# Radiobiological and dosimetric applications with proton/ion beams

Giada Petringa

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# Why the laser is interesting in medical applications?

# Some challenges in proton/ion therapy



Range uncertainties

The RBE is 1.1?

The increasing of biological effect

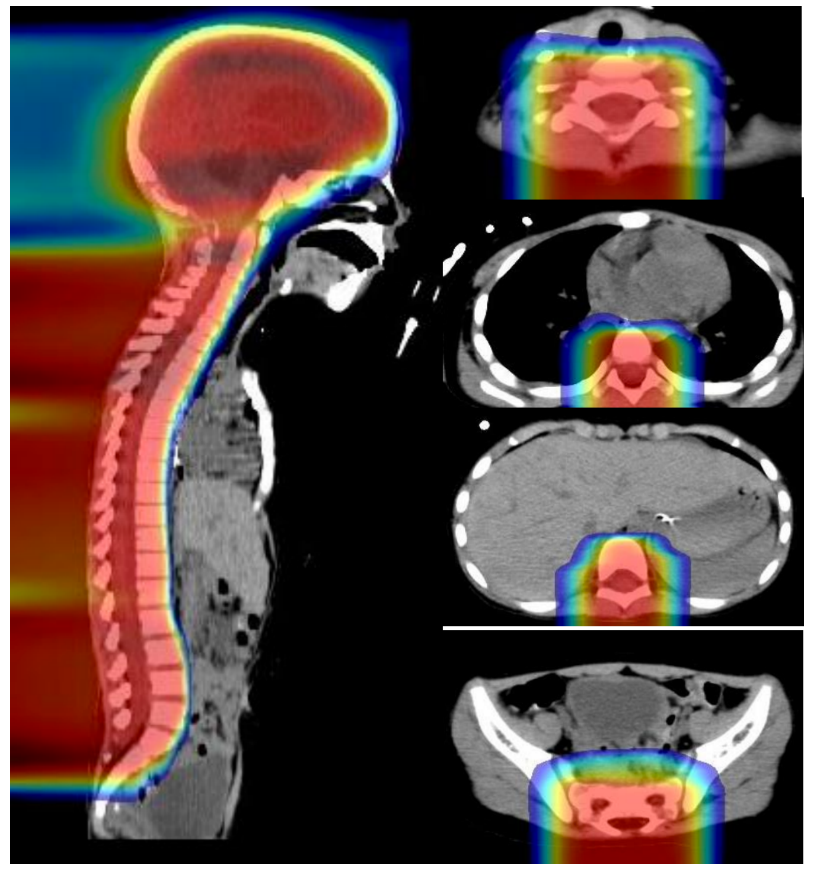
Radiotoxicity and healty tissue

# Some challenges in proton/ion therapy



Range uncertainties

The RBE is 1.1?



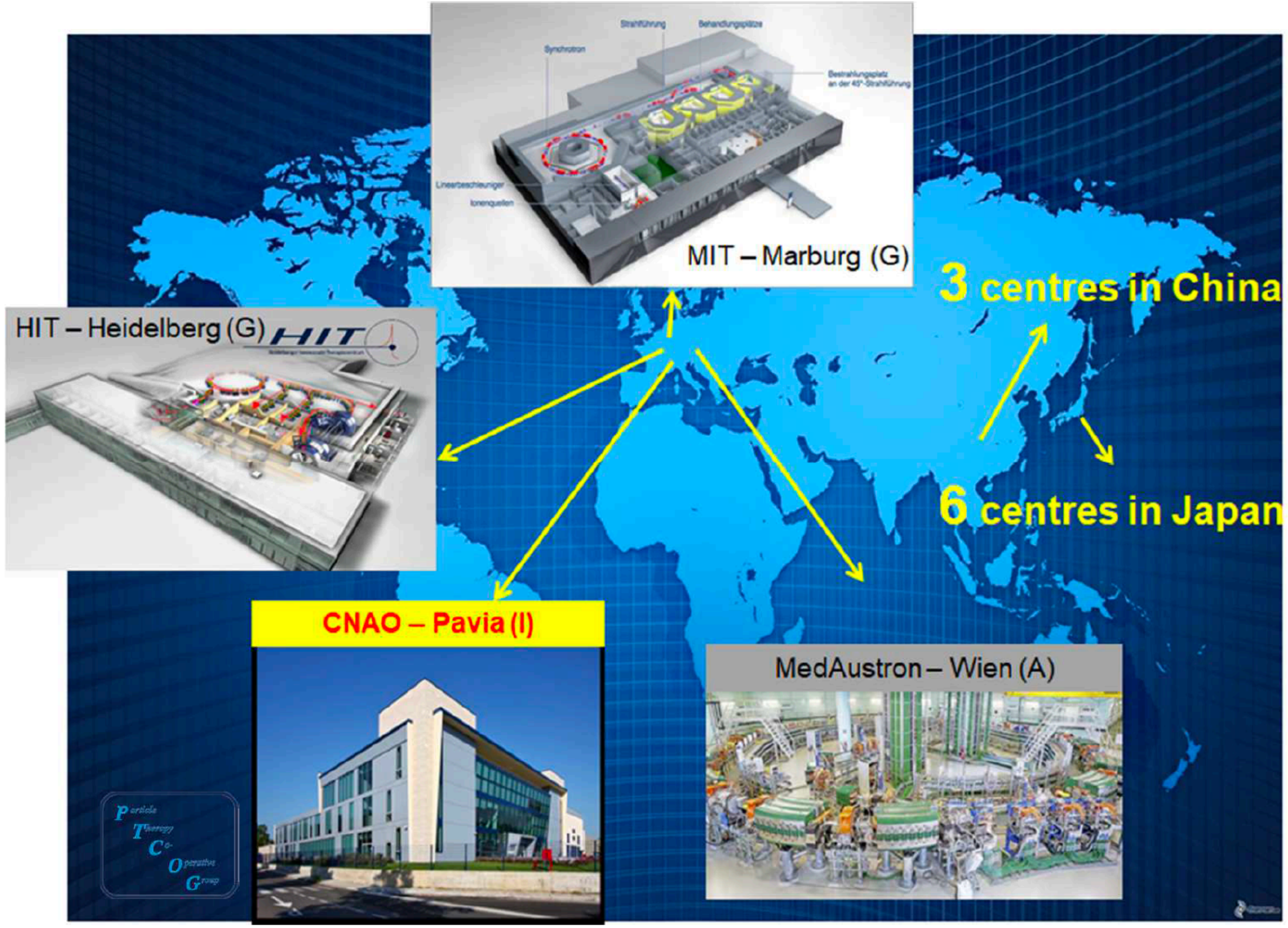
**The increasing of biological effect**

**Radiotoxicity and healty tissue**

# Increasing radiobiological effect



## HADRONTHERAPY IN THE WORLD




**14 carbon ions centres**
**(+5 in construction)**
**6 of them multi-particle**

4 in Europe
3 in China
7 in Japan

Under construction (update 2023): 5
1 China
1 France
2 South Korea
1 Taiwan

**47.000 patients treated**
**(+5.000/year)**

# Radiotoxicity and healty tissue



Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

First in Human

## Treatment of a first patient with FLASH-radiotherapy

Jean Bourhis [a,b,*], Wendy Jeanneret Sozzi [a], Patrik Gonçalves Jorge [a,b,c], Olivier Gaide [d], Claude Bailat [c], Fréderic Duclos [a], David Patin [a], Mahmut Ozsahin [a], François Bochud [c], Jean-François Germond [c], Raphaël Moeckli [c,1], Marie-Catherine Vozenin [a,b,1]

[a] Department of Radiation Oncology, Lausanne University Hospital and University of Lausanne; [b] Radiation Oncology Laboratory, Department of Radiation Oncology, Lausan University Hospital and University of Lausanne; [c] Institute of Radiation Physics, Lausanne University Hospital and University of Lausanne; and [d] Department of Dermatology, Lausan University Hospital and University of Lausanne, Switzerland


1a : Day 0

1b : 3 weeks

- lymphoma on skin
- FLASH-RT: 10 pulses (of 1 us duration) in 90 ms with 1.5 Gy/pulse

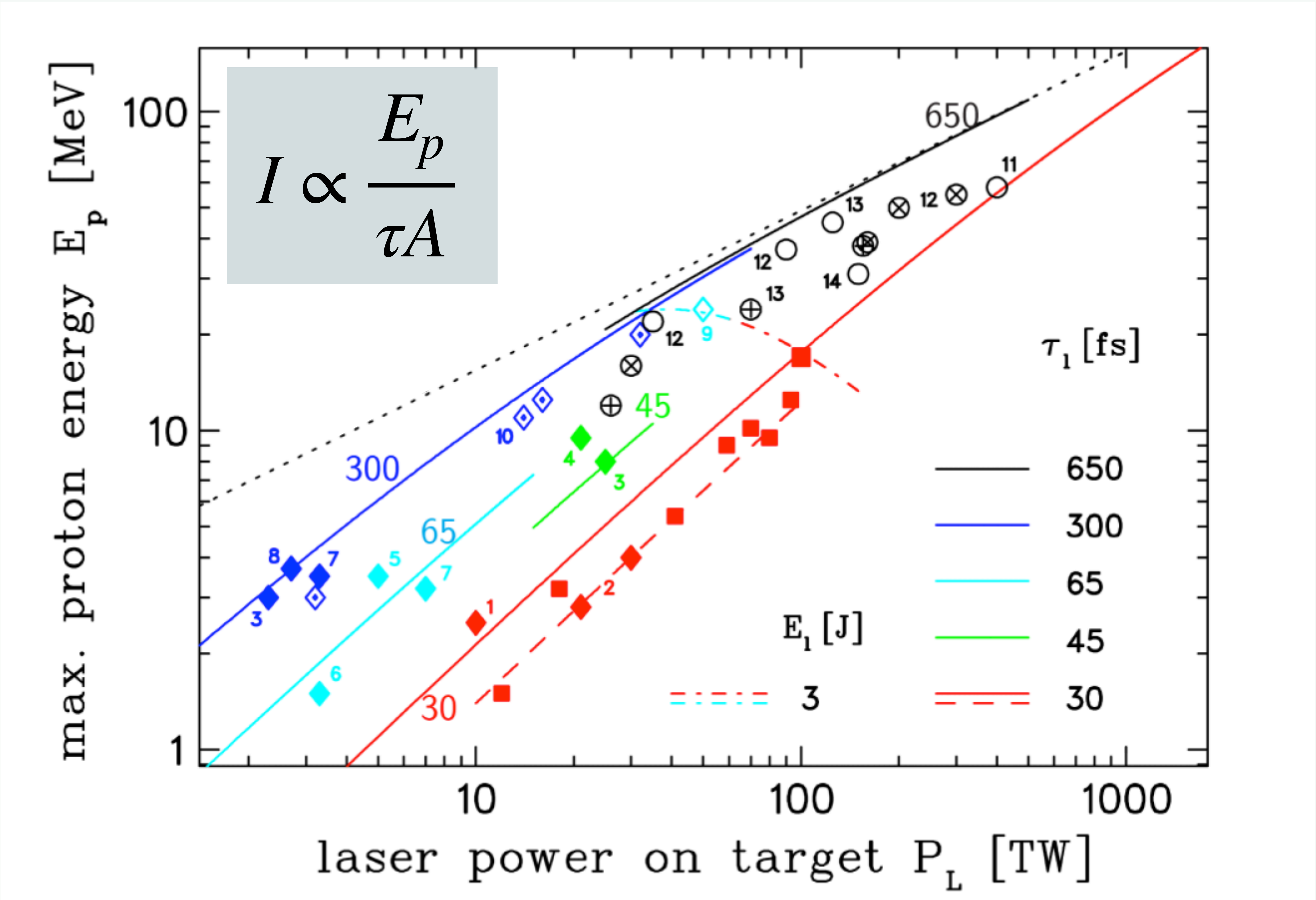
## Condition to have the flash effect

- Dose rate: >40 Gray/sec (possible); >100-150 Gray/sec (likely)
- Reproducible effect
  - Dose / pulse (> 1.5 Gy & few pulses)
  - Dose rate in the pulse (>= $10^6$ Gy /s)
  - Overall time (< 100 ms)
- Dose/fraction
  - Begins to show up at >10 Gray/fraction
  - No dose limiting effect observed in animal models between 25-41 Gray
- Radiation type
  - Most reproducible with electrons
  - Ongoing work on X-rays and protons

