

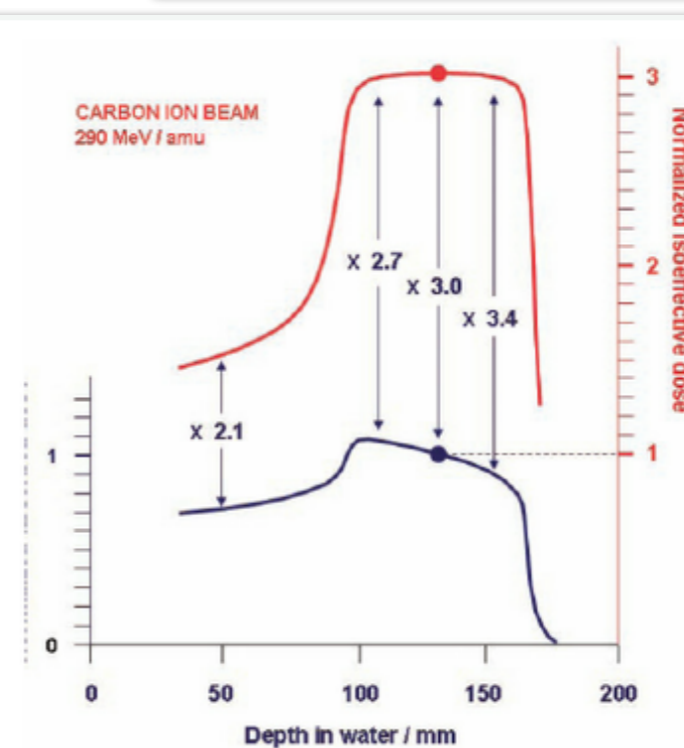
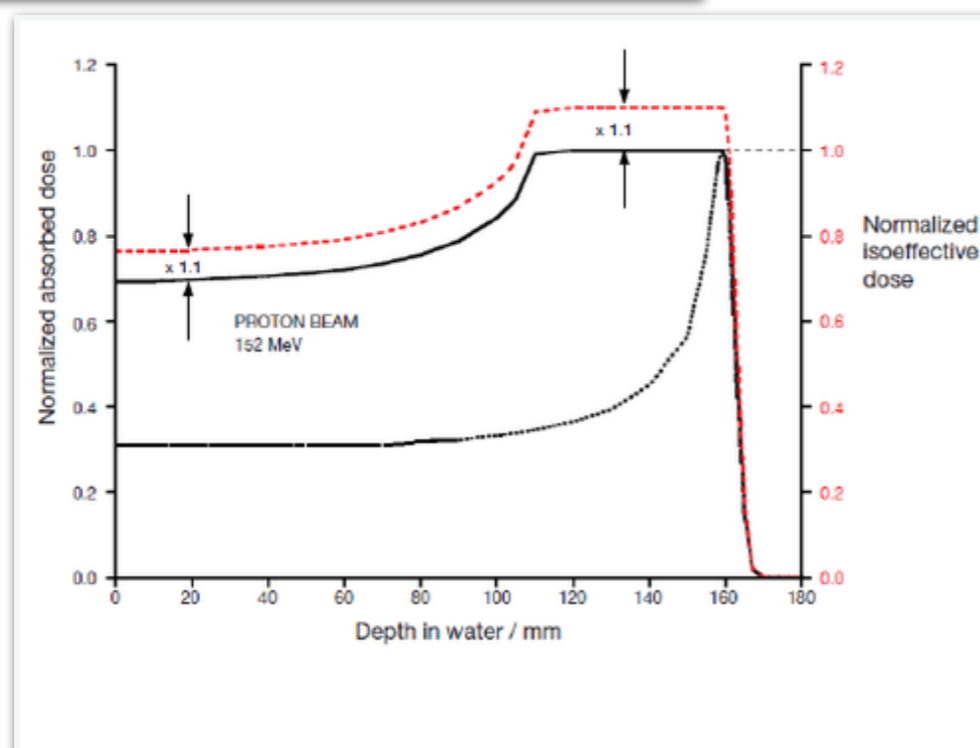
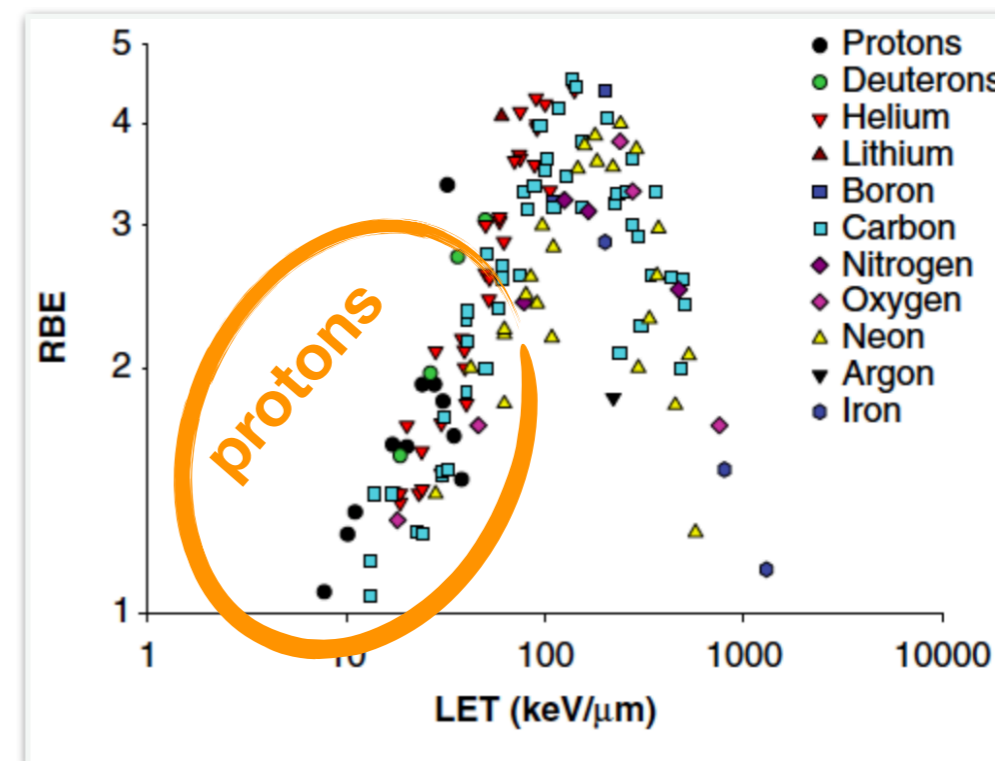
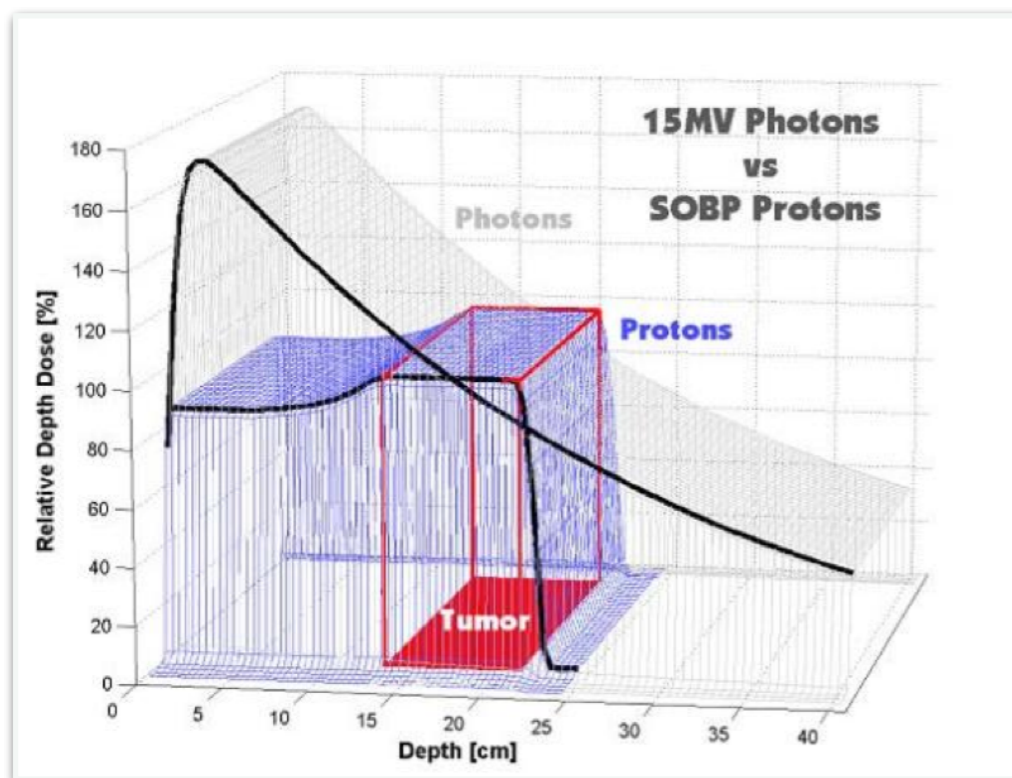


