



SAPIENZA  
UNIVERSITÀ DI ROMA



CENTRO RICERCHE  
ENRICO FERMI

## Bi-national conference on Detectors R&D LPNHE Paris



**EDR-DI2I**  
Groupement De Recherche  
DéTECTEURS et INSTRUMENTATION pour les 2 INFINIS

# Development and characterisation of an air-fluorescence-based beam monitor for ultra-high dose rates

Antonio Trigilio<sup>1</sup>, Bruno Buonomo<sup>1</sup>, Alberto Burattini<sup>2</sup>, Marina Carruezzo<sup>3</sup>, Domenico Di Giovenale<sup>1</sup>, Claudio Di Giulio<sup>1</sup>, Eleonora Diociaiuti<sup>1</sup>, Luca Foggetta<sup>1</sup>, Gaia Franciosini<sup>3,4</sup>, Laura Frassi<sup>3</sup>, Marco Garbini<sup>5</sup>, Marco Magi<sup>3</sup>, Vincenzo Patera<sup>3,4</sup>, Flaminia Quattrini<sup>4,2,6</sup>, Alessio Sarti<sup>3,4</sup>, Angelo Schiavi<sup>3,4</sup>, Clara Taruggi<sup>1</sup>, Luana Testa<sup>5,3</sup>, Marco Toppi<sup>3,4</sup>, Giacomo Traini<sup>4</sup>, Arianna Vannucci<sup>5,2</sup>, Michela Marafini<sup>5,4</sup>

<sup>1</sup> INFN, National Laboratories of Frascati

<sup>2</sup> Post-Graduate School in Medical Physics, Sapienza University of Rome

<sup>3</sup> Department of Basic and Applied Sciences for Engineering, Sapienza University of Rome

<sup>4</sup> INFN, Rome 1 Section

<sup>5</sup> "Enrico Fermi" Historical Museum of Physics and Study & Research Centre (CREF)

<sup>6</sup> Physics Department, Sapienza University of Rome



FLASH Radiotherapy with hIgh  
Dose-rate particle beAms



Antonio Trigilio

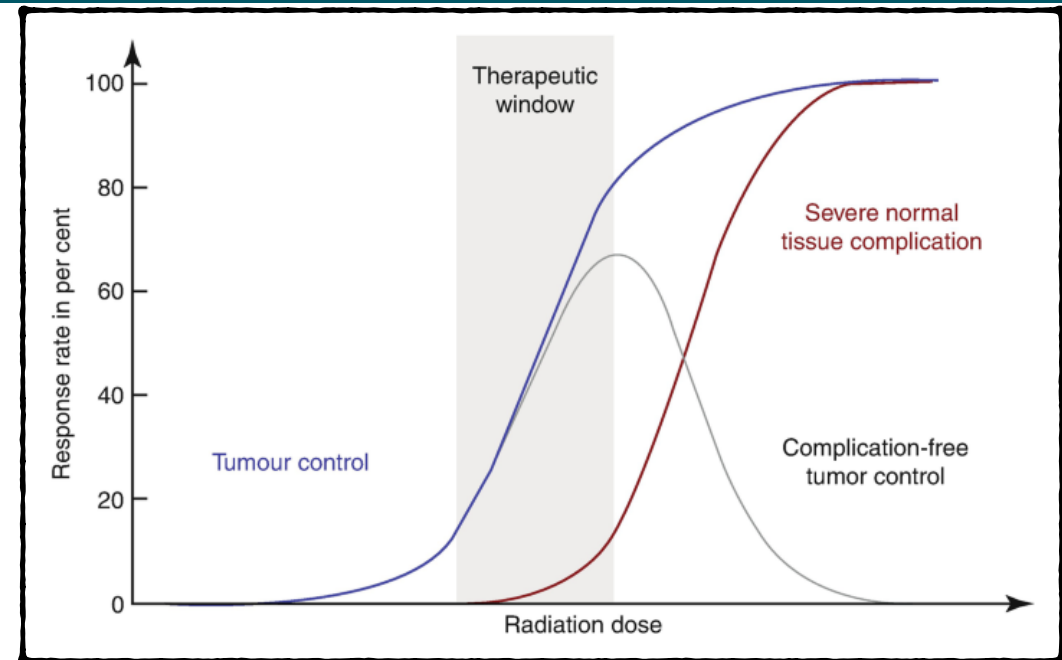
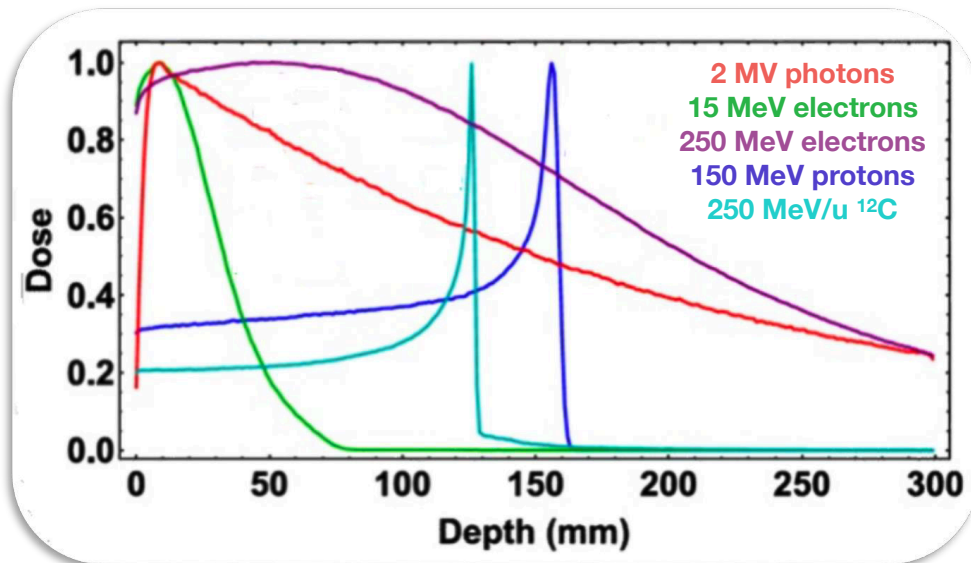
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# Radiotherapy challenge

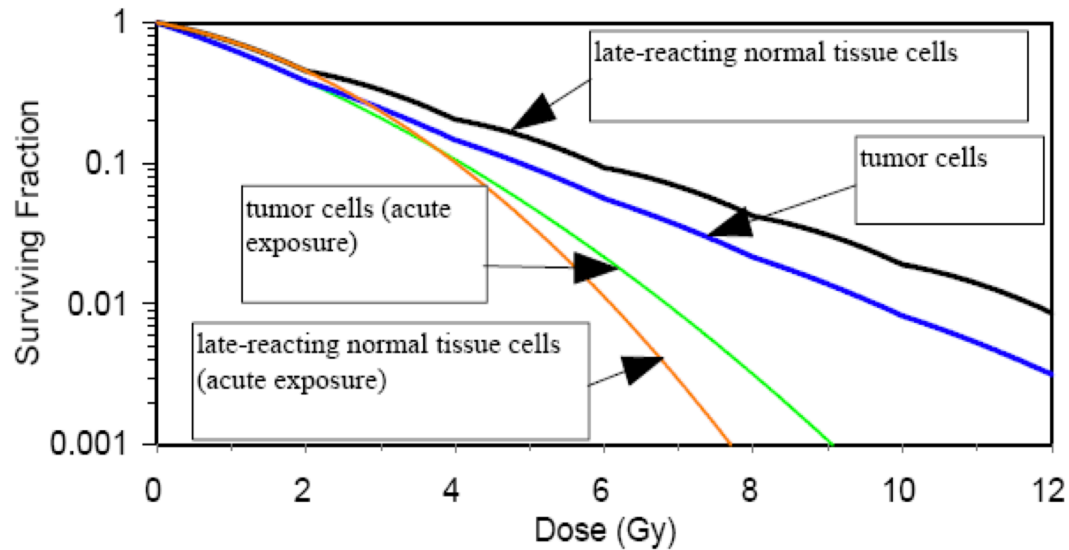
- **Therapeutical beam** release energy inside the human tissues — **dose** — following an optimized **treatment plan**.
- Wide number of untreatable pathologies due to an under-dosage to the tumor (**radio-resistance**) — need to **increase** the maximum dose deliverable.



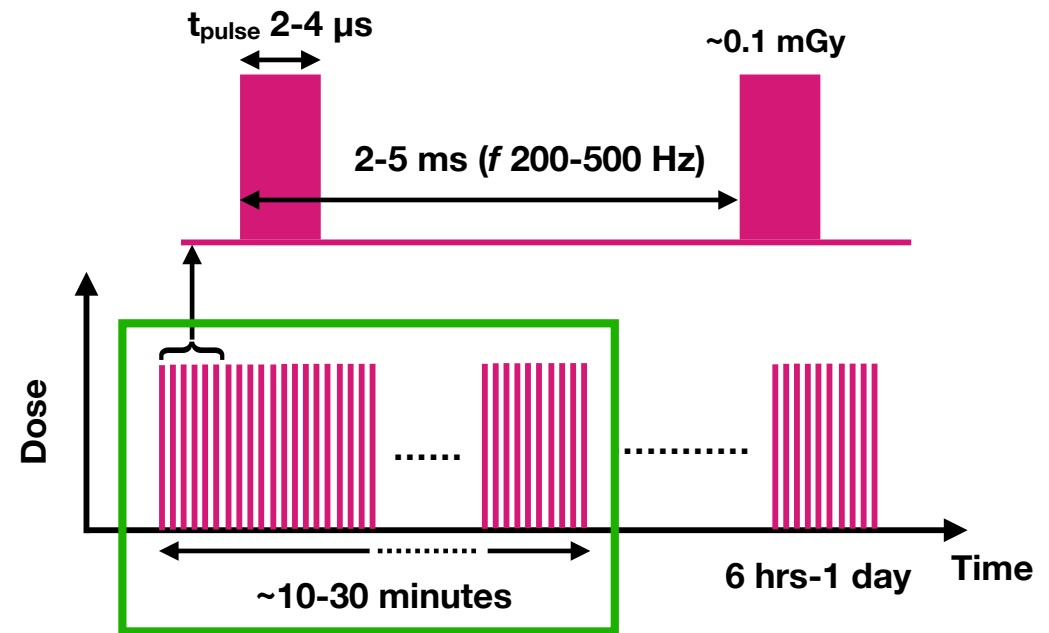
- **Conformality:** to give as much as possible dose to the tumor region, saving as much as possible the surrounding healthy tissues.
- **Limited** by protection against side effects to **organs at risk**.

# Beam characteristics in CONV-RT

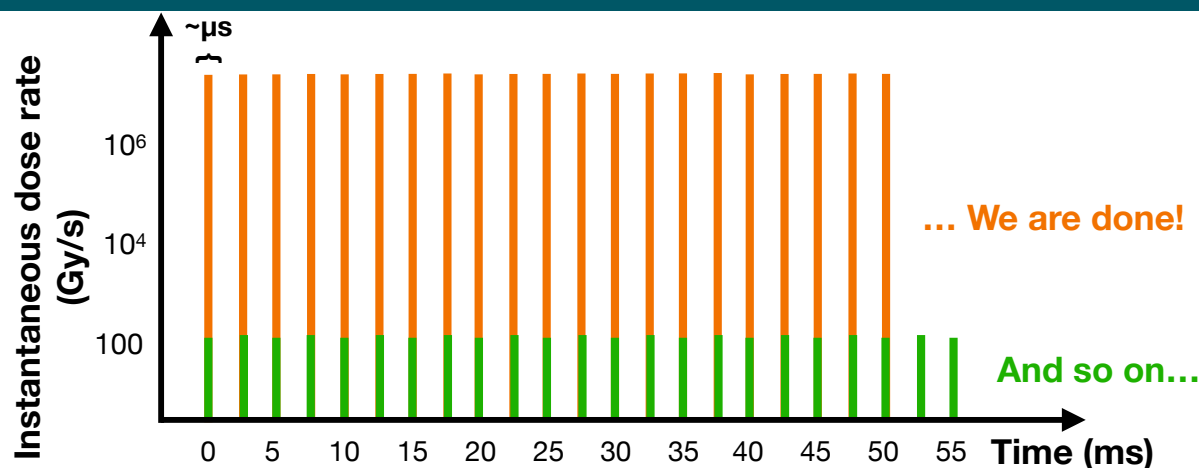
- Sublethal damages are repaired between fractions by **late-responding** tissues (normal). **Early-responding** tissues (tumors) are less efficient.
- Typical values: ~40 Gy delivered in ~20 fractions (2 Gy/fraction).