# Which is the current status?

# Proton and Ion beam acceleration

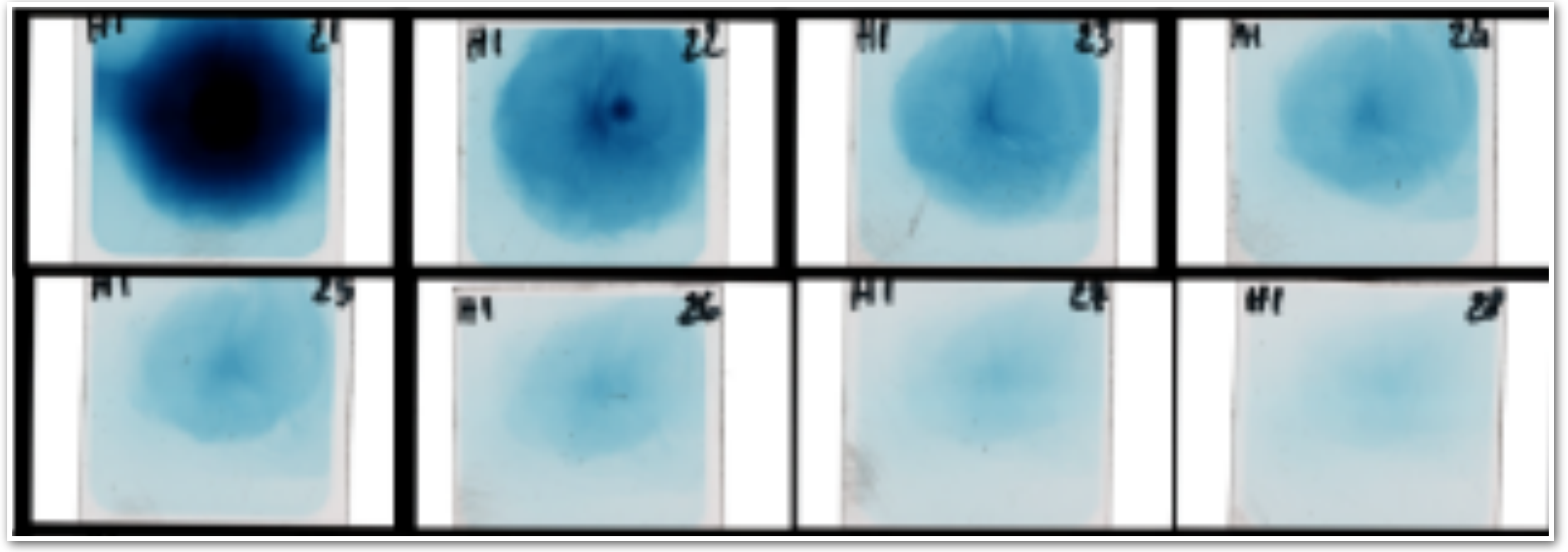


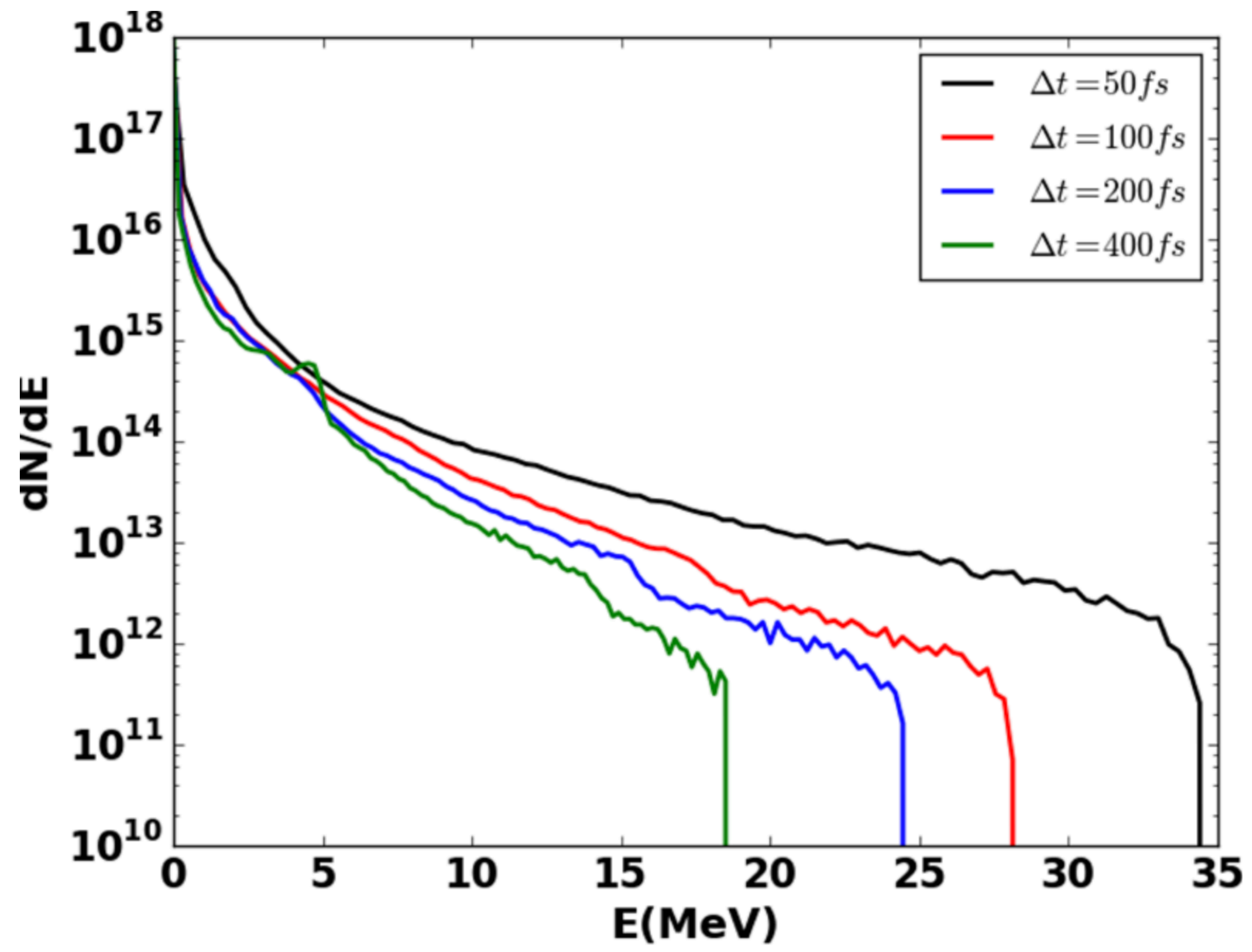



Divergency: ~ 10s degrees

Broad energy spectrum

Short duration source: ~ 1 ps






ARTICLE

DOI: 10.1038/s41467-018-03063-9 OPEN

Near-100 MeV protons via a laser-driven transparency-enhanced hybrid acceleration scheme

A. Higginson[1], R.J. Gray[1], M. King[1], R.J. Dance[1], S.D.R. Williamson[1], N.M.H. Butler[1], R. Wilson[1], R. Capdessus[1], C. Armstrong[1,2], J.S. Green[2], S.J. Hawkes[1,2], P. Martin[3], W.Q. Wei[4], S.R. Mirfayzi[3], X.H. Yuan[4], S. Kar[2,3], M. Borghesi[3], R.J. Clarke[2], D. Neely[1,2] & P. McKenna[1]

