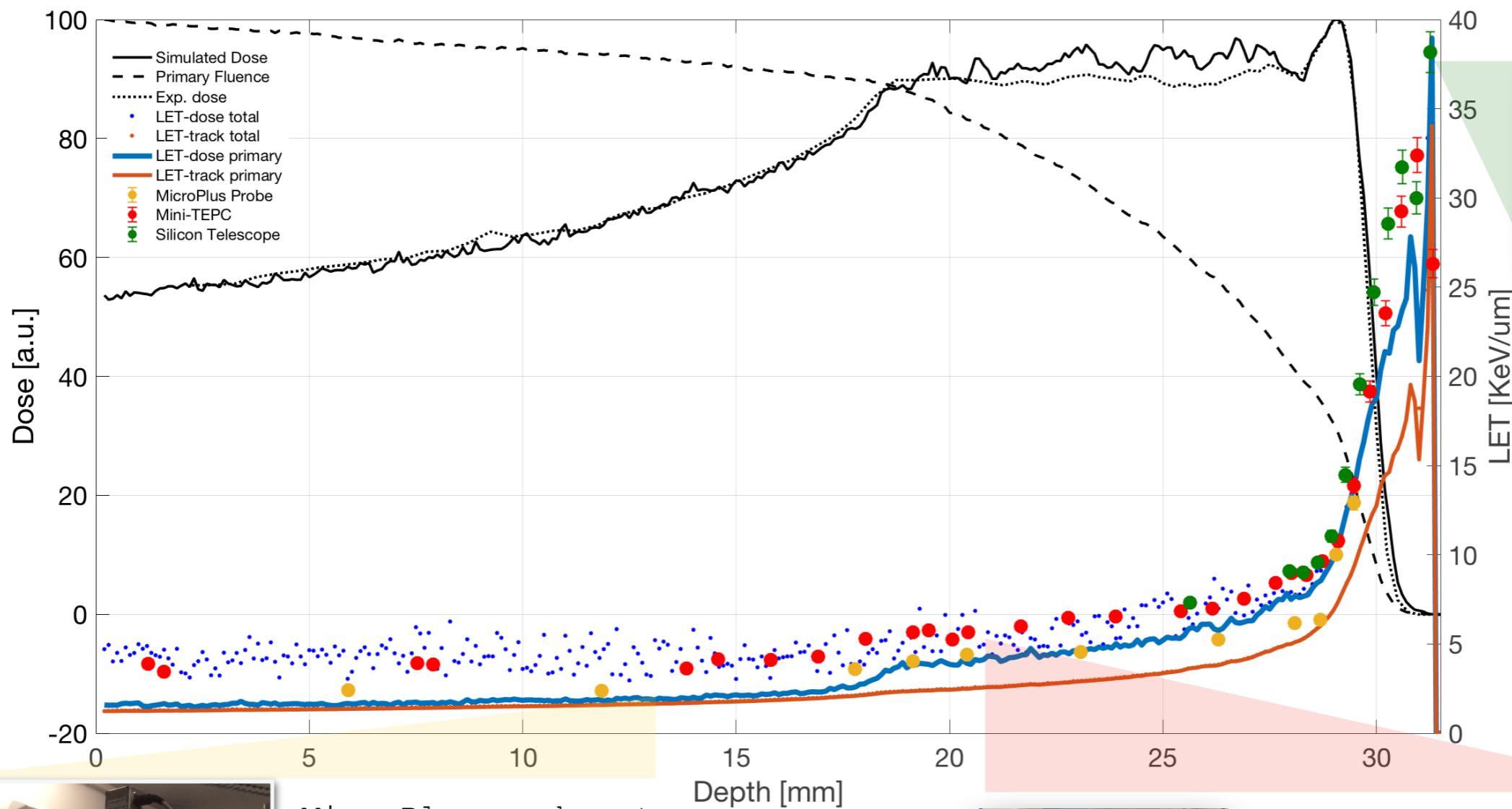
Position	Cut [mm]	\bar{L}_D [keV/ μ]	diff% L_D	\bar{L}_T [keV/ μ]	diff% L_T	\bar{L}_D^{TOT} [keV/ μ]	diff% L_D^{TOT}	\bar{L}_T^{TOT} [keV/ μ]	diff% L_T^{TOT}
P1	0.01	1.09	0.91	1.09	0.01	4.40	15.44	1.11	0.90
	0.1	1.09		1.09		4.79		1.11	
	1	1.10		1.09		4.05		1.10	
P2	0.01	3.70	0.27	3.46	0.29	4.43	1.81	3.48	0.29
	0.1	3.69		3.45		4.35		3.47	
	1	3.69		3.45		4.40		3.47	
P3	0.01	19.01	1.04	12.73	1.39	19.04	1.14	12.73	1.39
	0.1	19.15		12.86		19.18		12.86	
	1	19.21		12.91		19.26		12.91	

