FRIDA

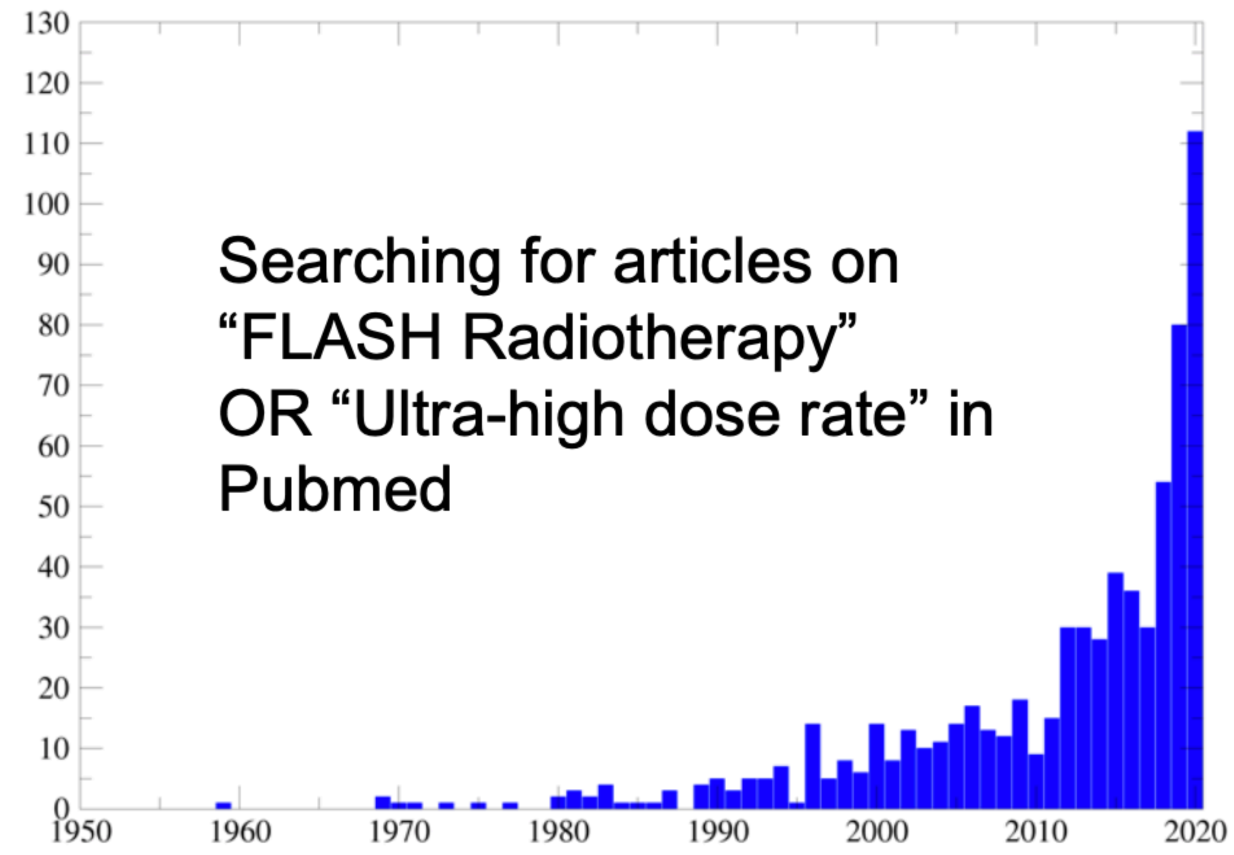
FLASH Radiotherapy with hIgh Dose-rate particle beAms

National: Dr A Sarti (Roma 1)
Local: Dr GAP Cirrone

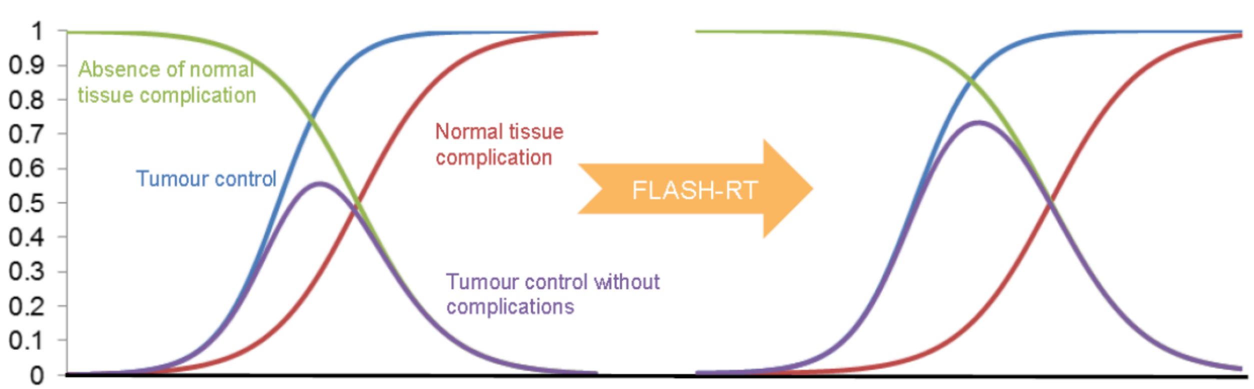
FRIDA motivations

- For a long time, one of the paradigm in External Beam Radio & Particle Therapy was the one indicating that 'the slower.. the better':
  => the overall dose to the patient had to be 'fractionated' to give enough time to the normal tissues (NT) to recover… as NT recovers better than the tumour ones..

- Actually, already sixty years ago a preliminary indication that, instead, going to very high dose rates could result in a better sparing of normal tissues was already obtained.. But the effect at that time was not considered to be significant enough to trigger dedicated investigations.