Record on the max protons energy

# Can be a high power laser competitive for ion acceleration?



1. Enhancing the maximum proton energy and flux

2. Reducing the beam angular divergence or improving the beam homogeneity

3. Reducing the ion contamination of the beam

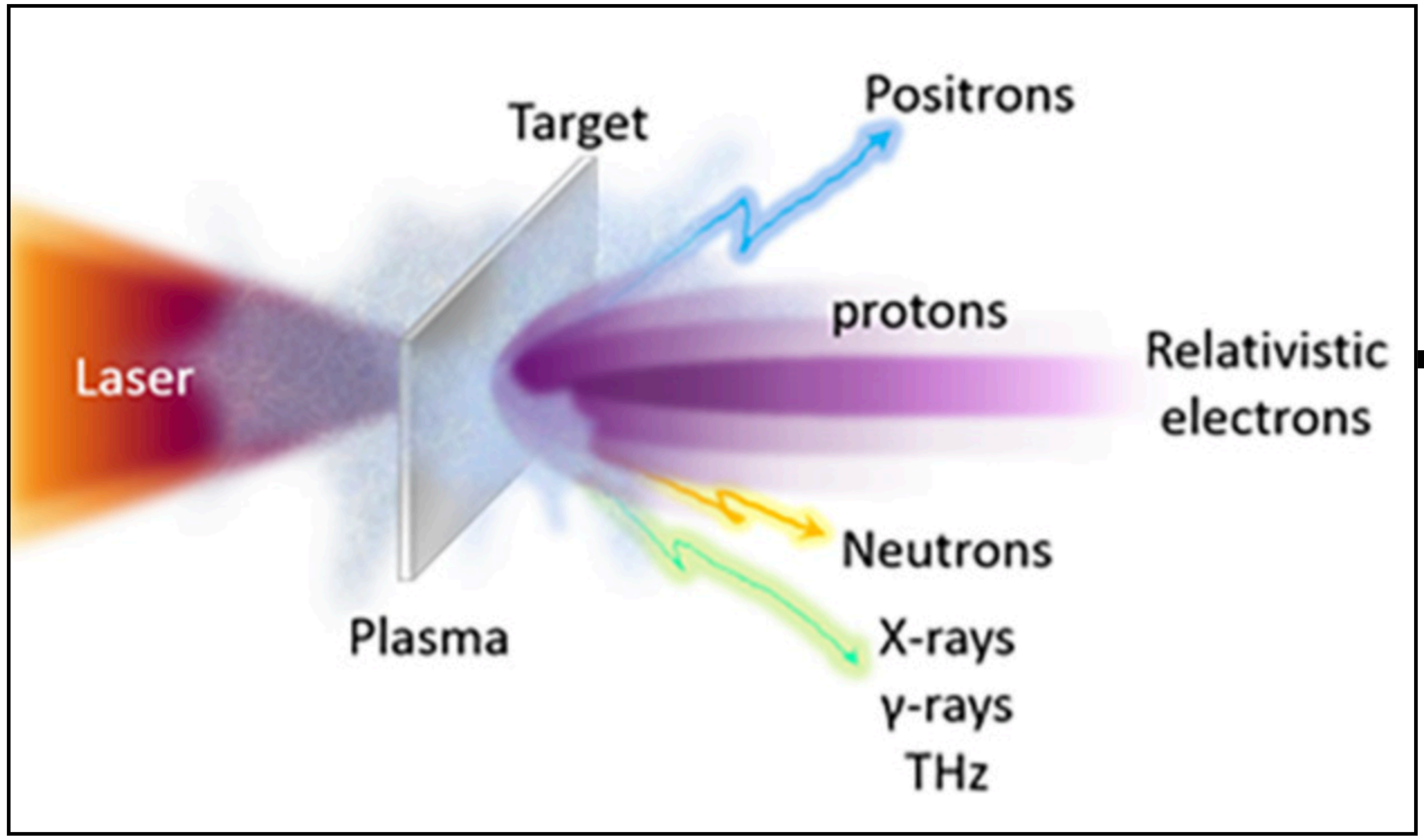
} Transport and selection system

} Target optimization

4. Developing new technologies and strategies for diagnostics and dosimetry

# Typical irradiation scheme

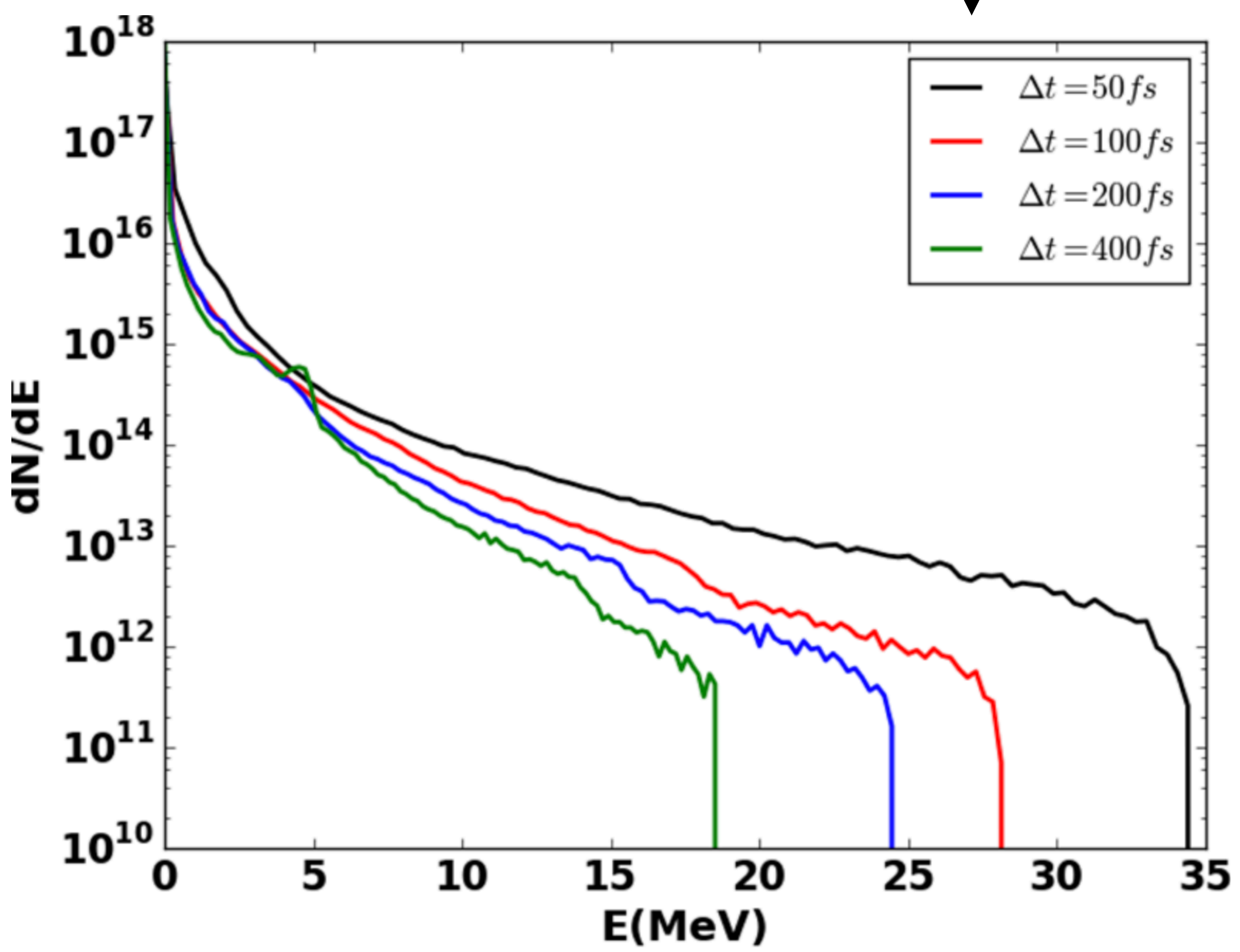


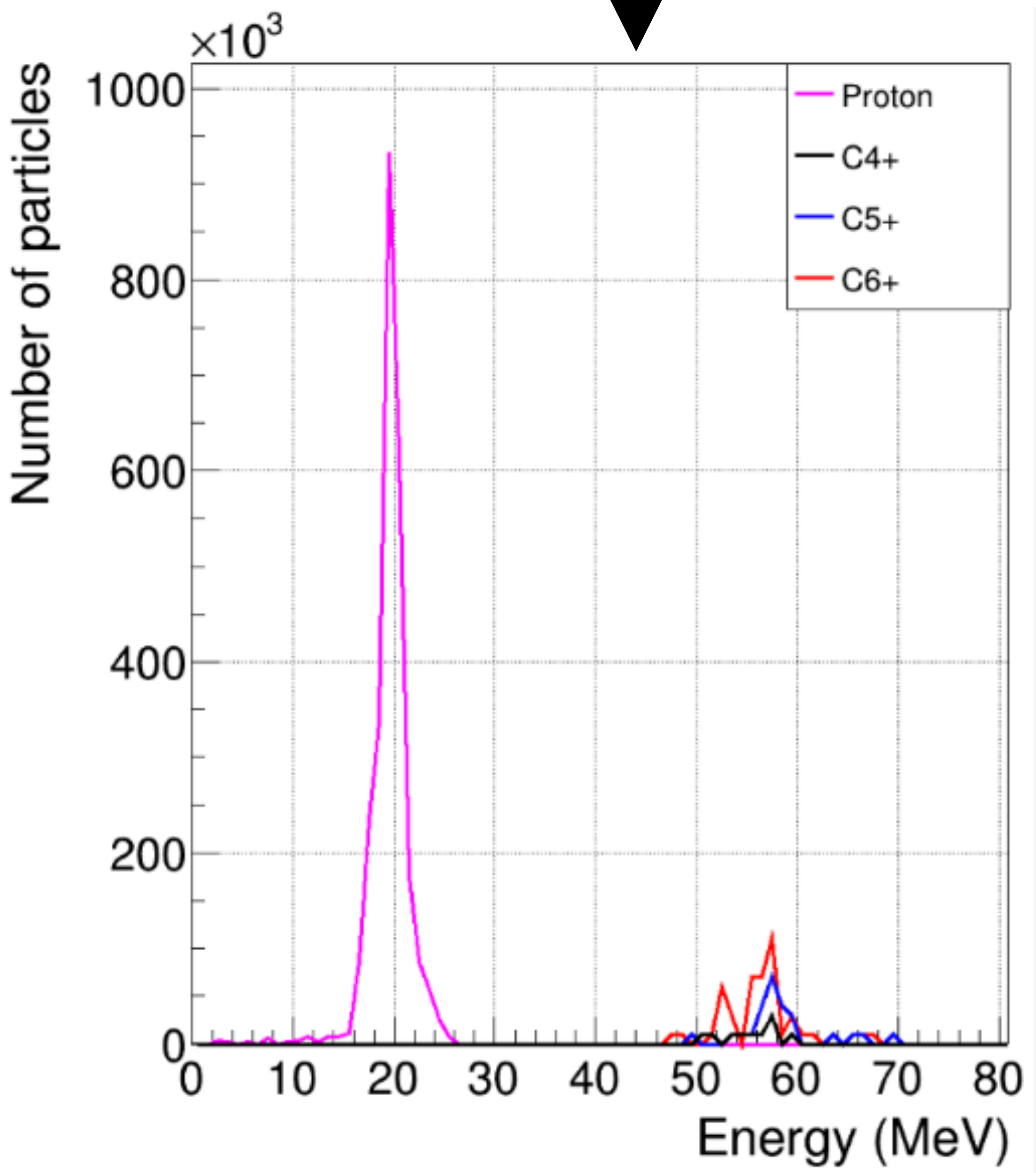


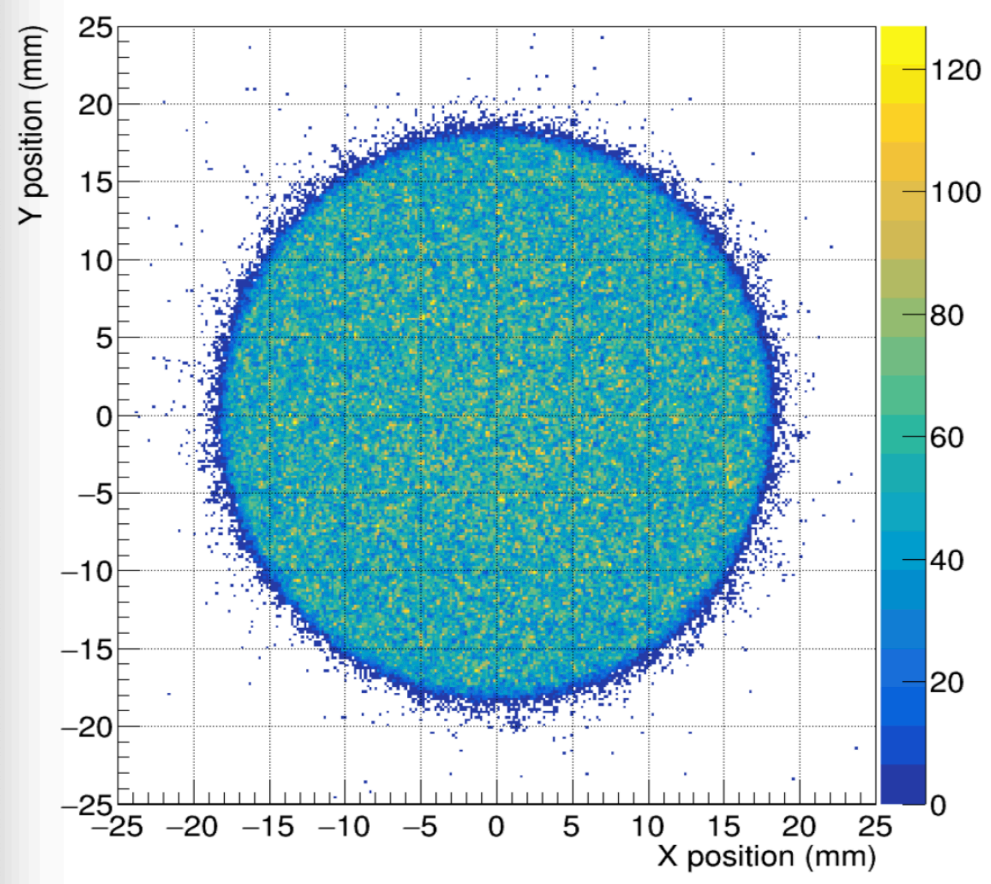

Focusing and Selection System

Diagnostic and Dosimetry

Sample Irradiation



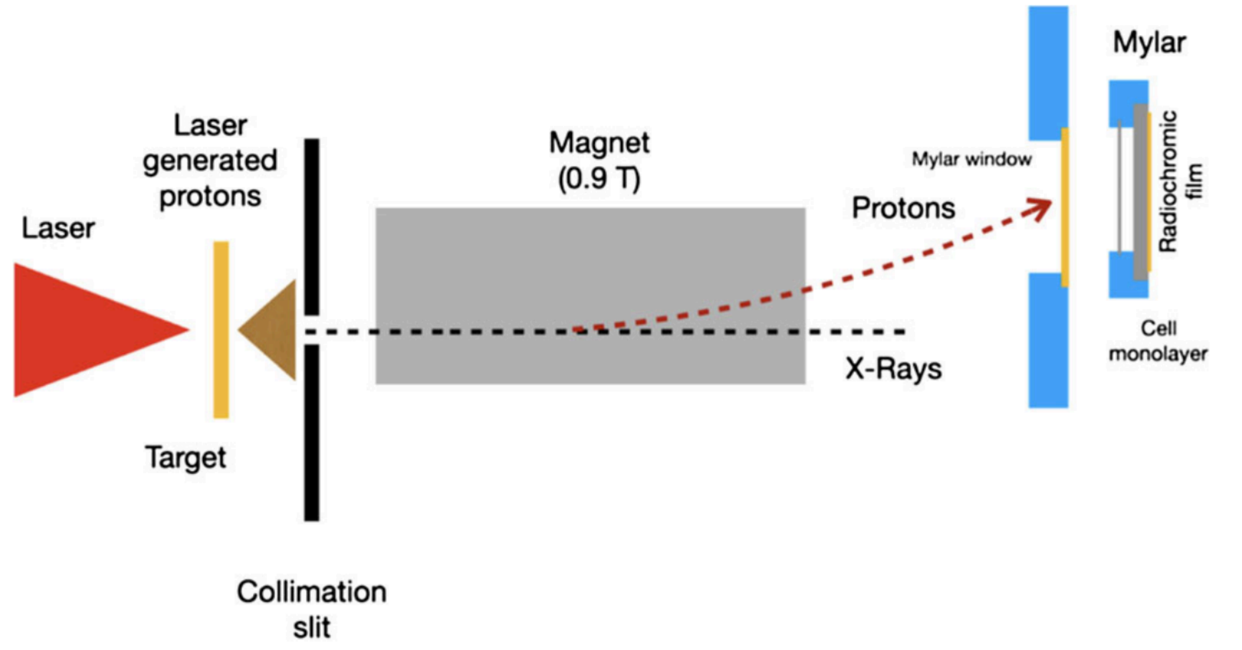




S. M. Barba, et al.
Appl.Sci. 11(21), 9623 (2021)

# Main adopted solutions to select and transport proton beam

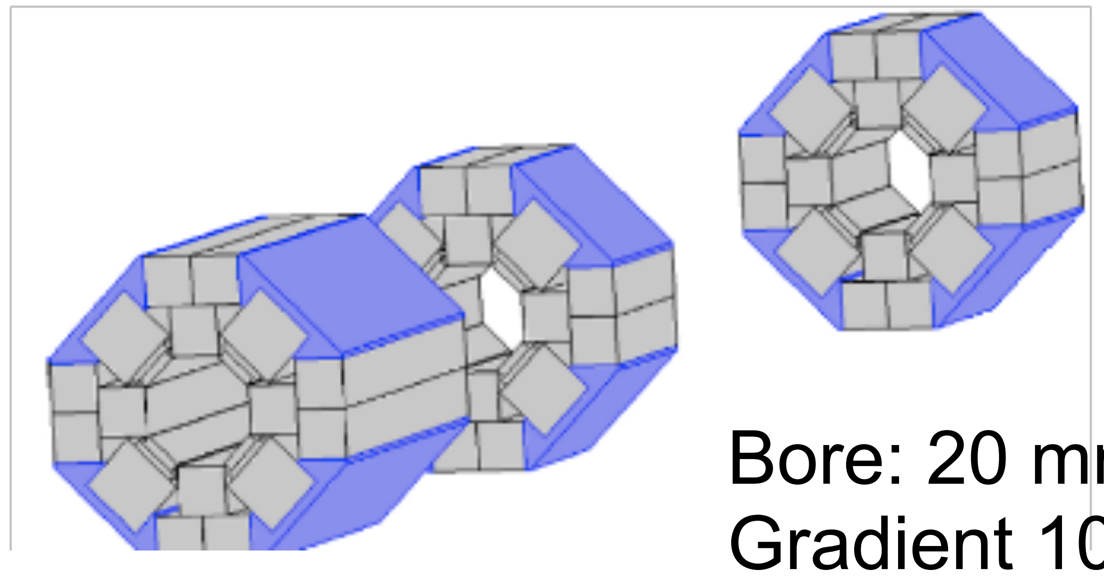




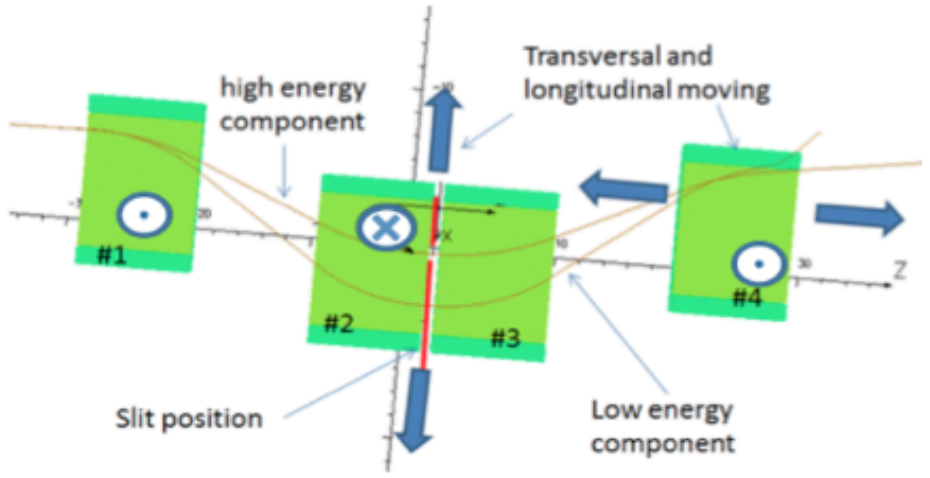

Dipole field: 0.9 T
Length: 100 mm
Energy selection:
up to 30 MeV proton

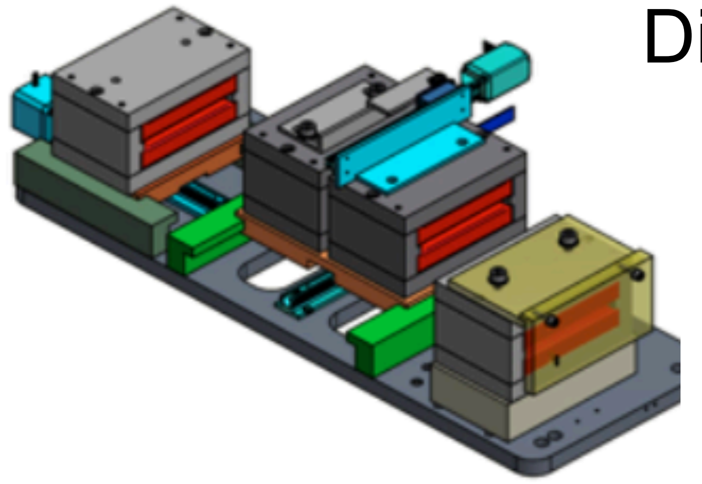
**Single dipole for energy selection**

F Hanton, et al.
Scientific Reports 9, 4471 (2019)



Bore: 20 mm;
Gradient 100 T/m

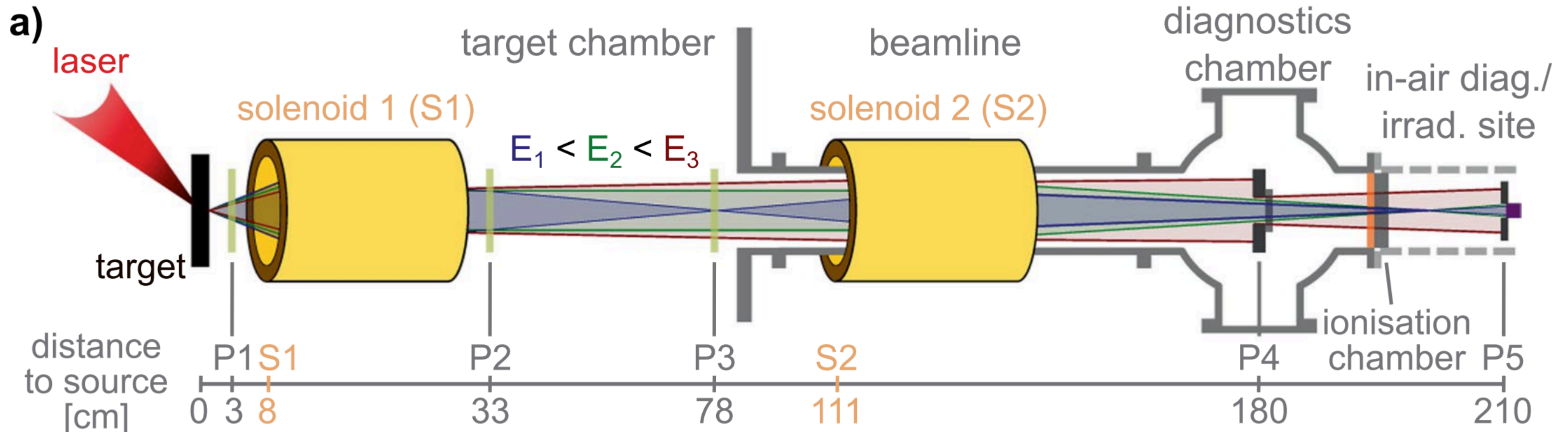


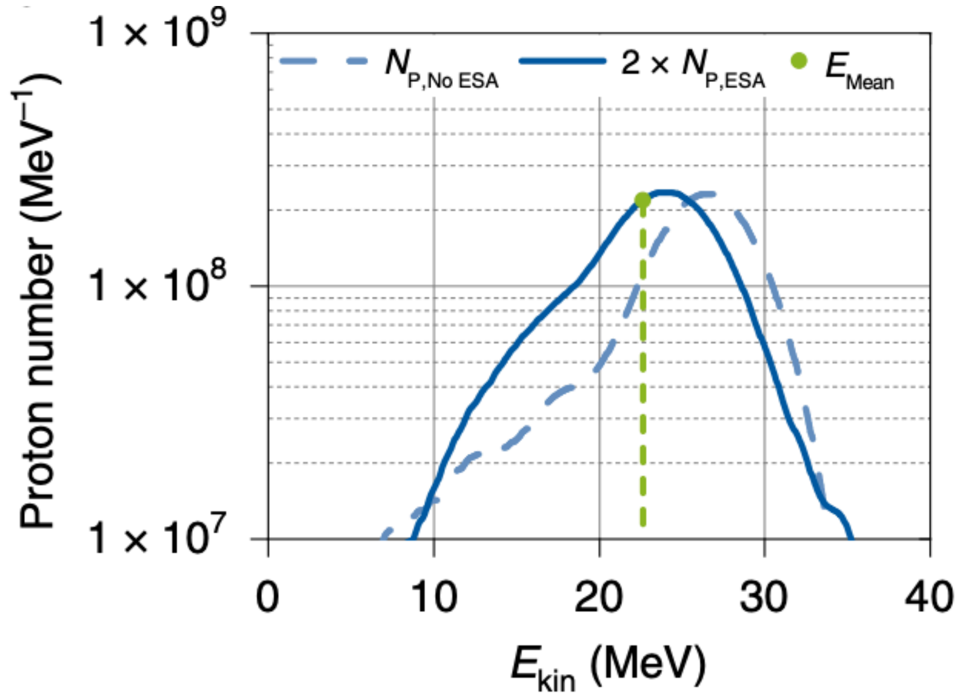
Dipole field: 0.8 T

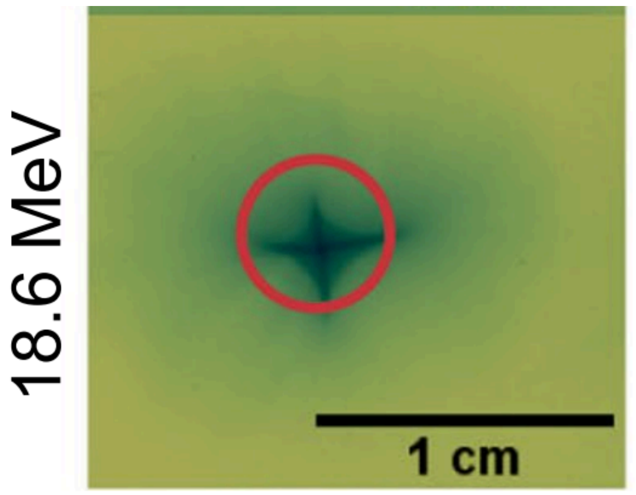
**Quadrupoles + energy selector**
Transport up to 30 MeV with an energy revolution of 5 %

F Schillaci, et al.
NIMA, 837, 80-87 (2016




On-axis magnetic field up to 19.5 T
Rep rate: up to 3 pulse per minute




**Pulsed solenoids**

F Kroll et al. Nature Physics 18, 316–322 (2022)

# Which diagnostic for laser-driven beams?



Diagnostic and dosimetry of laser-drive ion beams is still a challenge

**up to 10E11 ppb in 10 ns** → **up to 10E9 Gy/s**

## "Passive" detectors

- Reliable
- Not affected by the electromagnetic noise
- Not affected by the beam dose rate
- Easy to handle
- Not good for high repetition rate lasers

[Radiochromic films, CR39 track detectors, image plates ….]

