International Workshop on Radiation Imaging Detectors — 23rd iWoRiD

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

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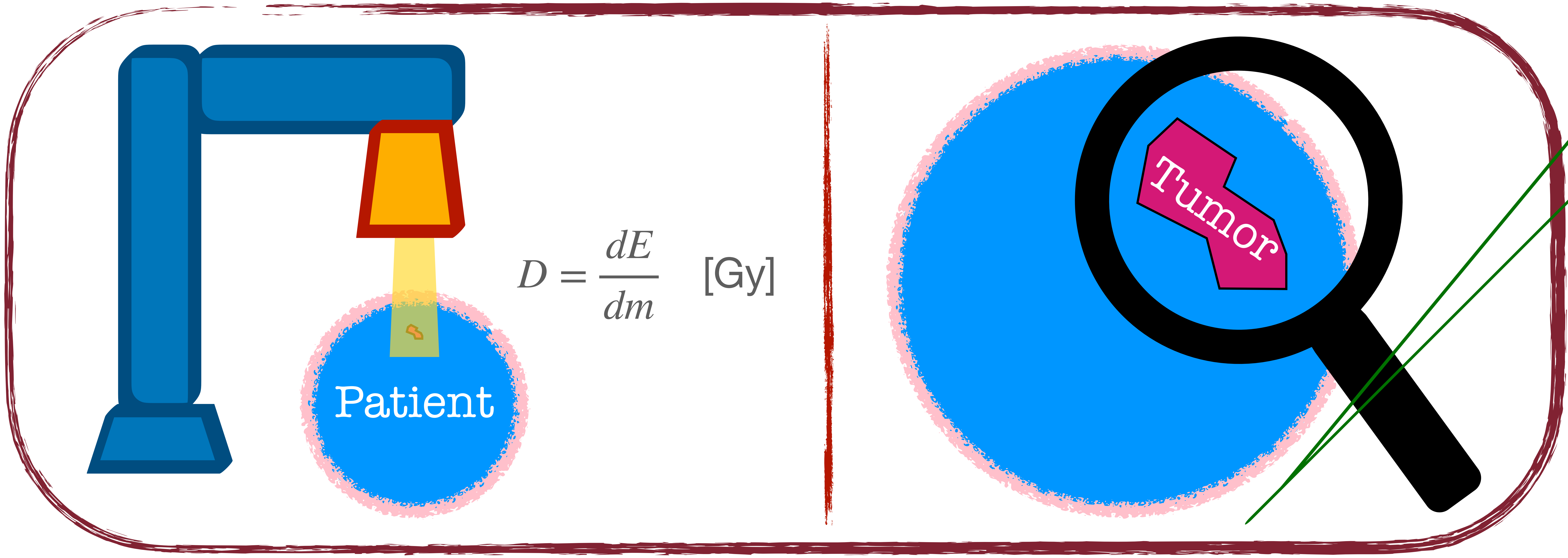
FLASH Radiotherapy with hIgh Dose-rate particle beAms

Sapienza Università di Roma — INFN — Centro Ricerche Enrico Fermi
Unione europea Fondo sociale europeo — Regione Lazio — 2014 2020 POR Programma Operativo Regione Lazio Fondo Sociale Europeo

Radiotherapy and Beam Monitoring



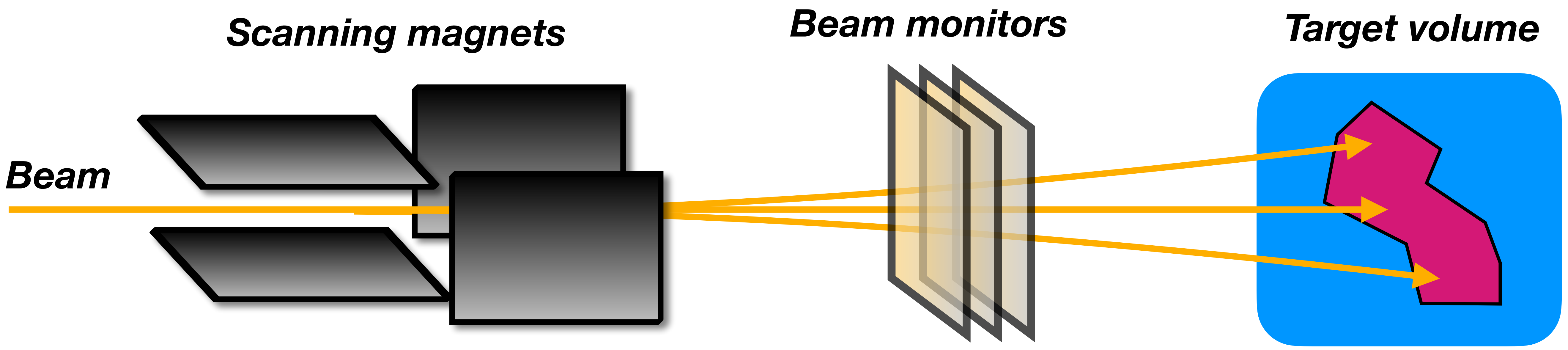
The key goal is to enhance the **therapeutic ratio**: **treatment efficacy** relative to **toxicity**.

Beam monitoring plays a crucial role in the various stages of planning and operation (commissioning, QA, **real-time** irradiation control…).

It is necessary to provide conclusive evidence on the optimal beam production and delivery strategies.

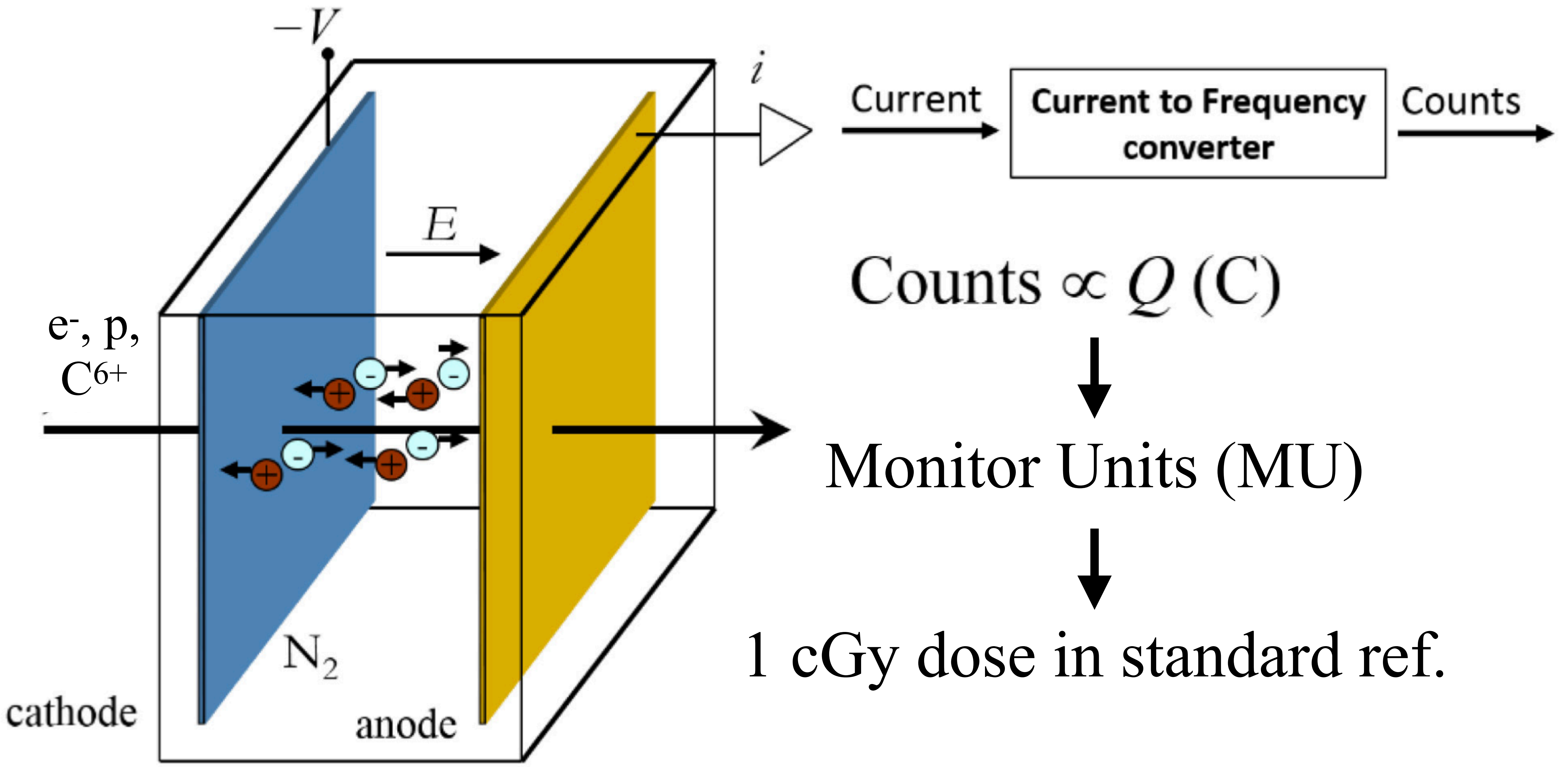
- **Therapeutical beam** (electrons, photons, light ions) release energy inside the human tissues — **dose** — following an optimized **treatment plan.**
- **Priority #1:** Spare healthy tissues surrounding the tumor — **Organs at Risk**.
- **Priority #2:** Maximize the damage to the tumor (control probability => avoid radio-resistance).

Radiotherapy and Beam Monitoring



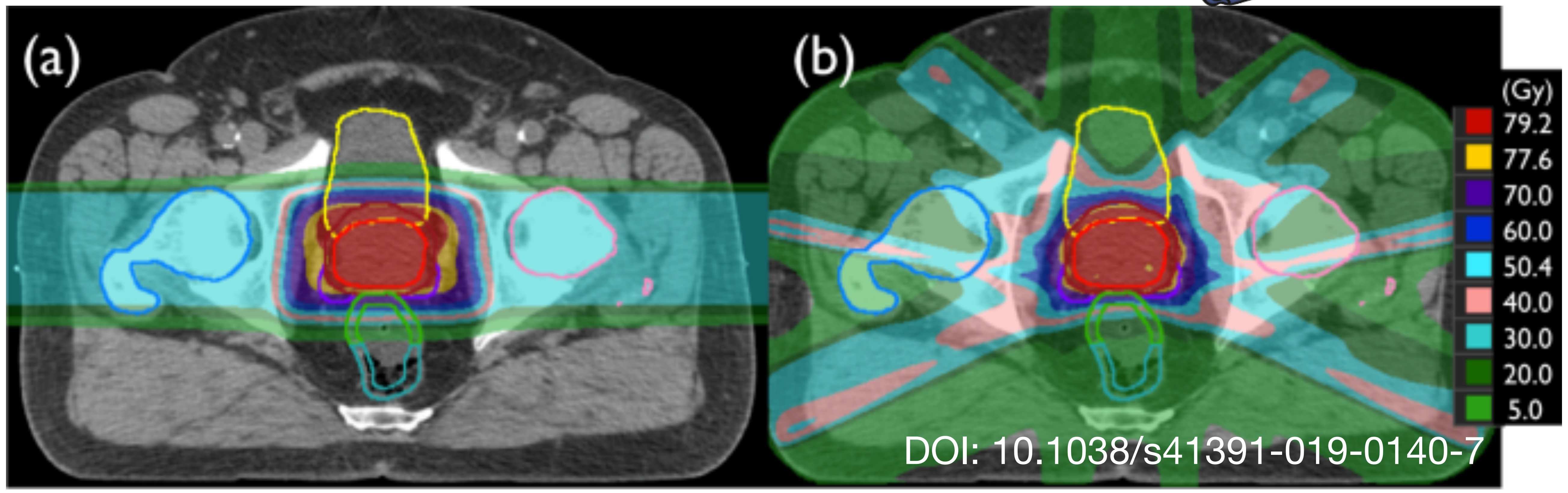
- In CONV-RT, the beam monitor system is a set of transmission ionization chambers, designed to measure **delivered dose**, dose-rate, beam flatness and symmetry and other additional parameters.
- The charge collected depends on the pressure and temperature of the gas, as well as on the voltage across the gap, and requires a dedicated calibration.
- To avoid sensitivity changes from fluctuations of *P* and *T*, chambers may be sealed or vented.

- ICs are easy to build and operate, and show no indication of performance degradation due to aging effects.
- They are thin and use low-*Z* materials to minimize interferences with the beam.



Radiotherapy and Beam Monitoring

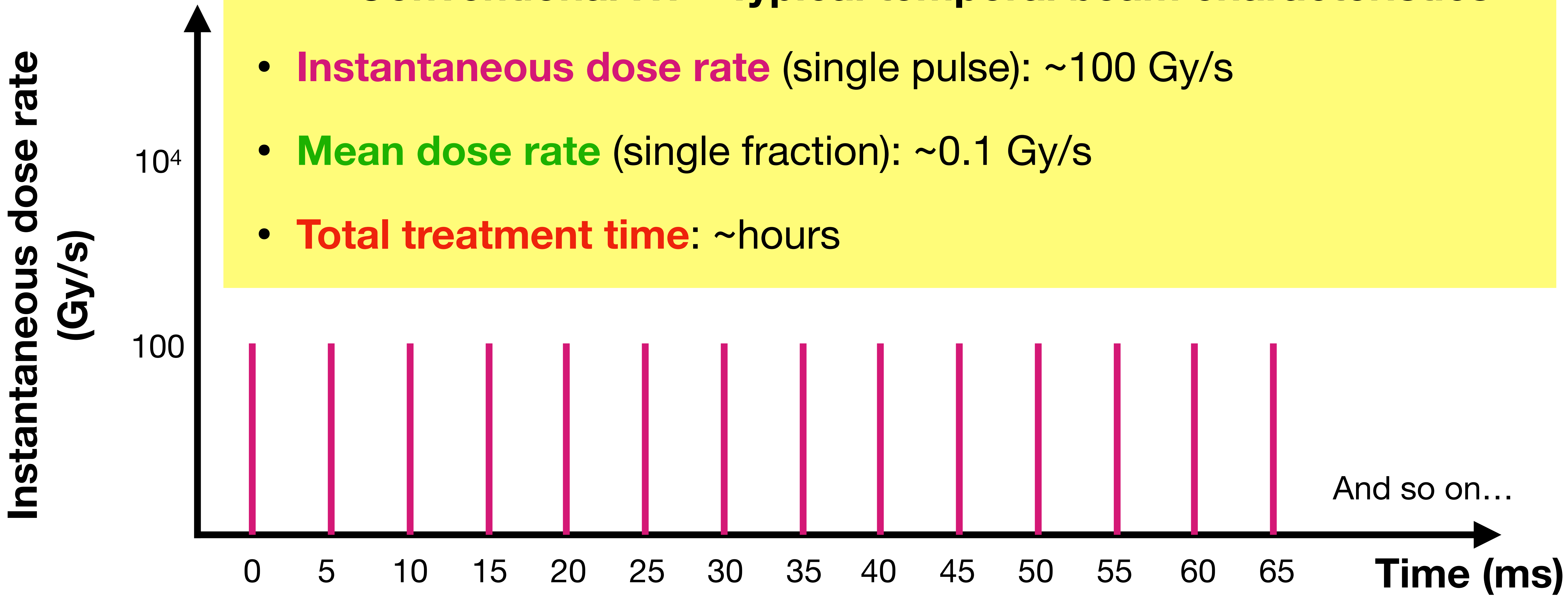
- Over the past decades, research has focused on increasing **spatial conformity** of the dose to the tumor volume
  - **(a)** Particle Therapy (protons and light ions)
  - **(b)** Multiple fields at different energies