- **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

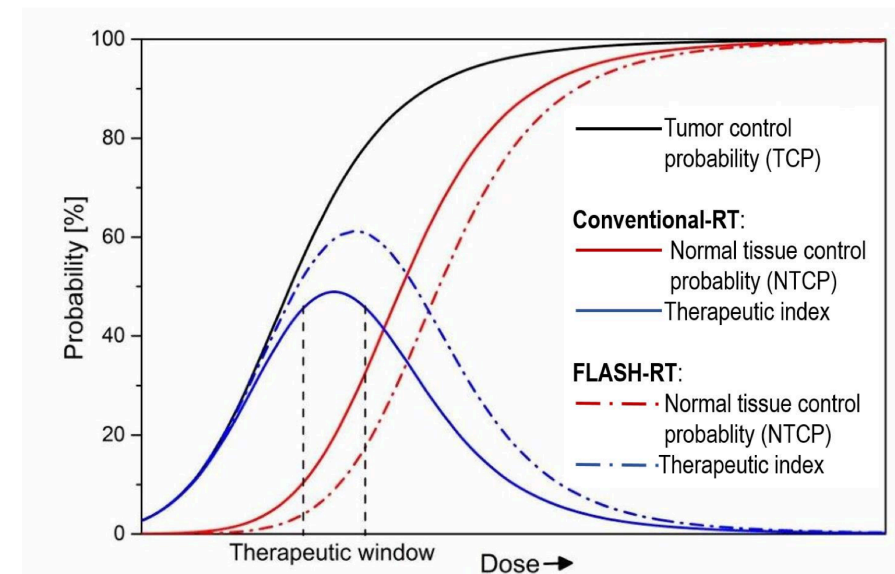


# Ultra high dose rate / FLASH effect



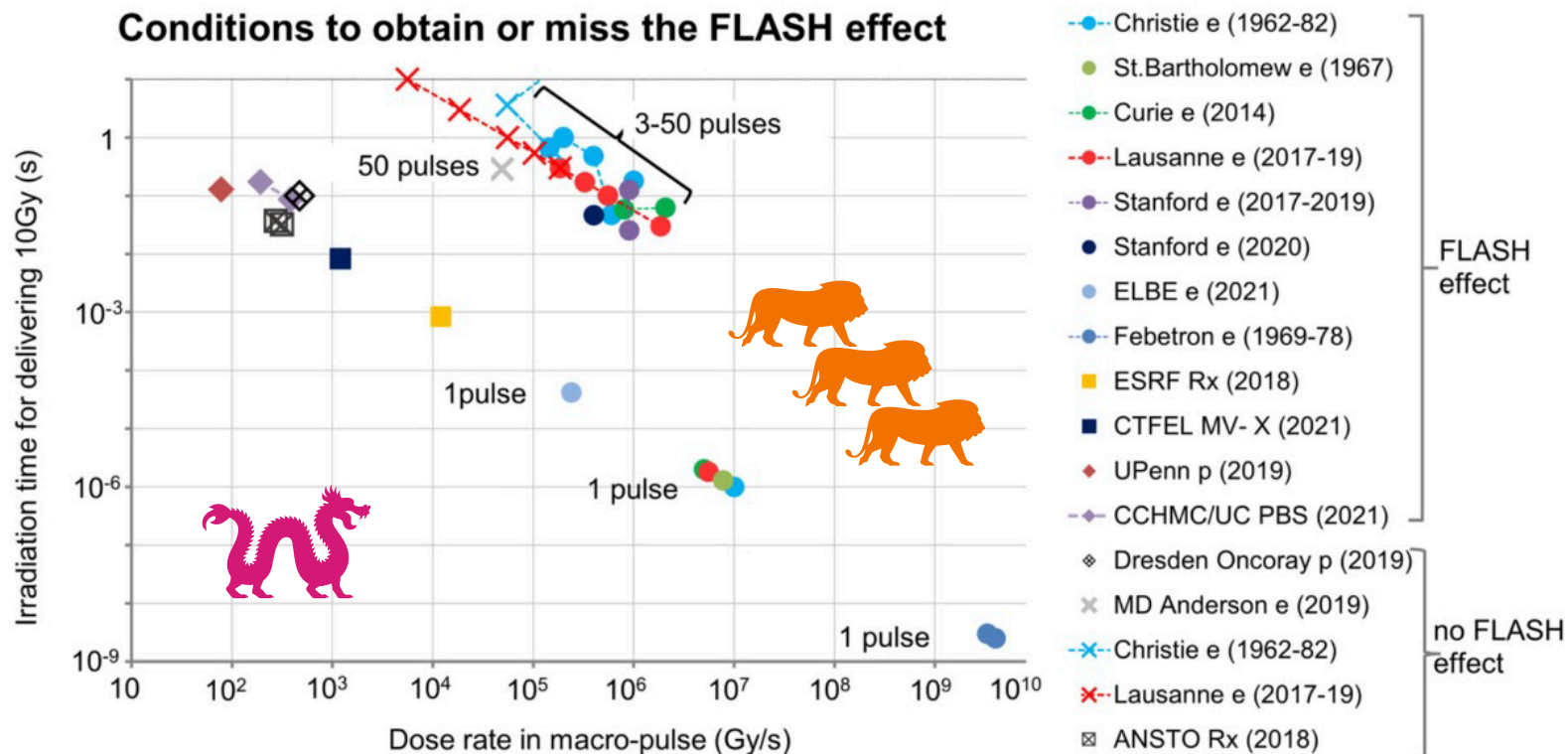
Beam characteristics	CONV	UHDR
Dose per pulse	~ 0.5 mGy	~1 Gy
Inst. dose rate (single pulse)	~ 100 Gy/s	> 10 <sup>6</sup> Gy/s
Mean dose rate (single fraction)	~ 0.1 Gy/s	> 100 Gy/s
Total fraction time	~ minutes	< 100 ms

- An increased radio-resistance — **reduced toxicity** — is measured **in normal tissues** (retaining anti-tumor efficacy) when delivering a single irradiation at **ULTRAHIGH** dose rates with **specific beam parameters**.
- This has been named **FLASH** effect. It has been observed **in vivo** with **electrons, photons, protons and carbon ions**.



# FLASH beam monitoring

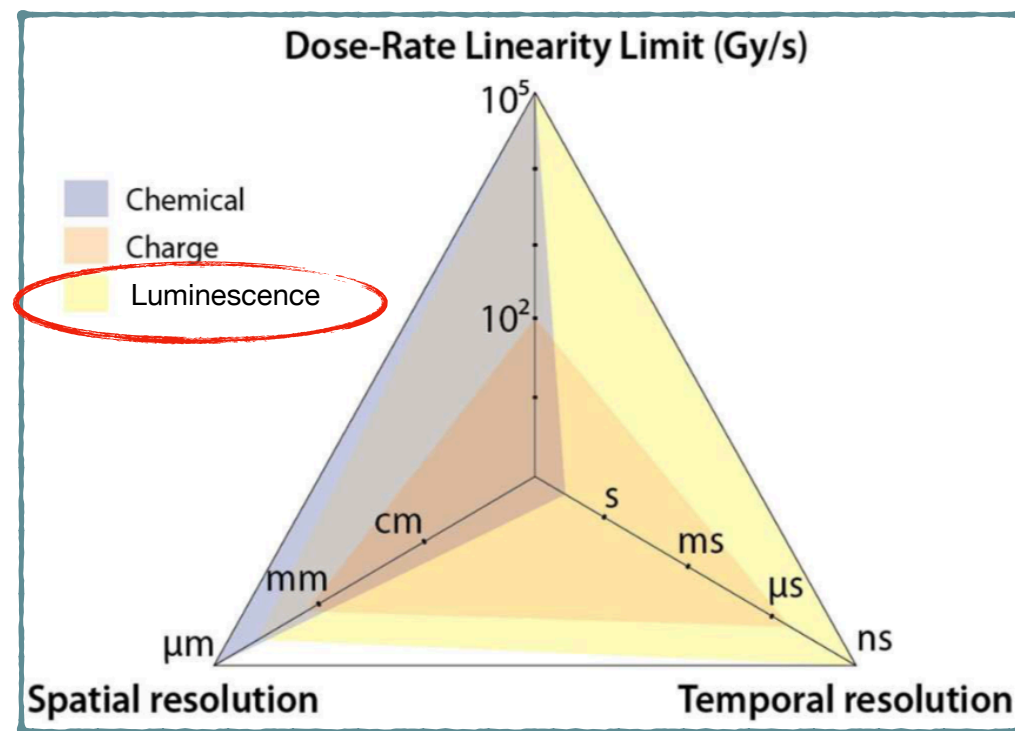
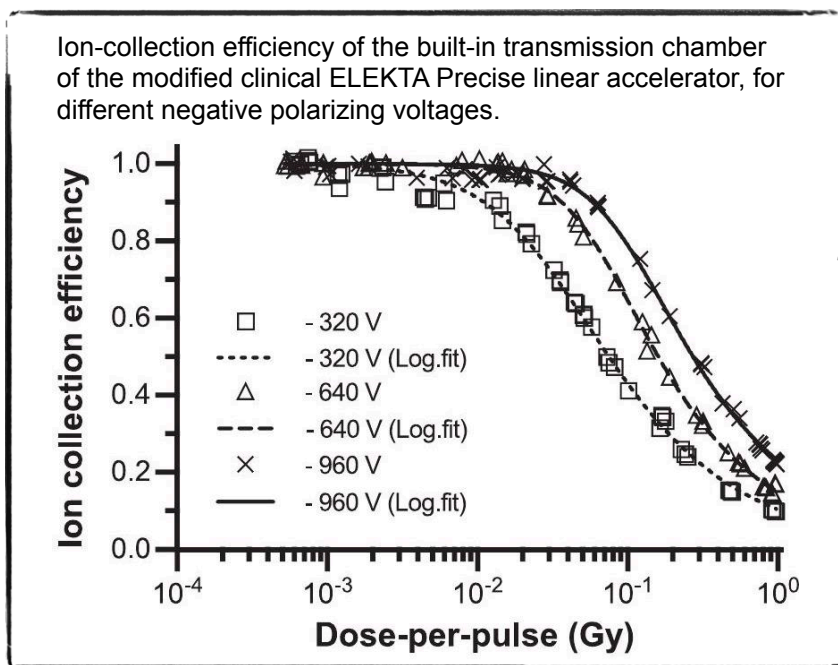
- A lot of parameters (mean dose rate, instantaneous dose rate, time structure of the beam, irradiation time, repetition frequency, pauses...).
- Beam monitoring devices which are able to **follow the temporal evolution** of the beam while maintaining an **adequate response to the dose per pulse** are eagerly needed.
  - **Dose rate linearity** (up to  $10^6$  Gy/s)
  - **Spatial resolution** ( $\sim$  mm)
  - **Temporal resolution** ( $< 1\mu\text{s}$ )
  - **Dose per pulse accuracy** (within 1%)



- New facilities are coming (SAFEST@Sapienza), and more experimental groups are entering the FLASH arena, particularly in the VHEE field (PITZ@DESY, SINBAD@DESY, BTF@LNF, ELBE@DRESDEN, CLARA@Daresbury...)

# FLASH beam monitoring

- Detectors commonly used in clinics (standard ionization chambers) undergo substantial energy dependencies due to **volume recombination** at UHDR.
- Many solutions are spreading in the community\*. Can we have a device with as little as possible material obstructing the beam?



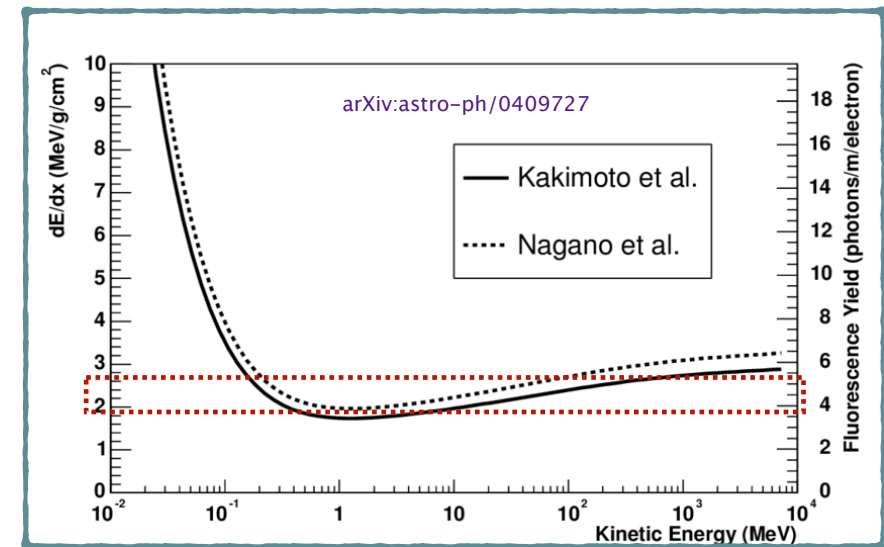
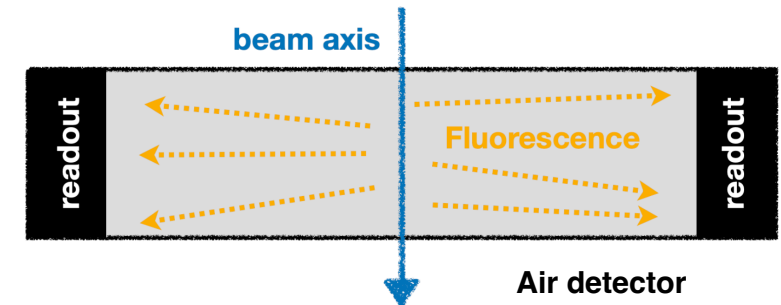
\* Ashraf MR et al, Dosimetry for FLASH Radiotherapy, doi: [10.3389/fphy.2020.00328](https://doi.org/10.3389/fphy.2020.00328)  
Romano F et al, Ultra-high dose rate dosimetry, doi: [10.1002/mp.15649](https://doi.org/10.1002/mp.15649)

# 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**.

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

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



# FLASH beam monitoring



REGIONE  
LAZIO

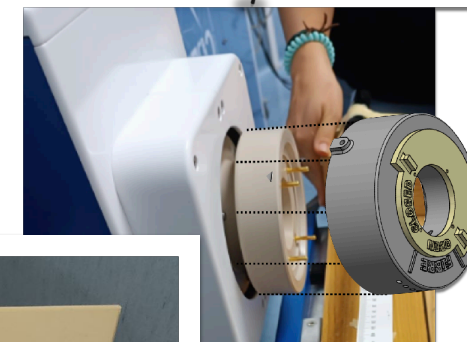
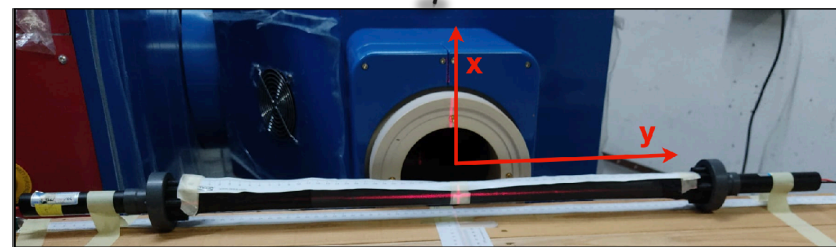
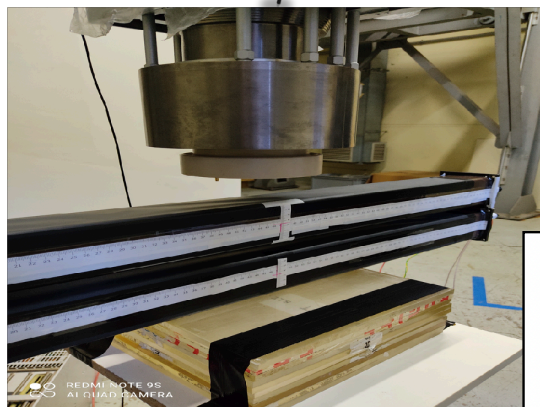


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Nuclear Inst. and Methods in Physics Research, A 1041 (2022) 167334

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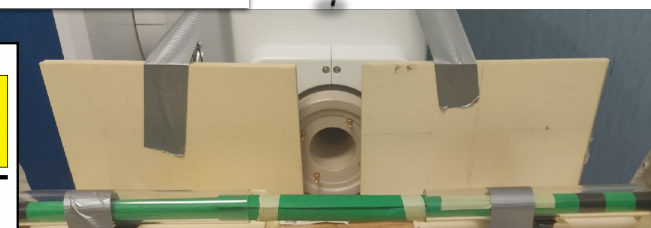
journal homepage: [www.elsevier.com/locate/nima](http://www.elsevier.com/locate/nima)

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

Antonio Triglio<sup>a,b</sup>, Angelica De Gregorio<sup>a,b,c</sup>, Marta Fischetti<sup>d,b</sup>, Gaia Franciosini<sup>a,b</sup>, Marco Garbini<sup>c</sup>, Gabriele Lippa<sup>d</sup>, Marco Magi<sup>d</sup>, Michela Marafini<sup>c,b</sup>, Annalisa Muscato<sup>c</sup>, Vincenzo Patera<sup>d,b</sup>, Alessio Sarti<sup>d,b</sup>, Angelo Schiavi<sup>d,b</sup>, Adalberto Sciubba<sup>d,b</sup>, Marco Toppi<sup>d,f</sup>, Giacomo Traini<sup>b</sup>, Micol De Simoni<sup>c,b,g</sup>

Check for updates



JINST\_036P\_1223

Antonio Triglio

"Test beam results of a fluorescence-based monitor for ultra-high dose rates"