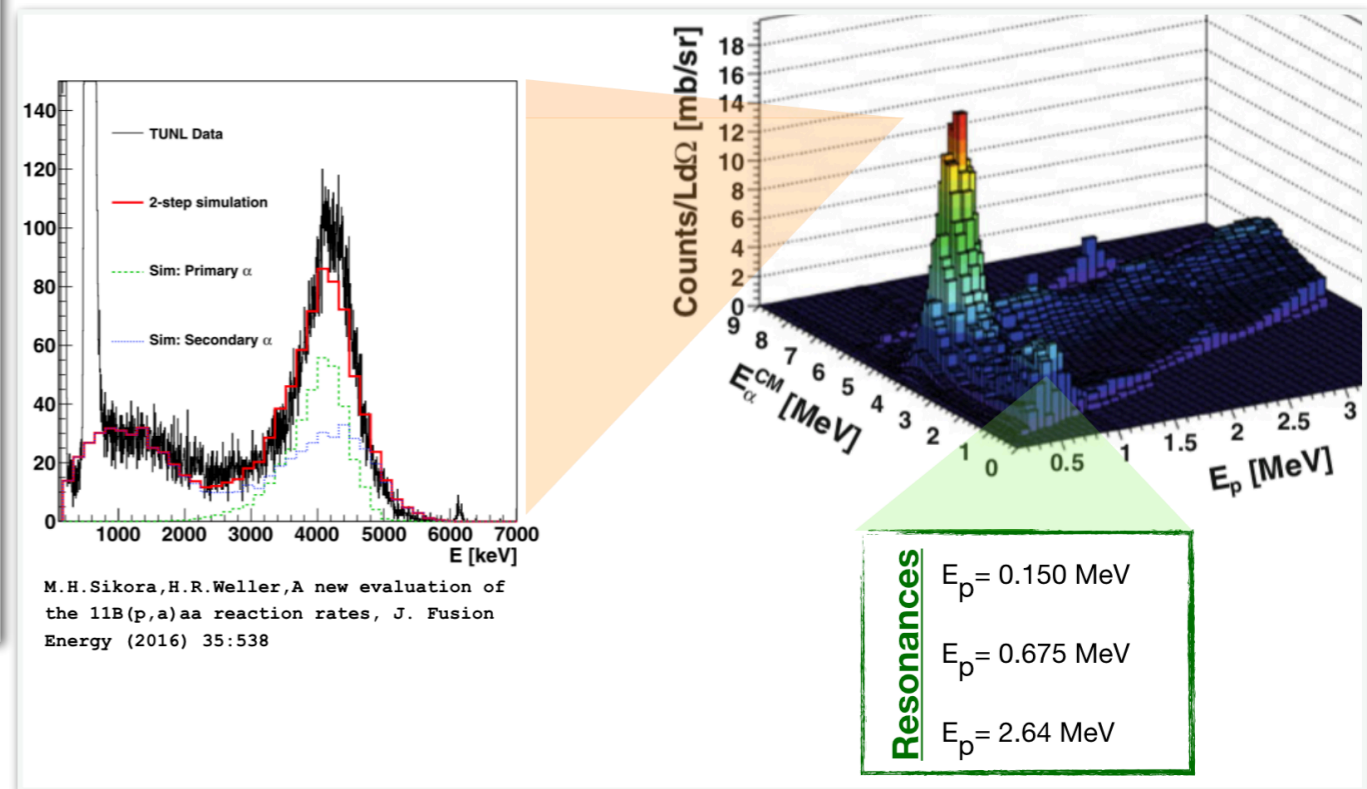
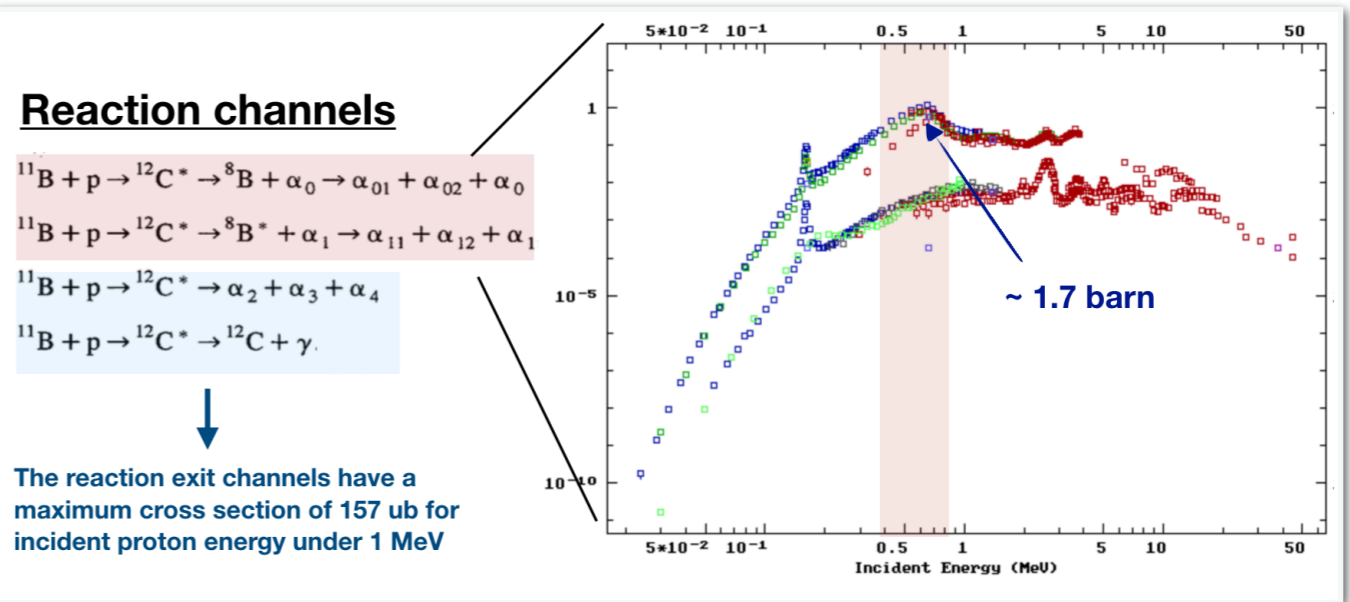
