ELIMED at ELIMAIA
A Users' open beam line for laser-accelerated ions

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

Motivations for laser-accelerated ions in therapy

INFN Istituto Nazionale di Fisica Nucleare

nature REVIEWS CLINICAL ONCOLOGY

Review Article | Published: 21 May 2013

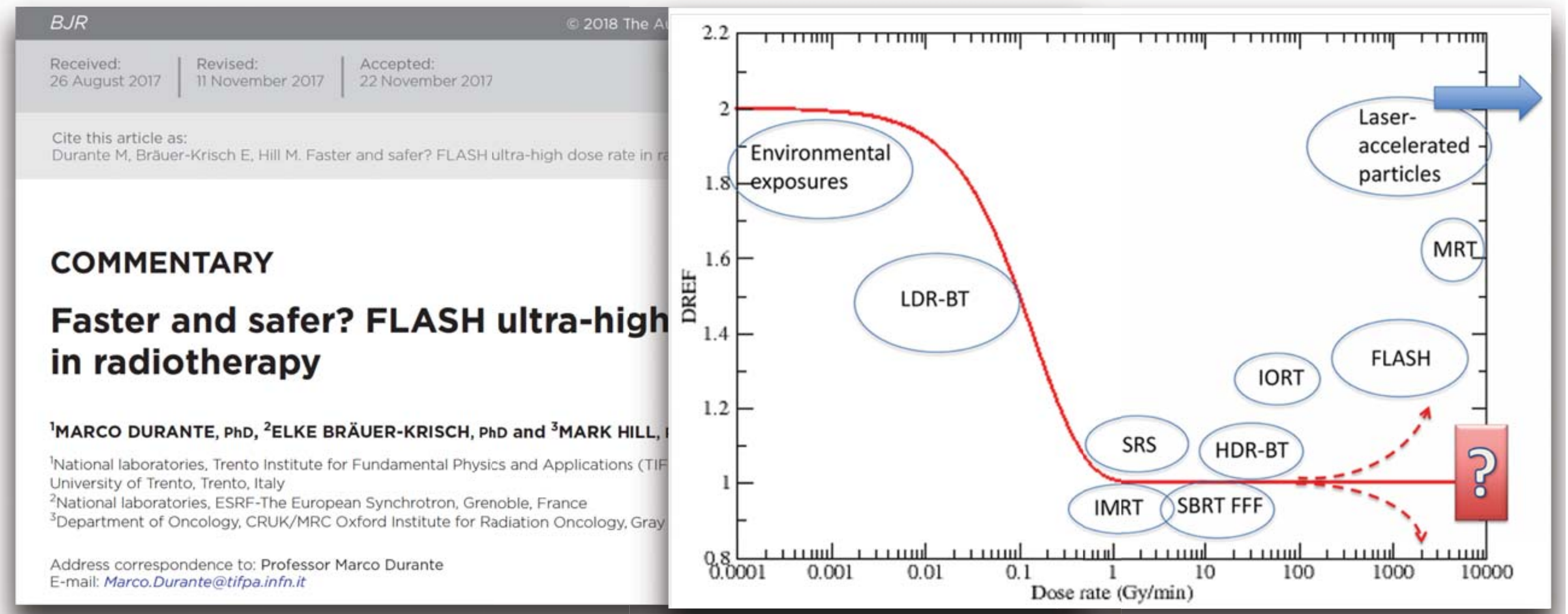
Charged particle therapy—opti
challenges and future directio

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]

Motivations for laser-accelerated ions in therapy



Motivations for laser-accelerated ions

- Potential reduction of dimensions and costs (more for Z > 1 ion beams)
- Study of unprecedented irradiation regimes
- Multi ions irradiation
- Space applications
- New schemes and approaches for radioisotope productions
- Cultural heritage (project funded by ELI)

INTERNATIONAL JOURNAL of PARTICLE THERAPY

New Ions for Therapy

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Life Sciences in Space Research 19 (2018) 68–75
Contents lists available at ScienceDirect
Life Sciences in Space Research
journal homepage: www.elsevier.com/locate/lssr

Dose calculations in a cell monolayer for high-throughput irradiation with proton beams generated by PW lasers for space applications

Mariana Bobeica[a,*,1], Sohichiroh Aogaki[a,1], Theodor Asavei[a], Mihail O. Cernaianu[a], Petru Ghenuche[a], Dan Stutman[a,b]
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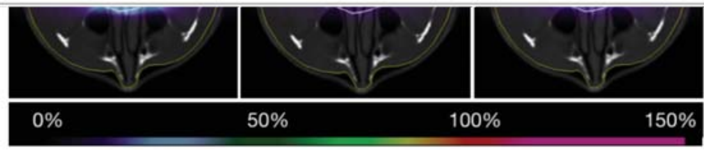
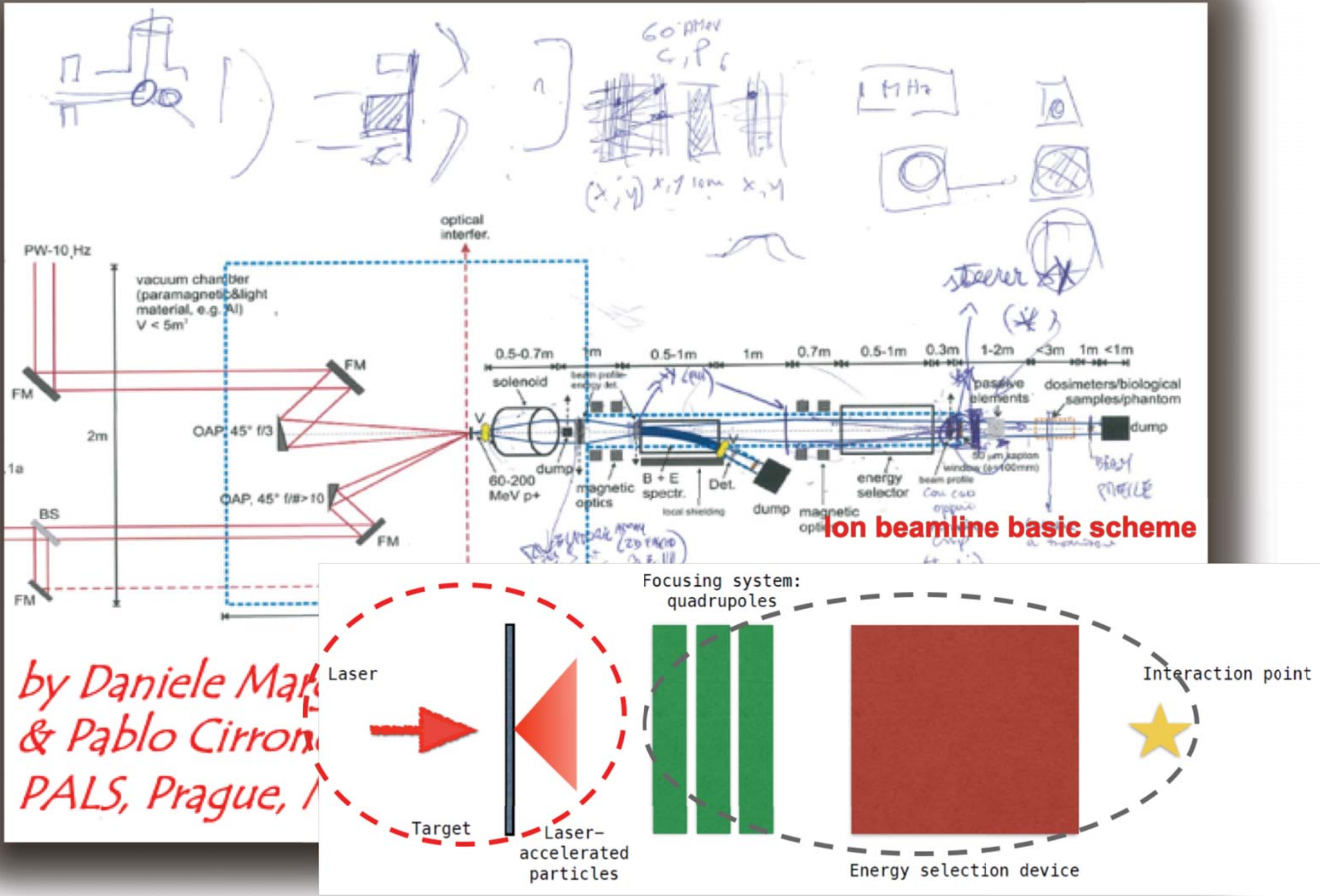


Figure 4.9.: Biologically optimized four-field ^{16}O + ^{4}He plan for a partially hypoxic skull base chordoma (scenario 1). The tumor and brainstem are marked with white and yellow lines, respectively. The scale represents the relative dose received by the tissue, compared to the prescribed biological dose of 2 Gy. (a) - total biological dose, (b) and (c) - contributions of ^{16}O and ^{4}He, (d) - total physical dose, (e) and (f) - contributions of ^{16}O and ^{4}He.

ELIMED beam line at ELIMAIA



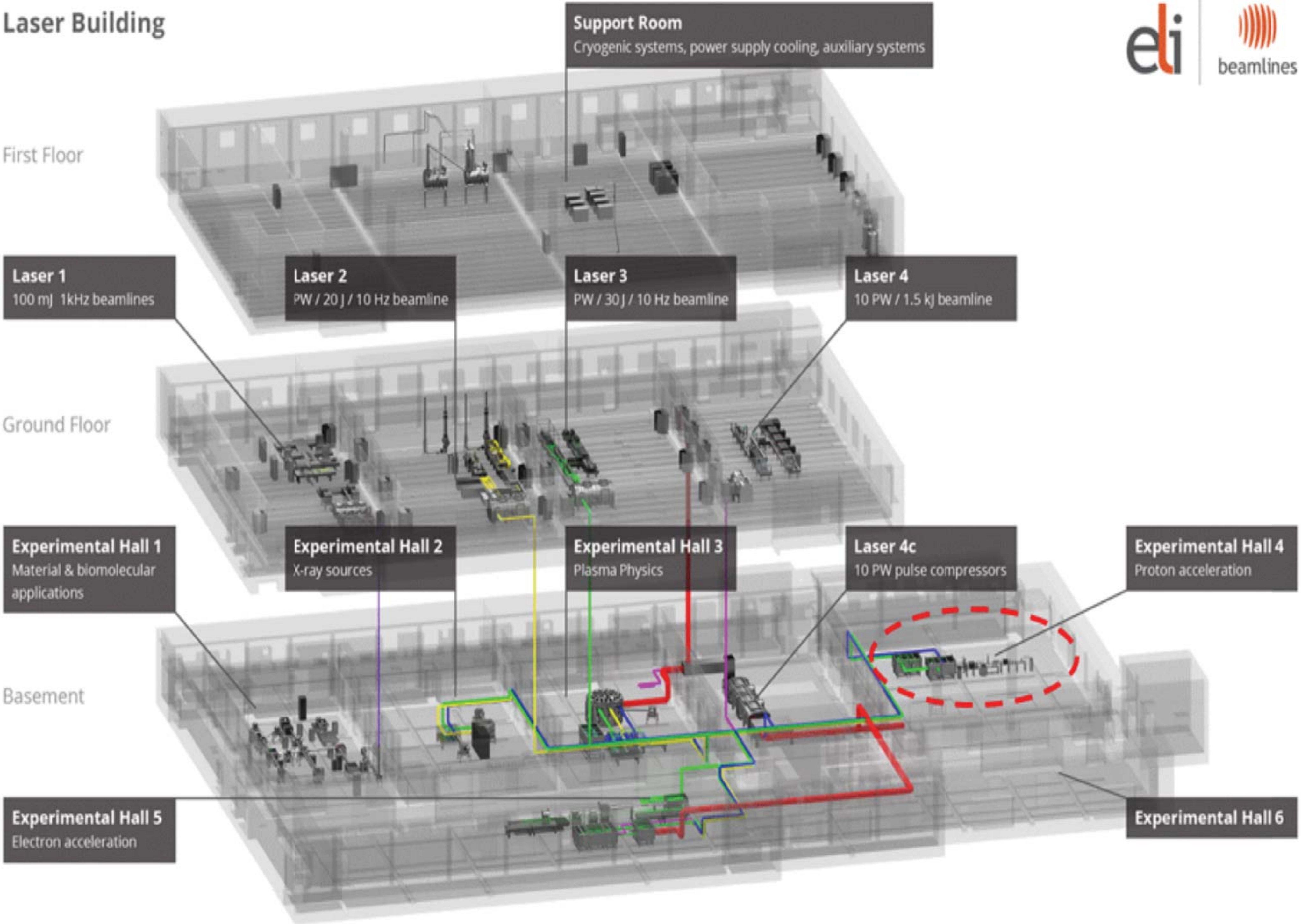
PW-10 Hz
vacuum chamber (paramagnetic&light material, e.g. Al) V < 5m³
optical interfer.
FM
2m
OAP, 45° f/3
OAP, 45° f/#>10
BS
FM
FM
0.5-0.7m
1m
0.5-1m
1m
0.7m
0.5-1m
0.3m
1-2m
<3m
1m
<1m
solenoid
60-200 MeV p+
dump
magnetic optics
B + E spectr.
Det.
dump
energy selector
passive elements
dosimeters/biological samples/phantom
dump
Ion beamline basic scheme
by Daniele Mar
& Pablo Cirron
PALS, Prague,
Focusing system: quadrupoles
Laser
Target
Laser-accelerated particles
Energy selection device
Interaction point

