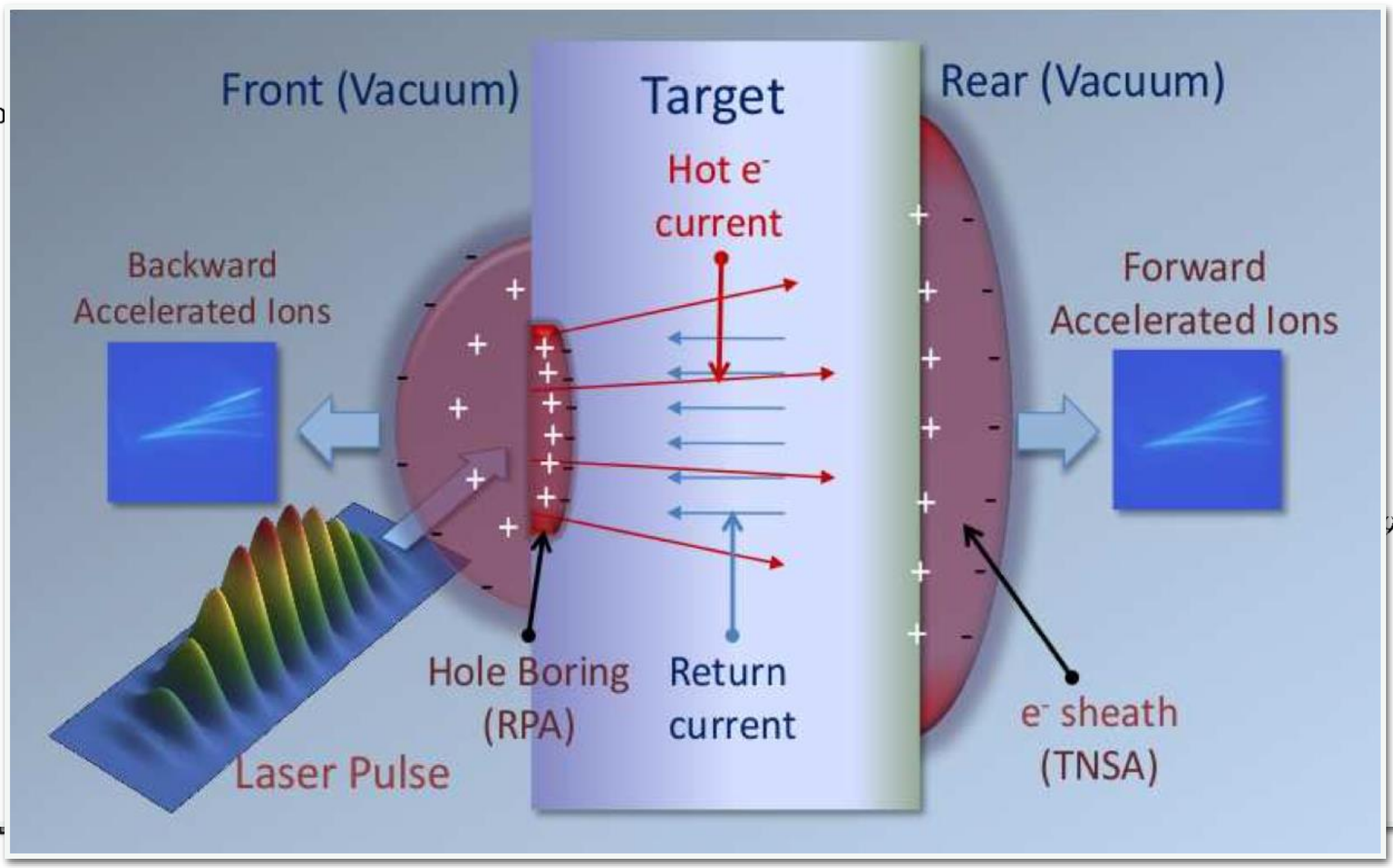
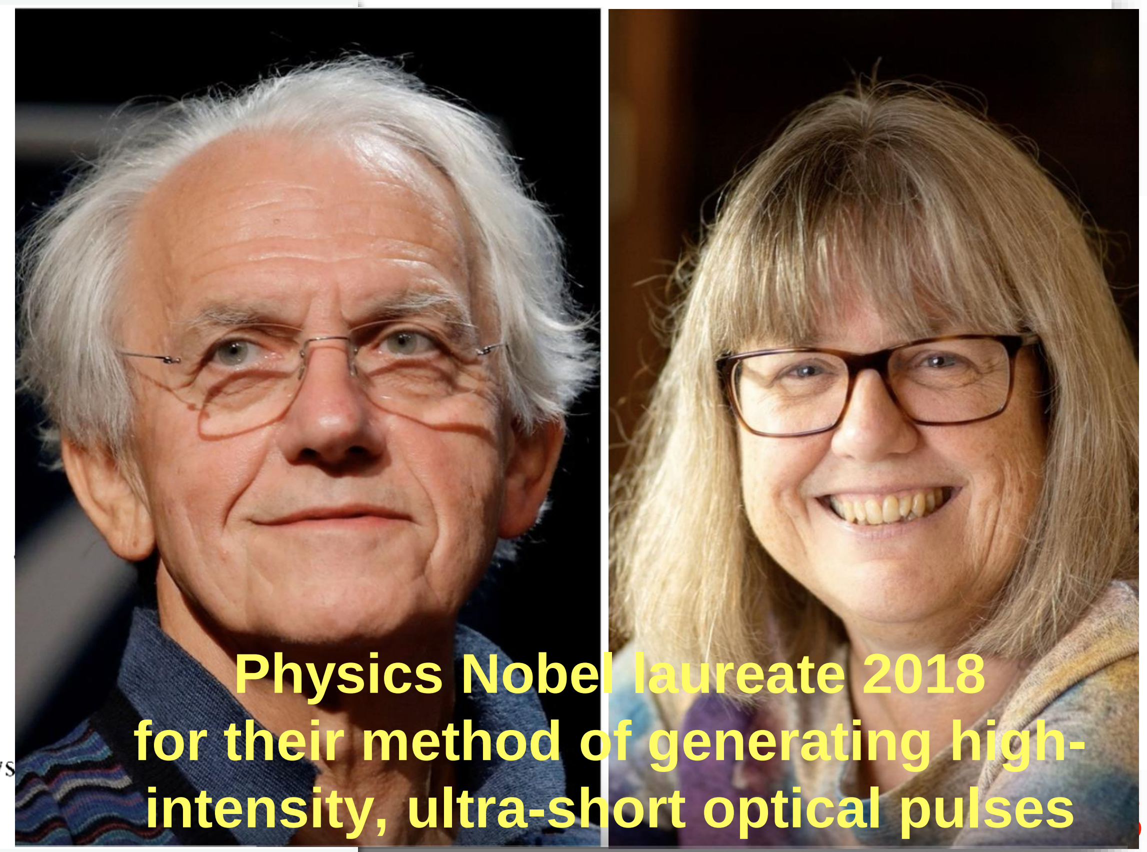
Hadrontherapy at LNS from the conventional approach to the frontiers of the biological enhancement and laser-driven applications

GAP Cirrone,
INFN-LNS , Italy
and
ELI-Beamlines project, Czech Republic

Hadrontherapy at LNS from the conventional approach to the frontier of biological enhancement and laser-driven applications

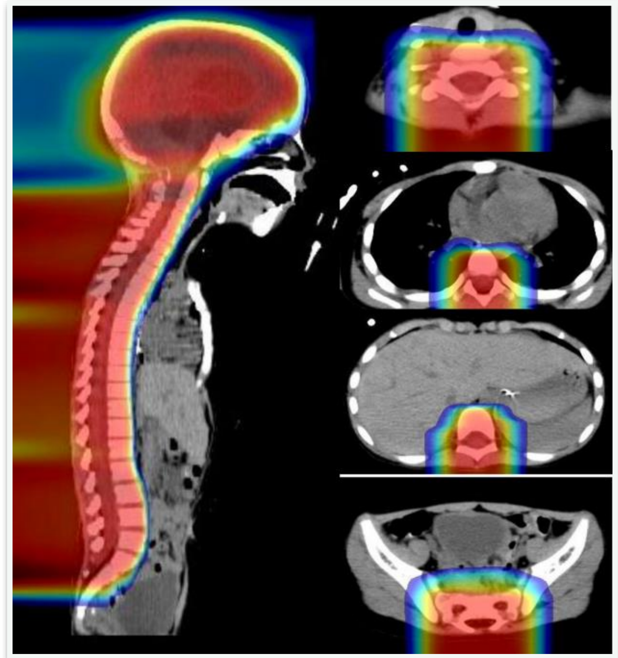




Conventional hadrontherapy

Clinical advantages of proton beams

x-Ray therapy



Protontherapy

Mirabell RA et al.
Potential reduction of the incidence of radiation-induced second cancers by using proton beams in the treatment of paediatric tumor,
Int. Jour. Rad. Onc. Phys. 2002, 54 (3) 824

Pediatric Medulloblastoma: The yearly risk of getting a secondary tumor was estimated to be 8 times greater with X-rays than with proton therapy [1]

Tumor Site	Proton Therapy	X-rays/IMRT
Stomach and esophagus	0%	11%
Colon	0%	7%
Breast	0%	0%
Lung	1%	7%
Thyroid	0%	6%
Bone and connective tissue	1%	2%
Leukemia	3%	5%
All Secondary Cancers	5%	43%

This chart compares the rates of secondary tumors for a pediatric patient treated for medulloblastoma.

Data shown are from a study that compared treatment plans.

IMRT = intensity modulated radiation therapy (a type of X-ray therapy)

Last Update: 2018

- **Facilities in operation: 70**
- **Patients: 190000**

Particle Therapy Cooperative Group (PTCOG). http://www.ptcog.ch

Hadrontherapy in Italy

Azienda Provinciale per i Servizi Sanitari
Provincia Autonoma di Trento

Cyclotron
protons up to 250 AMeV
Patient treated:387

fondazione CNAO
Centro Nazionale di Adroterapia Oncologica per il trattamento dei tumori

Syncrotron
protons and 12C up to 250 AMeV
Patient treated:
12C 1044
p 565

CATANA
INFN LNS
Istituto Nazionale di Fisica Nucleare
Laboratori Nazionali del Sud

Cyclotron
protons of 62 MeV
Patient treated:400

Hadrontherapy at LNS from the conventional approach to the frontier of biological enhancement and laser-driven applications

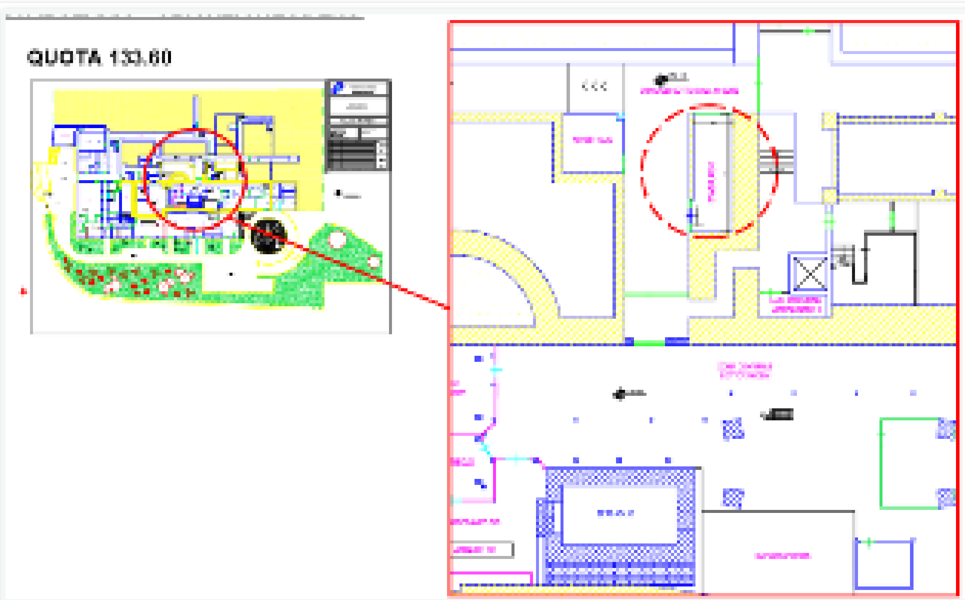
CATANA
Centro di AdroTerapia ed Applicazioni Nucleari Avanzate

First Italian proton therapy facility

- **First Patient treated on March 2002 - 400 treated**
- **Passive proton beam line - 62 MeV**

Dead Patients	4	
	Metastatis	3
	Other	1
Eye retention rate	92,68%	
Total survival	**95%**	
Local control	**97%**	

Hadrontherapy at LNS from the conventional approach to the frontier of biological enhancement and laser-driven applications



