Development of a radiobiology beam line at the 18 MeV proton cyclotron facility at CNA (Seville, Spain)

A. Baratto-Roldán[1,2,*], M. C. Battaglia[2], M. A. Cortés-Giraldo[2], M. C. Jiménez-Ramos[1], J. García-López[1,2], M. I. Gallardo[2], J. M. Espino[1,2]

(1) Centro Nacional de Aceleradores (Seville, Spain)

(2) Universidad de Sevilla (Seville, Spain)

(*) abaratto@us.es

2nd OMA Topical Workshop – Diagnostics for Beam and Patient Monitoring

CERN, Switzerland

June 4th-5th, 2018

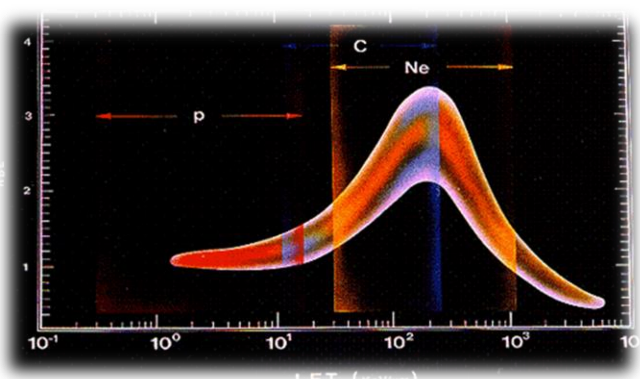
BIOLOGICAL EFFECT OF PROTON BEAMS

Preparation of beam lines at the National Centre of Accelerators (CNA) in Seville for radiobiology experiments with LOW ENERGY PROTON BEAMS

Low energy: **WHY**?

- **Uniform RBE of 1.1** assumed in treatment planning with SOBP.
- **RBE increases** with LET.

Radiobiology experiments at low proton energies are necessary to understand how RBE varies with LET.



CNA PROTON FACILITIES

Pelletron 9SDH-2 Tandem Accelerator

- Maximum terminal voltage 3MV

  ⇩

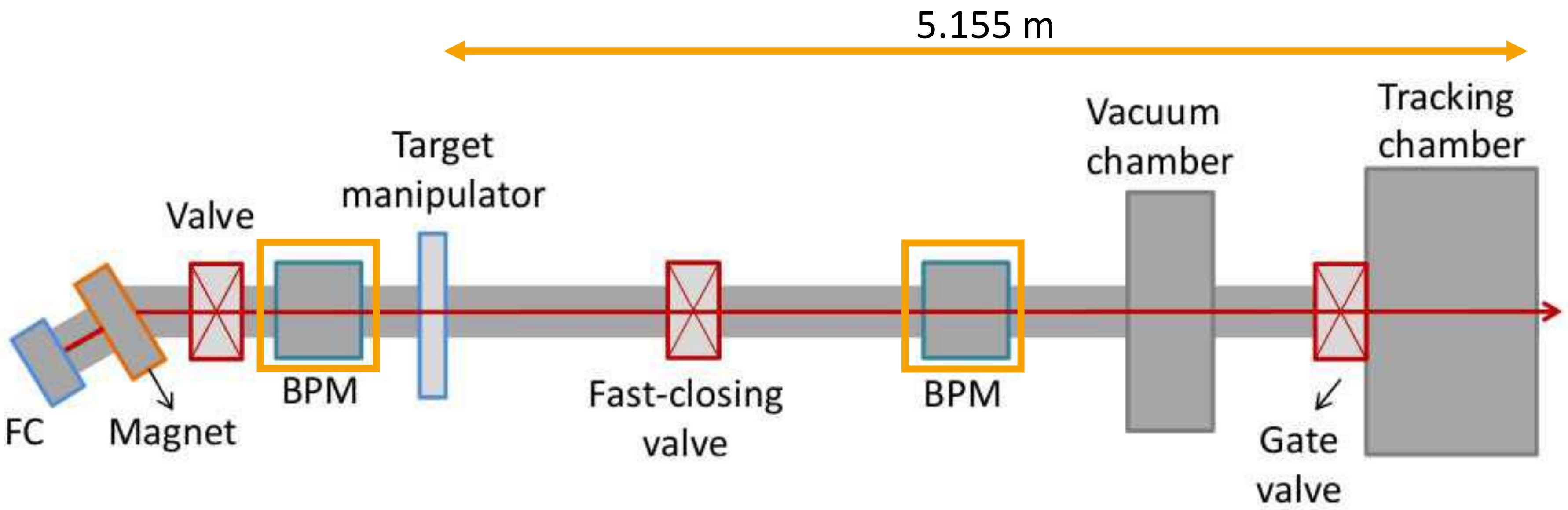
  Maximum proton energy of 6 MeV

- ***SNICS II source***: sputtering Cesium source (sputtering from solid targets)

Cyclone 18/9 Cyclotron Accelerator

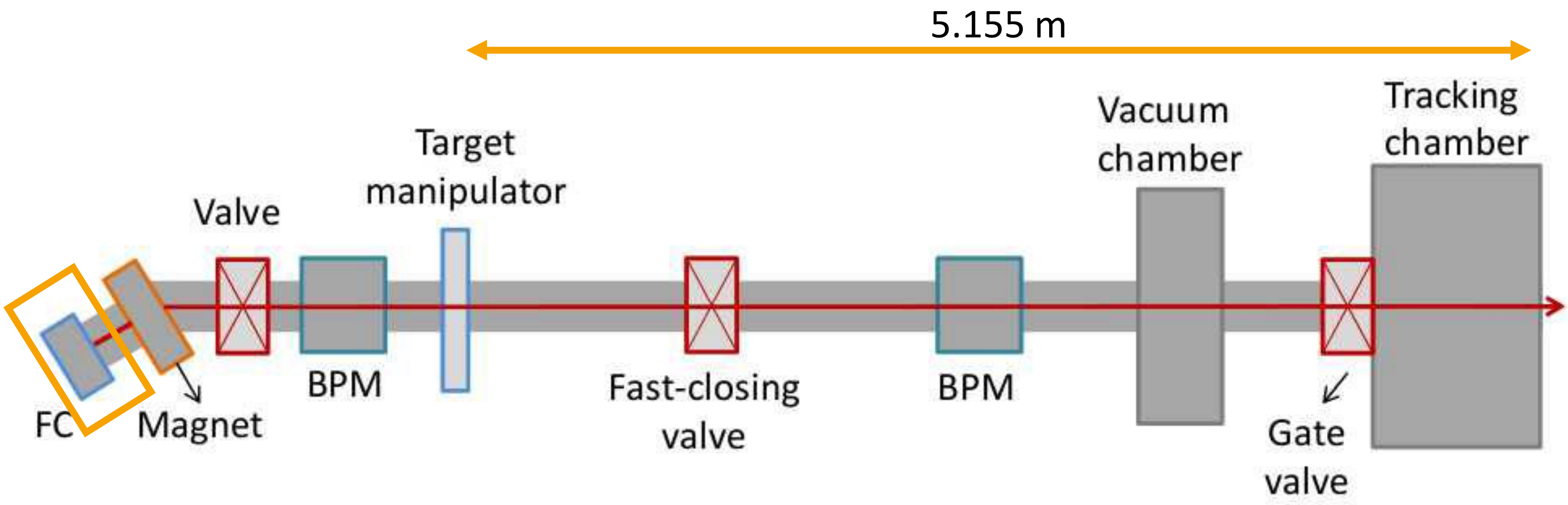
- Maximum proton energy of 18 MeV
- Extracted maximum beam intensity: 80 µA ± 10%
- Used for production of PET radioisotopes

EXPERIMENTAL SETUP: TANDEM BEAMLINE



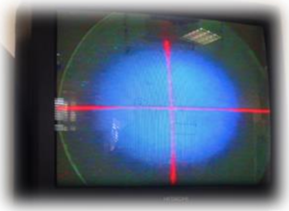
1. Beam Centering: Beam Profile Monitors (BPMs) with high beam current

EXPERIMENTAL SETUP: TANDEM BEAMLINE

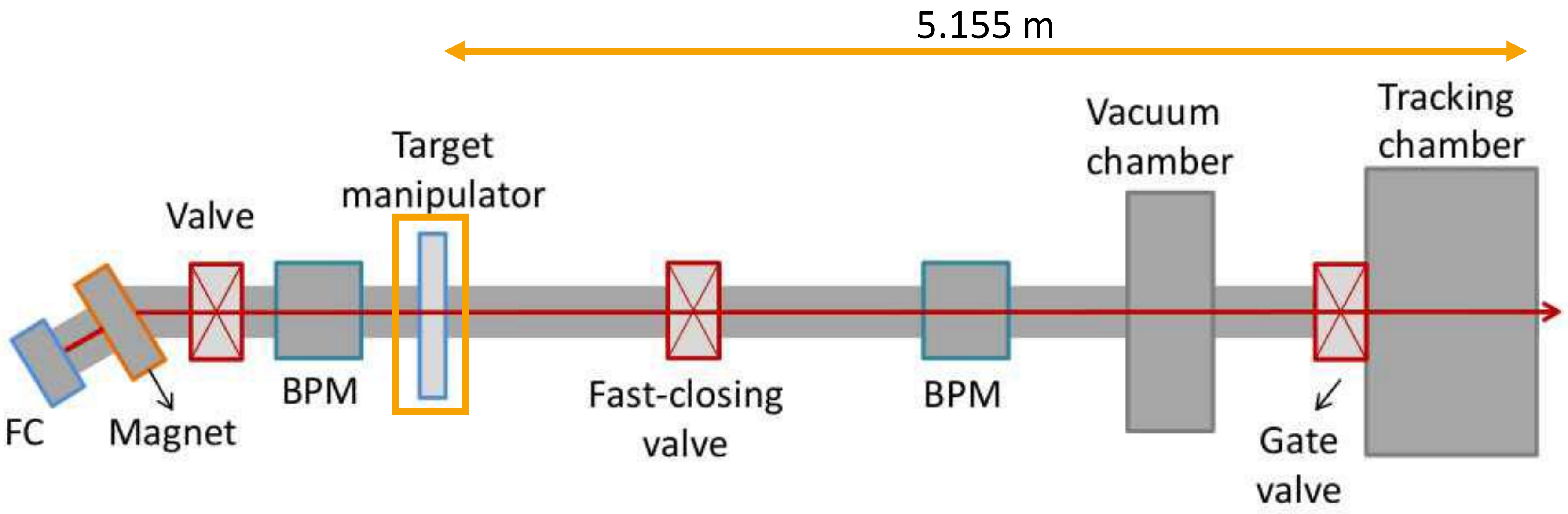


1. Beam centering: Beam Profile Monitors (BPMs) with high beam current;
2. Decreasing the current (tenths of nA in the Faraday Cup – FC):
   a. Defocusing the beam with the quadrupole magnets (fast procedure);
   b. Decreasing the pressure of the gas used for the stripping process (slow method)

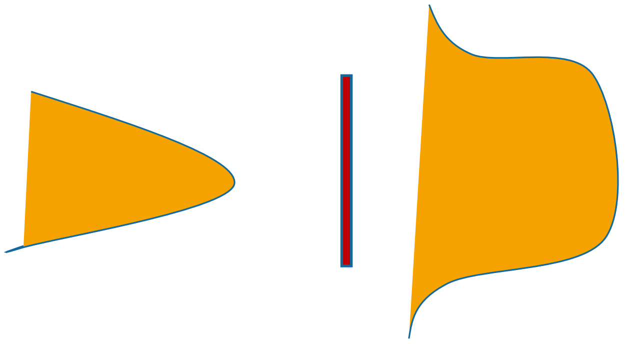
→ Beam optics unaltered and the maximum beam intensity maintained at the same position



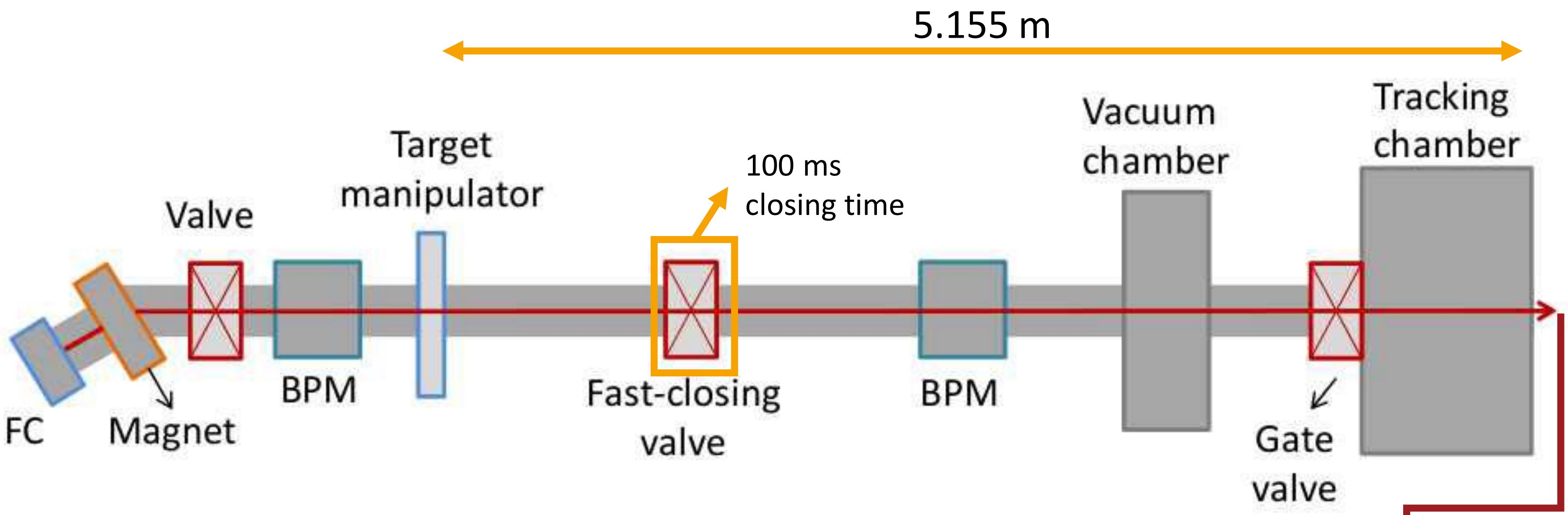
EXPERIMENTAL SETUP: TANDEM BEAMLINE



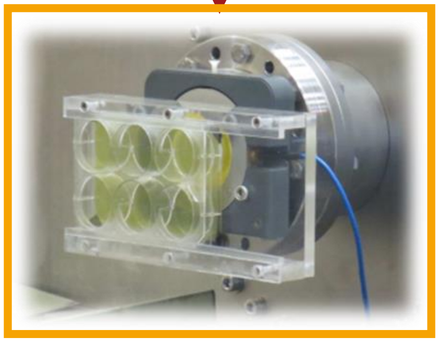
1. Beam centering: Beam Profile Monitors (BPMs) with high beam current;
2. Decreasing the current (tenths of nA in the Faraday Cup – FC);
3. Homogeneity: Beam scattering on heavy targets



EXPERIMENTAL SETUP: TANDEM BEAMLINE



1. Beam centering: Beam Profile Monitors (BPMs) with high beam current;
2. Decreasing the current (tenths of nA in the Faraday Cup – FC);
3. Homogeneity: Beam scattering on heavy targets;
4. Setup for sample irradiation.