2%



Linear Energy Transfer

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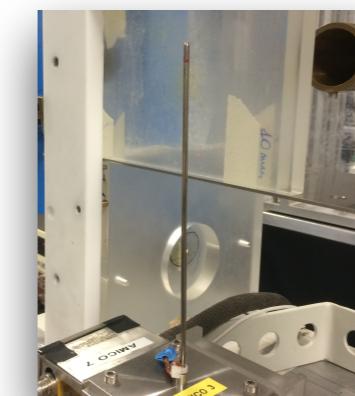


Silicon Telescope at the isocenter position of the CATANA protontherapy facility



MicroPlus probe at the isocenter position of the CATANA protontherapy facility

UNIVERSITY OF WOLLONGONG



Mini-TEPC at the isocenter position of the CATANA protontherapy facility

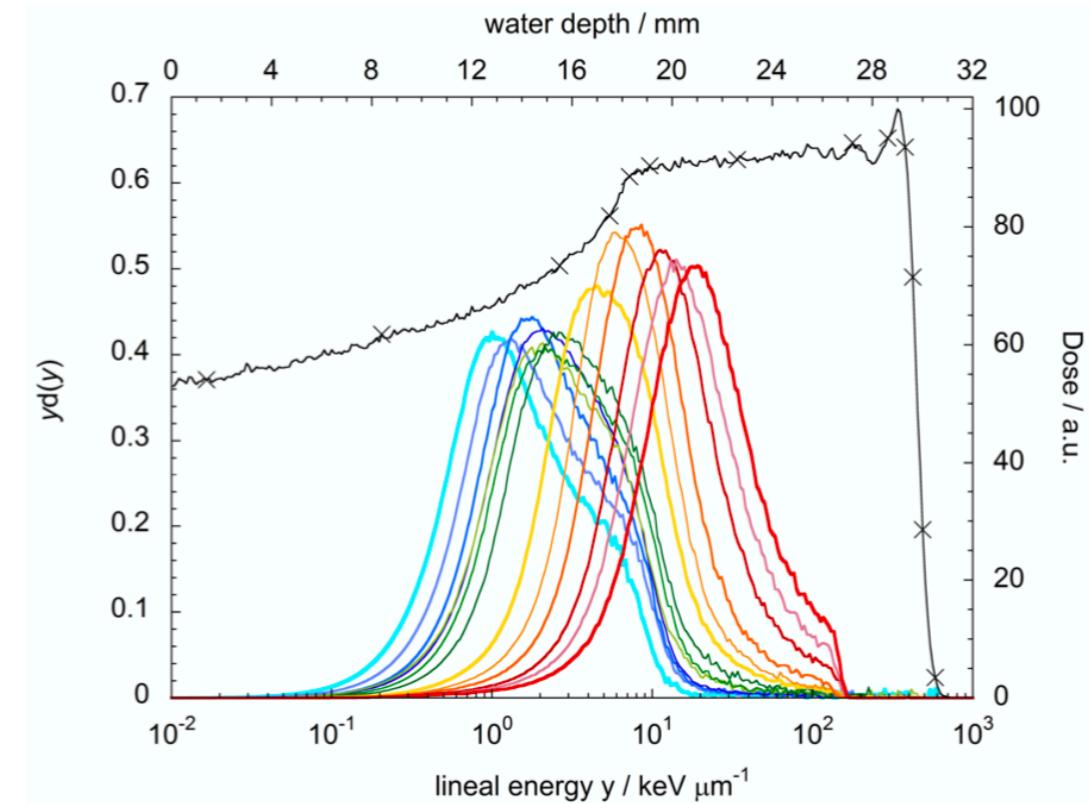
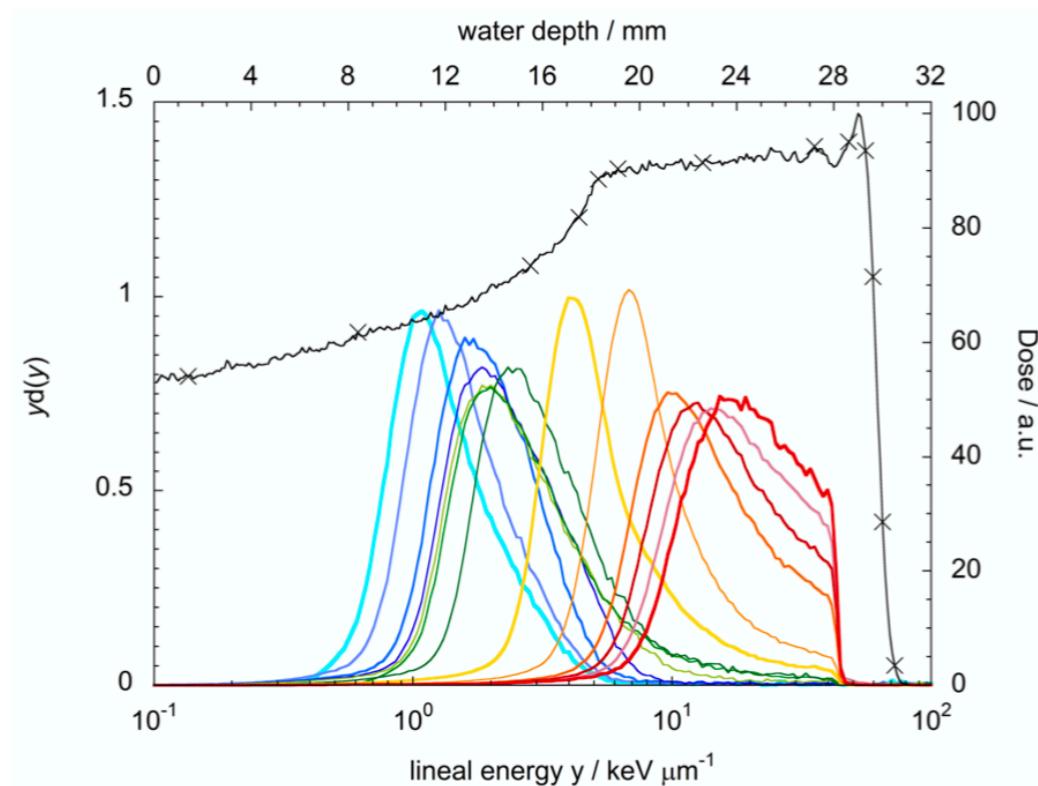

 Istituto Nazionale di Fisica Nucleare
 Laboratori Nazionali di Legnaro

Linear Energy Transfer

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Monte Carlo implementation of new algorithms for the averaged-dose and -track Linear Energy Transfer evaluation in 62 MeV clinical proton beams

G Petrigna¹, L Pandola¹, S Agosteo^{5,6}, P Colautti², V Conte²,
 G. Cuttone¹, K Fan³, Z Mei³, A Rosenfeld⁴, A Selva² and GAP Cirrone^{1,*}