Small animal facility room @LNS

Recovery unit

Transport unit

OSPEDALE CANNIZZARO

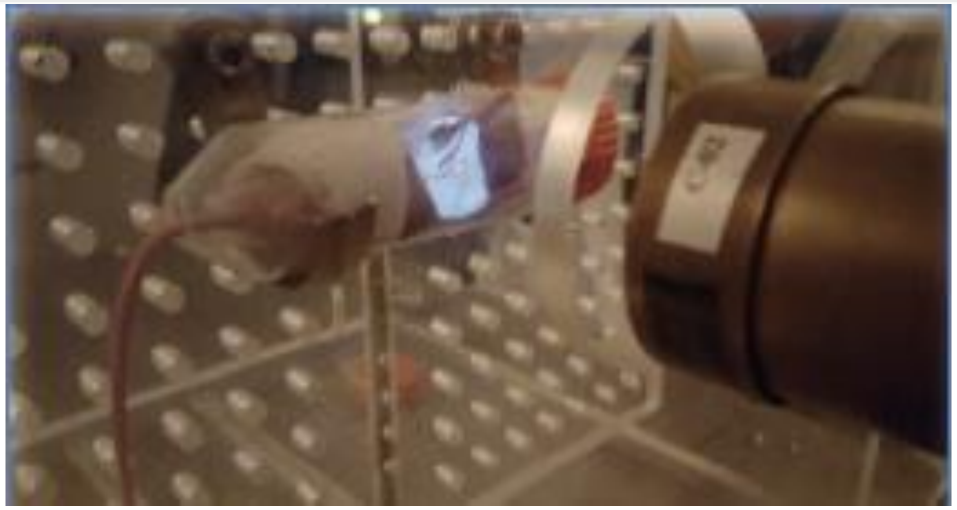
IBFM

INFN

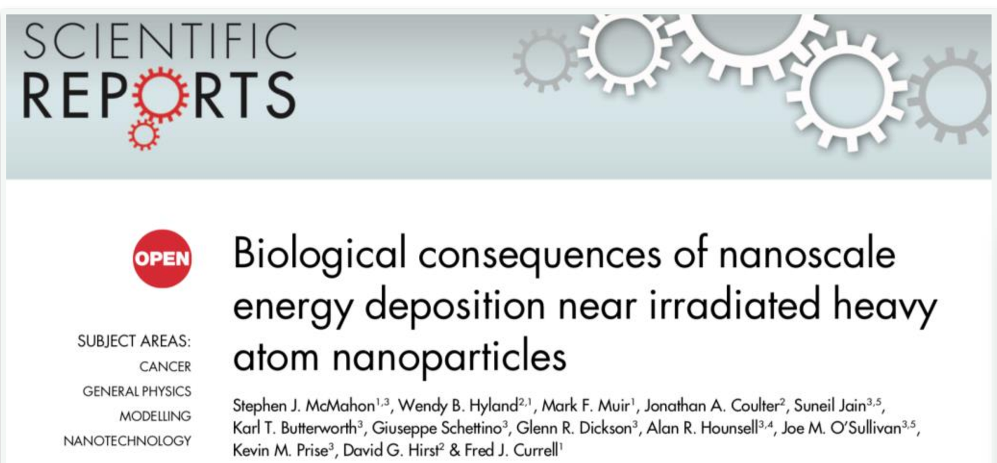
Istituto Nazionale di Fisica Nucleare

new in-vivo experiment dedicated to study the proton RBE in the distal part of Bragg Peak curve

MoVe IT



Hadrontherapy at LNS from the conventional approach to the frontier of biological enhancement and laser-driven applications



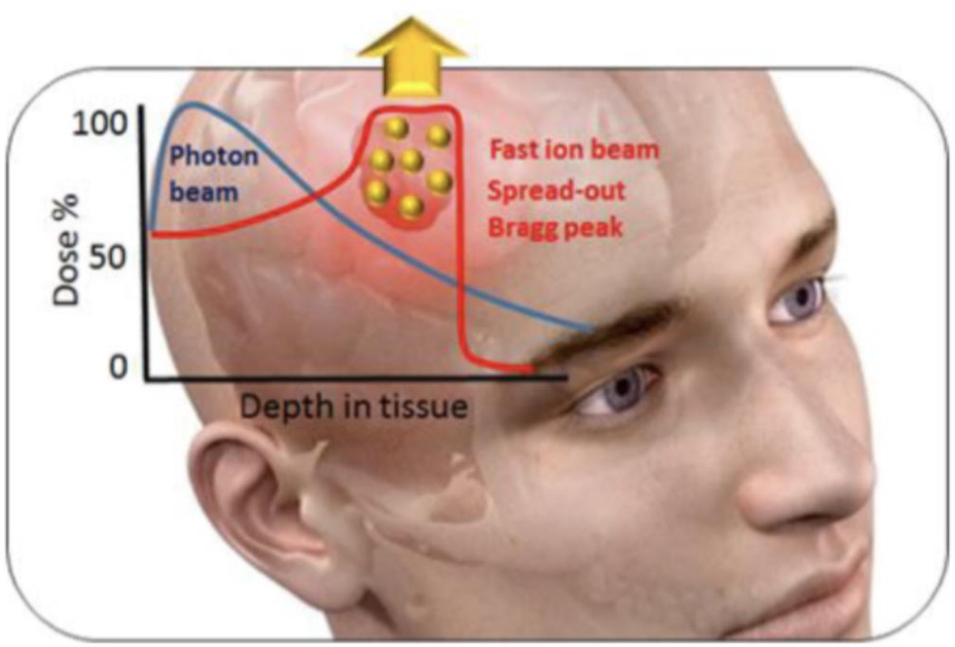
SCIENTIFIC REPORTS

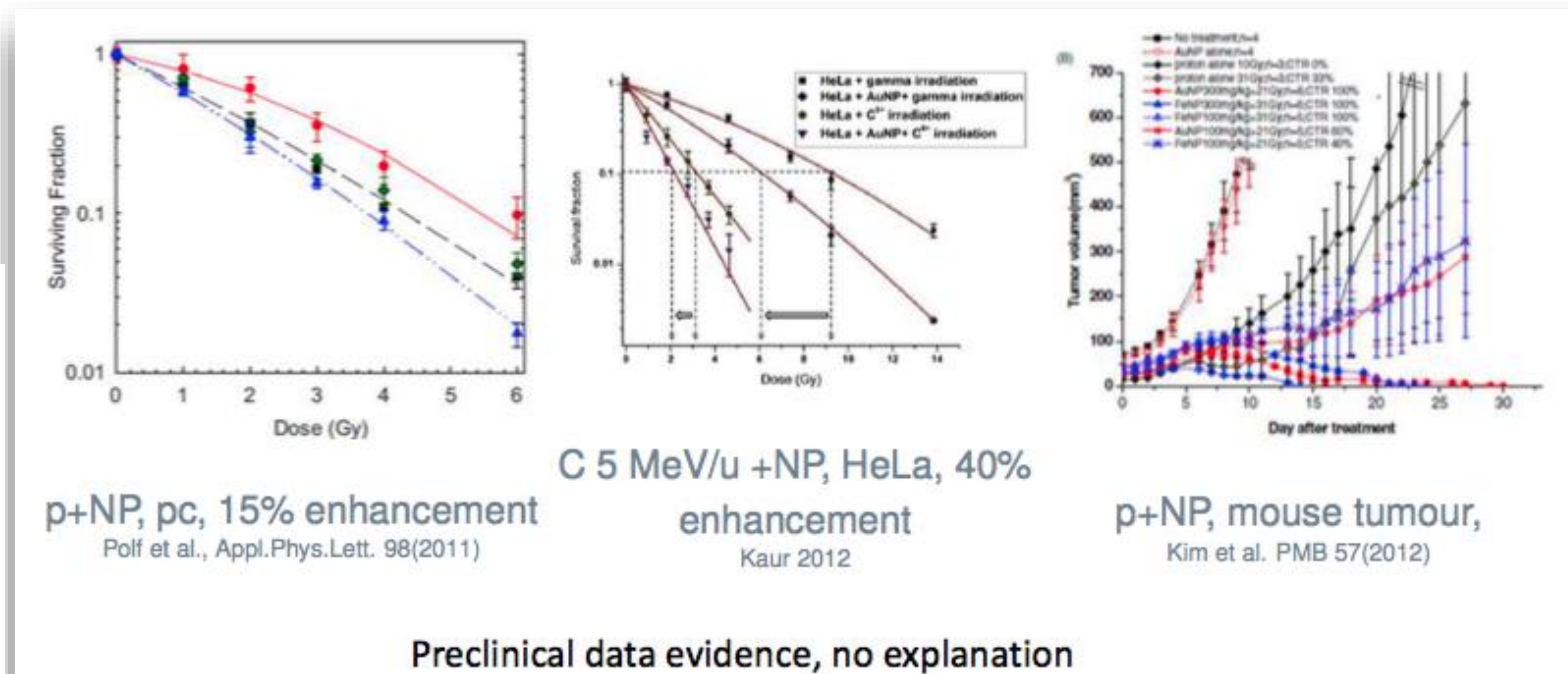
OPEN

SUBJECT AREAS:
CANCER
GENERAL PHYSICS
MODELLING
NANOTECHNOLOGY

Biological consequences of nanoscale energy deposition near irradiated heavy atom nanoparticles

Stephen J. McMahon[1,3], Wendy B. Hyland[2,1], Mark F. Muir[1], Jonathan A. Coulter[2], Suneil Jain[3,5], Karl T. Butterworth[3], Giuseppe Schettino[3], Glenn R. Dickson[3], Alan R. Hounsell[3,4], Joe M. O'Sullivan[3,5], Kevin M. Prise[3], David G. Hirst[2] & Fred J. Currell[1]





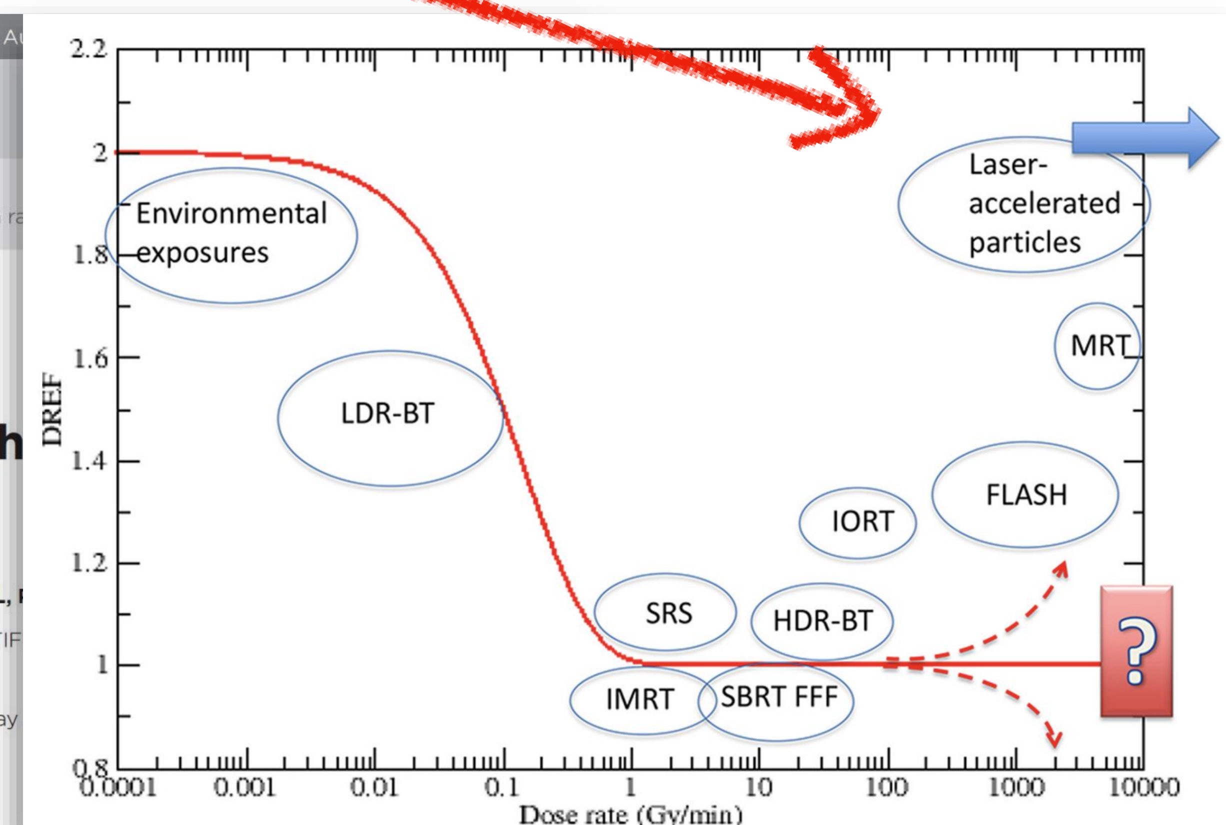
Hadrontherapy at LNS from the conventional approach to the frontier of biological enhancement and laser-driven applications


BJR © 2018 The A
Received: 26 August 2017 | Revised: 11 November 2017 | Accepted: 22 November 2017
Cite this article as:
Durante M, Bräuer-Krisch E, Hill M. Faster and safer? FLASH ultra-high dose rate in r

COMMENTARY

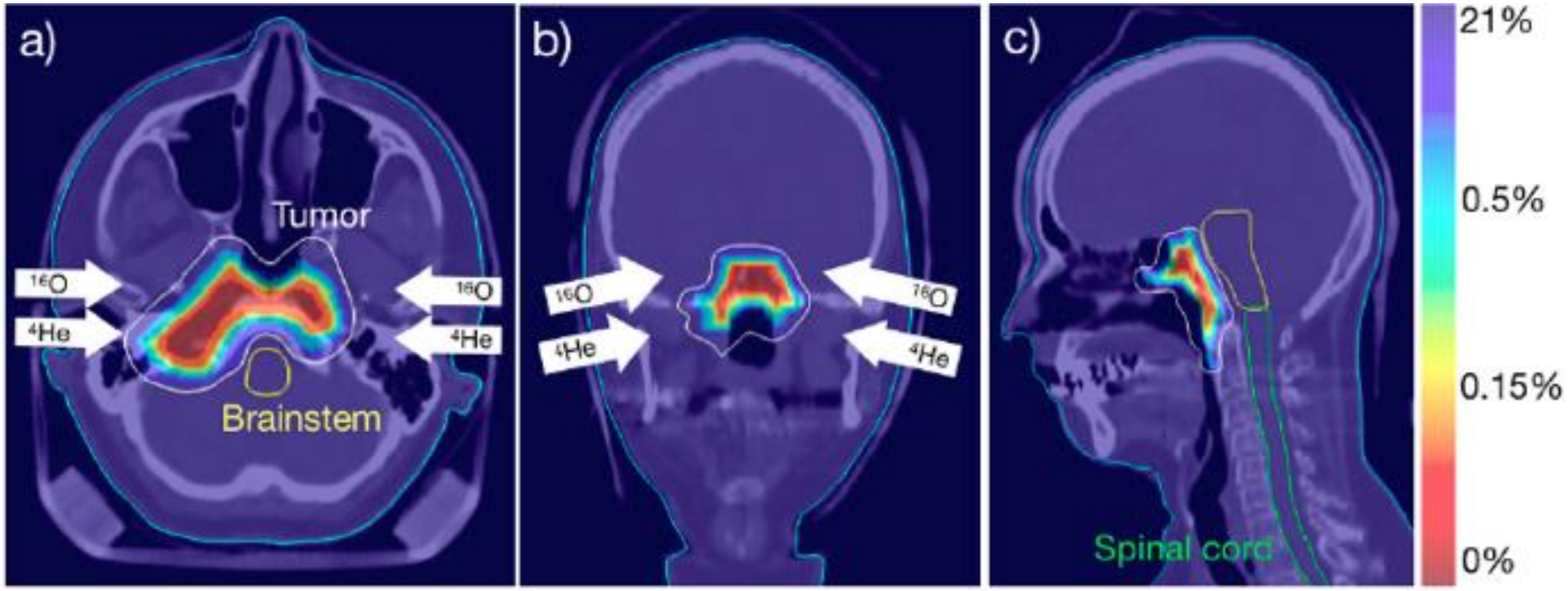
Faster and safer? FLASH ultra-high in radiotherapy

