SAPIENZA UNIVERSITÀ DI ROMA | INFN | ARPG Applied Radiation Physics Group | CENTRO RICERCHE ENRICO FERMI

Development of a fluorescence-based beam monitor and beam delivery studies for FLASH radiotherapy

Accelerator Physics PhD thesis defense

Antonio Trigilio

Supervisor: Prof. Alessio Sarti

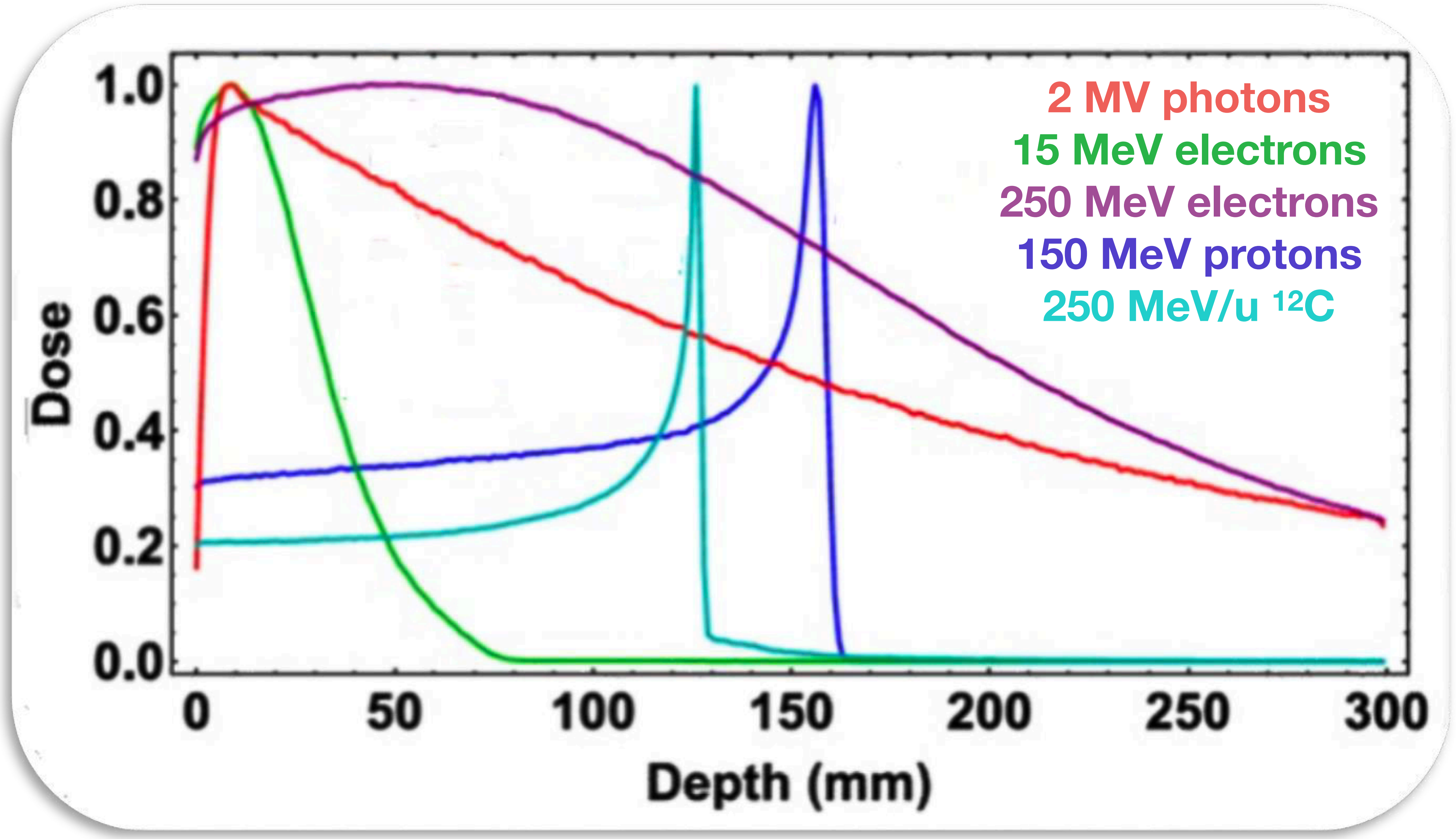
Co-Supervisor: Dr. Michela Marafini

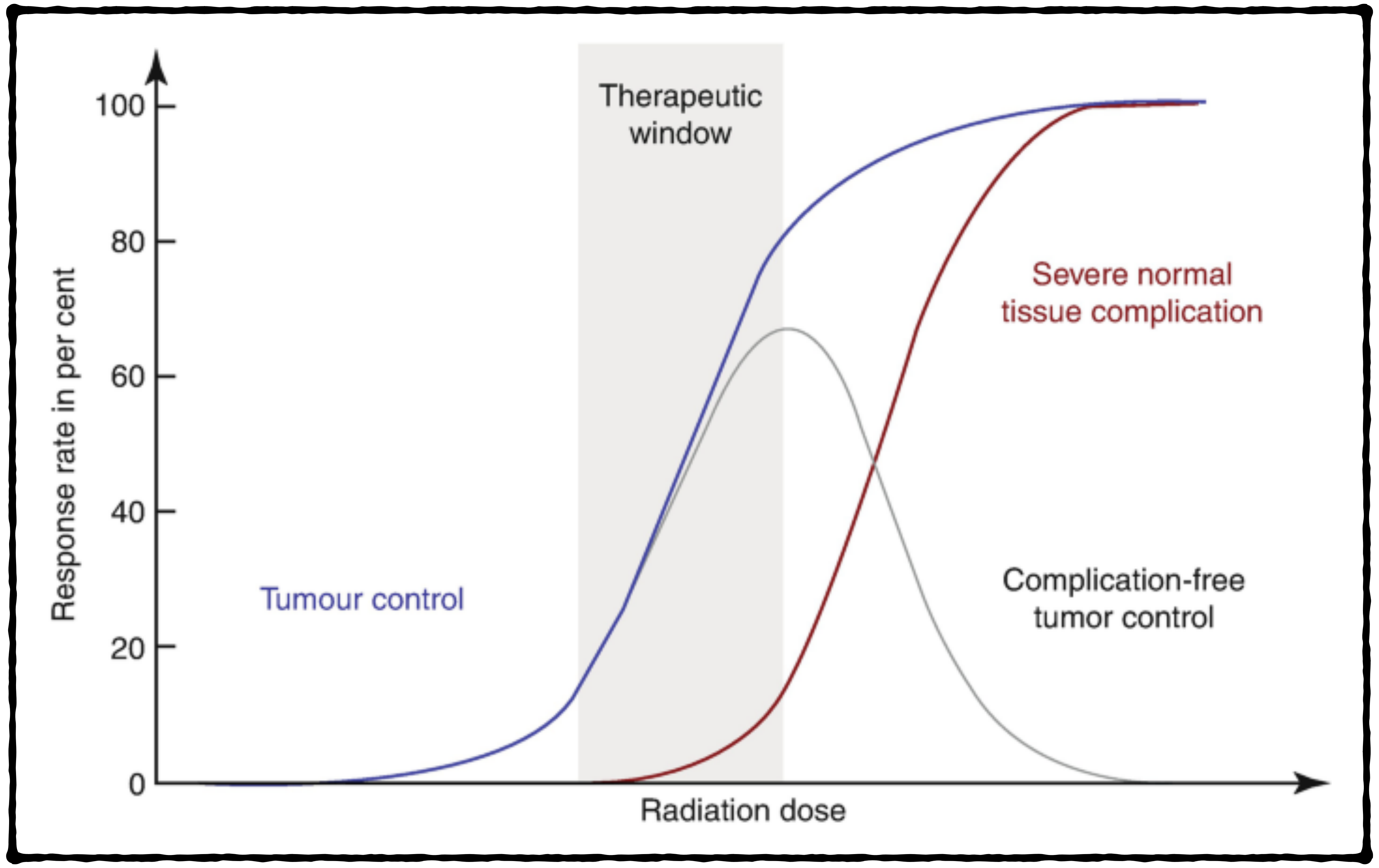
FLASH Radiotherapy with hIgh Dose-rate particle beAms

Radiotherapy

Goal: destroy tumors while saving the healthy tissue

- **Therapeutical beam** (electrons, photons, light ions) release energy inside the human tissues — **dose** — following an optimized **treatment plan**.
- **Limited** by protection against side effects to **organs at risk**.





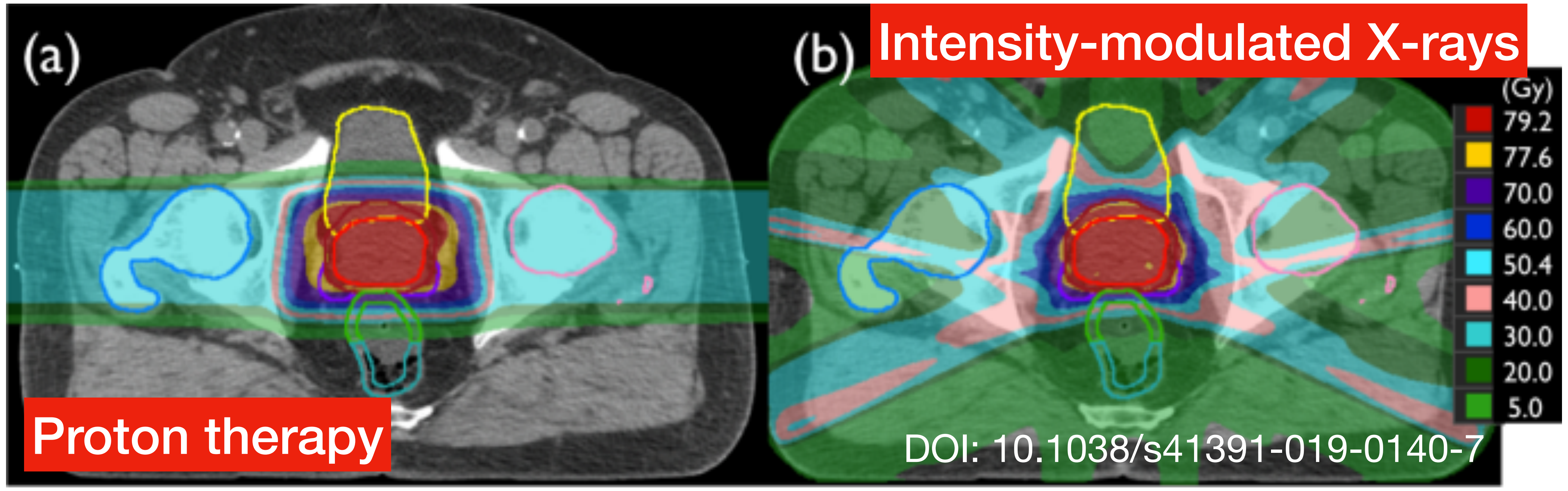
$$D = \frac{dE}{dm}\ [\mathrm{Gy}]$$

Dose: the amount of radiation we need to deliver during treatment (also as function of time).

- There is still a wide number of pathologies which are untreatable due to an under-dosage of radiation to the tumor, which leads to **radio-resistance**.
- The field of RT is constantly asking for new ways to widen the therapeutic window and **increase** the maximum dose deliverable.

Conventional Radiotherapy

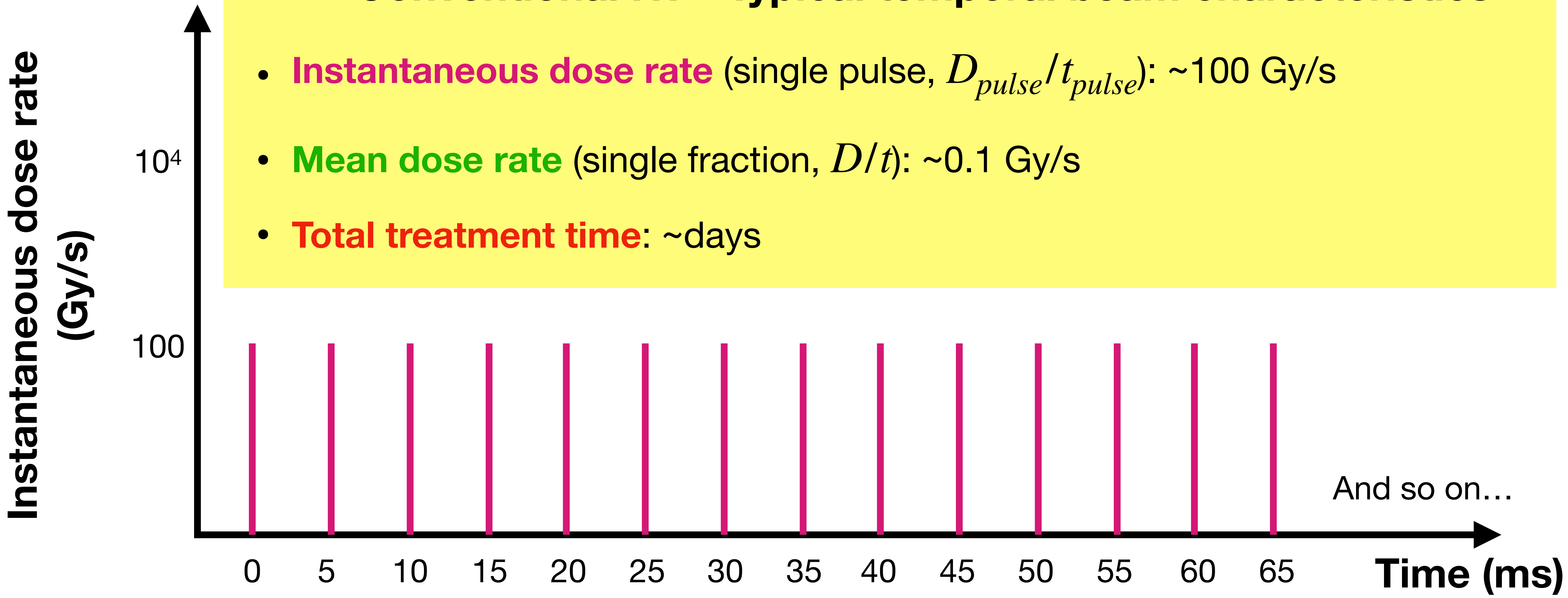
- Over the past decades, research has focused on increasing **spatial conformity** of the dose to the tumor volume.
  - Exploit the intrinsic properties of energy release in tissues (**protons**, **carbon** and other ions).
  - Address the tumor with many fields of different energies and directions (VMAT & techniques of intensity modulation).



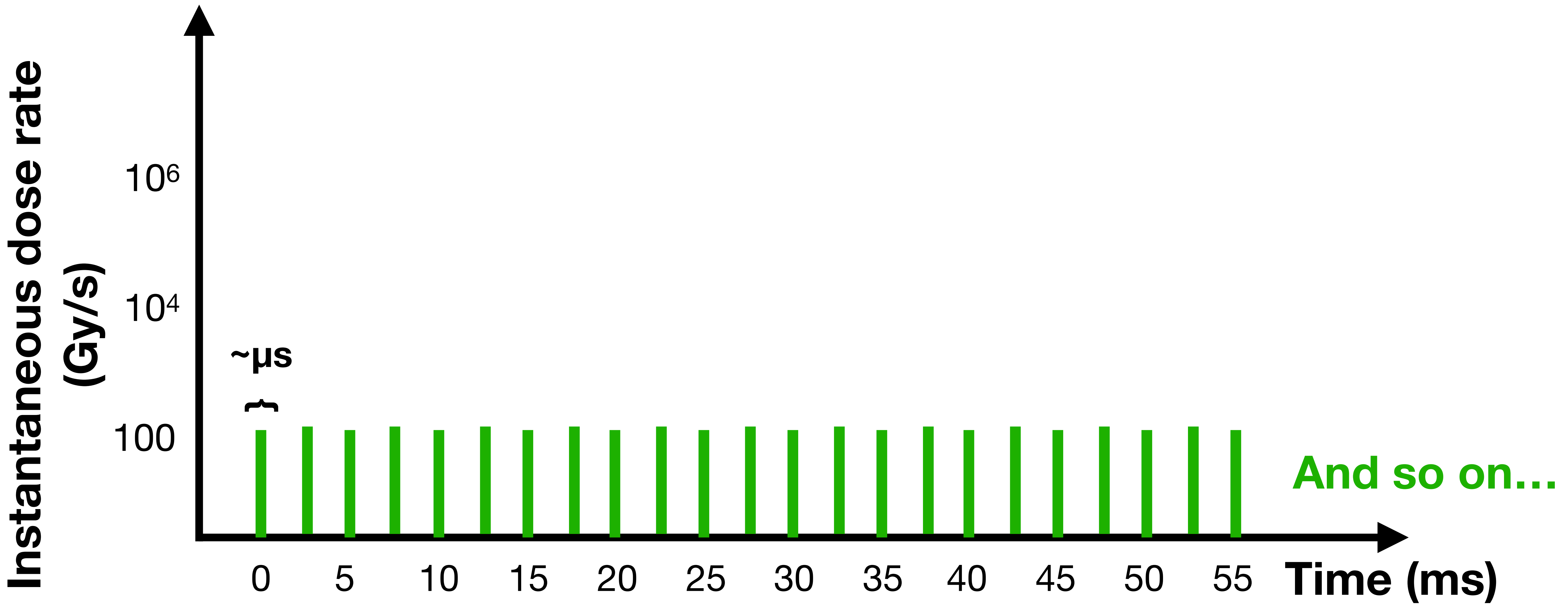
- What about **time**? The usual way a radiotherapy treatment is delivered is through a **pulsed** structure.
- **Pulse duration:** 2-6 μs
- **Repetition frequency:** 50-1000 Hz (strongly depends on the accelerator)
- The **total dose** is thus delivered in tens of **fractions** (~2 Gy, ~minutes), each made of a sequence of **pulses**.

Conventional RT - Typical temporal beam characteristics

- **Instantaneous dose rate** (single pulse, D_{pulse}/t_{pulse}): ~100 Gy/s
- **Mean dose rate** (single fraction, D/t): ~0.1 Gy/s
- **Total treatment time**: ~days



FLASH effect: Introduction



Beam characteristics	CONV
Dose per pulse	~ 0.5 mGy
Inst. dose rate (single pulse)	~ 100 Gy/s
Mean dose rate (single fraction)	~ 0.1 Gy/s
Total fraction time	~ minutes

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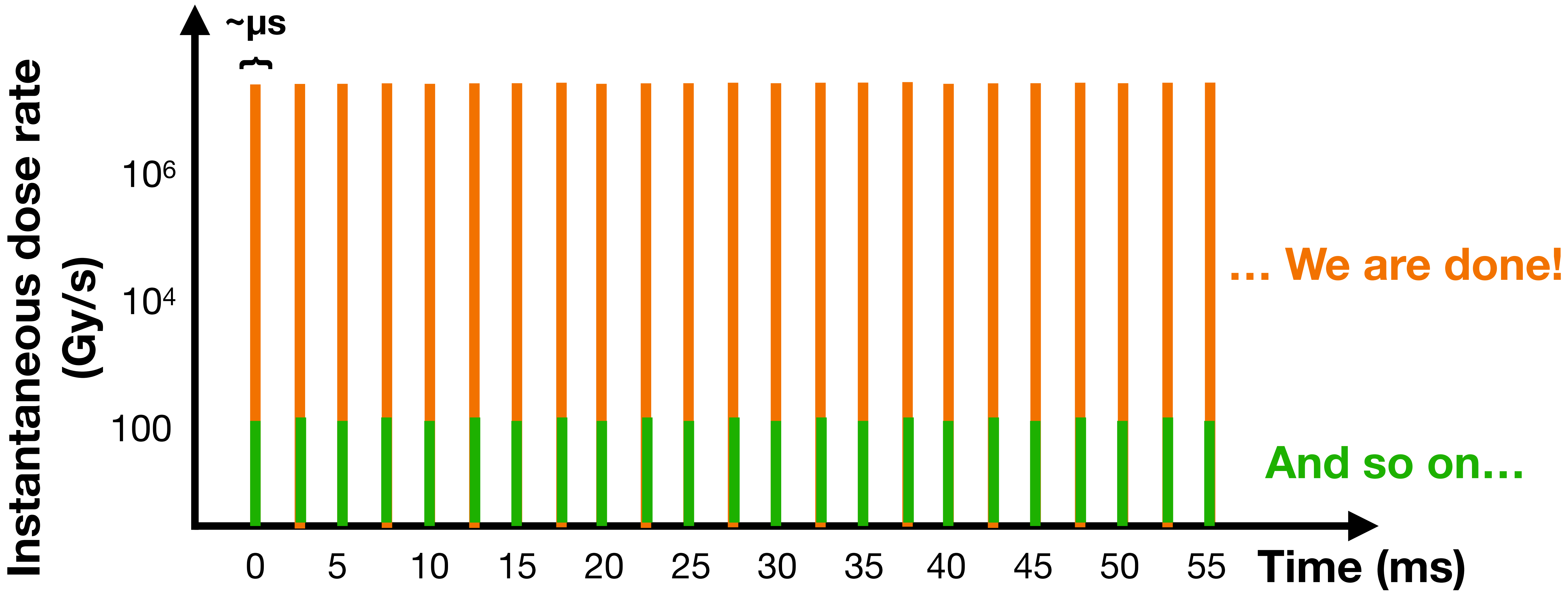

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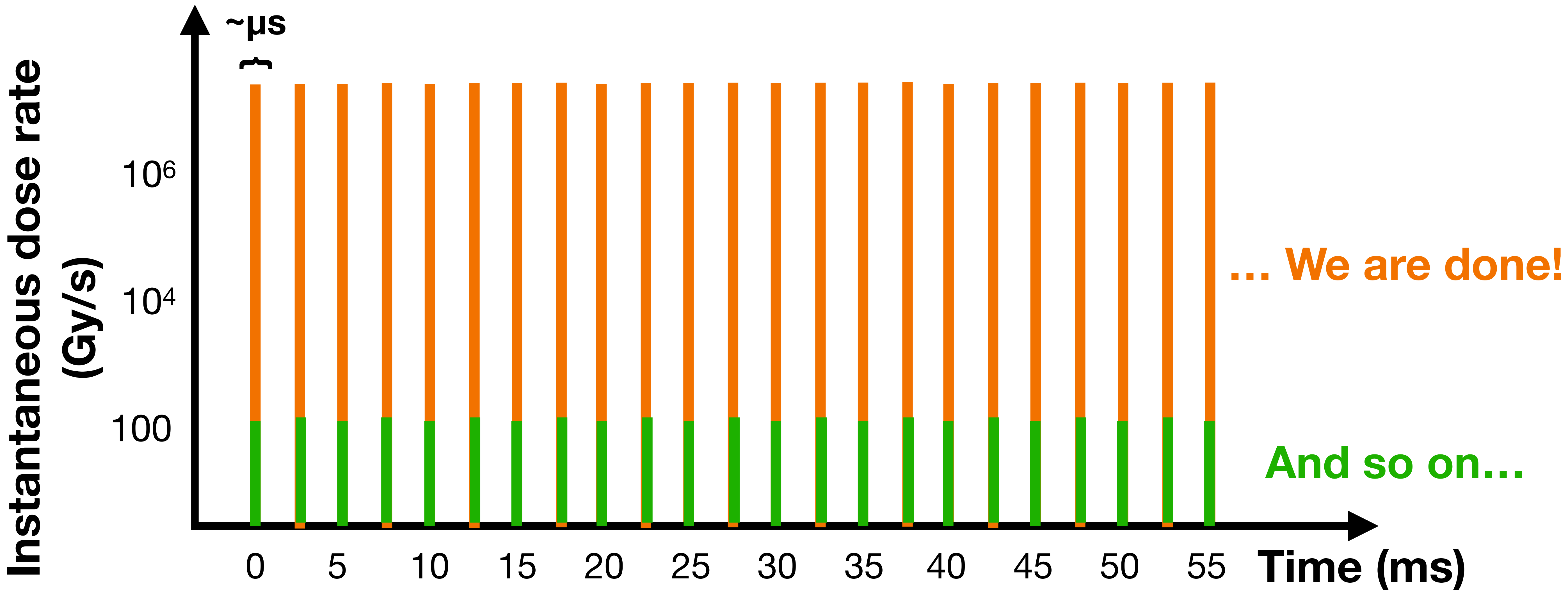
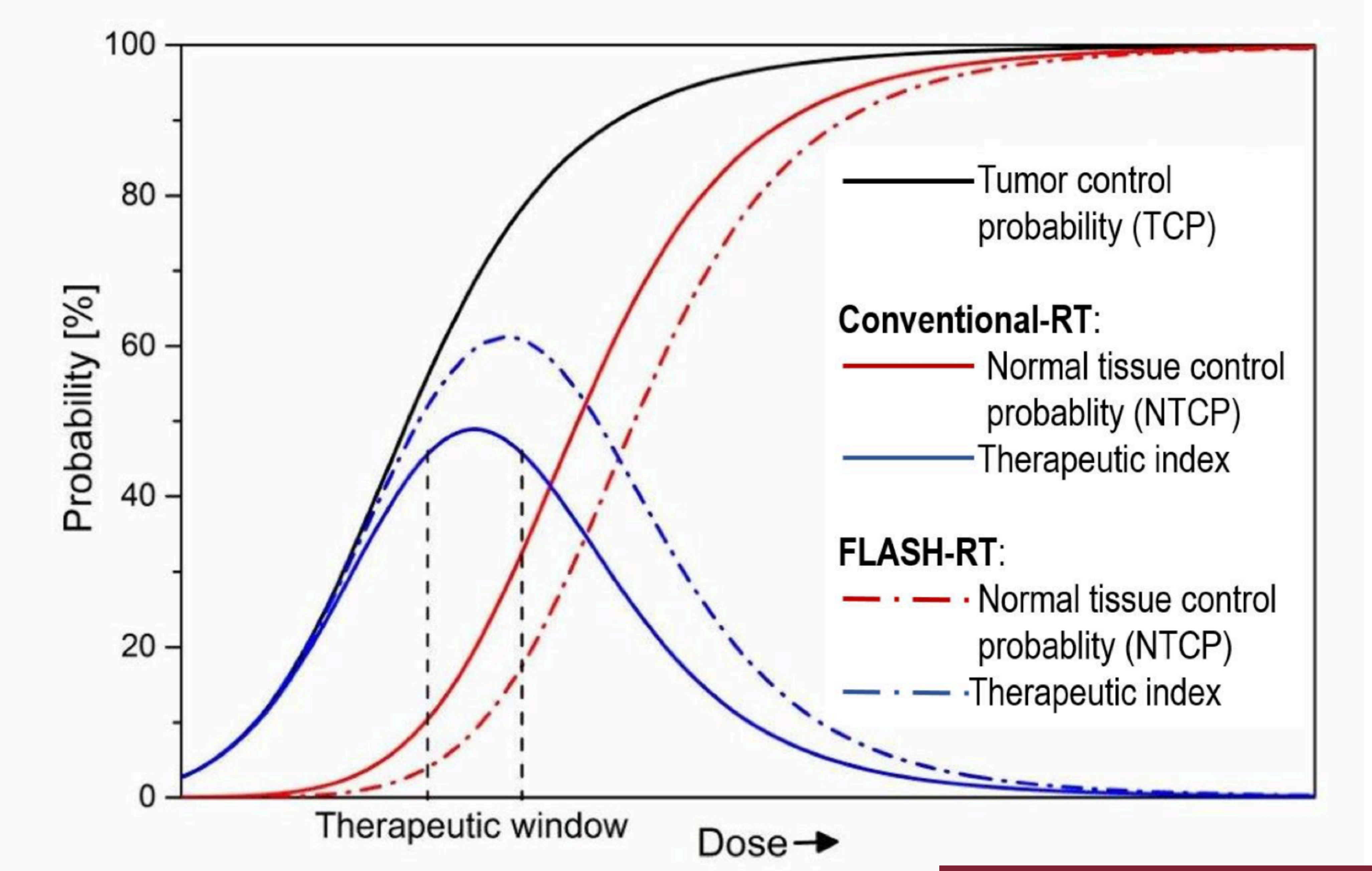
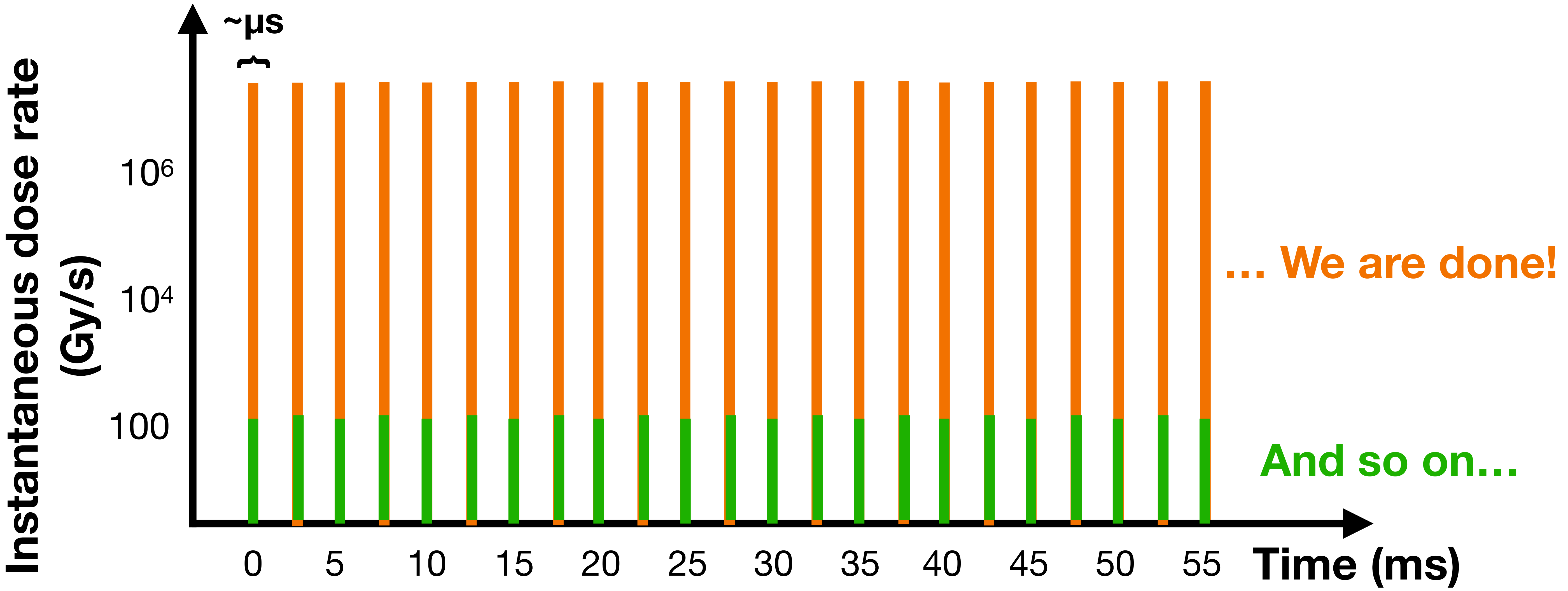


Beam characteristics	CONV	UHDR / FLASH-RT
Dose per pulse	~ 0.5 mGy	> 1 Gy
Inst. dose rate (single pulse)	~ 100 Gy/s	> 10^6 Gy/s
Mean dose rate (single fraction)	~ 0.1 Gy/s	> 100 Gy/s
Total fraction time	~ minutes	< 100 ms

FLASH effect: Introduction

- An increased radio-resistance — **reduced toxicity** — is observed **in normal tissues** when delivering a single irradiation at ***ULTRAHIGH*** dose rates in a very short time.
- This has been named **FLASH** effect. Its biological mechanisms are not yet understood, and there is a lot of investigation going on.
- It would be possible to treat the tumor with a **higher** (more efficient) dose, keeping an adequate **sparing** of the healthy tissues.





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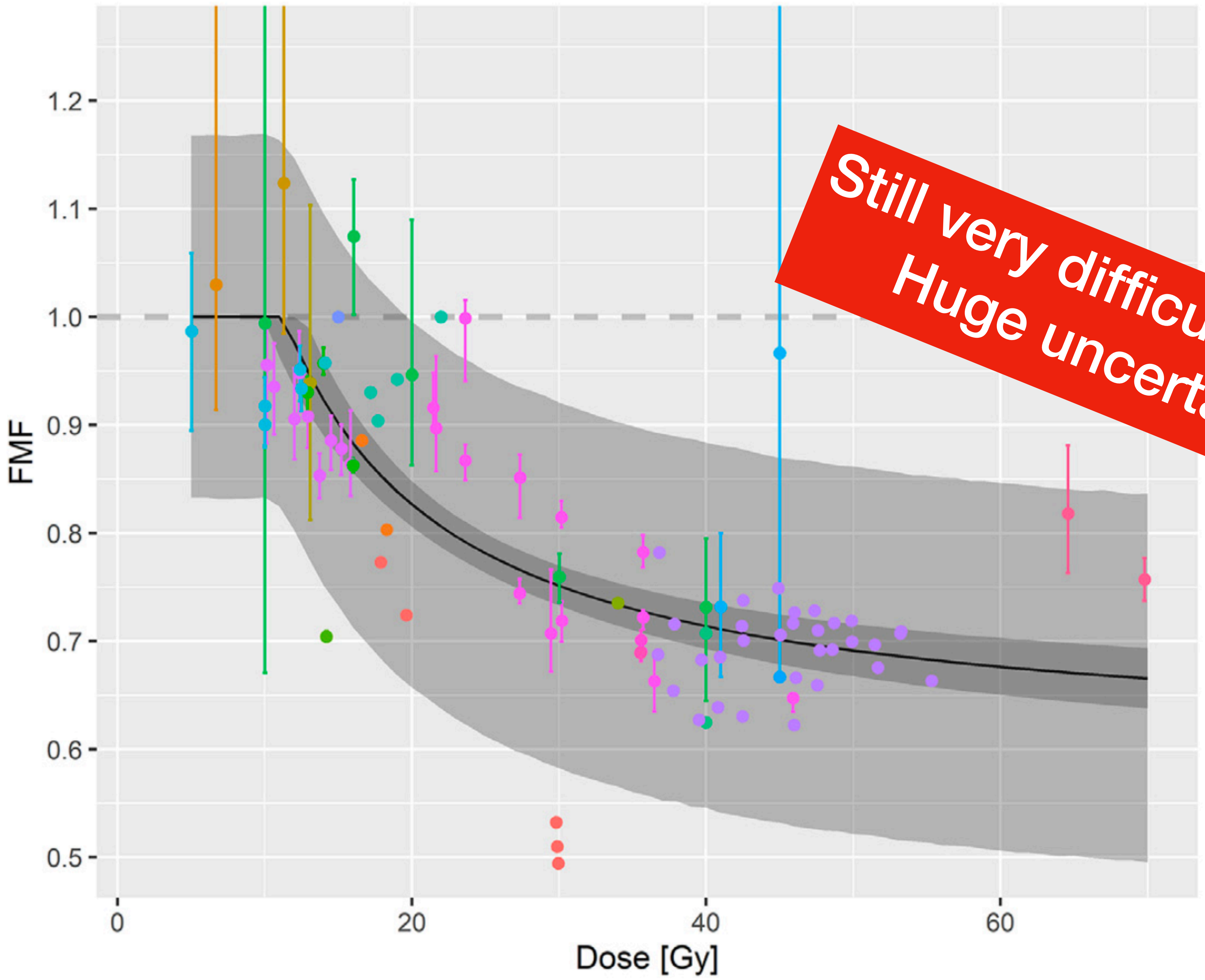
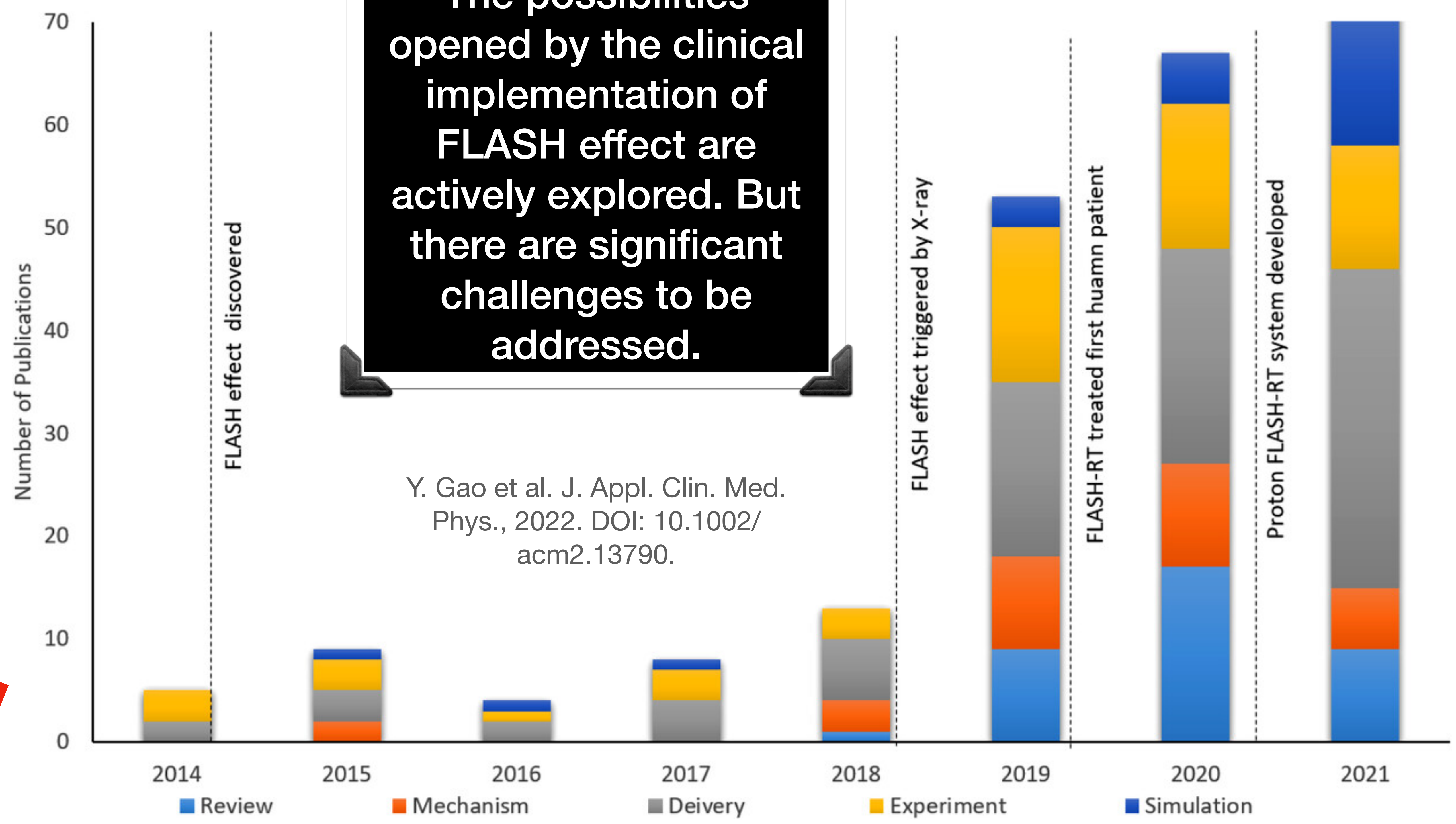
FLASH effect: Introduction

- 2023: the FLASH effect has been observed ***in vivo*** for different kinds of normal tissues (lungs, skin, brain…) and tumors (breast, H&N, lung…) and has been confirmed in several animal species (mice, cats, zebrafish…).
- The majority of studies use low-energy (4-7 MeV) electron beams, as of today the most widely available UHDR sources for pre-clinical research.



Still very difficult to quantify.
Huge uncertainties…



The possibilities opened by the clinical implementation of FLASH effect are actively explored. But there are significant challenges to be addressed.