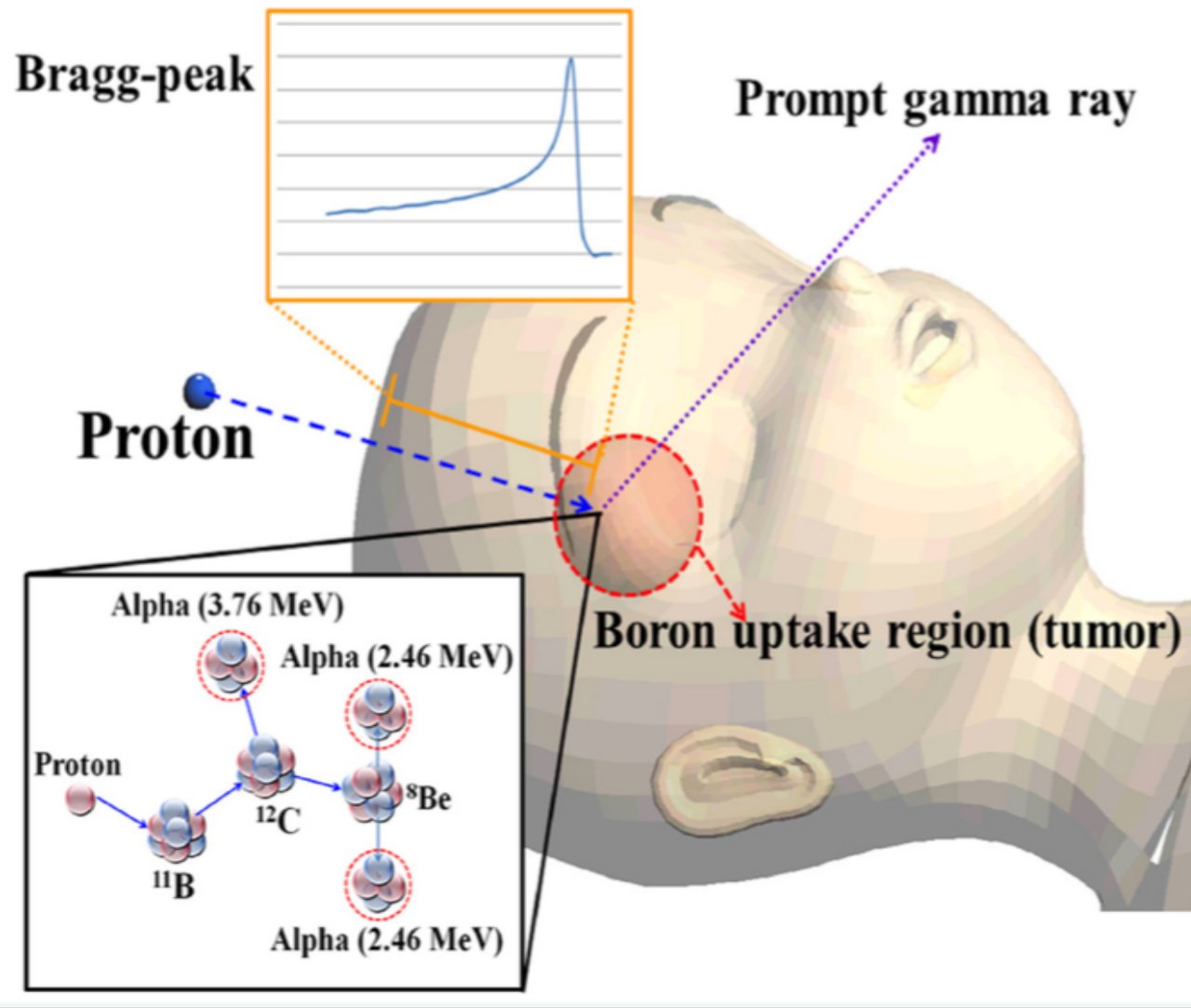
*Responsabile Nazionale: Giacomo Cuttone
Director of LNS*