Submitted: 8 December 2023

Accepted: 11 January 2024



FLASH Radiotherapy with high  
Dose-rate particle beams

Antonio Triglio

Bi-national conference on Detectors R&D

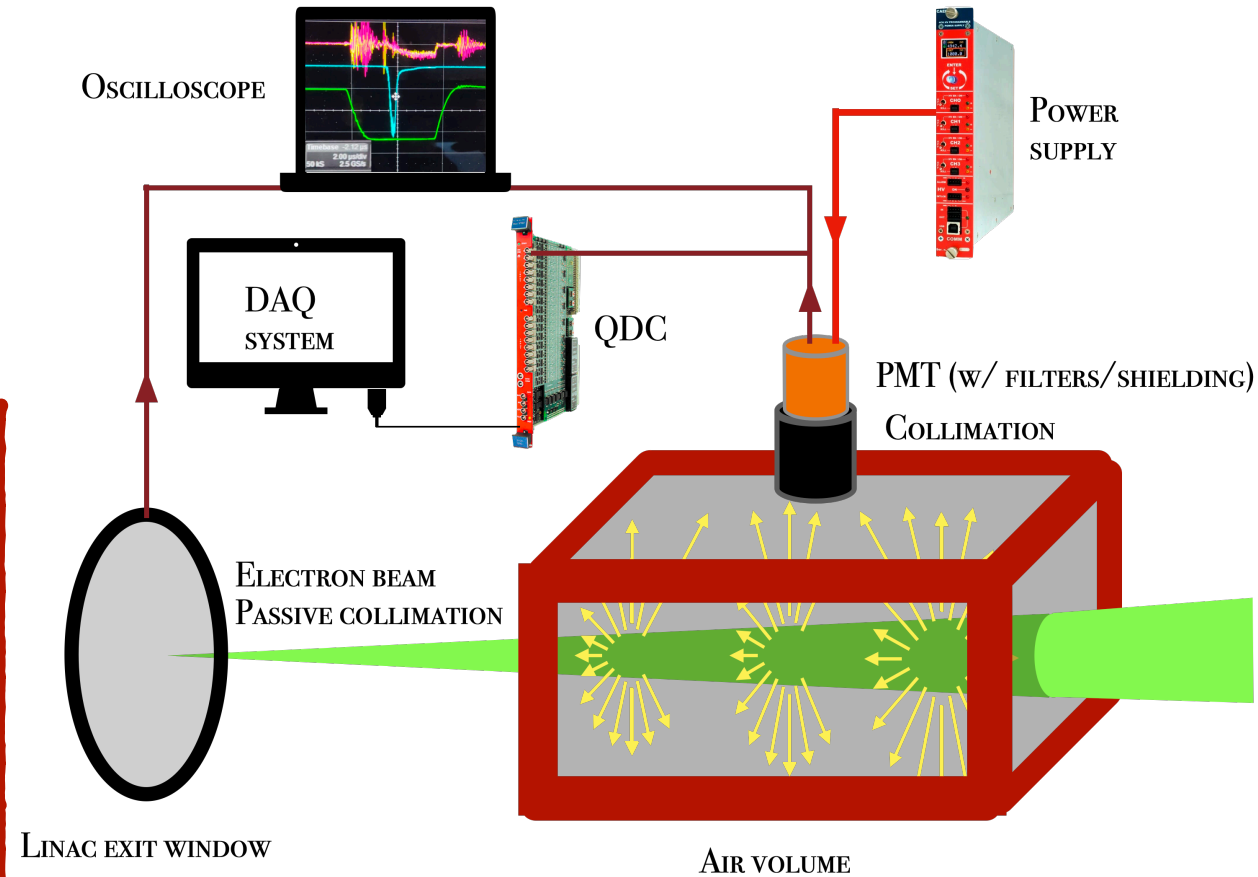
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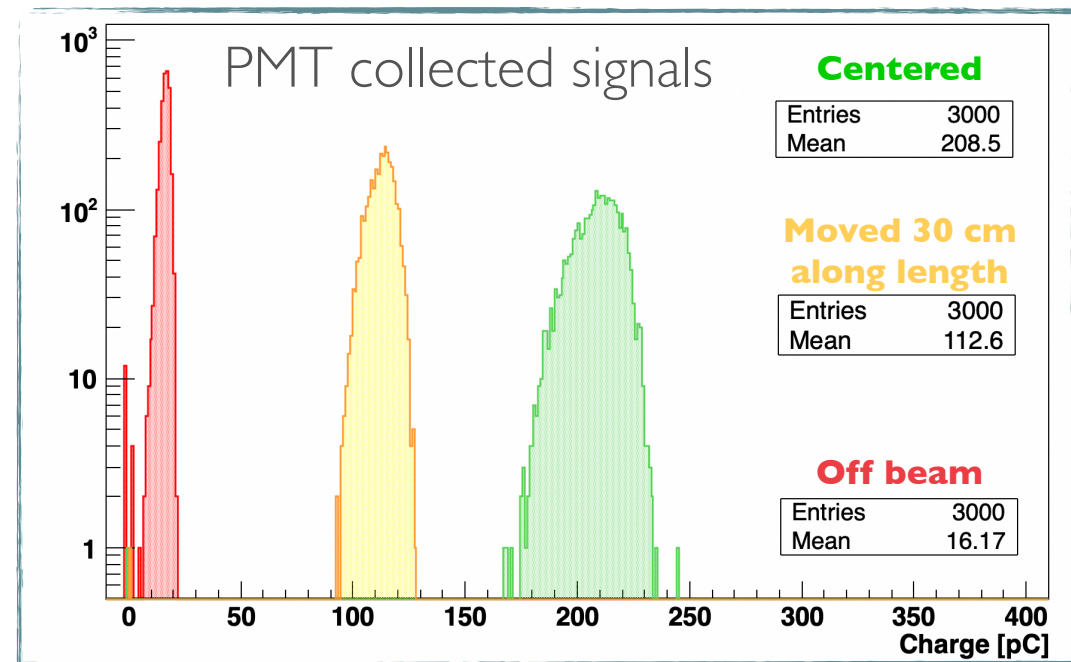
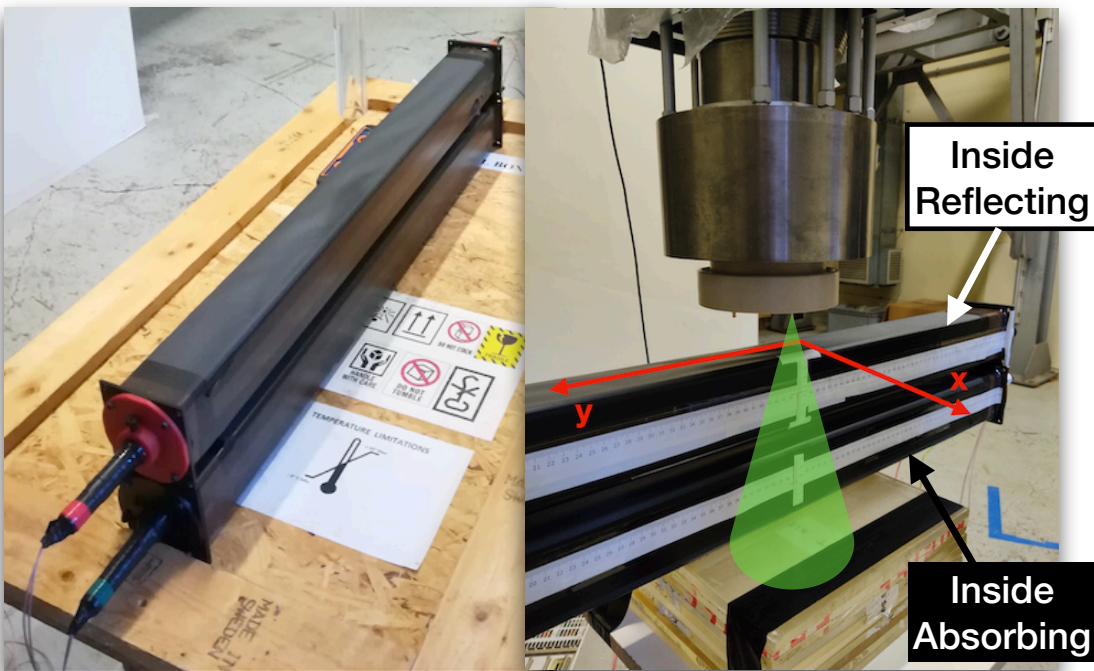
# FLASH beam monitoring

- Testing has been done on the (easily) available sources of beams with UHDR intensities: low energy (6-12 MeV) electrons usually used for intra-operative applications or dedicated to FLASH study



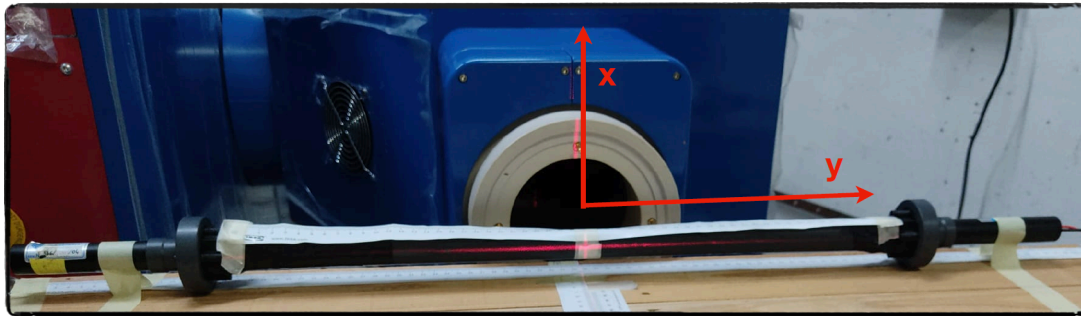
# First assessment

- **In-beam/off-beam** discrimination with a volume of **7x7x90 cm<sup>3</sup>** of air, enclosed by a thin layer of Teflon sheet, with a PVC supporting structure and two PMTs on the opposite squared faces.
- The results confirmed the expected signal sensitivity to the detector position with respect to the beam.

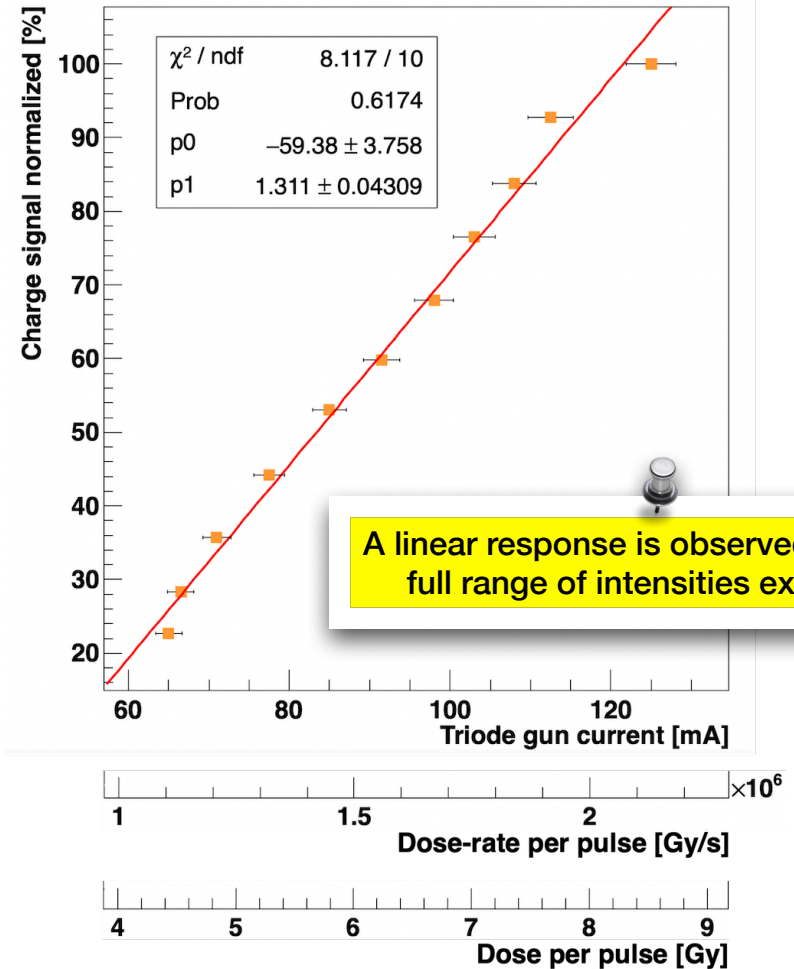
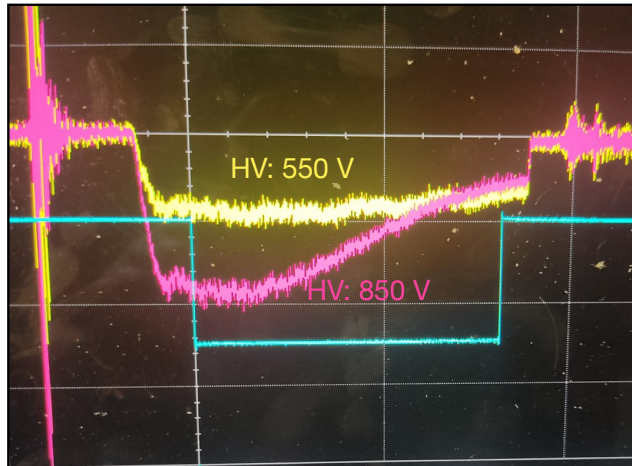


# Intensity sensitivity

- **ElectronFlash:** up to  $10^{12}$  electrons/pulse.
- **Dose(-rate) per pulse:** up to **20 Gy** ( $5 \cdot 10^6$  Gy/s).
- Field diameter: 5-6 cm at BEW (uncollimated).

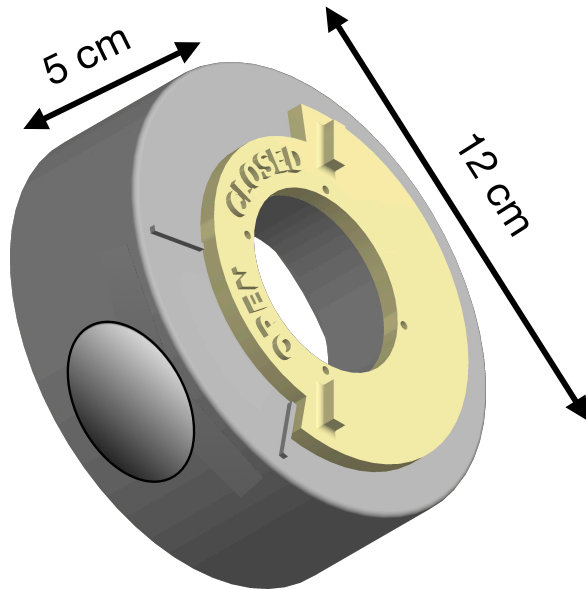


- New prototype: smaller dimensions ( $2 \times 2 \times 60$  cm<sup>3</sup>), with two PMTs on both ends equipped with **UV filters**, meant for studies on both position and **charge** sensitivity.



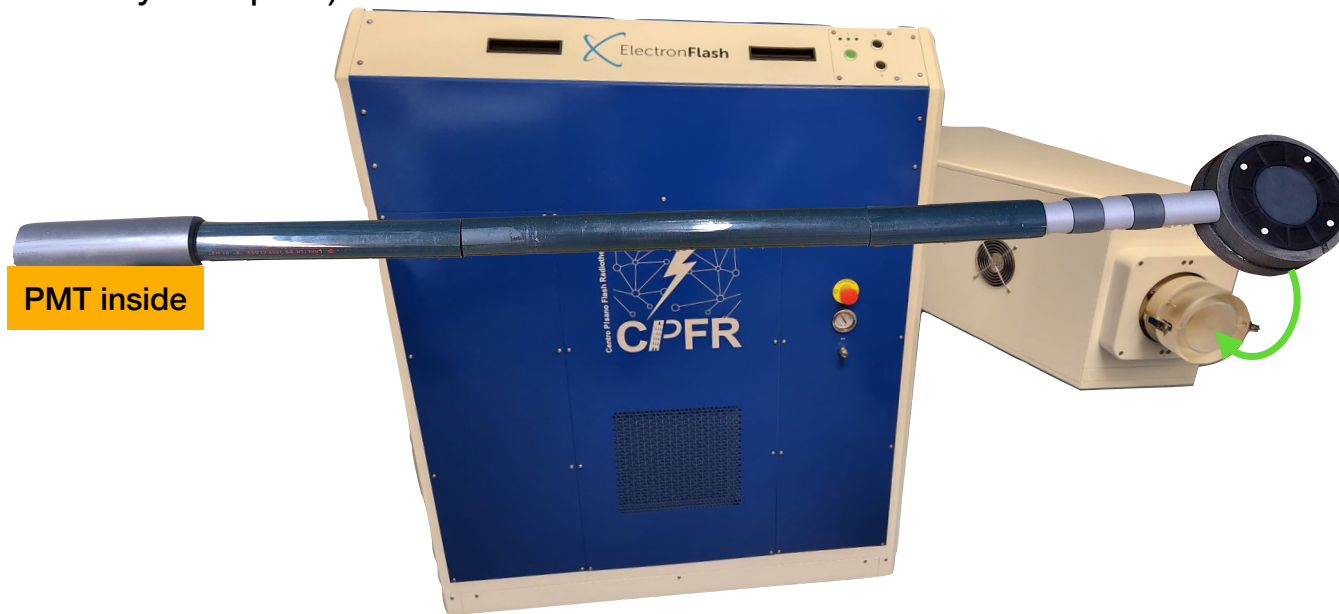
# FLASH beam monitoring

- Next step is to prove that the expected linearity of signal vs beam current is really due to fluorescence => subtract background.
- Detector **directly tailored** to the Beam Exit Window dimensions of the ElectronFlash at the Pisan Center for FLASH-RT studies (CPFR in Pisa, St. Claire University-Hospital).