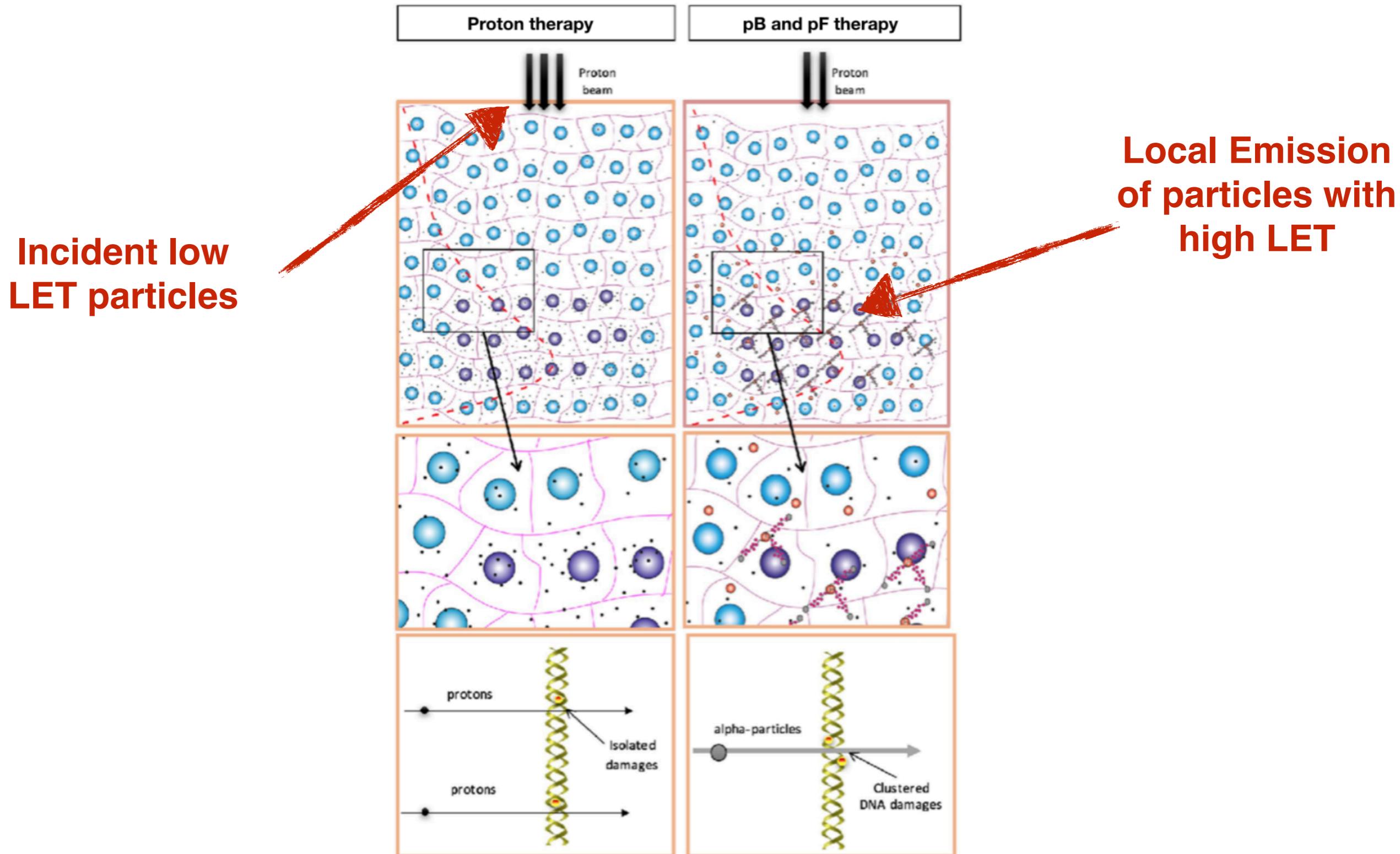


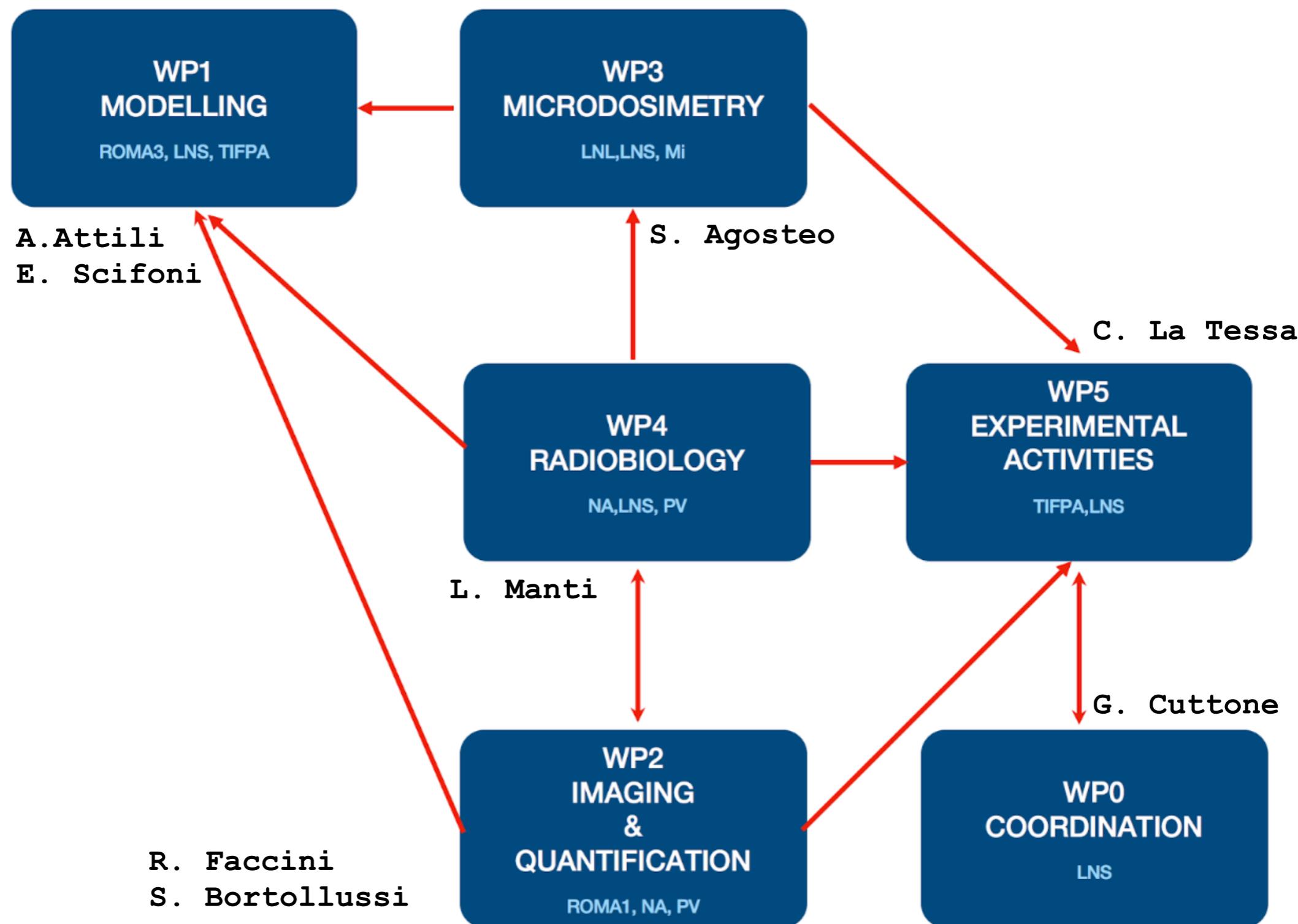


Responsabile Nazionale: Giacomo Cuttone

New binary reactions

21





Status of the project

Papers

24

- G. Petringa et al. "Radiobiological quantities in proton-therapy: estimation and validation using Geant4-based Monte Carlo simulations", Physica Medica 58, P72-80, (2019)
- F. Tommasino et al. "A new facility for proton radiobiology at the Trento proton therapy centre: design and implementation", Physica Medica 58, 99-106, (2019)
- F. Tommasino et al., "Study for a passive scattering line dedicated to radiobiology experiments at the Trento protontherapy center", Radiation protection dosimetry, 183.1.2. (2019)
- D. Mazzucconi et al. "Nano-microdosimetric investigation at the proton irradiation line of CATANA", Radiation Measurements 123, 26-33 (2019)
- L. Minafra et al. "Proton-irradiated breast cells: molecular points of view", Journal of Radiation Research, rrz032, <https://doi.org/10.1093/jrr/rrz032> (2019)
- F. Guida et al., "Dose intercomparison at Italian hadrontherapy centers", Physica Medica, Vol 68, 83-87 (2019)
- V. Conte et al., "Microdosimetry at the catana 62 mev proton beam with a sealed miniaturized tpc.", Physica Medica, Vol.64, 114-122, (2019)
- A. Selva et al., "Towards the use of nanodosimetry to predict cell survival", Radiation protection and dosimetry, 183-1-2 (2019)