- What about **<u>time</u>**? 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

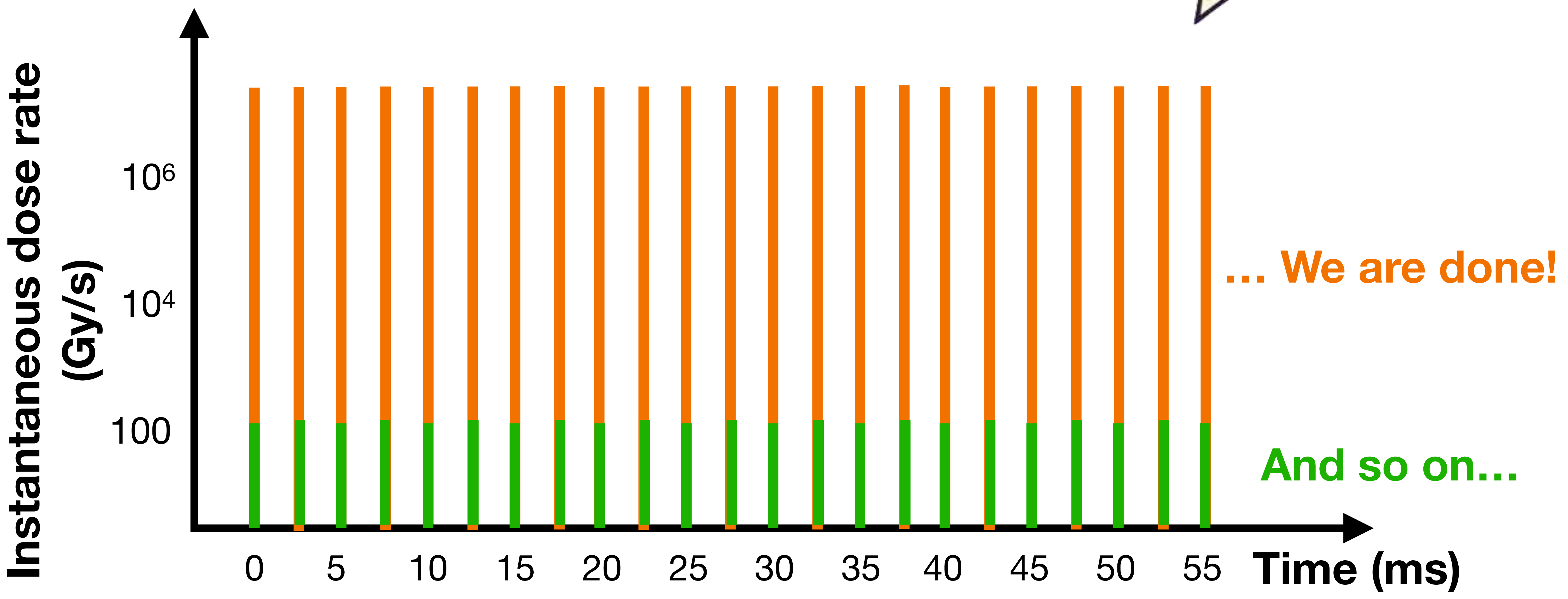
- **Instantaneous dose rate** (single pulse): ~100 Gy/s
- **Mean dose rate** (single fraction): ~0.1 Gy/s
- **Total treatment time**: ~hours



FLASH effect

- Recently, a new approach has gained great attention, to the point of being considered the next paradigm in the future of RT.
- 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.
- New accelerators (i.e. for IOeRT) are entering commissioning and operation, new theories are emerging awaiting validation…

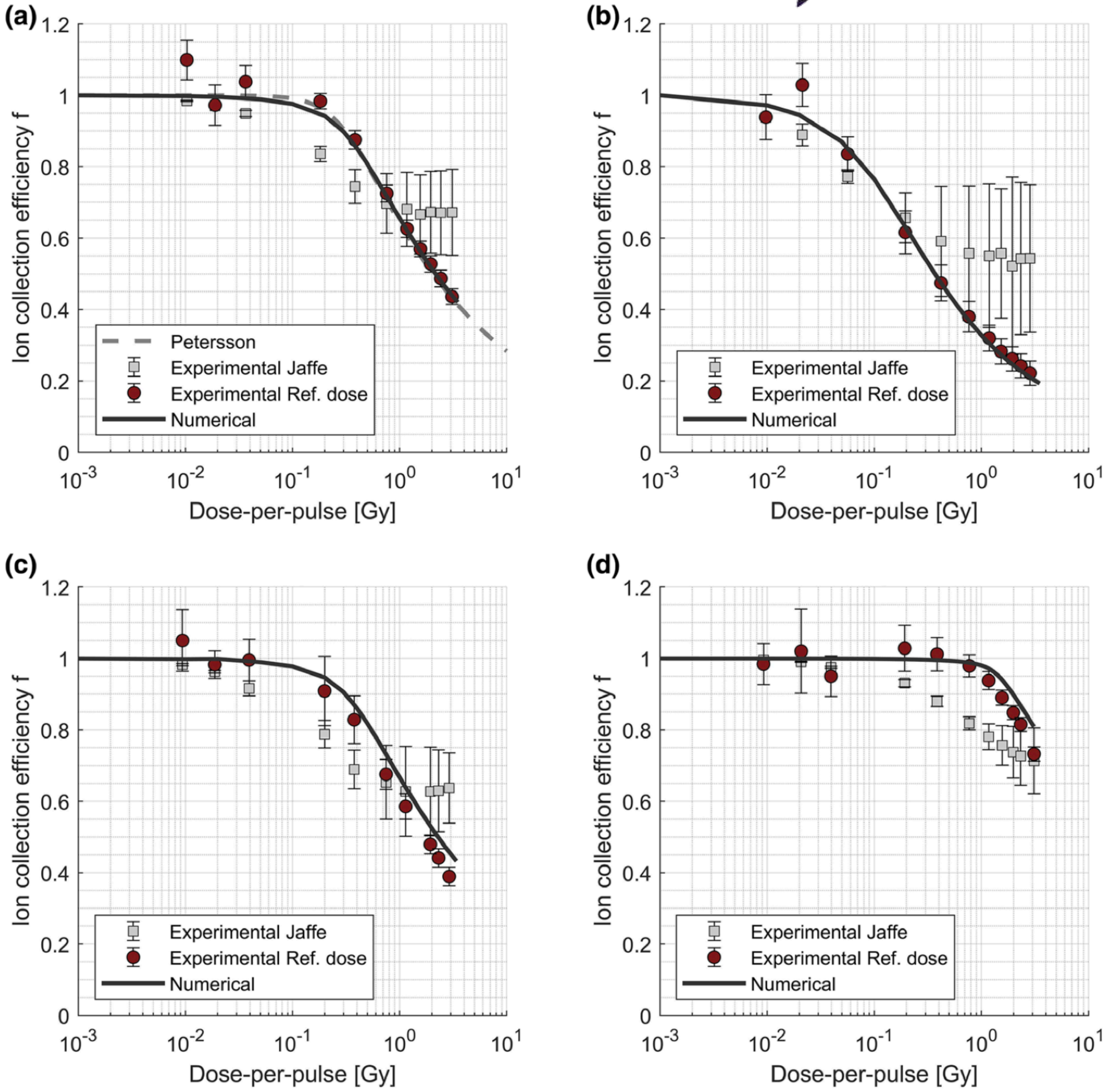
J. Wilson, et al., Ultra-high dose rate (FLASH) radiotherapy: Silver bullet or fool's gold?, Front. Oncol. 9:1563 (2020). doi:10.3389/fonc.2019.01563



Beam characteristics	CONV	FLASH
Dose per pulse	~ 0.4 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 treatment time	~ hours	< 100 ms

Beam Monitoring vs FLASH effect

- Beam monitoring is a cornerstone of this research, that must provide the reliable assessment of the (sometimes extreme) beam parameters.
- Problem is, BM can be hardly operated in FLASH environment. ICs undergo substantial energy dependencies due to **volume recombination**.
- (There are attempts to characterize this saturation effect by introducing correction factors.)



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

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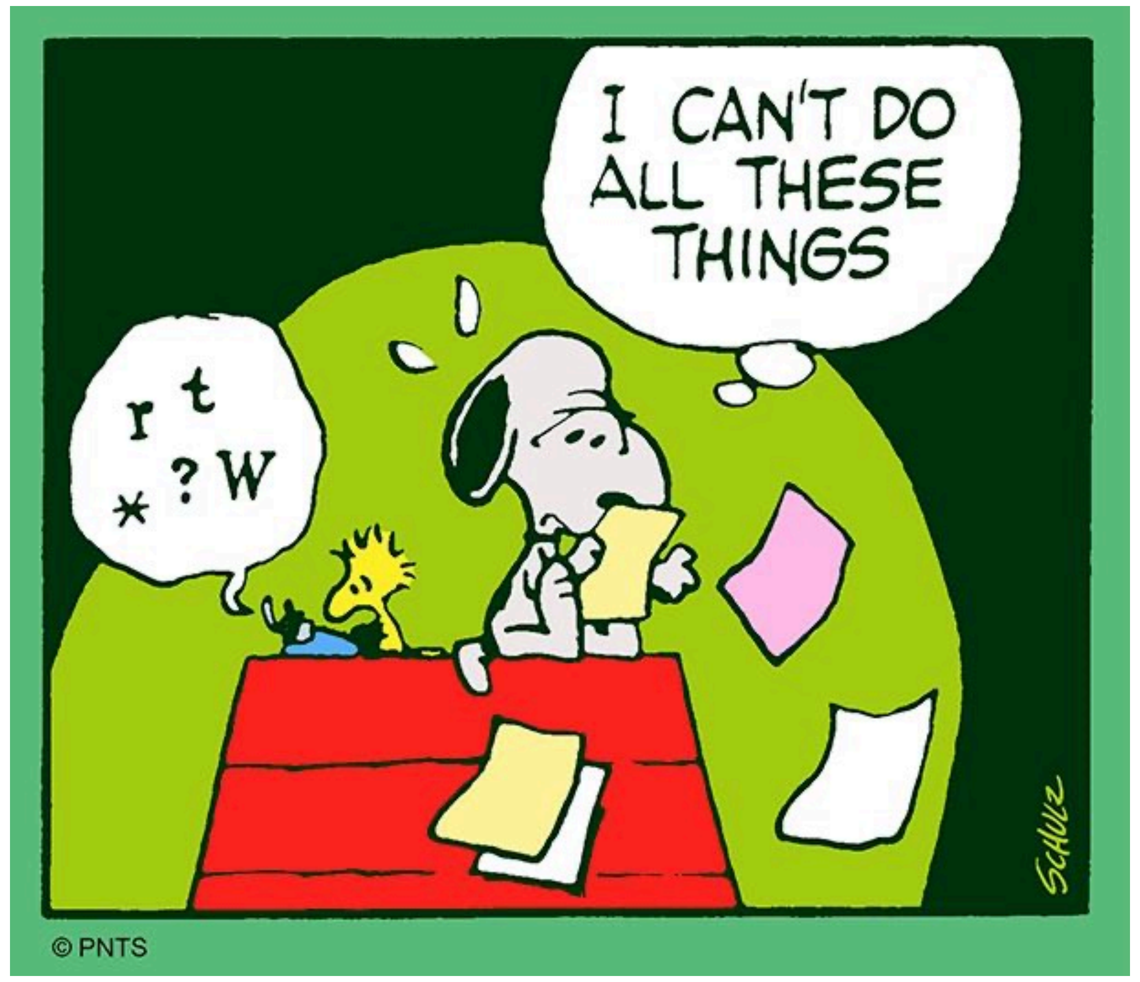
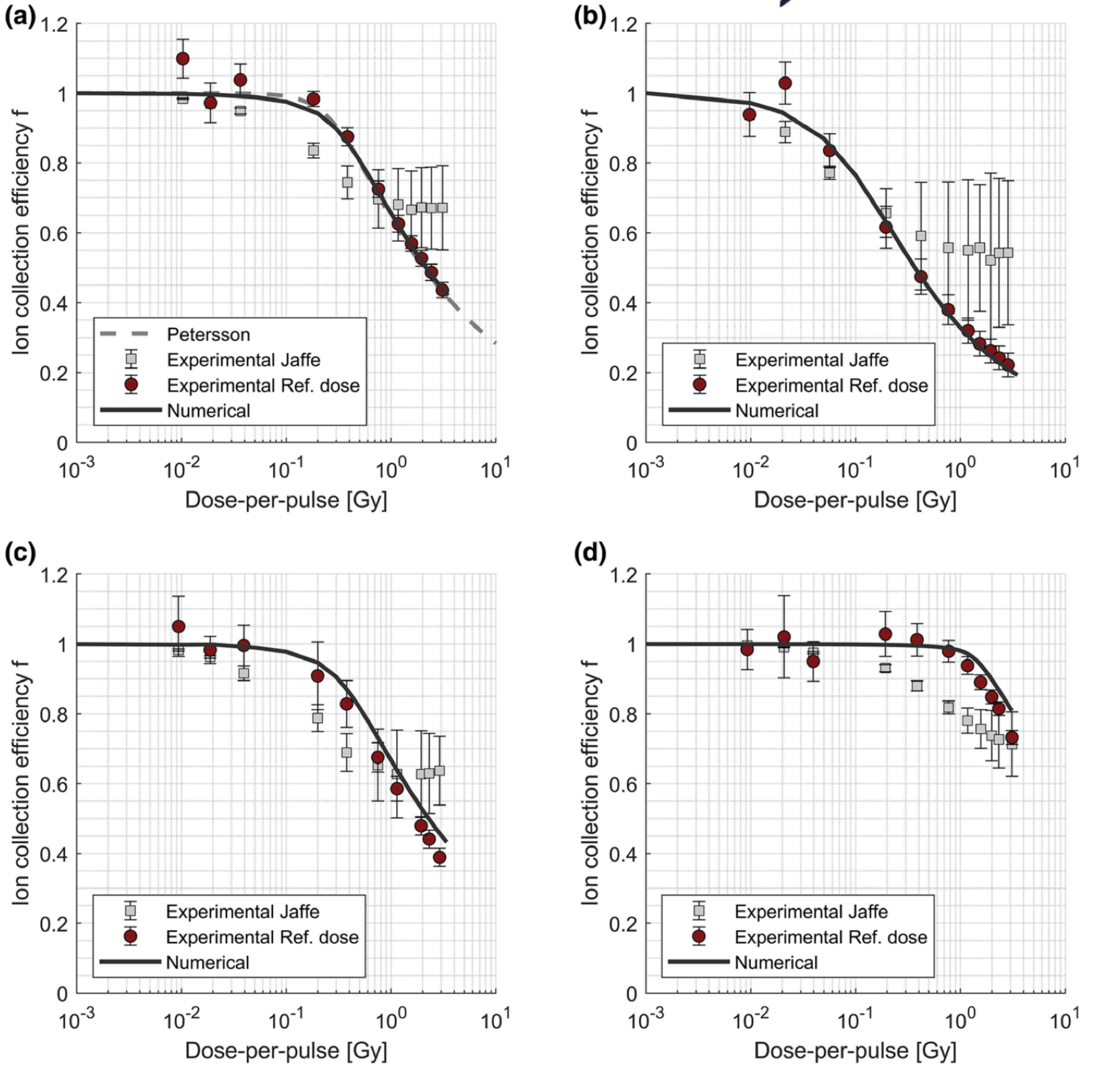
- Problem is, BM can be hardly operated in FLASH environment. ICs undergo substantial energy dependencies due to **volume recombination**.
- (There are attempts to characterize this saturation effect by introducing correction factors.)
- Moreover, ICs require <u>tens of μs</u> (30-300 μs for 0.5-5 mm air gap) to collect the charges, too slow to monitor FLASH beams (tens of Gy in a few μs).
- This is a limitation for FLASH experimental studies, that span **inst. dose-rates** from 10^3 up to 10^7 Gy/s (eventually reaching the whole prescribed dose in a single pulse).