[1]MARCO DURANTE, PhD, [2]ELKE BRÄUER-KRISCH, PhD and [3]MARK HILL,
[1]National laboratories, Trento Institute for Fundamental Physics and Applications (TIF University of Trento, Trento, Italy
[2]National laboratories, ESRF-The European Synchrotron, Grenoble, France
[3]Department of Oncology, CRUK/MRC Oxford Institute for Radiation Oncology, Gray
Address correspondence to: Professor Marco Durante
E-mail: Marco.Durante@tifpa.infn.it

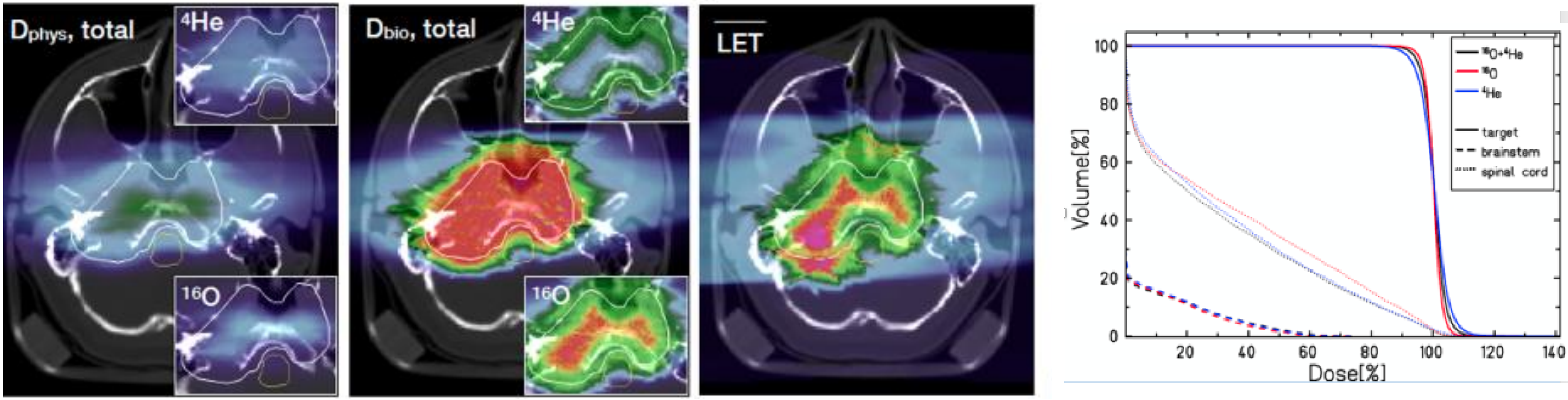


Multiple ions TPS

The beam spots are correctly selected by the optimization in order to concentrate high LET particles in the hypoxic regions

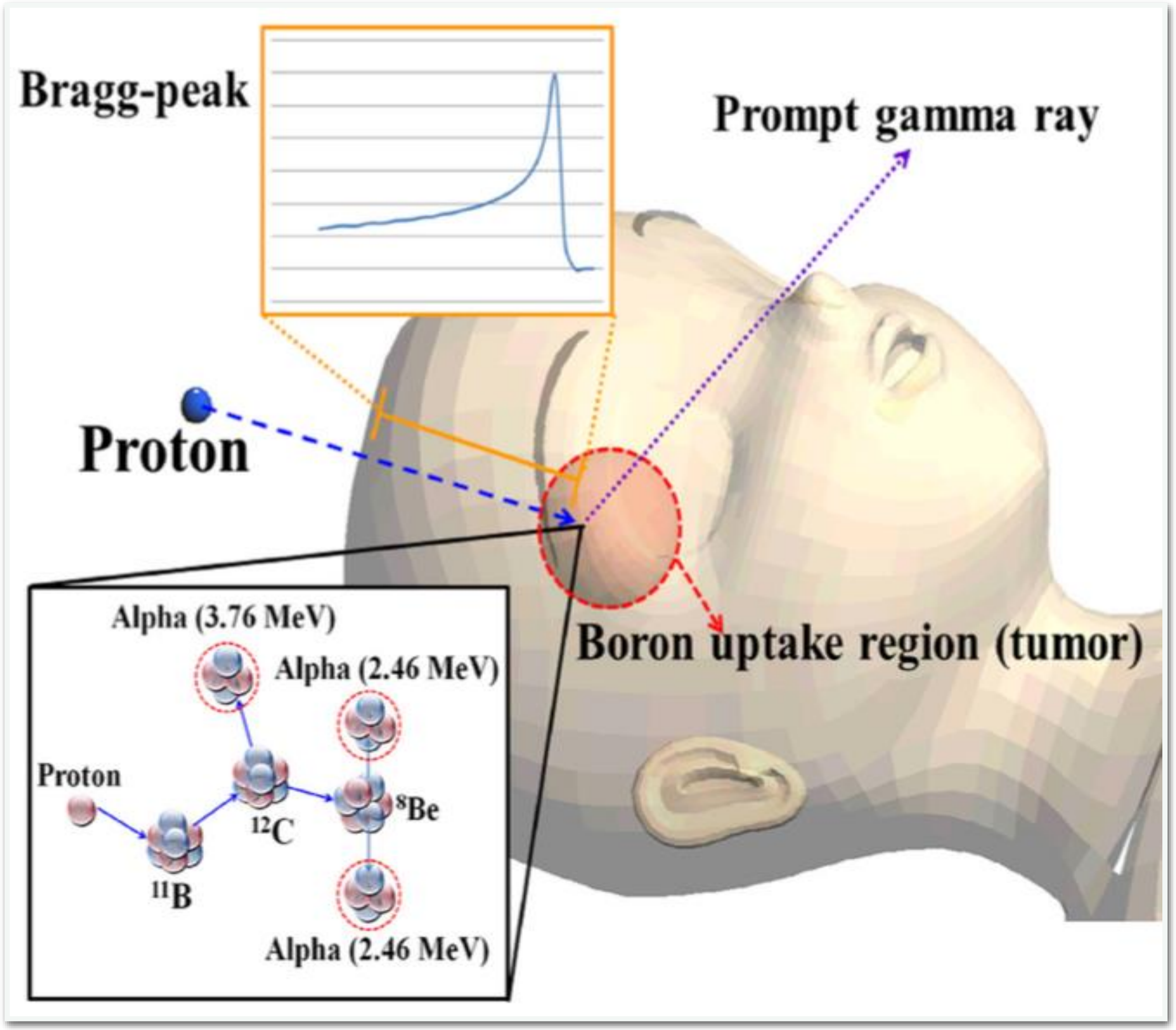


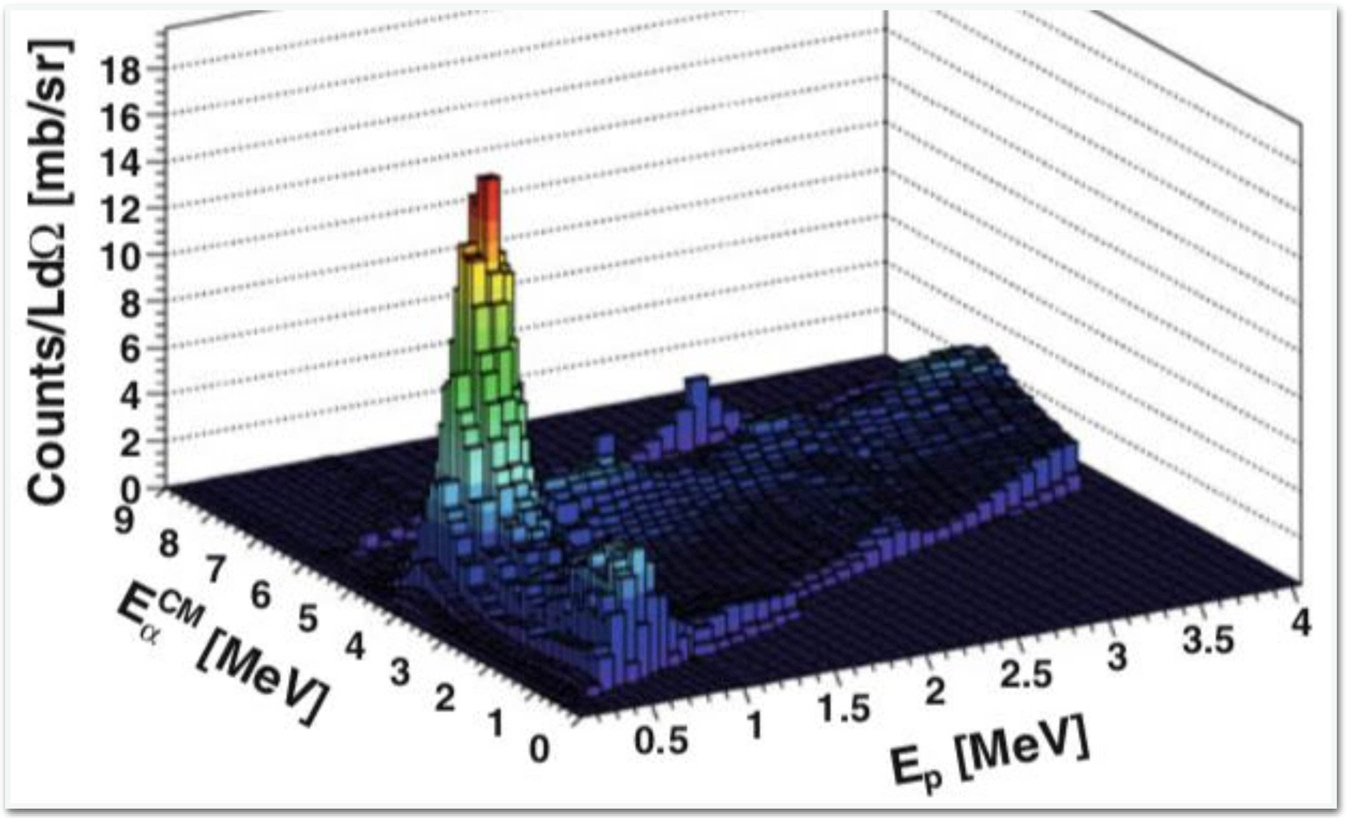
Sokol et al. to be subm PMB (2018) *100% dose = 2 Gy 100% LET = 65 keV/um



Exploiting the 11B(p,a)2a reaction

The proton-Boron capture therapy (PBCT)





M.H.Sikora,H.R.Weller,A new evaluation of the 11B(p,a)aa reaction rates, J. Fusion Energy (2016) 35:538

The idea:

D.-K. Yoon et al,
Application of proton boron fusion reaction to radiation therapy: A Monte Carlo simulation study
Applied Physics Letters 105,(2014);

Reaction channels

$$^{11}B + p \rightarrow ^{12}C^* \rightarrow ^{8}Be + \alpha_0 \rightarrow \alpha_{01} + \alpha_{02} + \alpha$$

$$^{11}B + p \rightarrow ^{12}C^* \rightarrow ^{8}Be* + \alpha_1 \rightarrow \alpha_{11} + \alpha_{12} + \alpha$$

The proton-Boron capture therapy (PBCT)