Y. Gao et al. J. Appl. Clin. Med. Phys., 2022. DOI: 10.1002/acm2.13790.

- Underlying bio-chemistry
- Beam delivery
- Beam monitoring and dosimetry
- Treatment planning

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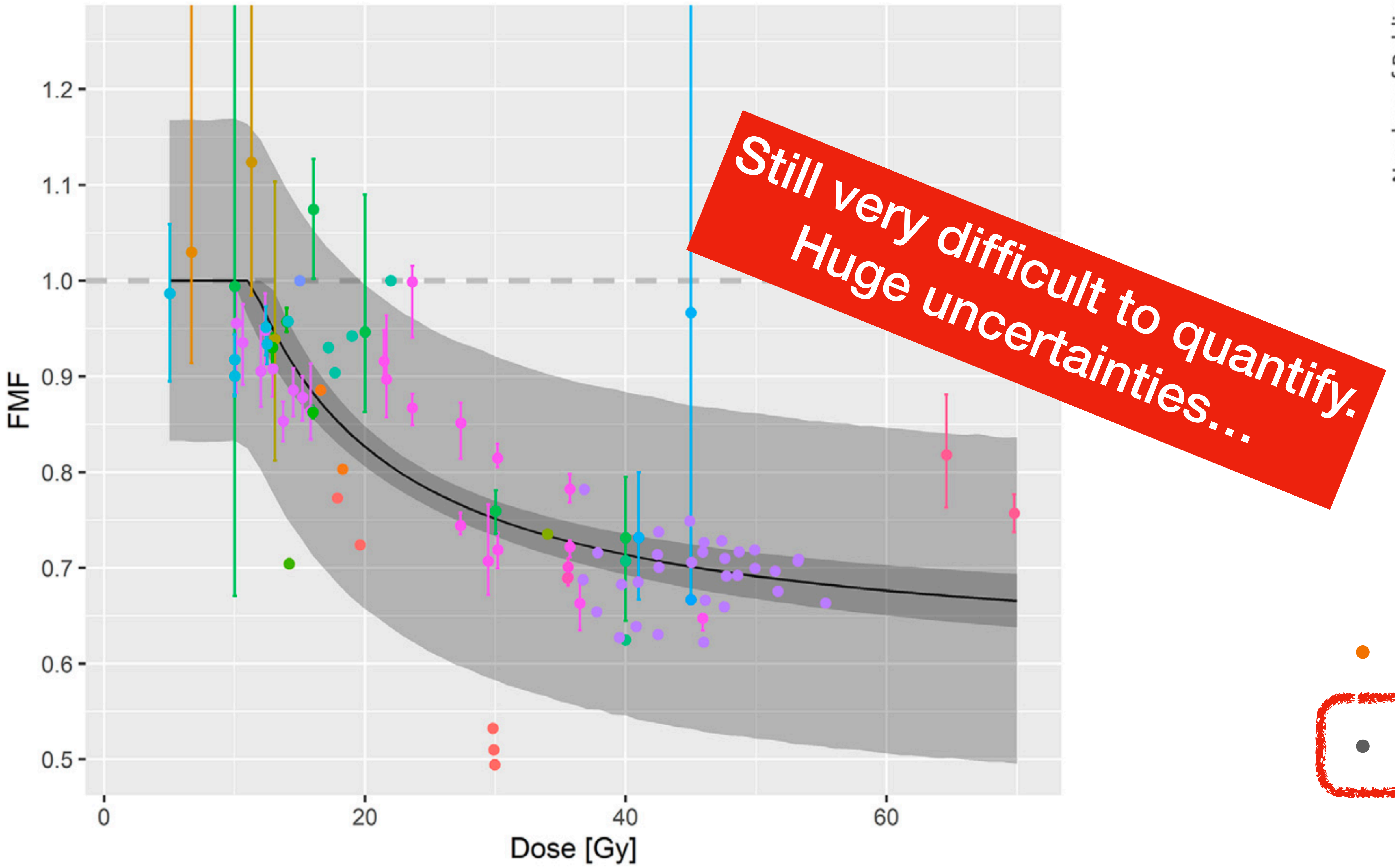

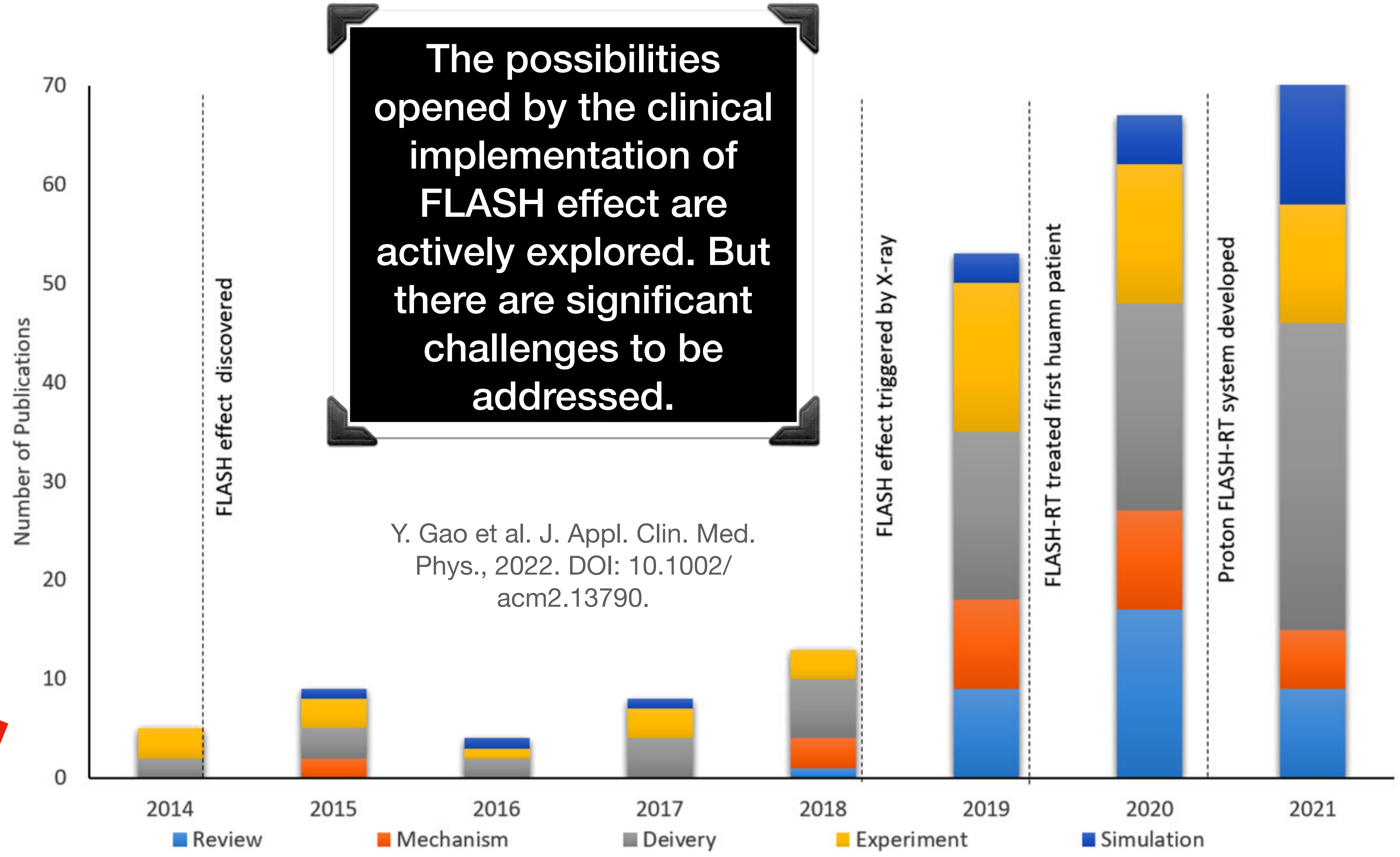

- Underlying bio-chemistry
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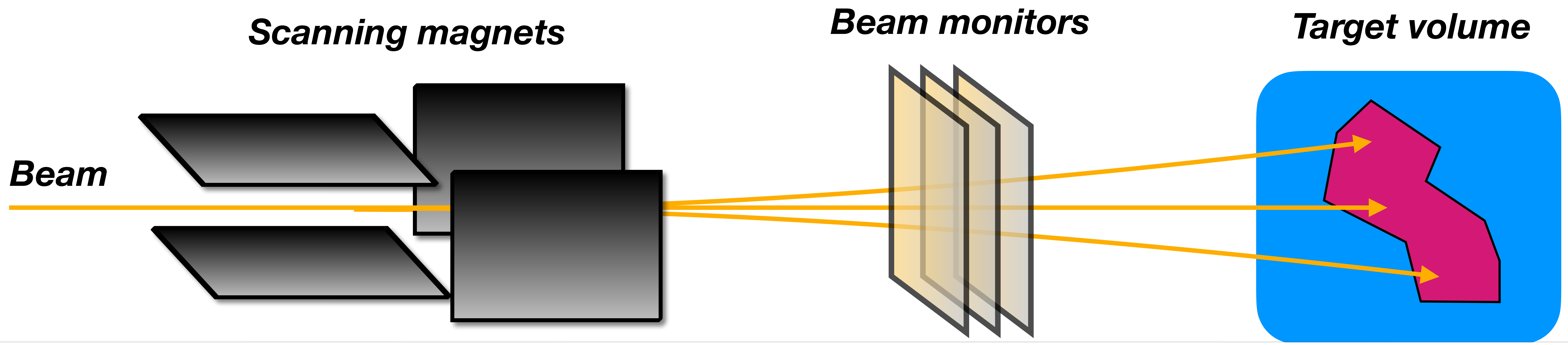
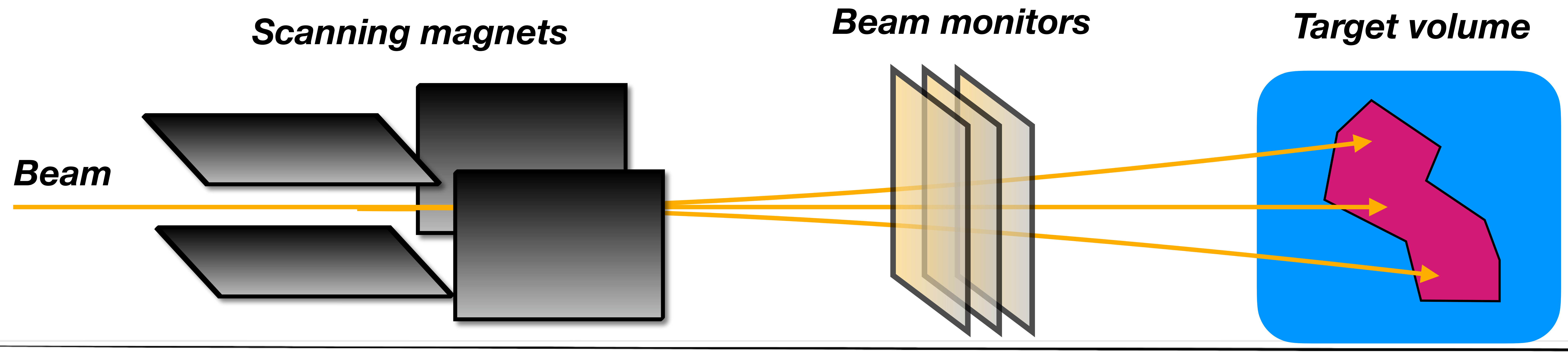
My thesis work



Ultra-High Dose Rate irradiation is full of uncharted territories. The goal of my PhD thesis is to explore two innovative techniques and test their feasibility for future implementation of the FLASH effect in clinical practice.

My thesis work



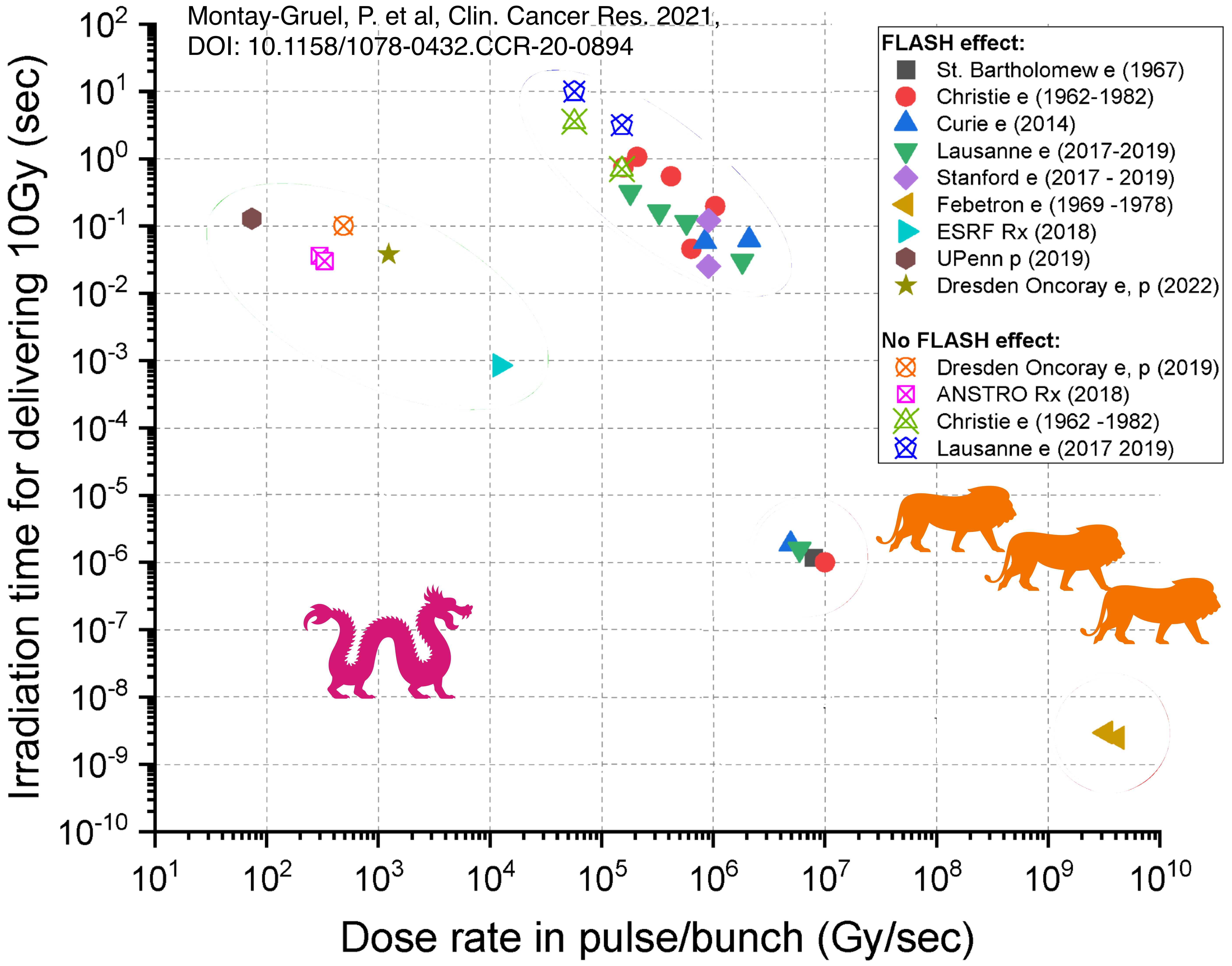
Ultra-High Dose Rate irradiation is full of uncharted territories. The goal of my PhD thesis is to explore two innovative techniques and test their feasibility for future implementation of the FLASH effect in clinical practice.

- How to safely deliver a FLASH beam? Is it possible to precisely target a solid tumor in such a short irradiation time? What are the technological challenges of an active scanning technique?

- How do we quantitatively characterize an UHDR beam? Do we have a system that can provide the adequate set of measurements ensuring irradiation is being delivered according to the desired outcome?

FLASH beam monitoring

- Currently the experimental evidence points to the description of FLASH as a **threshold** effect. However, its characterization is complicated by fundamental uncertainties.
- It is difficult to deconvolve the role played by the **dose within each pulse** and the **time of irradiation**.
- Beam monitoring devices which are able to **follow the temporal evolution** of the beam while maintaining an **adequate response to the dose per pulse** are eagerly needed.
  - **Dose rate linearity** (up to 10^6 Gy/s)
  - **Spatial resolution** (~ mm)
  - **Temporal resolution** (< 1μs)
  - **Dose per pulse accuracy** (within 1%)

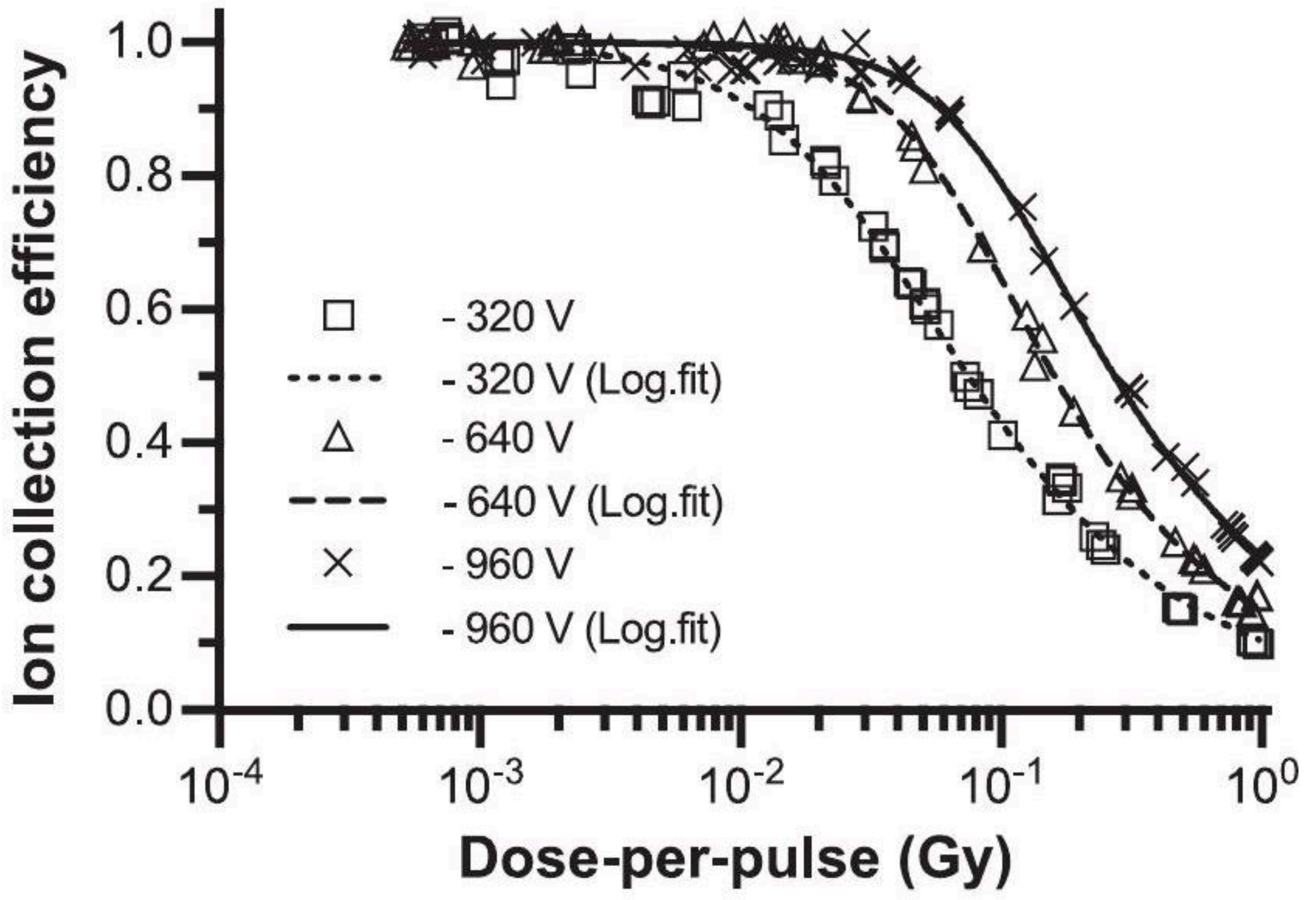


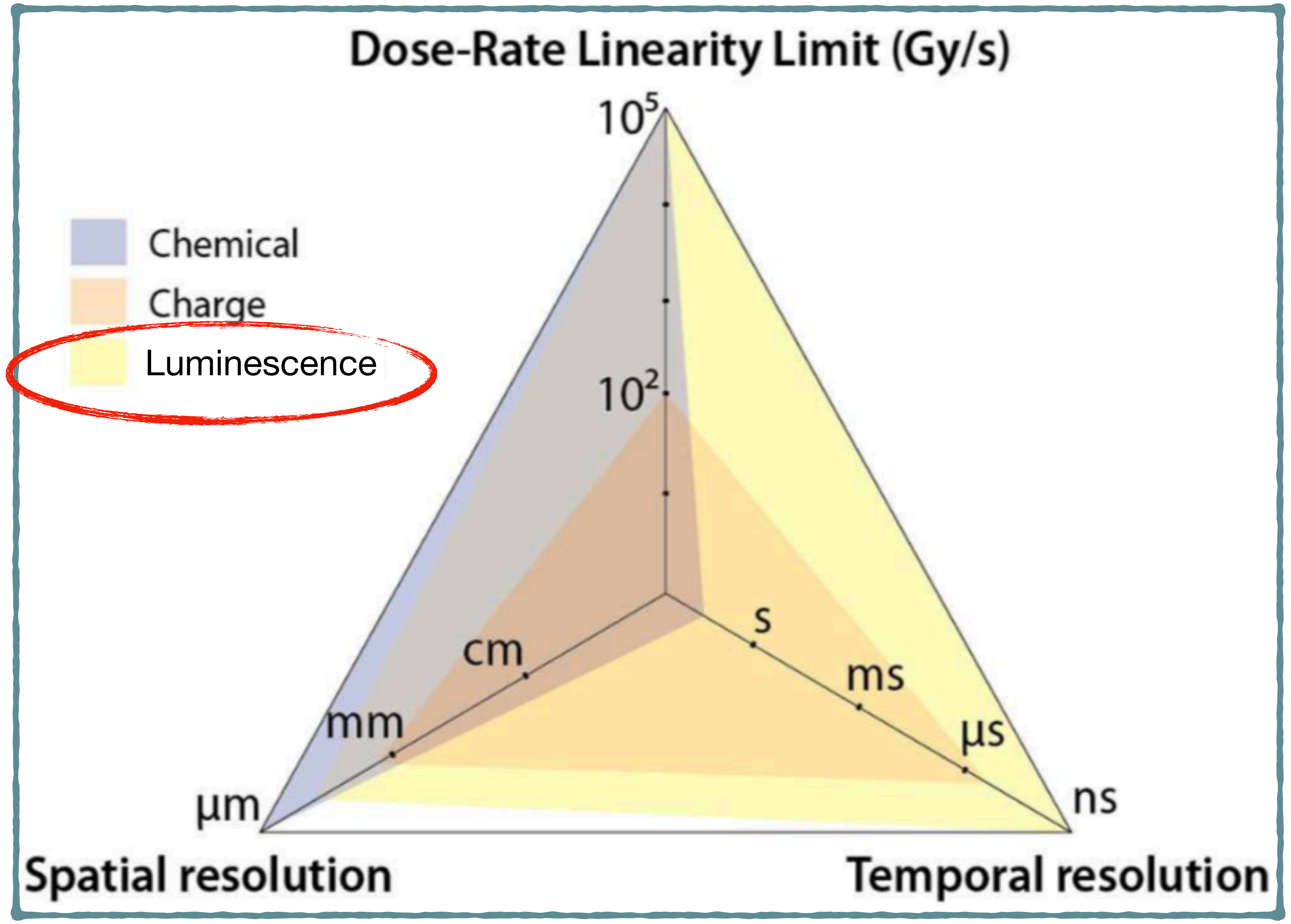
FLASH beam monitoring

- Problem is, BM can be hardly operated in FLASH environment. Detectors commonly used in clinics (standard ionization chambers) undergo substantial energy dependencies due to **volume recombination**.

- It is clear that we need *new monitoring devices*, essential to reach the degree of precision necessary to fully characterize the FLASH effect and determine its beneficial impact.

Ion-collection efficiency of the built-in transmission chamber of the modified clinical ELEKTA Precise linear accelerator, for different negative polarizing voltages.



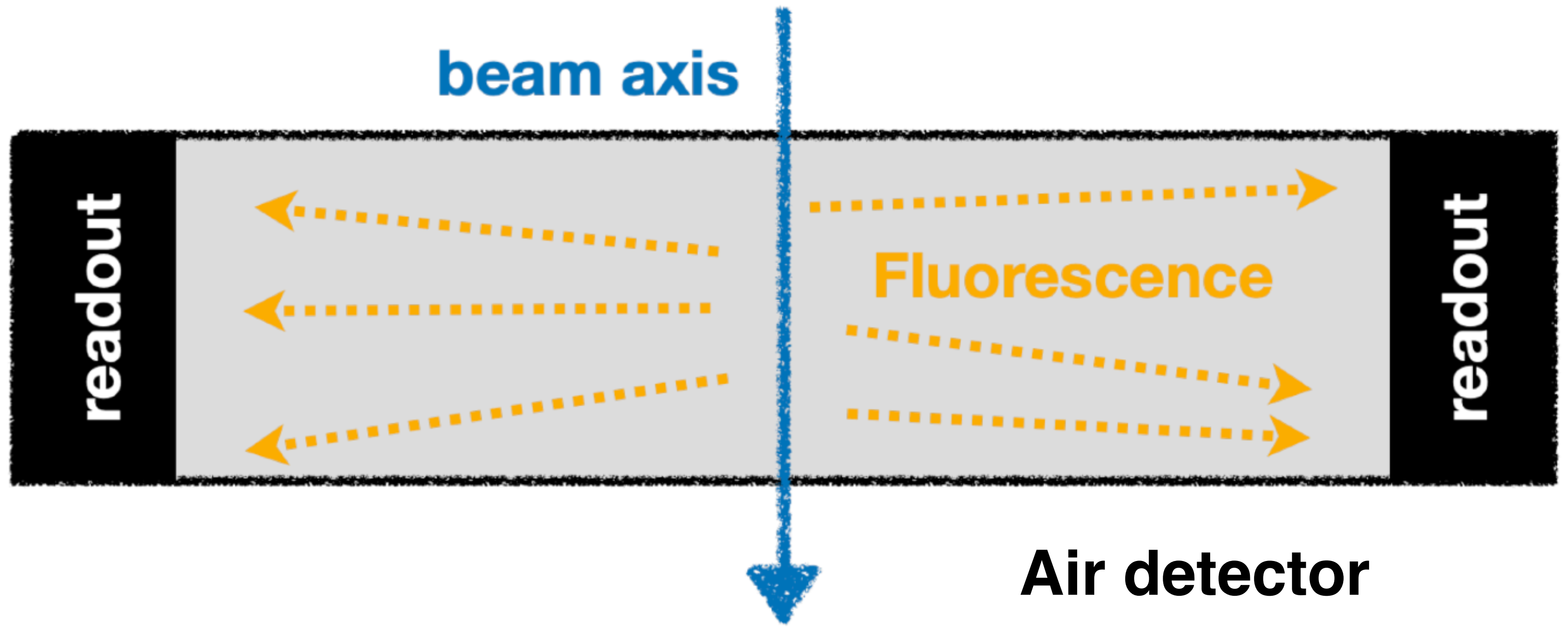


Ashraf MR et al, Dosimetry for FLASH Radiotherapy
doi: 10.3389/fphy.2020.00328

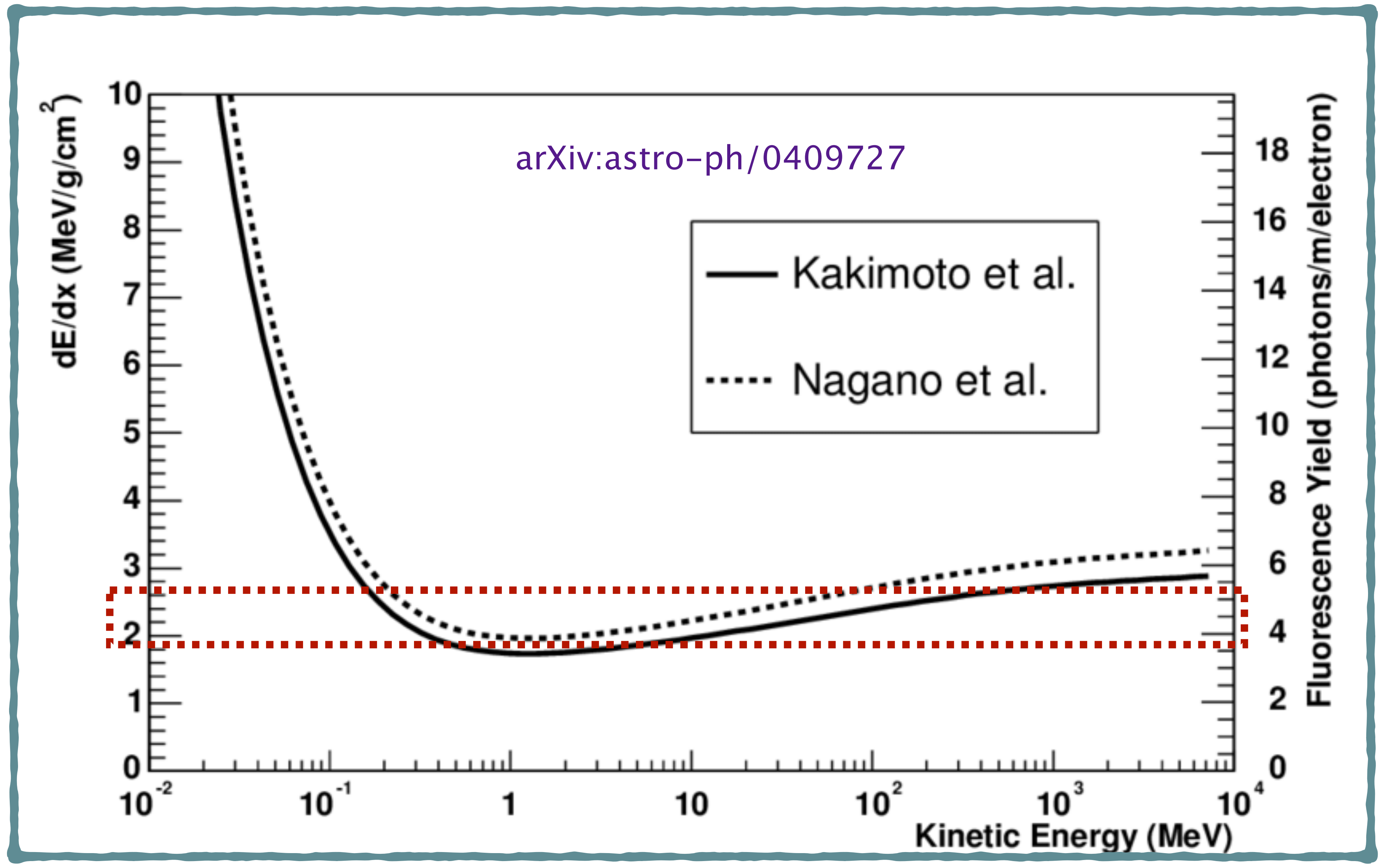
FLASH beam monitoring

- According to data in literature, **air fluorescence** can do the job for us.
- It happens when a charged particle crosses an air volume, exciting mainly **nitrogen molecules**, which release **optical photons**.
- It has many appealing features, but has never been investigated as a feasible beam monitoring technique.
- **Problems:** develop a proof-of-principle, perform studies of the signal in-beam and verify the expected performances.

Photon emission	Isotropic (3D)
Excited state lifetime	10 ns
Wavelength spectrum	290-430 nm
Fluorescence yield	$\propto dE/dx$ (~ 4 ph./m)
Signal-to-#e⁻ relation	**LINEAR**
Transparency wrt ref. cond.	100%
Radiation hardness	Optimal



Air detector



FLASH beam monitoring

Above all else, the philosophy of having a detector made out of air is to be as “invisible” to the beam as possible.

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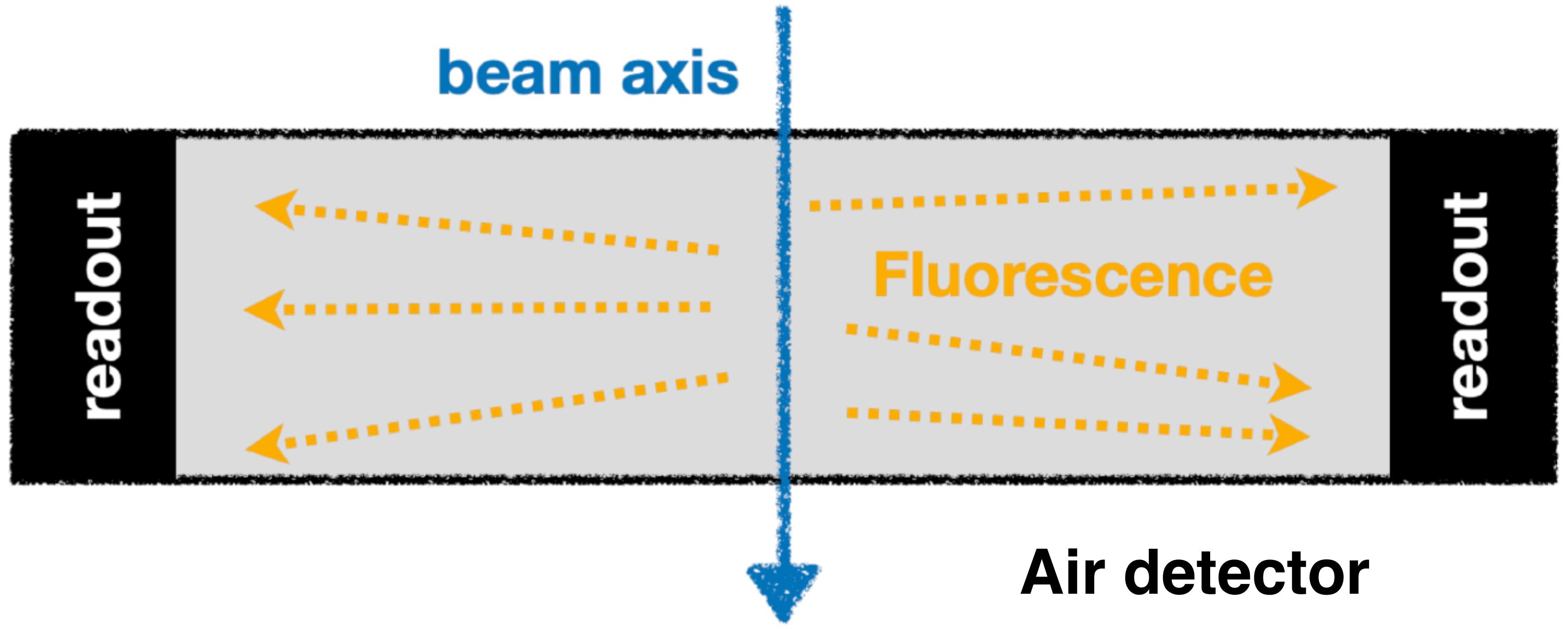

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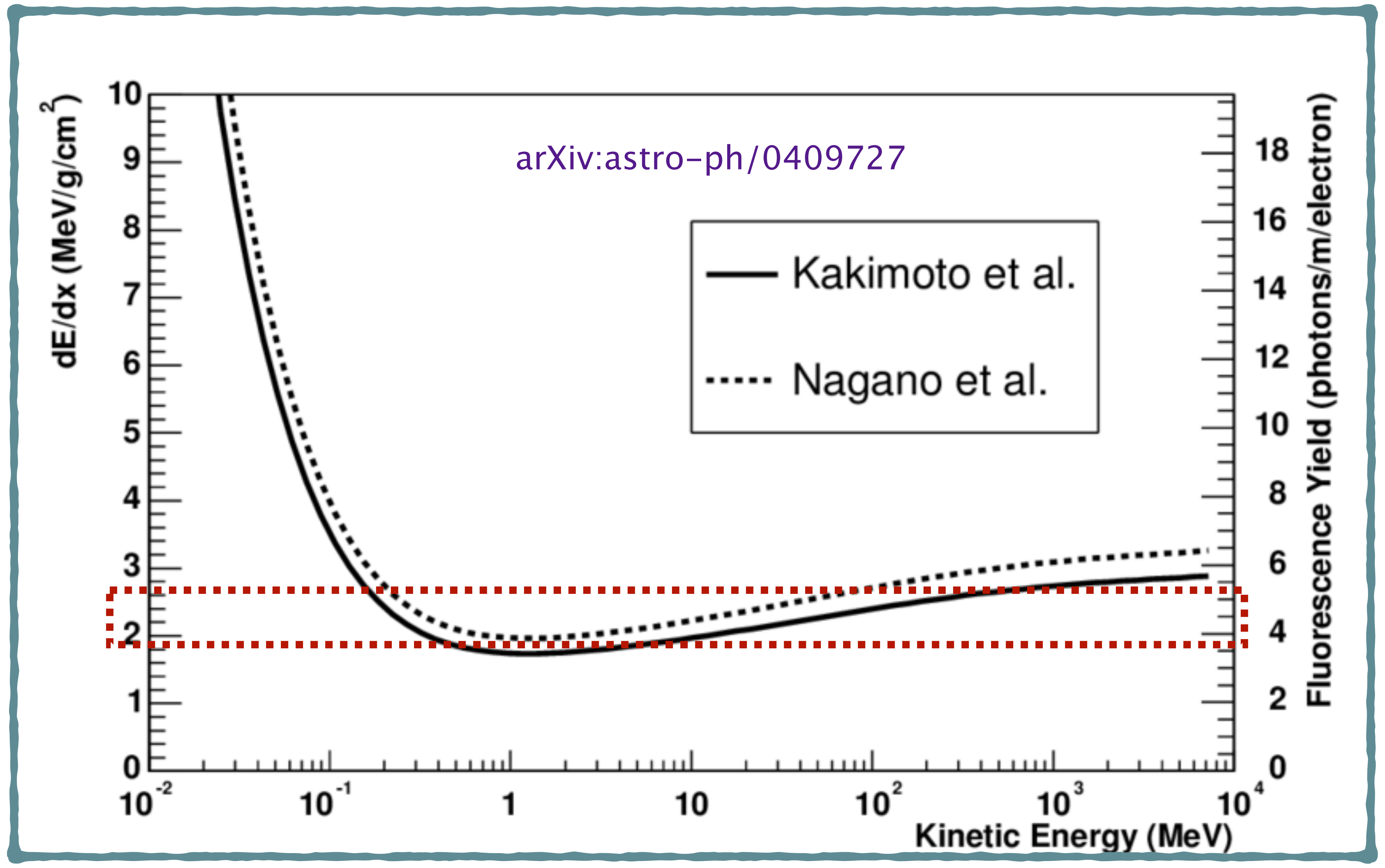