# FLASH beam monitoring

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- Detector **directly tailored** to the Beam Exit Window dimensions of the ElectronFlash at the Pisan Center for FLASH-RT studies (CPFR in Pisa, St. Claire University-Hospital).
- 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.

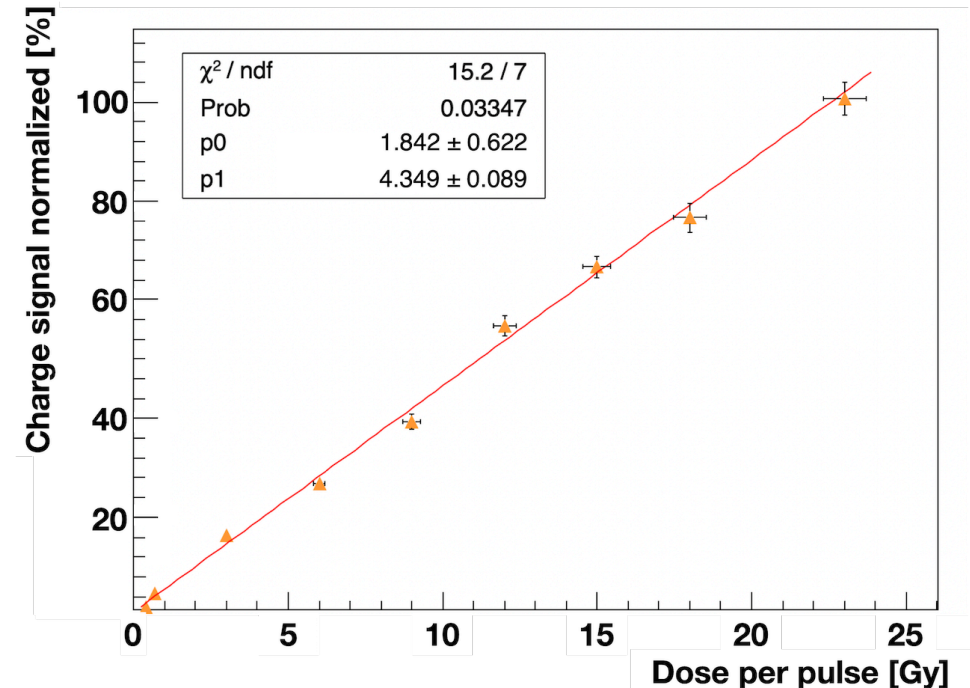
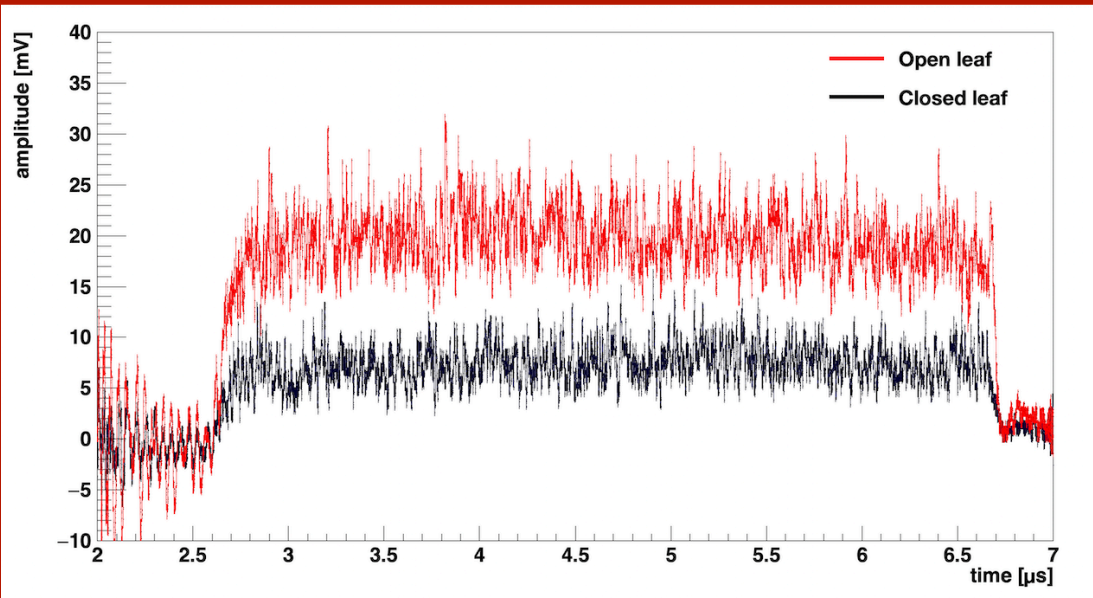


This is how the active volume support looks like once mounted on the beam exit window.  
N.B.: no material on the beam line! Just air...



# FLASH beam monitoring

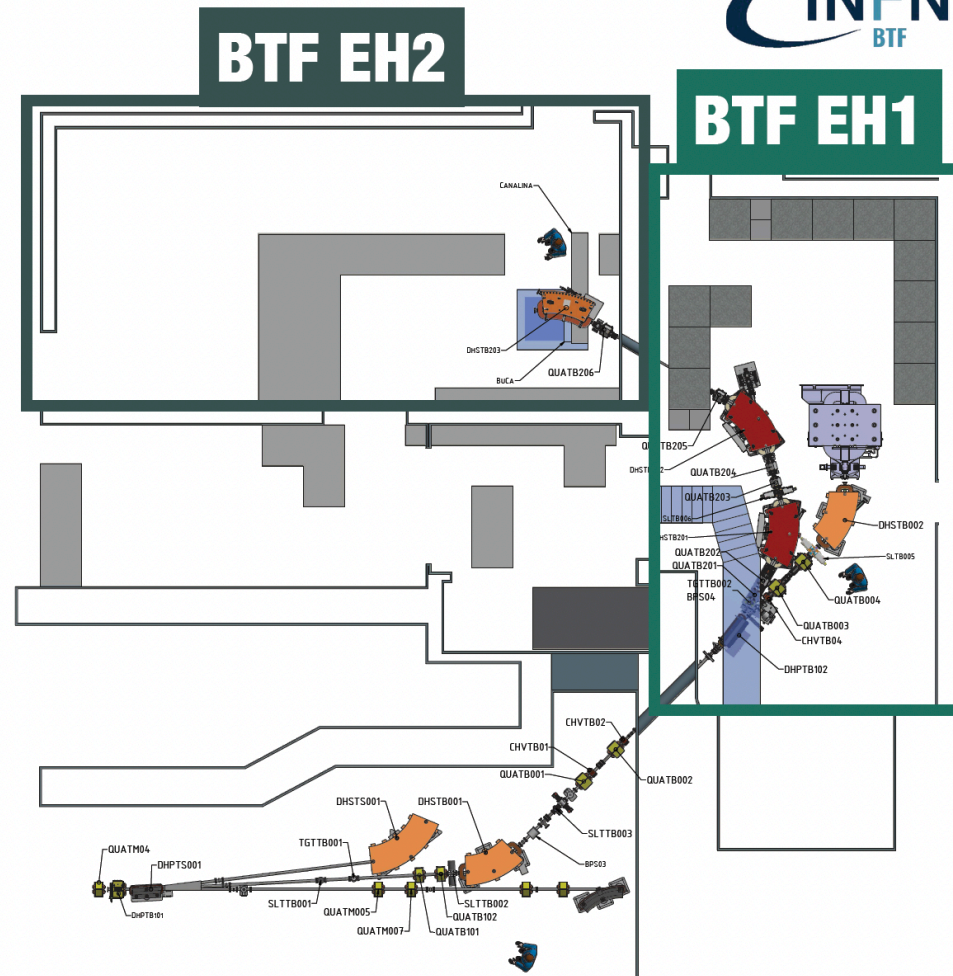
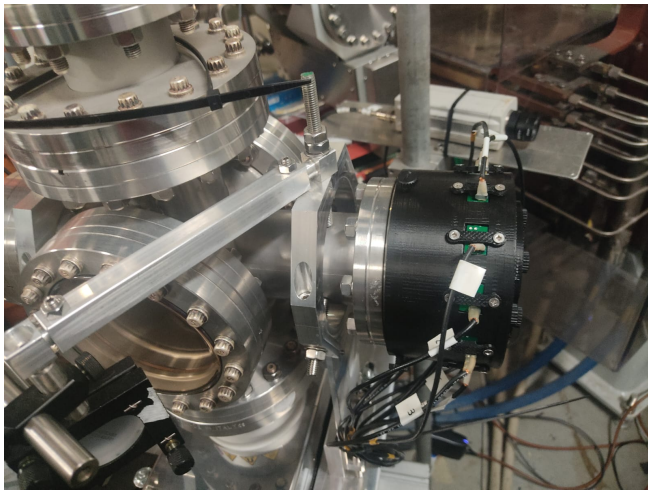
- Background can be successfully subtracted, although with this setup it is a sizable portion (~35%) of the total signal. Moreover, the gain of the PMT is still non-optimal for the fluctuations of the signal amplitude.
- The readout system and the geometry need to be optimized to increase the signal-to-noise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

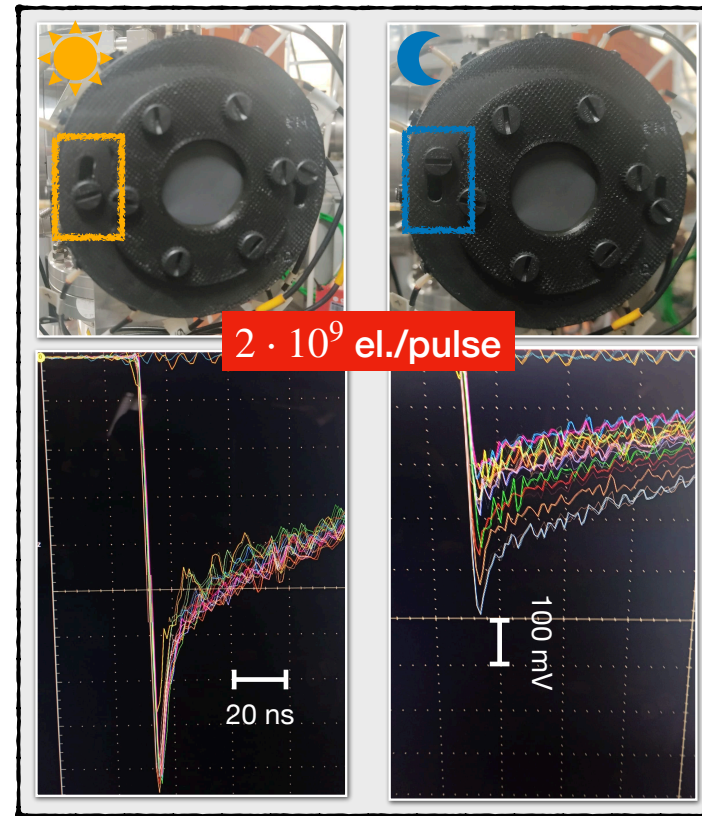
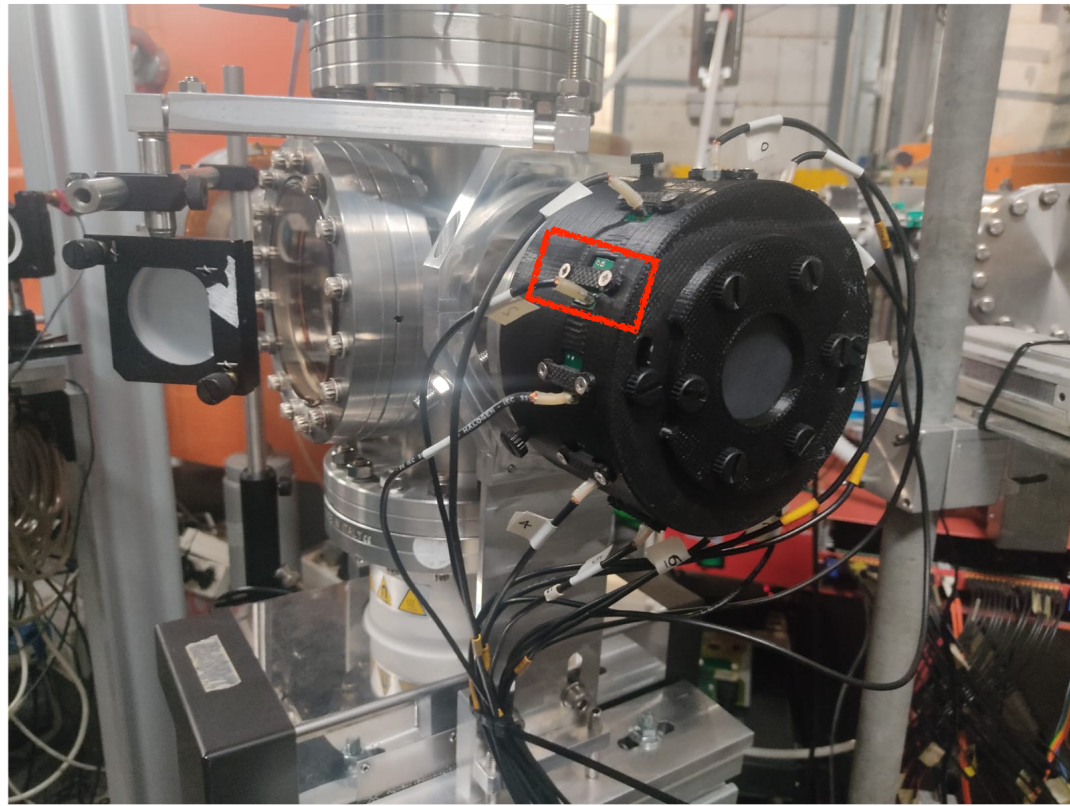
# Outside the clinic: BTF

- The LNF Beam Test Facility (BTF) experimental line 1 allows users to exploit a high intensity (up to  $10^{10}$  particles/pulse with minimum pulse length 1.5 ns) high energy (150 MeV) electron beam, with beam waist down to  $0.5 \times 0.5$  mm<sup>2</sup> and divergence down to 0.5 mrad.