Potential for widening the therapeutic window



FRIDA motivations

High dose rate beams represent one of the frontier of the external radiotherapy

Radiations (electrons, protons, X) with dose rates **exceeding the 40 Gy/sec**, show an increase in the NTCP (Normal Tissue Control Probability)-TCP (Tumour Control Probability) curves

The FLASH effect **has been already observed** in many conditions, in-vivo and in-vitro and clinical trials on patients are ongoing

But the FLASH effects **is not still understood** and the dosimetry and monitoring of such beams is a challenge

FRIDA main goals

WP1: FLASH effects understanding

G Forte (CNR-IBFM and LNS), E Scifoni (TIFPA)

Understanding the phenomena at chemical and biological level

WP2: FLASH beam delivery

GAP Cirrone (LNS), A Mostacci (RM1)

Implementing new solution to generate flash beam with conventional and laser-driven approaches

WP3: FLASH beam monitoring and dosimetry

G Bisogni (INFN-PI), A Vignati (INFN-TO)

Developing new approaches for the absolute dosimetry and the monitoring of these new beams

WP4: FLASH Treatment planning

A Schiavi (RM1), M Schwarz (TIFPA)

Implementing solutions for the FLASH-oriented treatment planning

INFN LNS
Istituto Nazionale di Fisica Nucleare
Laboratori Nazionali del Sud

FRIDA participant units and INFN-LNS role

INFN-CT

INFN-Mi

INFN-Pi

Roma1

TIFPA

Torino

INFN-LNS

Contribution on **WP1** for the understanding of the radiobiology models staying at the base of FLASH

Contribution ow **WP2**, for the development of new systems to delivery electron FLASH beams with conventional approaches and proton FLASH beams with laser-driven approaches

Contribution on **WP3** for the development of new, non-invasive techniques for the monitoring of proton FLASH beams

TOTAL FTE: 24.1

FRIDA involved people and funds requests

Requests

273.800 € - Three years

56.000 € personnel

57.000 € travel

160.800 € consumable and equipment

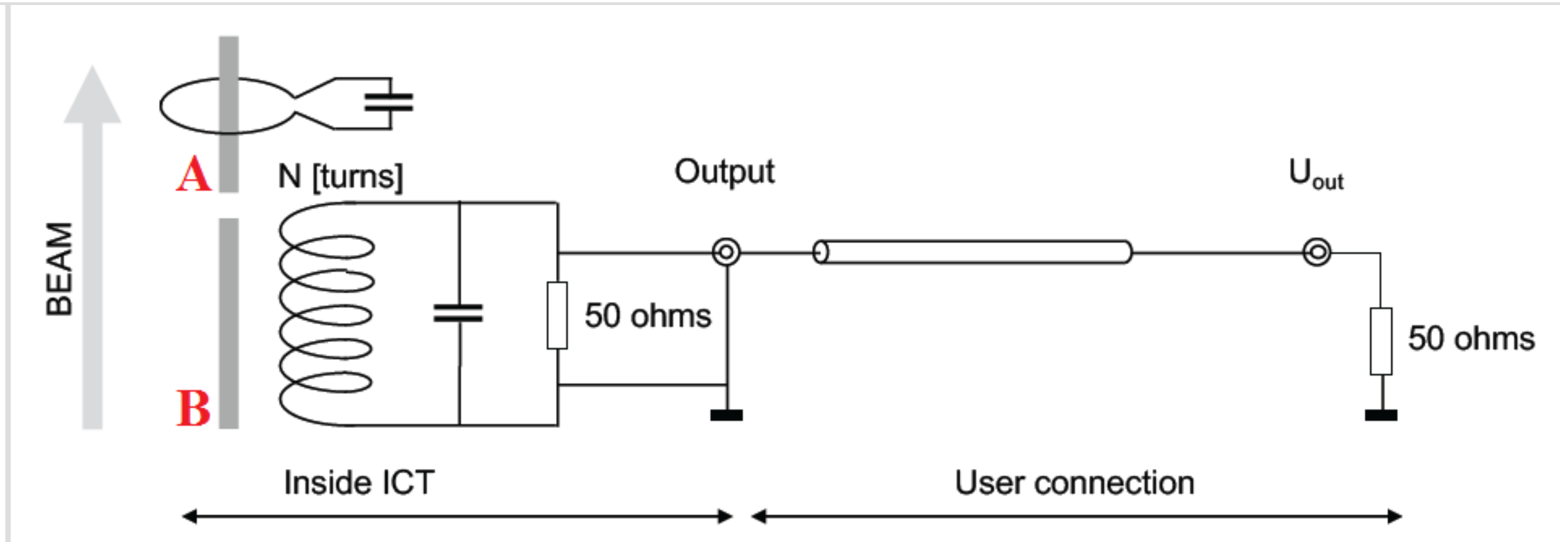
Bravatà	50
Calvaruso	50
Cammarata	10
Catalano	10
Cirrone	20
Cuttone	10
Ficarra	100
Forte	70
Patti	30
Minafra	10
Petringa	10
Russo	50
Torrisi	10

