FOOT (FragmentatiOn Of Target) Experiment

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FOOT

14th Nordic Meeting of Nuclear Physics

Longyearbyen, Norway

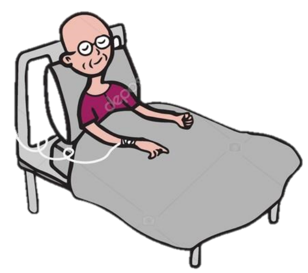
22-25 May, 2018

Cancer in the world

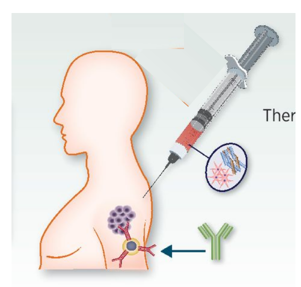
- 2015: **8.8 millions deaths** due to cancer (World Health Organisation Media Center)
- 2030: **13 millions** (projection)
- Five different methods of treatment:

Surgery

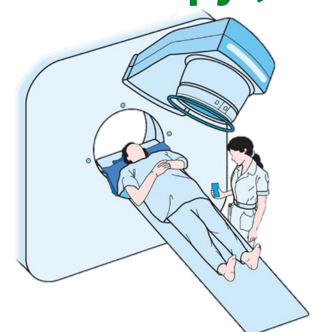
Chemotherapy



Immunotherapy

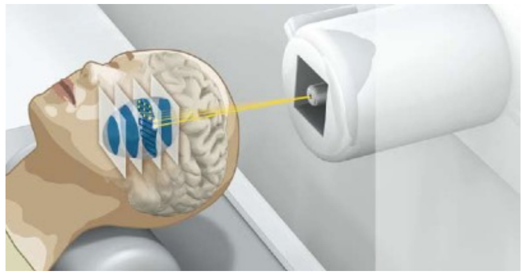


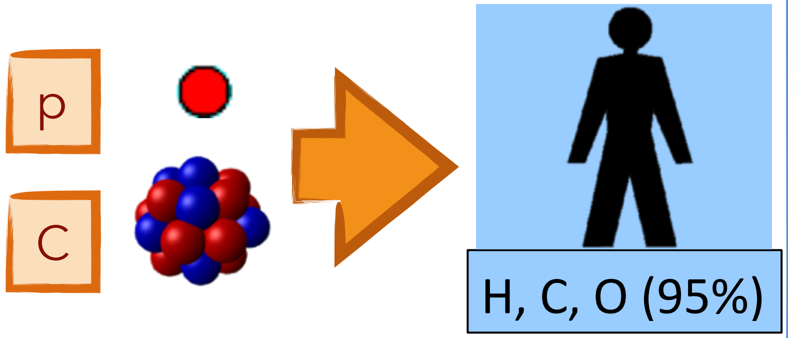
Radiotherapy (X-ray)

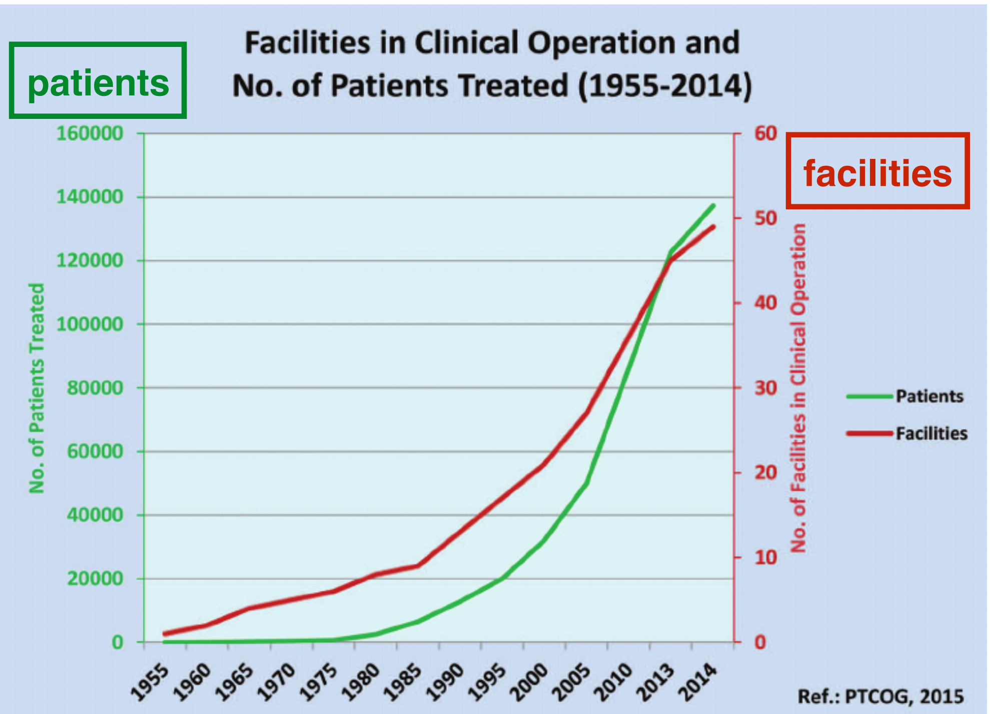


~50%
of all cancer patients

Hadrontherapy







Continuous expansion in the last 50 years

Facility (end of 2016):

- operative: 61 proton
  9 heavy ion centres

Treated patients (end of 2016):

- 149345 with proton (in USA 64516)
- 21580 with ^{12}C (in Japan 17331)

From 2010: 10000 patients per year

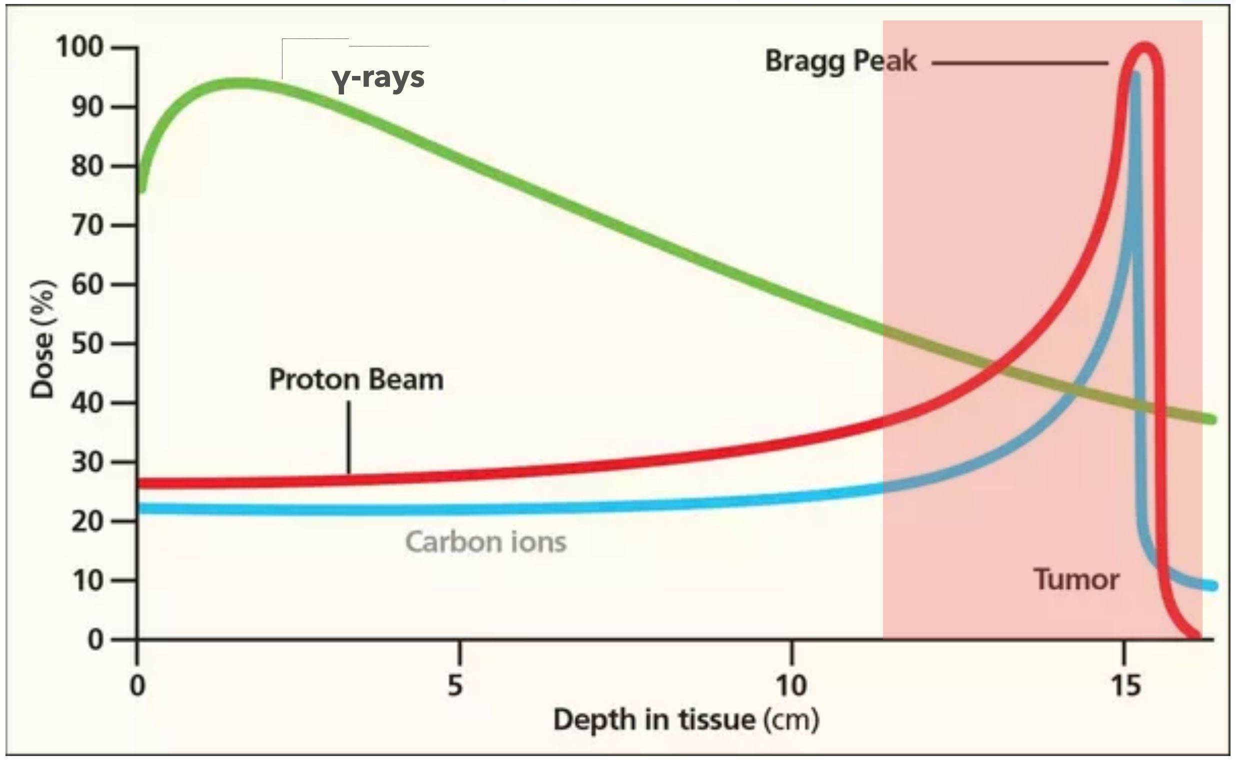
Hadrontherapy for cancer treatments

Radiotherapy

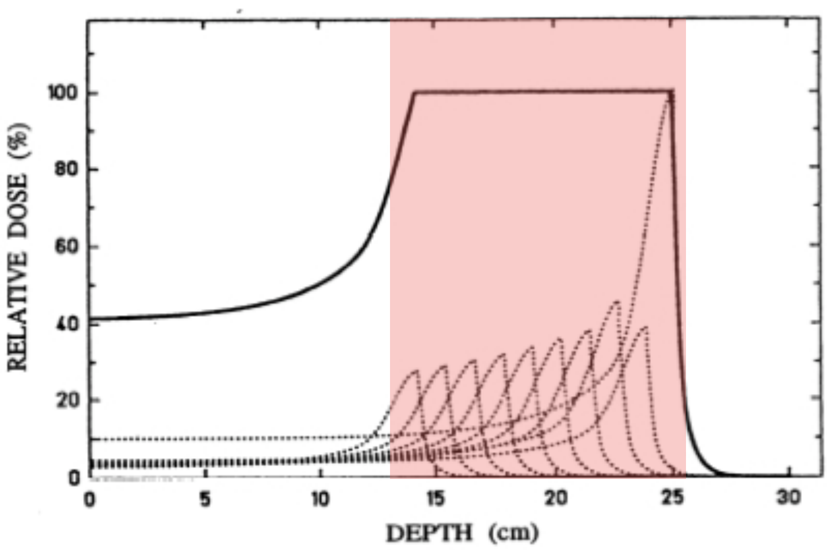
- large dose both in the entrance channel and beyond the tumour volume

Hadrontherapy

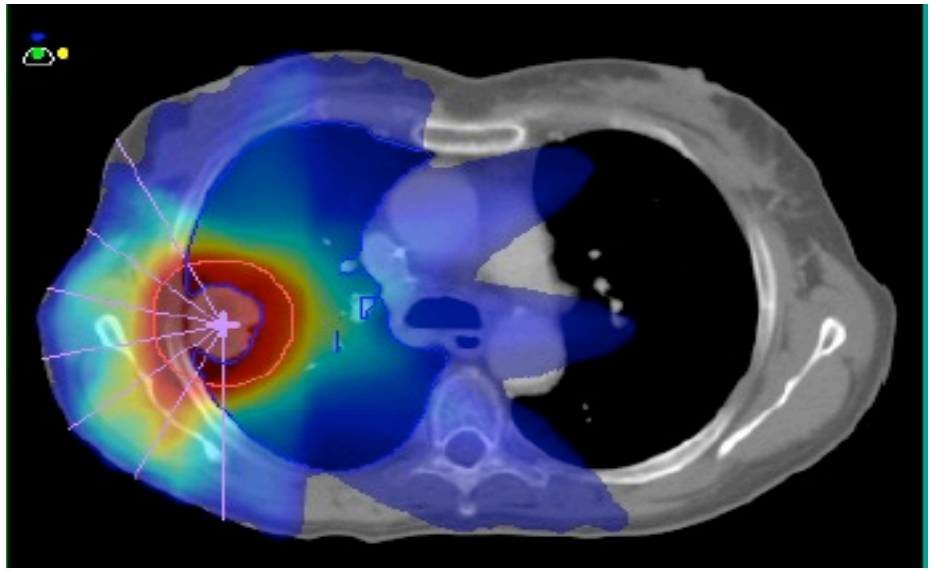
- Peak of dose release at the end of the path
- Beam penetration in tissue as a function of the beam energy
- High 3D precision



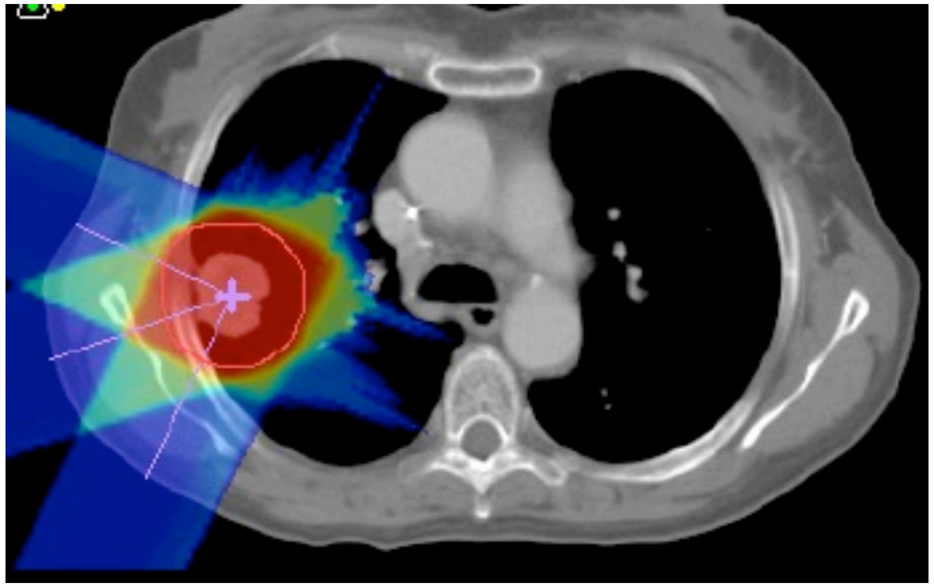
Accurate dose to tumour with Spread Out Bragg Peak (SOBP)



Radiotherapy



Hadrontherapy



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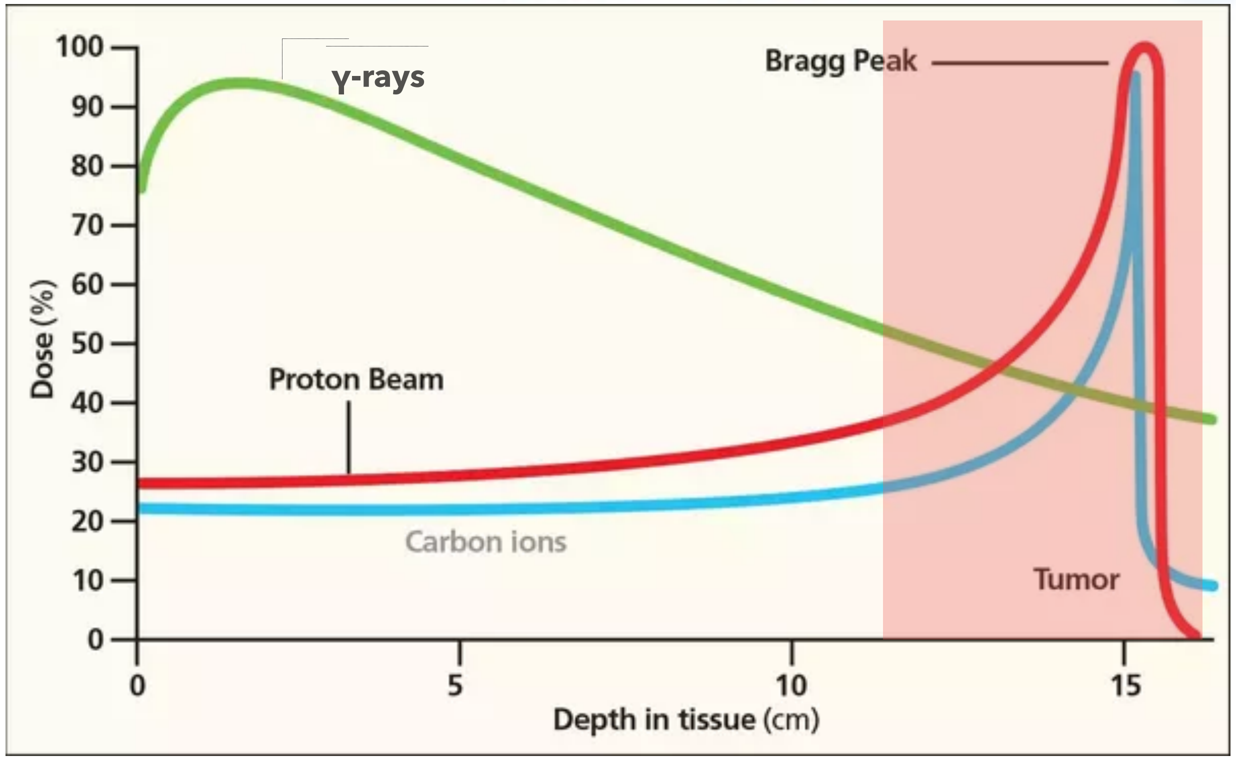

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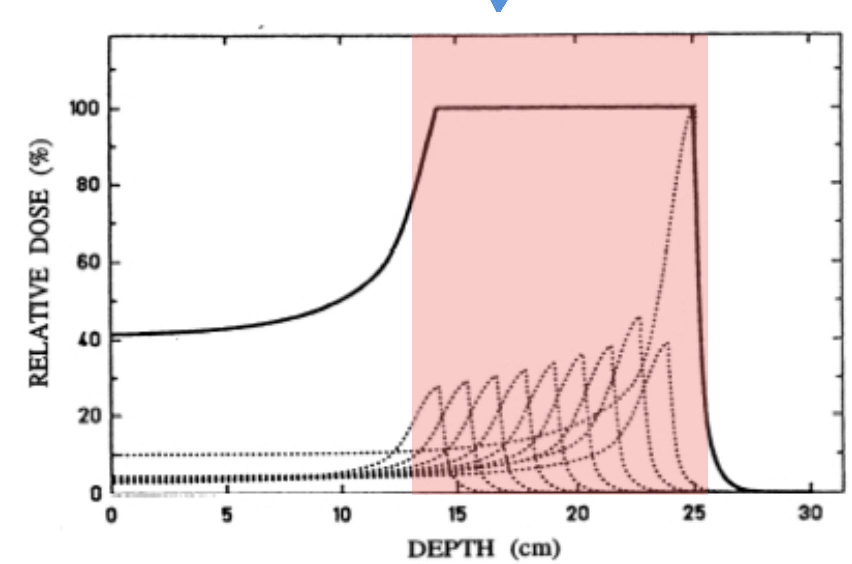
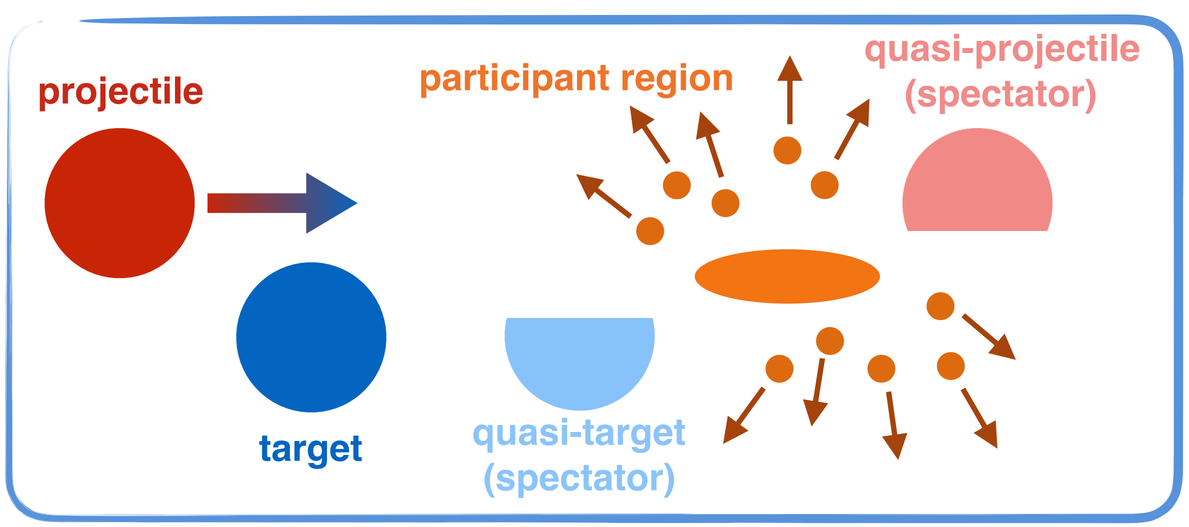


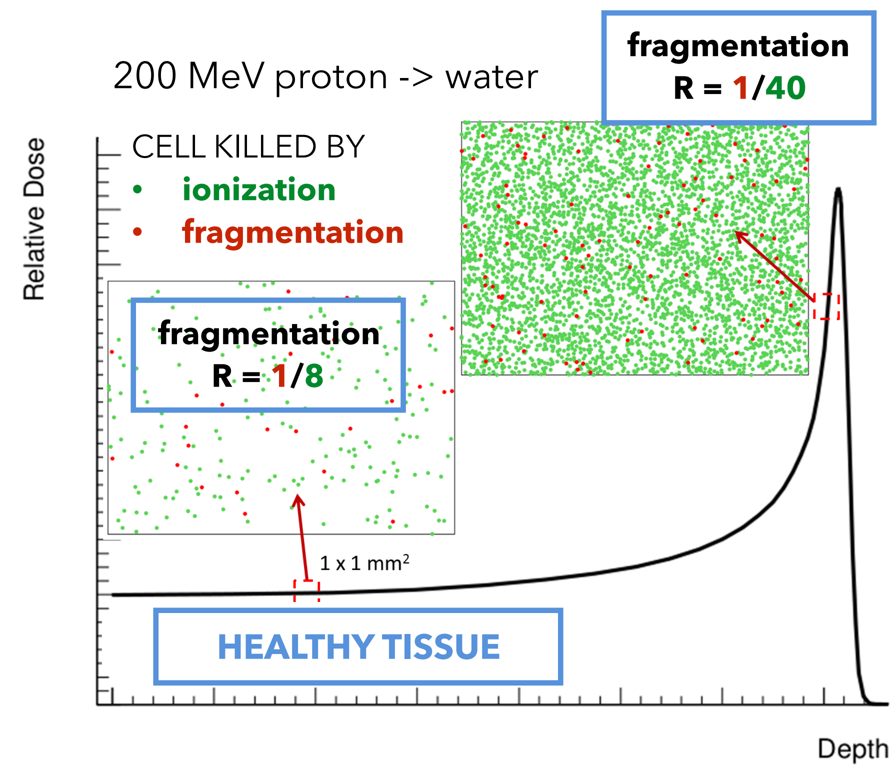
....BUT....