Courtesy of E. Diociaiuti on behalf of the BTF team

# Outside the clinic: BTF

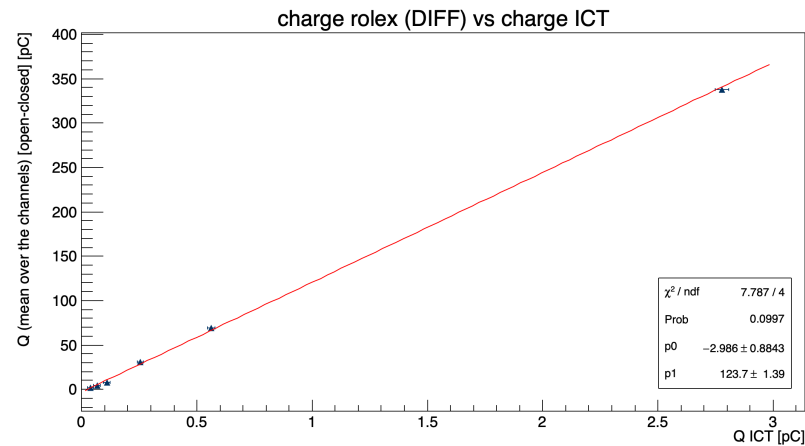
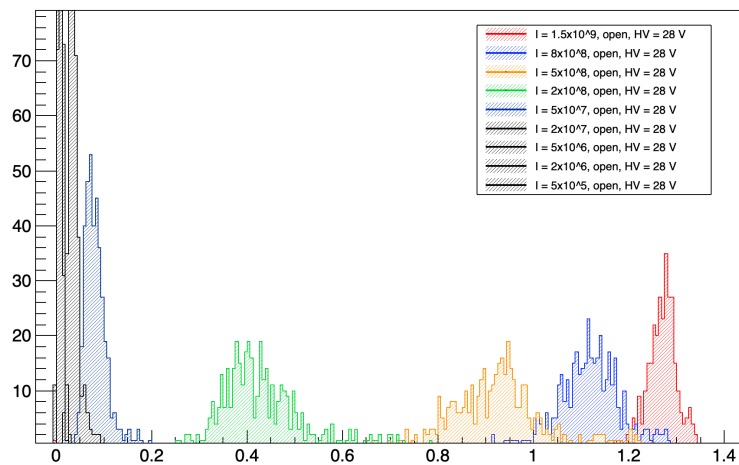


- A prototype (12 SiPMs arranged in a radial pattern) has been tested.
- We acquired data in a large range of possible currents values (from  $2 \cdot 10^9$  down to  $5 \cdot 10^5$  el./pulse).



# Outside the clinic: BTF

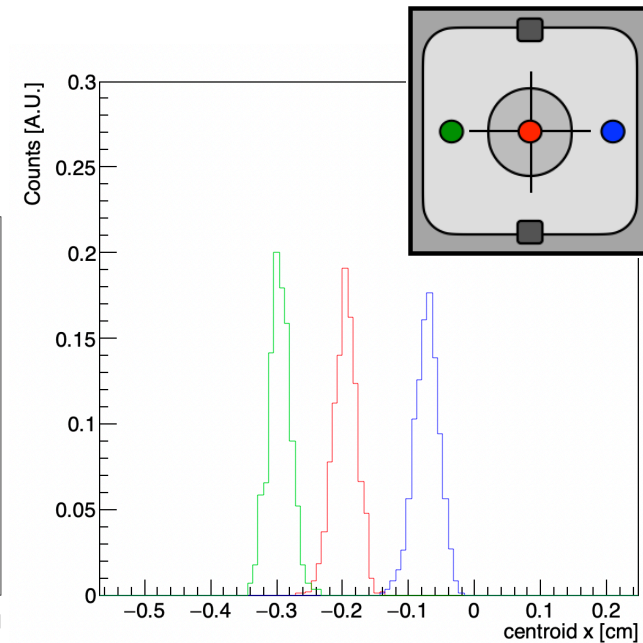
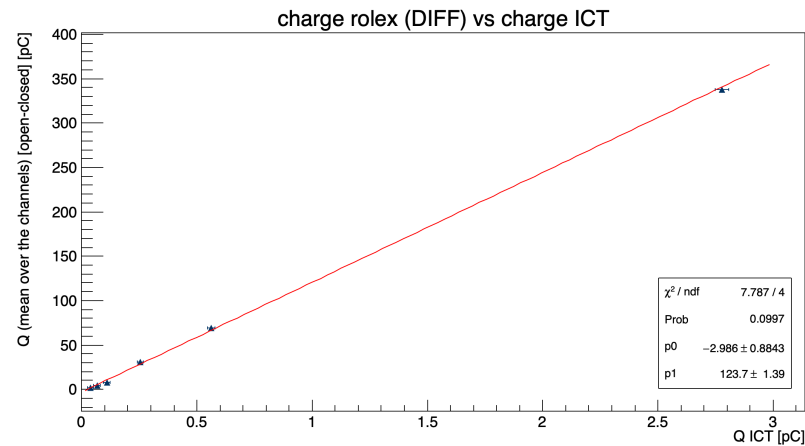
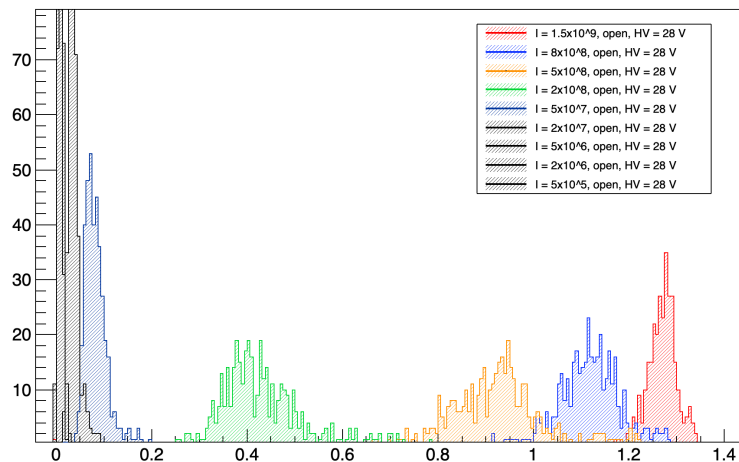
- Currently, there is a lack of feedback from a BTF monitoring system of the effective delivered currents within  $10^5$ - $10^7$  electrons/pulse beside the dose in the room (uncertainty of  $>30\%$ ).
- With the available SiPMs and a chosen gain optimised to ensure linearity in the BTF range of interest, the number of cells is not sufficient for pulses with more than  $10^8$  electrons.



# Outside the clinic: BTF

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- With the available SiPMs and a chosen gain optimised to ensure linearity in the BTF range of interest, the number of cells is not sufficient for pulses with more than  $10^8$  electrons.

- Charge centroid distributions obtained combining the response of the 12 SiPM channels.

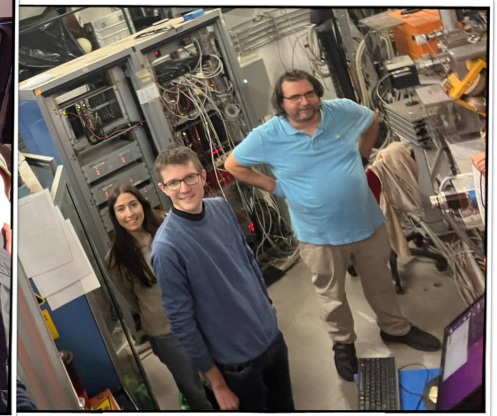


# Take-home messages

Links and contacts:  
[web.infn.it/FRIDA/](http://web.infn.it/FRIDA/)  
[antonio.trigilio@lnf.infn.it](mailto:antonio.trigilio@lnf.infn.it)  
[michela.marafini@roma1.infn.it](mailto:michela.marafini@roma1.infn.it)

- Fluorescence technique could be applied to FLASH monitoring but the clinical translation is still uncertain.
- FlashDC showed no saturation at the maximum intensity/energy available at electron FLASH machine → higher intensity can be explored. However, it seems to suffer from low S/N → could gain at narrower beams (VHEE, ions, protons).
- Beams with reduced transverse size opens to transverse position accuracy measurement using dedicated readout.
- In principle, it can be used in certain conditions of continuous current, and further studies could involve the variation of the signal with pressure, temperature, and different gas mixtures (e.g. radiative environment, high charge, certified fixed installations).

- Acknowledgements to Carlo Ligi and Giovanni Maccarrone for funding my trip :)



# Never underestimate an empty box...



**Merci beaucoup pour votre attention!**

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# Backup

# Backup

*M. Ave et al. / Astroparticle Physics 28 (2007) 41–57*

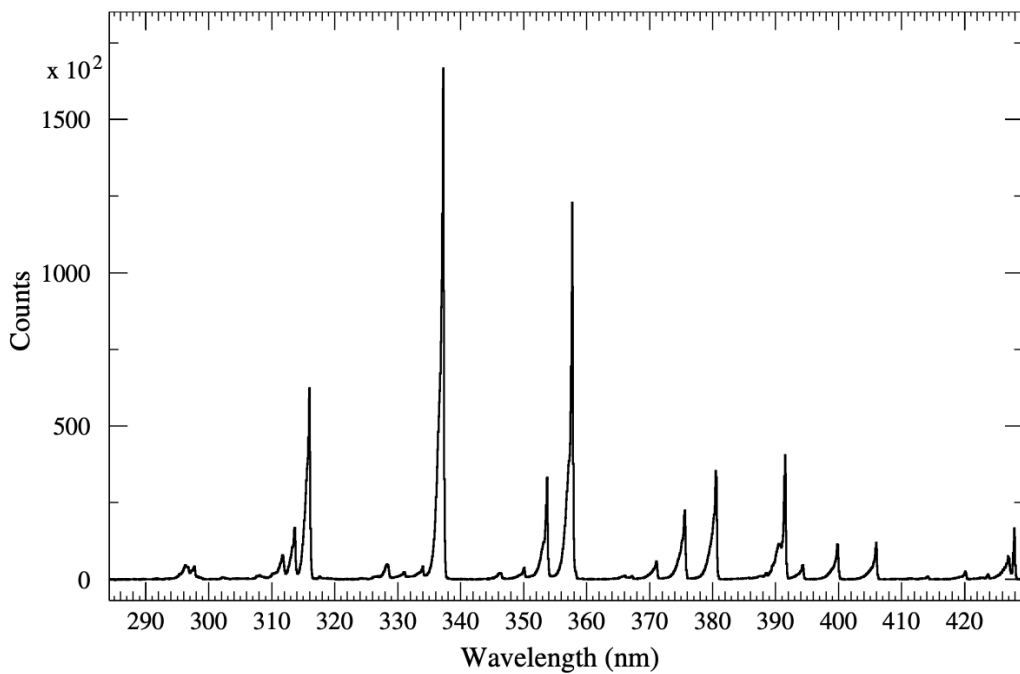
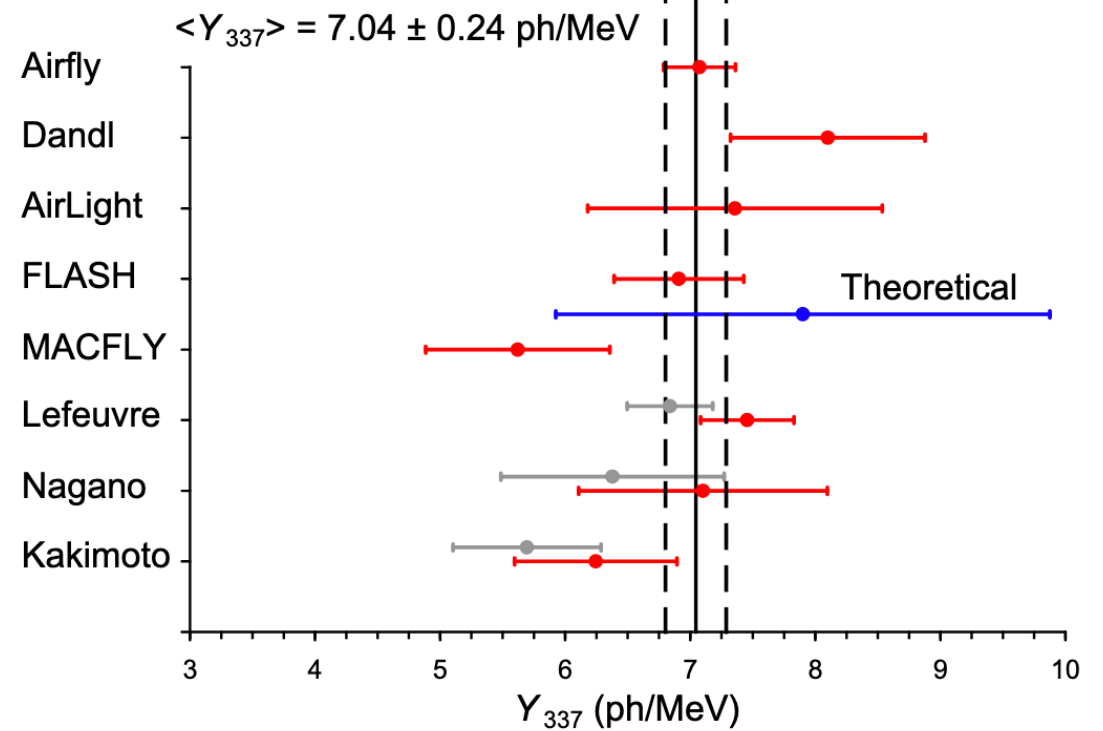
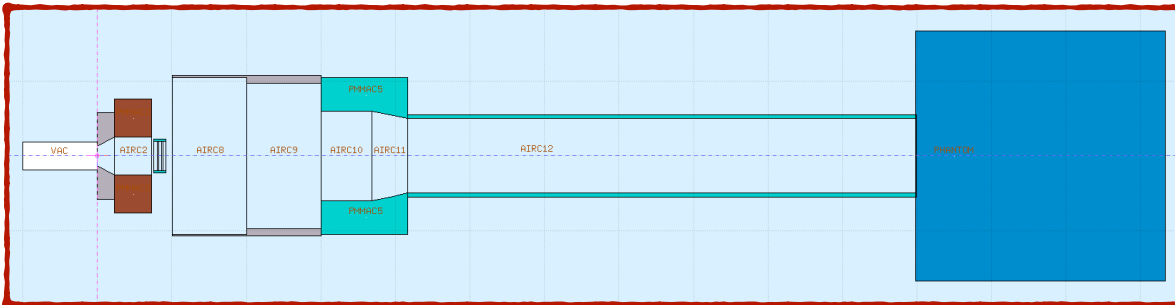


Fig. 4. Measured fluorescence spectrum in dry air at 800 hPa and 293 K.

