FOOT Collaboration:
Physics data for therapy

FOOT: **F**ragmentati**O**n **O**f **T**arget

An experiment for the measurement of nuclear fragmentation cross sections for Particle Therapy

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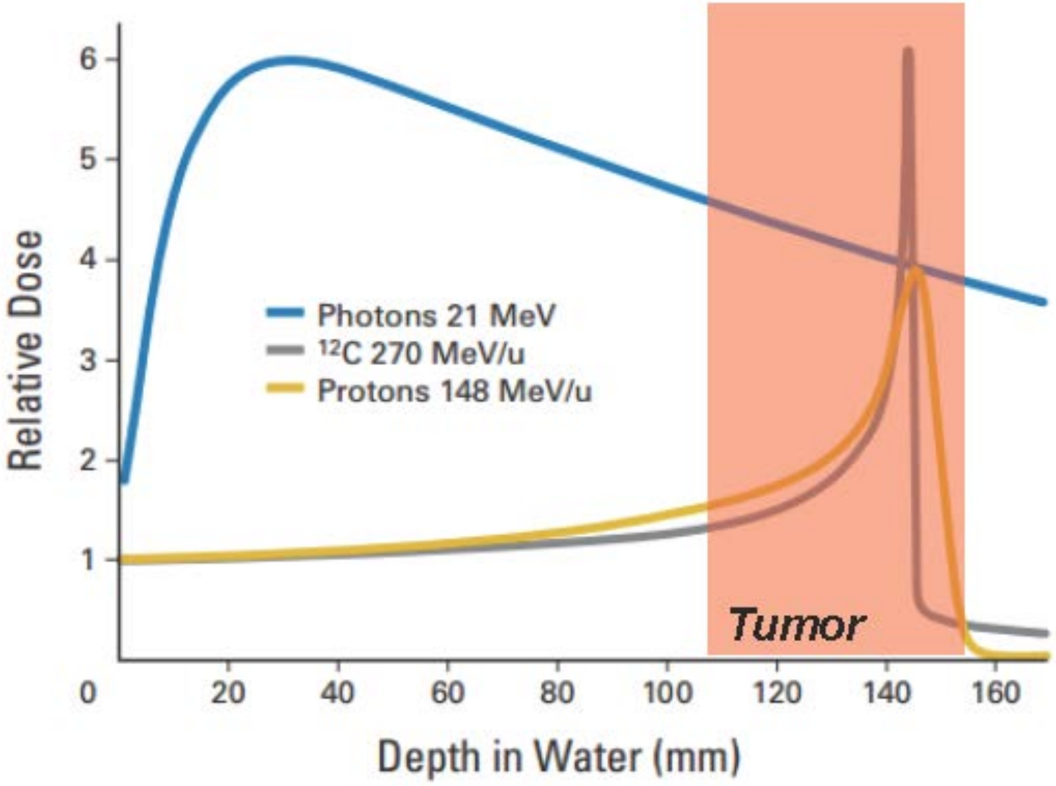
for the FOOT Collaboration

Workshop on Ions for Cancer Therapy, Space Research and Material Science
Chania 26-30 August 2017

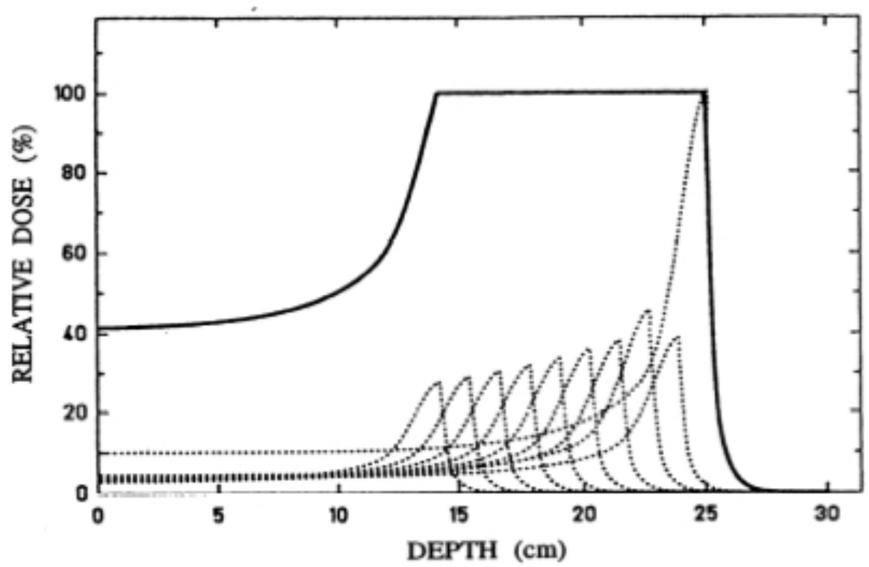
Charged Particle Therapy

Charged Particle Therapy vs "Conventional" radiotherapy (photons)

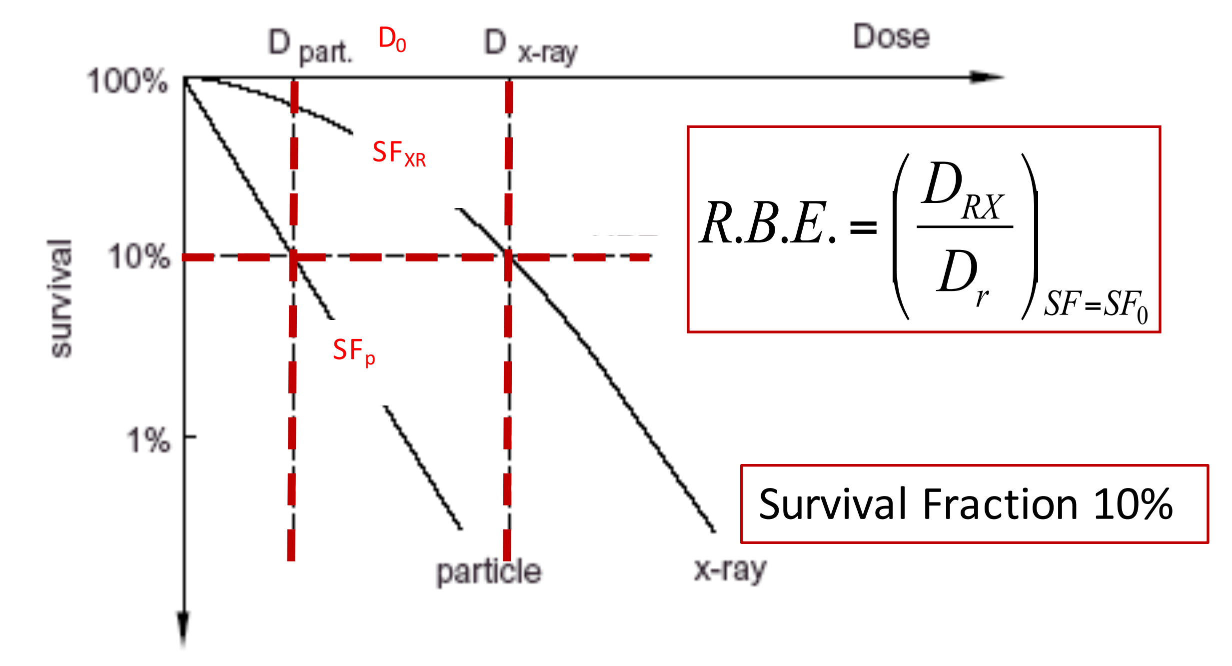
- ✓ Peak of dose released at the end of the track, **allowing sparing the normal tissue**
- ✓ Beam penetration in tissue is function of the beam energy
- ✓ Accurate conformal dose to tumor with Spread Out Bragg Peak



Schulz-Ertner et al. J. Clin. Oncol. (2007)



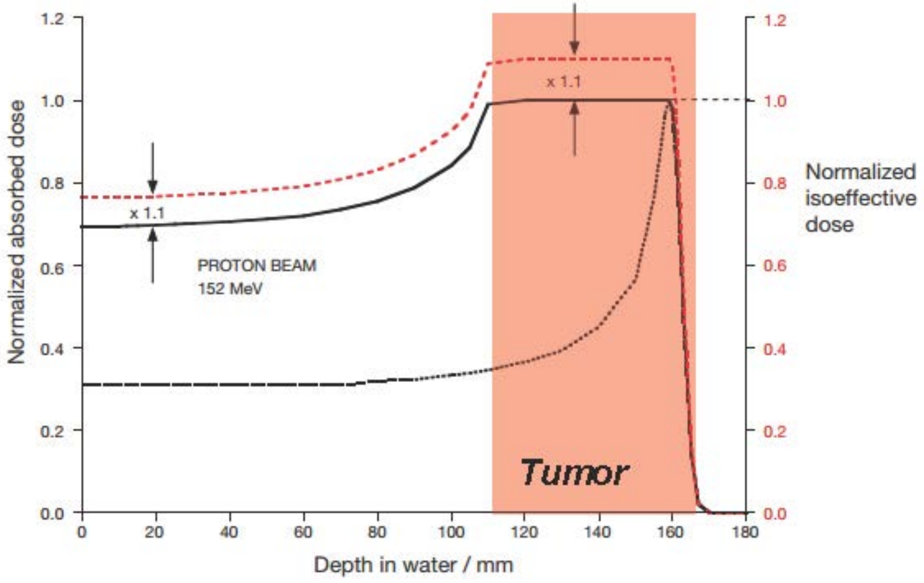
RBE: Relative Biological Effectiveness



$$R.B.E. = \left(\frac{D_{RX}}{D_r}\right)_{SF=SF_0}$$

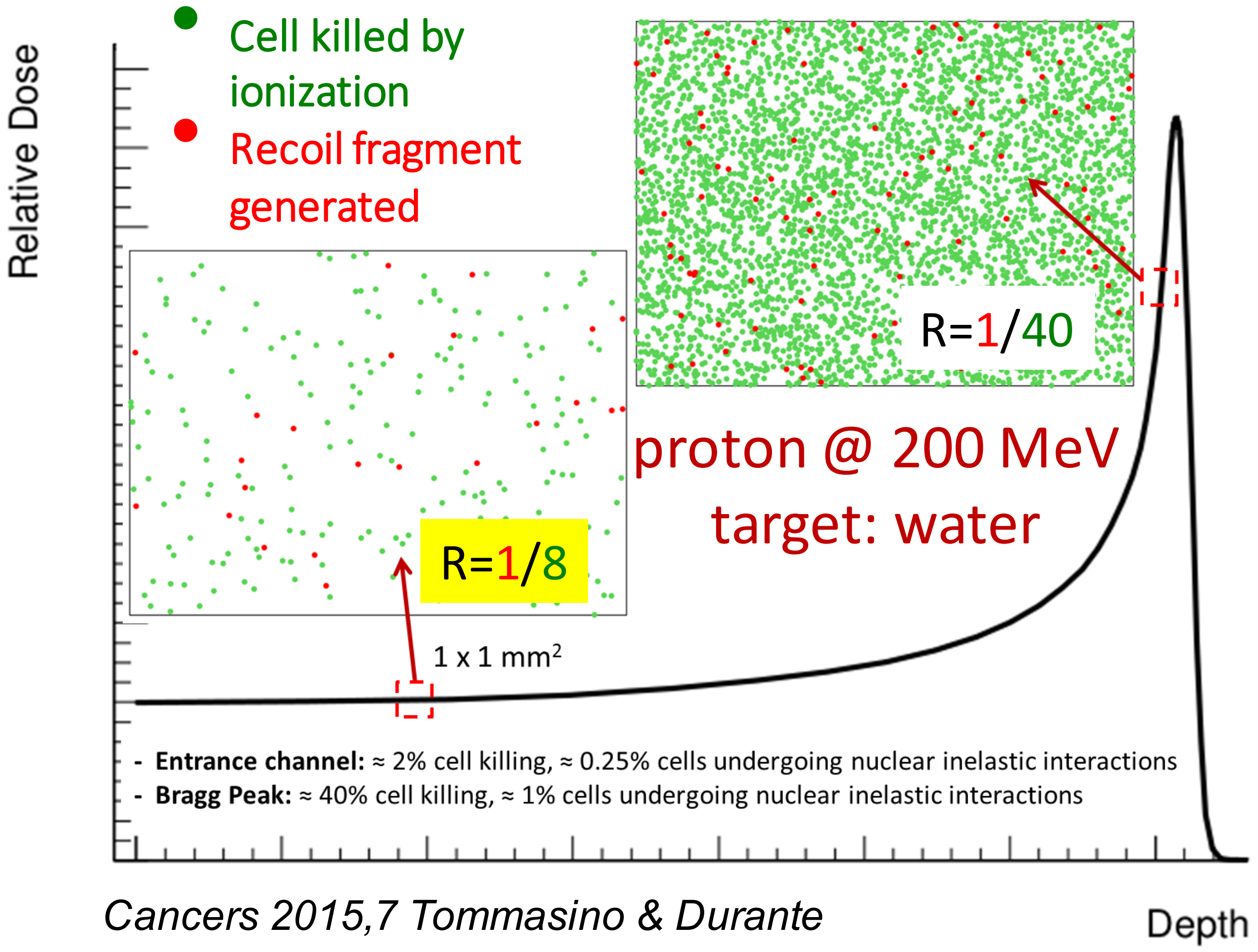
Survival Fraction 10%

$$D_{BIO} = R.B.E. * D_{phys}$$



In clinical practice protons RBE is a constant equal to 1.1, but experimental data show that RBE varies with Linear Energy Transfer (LET)!

