FOOT: a nuclear physics experiment focused on Particle therapy and Radioprotection in Space

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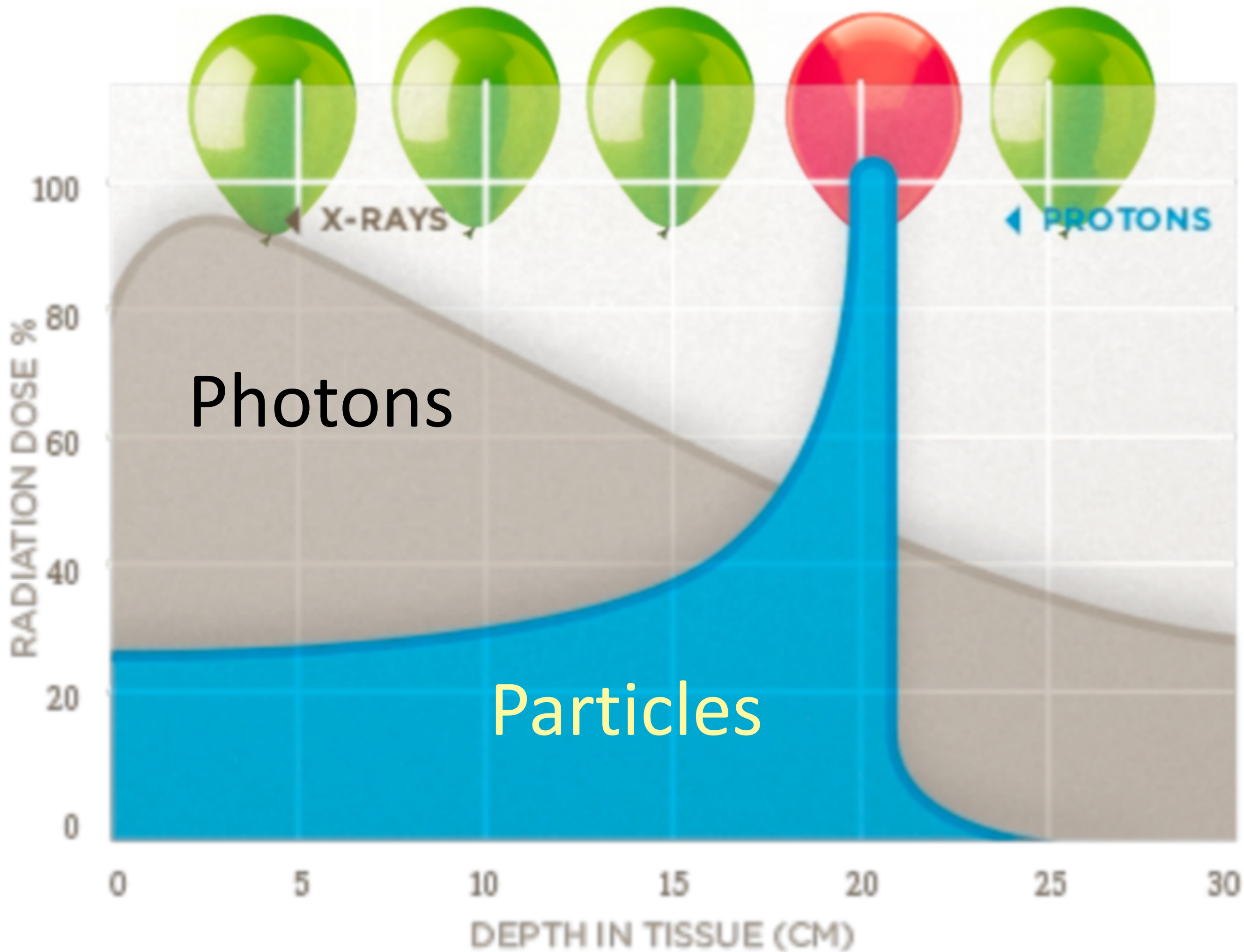
Particle Therapy for Dummies..

Healthy Tissue

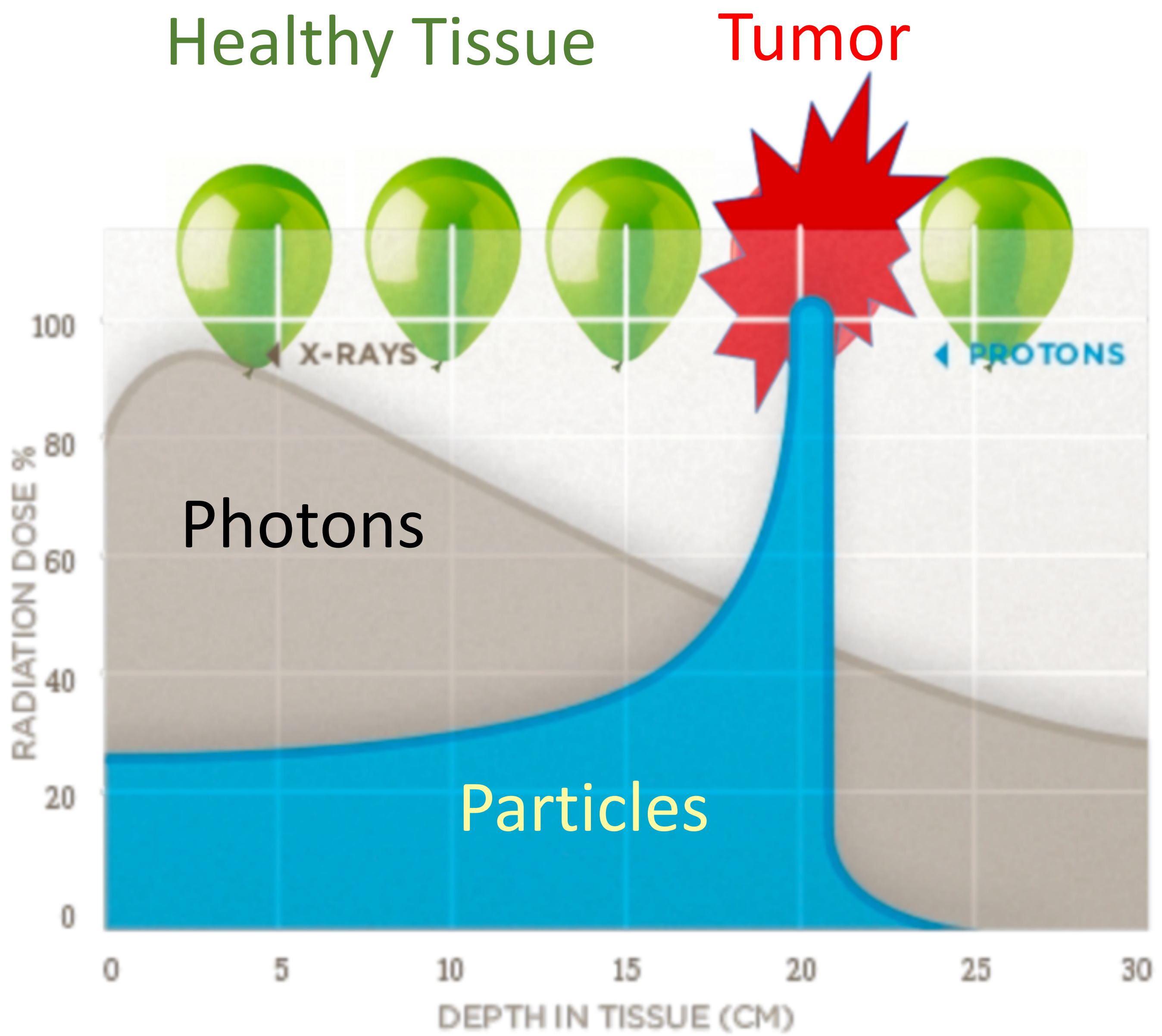
Tumor

Particle Therapy for Dummies..

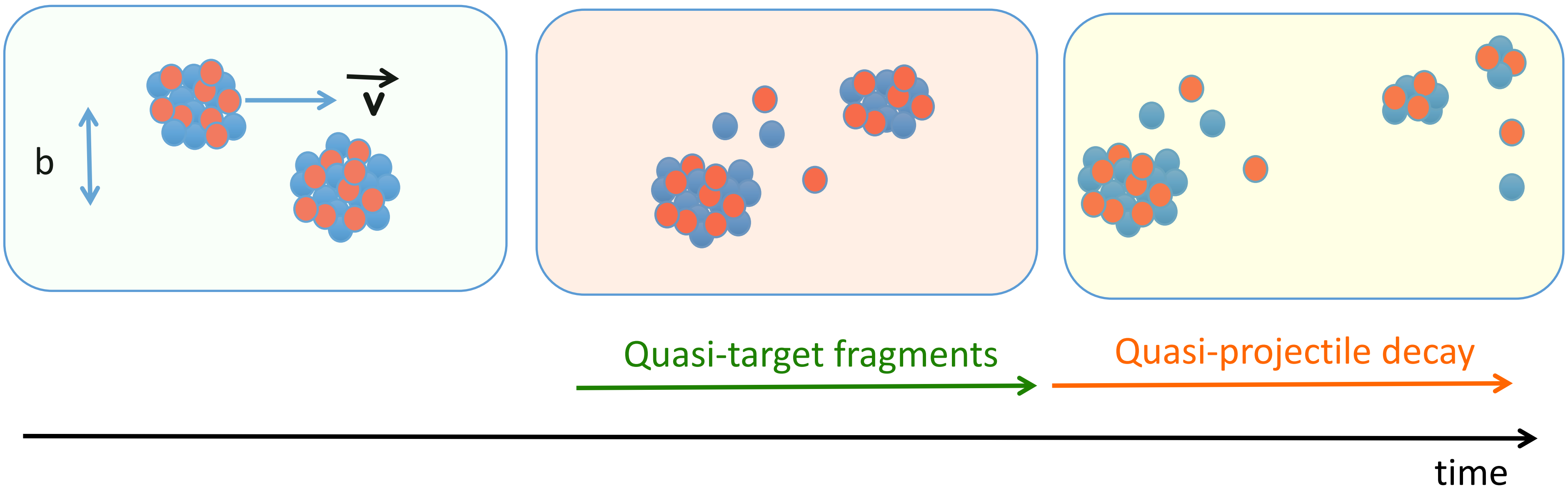
Healthy Tissue Tumor



Particle Therapy for Dummies..



PT as nucleus-nucleus interaction



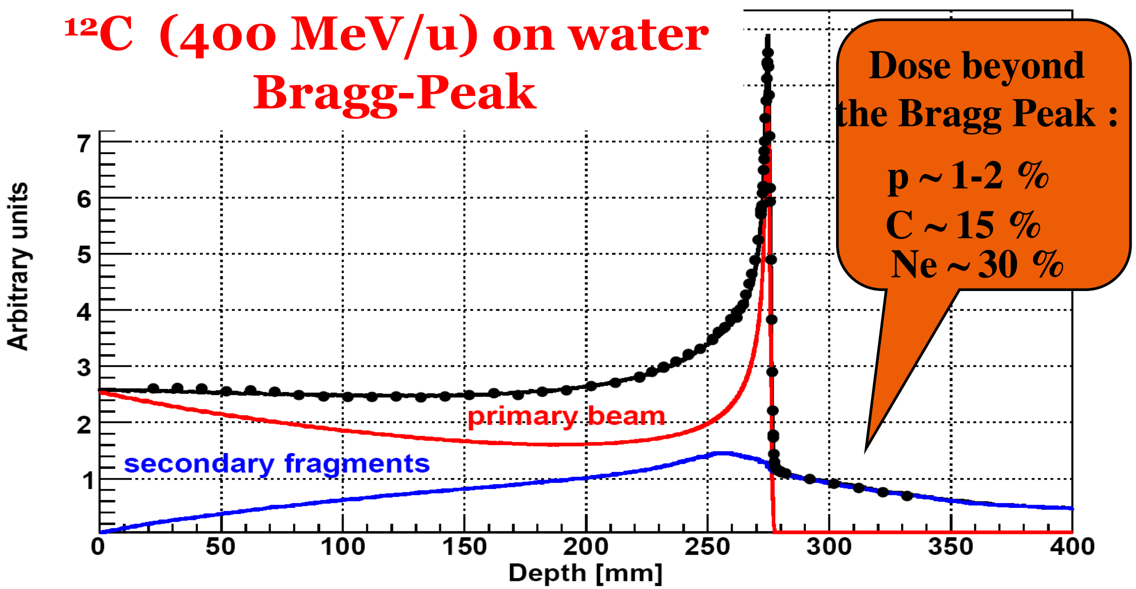
- Fragments from quasi-projectile have $V_{frag} \sim V_{beam}$ and narrow emission angle. Longer range then beam
- The target fragments have wider angular distribution and much lower energy.
- Proton and neutron fragments have both angular and energy wide distribution
- The dose beyond the distal part comes from the quasi projectile contribution. Wide angular halo from the rest of the process

Projectile Fragmentation: ^{12}C - ^{16}O

Dose release in healthy tissues with possible long term side effects → must be carefully taken into account in the Treatment Planning System

- ✓ Production of fragments with higher range vs primary ions
- ✓ Production of fragment with different direction vs primary ions

- ✓ Attenuation of the primary beam
- ✓ Different RBE of the fragments wrt the beam



Exp. Data (points) from Haettner et al, Rad. Prot. Dos. 2006

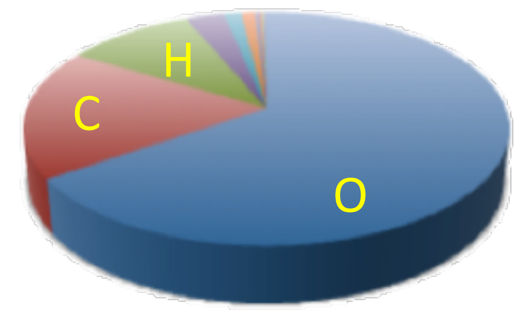
Simulation: A. Mairani PhD Thesis, 2007, Nuovo Cimento C, 31, 2008

proton on C,O (patient) @200 MeV

The elastic interaction and the forward Z=1,2 fragment production are quite well known. Uncertainties on large angle Z=1,2 fragments. Missing data on heavier fragments production.