2022 - Funds

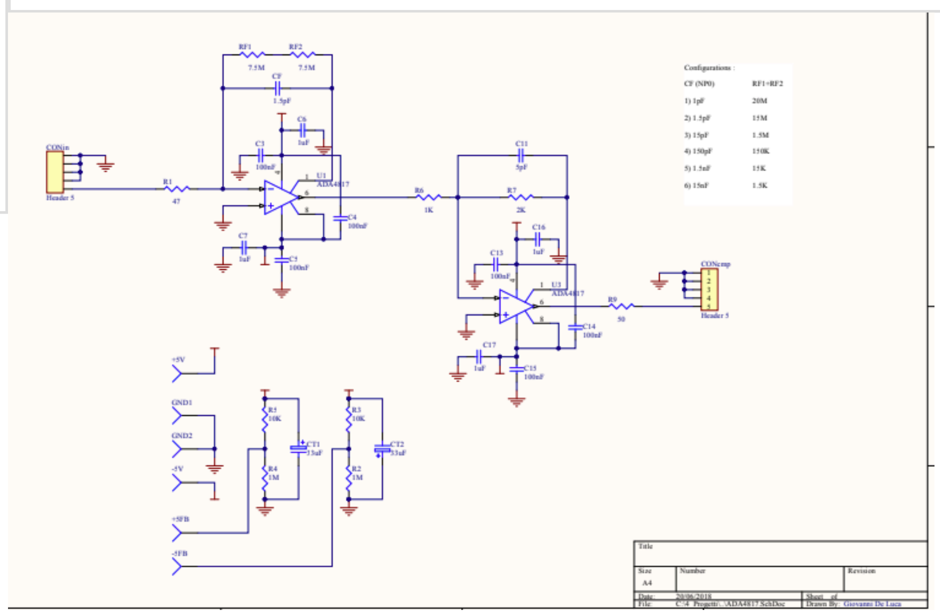
Sigla Loc.	Capitolo	Riunione	Note Alla Richiesta	Rich.	Rich. SJ	Assegn.	Assegn. SJ	Assegn. Dot.	Assegn. Ant.	Assegn. Ant. Dot.	Commento Alla Assegnazione
LNS	MISS	Assegnazioni	Experimental tests at Queens Univ., ELI-Beamlines (CZ) and other facilitiesÂ§	4.0	0.0	3.0					
		Assegnazioni	Experimnetal tests at INO-CNR (Pisa) and ELI- Beamlines (CZ)Â§	2.0	0.0	1.0					
		Assegnazioni	Radiobiology exp. at TifpaÂ§	8.0	0.0	0.0	6.0				SJ alla assegnazione del tempo macchina
		Totale MISS		14.0	0.0	4.0	6.0	0.0	0.0	0.0	
	CON	Assegnazioni	Needs for the experimental set-up preparationÂ§	3.0	0.0	0.0					
		Assegnazioni	Acquisto del 50% dei "coil target". La restante parte sarà acquistata dalla QUB University (Belfast). L'offerta dei coil target è allegata Â§	11.0	0.0	11.0					
		Assegnazioni	Meccanica di accoppiamento tra i coil target e il sistema di focalizzazione quadrupolareÂ§	2.0	0.0	2.0					
		Totale CON		16.0	0.0	13.0	0.0	0.0	0.0	0.0	
	TRA	Assegnazioni	Transport of detectors to Queens Univ (UK) and ELI- Beamlines (CZ)Â§	1.0	0.0	1.0					
		Assegnazioni	Transport of detectors to INO-CNR (Pisa) and ELI- Beamlines (CZ)Â§	2.0	0.0	1.0					
		Totale TRA		3.0	0.0	2.0	0.0	0.0	0.0	0.0	
	INV	Assegnazioni	Integrating Current Transformer Detector for beam monitoring Â§	18.0	0.0	0.0	18.0				SJ alla presentazione di una relazione da discutere coi referee
		Totale INV		18.0	0.0	0.0	18.0	0.0	0.0	0.0	
	SPSERVIZI	Assegnazioni	Assegno di ricerca biennale (quota per il primo anno)Â§	28.5	0.0	0.0					Concordato con il RL lo spostamento dell'assegno junior al 2023
		Totale SPSERVIZI		28.5	0.0	0.0	0.0	0.0	0.0	0.0	
Totale LNS				79.5	0.0	19.0	24.0	0.0	0.0	0.0	
Totale Generale FRIDA				79.5	0.0	19.0	24.0	0.0	0.0	0.0	

WP3 and WP2

=> experimental session @ELI-NP



1fs ≤ Tw ≤ 70 ns
Sensitivity: 5 Vs/C
N. of turns: 5
Electr. noise: 0,55 pC_{rms}



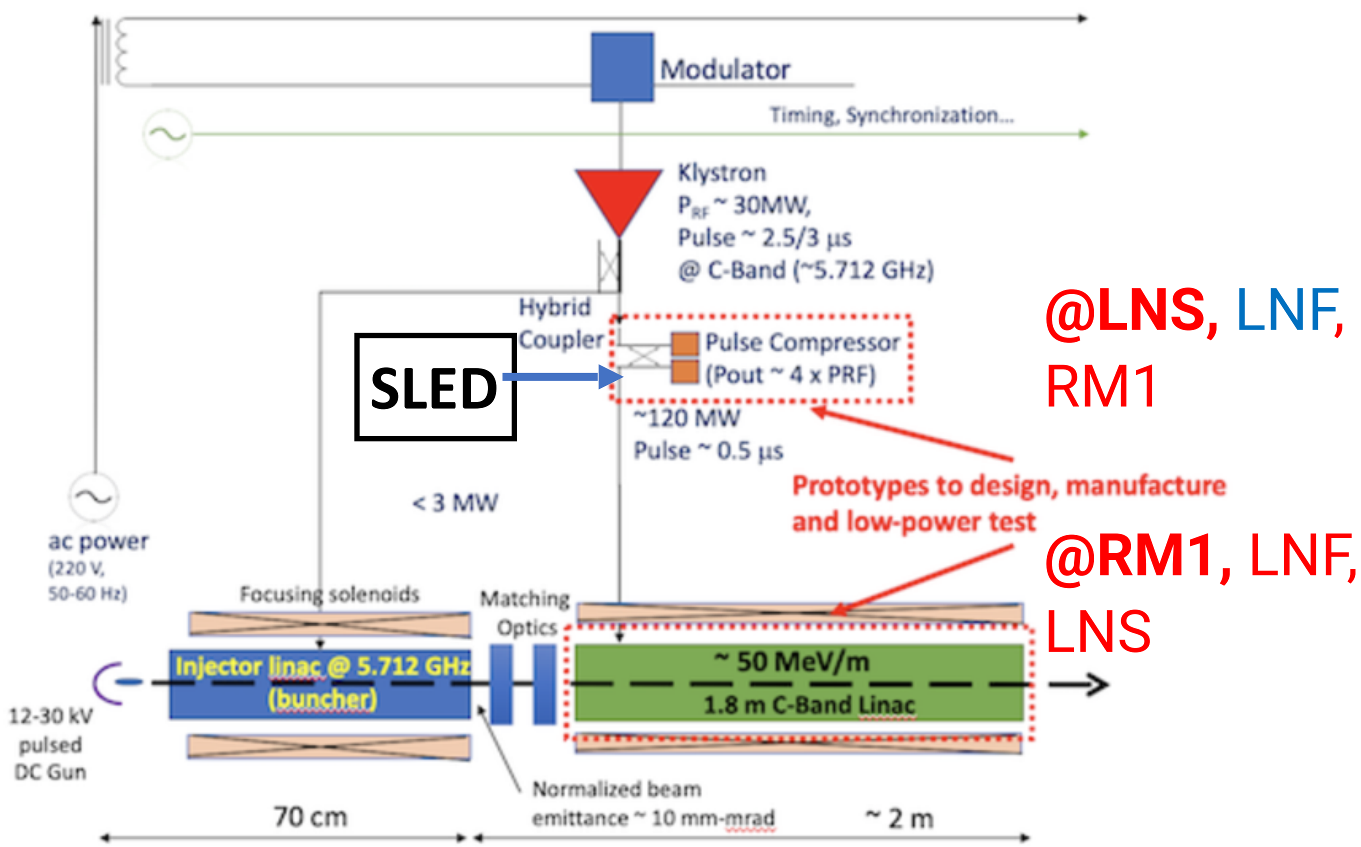
The electronical readout will be realized @LNS-INFN