Target fragmentation in proton therapy



Cancers 2015,7 Tommasino & Durante

- Target fragmentation in proton therapy gives higher contribution in healthy tissue, where beam is still energetic;
- About 10% of biological effect in the entrance channel due to secondary fragments (Grun 2013);
- Largest contributions of recoil fragments expected from **He, C, Be, O, N:** important issue concerning the Normal Tissue Complication Probability.

Target fragmentation in proton therapy

p on O_2 200 MeV/n

Tommasino and Durante *Cancers* - 2015

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

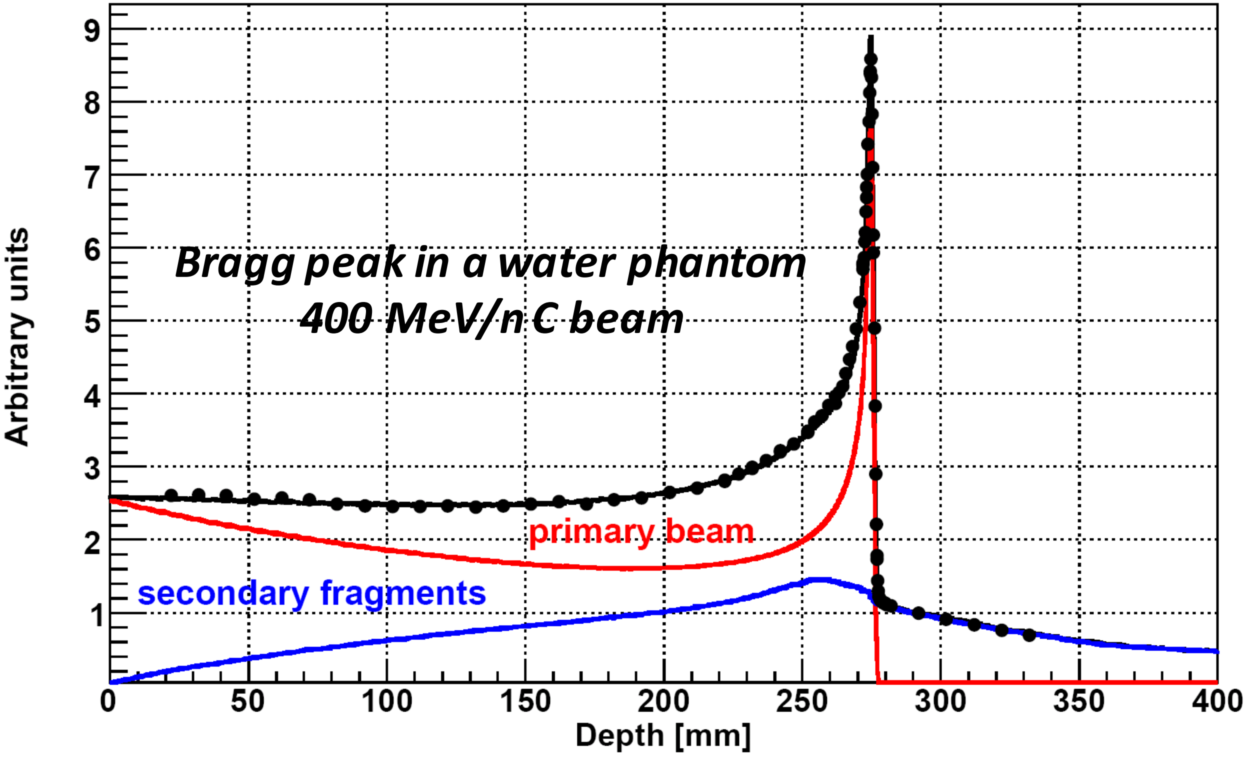
Analytic model to evaluate the fragments energies

We need to know the fragments cross section produced by proton on carbon or oxygen, the most common nuclei in tissue

- ✓ Missing data on heavy fragments
- ✓ Unreliable nuclear models

The FOOT project aims to measure the cross section of these fragments

Proton and Ion Therapy & FOOT



Exp. Data (points) from Haettner et al, Rad. Prot. Dos. 2006
Simulation: A. Mairani PhD Thesis, 2007, Nuovo Cimento C, 31, 2008

Proton Therapy:

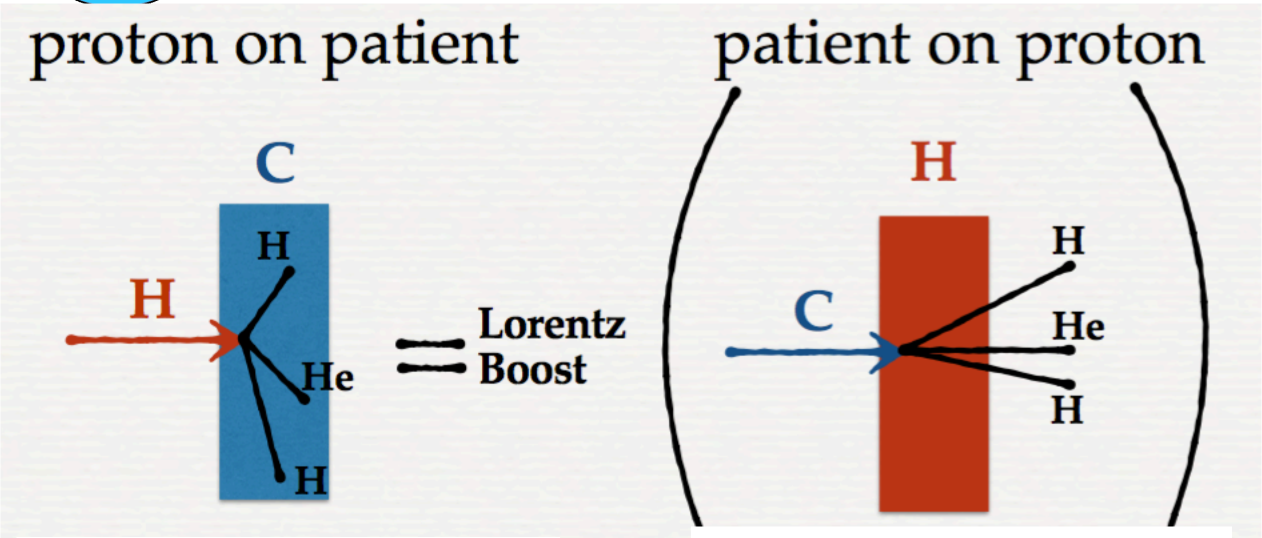
- Nuclear fragmentation of target
- Possible fragments contribution to RBE

Ion Therapy (He, C, O):

- Nuclear Fragmentation of Projectile and Target
- Scarce experimental/validation data
- Not well known contribution of varying RBE

The FOOT (FragmentatiOn Of Target) experiment aims to perform a set of measurements of nuclear fragmentation cross sections useful to develop a new generation of biologically oriented Treatment Planning Systems for proton and ion therapy.

FOOT: Inverse kinematic approach



Fragments with low energy and short range

Fragments with higher energy and longer range

- Protons @ E_{kin}= 200 MeV (β~0.6) on a "patient" (98% C, O, and H nucleus)

⬇

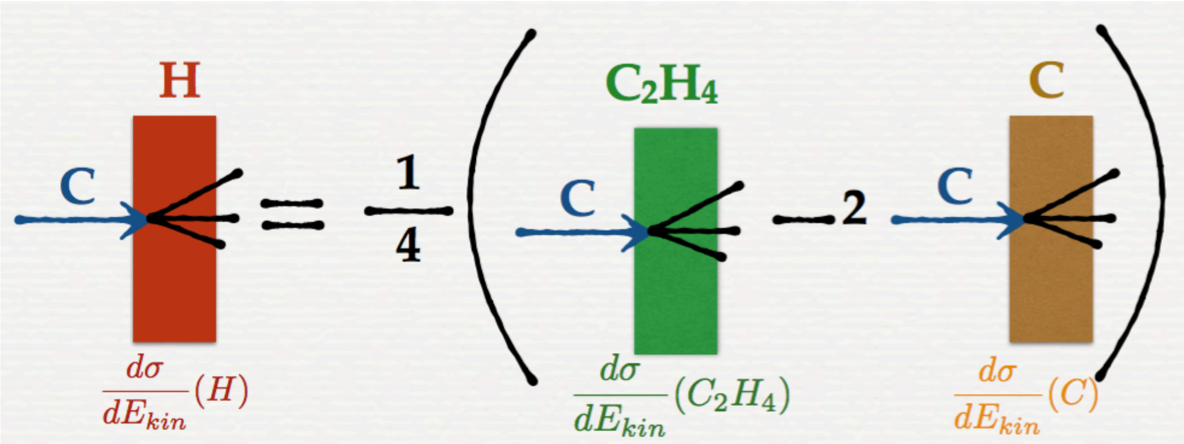
- can be replaced by ^{16}O, ^{12}C ion beams (E_{kin} ~ 200 MeV/n β~0.6) impinging on a target made of protons
- by applying the Lorentz transformation (well known β) it is possible to switch from the ***lab. frame*** to the ***patient frame***

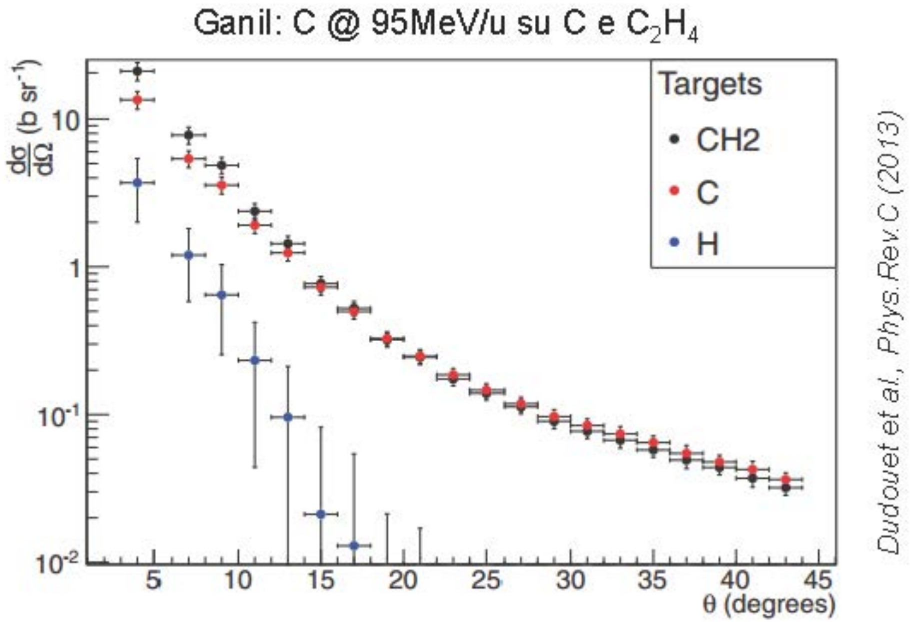
Requirements: the fragment direction must be well measured in the lab. frame to obtain the correct energy in the patient frame