hadrontherapy costs ~5-10 radiotherapy

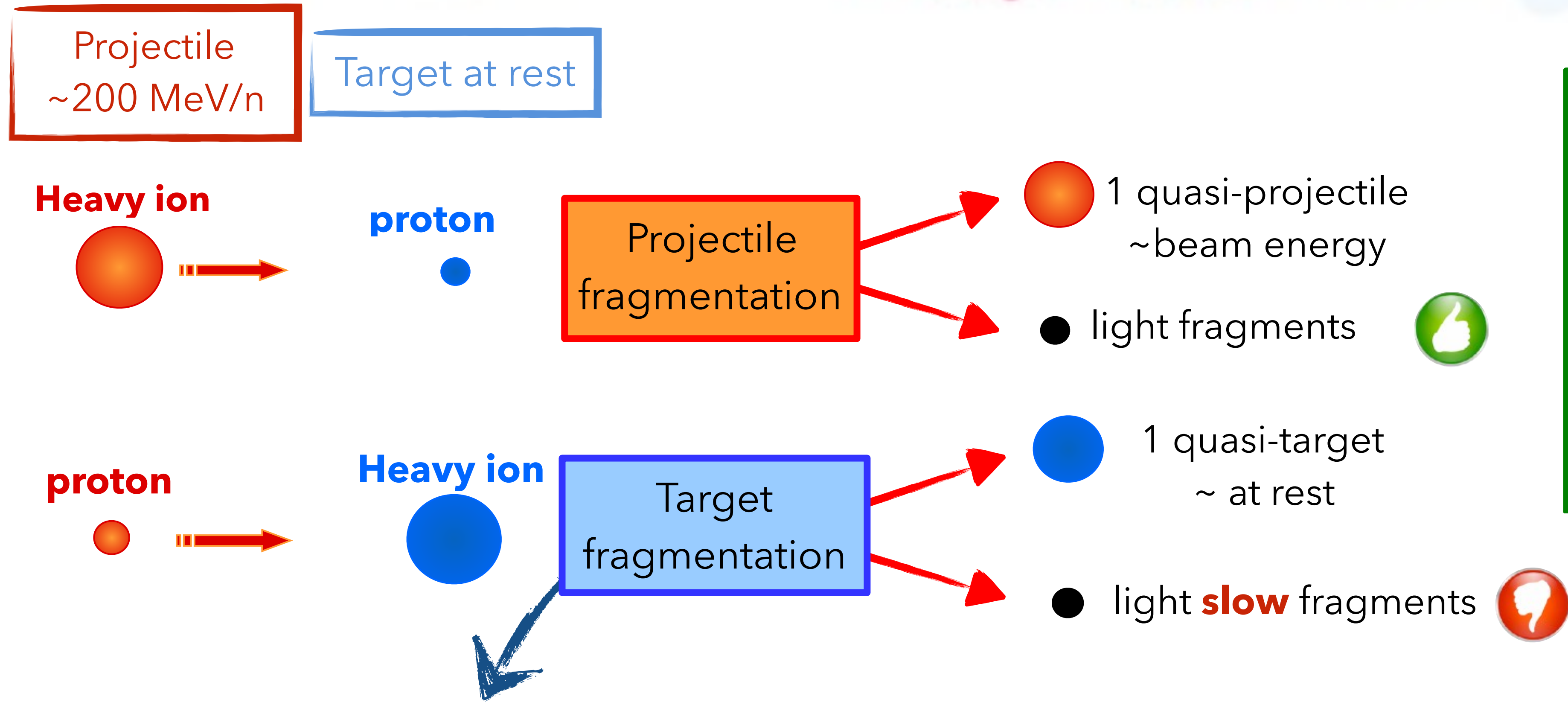
At the hadrontherapy energy (~ 10^2 MeV/nucleon), fragmentation is the most frequent nuclear interaction:

➡ peripheral collision, few nucleons participate, low multiplicity



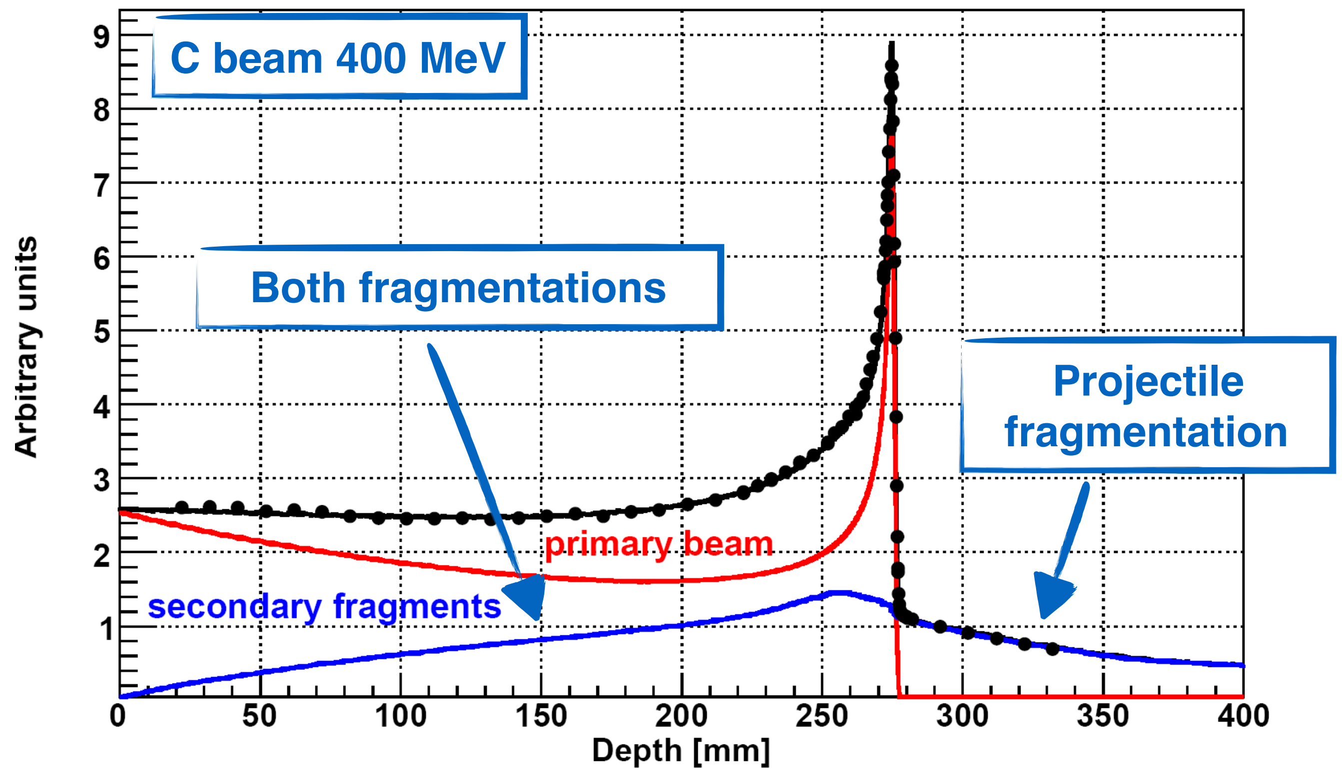


Fragmentation in hadrontherapy



Fragment	E (MeV)	LET (keV/μm)	Range (μm)
^{15}O	1.0	983	2.3
^{15}N	1.0	925	2.5
^{14}N	2.0	1137	3.6
^{13}C	3.0	951	5.4
^{12}C	3.8	912	6.2
^{11}C	4.6	878	7.0
^{10}B	5.4	643	9.9
^{8}Be	6.4	400	15.7
^{6}Li	6.8	215	26.7
^{4}He	6.0	77	48.5
^{3}He	4.7	89	38.8
^{2}H	2.5	14	68.9

Problem: Target fragments remain in the target



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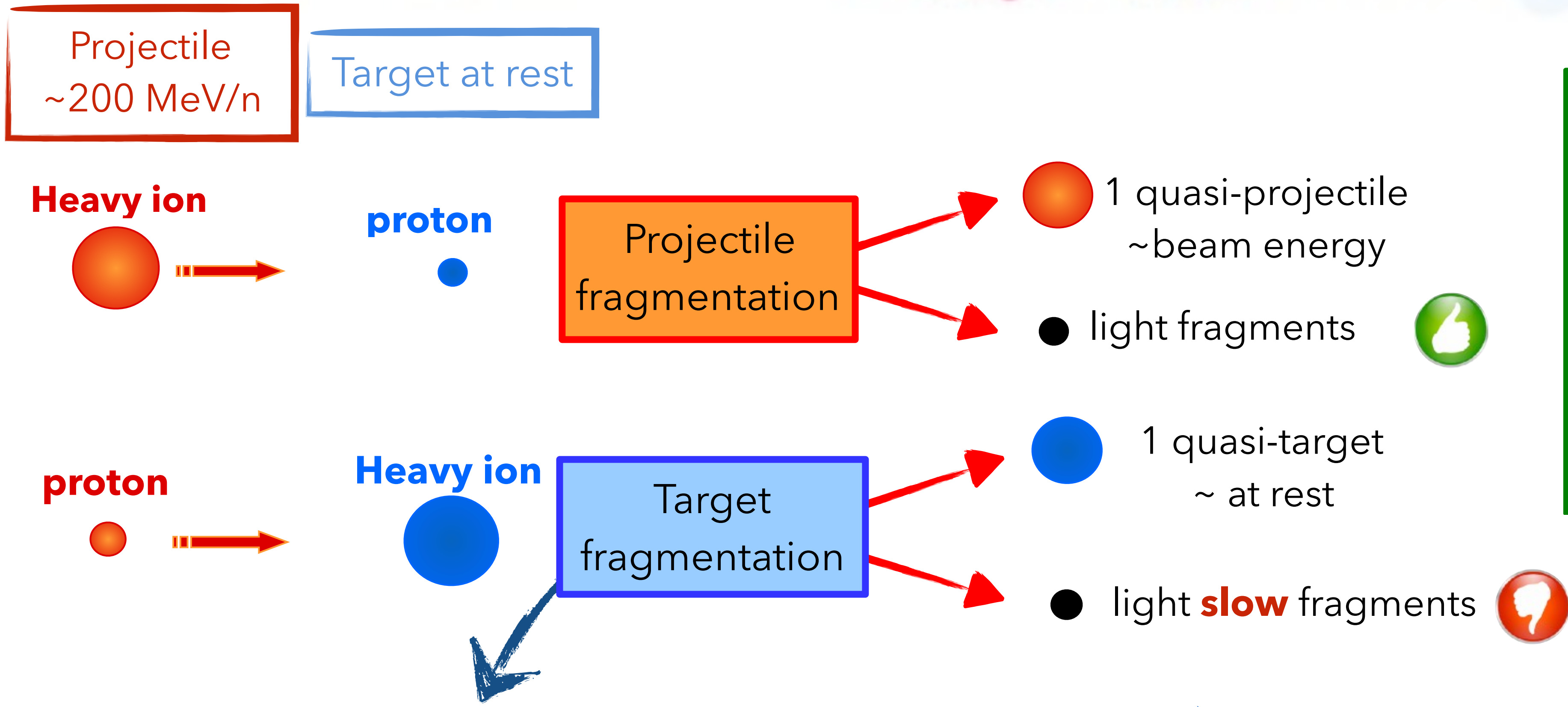

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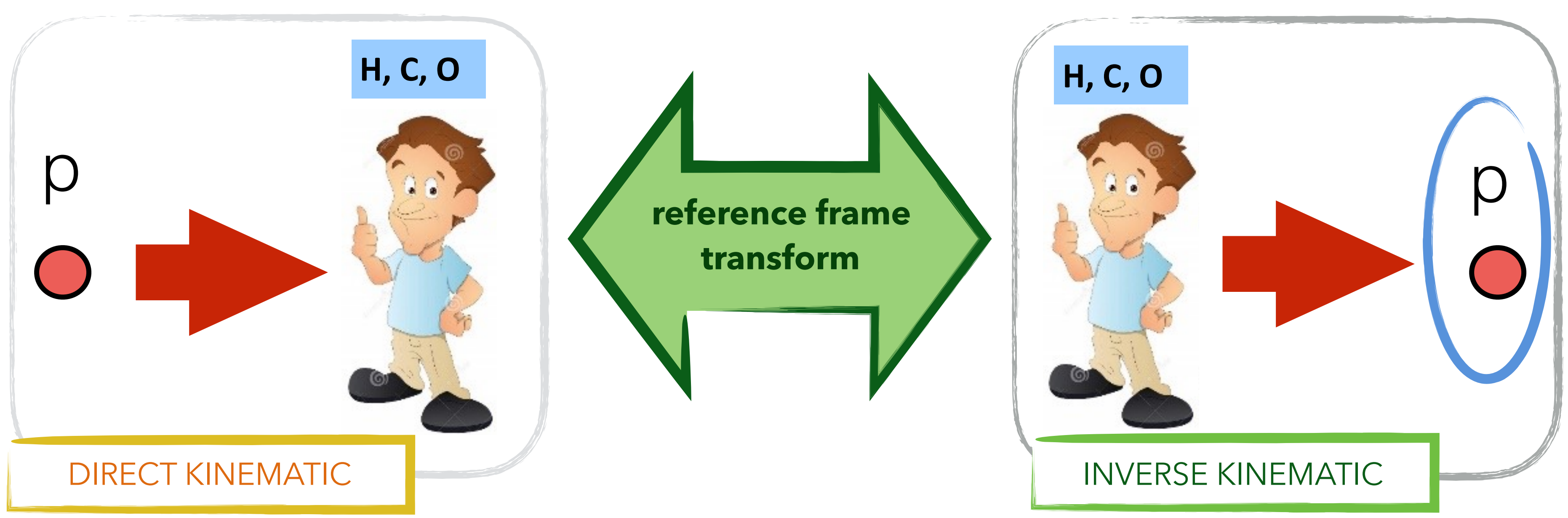
Problem: Target fragments remain in the target ⇨ **Solution:** Inverse kinematics

Shoot C,O (,He) on proton beam

Reference frame back-transformation = **Lorentz boost** to the final products



Fragmentation in hadrontherapy

Projectile ~200 MeV/n

Target at rest

Heavy ion → **proton** : Projectile fragmentation → 1 quasi-projectile ~beam energy; light fragments

proton → **Heavy ion** : Target fragmentation → 1 quasi-target ~ at rest; light **slow** fragments

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Problem: Hydrogen target

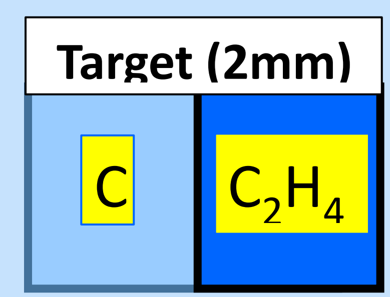
- gas is too sparse (too low cross sections)
- gas is not allowed in all the experimental rooms

Solution:

Polyethylene target C_2H_4 + Carbon target

- need to subtract the cross section on carbon to the one on polyethylene
- additional uncertainties to the final measurement

$$\frac{d\sigma}{dE_{kin}}(H) = \frac{1}{4}\left(\frac{d\sigma}{dE_{kin}}(C_2H_4) - 2\frac{d\sigma}{dE_{kin}}(C)\right)$$

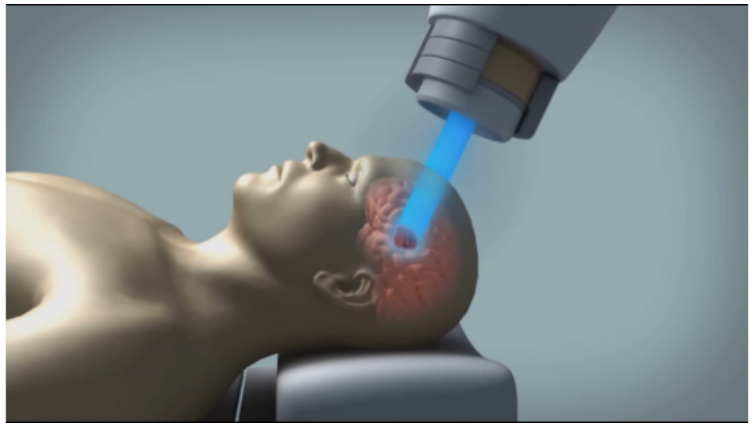


Fragmentation probability ~ 1%

The FOOT Experiment: goals

HADRONTHERAPY

- **Target fragmentation**
  - dσ/dE and dσ/dθ (with 5% precision) of all the fragments in inverse kinematics at hadrontherapy energies (~200-400 MeV) with p, C, O beams
- **Projectile fragmentation**
  - same but in direct kinematics



Radiobiology requests: to have a more precise **NTCP (Normal Tissue Complication Probability)** model on p+C,O @200-400 MeV/n

RADIOPROTECTION IN SPACE

- dσ/dE and dσ/dθ (with 5% precision) of all the fragments in inverse and direct kinematics at hadrontherapy energies with p, C, O beams

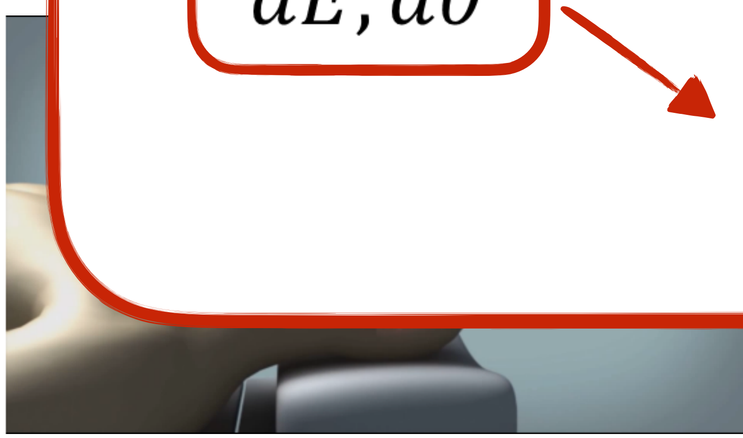
design and optimisation of the spacecraft shielding requires a detailed knowledge of the fragmentation processes

particles species currently available or considered in hadrontherapy (p,C or He,Li,O) are among **the most abundant in space!**

The FOOT Experiment: goals

HADRONTHERAPY

- **Target fragmentation**
  - dσ/dE and dσ/dθ (with 5% precision) of all th
    had
    Me
- **Project**
  - sam



RADIOPROTECTION IN SPACE

- dσ/dE and dσ/dθ (with 5% precision) of all the fragments in inverse and direct kinematics at
  beams
  ecraft
  edge

$$\frac{d\sigma}{dE, d\theta}$$

Identify all the different fragments
- Capability to reconstruct the charge
- Capability to resolve isotopes

1-2 MeV of **measurement accuracy**

angle spectrum accuracy important to correctly hit the tumour in the transverse plane

Radiobiology requests: to have a more precise **NTCP (Normal Tissue Complication Probability)** model on p+C,O @200-400 MeV/n

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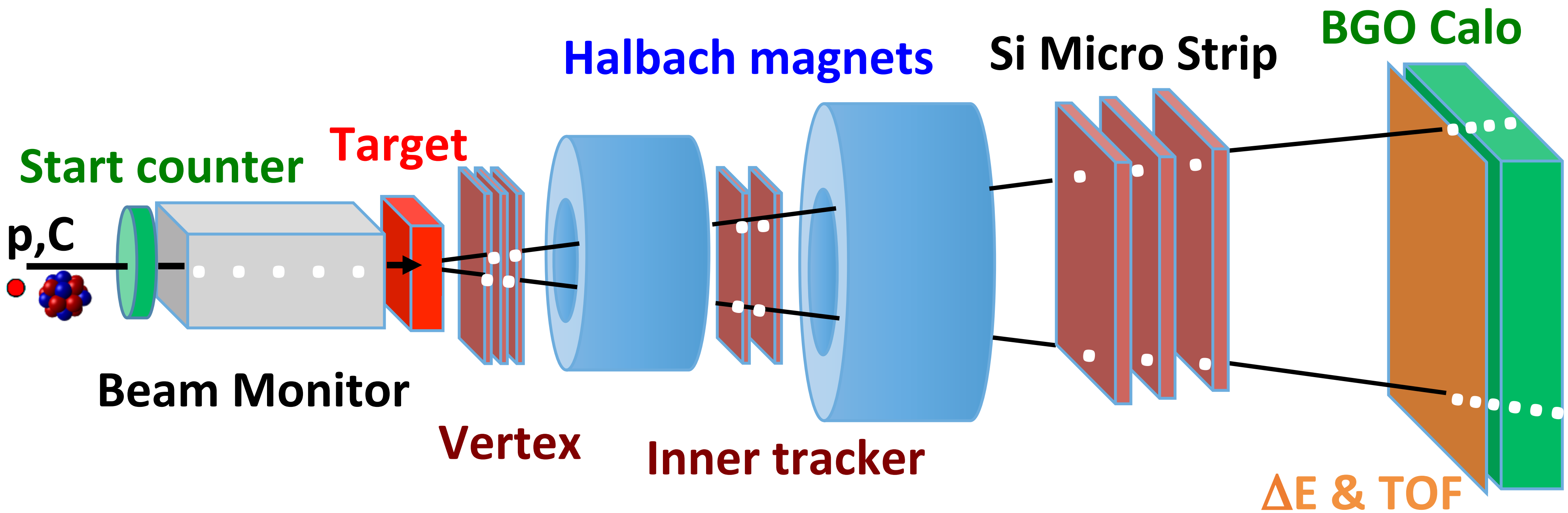
The FOOT Experiment: electronic setup

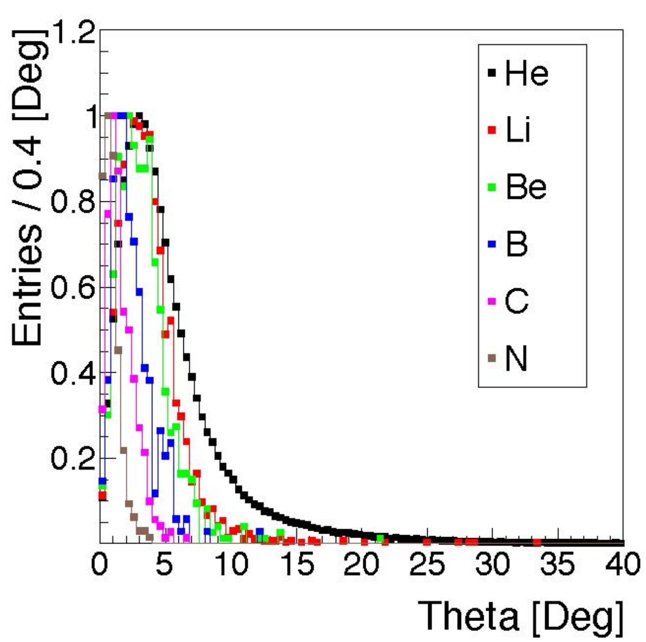


Needed detector performances

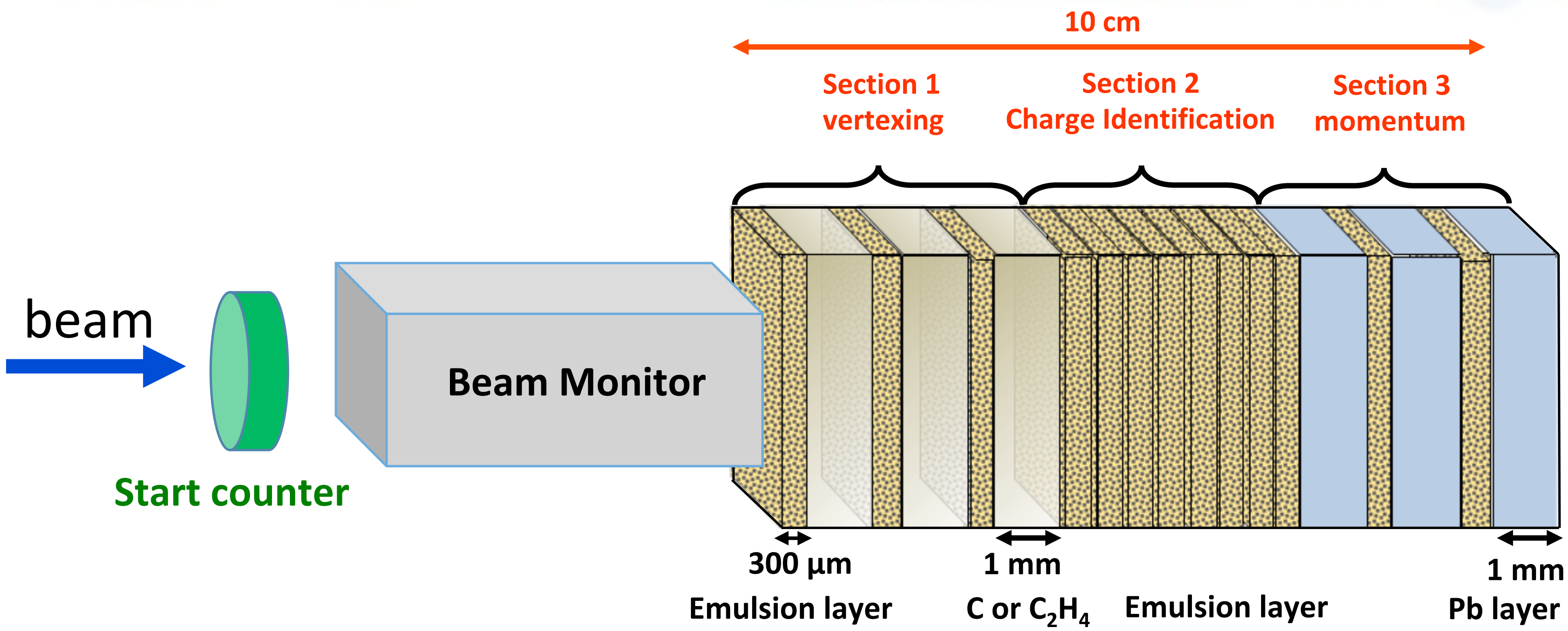
- **Δp/p** ~5%
- **TOF** resolution ~100ps
- **$\Delta E_{kin}/E_{kin}$** ~2%
- **Δ(dE)/dE** ~2%