FLASH beam monitoring

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2014 2020 POR

First round: LIAC-HWL
November 2020-June 2021

Second round: EF Antwerp
July 2021-June 2022

Third round: EF Pisa
July 2022-June 2023

2021

FLASH DC

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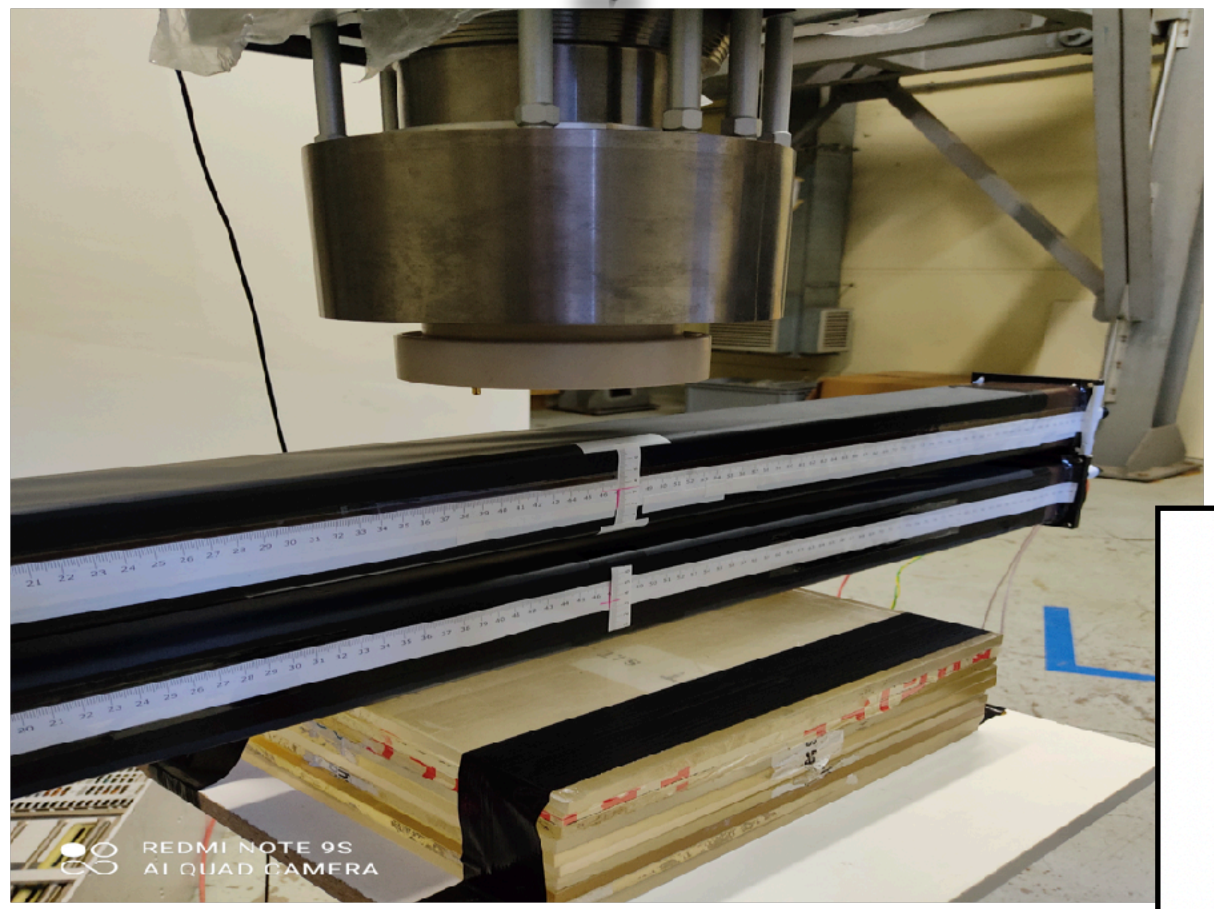

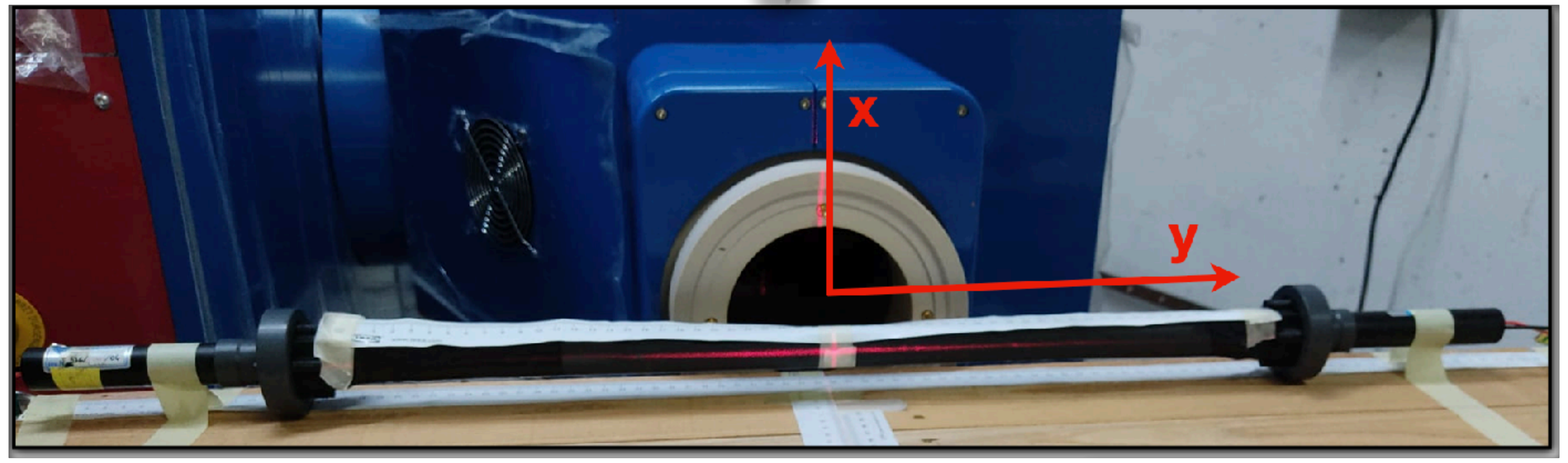

Nuclear Inst. and Methods in Physics Research, A 1041 (2022) 167334

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The FlashDC project: Development of a beam monitor for FLASH radiotherapy

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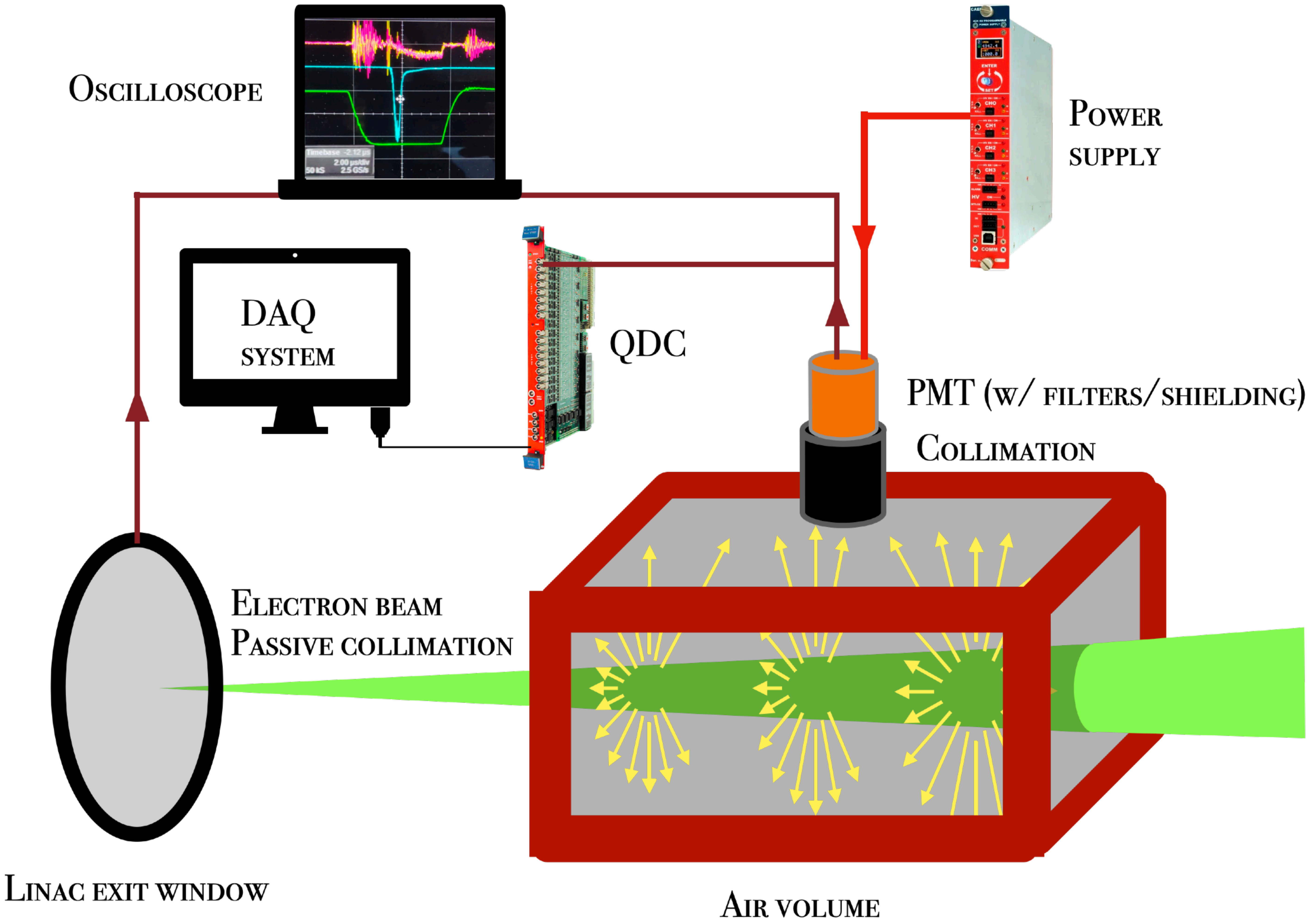
JINST_036P_1223

Antonio Trigilio
"Test beam results of a fluorescence-based monitor for ultra-high dose rates"
Submitted: 8 December 2023
Accepted: 11 January 2024

FLASH beam monitoring

First round: LIAC-HWL November 2020-June 2021	Second round: EF Antwerp July 2021-June 2022	Third round: EF Pisa July 2022-June 2023

- I worked with several prototypes testing the feasibility of a fluorescence-based beam monitor through different configurations and geometries.
- I have performed the design and testing focusing on the available sources of beams with UHDR intensities: low energy (6-12 MeV) electrons usually used for intra-operative applications.



FLASH beam monitoring

First round: LIAC-HWL
November 2020-June 2021

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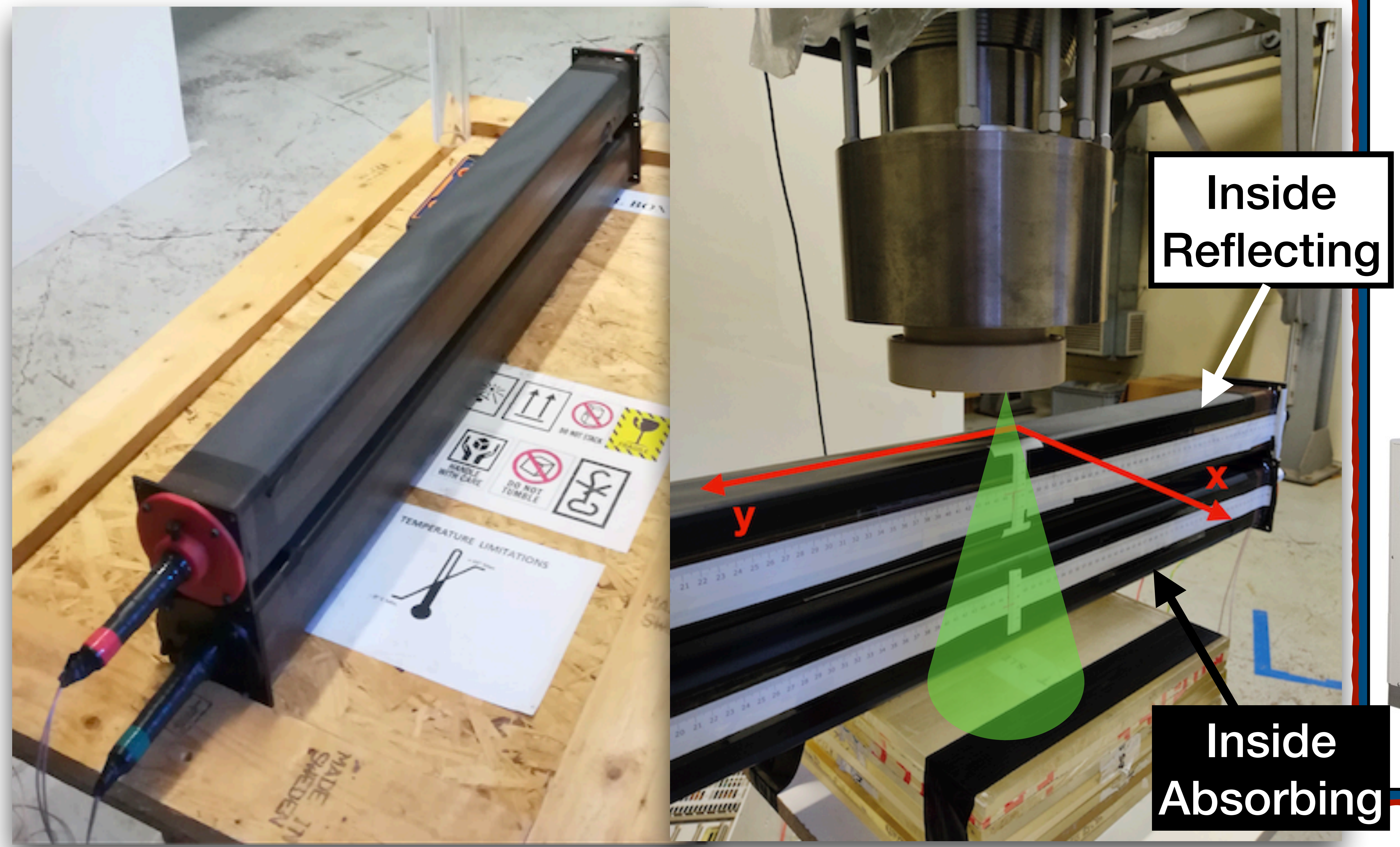
- The first objective is a successful **in-beam/off-beam** discrimination.
- The first prototype consisted in a volume of **7x7x90 cm³** of air, enclosed by a thin layer of Teflon sheet, with a PVC supporting structure and two PMTs on the opposite squared faces.



- **LIAC HWL**: linac for intra-operative electron RT **modified** to reach 10^{10} electrons/pulse.
- Electron energy: 6MeV.
- Pulse duration: 2 μs.
- Dose per pulse ~ 0.3 Gy.
- Mobile head: useful to test sensitivity to beam position.
- The accelerator delivery section and the detector geometries are implemented in a **FLUKA MC simulation**.
- The fluorescence production is activated using experimental data found in literature.

FLASH beam monitoring

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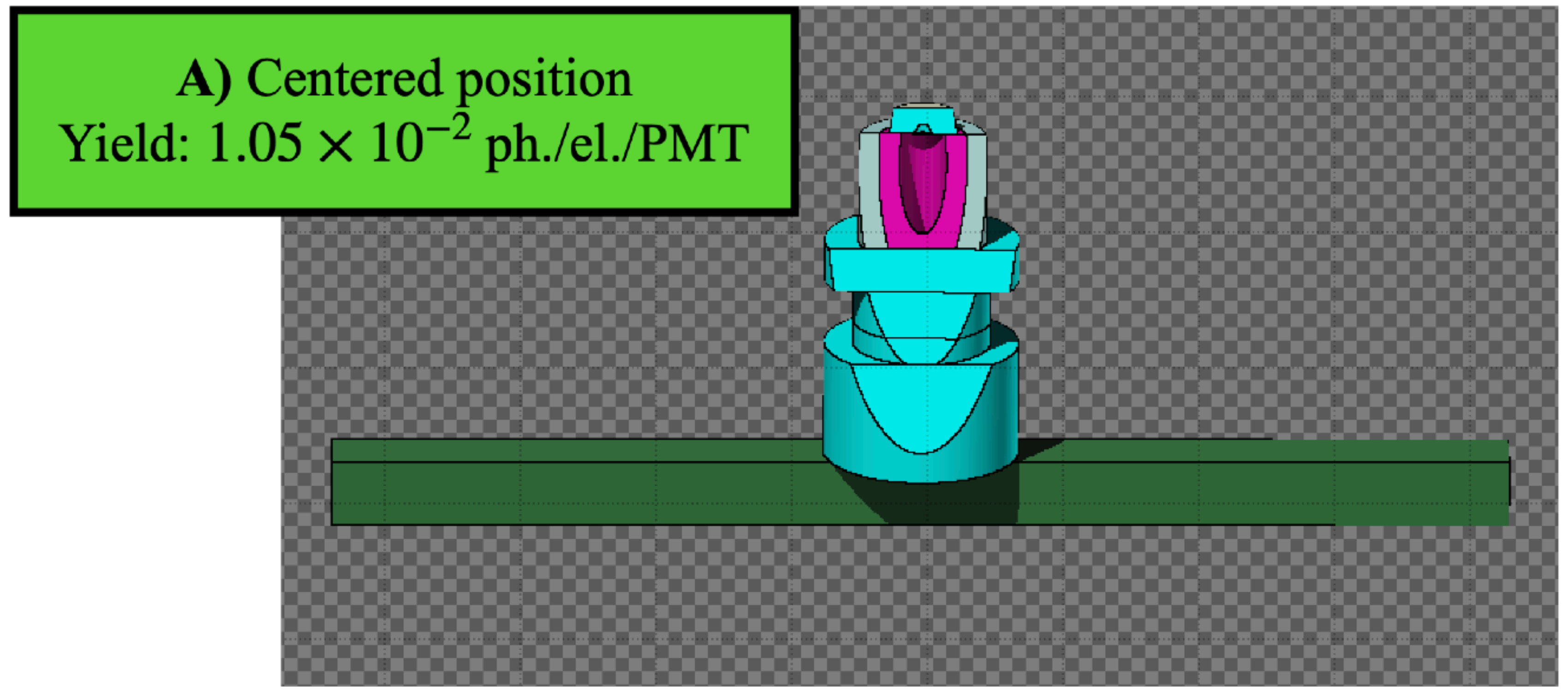
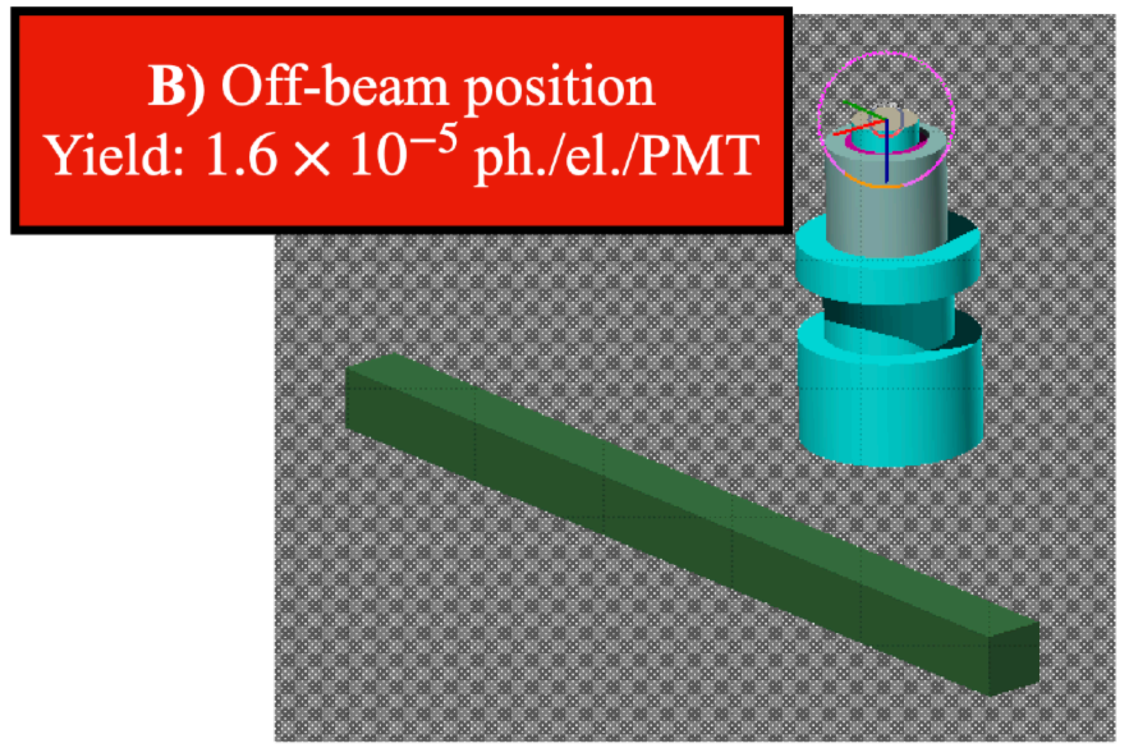
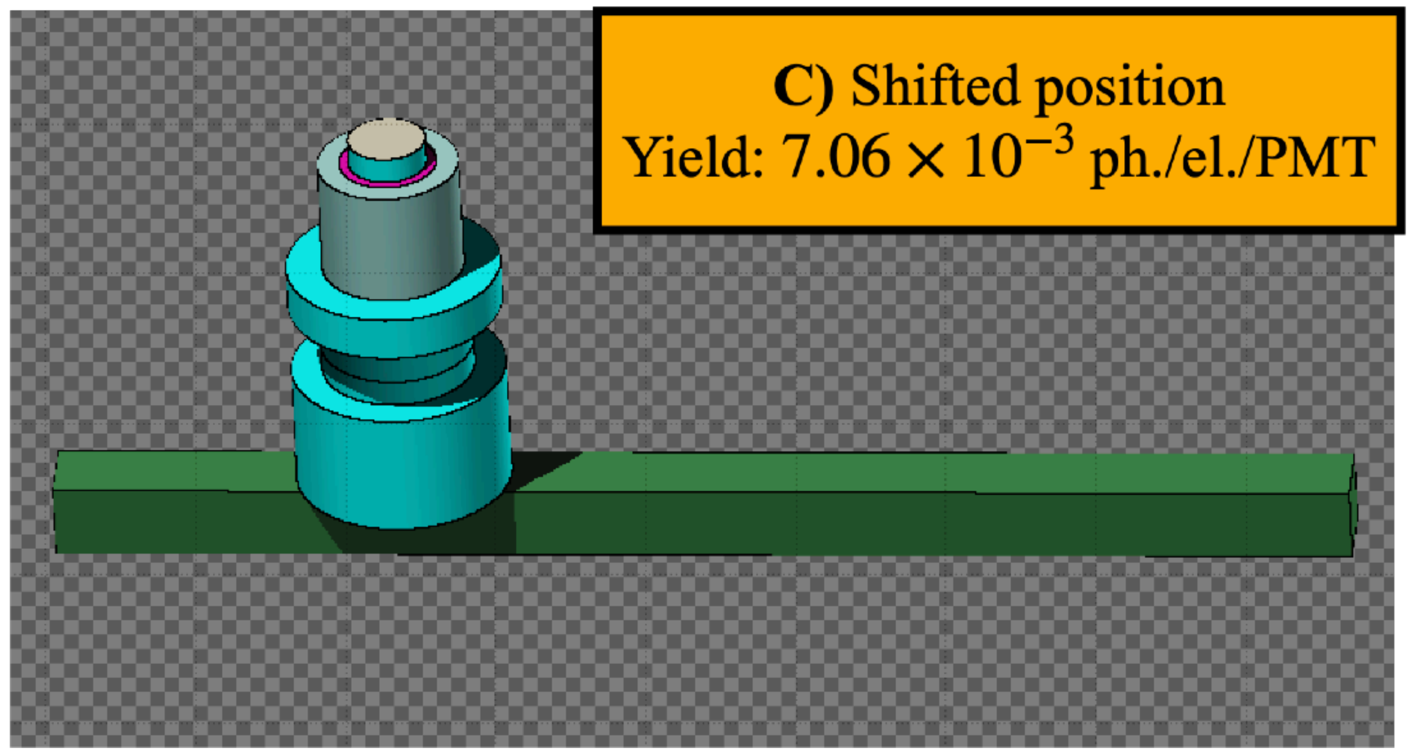
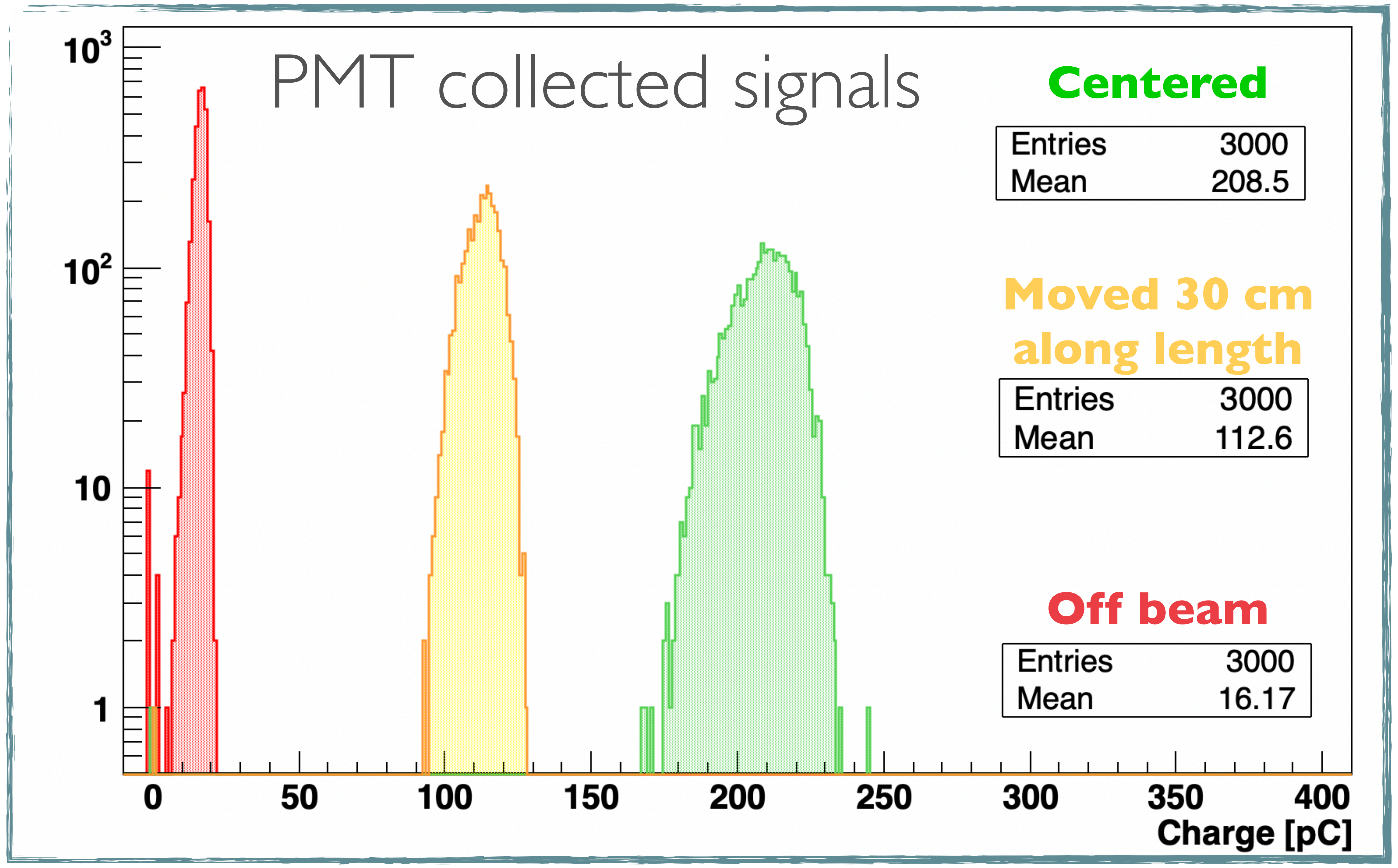






- I took part in the first data taking and performed the subsequent analysis.
- The results confirmed the expected signal sensitivity to the detector position with respect to the beam.



- I performed several runs of MC simulations to evaluate the expected signal (and background) in different configurations, and the **ratio** of optical photons reaching the PMTs when off-beam/in-beam.

FLASH beam monitoring

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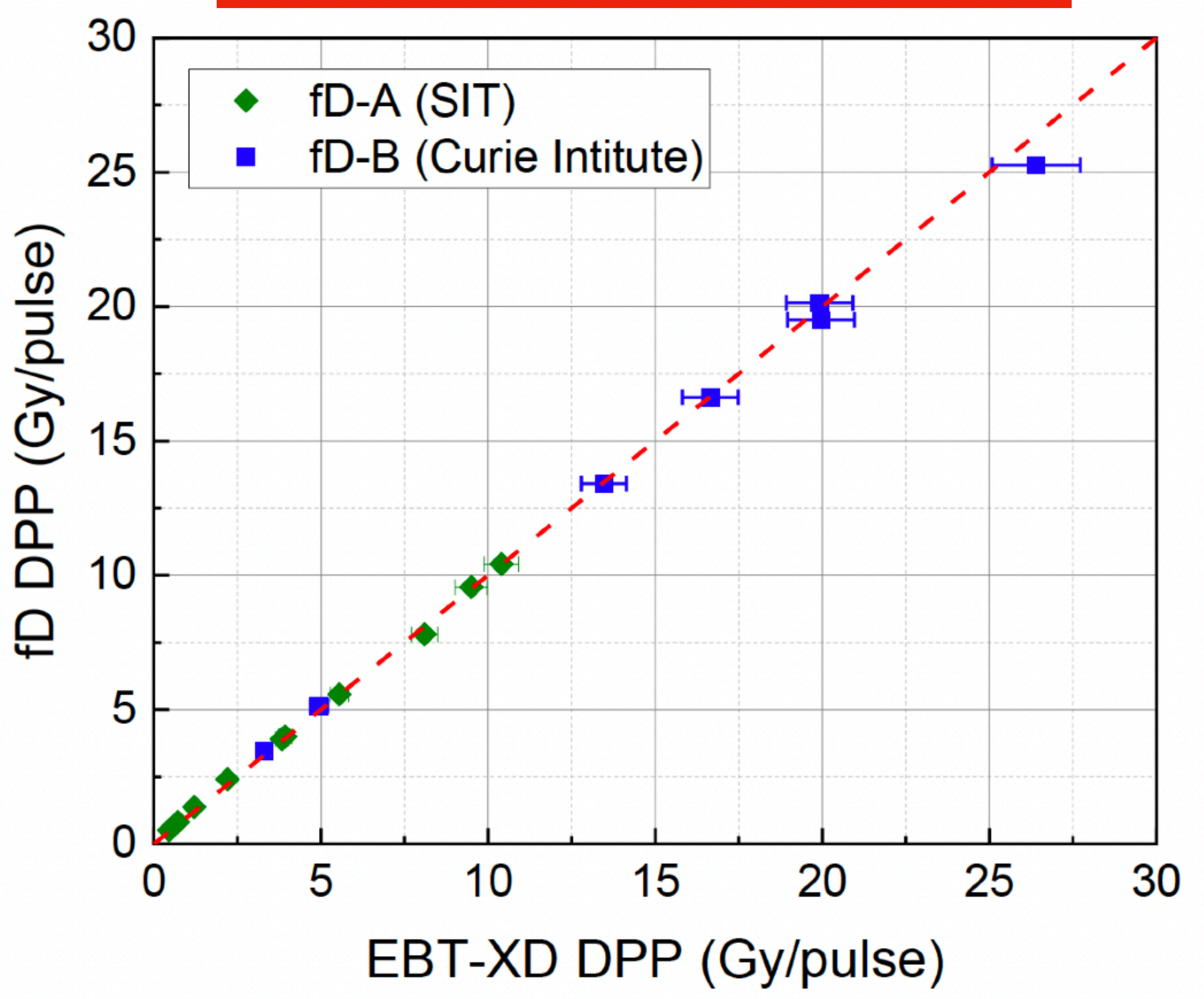
- **ElectronFlash**: up to 10^{12} electrons/pulse.
- Electron energy at the linac exit: 7MeV.
- **Dose(-rate) per pulse: up to 20 Gy ($5*10^6$ Gy/s).**
- Field diameter: 5-6 cm at BEW (uncollimated).

soiort.com/flash-rt-technology/

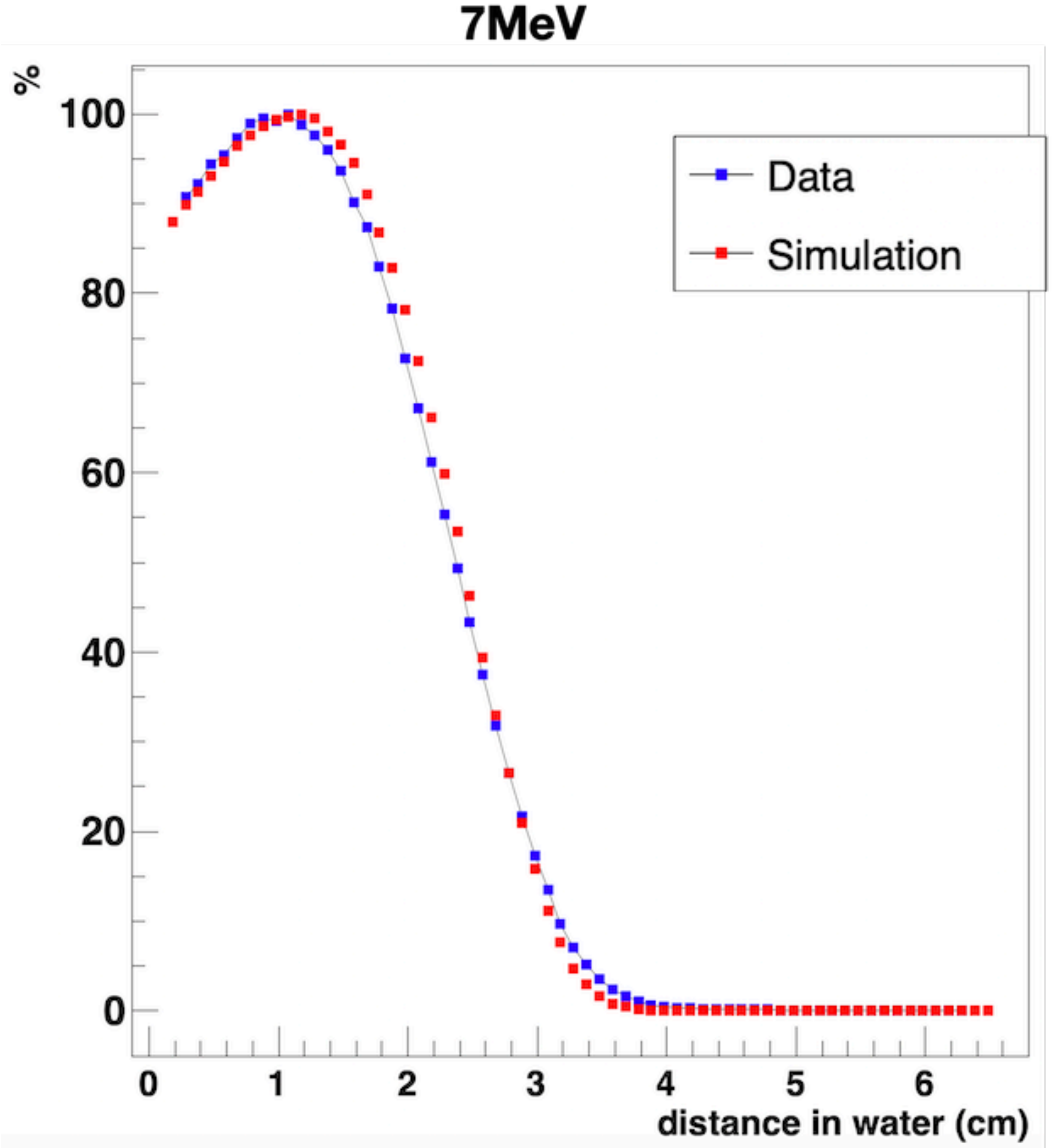
- The ElectronFlash, developed by S.I.T. Sordina, is a linac developed specifically to perform FLASH studies, and can provide different values of dose per pulse.
- **First tests in Aprilia**, before being shipped to the University of Antwerp. The dose per pulse had to be **manually set** by adjusting the ***injection beam current***.

flashDiamond: reference dosemeter



M. Marinelli et al. Medical Physics 2022, 1-9, DOI: 10.1002/mp.15473

PDDs of electrons delivered with the ElectronFlash in water (**fD** and **FLUKA MC simulation**).