Highly ionizing heavier fragment not included in dose evaluation in treatment planning: possible problem in healthy tissue where p beam ~ 200 MeV ?

Percent of Mass



Very low energy-short range fragments, almost isotropic.

MCs confirm this picture but…..

Nuclear model & MC not reliable at the needed level

Needed Z>2 fragment yields and emission energy

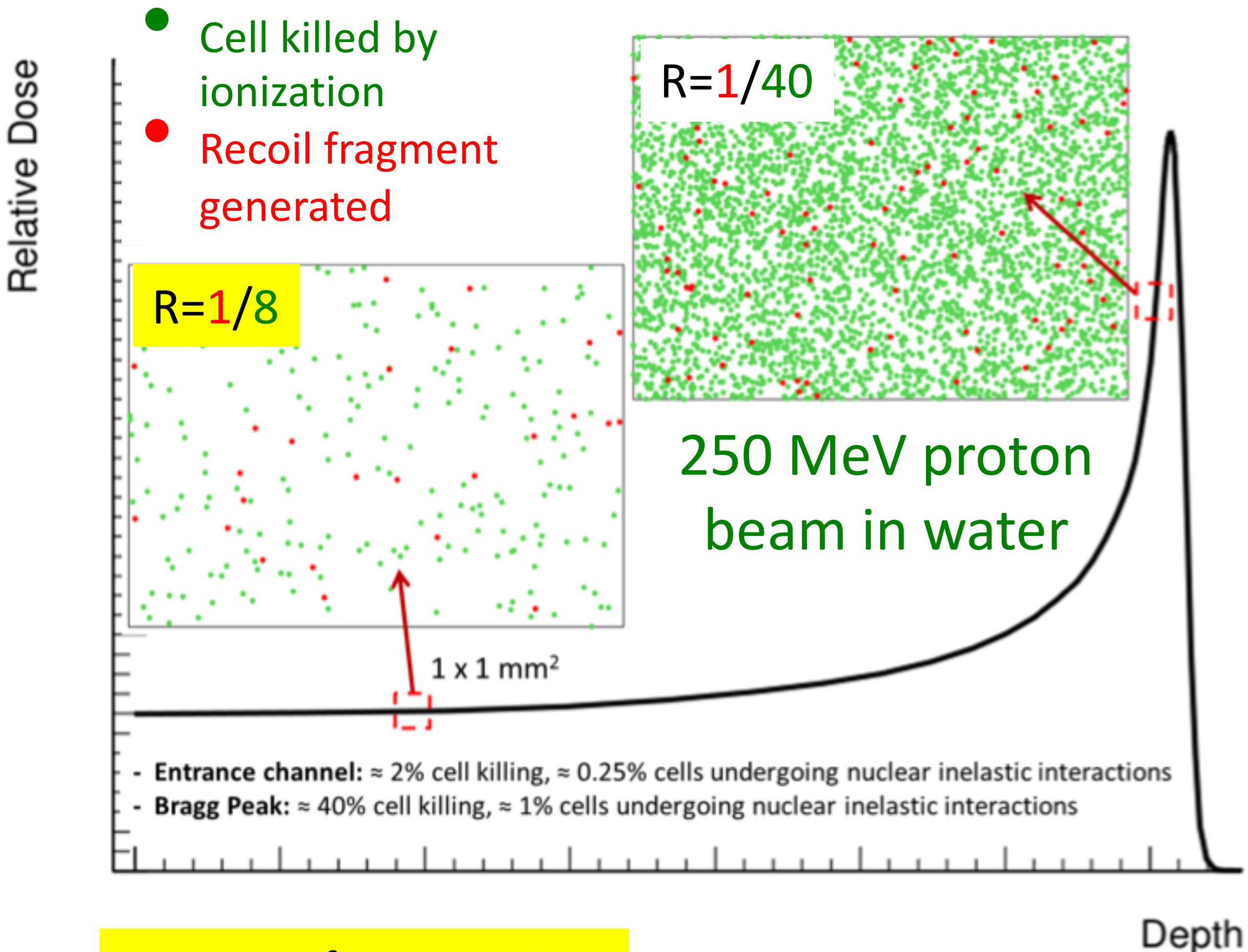
Analytic model results on p->O @200 MeV

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

Cancers 2015,7 Tommasino & Durante

Target fragmentation & PT

Target fragmentation in proton therapy: gives contribution also outside the tumor region!



About 10% of biological effect in the entrance channel due to secondary fragments

Largest contributions of recoil fragments expected from **He, C, Be, O, N**

See also dedicated MC studies:
- Paganetti 2002 PMB
- Grassberger 2011 PMB

Courtesy of F.Tommasino

Direct measurements : mission impossible

REMARK: For radiobiology effectiveness of proton beam the measurement of the fragment spectra is needed !!

- The fragments travel few μm in the target-> difficult to directly detect them, even for very thin target (10 μm?)
- The energy loss of the fragment in the target would be substantial and would be a severe systematic to be evaluated
- Such a very thin target produces very few events -> very careful control of the background.
- Possible solution from JET target techniques, where the target is a focused flux of gas crossing the beam in vacuum: difficult and expensive

Inverse kinematic strategy

Let's shoot a β=0.6 patient (C,O,N nuclei) on a proton at rest and measure how it fragments!! Then if we apply an inverse velocity transformation, we got the result.

DIRECT KINEMATIC

proton
200 MeV

C,O at rest

p + C,O → fragments

INVERSE KINEMATIC

C,O 200 MeV/A

Proton (H)
at rest

A the end Lorentz boost

C,O + p → fragments

The target can be thick as few mm, since now the fragments will have ~ 200 MeV/nucl with range larger than several cm.

But what about H target?

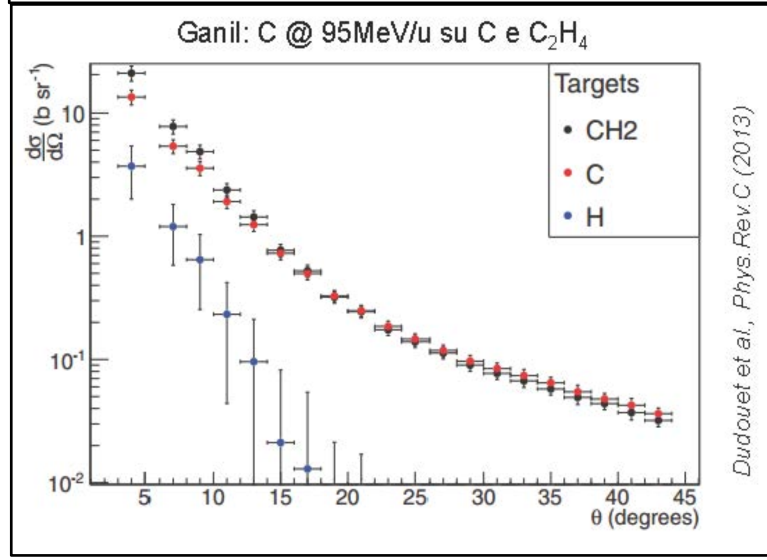
Inverse kinematics and the target

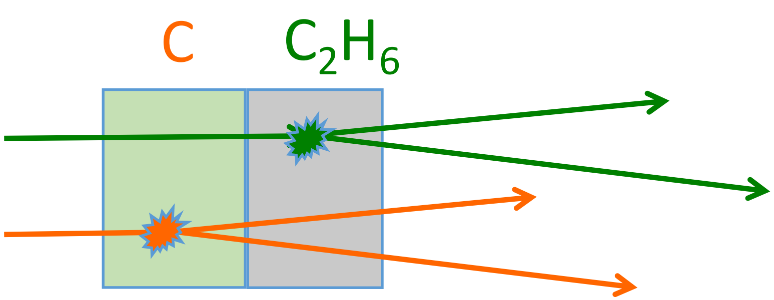
The target can be thick as few mm, since the fragment range is larger than several cm.

Fragmentation on H can be extracted by subtraction of twin C and C_2H_4 targets.

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

Ganil experimental data





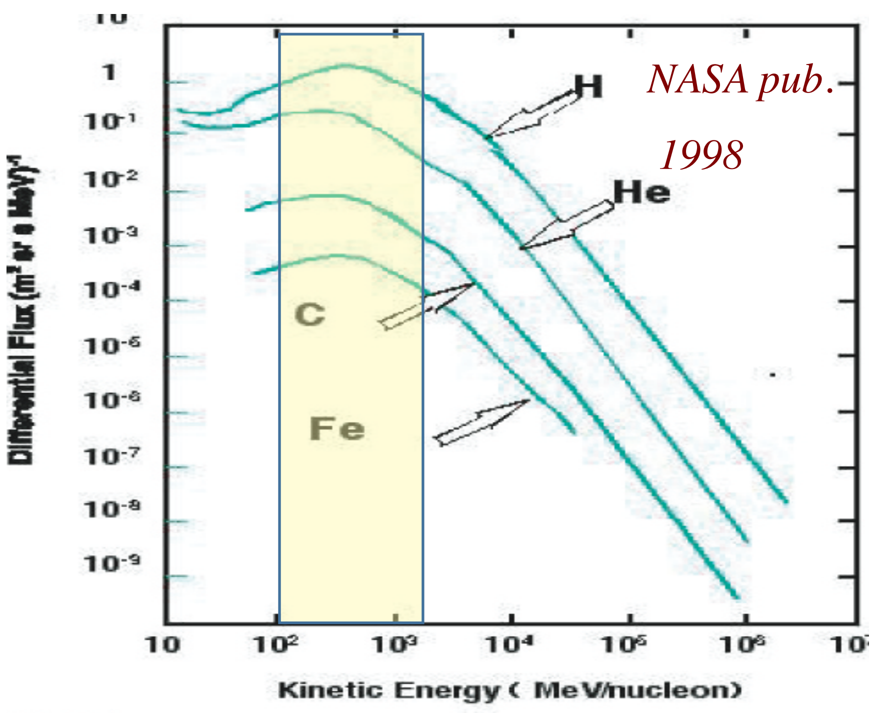
Simultaneous double target data taking can to minimize systematic, if the setup has good vertexing capability along beam line

From treatment room to space

Long term mission (Mars) : the astronauts will be exposed to Galactic Cosmic Ray for year(s) with daily equivalent dose of ~ 1 mSv/day

Threat also from Solar Particle Events: rare (~10 years) but with lethal dose: order of Sv from low energy protons

Shielding astronauths is compulsory in long range missions



87% protons, 12% He ions and 1% heavier ions (mainly O,C,N) with peaks at 700 MeV/n

Absorbed dose is driven by fragmentation on shields

"Best" shielding materials ?

- Liquid H_2
- Liquid CH_4
-
- Polyethylene (CH_2)
-
- H_2O
-
-
- Al—Inadequate shielding
-
-
- Pb
-

Best

Worst

Potential range for new and multi-functional shielding materials: CH_4 adsorption on carbon forms; polymer composites; hydrides and hydride/carbon o hydride/polymer composites

Trial and error approach based on measurements: no reliable data available

The best shield material is the same of that one needed to estimate the fragmentation effect in particle therapy.

FOOT can provide ^{4}He, ^{12}C, ^{16}O → C, C_2H_4 @ 700MeV/u

The FragmentatiOn Of Target (FOOT) experiment

- ✓The FOOT collaboration wants to tackle these issues of PT and RPS related to light nuclei fragmentation in the intermediate energy region (200-700 MeV/u)

- ✓The focus will be on fragment identification (Z,A) with corresponding angular and energy distributions

Nagoya University (Japan), GSI (Germany)

Aachen University (Germany), IPHC Strasbourg (France), CNAO (Italy)

10 INFN sections/labs & most of the funding

More than 90 researchers, 60% permanent, 45 FTE

Web site: https://web.infn.it/f00t/index.php/en/

FOOT physics program

Method of cross section difference is crucial to obtain X section on pure elements:

- Using C, C_2H_4 ➔ cross sections on C and H
- Using C, C_2H_4, PMMA ➔ cross sections on C, O and H

PMMA is a combination of C,O,H.