Sub-detector	Main characteristics
Start counter	plastic scintillator 250 μm
Beam monitor	drift chamber (12 layers of wires)
Target	$C+C_2H_4$ (2 mm)
Vertex	4 layers silicon pixel (20x20 μm)
Magnet	2 permanent dipoles (0.8 T)
Inner tracker	2 layers silicon pixel (20x20 μm)
Outer tracker	3 layers silicon strip (125 μm pitch)
Scintillator	2 layers of 20 bars (2x40x0.3 μm)
Calorimeter	360 BGO crystals (2x2x14 μm)

- optimised for heavy (Z≥3) fragments
- less than 2m: can be easily movable to fit the space limitations from experimental and treatment rooms
- angle setup: ±10°



The FOOT Experiment: emulsion setup



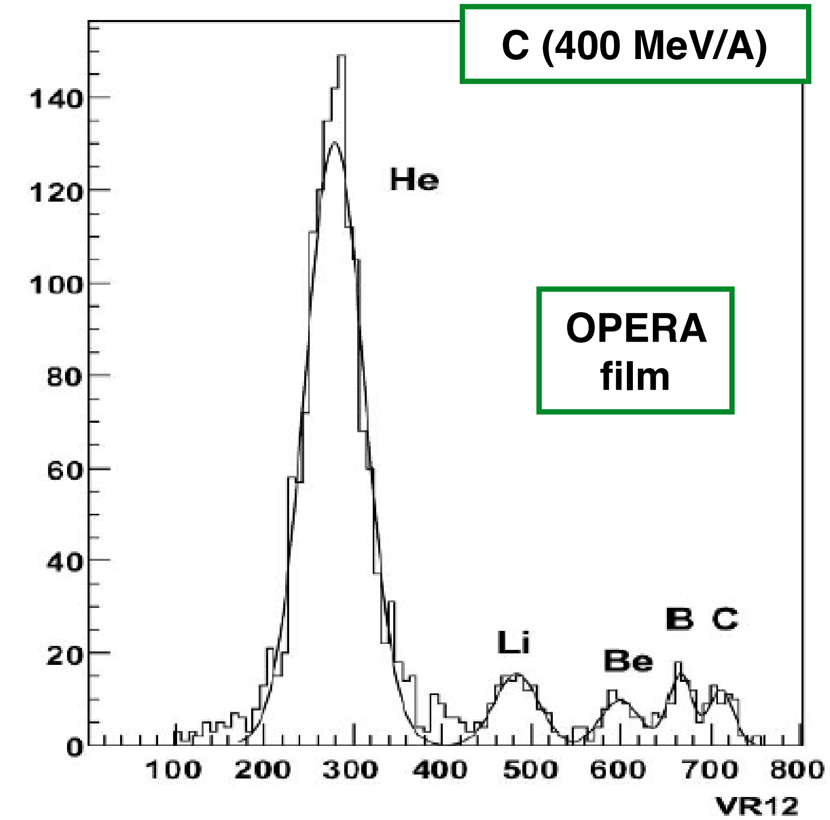
- optimised for light (Z≤3) fragments
- less than 1m: can be easily movable to fit the space limitations from experimental and treatment rooms
- angle setup: ±75°

Two complementary setups

- main reason: required angular precision of few mrad hard to achieve with an apparatus of limited size
- lower mass fragments (Z<3) can be emitted within a wider angular aperture wrt heavier nuclei

Main characteristics

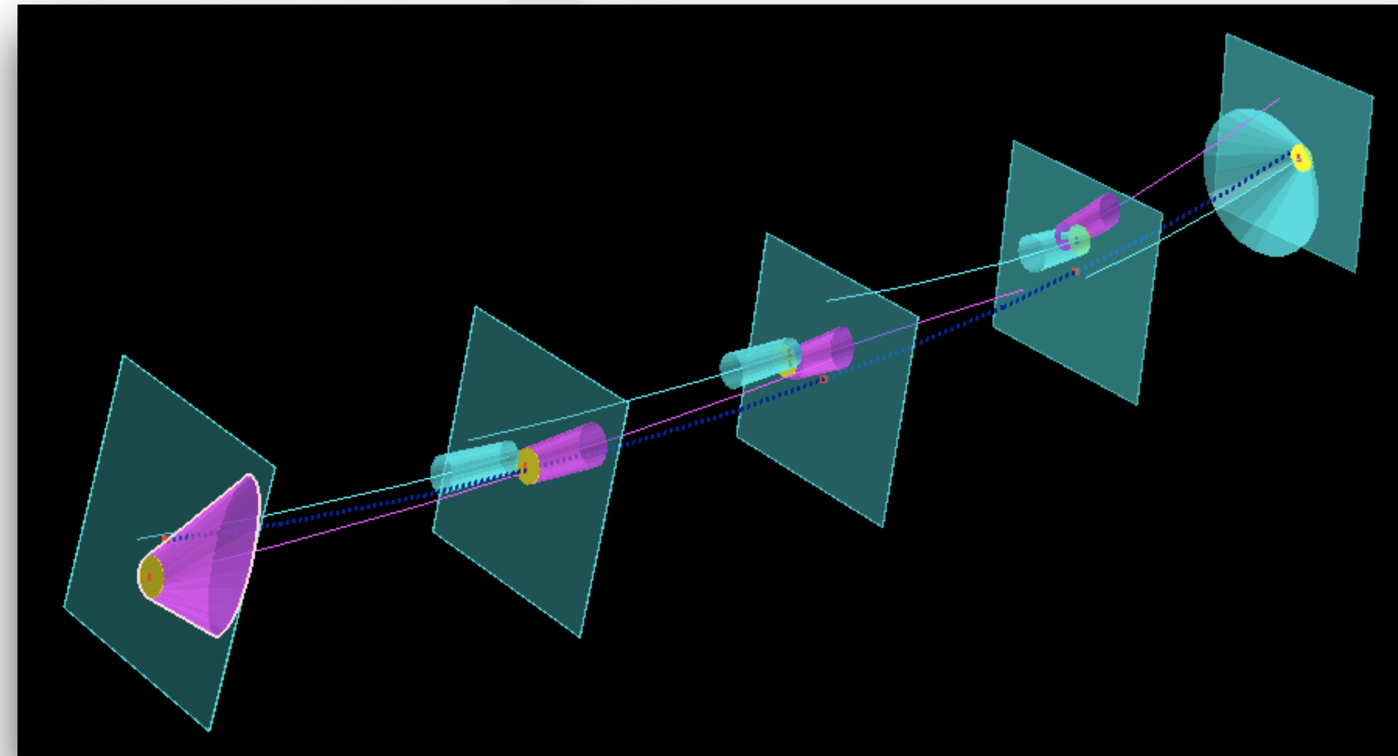
- both target and detector integrated in a very compact setup
- accurate reconstruction of the interactions inside the target (sub-micrometric resolution)
- fragment charge assessed with an efficiency > 99%
- automated scanning system technique: very fast and with wide angular acceptances



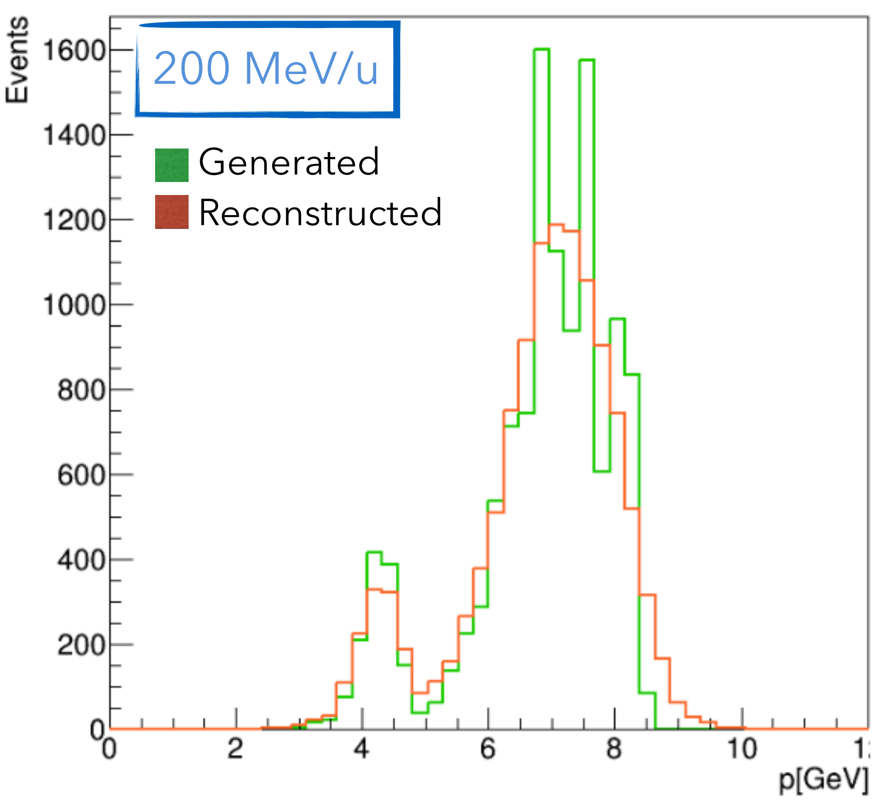
Fragmentation reconstruction

Fragmentation reconstruction uses

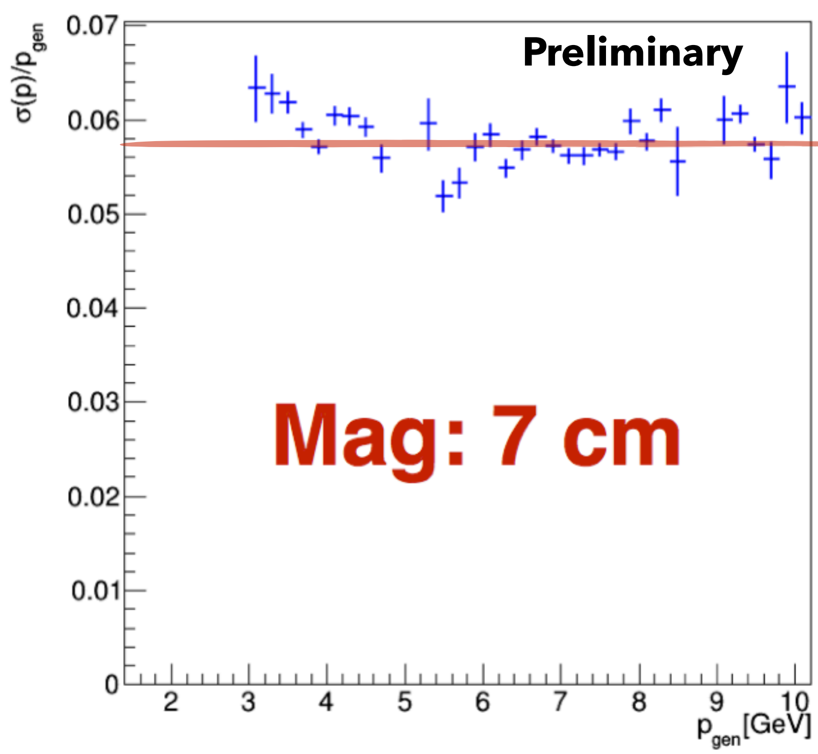
- ☑ global track fitting algorithm
- ☑ Vertex, Inner Tracker and Microstrip detectors simulated

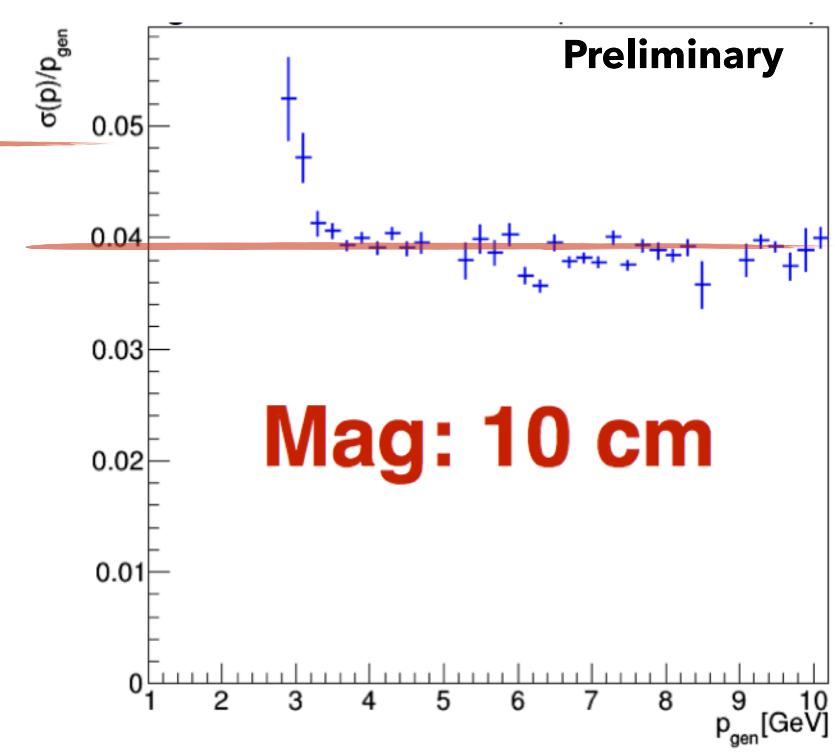


- Tracking using hits from a **single fragment at a time**.
- High filter reconstruction **efficiency** (when the fit converges over all processed)



- **Momentum resolution** determined with two different magnets options





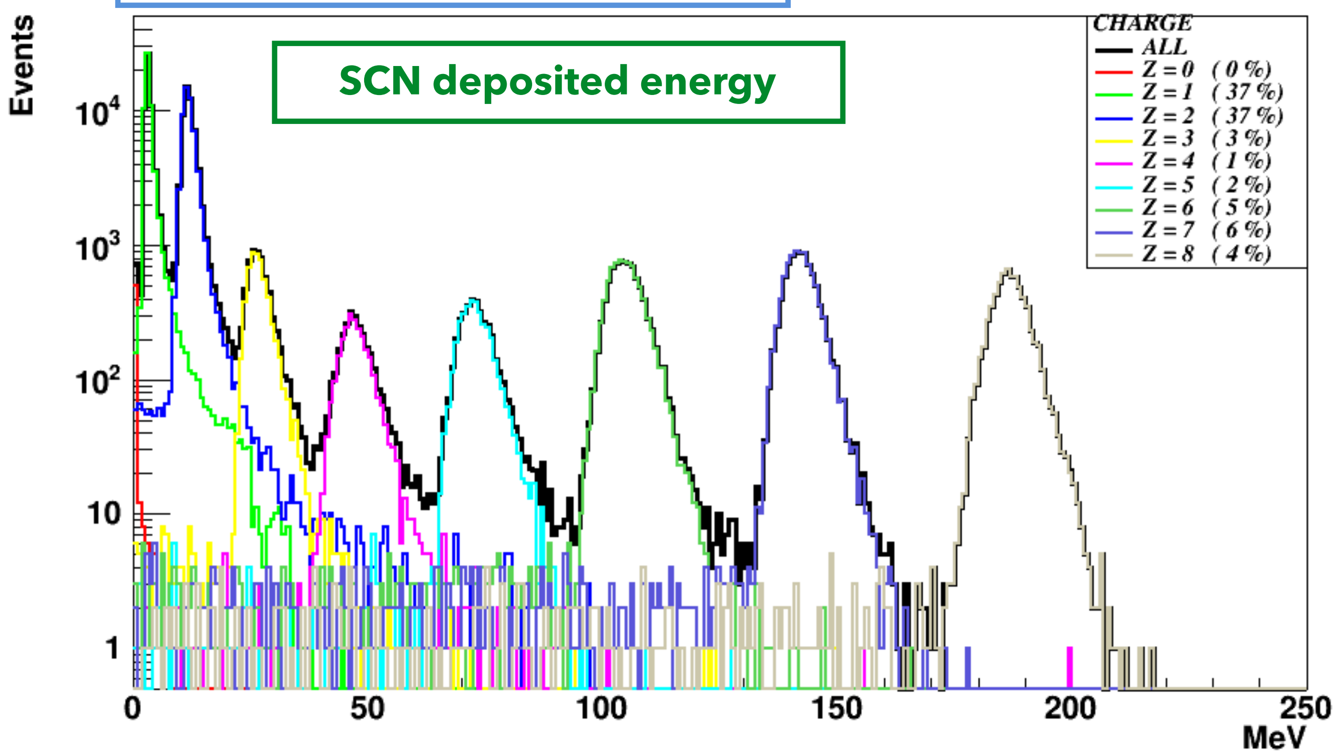
Fragmentation identification (I)

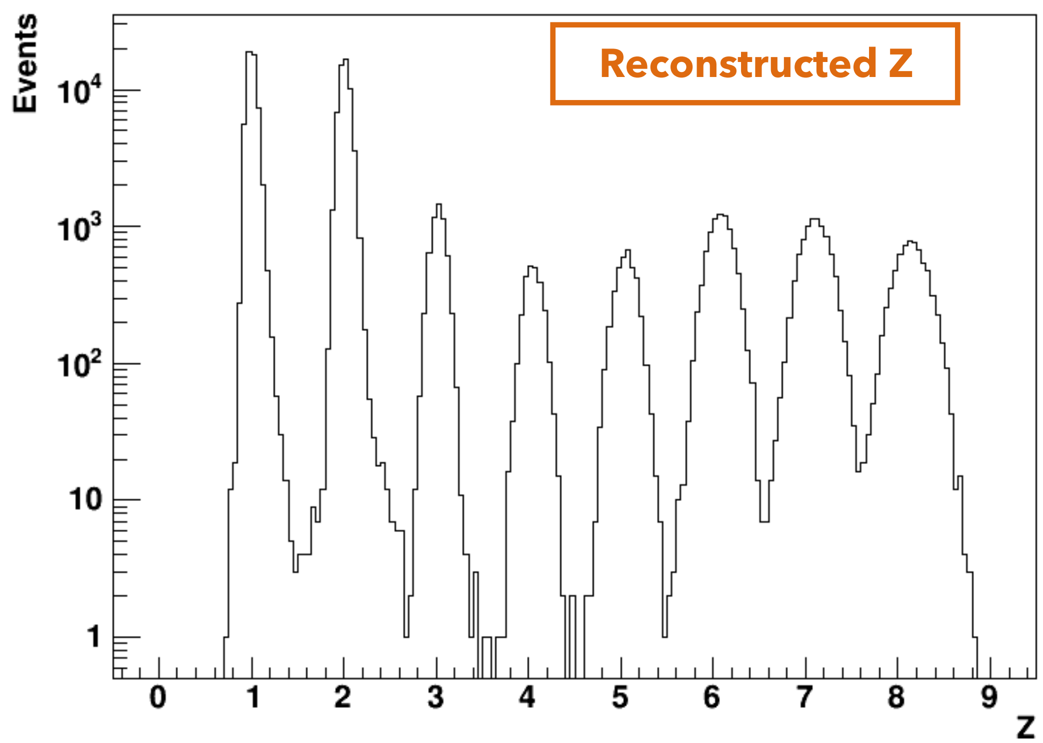
Fragments univocally defined by Z and A

- ☑ **reconstruction of Z**
- ☐ reconstruction of A

$$-\frac{dE}{dx} = \frac{\rho \cdot Z}{A} \frac{4\pi\, N_A\, m_e c^2}{M_U} \left(\frac{e^2}{4\pi\epsilon_0\, m_e c^2} \right)^2 \frac{z^2}{\beta^2} \left[\ln \left(\frac{2 m_e c^2 \beta^2}{I \cdot (1-\beta^2)} \right) - \beta^2 \right]$$

Beam: ^{16}O 200 MeV/n





Fragment	^{1}H	^{4}He	^{7}Li	^{9}Be	^{11}B	^{12}C	^{14}N	^{16}O
z	1	2	3	4	5	6	7	8
Reconstructed z	1.01 ± 0.06	2.01 ± 0.07	3.02 ± 0.08	4.05 ± 0.10	5.06 ± 0.12	6.08 ± 0.14	7.11 ± 0.16	8.15 ± 0.18
	5%	**3%**						**2.2%**

- **Z resolution: 2-5%** << minimum distance between charges (~10% between 7 and 8)

Fragmentation identification (II)

Fragments univocally defined by Z and A

☑ reconstruction of Z

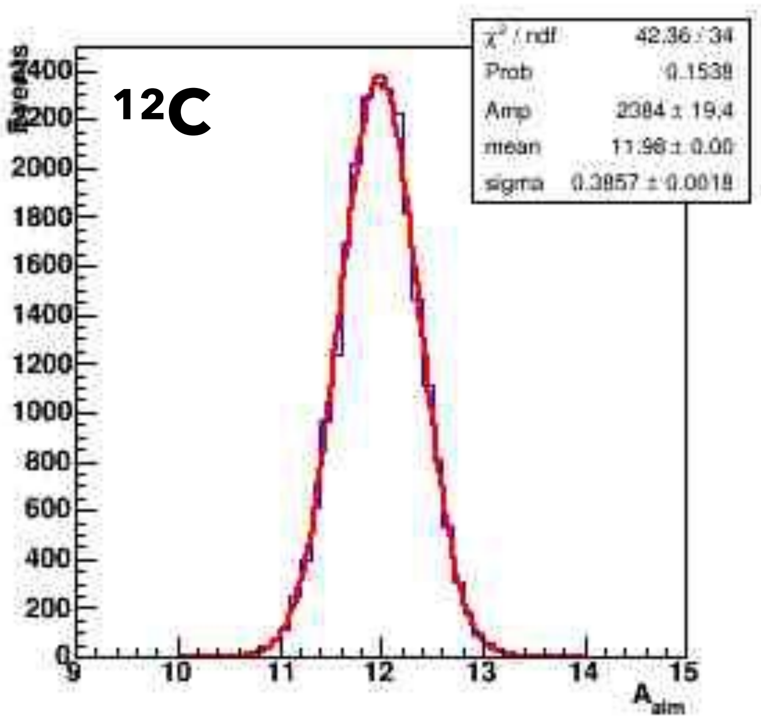
☑ **reconstruction of A**

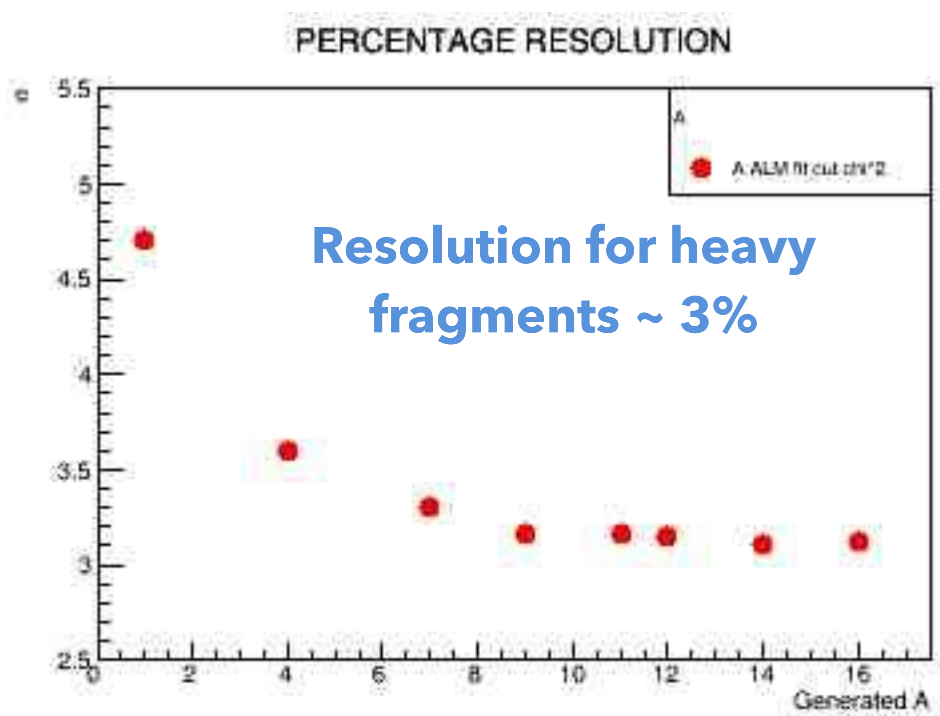
$$A_1 = \frac{m}{U} = \frac{p}{U\beta\gamma}$$ (p: TRACKER; $\beta\gamma$: TOF)