- **Protontherapy**
- **The idea**
 - ▶ **A proton enhancement technique**
- **A new project**
 - ▶ **NEPTUNE**
 - ▶ **WGs**
 - ▶ **INFN sections and other collaboration**
- **First deliverables**
- **Found request**
- **Beam request @LNS**
 - ▶ **WG3: Microdosimetry**
 - ▶ **WG4: Radiobiology**
- **The official web site**
- **Papers and conference**
- **Discussion with referee**
- **Next meeting**

Protontherapy: status of art

3





A proton enhancement technique

nature.com > scientific reports > articles > article

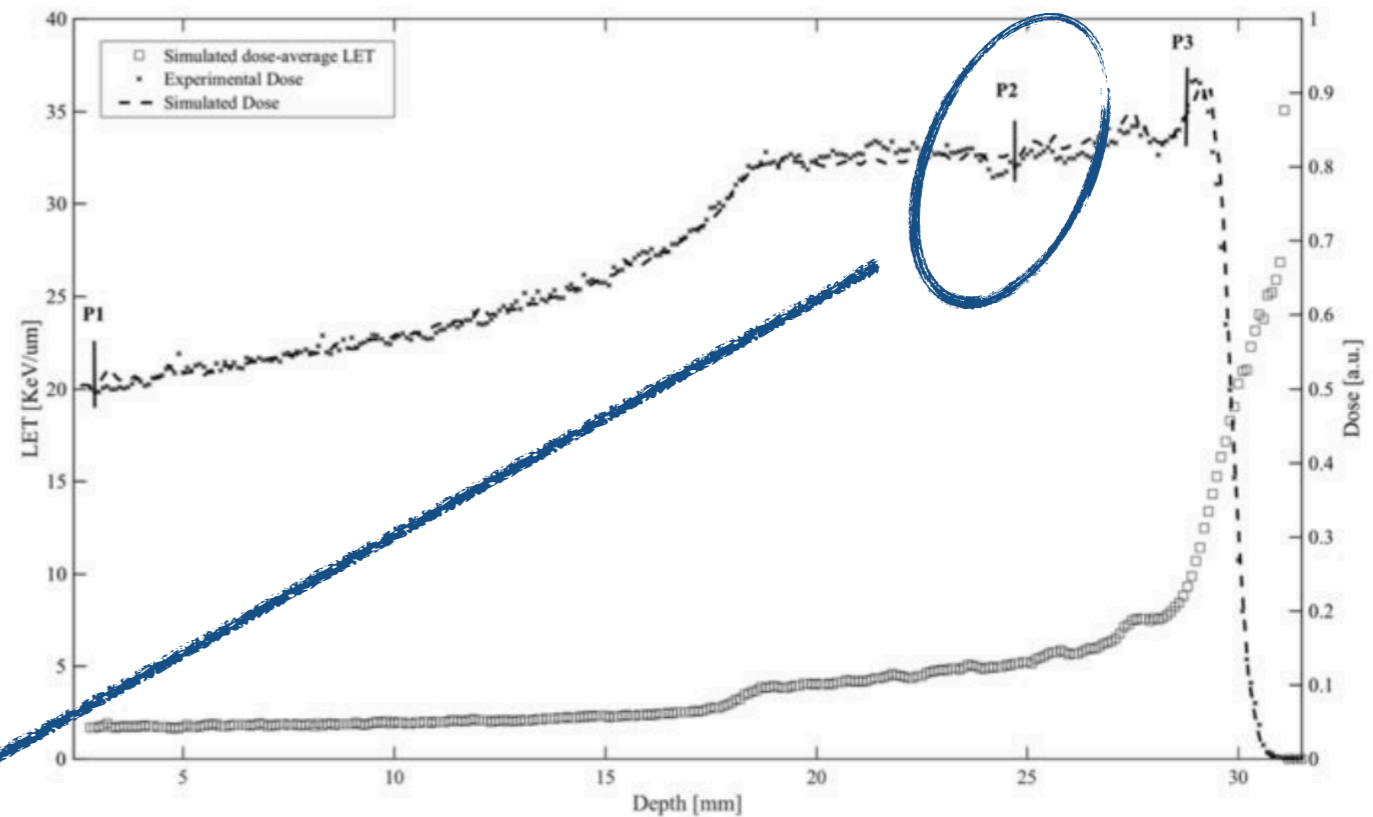
SCIENTIFIC REPORTS

Article | OPEN | Published: 18 January 2018

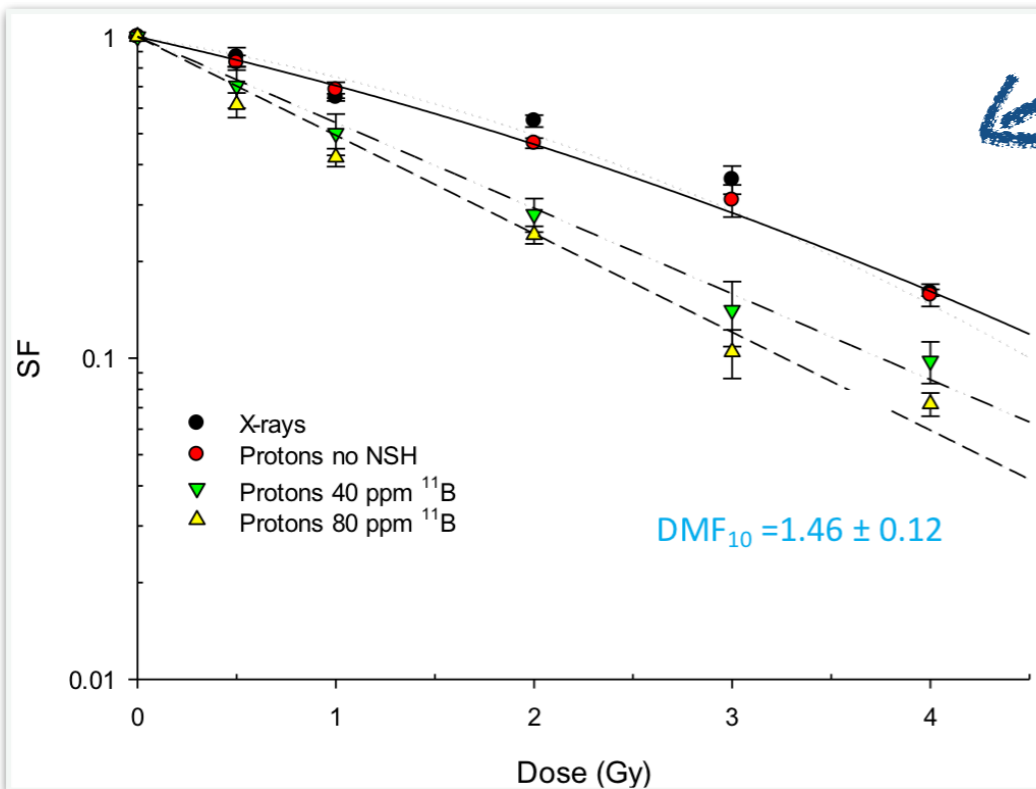
First experimental proof of Proton Boron Capture Therapy (PBCT) to enhance protontherapy effectiveness

