SPES Workshop Ferrara 30th Jan 2019

"Interdisciplinary aspects and applications related to the SPES project"

Nuclear fragmentation and Particle Therapy

Vincenzo Patera

Universita' di Roma "La Sapienza" & INFN

FOOT

SPES exotic beams for science

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"Interdisciplinary aspects and applications related to the SPES project"

i.e. "how you can have an impact on medicine doing basic, fundamental (FIS/01 for Italian colleagues) nuclear physics"

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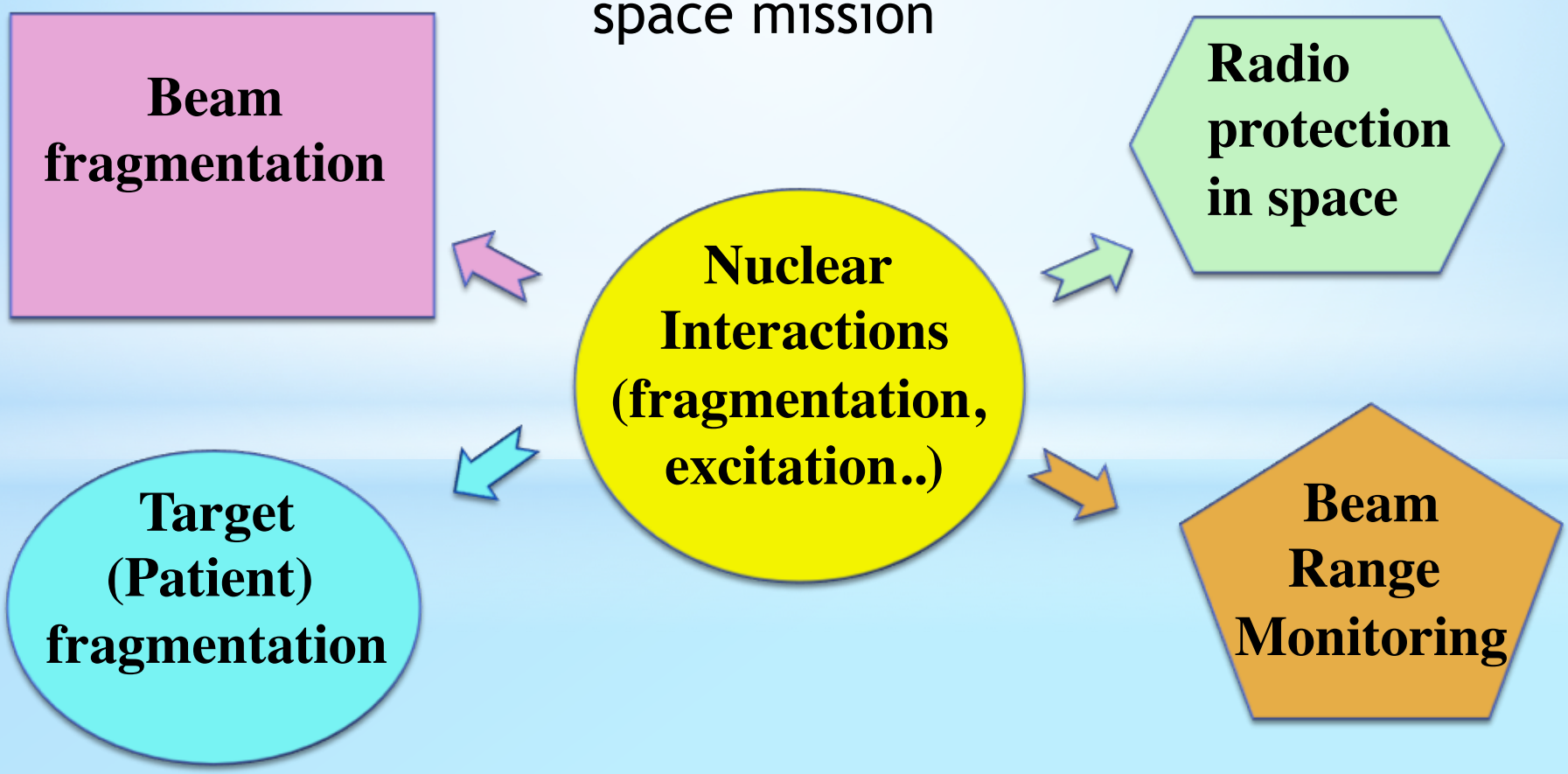
exotic beams for science