Phys	Beam	Target	Energy (MeV/u)	Inv/direct
Target Frag. PT	^{12}C	C, C_2H_4	200	inv
Target Frag. PT	^{16}O	C, C_2H_4	200	inv
Beam Frag. PT	^{12}C	C, C_2H_4, PMMA	350	dir
Beam Frag. PT	^{16}O	C, C_2H_4, PMMA	400	dir
Beam Frag. PT	^{4}He	C, C_2H_4, PMMA	250	dir
Rad. Prot.space	^{4}He	C, C_2H_4, PMMA	700	dir
Rad. Prot.space	^{12}C	C, C_2H_4, PMMA	700	dir
Rad. Prot.space	^{16}O	C, C_2H_4, PMMA	700	dir

These are specific measurements related with PT & RPS. But we are open to physics program enlargement..

Fragments from ^{12}C beam (E_{kin}=400 AMeV) on ^{12}C

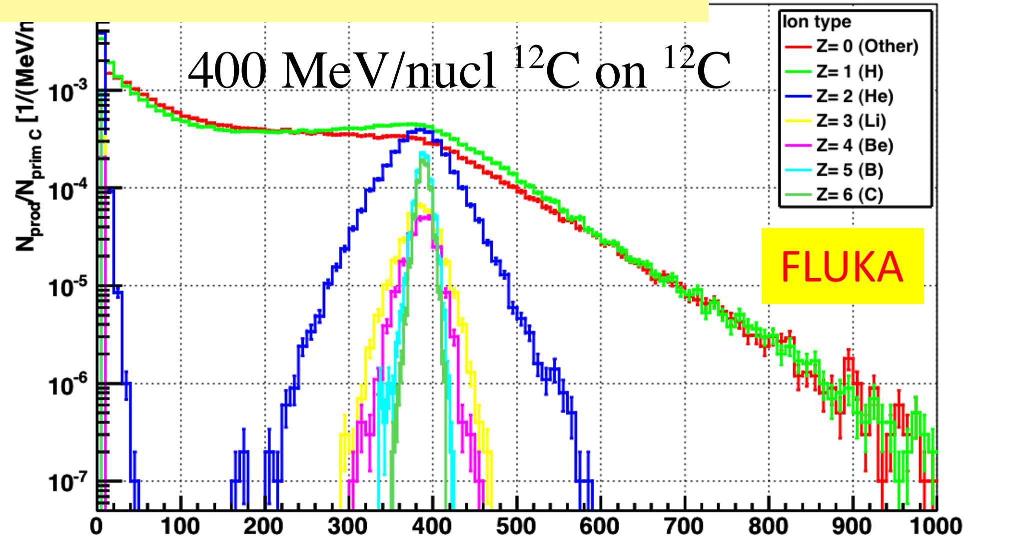
The Z>2 fragments have ~ same velocity of the beam and are emitted in the forward direction

The protons are the most abundant fragments with a wide angular and β spectrum

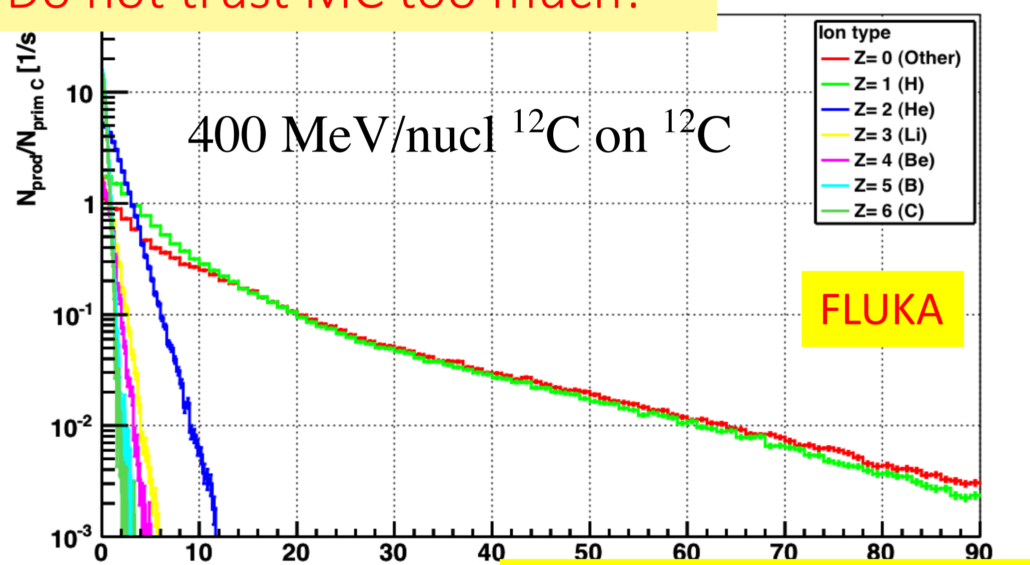
The Z<3 fragment are all emitted within 10^0 of angular aperture

- ✓ emulsion setup for Z<3, large angle fragments
- ✓ electronic setup== fixed target detector for Z>2, forward peaked fragments

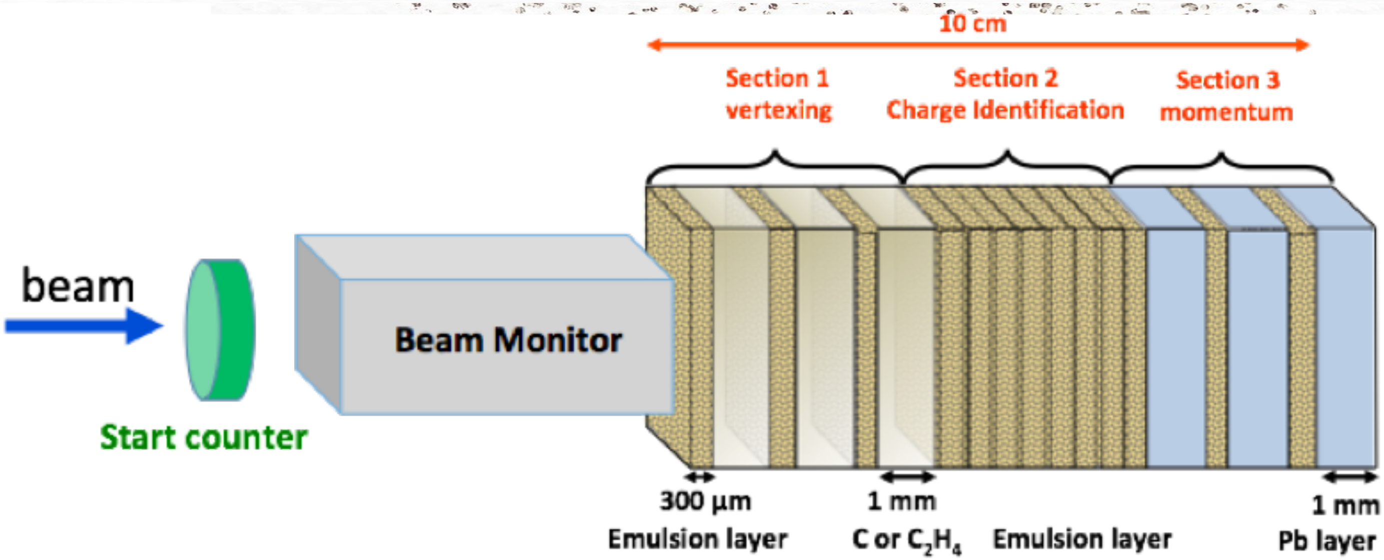
Do not trust MC too much!



Do not trust MC too much!



Light fragments:emulsion setup

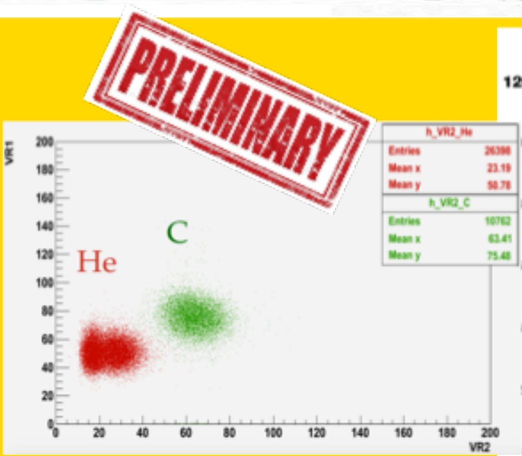


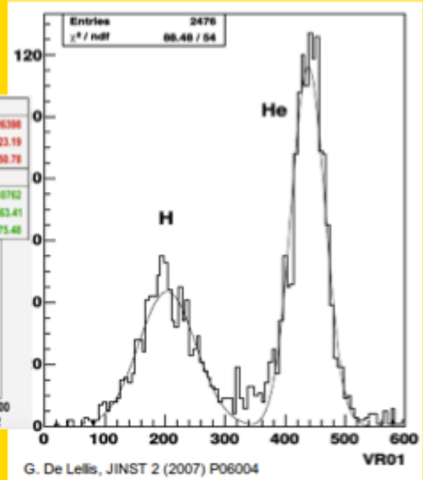
High speed automated scanning

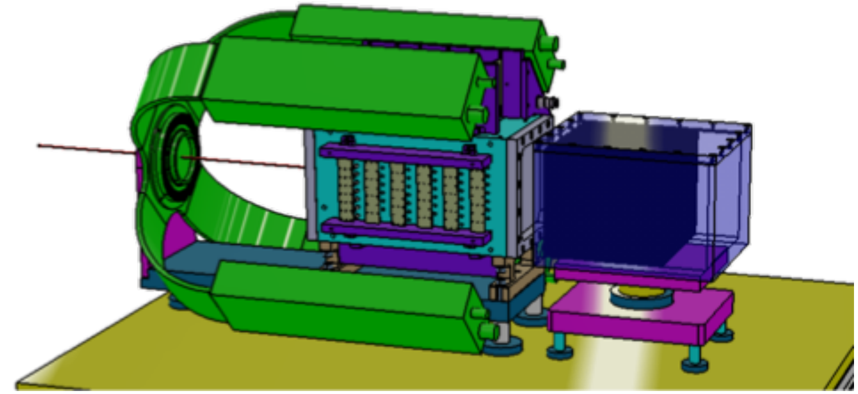
- ✓ Both target and detector integrated in a very compact setup
- ✓ Accurate reconstruction of the interactions inside the target (sub-micrometric resolution)
- ✓ Fragment charge detection eff > 99%
- ✓ Automated scanning system : very fast and with wide angular acceptances

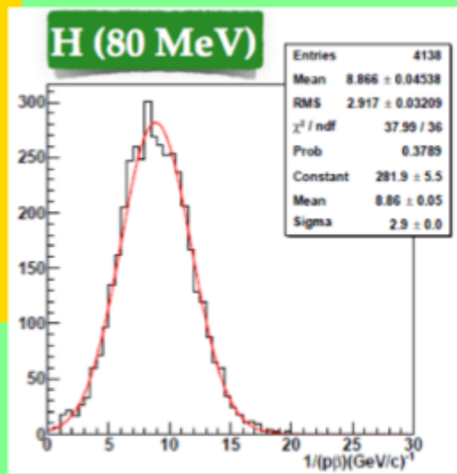
- optimised for light (Z≤3) fragments
- less than 1m: can be easily movable to fit the space limitations from experimental and treatment rooms
- angle setup: ±75°

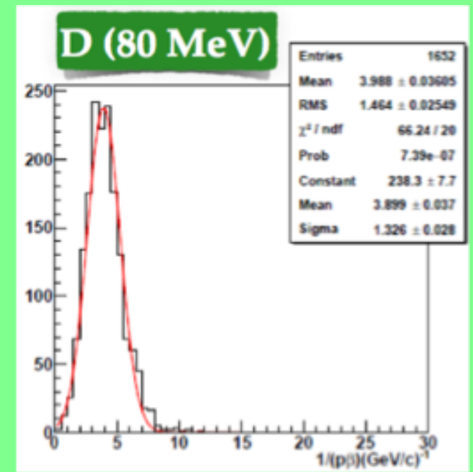
ECC performances









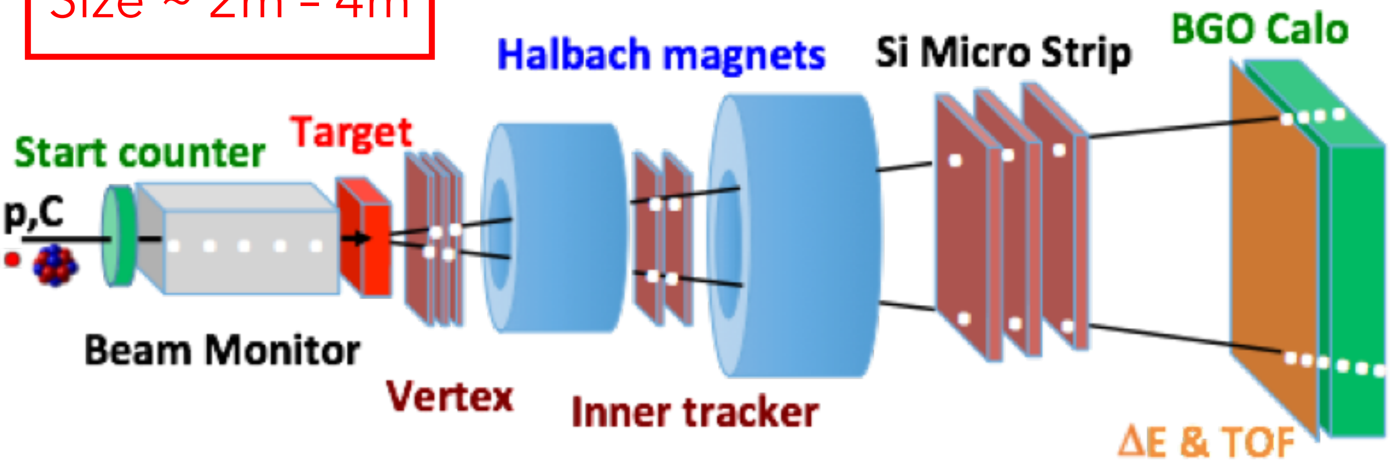


Test performed at LNS p, ^{4}He and ^{12}C beams

- **light isotope separation (preliminary study)**
- Particle range and multiple coulomb scattering measurements could provide a isotope identification