Fast Charge Amplifier
High Speed Peak Detector

Coil targets will be realized and optimized to perform experimental test with TW class laser @ ELI-NP (short pulses)

WP2: RF accelerator

Very High Energy Electron (VHEE) Linac modular Layout

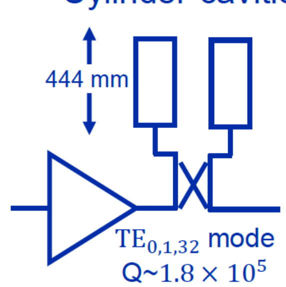


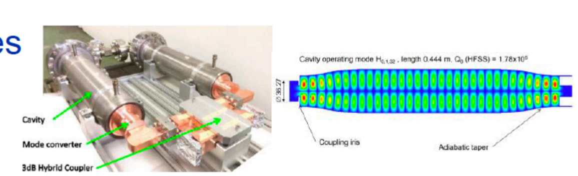
WP2 Milestones and Deliverables

D2.1.2	RF accelerating structure design	Design of the high gradient accelerating structure prototype	18
D2.2.1	RF compr. design	Design of the SLED RF pulse compressor.	18
D2.1.3	RF accel. structure manufacturing	Manufacturing high gradient accelerating prototype	24
D2.2.2	RF compressor manufacturing	Manufacturing of the pulse compressor prototype	24
D2.1.4	RF accelerating structure test	Low power RF tests of accelerating prototype	36
D2.2.3	RF compr. test	Low power RF tests of the SLED prototype	36

SLED-type PULSE COMPRESSOR: selected geometries for comparison

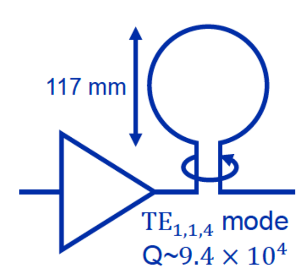
Cylinder cavities

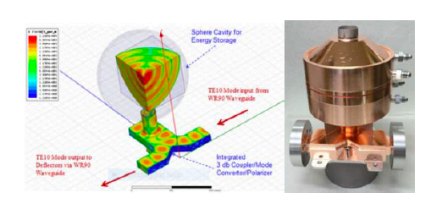




- ✓ Easy fabrication
- ✗ Not compact
  Dipole mode "breakdown"

Spherical cavity



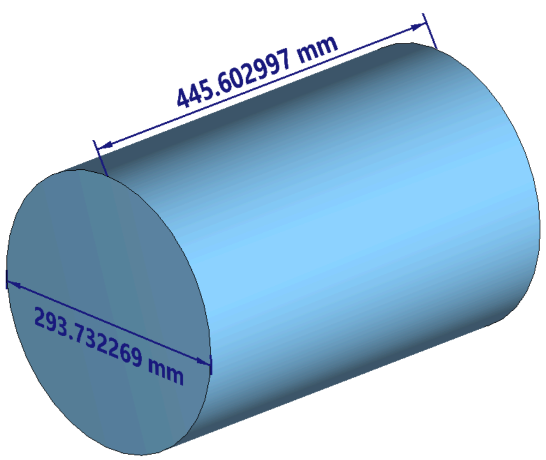


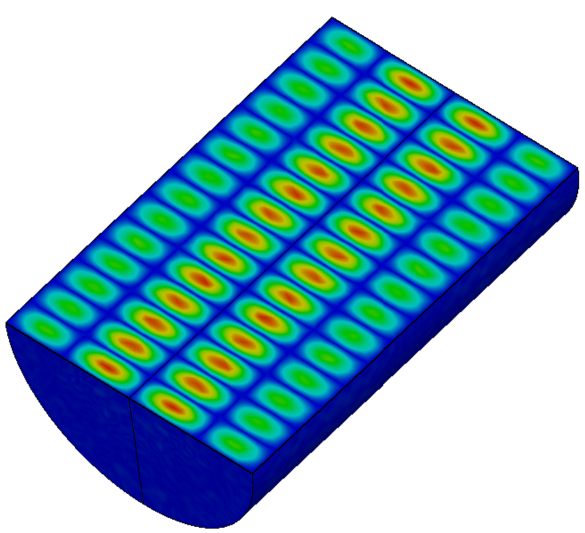
- ✓ Very compact
  Relatively easy fabrication
- ✗ Relatively low Q
  Dense mode spectrum