Double target strategy

- H target? Use twin targets made of C and polyethylene $(C_2H_4)_n$ and obtain the fragmentation results on H target from the difference
- C → H cross-section can be estimated by C→C_2H_4 and C→C cross-section

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





- GANIL experimental data

FOOT Detector goals

Which measurements for the knowledge of the H, C and O interaction @ 150 - 250 MeV/n:

- The fragment charge Z identification is the basis of the measurement
- The fragment mass A identification is a challenge. Wrong A assignment influences the range evaluation-> **less severe at high A**
- Particle identification achieved due to **combination** of measurements of **energy**, **momentum** and **TOF** measurement of fragments
- The fragmentation contribution due to detector material should be as low as possible and eventually subtracted
- **Detector portability to different beams is an absolute need: size of the detector should be in the 2 meters range**

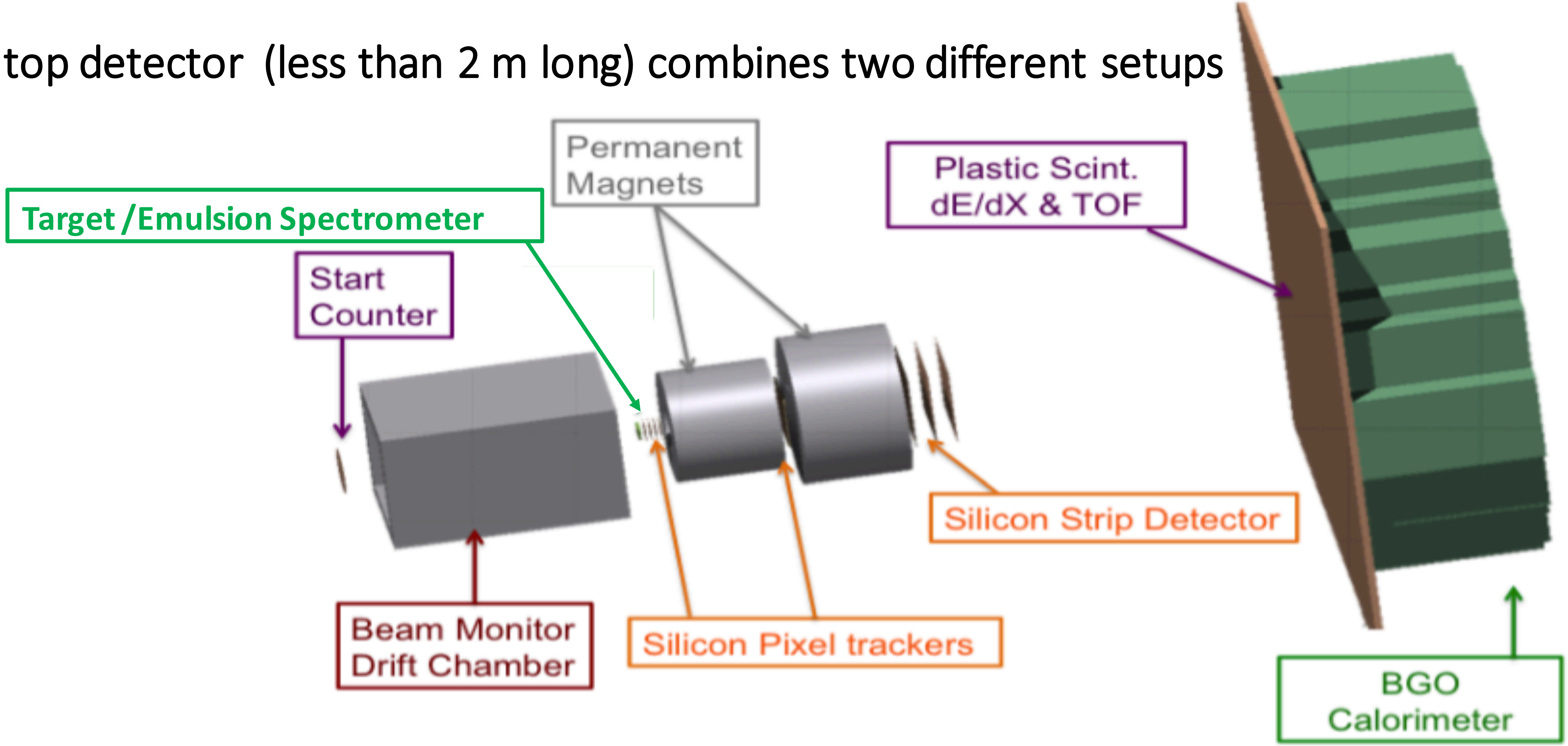
FOOT Detector: needed performances

- Momentum resolution σ_p/p ~ 5 % for E_{kin} ~ 200 MeV/n
- Time of flight resolution ~ 100 ps
- Energy resolution σ_E/E ~ 2 % for E_{kin} ~ 200 MeV/n
- $\sigma_{\Delta E}/\Delta E$ ~ 2 % (ΔE energy loss in a thin slab of material, dE/dx)

The achievement of this required resolutions will be possible by redundant measurements of the quantities of interest!

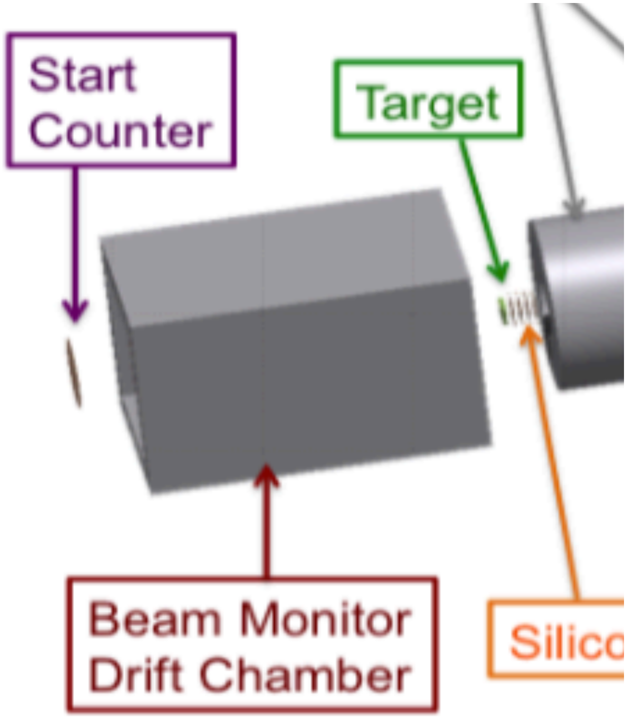
FOOT Detector

➢Table top detector (less than 2 m long) combines two different setups

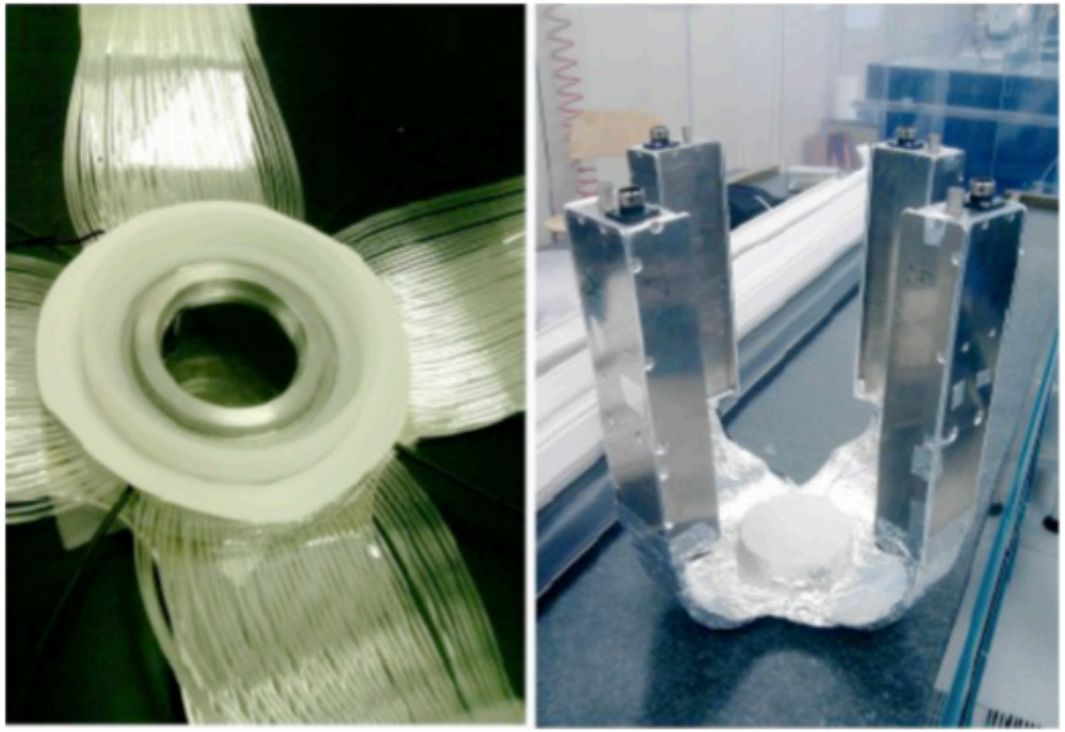


- electronic detectors and a magnetic spectrometer to identify and measure fragments heavier than ^{4}He (angular acceptance +/- 10°)
- emulsion spectrometer to measure the production of light charged fragments up to about 70°

FOOT Detector: upstream/target region

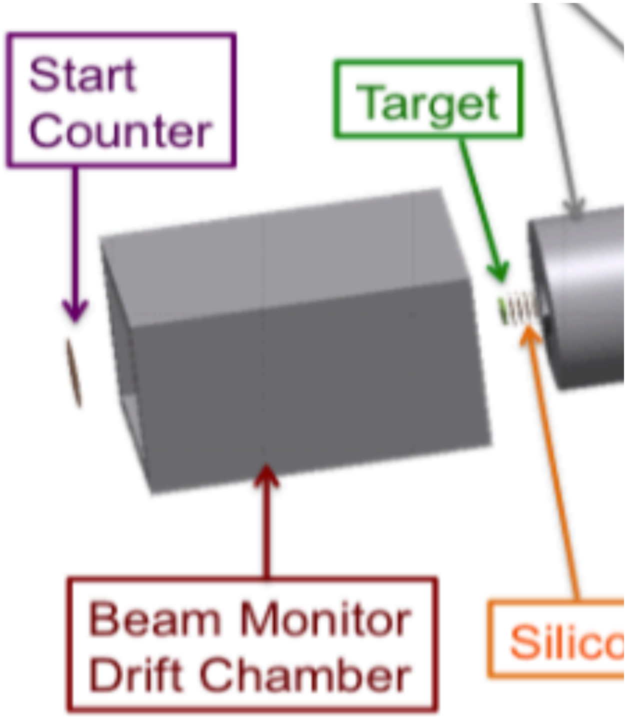


➢Start counter: thin plastic scintillator (250 μm) providing the start signal of the TOF (100 ps)