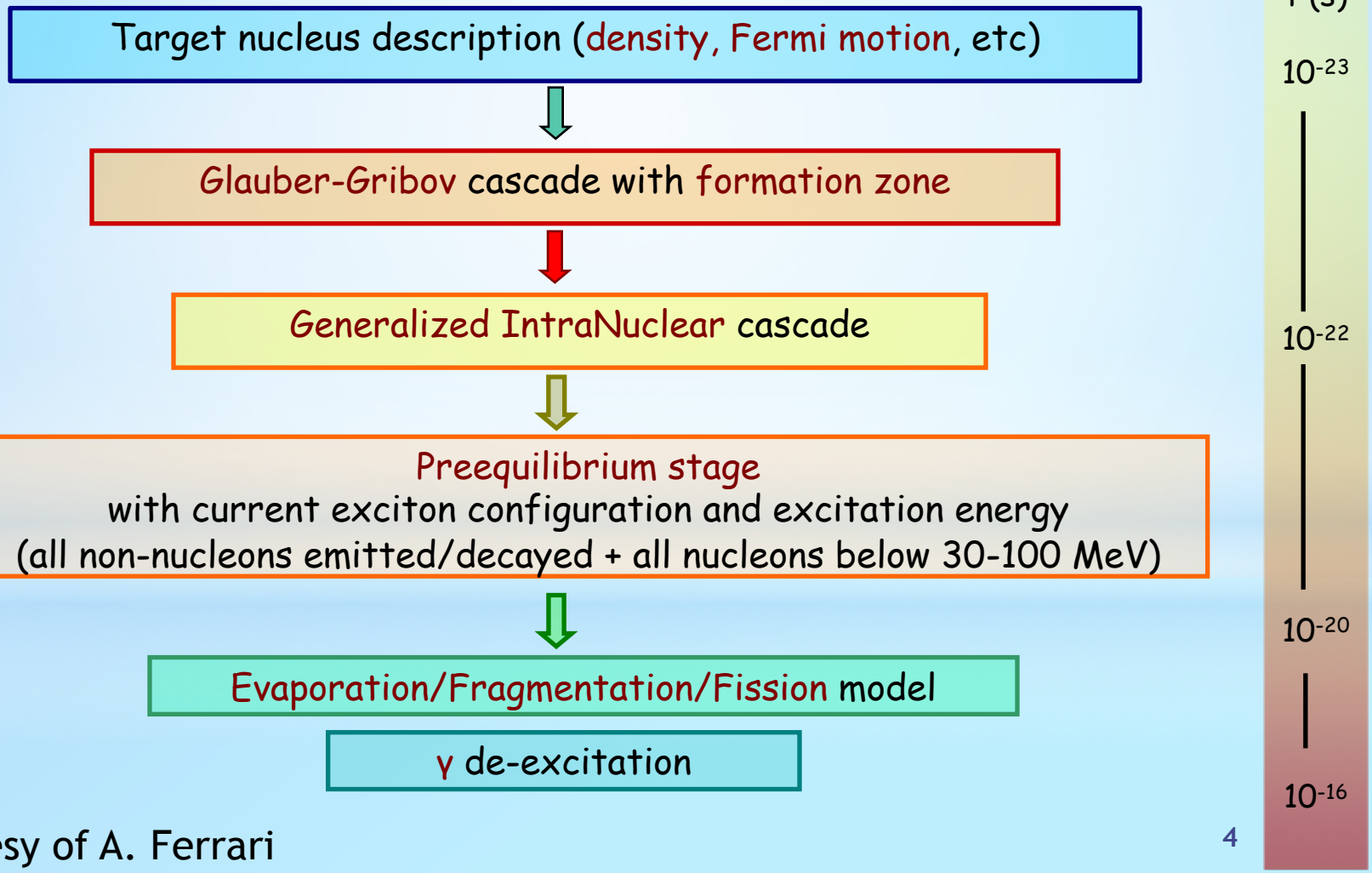
Nuclear fragmentation and Health (not only PT)

Nuclear fragmentation plays a role in several aspect of radiotherapy of tumor with proton of carbon beam (i.e. Particle Therapy) but also in radio protection in long term space mission



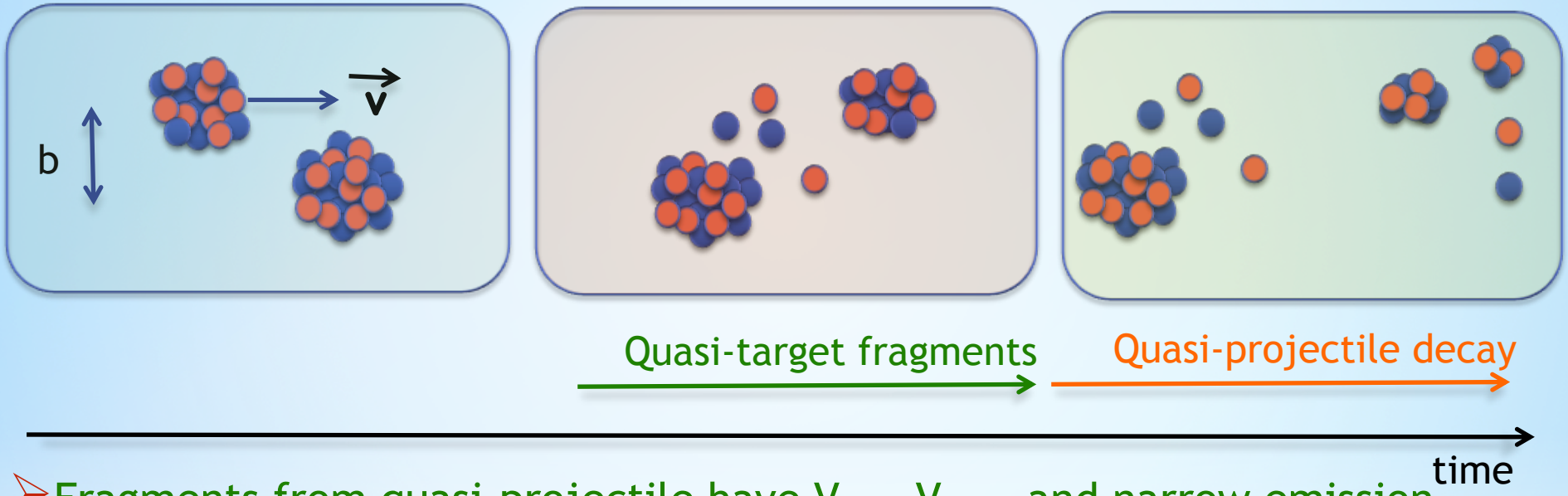
Nuclear Interactions and MC

The nuclear model embedded in MC try to reproduce the phenomenology of the nuclear interaction is generally very complex. Here we report the FLUKA scheme of the nuclear interaction