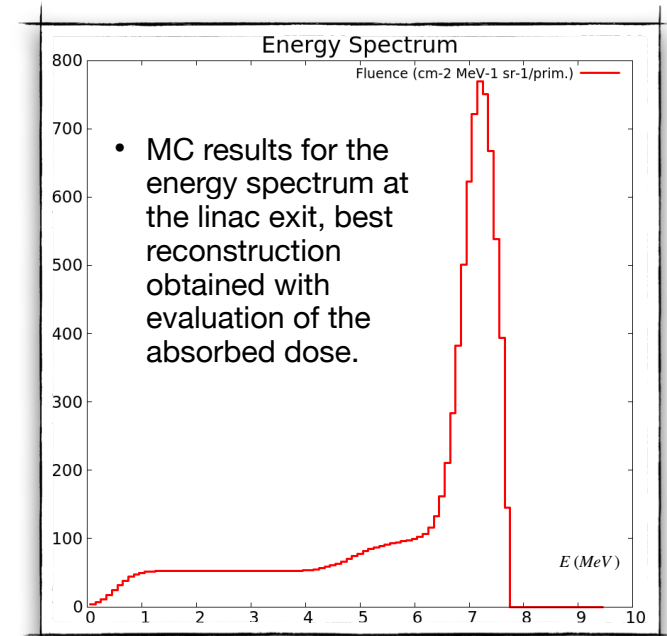
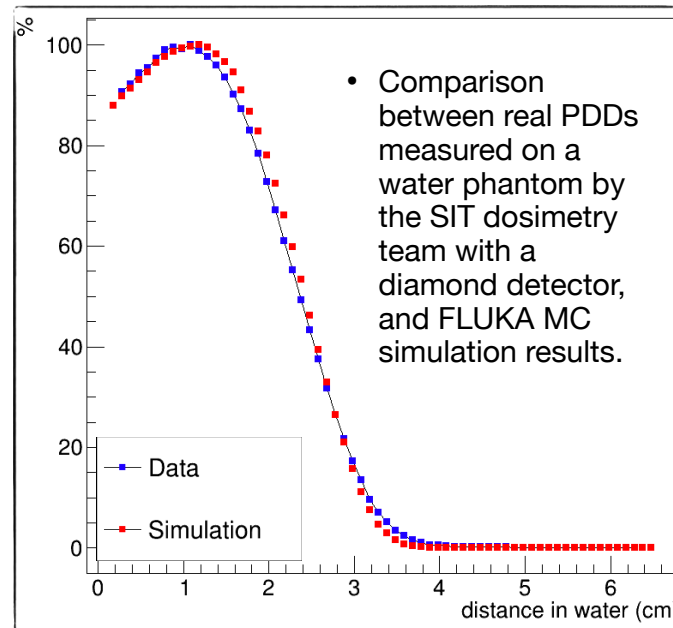


# Beam delivery studies

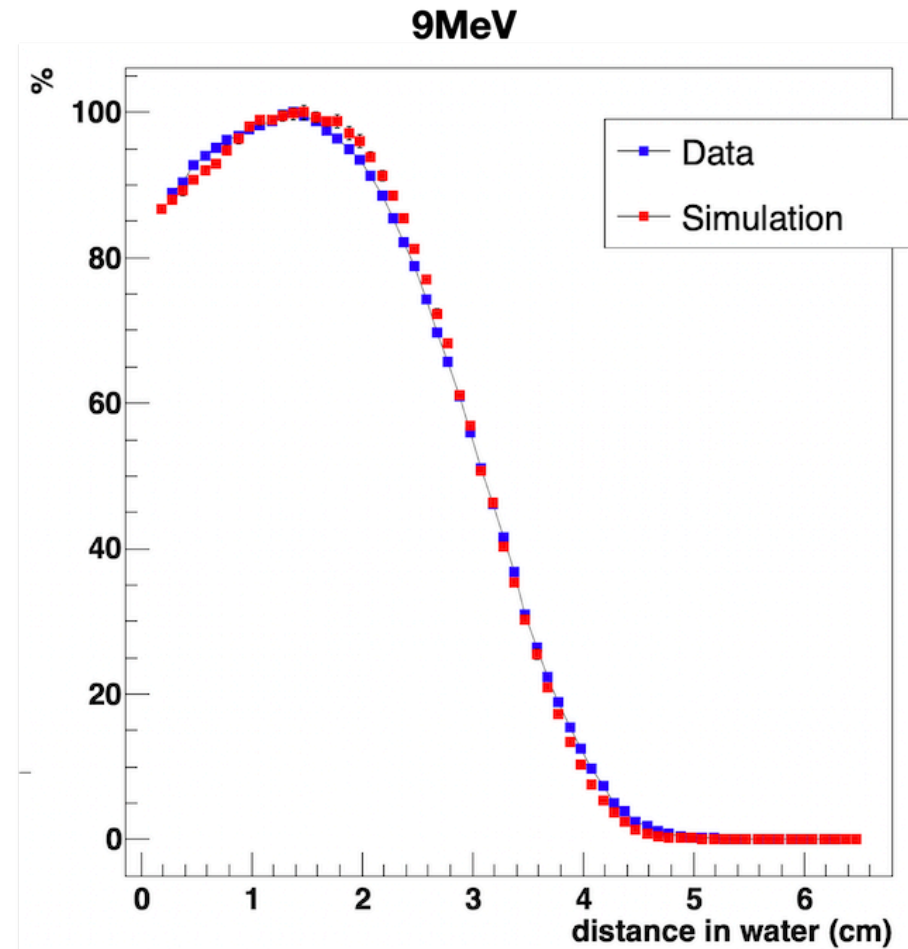
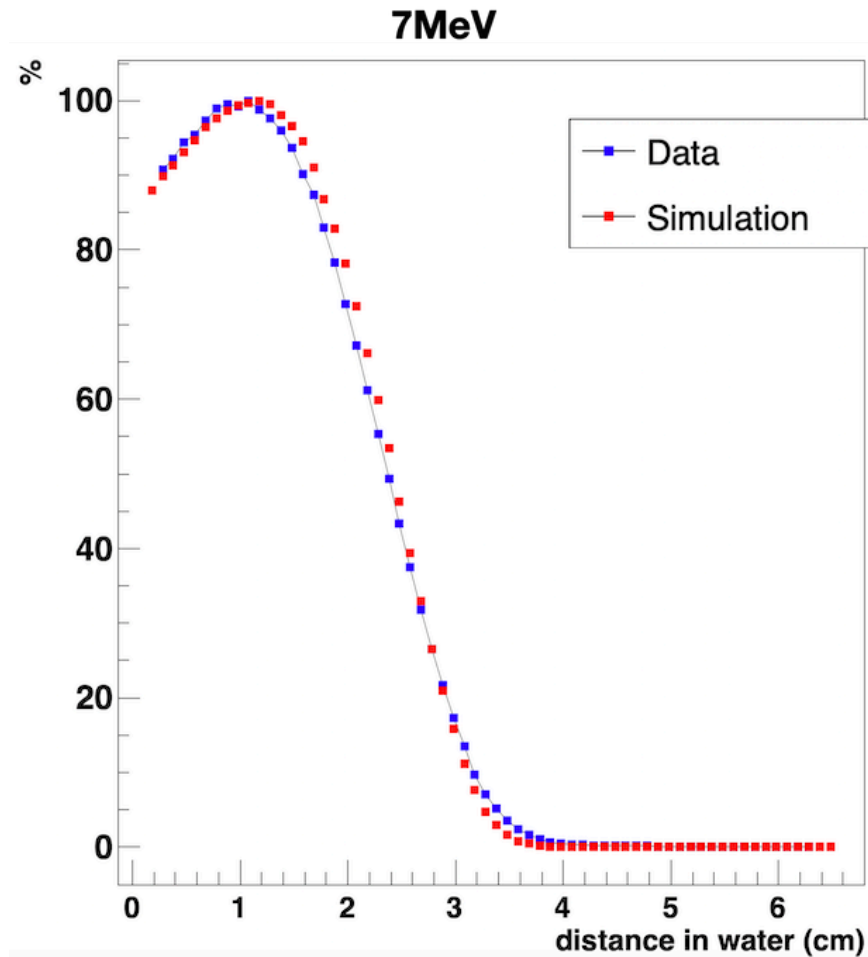


- Monte Carlo simulation provide a solid base to estimate the accuracy of the beam delivery system and the expected dosimetric qualities. It can also be a useful tool for the **optimization** of the hardware apparatus.
- I performed several validations with different applicator geometries comparing **Percentage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

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



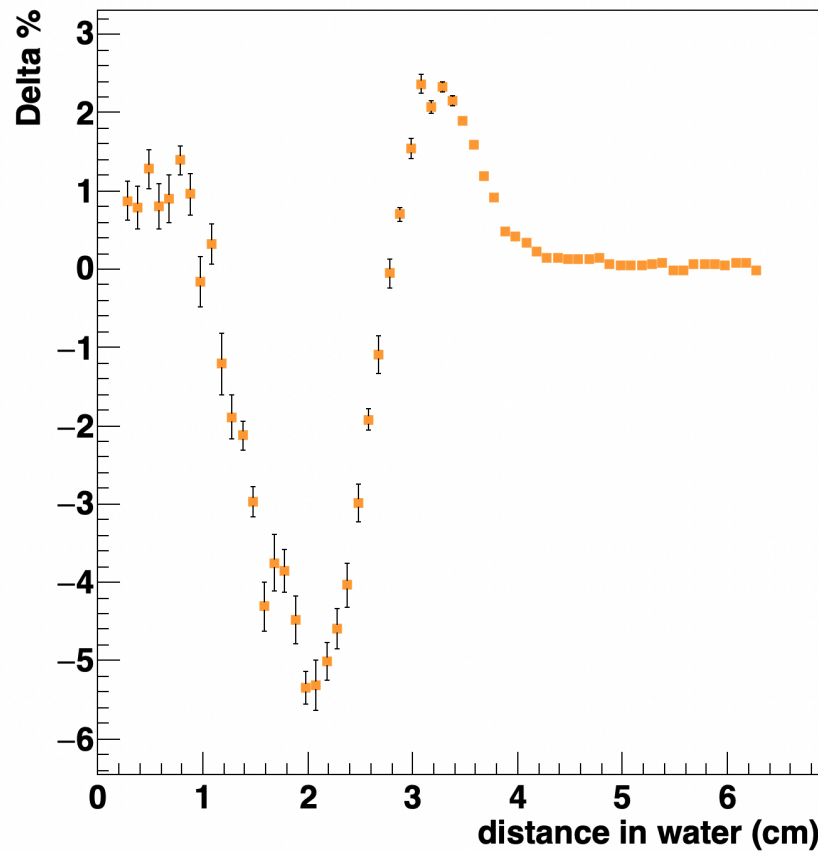
# Beam delivery studies



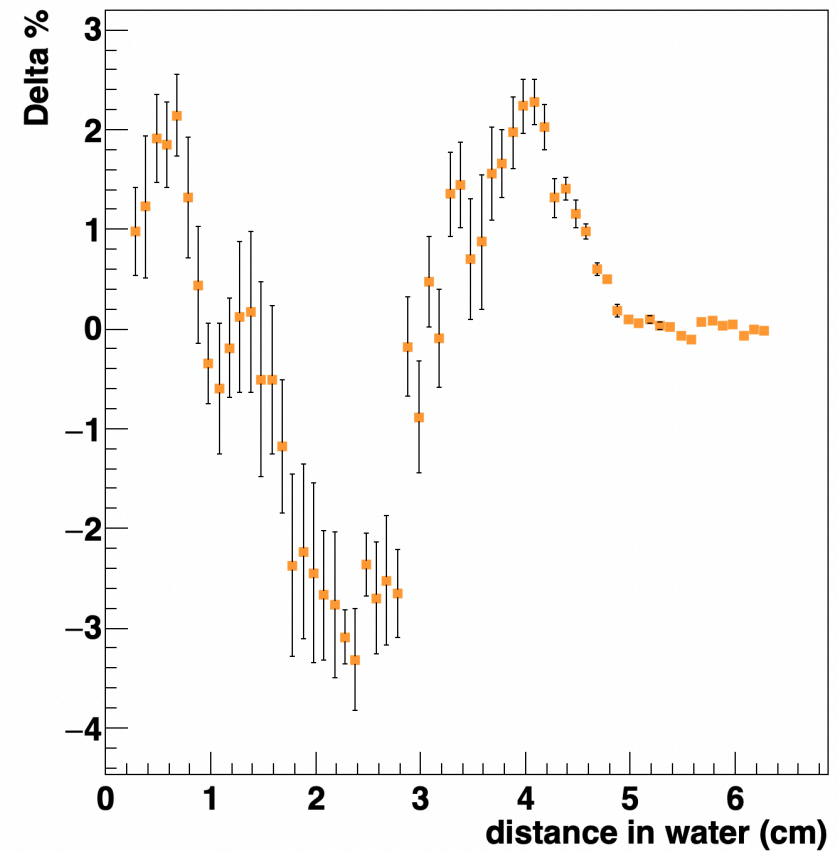


# Beam delivery studies

Percentage difference meas. vs sim. 7MeV

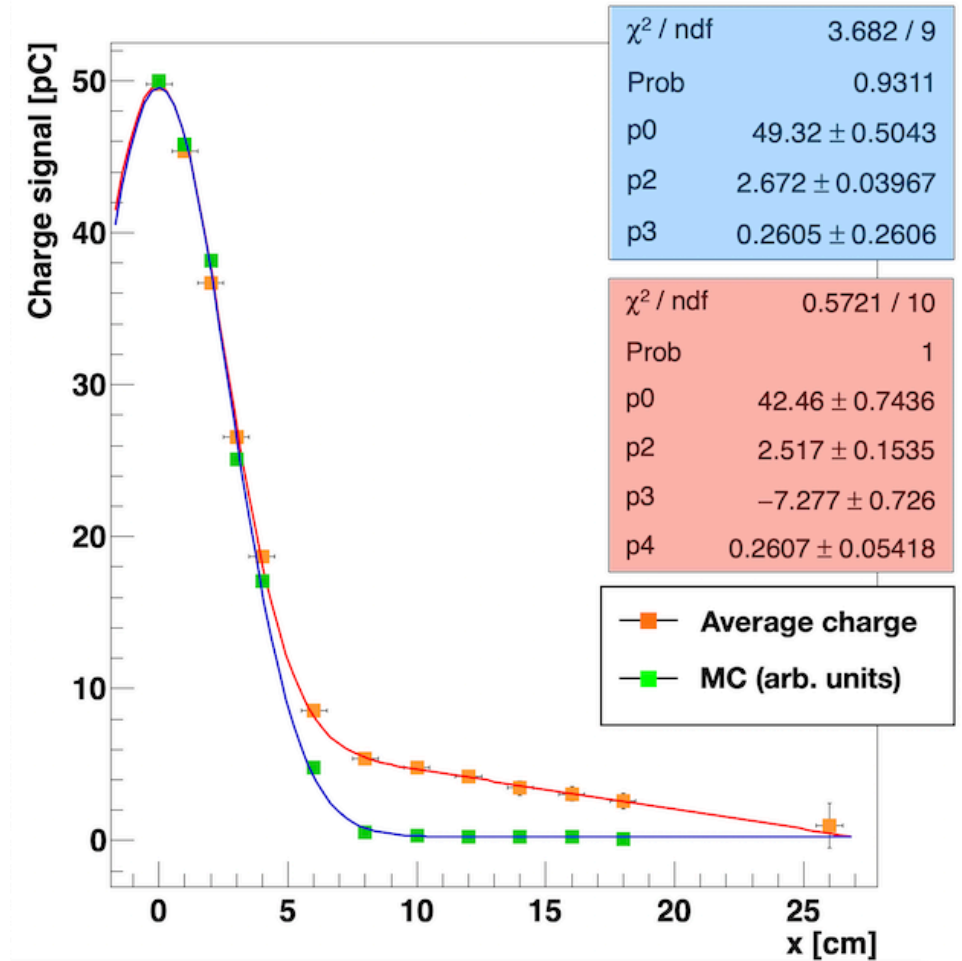


Percentage difference meas. vs sim. 9MeV



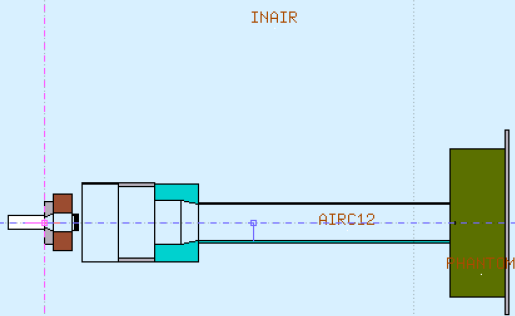
# Beam delivery studies

- 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

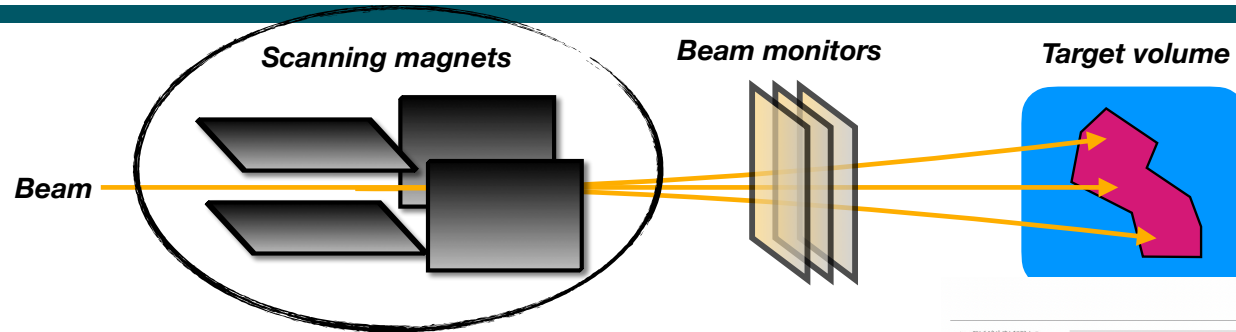
- Concerning **radio-protection** studies, I was asked to assess the adequacy of a set of ambient survey meters used to measure **stray radiation** inside the bunker where the ElectronFlash was installed in **University of Antwerp, Belgium**.
- It is one of the few facilities in the world where FLASH 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	$18.3 \pm 0.3 \mu\text{Sv/Gy}$	$16.8 \pm 0.2 \mu\text{Sv/Gy}$
STEP OD-02	$12.2 \pm 0.3 \mu\text{Sv/Gy}$	$13.1 \pm 0.2 \mu\text{Sv/Gy}$

# VHEE + FLASH: natural partners?



Description	value
Beam energy	> 130 MeV
RF frequency	5.712 GHz
Pulse repetition frequency	100 Hz
Pulse duration	< 3 $\mu$ s
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.