The FOOT electronic setup

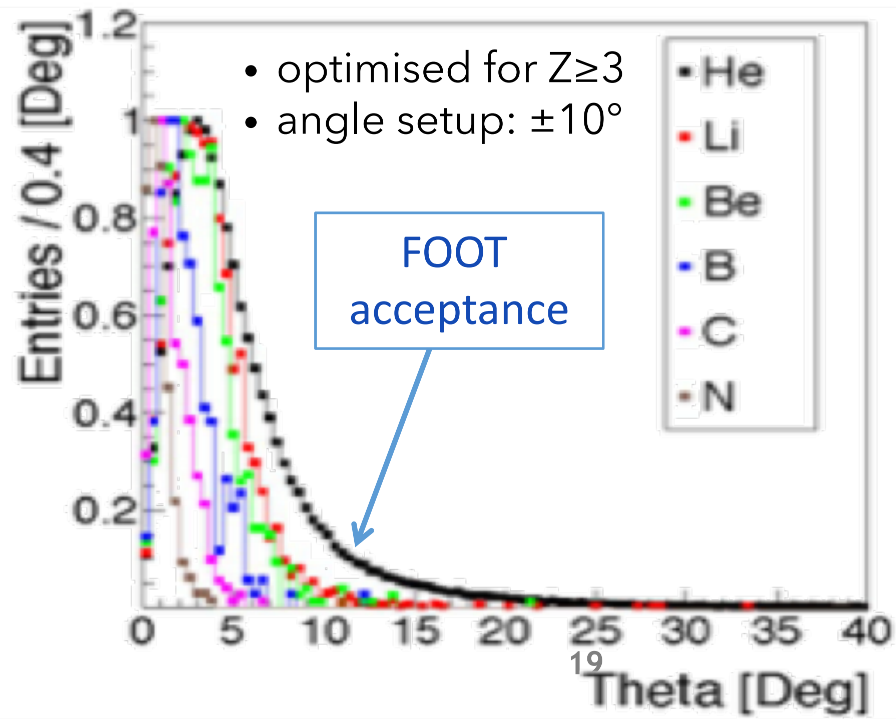
Size ~ 2m – 4m



Target performances

- **Δp/p** <3.5%
- **Δ_{TOF}** <70ps
- **ΔEkin/Ekin** <2%
- **Δ(dE)/dE** ~3%

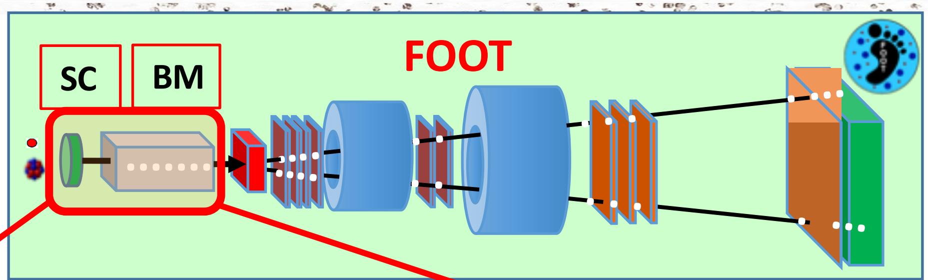
Sub-detector	Main characteristics
Start counter	plastic scintillator 250 μm
Beam monitor	drift chamber (12 layers of wires)
Target	$C+C_2H_4$ (2 mm)
Vertex	4 layers silicon pixel (20x20 μm)
Magnet	2 permanent dipoles (~ 1 T)
Inner tracker	2 layers silicon pixel (20x20 μm)
Outer tracker	3 layers silicon strip (125 μm pitch)
Scintillator	2 layers of 20 bars (2x40x0.3 μm)
Calorimeter	360 BGO crystals (2x2x14 μm)



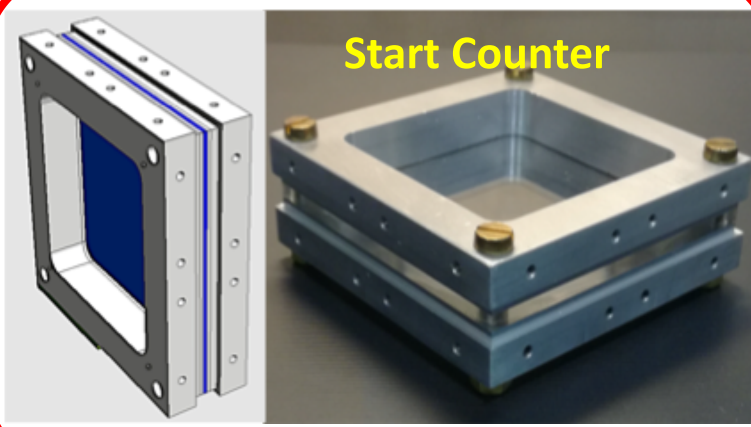
- optimised for Z≥3
- angle setup: ±10°

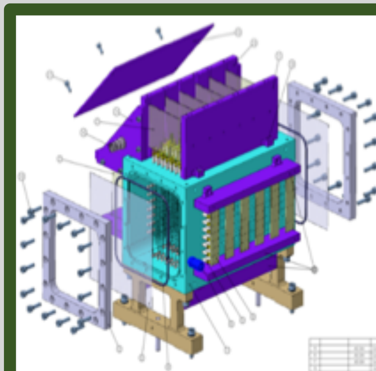
FOOT interaction region

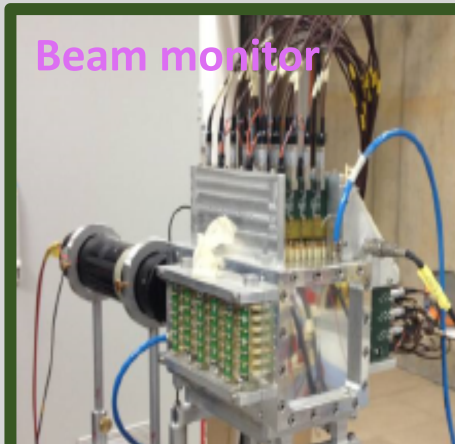
Accurate TOF start
Minimize beam fragmentation



Accurate beam position and direction measurements



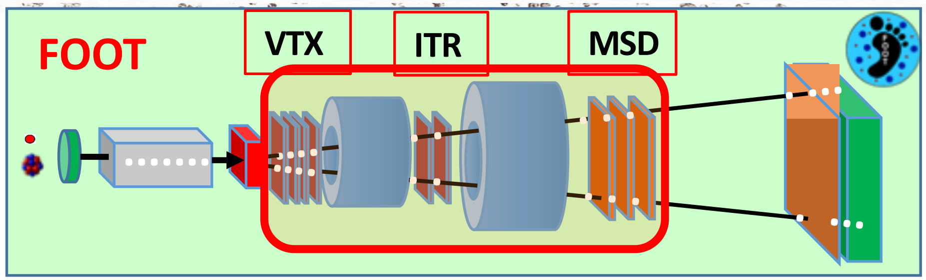




- 250 μm plastic scintillator read out by 48 SiPM (12/side)
- Readout by WFD at 5 Gsample/s.
- Time resolution: 65 ps for ^{12}C beam @ 200 MeV/nucl

- Drift chamber with 6+6 XY planes
- Gas: Ar/Co_2 (80/20%)
- Hit resolution on ^{12}C beam @ 400 MeV/nucl : <150 μm

Tracking region



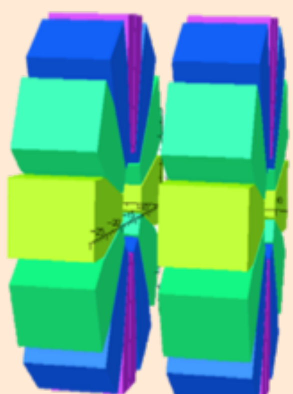
Vertex & Inner Tracker

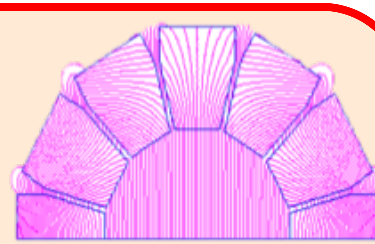
VTX: 4 layers of Silicon MAPS pixel (20 x 20 μm²)
ITR: 2 layers of Silicon MAPS pixel (20 x 20 μm²)
50 μm thickness

2 permanent dipole magnets in Hallbach geometry
B field in y direction
(max 1.1 T)

Micro Strip Detector

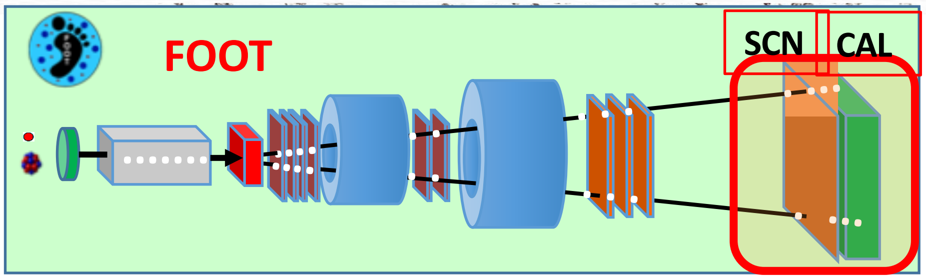
MSD:
3 layers of Silicon MicroStrips detectors (120 μm x 9 cm)
150 μm thickness

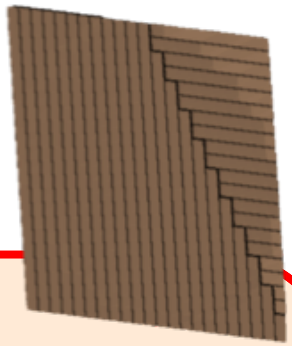


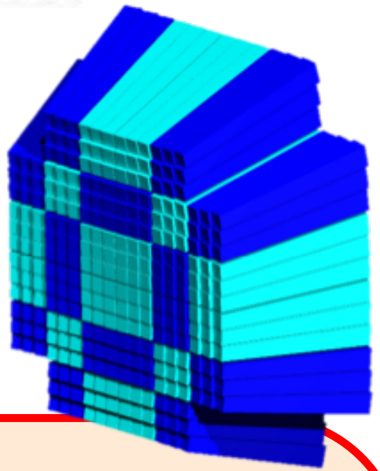


2 permanent Magnet

Downstream region

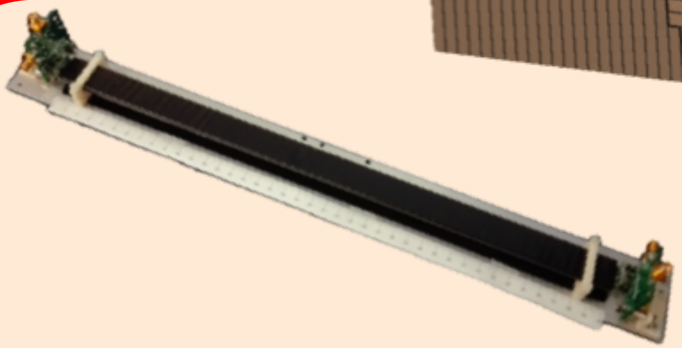




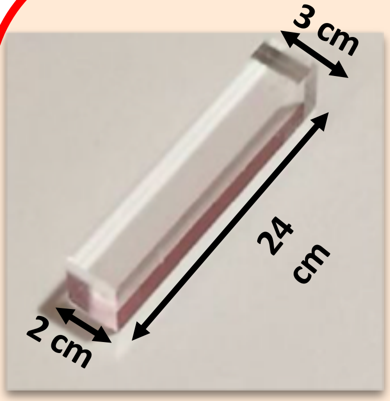


Plastic Scintillator
ΔE/TOF measurement

BGO Calorimeter

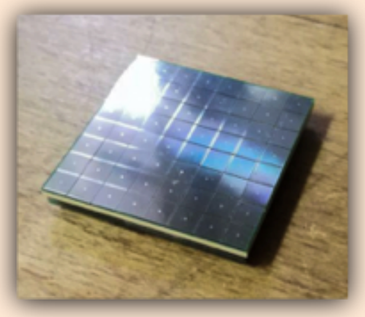


40 x 2 x 0,3 cm3 plastic scintillator bars
2 XY layers of 20 bars
Readout: 4 x 3mm² SiPM/bar
35 ps resolution @ 12C at 200 MeV/nucl (CNAO)