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

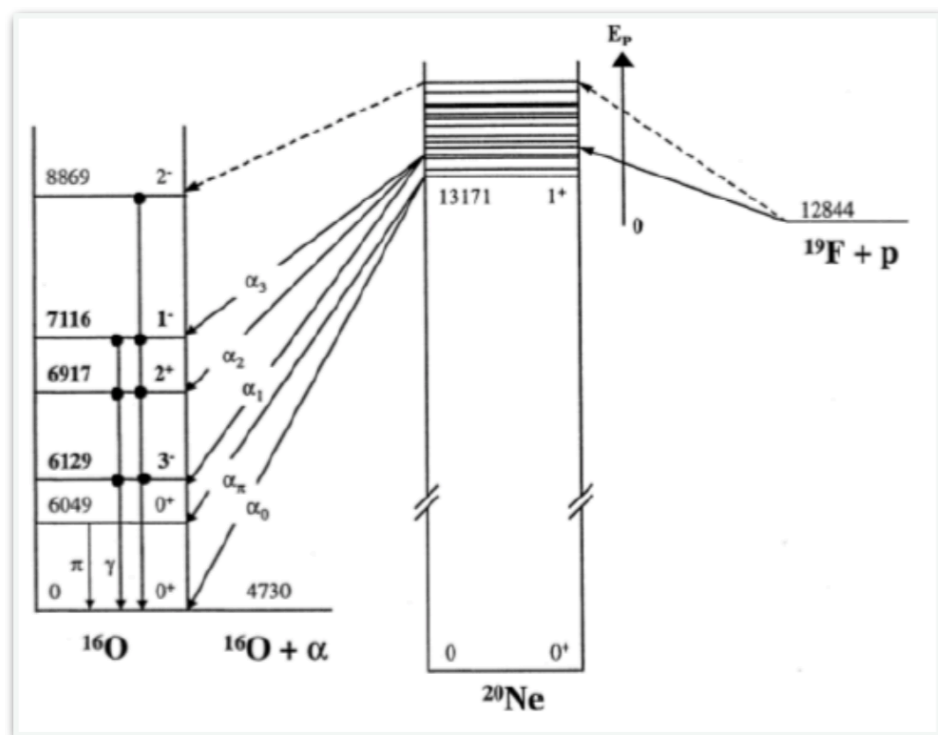


$$DMF_{10} (RBE_{10}) = 1.46 \pm 0.12$$

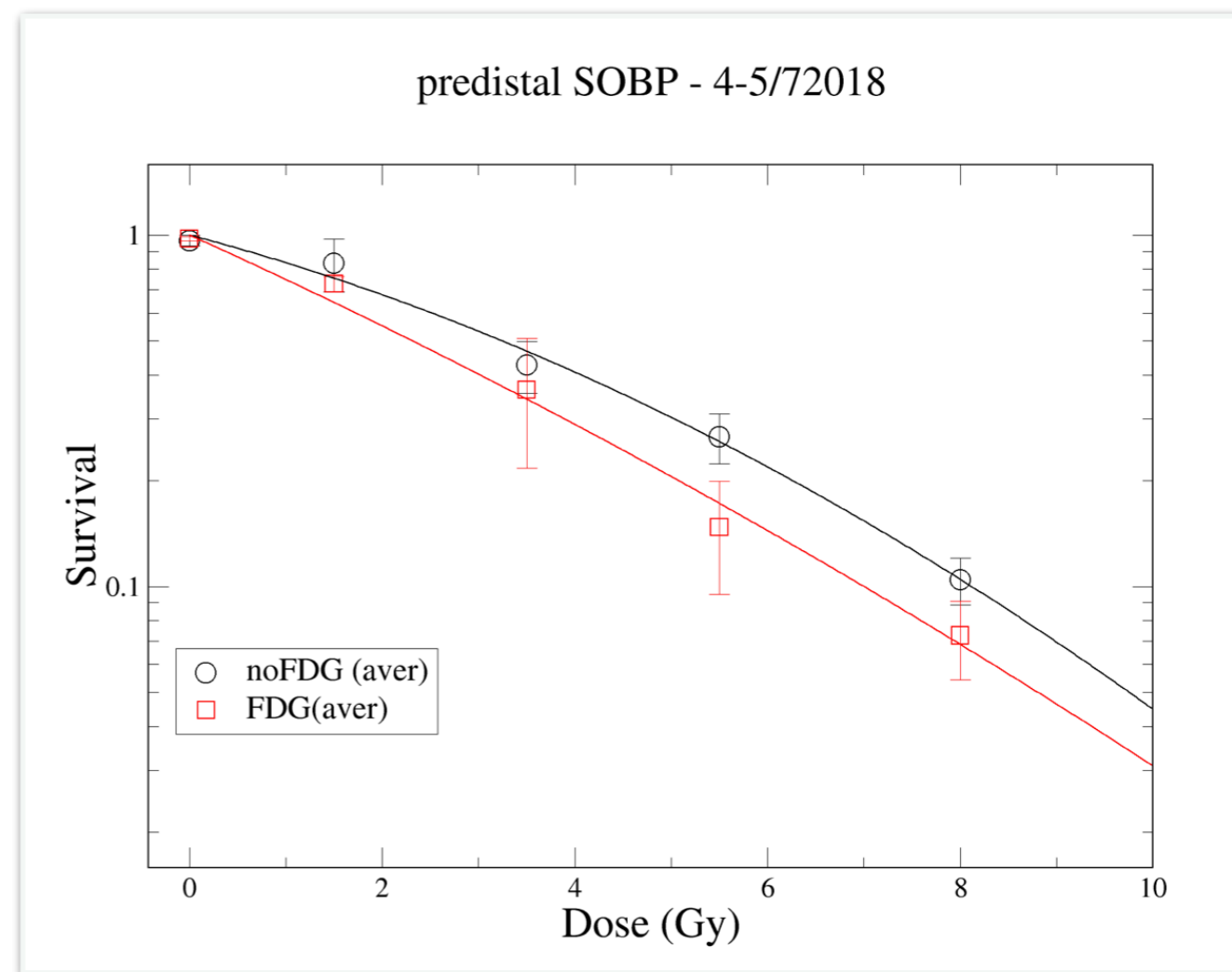


	α (Gy ⁻¹)	β (Gy ⁻²)
X ray irradiation	0.222 ± 0.062	0.064 ± 0.014