Courtesy of A. Ferrari

The abrasion-ablation view



- 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

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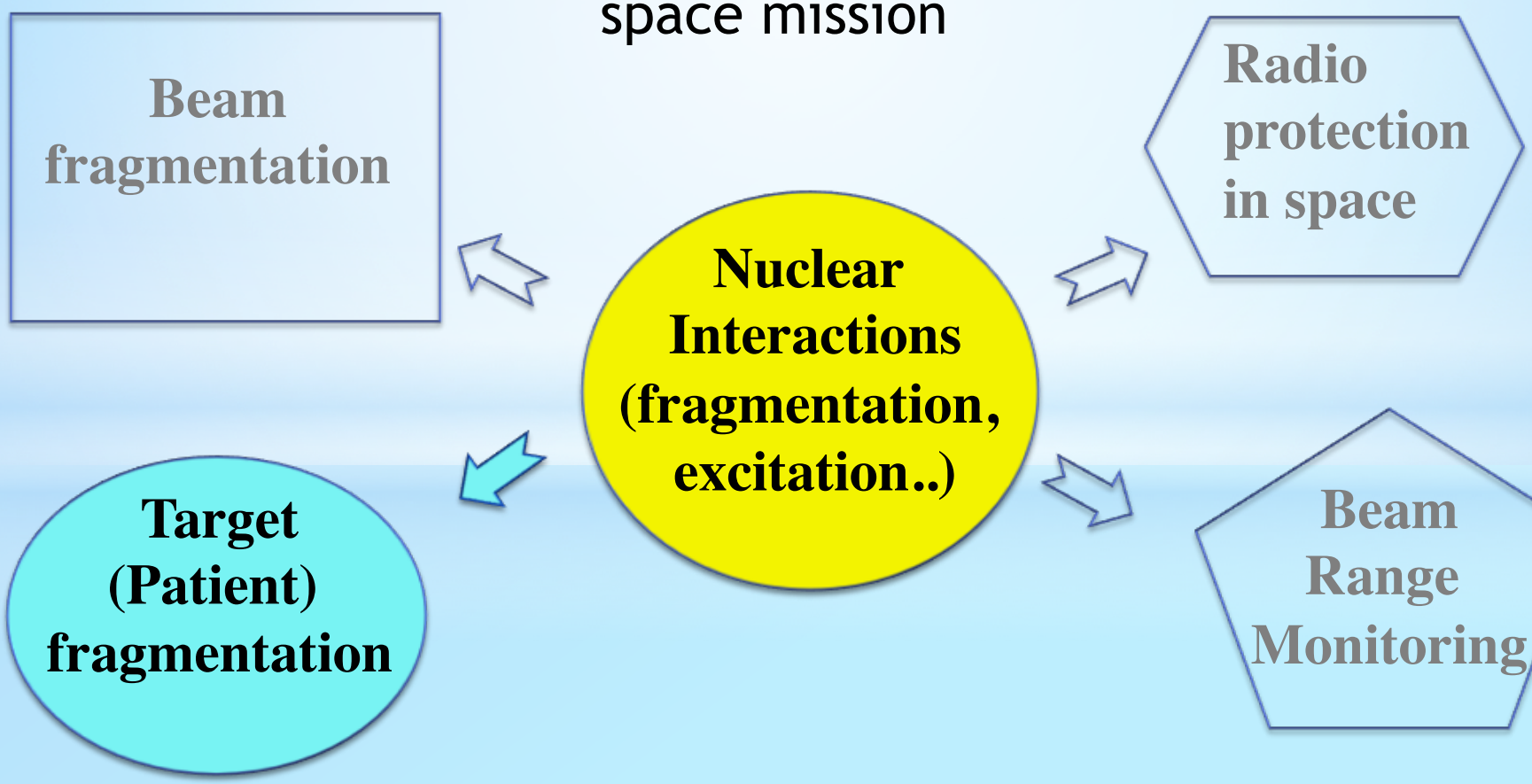
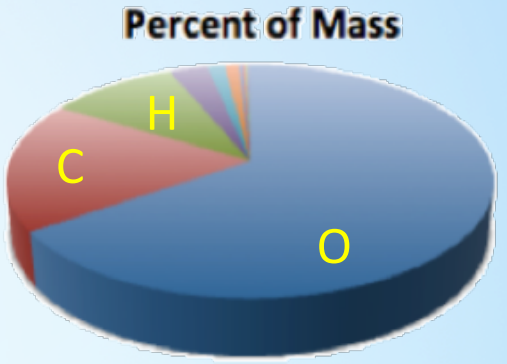


p on patient (O,C) @200 MeV

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 ?

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

Direct measurements : mission impossible

REMARK: For radiobiology effectiveness of p beam the measurement of the fragment spectra is compulsory !!

- 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

Proton (H) at rest

A the end Lorentz boost

C,O 200 MeV/A

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?