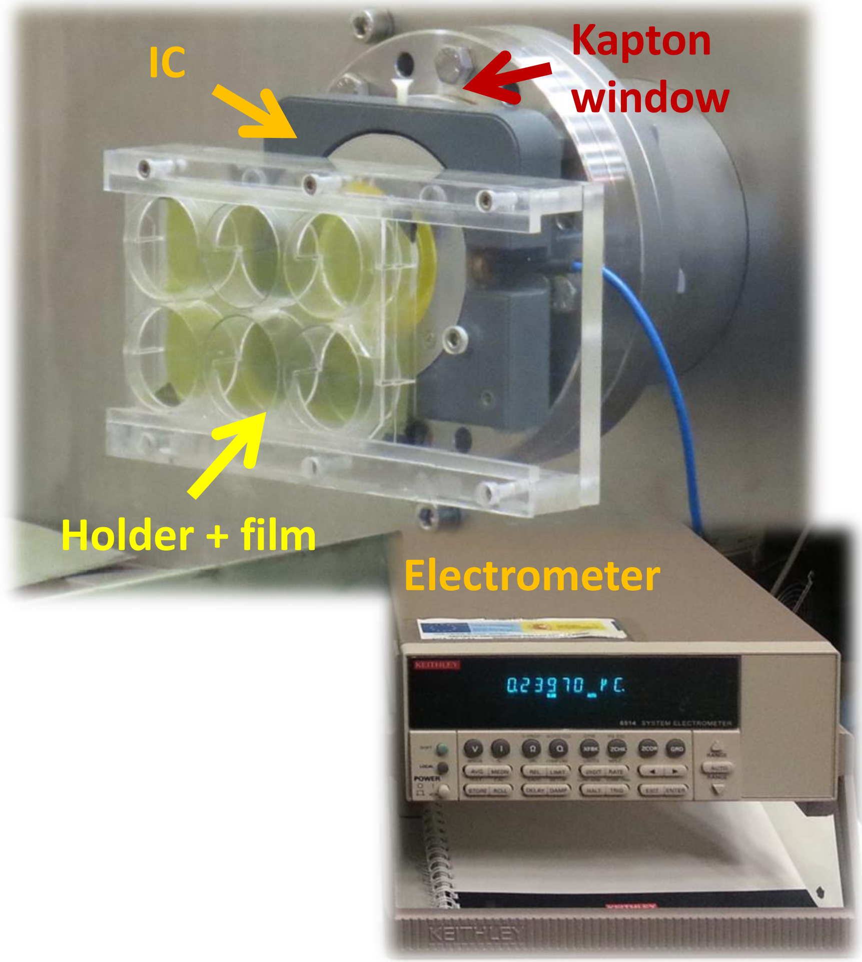


SETUP FOR SAMPLE IRRADIATION

- Thin vacuum exit window
  (kapton, thickness 50 µm, diameter 44 mm, P≈10^{-6} mbar vacuum pressure).

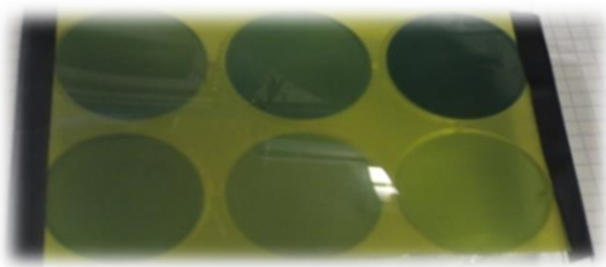
- Ionization chamber (IC)
  - three parallel electrodes 7.5 µm thick;
  - Two air gaps 6.75 mm thick;
  - V_{IC}=400 V;
  - connected to a Keithley electrometer.

- Holder with six positions designed for biological samples and also used for radiochromic films.



CHARACTERIZATION OF THE BEAM PROFILE WITH EBT3 FILMS

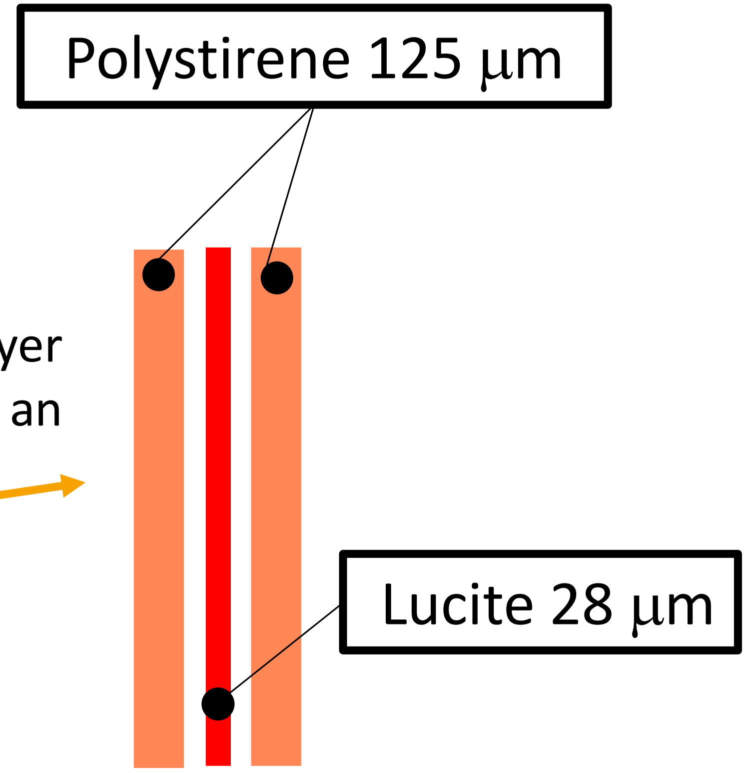
EBT3 Radiochromic fims:



EBT3 Films irradiated with different doses

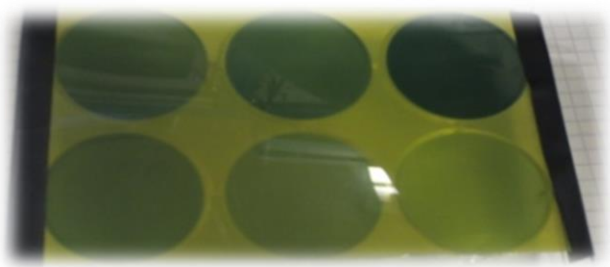
Mainly used for photon dosimetry:

- Under ionizing radiation, the sensitive gel layer polimerizes, and the film turns blue in an amount that is proportional to the dose.
- Symmetric construction.
- Energy independence.
- High spatial resolution (25μm).
- Tissue equivalence.
- No chemical, thermal or optical development.

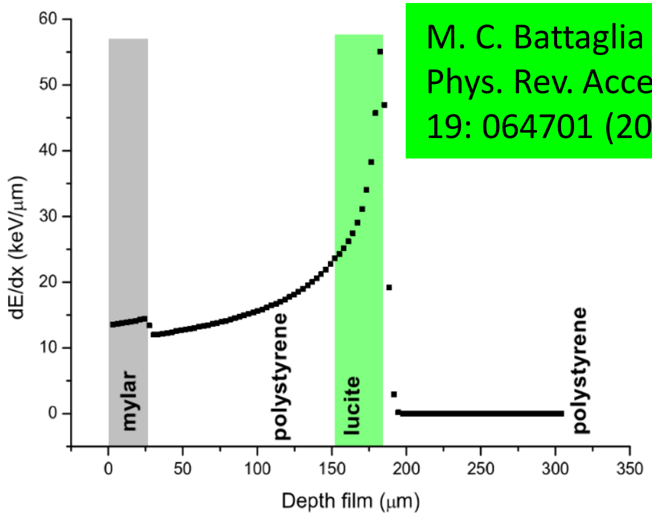


DOSIMETRY WITH EBT3 FILMS

EBT3 Radiochromic fims:



EBT3 Films irradiated with different doses



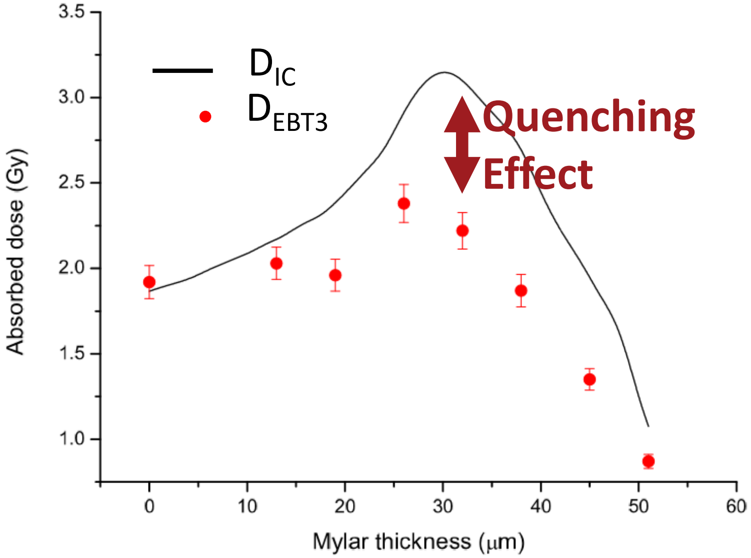
Proton dosimetry:

- Energy independence not necessarily true;
- Ionization chamber used to measure fluence and evaluate absorbed dose.

$$D_{IC} = F_{IC} \cdot \frac{dE}{\rho_{Lu} dx}$$

SIMULATION

$$F_{IC} = Q_{IC} \cdot \frac{W}{\Delta E_{IC}} \cdot \frac{1}{A}$$



CONCLUSIONS: TANDEM

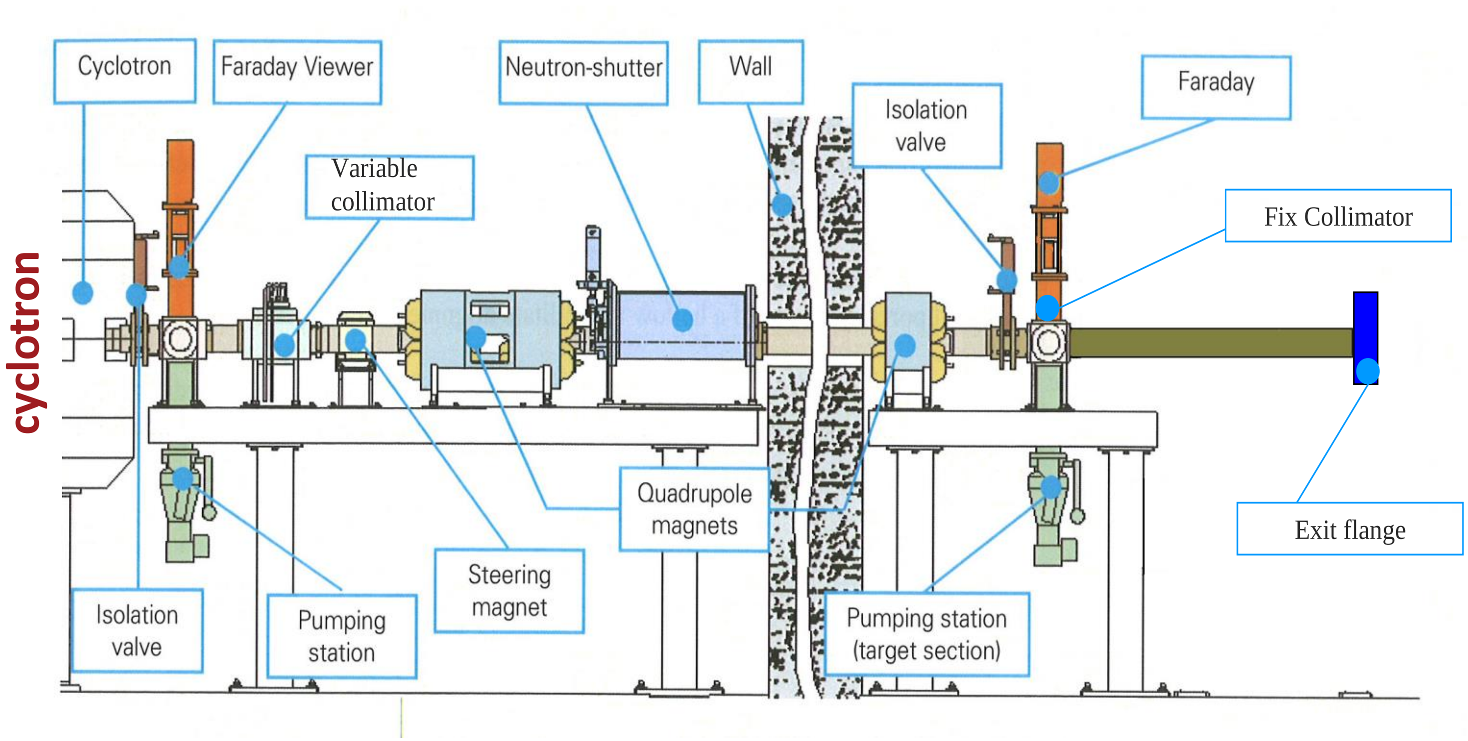
METHODOLOGY

- A dedicated setup which provides the best conditions to irradiate biological samples with low energy protons (E = 3.8 MeV).
- A protocol for the beam optimization has been established, to obtain low current beams and homogeneous beam profiles .

RESULTS

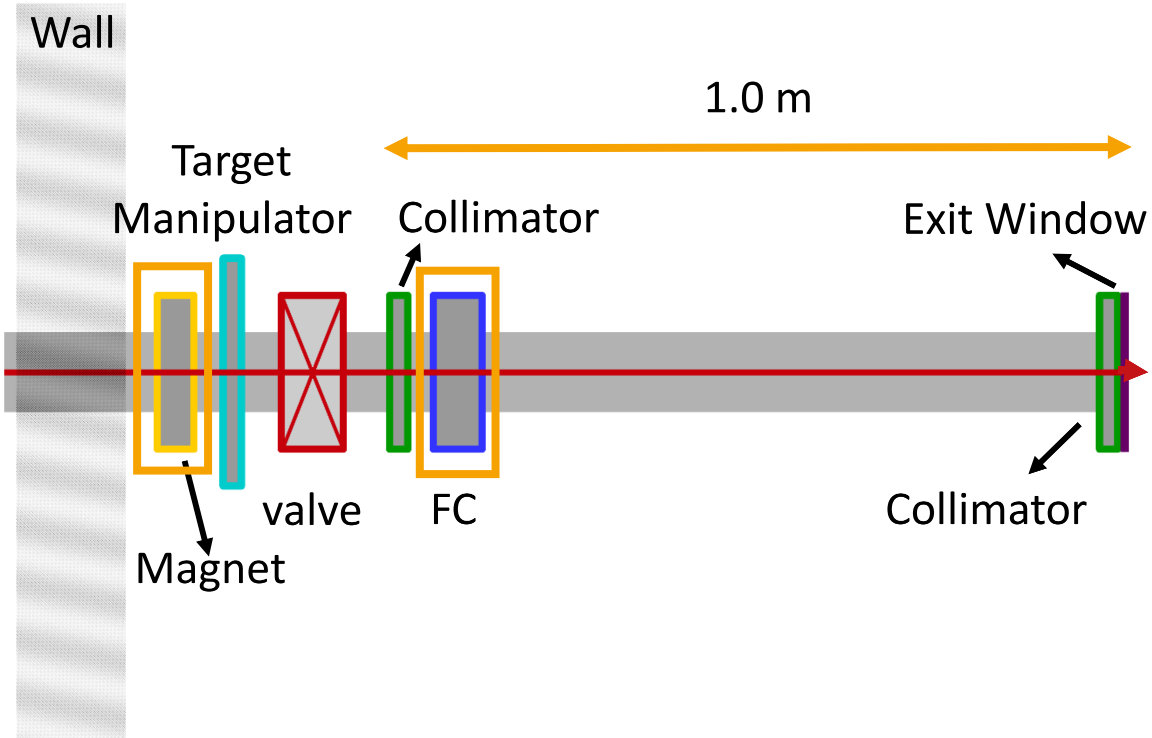
- Outside the Bragg peak region: dose calibration for the EBT3 film under photon irradiation, can be successfully adopted for low energy protons, as verified through the IC fluence measurements.
- Degrading the beam energy: effects of saturation in the EBT3 film response (LET increases). This effect is more remarkable for doses higher than 10 Gy.
- The protocol for the beam optimization and the dosimetry studies are necessary for the irradiation of cell cultures. First measurements were performed with breast cancer cells.