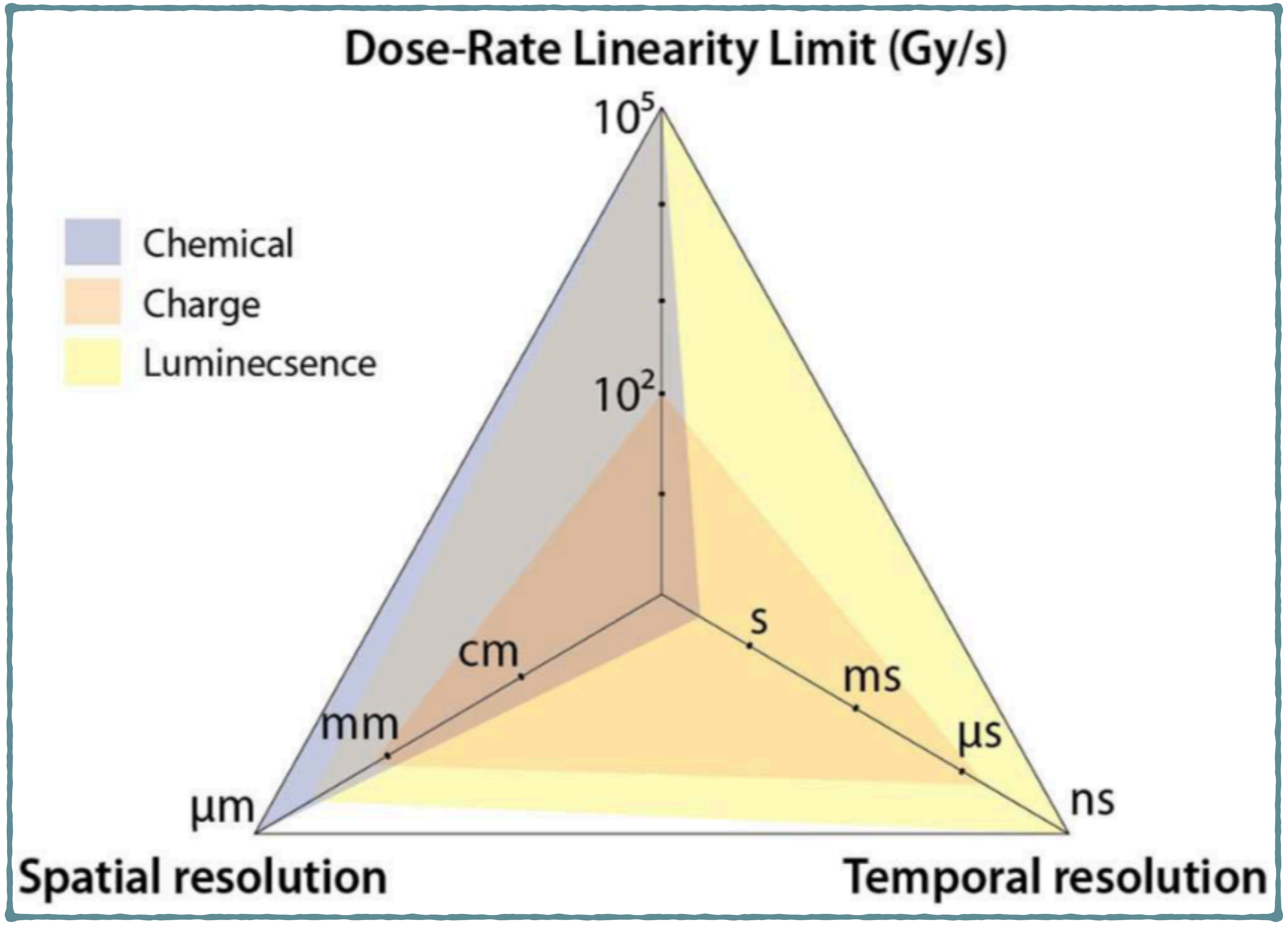
Ion collection efficiency for the ionization chambers with a polarizing voltage of 300 V. **(a)** Advanced Markus, **(b)** EWC2, **(c)** EWC1, **(d)** EWC05. doi: 10.1002/mp.14620

FLASH beam monitoring

- 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 (both for pre-clinical studies and in the perspective of clinical implementation).

- Most importantly, monitor **the rate of impinging particles per pulse** (real-time, position by position).

- The "perfect device" should have:
  - ☆ Dose Rate Linearity (up to 10^6 Gy/s)
  - ☆ Spatial Resolution (~ mm)
  - ☆ Temporal Resolution (< 1µs)
  - ☐ **Real-time** beam monitoring
  - ☐ Avoid **energy dependence**



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

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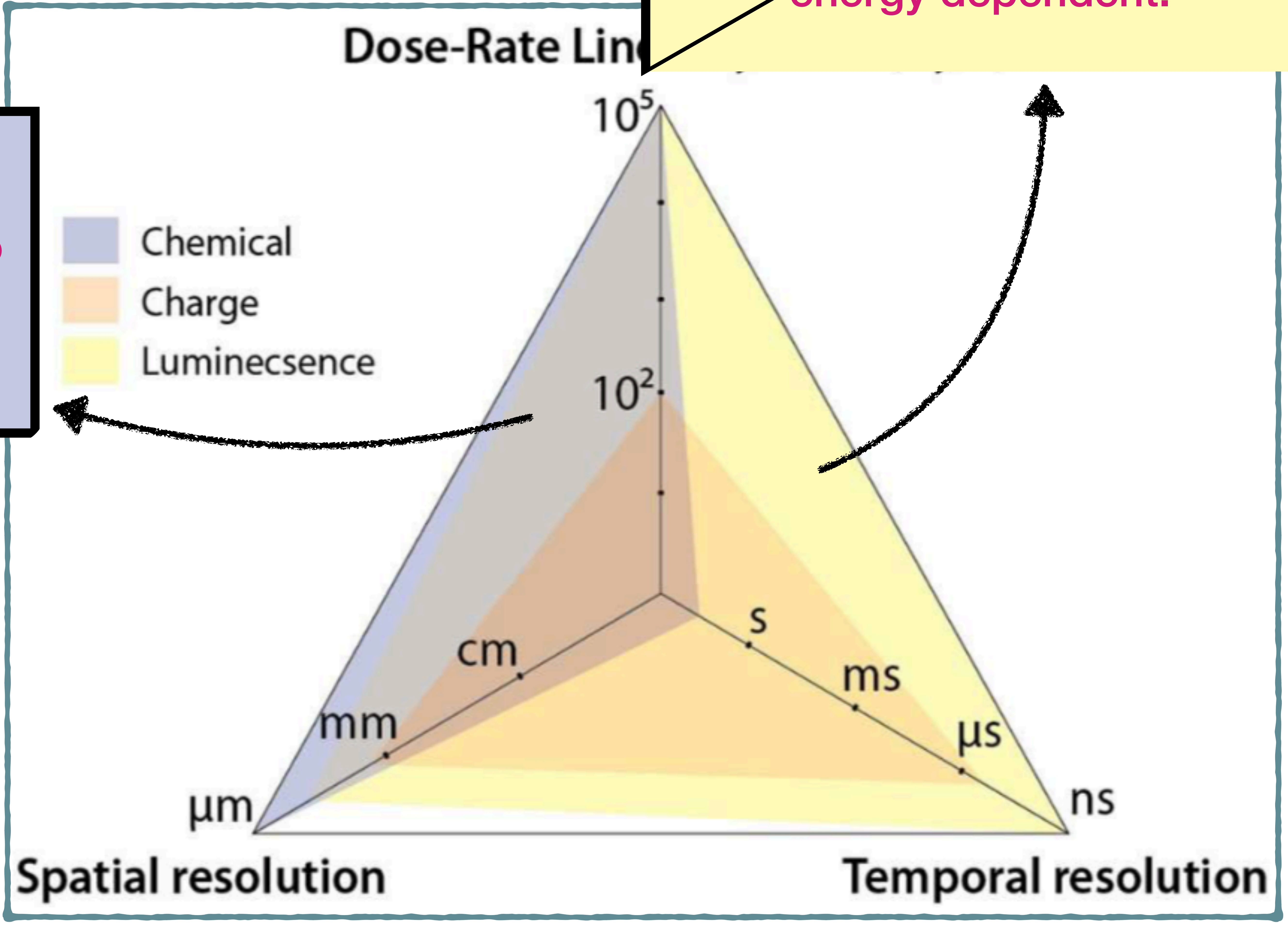
  - ☆ Temporal Resolution (< 1μs)
  - ☐ **Real-time** beam monitoring
  - ☐ Avoid **energy dependence**

Radiochromic films: Tissue equivalent, independent up to 10^9 Gy/s but only useful as passive detectors

Cherenkov detectors: best temporal resolution and independent up to 10^6 Gy/s but energy dependent.



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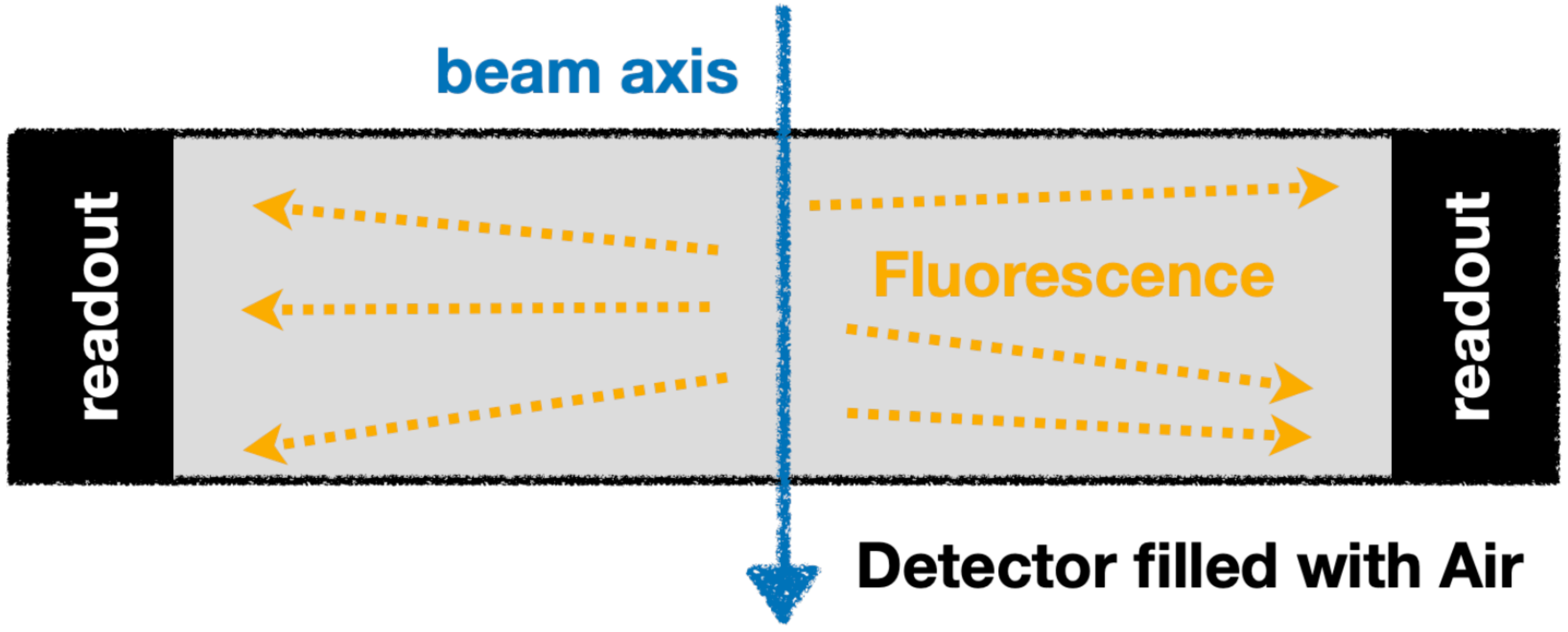
Fluorescence for FLASH BM

- **Fluorescence** is the emission of light from an excited atom or molecule, with a lifetime of the excited state **~ 10 ns**. It is already used to detect extensive air showers in atmosphere.

- In air, fluorescence occurs on nitrogen molecules excited via electron impact.

- Conceptually, a fluorescence based BM would require a **box filled with air**, with walls of thin black mylar and a photon readout at the end.