Proton irradiation in the absence of BSH	0.314 ± 0.022	0.035 ± 0.007
Proton irradiation with 40 ppm ¹¹ B	0.614 ± 0.069	—
Proton irradiation with 80 ppm ¹¹ B	0.705 ± 0.033	—

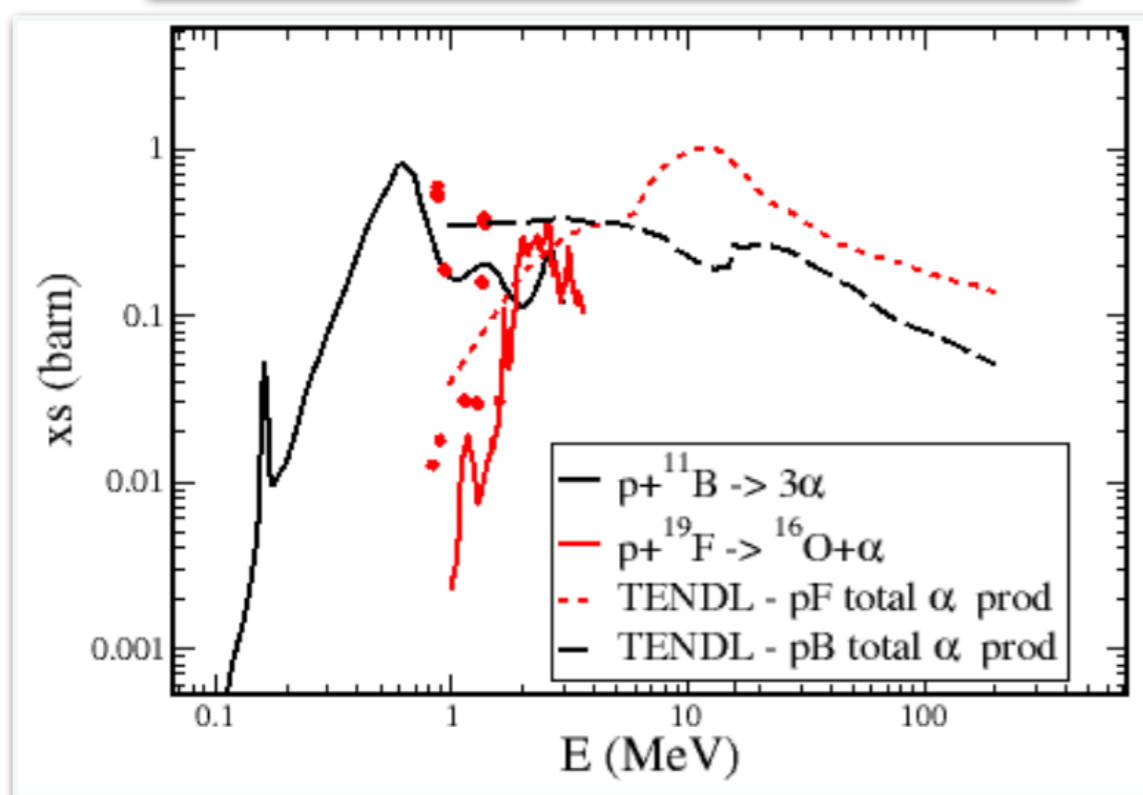
Irradiation @MID-SOBP



p + 19F → 16O + alpha (up to 13 MeV)