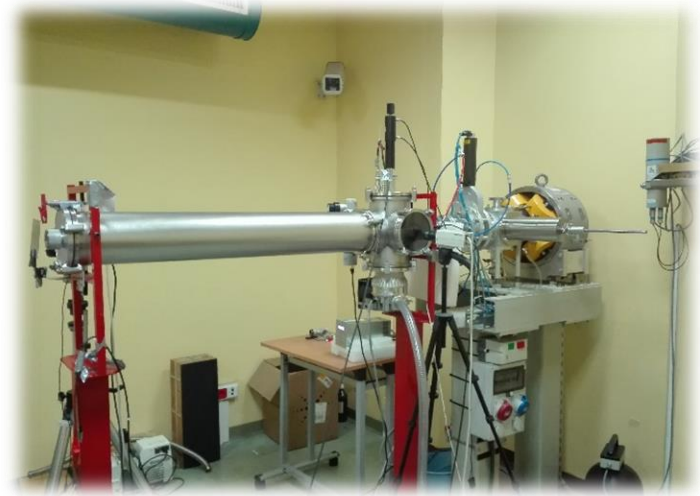
EXTENSION TO HIGHER ENERGIES: CYCLOTRON FACILITY

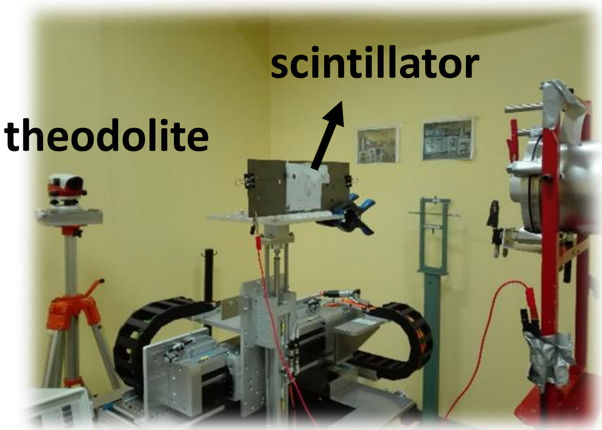


CYCLOTRON FACILITY: CHALLENGES

- Experimental beam line common to different research groups and devoted to interdisciplinary research activities.
- Beam time limited by normal workflow of PET radioisotopes production.
- Limited space in the experimental room.
- External beam in-air.

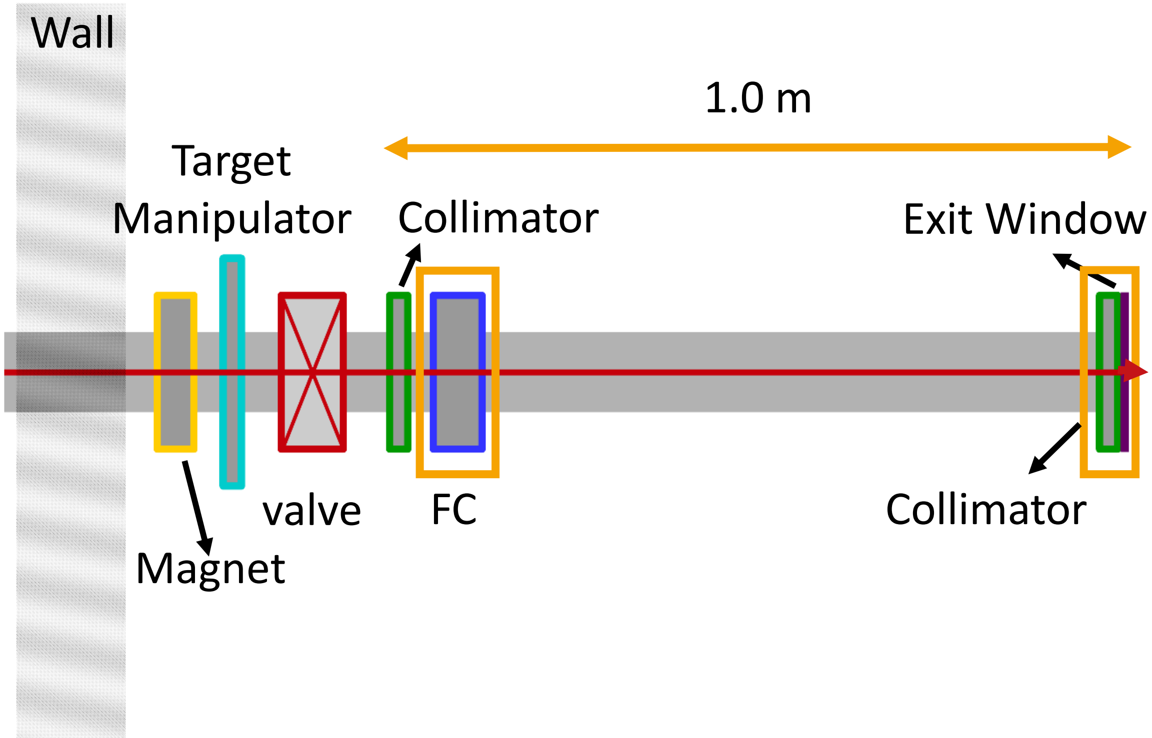


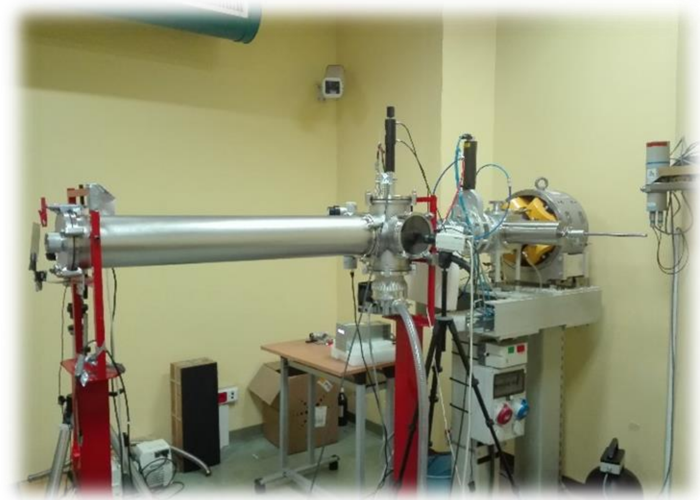




1. Beam centering:
   a. High beam current and focalized beam for centring procedure;
   b. Beam position checked with scintillating foils attached to the Faraday Cup and placed at the sample position.

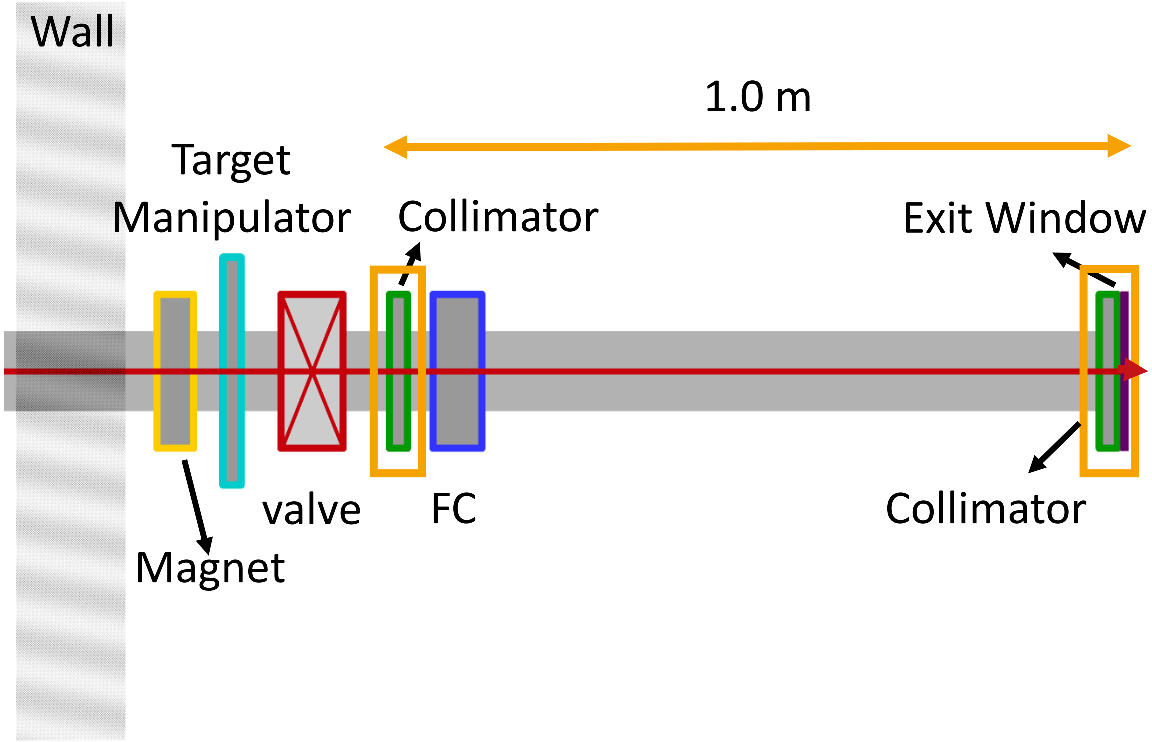
EXPERIMENTAL SETUP: CYCLOTRON BEAM LINE

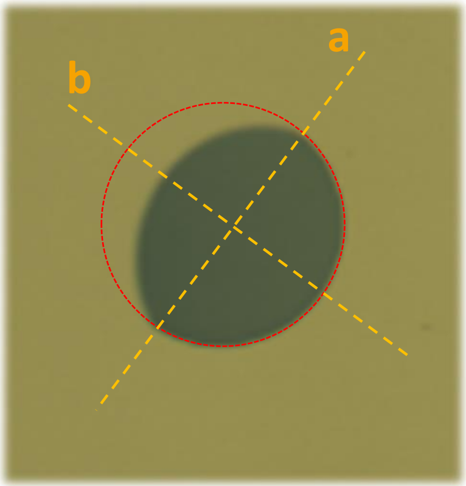




1. Beam centering;
2. Beam current:
    a. Ion source current set to the minimum ~5 mA;
    b. Completely **defocused** beam (detuned quadrupoles);
    c. Current in the Faraday Cup of the order of hundreds of pA;
    d. Approximately 80% of the beam intensity is lost after second collimation.

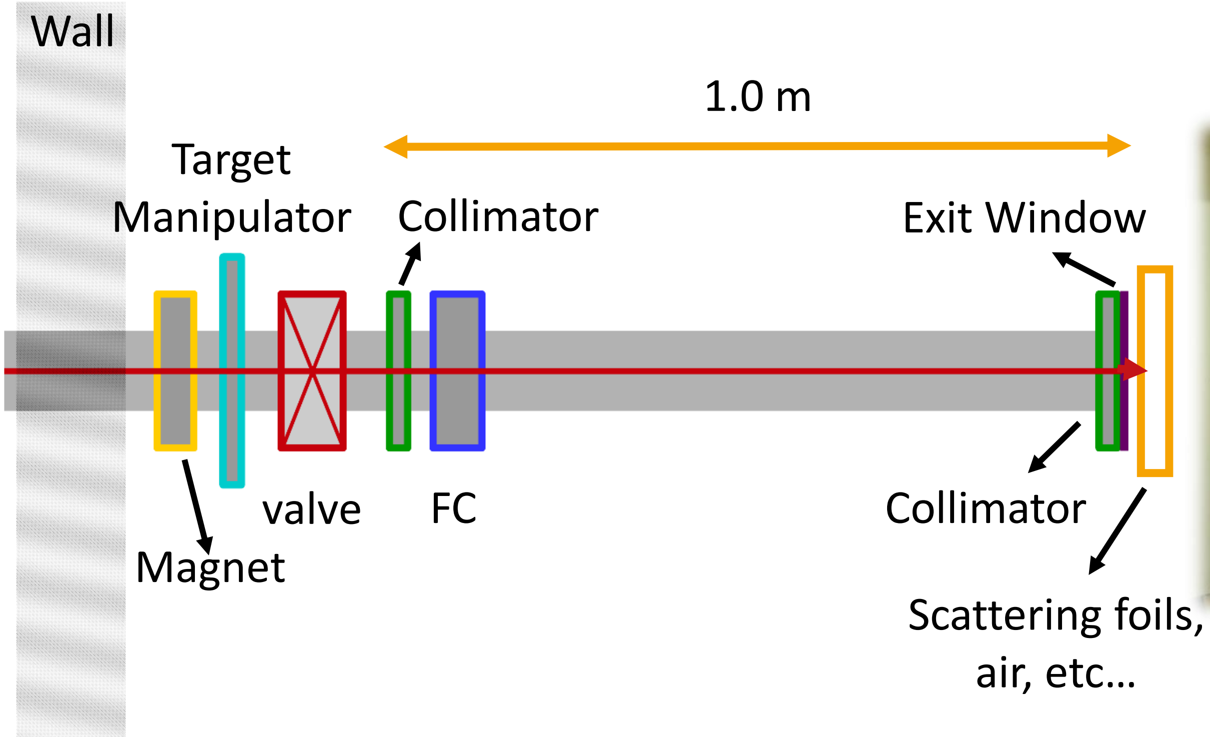
EXPERIMENTAL SETUP: CYCLOTRON BEAM LINE

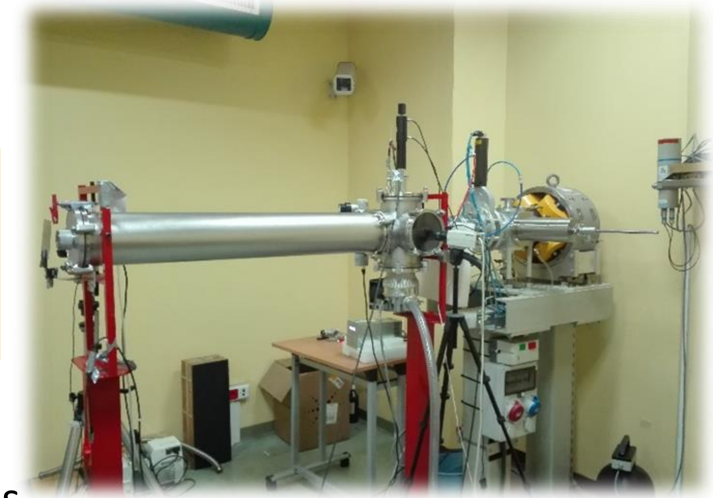




1. Beam centering;
2. Beam current;
3. Beam shape:
   a. Two collimators with diameter 1.5 cm at a distance of 1 m;
   b. Approximately elliptical (a ≈ 15 mm, b ≈ 12 mm).