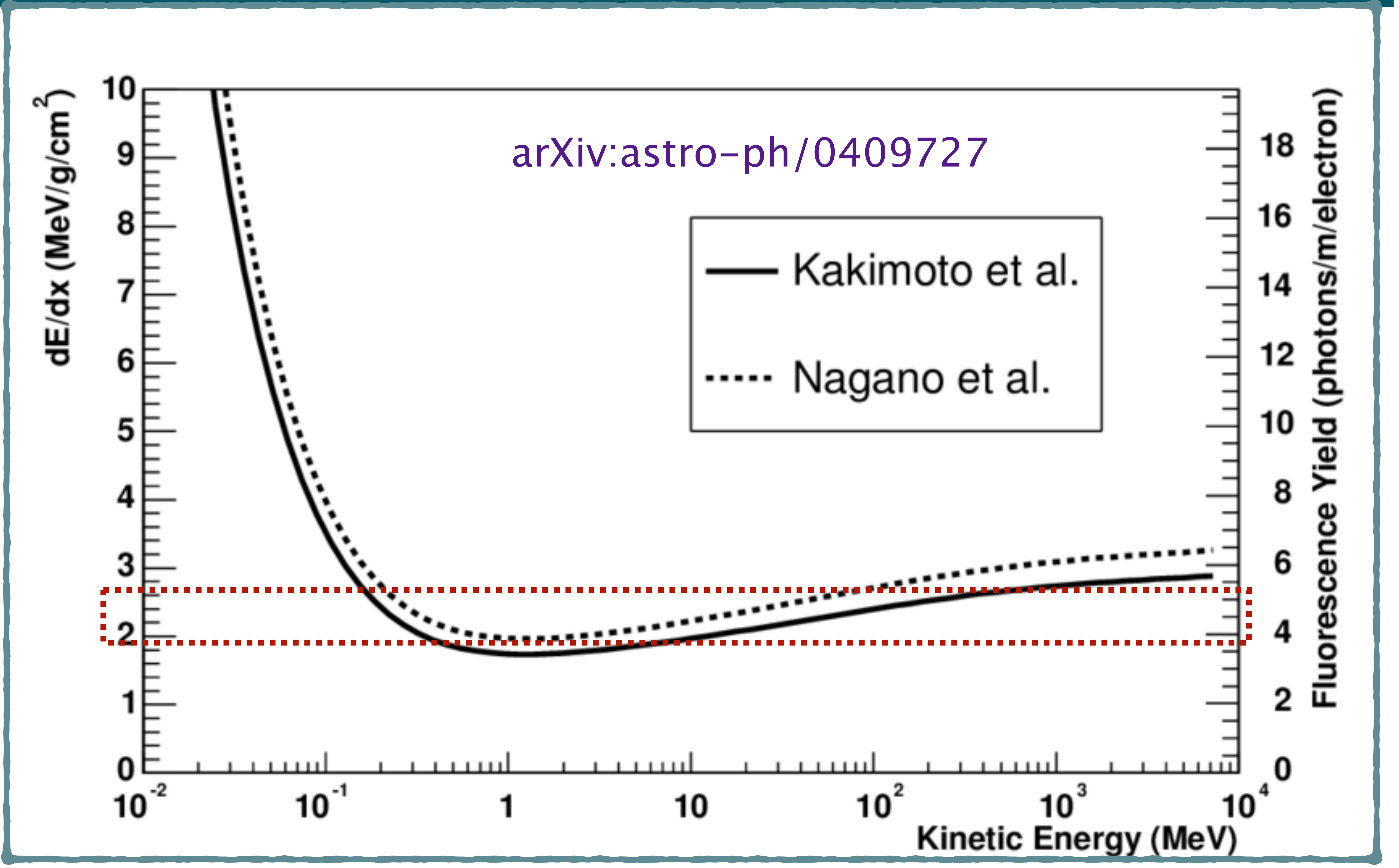
- Fluorescence has been rarely, if ever, exploited for BM purposes; it is thus a rather open field for research.



* Ultra High Energy Electrons

Fluorescence for FLASH BM

- It has been proven that the rate of molecular excitation is **proportional** to the deposited energy.
  - Fluorescence Yield (ph./m) ∝ *dE/dx*
- In a wide kinetic energy range (10-1000 MeV), of interest for CONV-RT and to UHEE* future applications, the photon yield is nearly constant (**4 ph./m**, ~1000 times less than organic scintillators).
- The detector would measure a photon signal directly proportional to the instantaneous dose-rate unaffected by energy dependence and with minimal risk of saturation at high intensity.



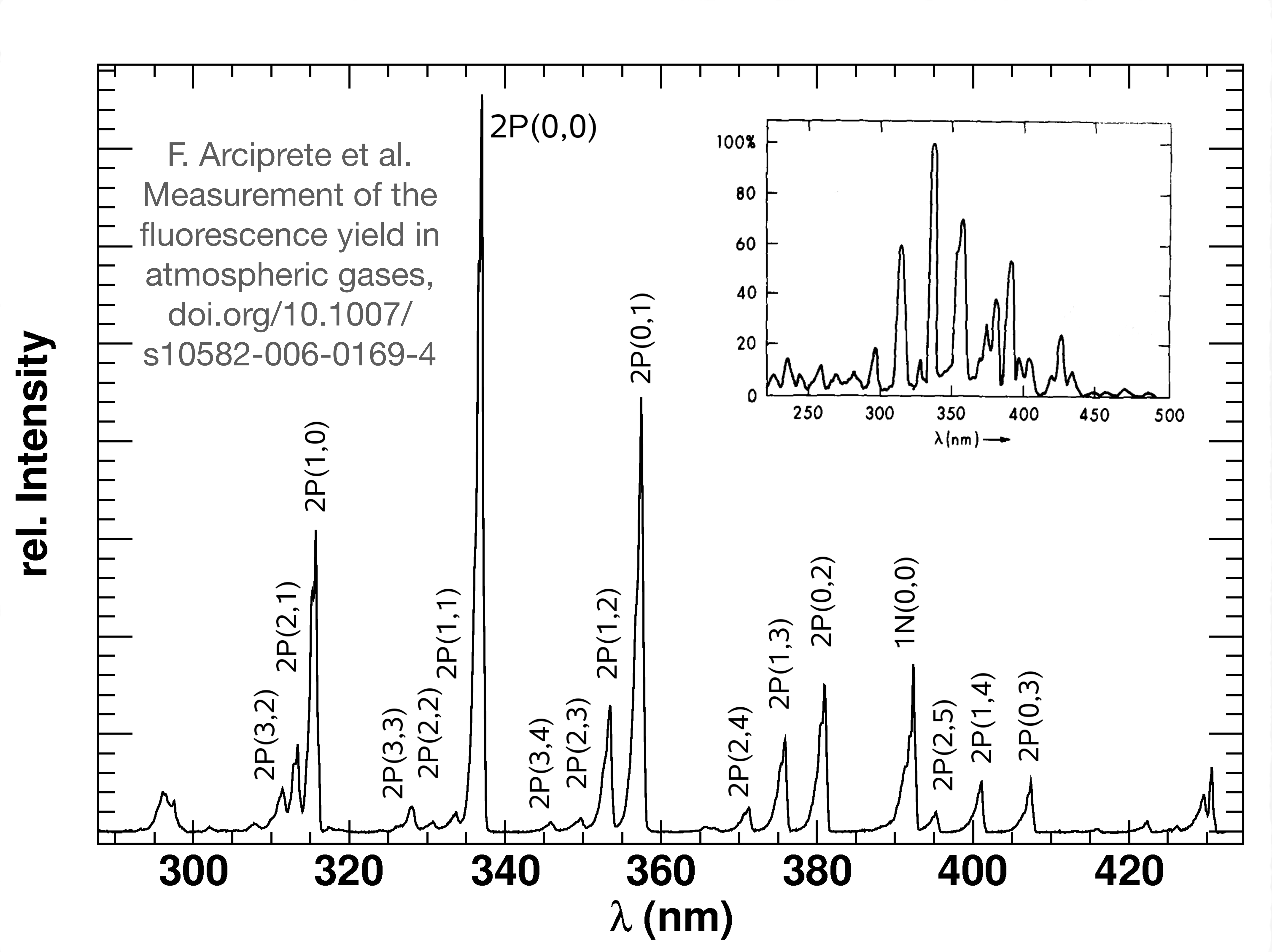
- Fluorescence yield ≈ 4 ph./m
- dE/dx ~ 2,25 MeV cm²/g
- dN/dE ≈ 15 ph./MeV

* Ultra High Energy Electrons

Fluorescence for FLASH BM

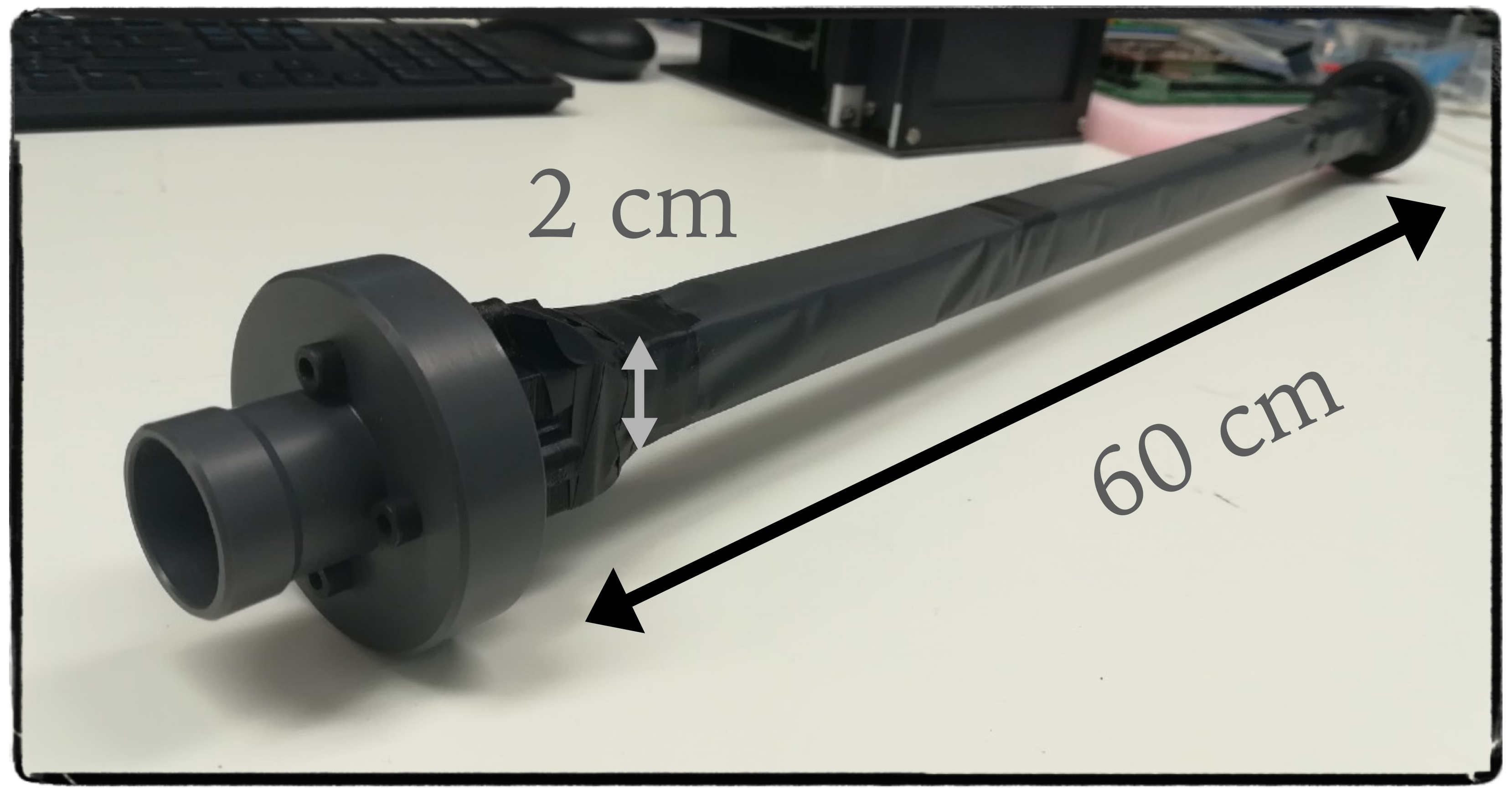
- The wavelength spectrum is known, and fits nicely with the response of standard photosensors.
- Pressure and temperature dependencies, as well as the impact of different percentages of quenching elements, are present in literature, and can be accounted for with detector calibration.
- **Appealing features**:
  - ☑ No energy threshold
  - ☑ Photons emitted isotropically
  - ☑ Fast signal ~ns
  - ☑ Simple and cheap to produce
  - ☑ **Minimal impact** on the irradiation of the patient

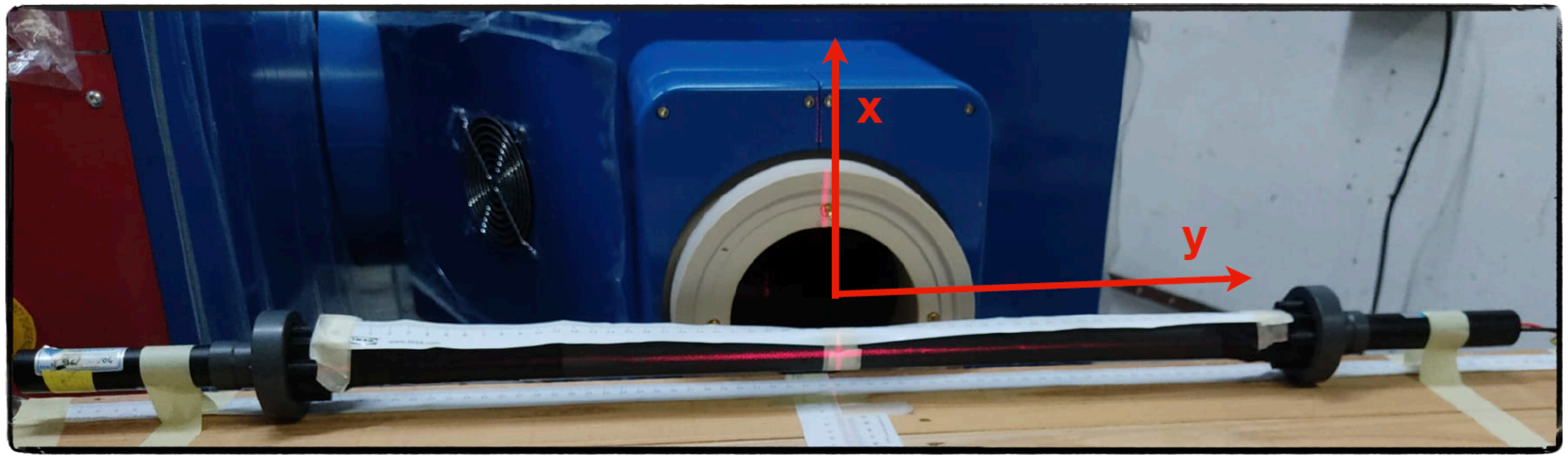
Figure 2.8: Fluorescence spectrum of air between 280 nm and 430 nm recorded by AIRFLY with transition labels. The gas was excited by 3 MeV electrons at a pressure of 800 hPa. In the right upper corner, the spectrum reported by Bunner (1967) is shown [15].