WP2: RF accelerator

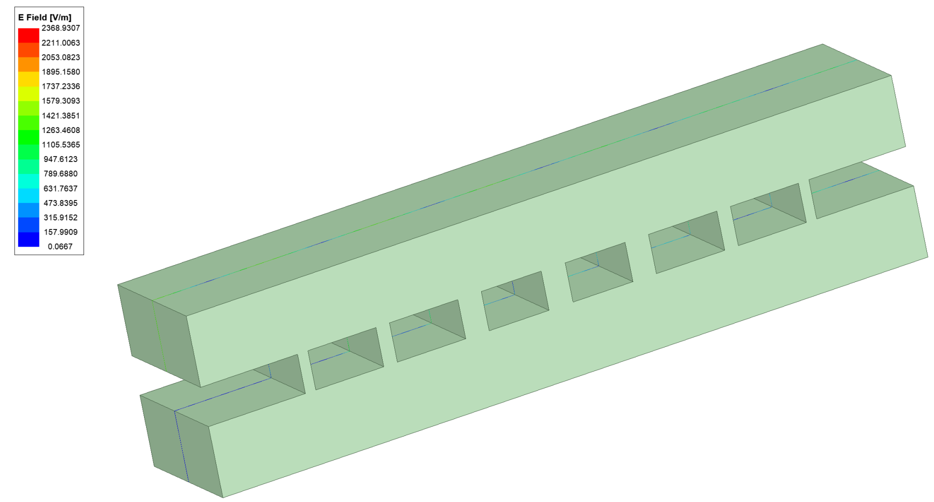
Design step:
1. Storage cavity design

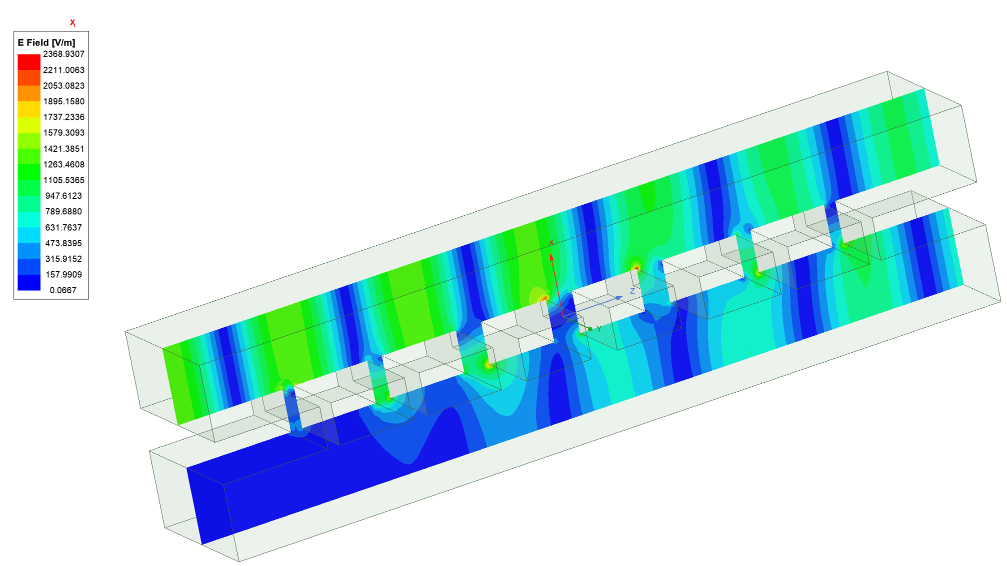
$TE_{0,2,14}$ mode (Q_0 = 2e5, f=5.235 GHz, Beta=2-8)



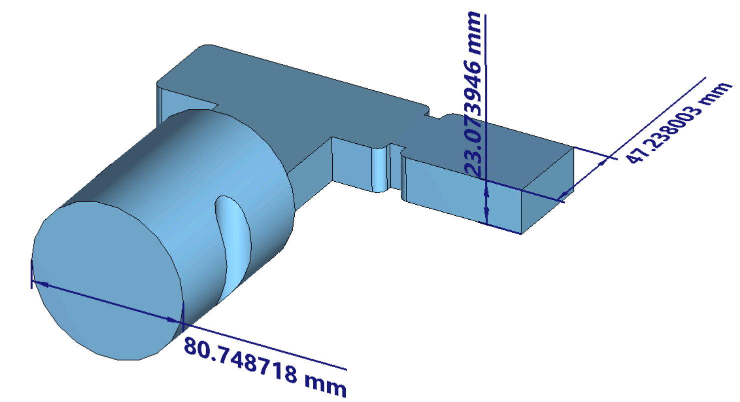


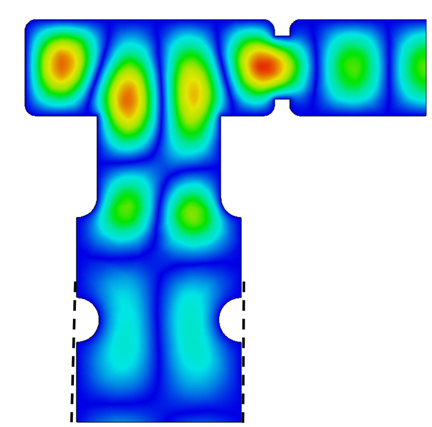
Design step:
2. NOVEL 3 dB hybrid RF design

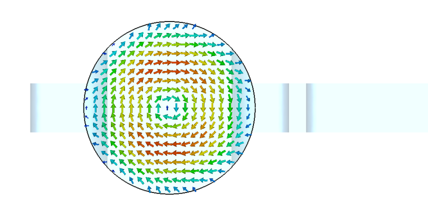




Design step:
3. rect TE_{10} to circ TE_{01} mode converter







Status - 2022

- resonant mode ✅
- Q-factor ✅
- coupling constant of the cavity ✅
- VSWR ✅
- machining accuracy required ongoing
- maximum peak surface ongoing
- coil target realization ongoing
- ICT realizzation ✅

Richieste 2023

FTE 2022 => verranno riconfermati nel 2023

consumo
11k€ coil target
50k€ SLED RF pulse compressor prototype
10k€ SLED compressor for low power test
5k€ radiobiological experiments

missioni
7k€ esperimenti facility lasers
8k€ esperimenti radiobiologia
2k€ meeting a LNF