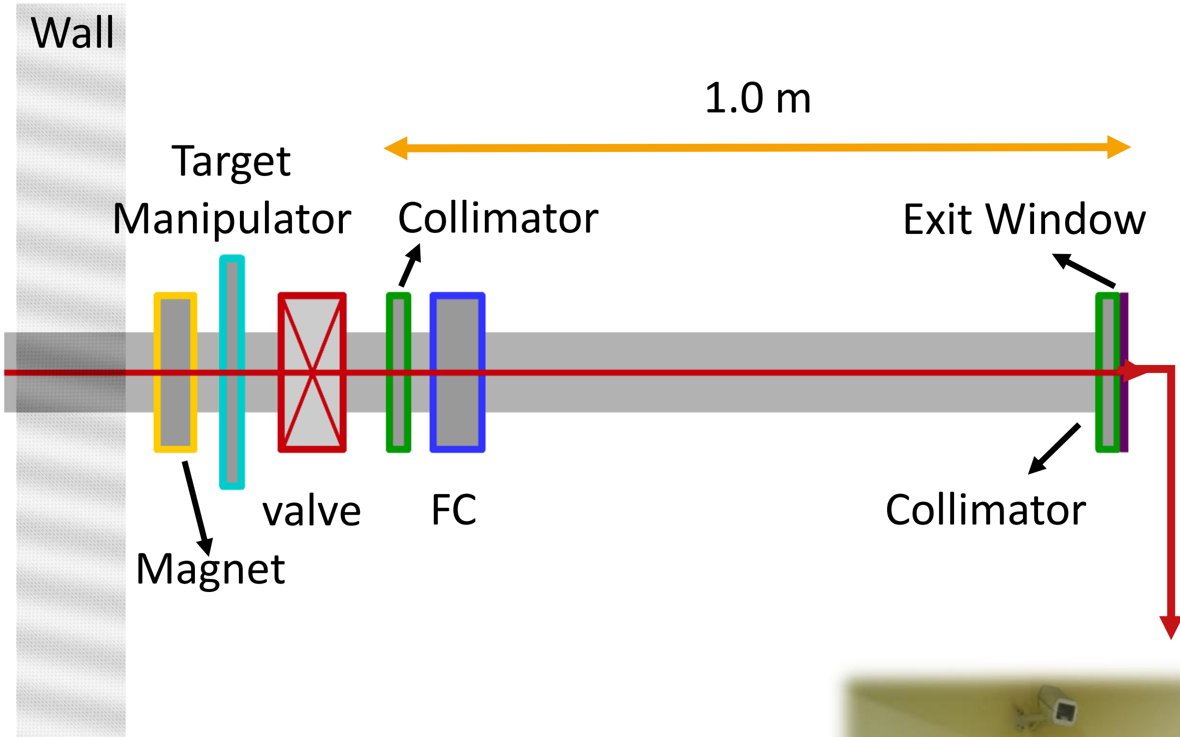
EXPERIMENTAL SETUP: CYCLOTRON BEAM LINE

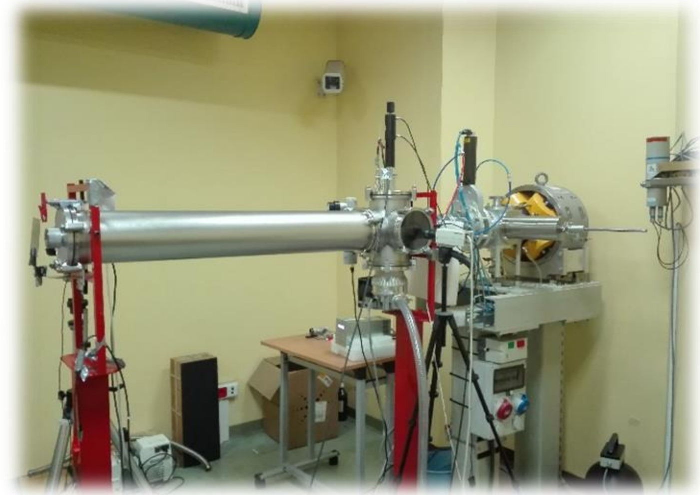




1. Beam centering;
2. Beam current;
3. Beam shape;
4. Homogeneity: Beam scattering on heavy targets and air.
    a. Tungsten foils of variable thickness;
    b. Variable distance between exit window and sample.

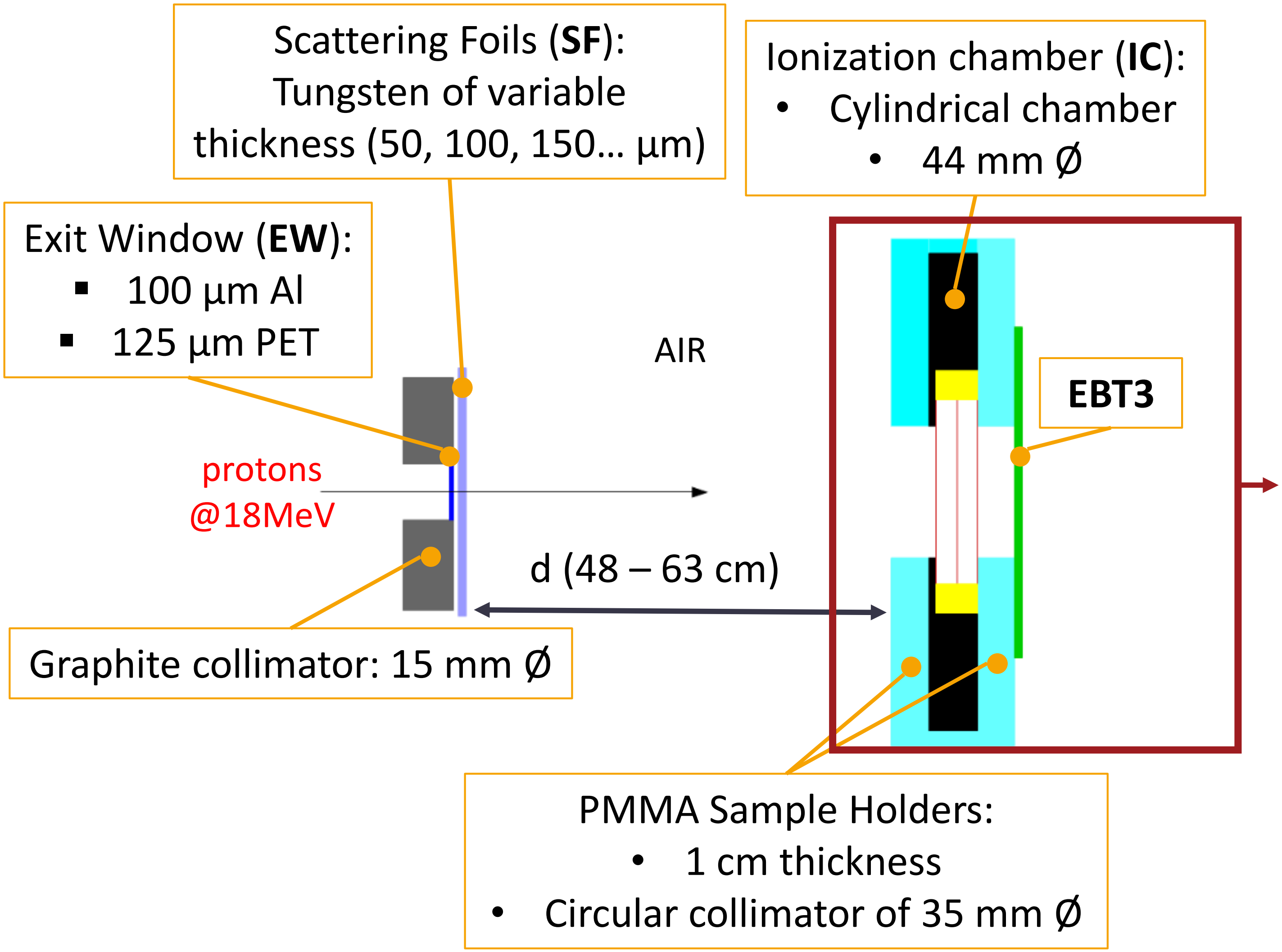
EXPERIMENTAL SETUP: CYCLOTRON BEAM LINE





1. Beam centering;
2. Beam current;
3. Beam shape;
4. Homogeneity;
5. Setup for sample irradiation.

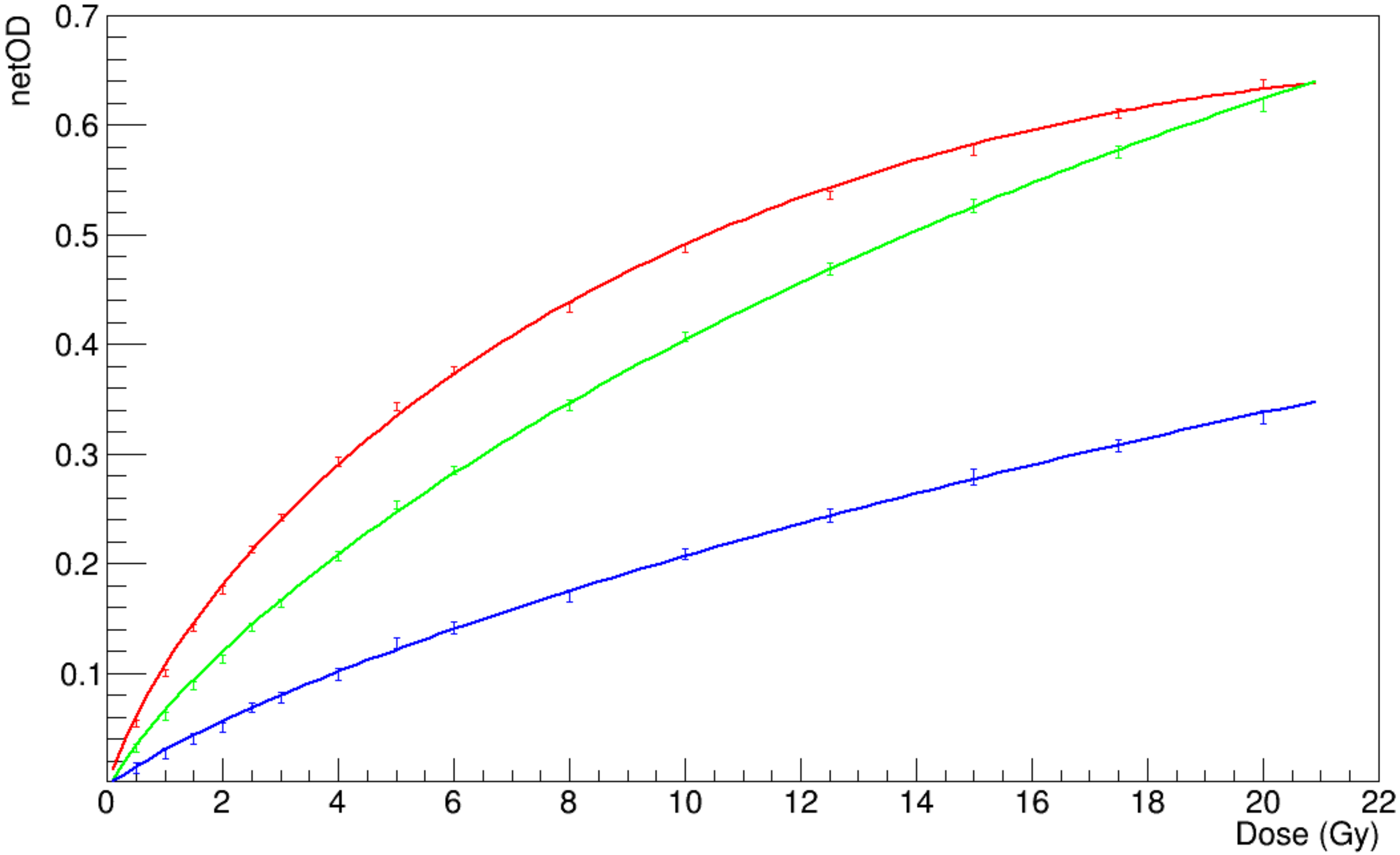
SETUP FOR SAMPLE IRRADIATION

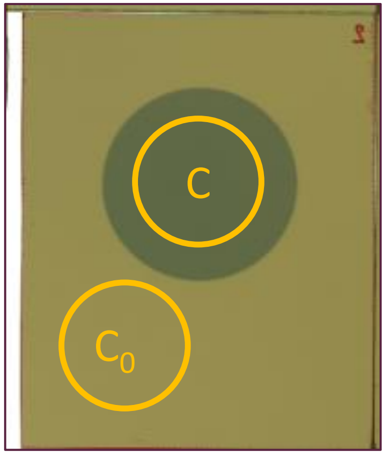


Mounted on a **moving table** with millimetric precision, which can be moved remotely from the control room.