The FlashDC project

- Ok… does it work??
  Objective: develop a monitor for FLASH-RT capable to simultaneously provide online the instantaneous rate of impinging particles per pulse and beam position.





- We built several prototypes for proof-of-principle studies and verify the degree of accuracy that can be reached with this technique.
- The one shown consists of a volume of air (**2x2x60 cm³**) enclosed by a ~5 μm thick layer of **black** mylar, with a PVC supporting structure (not crossed by the beam) and PMTs on the two opposite edges.
- Preliminary measurements have been performed at S.I.T. Sordina (Aprilia, Italy) with the **LIAC HWL** and the **ElectronFlash**.

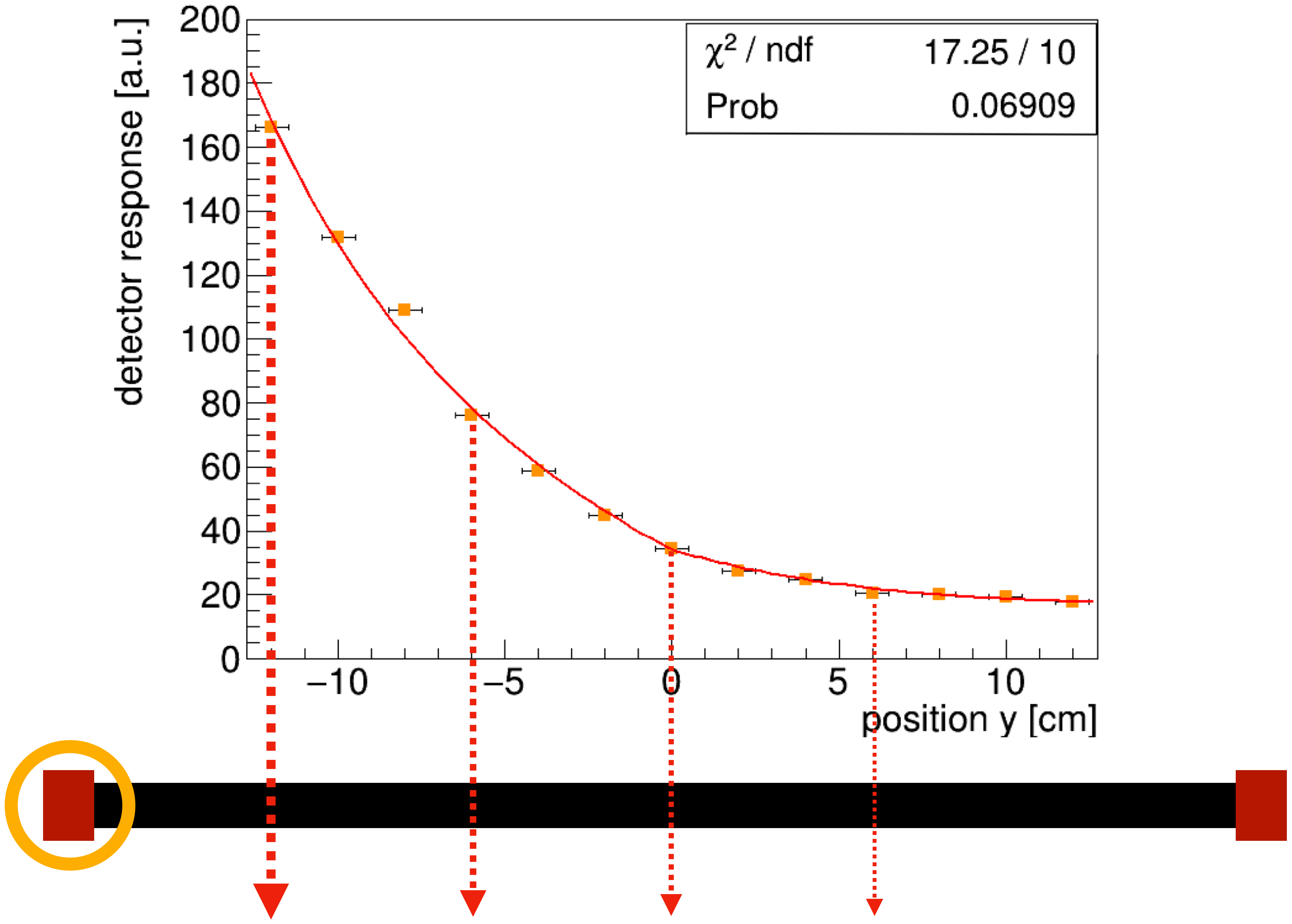
The FlashDC project

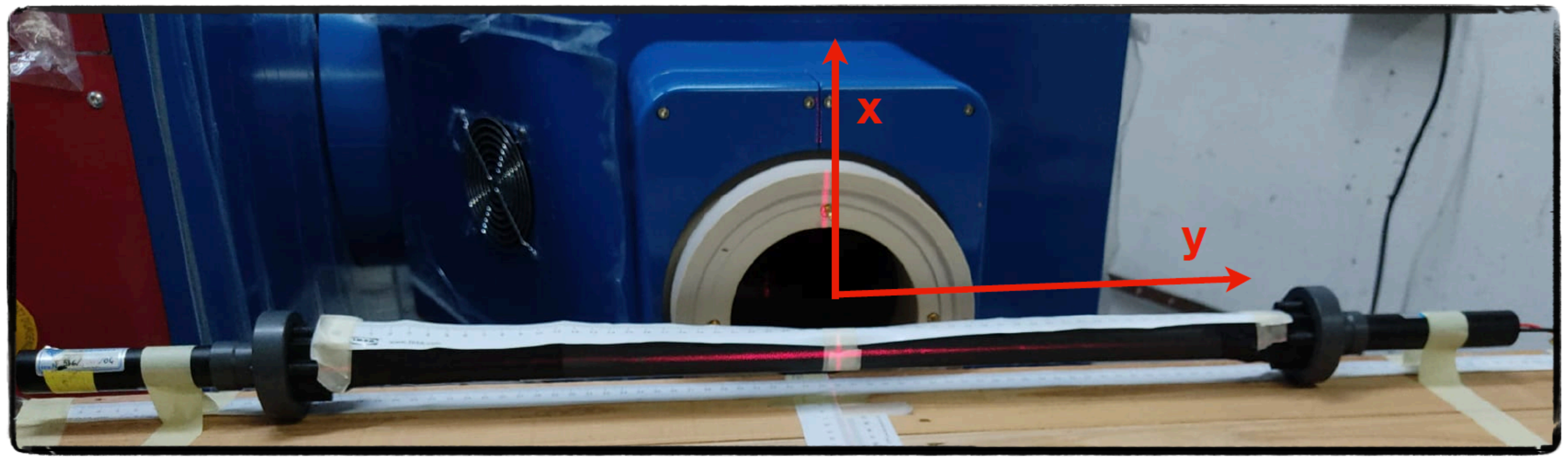
- **LIAC HWL**: 10^{10} electrons/pulse.
- Electron energy at the linac exit: 6MeV.
- Frequency: 10Hz.
- Design dose rate: 10÷30 Gy/min.
- **Field spread: ~1cm.**
- Mobile head: useful to test sensitivity to beam position.

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

Detector response - *y* axis

We studied the detector response as a function of the position (along the *x* and *y* directions), and intensity (beam current).



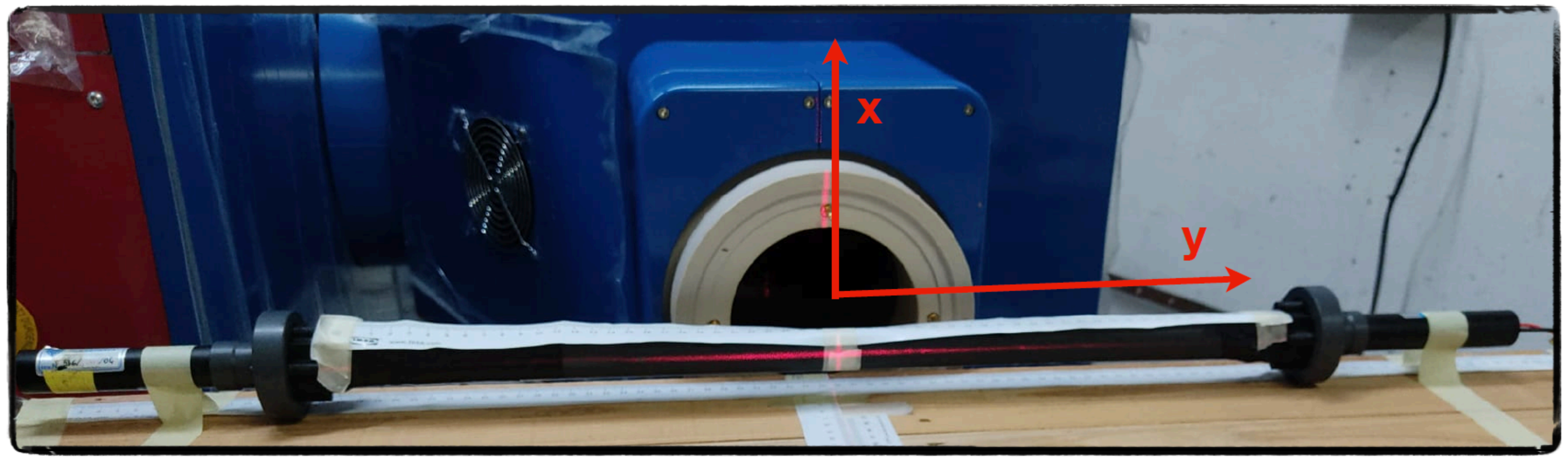


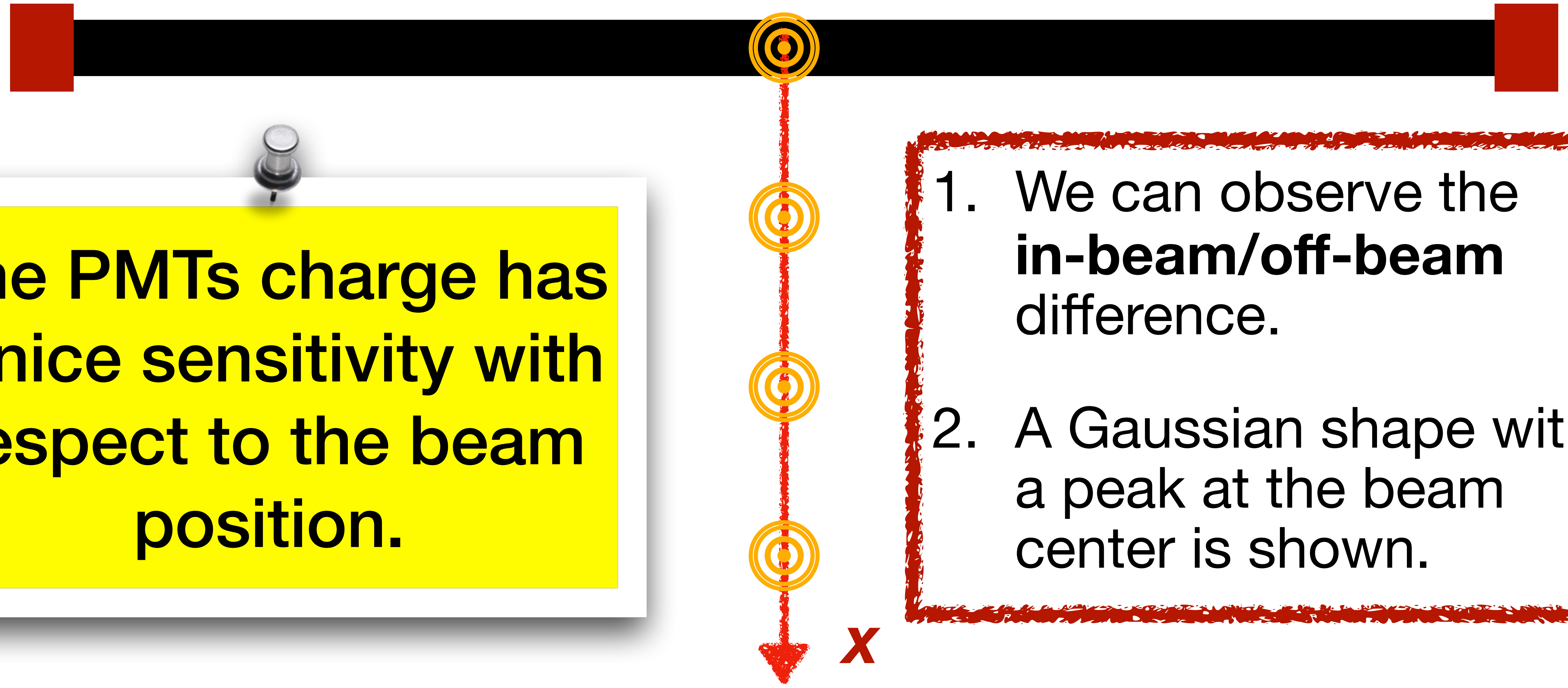
- The detector was initially positioned at distance 2 cm from the machine beam exit window.
- The beam entrance has been moved along the detector axis. The response is function of the solid angle (~$1/y^2$), as expected.
- Data taken with LIAC HWL accelerator (6 MeV). Beam size ~1 cm.

Beam transverse size monitoring

We studied the detector response as a function of the position (along the *x* and *y* directions), and intensity (beam current).