## "Active" detectors

- Reliable
- Could affected by the electromagnetic noise
- Could affected by the beam dose rate
- Real-time acquisition and analysis
- Necessary for high repetition rate laser systems

[Thomson-like spectrometers, Time-of-Flight detectors, Integrated Current Transformer … ]

# Some example of irradiation systems

# DRACO, DRESDEN (D)



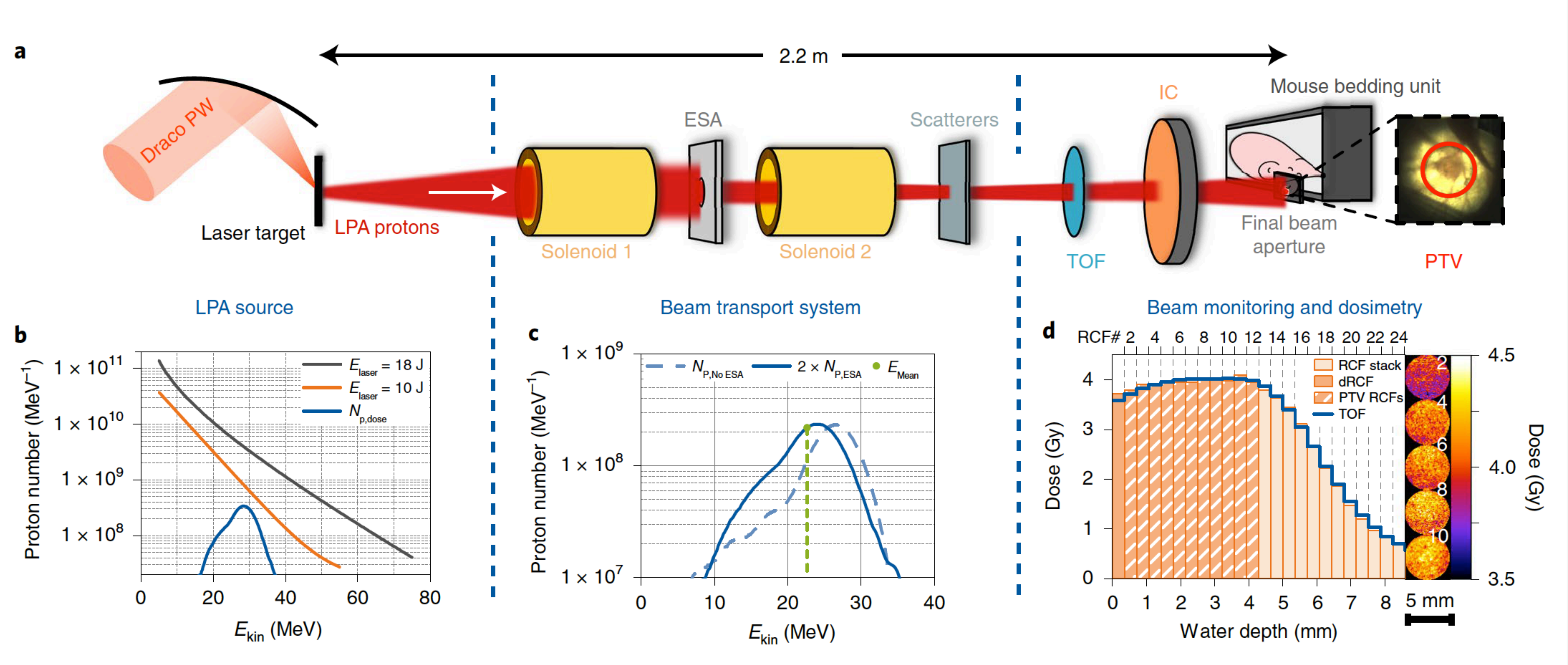
Helmholtz-Zentrum Dresden-Rossendorf D
18 J in 30 fs on the target.
Protons are emitted from plastic foils of ~220 nm thickness,
cut-off energy of up to ~70 MeV.

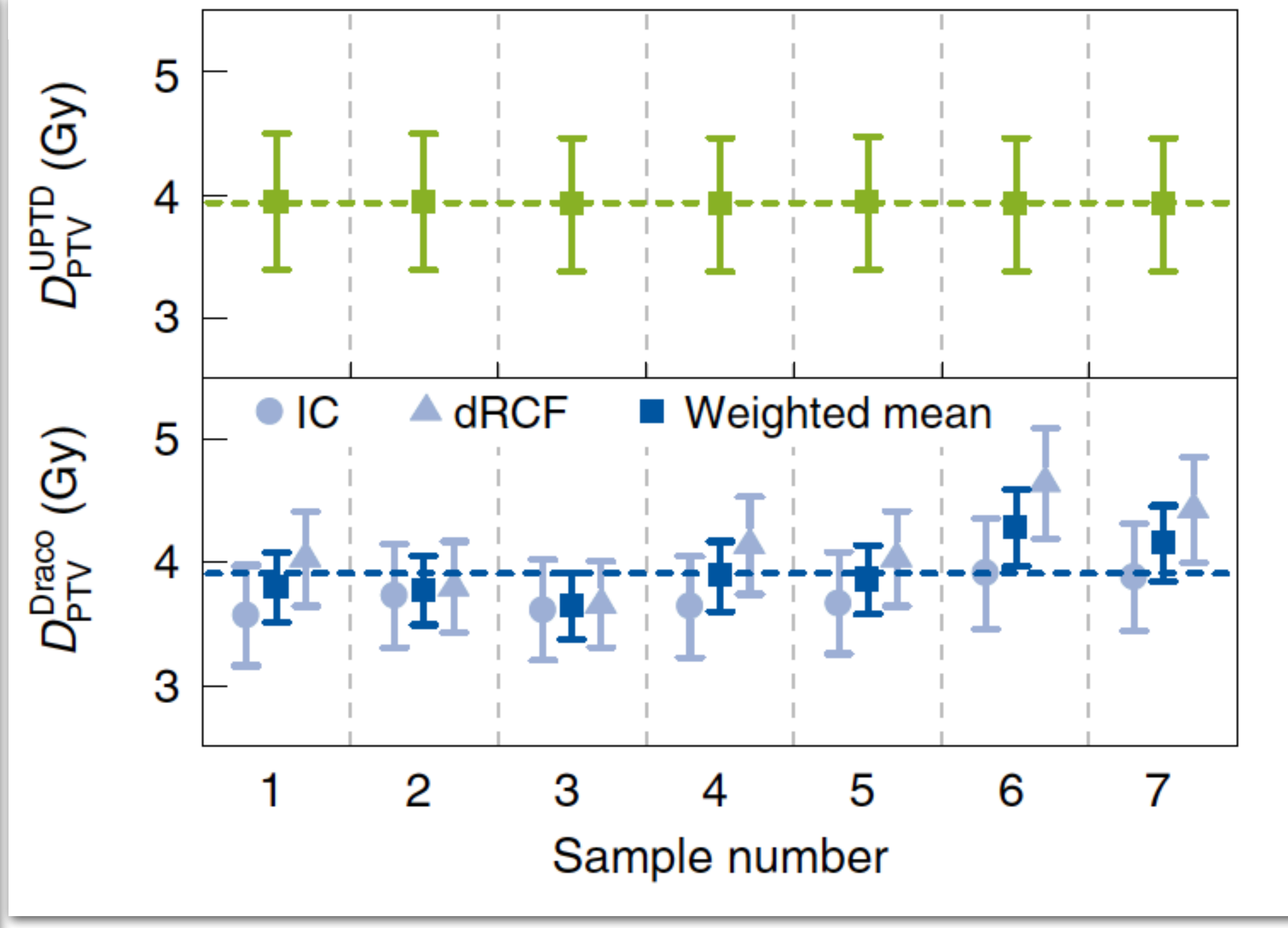
ARTICLES
https://doi.org/10.1038/s41567-022-01520-3
nature physics
Check for updates
OPEN

**Tumour irradiation in mice with a laser-accelerated proton beam**

Florian Kroll[1✉], Florian-Emanuel Brack[1,2], Constantin Bernert[1,2], Stefan Bock[1], Elisabeth Bodenstein[3], Kerstin Brüchner[1,2,3], Thomas E. Cowan[1,2], Lennart Gaus[1,2], René Gebhardt[1], Uwe Helbig[1], Leonhard Karsch[1,3], Thomas Kluge[1], Stephan Kraft[1], Mechthild Krause[1,3,4,5,6,7], Elisabeth Lessmann[1], Umar Masood[1], Sebastian Meister[1], Josefine Metzkes-Ng[1], Alexej Nossula[1], Jörg Pawelke[1,3], Jens Pietzsch[1,2], Thomas Püschel[1], Marvin Reimold[1,2], Martin Rehwald[1,2], Christian Richter[1,3,4,5,6], Hans-Peter Schlenvoigt[1], Ulrich Schramm[1,2], Marvin E. P. Umlandt[1,2], Tim Ziegler[1,2], Karl Zeil[1] and Elke Beyreuther[1,3]

Nature Physics I VOL 18 I 316 March 2022 I 316–322 I www.nature.com/naturephysics



# ELIMAIA, ELIBEAMLINES (CZ)



| Beamline | L3 HAPLS | L4 ATON |
|---|---|---|
| Peak power | ≥1 PW | 10 PW |
| Energy in pulse | ≥30 J | ≥1.5 kJ |
| Pulse duration | ≤30 fs | ≤150 fs |
| Rep rate | 10 Hz | 1 per min |
| Supplier | LLNL | National Energetics |
| **ELI-Beamlines** | **Compressor, short pulse diagnostics, controls & timing systems** | **Compressor design, OPCPA design, short pulse diagnostics, timing system** |

**ELIMAIA experimental area**

30J / 30fs

Protons are emitted from metallic/plastic foils um thickness

cut-off energy of up to ~40 MeV.

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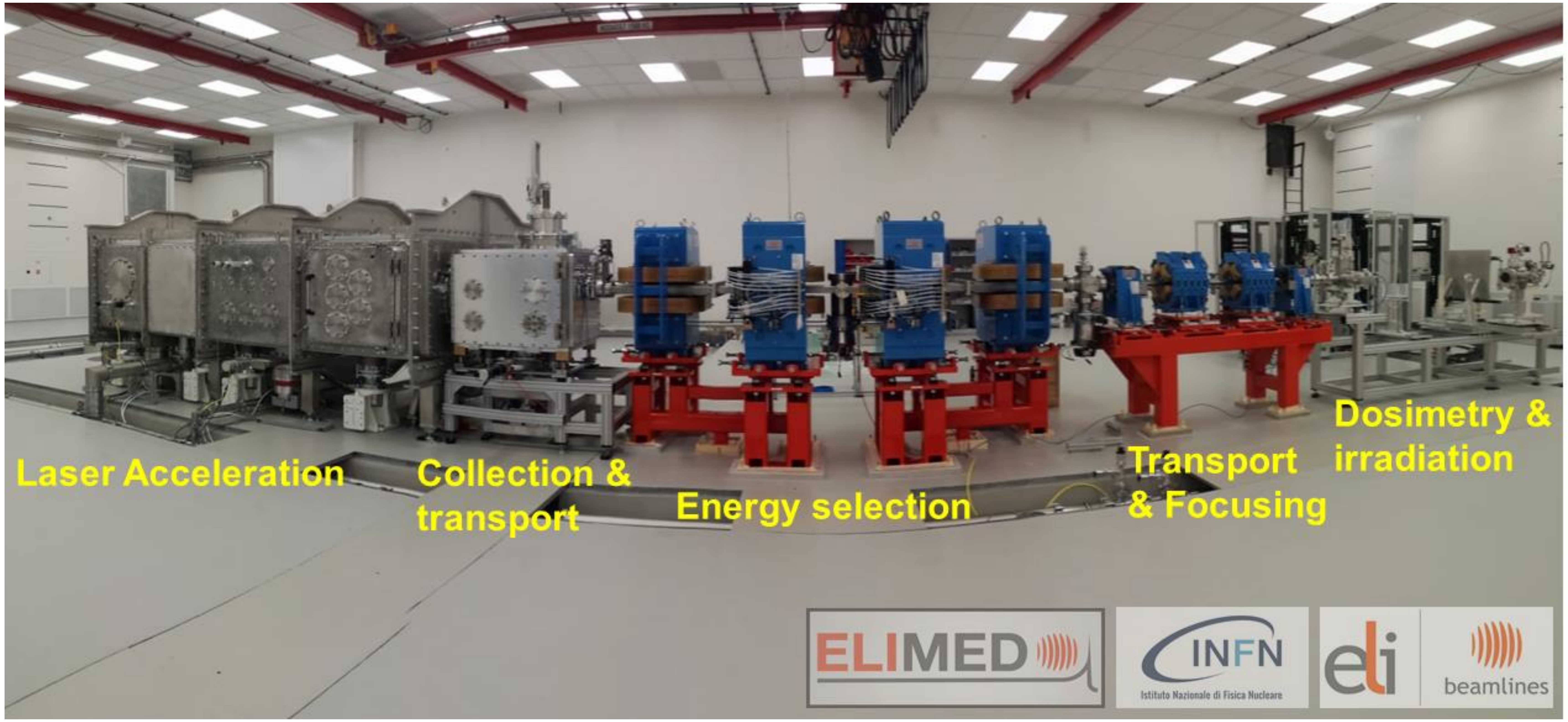
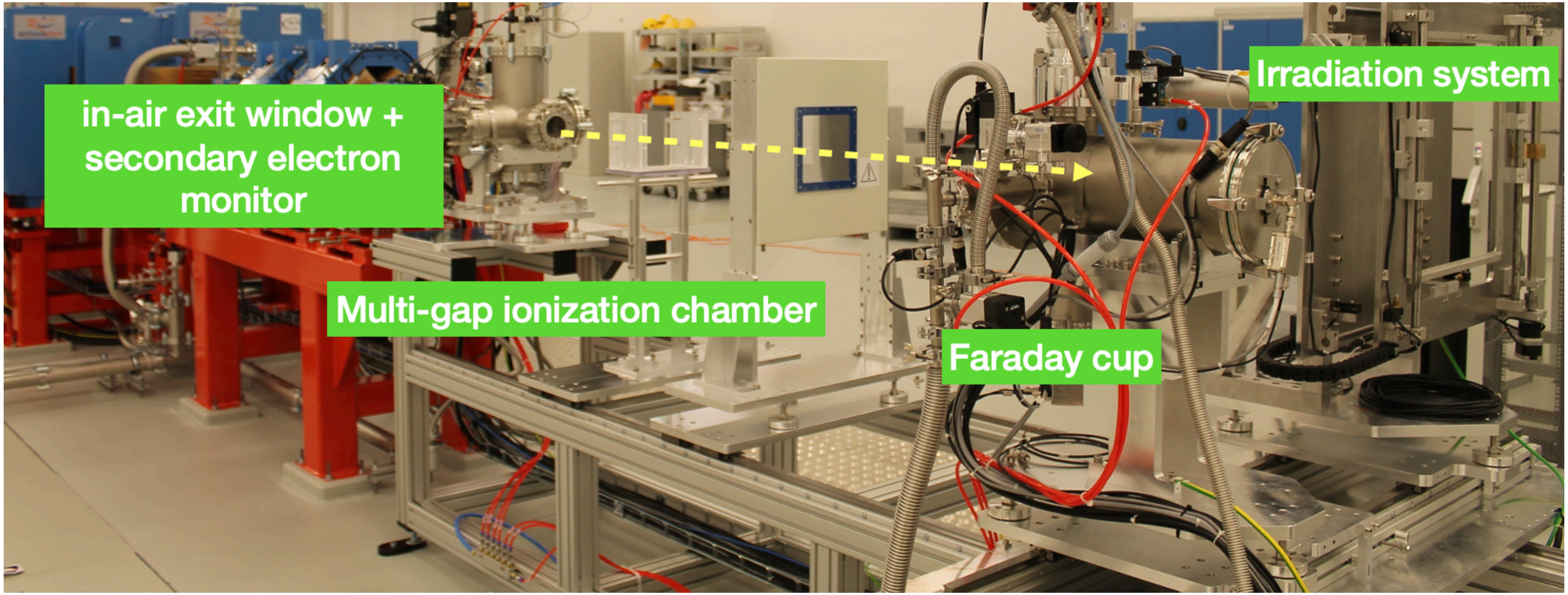