- D. Mazzucconi et al., "Micorodosimetry at nanometric scale with an avalanche-confinement TEPC: Responce against a helium ion beam", Radiation Protection Dosimetry 183-1-2 (2019)
- V.P. Bonanno et al., "A radiation hardness test facility at INFN-LNS in the framework of ASIF project", NIMB, Volume 461, Pages 114-117 (2019)
- M. Rebai et al, "New thick silicon carbide detectors: Response to 14 MeV neutrons and comparison with single-crystal diamonds", NIM A 946 (2019)
- S. Tudisco et al., "Silicon carbide for future intense luminosity nuclear physics investigations", Nuovo Cimento C (2019)
- C. Ciampi et al., "Nuclear fragment identification with Delta E-E telescopes exploiting silicon carbide detectors", NIMA 925 (2019)
- M. Cesaire et al., "Sensitization of chondrosarcoma cells with PARP inhibitor and high-LET radiation", Journal of Bone Oncology, 17, 100246 (2019)
- G.A.Malfa et al., "Betula etnensis Raf. (Betulaceae) Extract Induced HO-1 Expression and Ferroptosis Cell Death in Human Colon Cancer Cells", INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES, 20-11, 2723 (2019)
- M. Lasalvia et al., "Raman spectroscopy for the evaluation of the radiobiological sensitivity of normal human breast cells at different time points after irradiation by a clinical proton beam", ANALYST, 144-6, (2019)