400 BGO crystals
$Z_{eff} = 74$
$P_{BGO} = 7.13\ g/cm^3$
Weight = 1.027 kg
Total weight 330 Kg

Readout:
SiPM 8x8 mm²
cell 20 µm
Voltage breakdown
53 V



Estimated performances: charge Z reconstruction

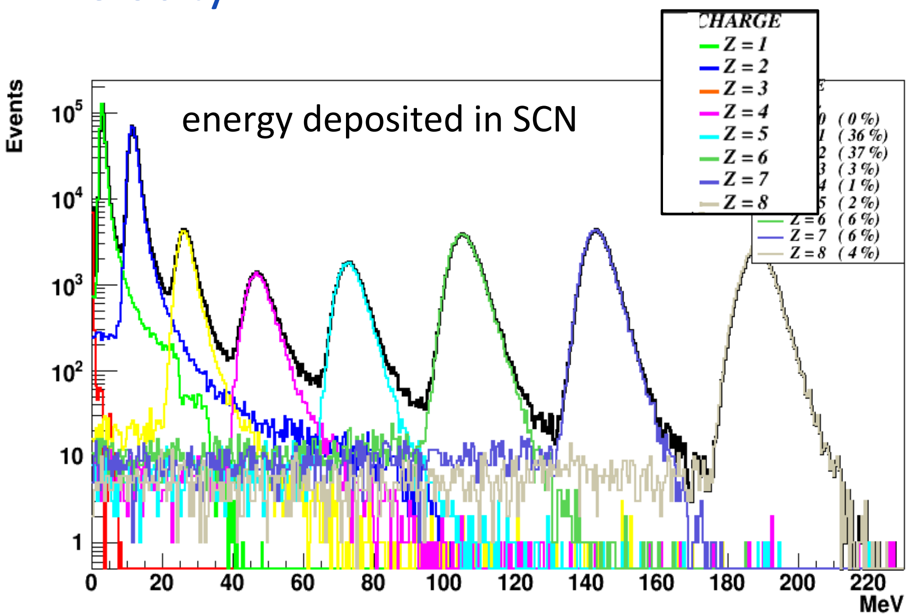
Fragment charge are derived from energy release in DE/TOF scintillator and from the fragment velocity

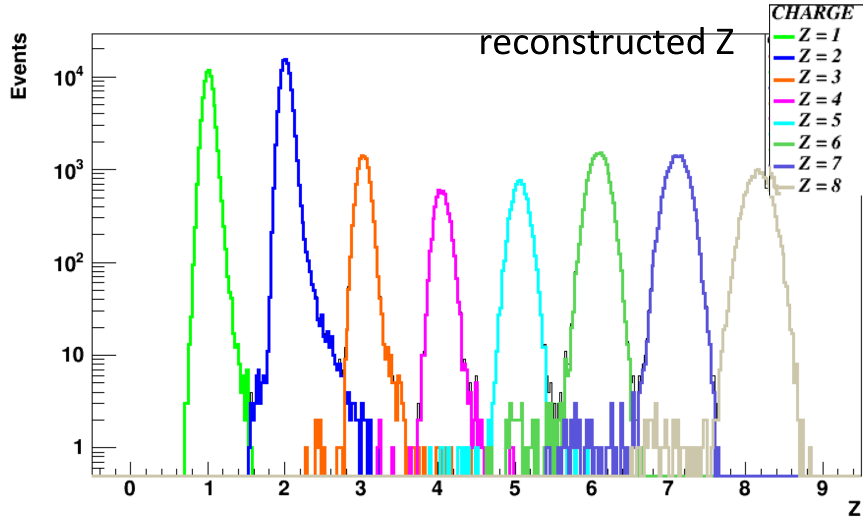
FLUKA simulation : ^{16}O (200 MeV/u) → C_2H_4

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

ΔE

TOF





	^{1}H	^{4}He	^{7}Li	^{9}Be	^{11}B	^{12}C	^{14}N	^{16}O
	1	2	3	4	5	6	7	8
Z Resolution :	1.01±0.09	2.01±0.06	3.03±0.08	4.05±0.09	5.06±0.10	6.09±0.12	7.11±0.14	8.15±0.15

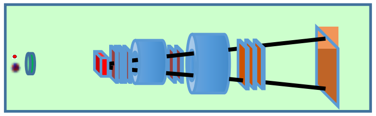
Estimated wrong charge assignment < 1%

Isotopic mass identification

The redundancy in the A measurement allows to use a constrained fit to obtain both fragment mass and the emission 4-momentum.

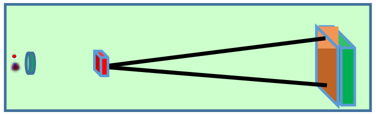
TOF (β) & TRACKER (p)

$$A_1 = \frac{p}{U\beta\gamma}$$



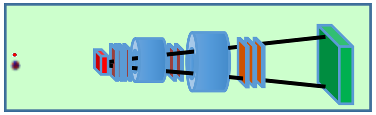
TOF (β) & CALO (Ekin)

$$A_2 = \frac{E_{kin}}{U(\gamma - 1)}$$



TRACKER (p) & CALO (Ekin)

$$A_3 = \frac{p^2 - E_{kin}^2}{2UE_{kin}}$$



$$L = \frac{(P_{fit} - P_{meas})^2}{\sigma_p^2} + \frac{(TOF_{fit} - TOF_{meas})^2}{\sigma_{TOF}^2} + \frac{(E_{fit} - E_{meas})^2}{\sigma_E^2} - \sum_i^{1,3} \lambda_i C_i\left(P, TOF, E\right) + \sum_i^{1,3} C_i^2 (P, TOF, E)$$

$$C_1 = AU\beta\gamma - p = 0$$

$$C_2 = AU(\gamma - 1) - E_{kin} = 0$$

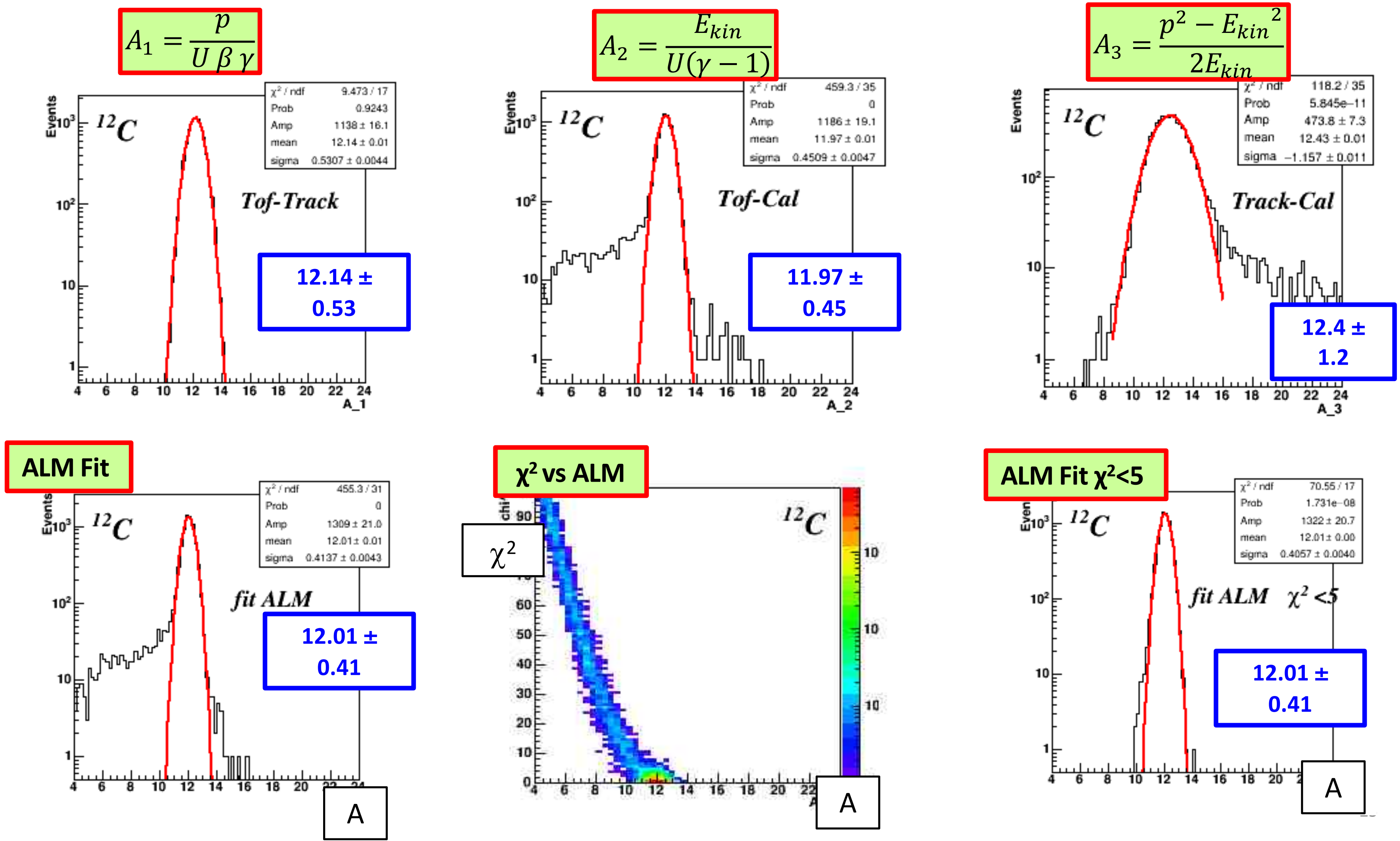
$$C_3 = 2AUE_{kin} - p^2 - E_{kin}^2 = 0$$

The PID performance evaluation on a 200 MeV/u ^{12}C fragment make use of quite conservative accuracy (with respect to test beam results)

Kinetic energy: $\sigma_E/E \sim 2\%$, Tof: $\sigma_{TOF} \sim 100$ ps, Momentum: $\sigma_p/p \sim 3.5\ \%$

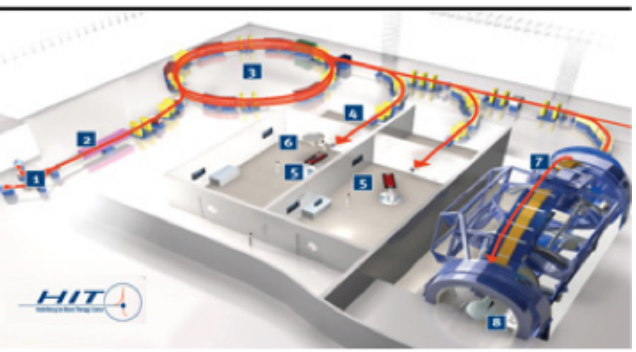
^{12}C mass ID: ^{16}O on C_2H_4 @200 MeV/u

The tails in the A_2 and A_3 distribution are due to neutron leakage in BGO calo: wrong reconstructed events can be filtered using fit χ^2



beams, data taking & schedule

FOOT detector can be moved !!!