# Dosimetric approaches in E4





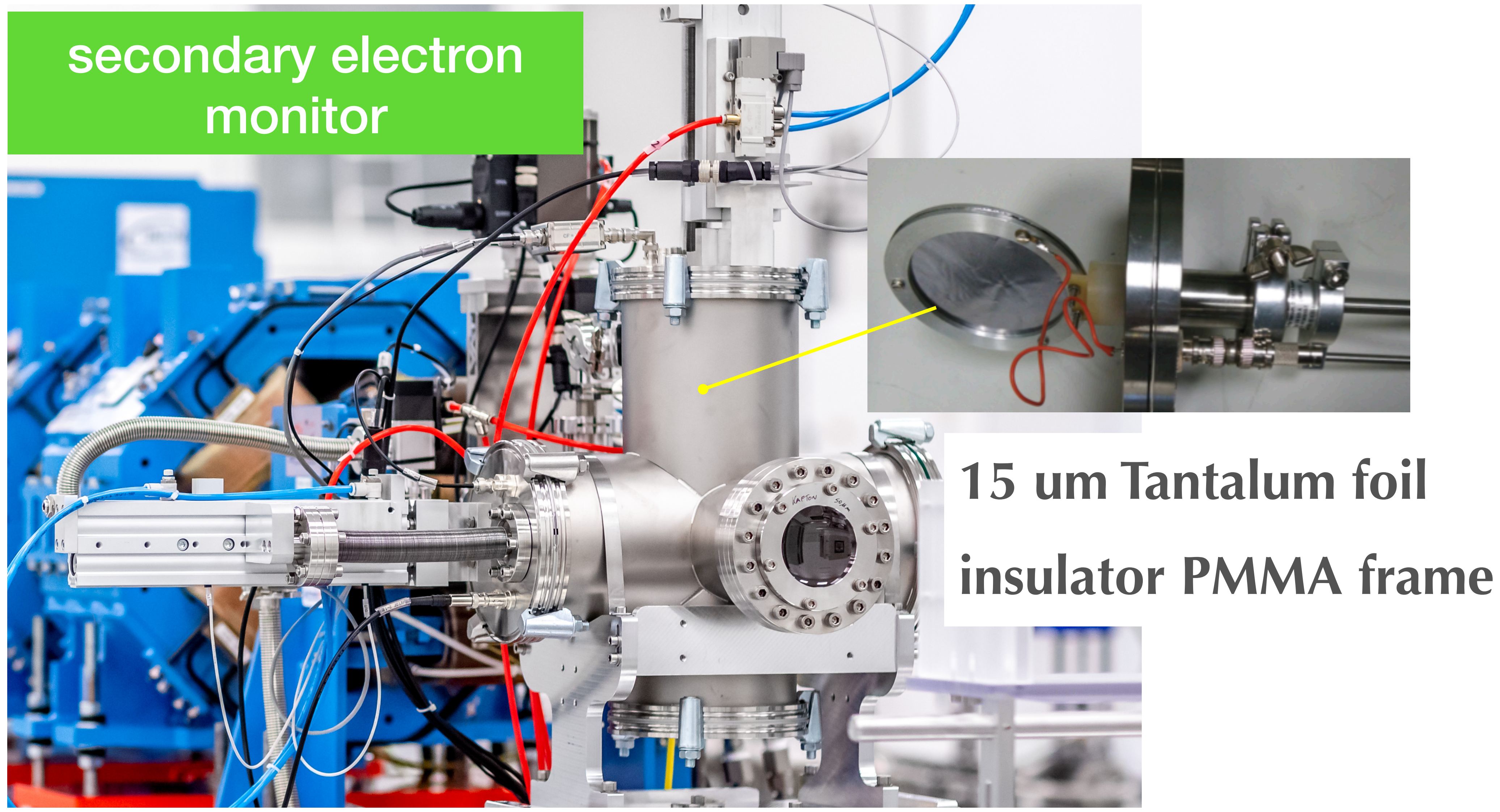

Faraday cup in a special design for absolute dosimetry

Dual gap ionisation chamber for ion recombination correction

Radiochromic films and plastic detector for spectroscopy(first phase, low-energy)

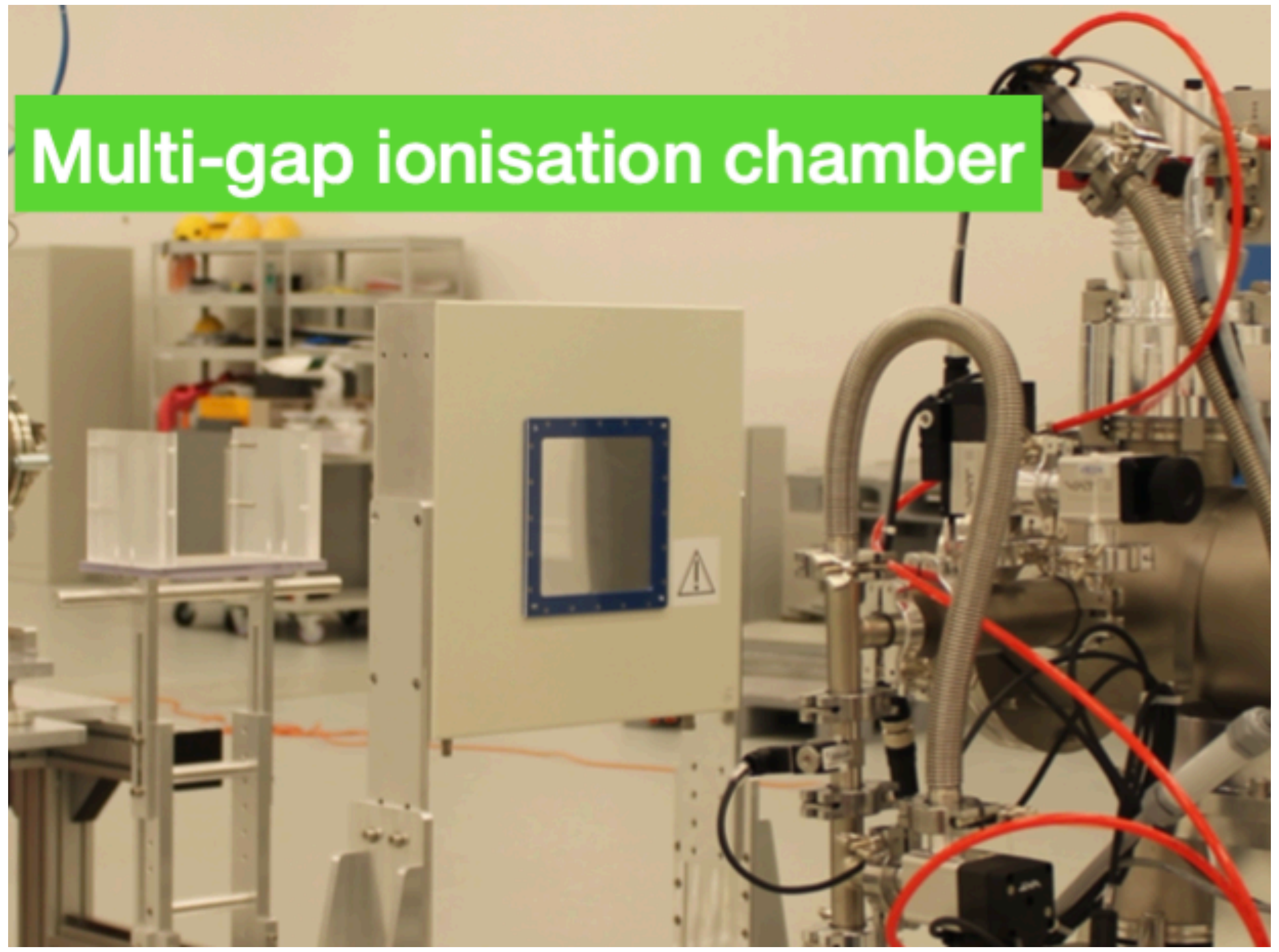
# Relative dosimetry






- Time Of Fligth configuration
- Charge integration for normalisation purposes
- Scattering foil for beam diffusion

Supplied by DE.TEC.TOR. Devices & Technologies Torino Srl, Italy

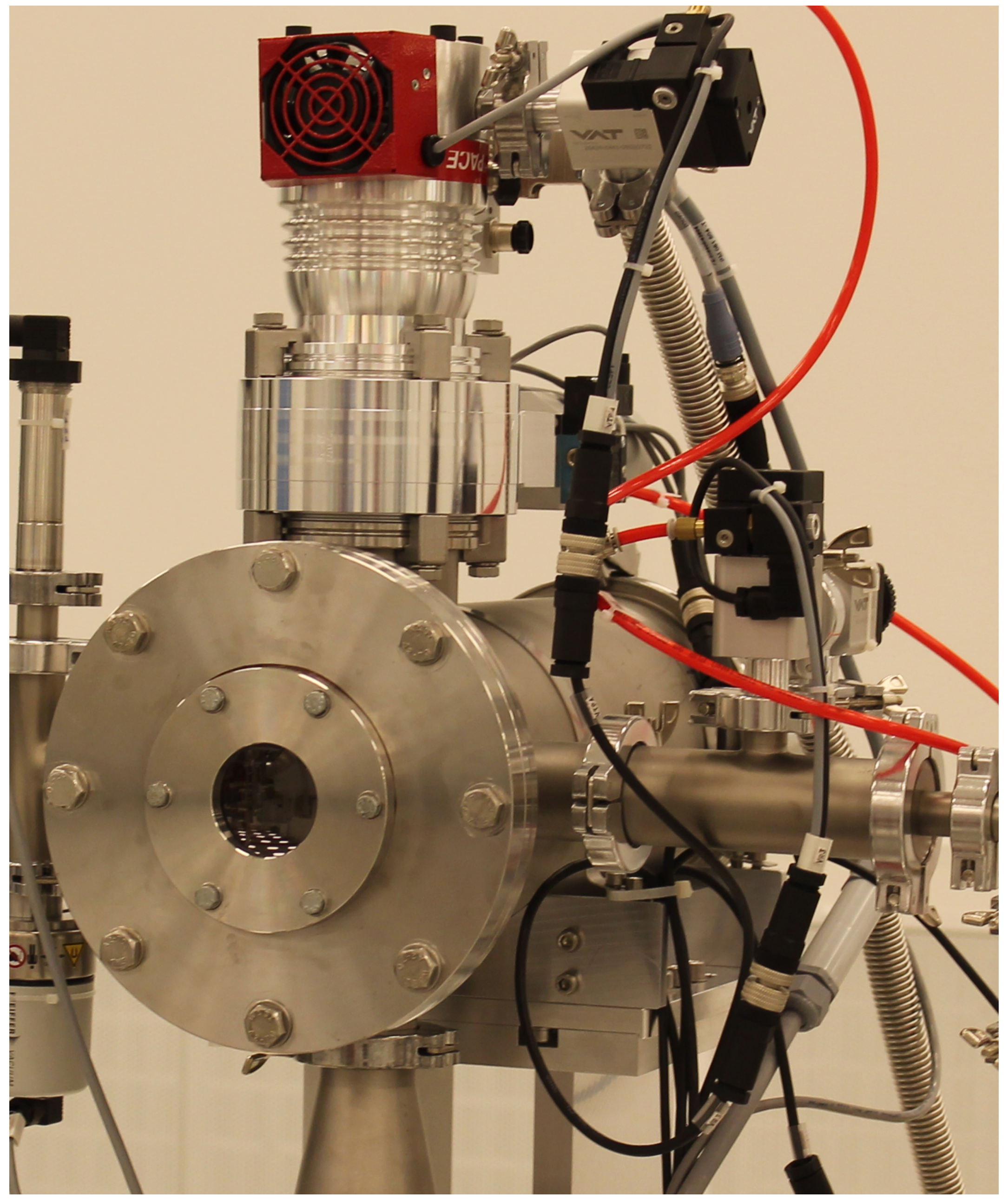


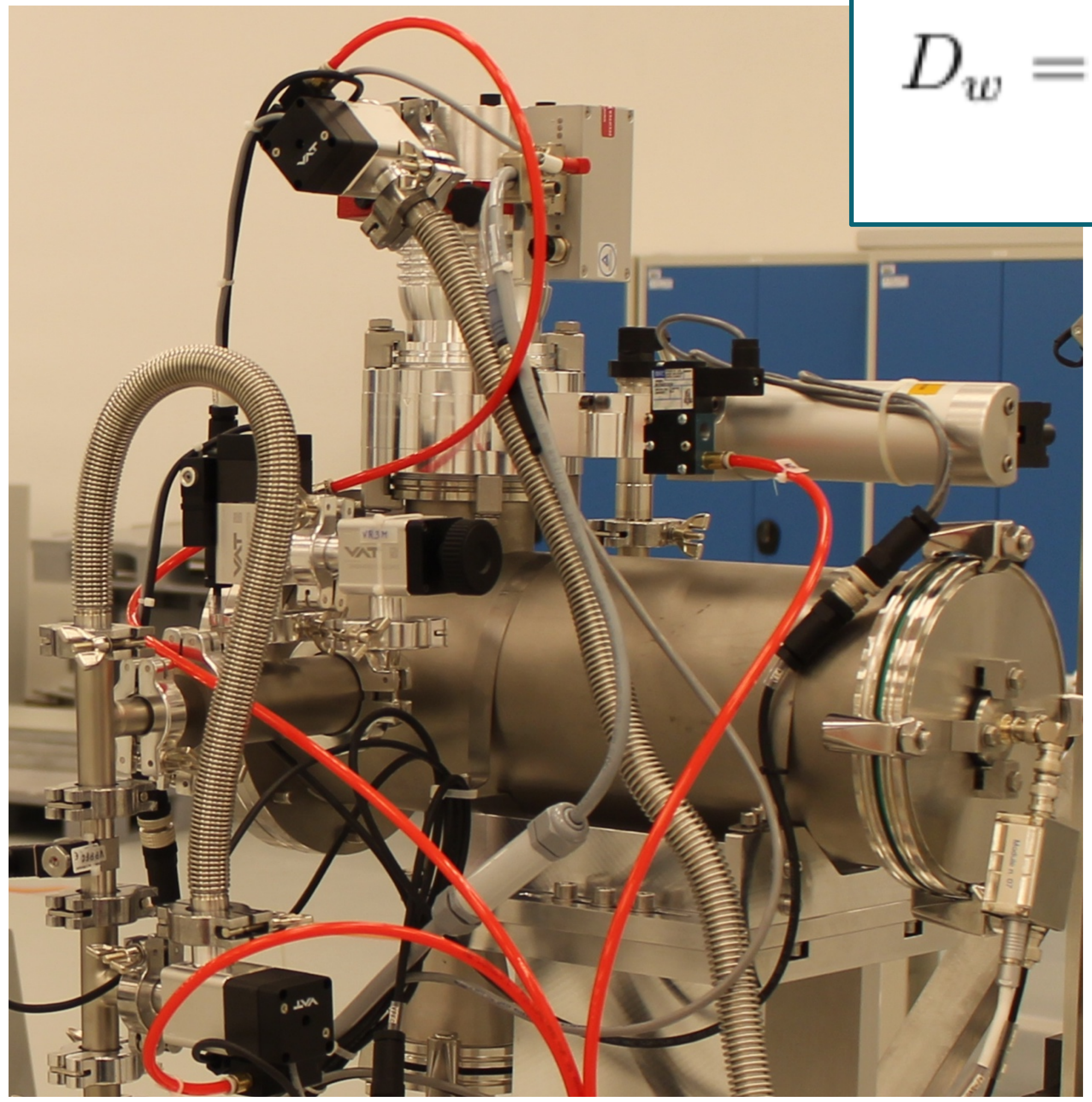

- Two adjacent IC, gaps of 5 mm and 10 mm, independently biased (maximum applied voltage ± 1000 V and ± 2000 V, respectively)
- Anode: thin layers of 5 μm of copper and 2 μm of nickel, deposited on a 25 μm layer of kapton
- Cathode:12 μm-thick layer of aluminized mylar

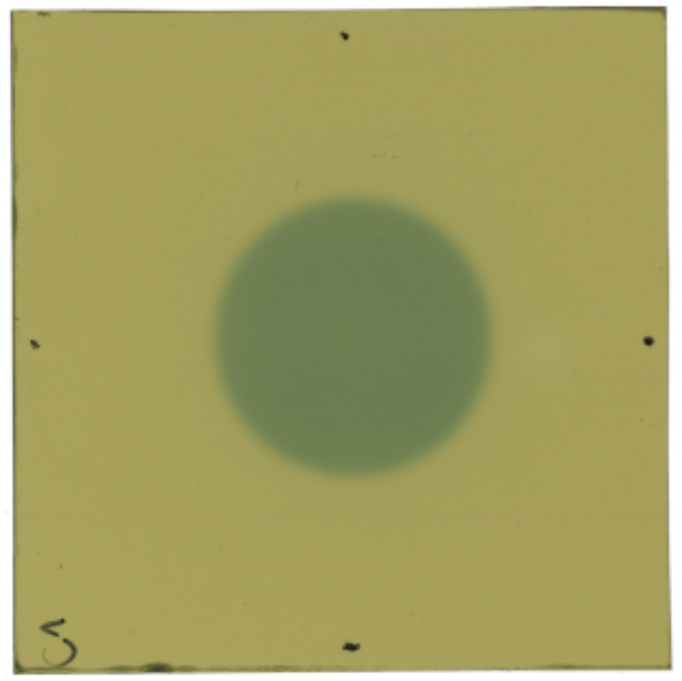
# Absolute dosimetry: Faraday cup

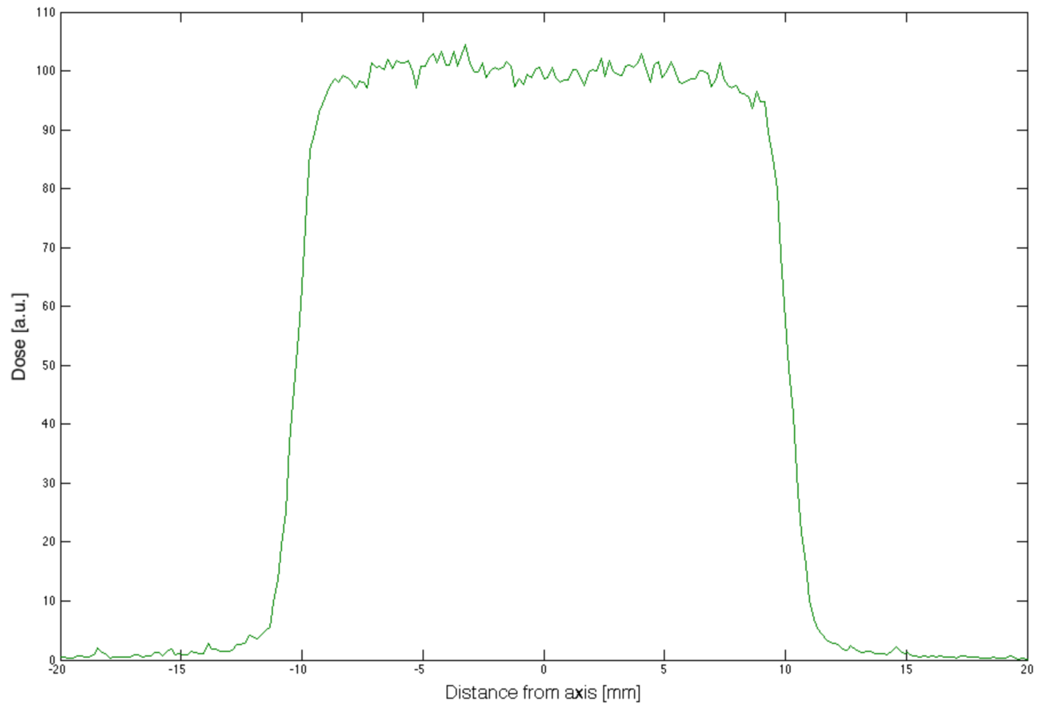


$$D_w = \frac{1}{A} \cdot \frac{\int (S(E))_w N(E) dE}{\int N(E) dE} \cdot \frac{Q}{e} \cdot 1.602 \cdot 10^{-10} \quad (Gy)$$