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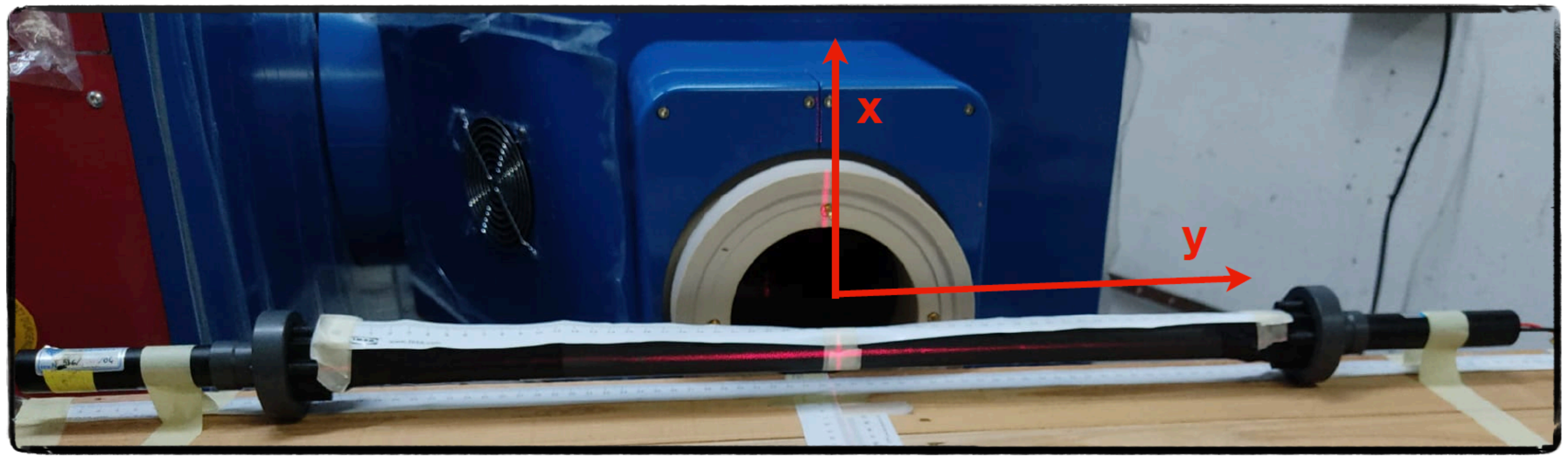
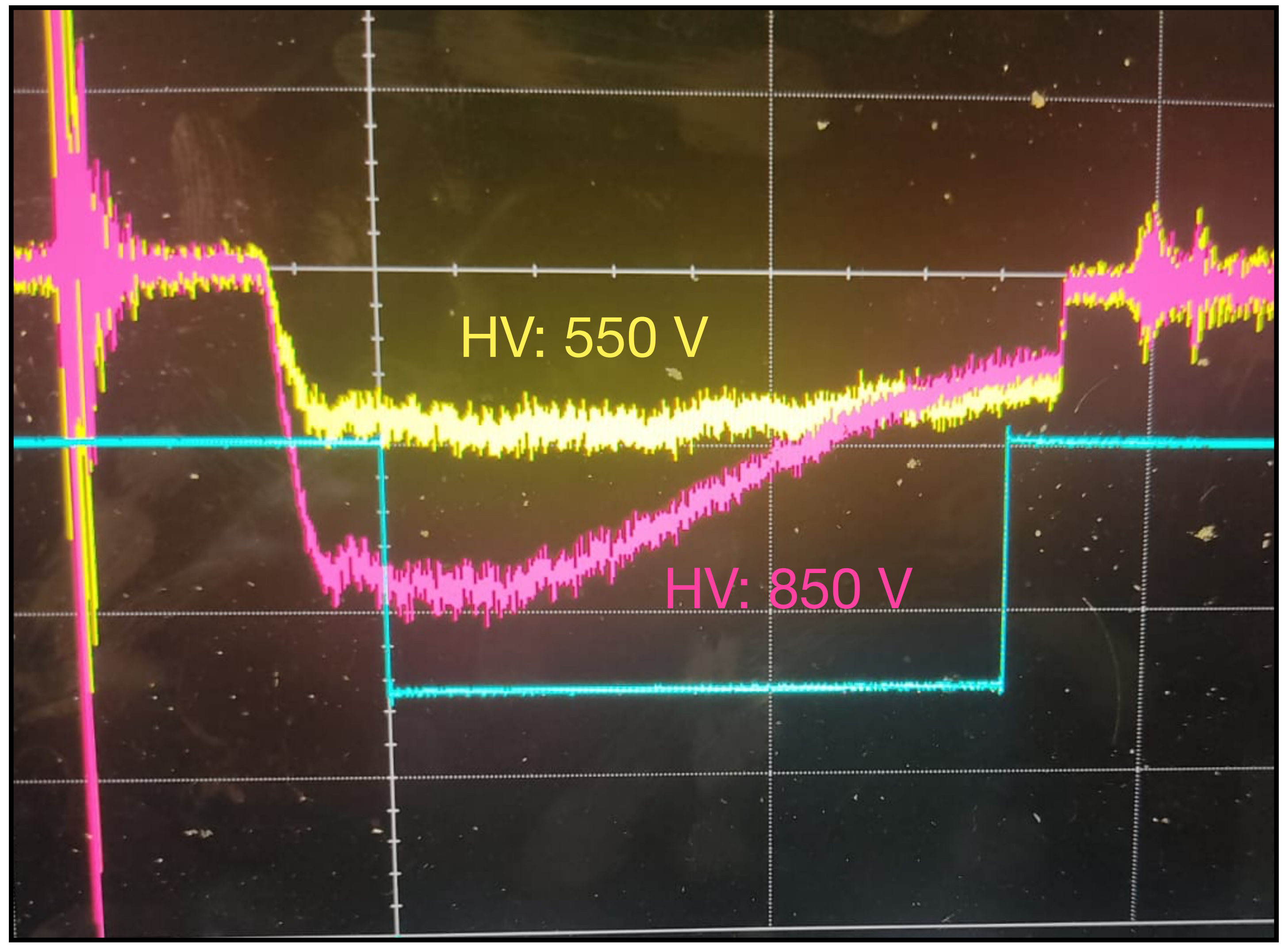
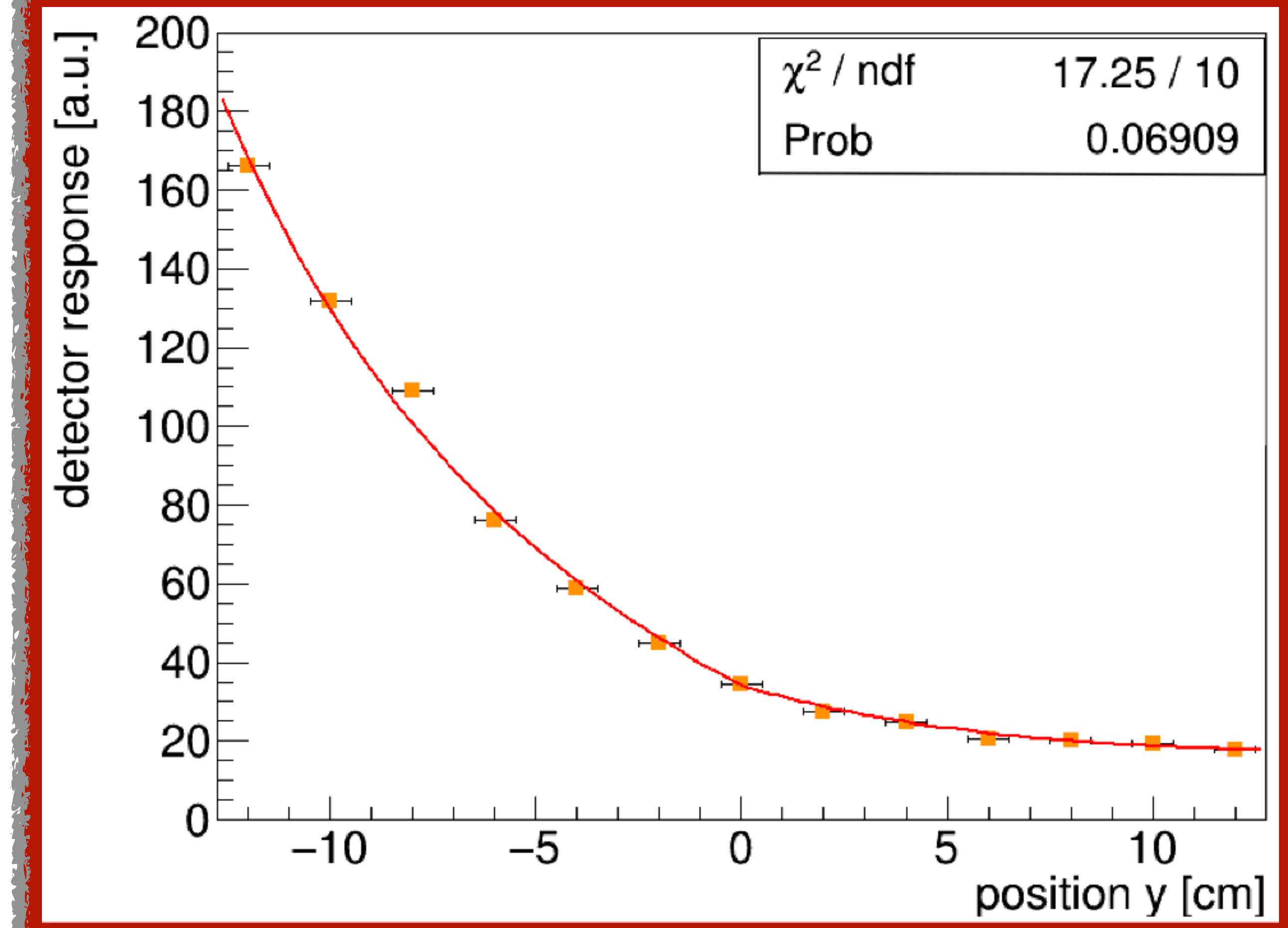


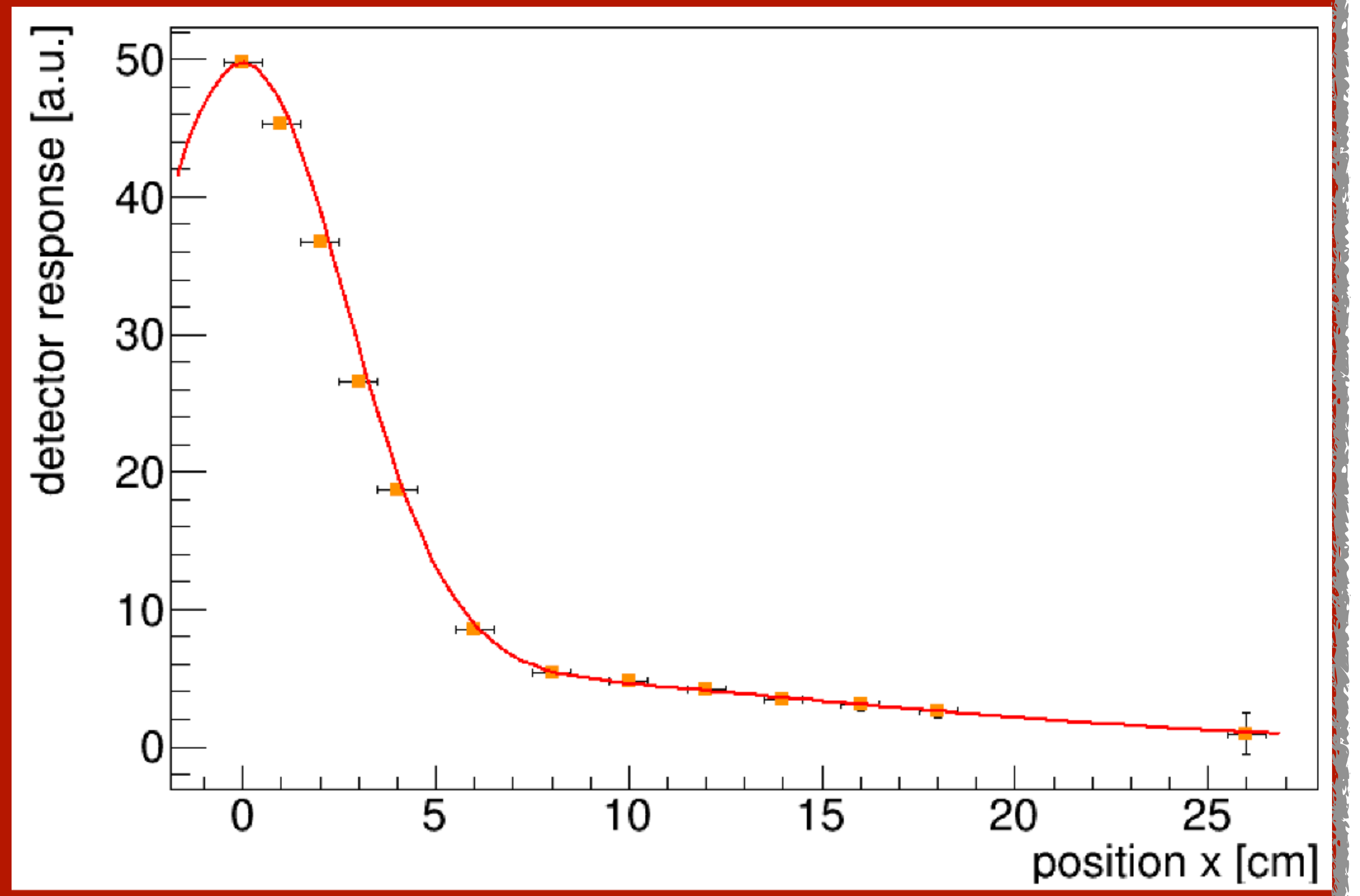
- The new prototype is still an air volume, with smaller dimensions (**2x2x60** cm³), with two PMTs on both ends equipped with **UV filters**, meant for studies on both position and ***charge*** sensitivity.





- I performed the analysis verifying the expected geometry dependencies of the detector response in different positions.
- Further indication that the signal is indeed due to the production of optical photons **inside** the active volume.

- Plot obtained gradually moving the detector off the beam to reconstruct the transverse shape.
- The in-beam/off-beam difference is observed.



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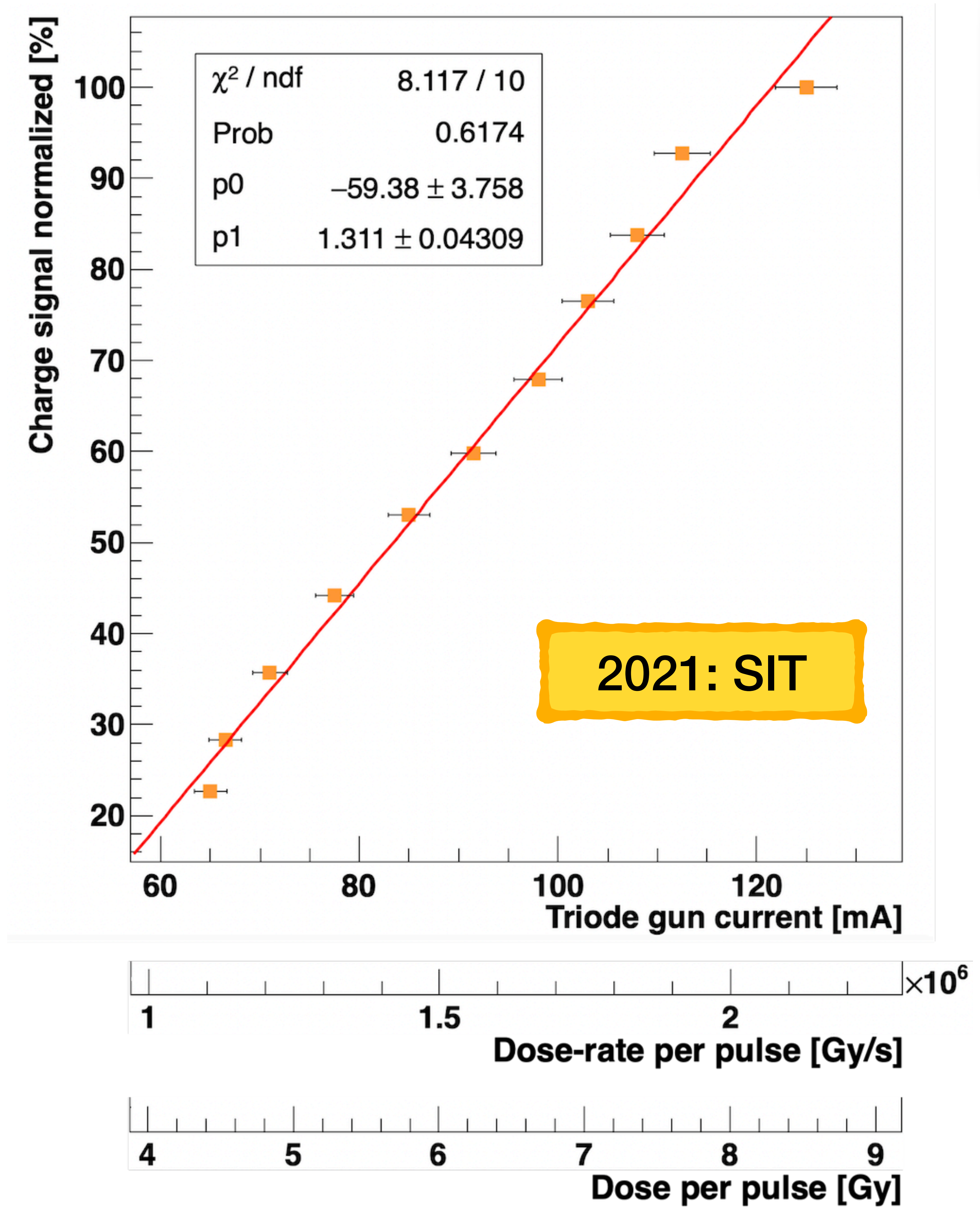

A linear response is observed over the full range of intensities explored.

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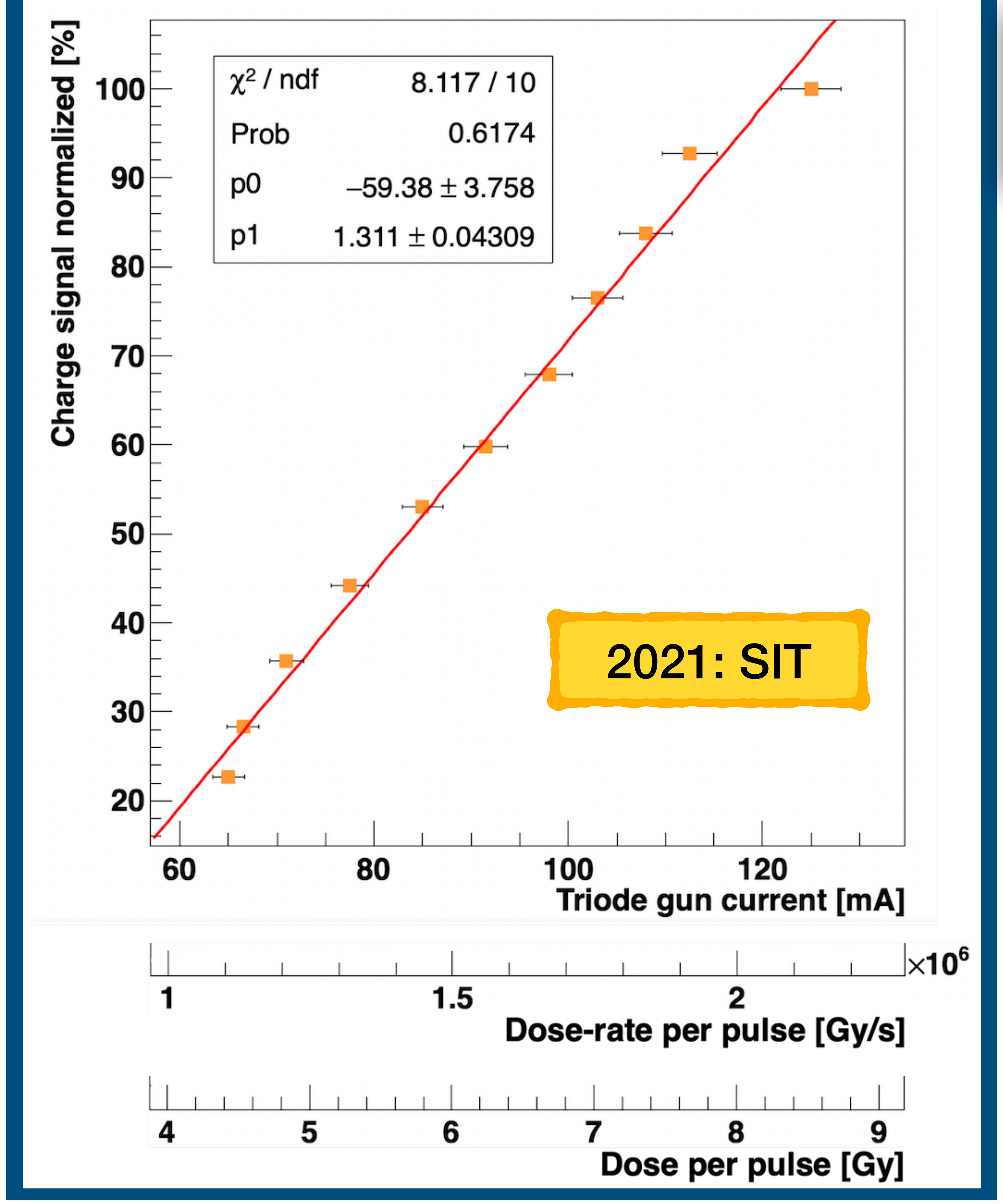

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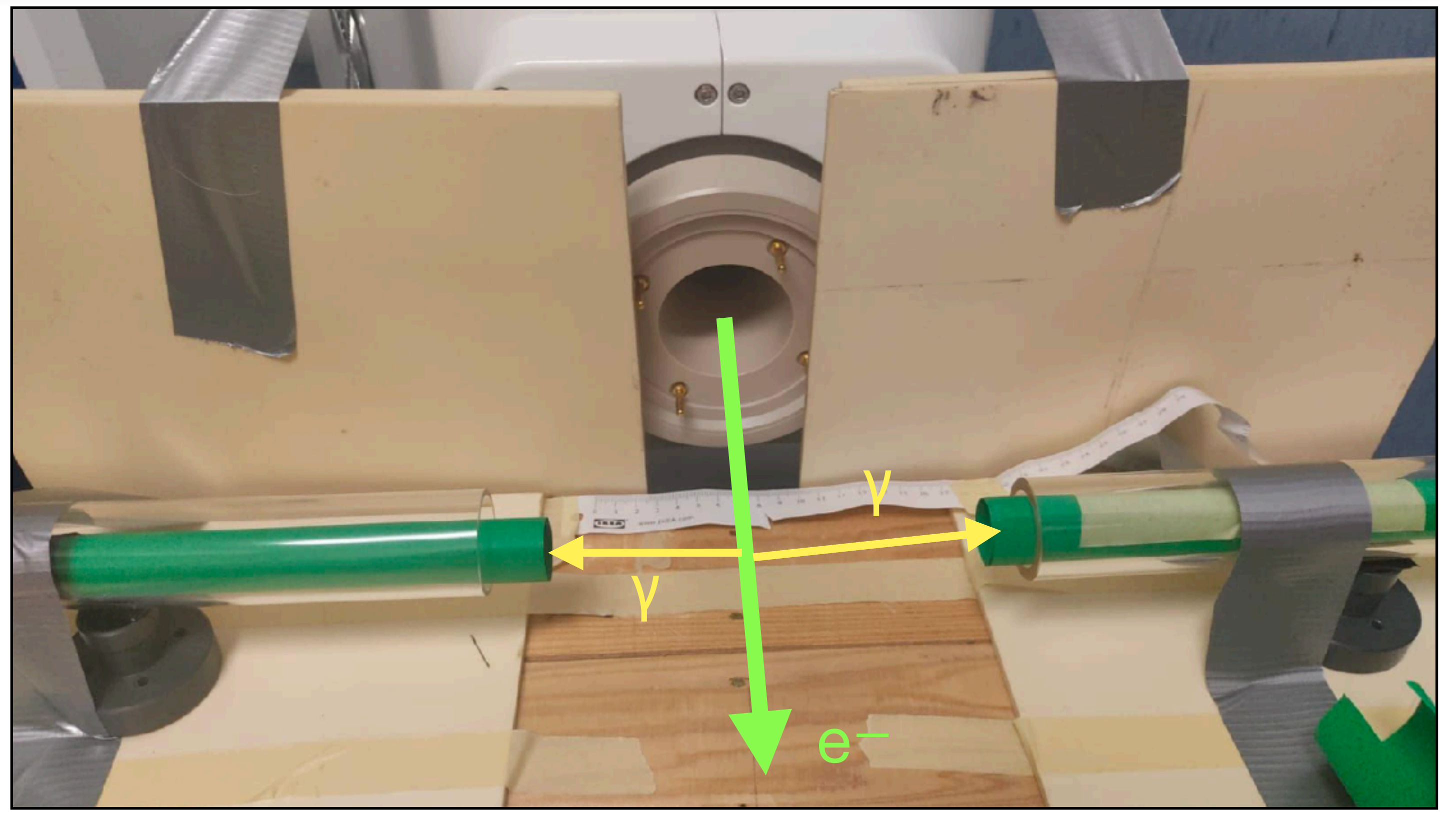
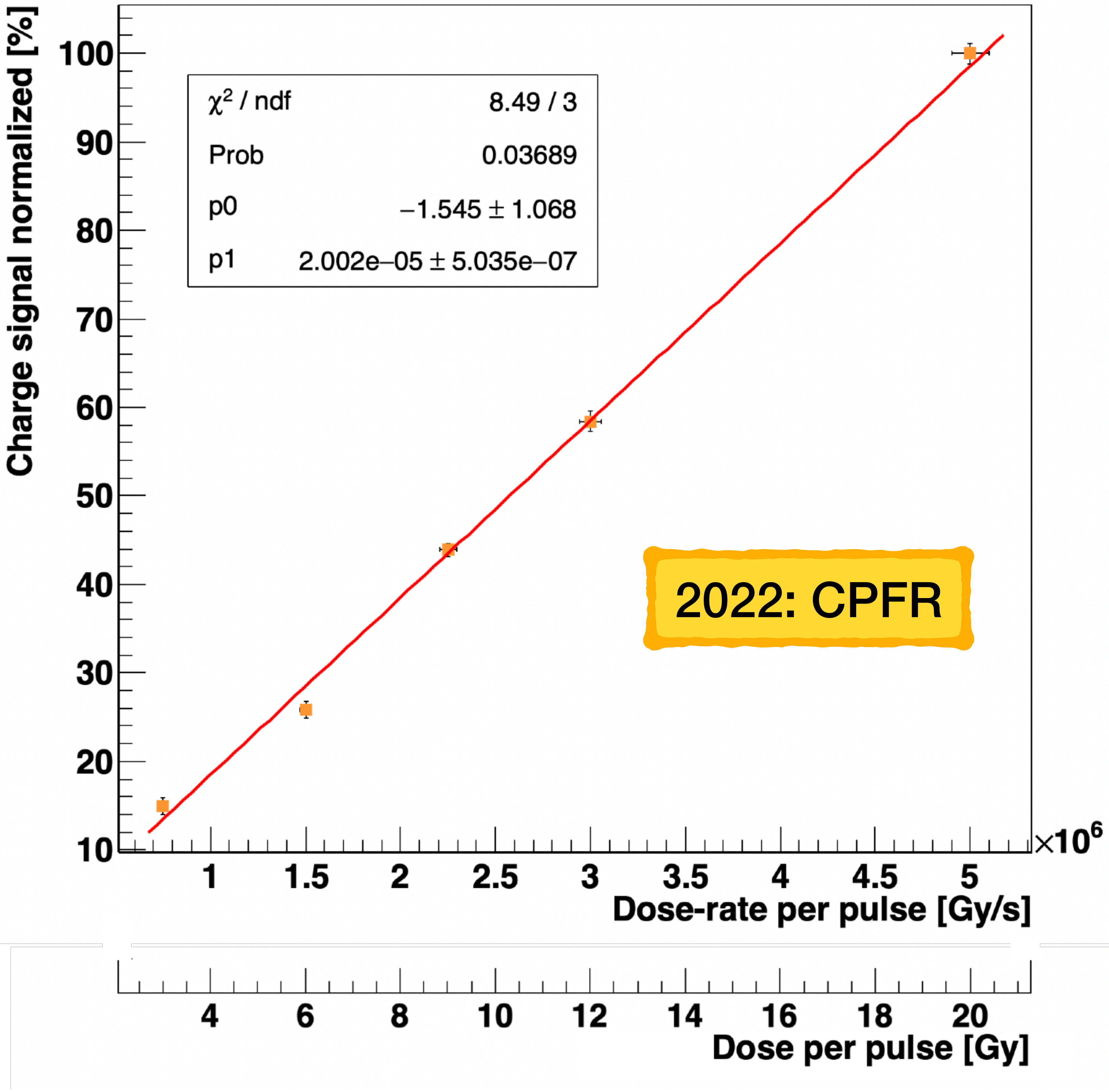


- The ElectronFlash is now available at **<u>CPFR in Pisa (St. Claire University-Hospital)</u>**.
- I repeated the measurement, also starting to modify the geometry in order to perform background subtraction studies.



FLASH beam monitoring

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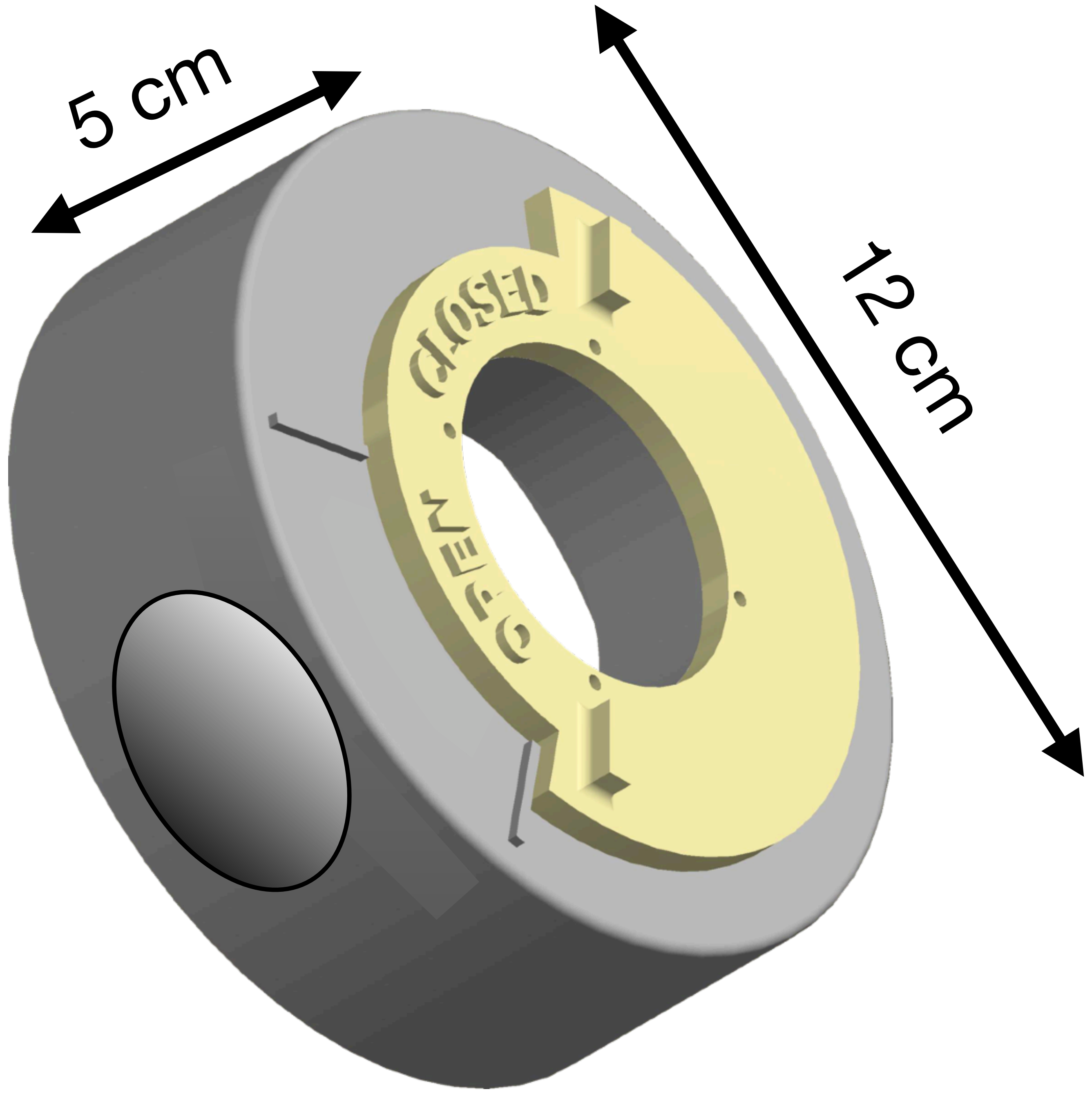
- Next step is to prove that the expected linearity of signal *vs* beam current is really due to fluorescence => subtract background.
- Taking advantage of the direct access to the Pisan ElectronFlash technical design, the next detector is **directly tailored** to the Beam Exit Window dimensions.



FLASH beam monitoring

First round: LIAC-HWL November 2020-June 2021	Second round: EF Antwerp July 2021-June 2022	Third round: EF Pisa July 2022-June 2023

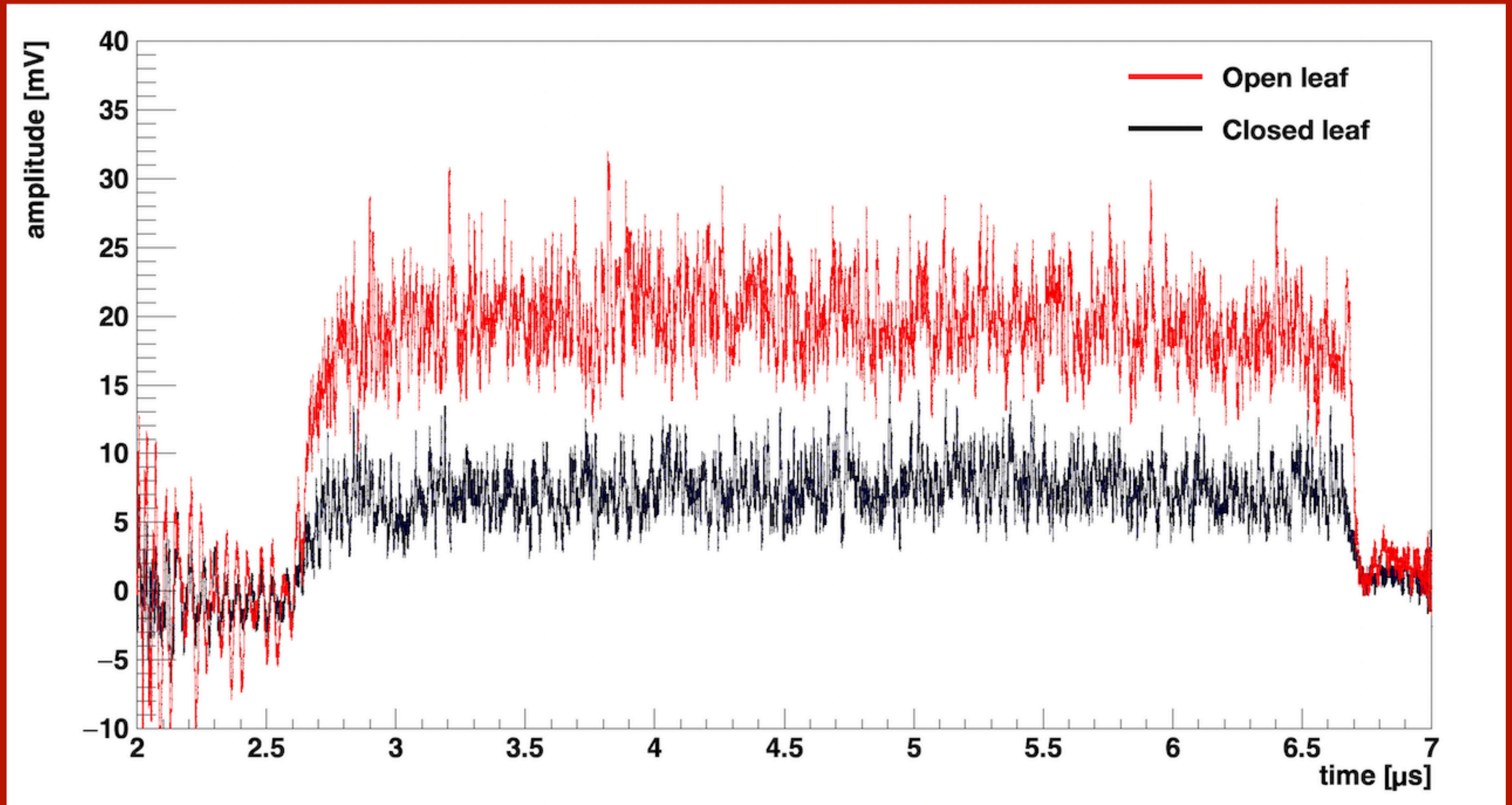
- Next step is to prove that the expected linearity of signal *vs* beam current is really due to fluorescence => subtract background.
- Taking advantage of the direct access to the Pisan ElectronFlash technical design, the next detector is **directly tailored** to the Beam Exit Window dimensions.
- The active volume is the air immediately after the BEW, enclosed in a cylindrical case. A sliding leaf on the external face can be closed and opened for background measurement.
- In this configuration, the PMT is wrapped in a plastic shield with thickness of 2 cm, at 1.2 m from the beam exit window.

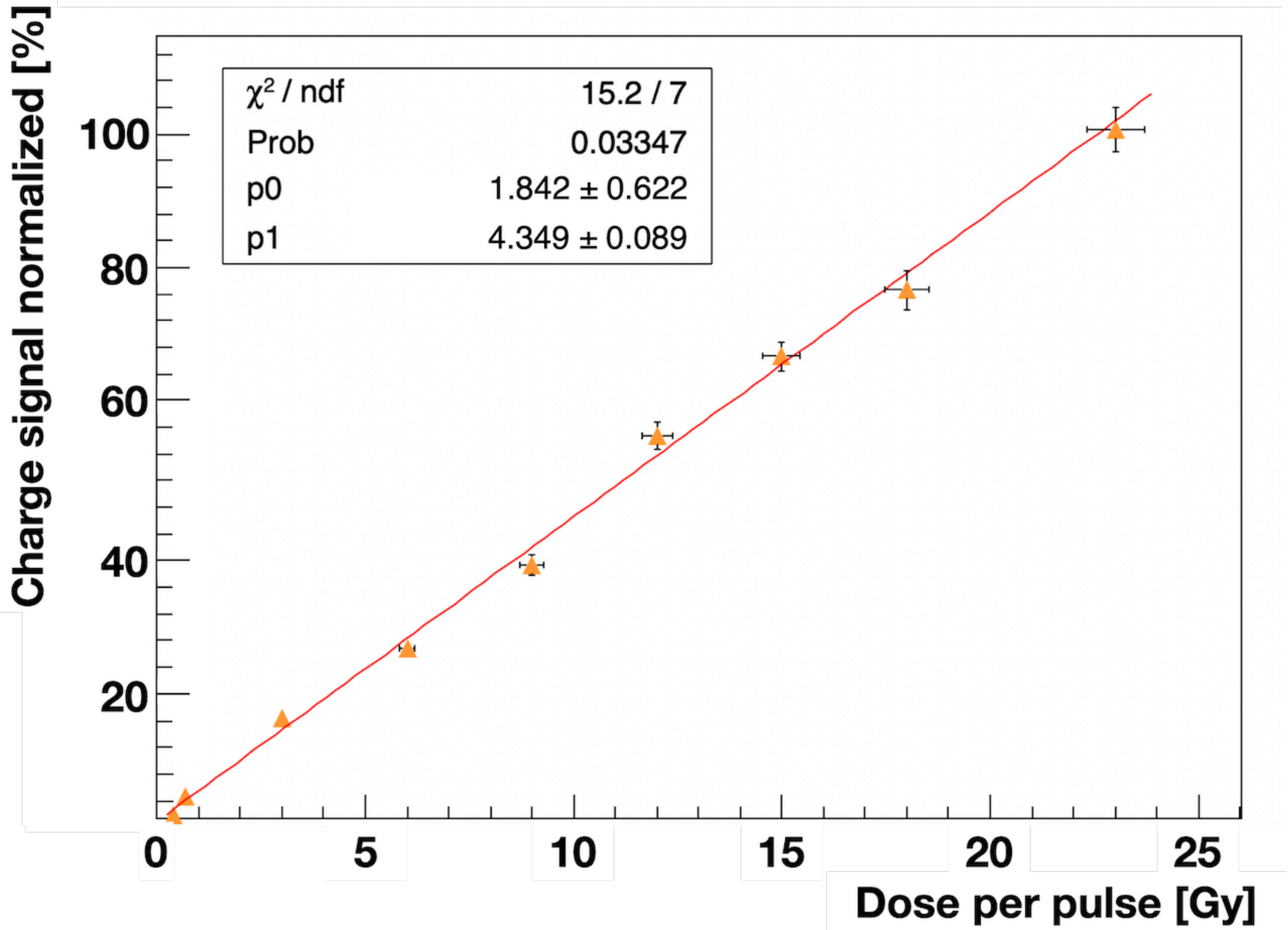
This is how the active volume support looks like once mounted on the beam exit window. N.B.: <u>**no material on the beam line!**</u> Just air…

FLASH beam monitoring

First round: LIAC-HWL November 2020-June 2021 → Second round: EF Antwerp July 2021-June 2022 → **Third round: EF Pisa July 2022-June 2023**

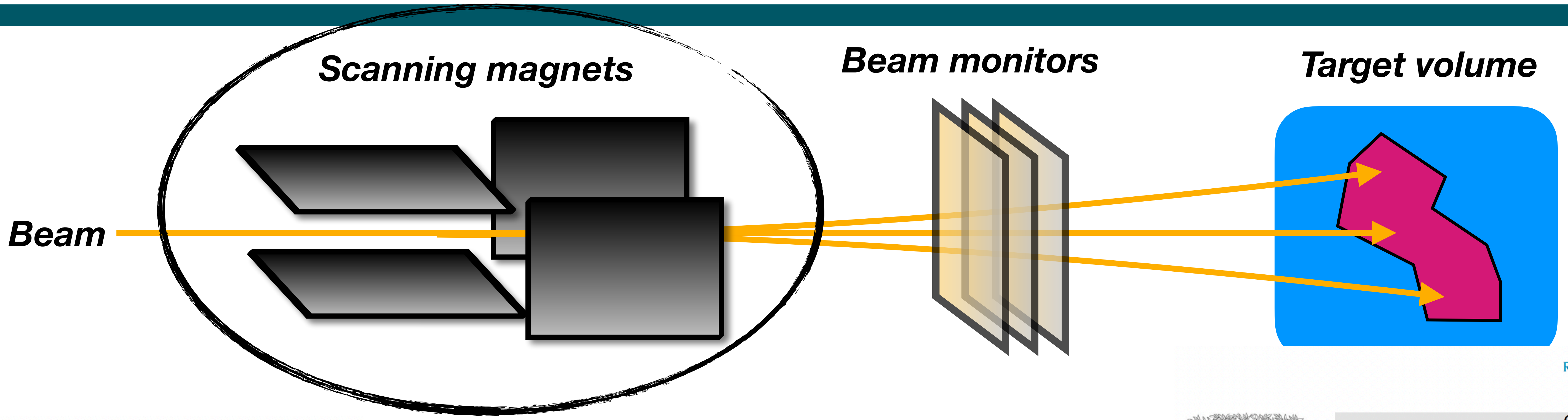
- Background can be successfully subtracted, although with this setup it is a sizable portion (~35%) of the total signal. Moreover, the gain of the PMT is still non-optimal for the fluctuations of the signal amplitude.
- The readout system and the geometry need to be optimized to increase the signal-to-noise ratio.