ELIMAIA and ELIMED mission

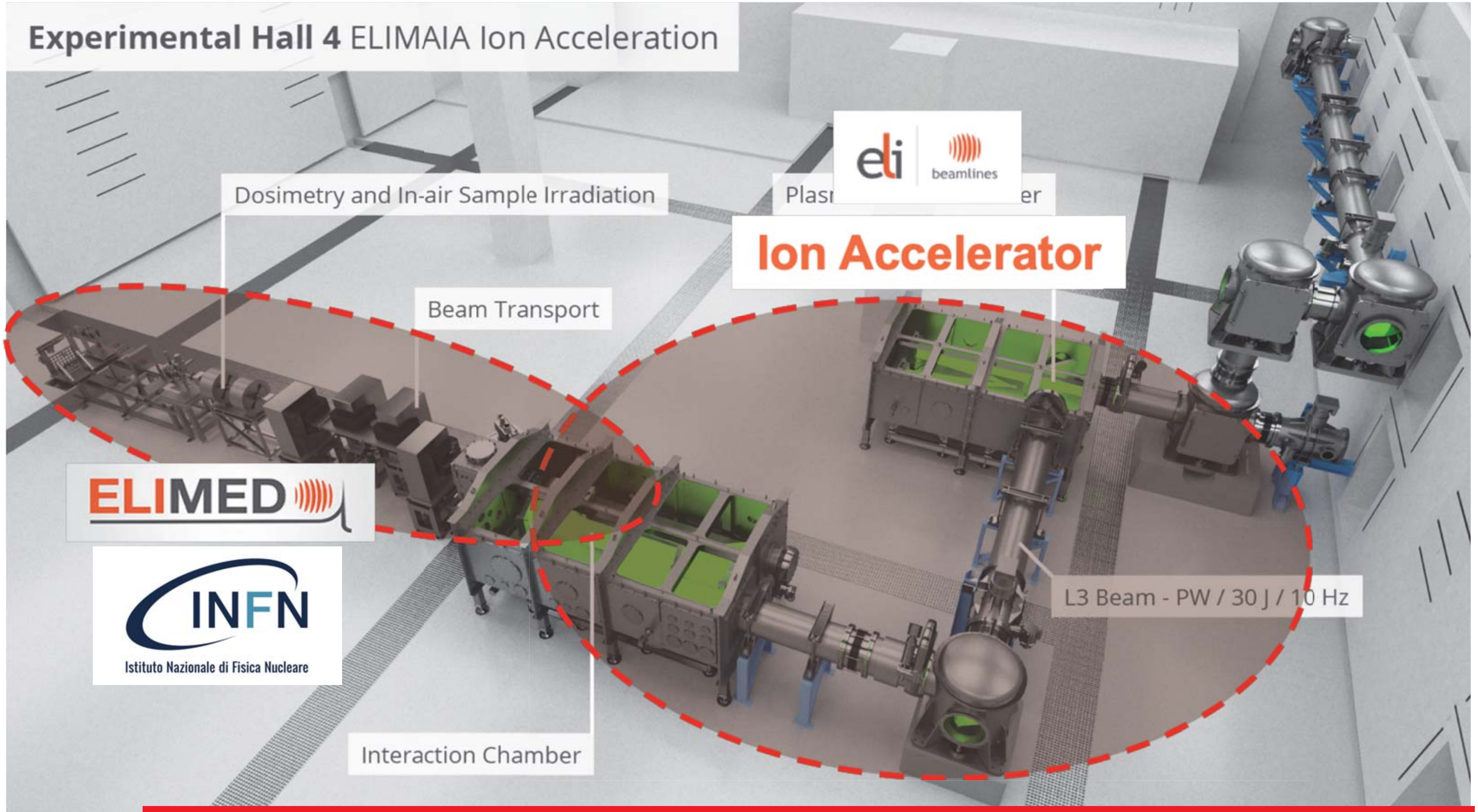
- **The ELIMAIA beamline *(ion accelerator + user station)***
  ELI Multidisciplinary Applications of laser-Ion Acceleration
  Dual bid:
  - provide an experimental platform to users who want to develop laser driven ion accelerators using multi-PW, high rep. rate lasers
  - provide laser driven ion beams with unique features to a broad user community for applications in biomedicine, chemistry, material science

- **The ELIMED line *(transport and dosimetry)***
  ELI MEDical applications
  Dual bid:
  - carry out transport and absolute dosimetry of laser-accelerated ion beams with ultrahigh dose rate
  - gather a user community with future goal of clinical applications using a compact approach to cancer therapy (radiobiologists, medical doctors)

Laser Building



ELIMAIA: a Users' beam line

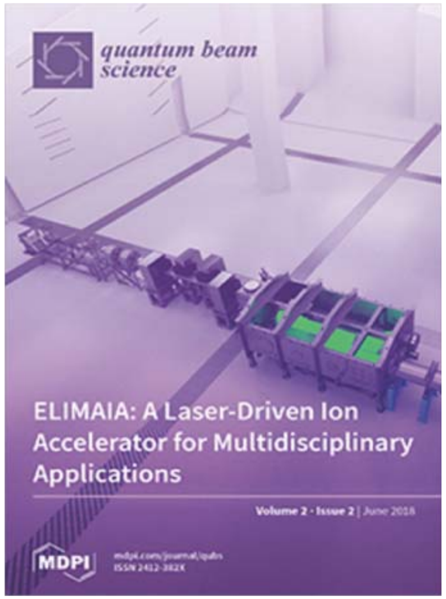


See the invited talk by Dr Daniele Margarone Laser-driven ion acceleration and applications at the Extreme Light Infrastructure (ELI) Session 8, Wednesday 8

Let focus on the ELIMED section of ELIMAIA (transport and dosimetry)

ELIMED installation time-elapse

The beamline installation was completed in July 2018



D. Margarone, G.A.P. Cirrone et al.,

"ELIMAIA: A Laser-Driven Ion Accelerator for Multidisciplinary Applications", Quantum Beam Sci. 2 (2018) 8

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
Renata Leanza

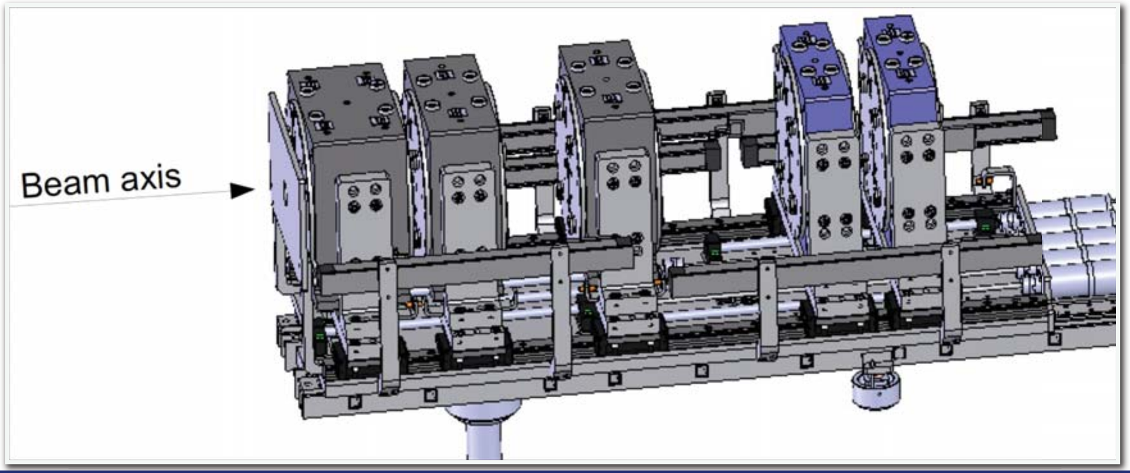
November 2018

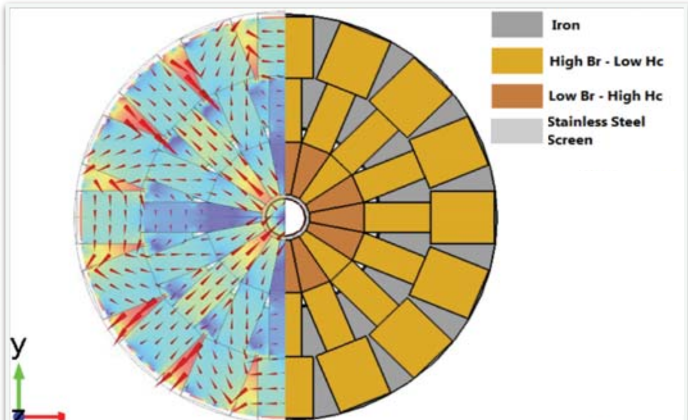
Mario Maggiore
Rosanna Manna
Letizia Marchese
Nino Maugeri
Giuliana Milluzzo
Nello Salamone
Roberto Pellegrini
Giada Petringa
Pietro Pisciotta
Salvo Pulvirenti
Daniele Rizzo
Francesco Romano
Francesco Schillaci
Valentina Scuderi
Salvatore Vinciguerra
Emilio Zapallà

See work by Francesco Schillaci on the Wednesday poster session:
Advanced beam transport solutions for ELIMAIA: a user oriented laser-driven ion beamlines

Focusing and collecting

five permanent magnets quadrupoles, 100 T/m gradient



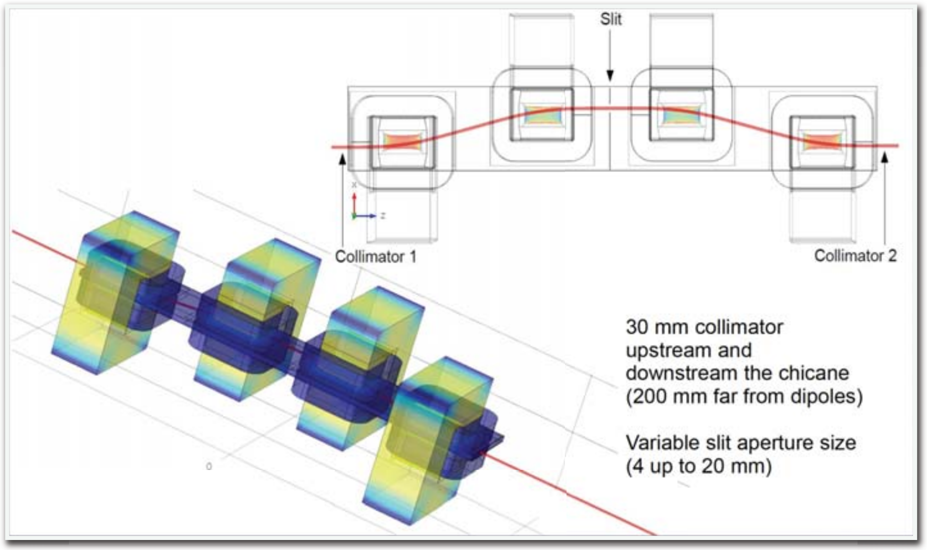


F. Schillaci et al., JINST 10 T12001 (2015)

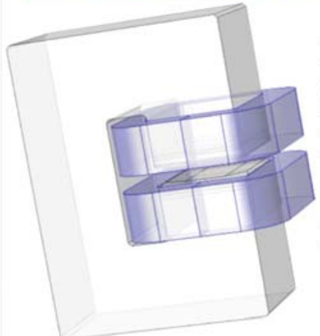
Proton and carbon beams up to 250 MeV and 70 AMeV, respectively

See work by Francesco Schillaci on the Wednesday poster session:
Advanced beam transport solutions for ELIMAIA: a user oriented laser-driven ion beamlines

Energy selection

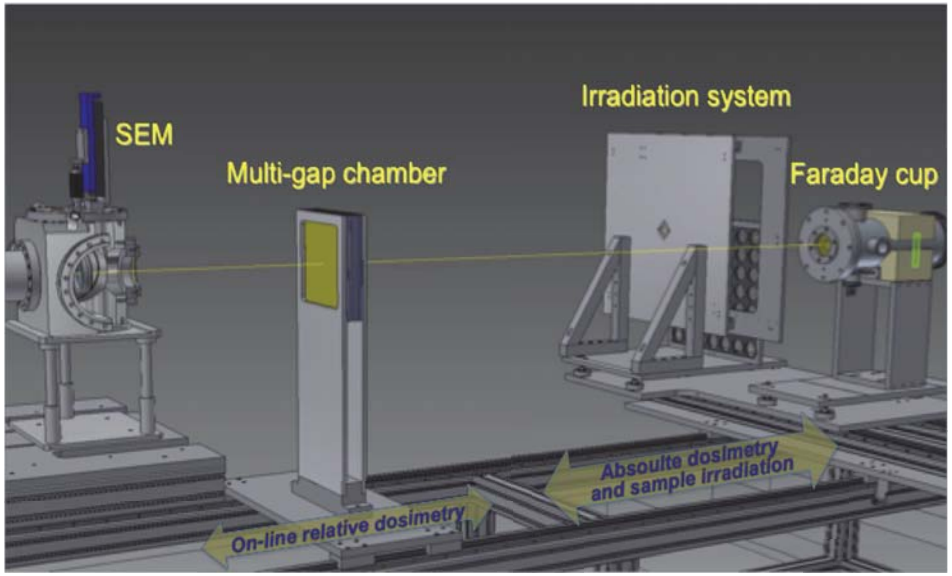


n° of Dipoles	B field	Geometric length	Effective length	Gap
4	0,085 – 1,2 T	400 mm	450 mm	59 mm
Good Field region (GFR)	**Field uniformity**	**Curvature radius**	**Bending angle**	**Drift between dipoles**
100 mm	< 0,5 %	2,5293 m	10,10° (176,3 mrad)	500 mm