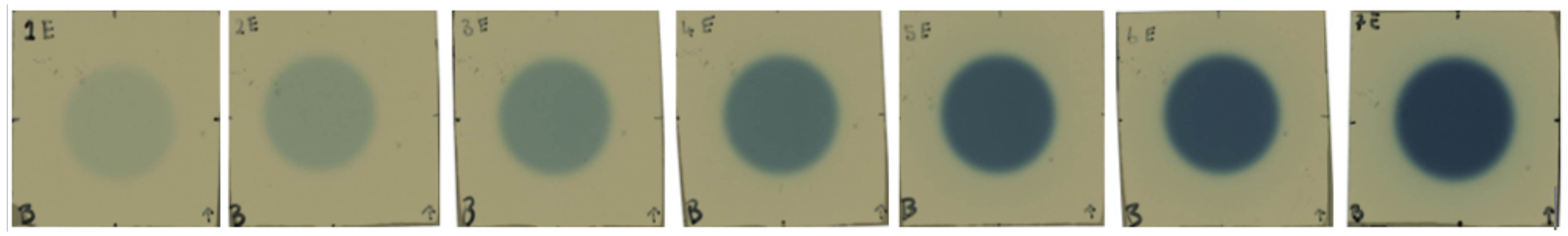


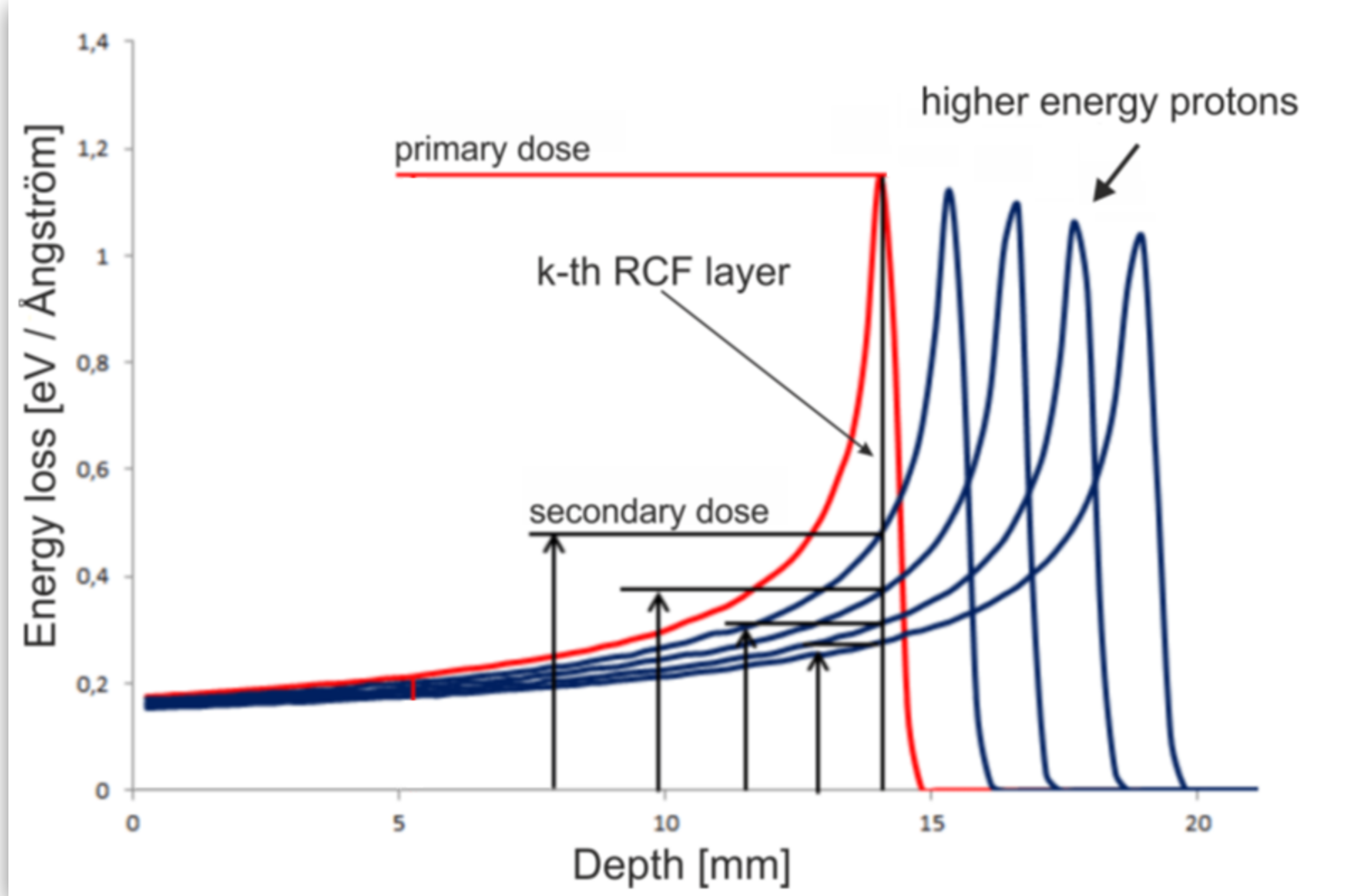

The cylindrical symmetry of the electric field provided by the external electrode is broken due to the presence of the internal one.

The resulting effect is a strongly asymmetric electric field, characterized by a significant transversal component able to maximize the deflection of the secondary electrons generated by both the entrance window and the cup.

# The unfolding approach to reconstruct the proton spectra

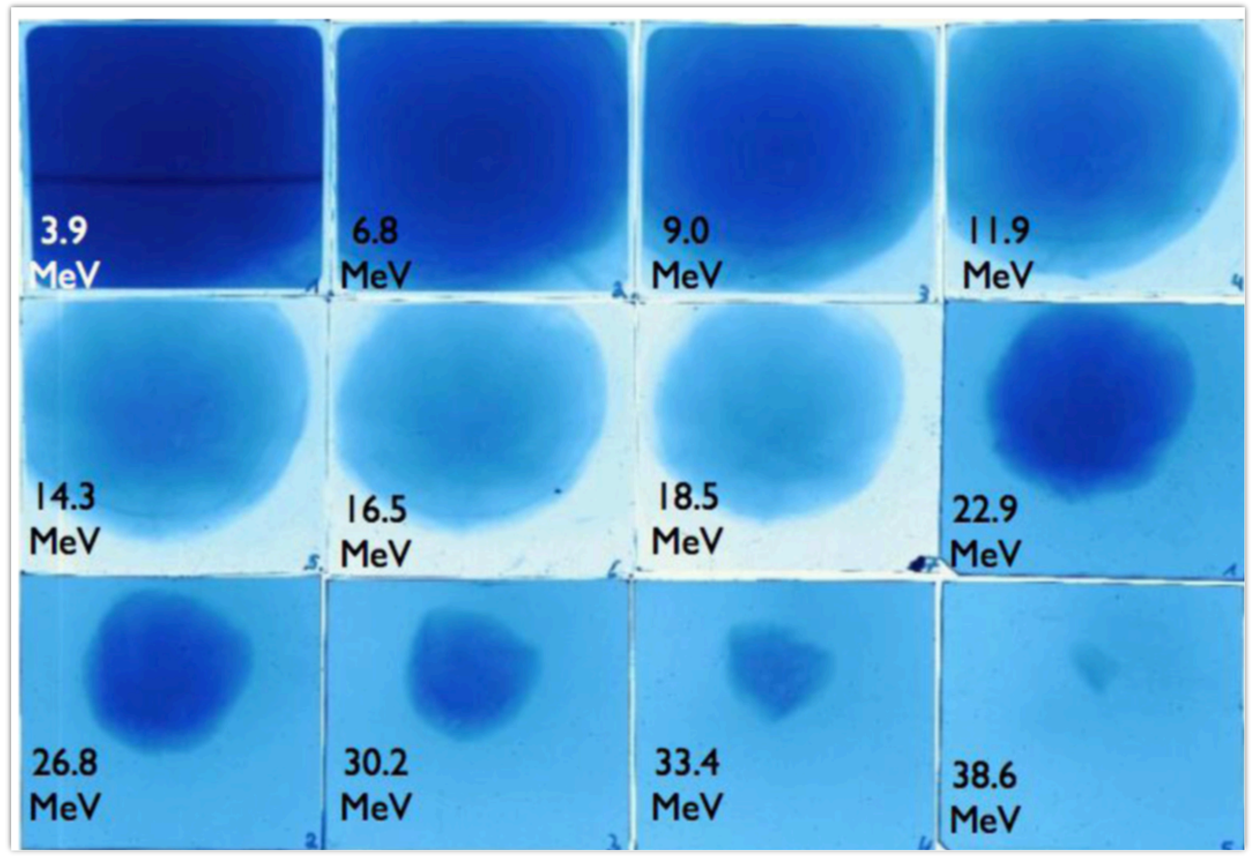


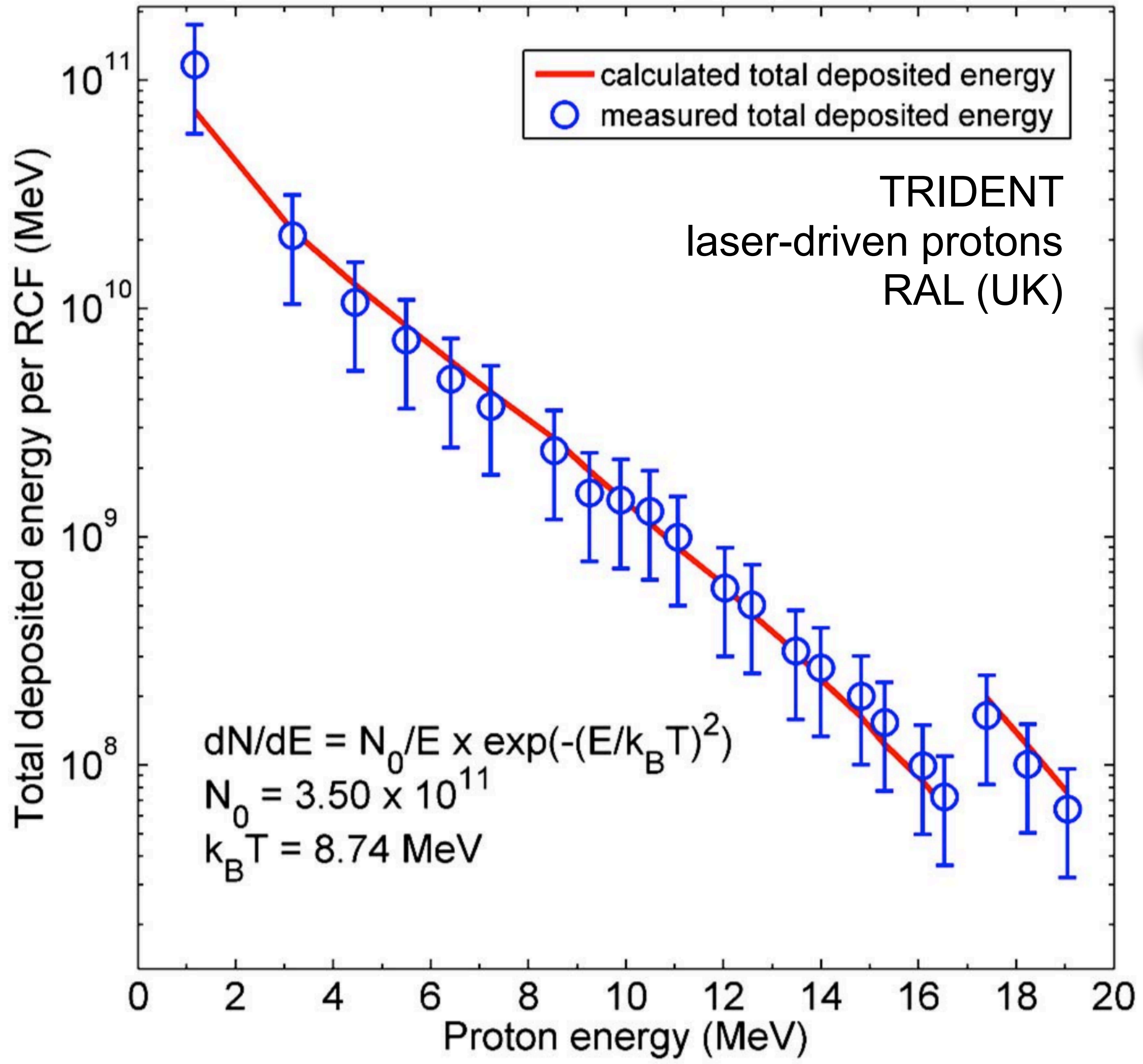





$$D_{prim}^{(k)} = D_{tot}^{(k)} - \sum_{i=k+1}^{N} \frac{D_{prim}^{(i)}}{w_{ii}} w_{ki}$$

F Nürnberg, et al.
Review of Scientific Instruments 80, 033301 (2009);



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# Some interesting results

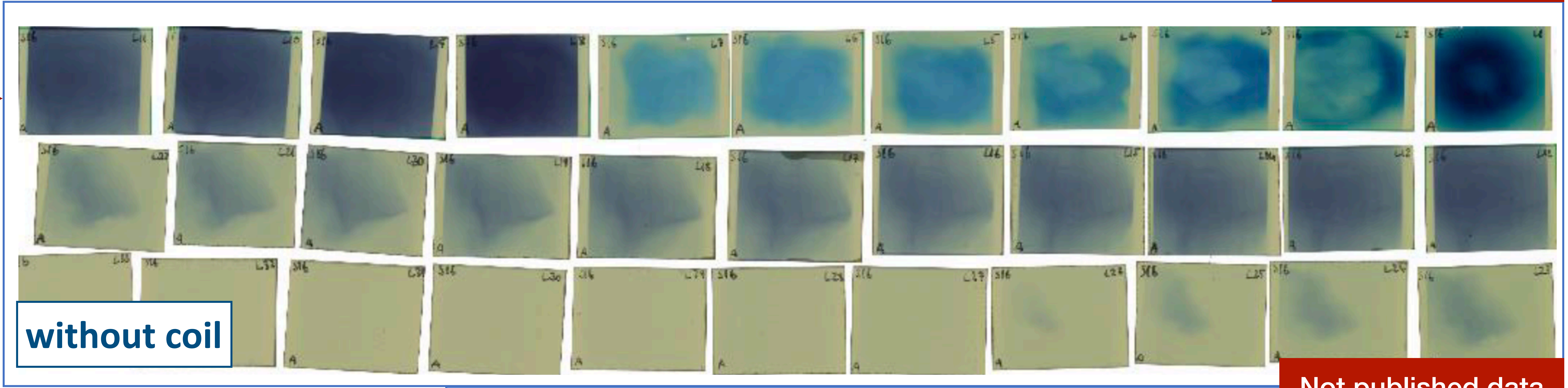
# Energy on target: 10 J - Target thickness: 4.5 um Al