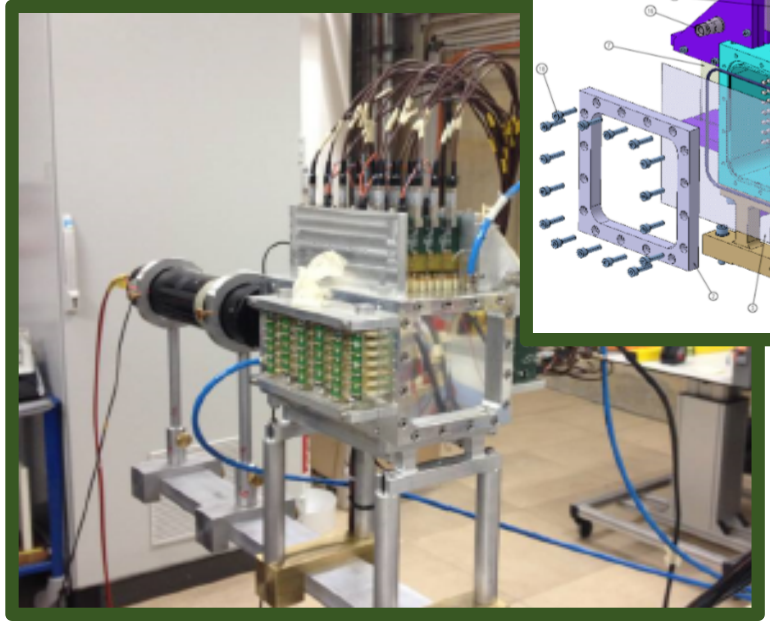


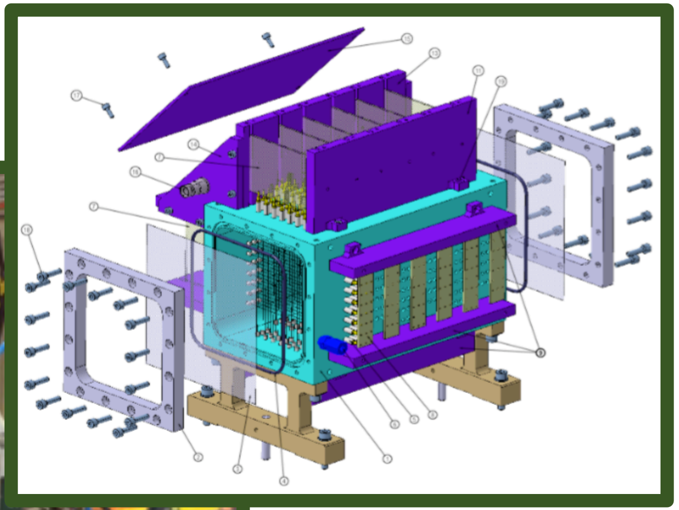
• scintillator foil and 160 optical fibers grouped in four different arms

FOOT Detector: upstream/target region



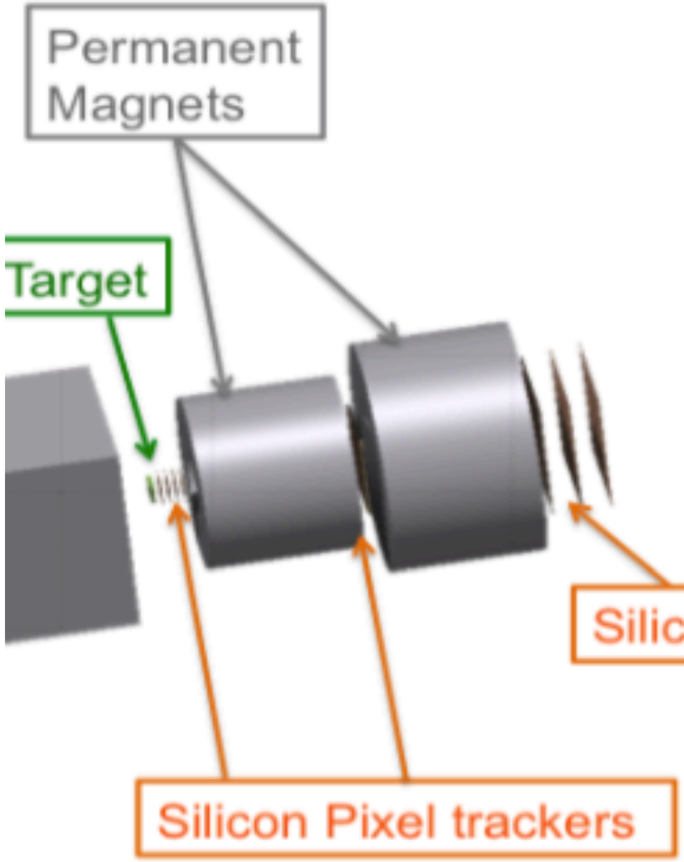
- Drift chamber acting as beam monitor: twelve layers of wires, with three drift cells per layer
- measure the direction and the position (spatial resolution ~140 μm) of the impinging beam on the target
- looks for fragmented primaries





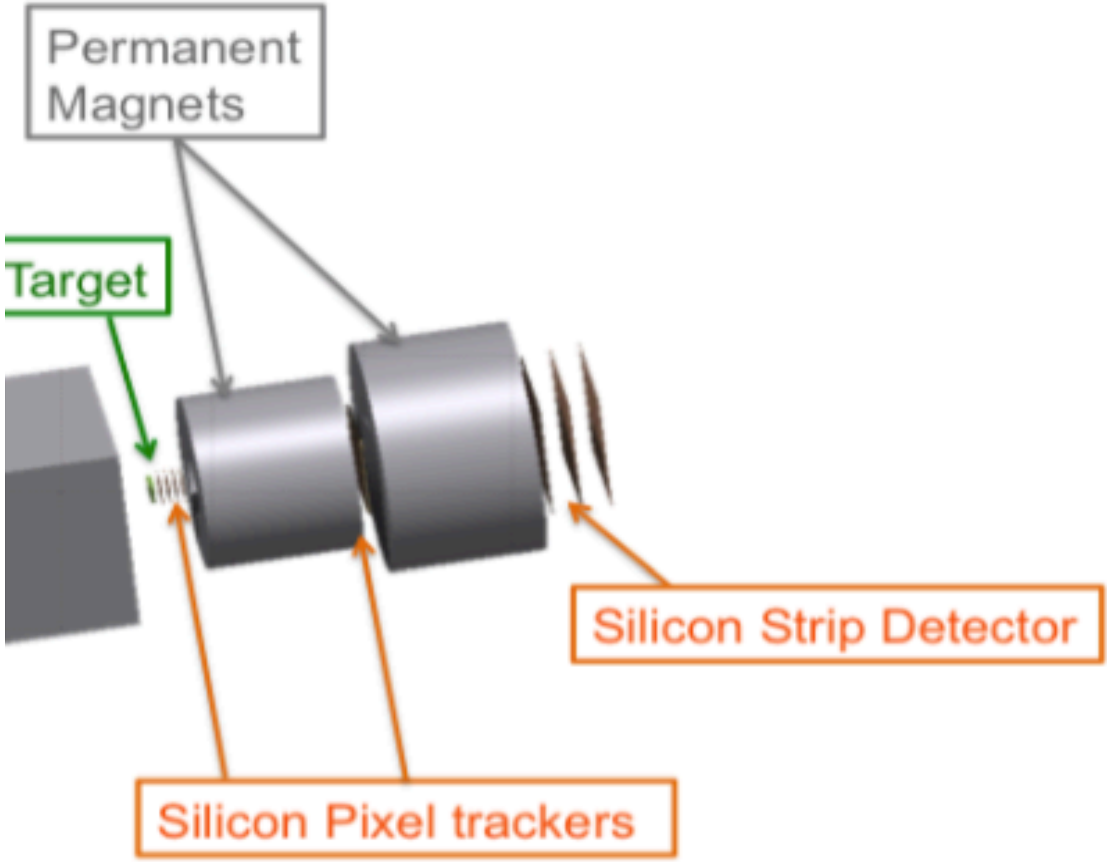
FOOT Detector: magnetic spectrometer

- Region dedicated to the **vertex** and **traking reconstruction** and to the **measurement of the fragment momentum**



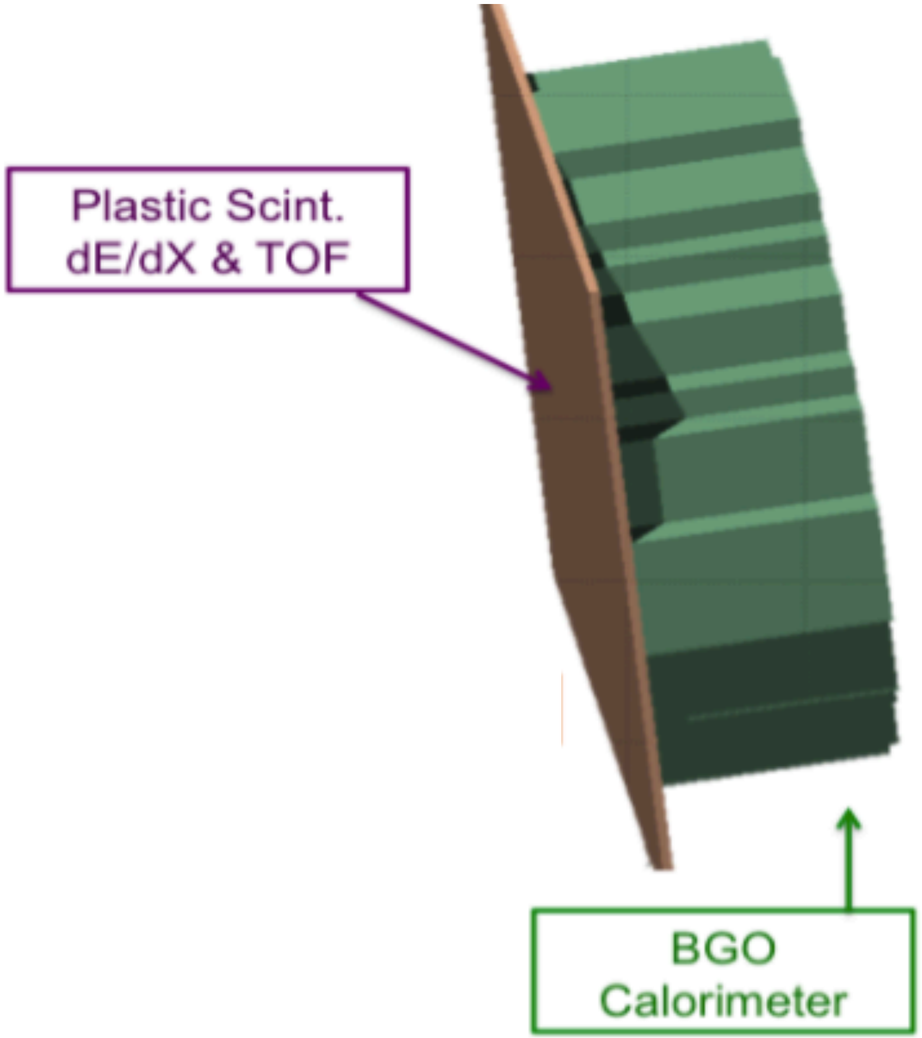
- A telescope of **silicon pixel trackers** provides the vertex reconstruction: four tracking layers (CMOS Monolithic Active Pixel Sensors, matrix of 928 x 960 pixels of 20 μm pitch, 2 x 2.2 cm^2)
- The magnetic region (two permanent dipole magnets in Hallbach geometry) bends the fragments trajectory
- Between the two magnets, the fragment direction is measured by two additional layers of silicon pixel trackers (8 x 8 cm^2)
- At the exit of the magnet systems, a **telescope of silicon microstrips** provides a further precision tracking (3 x-y planes, 9 x 9 cm^2, strip pitch = 125 μm, spatial resolution < 35 μm)
- momentum resolution $\Delta p/p$ about 3 %