DOSIMETRY WITH EBT3 FILMS: PHOTON CALIBRATION

PHOTON CALIBRATION @HOSPITAL: "Hospital Universitario Virgen Macarena"

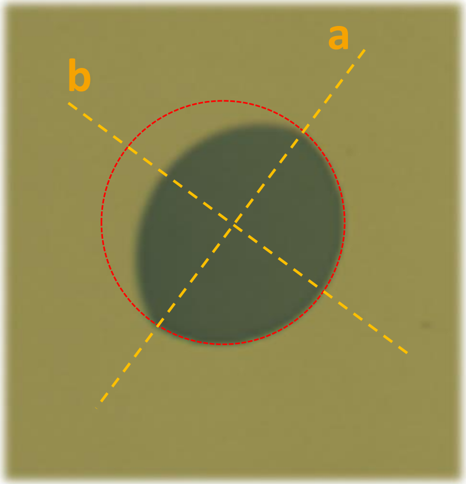




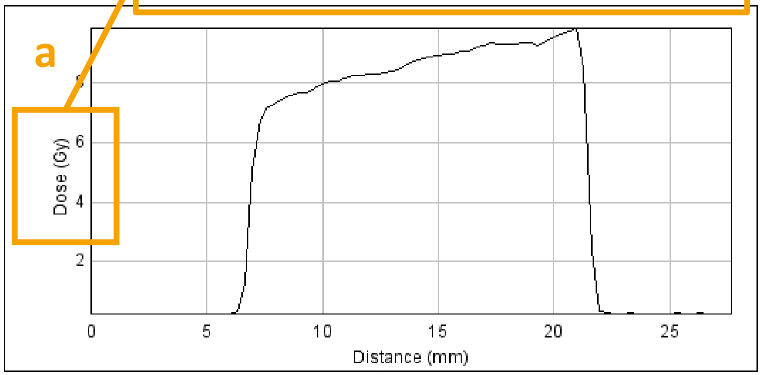
$$\mathrm{netOD} = -\log_{10}\frac{C}{C_0}$$

- Films irradiated with a 6 MV linac under reference conditions (0 – 20 Gy);
- Calibration curves of the form: $D = a + b \cdot \mathrm{netOD} + c \cdot \mathrm{netOD}^d$

FULL-BEAM PROFILES

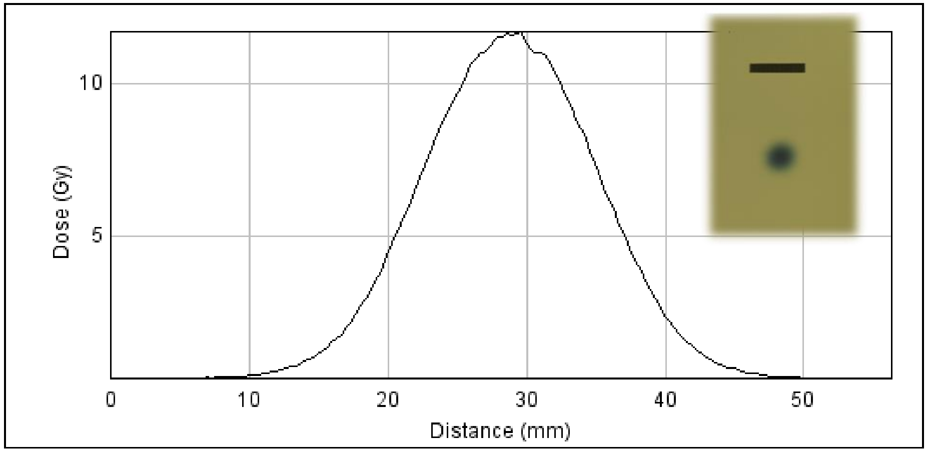


Dose from photon calibration

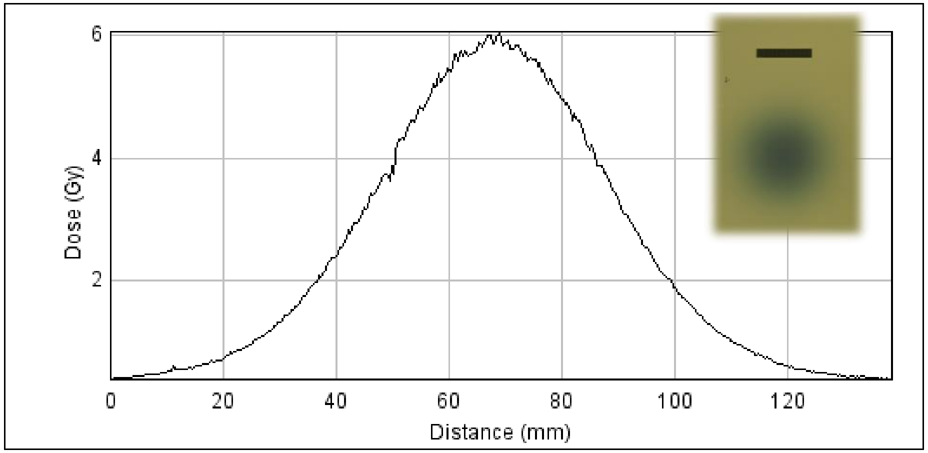


Effect of asymmetry not visible
anymore after scattering in air (+ foils)

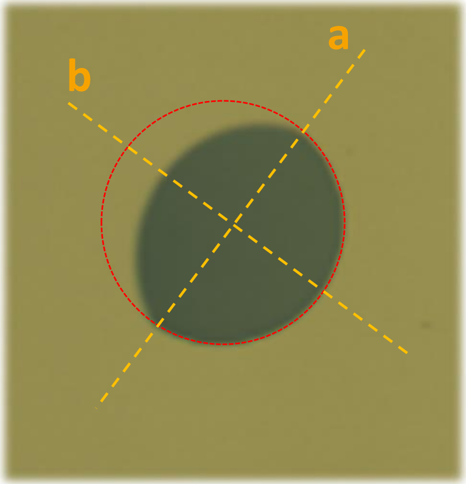
125 µm PET + 48.4 cm Air + EBT3

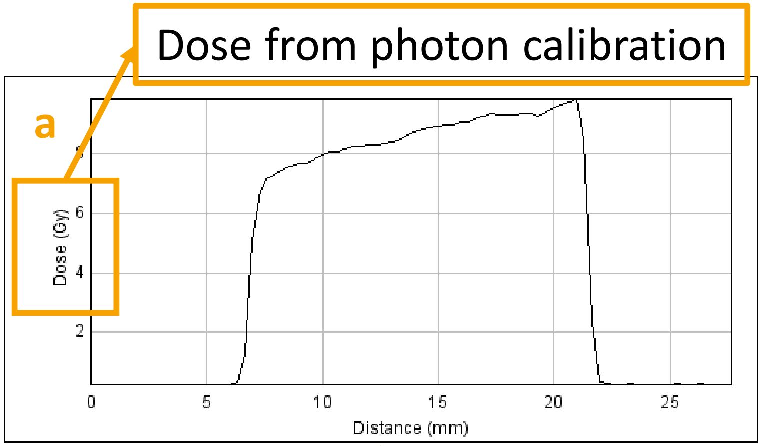


125 µm PET + 50 µm W + 48.4 cm Air + EBT3



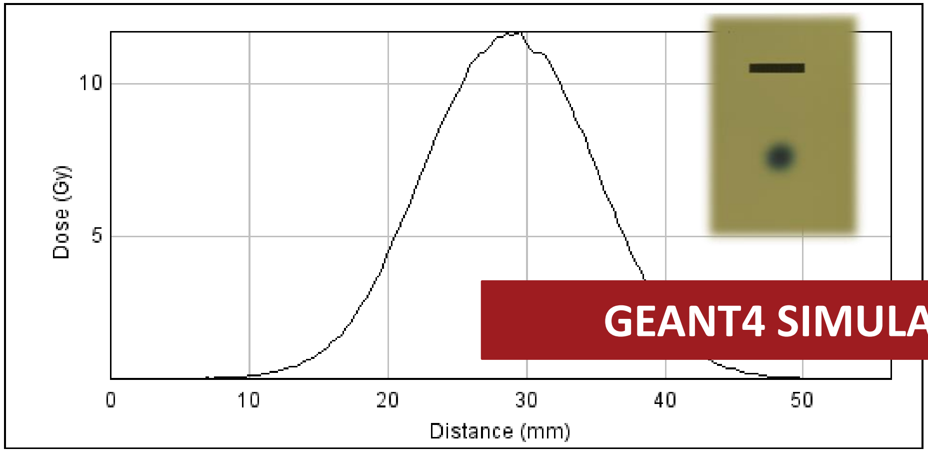
FULL-BEAM PROFILES



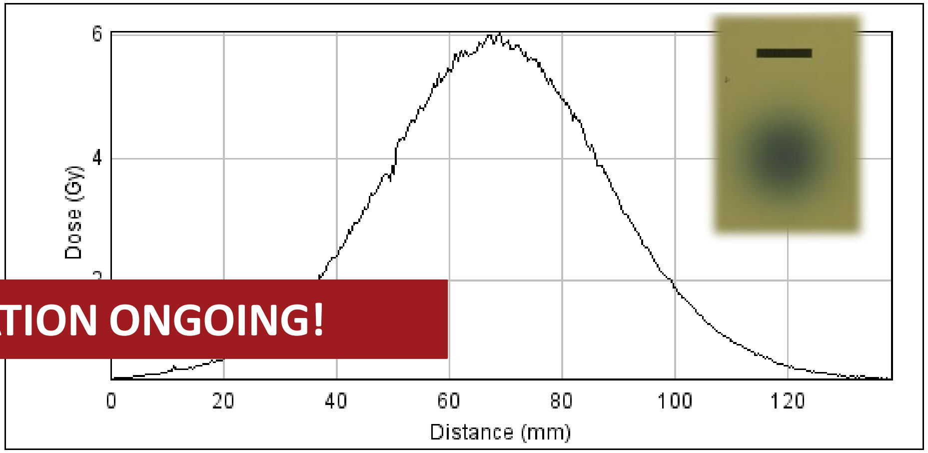


Effect of asymmetry not visible anymore after scattering in air (+ foils)

125 µm PET + 48.4 cm Air + EBT3



125 µm PET + 50 µm W + 48.4 cm Air + EBT3

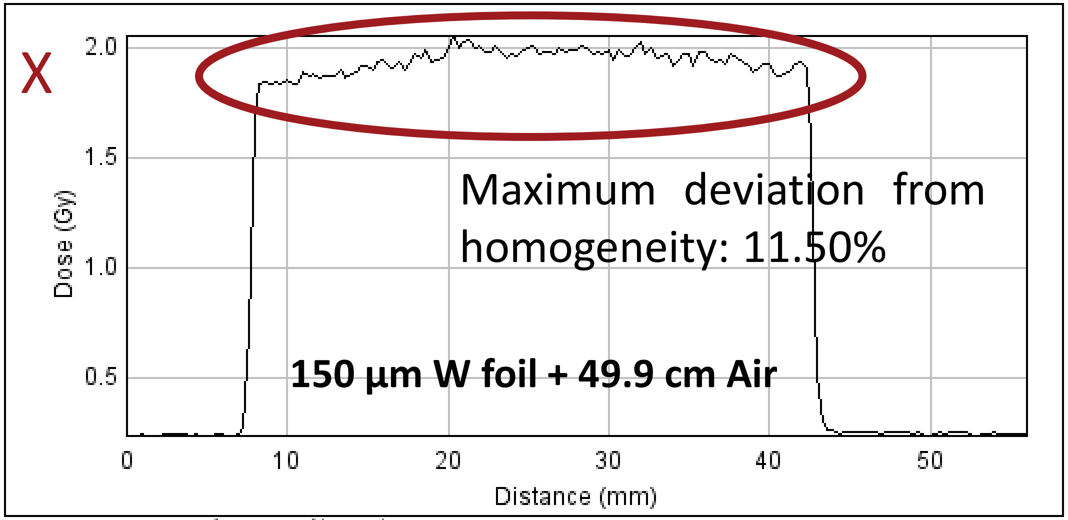


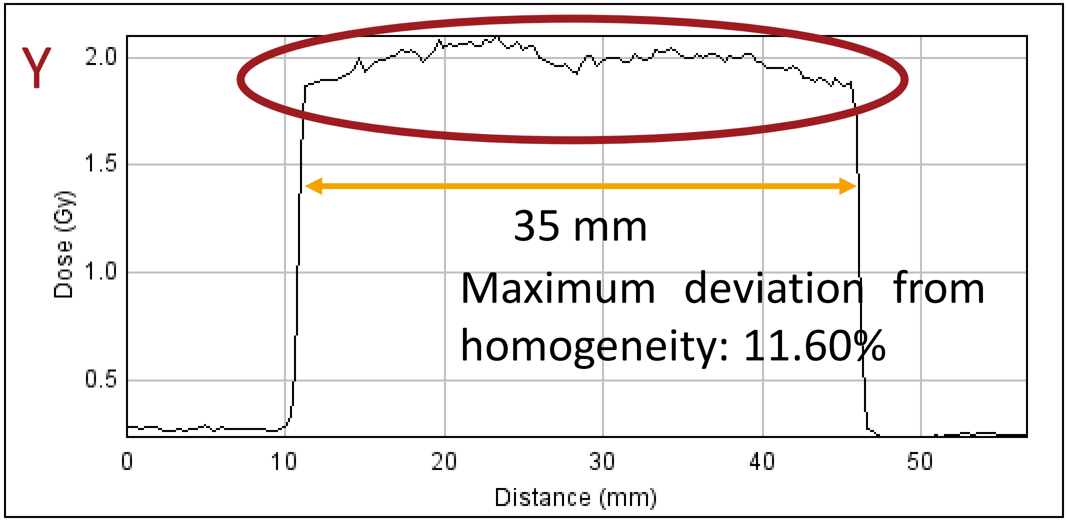
GEANT4 SIMULATION ONGOING!

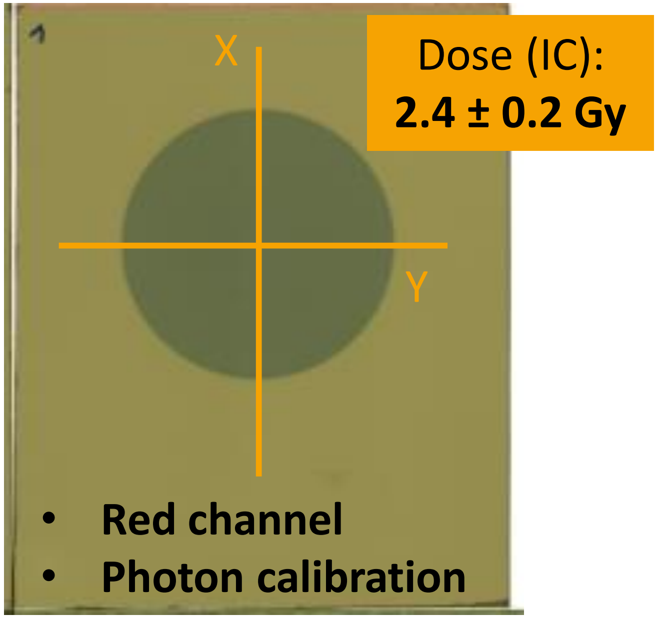
CHARACTERIZATION OF THE BEAM PROFILE

1. Decreasing the current: minimum beam intensity settable (pA) + defocusing;

2. Homogeneity: Beam scattering on heavy targets placed after the exit window in air.







Mean value and standard deviation of the sample (σ):

X : 1.99 ± 0.04 Gy

Y : 2.04 ± 0.04 Gy

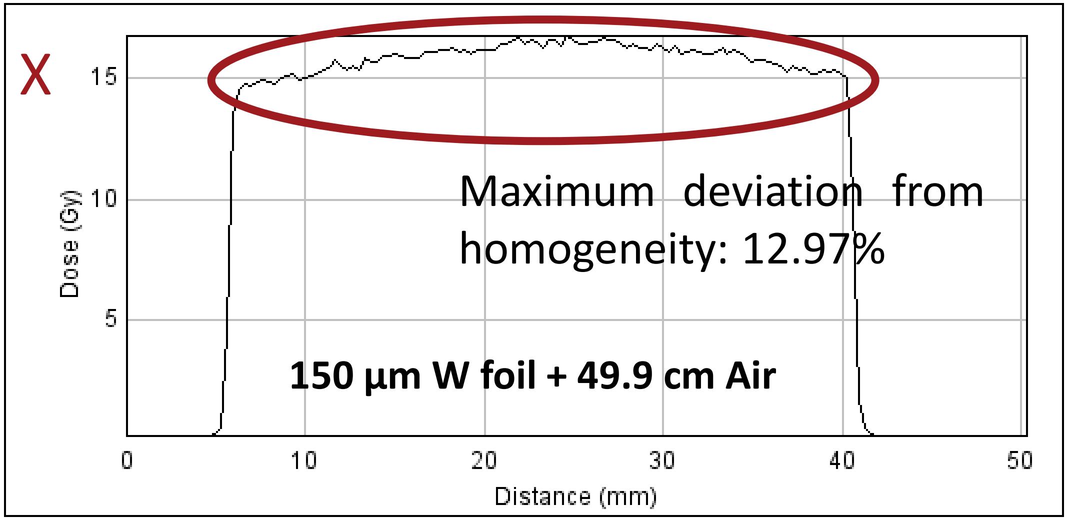
Max deviation from mean value:

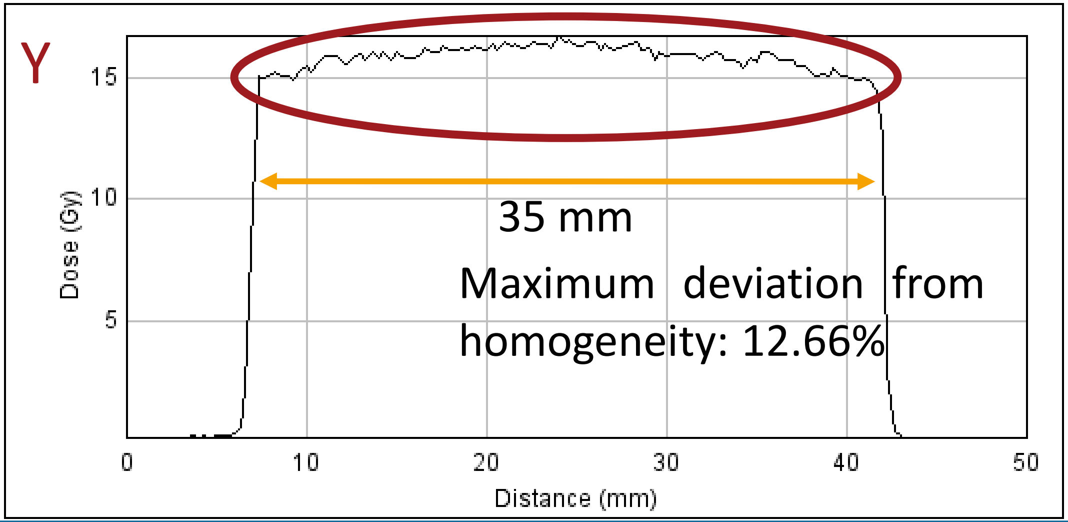
X : 2.8 σ

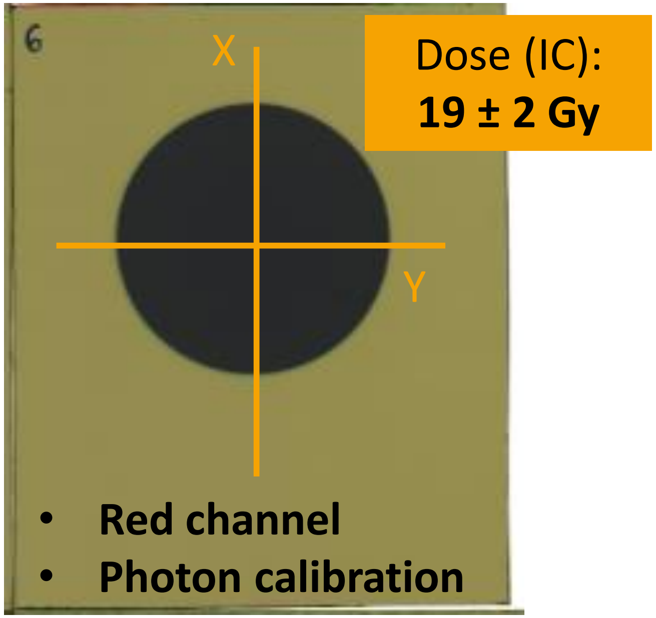
Y : 2.7 σ

CHARACTERIZATION OF THE BEAM PROFILE

1. Decreasing the current: minimum beam intensity settable (pA) + defocusing;
2. Homogeneity: Beam scattering on heavy targets placed after the exit window in air.







Mean value and standard deviation of the sample (σ):

X : 16.32 ± 0.03 Gy

Y : 16.33 ± 0.04 Gy

Max deviation from mean value:

X : 2.3 σ

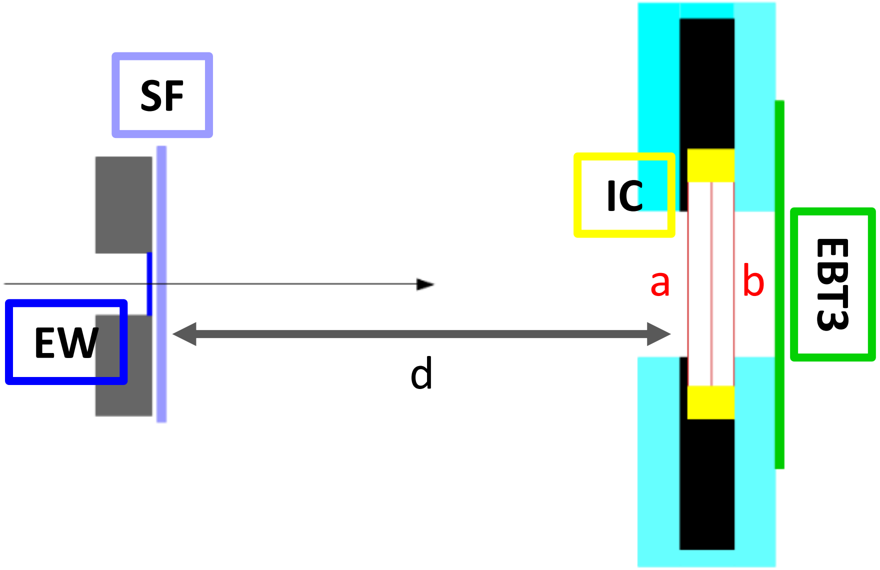
Y : 2.2 σ

Proton dose evaluation with the ionization chamber coupled with EBT3 films

$$D = f\frac{N_{\mathrm{p}}^{\mathrm{IC}}}{A}\cdot\frac{\mathrm{d}E}{\rho_{\mathrm{Lu}}\mathrm{d}x}$$

$$N_{\mathrm{p}}^{\mathrm{IC}} = \frac{Q_{\mathrm{IC}}}{e}\cdot\frac{W}{\Delta E_{\mathrm{IC}}}$$

$$f = \frac{N_{\mathrm{p}}(\mathrm{b})}{N_{\mathrm{p}}^{\mathrm{IC}}(\mathrm{a})}$$

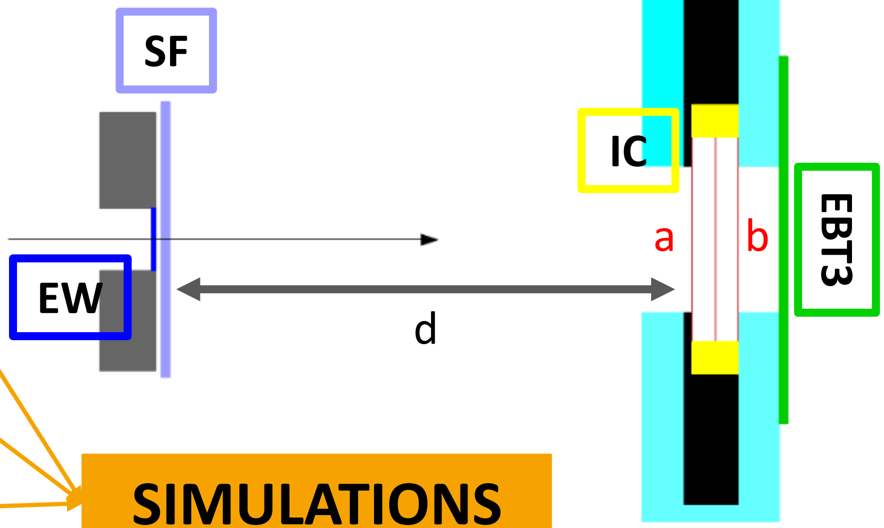


Proton dose evaluation with the ionization chamber coupled with EBT3 films

$$D = f \frac{N_{\mathrm{p}}^{\mathrm{IC}}}{A} \cdot \frac{\mathrm{d}E}{\rho_{\mathrm{Lu}} \mathrm{d}x}$$

$$N_{\mathrm{p}}^{\mathrm{IC}} = \frac{Q_{\mathrm{IC}}}{e} \cdot \frac{W}{\Delta E_{\mathrm{IC}}}$$

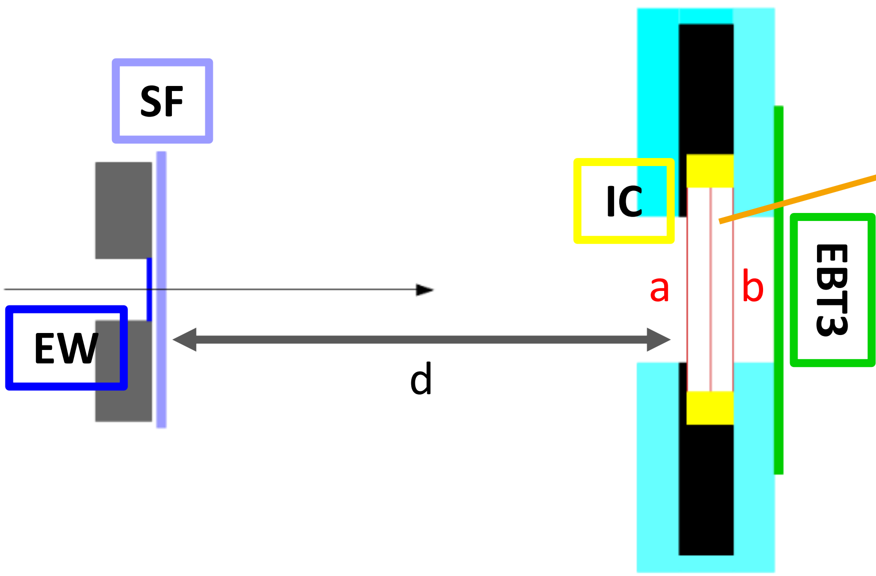
$$f = \frac{N_{\mathrm{p}}(\mathrm{b})}{N_{\mathrm{p}}^{\mathrm{IC}}(\mathrm{a})}$$

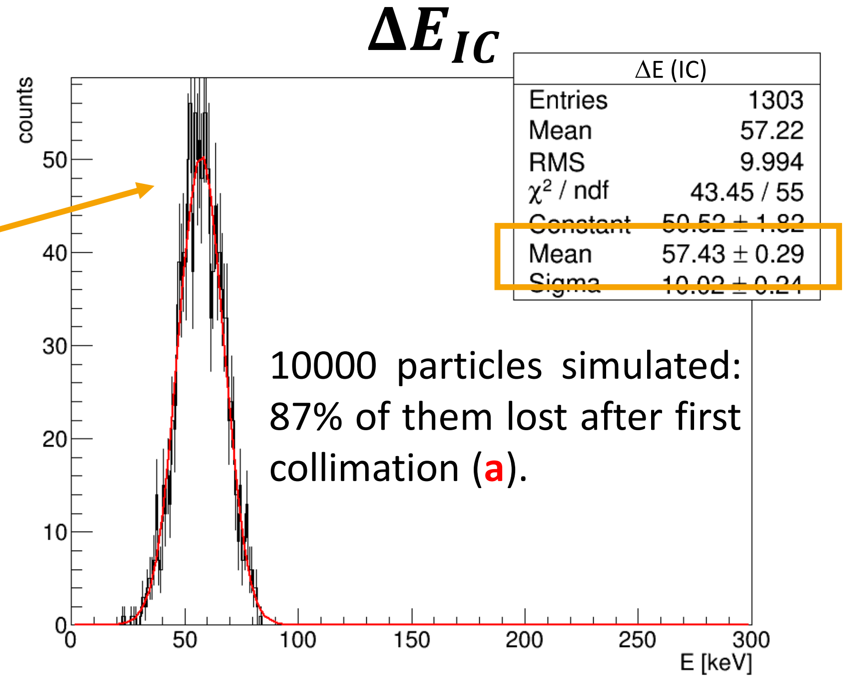


SIMULATIONS

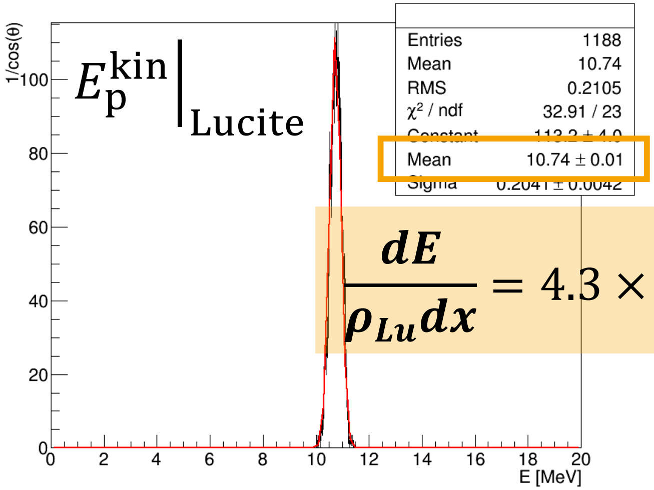
MONTE CARLO SIMULATIONS: SRIM

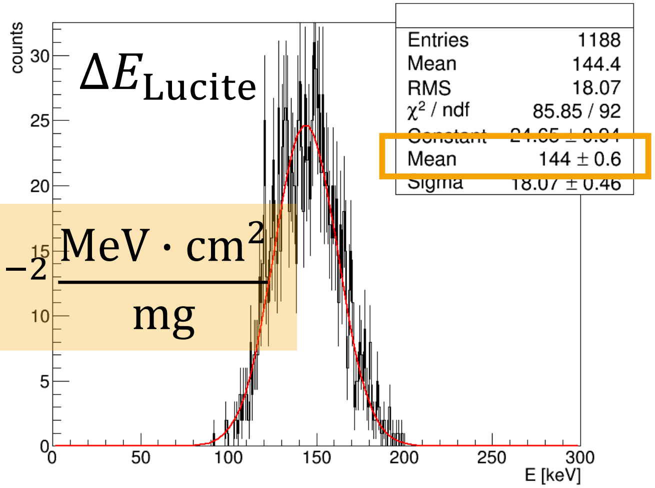
125 µm PET + 150 µm W + 49.9 cm Air + IC + EBT3





10000 particles simulated: 87% of them lost after first collimation (**a**).