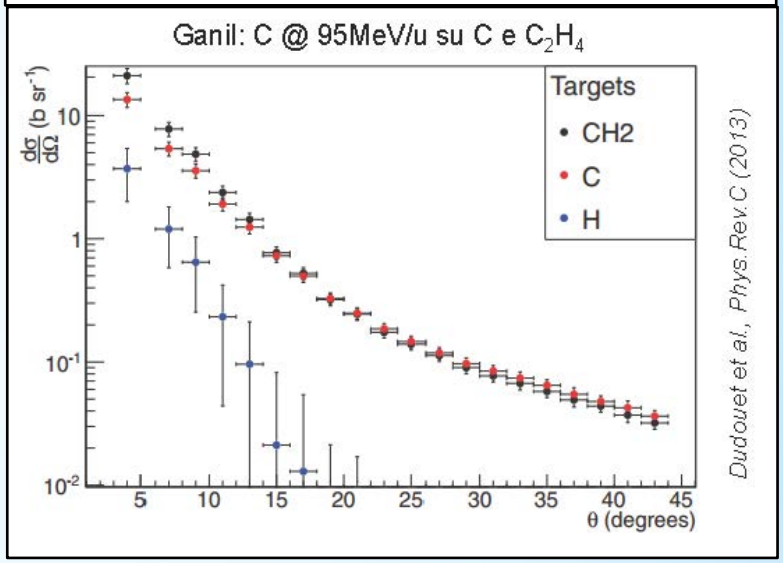
Inverse kinematics and the target

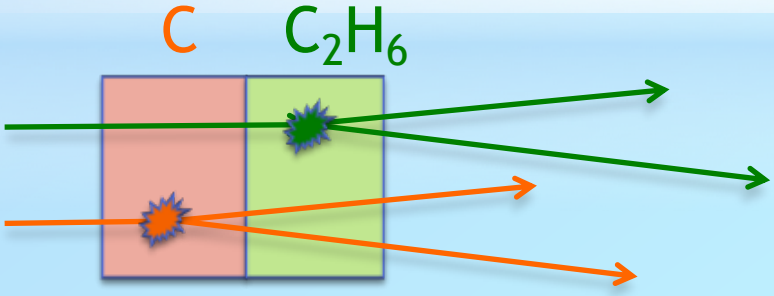
The target can be thick as few mm, since the fragment range is larger than several cm.

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

Nuclear fragmentation and Health (not only PT)