- F.P. Cammarata et al., "Proton Therapy and Src Family Kinase Inhibitor Combined Treatments on U87 Human Glioblastoma Multiforme Cell Line", INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES, 20-19, 4745 (2019)
- R. Ferrari et al., "MR-based artificial intelligence model to assess response to therapy in locally advanced rectal cancer"EUROPEAN JOURNAL OF RADIOLOGY, 118-, (2019)

Talks and Thesis

Titolo		Autore	Tipo	Univ.	Sez.	Relatori
1	Analisi UHPLC HR-MS/MS per lo studio di carriers del boro nella Proton...	✓ Cusano E.	S	Seconda Universita' Di Napoli	NA	Severina Pacifico
2	Caratterizzazione dosimetrica di un fascio di protoni accelerati press...	✓ Riccio C.	T	Seconda Universita' Di Napoli	NA	Lucio Gialanella et al.
3	Microdosimetric investigation of the p-11B reaction through a silicon ...	✓ Cazzola L.	S	Politecnico Di Milano	MI	Stefano Agosteo et al.
4	Preliminary Modelling for the Proton Boron Capture Therapy (PBCT)	✓ Chiappara D.	V	Universita' Di Padova	PD	Marco Mazzocco et al.
5	Preliminary study with a silicon microdosimeter for future application...	✓ Gigliuto C.	S	Universita' Di Catania	LNS	Giacomo Cuttone et al.
6	Progettazione di un'antenna a radio frequenza per applicazioni di riso...	✓ Fontanella M.	T	Universita' Di Roma 1	RM1	Luca Ficcadenti
7	STUDY ON EFFICACY IMPROVEMENTS AND QUALITY OF THE PROTONTHERAPY TREATMENTS	✓ Petringa G.	D	Universita' Di Catania	LNS	Pablo Cirrone et al.