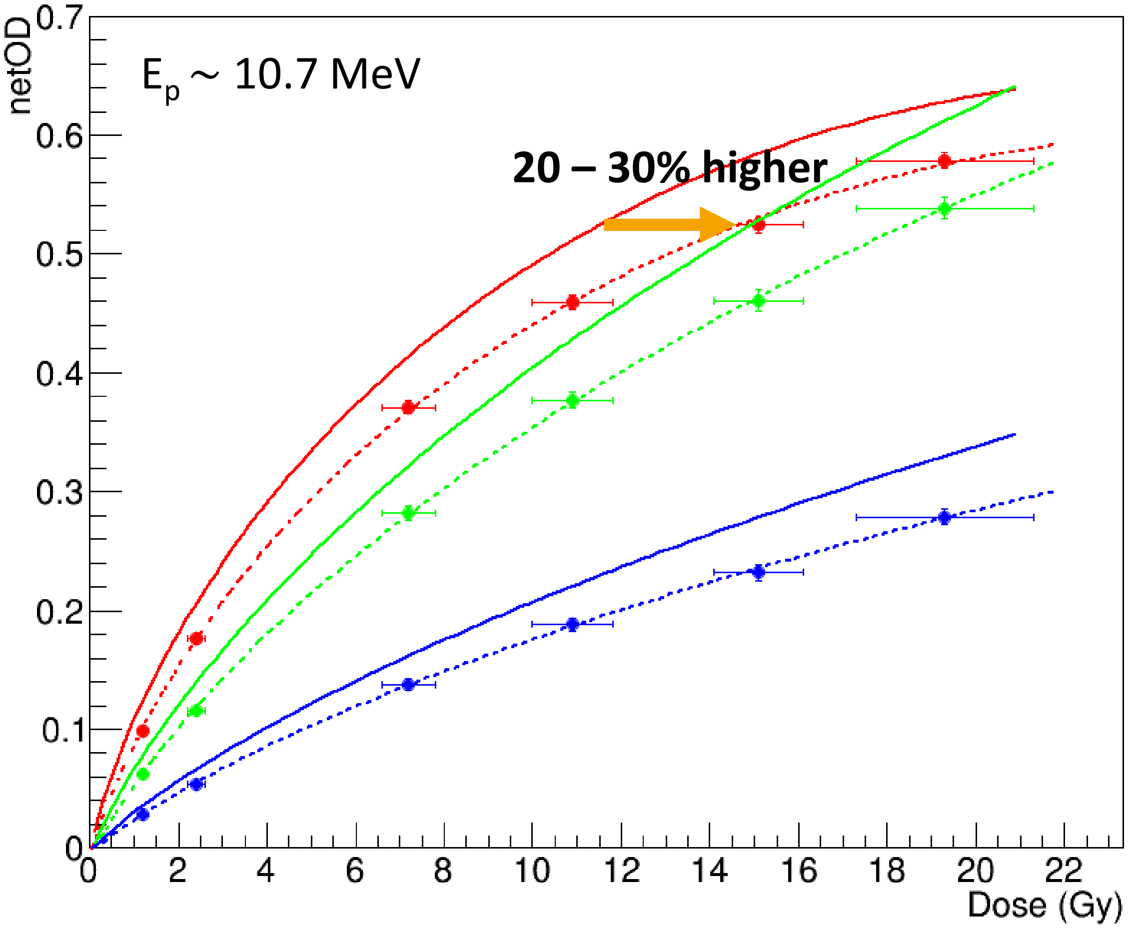


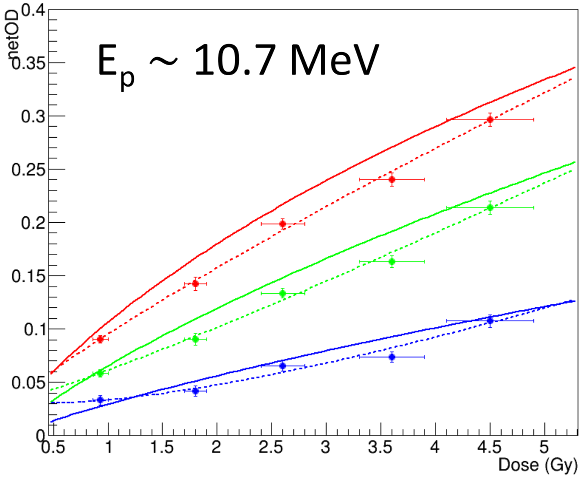
$$\frac{dE}{\rho_{Lu}dx} = 4.3 \times 10^{-2}\,\frac{\mathrm{MeV}\cdot\mathrm{cm}^2}{\mathrm{mg}}$$

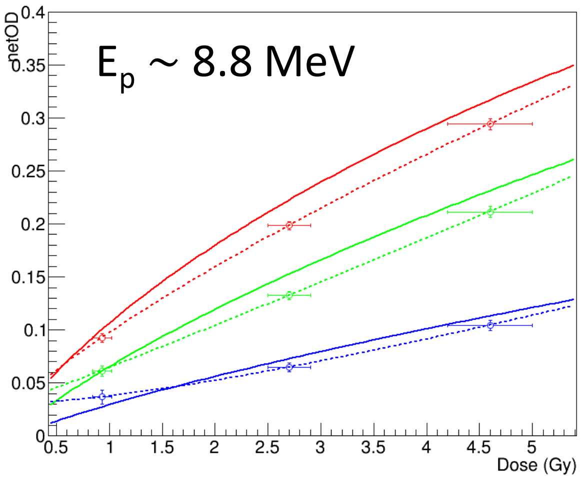
8% of simulated particles lost after second collimation (**b**).

$$f = \frac{1188}{1303} = 0.91$$

DOSIMETRY WITH EBT3 FILMS: PROTON CALIBRATION



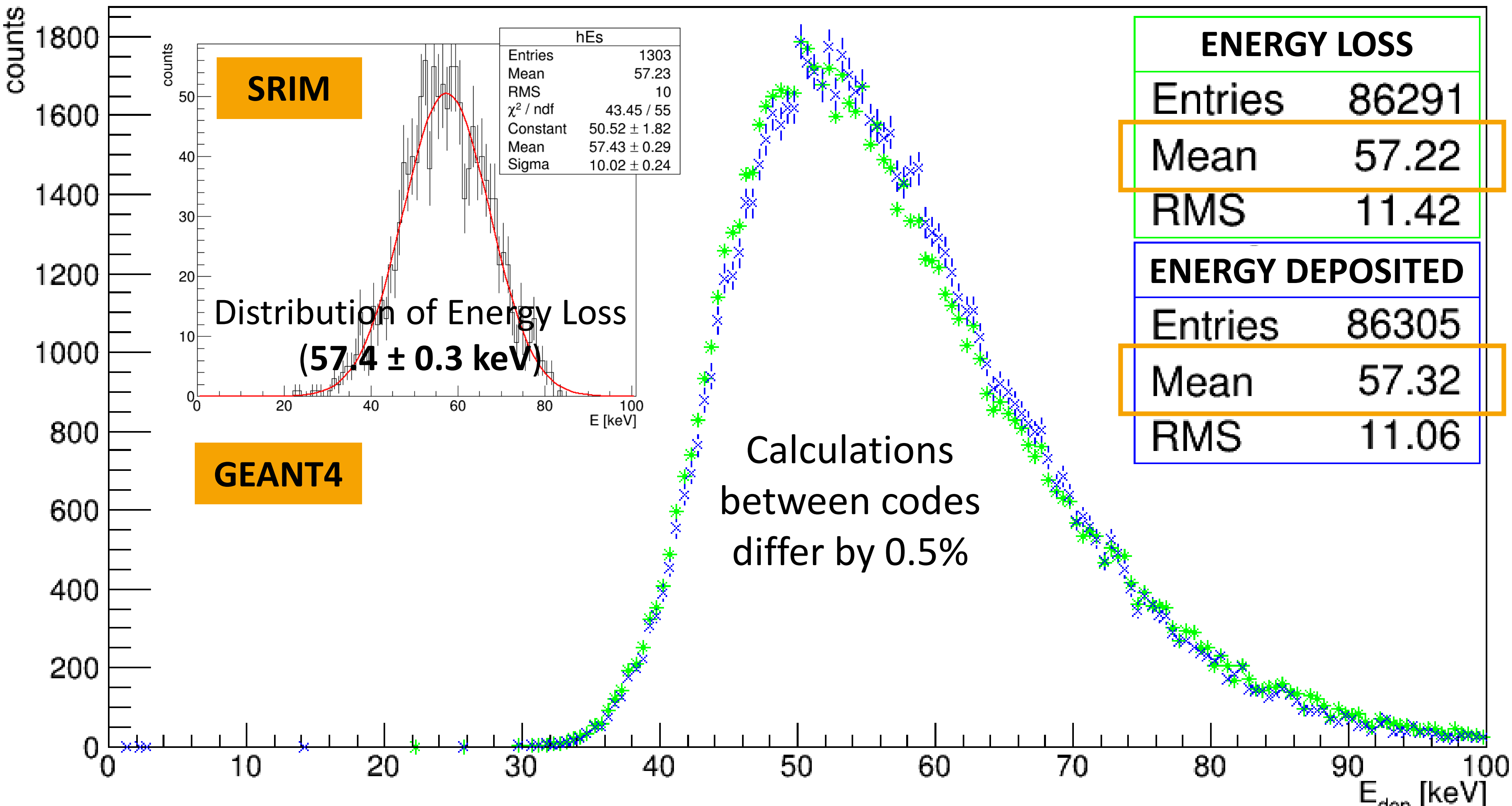




MONTE CARLO SIMULATIONS: COMPARISON SRIM – GEANT4

125 μm PET + 150 μm W + 49.9 cm Air + IC + EBT3

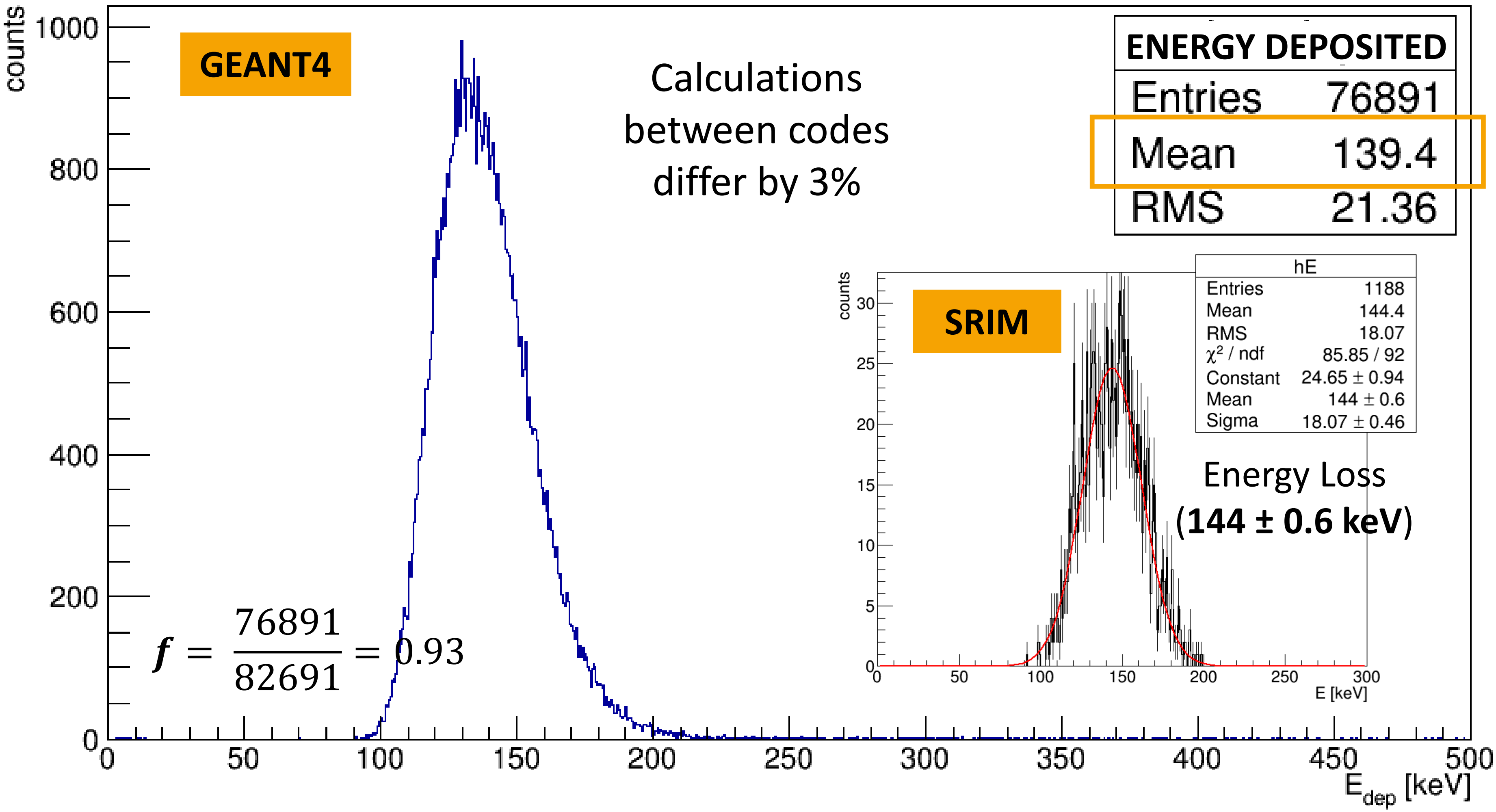
IONIZATION CHAMBER



MONTE CARLO SIMULATIONS: COMPARISON SRIM – GEANT4

125 µm PET + 150 µm W + 49.9 cm Air + IC + EBT3

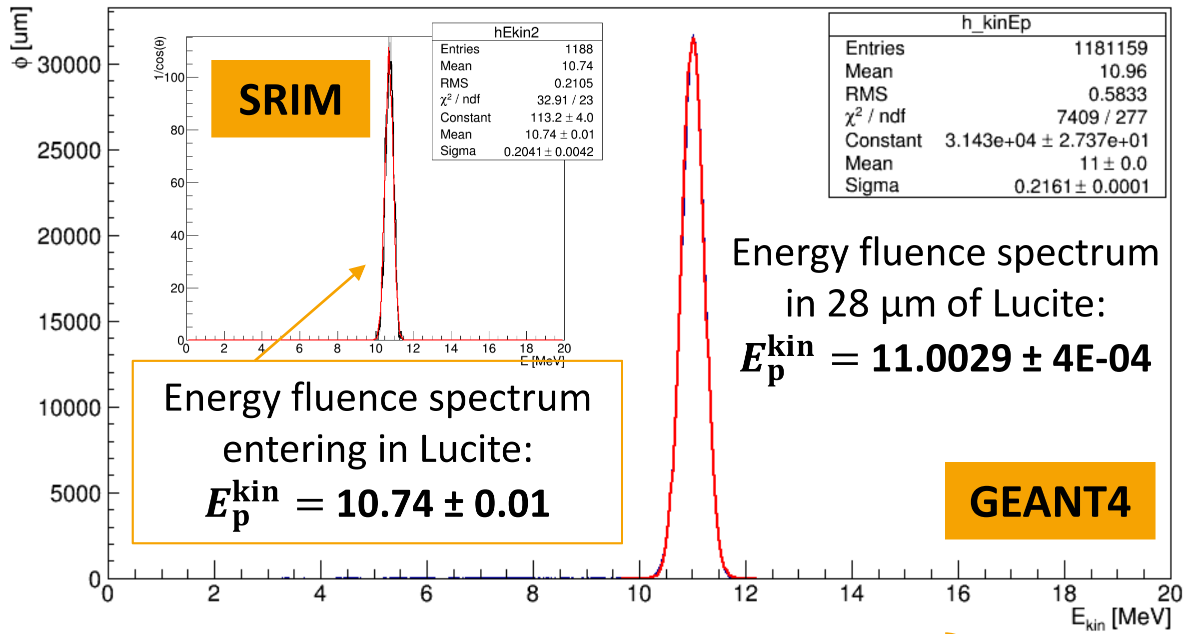
ENERGY DEPOSITED WITHIN ACTIVE VOLUME OF THE EBT3 FILM (LUCITE)

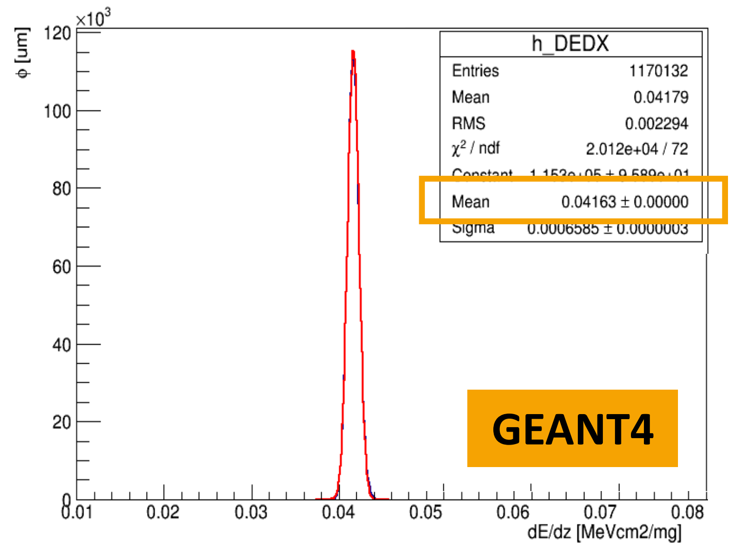


MONTE CARLO SIMULATIONS: COMPARISON SRIM – GEANT4

125 µm PET + 150 µm W + 49.9 cm Air + IC + EBT3

FLUENCE SPECTRA AND AVERAGE LET IN EBT3 FILM (LUCITE)





$$\left.\frac{dE}{\rho_{Lu}dx}\right|_{\mathrm{SRIM}} = 4.3 \times 10^{-2}\,\frac{\mathrm{MeV}\cdot\mathrm{cm}^2}{\mathrm{mg}}$$

$$\left.\frac{dE}{\rho_{Lu}dx}\right|_{\mathrm{GEANT4}} = 4.2 \times 10^{-2}\,\frac{\mathrm{MeV}\cdot\mathrm{cm}^2}{\mathrm{mg}}$$

Energies slightly higher in Geant4.