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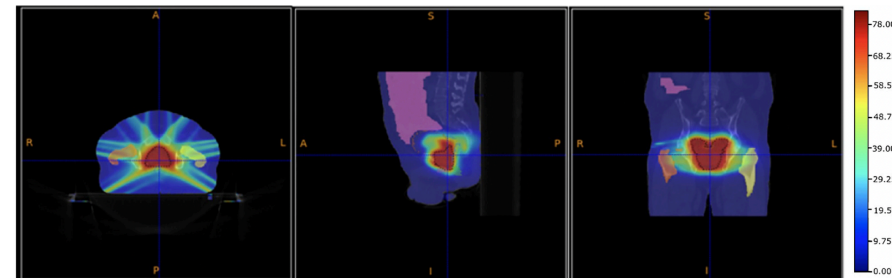


Review Article

FLASH radiotherapy treatment planning and models for electron beams

Mahbubur Rahman<sup>a,1</sup>, Antonio Trigilio<sup>b,c,1</sup>, Gaia Franciosini<sup>b,c</sup>, Raphaël Moeckli<sup>d,\*</sup>, Rongxiao Zhang<sup>a,e</sup>, Till Tobias Böhlen<sup>d</sup>

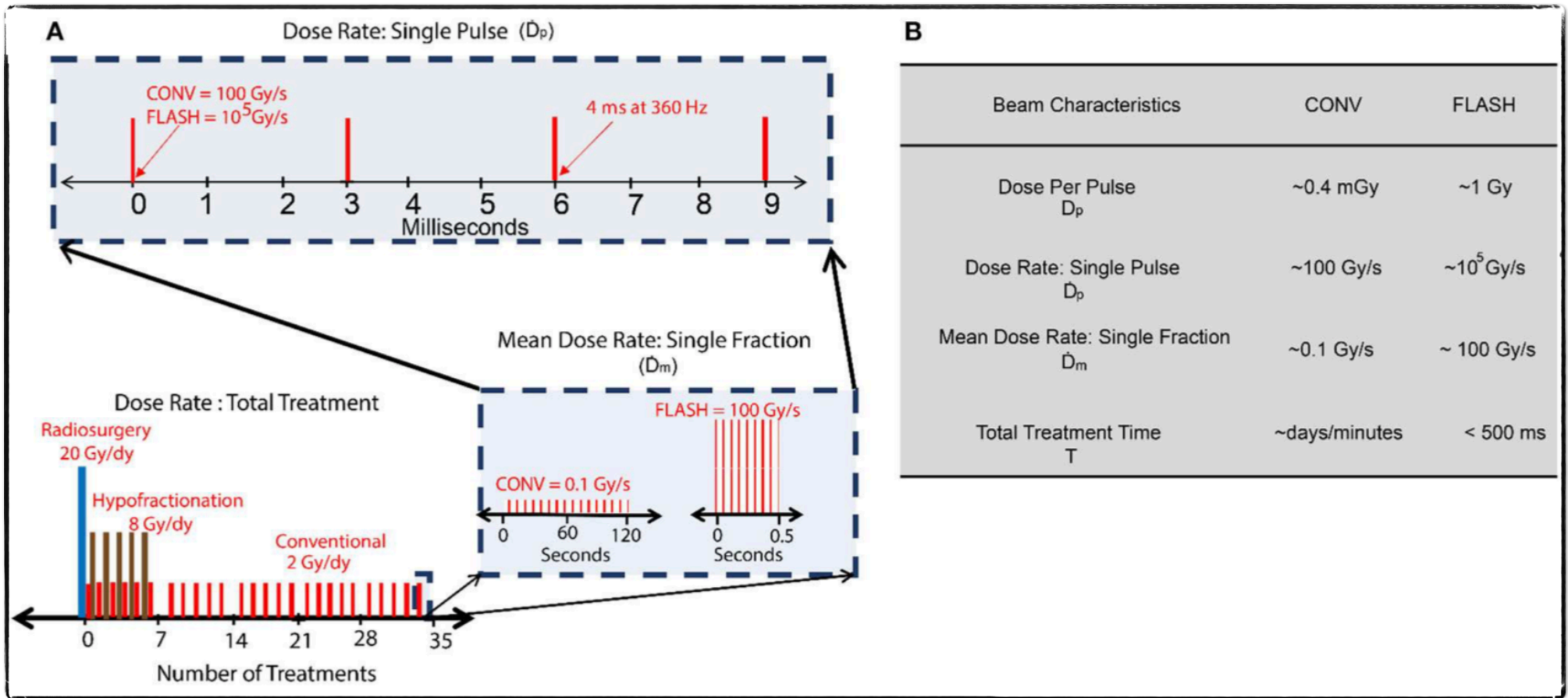
<sup>a</sup>Thayer School of Engineering, Dartmouth College, Hanover, NH, USA; <sup>b</sup>Physics Department, "La Sapienza" University of Rome; <sup>c</sup>INFN National Institute of Nuclear Physics, Rome Section, Rome, Italy; <sup>d</sup>Institute of Radiation Physics, Lausanne University Hospital and Lausanne University, Lausanne, Switzerland; <sup>e</sup>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

# 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



# Backup

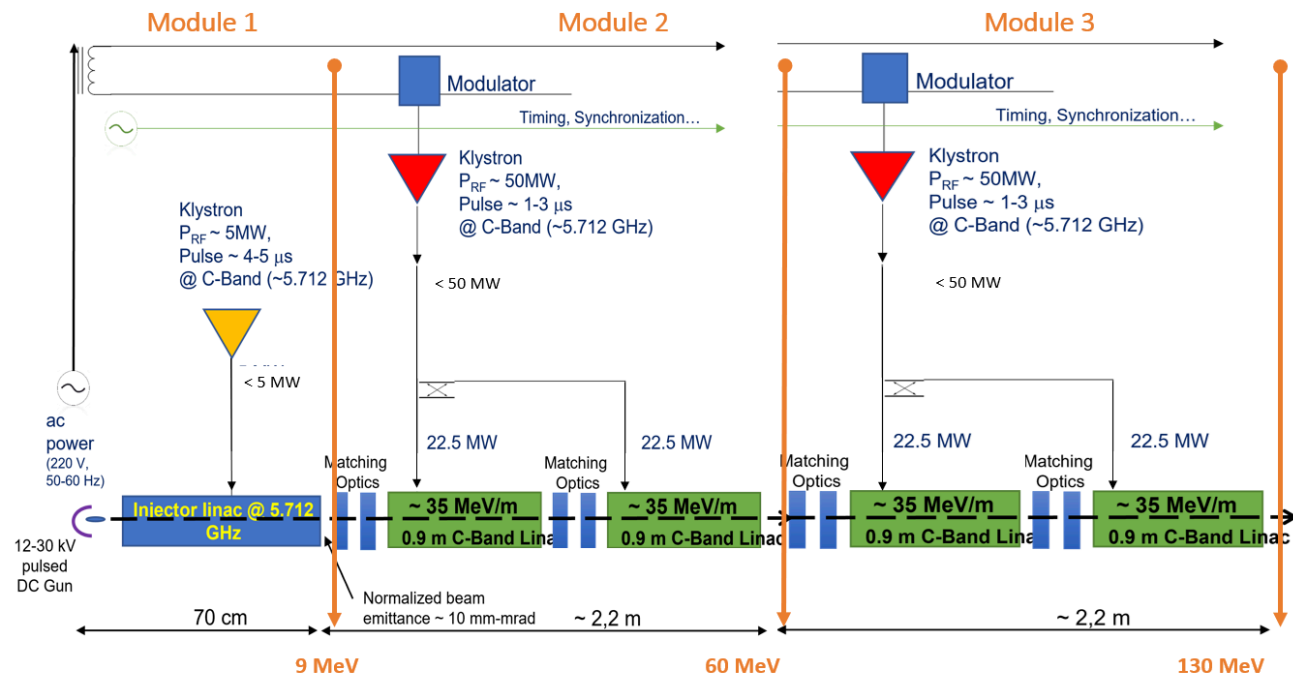
Response	Detectors	Measurement type	FLASH study	Instantaneous dose-rate/dose per pulse ( $D_p$ ) dependence	Spatial resolution	Time-resolution	Energy dependence
Luminescence	TLD/OSLD	1D, 2D	e [15, 37, 71]	Independent ( $\sim 10^9$ Gy/s) [80, 137]	$\sim 1$ mm	Passive	Tissue-equivalent
	Scintillators	1D,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

# Devices using FLASH irradiation modalities

Devices	Dose rate [Gy/s]	Pulse width [ $\mu$ s]	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 $\sim 0.05$	/	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 world, 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%.
- The injector is a standing-wave (SW), biperiodic, magnetic coupling structure. The accelerating mode is the  $\pi/2$  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.

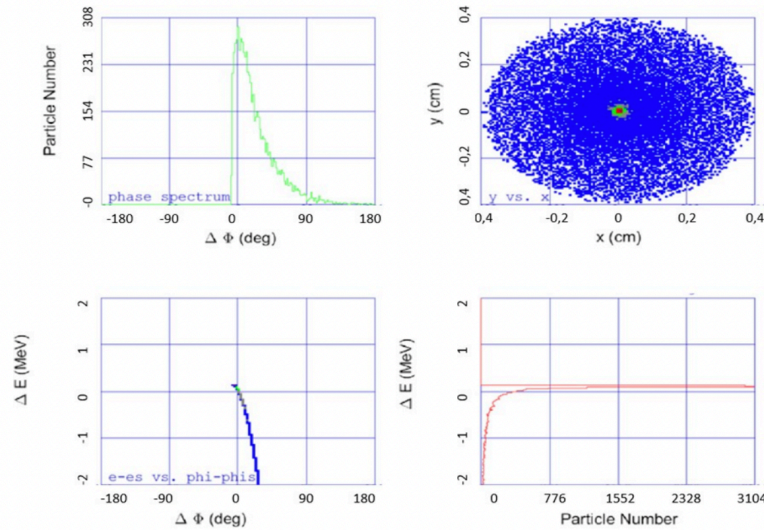
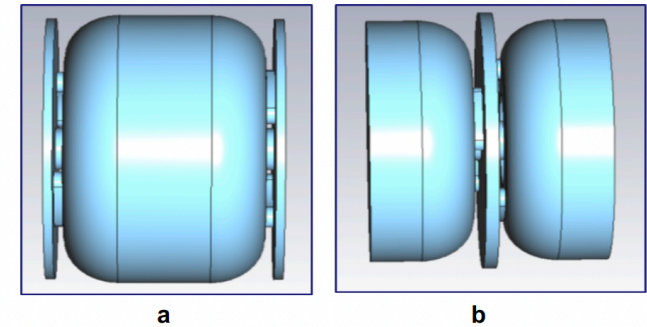


Figure 5.5: TSTEP output electron beam parameters at the exit of the Module 1.



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

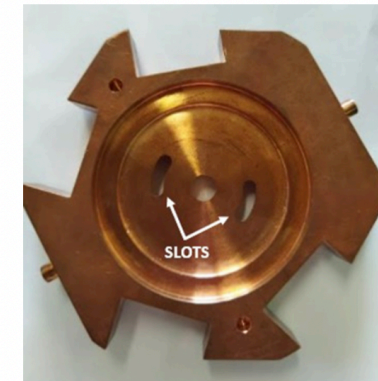


Figure 5.3: Off axis slots for the magnetic coupling.

# 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 ( $\phi''$ ) 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.