trasporto
3k€

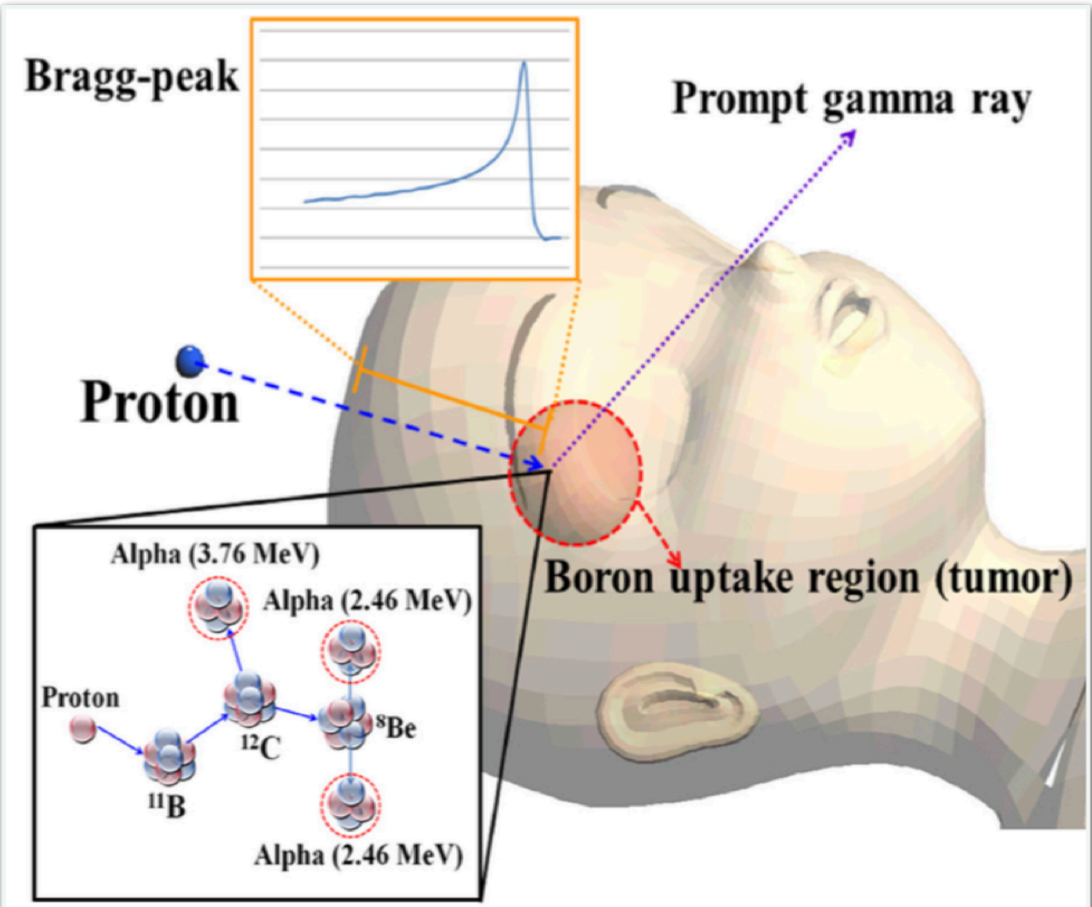
Istituto Nazionale di Fisica Nucleare

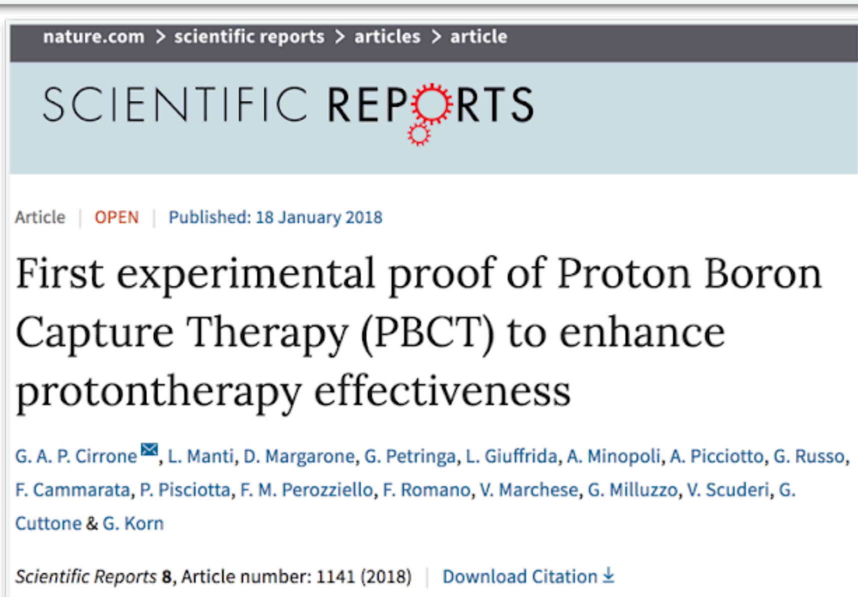
NEPTUNE

Nuclear process driven Enhancement of Proton Therapy Unraveled

National: Dr Giacomo Cuttone
Local: Dr Giacomo Cuttone

NEPTUNE Main Goal




nature.com > scientific reports > articles > article

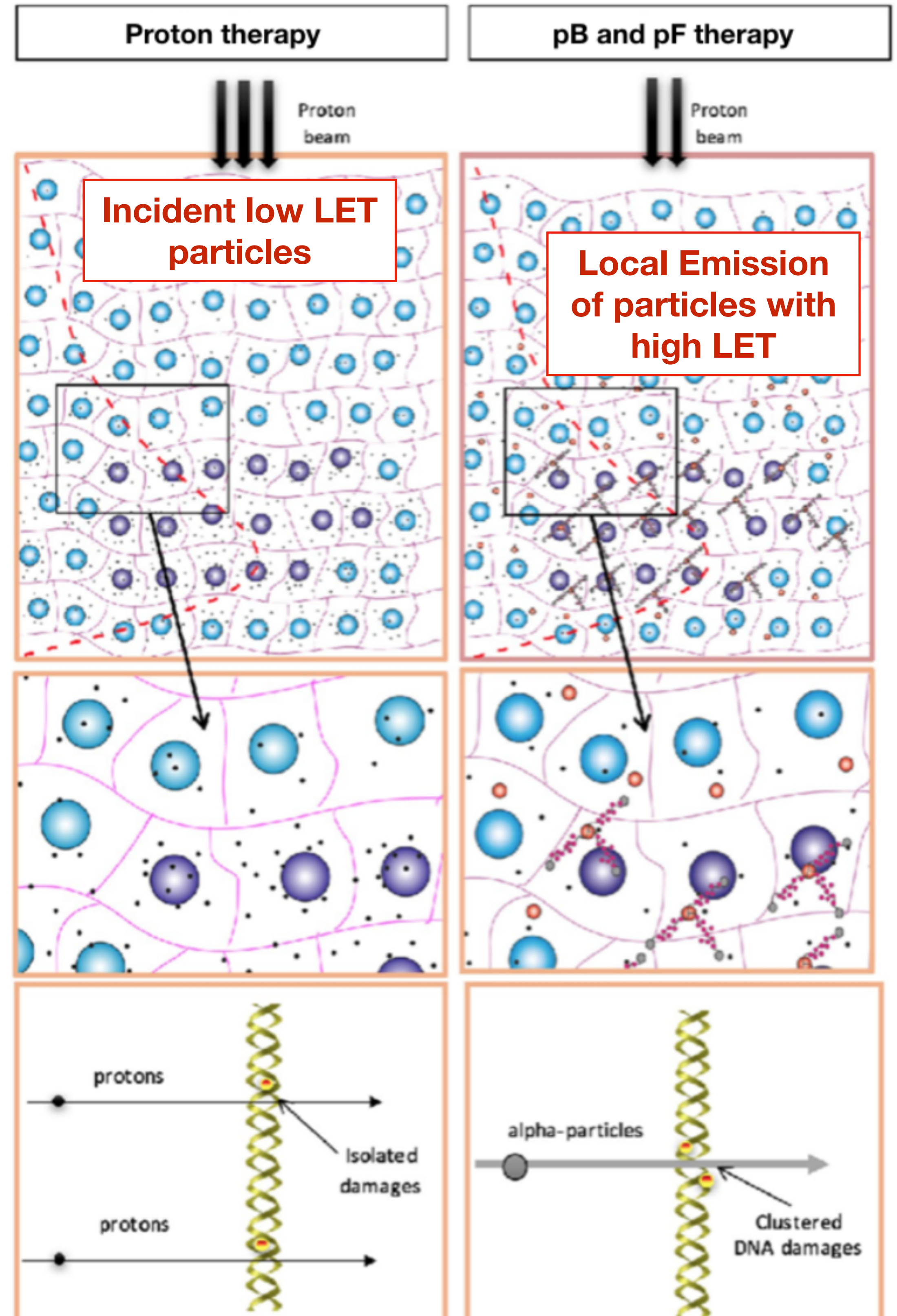
SCIENTIFIC REPORTS

Article | OPEN | Published: 18 January 2018