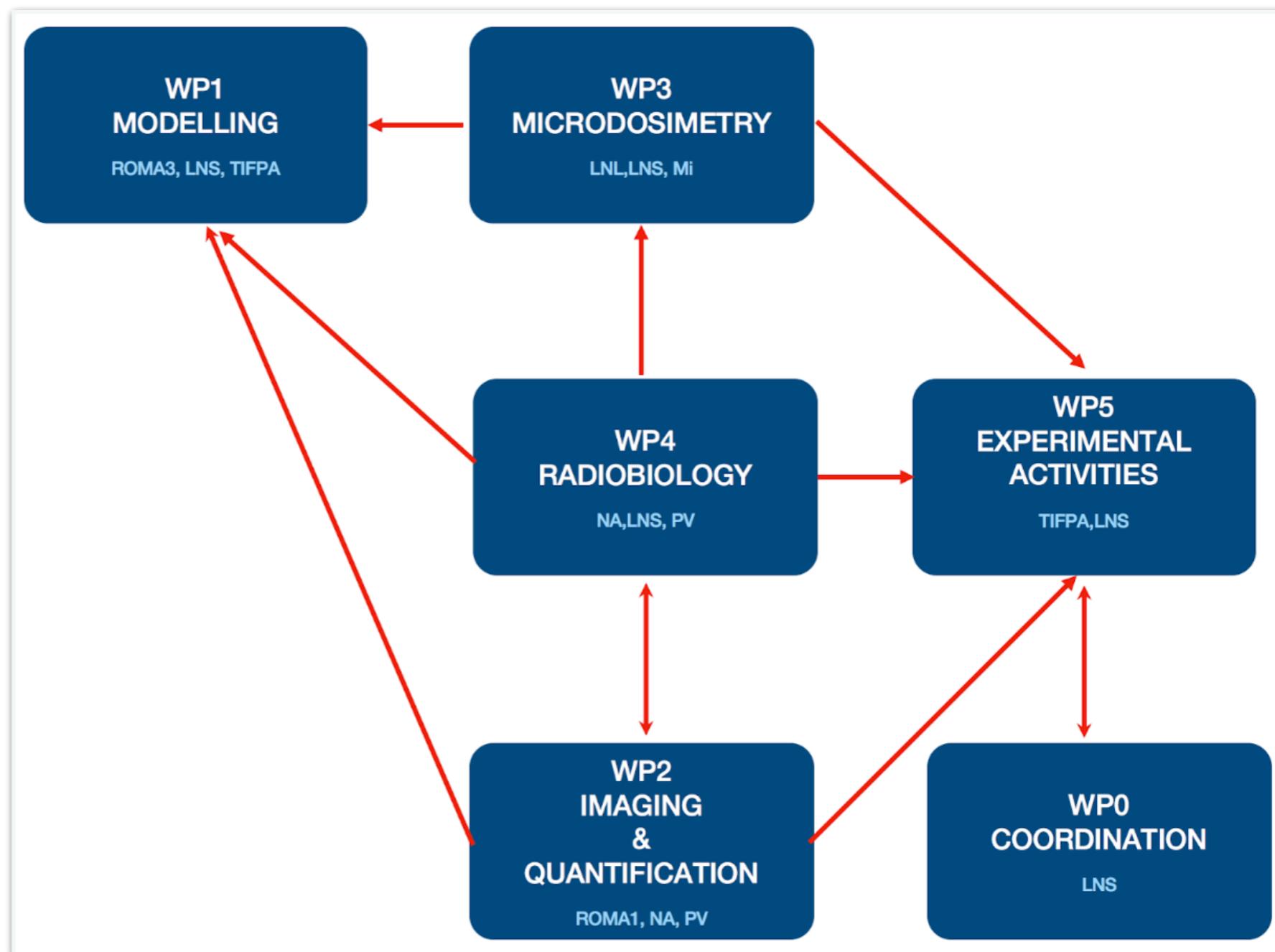
First Experimental results with FDG@ATREP (Trento)





Understanding the effect from different point of views

- ▶ Nuclear
- ▶ Microdosimetric
- ▶ Radiobiological
- ▶ Functional uptake (of ^{11}B or ^{19}F)
- ▶ Modelling



INFN Sections

- ▶ INFN-LNS (WP0 - WP1- WP3 - WP5)
- ▶ INFN-NA (WP4 - WP2 (Caserta))
- ▶ INFN-MI (WP3)
- ▶ INFN-RM3 (WP3)
- ▶ INFN-RM1 (WP2)
- ▶ INFN-PV (WP2)
- ▶ INFN-TIFPA (WP1- WP5)
- ▶ INFN-LNL (WP3)

FTE: 18.35

External Collaborations



Istituto Superiore di Sanità



		Month	Description
WP1	D1.1	1-6	Implementatiton of MC simulations (Geant4) for p+11B and p+19F nuclear reaction spectra generated in the experimental setup
WP2	D2.1	1-16	Establish of a procedure for the measurement of the concentration of borated and fluorinated compound in-vitro tests
WP3	D3.1	12	Microdosimetric spectra from the measurement at LNS with the already available detectors (for WP1 and WP4)
WP4	D4.1	6	Corroboration of proton biological enhancement by p-B on previously tested cell systems (MCF-10 and DU145 cells)
WP5	D5.1	6	Report on experimental criteria to be followed

Critical points?

Found Request



primo anno

	ITEM	I anno	GROUP	WP
Personale	2 years of grant on radiobiological modeling and experimental activity	0,00 €	LNS	1 and 5
	2 years of grant	0,00 €	RM1 + PV	2
	2 years of grant on experimental microdosimetry	0,00 €	LNL	3
	2 years of grant for dedicated personnel	28.500,00 €	NA	4

secondo e terzo anno

	ITEM	II anno	III anno	GROUP	WP
Personale	2 years of grant on radiobiological modeling and experimental activity	€28.500,00	€28.500,00	LNS	1 and 5
	2 years of grant	€28.500,00	€28.500,00	RM1 + PV	2
	2 years of grant on experimental microdosimetry	€28.500,00	€28.500,00	LNL	3