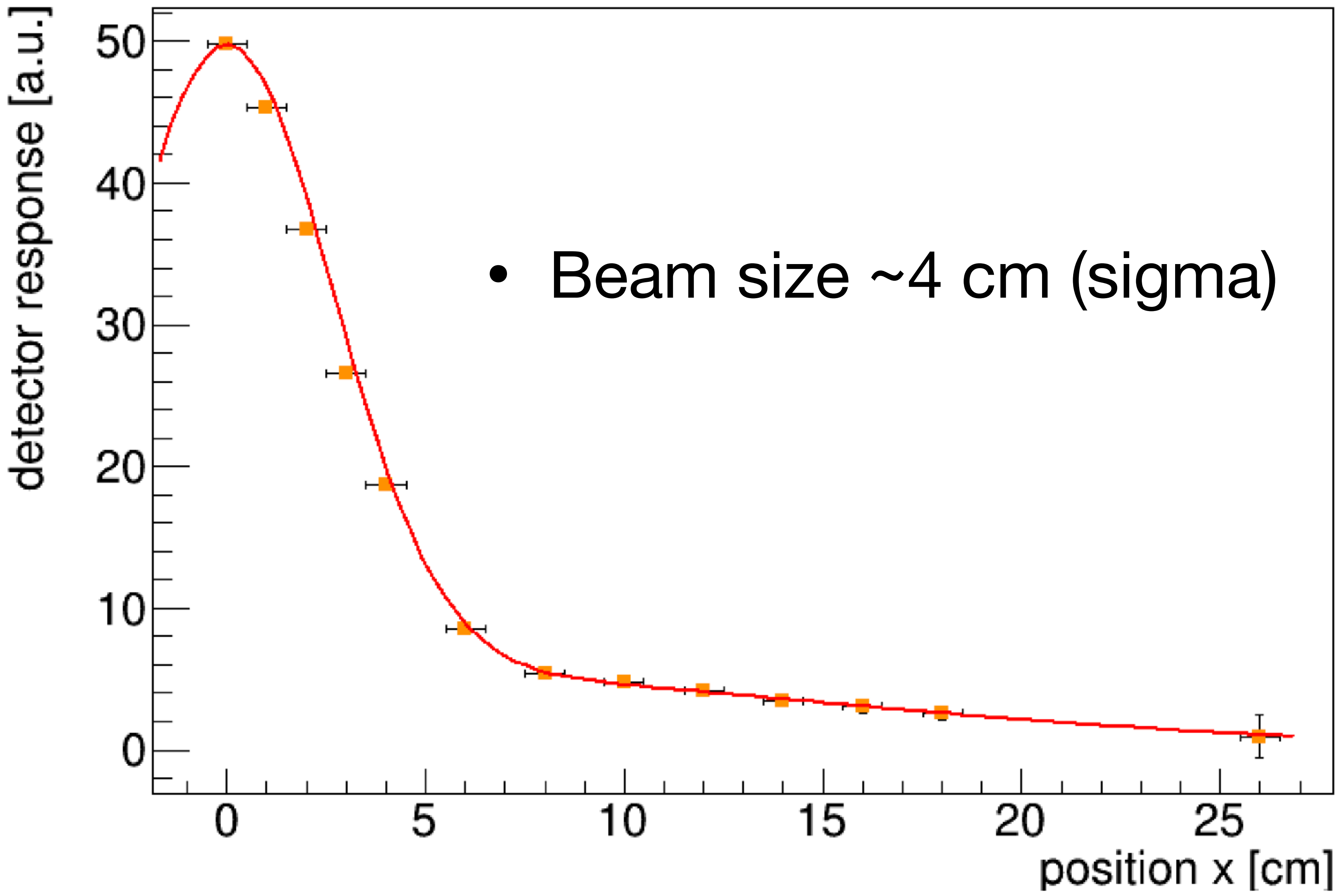
- The detector was initially positioned at distance 2.5 cm from the machine beam exit window.
- It was then gradually moved off the beam to reconstruct the transverse shape.





The PMTs charge has a nice sensitivity with respect to the beam position.

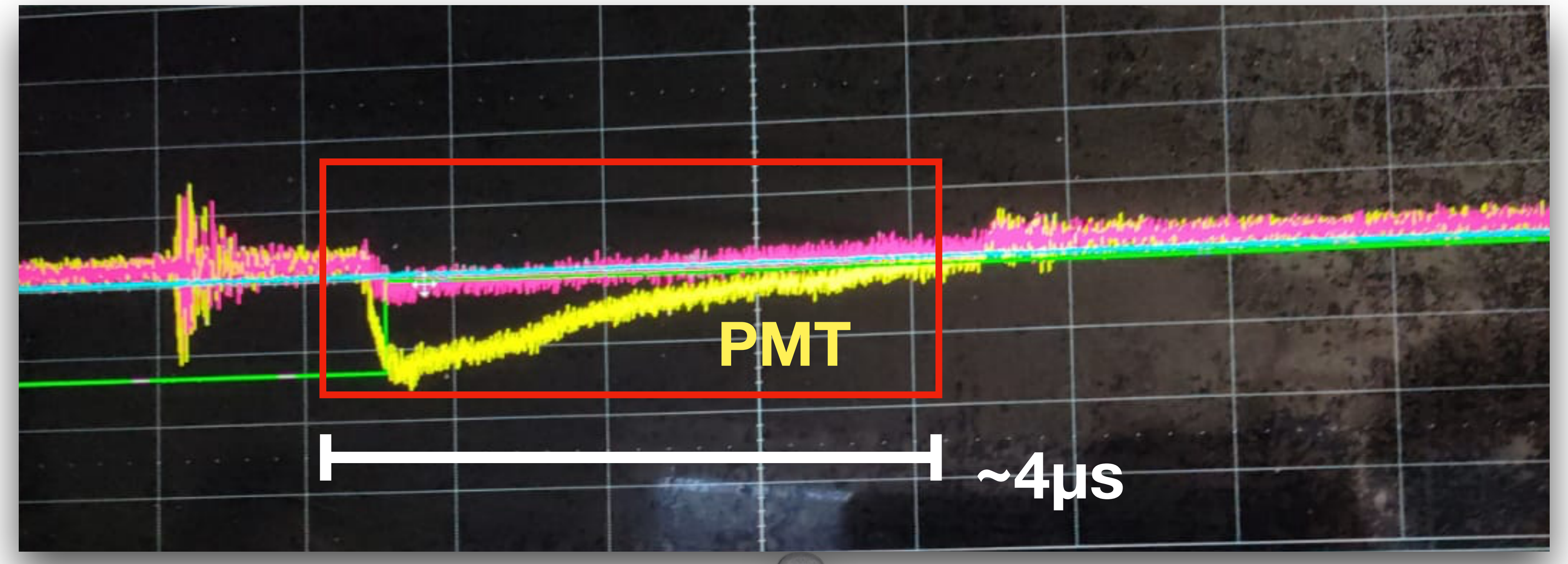
1. We can observe the **in-beam/off-beam** difference.
2. A Gaussian shape with a peak at the beam center is shown.

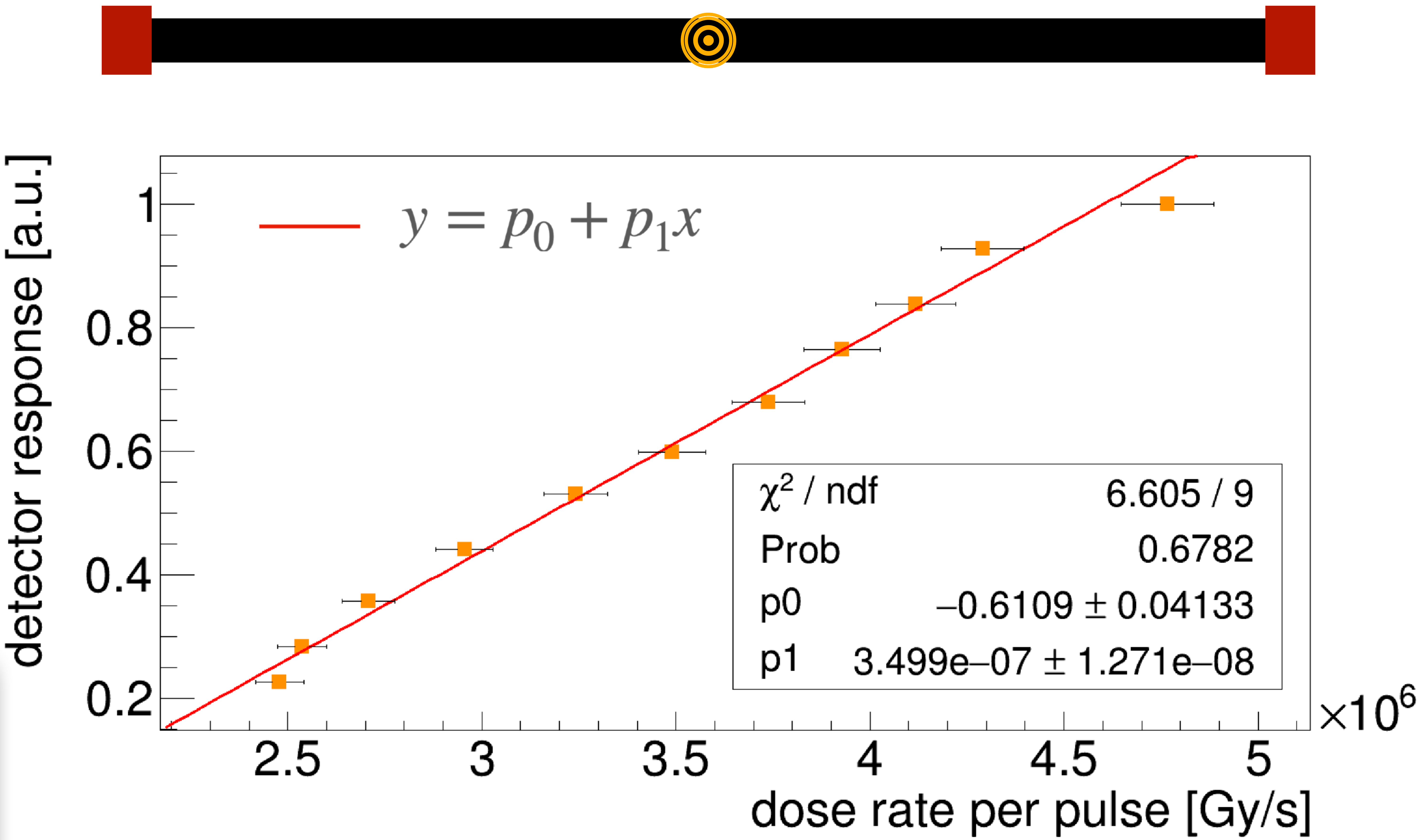


BM response vs beam current

We studied the detector response as a function of the position (along the *x* and *y* directions), and intensity (beam current).

- The beam current is an adjustable parameter proportional to the instantaneous dose rate. The ElectronFlash can deliver pulsed beams of electrons with peak energy 7 MeV, in the range 60-130 mA, with a fixed pulse duration of 4μs.





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

Conclusions

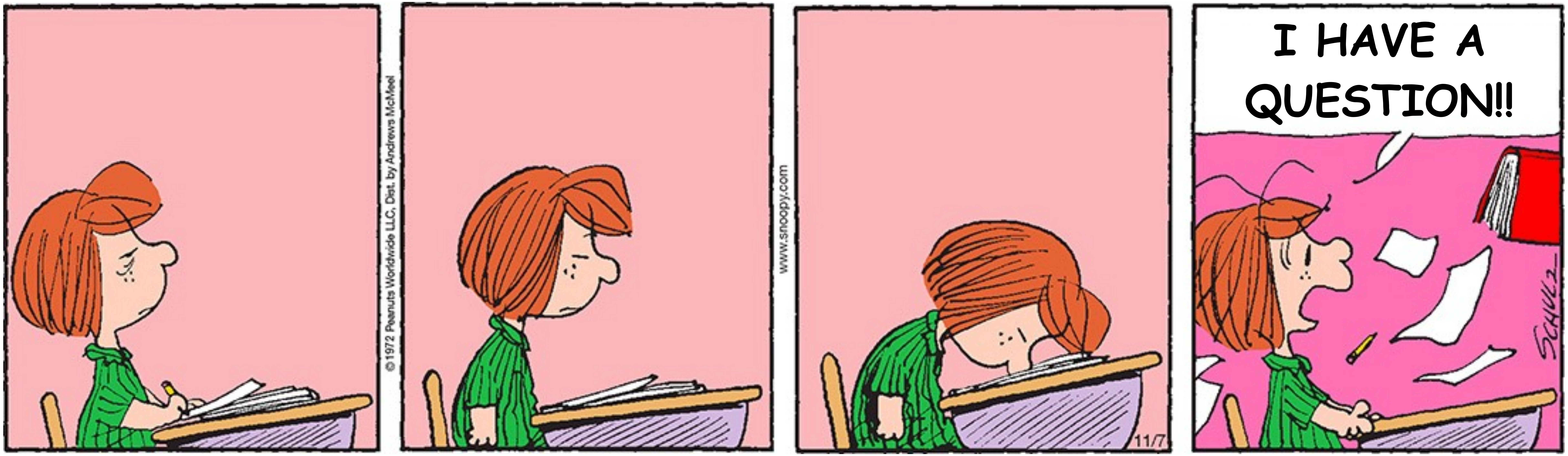
The PMTs charge has a nice sensitivity with respect to the beam position.

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

- A set of preliminary measurements with FLASH electron beams has given promising results on the feasibility and the performances of a fluorescence-based BM.
- With the help of a FLUKA-MC simulation, we are starting to imagine the final device, optimized for BM in 2D.
- Another round of tests, taking advantage of a high intensity strongly-focused beam, is planned for final months of 2022 (new detector in 2023).