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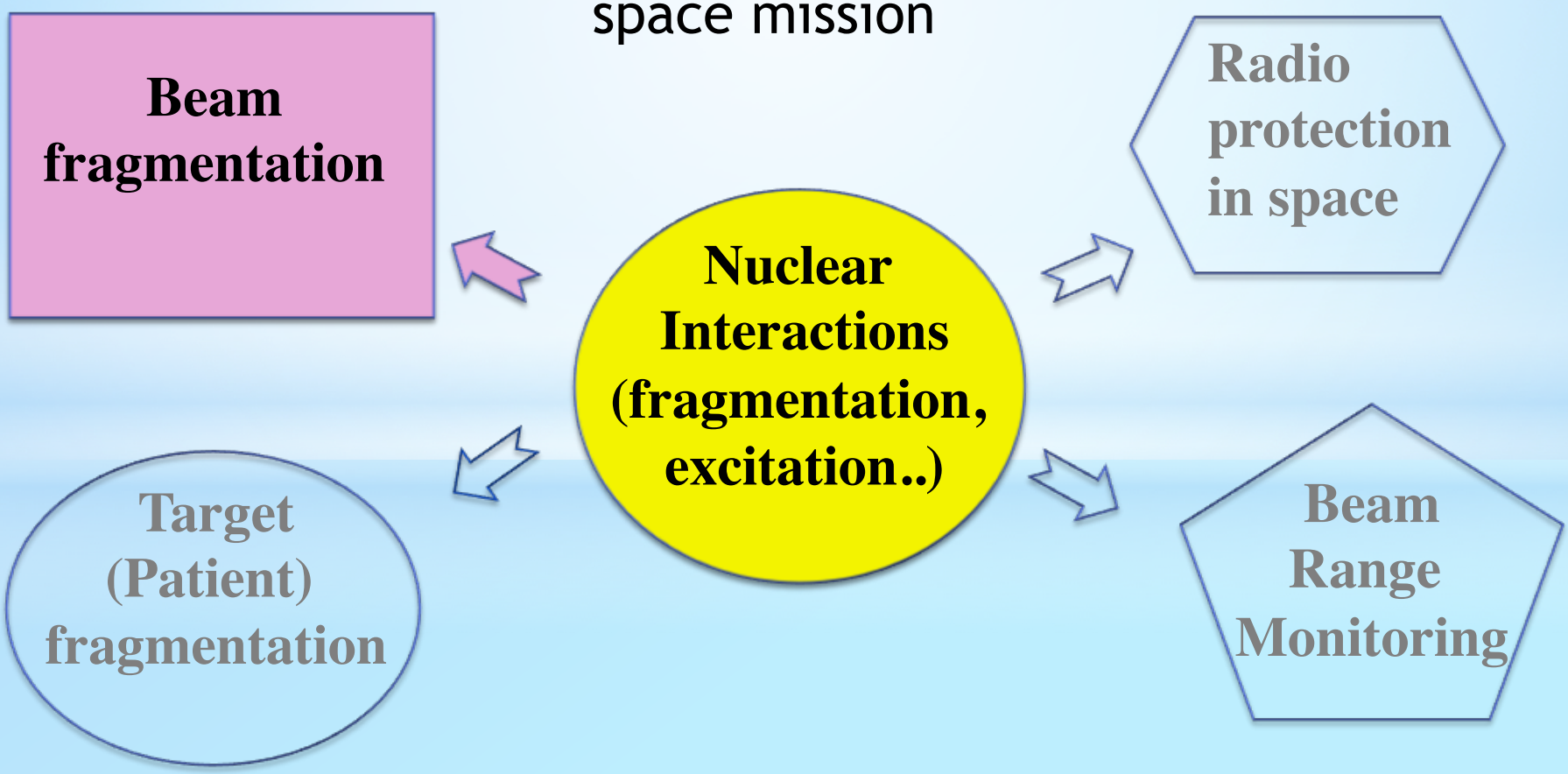
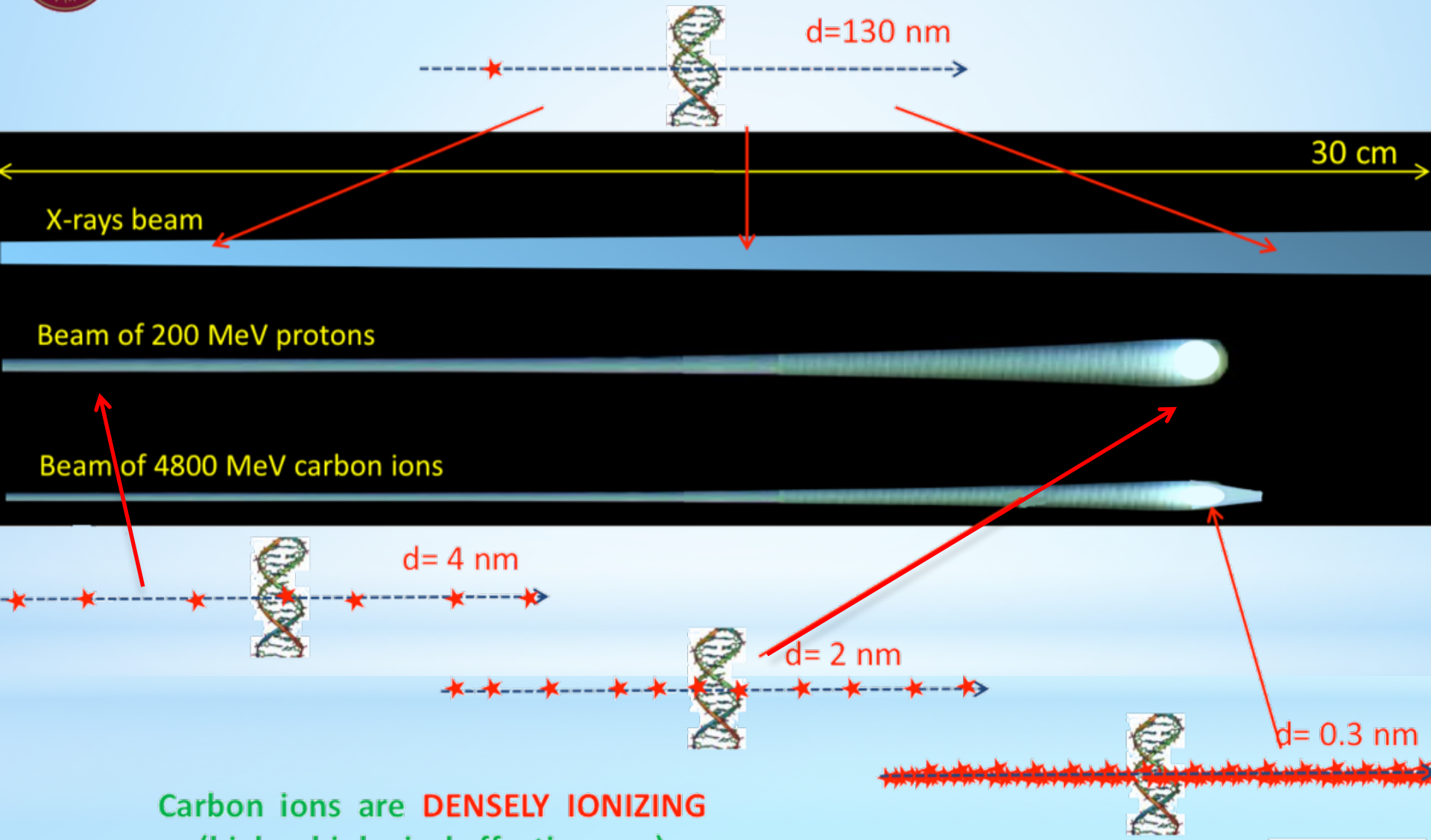


Different bullet, different effects



Carbon ions are DENSELY IONIZING
(higher biological effectiveness)