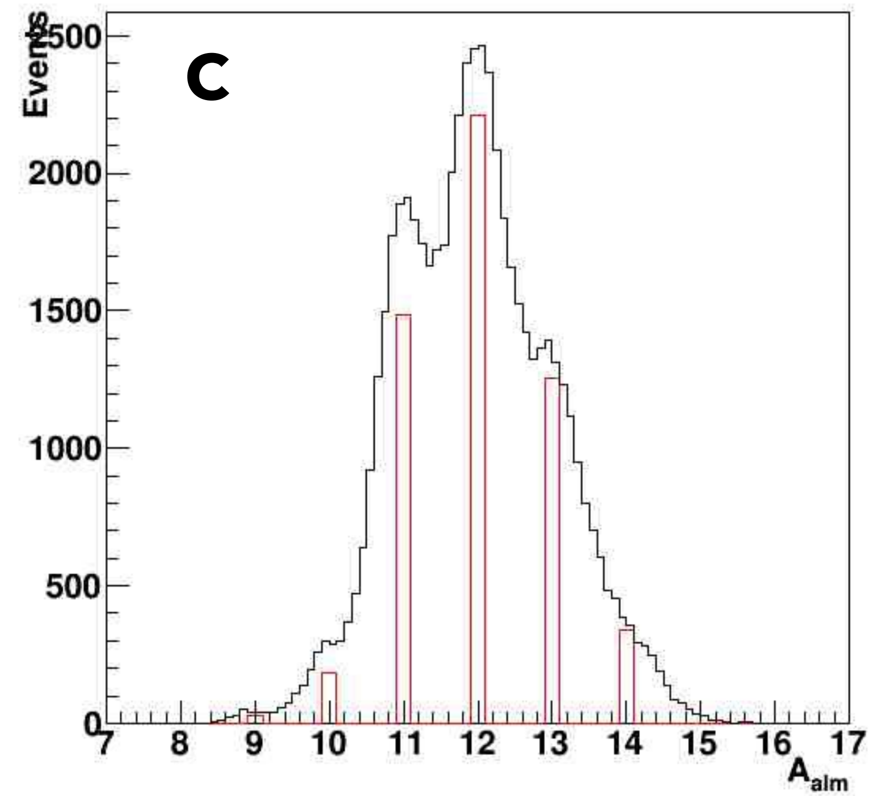
$$A_2 = \frac{m}{U} = \frac{E_{kin}}{U(\gamma - 1)}$$ (E_{kin}: CALO; γ: TOF)

$$A_3 = \frac{m}{U} = \frac{p^2 - E_{kin}^2}{2E_{kin}}$$ (p: TRACKER; E_{kin}: CALO)

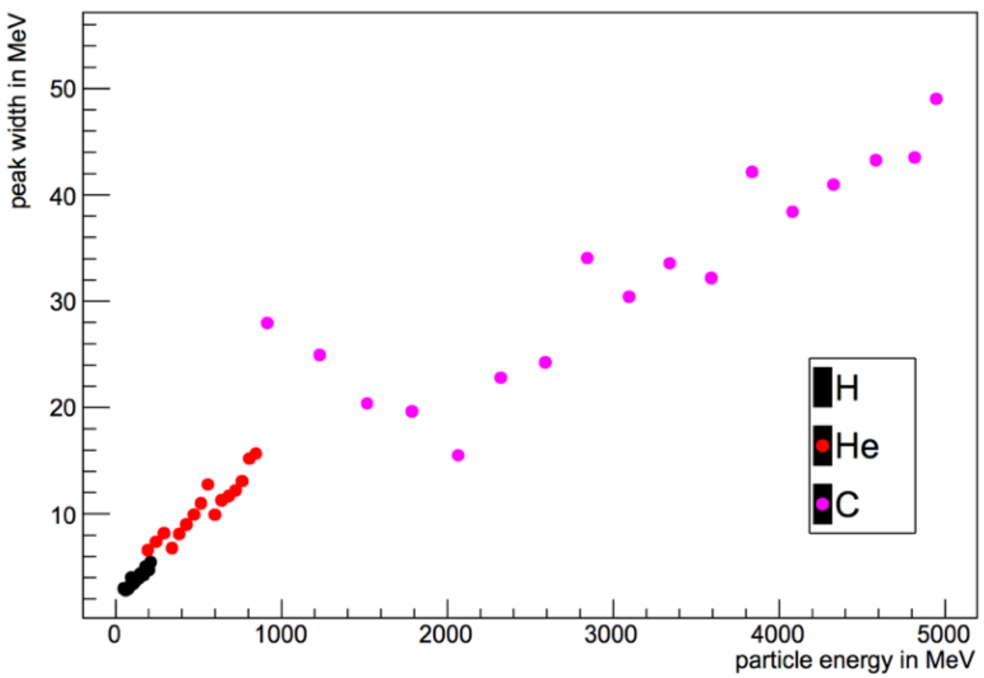
- 3 different methods to determine A, thanks to the redundant experimental apparatus
- 2 different fit methods: **standard χ²** and **Augmented Lagrangian Method (ALM)**



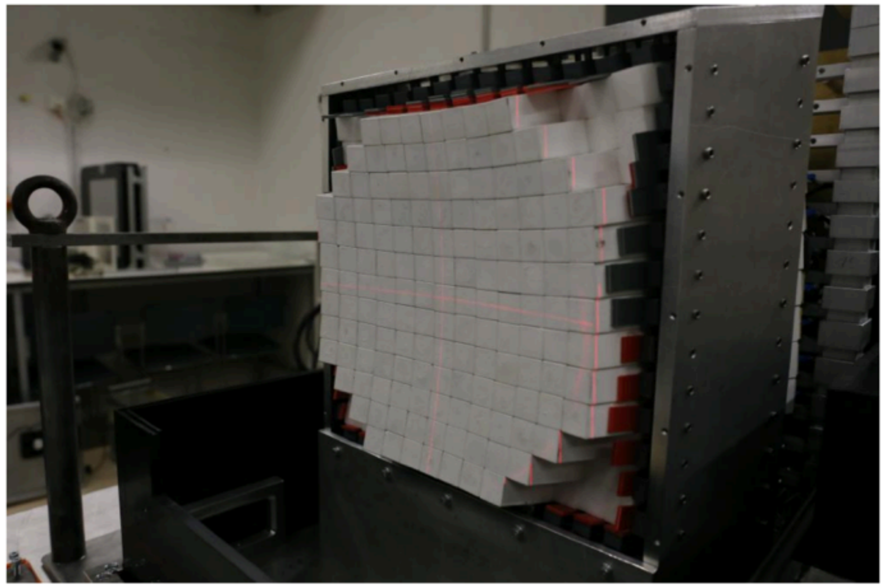




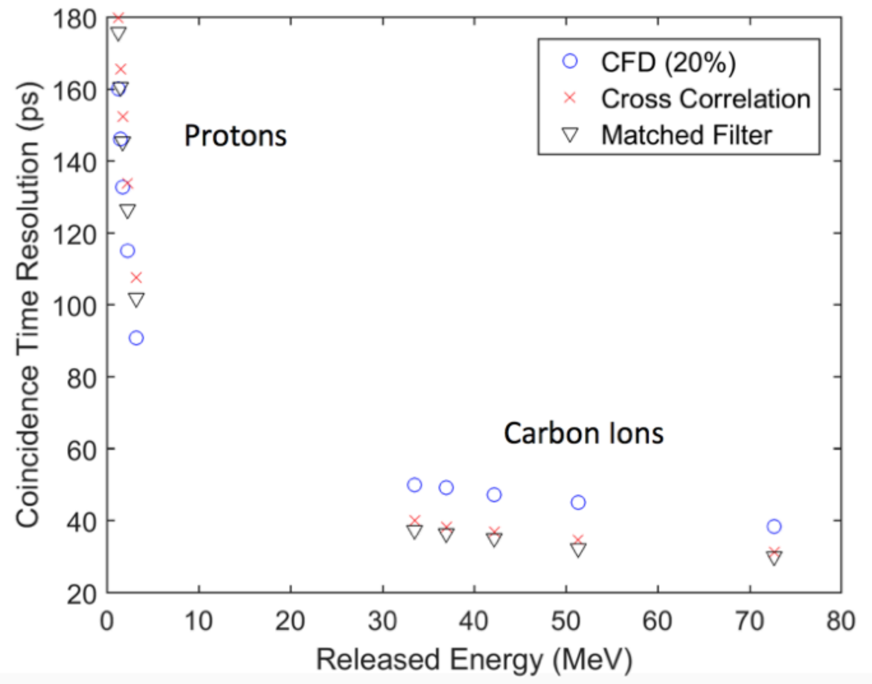
Test beams - Calorimeter & Scintillator

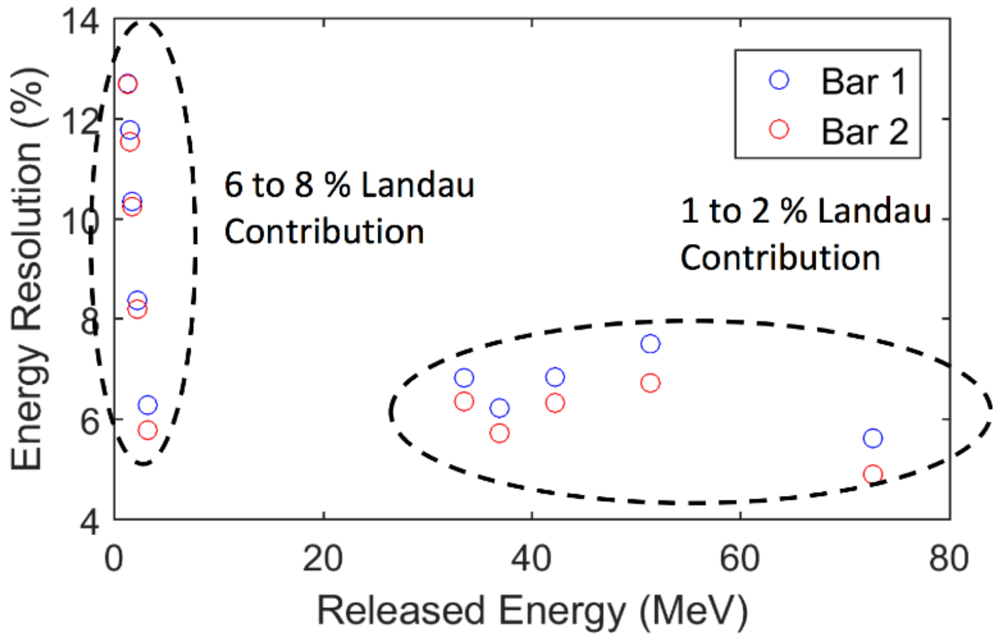


- 145 BGO crystals
- different particles with different energies on one cell
  - **H and He:** 50 MeV/n to 220 MeV/n
  - **C:** 100 MeV/n to 430 MeV/n
- Contributions from beam energy spread, detector and electronics included
- **from 1% to 3%**

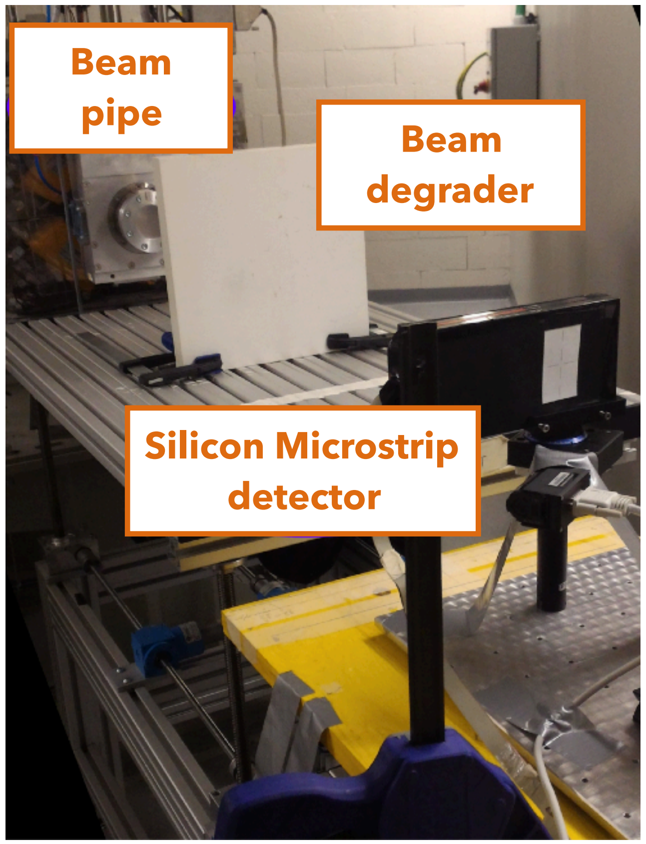


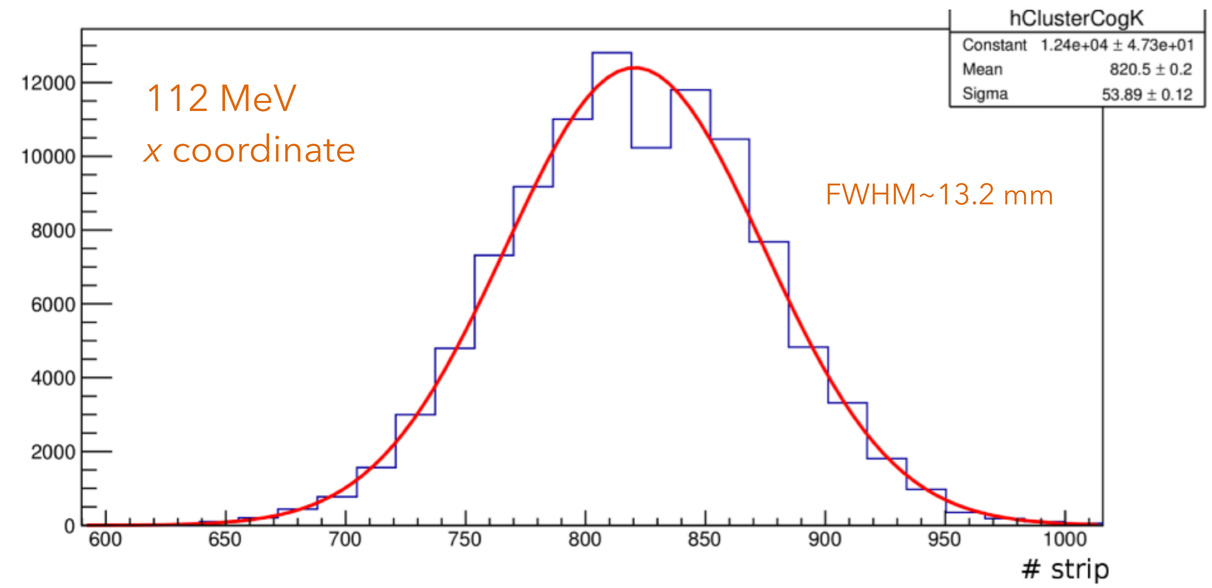
- Time resolution
  - **100-180 ps** for protons
  - **~ 50 ps** for C ions
- Energy resolution
  - Landau fluctuation included
  - **5-12%** for protons
  - **~7%** for C ions

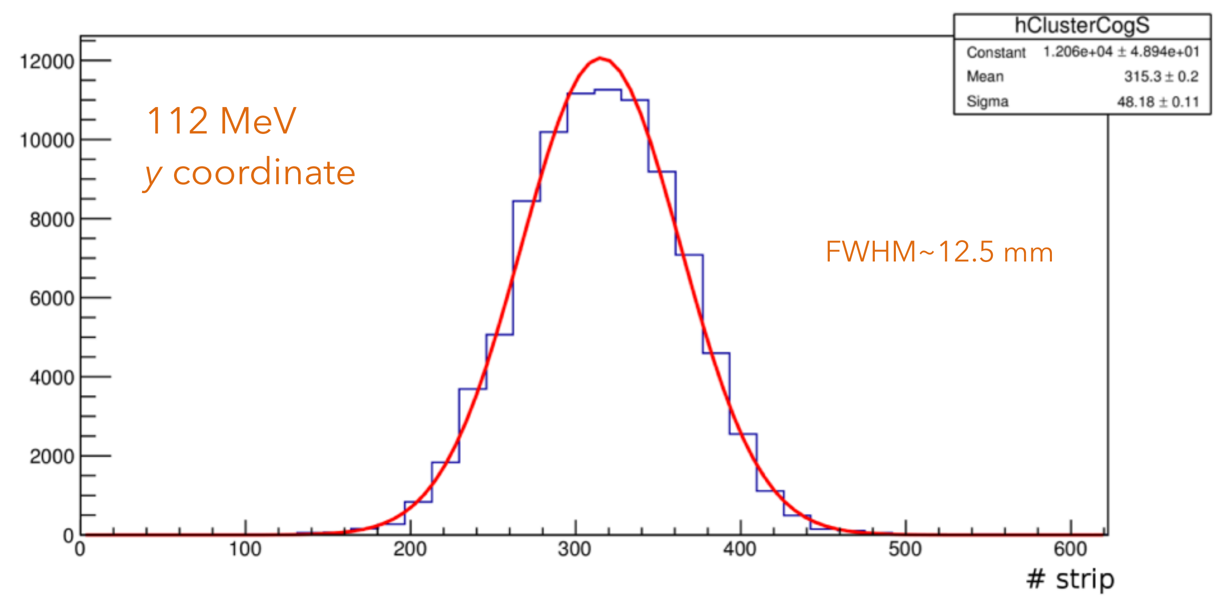




Test beams - Microstrip







- Hadrontherapy Center (TN)
  - **50, 70, 80, 112, 159, 200, 228 MeV protons**
  - sensor positioned at the **isocenter**
- Beam characteristics:
  - for 112 MeV: $\sigma_x = 5.2$ mm, $\sigma_y = 5.4$ mm
- Profile beam measured
  - agreement with beam size provided by the facility

Conclusions

- The FOOT experiment is **under development**, simulations and test beams are ongoing for each detector
  - **Simulation** phase is well advanced
  - **Detector setup** almost established
  - Many **test beams** already made
- Large physics panorama:
  - **hadrontherapy**: both target and projectile fragmentation
  - **radioprotection in space**
- **CDR** presented and approved
- **Future perspectives**:
  - data taking in 2020
  - usage of different beams (O, He, …)

THANKS FOR THE ATTENTION!