- The statistics is quite low (30 events per point), and the uncertainty has been put to 3% considering a systematic uncertainty on the D_p value.
- Linearity plot obtained with signal background-subtracted. **Fluorescence linearity is verified.**

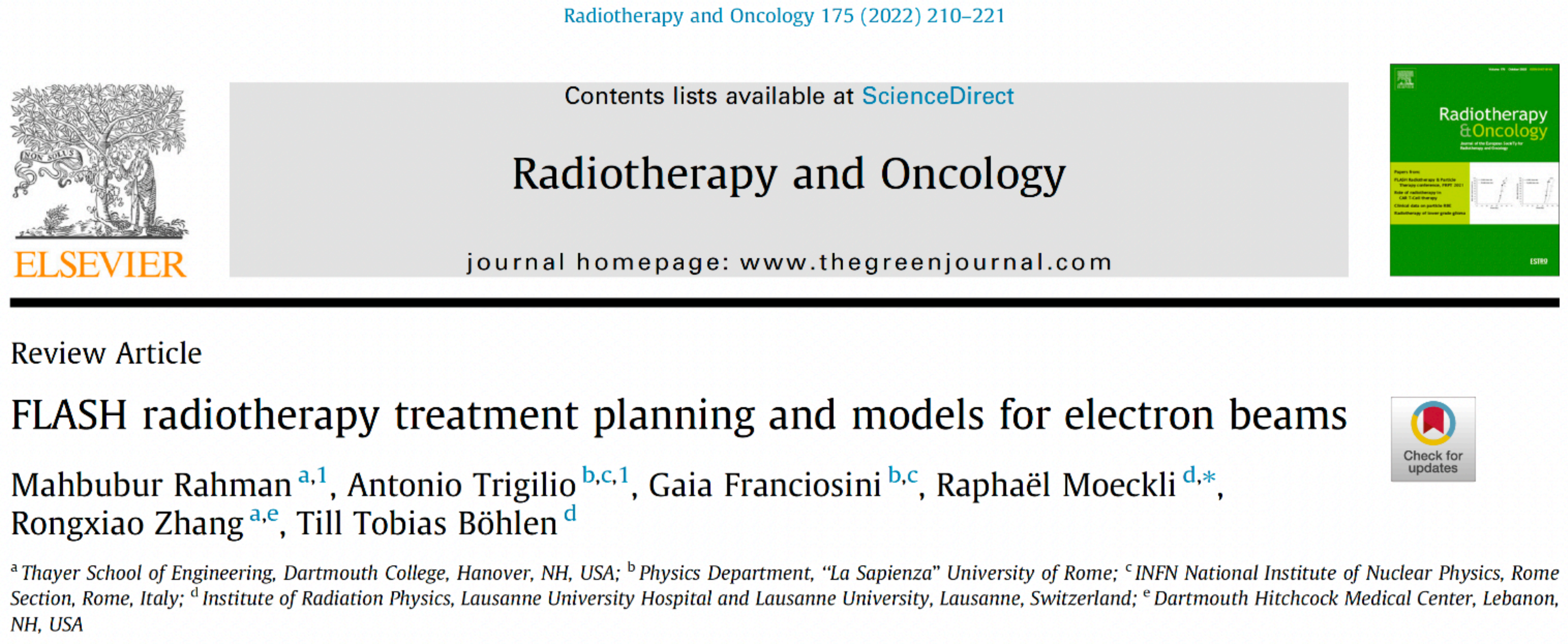
VHEE + FLASH: natural partners?



Description	value
Beam energy	> 130 MeV
RF frequency	5.712 GHz
Pulse repetition frequency	100 Hz
Pulse duration	< 3 μs
Max charge per pulse	600 nC
Max pulse current	200 mA
In-pulse dose-rate	> 10^7 Gy/s
Dose per pulse	>> 1Gy
Total treatment time	<100 ms
Average dose rate	>100 Gy/s

Parameter list of the VHEE LINAC.

- As of today, only electrons of **low-to-intermediate** energy (<20 MeV) are used to treat **superficial tumors** or for IOeRT applications.
- The idea to use electron beams with E > 50 MeV (***Very High Energy Electrons - VHEE***) to cure deep seated tumors has gained interest.
- A VHEE linac has been proposed as a collaboration between Sapienza and INFN, the ***SAFEST*** project.
- Beam delivery is an issue: FLASH does not allow for the loss of spatial conformity.



Radiotherapy and Oncology 175 (2022) 210–221
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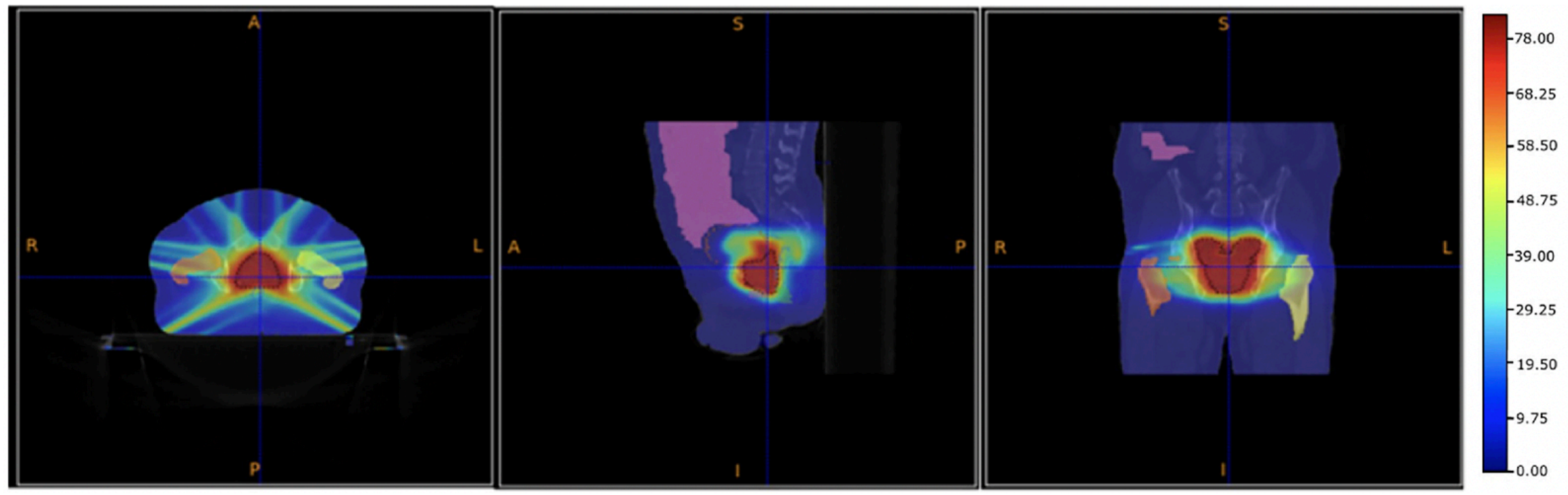
Review Article
FLASH radiotherapy treatment planning and models for electron beams

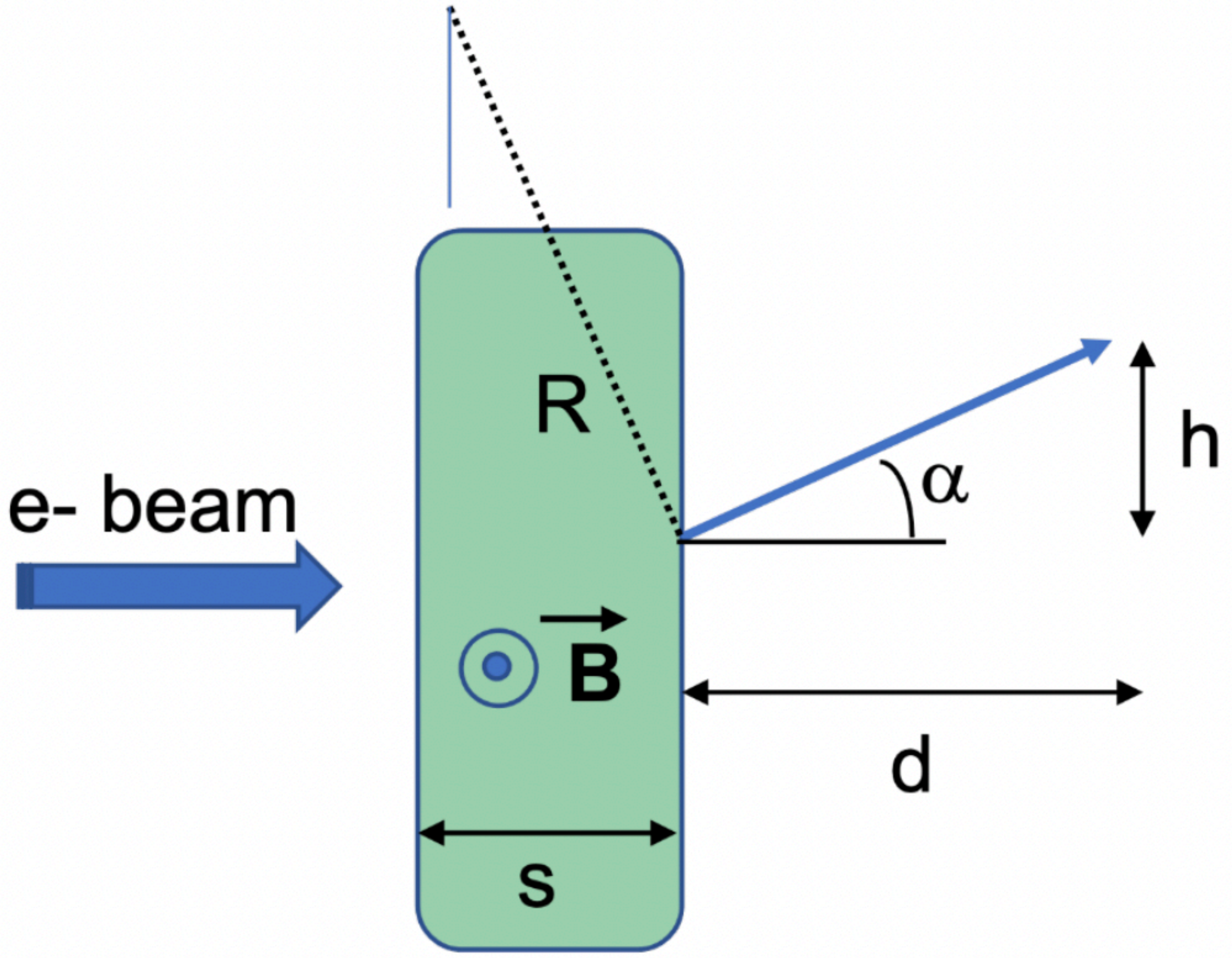
Mahbubur Rahman [a,1], Antonio Trigilio [b,c,1], Gaia Franciosini [b,c], Raphaël Moeckli [d,*], Rongxiao Zhang [a,e], Till Tobias Böhlen [d]
[a] Thayer School of Engineering, Dartmouth College, Hanover, NH, USA; [b] Physics Department, "La Sapienza" University of Rome; [c] INFN National Institute of Nuclear Physics, Rome Section, Rome, Italy; [d] Institute of Radiation Physics, Lausanne University Hospital and Lausanne University, Lausanne, Switzerland; [e] Dartmouth Hitchcock Medical Center, Lebanon, NH, USA



Sarti A et al (2021) Deep Seated Tumour Treatments With Electrons of High Energy Delivered at FLASH Rates: The Example of Prostate Cancer. Front. Oncol. 11:777852. doi: 10.3389/fonc.2021.777852

Magnetic scanning system

- Due to the intrinsic technological features of a compact VHEE-LINAC, the resulting beam is a collimated, narrow "**pencil beam**".
- Requires either passive or **active** scanning system to cover the full target volume.
- Option: Two-dimensional dipole shifting the beam direction at each pulse changing the current, to be evaluated for a 100 MeV electron.



- **Time factor:** The magnetic sweeping should not introduce any **delay** in the dose delivery to keep the high dose rate needed in the FLASH modality.
- The beam sweeping must take less time than the inverse of the pulse repetition frequency of the LINAC.
- Using the scanning system for the CNAO center of oncological hadron therapy as reference, the upper limit is ~5 kHz.

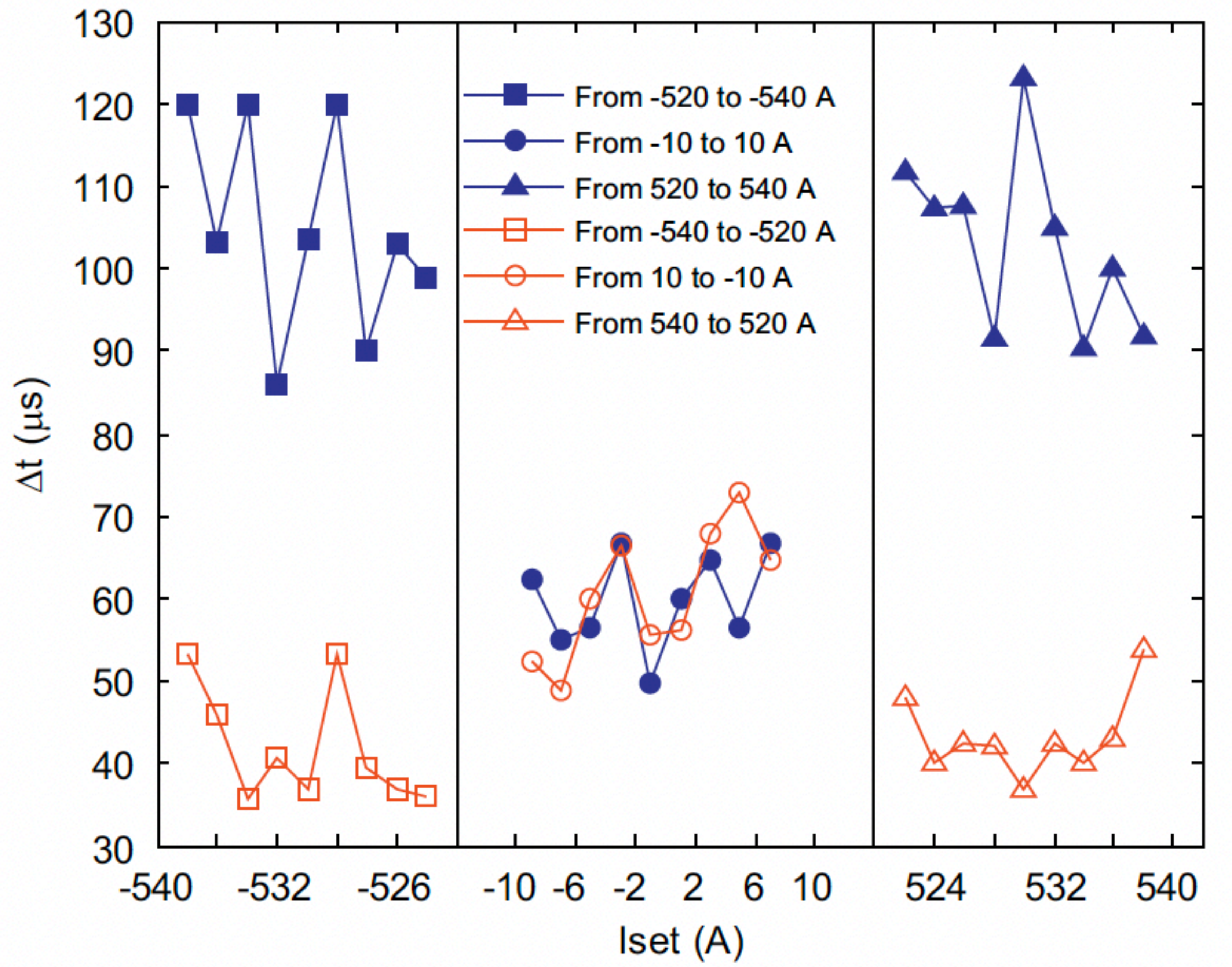


Fig. 10. Transient time (Δt) between 20% and 80% of 2 A steps as a function of I_{set} for increasing and decreasing currents.

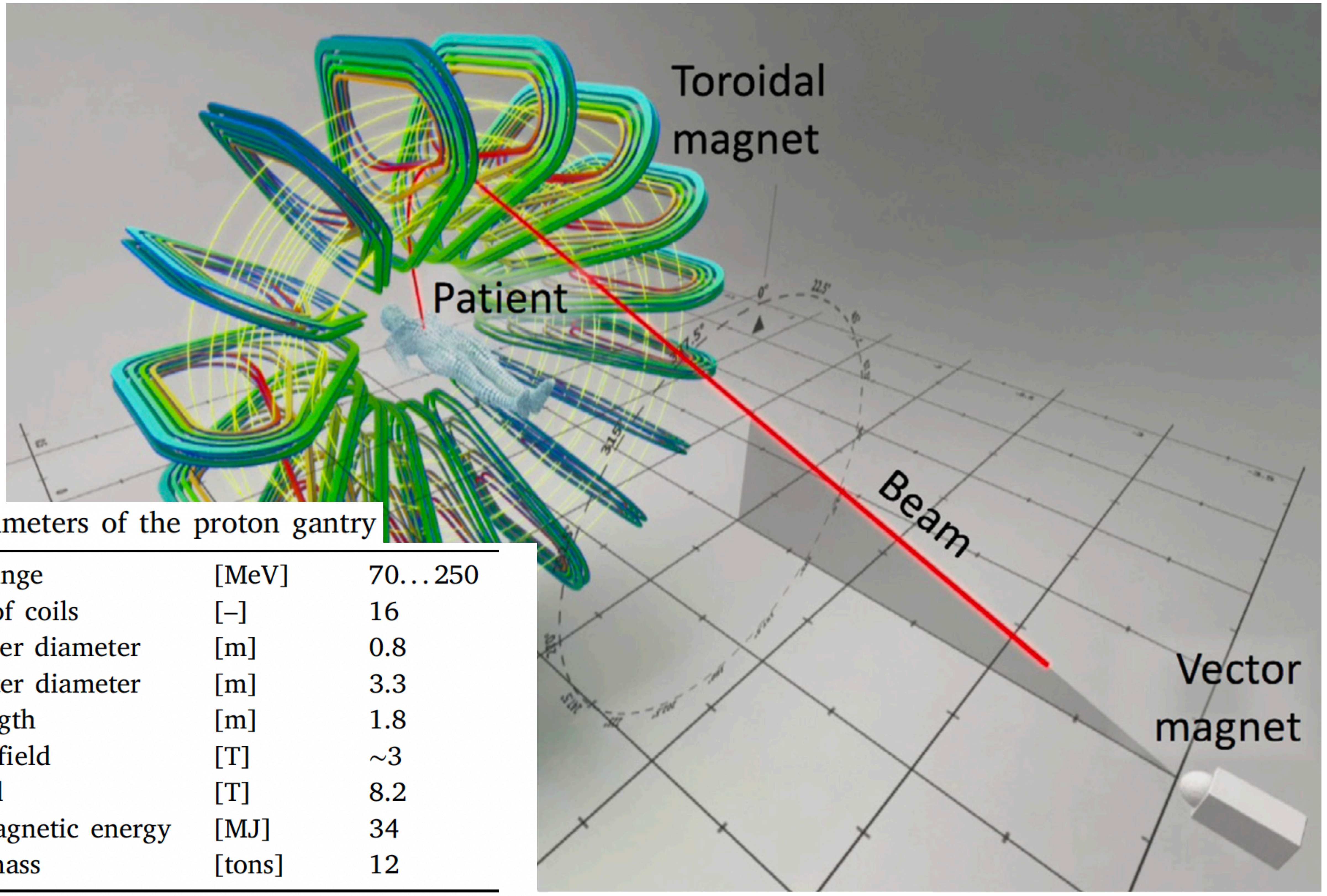
S. Giordanengo et al., Nucl. Instrum. Methods Phys. Res. A 613 (2010) 317–322

Considering a $2h \times 2h$ field of view ($h = 10$ cm) and a distance $d = 0.5$ m between the magnet and the patient, with a $B_{max} = 0.3$ T the result will be $R = 1.7$ m and $s = 20$ cm.

Magnetic scanning system

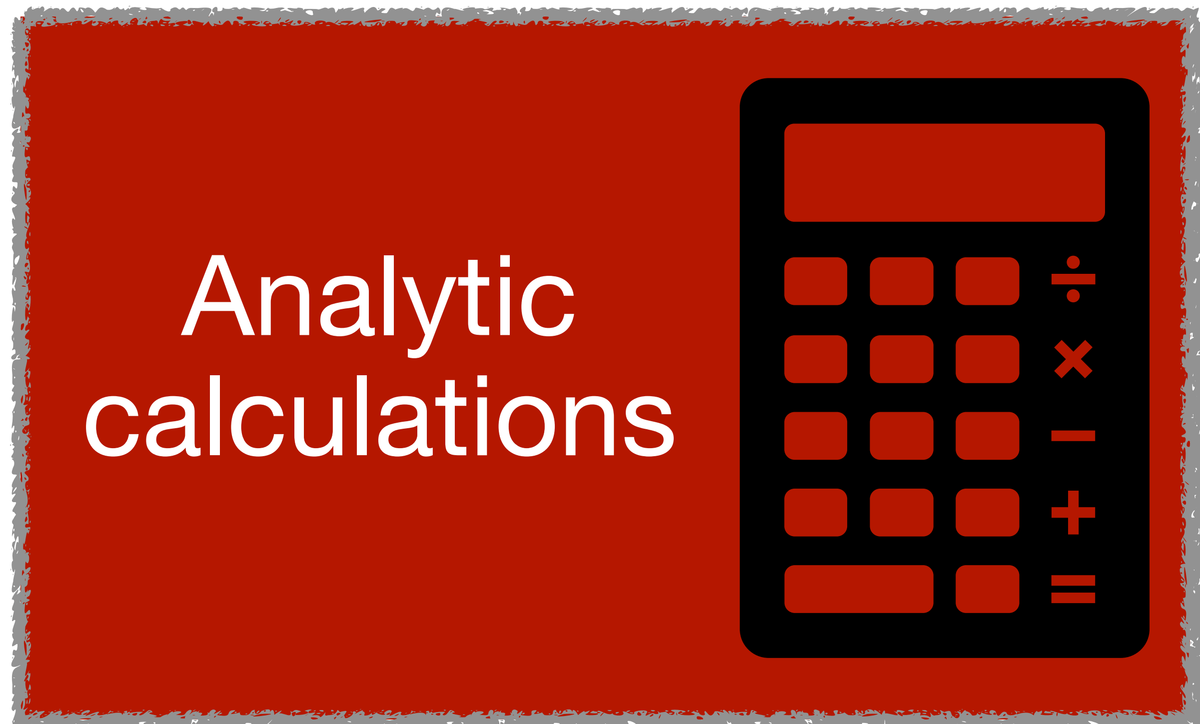
- In the larger perspective of a clinical implementation of VHEE-FLASH to treat deep seated tumors, there is the issue of **multi-directional treatments**.
- The idea is to use a **static gantry**, bending the beam towards the patient with a toroidal system, located after the initial kicker magnet.
- **<u>Not new</u>**: GaToroid concept for PT. Requires superconducting, **large** and **heavy** structure.
- I studied the possibility to scale down GaToroid and have a *<u>lightweight</u>* gantry that, on top of the field transversal scanning, will bend magnetically the electron beam to reach the patient from **<u>different directions</u>**, providing the field entrances chosen in the TPS.

L. Bottura, E. Felcini, G. De Rijk et al., Nucl. Inst. Methods Phys. Res. A 983 (2020) 164588



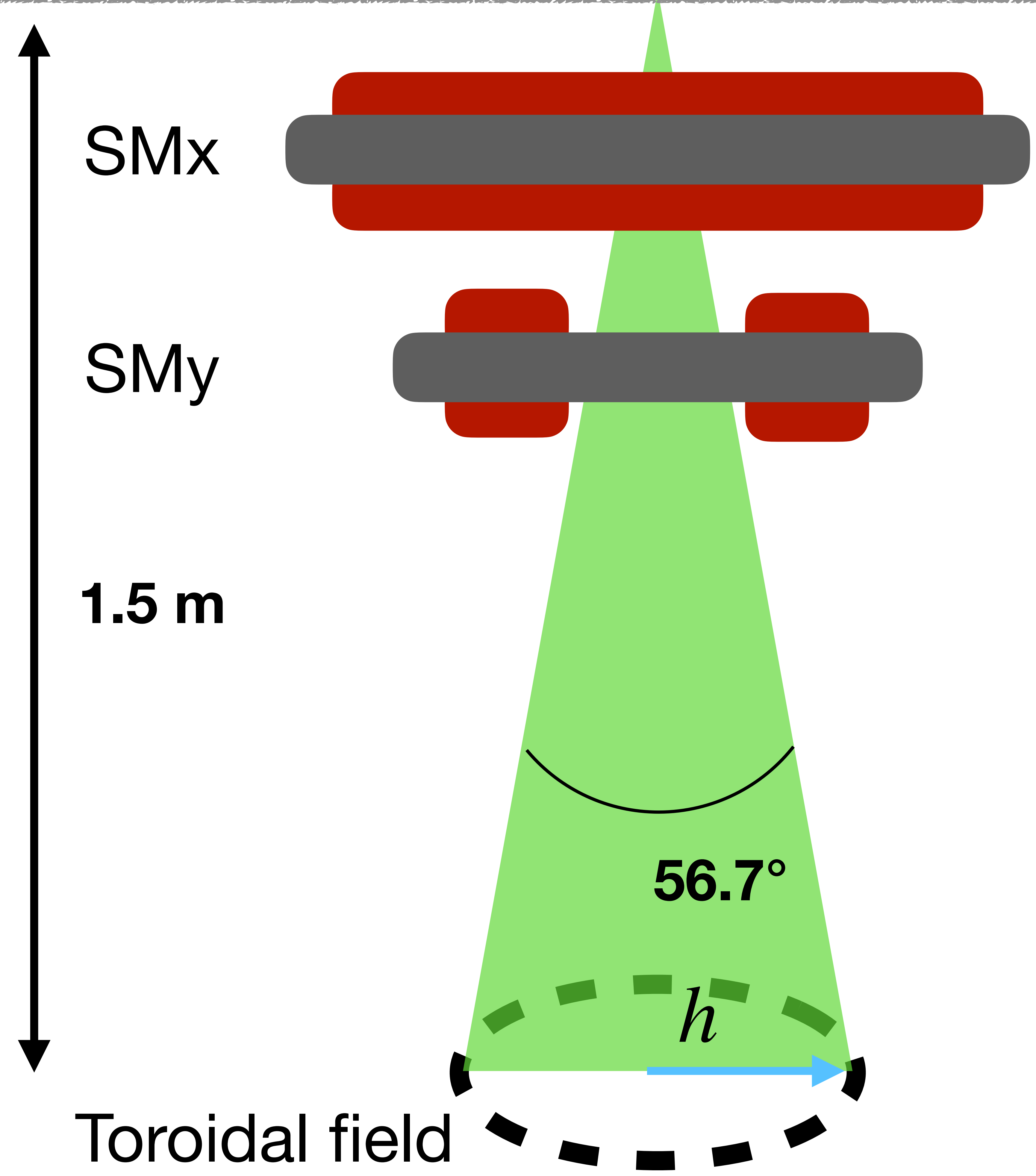
Main parameters of the proton gantry

Energy range	[MeV]	70...250
Number of coils	[–]	16
Torus inner diameter	[m]	0.8
Torus outer diameter	[m]	3.3
Torus length	[m]	1.8
Effective field	[T]	~3
Peak field	[T]	8.2
Stored magnetic energy	[MJ]	34
Magnet mass	[tons]	12

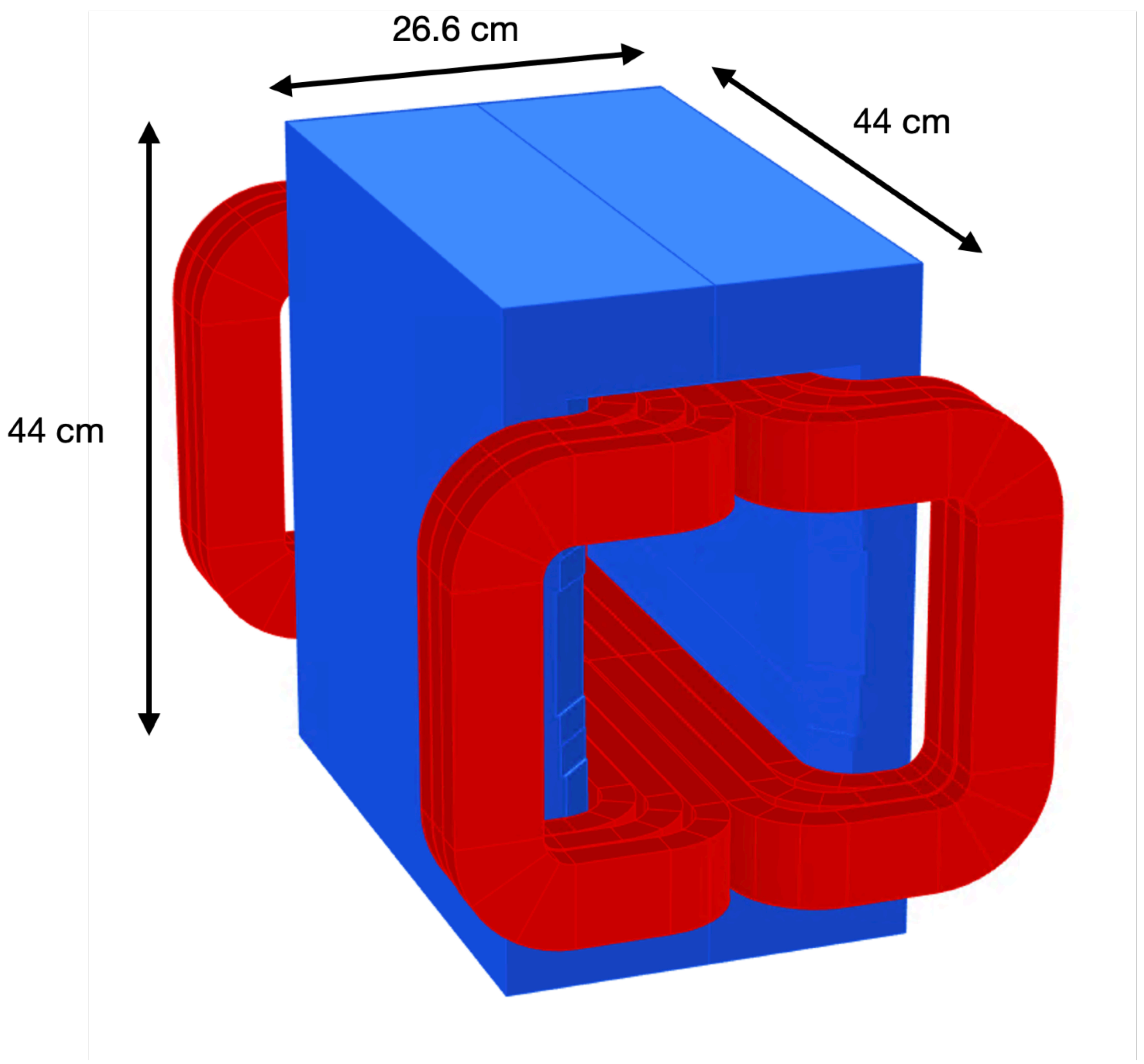


Magnetic scanning system

Analytic calculations



- For the scanning dipoles, I computed the magnet current and geometric features based on data similar to what already in use at CNAO.
- Based on the existing cross-section of the coils, the power converter would need to operate at **42.6 kW** about **12%** its maximum value.
- The existing dipoles are **oversized**: an active scanning of the beam at UHDR is achievable.



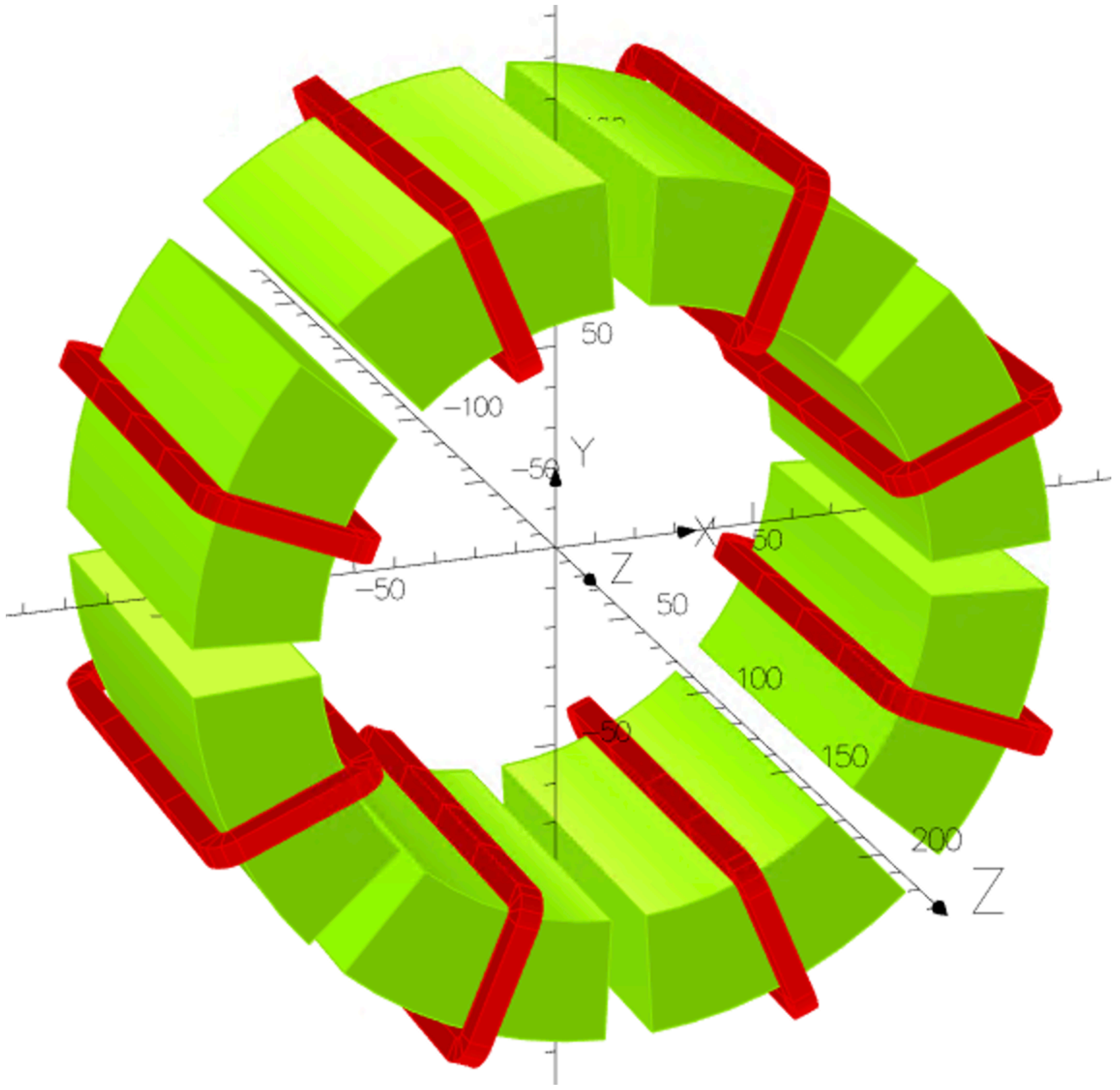
Magnetic scanning system

Analytic calculations	OPERA 3D simulation

- The values of the number of coils have been taken from the original Gatoroid optimization, but they could be reduced.
- Parameters to be analyzed for future optimization: magnet length and cooling circuits (work in progress).
- The field computed can be passed as input to FLUKA => dosimetric validation.