Speaker	Conference	Contr. Title
1 Mancini-Terracciano Carlo (M)	<i>Ciclo di seminari AI-at-SLAC</i>	Machine learning for medical applications of Physics.
2 Manti Lorenzo (M)	<i>Proton Physics Research and Impleme...</i>	 Proton-Boron Capture Therapy (PBCT): enhancing clinical proton biological e...
3 Scifoni Emanuele (M)	<i>International School Detectors and ...</i>	 Research and development for Hadrontherapy in Italy
4 Petrica Giada (F)	<i>Giornata monotematica SIRR (Società...</i>	 Modelli radiobiologici e simulazioni Monte Carlo in adroterapia ...
5 Petrica Giada (F)	<i>1st International Biophysics Collab...</i>	 Relative Biological Effectiveness (RBE) of a clinical eye proton therapy be...
6 Petrica Giada (F)	<i>The International Conference on the...</i>	 MIRTO: A microdosimetric study and RBE measurement with 62 MeV clinical pro...
7 Petrica Giada (F)	<i>The International Conference on the...</i>	 Improvement of ParticleHP with proton-boron fusion reaction in GEANT4 for m...
8 Cirrone Giuseppe (M)	<i>The International Conference on the...</i>	 Monte Carlo in Hadrontherapy
9 La Tessa Chiara (F)	<i>2019 African Nuclear Physics Confer...</i>	 What do cancer therapy and Mars exploration have in common? ...
10 Manti Lorenzo (M)	<i>International Conference of Radiati...</i>	 Enhancement of clinical proton effectiveness by nuclear fusion reactions ...
11 Colautti Paolo (M)	<i>19th International Conference on So...</i>	 LET and RBE of Therapeutic Proton Beams Monitored With Microdosimeters ...
12 Voena Cecilia (F)	<i>Advanced Physics for Medicine</i>	 Development of 19F Magnetic Resonance Imaging
13 Blaha Pavel (M)	<i>Radiobiological Fundamentals of Rad...</i>	 Proton Boron Capture Therapy:: A novel approach to proton therapy-awarded a...
14 Blaha Pavel (M)	<i>ELI User Workshop on Laser-Driven A...</i>	 Radiobiology and in vitro irradiation at ELIMAIA

Important results

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- Molecula: BPA was identified as best molecula in terms of toxicity and 11B concentration;
- Radiobiological experiments: was studies different radiobiological endpoints (survival, ROS, chromosome aberrations, pathway repairs) with different incident proton energies (60 MeV and 150 MeV) and different LET (1 keV/um up to 20keV/um);
- Microdosimetric measurements: experimental campaigns were performed adopted 3 different detectors along the same SOBP adopted for the radiobiological experiments;
- Neutron contamination: the flux of neutron was experimentally evaluated;

Milestones 2020 and Covid-19 impact

Deliverables 2020		Deadline	Details	Delay
D1.2	Implementation of Geant4-DNA and TRAX-CHEM simulations starting from the spectra previously obtained (E. Scifoni, A. Attili)	30-06	Rimodulazione in corso	/
D2.2	Establishment of a procedure for the measurements of the concentration of borated and fluorinated compound in-vitro tests (R Faccini, C Voena, S Bortolussi)	30-04		No
D3.2	Microdosimetric spectra with the avalanche confinement detectors simulating different site sizes (for WP1) (S Agosteo)	31-12	Lo shift è dettato dal fatto che ci sono stati dei <u>ritardi nella realizzazione dei preamplificatori della TEPC-borata e la sua consequenziale caratterizzazione.</u> Una volta che la sua realizzazione verrà ultimata verrà fatta una campagna di misura a Trento per investigare le configurazioni con/senza boro con tutti i rivelatori adottati per i test.	6 mesi

Milestones 2020 and Covid-19 impact

	Deliverables 2020	Deadline	Details	Delay
D4.2	Results on high-LET radiation induced CL as an effector of proton biological enhancement by p-B and p-F reactions. Cell survival studies with BNCT (L Manti)	31-12	Ci sono dei <u>ritardi nel completamento delle milestone M4.2 ed M4.3</u> . In particolare non sono ancora stati effettuati i test a bassa energia di protoni incidenti (M4.3). Finora è stato fatto soltanto un test preliminare a Caserta ma è necessario effettuare almeno altri due turni di misura in cui poter completare appieno la milestone. Per quanto concerne, invece, i test ad alta energia, questi sono stati effettuati con entrambe le molecole (BSH e BPA). Manca soltanto l'ultimo turno sperimentale a CNAO (M4.2). Mario Ciocca è già stato contattato dando la disponibilità per il beam time anche nel 2020. <u>Infine, occorre ricordare che al momento il WP4 ha dato priorità al completamento degli esperimenti con il boro. Una volta che questi verranno terminati si procederà alla caratterizzazione con il fluoro.</u> Questi testa avverranno tutti nella stessa facility, ovvero a Trento, e verranno effettuati a partire dalla seconda metà del 2021 fino a tutto il 2022.	6 mesi
D0.2 e D5.3	Summary report of all experimental activities (C La Tessa)	31-12		No

Thanks for listening