Supporting material

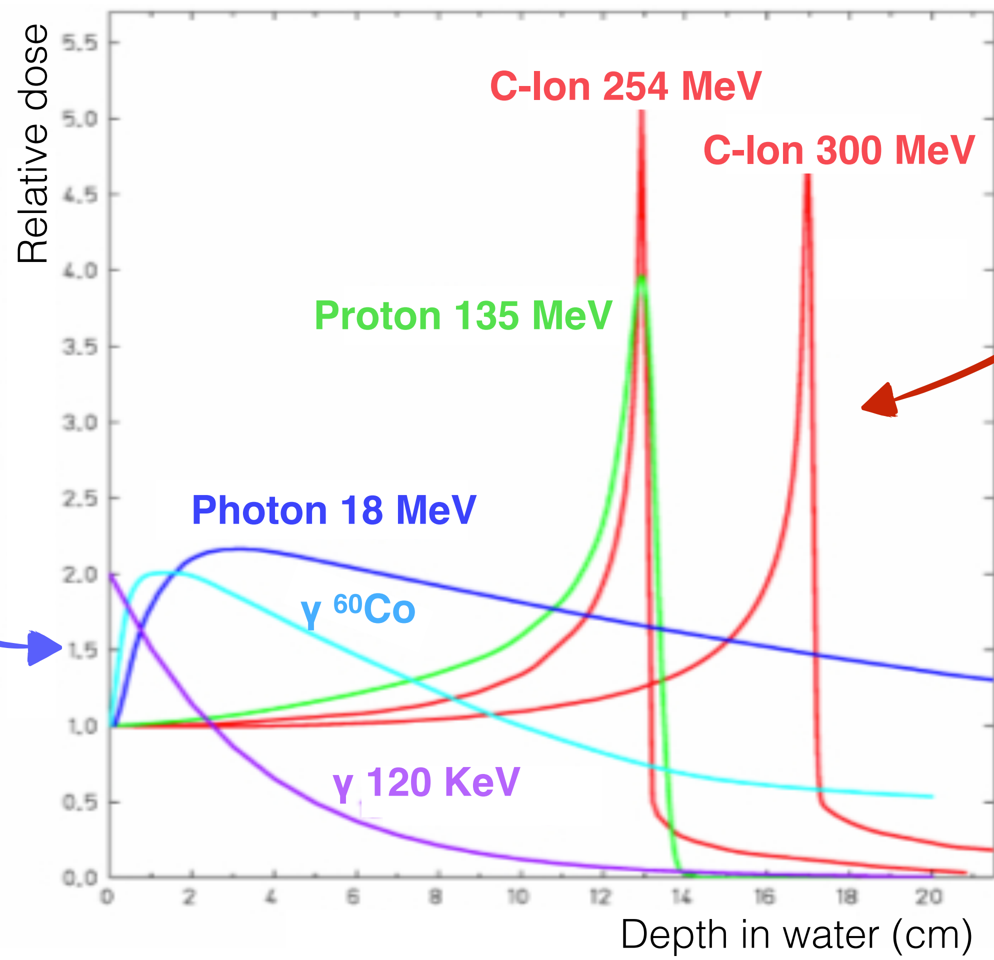
Interaction with matter

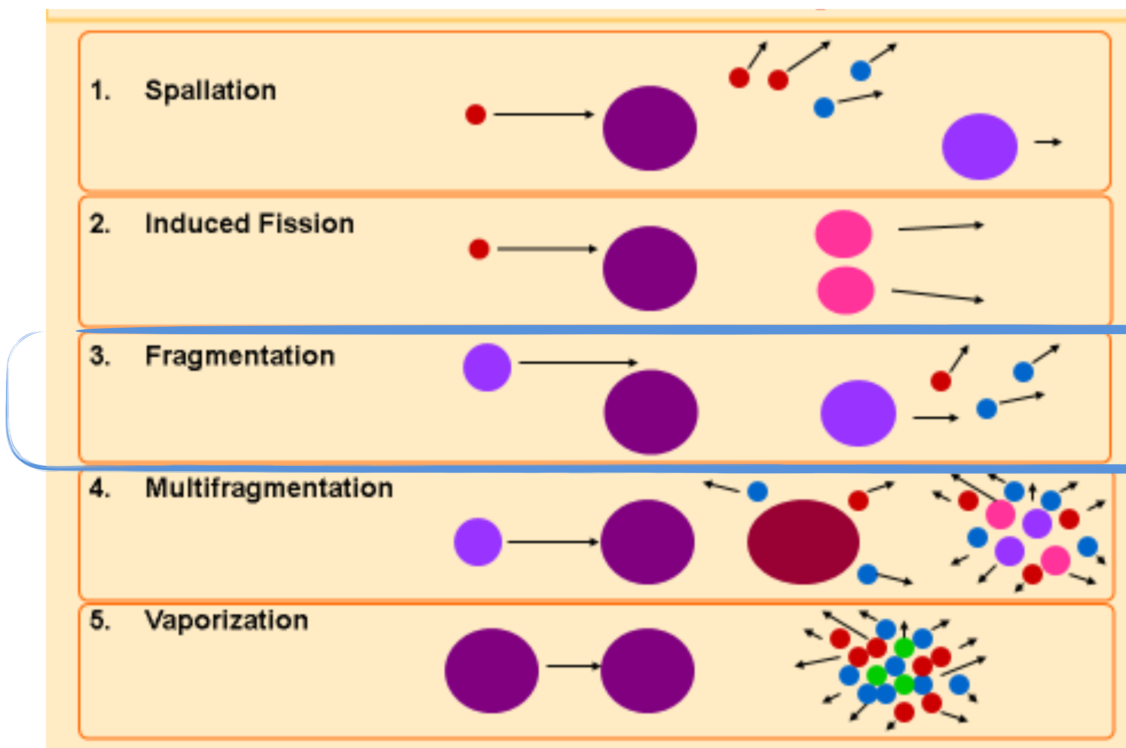
Photons

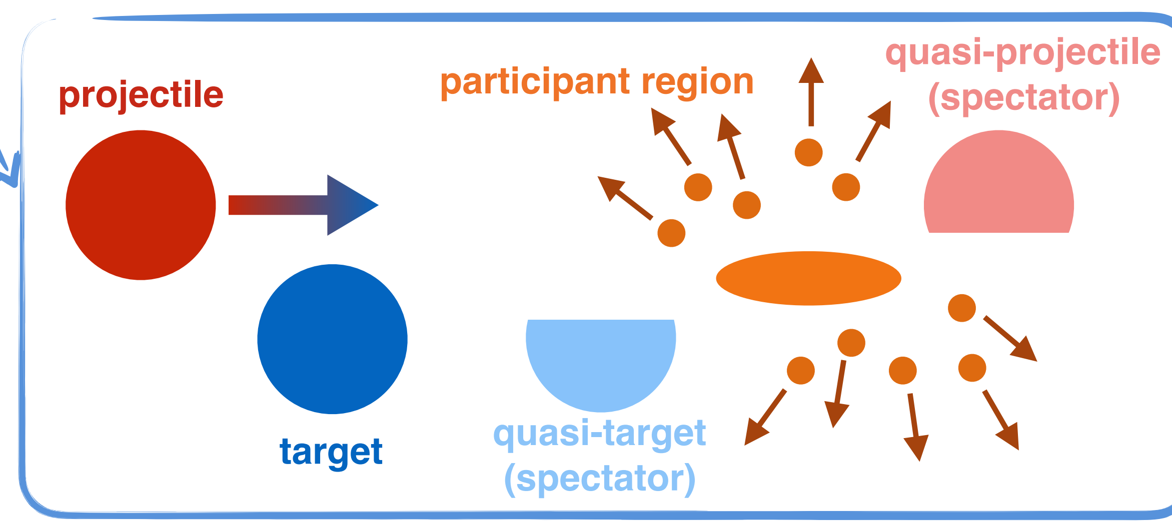
- Photoelectric: $\sigma \propto Z^4/E^3$
- Compton: $\sigma \propto Z/E$
- Pair production: $\sigma \propto Z^2/\ln(E)$

Charged particles (protons, ions)

- EM interaction: ionization, excitation, Bremsstrahlung and Cherenkov radiation;
- Nuclear interaction: projectile energy higher than the Coulombian barrier.







At the hadrontherapy energy (~ 10^2 MeV/nucleon), fragmentation is the most frequent nuclear interaction:

➡ peripheral collision, few nucleons participate, low multiplicity

Biological effects on cancers

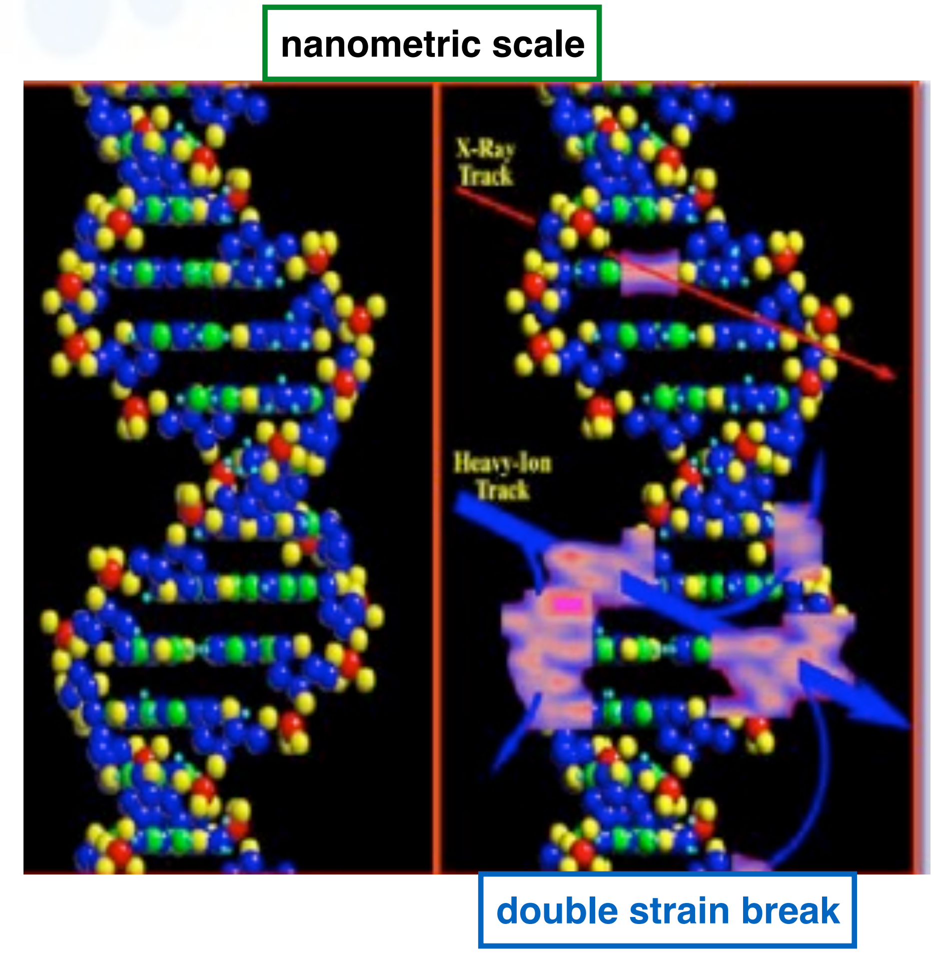
Goal: to kill a tumour cell an irreparable damage at DNA is needed (this way it cannot reproduce itself)

How: higher projectile charge makes a higher damage

But: important to have a good knowledge of nuclear interactions at "medical" energies

↓

To design biologically driven Treatment Planning Systems (BioTPS) aiming at accounting as much as possible the biological effect



Linear Energy Transfer

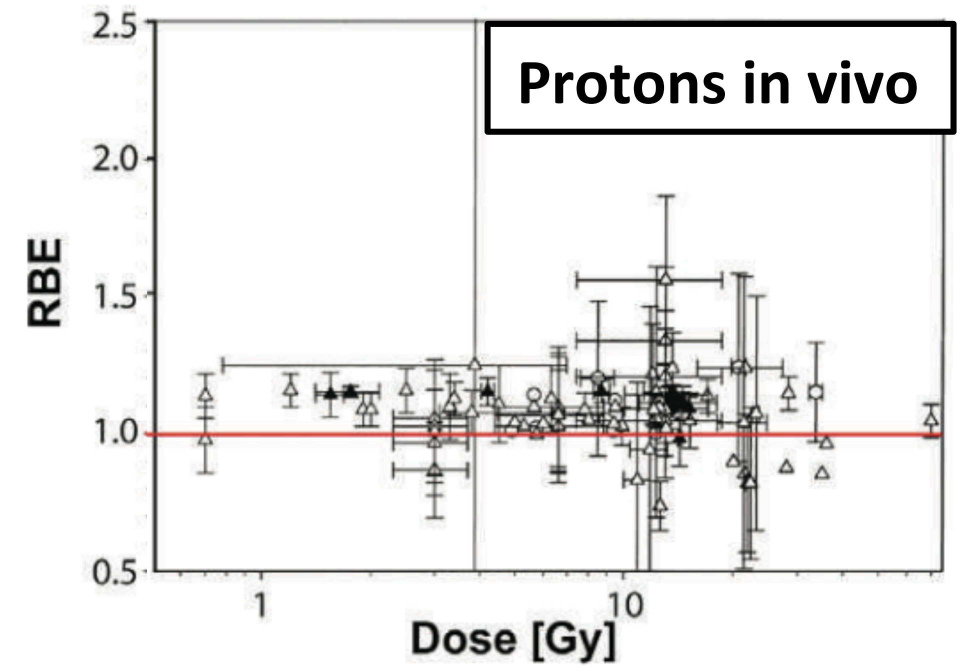
$$\text{L.E.T.} = \left(\frac{dE}{dx}\right)$$

enhanced biological effectiveness in cell killing wrt conventional photon radiation

Relative Biological Effectiveness

$$\text{R.B.E.} = \left(\frac{D_{X-ray}}{D_H}\right)_{\text{same effect}}$$

→ constant RBE = 1.1 for protons in clinical practice



PROBLEM: large fluctuation on the measurement

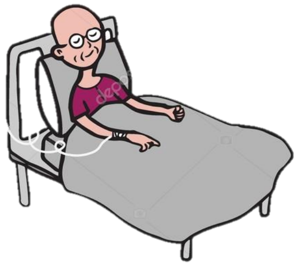
- considering a constant RBE = 1.1 probably leads to an underestimation of dose in healthy tissue region

Cancer therapies

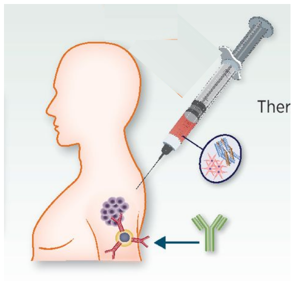
Cancer definition: cellular mutation that indefinitely proliferates

Cancer therapies

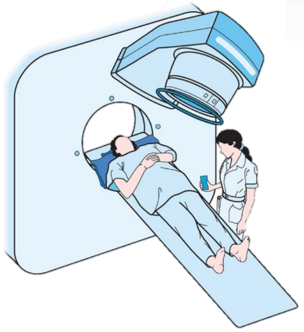
- Surgery: removal part of the body containing the diseased cells



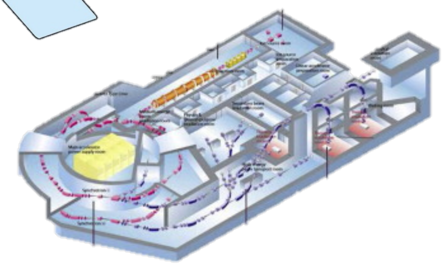
- Chemotherapy: non localised somministration of medication to destroy or to prevent the cell reproduction



- Immunotherapy: instructs the immune system to recognise and eliminate diseased cells



- Radiotherapy: e.m. irradiation of cancer region to destroy or to prevent the cell reproduction
- Hadrontherapy: hadron irradiation of cancer region to destroy or to prevent the cell reproduction



Radiation as cure of cancer

To cure a cancer, it is not necessary to kill a cell, but it is enough to prevent its reproduction

↓

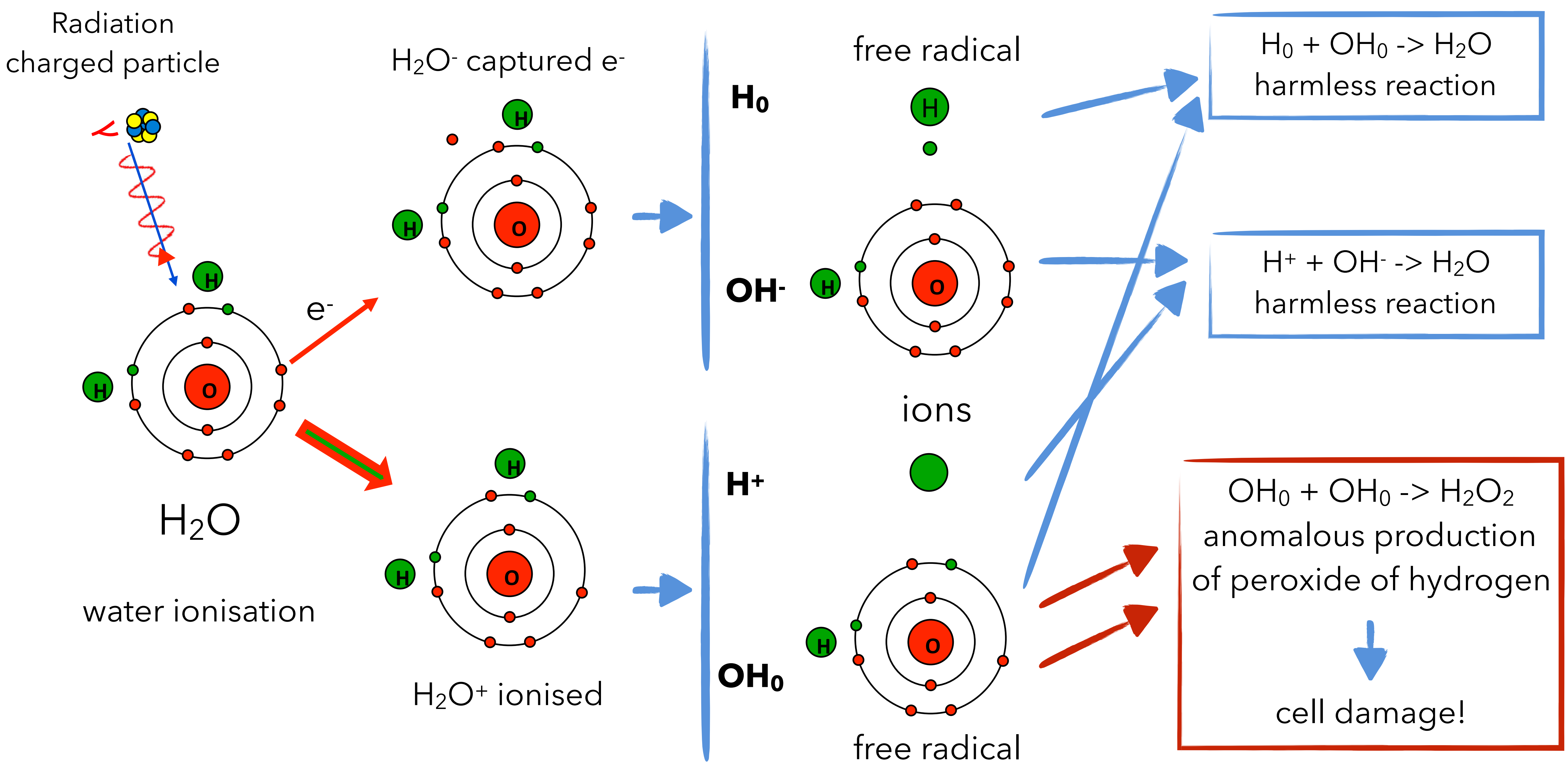
damage the DNA of the cell that is the core of the cell reproduction

two possible ways

Indirect way: radiation hits the water copiously present in the cell, production of free radicals (very reactive neutral atoms or molecules due to a odd electron), damage the DNA

Direct way: radiation hit the strand of the DNA

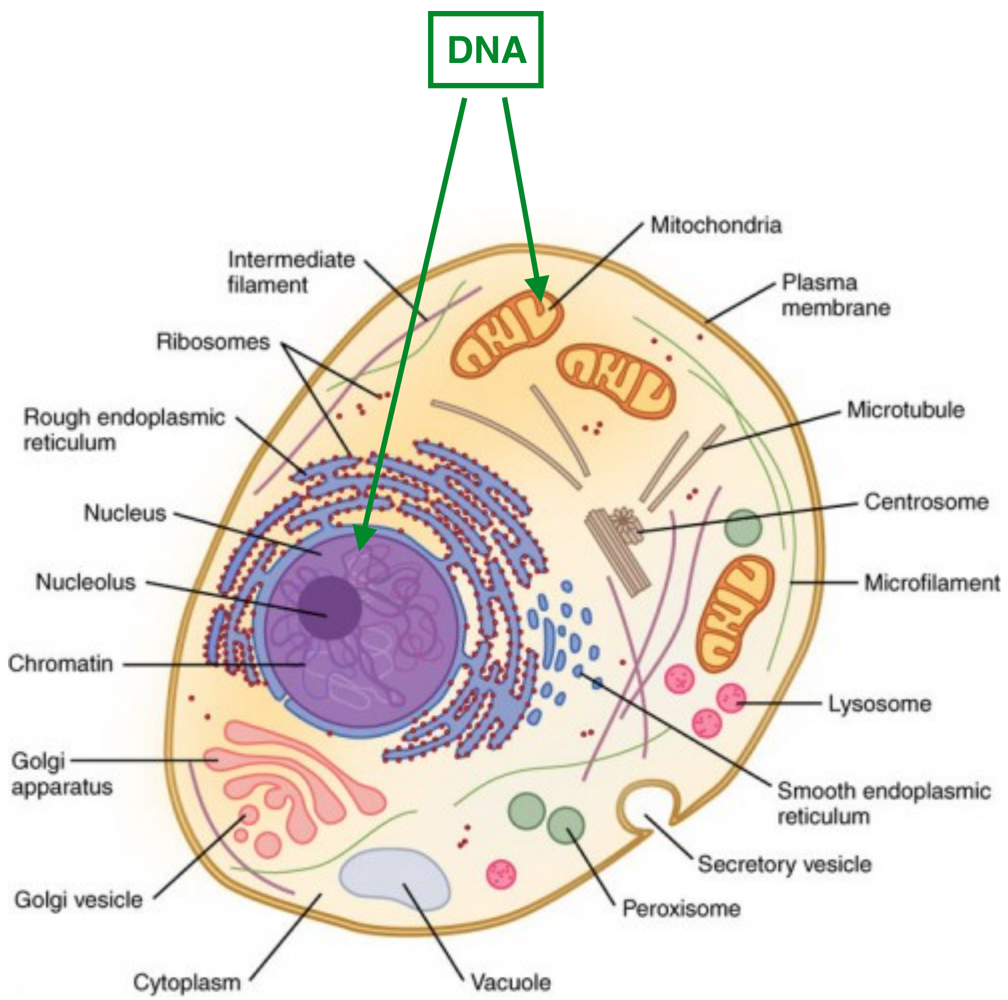
Indirect way (a possibility)



Oxygen concentration increases the free radicals activity

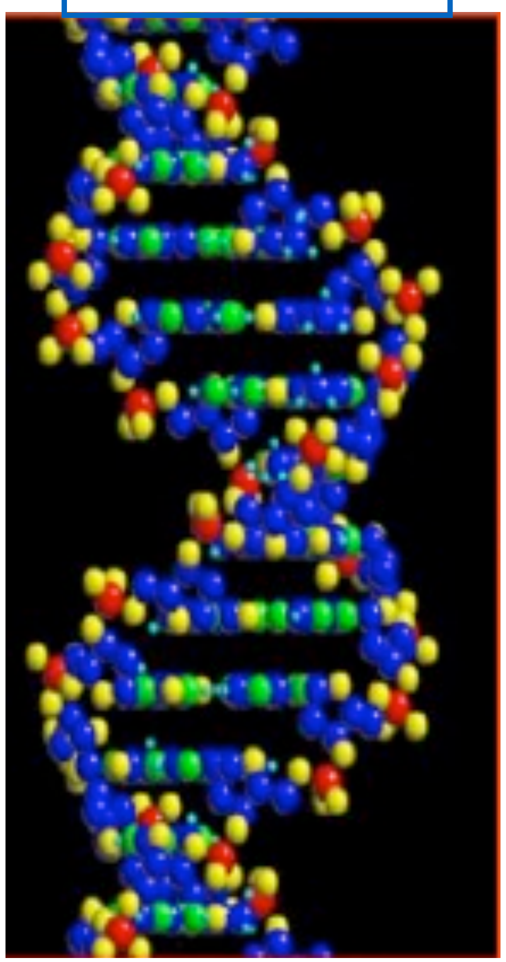
Direct way

DNA is insed nucleus (chromatin in chromosomes) and in mitochondria



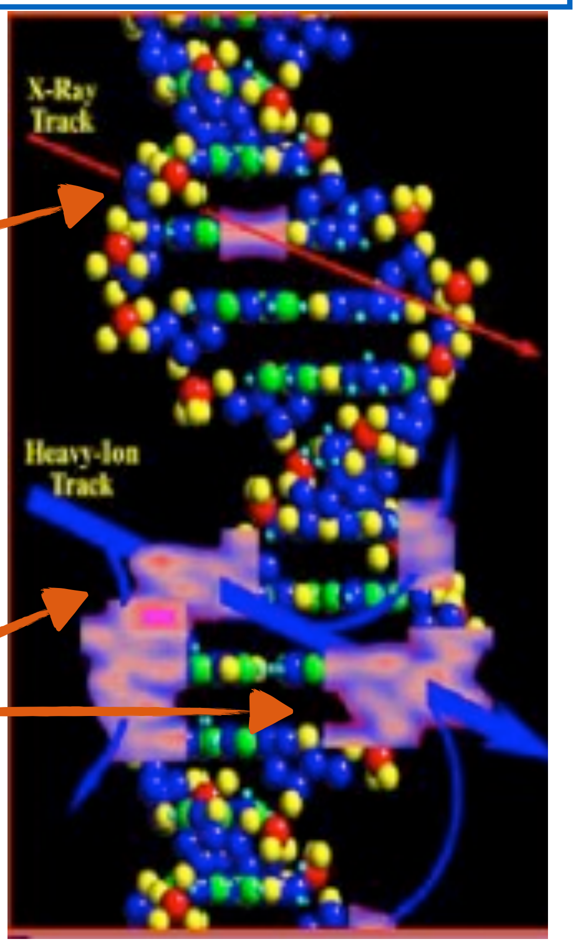
10 µm

double strand break



ionisation from radiation (e.m. or hadron)

double and single strand break



reparable damage

NOT reparable damage

nanometric scale

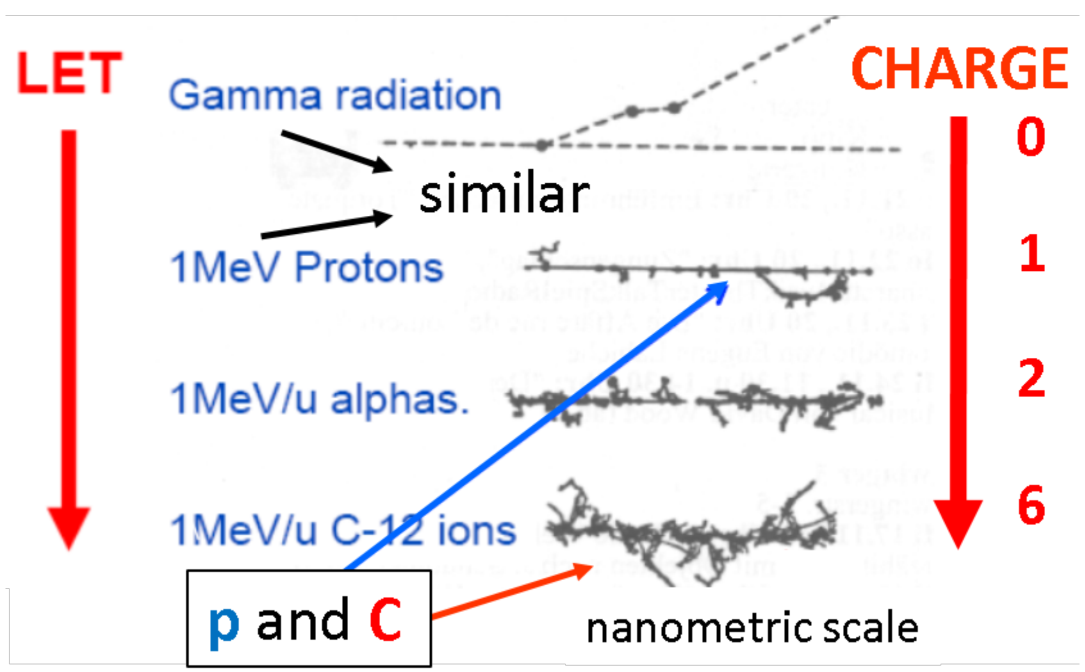
reproduction forbidden!