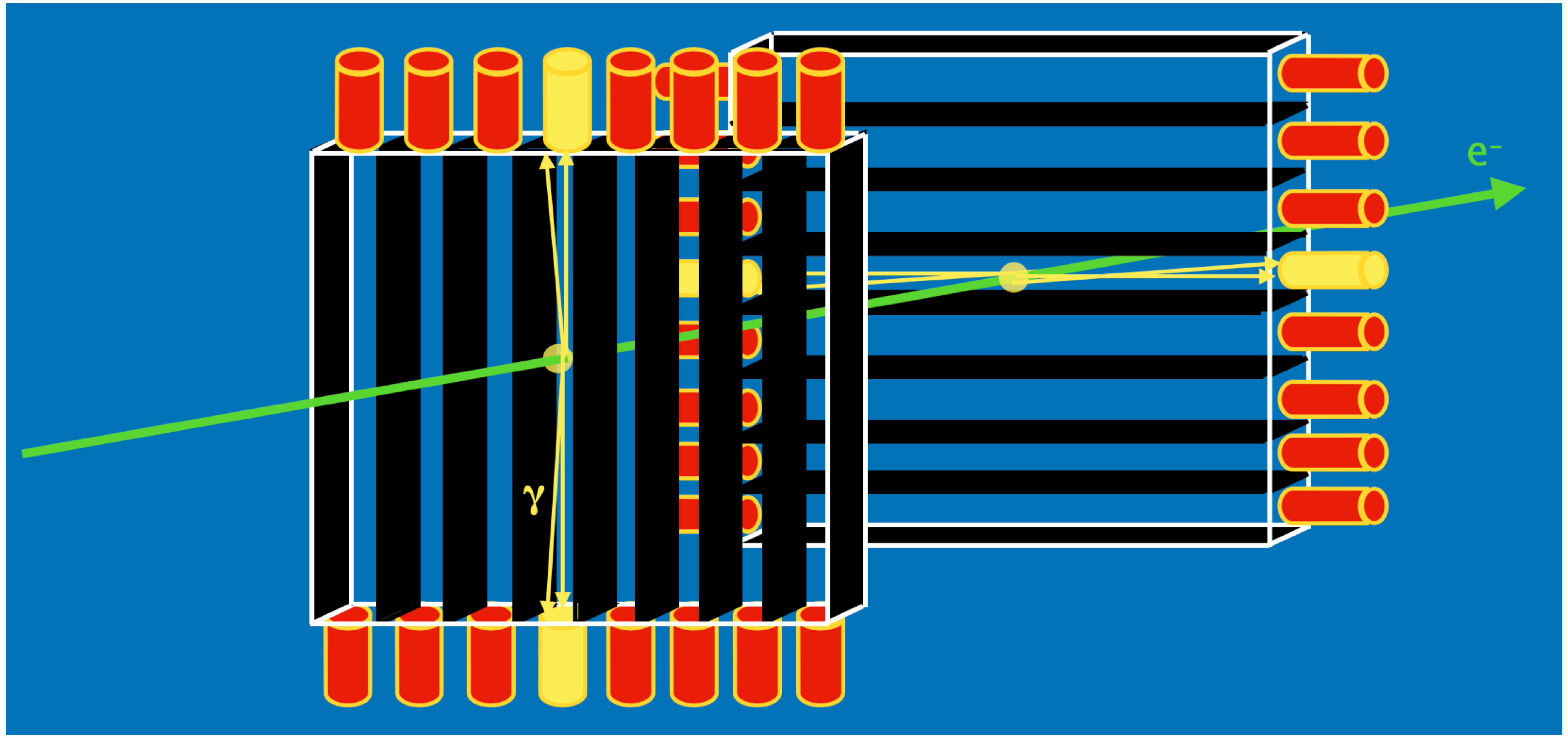
Links:
arpg-serv.ing2.uniroma1.it/arpg-site/
web.infn.it/FRIDA/

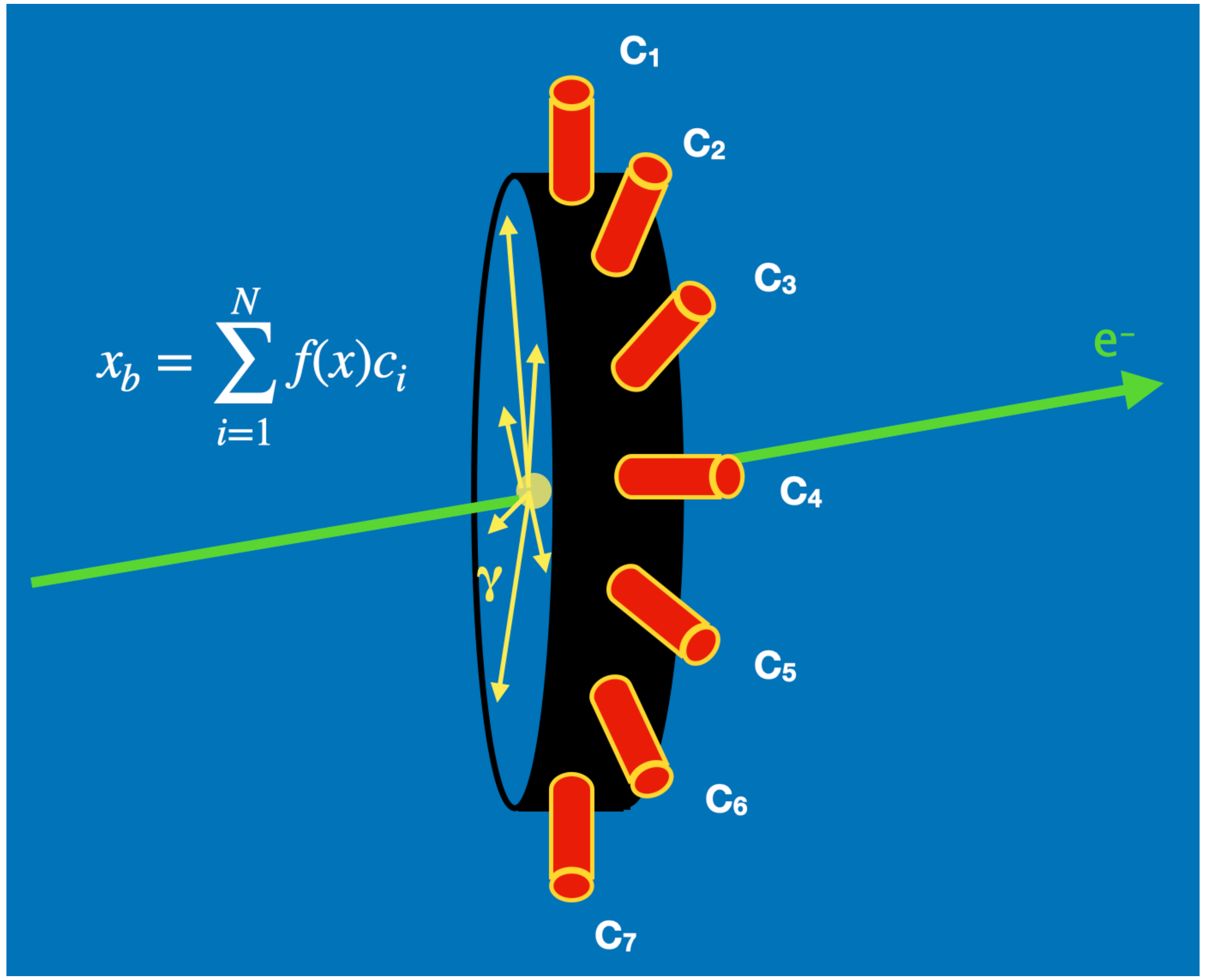
Thank you for your attention!