First experimental proof of Proton Boron Capture Therapy (PBCT) to enhance protontherapy effectiveness

G. A. P. Cirrone, L. Manti, D. Margarone, G. Petringa, L. Giuffrida, A. Minopoli, A. Picciotto, G. Russo, F. Cammarata, P. Pisciotta, F. M. Perozziello, F. Romano, V. Marchese, G. Milluzzo, V. Scuderi, G. Cuttone & G. Korn

Scientific Reports **8**, Article number: 1141 (2018) | Download Citation

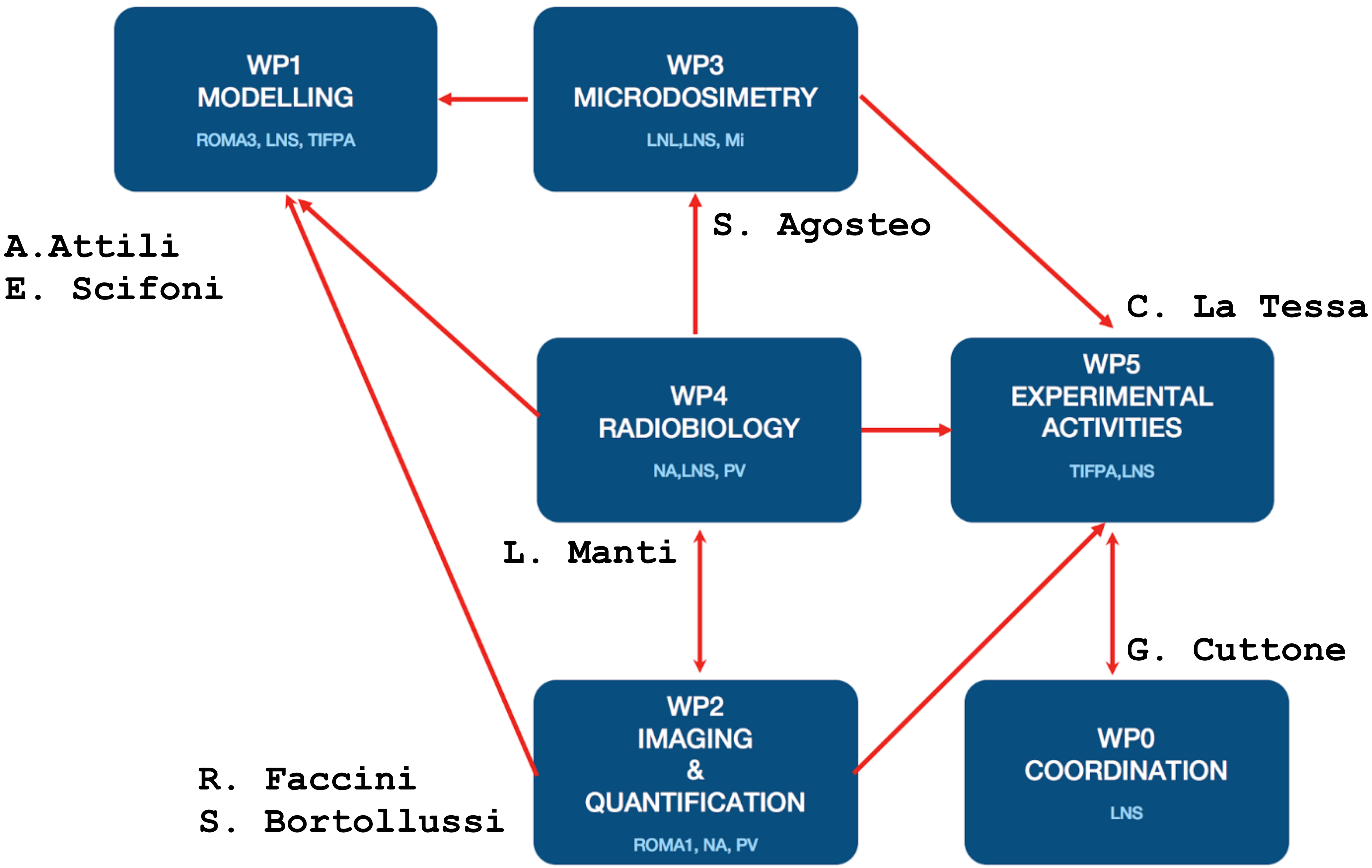


NEPTUNE Structure

Call-Project

Project duration: 3 years (2019-2021)