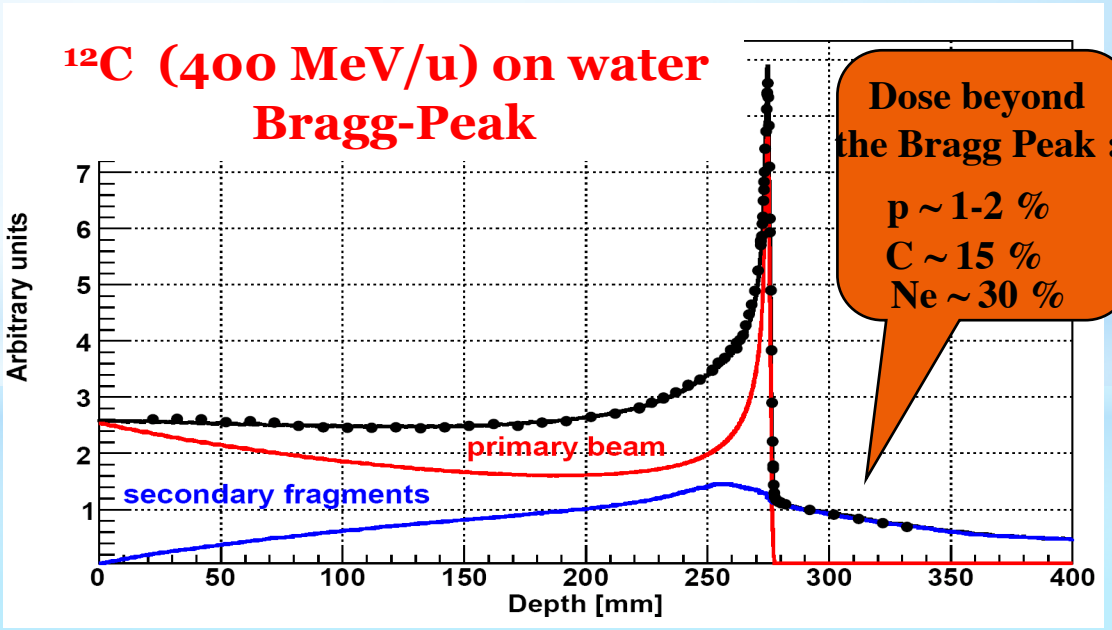
Courtesy U.Amaldi

^{12}C (^{16}O) Beam Fragmentation

Dose release in healthy tissues with possible long term side effects, in particular in treatment of young patients ➔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

- ✓ Mitigation and attenuation of the primary beam
- ✓ Different biological effectiveness of the fragments wrt the beam



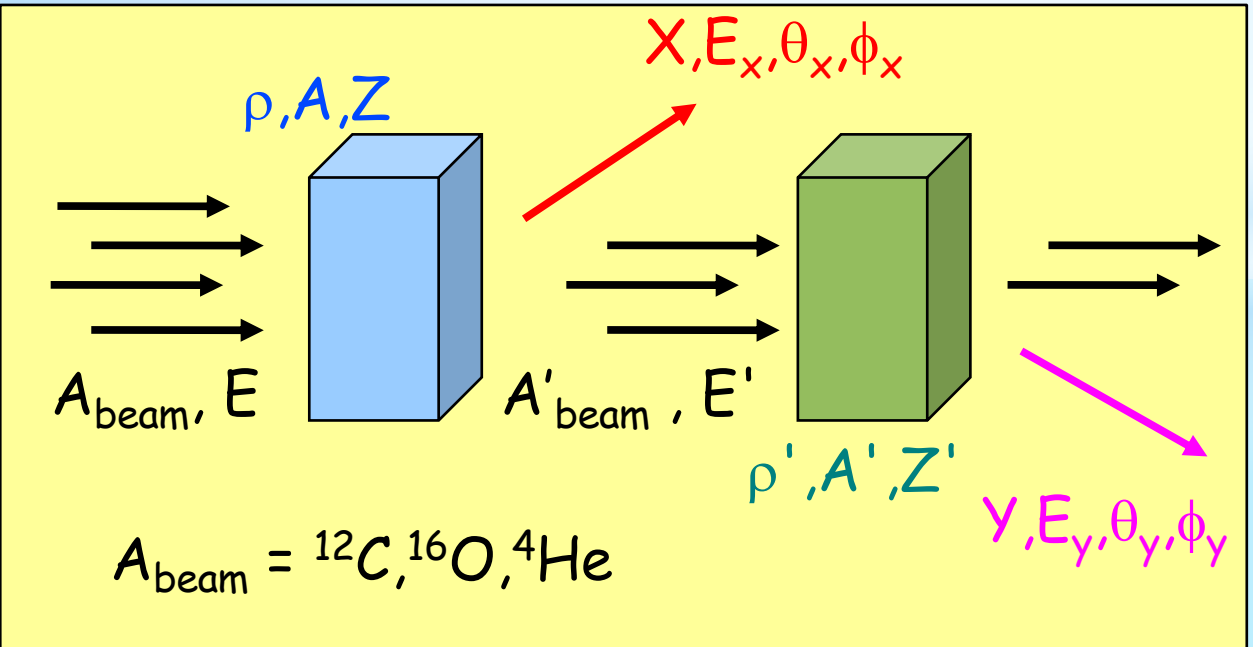
Exp. Data (points) from Haettner et al, Rad. Prot. Dos. 2006
Simulation: A. Mairani PhD Thesis, 2007, Nuovo Cimento C, 31, 2008

Courtesy of Andrea Mairani

What we still miss to know about light ions fragmentation in 2019?

We need to know, for any beam of interest and on thin target:

- Production yields of all $Z \leq Z_{beam}$ fragments, if possible of all $A \leq A_{beam}$
- $d^2\sigma/d\Omega dE$ wrt angle and energy, with large angular acceptance
- For any beam energy of interest (100-300 AMeV)
- Thin target measurement of all materials crossed by beam



Not possible a complete DB of measurements

We need to train a nuclear interaction model with the measurements!!