Next Step:

- Check differences for each simulation step and material.
- Compare with measured energy

Preparation of beam line: Next steps

- Accurate measurement of beam energy at the position of IC and EBT3 films, to be compared with SRIM and Geant4 simulations;
- Understand source of the differences between Geant4 and SRIM simulations;
- Complete Geant4 simulation of the beam characteristics and compare simulation results with full beam profile mesurements;
- Improve proton calibration with EBT3 films.
- Improve beam profile homogeneity (insertion of scattering foils in vacuum, change collimation system…)

AKNOWLEDGMENTS

- Thanks to Dr. M. Cristina Battaglia, who generously gave me material for this talk.

- This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No 675265, OMA – Optimization of Medical Accelerators, and from the Spanish Ministry of Economy and Competitiveness under grant No FPA2016-77689-C2-1-R. The Monte Carlo simulations were carried out at the FIS-ATOM cluster hosted at CICA (Seville, Spain).

MARIE CURIE ACTIONS

CSIC

THANK YOU FOR YOUR ATTENTION!

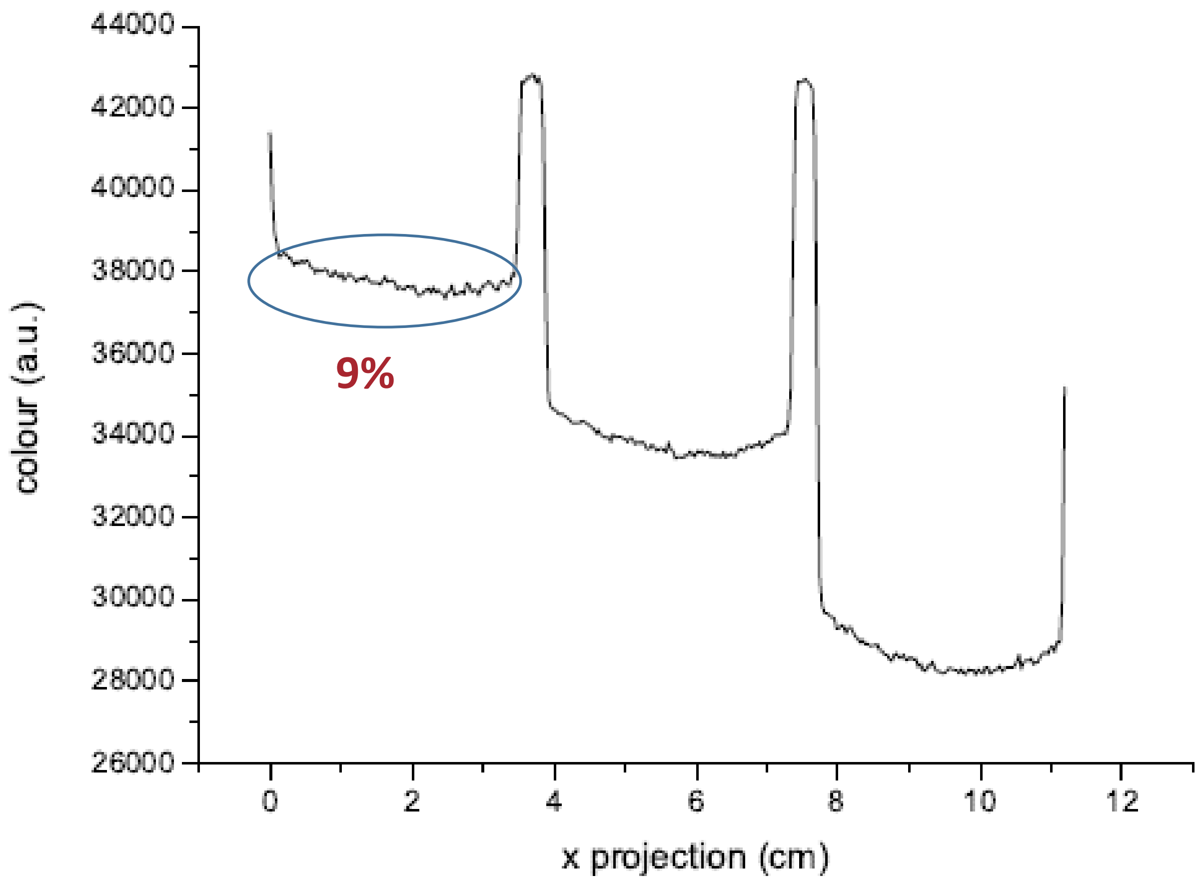
SPARE SLIDES

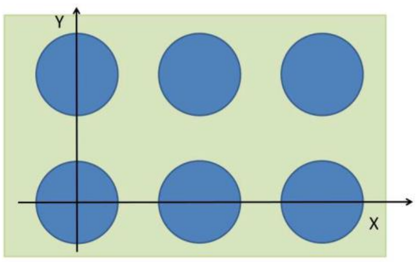
OUTLINE

- Goal of the project and CNA facilities;
- Previous experiments at Tandem;
- Extension to higher energies: the Cyclotron;
- Results;
- Conclusions.

CHARACTERIZATION OF THE BEAM PROFILE

Preliminary analysis of radiochromic films to identify the best Au scatterer:

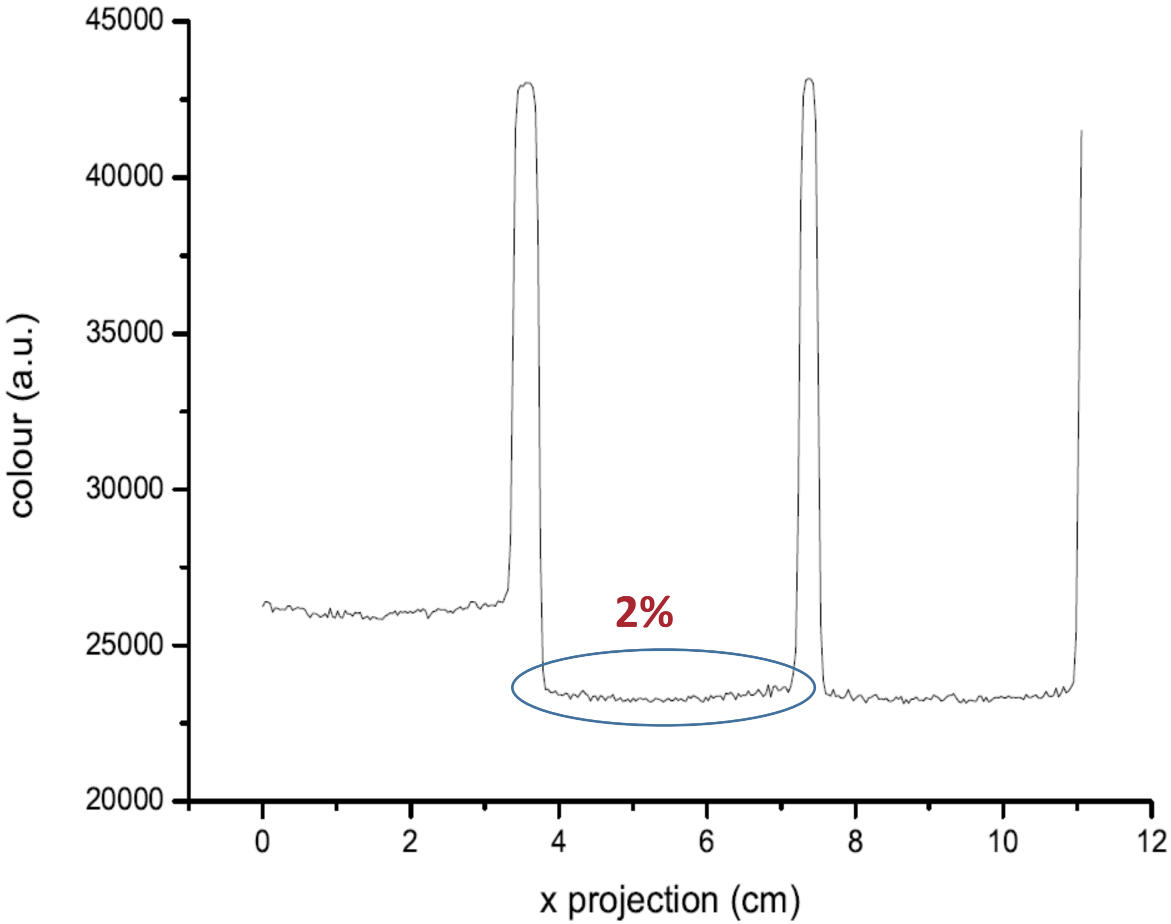


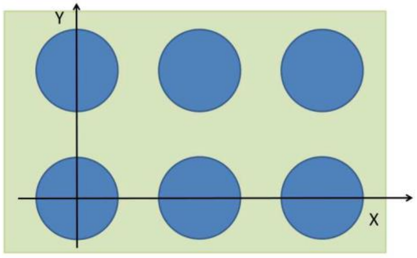


Raw response for three values of irradiation with a gold target of 2.0 mg/cm^2: curved profile, not suitable for the measurements

CHARACTERIZATION OF THE BEAM PROFILE

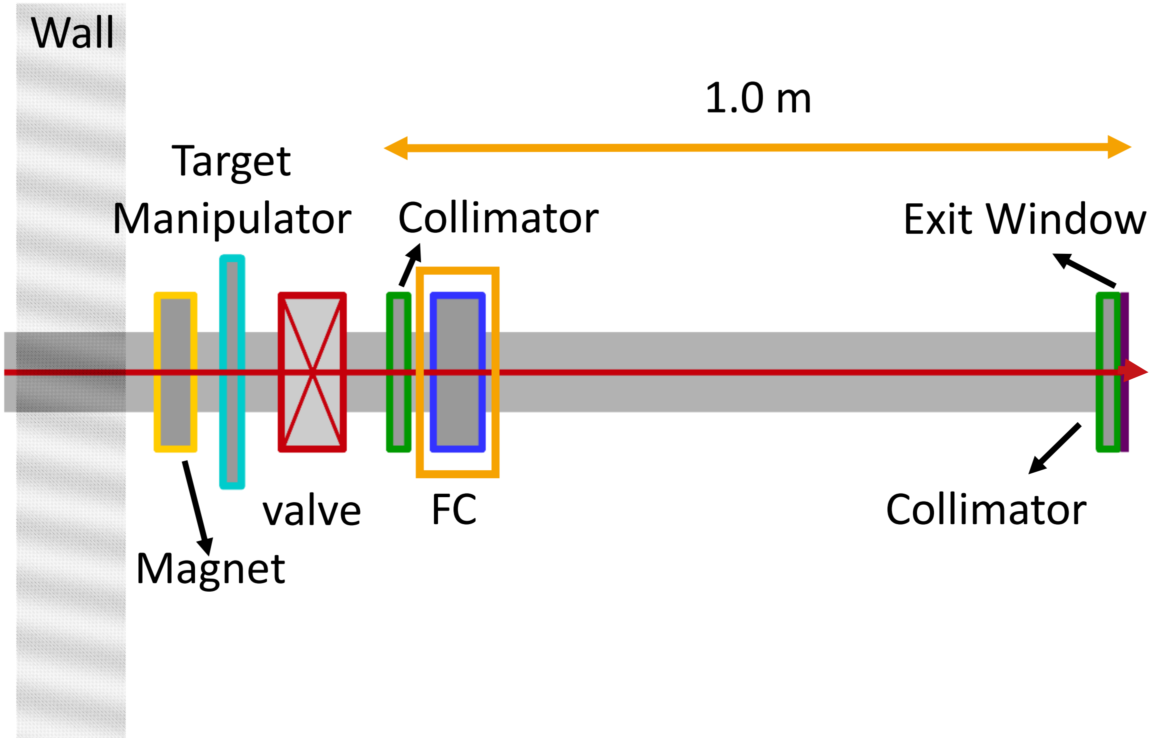
Preliminary analysis of radiochromic films to identify the best Au scatterer:

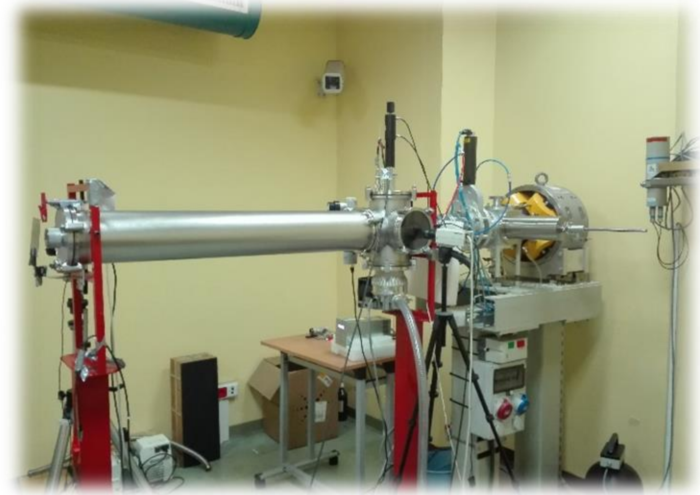




Raw response for three values of irradiation with a gold target of 5.4 mg/cm^2: flat profile, **suitable** for the measurements

EXPERIMENTAL SETUP: CYCLOTRON BEAM LINE





1. Beam centering;
2. Beam current;
3. Beam shape;
4. Sample centering:
    a. Samples placed on a moving table with millimetric precision;
    b. Samples centred at the beam position.

SETUP FOR FULL BEAM PROFILES MEASUREMENT