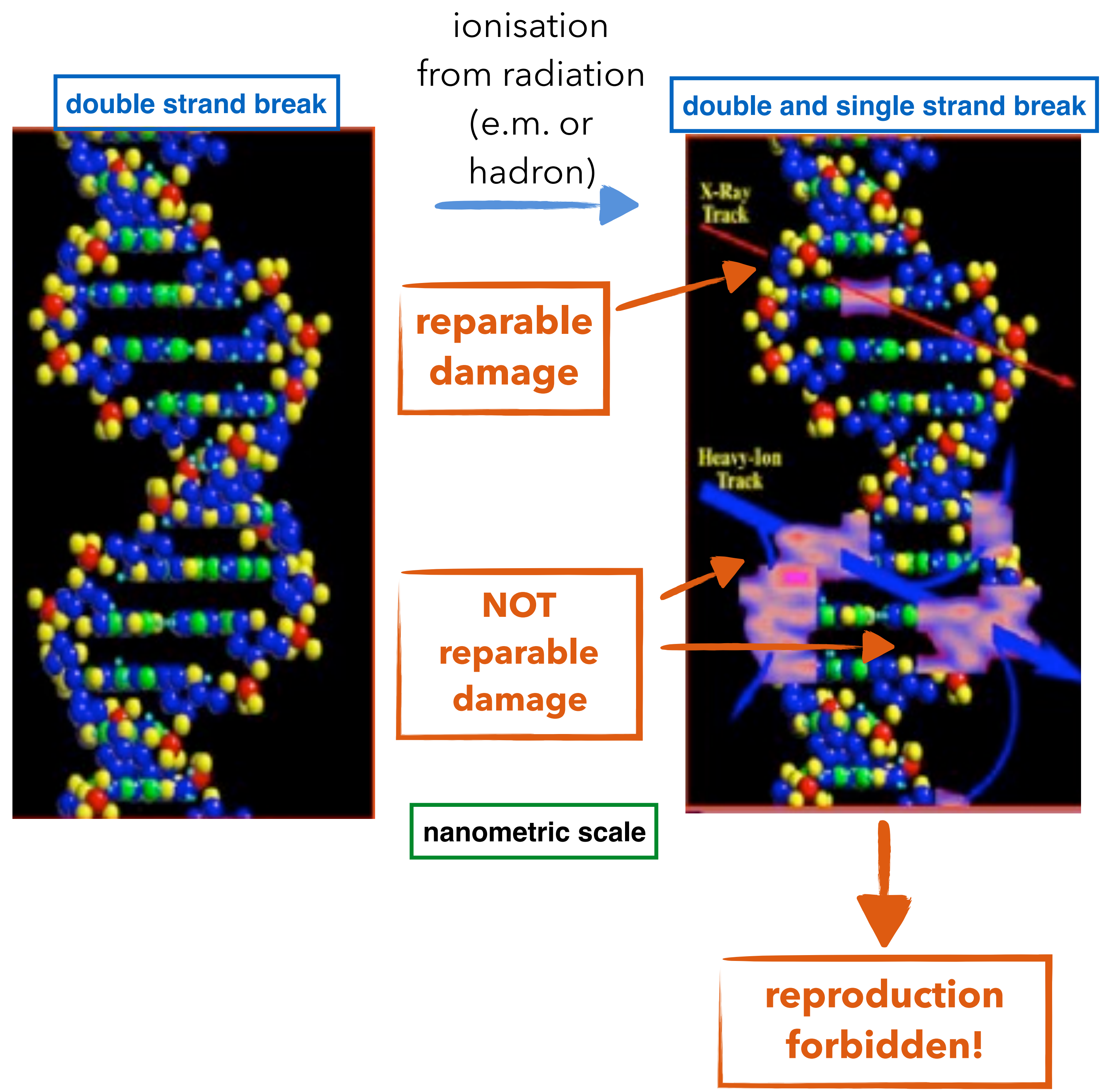
Goal: to find a radiation capable to make a multiple ionisation on DNA

Direct way

Goal: to kill a tumour cell an irreparable damage at DNA is needed (this way it cannot reproduce itself)

How: higher projectile charge makes a higher damage





Hadronterapy in Italy

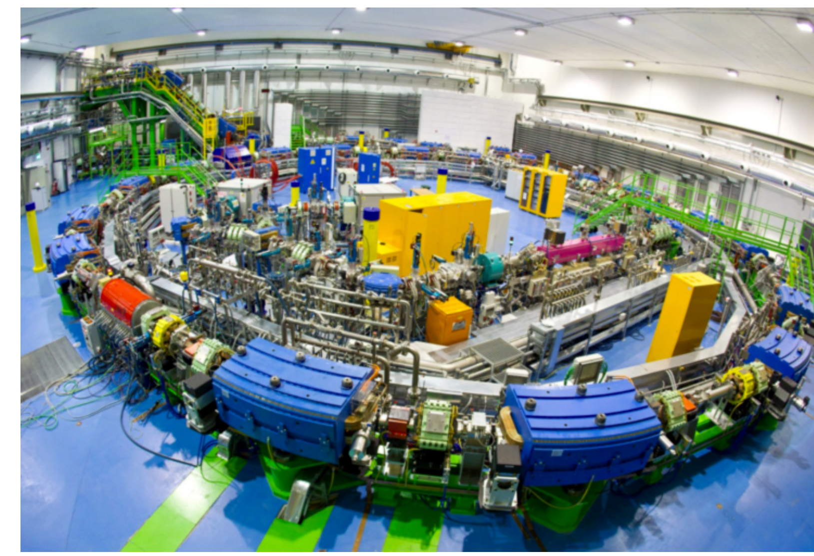
April 2017: hadrontherapy entered in LEA (Essential Levels of Assistance) allowing the treatment of 10 tumour pathologies

CATANA - Catania
Proton Therapy beam line

- Proton beam (up to 60 MeV)
- Active since 2002
- Eye tumour: 363 patients (98% survived)

CNAO - Pavia
Centro Nazionale di Adroterapia Oncologica

- Proton beam (up to 250 MeV)
- Carbon beam (up to 400 MeV)
- Active since 2011
- First 5 years: 828 patients (70-90% success)
- ~1200 patients now

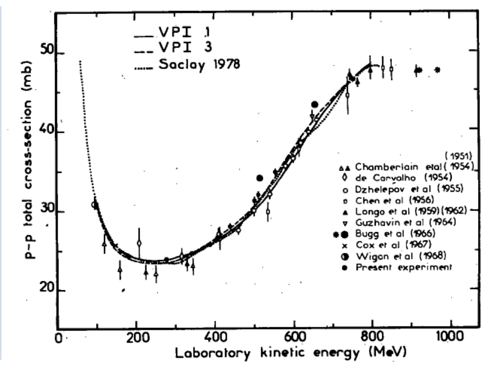


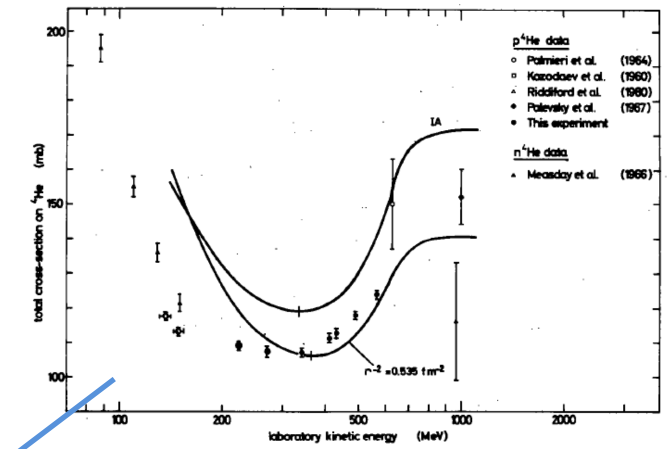
APSS - Trento
Proton Therapy Center

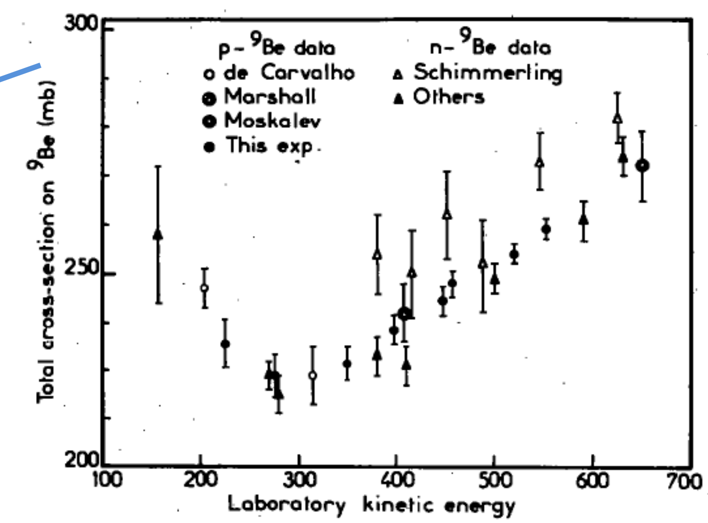
- Proton beam (60-230 MeV)
- Active since 2015
- Full body treatment
- Experimental halls

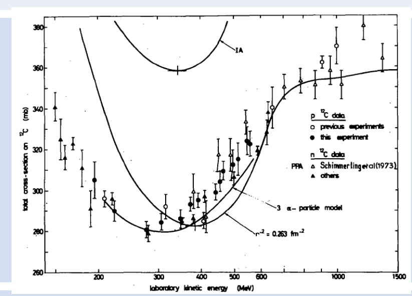
Experimental panorama on proton cross section

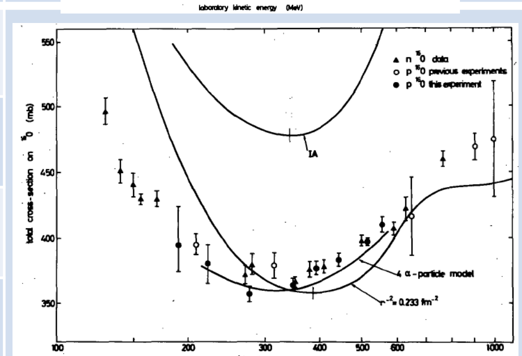
Reaction	E_{Kin} (MeV)	σ_{TOT} (mb)
p -> p	10	300
	100	30
	180-500	25-35
	600-2000	45-50
P -> ^{4}He	150-600	110-120
P -> ^{9}Be	200-600	230-250
P -> ^{12}C	50	450
	100-200	230
	200-1000	280-350
P -> ^{16}O	20	550
	50	400
	200	350
	200-600	350-400
P -> ^{40}Ca	30	900
	100-200	500

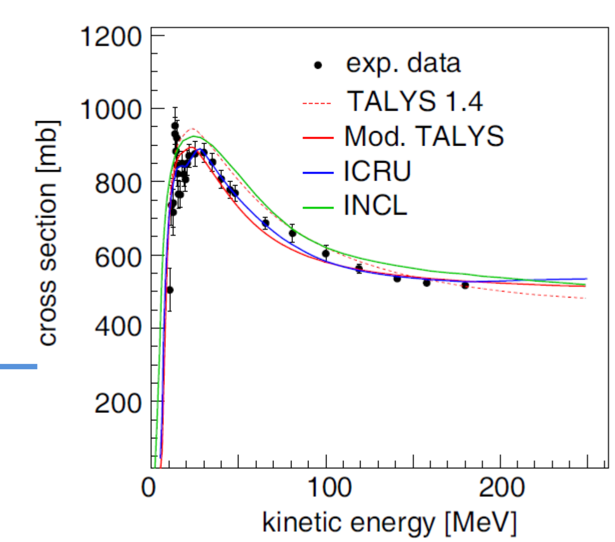










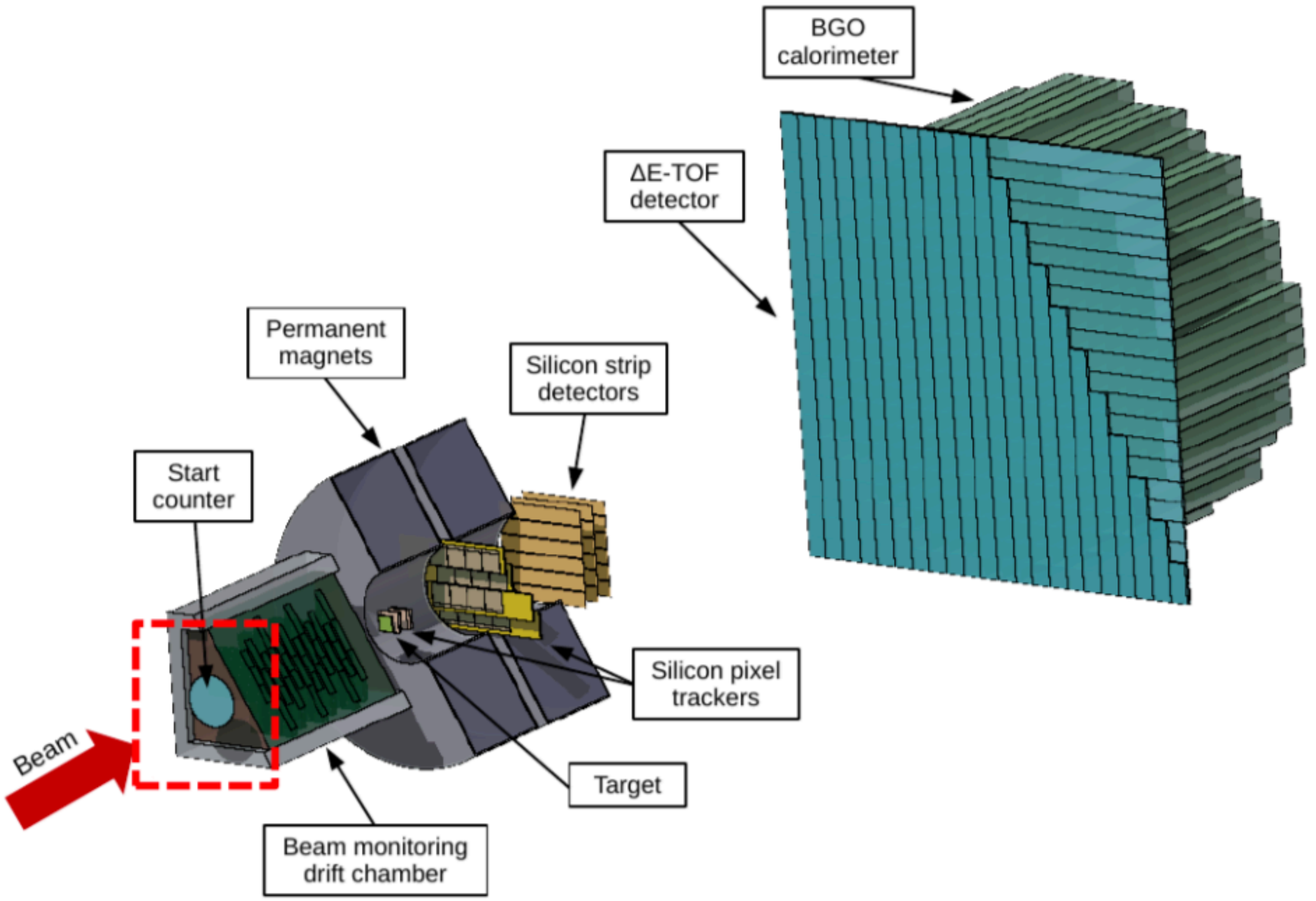


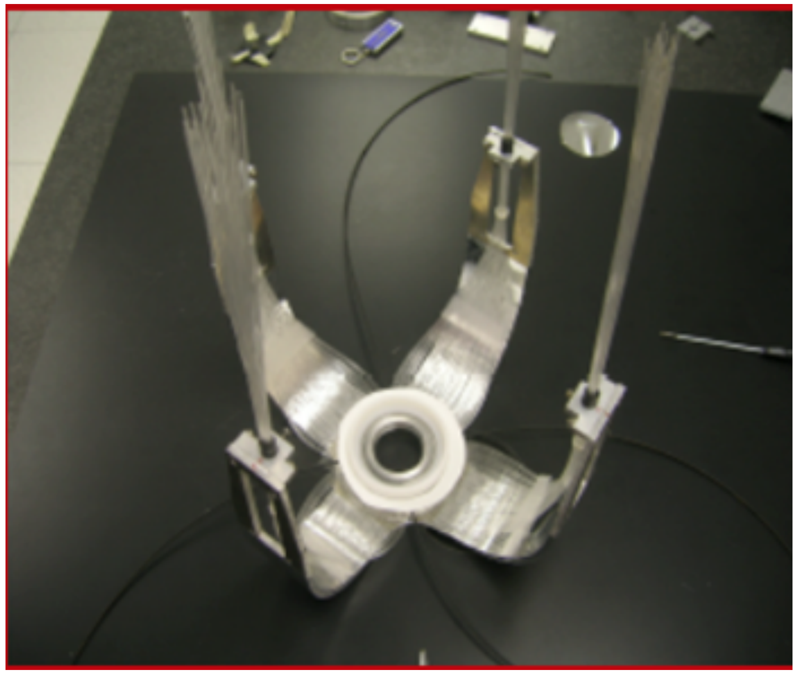
Start counter

Provides:

- first time-stamp for the Time Of Flight measurement
- incoming ion counter

thin plastic scintillator layer (about 250 μm) with side read-out



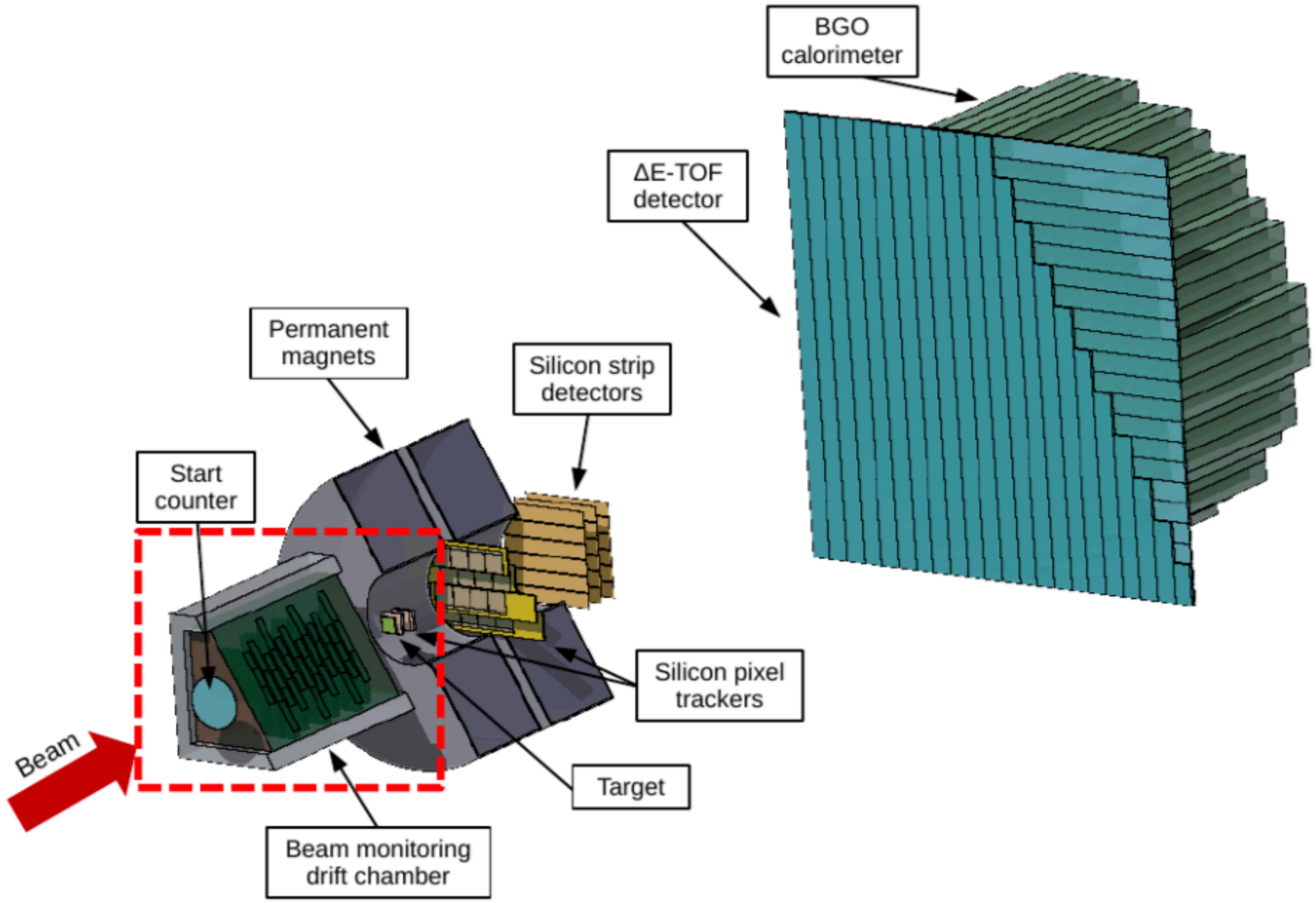


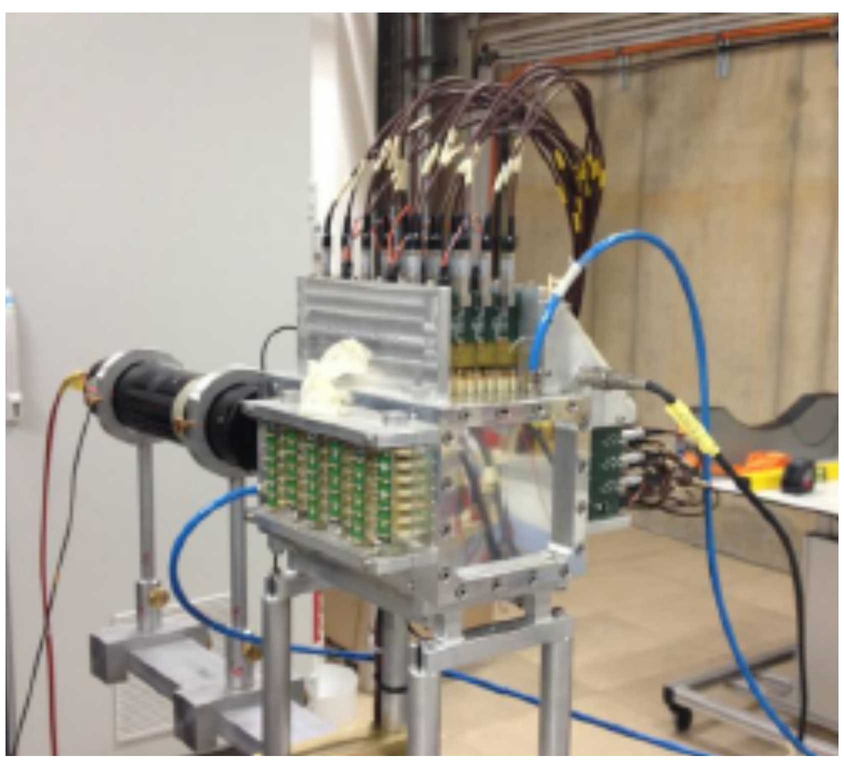
A first prototype equipping PMTs already running, a second detector with SiPMs is under construction