European Patent 3266470A1

nature.com > scientific reports > articles > article

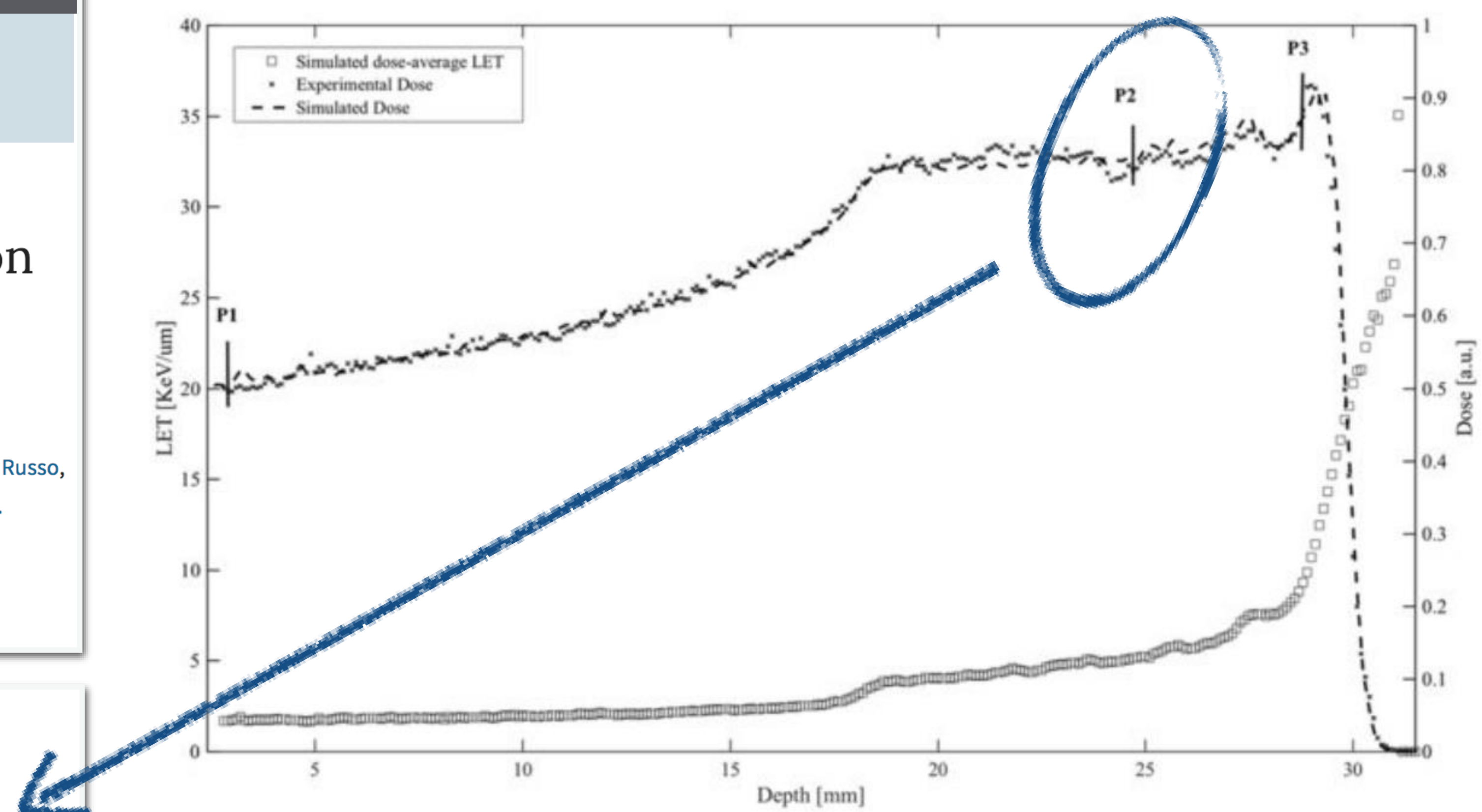
SCIENTIFIC REPORTS

Article | OPEN | Published: 18 January 2018

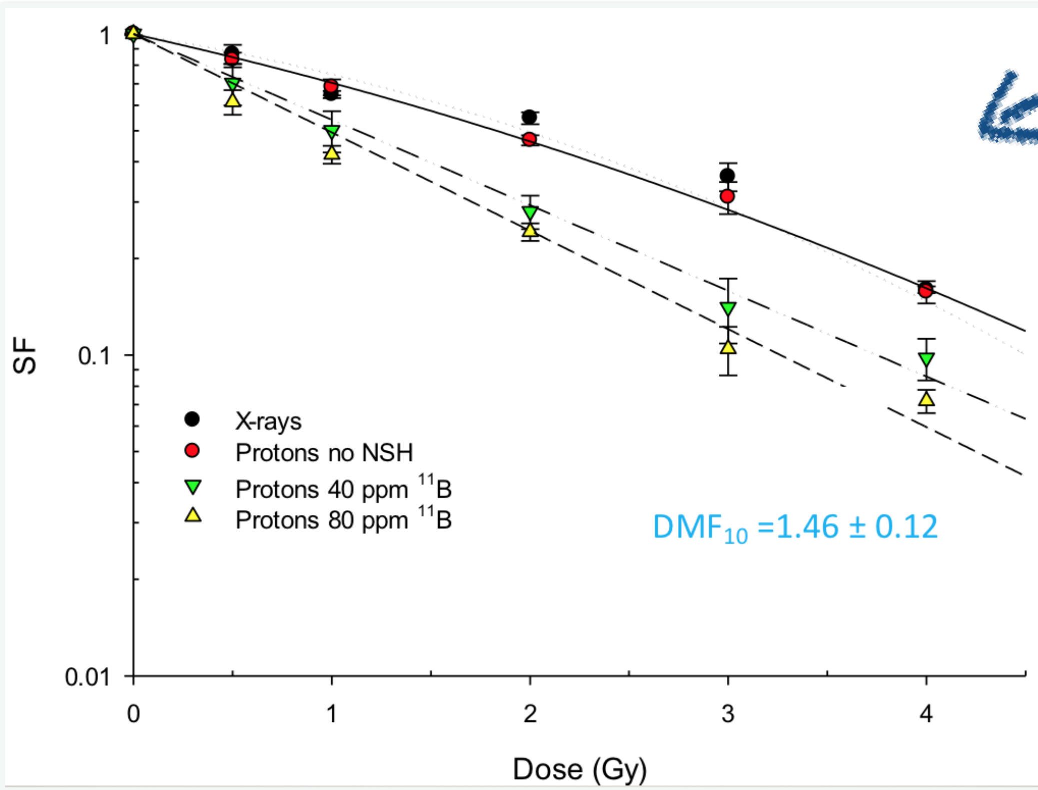
First experimental proof of Proton Boron Capture Therapy (PBCT) to enhance protontherapy effectiveness

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



Irradiation @MID-SOBP

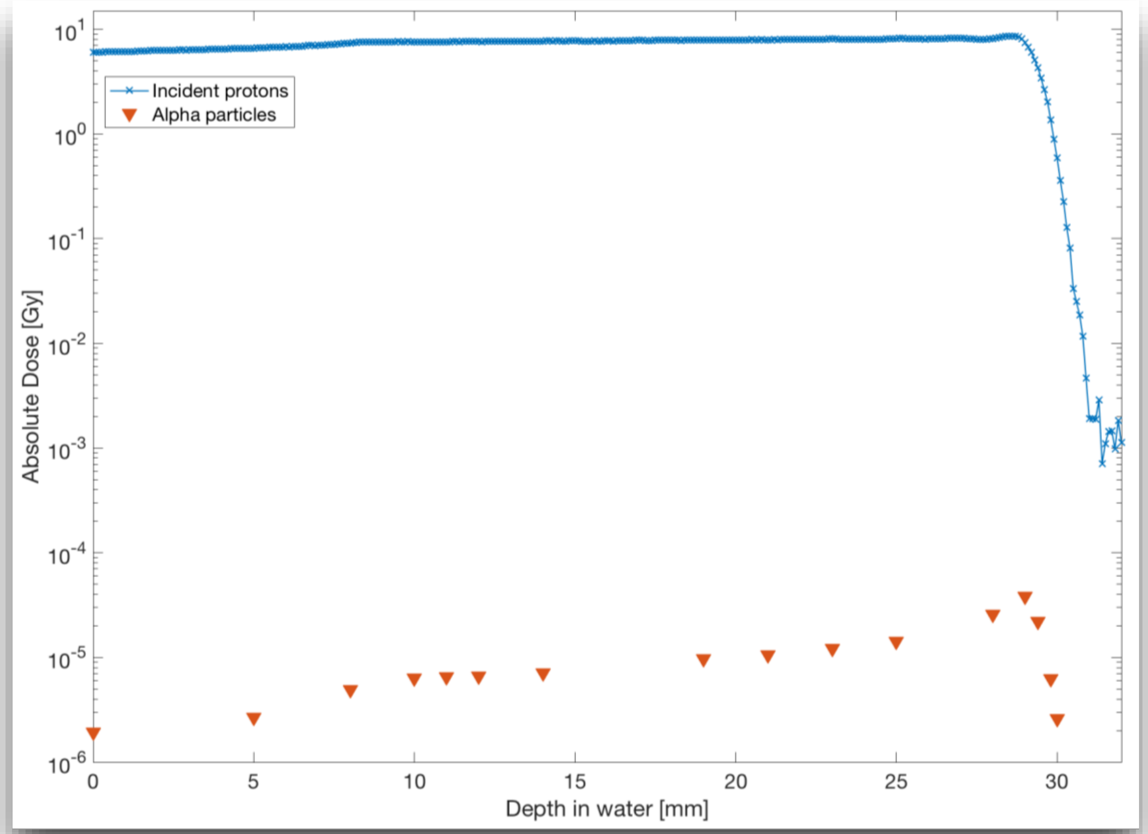


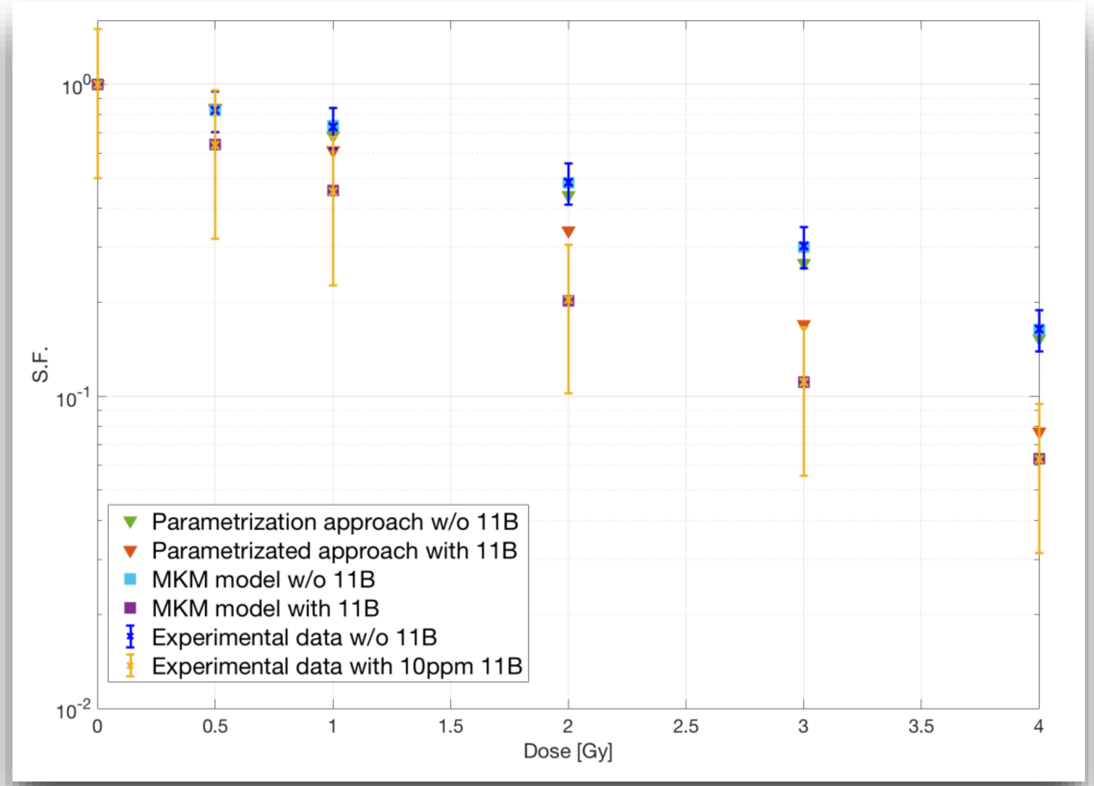
DMF_{10} (RBE_{10})= 1.46 ± 0.12

	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	—

…. but

Are nuclear physics considerations and analytical/Monte Carlo calculations able to explain these results?





An increment of the order of 40% correspond to ~10^5 alpha particels emitted

The proton-Boron capture therapy (PBCT)

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

On the (un)effectiveness of Proton Boron Capture in Proton Therapy

Annamaria Mazzone, Paolo Finocchiaro, Sergio Lo Meo, Nicola Colonna

(Submitted on 26 Feb 2018 (v1), last revised 3 Mar 2018 (this version, v2))

We present calculations and simulations on the role of the p+^{11}B\to3\alpha reaction in proton therapy. This reaction has been recently suggested to be responsible for a decrease in the survival probability of tumor cells, when they are irradiated with low-energy protons. However, at the concentration levels typical of the proposed boron carrier (sodium borocaptate, Na_{2}B_{12}H_{11}SH, in short BSH), i.e. less than 100 ppm, both calculations and Monte Carlo simulations suggest that the dose related to this reaction is orders of magnitude lower than the dose delivered by the primary proton beam inside the tissues. These calculations cast some doubts on the claim of an important role played by Proton Boron Capture in enhancing the therapeutic effectiveness of proton therapy, and suggest that other mechanisms should be investigated in order to explain the observed decrease in the survival probability.

Study of gamma-ray emission by proton beam interaction with injected Boron atoms for future medical imaging applications

G. Petringa,[a,b,1] G.A.P. Cirrone,[a] C. Caliri,[a] G. Cuttone,[a] L. Giuffrida,[c] G. Larosa,[a] R. Manna,[a] L. Manti,[e] V. Marchese,[a] C. Marchetta,[a] D. Margarone,[c] G. Milluzzo,[a,b] A. Picciotto,[d] F. Romano,[a] F.P. Romano,[a,g] A.D. Russo,[a] G. Russo,[a,f] D. Santonocito[a] and V. Scuderi[a,c]

DISCUSSING THE DISCREPANCY BETWEEN ANALYTICAL CALCULATIONS AND THE OBSERVED BIOLOGICAL EFFECTIVENESS IN PROTON BORON CAPTURE THERAPY (PBCT)

G.A.P. Cirrone[1,2], G. Petringa[1,*], A. Attili[3], D. Chiappara[1,6], L.Manti[4,5], V. Bravatà[7], D. Margarone[2], M.Mazzocco[6,8] and G. Cuttone[1]

Accepted in RADIATION&APPLICATIONS In Physics, Chemistry, Biology, Medical Sciences, Engineering and Environmental Sciences

Prompt gamma ray diagnostics and enhanced hadron-therapy using neutron-free nuclear reactions

AIP Advances 6, 105204 (2016); https://doi.org/10.1063/1.4965254

L. Giuffrida[1], D. Margarone[1], G. A. P. Cirrone[2], A. Picciotto[3], G. Cuttone[2], *and* G. Korn[1]

The proton-Boron capture therapy (PBCT)

NEPTUNE

Nuclear process driven Enhancement of Proton Therapy UNravEled

- **Radiobiology (INFN-NA; CNR-IBFM)**
- **Simulation and modeling (INFN-LNS; INFN-RM3; INFN-TIFPA)**
- **Imaging (INFN-RM1; INFN-PV)**
- **Microdosimetry (INFN-LNL; INFN-MI; INFN-LNS)**

Hadrontherapy at LNS from the conventional approach to the frontier of biological enhancement and laser-driven applications

nature > nature reviews clinical oncology > review articles > a

nature REVIEWS CLINICAL ONCOLOGY

Review Article | Published: 21 May 2013

Charged particle therapy—opti challenges and future directio

Jay S. Loeffler & Marco Durante

Nature Reviews Clinical Oncology **10**, 411–424 (2013) | Download Citati

Research and development in the field of accelerators should be towards a reduction of costs, while maintaining or improving the performances of the current machines. Possible new accelerators for CPT[122] include synchrocyclotrons, rapid cycling synchrotrons, fixed-field alternating gradient rings, cyclotron–linac combinations, dielectric wall accelerators, and laser-driven plasma accelerators.[123] These options are at very different stages of design maturity, but all offer promising design features to offset the shortcomings of current synchrotrons, including fast scanning capabilities, reduced size, complexity and power consumption, increased dose rate capability, and ultimately a lower cost and a shorter treatment time.[14]

ELI (Extreme Light Infrastructure)

new type of European large scale laser infrastructure specifically designed to produce the highest peak power (10 PW) and focused intensity;

ELI-Beamlines (Czech Rep.)