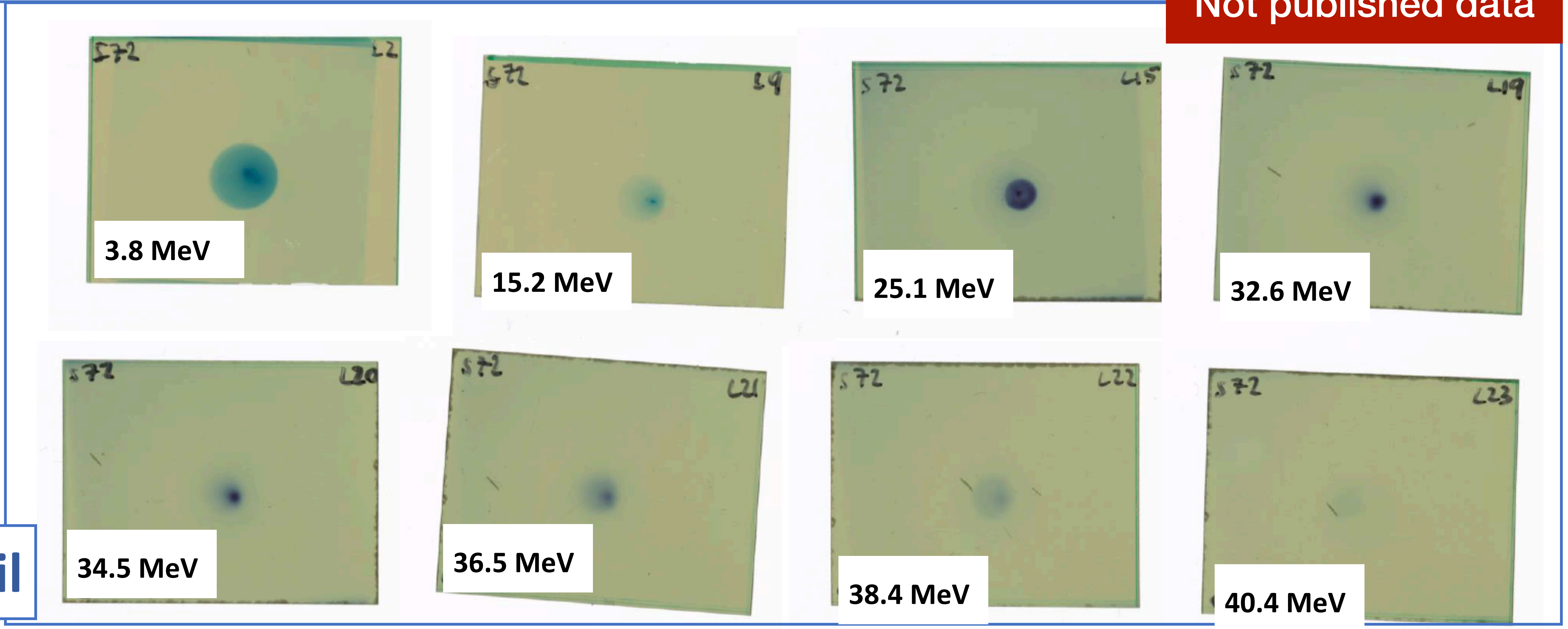
**PI Satya Kar (QUB)**

Preliminary results

proton beam




Not published data




with coil

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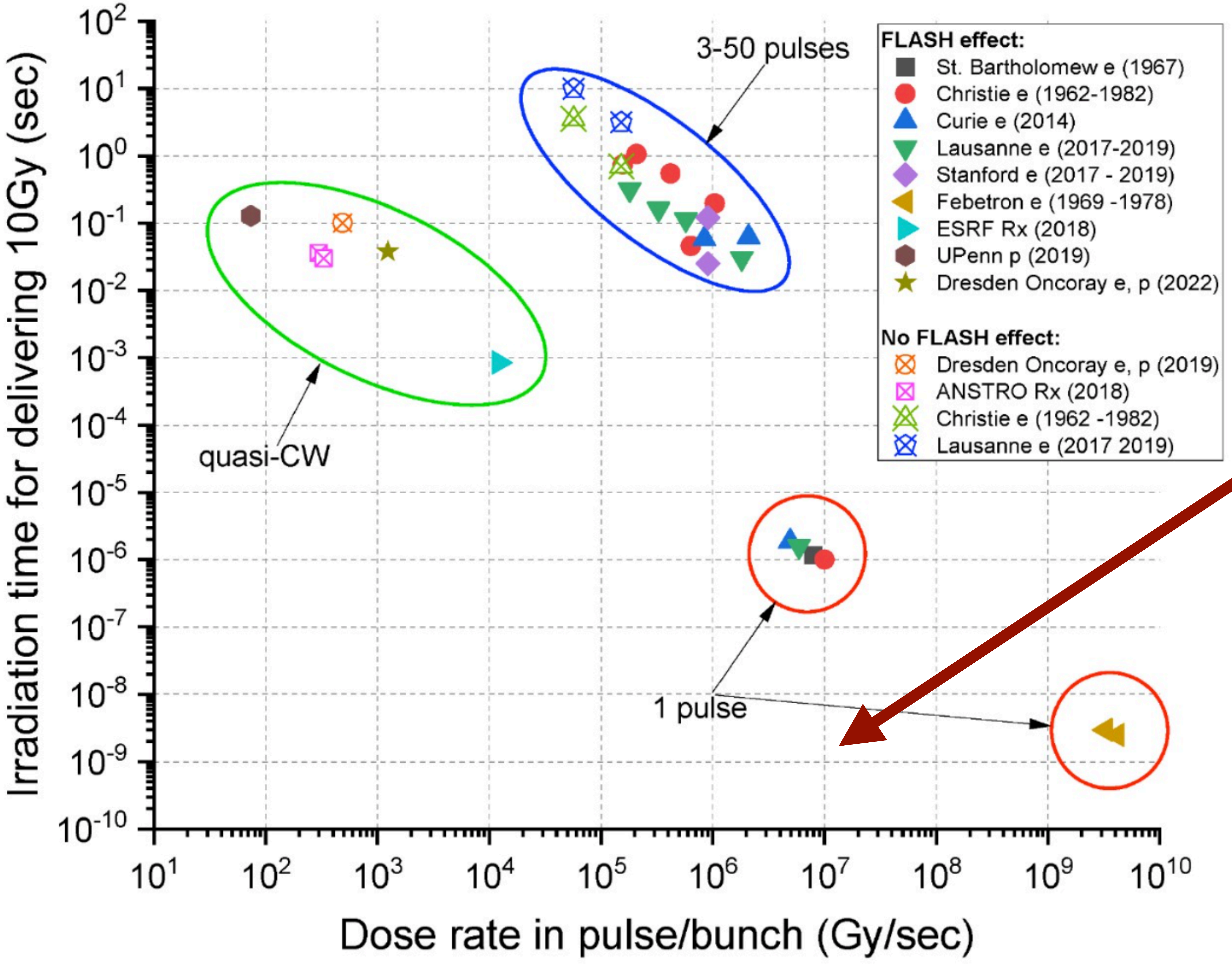
# Coil target

## Energy: 10 J - Target: 2um Cu




| Dose [Gy] | Energy [MeV] |
|---|---|
| 69,47 | 16,9 |
| 28 | 17,8 |
| 12 | 19,3 |
| 10,53 | 21,4 |
| 9,35 | 23,3 |
| 11,85 | 25,1 |
| 10,8 | 27 |
| 13,5 | 28,8 |
| 11,08 | 30,7 |
| 10,69 | 32,6 |
| 8,74 | 34,5 |

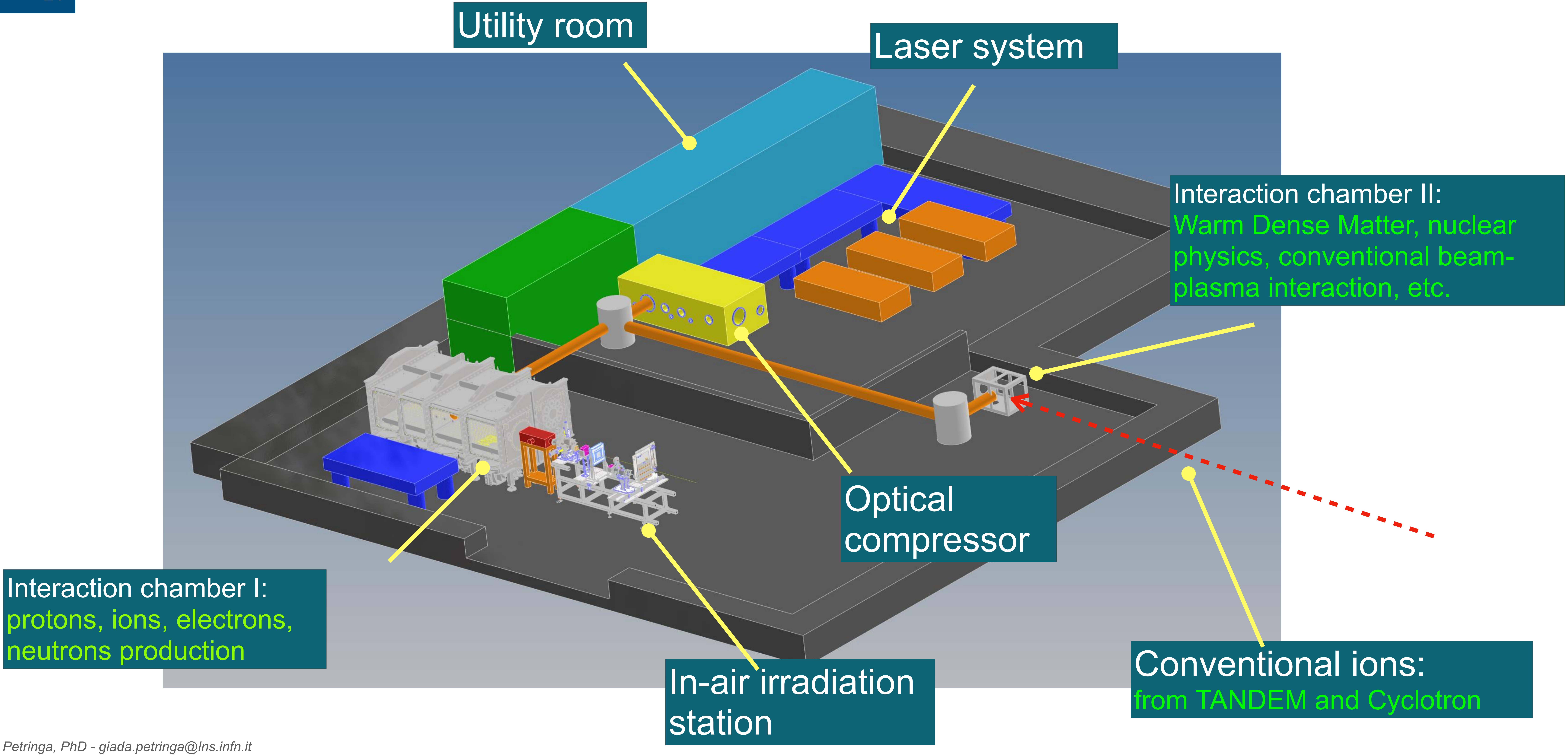
Preliminary results

# INFN - Laser indUCEd radiation production

The objective is to establish an operational laser facility at Laboratori Nazionali del Sud for studies in nuclear physics, plasma physics, development of new detectors, applications in medical physics and cultural heritage."