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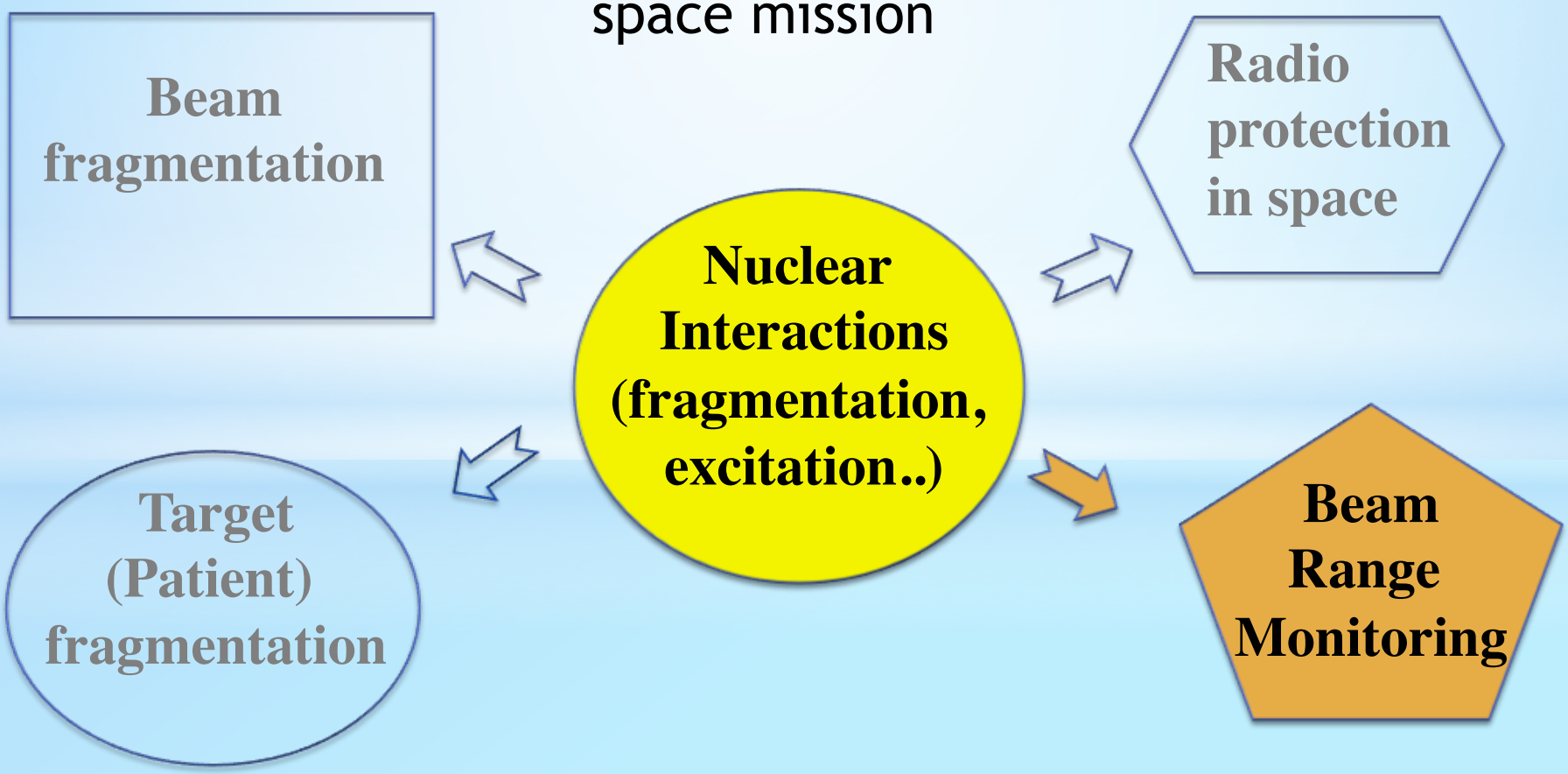
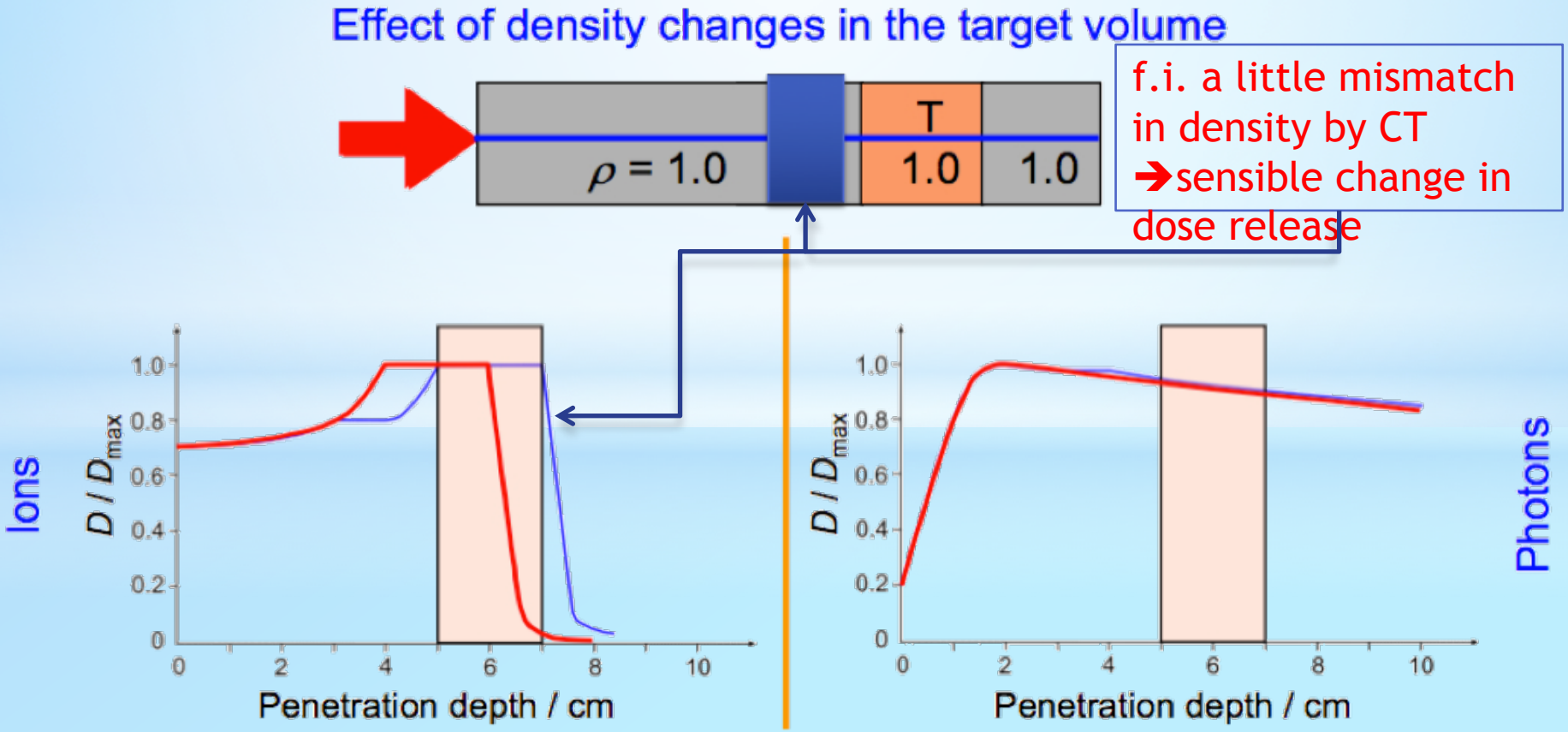