- 400 mm length
- 300 mm pole width
- 59 mm gap
- 100 mm GFR
- Magnet efficiency 98%
- 115.5x168 coil section (11x16turns, 0,5 mm of insulator, 6 mm water channel)
- Max current ~200 A/turn
- Total weight ~3 Tons

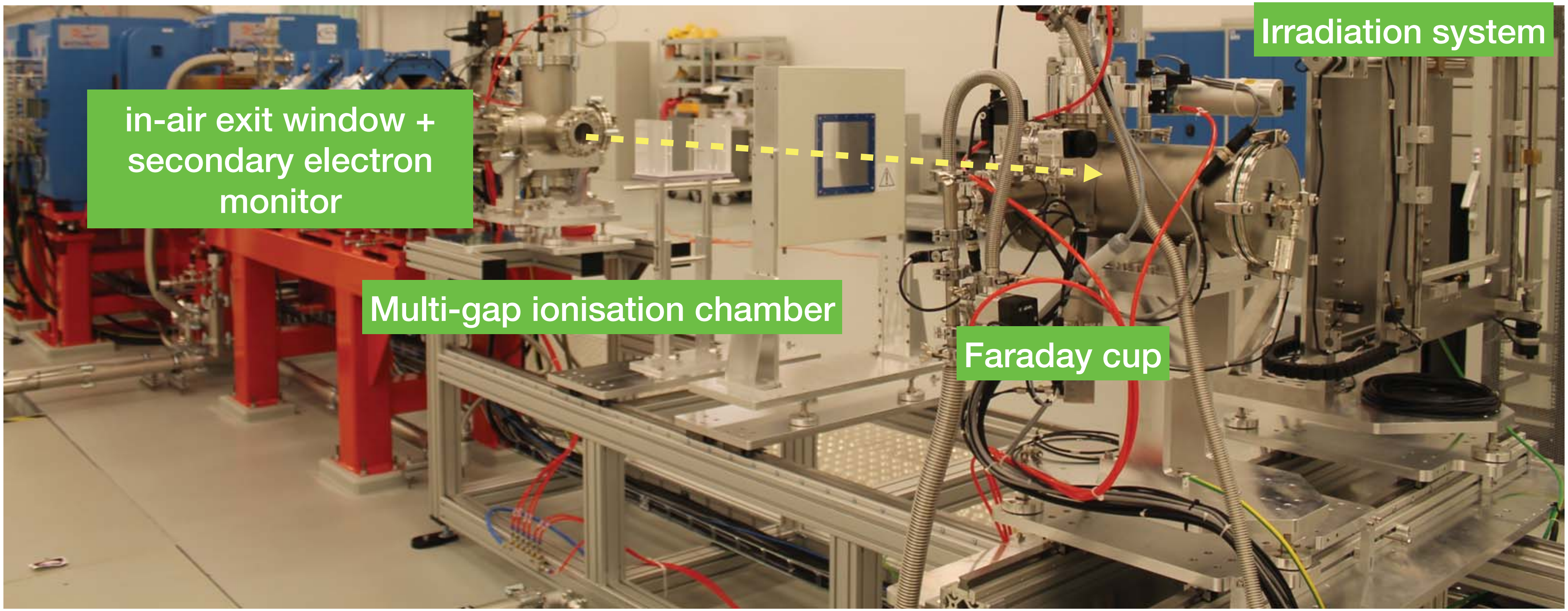
Relative and absolute dosimetry



Dose-rate independent approaches
Correction of recombination effects
Off-line and real-time measure of depth dose distributions
No code of practice available, at moment

Dosimetric approaches at ELIMED

Dosimetric section in-air



Particle fluence and spectroscopy with CR39 (first phase, low-energy)

Energy spectra with Gafchromic films (calibrated with protons between 15 and 100 MeV)

Silicon Carbide telescope for real-time, shot-to-shot measure of the Bragg peak

Phase 1, playing with PIC simulations and Monte Carlo

Flat plastic 300 nm thick target

3D PIC simulation by Martina Zakova (ELI-Beamlines)

Space and time profile: gaussian

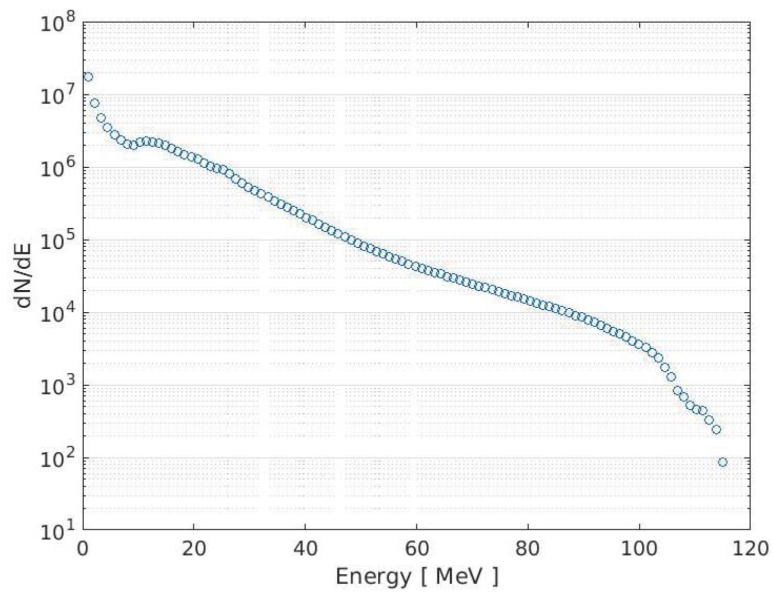
Pulse duration 30 fs

Beam width (FWHM) 3 um

Intensity 5E21 W/cm2

Laser wavelength 800 nm

Laser incidence 15°



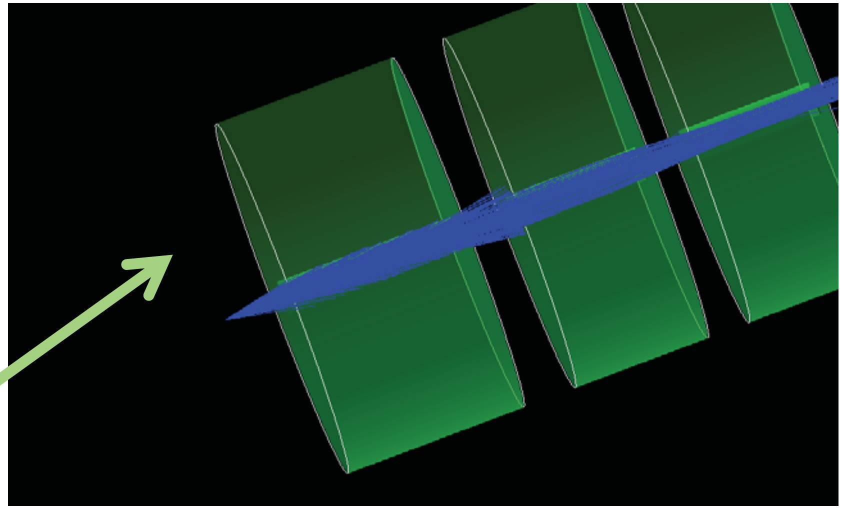
Phase 1, playing with PIC simulations, 60 MeV case

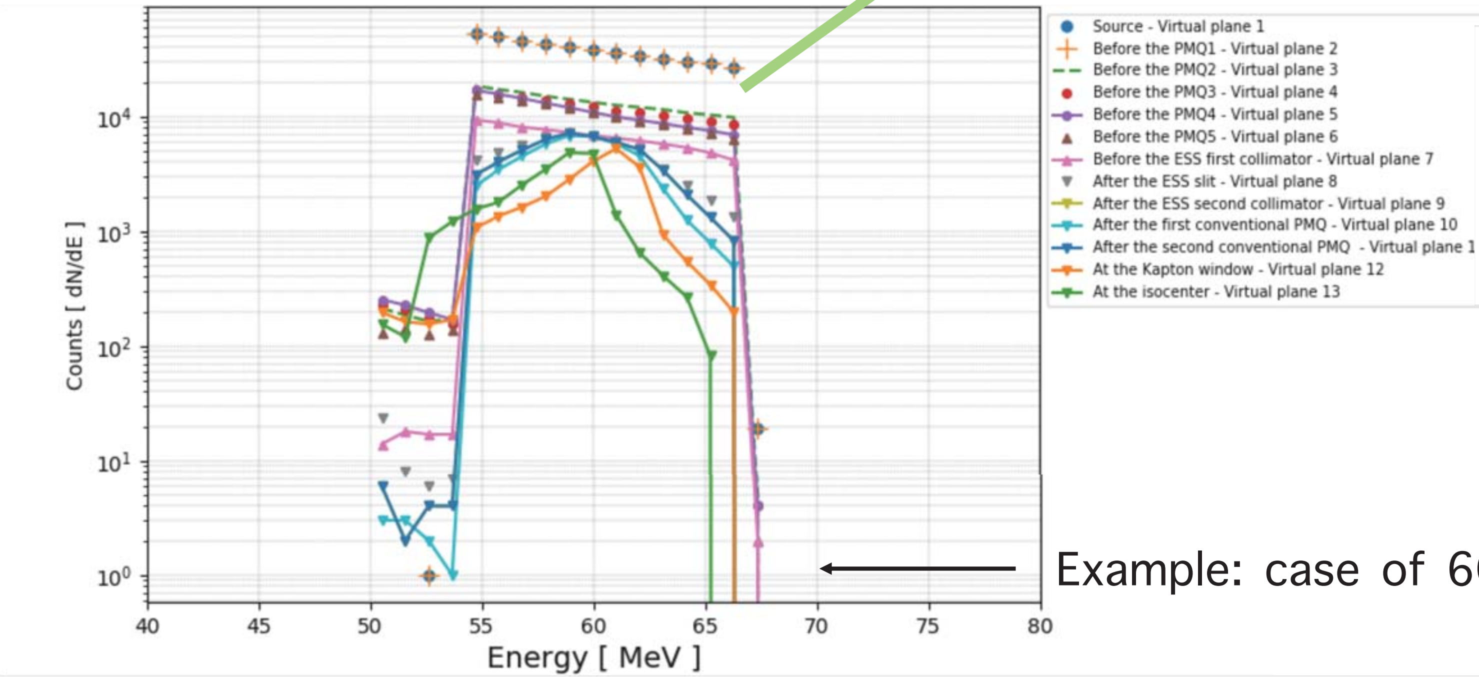
More than 80% is loss on the first quadrupole

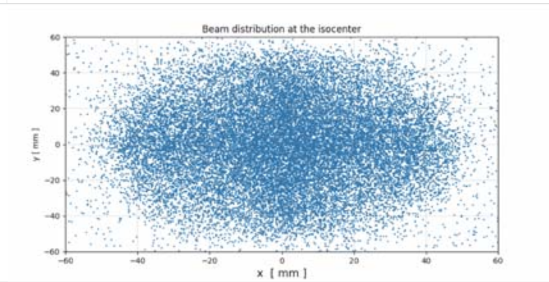
Around than 10 % in the rest of beamline