Found Request

II

ITEM		I anno	GROUP	WP
Inventariabile	Multicore	4.000,00 €	RM3	1
	Software Define Radio (SDR)	15.000,00 €	RM1	2
	Criogenerator for MRI electronics	0,00 €	RM1	2
	PC for data acquisition and analysis	2.000,00 €	RM1	2
	moderno HPLC per analisi metabolomiche	48.356,69 €	NA	2
	CAEN HV 4 channels (see offer)	6.000,00 €	MI	3
	2 ORTEC Amplifiers (see offer)	11.500,00 €	MI	3
	Microdosimetry detectors for alpha particles measurements FROM UOW (see offer)	30.000,00 €	LNS	3
	Stand replacement for motorized fluorescence microscope dedicated to automated search of metaphases and micronuclei	10.000,00 €	NA	4
	Ionization chamber for dosimetry for x ray irradiation with radiogen tube of cell cultures as low LET reference	5.500,00 €	NA	4
	PhMeter and thermocouple to be used for reagents in cytogenetic assay procedures	1.000,00 €	NA	4
	Consumabile	Tracers for imaging	4.000,00 €	RM1
Material for antenna development		4.000,00 €	RM1	2
FPGA with PCIe interface fo optimal imaging		0,00 €	RM1	2
Solventi ed altri consumabili per HPLC e LC/MS		4.500,00 €	NA	2
Materiali consumabili per colture cellulari		3.000,00 €	PV	2
Materiali consumabili per autoradiografia neutronica (CR39, reagenti)		1.500,00 €	PV	2
consumables for tests on 40 NOD/SCID mice (animals+plastic+reagent+caratteriz. cellulare)		10.000,00 €	RM1	2
Development and construction of PCBs for low-noise front-end electronics for new configurations of silicon microdosimeters		10.000,00 €	MI	3
Construction of a new preamplifier (low-noise and wide dynamics) for the the multi-shell borated TEPC		0,00 €	MI	3
Boron foil (see offer)		710,00 €	MI	3
TE gas (see offer)		3.000,00 €	MI	3
Borated plastic (see offer)		10.000,00 €	LNL	3
Development and construction of PCBs for SiCs mounting		4.000,00 €	LNS	3
Front-end electronics for SiC microdosimeters		4.000,00 €	LNS	3
Fluorated plastic		3.000,00 €	LNL	3
TE gas (see offer)		12.000,00 €	LNL	3
Laboratory consumables for cell culture, antibodies, kits for DNA damage and ROS quantification		14.000,00 €	LNS	4
Laboratory consumables for cell culture, apoptosis (caspase) quantification,		18.000,00 €	NA (Caserta)	4
Laboratory consumables, purchase of cell lines, cell culture media, reagents for DNA damage and senescence, boron carrier		10.000,00 €	NA	4
Chromosome painting probes, reagents for chromosome (calyculin A) and micronuclei (Cytochalasin B)		3.000,00 €	NA	4
Liquid nitrogen and CO2 for cell cryopreservation & incubator for cell culture, mylar for low-energy proton irradiation		4.000,00 €	NA	4
Laboratory consumables for cell cultures		500,00 €	PV	4
Laboratory consumables for neutron autoradiography		8.000,00 €	PV	4
Beam Time	10.000,00 €	TIFPA	5	
Apparati	Dedicated support structures for experiments	10.000,00 €	TIFPA	6

=> WP3

Beam-time requested

8 BTUs (2 runs of 4 BTUs each) are requested for the described measurements
(≈ 2 BTUs for each detector)

1st run

- Accelerator: Cyclotron
- Beam: **protons**
- Energy: 62 MeV
- Beamline: CATANA
- Beam time requested: **4 BTUs**
- Desired period: June and 1-15 July 2019
- Excluded periods: from January to May 2019

2nd run

- Accelerator: Cyclotron
- Beam: **protons**
- Energy: 62 MeV
- Beamline: CATANA
- Beam time requested: **4 BTUs**
- Desired period: 1-15 Sept. and December 2019
- Excluded periods: from Oct. to November 2019

=> WP4

END POINTS

- 1) Cell death in pancreatic radioresistant cancer cells and in fibroblasts as normal cell reference will be evaluated by clonogenic assay.
- 2) Cytogenetic damage in form of chromosome aberrations (CA) and micronuclei (MN) will be tested and quantified by immunofluorescence analysis.
- 3) Characterization of High-LET signature by identification of clustered lesions (CL), made of double strand breaks (DSB) and non-DSB lesions, will be studied by specific DNA repair pathways (ATR-activated Homologous Recombination (HR) by ATM/ATR kinase ratio; measurement of initial and residual CLs by the gamma-H2AX/53BP1 assay).
- 4) Estimation of Radical Oxygen Species (ROS) generation will be performed by means of immunofluorescence through the assessment of the redox state of irradiated cells at different time points, immediately after proton irradiation.
- 5) Premature senescence which is linked with the occurrence of CLs, will be quantified by beta-galactosidase assay.
- 6) Bystander effects, i.e. non-DNA effects, will be tested by using the ^{11}B - and ^{19}F -free medium from irradiated cells transferred onto unirradiated cells, and then assayed for clonogenic death and DNA damage.

=> WP4

AIMS

- 1) To corroborate the proton biological enhancement by p-B in previously tested cell line systems (breast and prostate cancer cell lines).
- 2) To extend such findings to novel biological systems of relevance for protontherapy such as pancreatic and lung cancers and to test fluorinated compounds in order to exploit a similar binary approach based on the $p+^{19}\text{F}$ (p-F) reaction.
- 3) To provide radiobiological insights into the mechanisms underlying the observed enhancement of proton efficiency at damaging cellular DNA by p-B and p-F reactions.

Beam type	Beam time (BTU)	Measurements
Proton 62 MeV	8	Radiobiology (cell death, cytogenetic damage, ROS production, DNA repair pathways, bystander effects)

Beam time request

15

▶ Other facilities?

CNAO...?

TIFPA...?

▶ and when?

The official web site



- ▶ Which platform? google - joomla - simple PHP, other...
- ▶ Deadline?
- ▶ A contribute for each WP
- ▶ Two sections: public and private

- ▶ Mailing list for information sharing

PTCOG <https://ptcog58.org>

MCMA <http://iccr-mcma.org>

.....

- ▶ don't forget! => Acknowledge the NEPTUNE project

IEEE Transaction on Radiation and Plasmas

IMPORTANT DATES!

- **July 2019:** sottomissione preventivi
==> prima discussione con i referee
da fare max entro in primi 10 gg di
giugno
- **September 2019:** audizione in
commissione



Next meetings

- Every six months: upgrade (via Skype)
- Annually: collaboration meeting

meeting minutes always online on the official website!