The FOOT construction has been approved and funded

Needed facilities providing ^{4}He, ^{12}C, ^{16}O ions in the 200-700 MeV/u energy range. Possible (affordable) choices are

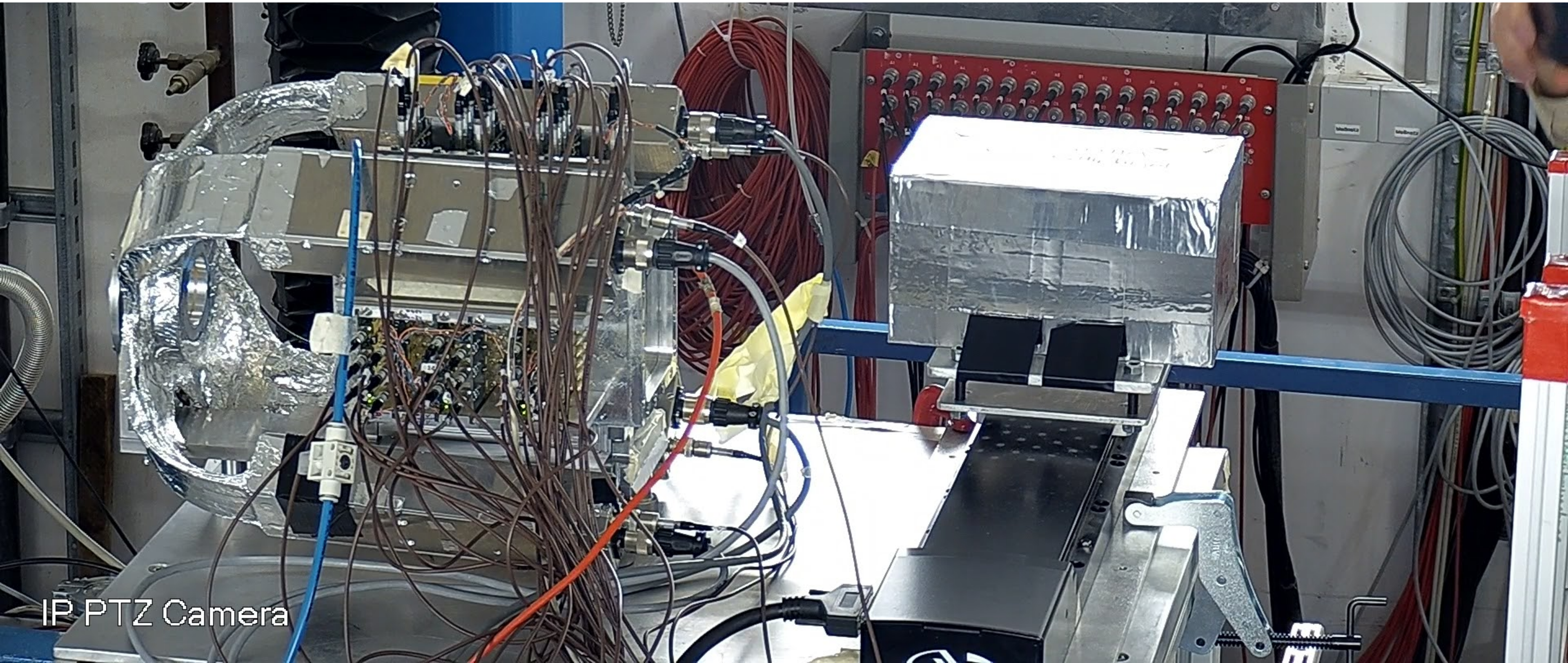
GSI : all beams and energies needed available
HIT : all beams needed only up to 400 MeV/u
CNAO : only p and ^{12}C up to 400 MeV/u

- First data taking at GSI performed in April 2019 with ^{16}O beam 200-400 MeV/u focused on emulsion
- The electronic setup will be completed mid 2020. (first engineering run was in April 2019 at GSI)
- Electronic setup data taking campaign will start late 2020. It will last at least till 2022

Emulsion runs: ^{16}O@200 & 400 MeV/u on C,CH_2

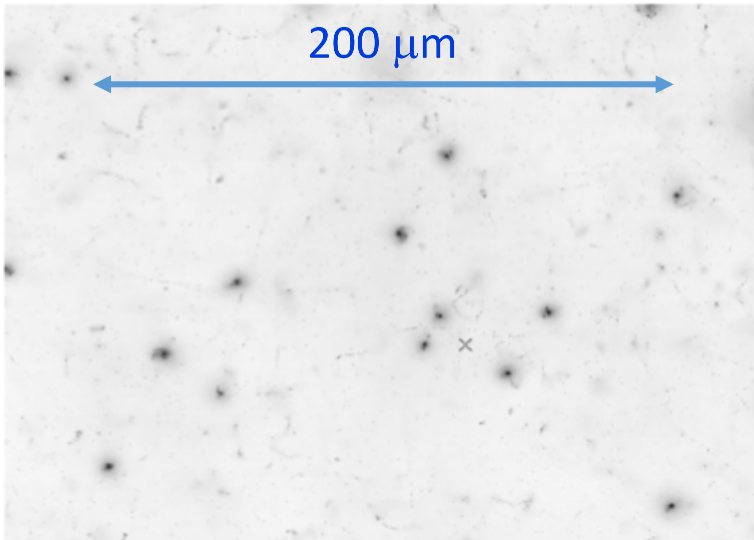
The emulsion exposure must be carefully handled: only few ions ($3x10^4$) must be shot in the target to avoid event pileup in reconstruction.

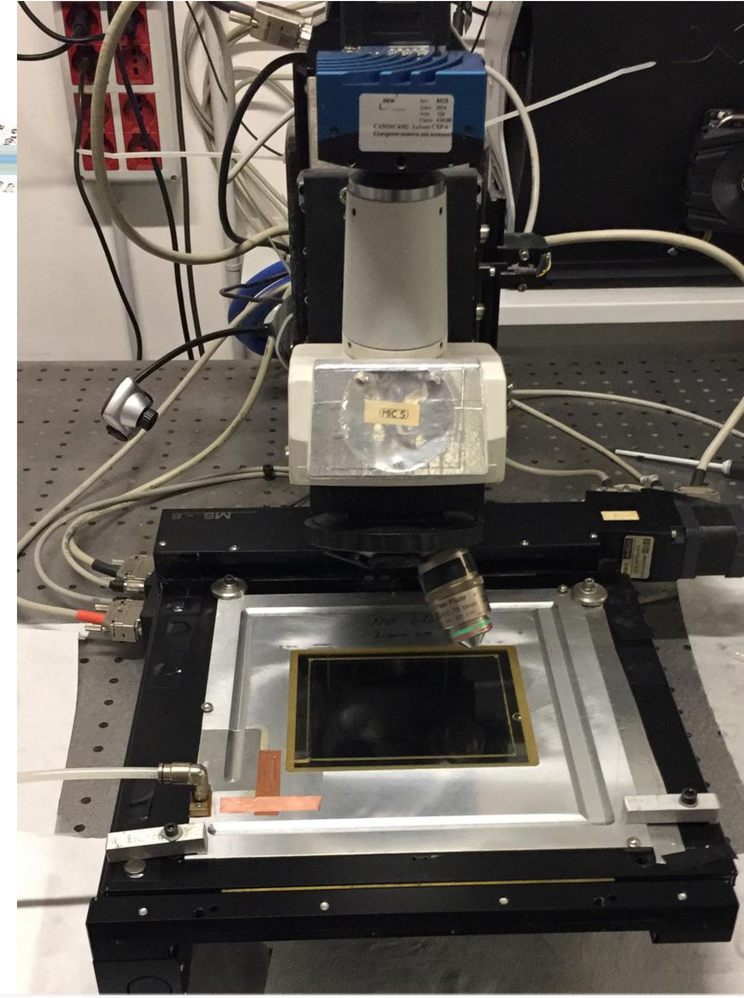
Before exposing the emulsion «dry» runs have been taken with Scintillator and beam monitor (Drift chamber) to check the beam flux



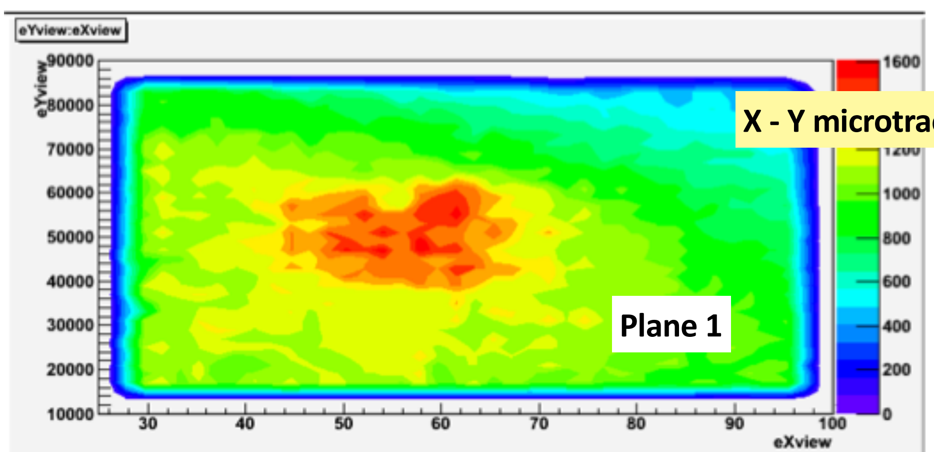
Emulsions Scanning

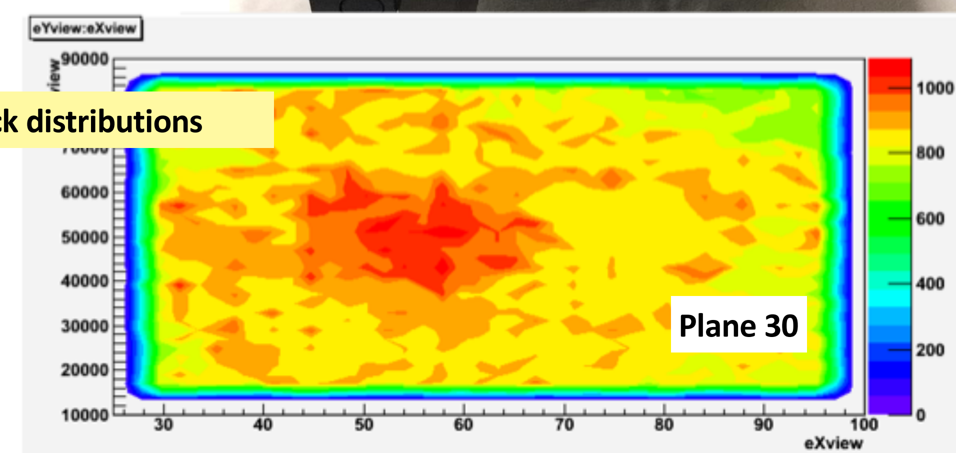
- Scanning parameter optimization on-going
- 30 emulsions (GSI2, stack 1) have been already scanned





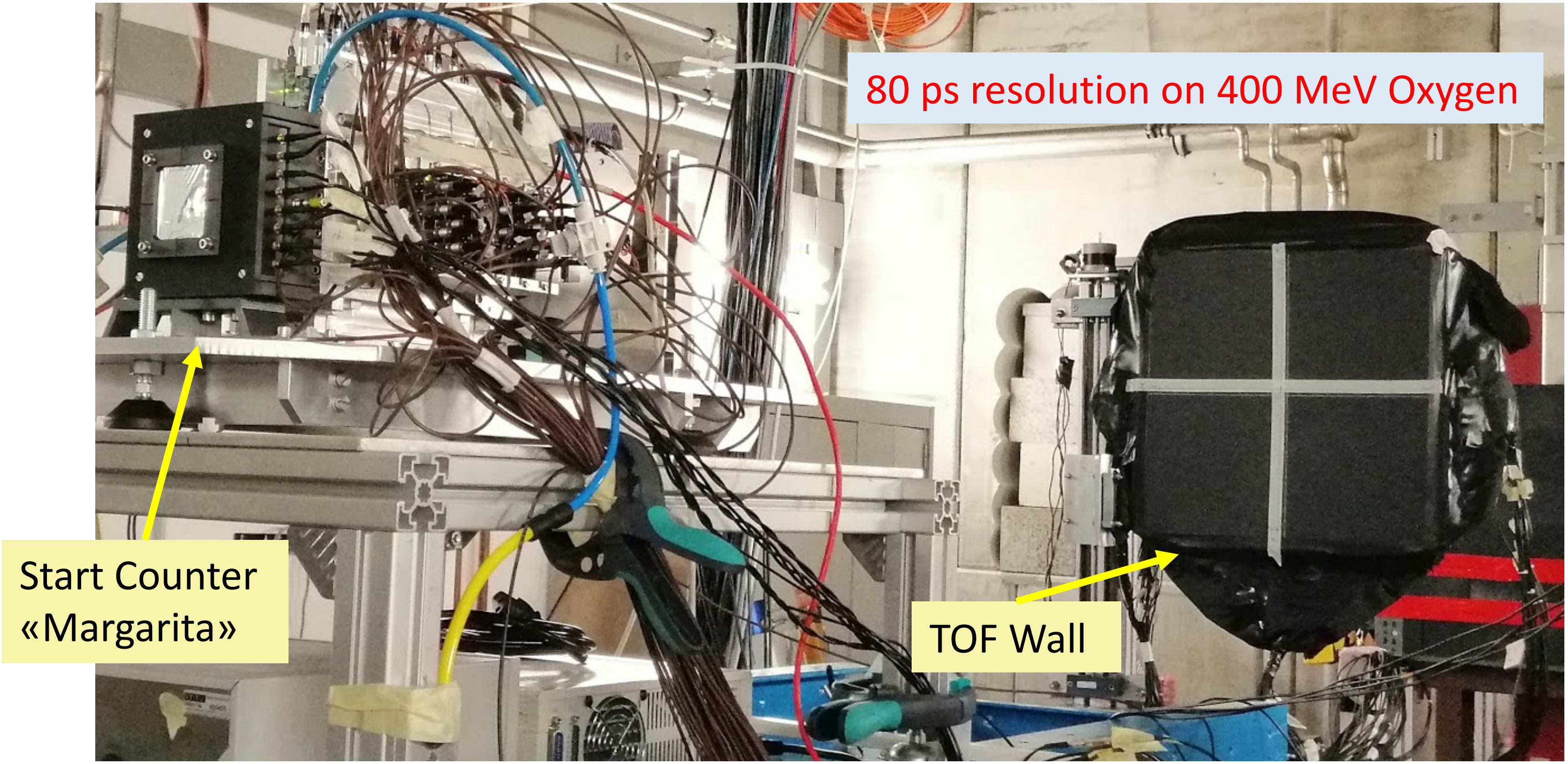
X - Y microtrack distributions





Test of TOF system @ GSI

- Start provided by 250 μm thick plastic scintillator read out by 48 SiPMs
- Stop provided by TOF Wall: 2 planes (X-Y) made of 20 plastic scint. rods (20x2x0.3 cm) each read by 2+2 SiPMs
- FEE from MEG experiment with 5 Gsamples Waveform Digitizers