10 % total transmission

In the worst simulated conditions: **0.1 Gy per shot**

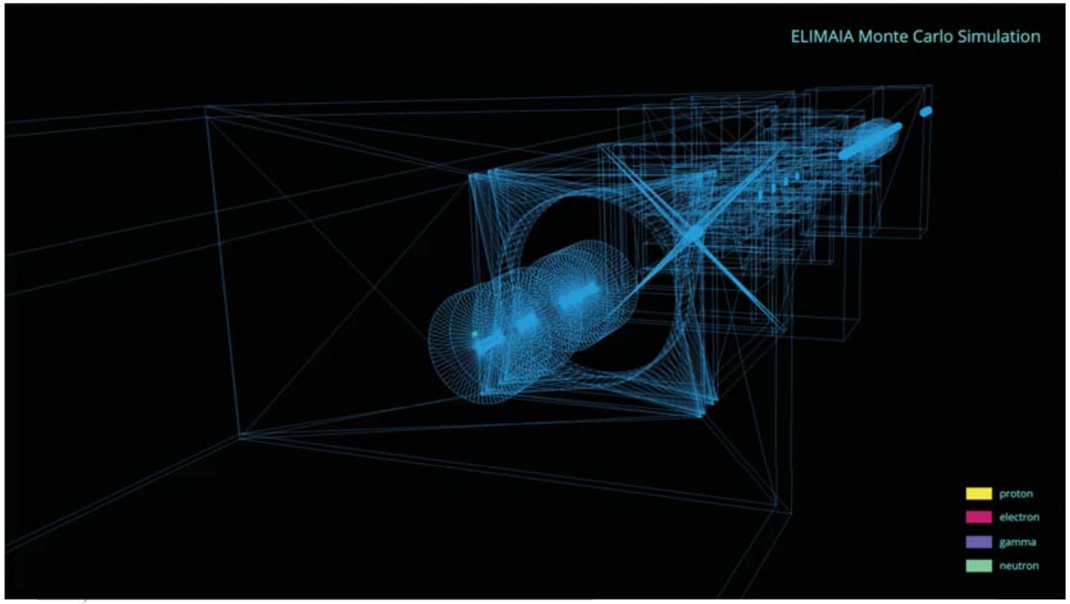


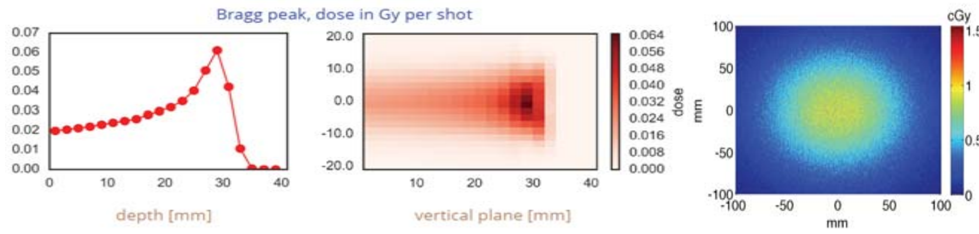


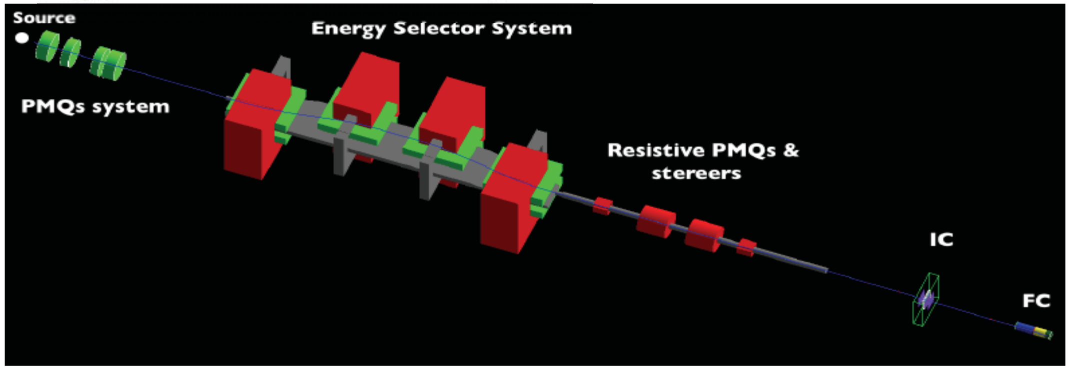


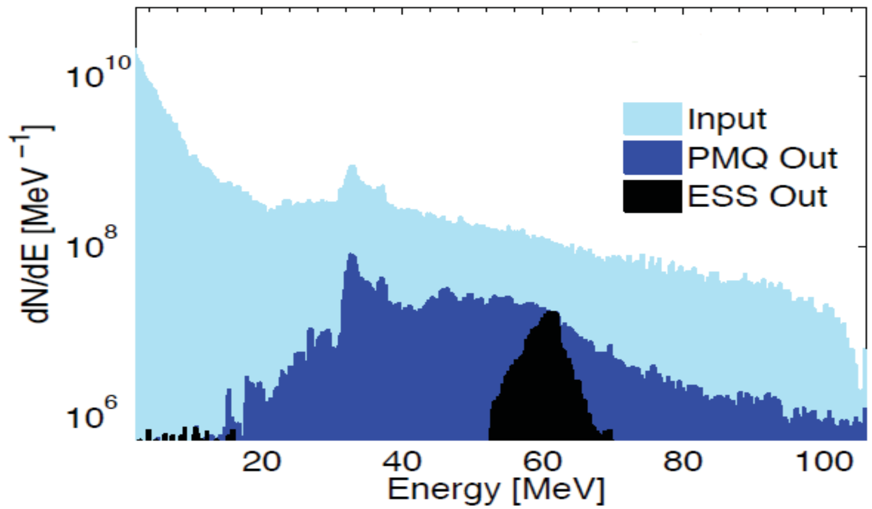
Example: case of 60 MeV protons selected

Coupling PIC with Monte Carlo

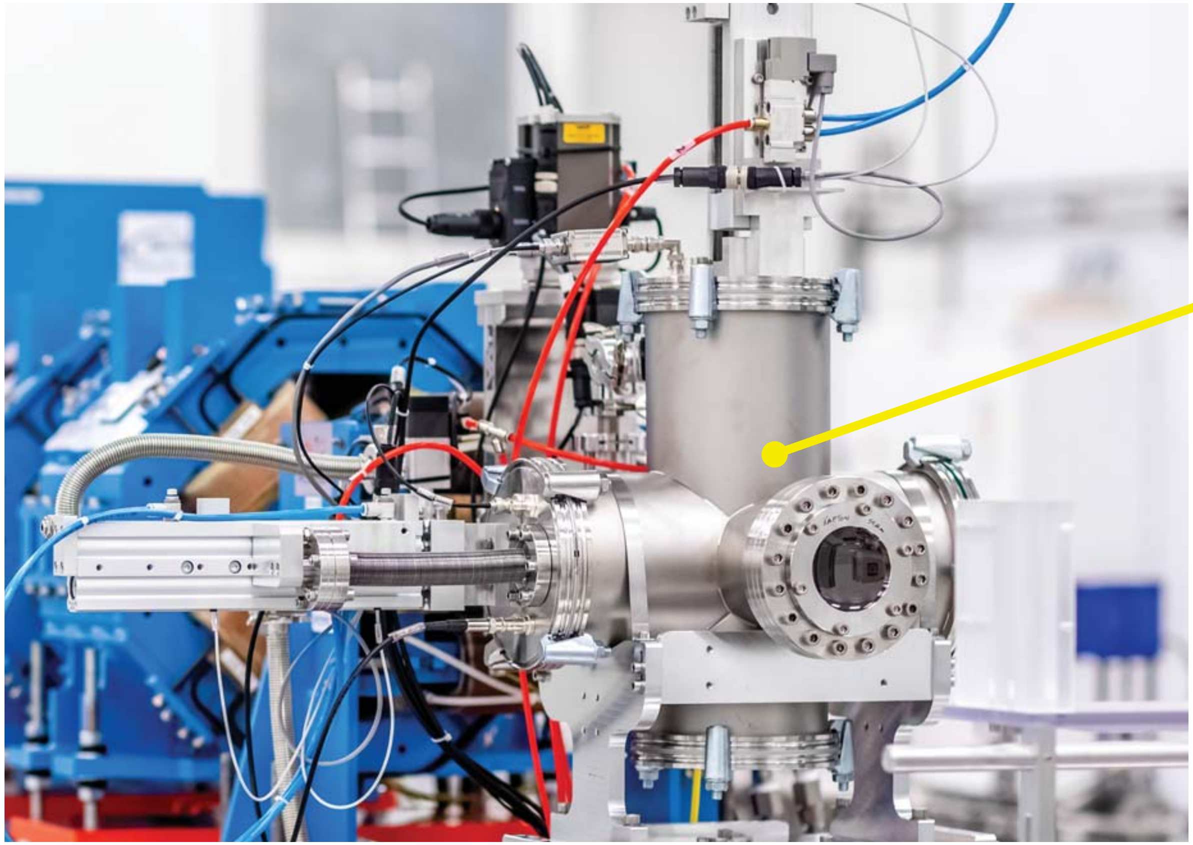


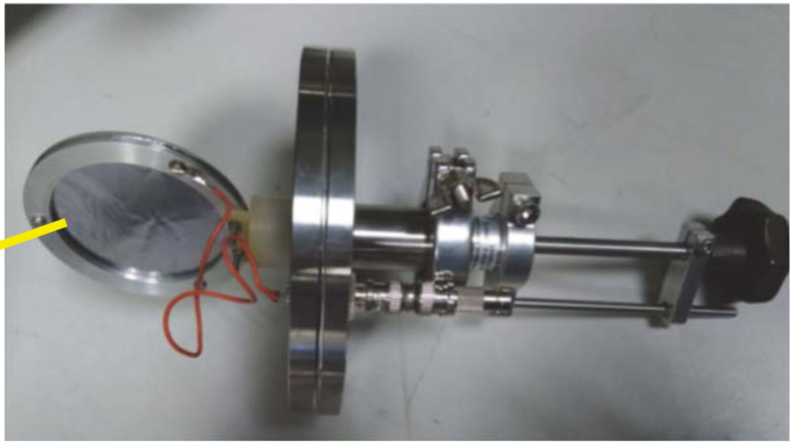






Secondary Electron Monitoring (SEM)





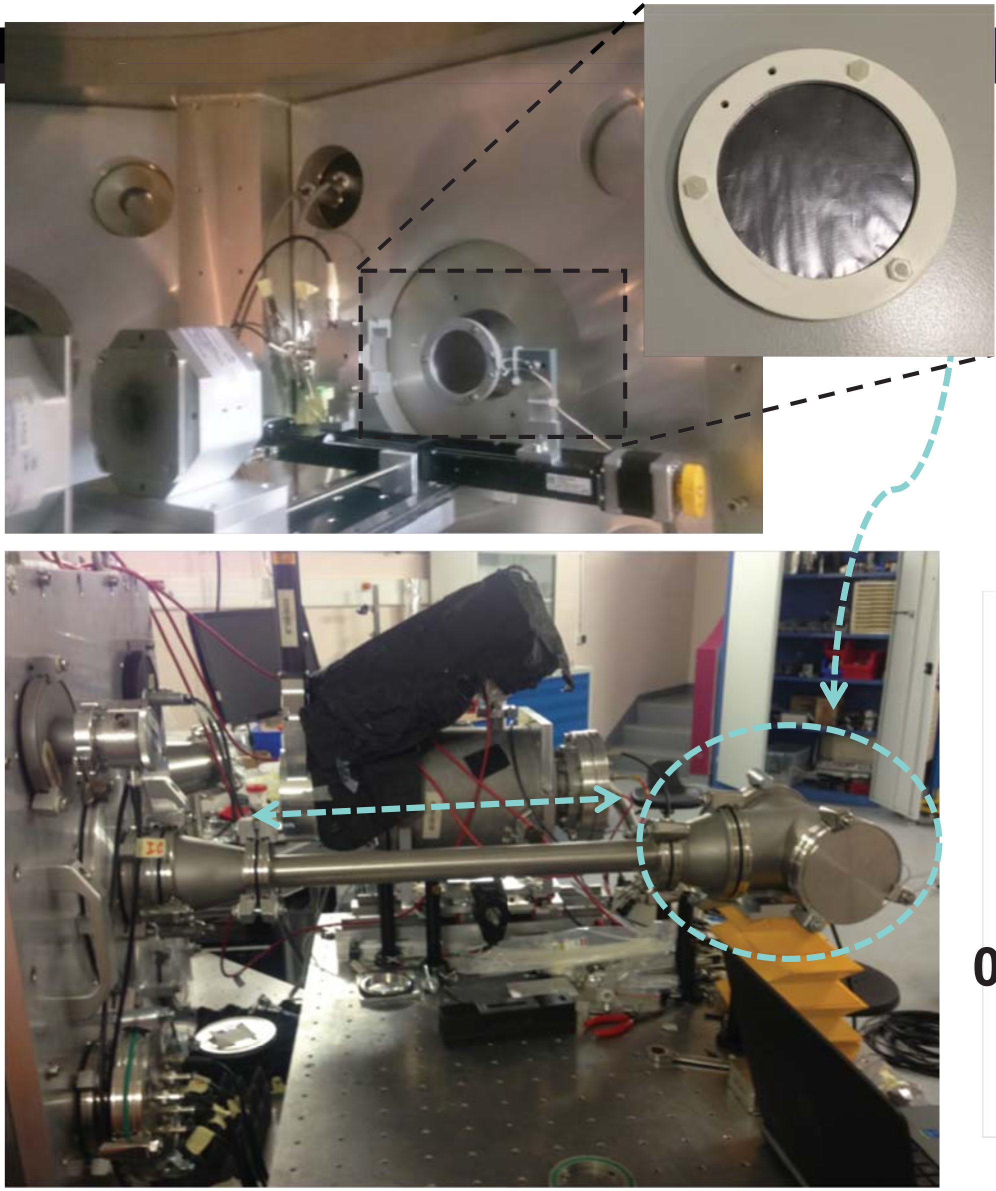
15 um Tantalum foil; it will act:

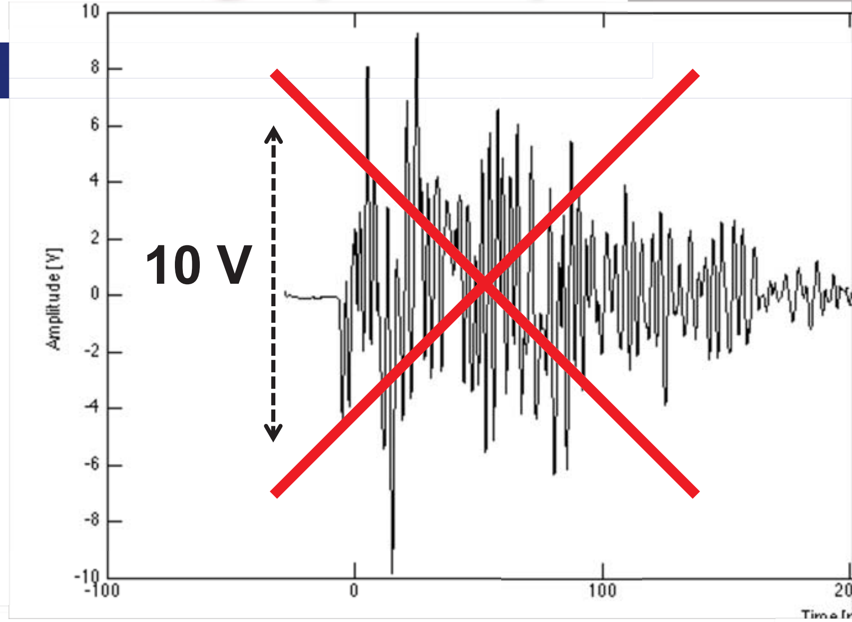
Time Of Fligth configuration

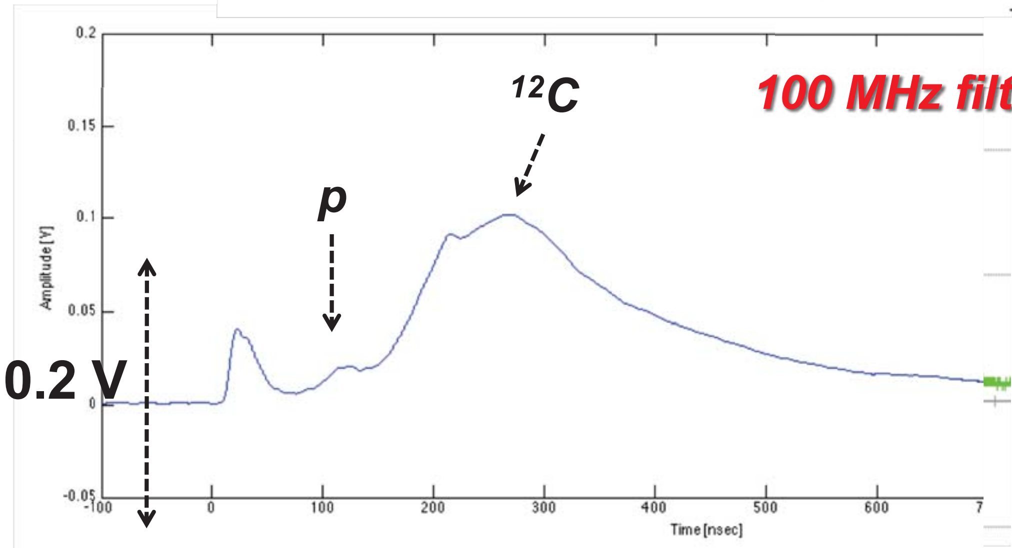
Charge integration for normalisation purposes

Scattering foil for beam diffusion

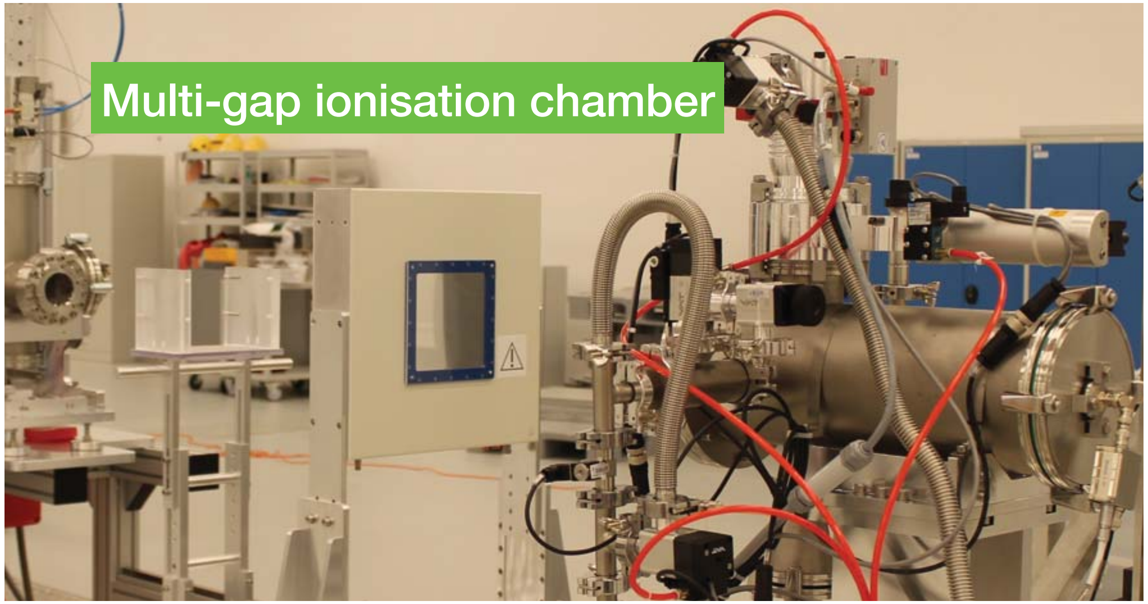
Secondary Electron Monitoring (SEM)







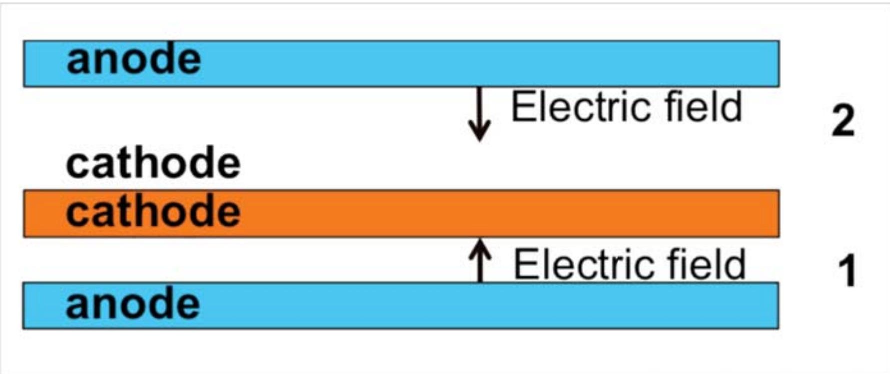
Multi-gaps chambers + Faraday cup



$$f_1 = \frac{Q_1}{Q_1^{sat}} \qquad f_2 = \frac{Q_2}{Q_2^{sat}}$$

$$\frac{f_1}{f_2} = \frac{Q_1}{Q_1^{sat}} \cdot \frac{Q_2^{sat}}{Q_2} = \frac{Q_1}{Q_2} \cdot \frac{Q_2^{sat}}{Q_1^{sat}} = \frac{Q_1}{Q_2} \cdot const$$

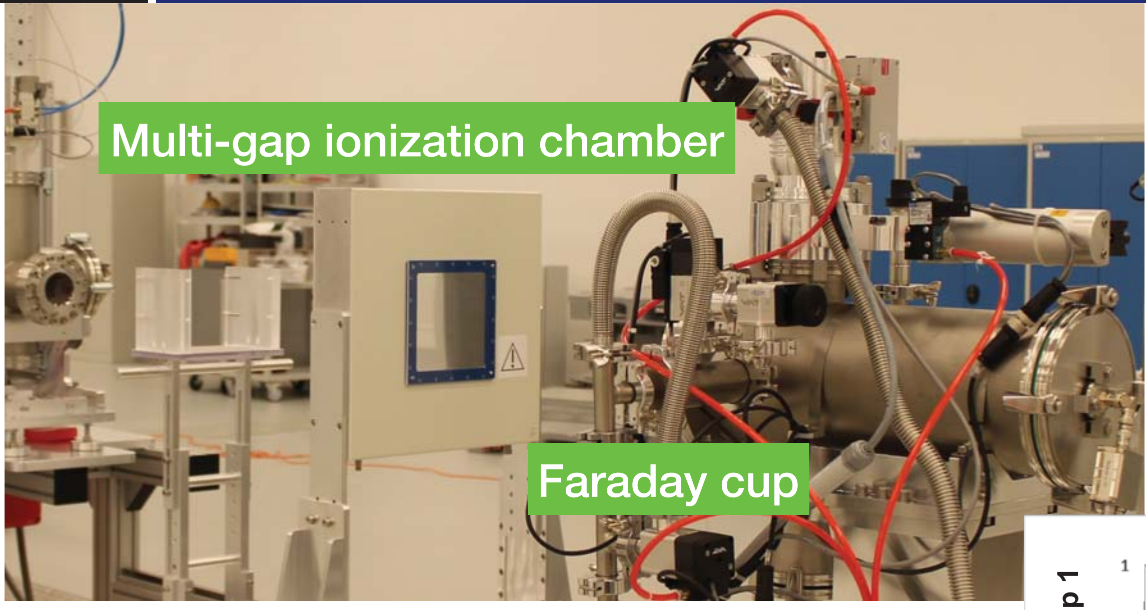
Q_1^{sat} and Q_2^{sat}
are derived from a fit of the
Boag-theory for pulsed beams



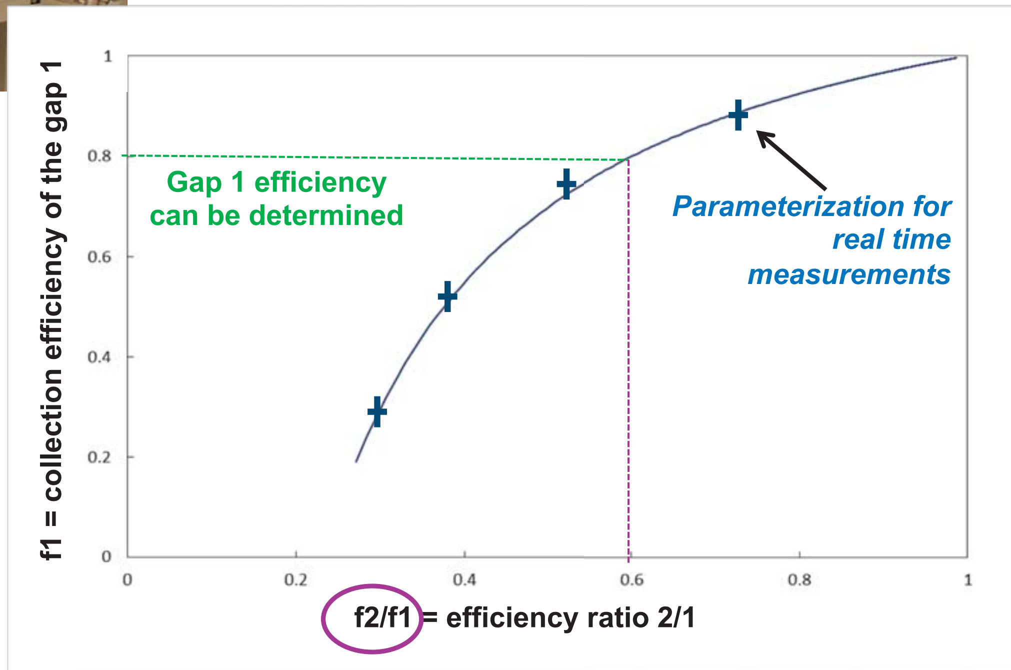
$$f = \frac{1}{u}\ln(1+u)$$

$$u = \frac{\alpha/e}{K1+K2} \frac{n_0 d^2}{V}$$

Multi-gaps chambers + Faraday cup



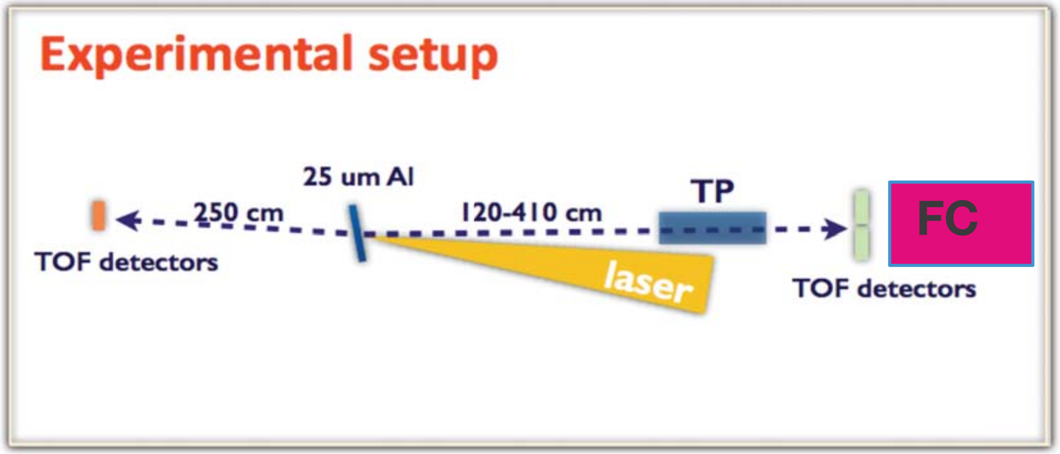
Once f1 is calculated
Q1, for that shot, is evaluated
And f1 is connected to an absolute dose thanks to the Faraday cup measure