Backup

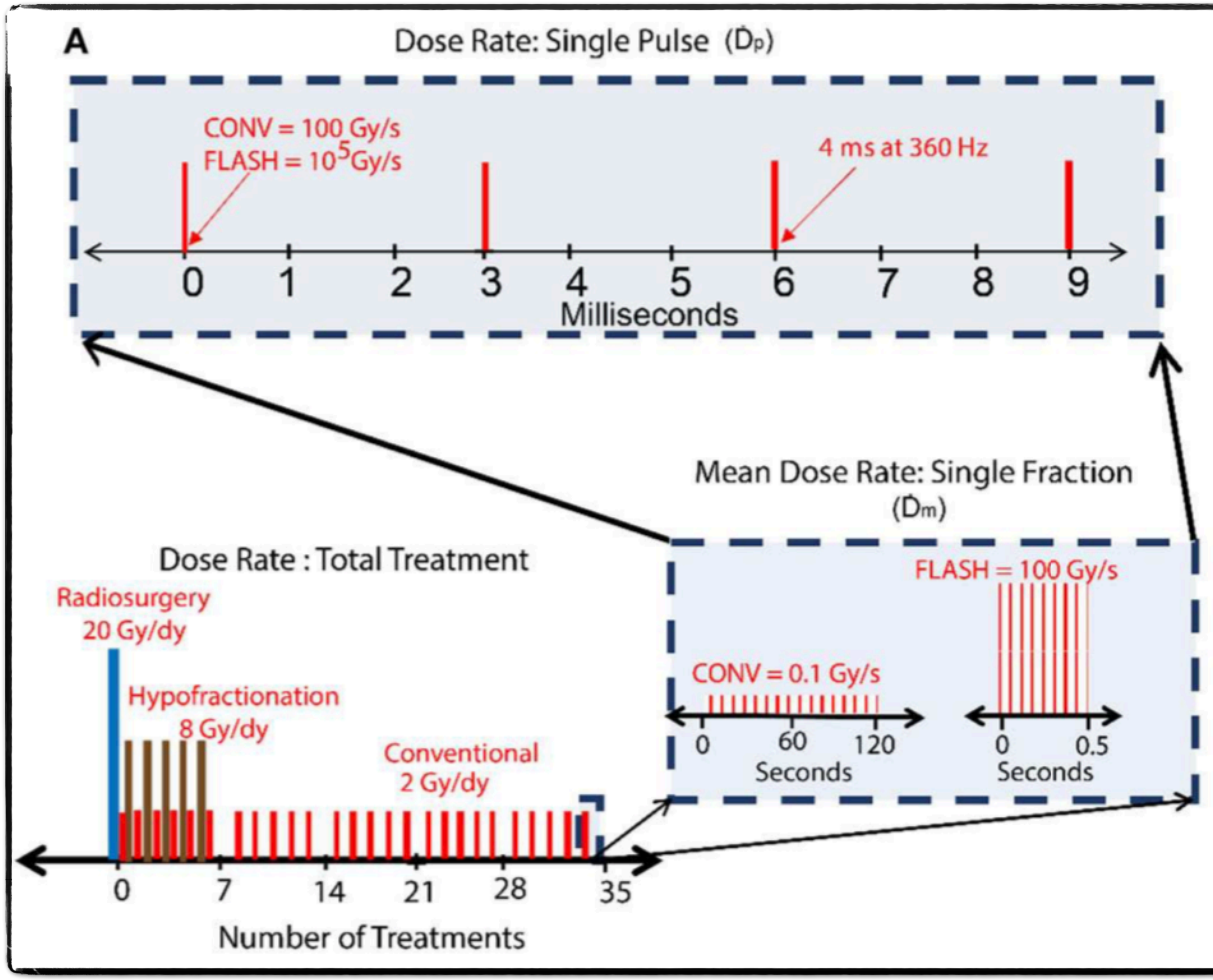
- Possible models for the new geometry





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



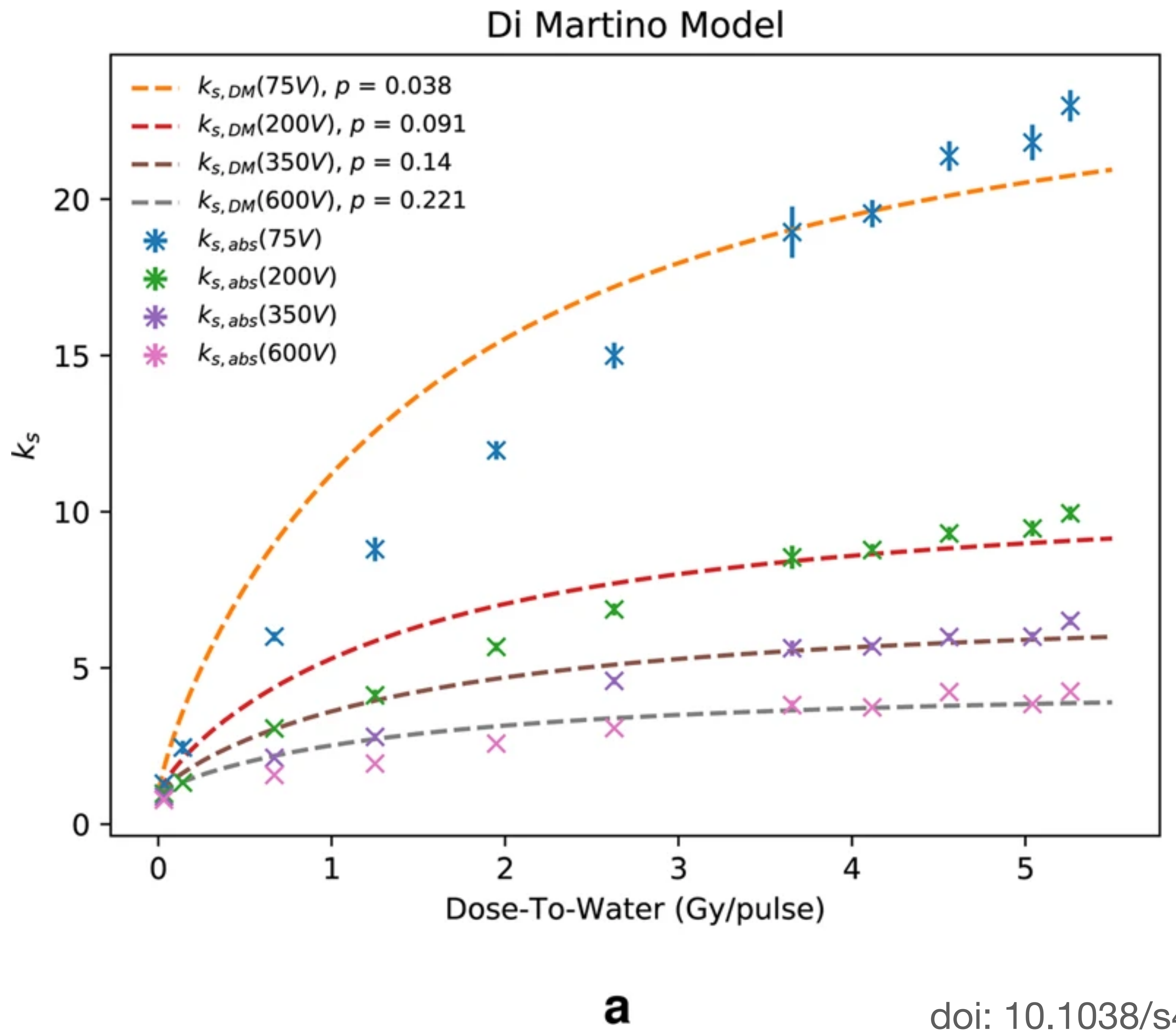
B

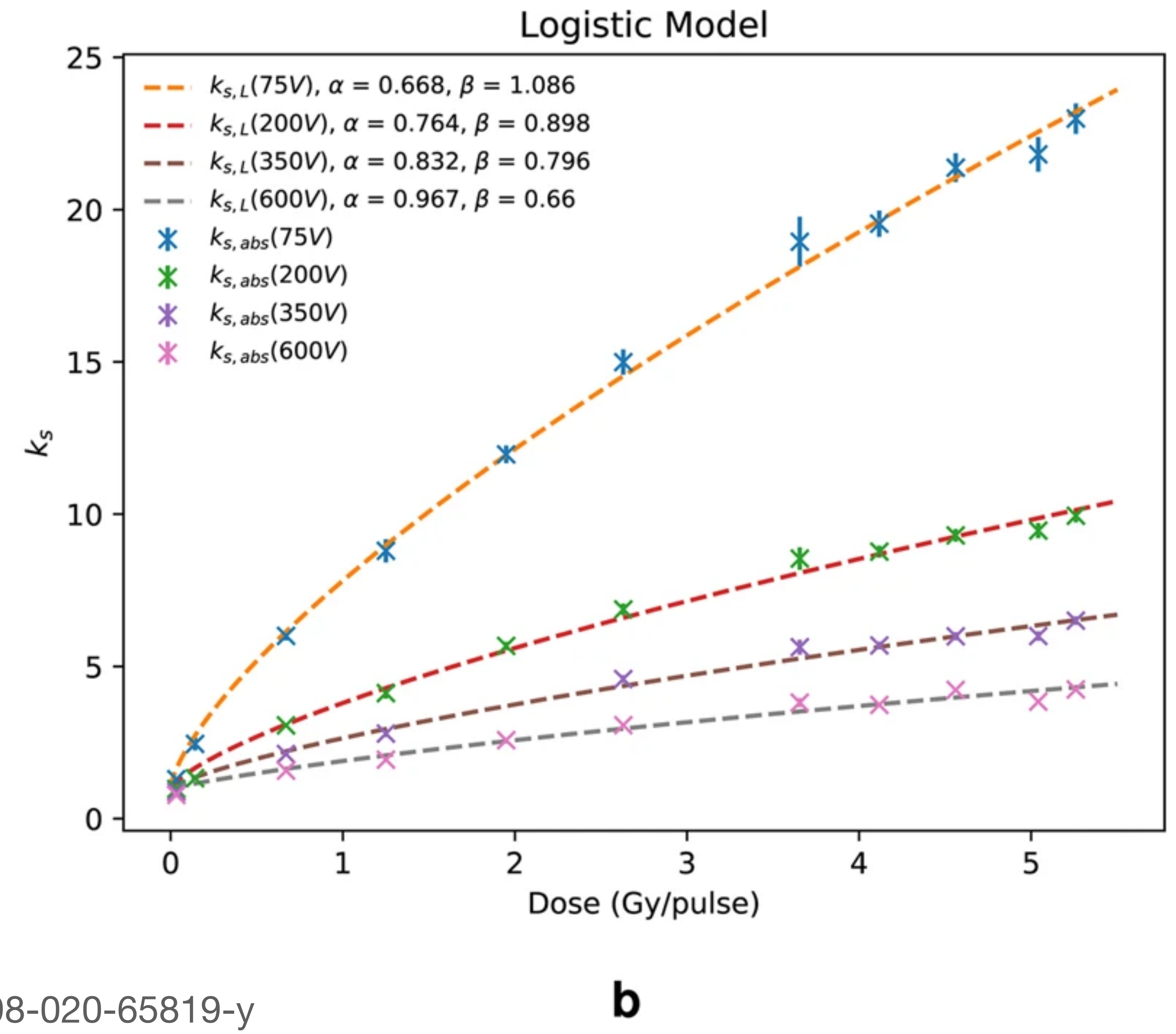
Beam Characteristics	CONV	FLASH
Dose Per Pulse D_p	~0.4 mGy	~1 Gy
Dose Rate: Single Pulse $\dot{D}_p$	~100 Gy/s	~10^5 Gy/s
Mean Dose Rate: Single Fraction $\dot{D}_m$	~0.1 Gy/s	~ 100 Gy/s
Total Treatment Time T	~days/minutes	< 500 ms

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

Backup



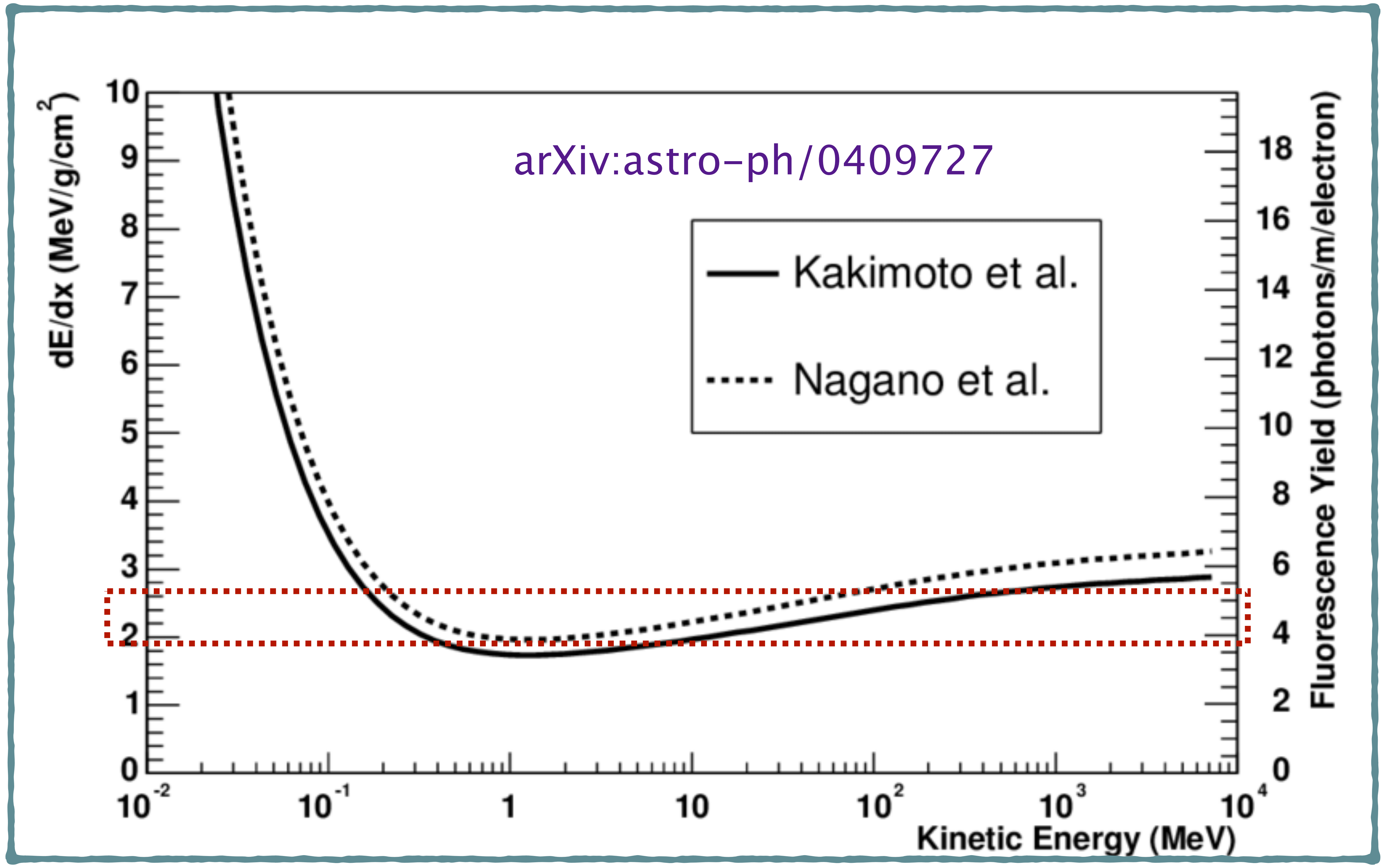


doi: 10.1038/s41598-020-65819-y

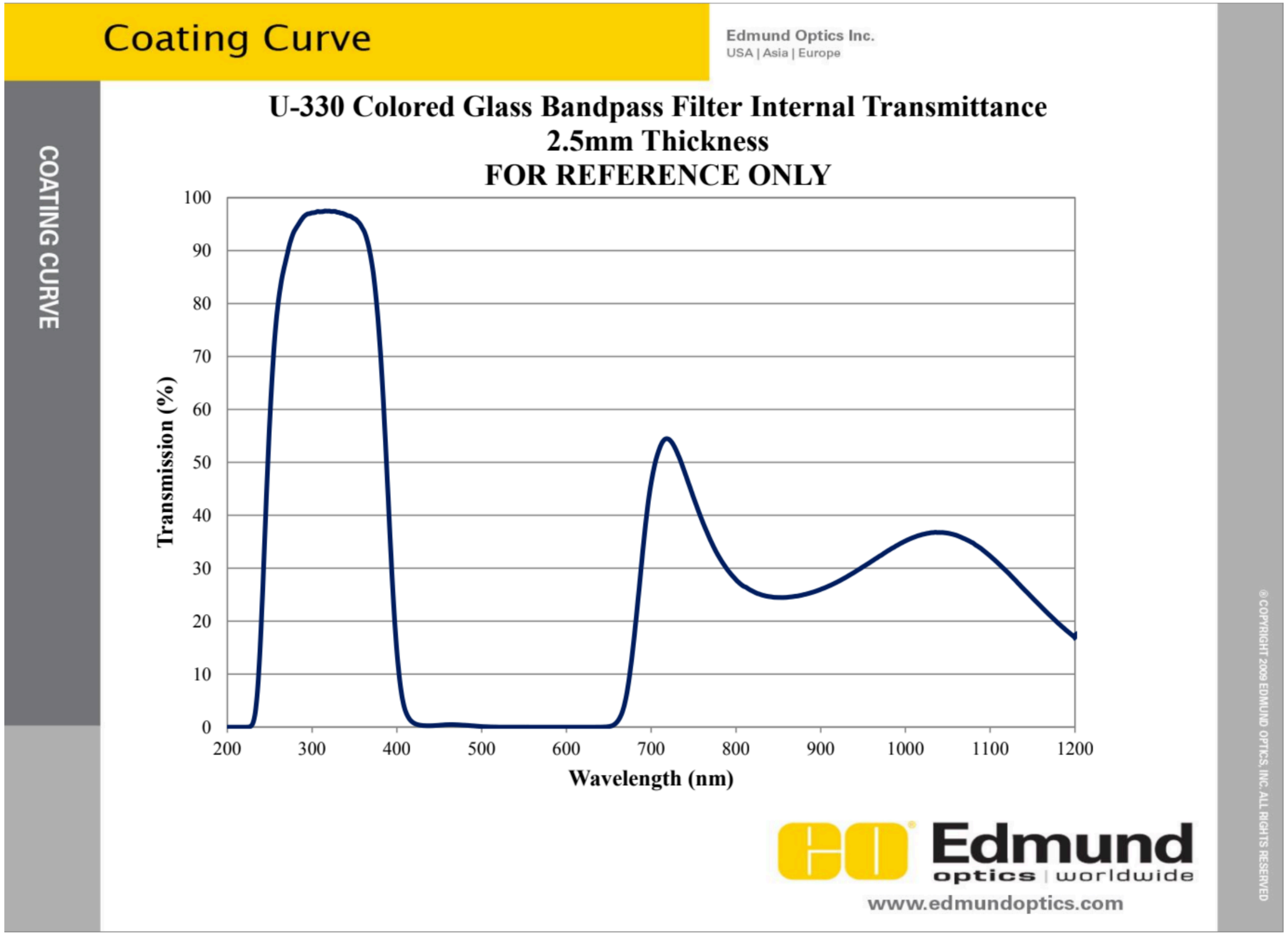
Backup

- 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



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)
0
10
20
30
40
50
60
70
80
90
100
200
300
400
500
600
700
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900
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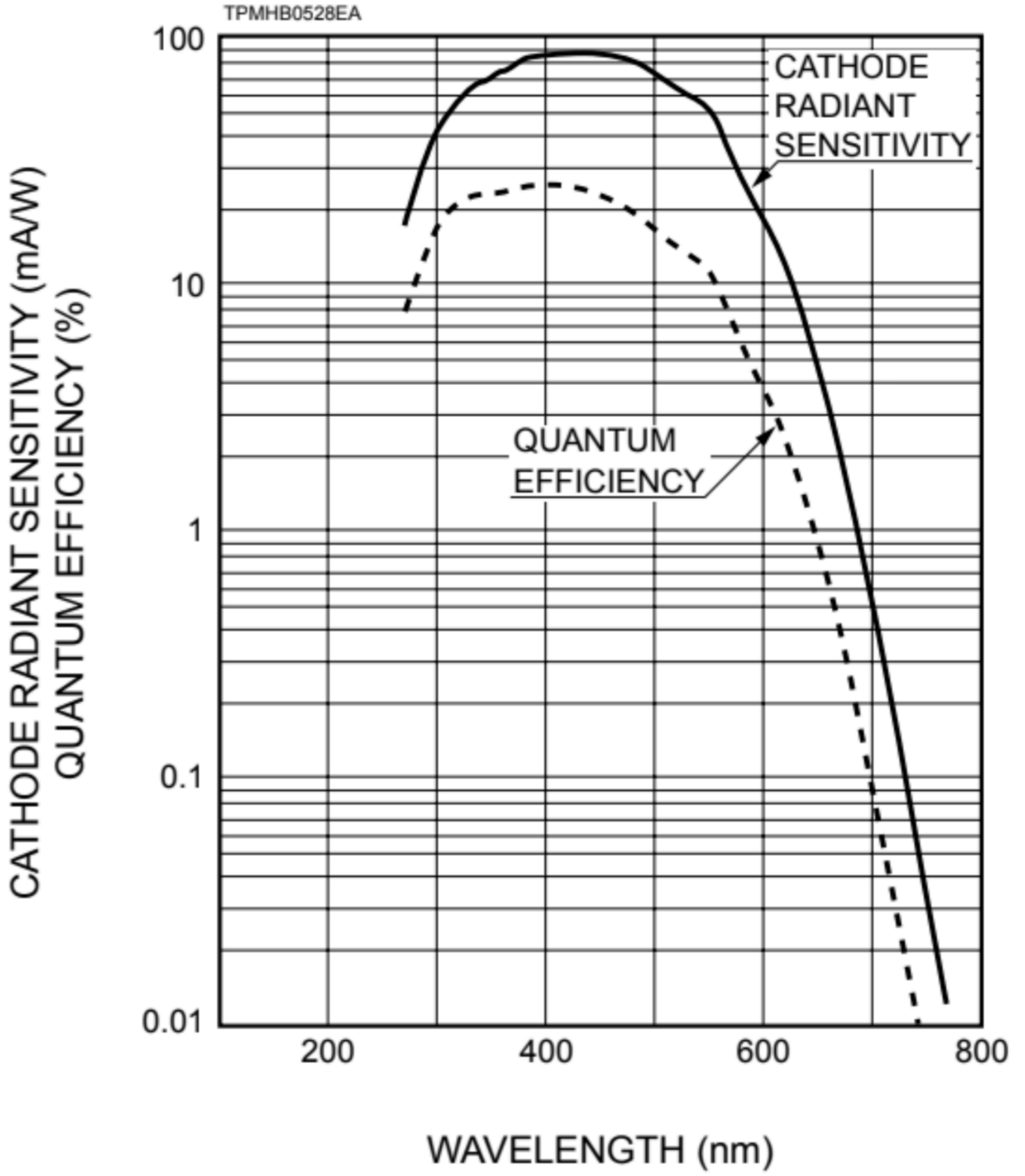

TPMHB0528EA
CATHODE RADIANT SENSITIVITY (mA/W)
QUANTUM EFFICIENCY (%)
100
10
1
0.1
0.01
CATHODE
RADIANT
SENSITIVITY
QUANTUM
EFFICIENCY
200
400
600
800
WAVELENGTH (nm)

Backup

- A MC simulation has been developed to perform a model of the detection technique.
- It works well with the expected beam parameters (some of which are not present in the simulation, secondaries and uncertainties in the energy and angular divergence…)
- Introducing the measured parameters in this model we will continue with the optimization of the geometry.