Summary & conclusions

- Nuclear fragmentation plays a role in target fragmentation in proton therapy and in beam fragmentation in carbon (oxygen) therapy
- The radio protection in space (a show-stopper for human exploration of solar system) needs the same knowledge on fragmentation of light ion at intermediate energy of PT
- The FOOT experiment is a medium size particle physics experiment and can address these PT and RPS related issues measuring the relevant fragmentation cross section

Foot has an open and evolving physics program and collaboration. Proposal to move the focus on neutron production in future


Start counter
Target
p,C
Beam Monitor
Vertex
Halbach magnets
Inner tracker
Si Micro Strip
BGO Calo
ΔE & TOF
FOOT

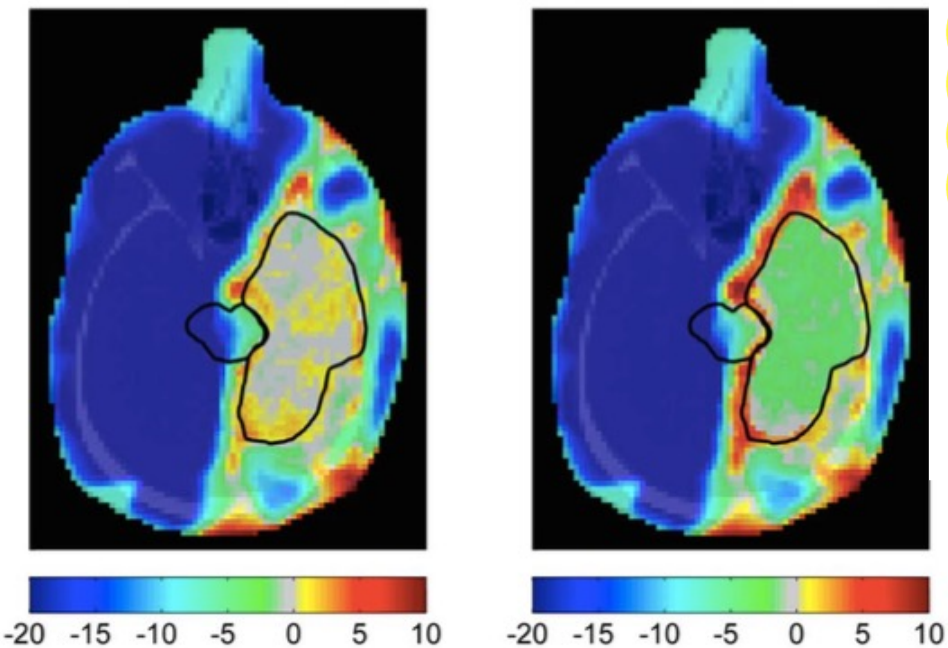
Thanks...

Target fragmentation & proton RBE

Currently the contribution of target fragments and of the increasing RBE near the PB is implicit (ICRU reccommendation RBE=1.1)

Lately has been pointed out possible impact of variable proton RBE on clinical NTCP values

RBE=1.1 | Variable RBE

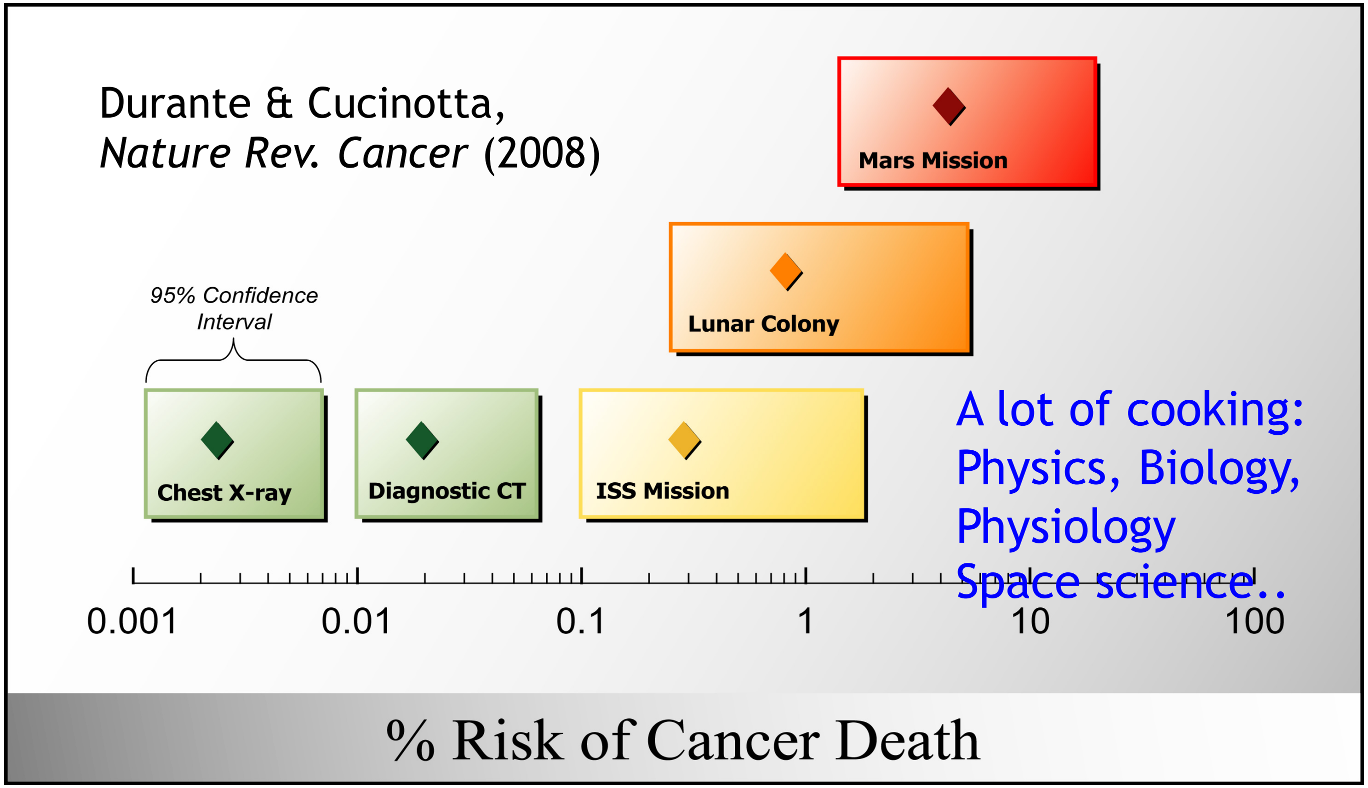


The differences in DVHs and dose distributions are also translated into different NTCP values, shown in Table III. As an example, the probability of necrosis in the brain stem is estimated in case1 to 0.84% for the IMRT plan and 0.57% for the proton plan when assuming a RBE equal to 1.1. However, when assuming a variable RBE the probability increases to 2.13%. Equivalently, the probability for blindness increases from 1.13% (RBE = 1.1) to 4.21% (variable RBE) for protons compared to 1.21% for photons for the optic nerve. The same tendency of estimating a lower NTCP for protons compared to photons when having RBE equal to 1.1, but obtaining a higher NTCP compared to photons when assuming a RBE distribution is also observed for the chiasm and for the other brain cases (see Table III).

Wedenberg 2014 Med Phys

Death from the star?

- Long term mission in space expose the astronauths to a huge dose release: shielding is compulsory
- He, C, O, Fe components of the Galactic Cosmic Rays fragment on the shields and contribute to the integrated dose: material of shielding matters



To choose the shielding material He, C, O fragmentation X section on shields are needed at 0.7-1 GeV/nucl

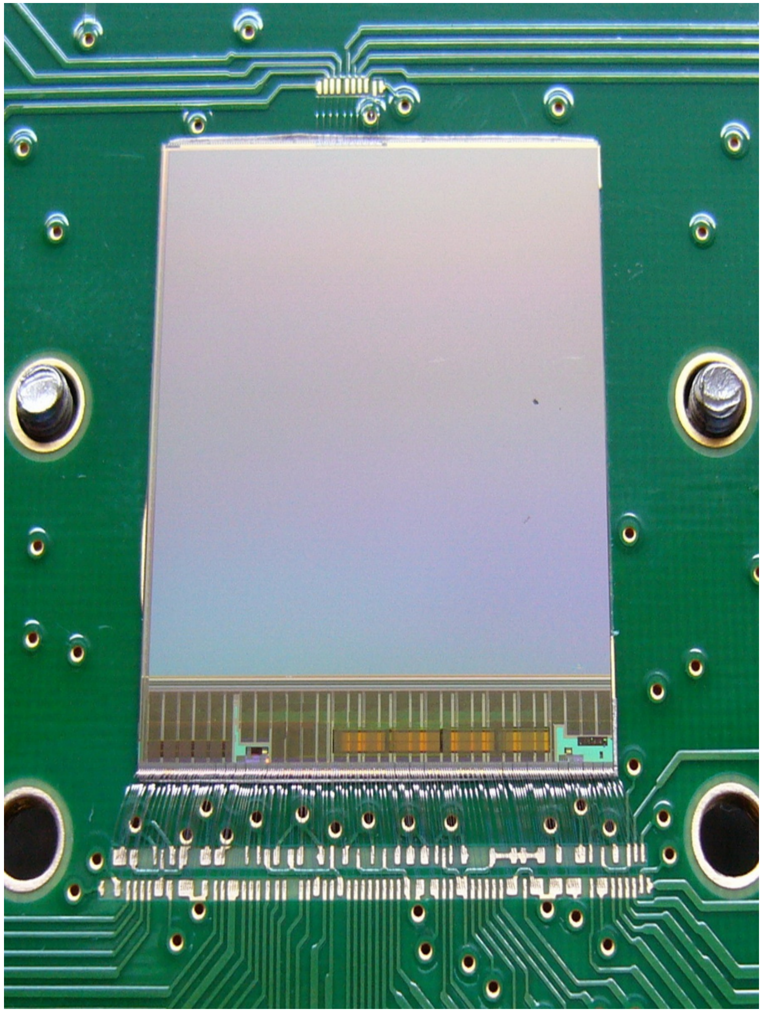
Radiobiology requests & detector constraints for Target Fragmentation

To implement Normal Tissue Complication Probability models requirements are very strict. Lorentz boost in the patient frame asks for good energy and angular accuracy in the lab frame

- Heavy fragment (Z>2) production cross section with uncertainty of 5%
- Relative accuracy on fragment energy of the order of few %
- Good charge and isotopic identification capability of fragments
- Accuracy on light ions production also at large angle
- Angular resolution on the beam-fragment emission angle at mr level

TOO MUCH ?!?!