FOOT Detector: magnetic spectrometer

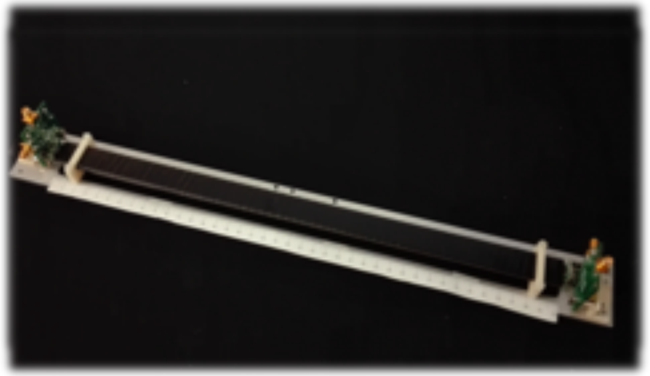


Target and vertex tracker

FOOT Detector: plastic scintillator & calorimeter



- Two orthogonal layers of 20 plastic scintillator rods (2 cm large and 40 cm long for a total area of 40×40 cm^2, tickness 3 mm – *to be optimized*)
- It will provide the stop signal for the TOF measurement and the measurement of the energy loss ΔE to identity the charge of the fragments
- The calorimeter will be formed by about 360 BGO crystals (2x2 cm^2 transverse size) covering a circular surface of about 20 cm radius: it will be measure the fragments energy



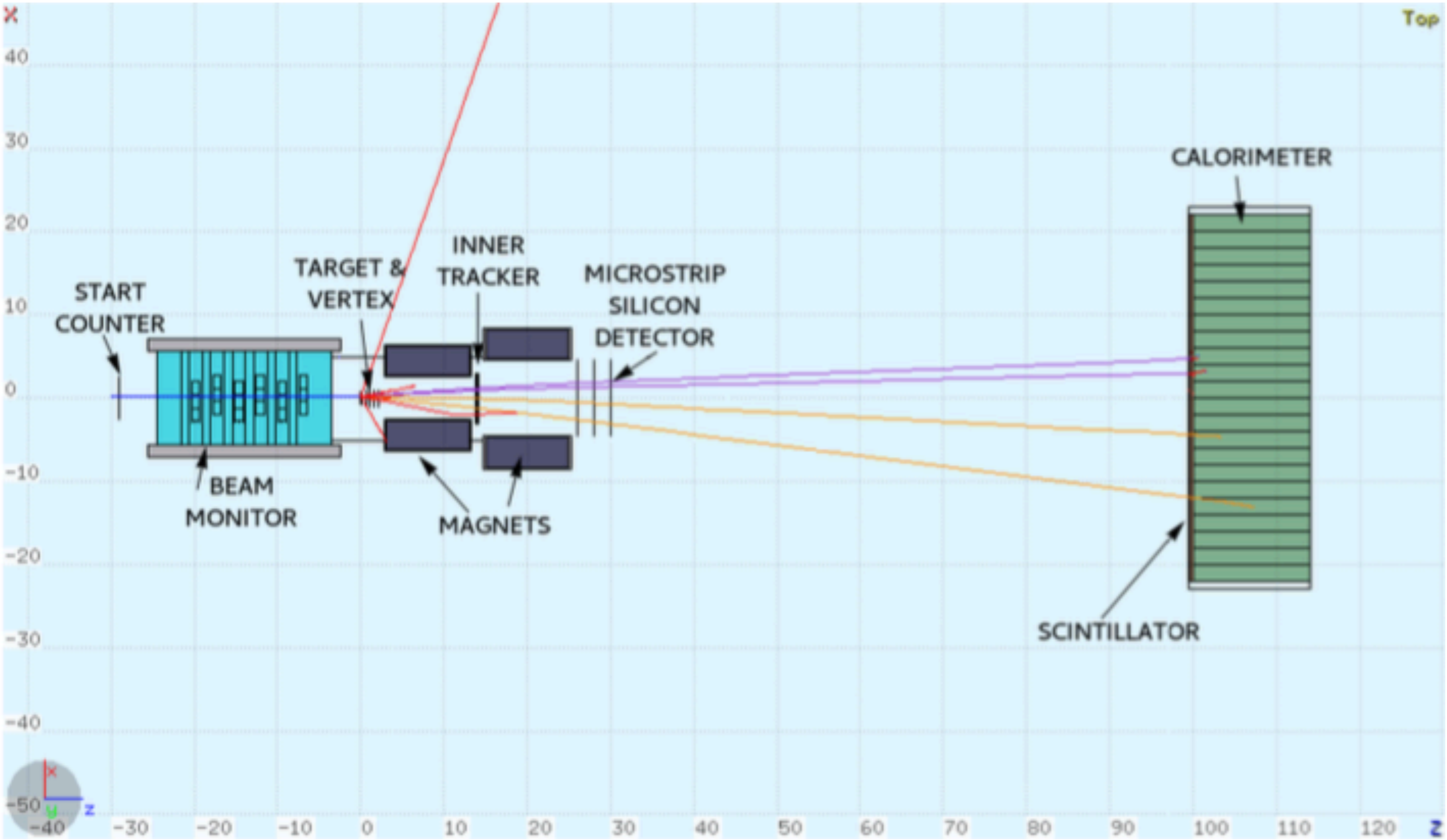
Plastic scintillator detector prototype

FOOT Detector: redundant measurements

The fragments mass A can be determined by:

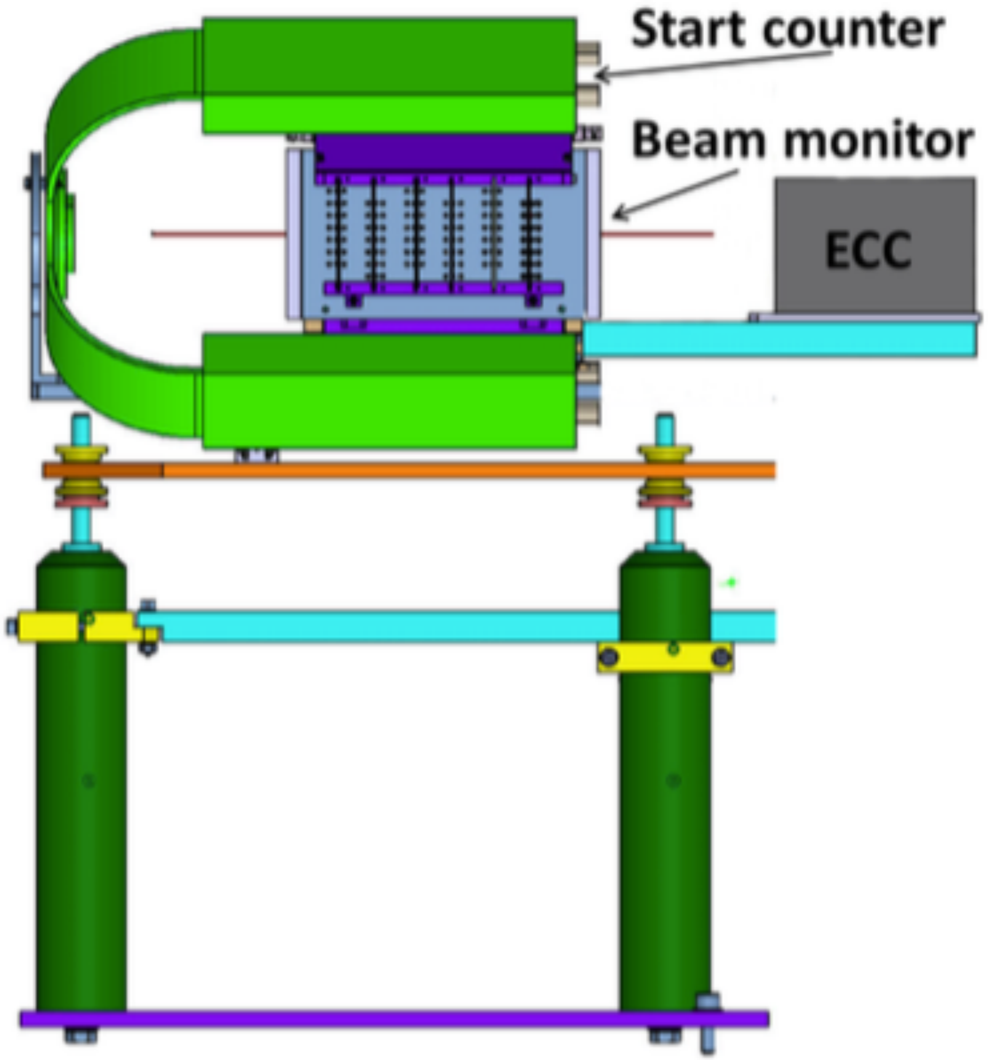
- measuring β and p respectively from the TOF and the magnetic spectrometer
- measuring β and E_{kin} respectively from the TOF and the calorimeter
- measuring p and E_{kin} respectively from the magnetic spectrometer and the calorimeter

FOOT Detector: simulation with FLUKA



Schematic 2D event display of a primary ^{16}O ion interacting in a polyethylene target

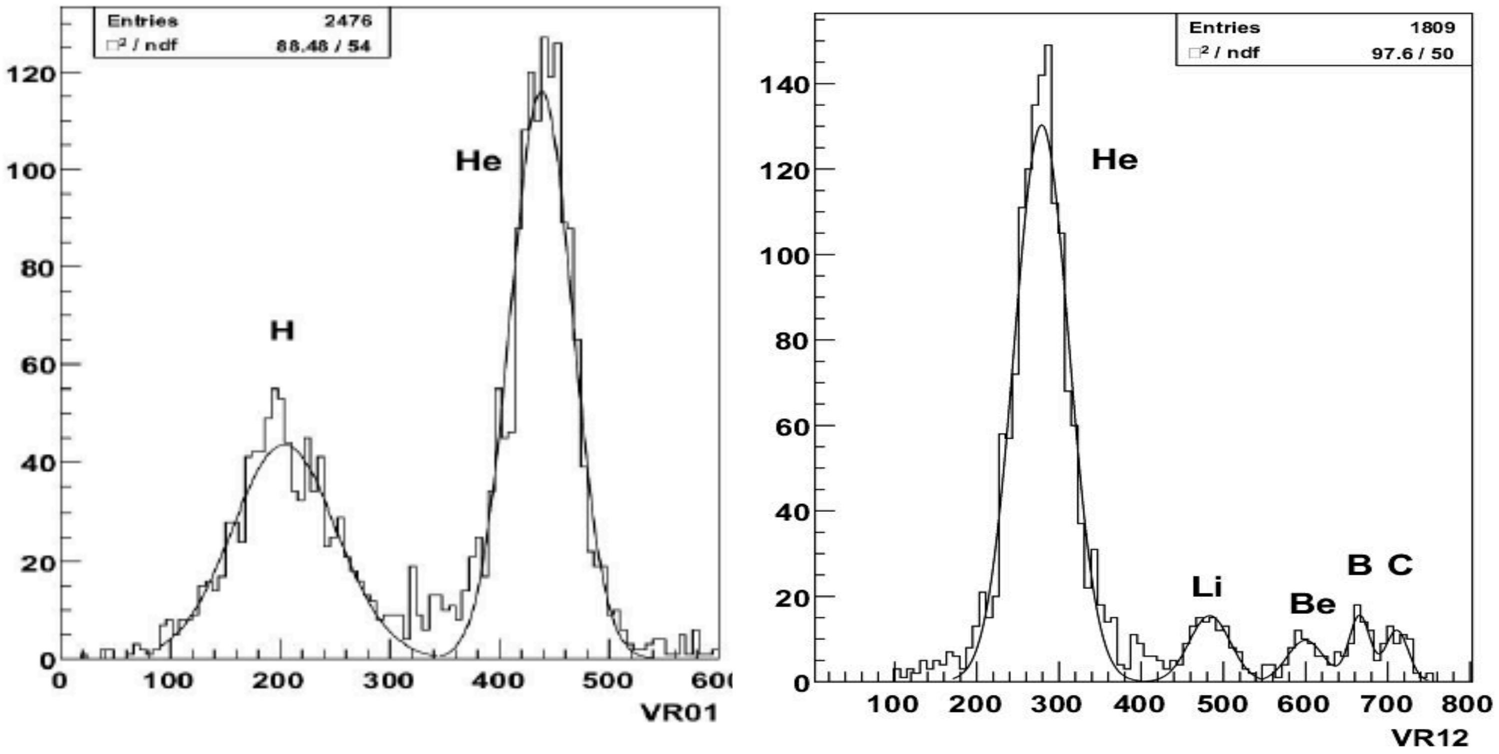
FOOT Detector: Emulsion spectrometer



- To measure fragments as protons, deuterons, ^{4}He and Li emitted within a wider angular aperture (up to 70 degrees) with respect to heavier nuclei
- Detector based on the concept of Emulsion Cloud Chamber - ECC (nuclear emulsion sensitive to ionizing particle interleaved with passive material)
- ECC integrates target and detector in a very compact setup and provides a very accurate reconstruction of the interactions occurring inside the target
- New generation microscopes with automated fast scanning systems allow to analyze and to reconstruct the fragments interaction occured in the ECC