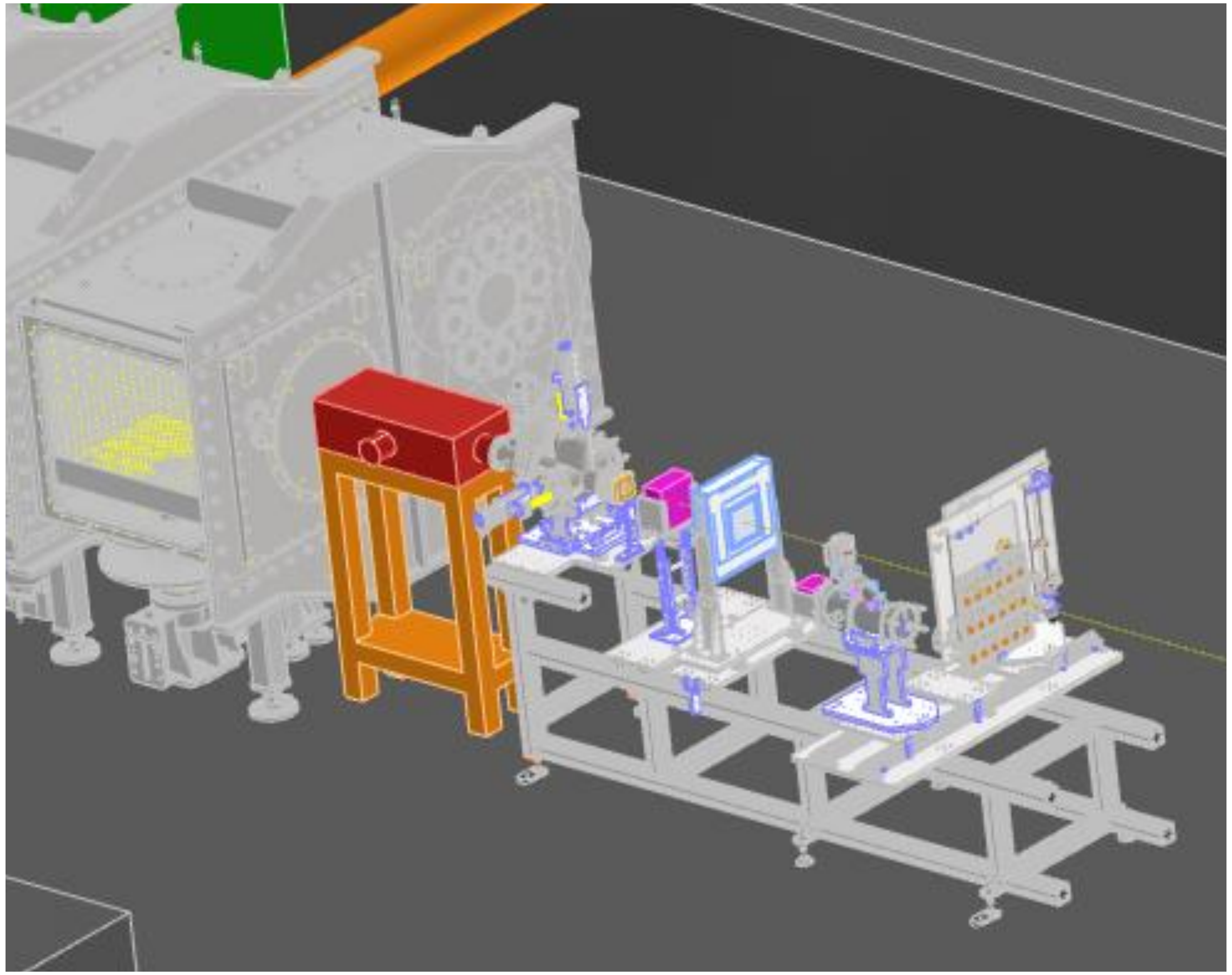
# I-LUCE facility @LNS



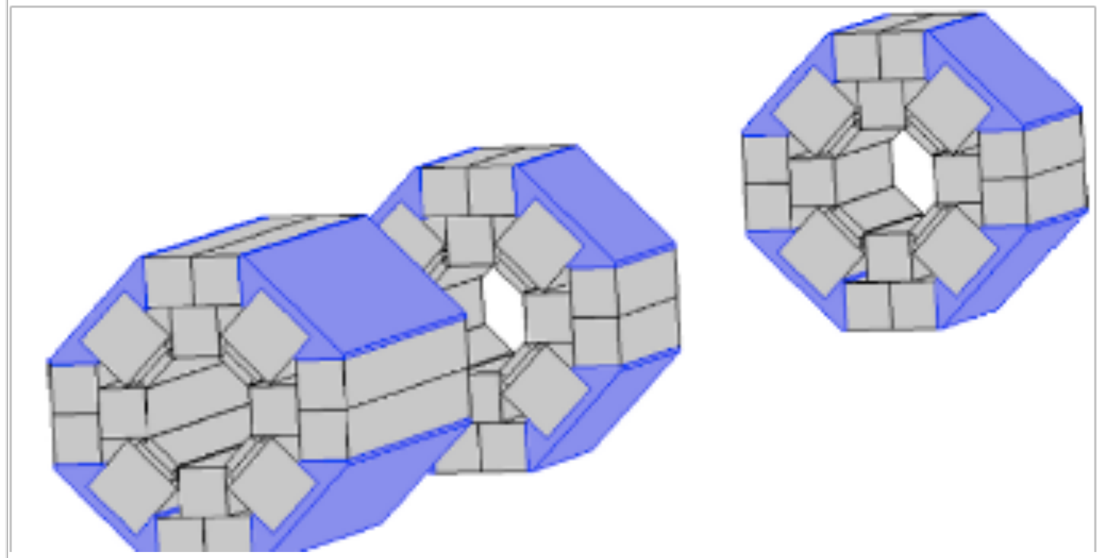


# BIOLOGICAL SAMPLE IRRADIATION

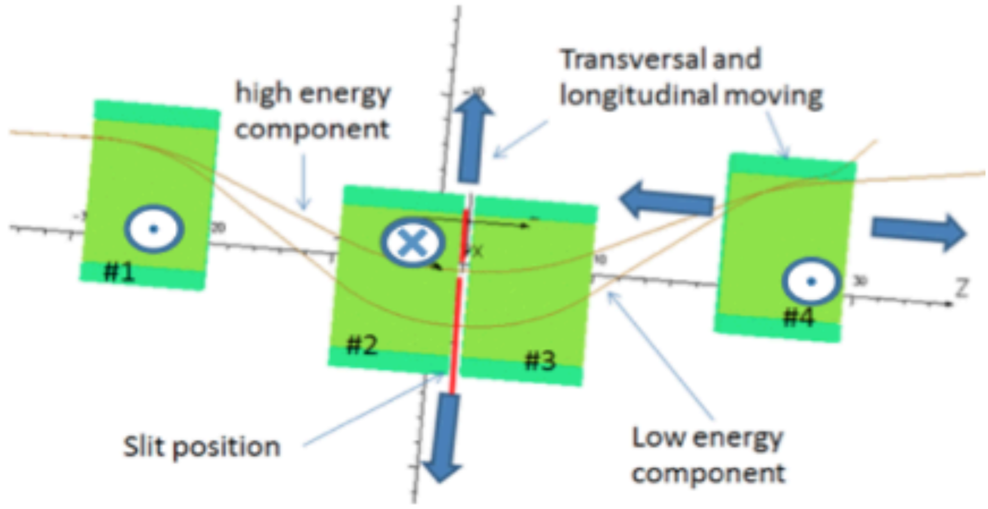


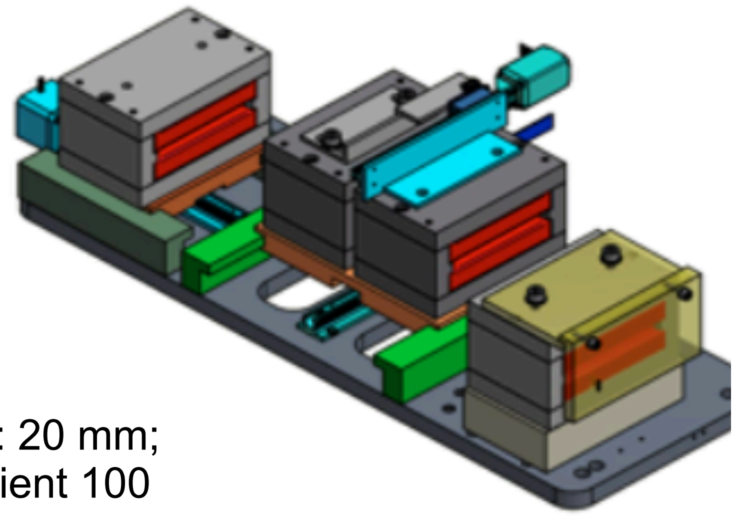


| | | |
|---|---|---|
| Protons / Ions | Max energy | 50 MeV |
| | Particle per pulse (at 30 MeV) | $10^{11}$ MeV$^{-1}$ Sr$^{-1}$ |
| Eletrons | Max energy | 3 GeV |
| | Particles per pulse | $10^{9}$ |



Dipole field: 0.8 T

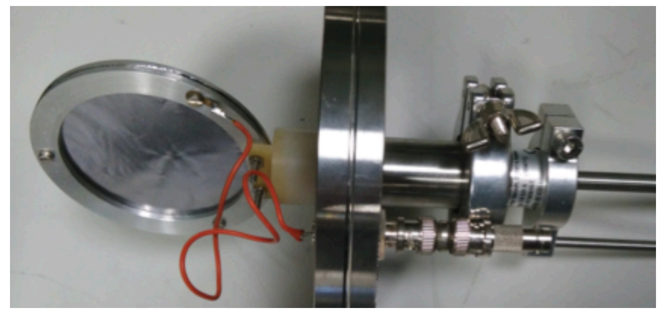


Bore: 20 mm;
Gradient 100
T/m

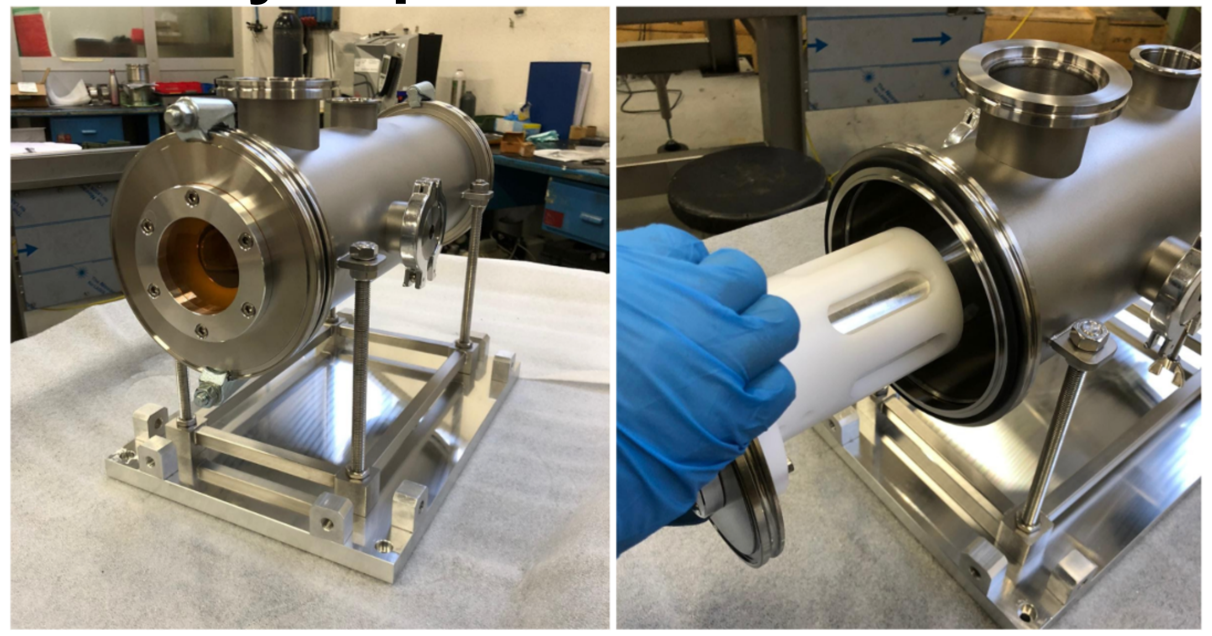
**Quadrupoles + energy selector**
Transport up to 30 MeV with an energy revolution of 5 %

**SEM**



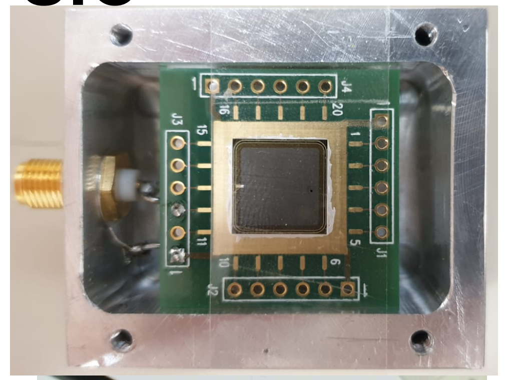
**ICT**

**Faraday cup**



**Scintillator**


**SiC**

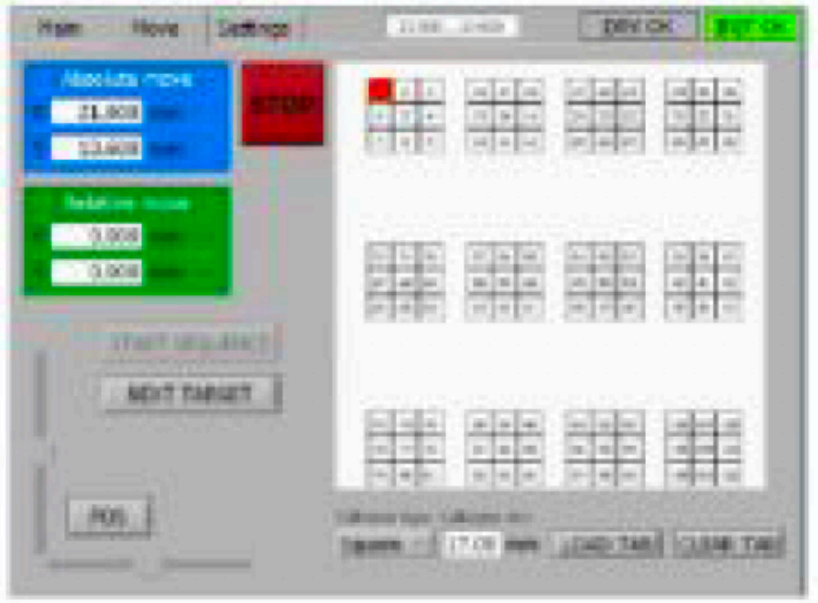


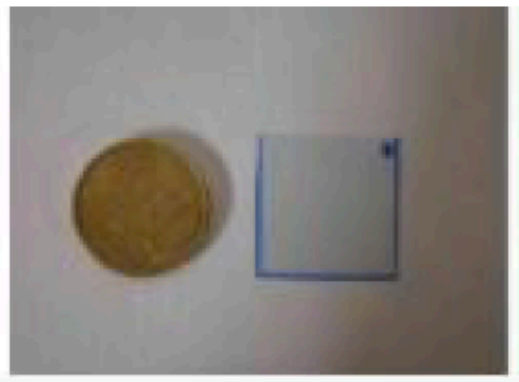
**Diamond**

# BIOLOGICAL SAMPLE IRRADIATION

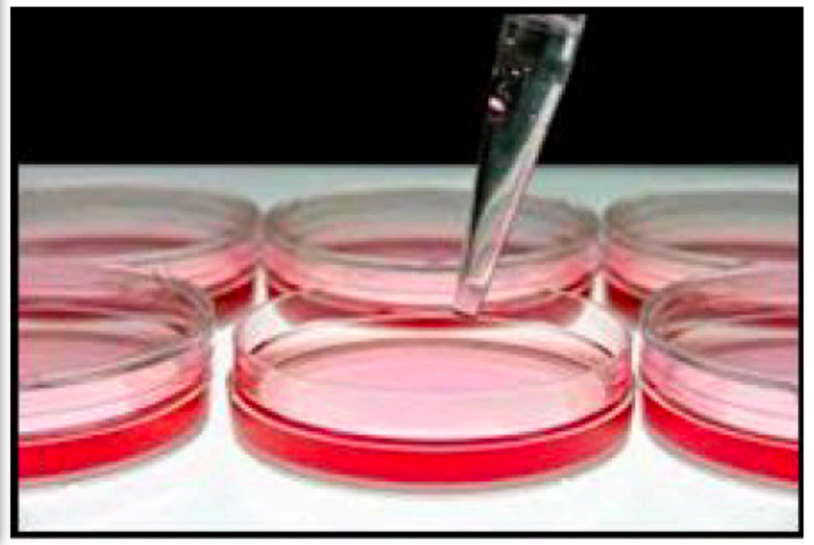


In-vitro positioning system

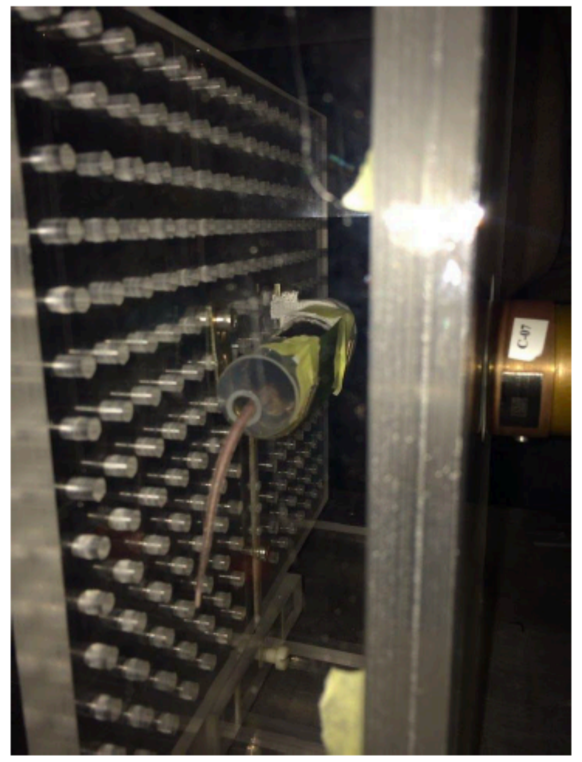




Analysis pre and post irradiation



In-vivo positioning system



Small animals storage

**Types of equipment into the Bio-Lab:**

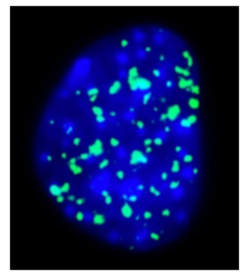
- ✓Laboratory Hood
- ✓Inverted microscopy
- ✓Centrifuge
- ✓Incubator
- ✓-80°C for storage of biological samples
- ✓Dewar for long term storage of different cellular batch

*Fluorescence Microscopy*


**16.25 megapixel CMOS image sensors for microscopy**

**High sensitivity**
**Excellent linearity**
**High – frame rate**
**Low Noise**

**Integration with imaging SF**



eli beamlines

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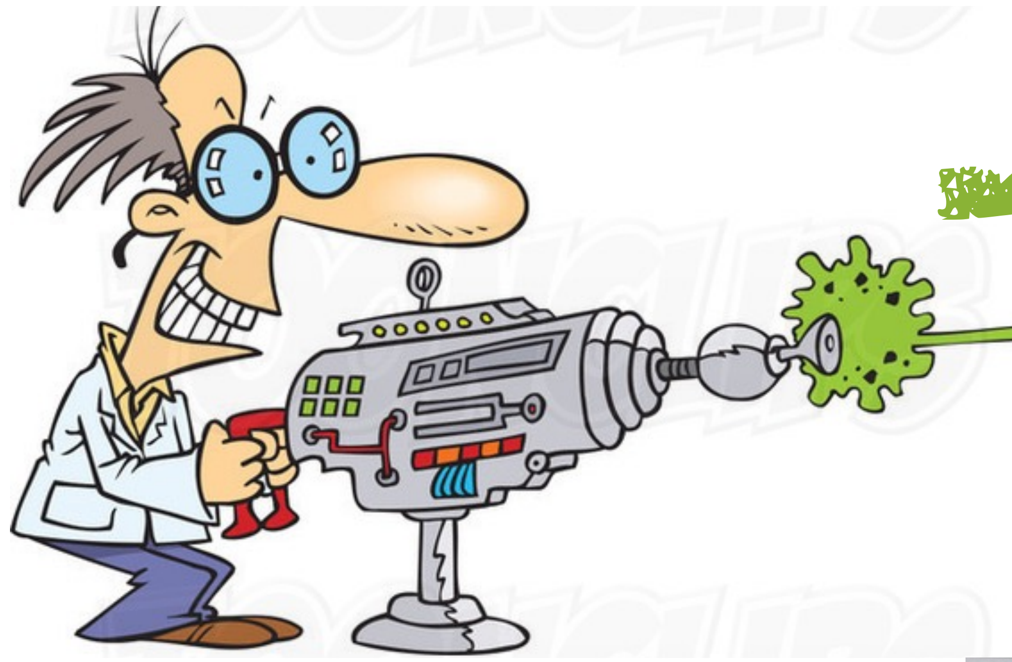

# Thanks for listening