Ungary

Romania

tbd

protons/ions

X-ray sources

Electrons

ELIMAIA

ELIMAIA: (ion accelerator + user station)
ELI Multidisciplinary Applications of laser-Ion Acceleration

ELIMED

ELIMED: (transport and dosimetry)
ELI MEDical and multidisciplinary applications

Laser Building

Support Room
Cryogenic systems, power supply cooling, auxiliary systems

eli beamlines

First Floor

Laser 1
100 mJ 1kHz bea

Ground Floor

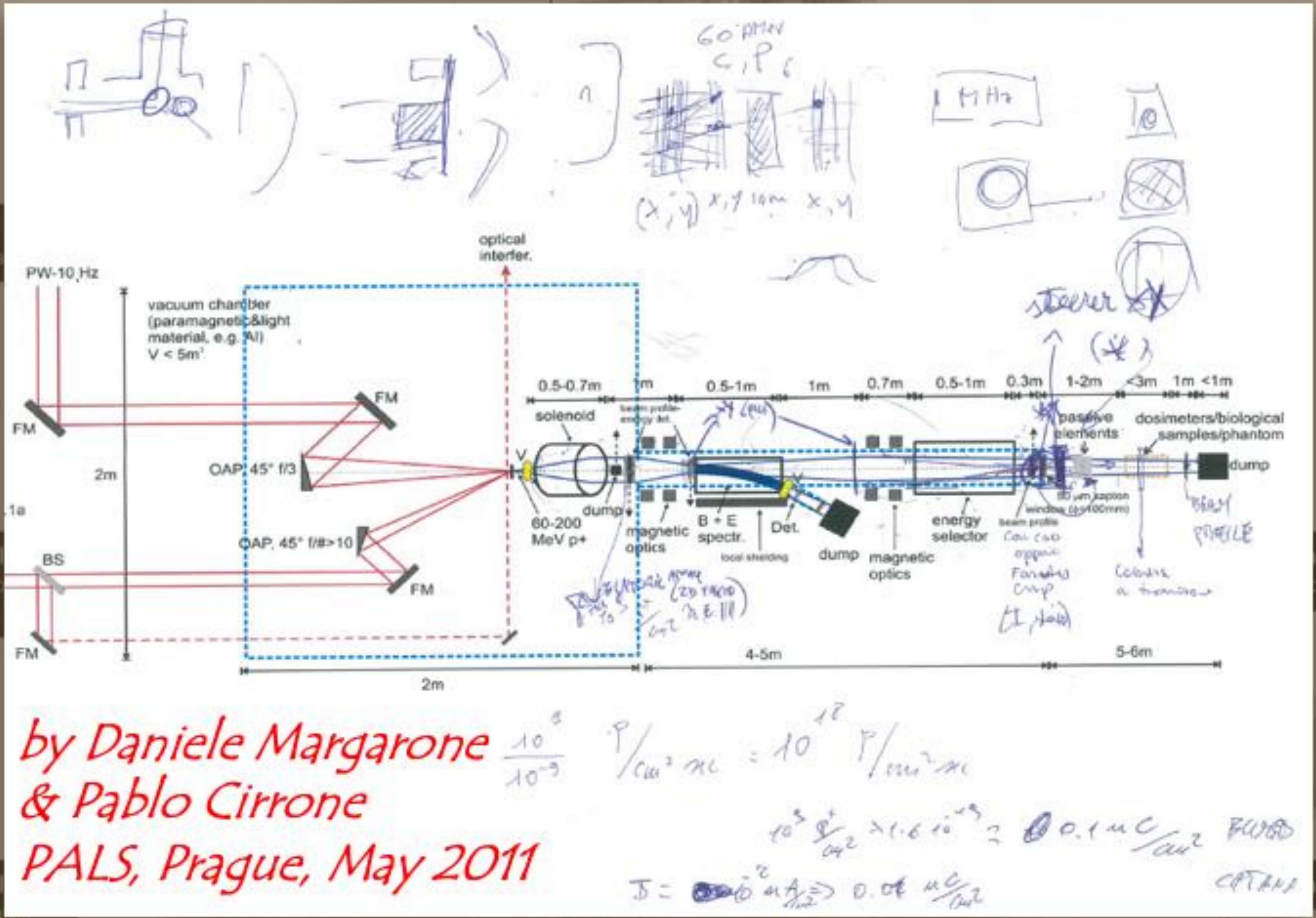
Experimental
Material & biom
applications

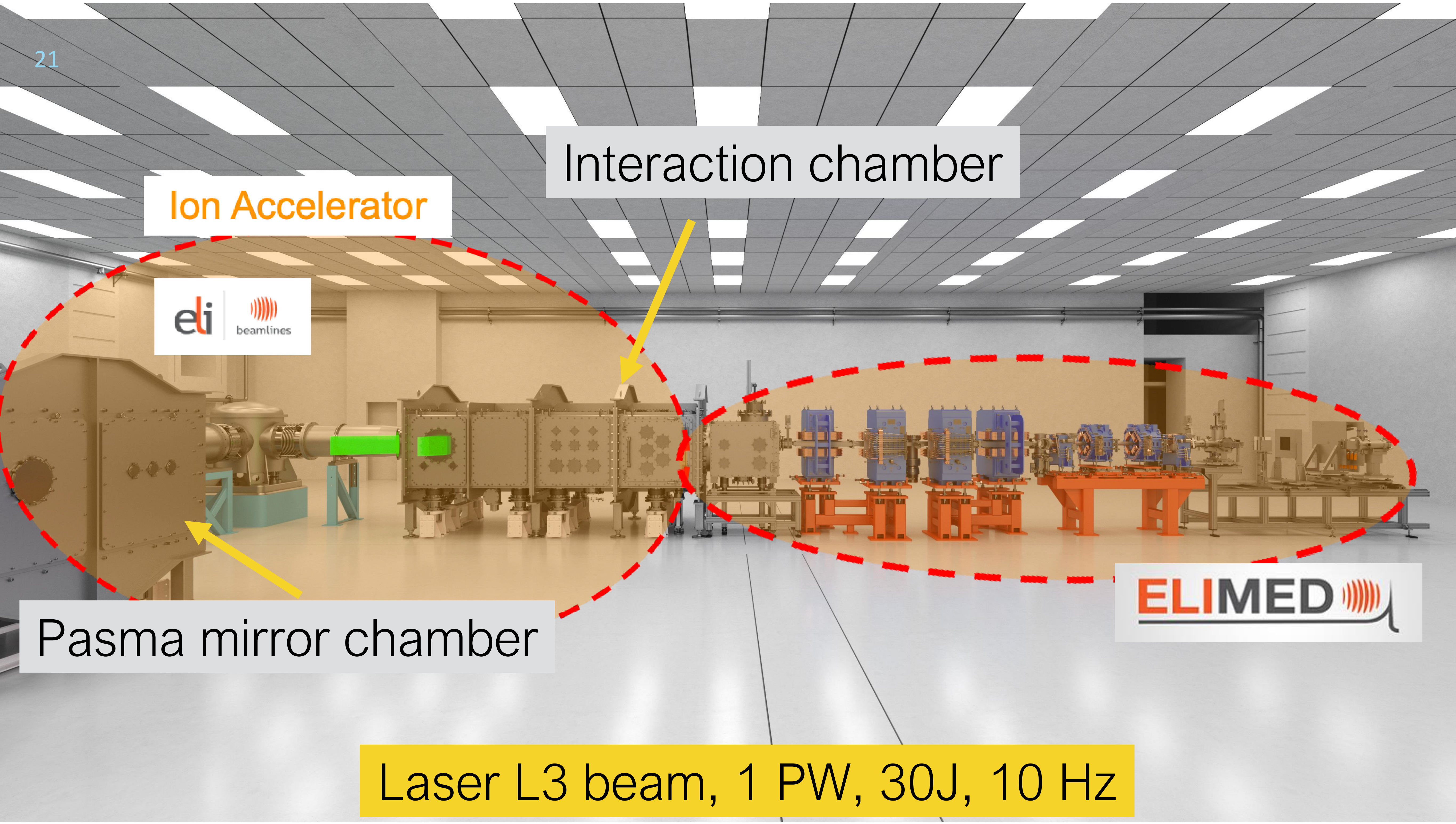
Basement

Experimental
Electron accelera

ental Hall 4
eleration

ental Hall 6




Interaction chamber
Ion Accelerator
eli beamlines
ELIMED
Pasma mirror chamber
Laser L3 beam, 1 PW, 30J, 10 Hz