INFN Participant units: LNS,Roma3, Milano,LNL, Roma1,Pavia,Napoli,TIFPA,



Important Results

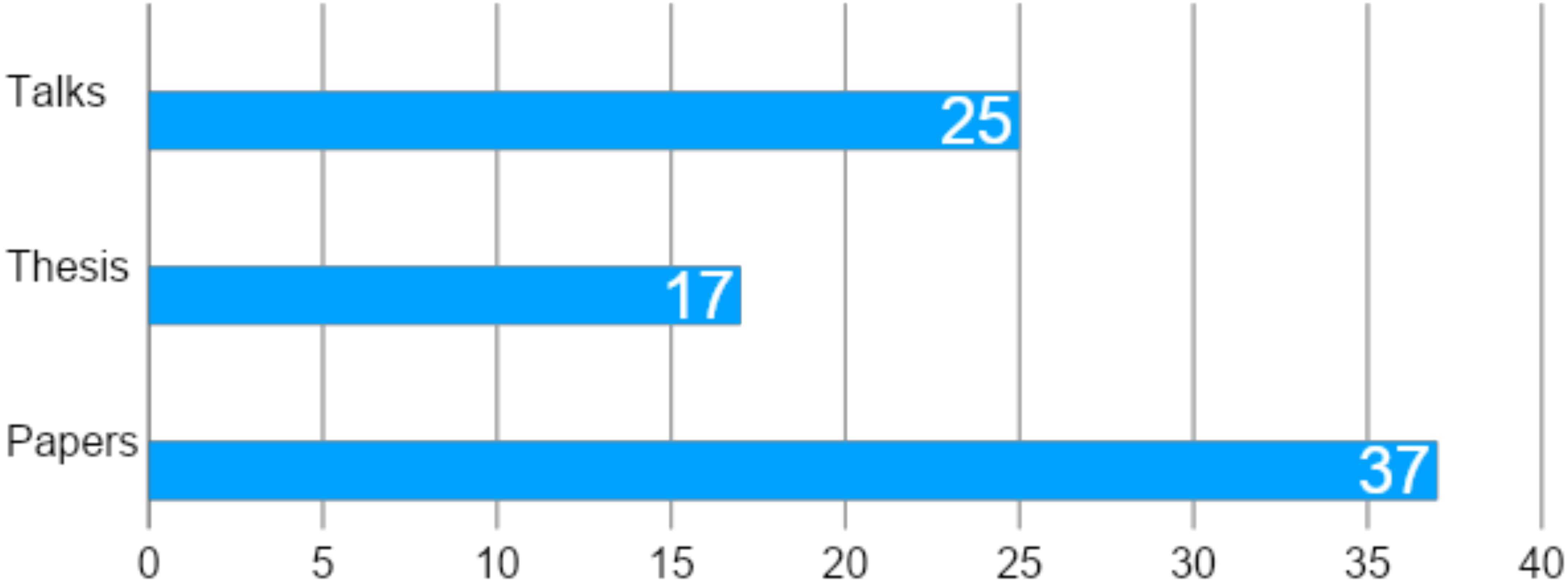
- **Molecula:** BPA was identified as best molecula in terms of toxicity and 11B concentration;

- **Radiobiological experiments:** 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) was studied;

- **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;

Scientific production



MAECI - Grande rivelanza project (2019-2021) melanoma cells
PRIN - PBCT (2020-2023) melanoma cells

pB

Richiesta prolungamento

La richiesta di estensione di un anno è stata dettata dall'esigenza di completare l'attività che era stata prevista per l'anno 2020-2021. A causa della situazione epidemiologica non è stato possibile condurre gli esperimenti radiobiologia e microdosimetria volti a quantificare l'effetto biologico del 19F (WP4 e WP3).

Il 2022 è dedicato alle misure sperimentali con F-BPA e target di 19F. Inoltre, il WP2 si sta dedicando allo studio di tossicità della molecola FDG, un potenziale carrier adottabile per la reazione p-19F.

Infine il WP1 si sta occupando di simulare il danno indotto dalla presenza nelle cellule di atomi di 19F e nel contempo completerà gli studi sui radicali liberi e sulla modellizzazione del bystander effect.

Project Status - Third year

Deadline	Description	%
30/06	WP4 - Cellular and biomolecular studies on the possible enhancement of clinical proton biological effectiveness due to combined proton-boron and proton-fluorine reactions	80%
30/06	WP4 - Pre-clinical relevant effects and elucidation of the radiobiological mechanisms underlying the potential use of proton- boron and/or proton-fluorine nuclear fusion reaction to enhance protontherapy efficacy	?
31/12	WP3 - Measurement of microdosimetric spectra across the proton Bragg peak at TIFPA and CNAO with the 4 microdosimeters with tissue-equivalent (TE) walls/converters unloaded and loaded with natural B, B-11 and F	40%
31/12	WP3 - Development of tissue-equivalent plastics enriched with F	?
31/12	WP0 - Final report	50%
31/12	WP2 - test ex-vivo on mice models with 19F-BPA	?
31/12	WP2 - complete the laboratory tests to assess the improvements achievable with the new antenna and SDR	?
31/12	WP1 - Implementation of MC simulations and full biophysical treatment for p+19F nuclear process generated in the experimental setup	20%
31/12	WP1 - Evaluation of themicro/nanodosimetric spectra and reactive species by means of Geant4-DNA/Trax-Chem	80%