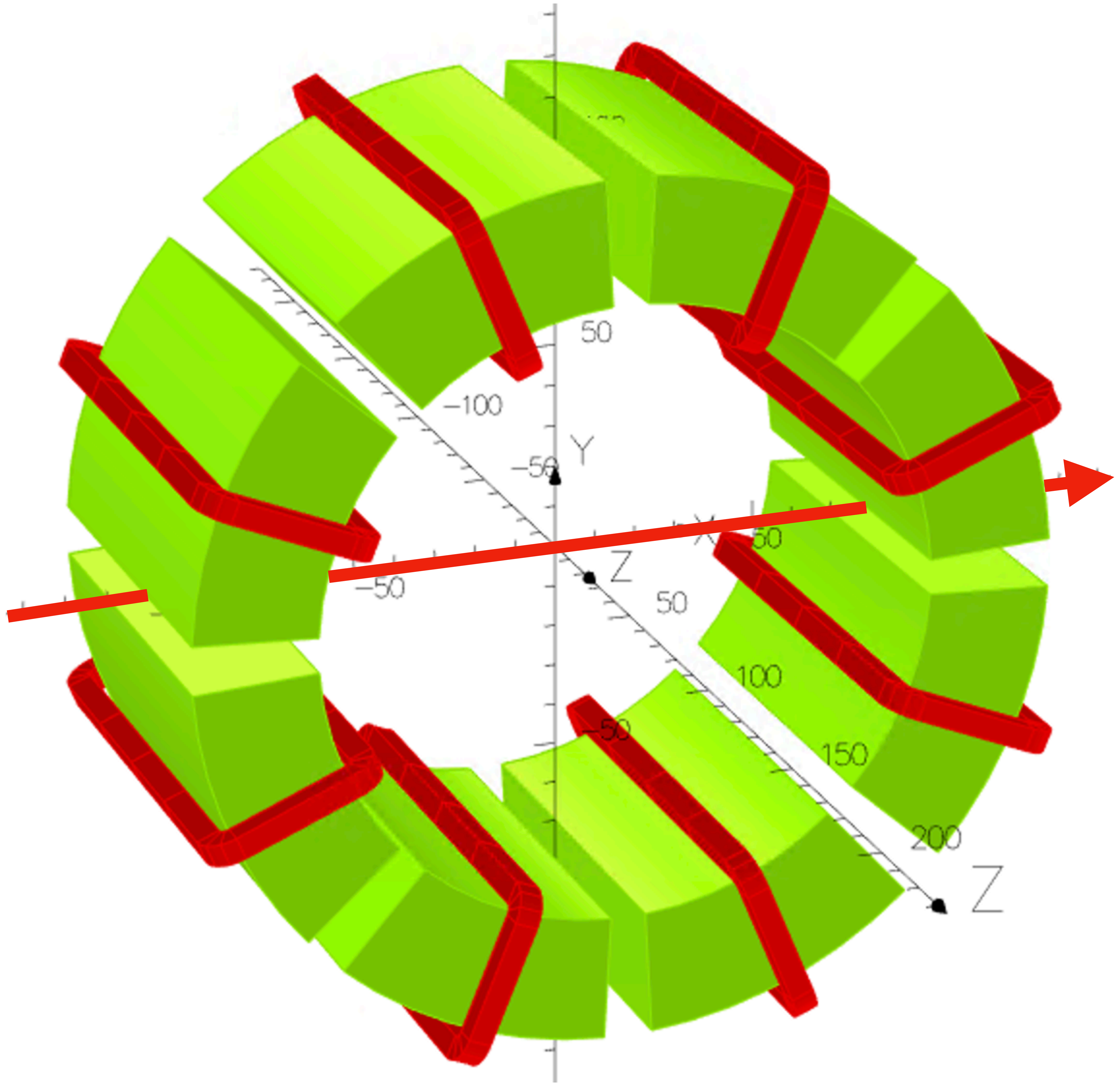
Deflection angle	90° (test)
Effective length	1 m
Torus outer radius	1.5 m
Number of directions	8
Number of coils	16 (test)
Ampereturns NI per coil	45’863.9 A
Effective field	0.524 T
Air aperture	0.11 m

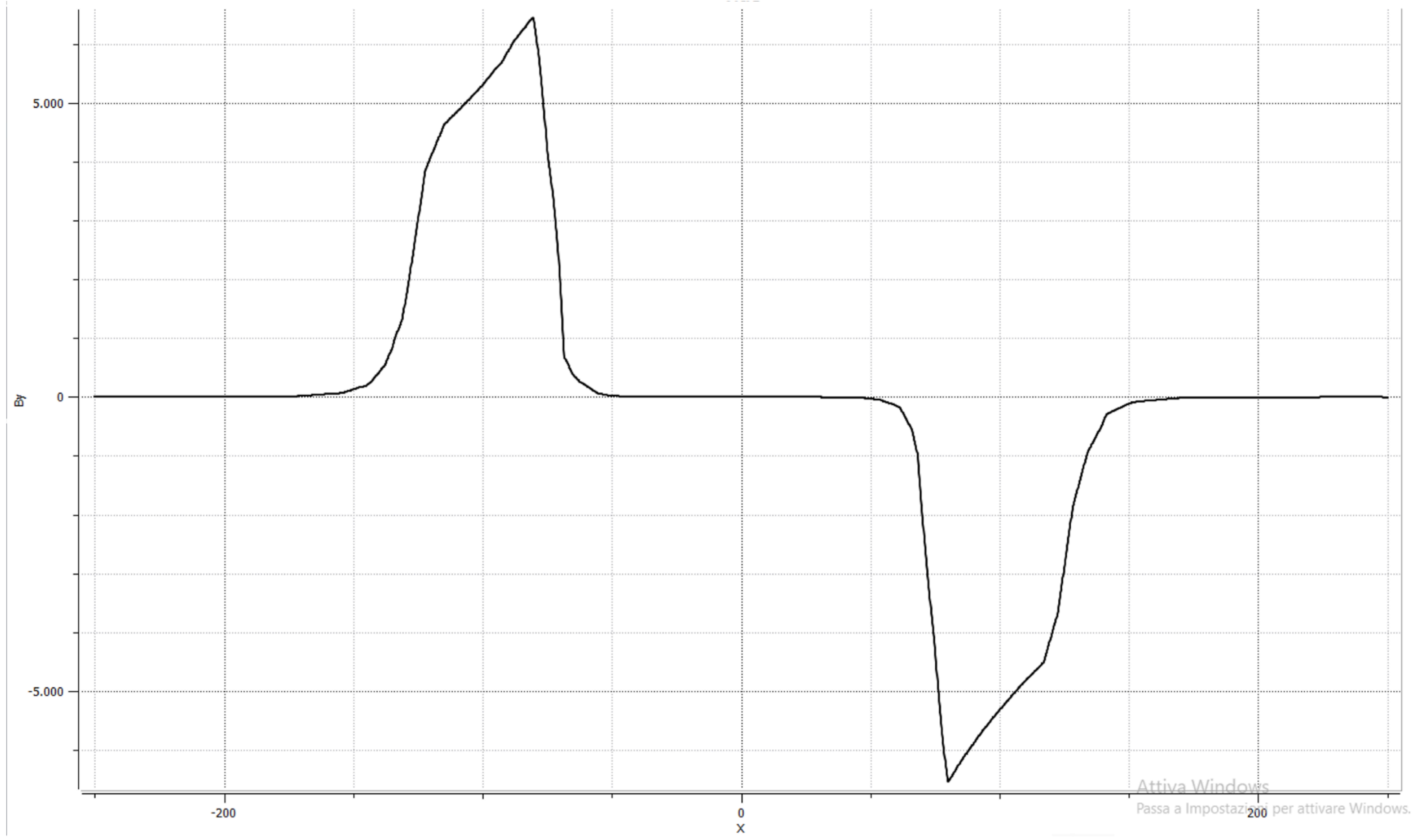
Effective cross-section	60 mm²
Current per coil	327.6 A
Length per turn	3 m
N of turns per coil	140
Current density	5.34 A/mm²
Resistance	0.15 Ω
Power loss	16.16 kW



Magnetic scanning system

OPERA 3D simulation





- Graph of B_y (vertical field) calculated over the horizontal direction.
- Peak value of 0.65 T (slightly above prediction, but this is due to simplified geometry in the analytical model)

Summary and Conclusions

- I dedicated my PhD research to the investigation of major topical issues in FLASH effect and UHDR studies.
- I actively explored air fluorescence as a beam monitoring technique, verifying the linear response with respect to the dose-rate per pulse and obtaining promising results.
- With FLUKA-MC simulation, I have started the design and development of a 2D BM device. New detector and first round of tests are foreseen at BTF in Frascati in 2024.
- I performed a preliminary evaluation on the feasibility for a beam delivery to the target exploiting both scanning dipole magnets and a static toroidal magnetic field.
- The OPERA 3D simulation has been validated. I will perform a geometry optimization and detailed description of technical requirements.
- **Acknowledgements to the FlashDC team:** Michela Marafini, Angelica De Gregorio, Gaia Franciosini, Marco Garbini, Vincenzo Patera, Alessio Sarti, Adalberto Sciubba, Marco Toppi, Giacomo Traini.
- **Acknowledgements to the LNF Magnetic Measurement Laboratory team:** Alessandro Vannozzi, Lucia Sabbatini, Ilaria Balossino, Lucas Capuano, Luca Petrucciani, Andrea Selce.


Nuclear Inst. and Methods in Physics Research, A 1041 (2022) 167334

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journal homepage: www.elsevier.com/locate/nima

The FlashDC project: Development of a beam monitor for FLASH radiotherapy

Antonio Trigilio [a,b], Angelic
Marco Garbini [c], Gabriele I
Vincenzo Patera [d,b], Alessio
Giacomo Traini [b], Micol De

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Review Article

FLASH radiotherapy treatment planning and models for electron beams

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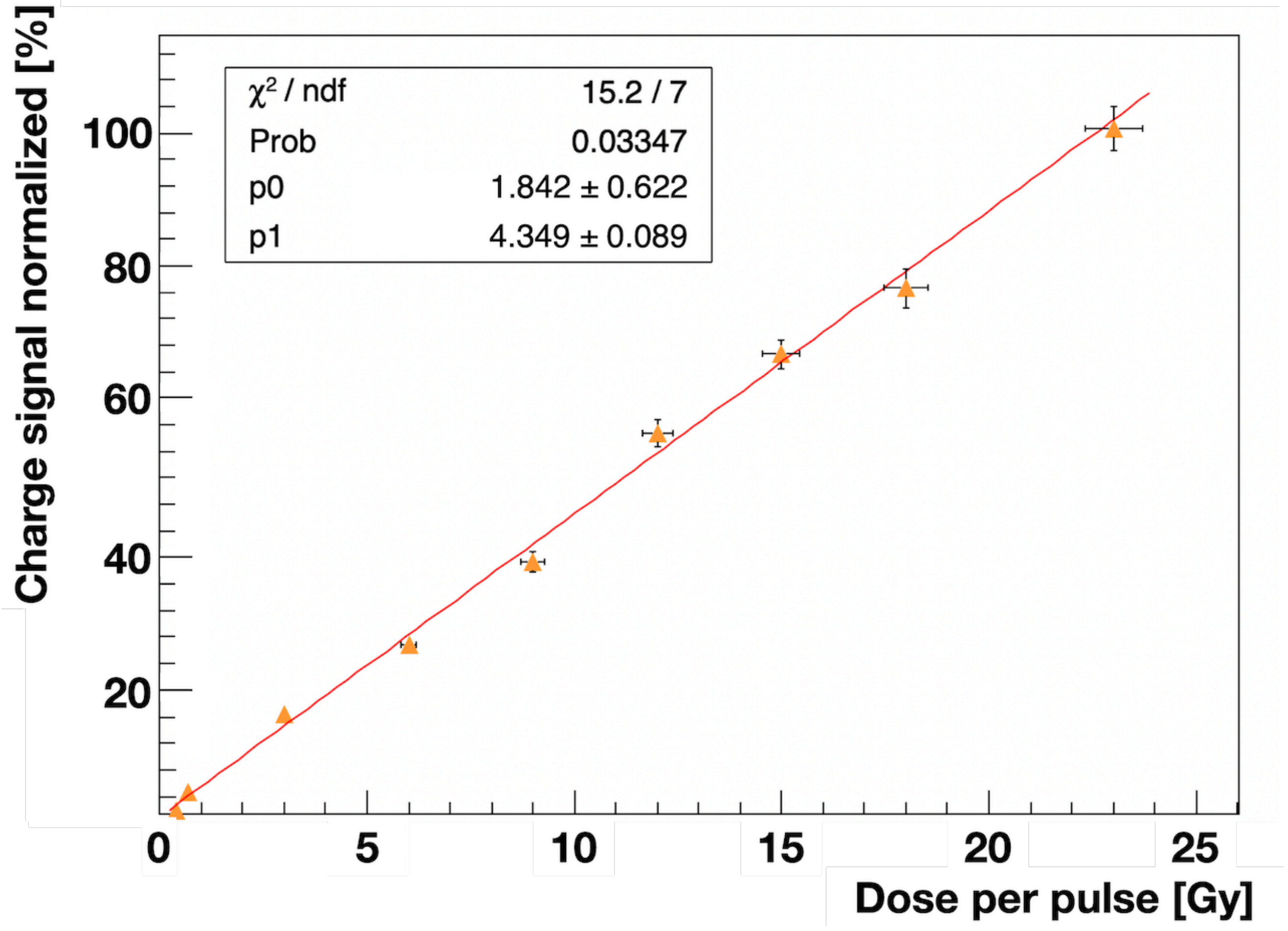
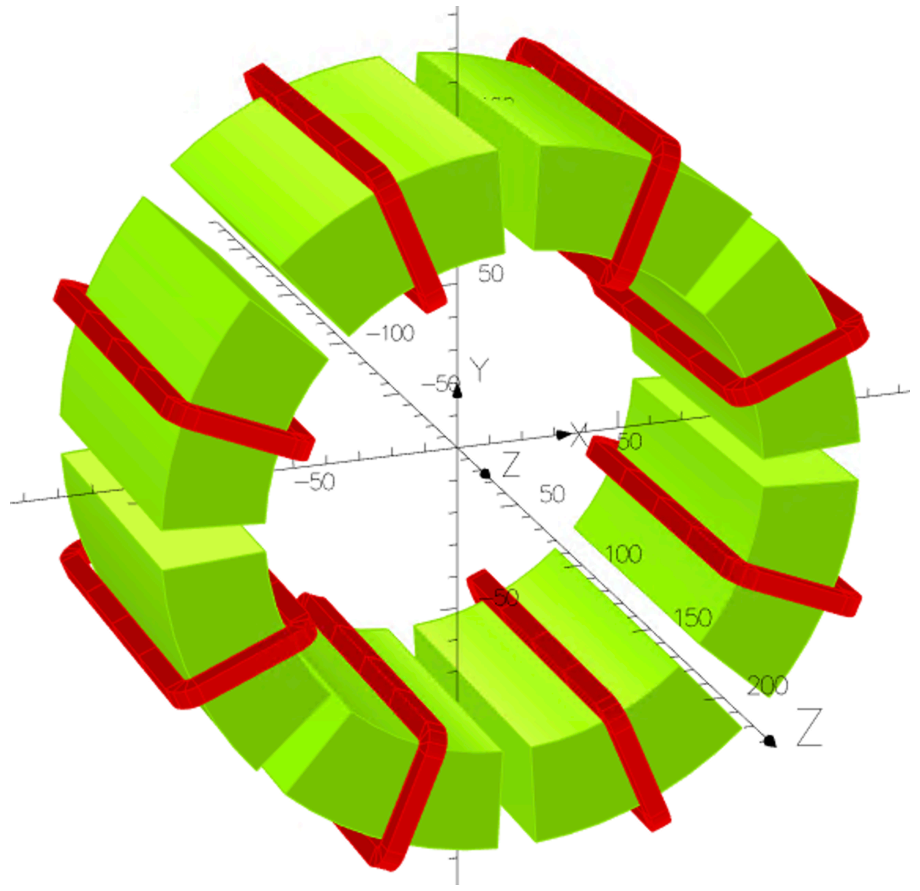
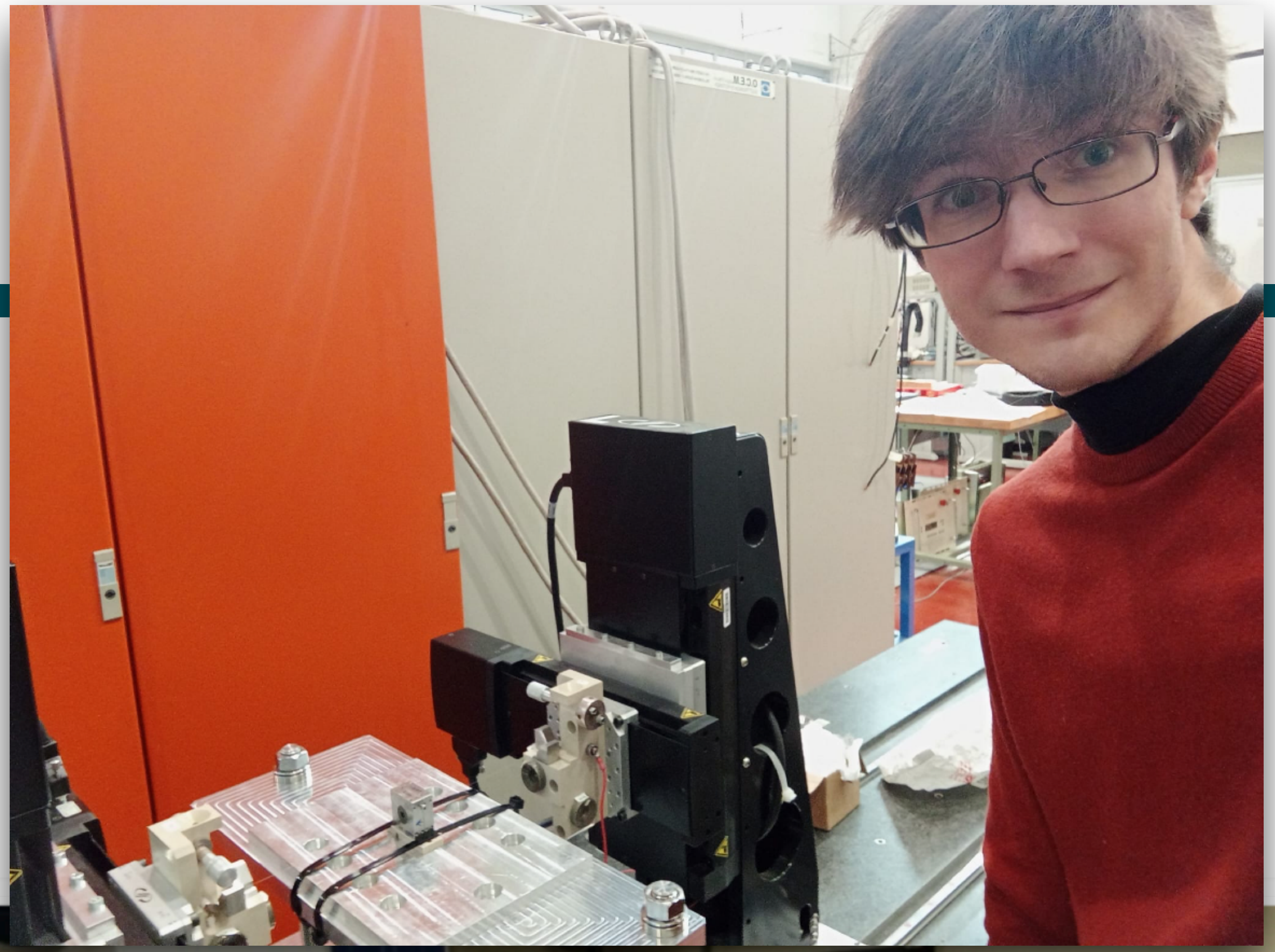




Thank you for your attention!

Links:
arpg-serv.ing2.uniroma1.it/arpg-site/index.php/research-projects/current-project/flashdc
web.infn.it/FRIDA/

3-year book



Scientific products

1. Rocco D., et al., "TOPS fast timing plastic scintillators: Time and light output performances", Nuclear Inst. and Methods in Physics Research A, 2023, 1052, 168277, DOI: 10.1016/j.nima.2023.168277.
2. Franciosini G., et al., "GPU-accelerated Monte Carlo simulation of electron and photon interactions for radiotherapy applications", Phys. Med. Biol., 2023, 68(4), 044001, Open Access, DOI: 10.1088/1361-6560/aca1f2.
3. Muscato A., et al., "Treatment planning of intracranial lesions with VHEE: comparing conventional and FLASH irradiation potential with state-of-the-art photon and proton radiotherapy", Front. Phys., 2023, 11:1185598, Open Access, DOI: 10.3389/fphy.2023.1185598.
4. Silvestre G., et al., "Characterization of 150 μm thick silicon microstrip prototype for the FOOT experiment", JINST, 2022, 17(12), P12012, DOI: 10.1088/1748-0221/17/12/P12012.
5. Toppi M., Sarti A., Alexandrov A., et al., "Elemental fragmentation cross sections for a ^{16}O beam of 400 MeV/u kinetic energy interacting with a graphite target using the FOOT ΔE-TOF detectors", Front. Phys., 2022, 10:979229, Open Access, DOI: 10.3389/fphy.2022.979229.
6. Trigilio A., De Gregorio A., Fischetti M., et al., "The FlashDC project: Development of a beam monitor for FLASH radiotherapy", Nuclear Inst. and Methods in Physics Research A, 2022, 1041:167334, DOI: 10.1016/j.nima.2022.167334.
7. Rahman M., Trigilio A., et al., "FLASH radiotherapy treatment planning and models for electron beams", Radiother. Oncol., 2022, 175, pp. 210–221, Open Access, DOI: 10.1016/j.radonc.2022.08.009.
8. Moglioni M., Kraan A.C., Baroni G., et al., "In-vivo range verification analysis with in-beam PET data for patients treated with proton therapy at CNAO", Front. Oncol., 2022, 12:929949, Open Access, DOI: 10.3389/fonc.2022.929949.
9. De Simoni M., et al. "A data-driven fragmentation model for carbon therapy GPU-accelerated Monte-Carlo dose recalculation", Front. Oncol., 2022, 12:780784, Open Access, DOI: 10.3389/fonc.2022.780784.
10. Sarti A., De Maria P., Battistoni G., et al. "Deep seated tumour treatments with electrons of high energy delivered at FLASH rates: the example of prostate cancer", Front. Oncol., 2021, 11:777852, Open Access, DOI: 10.3389/fonc.2021.777852.
11. Trigilio A. "New reconstruction algorithm for the fast neutron MONDO tracker", Il Nuovo Cimento C, 2021 44(1), Open Access, DOI: 10.1393/ncc/i2021-21016-7.

Contributions to International Conferences

Oral Presentations

25-29 Sept. 2023	**16th Topical Seminar on Innovative Particle and Radiation Detectors - Siena, Italy.** *Test beam results of a fluorescence-based monitor for ultra-high dose rates.*
25-29 June 2023	**24th International Workshop on Radiation Imaging Detectors - Oslo, Norway.** *Test beam results of a fluorescence-based monitor for ultra-high dose rates.*
17-20 Aug. 2022	**4th European Congress of Medical Physics - Dublin, Ireland.** *FlashDC: development of a beam monitoring system for FLASH radiotherapy.*
26-30 June 2022	**23rd International Workshop on Radiation Imaging Detectors - Riva del Garda, Italy.** *The FlashDC project: development of a beam monitor for FLASH radiotherapy.*
12-16 Sept. 2021	**Applied Nuclear Physics Conference - Prague, Czech Republic.** *MONDO: A scintillating fibre tracker for secondary neutron measurements in Particle Therapy.*
10 Sept. 2021	**Workshop S.I.R.R. Società Italiana per la Ricerca sulle Radiazioni - Napoli, Italy.** *FlashDC project: development of a beam monitor for FLASH therapy.*
14-18 June 2021	**9th International Conference on Radiation in Various Fields of Research - Herceg Novi, Montenegro.** *Prostate cancer FLASH therapy treatments with electrons of high energy: a feasibility study.* Abstract DOI: 10.21175/rad.abstr.book.2021.36.9
14-18 Sept. 2020	**106th National Congress of the Italian Physical Society - online.** *Preliminary characterization of a SPAD based sensor for the MONDO neutron tracker.* Awarded as best communication in the Biophysics and Medical Physics section by the scientific committee.

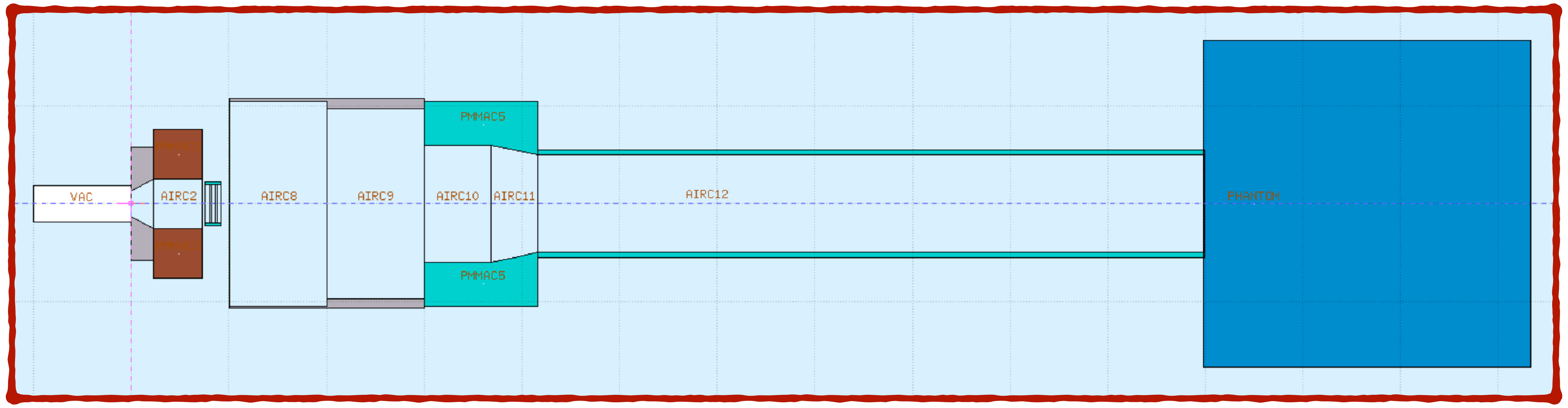
E-Posters

1-3 Dec. 2021	**Flash Radiotherapy and Particle Therapy Conference - online.** *FlashDC project: development of a beam monitor for FLASH radiotherapy.*

Come fai..SBAI

Backup

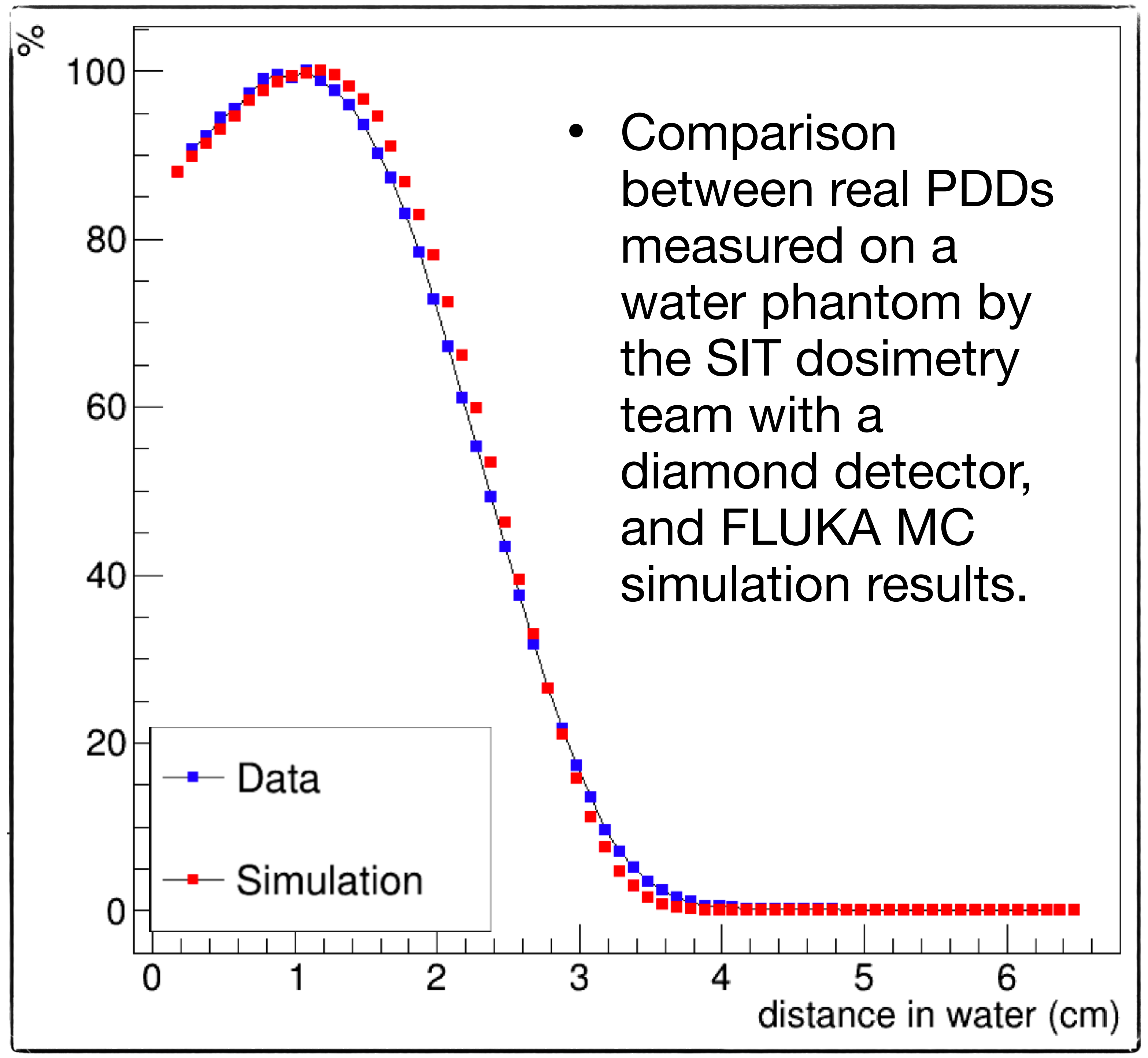
Beam delivery studies



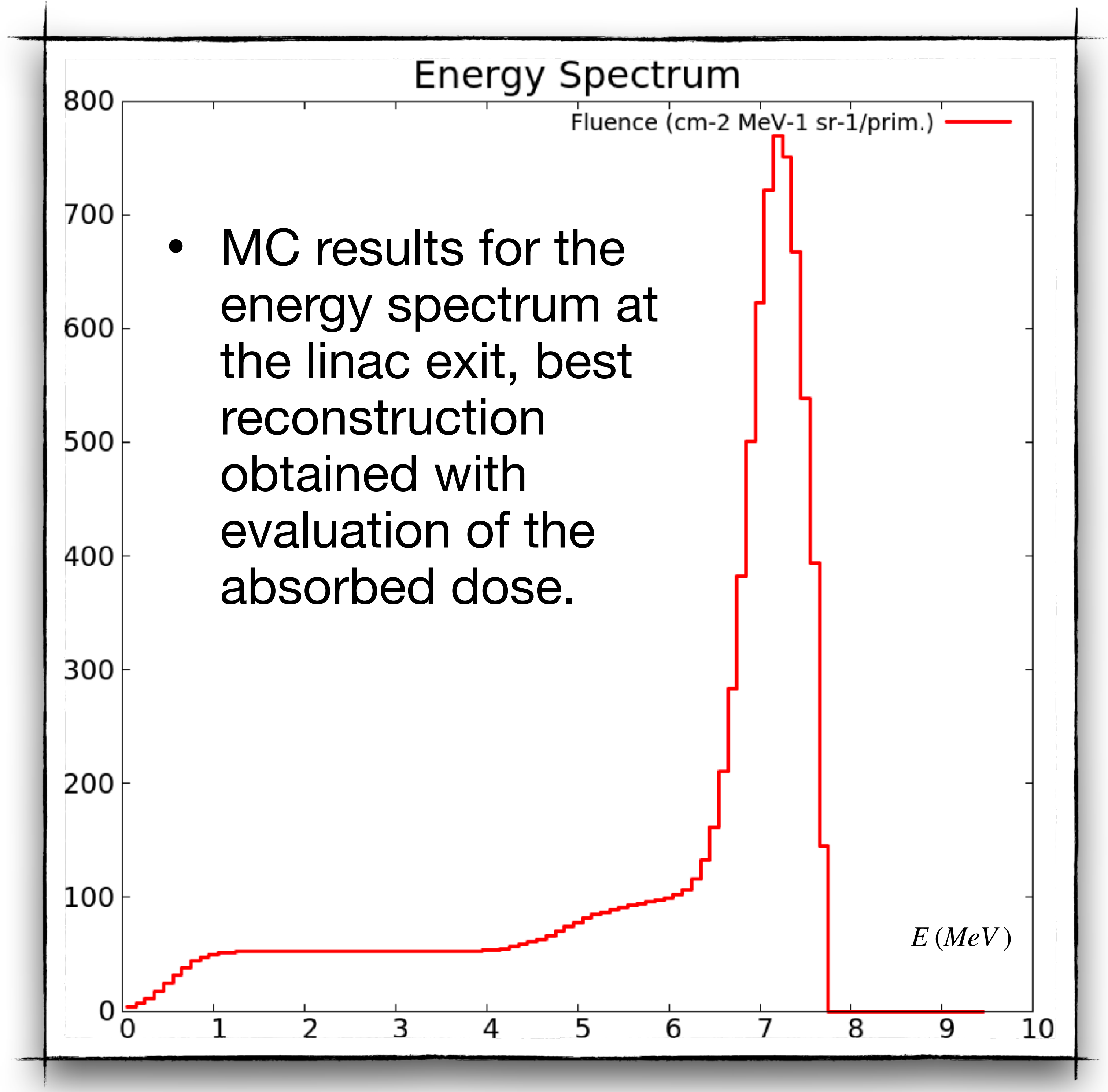
- Monte Carlo simulation provide a solid base to estimate the accuracy of the beam delivery system and the expected dosimetric qualities. It can also be a useful tool for the **optimization** of the hardware apparatus.
- I performed several validations with different applicator geometries comparing **Percentage Dose Depth** and dose profile measurements.

- **ElectronFlash**: ~10^{12} electrons/pulse.
- Electron energy at the linac exit: 7MeV.
- **Dose rate (single pulse): up to 5*10^6 Gy/s.**
- Field spread: 4-5 cm at BEW (uncollimated).

soiort.com/flash-rt-technology/



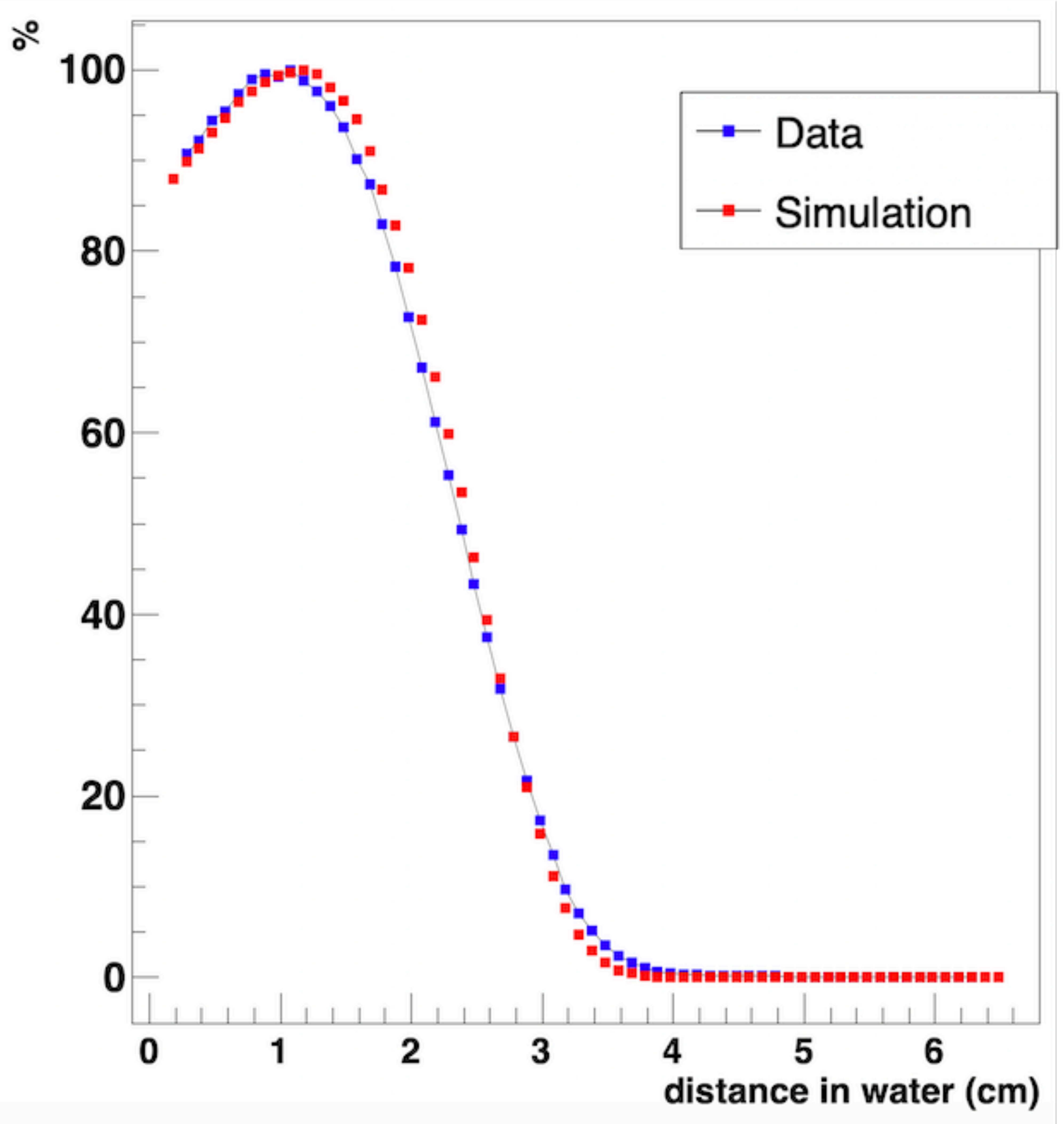
- Comparison between real PDDs measured on a water phantom by the SIT dosimetry team with a diamond detector, and FLUKA MC simulation results.



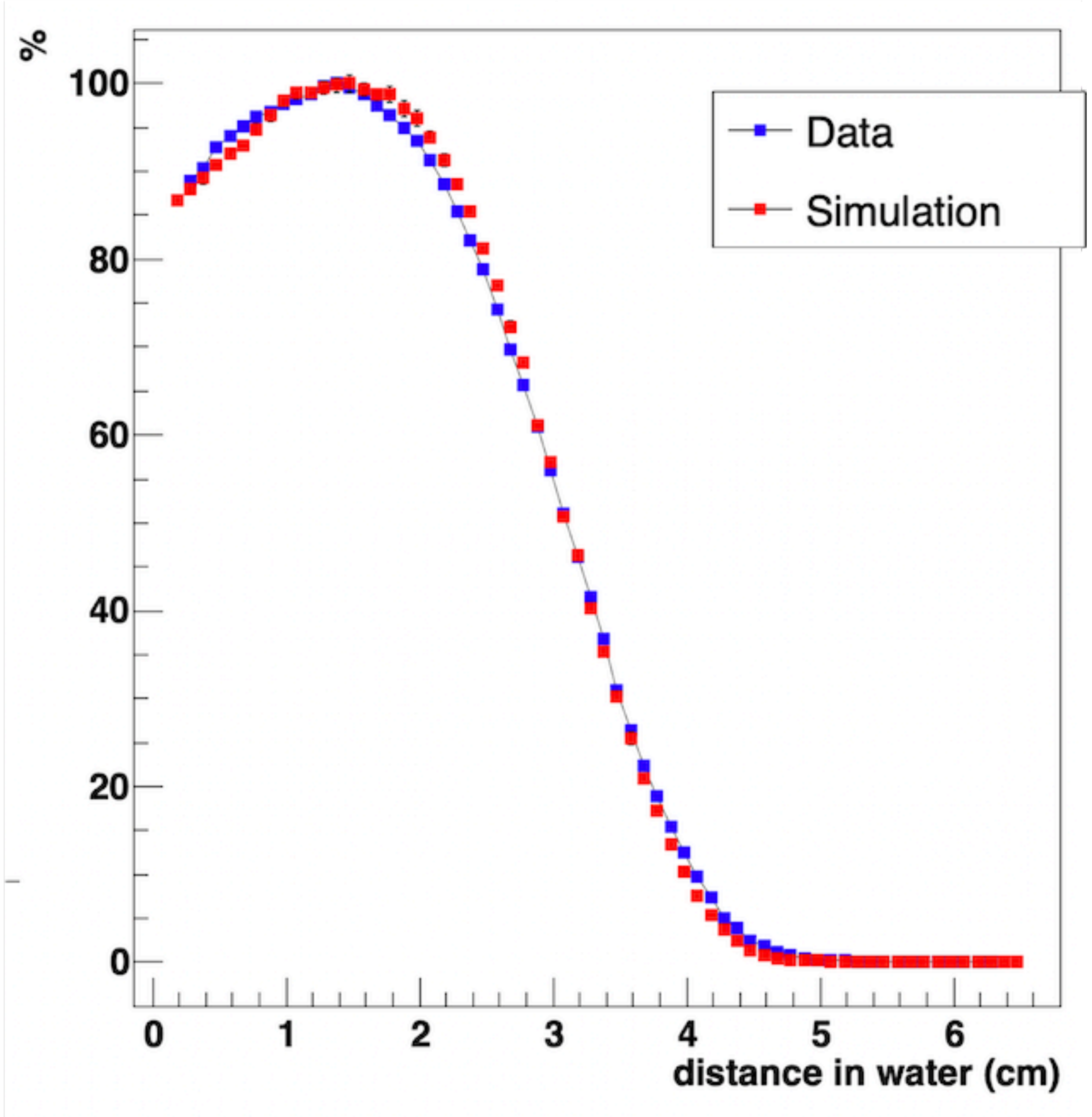
- MC results for the energy spectrum at the linac exit, best reconstruction obtained with evaluation of the absorbed dose.