July 2018

Luciano Allegra

Antonio Amico

Nino Amato

Simona Argentati

Renato Avolio

Luciano Calabretta

Giacomo Candiano

Carmelo Caruso

Fausta Caruso

Sarah Cesare

Giacomo Cuttone

Dora Di Nunzio

Enzo Lo Vecchio

Santo Gammino

Giusi Larosa

Mario Maggiore

Rosanna Manna

Letizia Marchese

Nino Maugeri

Giuliana Milluzzo

Nello Salamone

Roberto Pellegrini

Giada Petringa

Pietro Pisciotta

Salvo Pulvirenti

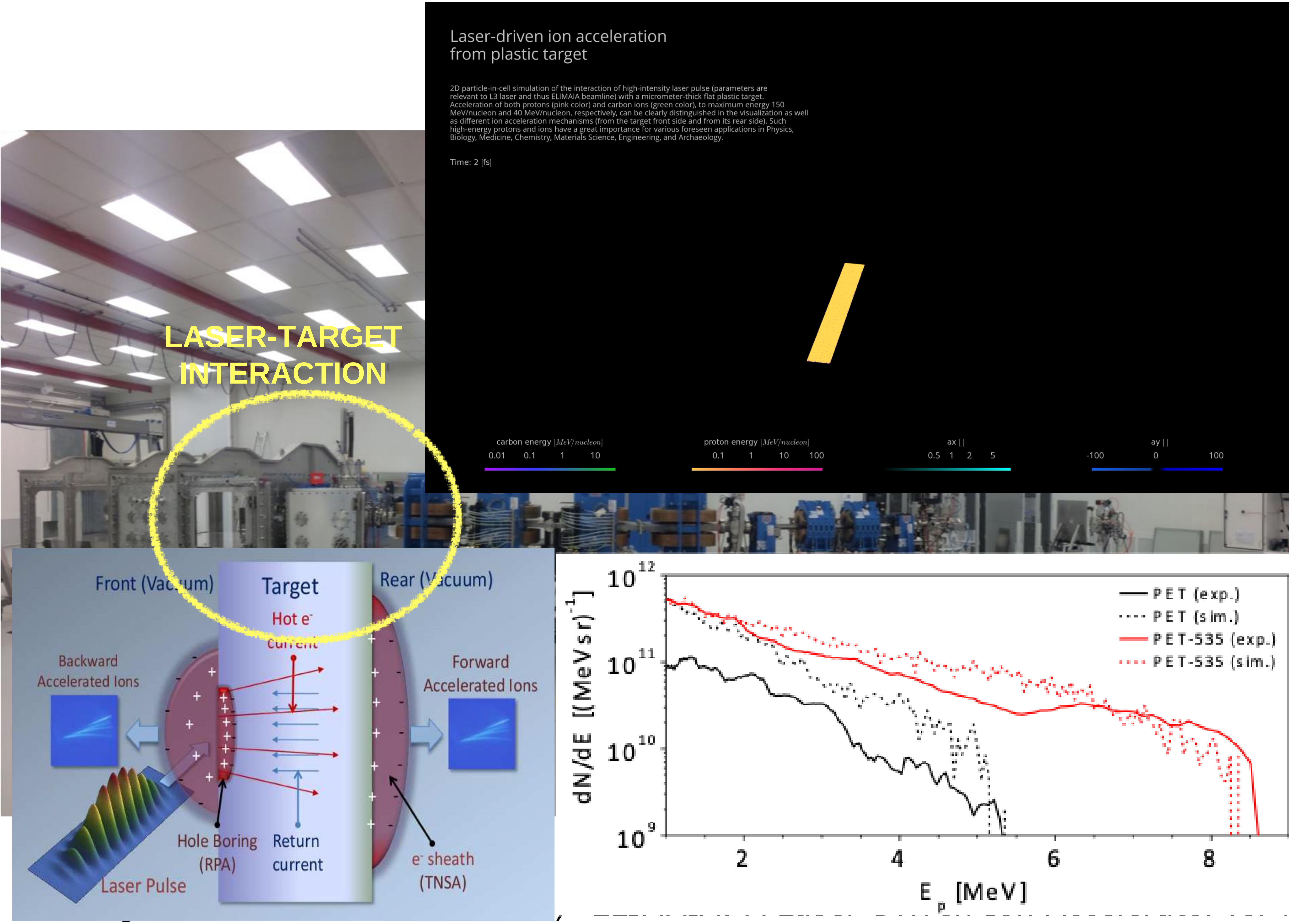
Daniele Rizzo

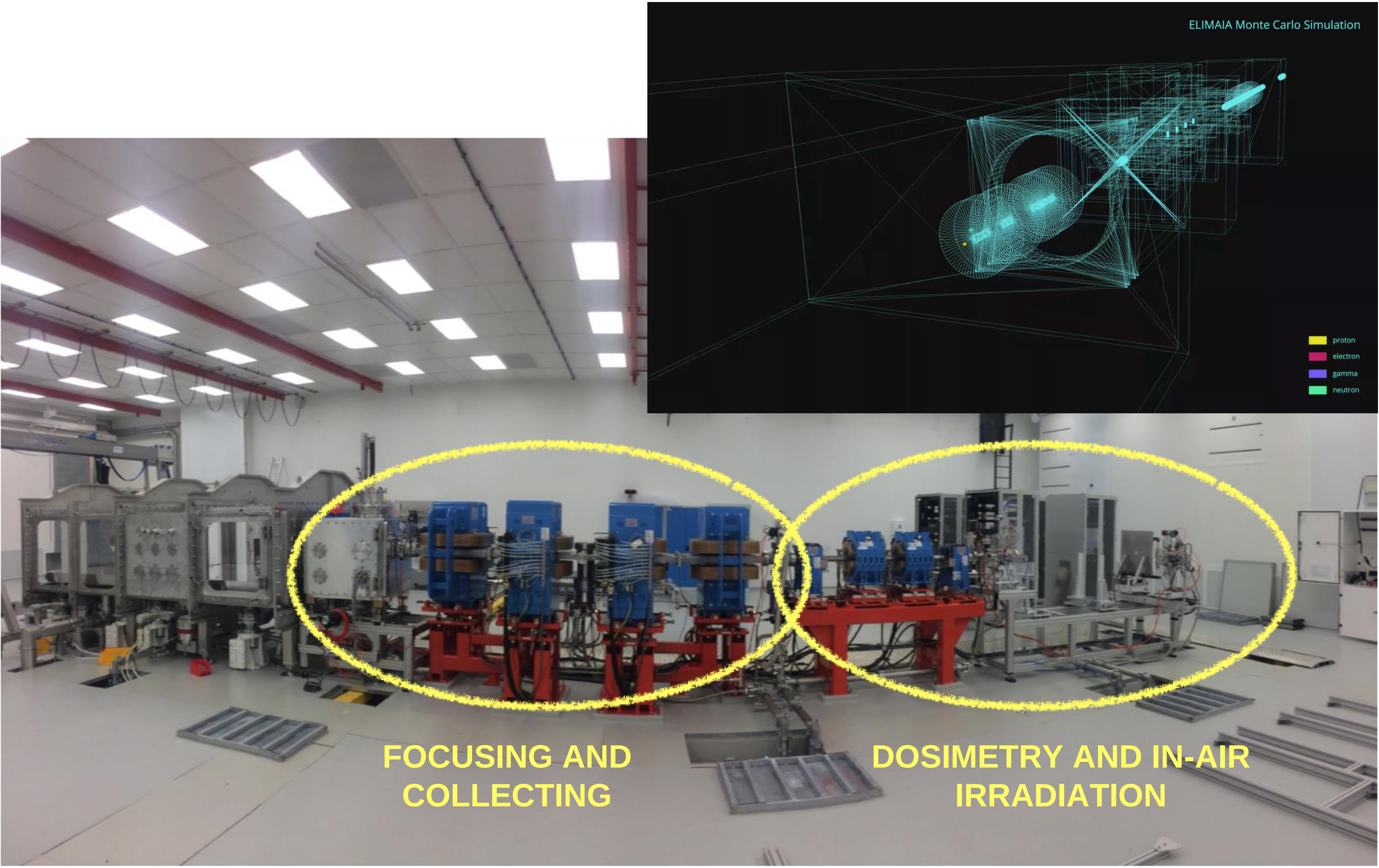
Francesco Romano

Francesco Schillaci

Valentina Scuderi

Salvatore Vinciguerra

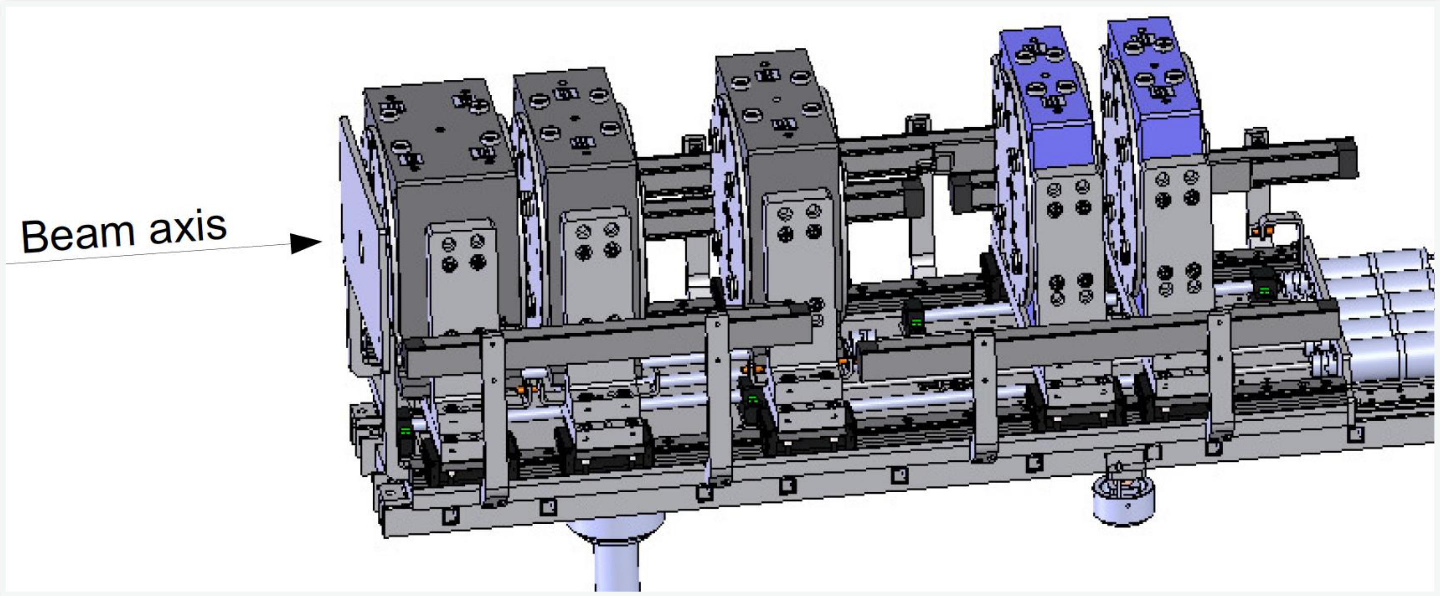

Laser-driven ion acceleration
from plastic target
2D particle-in-cell simulation of the interaction of high-intensity laser pulse (parameters are relevant to L3 laser and thus ELIMAIA beamline) with a micrometer-thick flat plastic target. Acceleration of both protons (pink color) and carbon ions (green color), to maximum energy 150 MeV/nucleon and 40 MeV/nucleon, respectively, can be clearly distinguished in the visualization as well as different ion acceleration mechanisms (from the target front side and from its rear side). Such high-energy protons and ions have a great importance for various foreseen applications in Physics, Biology, Medicine, Chemistry, Materials Science, Engineering, and Archaeology.
Time: 2 [fs]
carbon energy [MeV/nucleon]
0.01 0.1 1 10
proton energy [MeV/nucleon]
0.1 1 10 100
ax [ ]
0.5 1 2 5
ay [ ]
-100 0 100
LASER-TARGET
INTERACTION
Front (Vacuum)
Target
Rear (Vacuum)
Hot e⁻
current
Backward
Accelerated Ions
Forward
Accelerated Ions
Hole Boring
(RPA)
Return
current
e⁻ sheath
(TNSA)
Laser Pulse
10^{12}
10^{11}
10^{10}
10^{9}
dN/dE [(MeV sr)$^{-1}$]
2
4
6
8
E_p [MeV]
PET (exp.)
PET (sim.)
PET-535 (exp.)
PET-535 (sim.)