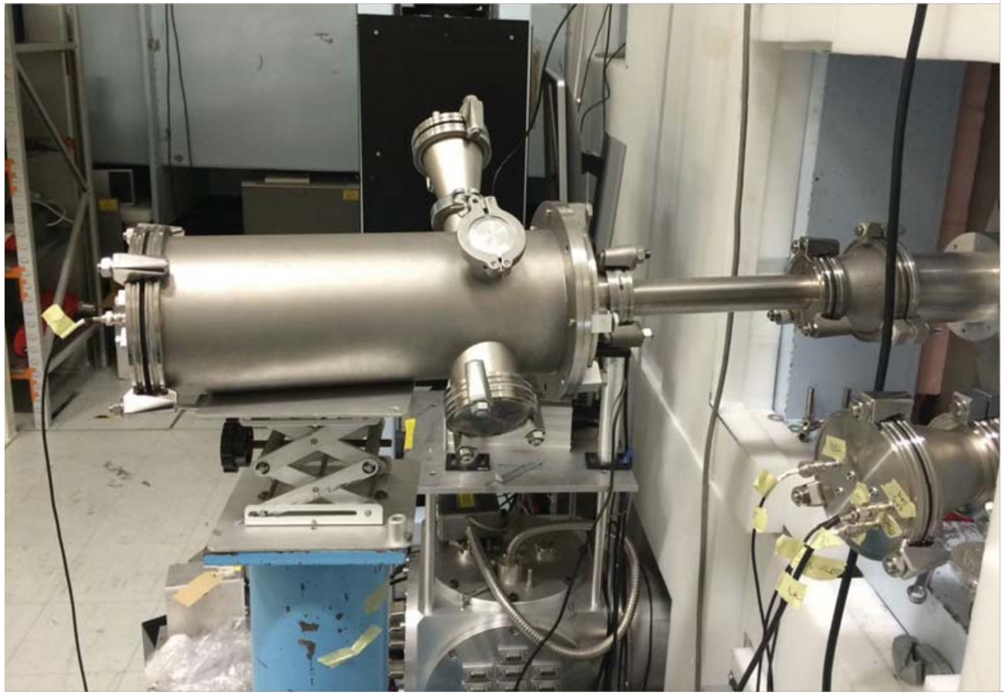


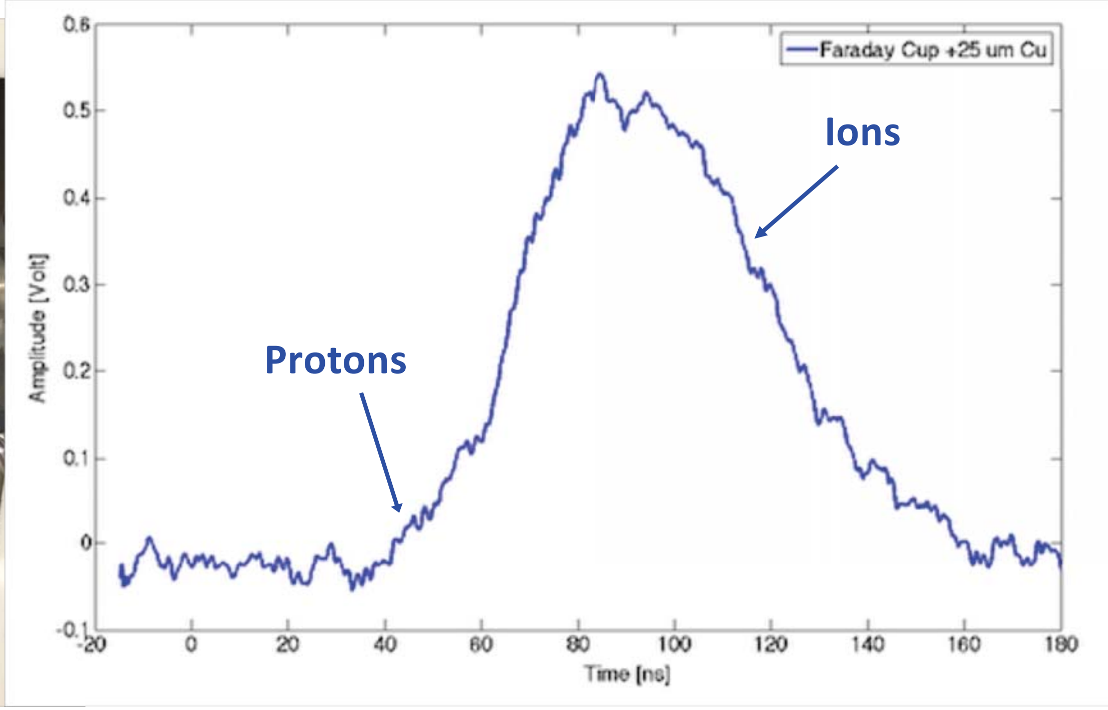
This curve is experimentally derived for different beam dose-rates

FC preliminary test with the VULCAN PW laser @ RAL (UK)

VULCAN Laser parameters
Power: 1 PW
Intensity:10^{21} W/cm^2
Energy: 650 J
Time pulse: 500 fs
Target: 25 um Al





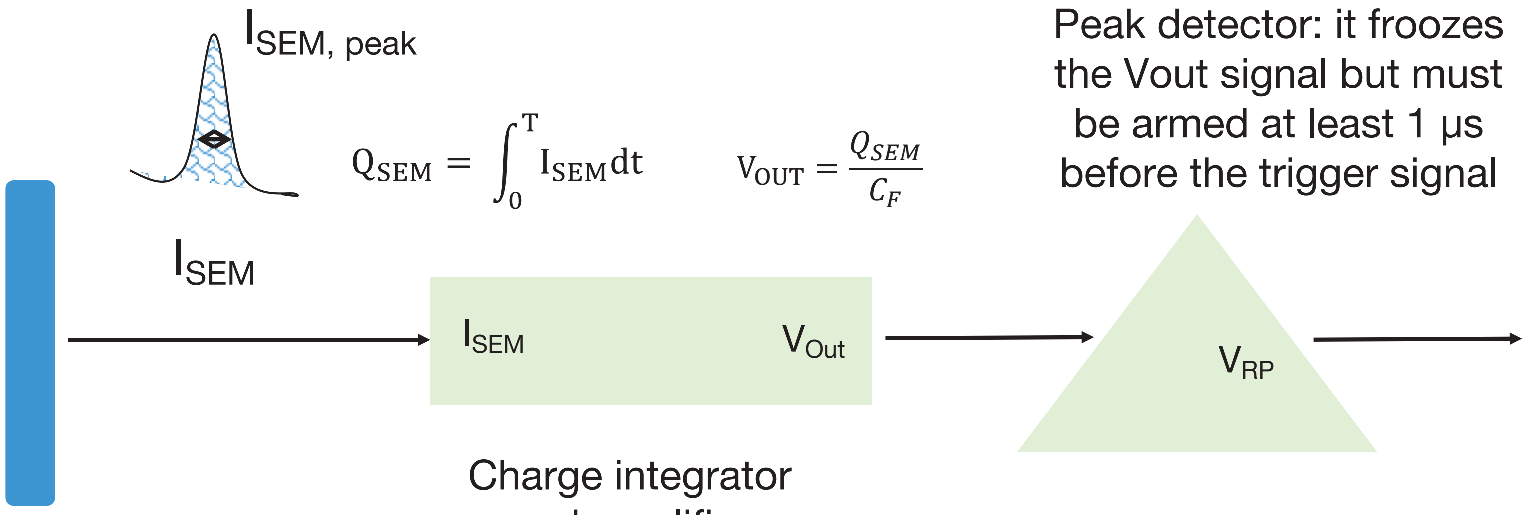


Data acquisition for absolute dosimetry

Δt must be < 1 µs

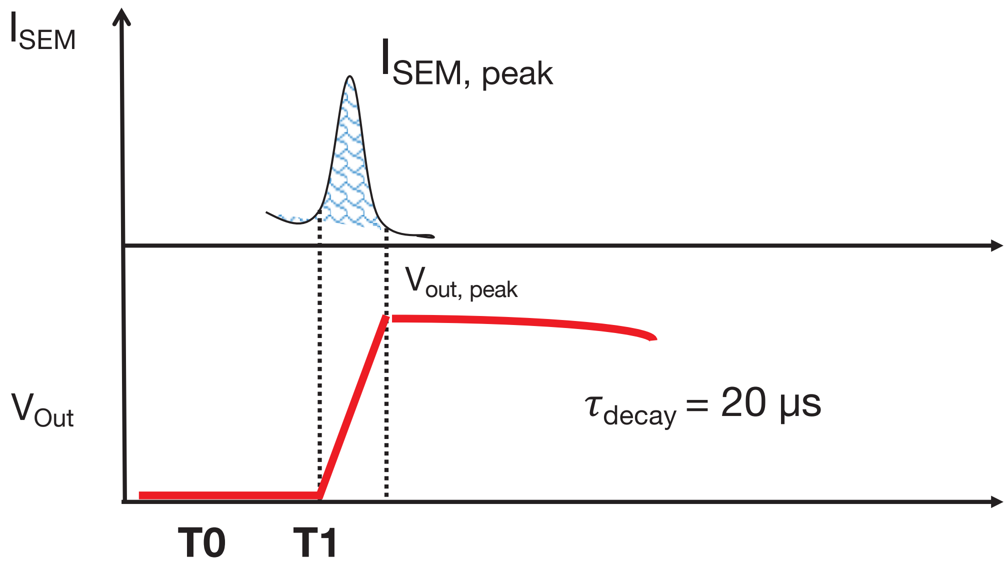
$$Q_{SEM} = \int_0^T I_{SEM}\,dt \qquad V_{OUT} = \frac{Q_{SEM}}{C_F}$$

Peak detector: it froozes the Vout signal but must be armed at least 1 µs before the trigger signal



$-1.7\ V \leq V_{OUT}^{Range} \leq 1.7\ V$

$0\ V \leq V_{RP}^{Range} \leq 10\ V$

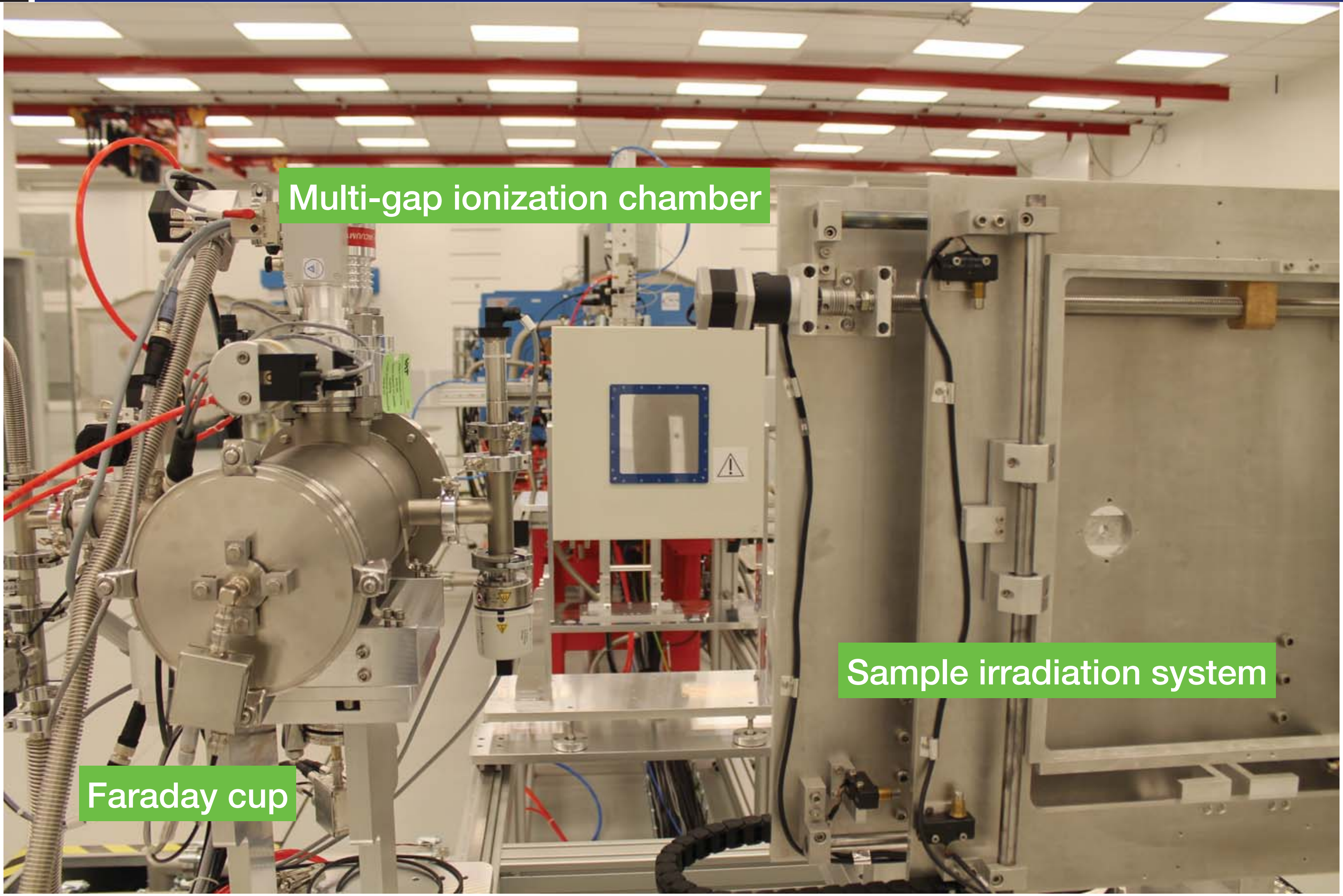


The avallabile nominal C_F are: 1pF, 1.5pF, 15pF, 150pF, 1.5nF and 15 nF

The measured C_F are: (1.16pF and 1.22pF), (1.77pF and 1.78pF), (15.40pF and 15.40pF), (149,51pF and 153.55pF), (1.73nF and 1.73nF), and (14.28 nF and 15.82 nF)