Beam delivery studies

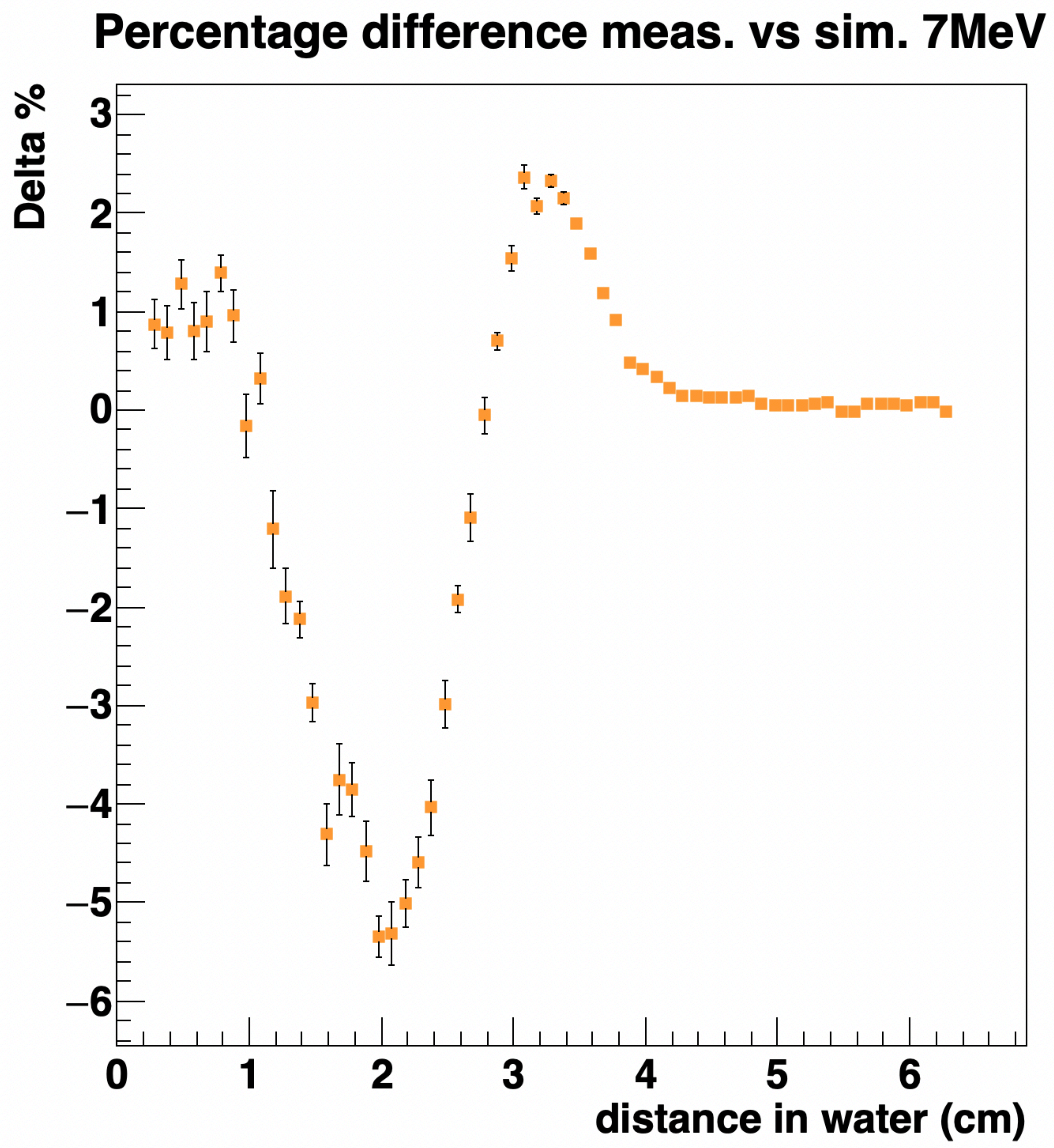
7MeV

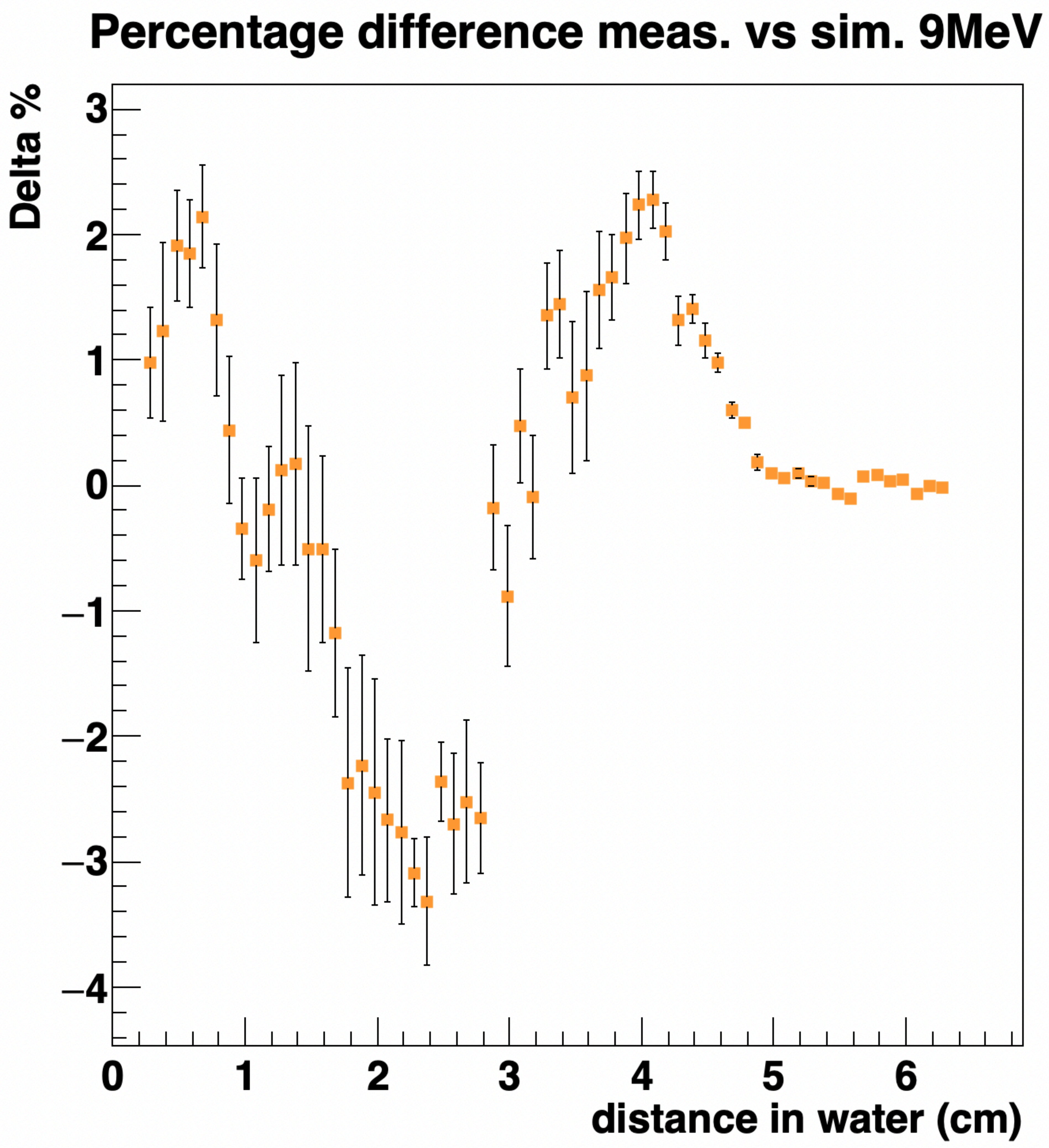


9MeV



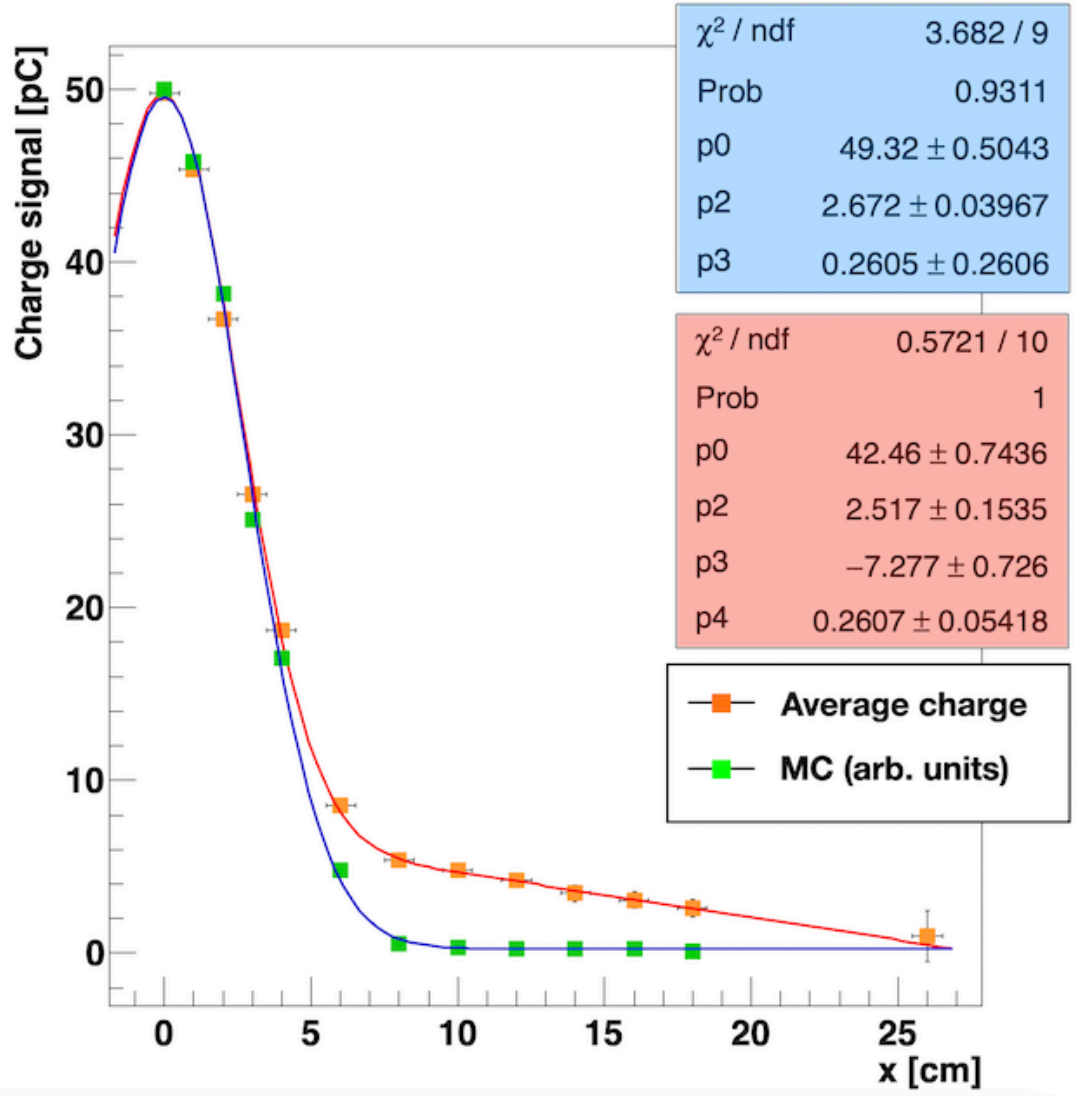
Beam delivery studies





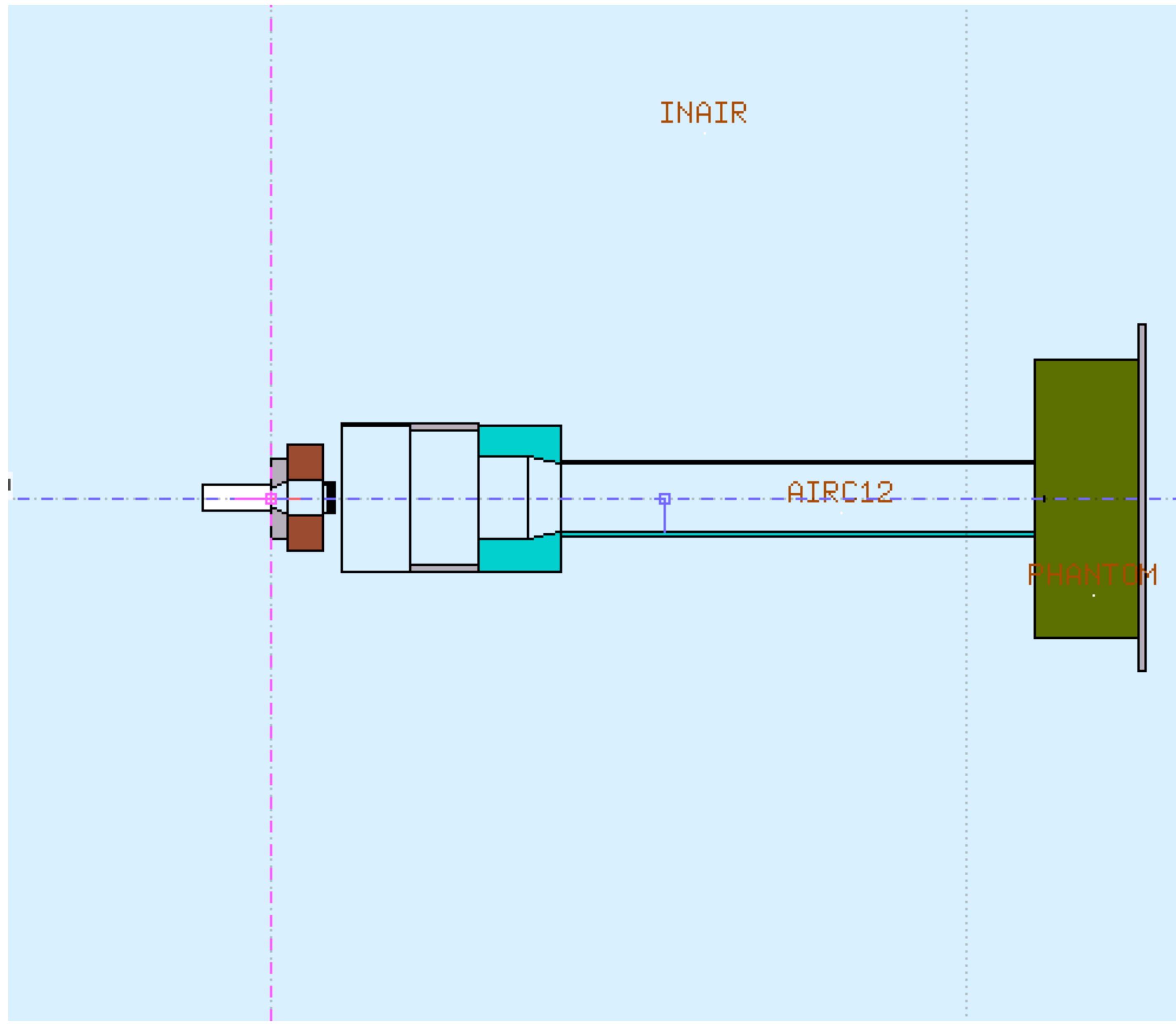
Beam delivery studies

- The MC simulation was used to estimate the amount of missing background produced at the beam edges.
- In order to study this spurious signal, we need a new system with a better repeatability that can further minimize the impact of the material along the beam line and measure the **signal-to-noise** ratio.



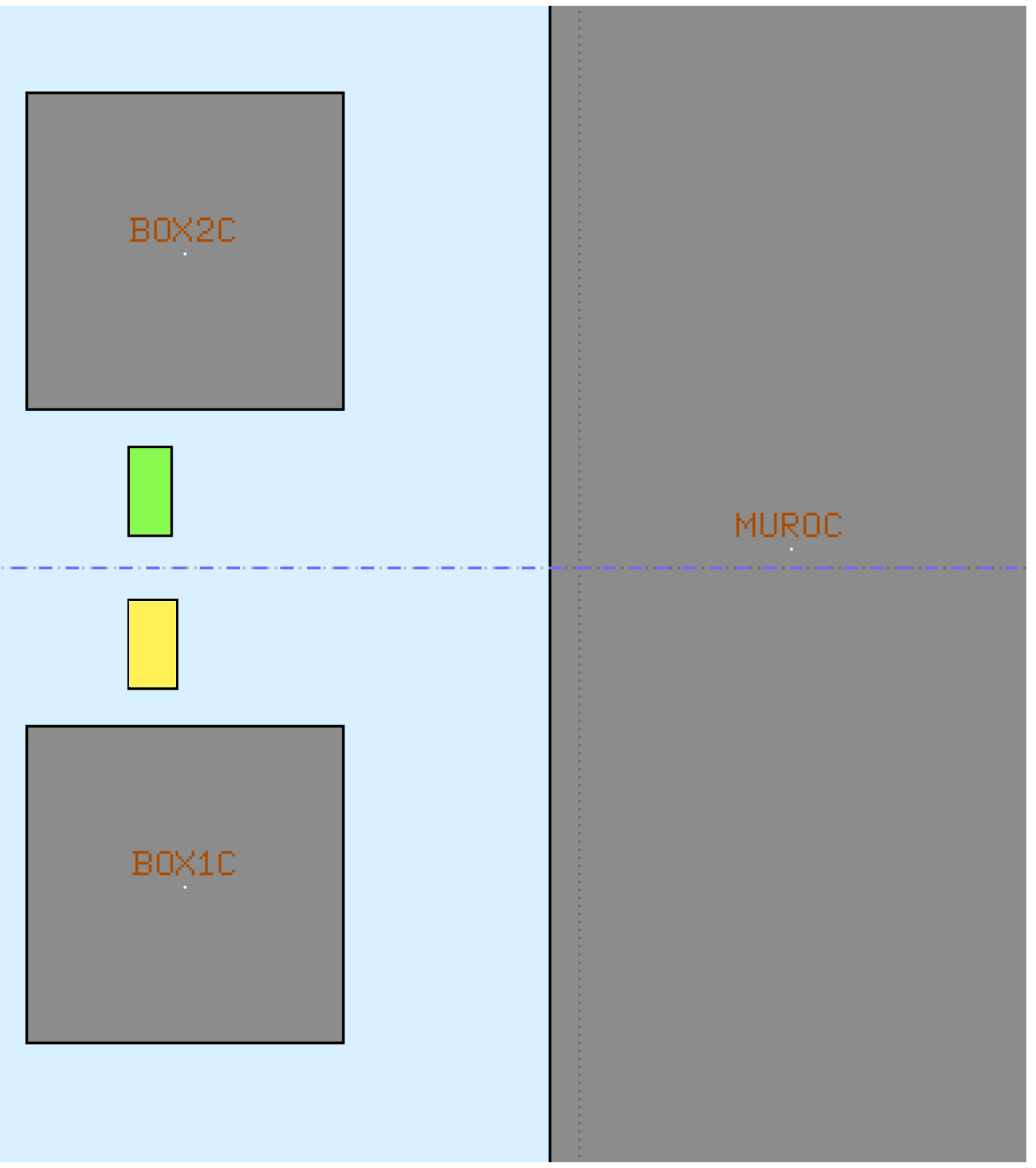
Beam delivery studies

- Concerning **radio-protection** studies, I was asked to assess the adequacy of a set of ambient survey meters used to measure **stray radiation** inside the bunker where the ElectronFlash was installed in **University of Antwerp, Belgium**.
- It is one of the few facilities in the world where FLASH pre-clinical studies are performed with dedicated machines.
- In this case, no optimization required. Instead, a careful modeling of the **geometry** of the bunker / **scoring** of the particle fluences.



- The beam hits a target of RW3. Secondary radiation is stopped by a lead block. The walls are concrete and show no significant leakage.
- At FLASH intensities, the simulation was found in reasonable agreement with the experimental results.

Survey meter	Exp.	MC
Babyline	18.3 ± 0.3 μSv/Gy	16.8 ± 0.2 μSv/Gy
STEP OD-02	12.2 ± 0.3 μSv/Gy	13.1 ± 0.2 μSv/Gy



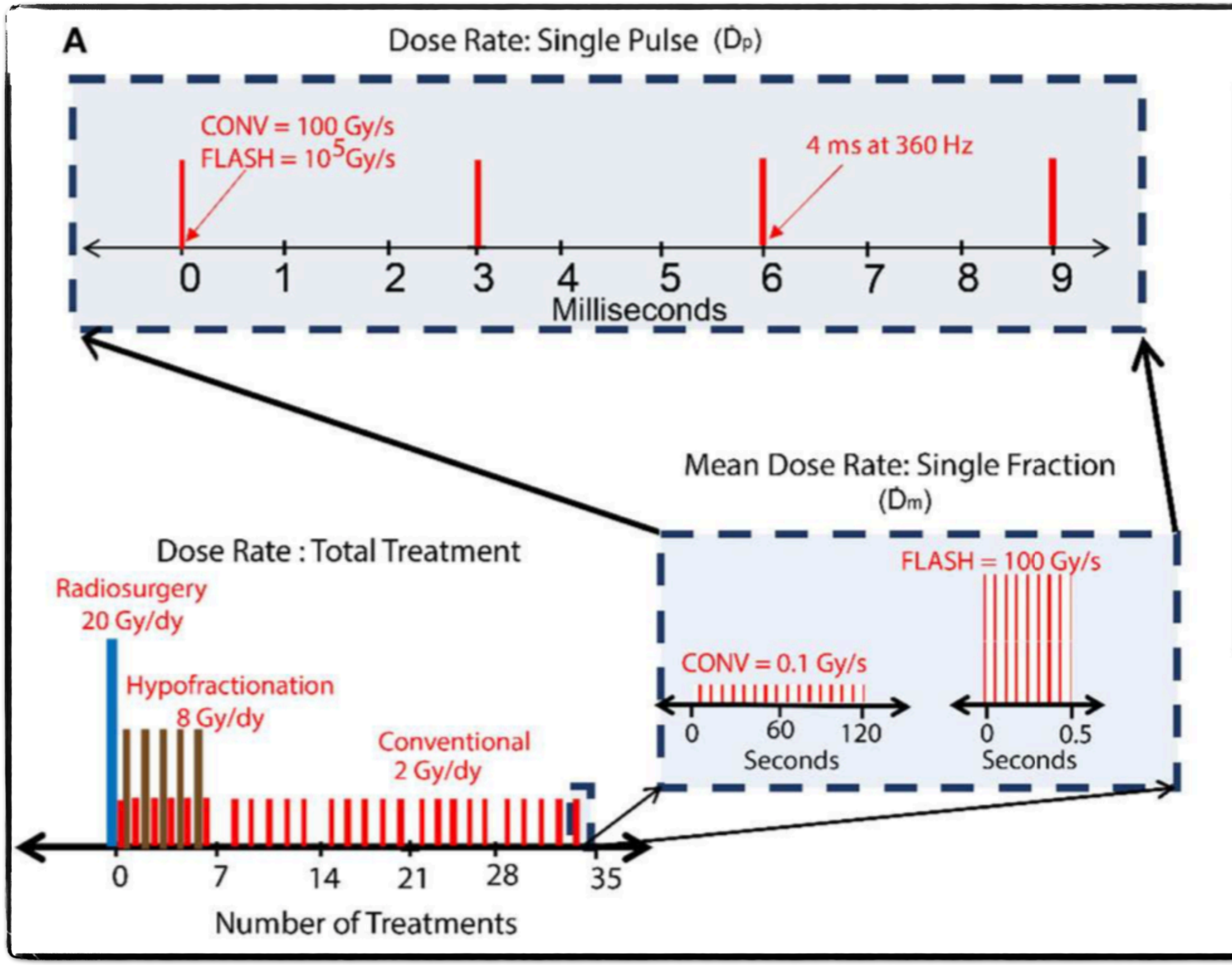
FRPT 2022
FLASH RADIOTHERAPY & PARTICLE THERAPY
BARCELONA & ONLINE
30 NOVEMBER - 2 DECEMBER 2022

Radiation protection and other stories on the installation of ultra-high dose rate electron beam systems

A. Gasparini[1,2], A. Trigilio[3], F. Di Martino[4], S. Heinrich[5], G. Felici[6], G. Mariani[6], M. Pacitti[6], R. Pain[5], V. Vanreusel[1,7], V. Patera[3], D. Verellen[1,2]
[1]University of Antwerp, AReRO, Belgium; [2]Iridium Netwerk, Physics, Belgium; [3]Sapienza University of Rome, Italy; [4]CPRF, Italy; [5]Institut Curie, France; [6]S.I.T., R&D, Italy; [7]SCK CEN, RDA, Belgium

Backup

Ashraf MR, Rahman M, Zhang R, Williams BB, Gladstone DJ, Pogue BW and Bruza P (2020) Dosimetry for FLASH Radiotherapy: A Review of Tools and the Role of Radioluminescence and Cherenkov Emission. Front. Phys. 8:328. doi: 10.3389/fphy.2020.00328



B

Beam Characteristics	CONV	FLASH
Dose Per Pulse D_p	~0.4 mGy	~1 Gy
Dose Rate: Single Pulse $\dot{D}_p$	~100 Gy/s	~10^5 Gy/s
Mean Dose Rate: Single Fraction $\dot{D}_m$	~0.1 Gy/s	~ 100 Gy/s
Total Treatment Time T	~days/minutes	< 500 ms

Backup

Response	Detectors	Measurement type	FLASH study	Instantaneous dose-rate/dose per pulse (D_p) dependence	Spatial resolution	Time-resolution	Energy dependence
Luminescence	TLD/OSLD	**1D,** 2D	e [15, 37, 71]	Independent (~10^9 Gy/s) [80, 137]	~ 1 mm	Passive	Tissue-equivalent
	Scintillators	1D, **2D**, 3D	p [13, 18]	Independent (~10^6 Gy/s) [29]	~ 1 mm	~ns	Tissue-equivalent
	Cherenkov	**1D**, 2D, 3D	e [29]	Independent (~10^6 Gy/s) [29]	~ 1 mm	~ps	Energy dependent
	FNTD	2D	NA	Independent (~10^8 Gy/s) [85]	~ 1 μm	Passive	Energy dependent
Charge	Ionization chambers	**1D**, **2D**	p [13, 18, 19] e [15, 37, 71] ph [16, 17]	Dependent on D_p [48, 52] (> 1 Gy/pulse),	~3–5 mm	~ms	Energy dependence shows up > 2 MeV
	Diamonds	**1D**	p [18]	Dependent on D_p (> 1 mGy/pulse) [49]	~ 1 mm	~μs	Tissue-equivalent
	Si diode	**1D**, 2D	NA	Dependent on D_p [54] (Independent ~0.2 Gy/s) [138]	~ 1 mm	~ms	Energy dependent
Chemical	Alanine pellets	**1D**	e [12, 15, 37, 139]	Independent (10^8 Gy/s) [69]	~ 5 mm	Passive	Tissue-equivalent
	Methyl viologen/fricke	**1D**	e [29, 48]	Depends on the decay rate and diffusion of radiation induced species	~ 2 mm	~ns	Tissue-equivalent
	Radiochromic film	**2D**	p [18, 19] e [10–12, 15, 30, 37, 71, 140] ph [16]	Independent (10^9 Gy/s) [70, 71]	~1 μm	Passive	Tissue-equivalent
	Gel dosimeters	3D	NA	Strong dependence below 0.001 Gy/s [141] and above 0.10 Gy/s [142]	~1 mm	Passive	Tissue-equivalent

Devices using FLASH irradiation modalities

Devices	Dose rate [Gy/s]	Pulse width [µs]	Energy [MeV]	Particle
Oriatron e6, CHUV (Losanne)	10^{-2} - 10^{7}	0.05 - 2.7	4.9 - 6	Electrons
Modified Elekta SL75 (Oxford UK)	200	3.4	6	Electrons
Modified Elekta Precise (Sweden)	220	1	8	Electrons
Varian Clinac 21EX, Cancer Institute (Stanford)	280	5	16	Electrons
ElectronFlash, Institut Curie (Orsay), Pisa University and Antwerp University	0.05 - 10^{6}	0.5 - 4	5 - 9	Electrons
Modified proton cyclotron (IBA), Institut Curie (Orsay)	40	/	230	Protons
Proton-Therapy Centers with PBS	Inst. up to 200 Mean dose rate ~0.05	/	TBD	Protons

SAFEST

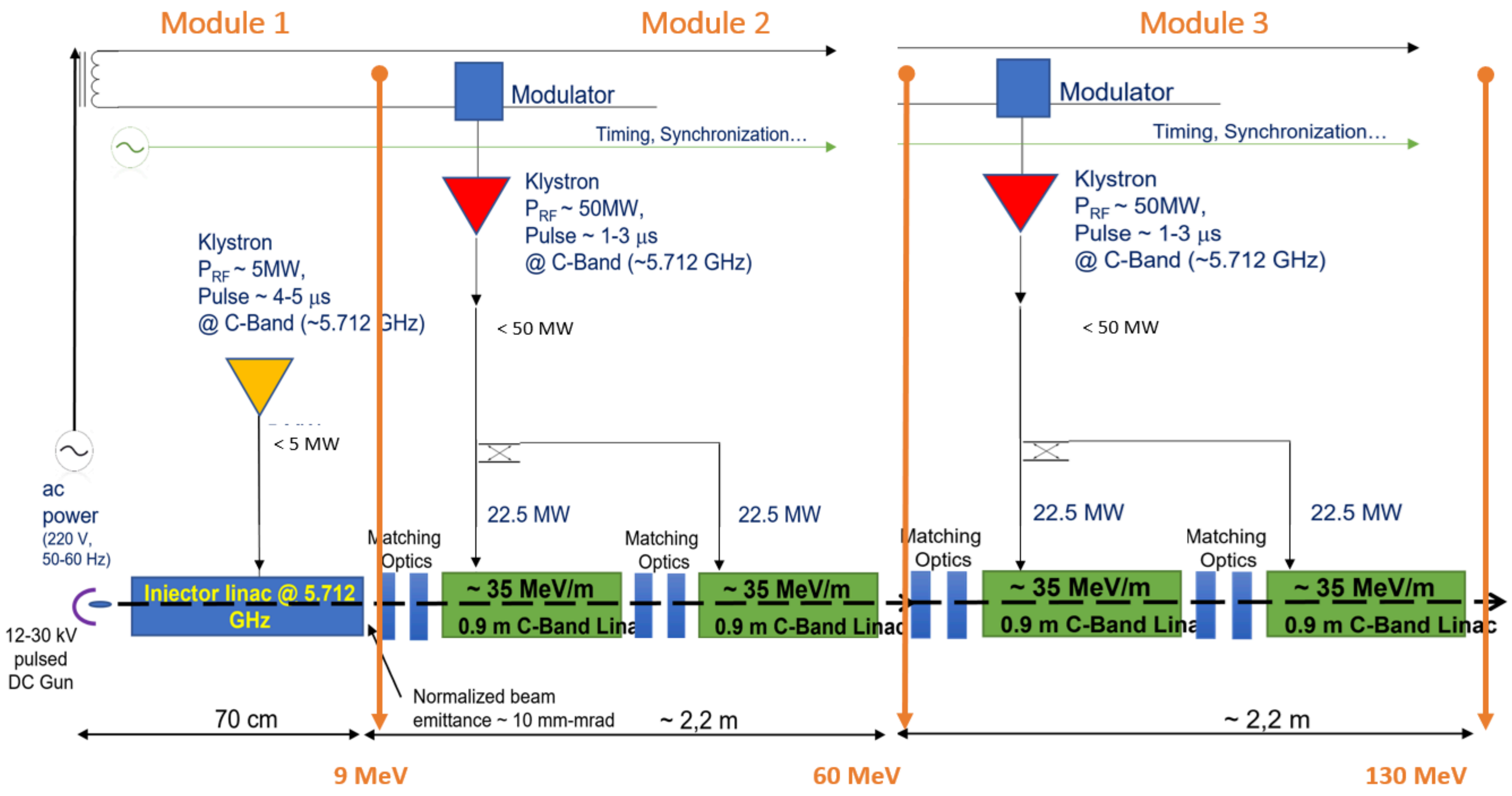
- **Proposal:** Research Facility based on an innovative VHEE LINAC operating in C-band (5.712 GHz), able to deliver the high current required by the FLASH irradiation regime, with a higher accelerating gradient which, compared with the existing traditional machines in the word, is more compact in terms of weight and size. The length of accelerating cells is approximately half of those of S-band (2.998 GHz).

- The electron source for the VHEE LINAC is a thermionic DC gun operated at a maximum voltage of 30 kV. The VHEE LINAC system comprises one standing wave (SW) injector and four traveling wave (TW) high-gradient accelerating structures. It is divided into 3 main modules:

- In Module 1 we can distinguish, on the left, the first accelerating SW injector capable of accelerating a current exiting from a pulsed DC gun up to 200 mA at an energy of 9-12 MeV.

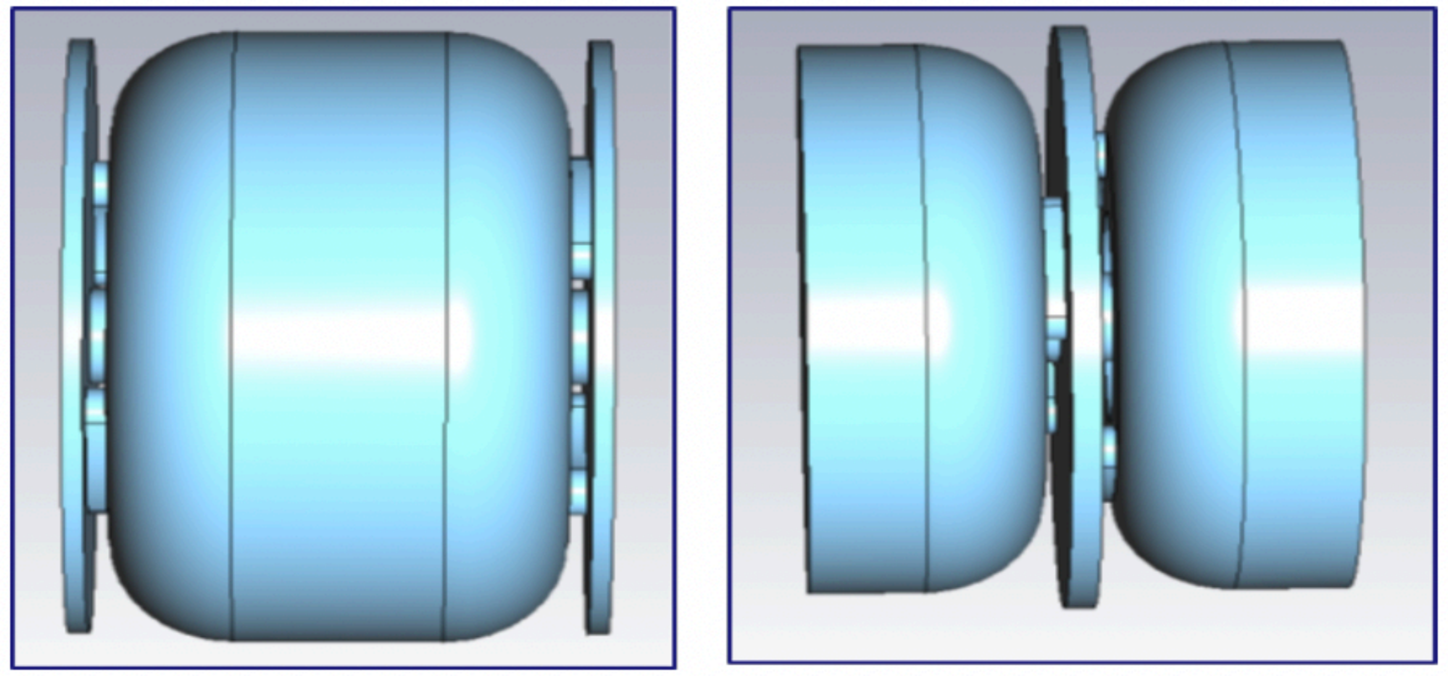
- In Module 2 the beam is matched by means of quadrupoles (matching optics) and injected into a compact linear TW accelerating structure characterized by a high accelerating gradient (up to about 40 MeV/m) able to bring the energy of the electron beam up to about 60 MeV.

- In Module 3 the beam energy is finally brought up to 130 MeV by means of a total of four 90 cm long accelerating structures, each one followed by quadrupoles for matching conditions. Solenoids around the accelerating structures guarantee the necessary focusing to the beam.



SAFEST

- **Module 1:** In the gun, electrons are generated by producing a potential difference between the thermionic emitter (cathode) and a plate (anode) with an hole to permit the electron beam to exit.
- For this project we used a commercial Electron Gun triode, in which the emission of the electrons from the cathode are tuned by utilizing a grid between the cathode and anode. The optimal distance between cathode and the LINAC entry plate is 0.5 cm for a maximum beam capture larger than 40%.



celerating cell with two half coupling cells (b) and coupling cell with two half accelerating cells.

- The injector is a standing-wave (SW), biperiodic, magnetic coupling structure. The accelerating mode is the π/2 mode, it has an electric null field in the coupling cavities and alternating field in the accelerating cells.
- For the magnetic coupling, holes off axis are used to connect the accelerating cells with the coupling ones. The first and last cell has only one pair of slots, while other cells have two pairs of slots on both ends.

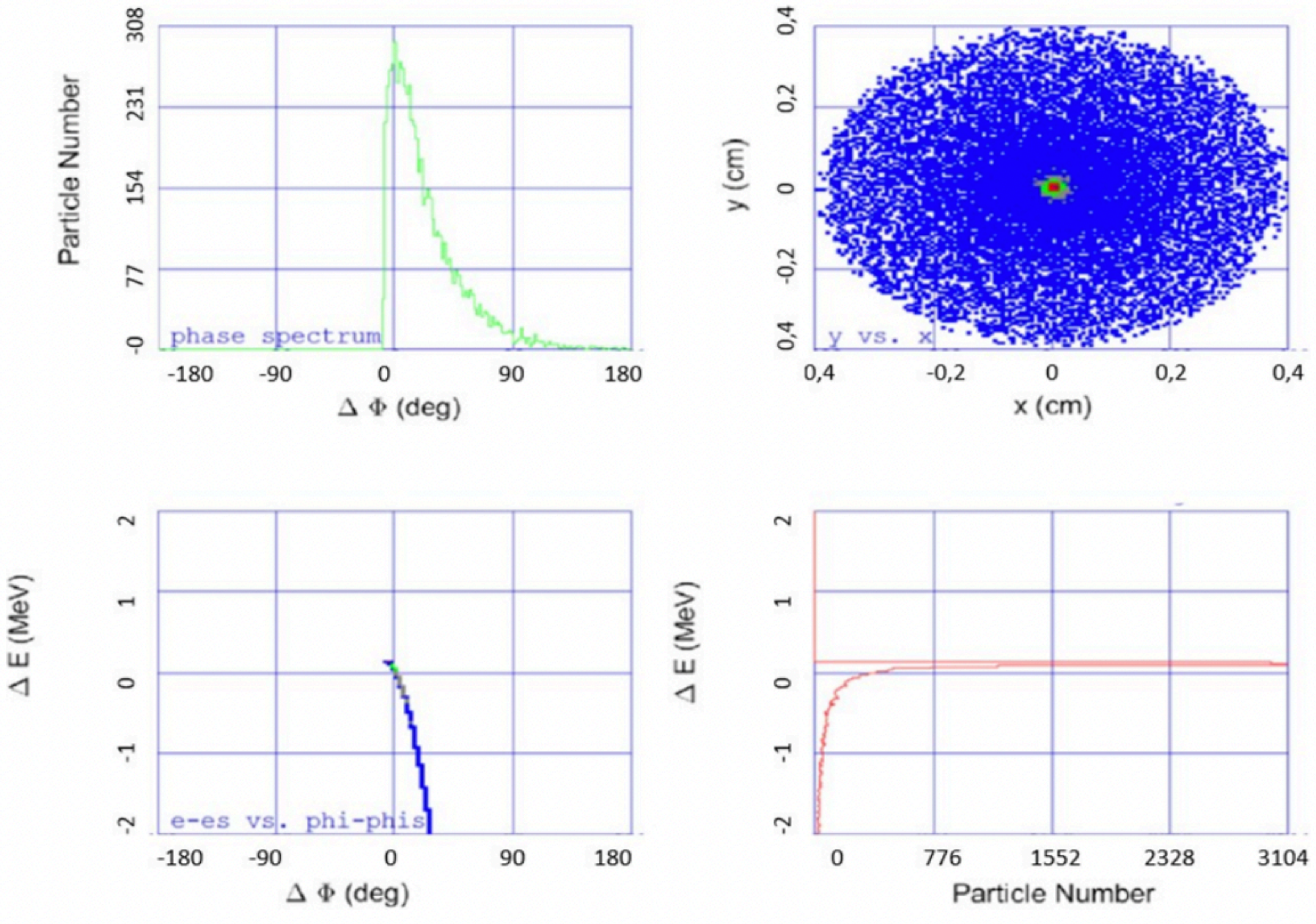


Figure 5.5: TSTEP output electron beam parameters at the exit of the Module 1.