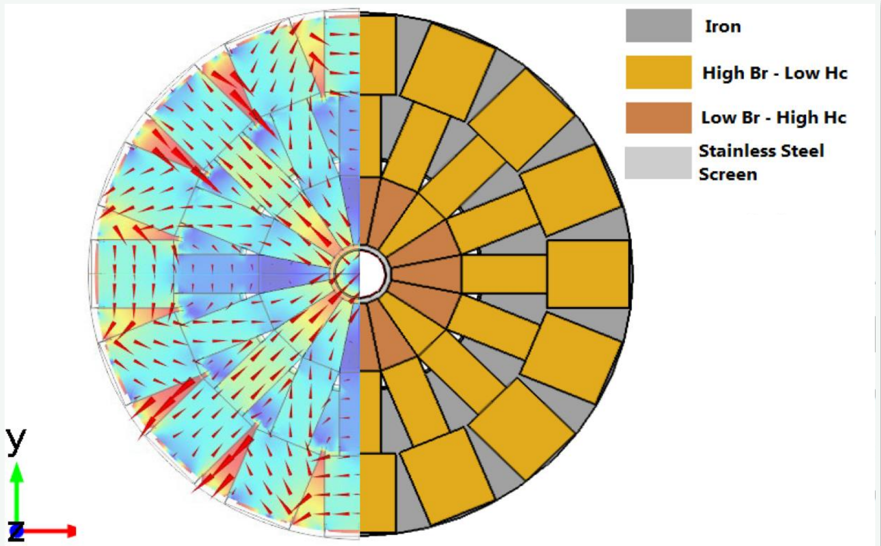


D. Margarone, G.A.P. Cirrone et al., "ELIMAIA: A Laser-Driven Ion Accelerator for M

Focusing and Collecting

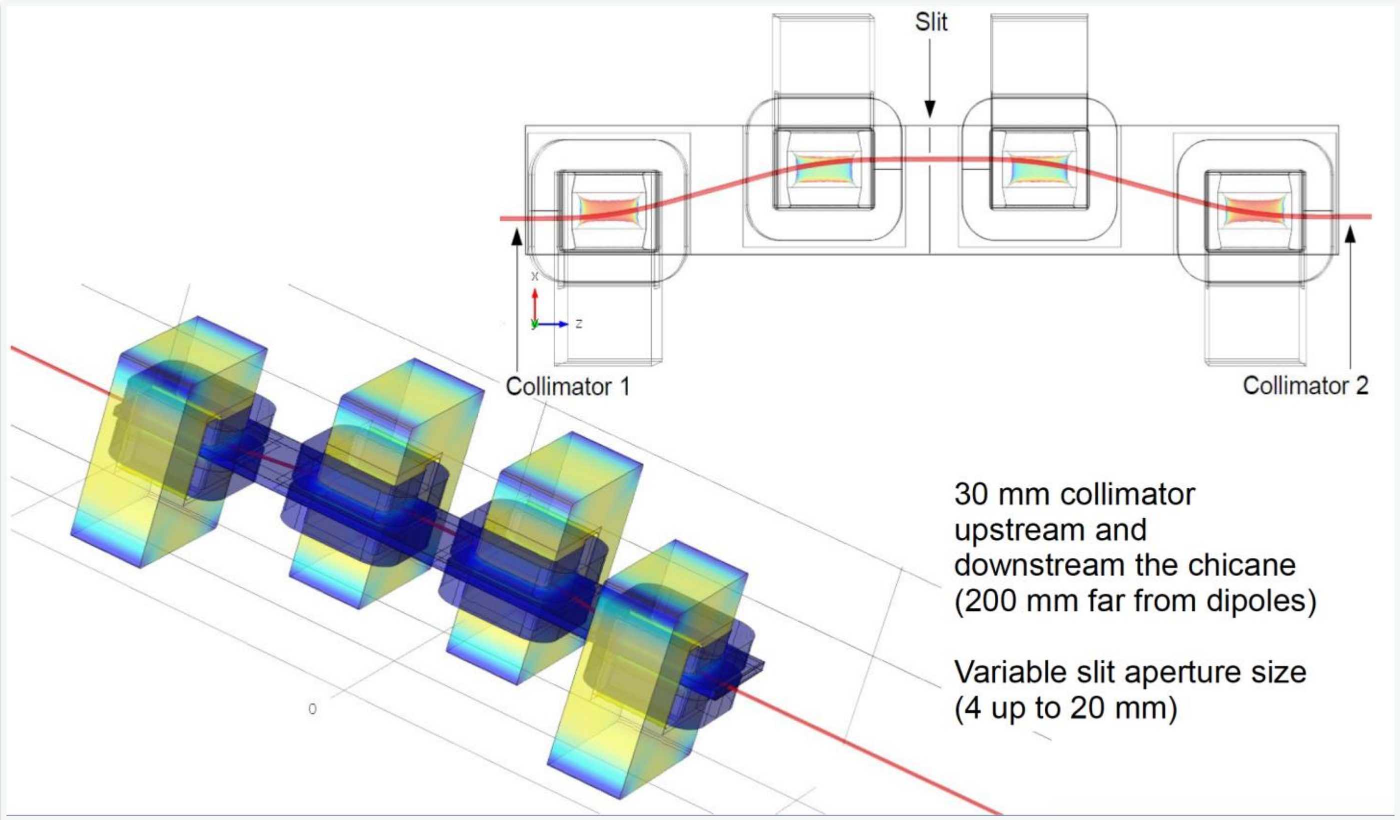
Permanent magnets: Quadrupoles

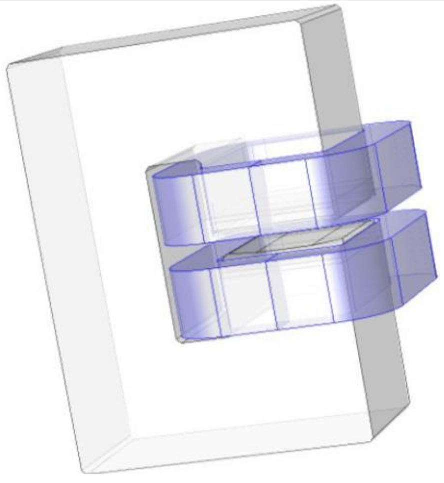




F. Schillaci et al., JINST 10 T12001 (2015)

Energy Selector System



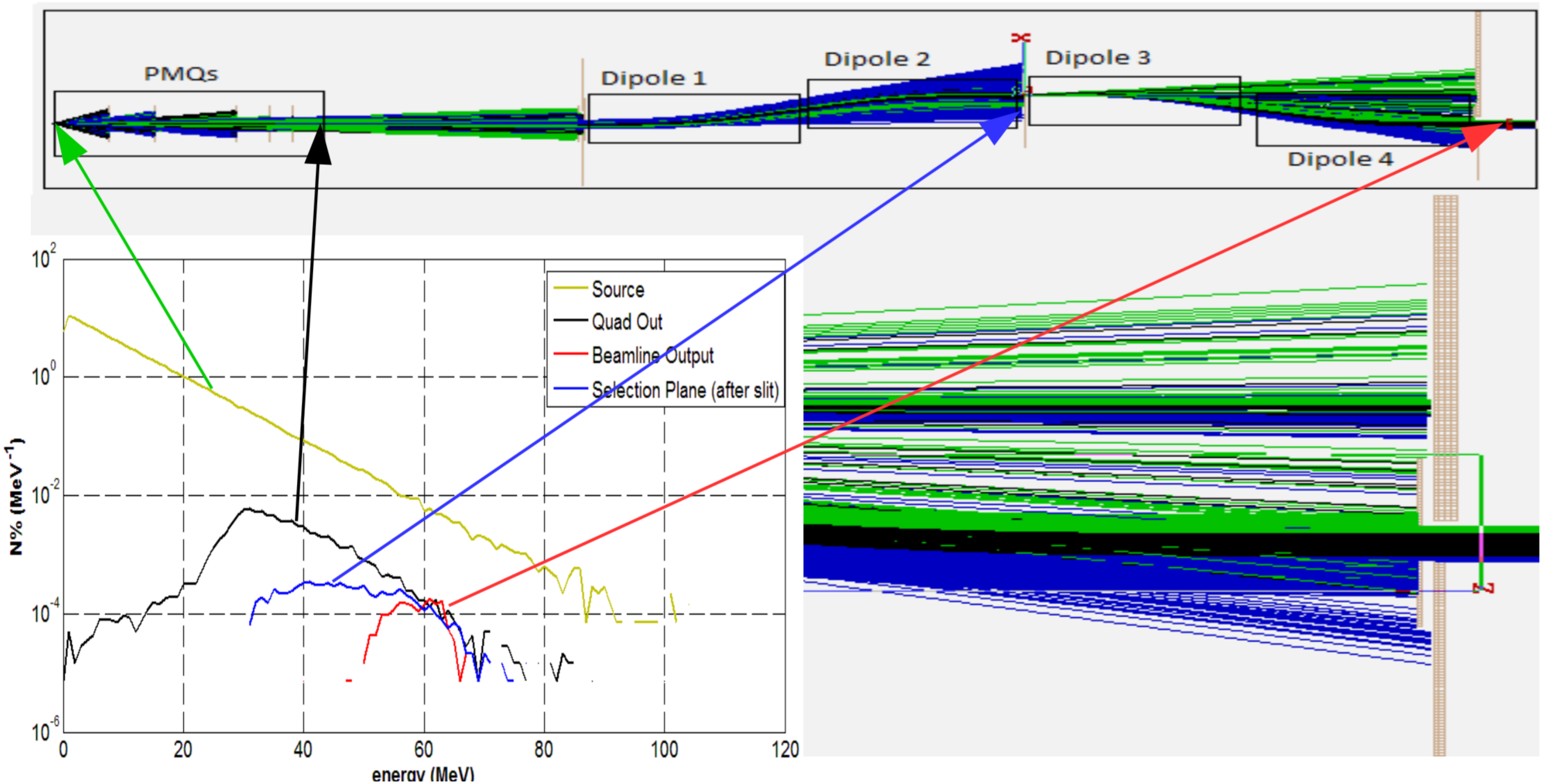


- Magnet efficiency 98%
- Packing factor 98%
- 115.5x168 coil section (11x16turns, 0,5 mm of insulator, 6 mm water channel)
- Max current ~200 A/turn
- Total weight ~3 Tons
- 40 kWatt in total

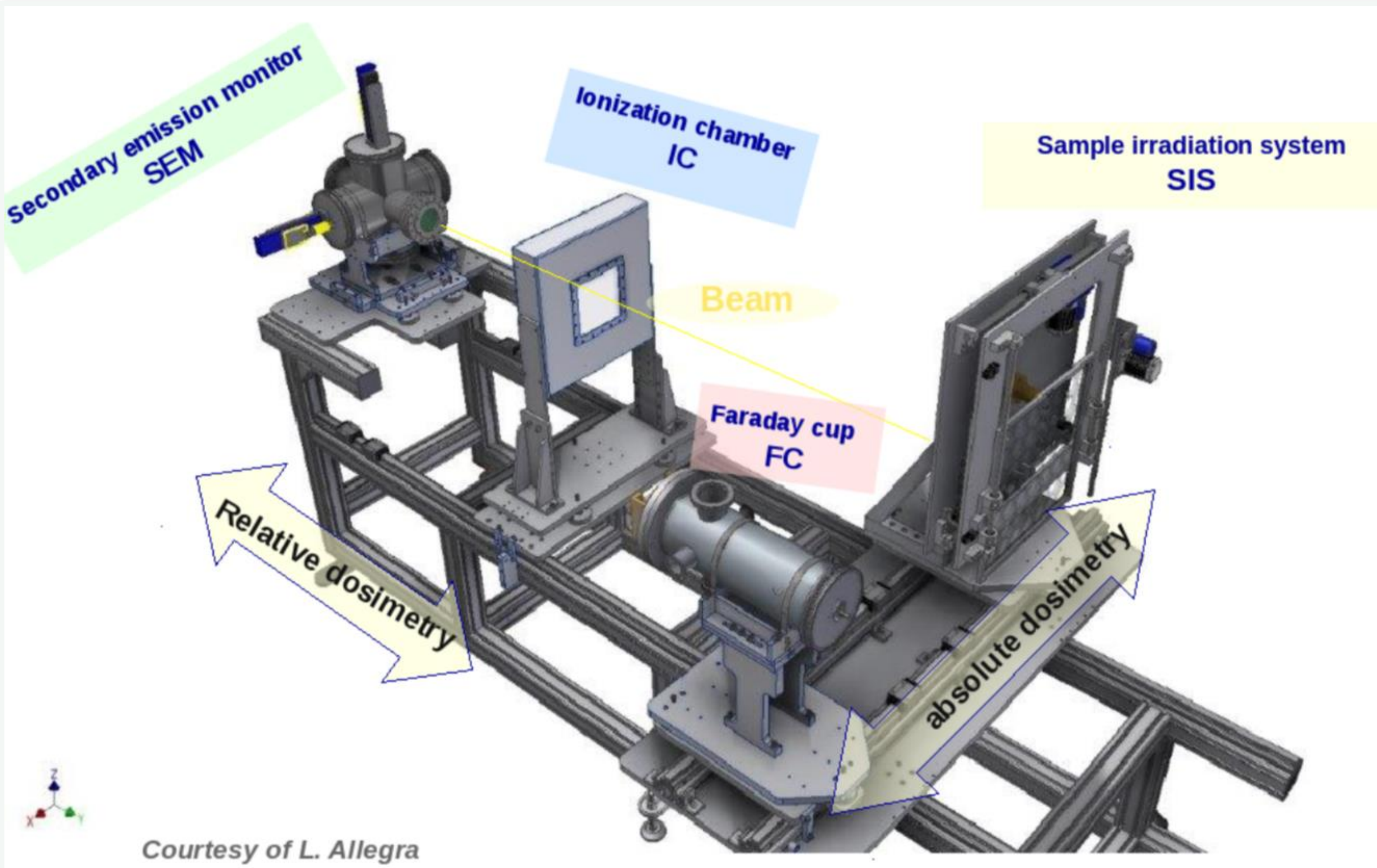
Focusing and Collecting

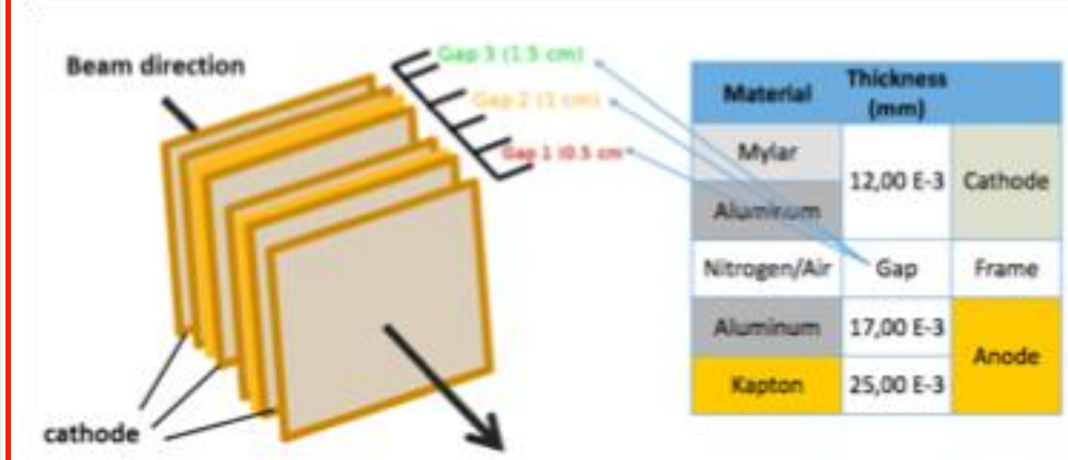
Angular divergence = 5° (FWHM)

Transmission efficiency ~12% (9,2e7 H^+/bunch)