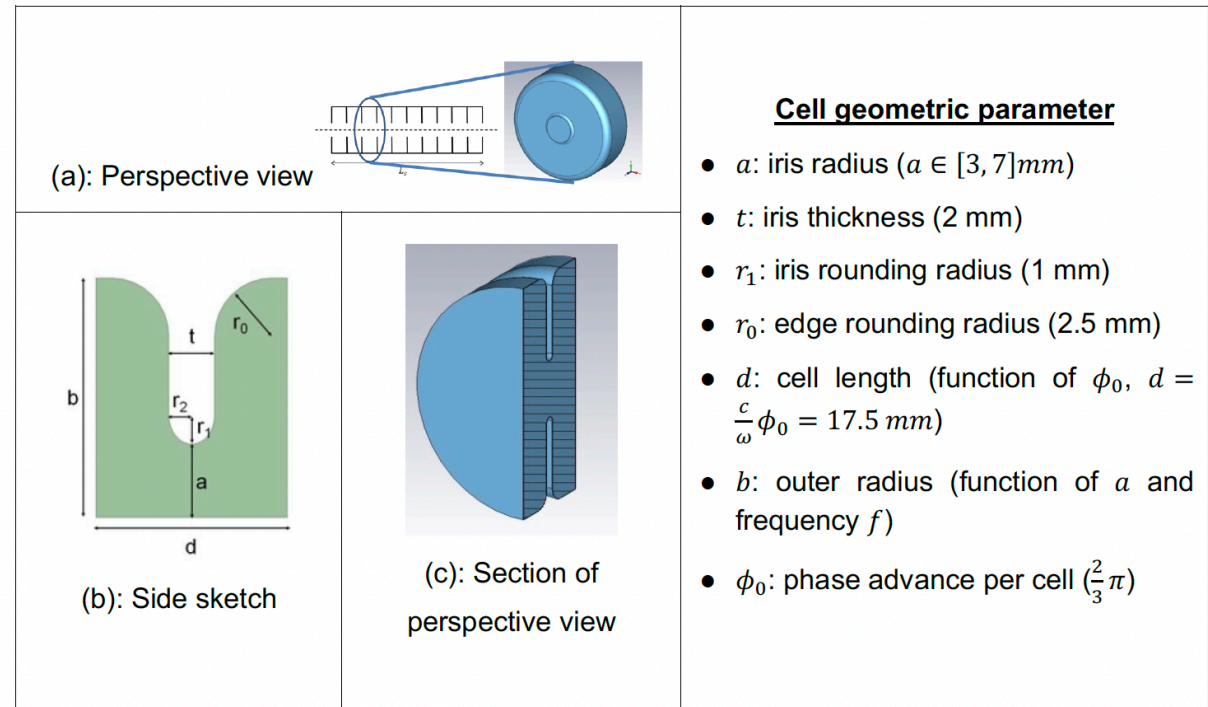
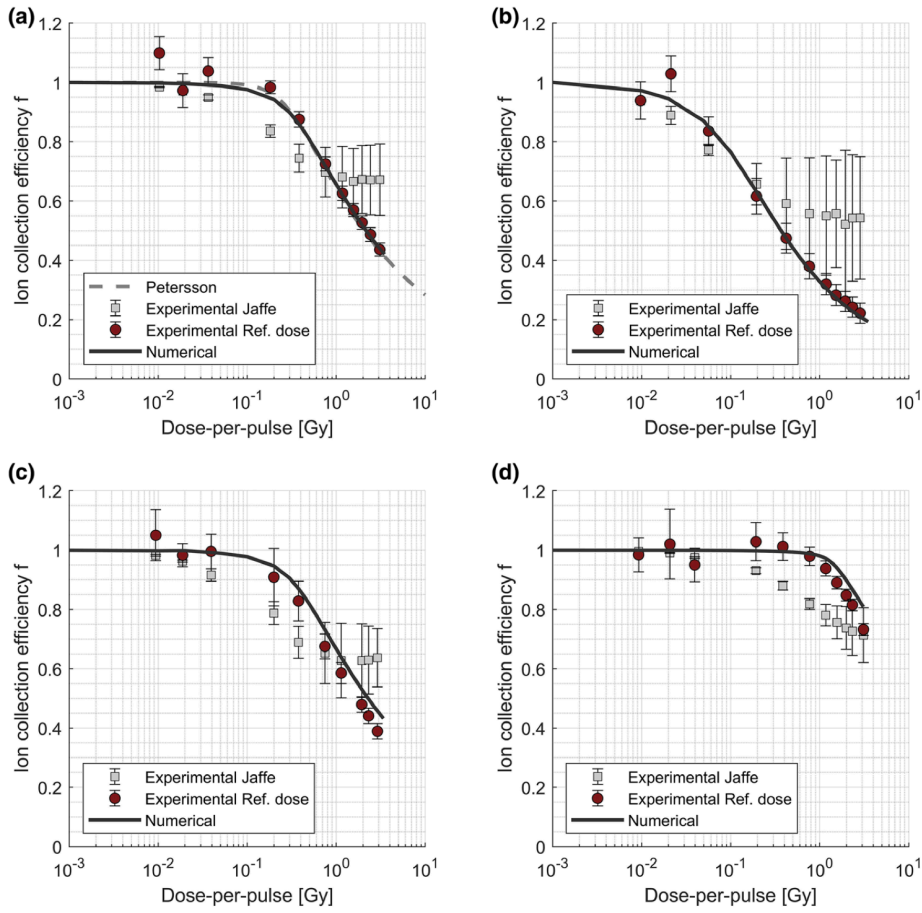


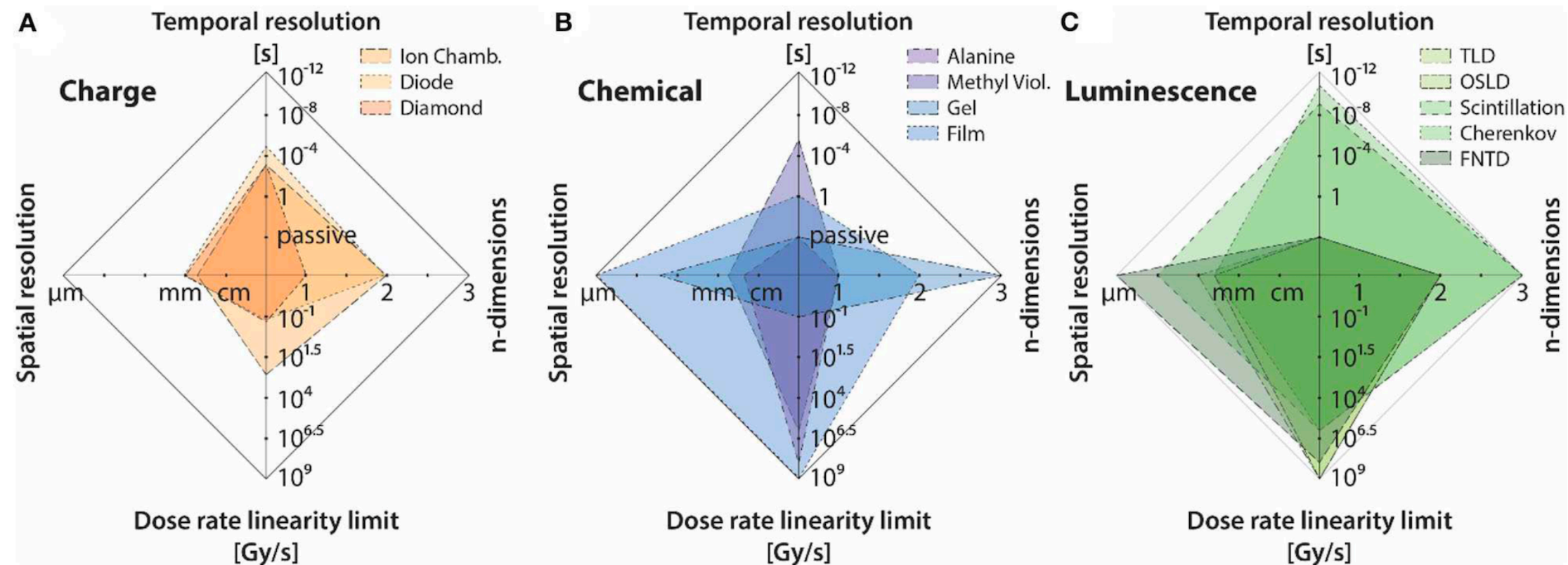
Figure 5.6: TW cell and its geometric parameters. (a): Perspective view; (b): Side sketch with main dimensions; (c): Section of perspective view.

# 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

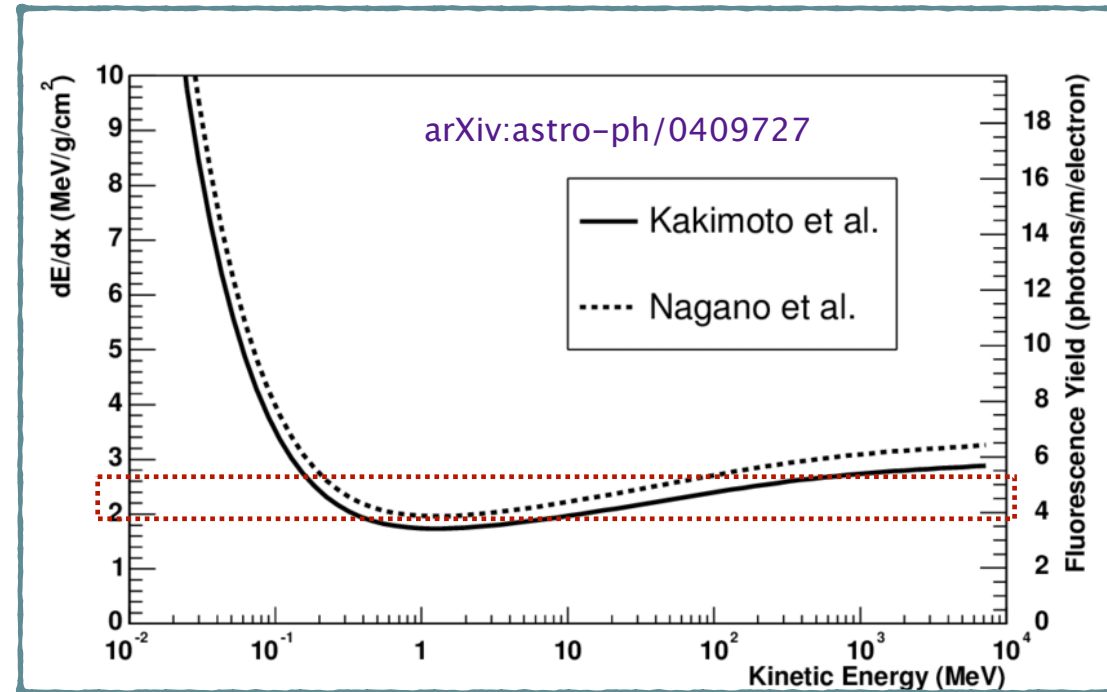
# FLASH beam monitoring



# Backup

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

$E_k$	ph./m (Fluor.)	ph./m (Ch.)
10 MeV	4 (@4 $\pi$ )	Under thr.
20 MeV	4 (@4 $\pi$ )	6 (@0.1°)
130 MeV	5 (@4 $\pi$ )	70 (@1.4°)

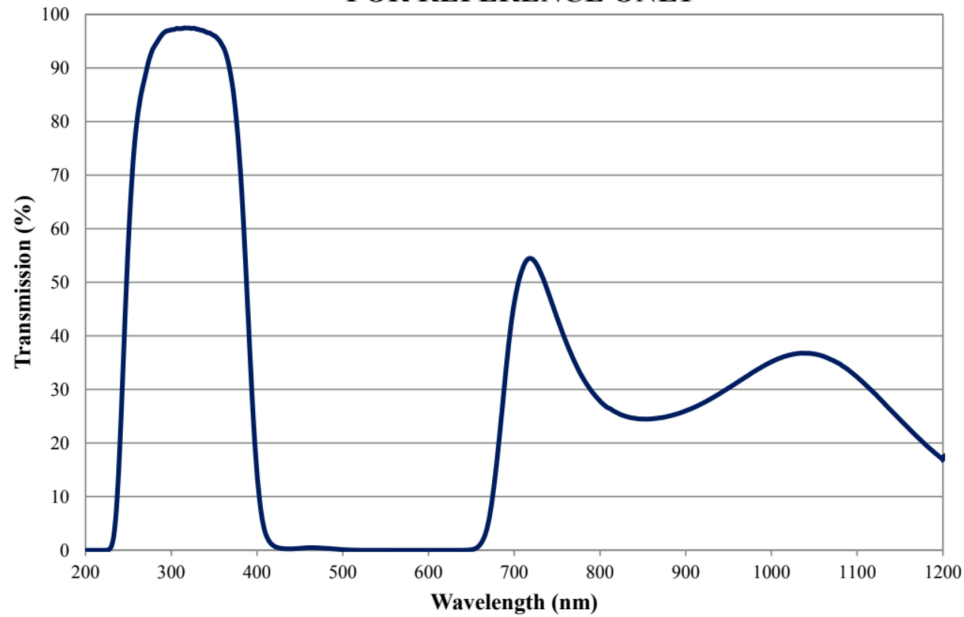


# Backup

## Coating Curve

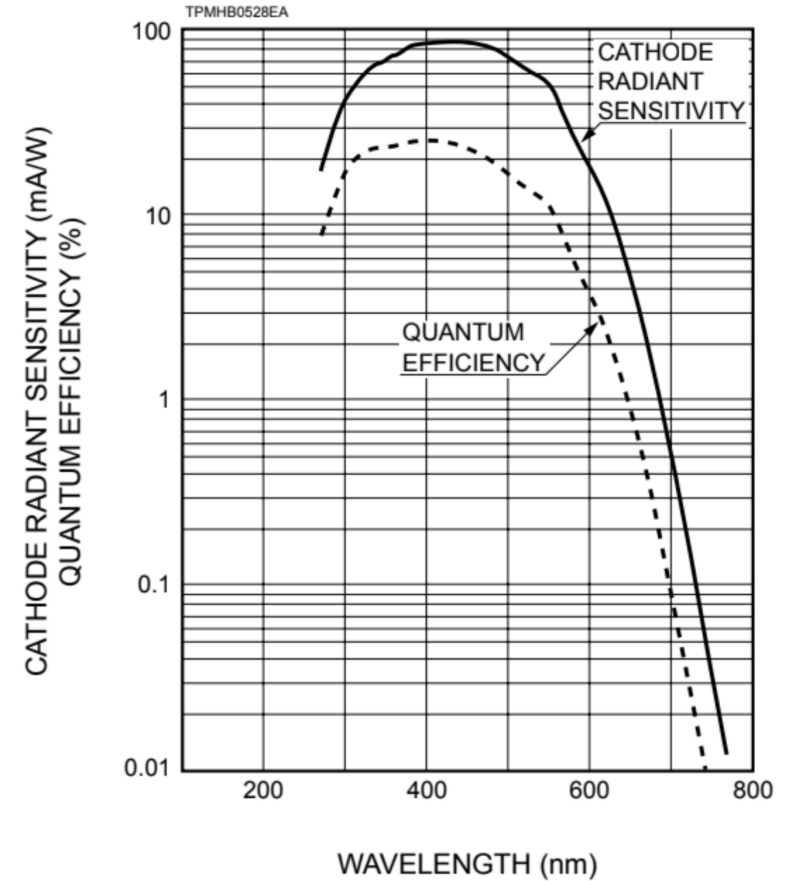
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U-330 Colored Glass Bandpass Filter Internal Transmittance  
2.5mm Thickness  
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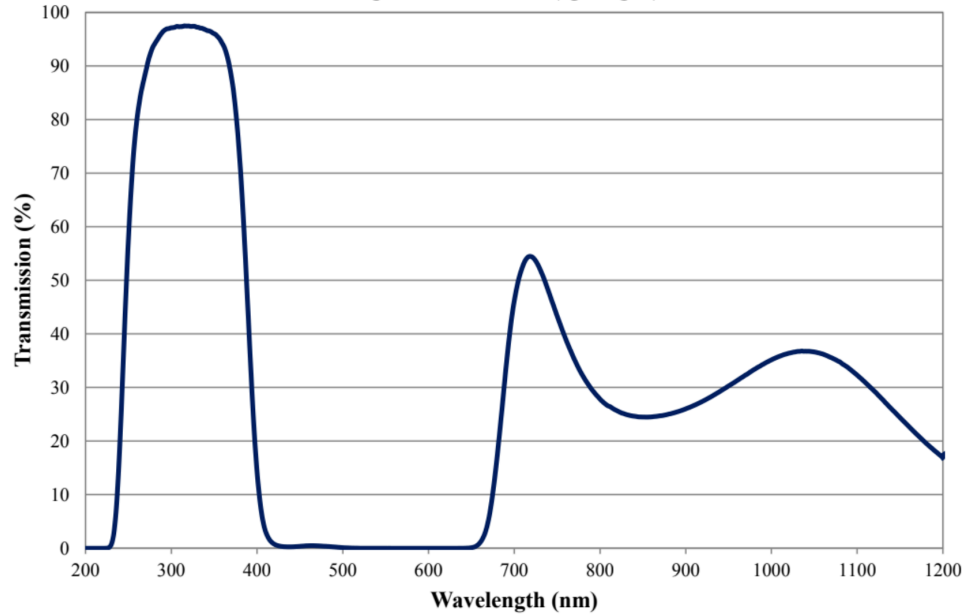


# Backup

## Coating Curve

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Figure 2: Typical Gain Characteristics