Beam monitor

Provides:

- Position and direction of the primary particle, essential to apply inverse kinematic with the required resolution

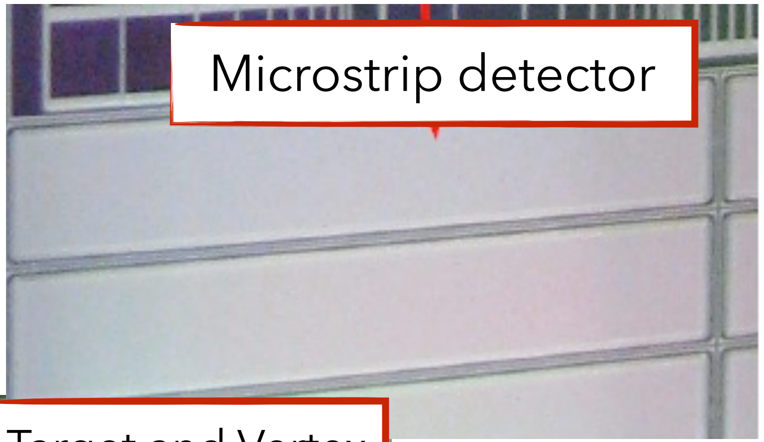


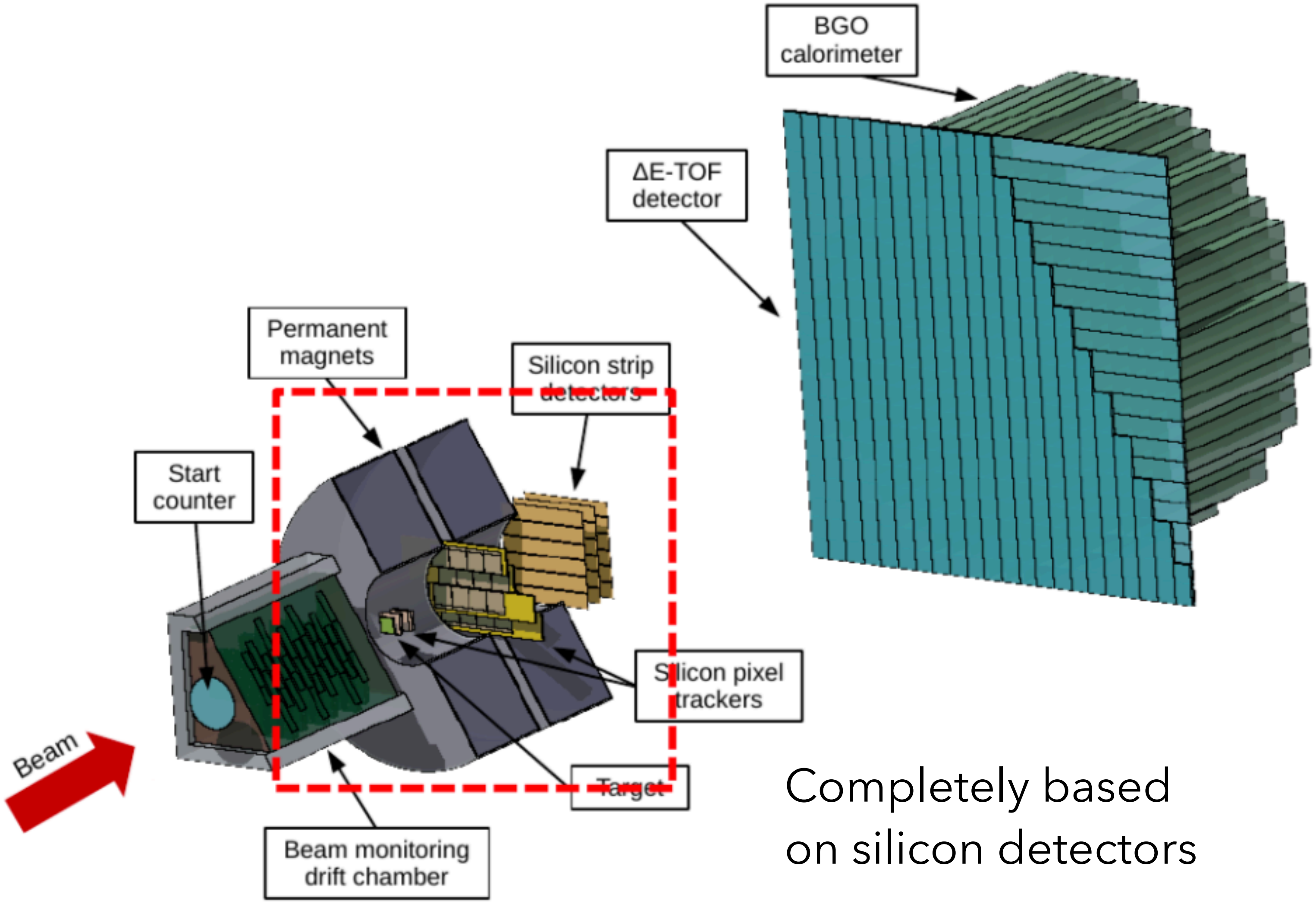


Drift chamber of 11 cm x 11 cm x 20 cm dimension composed of 12 orthogonal layers of wires.

Magnetic Spectrometer

Provides:
- the track of the fragment before and inside the magnet
- the dE/dx in the strips with a large dynamic range





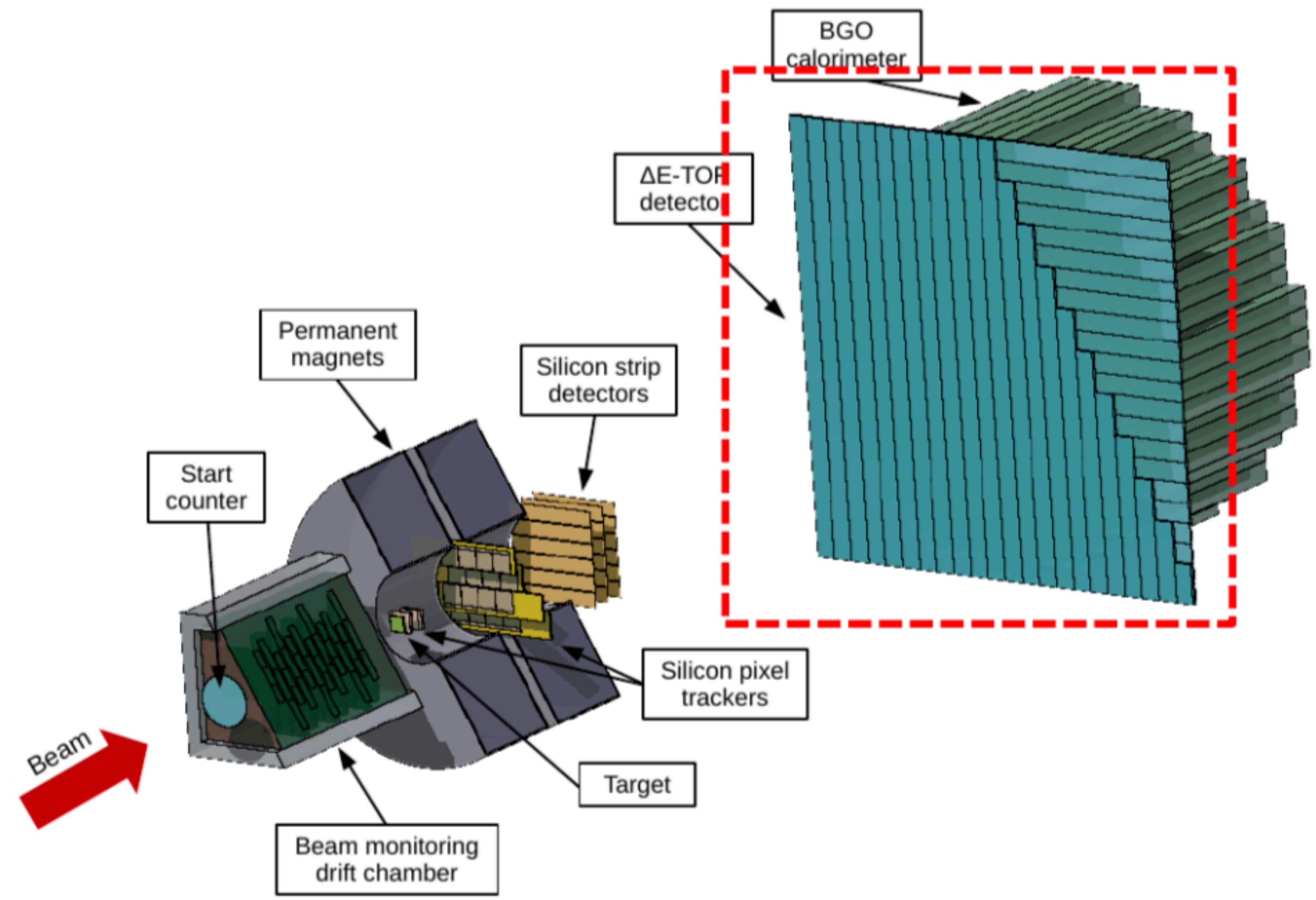
Completely based on silicon detectors

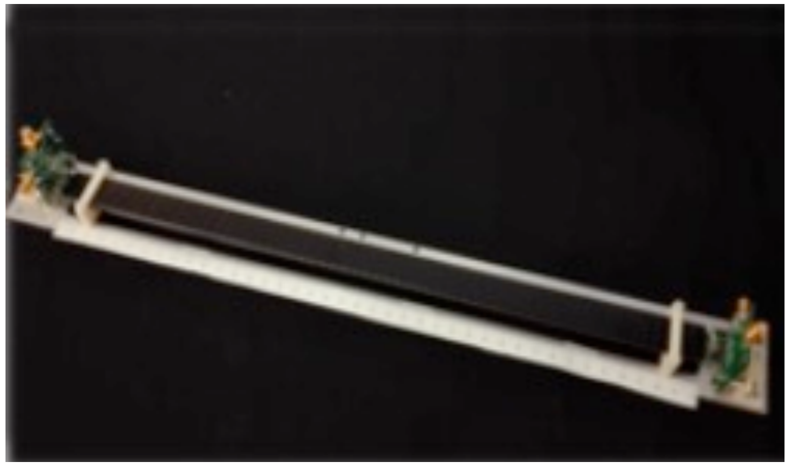
- **Vertex tracker:** 4 tracking layers of M28 MAPS, 20.7 μm pitch and 50 μm thickness
- **Inner Tracker:** 2 layers of M28 sensors
- **Downstream Tracking:** 3 layers of x-y silicon strips, 100-150 μm width and 9 x 9 cm^2 area

ΔE-TOF detector

Provides:

- Second time-stamp for the TOF measurement
- dE/dx information



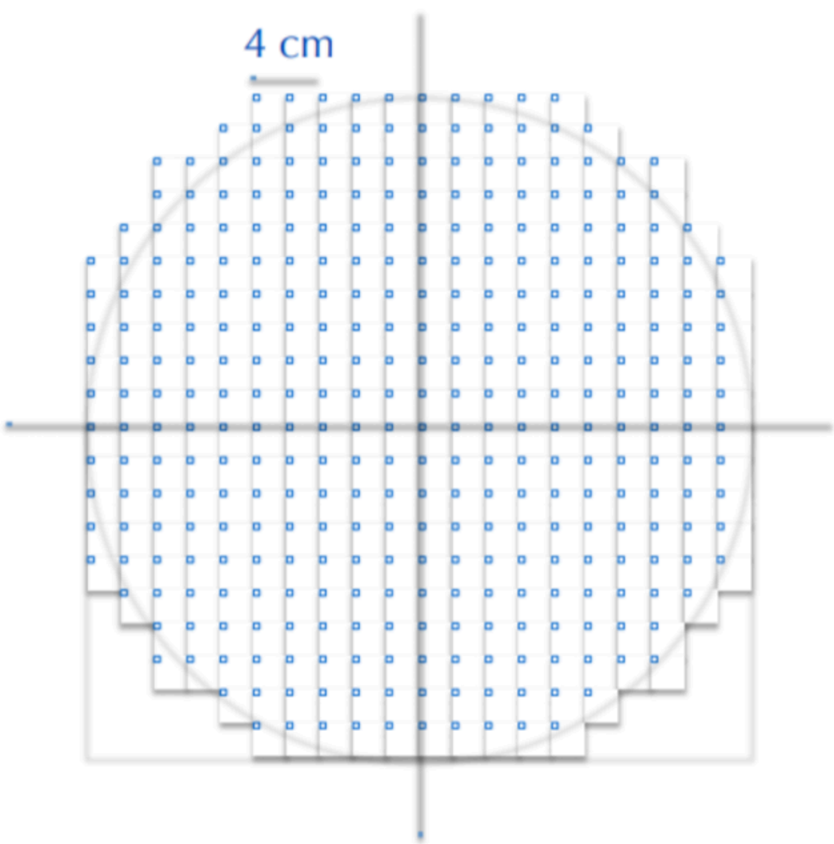


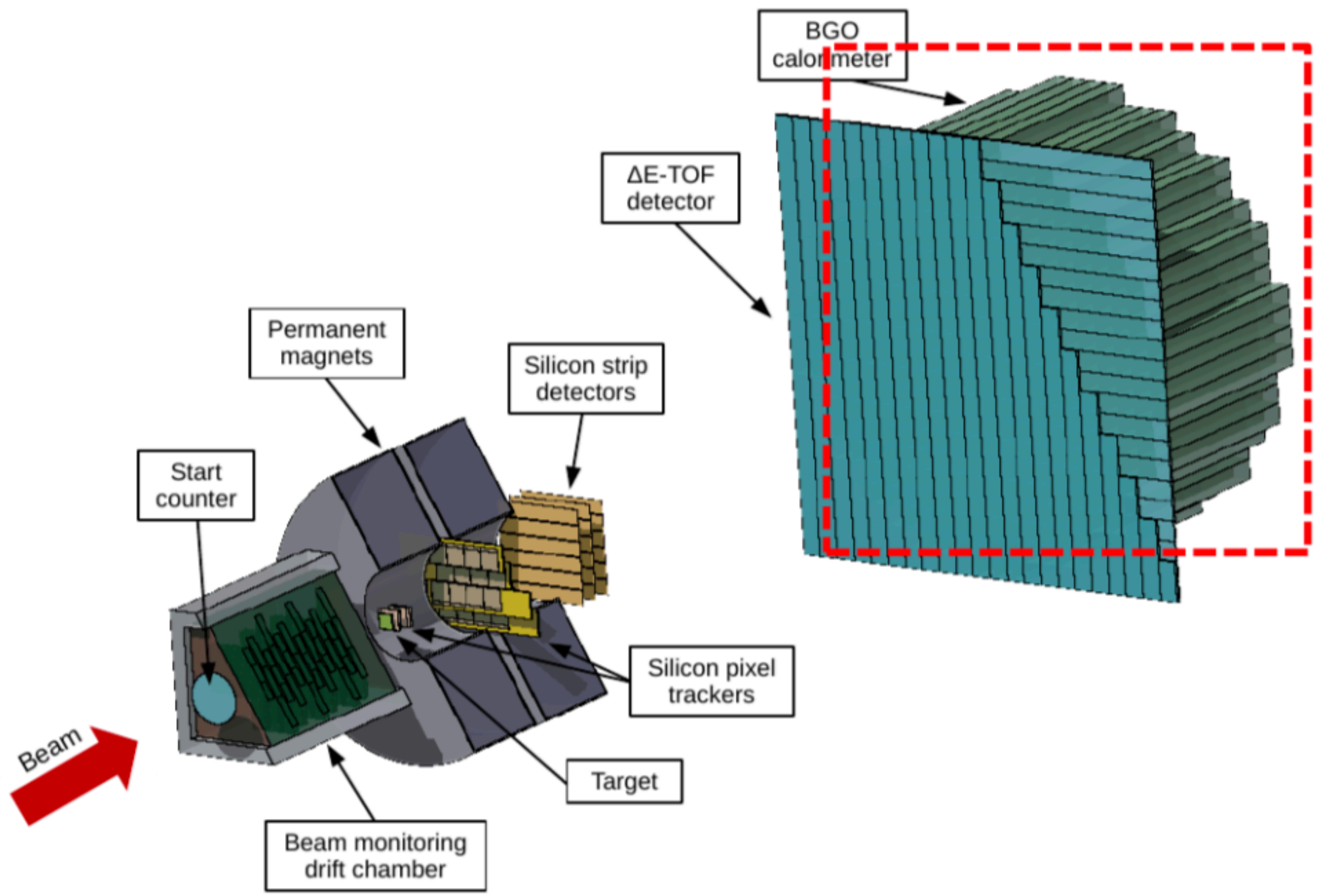
Plastic scintillator wall composed of two layers of bars read-out by SiPMs

Calorimeter

Provides:

- the kinetic energy of the particle
- interaction position





BGO calorimeter with 20 cm radius (344 pixels)
2 x 2 cm pitch (same as the ΔE/TOF).

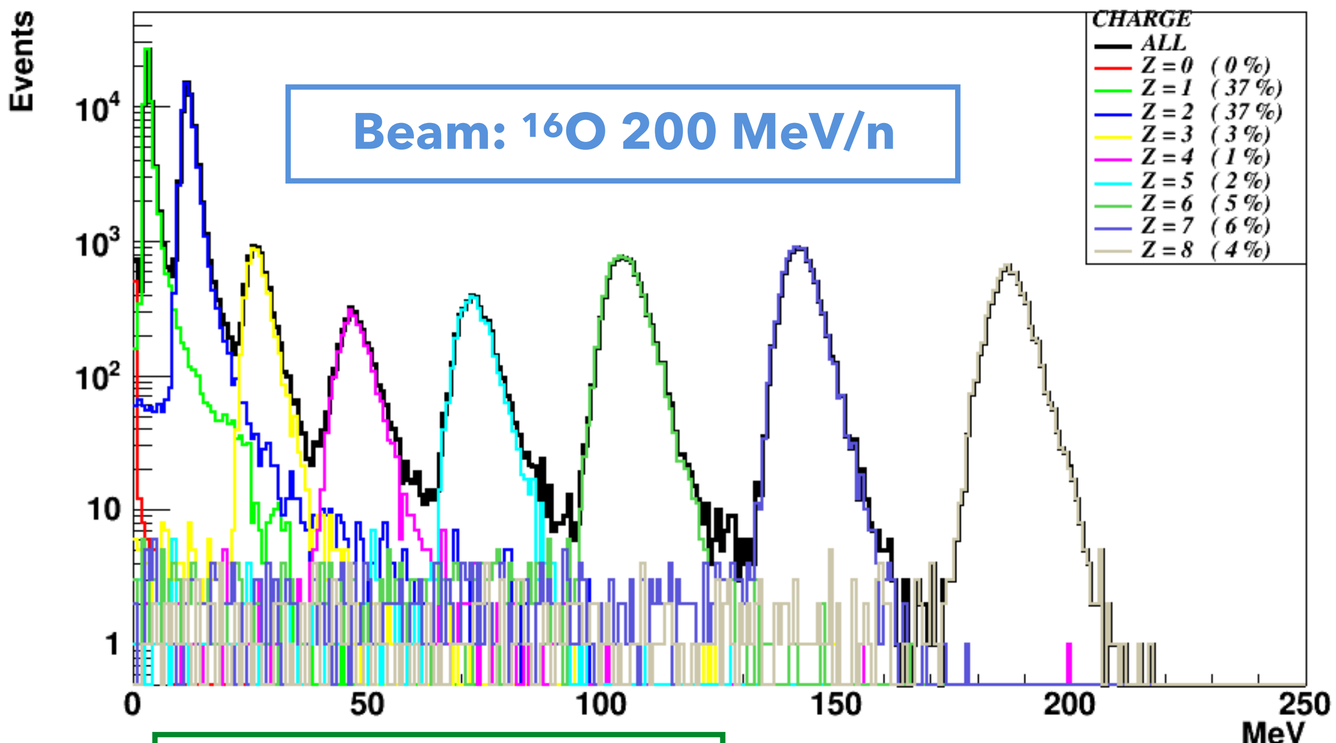
Fragmentation identification (I)

Fragments univocally defined by Z and A

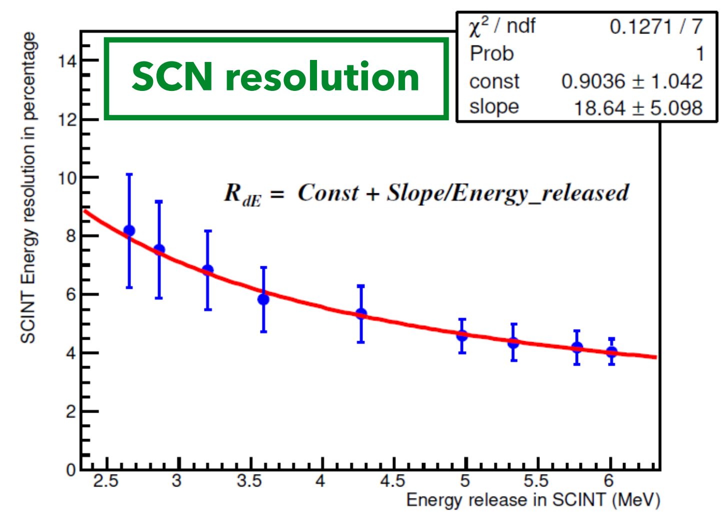
- ☑ **reconstruction of Z**
- ☐ reconstruction of A

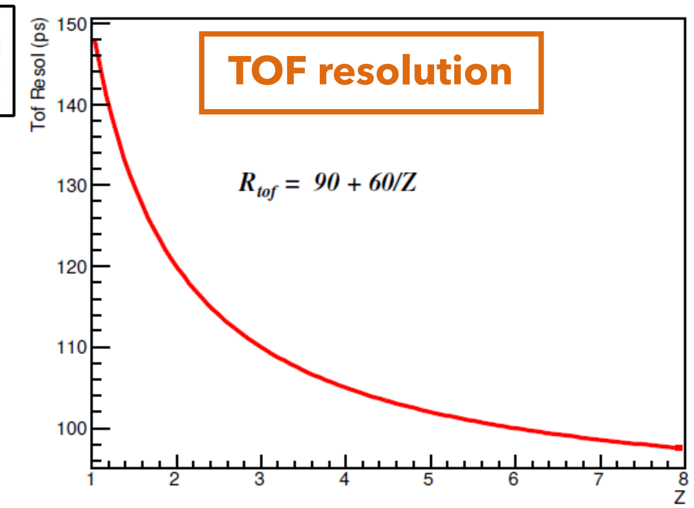
$$-\frac{dE}{dx} = \frac{\rho \cdot Z}{A} \frac{4\pi N_A m_e c^2}{M_U} \left(\frac{e^2}{4\pi\epsilon_0 m_e c^2}\right)^2 \frac{z^2}{\beta^2} \left[\ln\left(\frac{2 m_e c^2 \beta^2}{I \cdot (1-\beta^2)}\right) - \beta^2\right]$$