The error on CF is of 2%

Summarising the dosimetric procedure



In preparation of the first radiobiological measure

Minimal irradiation conditions

Energy 20 MeV, at minimum (Range in water:)

Best: 30 MeV

Bragg peak-plateau ratio: 4, at least

Energy spread: < 7 %

Beam spot size: circular, 1 cm2, at minimum

Trasversal dose homegeneity: < 10%

Lateral penumbra: < 1 mm

Dose accuracy < 5%

Dose statbility < 5%

Dose per bunch >= 10 cGy

Ongoing calibrations with continuous and pulsed beams

DUAL GAP CHAMBER & FARADAY CUP IRRADIATION

Dosimetric study and characterization with proton beam of 35MeV, D= 5 Gy.

A. Study of the response of the DG according to the voltage variation:

$I_{FC1} = 0{,}74\, nA$

$$\mathbf{-20\,V \leq V\,(ICh1) \leq 1800\,V}$$
$$\mathbf{-10\,V \leq V\,(ICh2) \leq 900\,V}$$

B. Study of the response of the DG according to the dose rate variation, in tw configurations:

1. $V\,(ICh1) = 1200\,V, V\,(ICh2) = 600\,V$
2. $V\,(ICh1) = 140\,V,\ V\,(ICh2) = 600\,V$

$$\mathbf{I_{FC1} = 0,21\ - 0,41\ - 1,2\ - 1,8\ - 2\,nA}$$

C. Study of the response of the CF according to the voltage variation:

$V\,(ICh1) = 1200\,V,\quad V\,(ICh2) = 600\,V,\quad I_{FC1} = 0{,}73\,nA$

$$\mathbf{-2000\,V \leq V_{FC}^{external} \leq 0\,V}$$
$$\mathbf{-2000\,V \leq V_{FC}^{internal} \leq 2000\,V}$$

D. Study of the response of the FC according to the dose rate variation:

$V\,(ICh1) = 1200\,V,\qquad V\,(ICh2) = 600\,V$

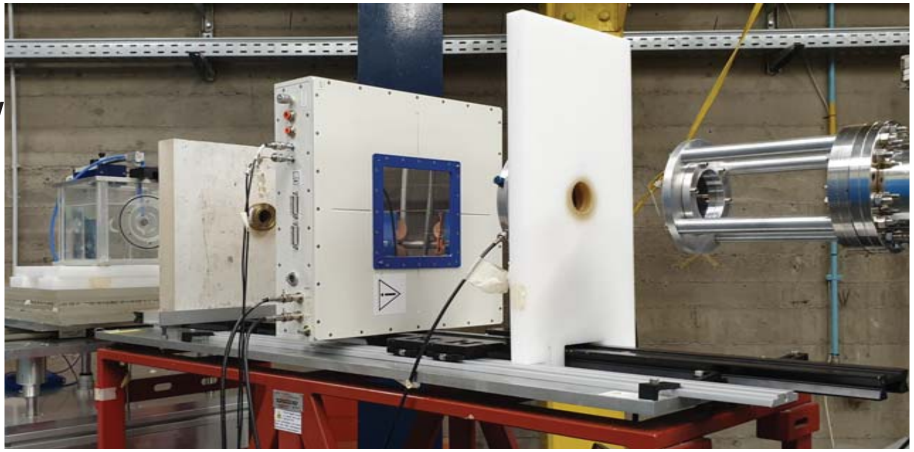
$V_{FC}^{external} = -800\,V,\qquad V_{FC}^{internal} = 0\,V$

$$\mathbf{I_{FC1} = 0,22\ - 0,44\ - 1,15\ - 1,75\ - 1,85\,nA}$$

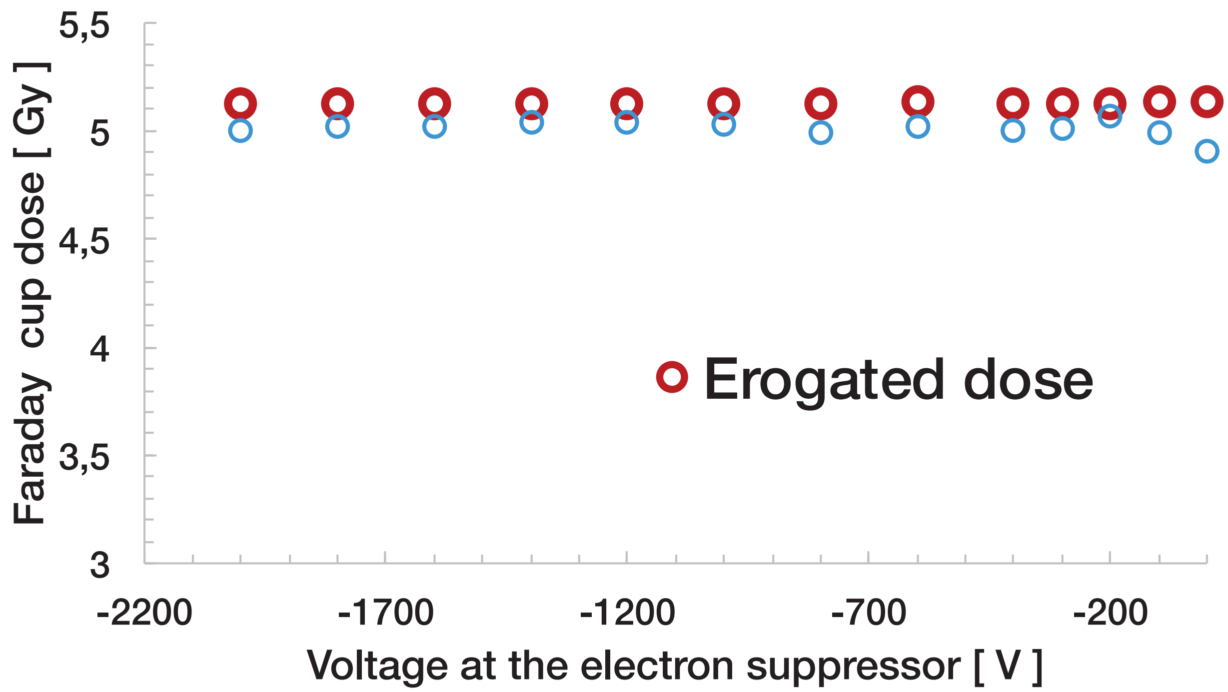
Next tests:

Very high dose rates (up to 200 Gy/min)

Pulsed beams



FC absolute dose, continuous beam



35 MeV proton beam, arojnd 20 Gy/min

Max difference in dose 2.4 %

Test in pulsed beam, high dose rates in the next months

Monte Carlo work, selecting 30 MeV protons

Flat plastic 300 nm thick target

3D PIC simulation by Martina Zakova (ELI-Beamlines)

Space and time profile: gaussian

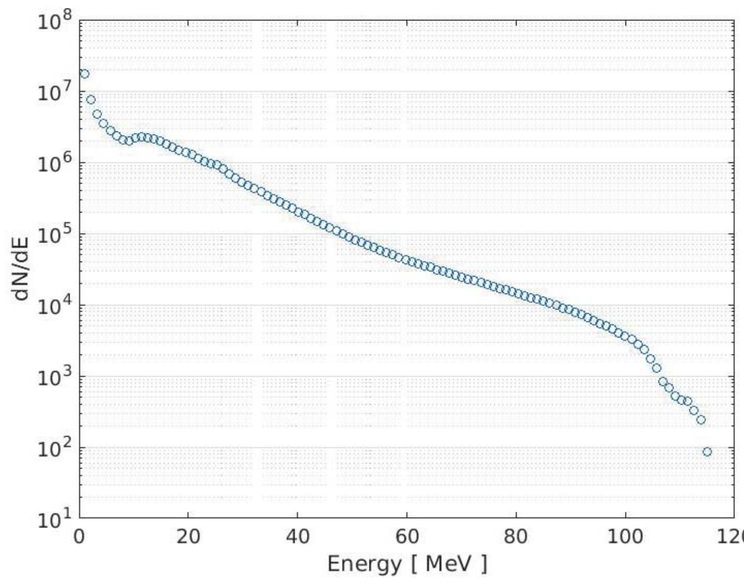
Pulse duration 30 fs

Beam width (FWHM) 3 um

Intensity 5E21 W/cm2

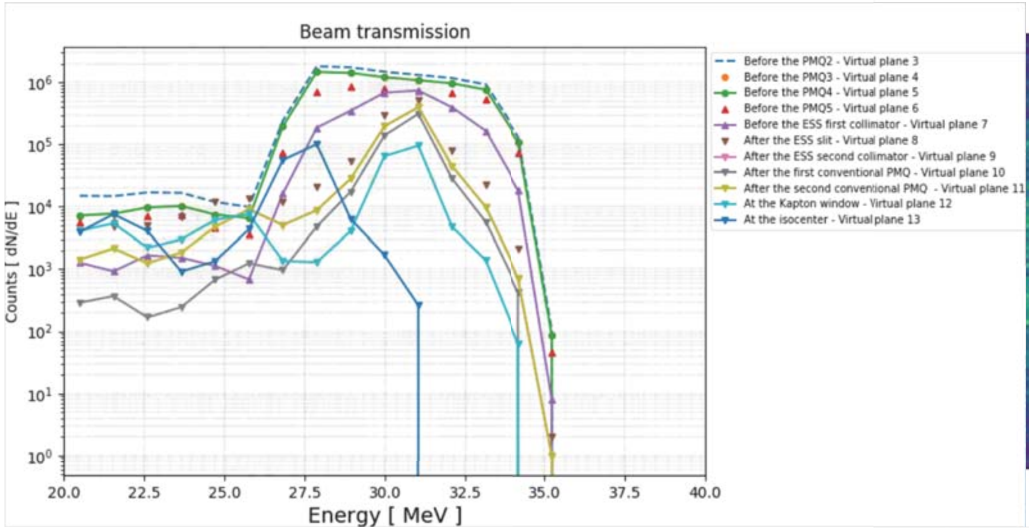
Laser wavelength 800 nm

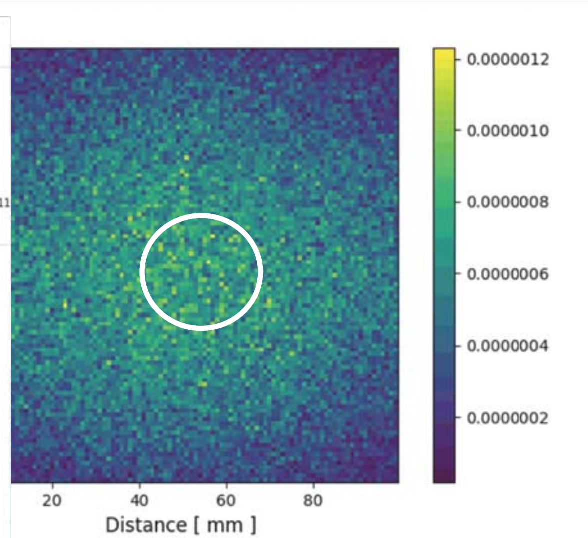
Laser incidence 15°



Example: case of 30 MeV protons selected

5% transmission





0.58 cGy per bunch

12 % homogeneity in 1.0 cm diam. spot

Thoughts on radiobiology of laser-driven particle beams

Biological action of ionizing radiation is driven by the interaction of DNA lesions in spatial and temporal proximity

In radiation biology, a dose-rate effect is well known to occur when dose is administered below 0.1 Gy per min, leading to increased cell survival because of concomitant repair

Little is known at the exceedingly high dose rates allowed by optical beam acceleration: It is postulated that oxygen depletion may become significant under such regimes leading to cell radioresistance

This may be the mechanism(s) underlying the apparent enhanced sparing effect on normal tissues observed with very high-dose rate photons/electrons (FLASH RT)

However, therapeutically meaningful applications of laser-driven particle beams require to verify that cancer cell death occurs at the same levels per dose as observed with conventionally accelerated beams. This is in fact what existing data seem to indicate thus far.