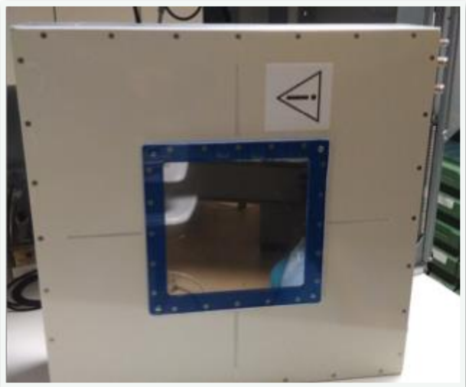


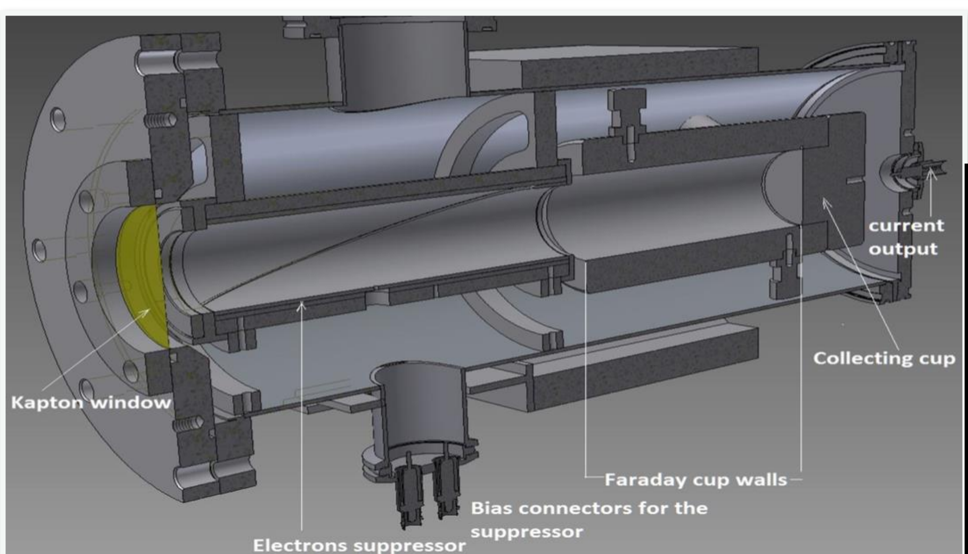
Dosimetric System



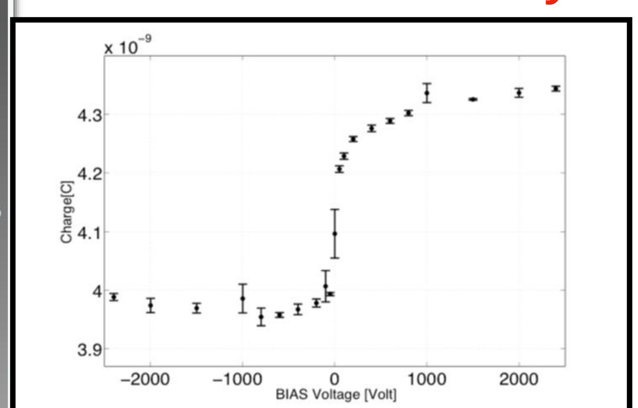


Transmission monitor chambers for relative dosimetry



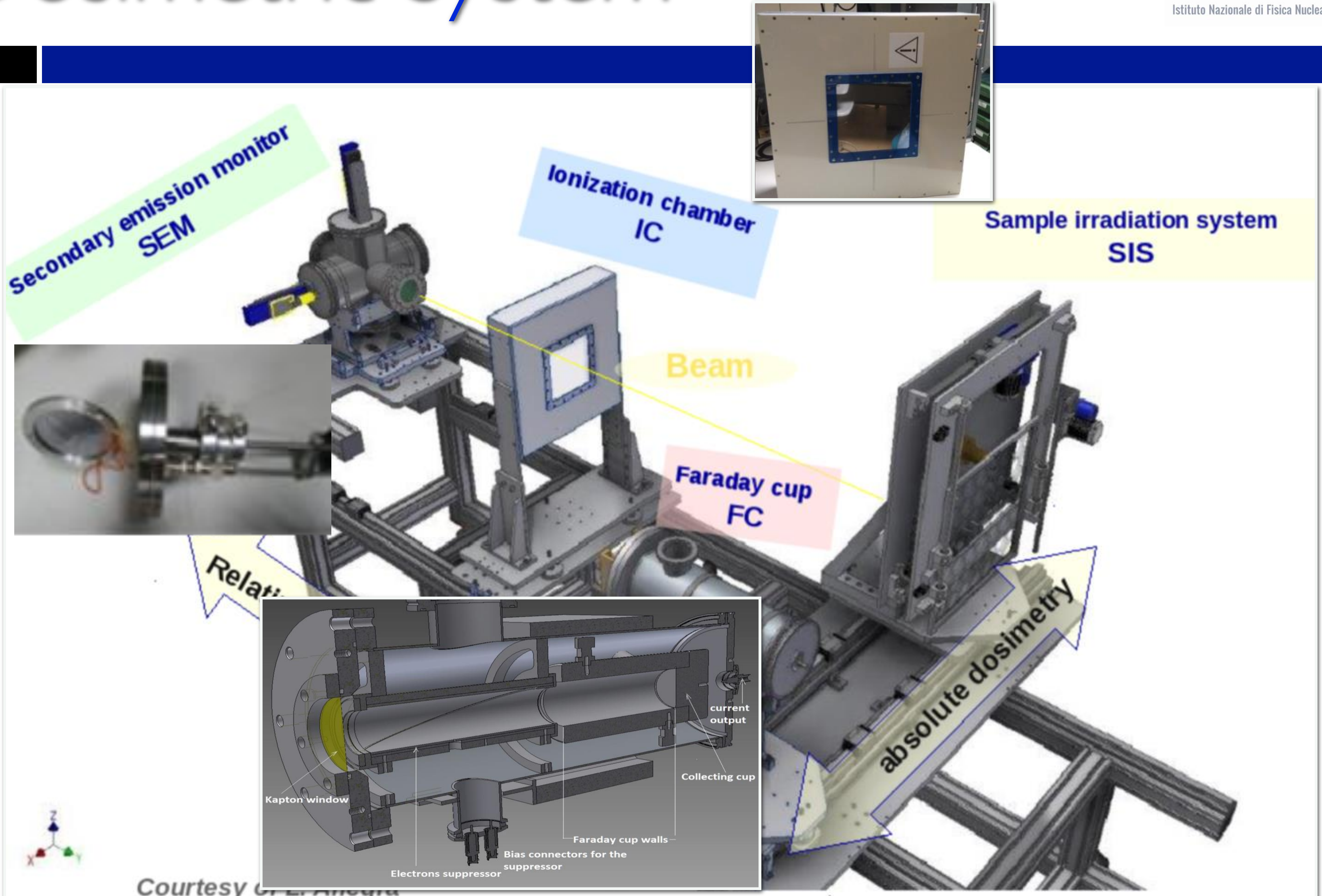


Faraday Cup for absolute dosimetry



Secondary Emission Monitor

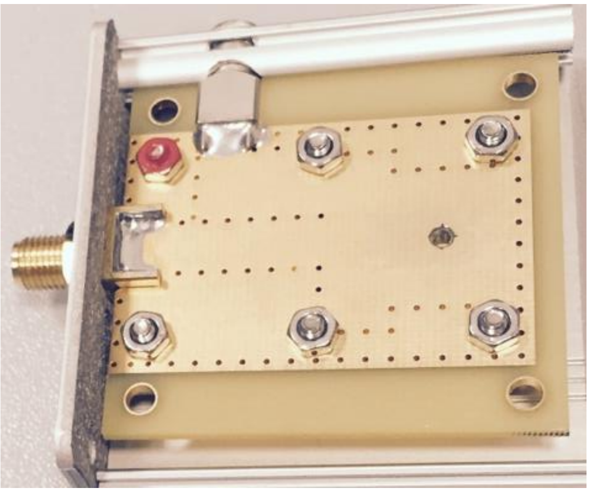
Dosimetric System

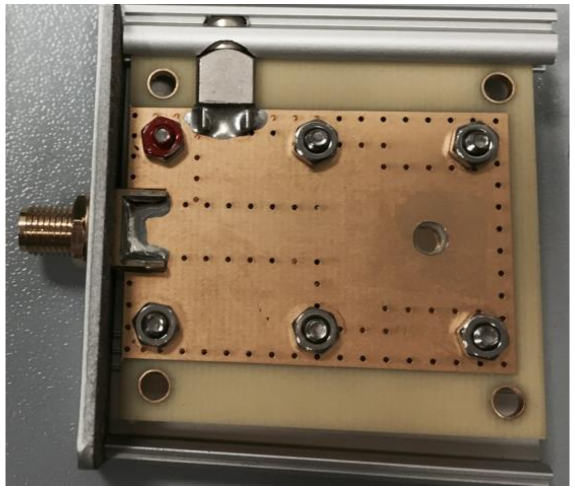


Monitoring System: TOF detectors

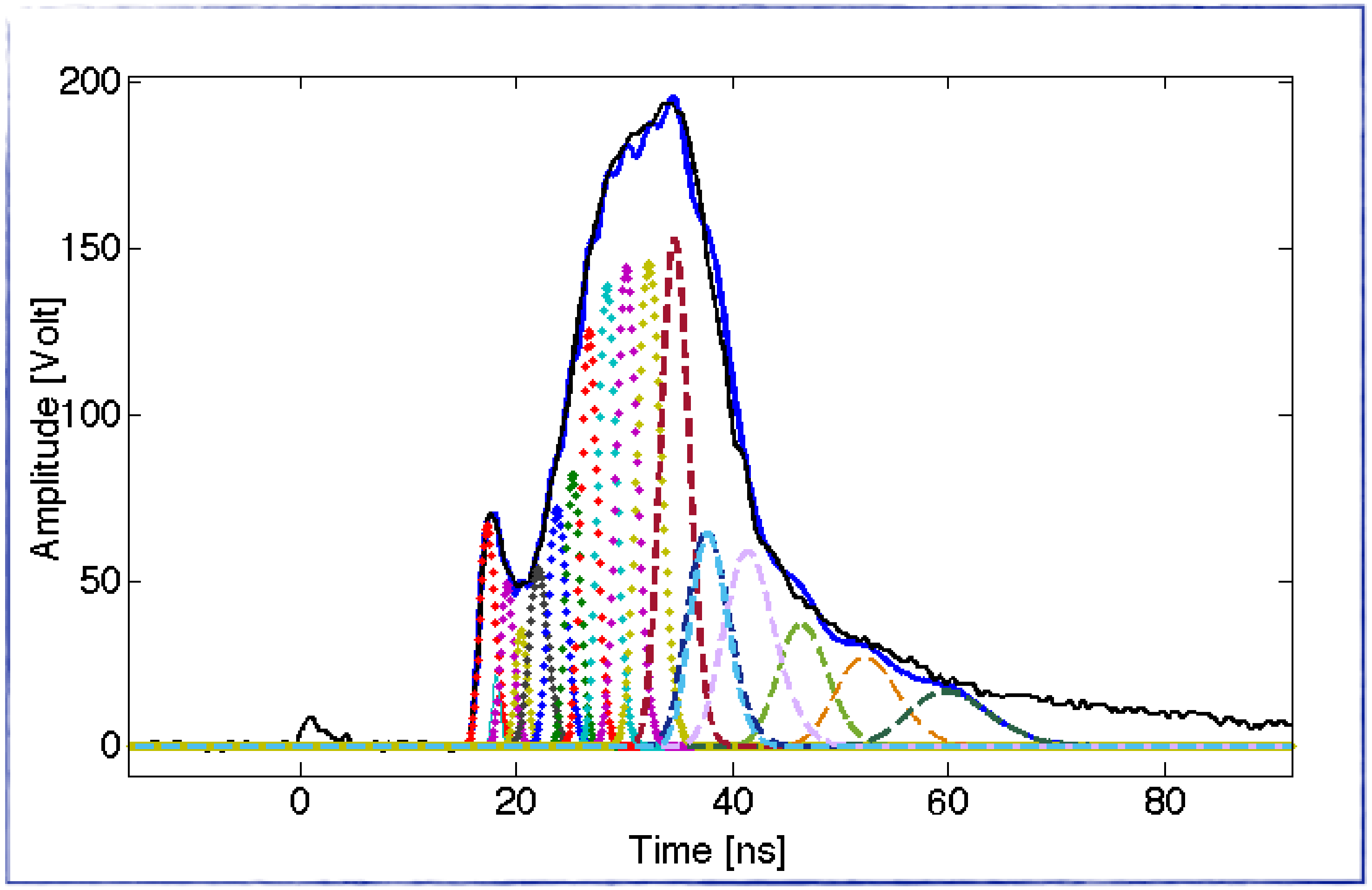
Main goal: *ONLINE proton energy spectrum and fluence measurement along the beam line*

pCVD **sCVD**





- *high radiation diamond detector*
- *linear response for very high intensity (up to 10^9 ppp)*
- *good time resolution*
- *excellent signal-to-noise ratio (low noise)*



Laser-beam hadrontherapy: potential advantages

Reduced cost/shielding

•Laser transport rather than ion transport

(vast reduction in radiation shielding)

•Possibility to reduce size of gantry

Flexibility/modularity

•Possibility of controlling output energy and spectrum

•Possibility of varying accelerated species

•Spectral shaping for direct "painting" of tumor region (no degrader needed)

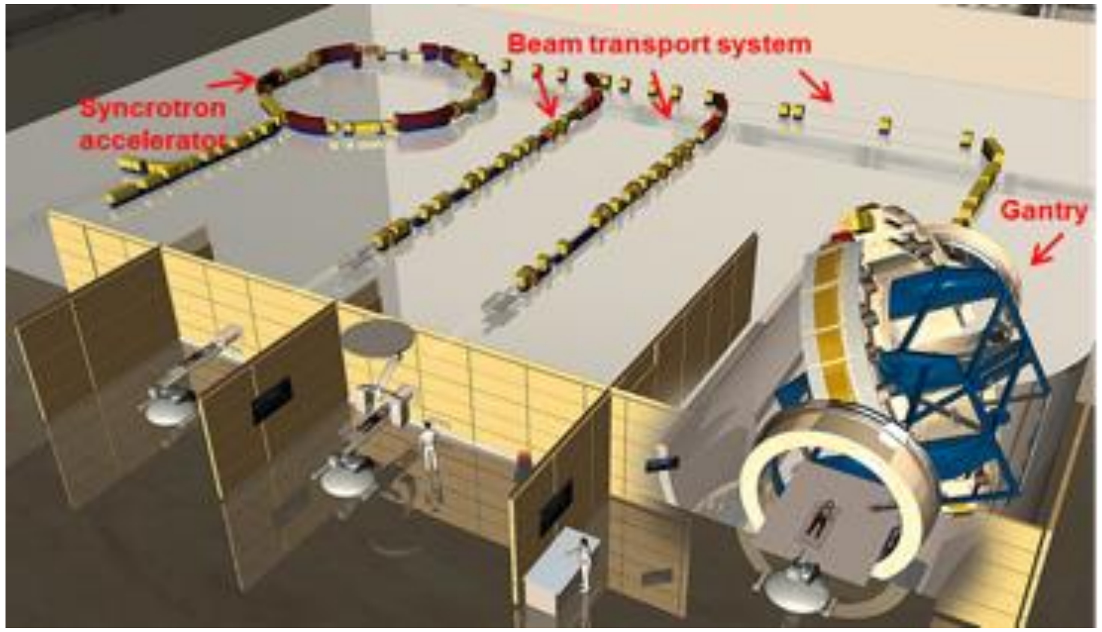
Novel therapeutic/diagnostic options

•Mixed fields: ions, X-rays, electrons, neutrons

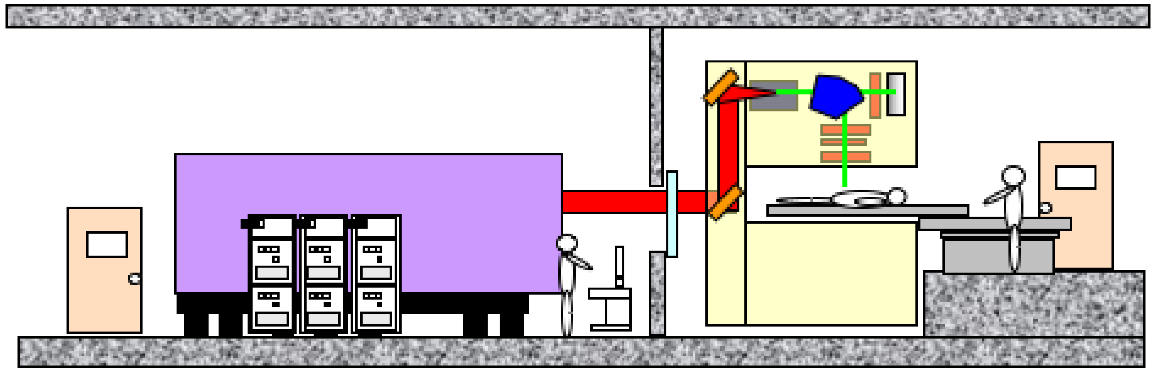
•In-situ diagnosis (PET, X-rays)

Radiobiological advantages

Conventional hadrontherapy



Laser-based hadrontherapy



…. can be of interest for the community

First dosimetry and radiobiology irradiation with laser-driven fast beams

Within June 2020, 30 MeV, 20 ns protons

We are discussing the participation of ELI with ELIMED in the next ENSAR program

A radioisotopes production study is ongoing for new more advantageous schemes and modalities

gliuto, Giuseppina La Rosa, Renata Leanza, Piero Lojacono, Valentina Marchese, Luigi Mi
Salvatore, Tudisco, Filippo Torrisi