FOOT Detector: Emulsion Spectrometer

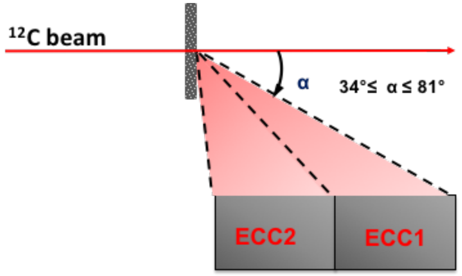
- The emulsion technique has been already exploited to study the fragmentation of Carbon ions in polycarbonate: identification of the secondary nuclei produced by fragmentation of 400 MeV/n ^{12}C can be achieved with high significance

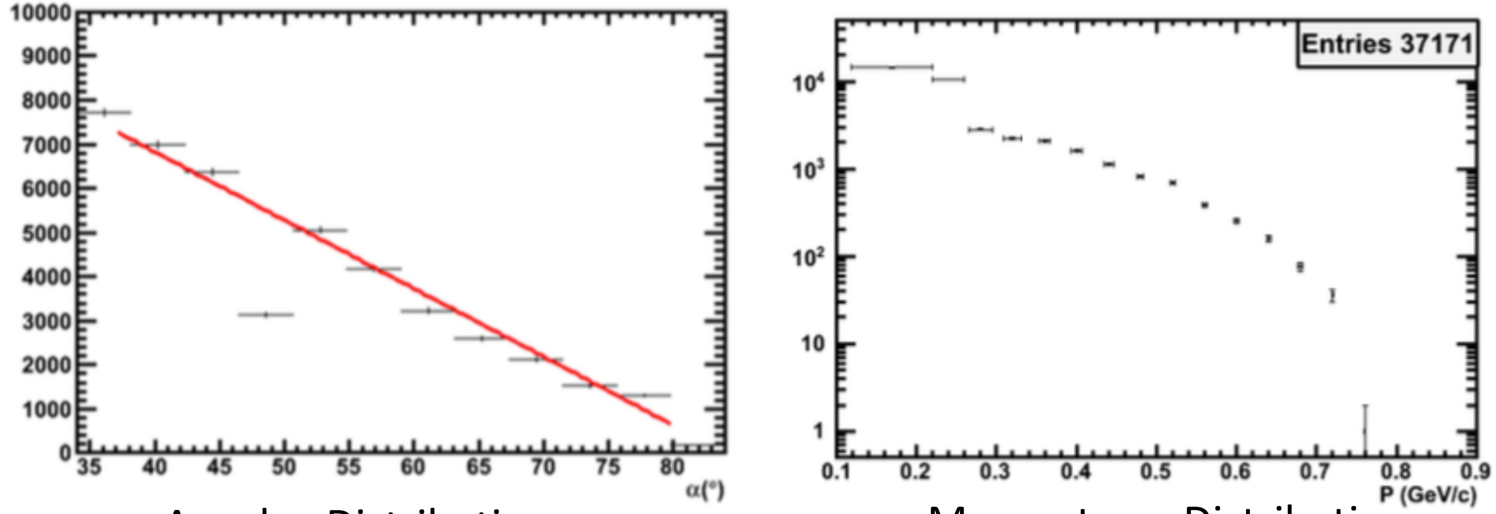


G. De Lellis et al. JINST 2, 2007, P06004

FOOT Detector: Emulsion Spectrometer

- Other study: large angle fragmentation and momentum measurements of a 400 MeV/n ^{12}C beam impinging on a composite target has been performed by using two ECC detectors to cover a range from 34° to 81° with respect to the beam axis





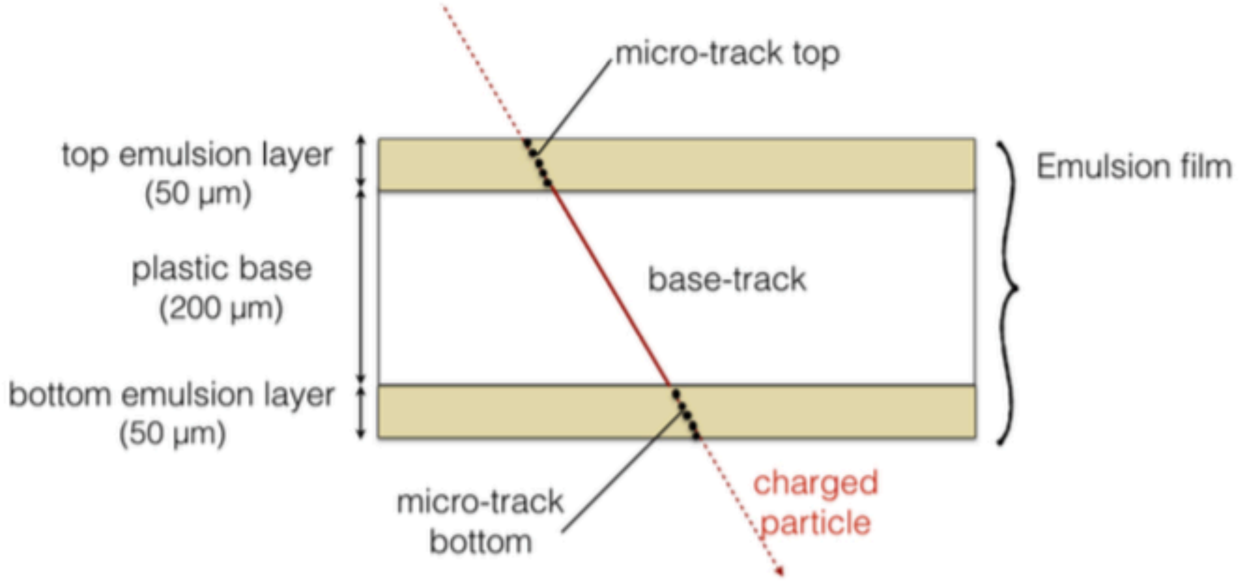
Angular Distribution

Momentum Distribution

A. Alexandrov et al., JINST 12 (2017) P08013

FOOT: Emulsion film – how it works

Istituto Nazionale di Fisica Nucleare



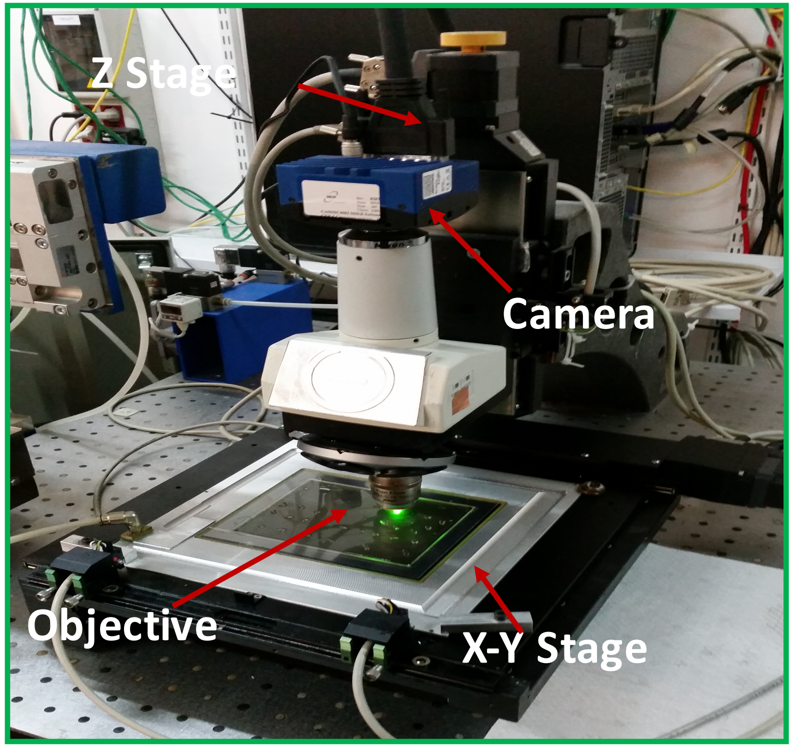
- ✓ The emulsion films exhibits:
  - Spatial resolution: ~ 0.3 μm
  - Angular resolution: ~ 2 mrad
  - Detection efficiency of the tracks: ~ 95%
- ✓ The trajectory of a charged is recorded by all AgBr crystals along its path

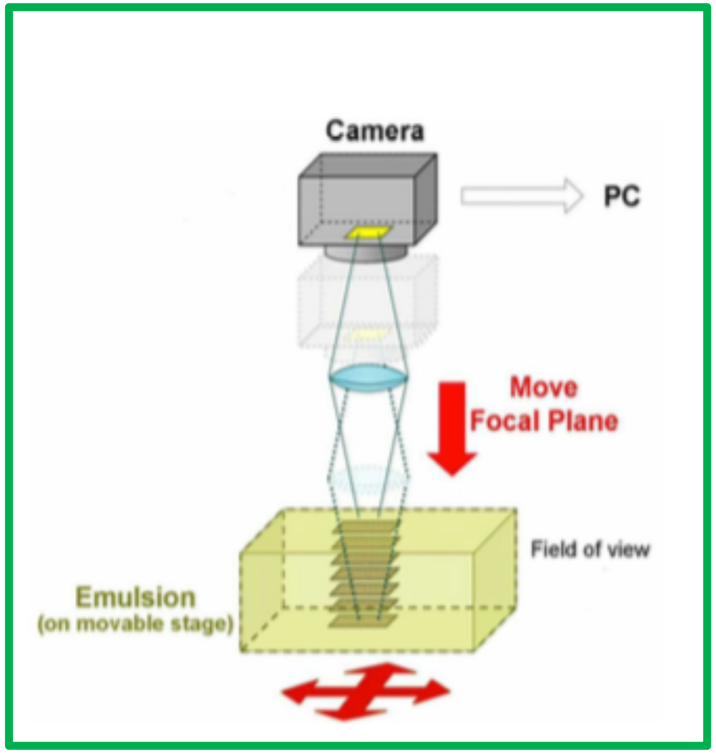
- ✓ The developed emulsions are scanned by an automated microscope
- ✓ The image are analyzed by a dedicated software to recognize clusters of dark pixels aligned (i.e. track produced by ionizing particle)
- ✓ A straight sequence of pixels in one emulsion layer defines a "micro-track": two aligned micro-tracks belonging to the top and bottom layers of an emulsion film form a "base-track"
- ✓ Base-tracks belonging to a straight line along different films, are connected to form volume-tracks.