Scintillator (dE/dx) — **TOF** (z^2/β^2)

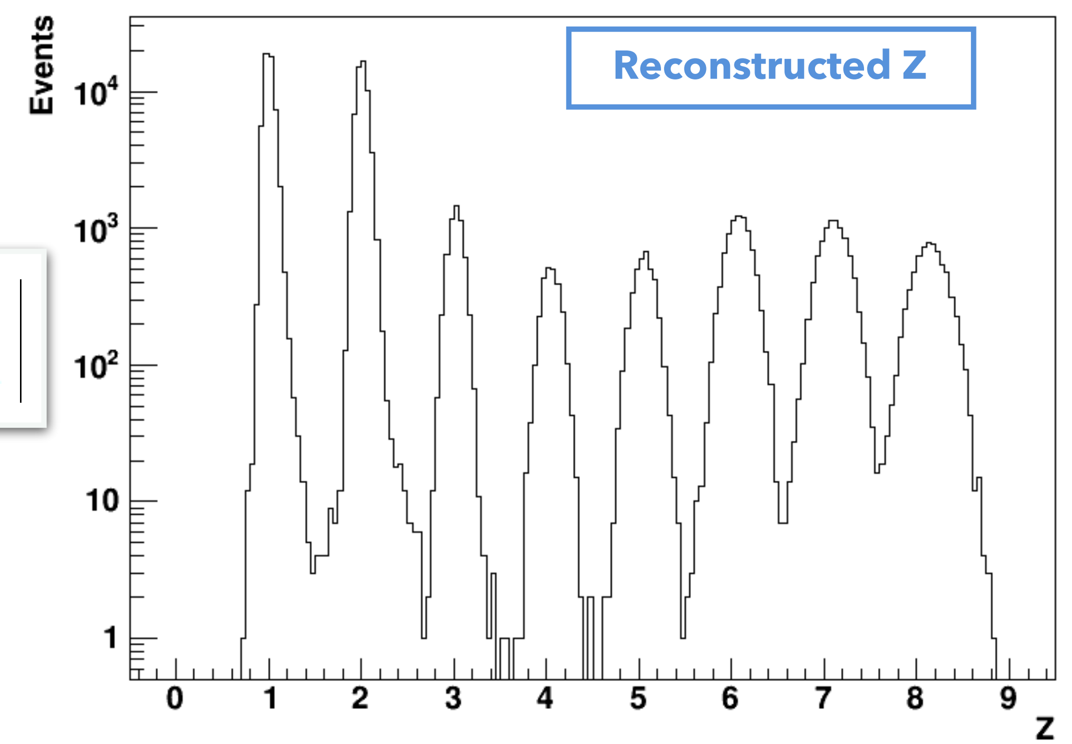


SCN deposited energy





^{1}H	^{4}He	^{7}Li	^{9}Be	^{11}B	^{12}C	^{14}N	^{16}O
1	2	3	4	5	6	7	8
1.01 ± 0.05	2.02 ± 0.06	3.03 ± 0.08	4.05 ± 0.10	5.07 ± 0.11	6.09 ± 0.14	7.11 ± 0.16	8.15 ± 0.18
5%	**3%**						**2.2%**



- **Z resolution: 2-5%** << minimum distance between charges (~10% between 7 and 8)

χ2 method

- χ^2 minimisation method based on a function f
- TOF, p, E_k, A_1, A_2, A_3 are the reconstructed quantities (gaussian smearing to simulate the reconstruction efficiencies)
- σ_{TOF}, σ_p, σ_{Ek} are the uncertainties
- T, P, K, A are the fit output parameters

$$f = \left(\frac{TOF - T}{\sigma_{TOF}}\right)^2 + \left(\frac{p - P}{\sigma_p}\right)^2 + \left(\frac{E_k - K}{\sigma_{E_k}}\right)^2 +$$
$$\left(A_1 - A, \quad A_2 - A, \quad A_3 - A\right) \begin{pmatrix} B_{00} & B_{01} & B_{02} \\ B_{10} & B_{11} & B_{12} \\ B_{20} & B_{21} & B_{22} \end{pmatrix} \begin{pmatrix} A_1 - A \\ A_2 - A \\ A_3 - A \end{pmatrix}$$

- The evaluation of the uncertainties associated to A_1, A_2, A_3 has to take into account their correlation which is generically expressed by the matrix B, related to the correlation matrix C by the function $B = (C \cdot C^T)^{-1}$
- The correlation matrix is expressed as

$$C = \begin{pmatrix} \frac{\partial A_1}{\partial T} dT & \frac{\partial A_1}{\partial P} dP & 0 \\ \frac{\partial A_2}{\partial T} dT & 0 & \frac{\partial A_2}{\partial K} dK \\ 0 & \frac{\partial A_3}{\partial P} dP & \frac{\partial A_3}{\partial K} dK \end{pmatrix}$$

Augmented Lagrangian Method

- The **ALM** approach performs a constrained minimization in a large parameter space
- Minimisation of a Lagrangian function:

$$L(\vec{x}, \lambda, \mu) \equiv f(\vec{x}) - \sum_a \lambda_a c_a(\vec{x}) + \frac{1}{2\mu} \sum_a c_a^2(\vec{x})$$

$$f(\vec{x}) = \left(\frac{TOF - T}{\sigma_{TOF}}\right)^2 + \left(\frac{p - P}{\sigma_p}\right)^2 + \left(\frac{E_k - K}{\sigma_{E_k}}\right)^2$$

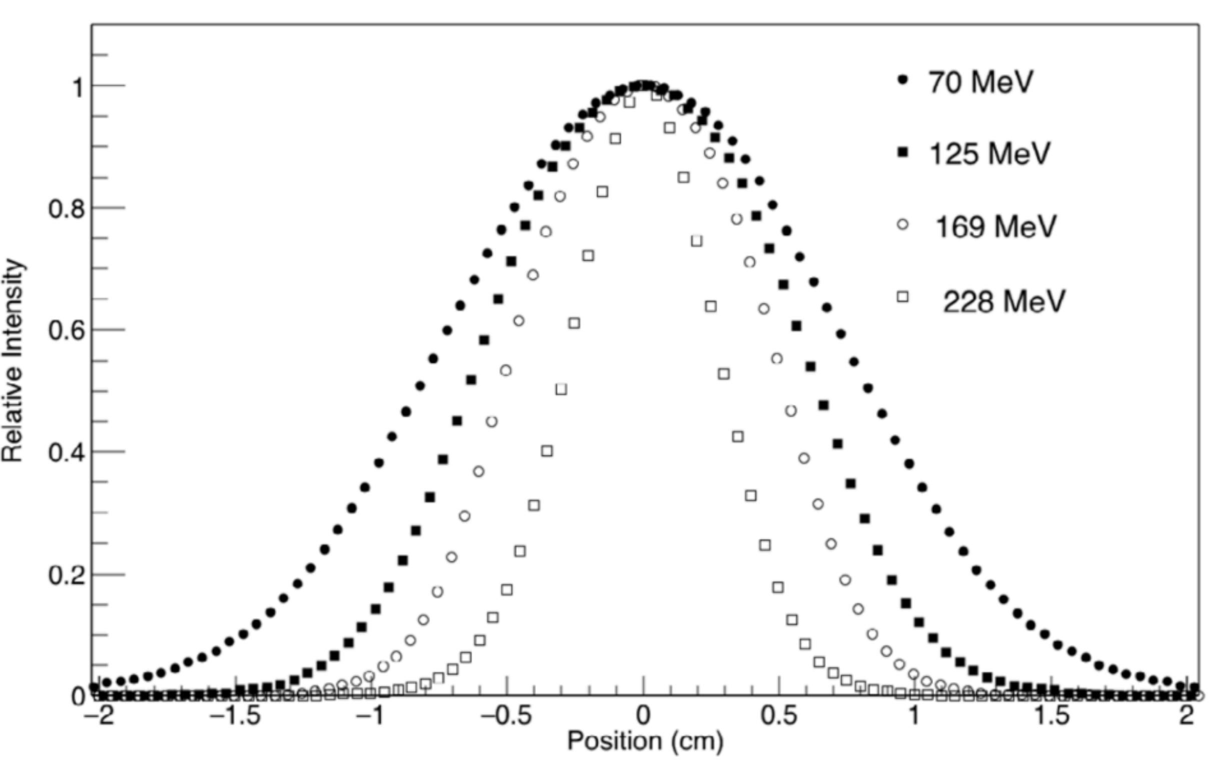
- Both the summation run over the three constraints (A_1, A_2 and A_3) with the relation:

$$\sum_a \lambda_a c_a(\vec{x}) + \frac{1}{2\mu} \sum_a c_a^2(\vec{x}) = \lambda_1 (A_1 - A) + \lambda_2 (A_2 - A) + \lambda_3 (A_3 - A) + \frac{1}{2\mu}\left((A_1 - A)^2 + (A_2 - A)^2 + (A_3 - A)^2\right)$$

- λ = variable Lagrange multiplier parameters
- μ = penalty term fixed to 0.1
  - this forces the fit to give more strength to the constraints: the lower is μ, the greater is the effect of the constraints

Trento Proton Therapy facility

- Below: beam spot profiles measured at different energies with the Lynx detector placed at the Isocenter position.
- Right: beam spot size estimated from a Gaussian fit on the profiles measured in the X–Y plane perpendicular to the beam direction.

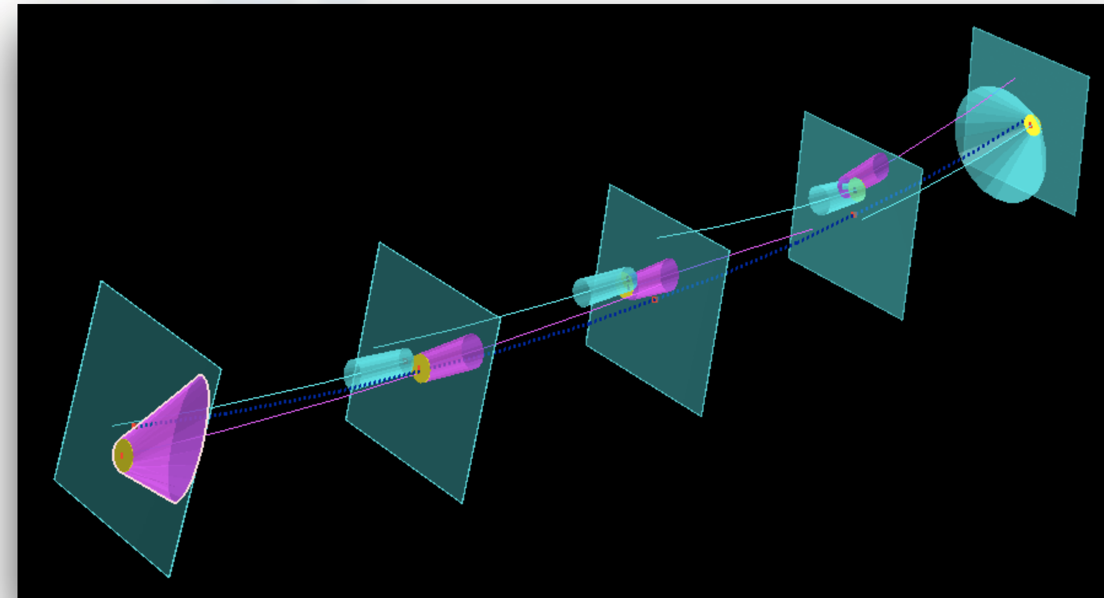


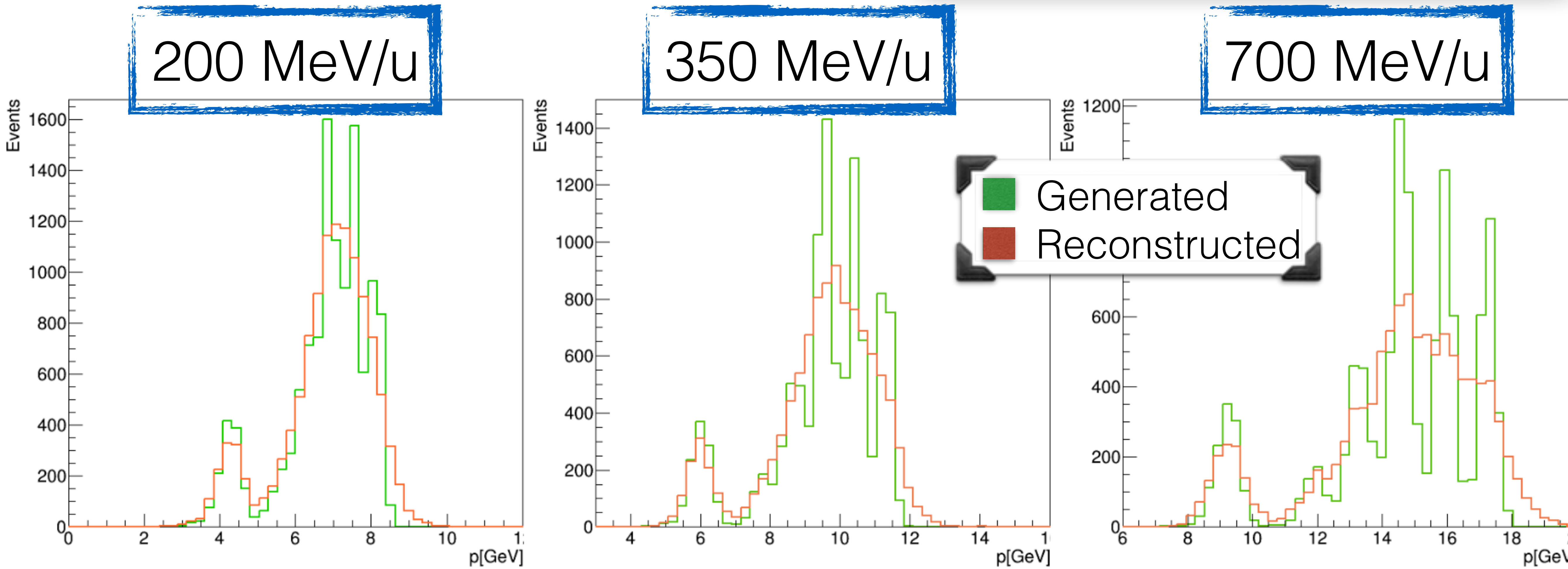
E (MeV)	σ_x (mm)	σ_y (mm)	Asymmetry (%)
70.2	6.93	6.91	0.1
73.9	6.63	6.74	0.8
82.7	6.28	6.41	1.0
90.8	6.04	6.15	0.9
100.0	5.63	5.73	0.8
105.6	5.42	5.63	1.8
112.4	5.26	5.43	1.6
119.0	5.05	5.24	1.9
125.3	4.90	5.09	1.9
131.3	4.70	4.88	1.9
137.2	4.49	4.79	3.2
142.9	4.50	4.62	1.3
148.5	4.39	4.52	1.4
153.9	4.23	4.41	2.0
159.2	4.10	4.31	2.5
164.4	4.02	4.19	2.0
169.4	3.93	4.08	1.8
174.4	3.85	4.07	2.7
179.3	3.76	3.92	2.1
184.1	3.71	3.84	1.7
188.8	3.66	3.83	2.2
193.4	3.57	3.74	2.2
197.9	3.48	3.64	2.3
202.4	3.44	3.52	1.1
206.9	3.33	3.44	1.5
211.2	3.33	3.31	0.4
215.5	3.18	3.19	0.1
219.8	3.10	3.08	0.5
224.0	3.04	2.97	1.0
228.2	2.74	2.72	0.2

Fragmentation reconstruction

Fragmentation reconstruction uses

- ☑ global track fitting algorithm
- ☑ Vertex, Inner Tracker and Microstrip detectors simulated





Kalman filter in pills

1. Take an ideal particle in vacuum. If we add air + detector layers, trajectory changes due to M.S. and energy loss.

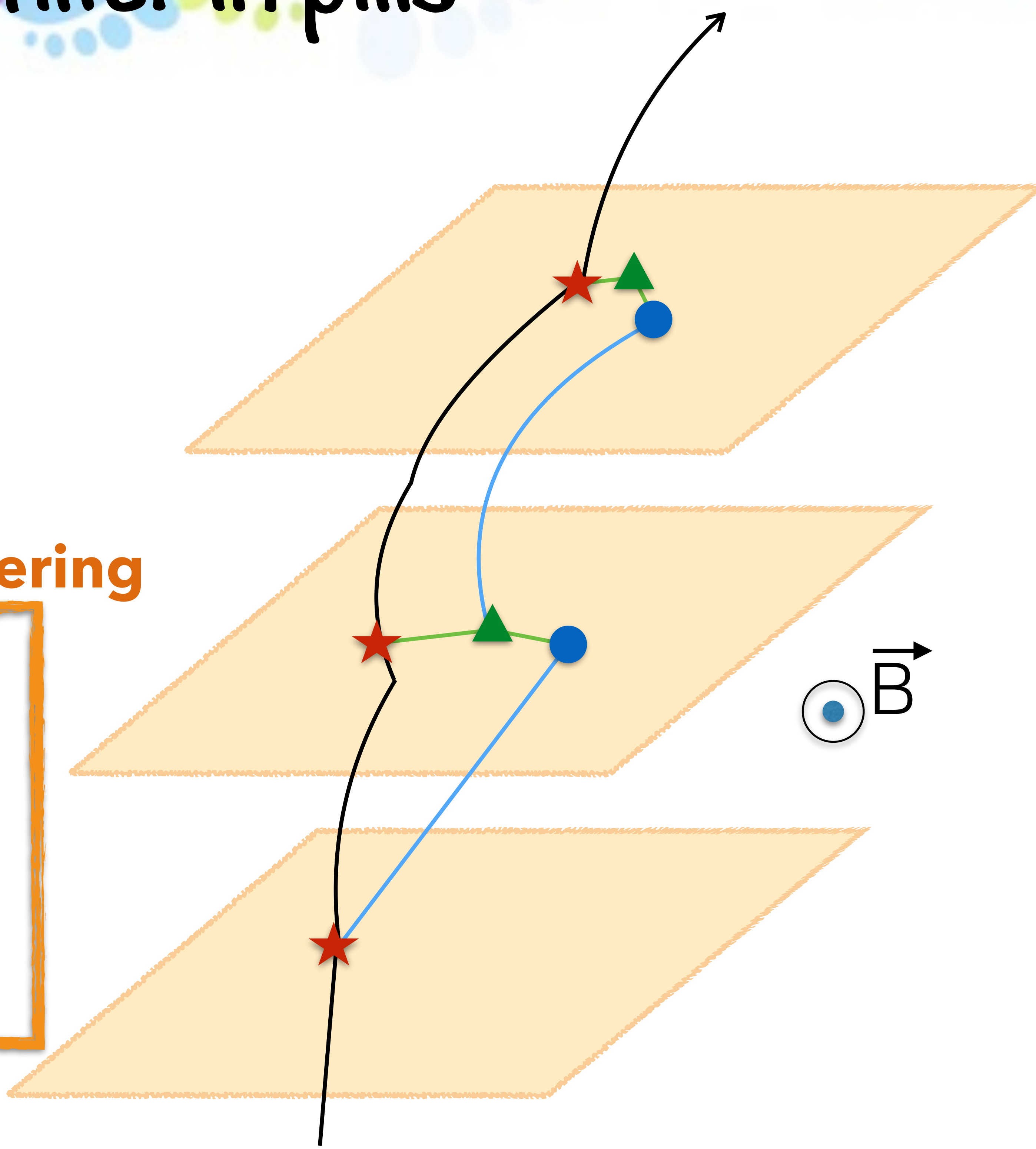
2. We'll see some measurement hits on the detector layers (considering finite detector uncertainty).

Filtering

3. Propagate the first hit to the next layer. Propagator Matrix F.

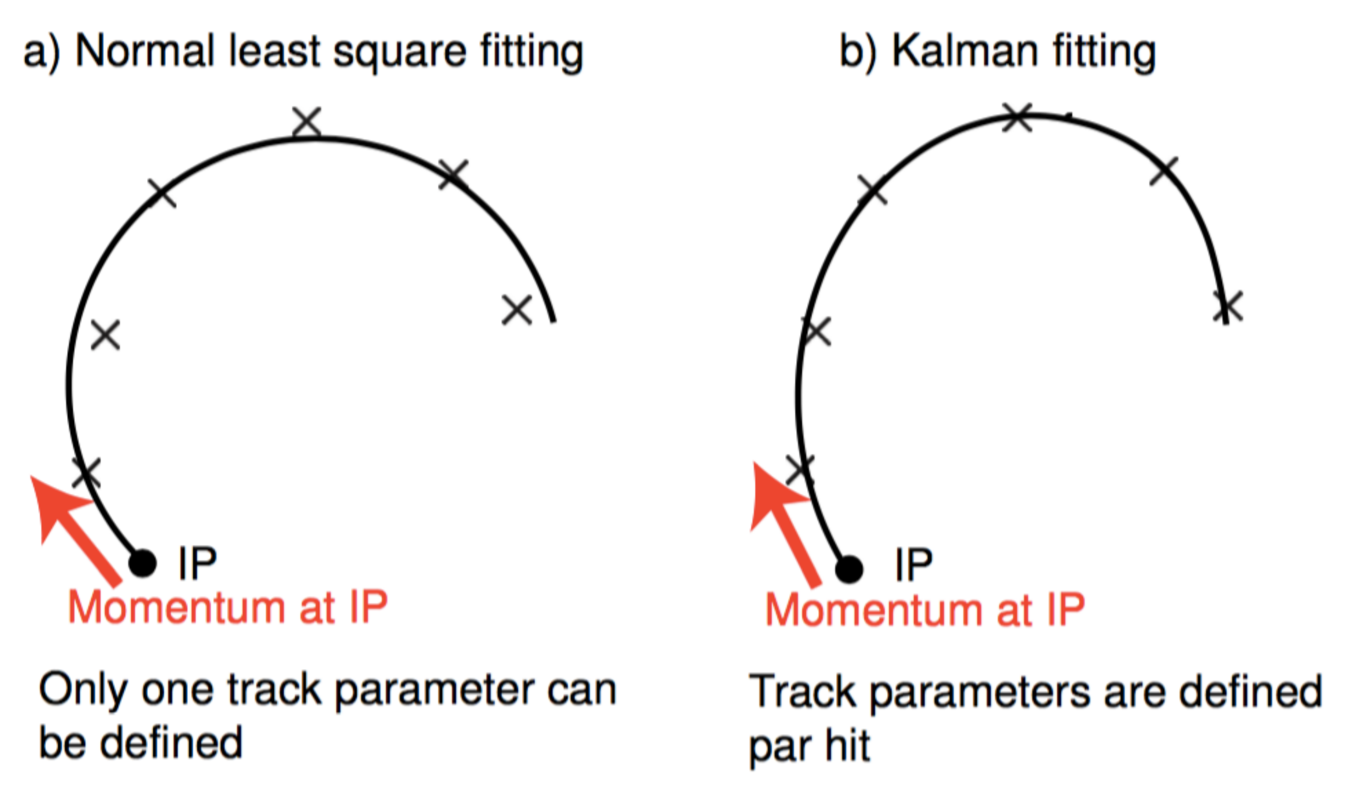
4. Find the best compromise between the propagated point and the closest hit on the 2^{nd} layer. Use a Chi2 and a Projection Matrix H.

5. **Iterate** 3 and 4 for the next layers.



Kalman filter in pills

- R.E.Kalman proposed an iterative method to estimate the states of a dynamic system starting from a series of measurement points on N surfaces.
- Initially used to calculate the trajectory of ballistic missiles. Later introduced in particle physics (1984).
- Precise as a global χ^2 fitting;
- ***Fast***;
- Best ***track parameter*** found ***for each hit!!!***



“A new approach to linear filtering and prediction problems” Trans. ASME J. Basic Eng. 82 (1960), 35