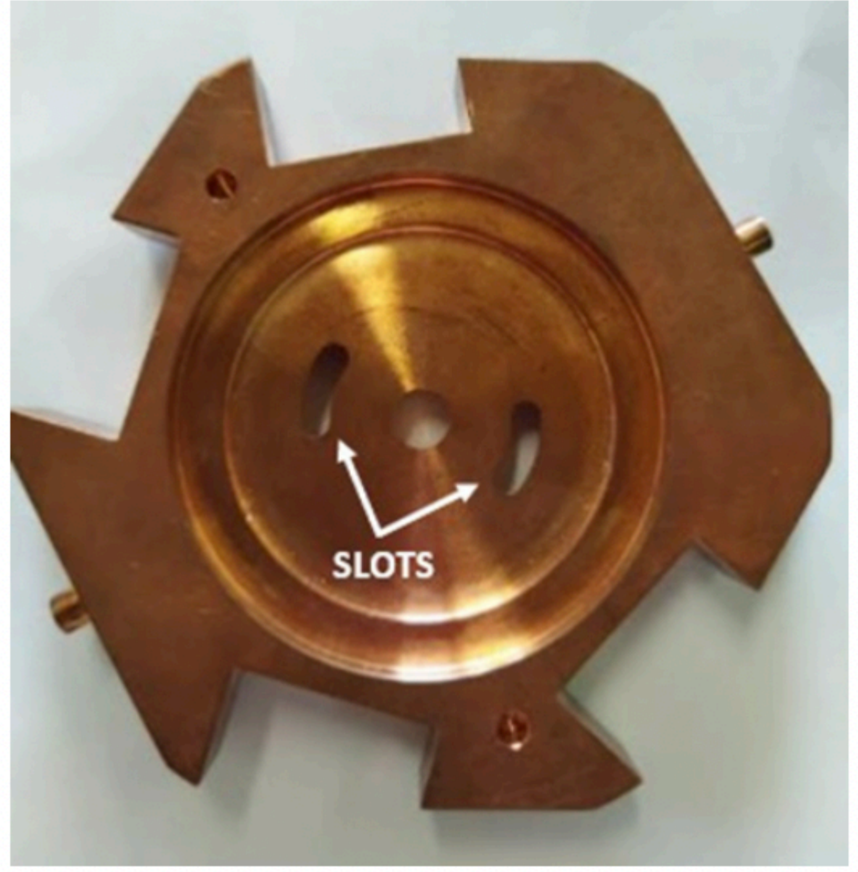
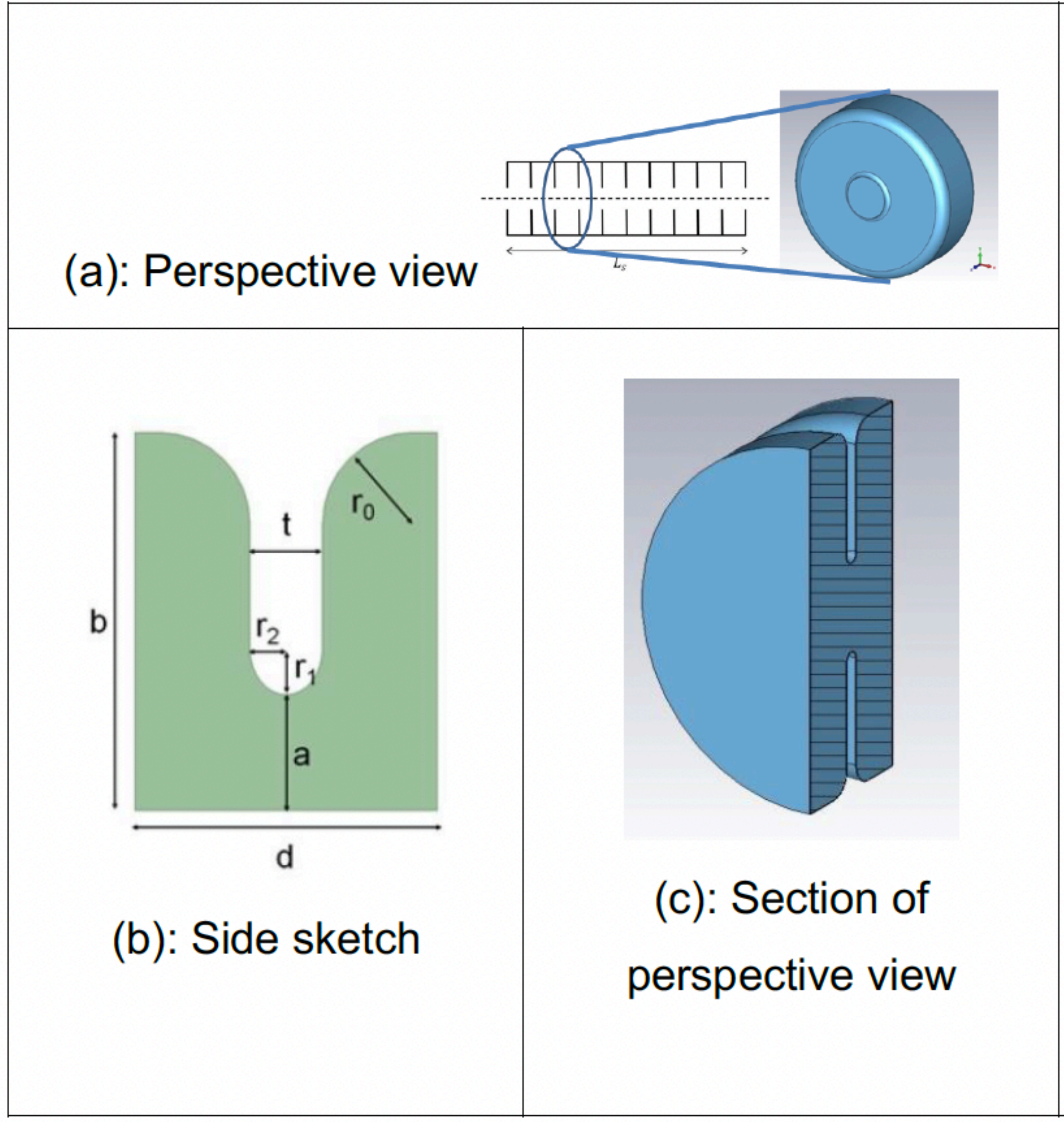


Figure 5.3: Off axis slots for the magnetic coupling.

SAFEST

- **Modules 2 and 3:** The C-band high gradient TW accelerating structures (Modules 2 and 3) operate in the TM_{01}-like mode with a phase advance per cell (ϕ") of $2\pi/3$ which guarantees the best efficiency for this type of accelerating cavities.
- A single RF structure increases the beam energy up to about 35 MeV in a space of about 90 cm, thus respecting the available space constraints.
- The electron beam transverse size exiting from the LINAC can be easily modified. For the case of operation with a fixed field, a magnet quadrupole duplet can be located after 50 cm from the LINAC exit.
- The beam size is enlarged by one order of magnitude, from 4 mm to 4 cm, by utilizing a normal conducting magnet quadrupole with 47 T/m gradients. In alternative to quadrupoles, it is also possible to use scattering materials.

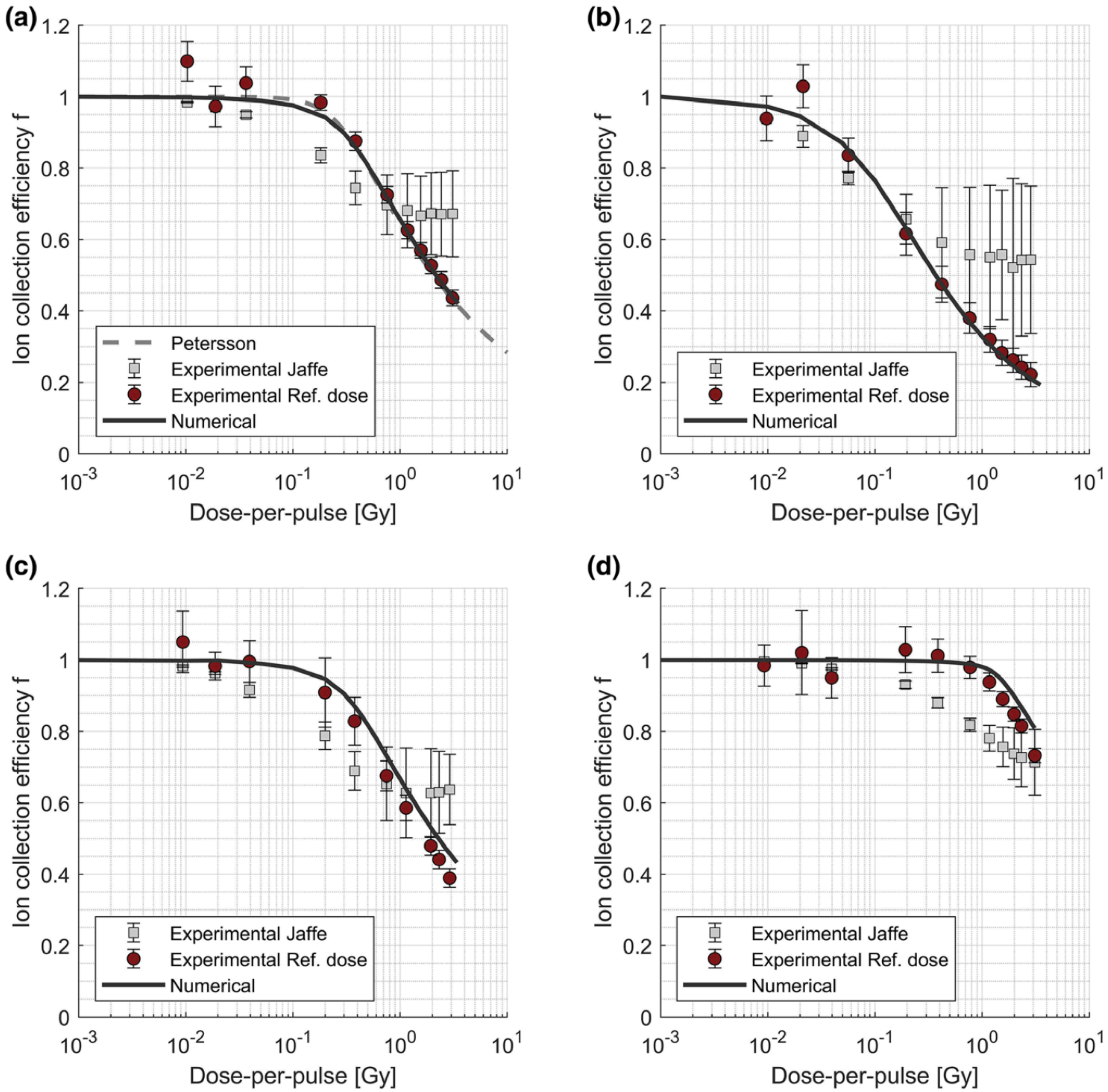


Cell geometric parameter

- a: iris radius ($a \in [3,7]mm$)
- t: iris thickness (2 mm)
- r_1: iris rounding radius (1 mm)
- r_0: edge rounding radius (2.5 mm)
- d: cell length (function of ϕ_0, $d = \frac{c}{\omega}\phi_0 = 17.5\,mm$)
- b: outer radius (function of a and frequency f)
- ϕ_0: phase advance per cell ($\frac{2}{3}\pi$)

Figure 5.6: TW cell and its geometric parameters. (a): Perspective view; (b): Side sketch with main dimensions; (c): Section of perspective view.

Beam Monitoring vs FLASH effect



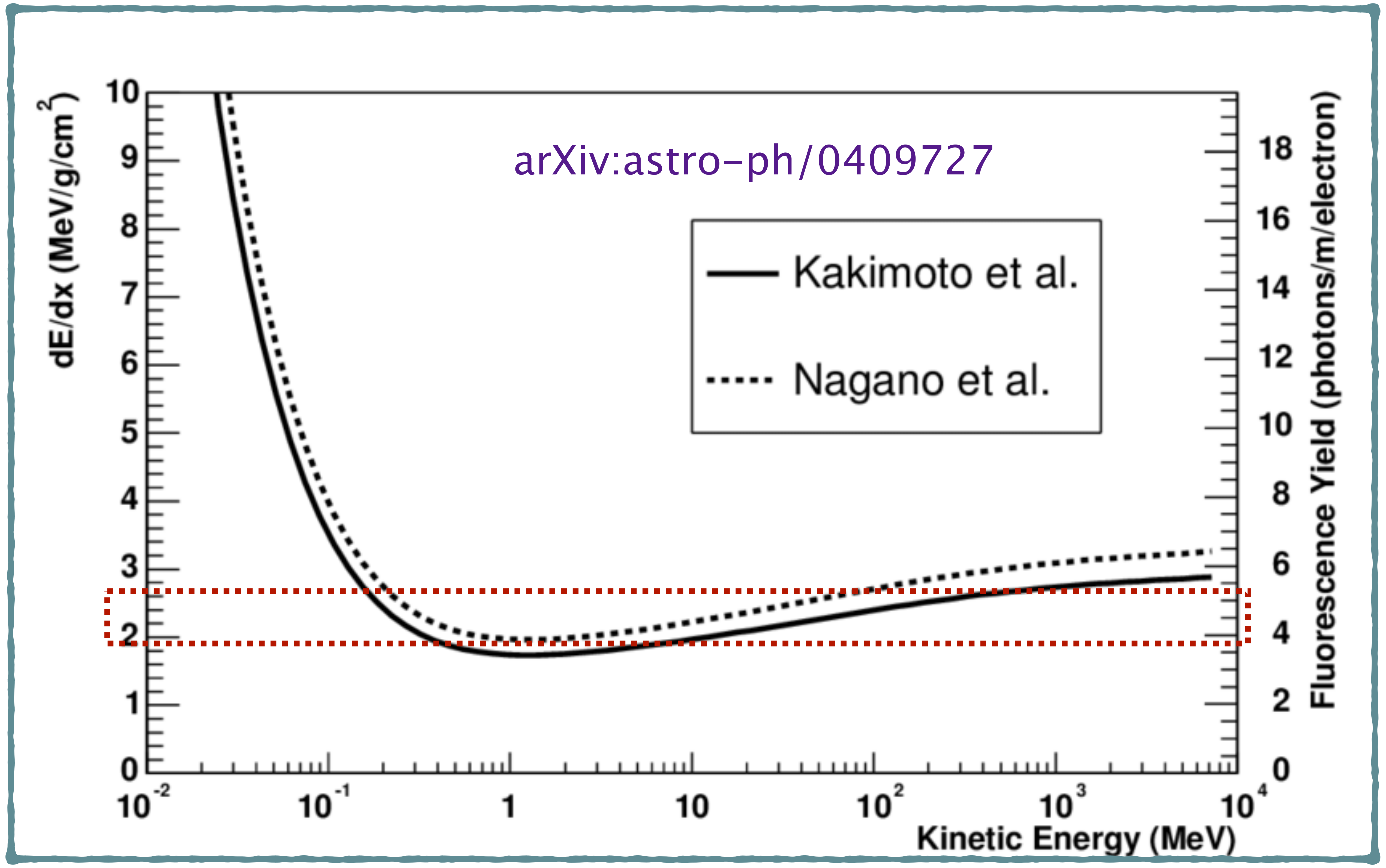
Ion collection efficiency for the ionization chambers with a polarizing voltage of 300 V.
(a) Advanced Markus, **(b)** EWC2, **(c)** EWC1, **(d)** EWC05. doi: 10.1002/mp.14620

FLASH beam monitoring

Backup

- How many photons we expect at typical IOeRT and VHEE energies?

E_K	ph./m (Fluor.)	ph./m (Ch.)
10 MeV	4 (@4π)	Under thr.
20 MeV	4 (@4π)	6 (@0.1°)
130 MeV	5 (@4π)	70 (@1.4°)



Backup

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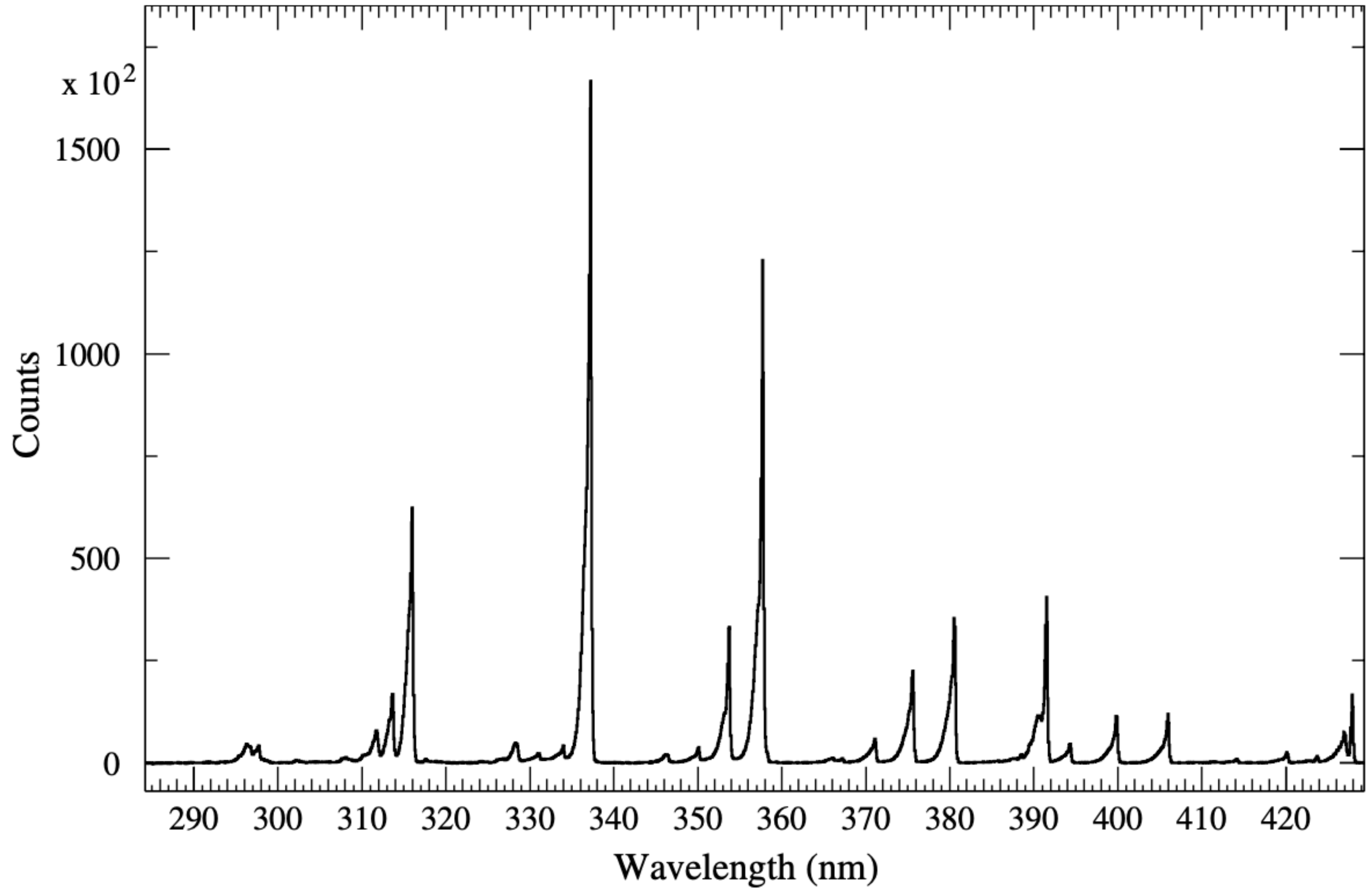
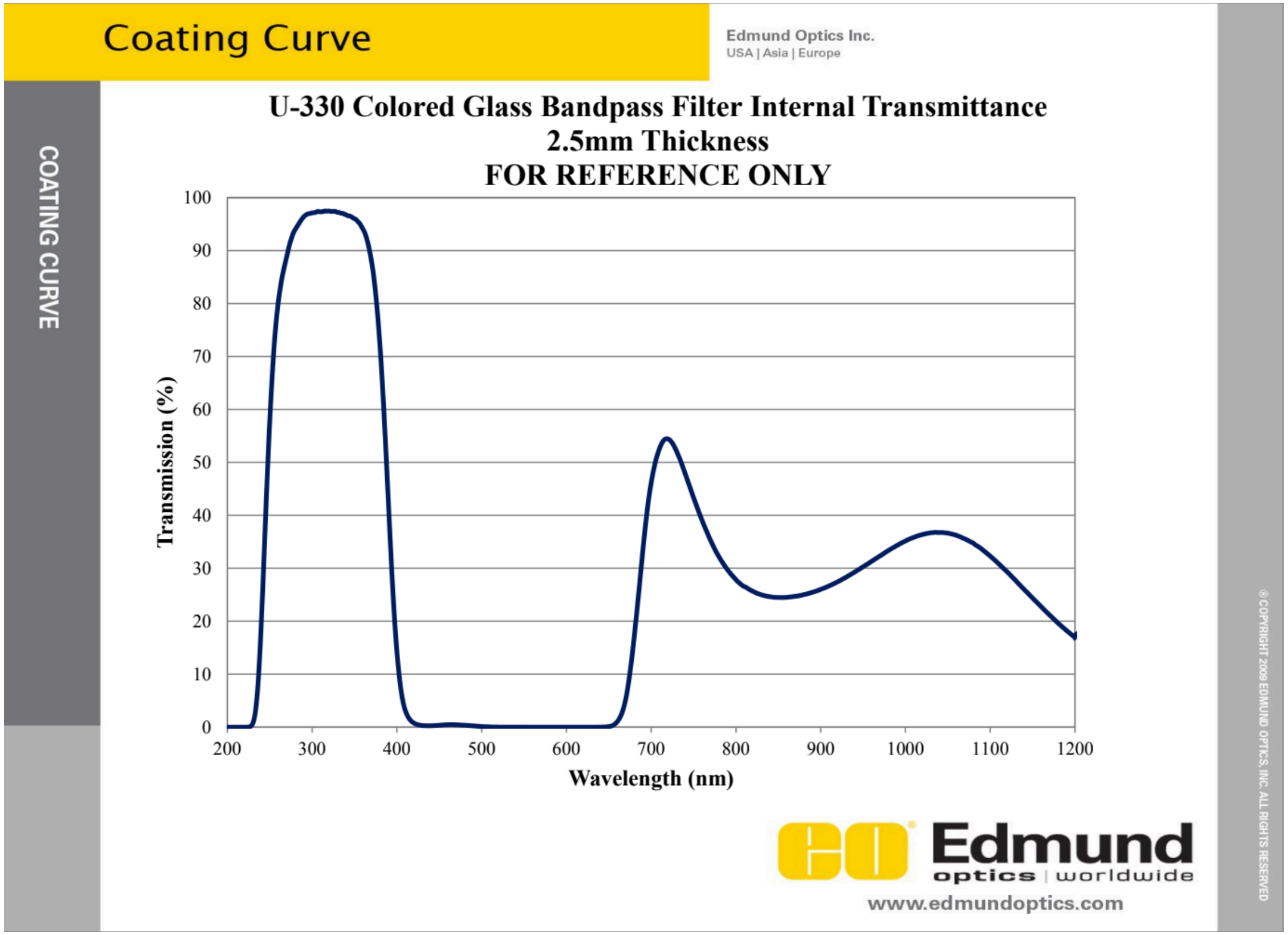
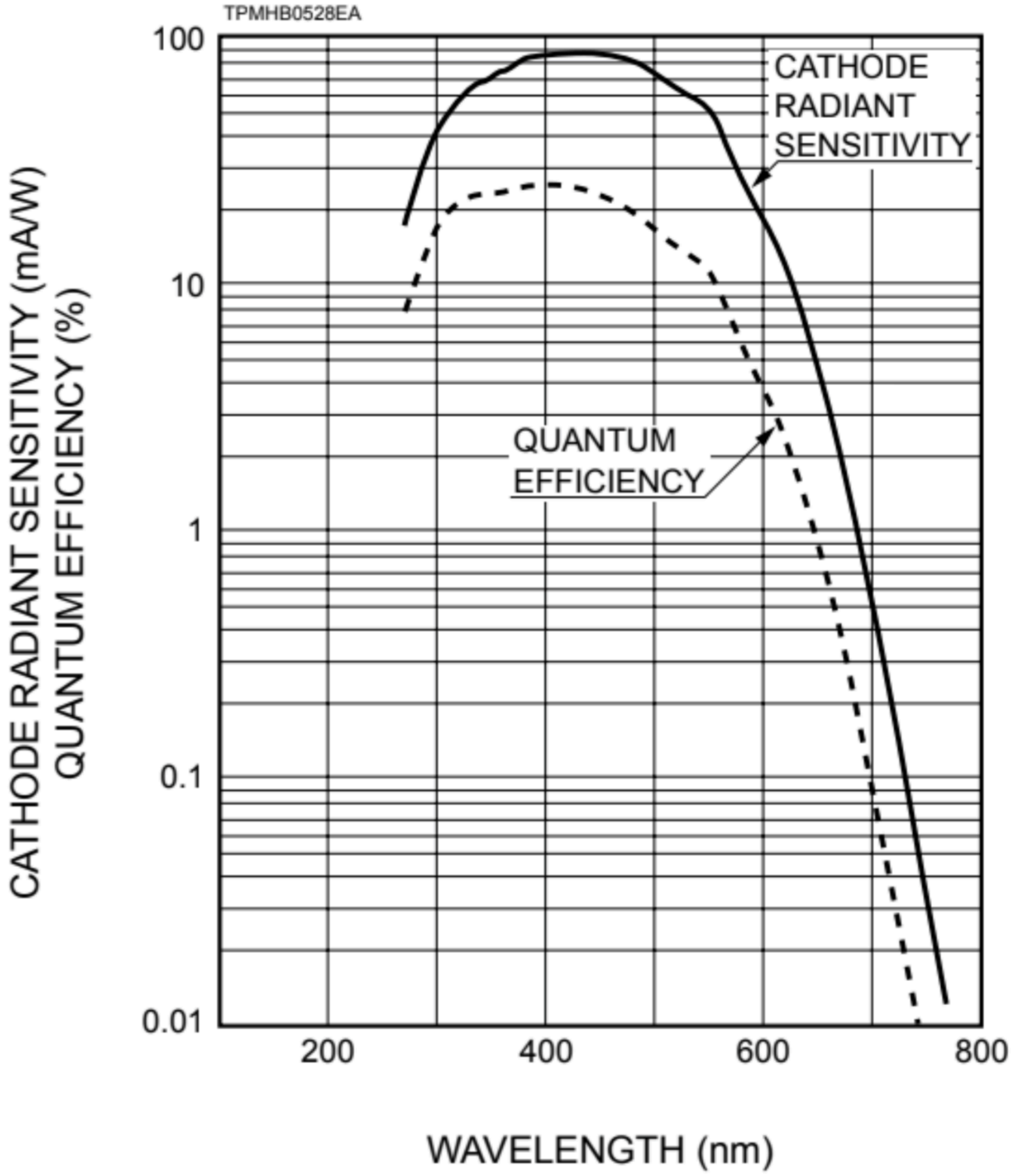


Fig. 4. Measured fluorescence spectrum in dry air at 800 hPa and 293 K.

Backup



Coating Curve
Edmund Optics Inc.
USA | Asia | Europe
COATING CURVE
U-330 Colored Glass Bandpass Filter Internal Transmittance
2.5mm Thickness
FOR REFERENCE ONLY
Transmission (%)
Wavelength (nm)
Edmund
optics | worldwide
www.edmundoptics.com



TPMHB0528EA
CATHODE RADIANT SENSITIVITY
QUANTUM EFFICIENCY
CATHODE RADIANT SENSITIVITY (mA/W)
QUANTUM EFFICIENCY (%)
WAVELENGTH (nm)

Backup

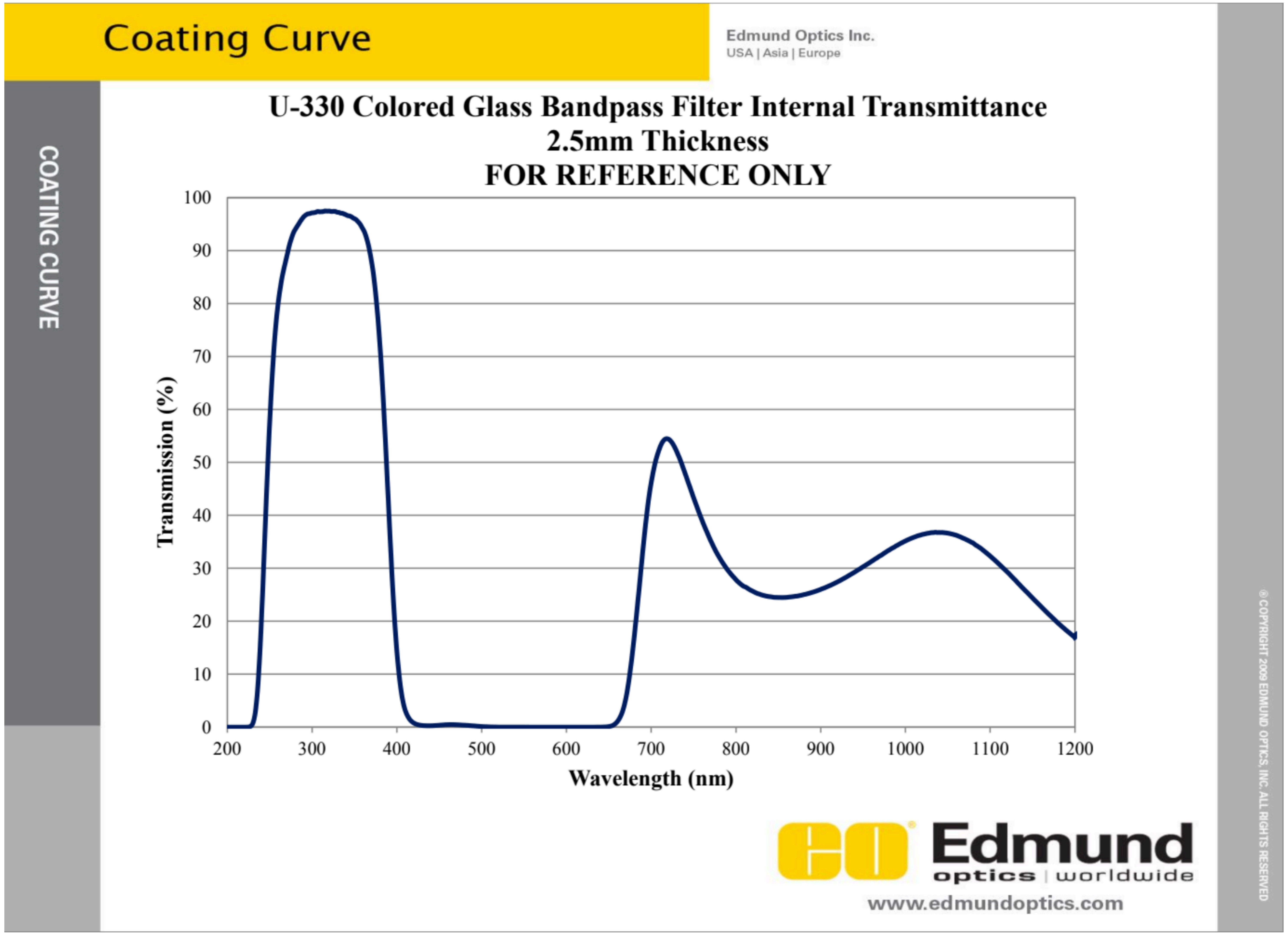
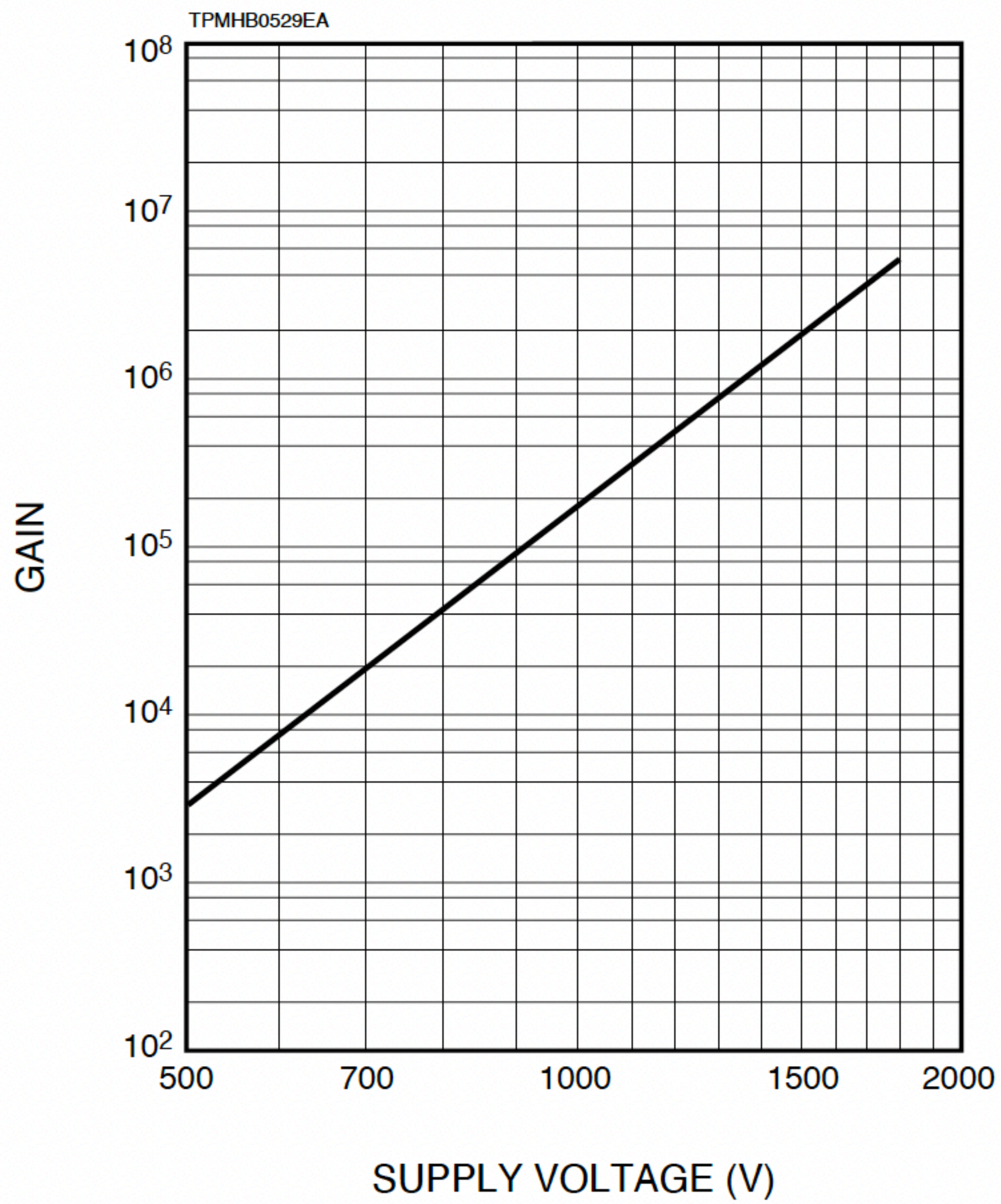
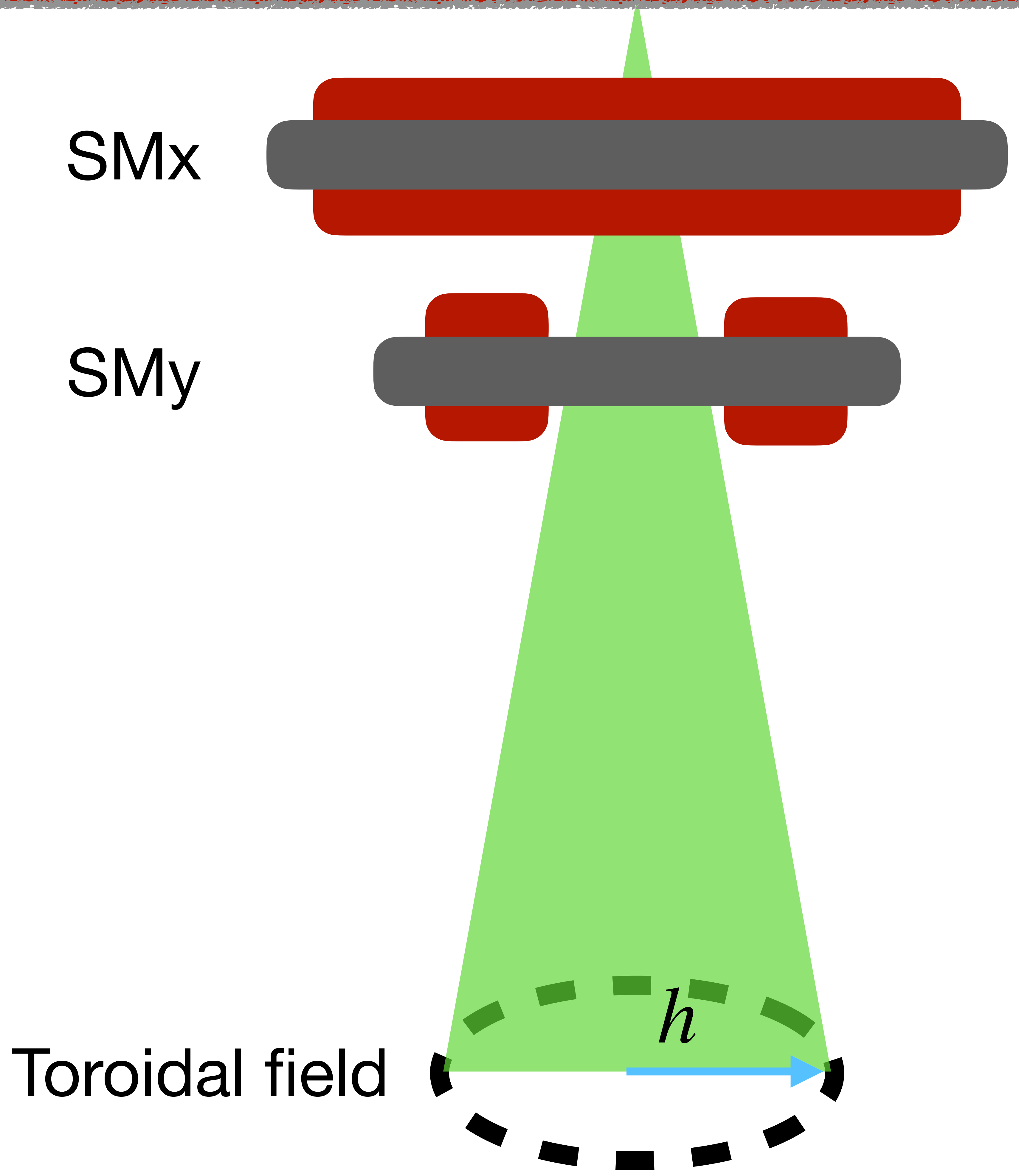


Figure 2: Typical Gain Characteristics



Magnetic scanning system

Analytic calculations



- For the scanning dipoles, I computed the magnet current and geometric features based on data similar to what already in use at CNAO.
- Based on the existing cross-section of the coils, the power converter would need to operate at about <u>**12%**</u> its maximum value.
- The existing dipoles are <u>**oversized**</u>: an active scanning of the beam at UHDR is achievable.

Electron Energy	100 MeV
Mag. Rigidity	0.33 Tm
Dipole Peak field	0.31 T
Field rate	6.6 T/s
Vector magnets length	0.55 m
Gap between poles	0.05 m
Distance source/toroid	1.5 m
Deflection angle	28.34°
Beam distance w/ toroid center (h)	0.81 m

Effective cross-section	79.5 mm^2
Length	123.04 m
Ampereturns NI per coil	17’603.5 A
Inductance	4.4 mH
Max. current ramp	121256 A/s
Current density	7.38 A/mm^2
Power	42.6 kW (maximum 335 kW)