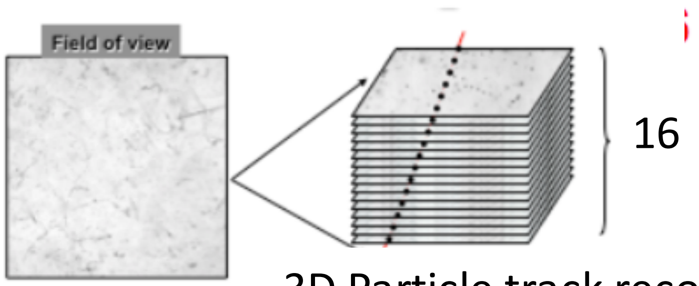
FOOT: automated microscope for emulsion read-out

INFN
Istituto Nazionale di Fisica Nucleare

- The improvements in the read-out technology for emulsion films have allowed to extend their application (neutrino physics, the dark matter search, muon radiography/tomography, hadron-therapy)



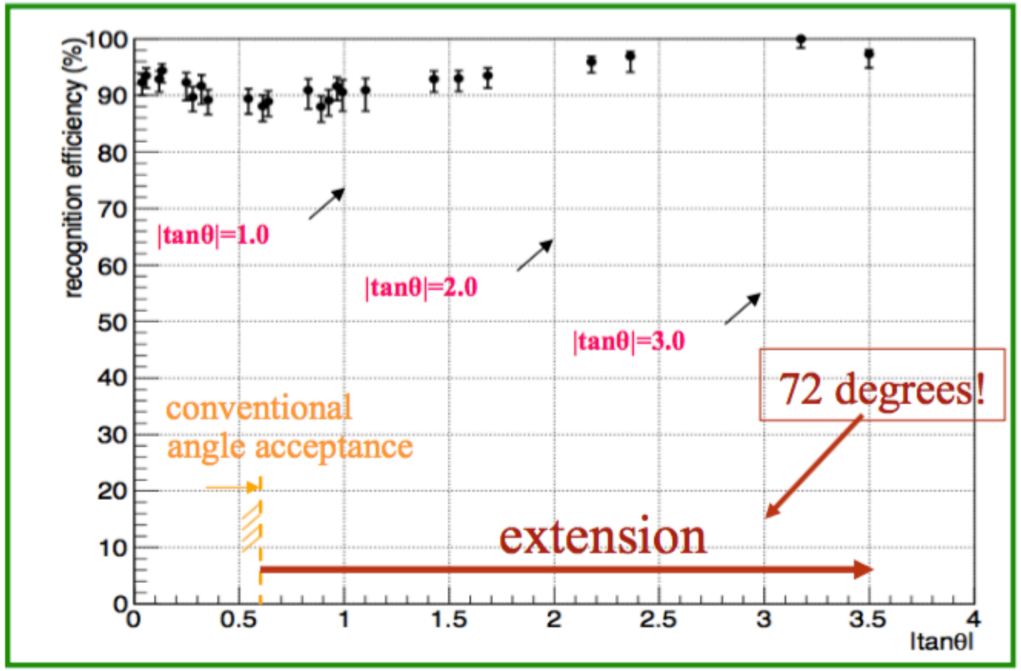




3D Particle track recon.

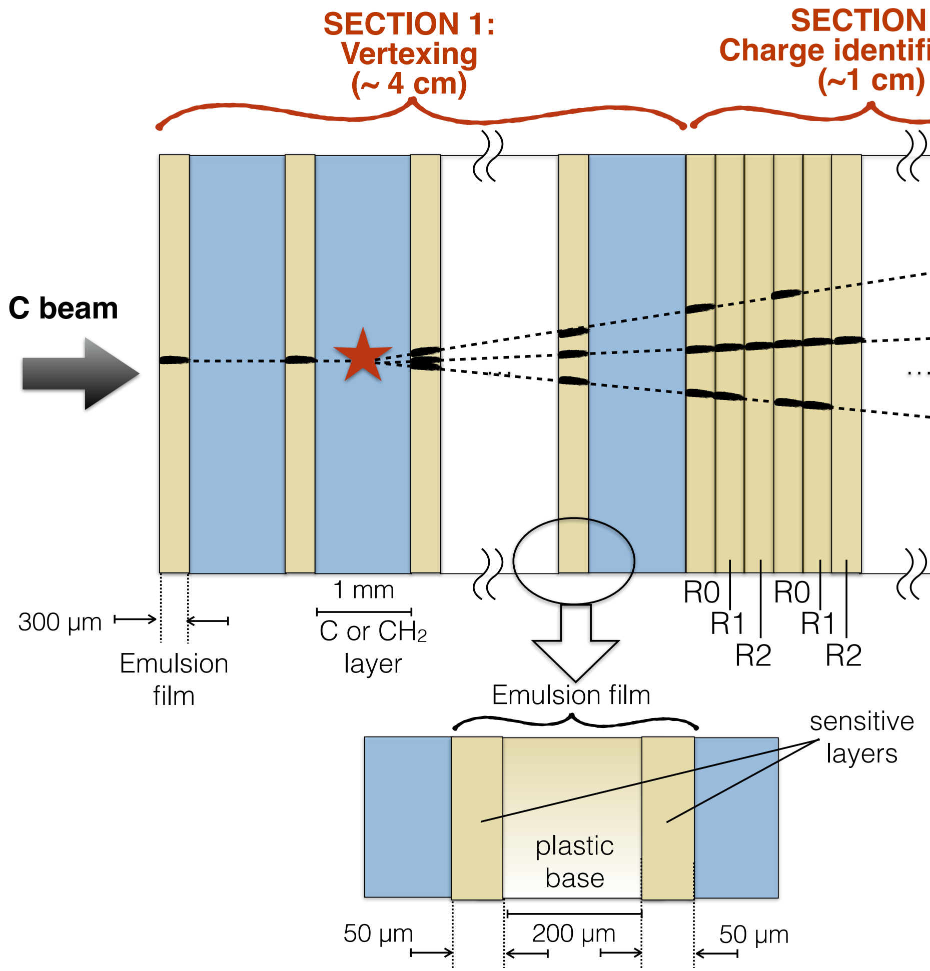
FOOT: automated microscope R&D

- New reconstruction software (LASSO -Large Angle Scanning System for OPERA experiment) to extend track recognition angular acceptance from θ = 30° to θ = 72° (A. Alexandrov et al., JINST 10 (2015) no.11 P1100)



- Development of a new generation scanning system by upgrading the objective lens (Nikon Plan Fluor 20X 0.75 NA) and the CMOS digital camera (Mikrotron MC-4082camera) and implementing a processing approach based on GPU (Graphics Processing Unit) extend the scanning speed up to **190 cm^2/h** (A. Alexandrov et al., JINST 11 - 2016 - 6002, A. Alexandrov et al., *Nature Scientific Reports* **7** - 2017 - 7310)

FOOT: Emulsion Spectrometer Layout



Section 1: alternated layers of emulsions and target (C/C_2H_4)

- vertex detector

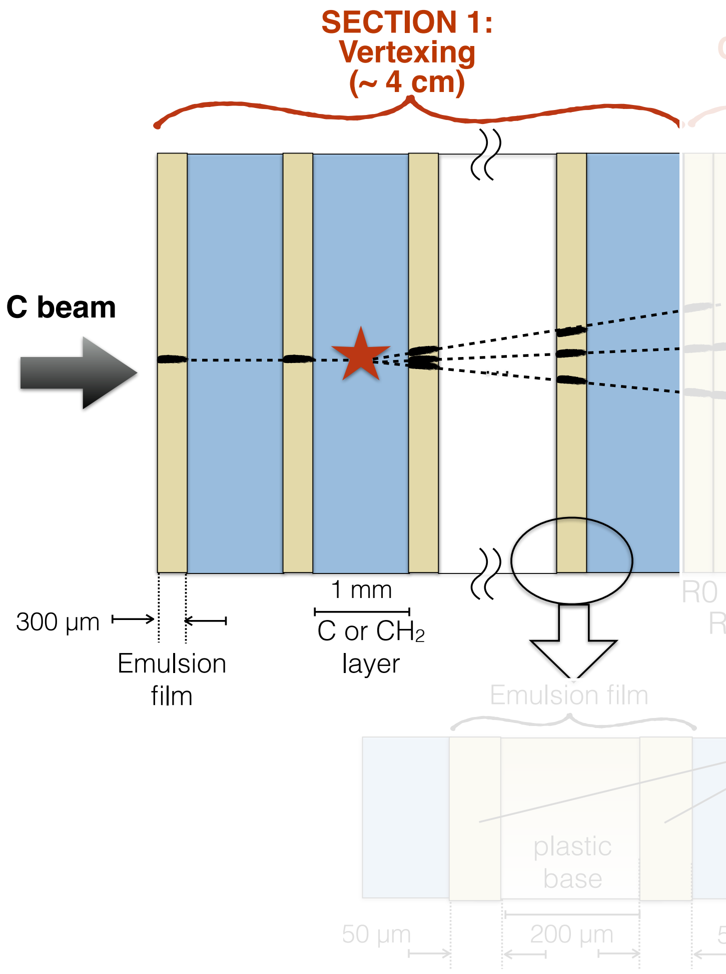
Section 2: made of emulsion films only

- charge identification for low Z fragments (H, He, Li)

Section 3: alternated layers of emulsions and lead

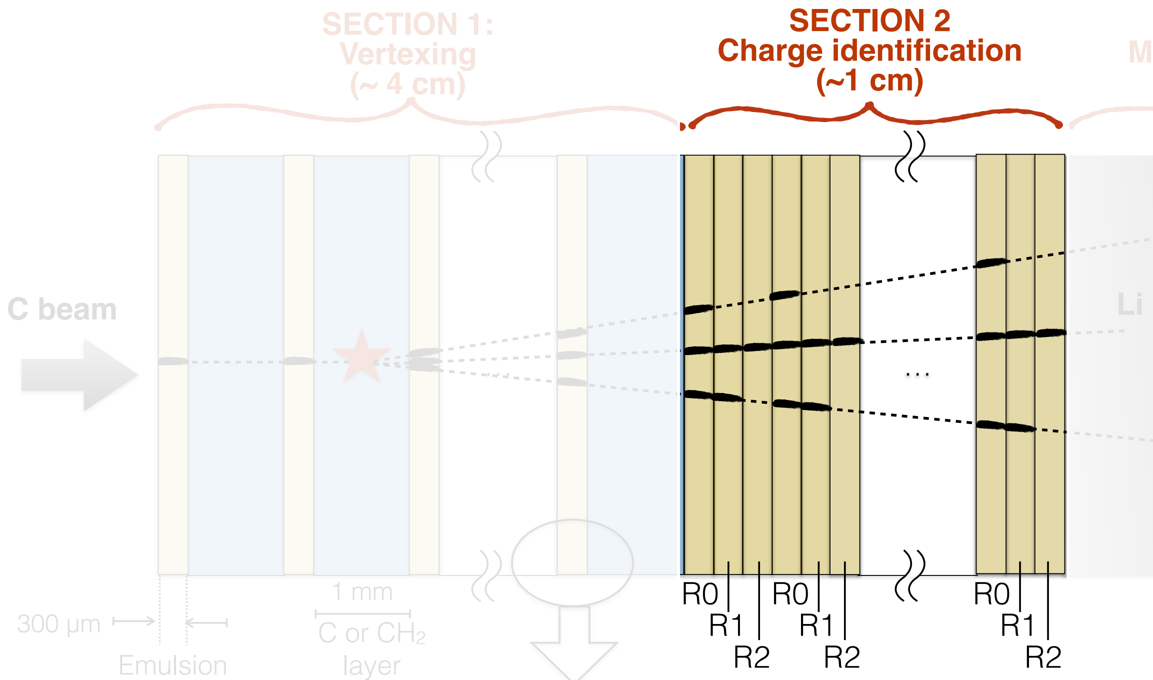
- Momentum measurement by range and Multiple Coulomb Scattering (MCS)
- Isotopic identification