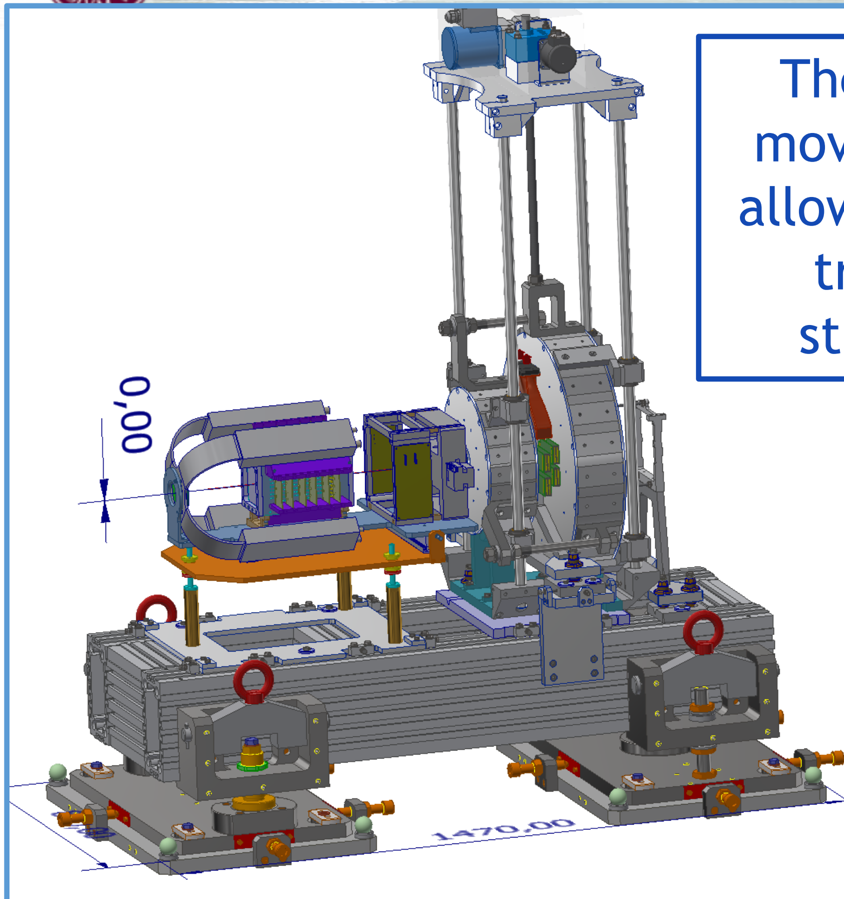
M28 pixel sensor main characteristics



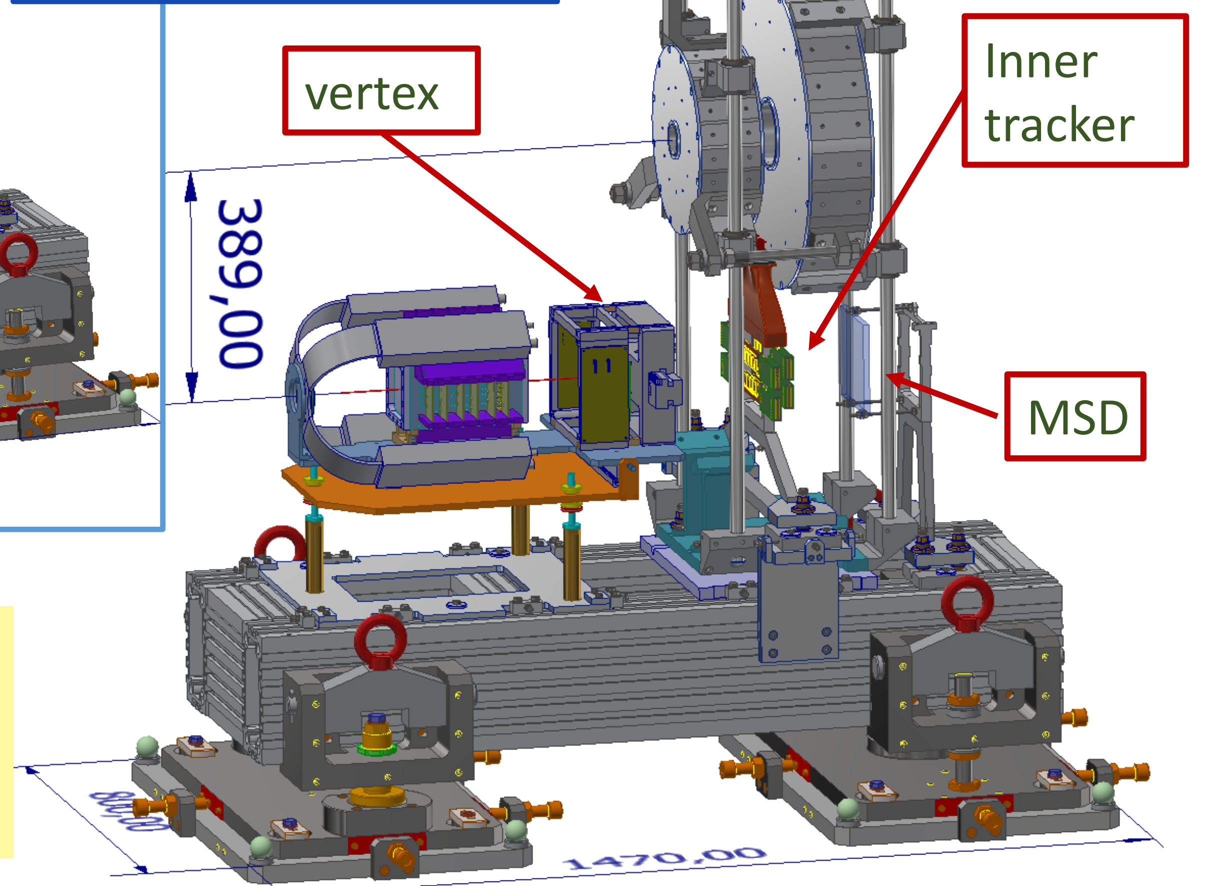
- MAPS (AMS 0.35 μm, 15 μm epi-layer)
- 50 μm thickness
- 928 (rows) x 960 (columns) pixels
- 20.7 μm pitch
- Size 20.22 mm x 22.71 mm
- chip readout time 185.6 μs
- Digital Zero Suppressed Output

By IPHC In2p3 Strasbourg

Calibration with straight tracks



The magnet can move rigidly up to allow calibration of trackers with straight tracks



Mechanical structure derived from the ELI beam line mechanics

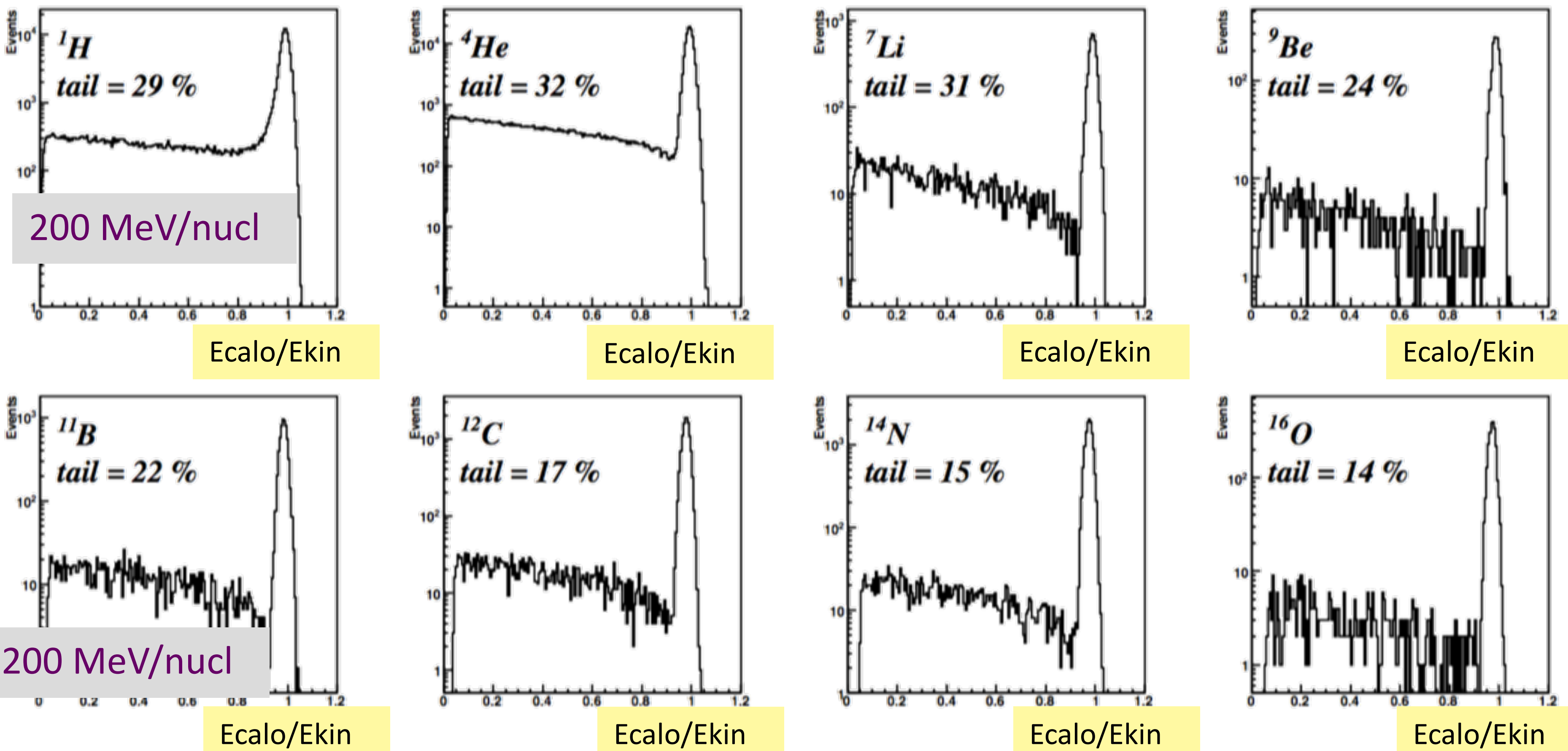
BGO calo VS neutron leakage

The neutron leakage in BGO seems to be important for energy higher than 200 MeV/nucl and for light fragments

The fit constrained can tag such events, but they must be minimized to keep the systematic under control.

Neutron int. length in BGO at this energy ~ 30-40 cm

FLUKA 2017: 14 cm length crystal (NB final FOOT crystal are 24 cm)

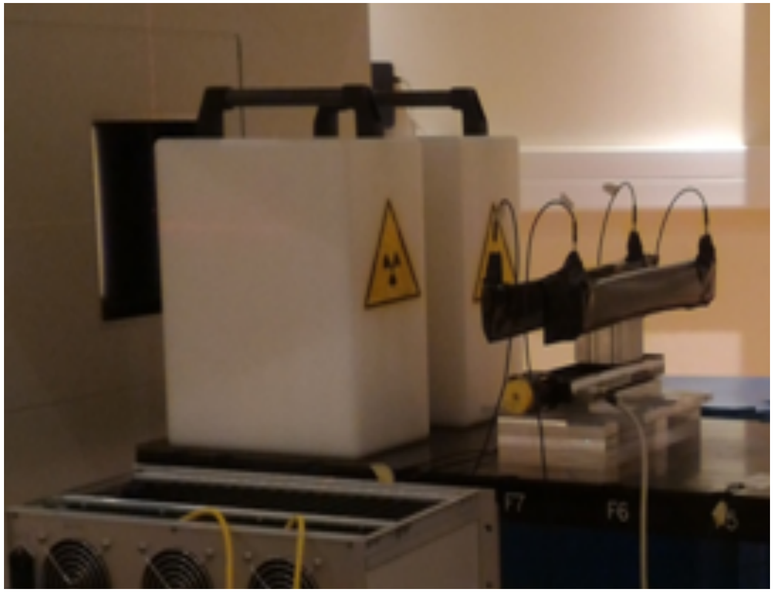


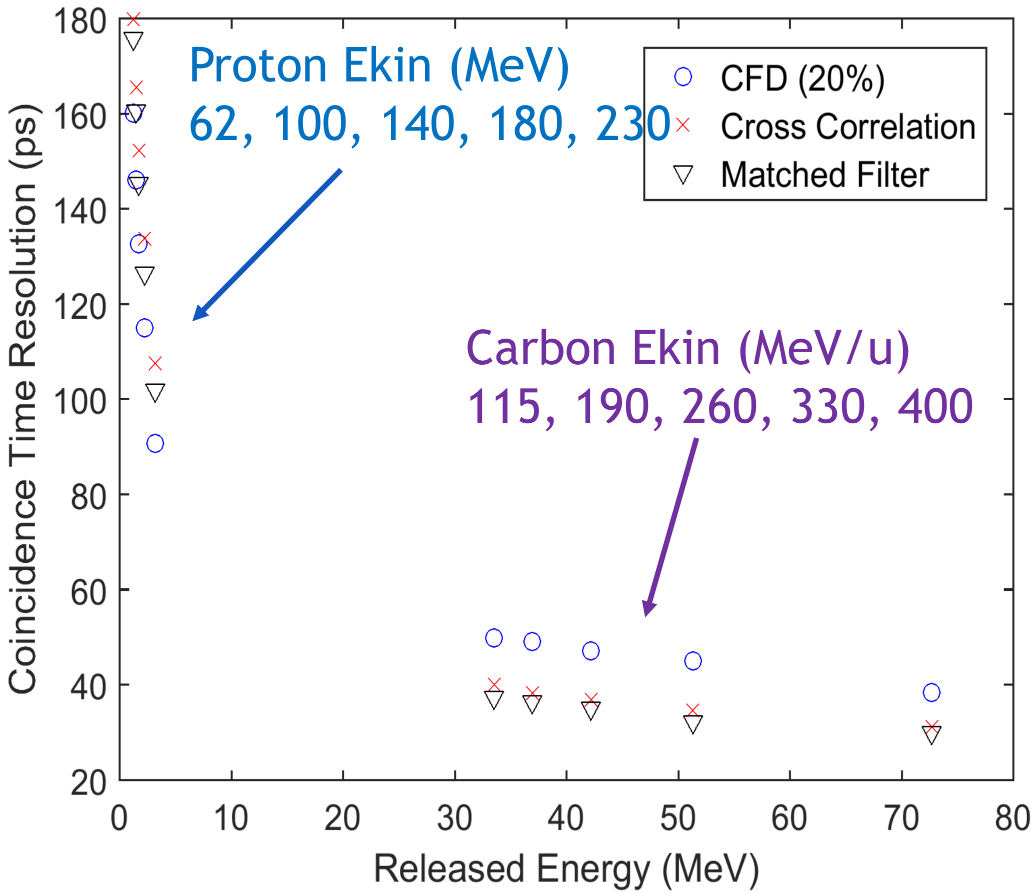
ΔE/TOF test @ CNAO p & ^{12}C beam

- Each bar side readout by 2 parallel of 2 SiPM powered in series (Hamamatsu SiPM 25 um cell size)
- Each bar side readout by 4 SiPMs powered in series (Avant SiD 40 um cell size)

Tested 2 EJ-200 Scintillator bars 20 x 3 x 400 mm^3

Time resolution 30-40 ps for ^{12}C beam





BGO crystal test @ HIT& CNAO

- The data confirmed that resolution in the range of 1-2% can be obtained for carbon fragment at 200-400 MeV/u
- The energy resolution seems to scale as sqrt(E_{kin}) as expected
- The neutron contribution is sizeable (higher for lighter fragments)