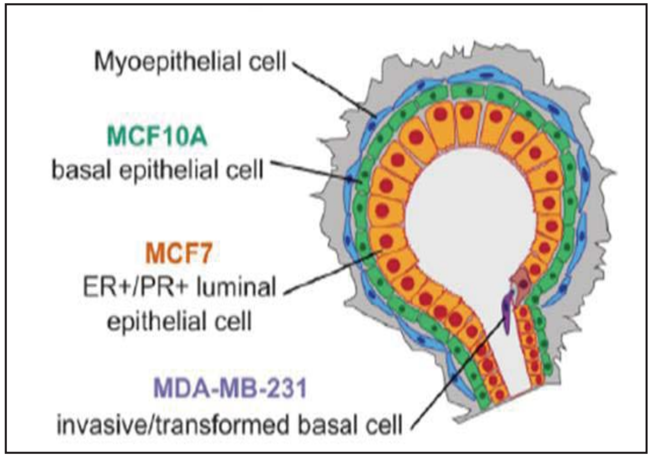
First radiobiological experiment at ELIMED

- **Breast cancer** is currently explored as a possible target for protontherapy because of expected reduction of cardiovascular damage due to its greater precision.
- Irradiation of **Breast Cancer and normal cell lines previously irradiated with conventionally accelerated beams** (x-rays and proton).

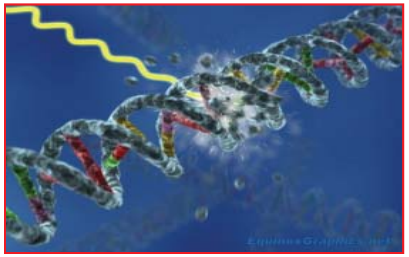
AIMS

Radiobiological characterization of the ELIMED beam line in terms of:

- Quantification of cancer cell death
- Study of sublethal cytogenetic damage in normal cells
- Possible reduction of normal cell damage while efficiently killing cancer cells?



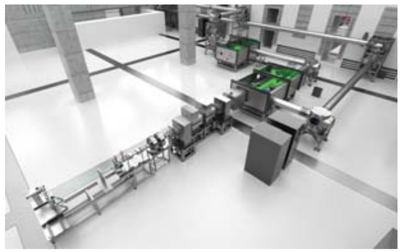
Conventional



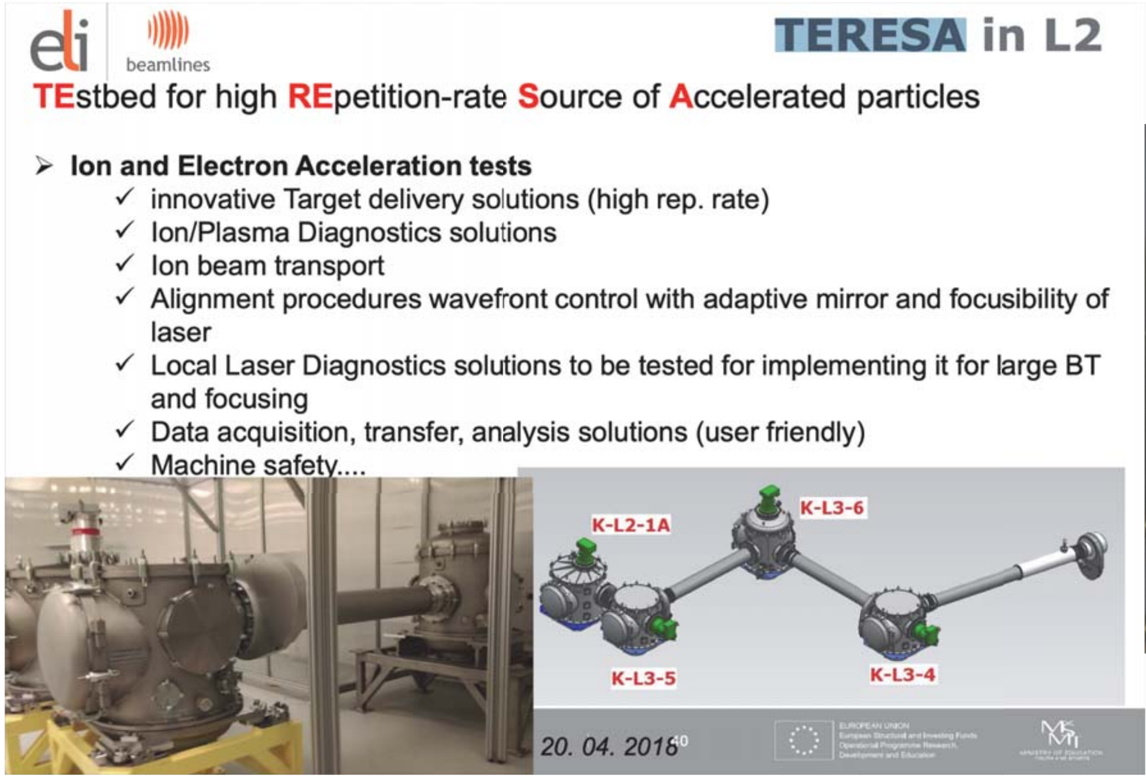
Hadrontherapy

VS

Laser-driven protontherapy



Preliminary tests in 2019



INFN quadrupoles, 30 T/M field

…. finally

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

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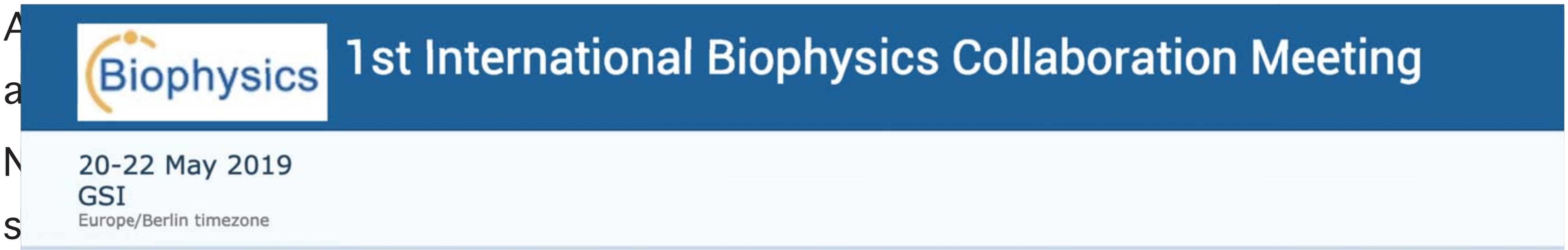

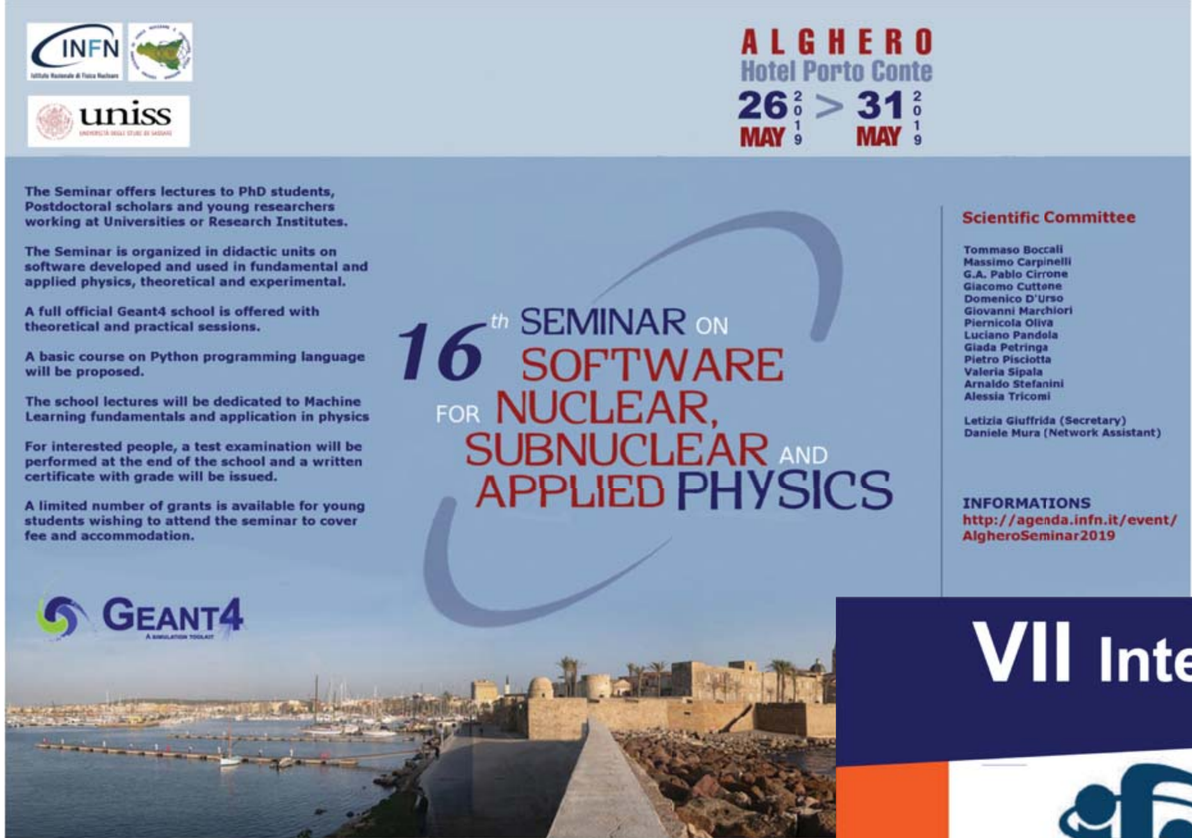
INFN
uniss
ALGHERO
Hotel Porto Conte
26 MAY 2019 > 31 MAY 2019
The Seminar offers lectures to PhD students, Postdoctoral scholars and young researchers working at Universities or Research Institutes.
The Seminar is organized in didactic units on software developed and used in fundamental and applied physics, theoretical and experimental.
A full official Geant4 school is offered with theoretical and practical sessions.
A basic course on Python programming language will be proposed.
The school lectures will be dedicated to Machine Learning fundamentals and application in physics
For interested people, a test examination will be performed at the end of the school and a written certificate with grade will be issued.
A limited number of grants is available for young students wishing to attend the seminar to cover fee and accommodation.
16th SEMINAR ON SOFTWARE FOR NUCLEAR, SUBNUCLEAR AND APPLIED PHYSICS
Scientific Committee
Tommaso Boccali
Massimo Carpinelli
G.A. Pablo Cirrone
Giacomo Cuttone
Domenico D'Urso
Giovanni Marchiori
Piernicola Oliva
Luciano Pandola
Giada Petringa
Pietro Pisciotta
Valeria Sipala
Arnaldo Stefanini
Alessia Tricomi
Letizia Giuffrida (Secretary)
Daniele Mura (Network Assistant)
INFORMATIONS
http://agenda.infn.it/event/AlgheroSeminar2019
GEANT4


VII International Geant4 School
July 1-5, 2019
THE HENRYK NIEWODNICZAŃSKI
INSTITUTE OF NUCLEAR PHYSICS
POLISH ACADEMY OF SCIENCES
INFN
GEANT4
ORGANIZERS
Pablo Cirrone (LNS-INFN)
Luciano Pandola (LNS-INFN)
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Antoni Rucinski (IFJ PAN)
Jakub Baran (IFJ PAN)
Jan Gajewski (IFJ PAN)
Magdalena Garbacz (IFJ PAN)
Monika Pawlik-Niedźwiecka (IFJ PAN)
TOPICS
Basic overview on the main aspects of the Geant4 Monte Carlo toolkit
Lectures on the Geant4 code complemented by hands-on pratical sessions
Basic course on C++
Maximum 50 participants will be admitted
Krakow university students will be admitted with a reduced fee
http://www.facebook.com/softwareandGeant4School/timeline
http://agenda.infn.it/event/VIIInternationalGeant4School

Thank you

Left to right: Roberto Catalano, Giovanni Manno, Emilio Zappalà, Antonio Russo, Gustavo Messina, Pablo Cirrone, Milene Ficarra, Gaetano Savoca, Cristina Guarrera, Giusi Larosa, Antonio Amato, Giada Petringa, Giacomo Cuttone, Ruhani Khanna, Giuseppe Fustaino, Beatrice Cagni, Chidera Opara, Daniele Rizzo, Giuseppe Pastore, Salvo Tudisco, Nelly Puglia, Marco Calvaruso, Luigi Minafra, Francesco Cammarata, Giorgio Russo, Piero Lojacono