FOOT: Emulsion Spectrometer – section 1



- ✓ Alternate target layers of C or C_2H_4 (1 mm) and emulsion films (300 μm)
- ✓ Vertex detector and particle tracking
- ✓ Chamber thickness defined by the interaction length → obtain a sufficiently high number of interactions
- ✓ 20% of Carbon ions interacting in 3 cm Lexan (G. De Lellis, Nucl. Phys. A Vol. 853, 2011)
- ✓ Total length ~ 30 cells = 39mm

FOOT: Emulsion Spectrometer – section 2



✓ Charge identification for low Z fragments (H, He, Li)

✓ Emulsion will have a different thermal treatment according to its position in the elementary cell:

- **R0:**
  - Not refreshed
  - **Sensitive to m.i.p.**
- **R1:**
  - Appropriate refreshing for protons
  - **Sensitive to protons**
- **R2:**
  - Appropriate refreshing for He
  - **Sensitive to He**

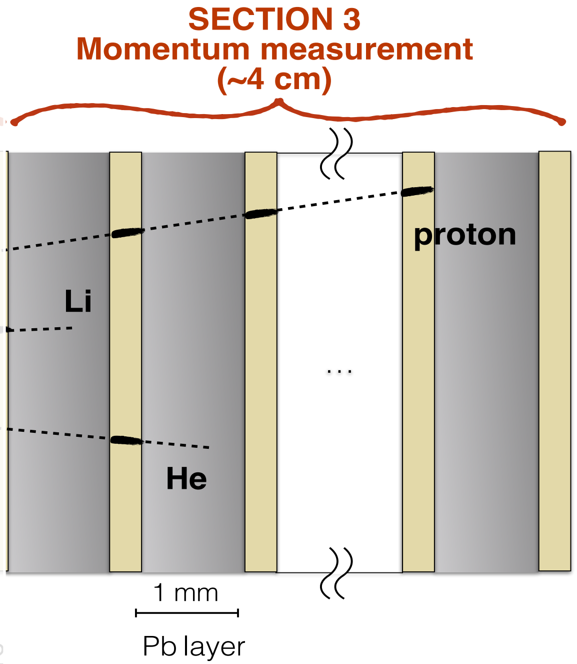
To obtain a 3σ He-Li separation, 9 cells are necessary

G. De Lellis et al. JINST 2, 2007, P06004

✓ New emulsion batches are under characterization (beam exposure at LNS – Catania, IT – and at Proton Therapy Center – Trento, IT) to tune the thermal treatment required for the charge separation at $Z \leq 3$

FOOT: Emulsion Spectrometer – section 3

- ✓ Emulsion films interleaved with 1 mm thick lead layers
- ✓ Dedicated to the momentum measurements by using the range method and the Multiple Coulomb Scattering (MCS)
- ✓ Range Method: the kinetic energy of the particle is estimated on the basis of the range measurements (NIST data)
- ✓ The MCS estimates the particles momuntum through the measurements of the position and the slope of the particles trajectory
- ✓ Isotopic identification: by means two indipendent methods for the momuntum measurements



Emulsion Spectrometer will perform the the first FOOT data taking in 2018

FOOT: which experimental facilities?

- ✓ CNAO (Pavia, Italy) Experimental room is our choice (Exp. Hall ready by 2019)
- ✓ Heidelberg Ion-Beam Therapy Center (HIT, Germany): first test in 2018
- ✓ GSI (Darmstadt, Germany): beam request for 2019
- ✓ Proton Therapy Center (Trento, Italy) and Laboratori Nazionali del Sud (INFN-LNS, Catania, Italy) for calibration purpose with protons and ion beams respectively

FOOT experimental program

- Target fragmentation of p on O and C @100-200 MeV/n
- Projectile fragmentation of O on C @200-400 MeV/n
- Projectile fragmentation of C on C @200-350 MeV/n
- Evaluation of production of some β^+ emitters (for example ^8B) from C, O on C @200-400 MeV/n: *useful for range monitoring of Particle Therapy*
- Fragmentation measurement of several beams (e.g. He) on (C_2H_4) of interest for radioprotection in space

FOOT collaboration

- ✓ Funded by INFN for 2017, with contribution of Centro Fermi Institute
- ✓ FOOT Conceptual Design Report presented in June 2017
- ✓ 10 INFN Sections/Labs: Bologna, Frascati, Milano, Napoli, Perugia, Pisa, Roma1, Roma2, Torino, Trento
- ✓ CNAO Foundation joined
- ✓ People: ~70 researcher
- ✓ International collaborations: Nagoya Univ.; GSI Darmstadt, IPHC Strasbourg, RWTH University Achen

Conclusions

- Target fragmentation and proton RBE are ”hot” topics in Charged Particle Therapy
- The FOOT detector will measure both target fragmentation in proton therapy and projectile fragmentation in charged particle therapy (He, C and O)
- The FOOT experiment has been approved and funded by INFN as R&D in 2017. In September 2017 final approval for the 2018-2021
- FOOT emulsion spectrometer data taking in 2018 (CNAO/Heidelberg)
- Whole detector data taking foreseen in late 2019 – 2020 (CNAO/Heidelberg/GSI)

FOOT collaboration

http://web.infn.it/f00t/index.php

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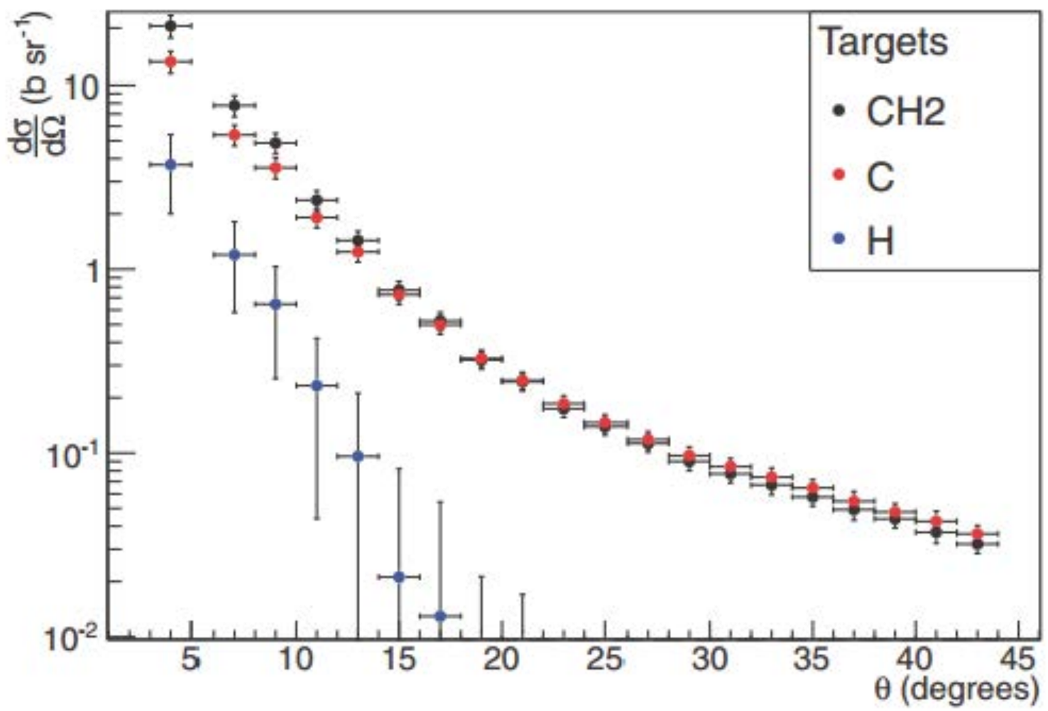
Back-up slides

Double target strategy: preliminary results

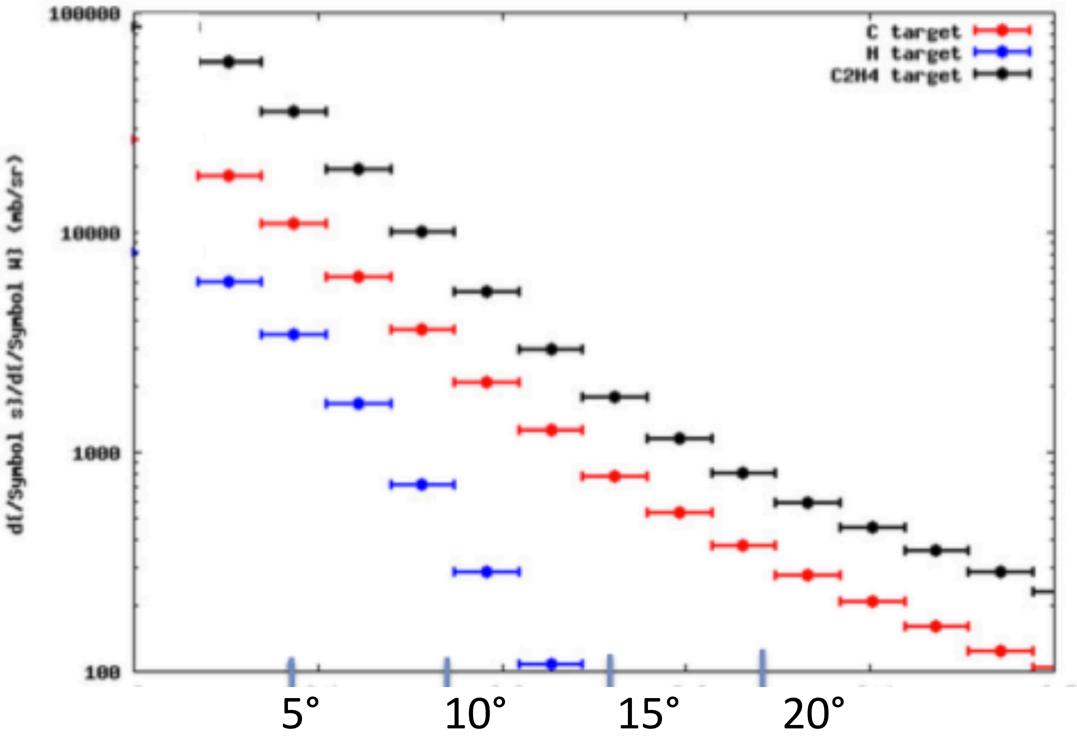
C @ 95 MeV/n on C and C_2H_4



Dudouet et al., Phys.Rev.C (2013)

- ➢GANIL experimental data

C @ 200 MeV/n on C and C_2H_4



- ➢Fluka simulation in the FOOT experiment

FOOT Detector: redundancy

1. Simultaneous determination of β and p respectively from the TOF and the magnetic spectrometer:

$$A_1 = \frac{p}{U\beta c\gamma}$$ where $$\gamma = \frac{1}{\sqrt{1-\beta^2}}$$ and U = 931.5 MeV (Unified Atomic Mass)

2. Simultaneous determination of β and E_{kin} respectively from the TOF and the calorimeter:

$$A_2 = \frac{K}{Uc^2(\gamma - 1)}$$

3. Simultaneous determination of p and E_{kin} respectively from the magnetic spectrometer and the calorimeter:

$$A_3 = \frac{p^2c^2 - K}{2\ U\ c^2 E_K}$$

FOOT Conceptual Design Report

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