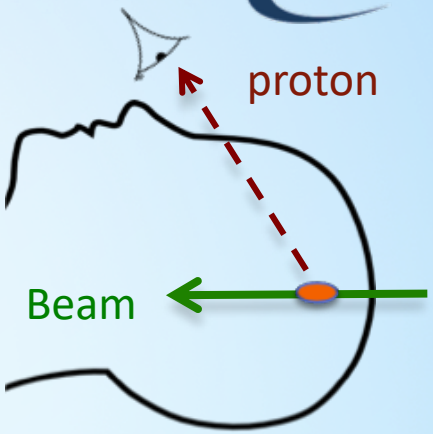
Beam monitoring in PT

Beam monitor in PT is crucial with respect to photon RT. It is like firing with machine-gun or using a precision rifle..

Inhomogeneities, implants, CT artifact, HU conversion, inter session physiological changes-> can cause range variations

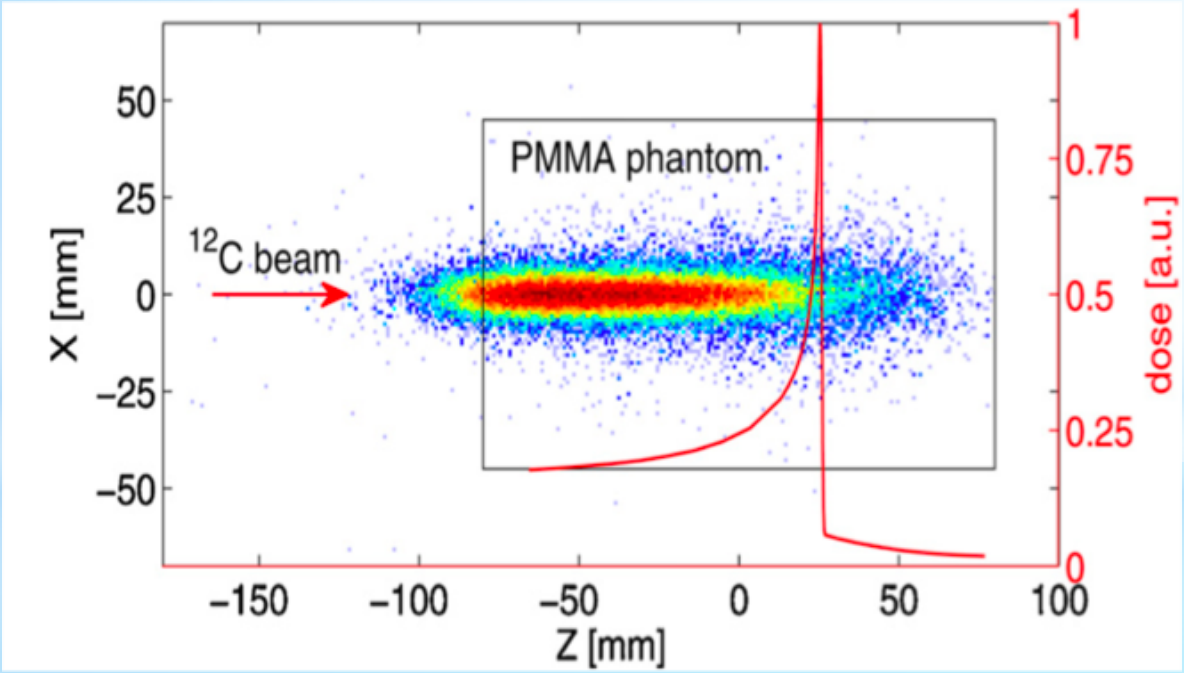


^{12}C beam beam monitor : exploiting charged fragments



Charged secondaries have several nice features as

- The detection efficiency is almost one
- Can be easily back-tracked to the emission point-> can be correlated to the beam profile

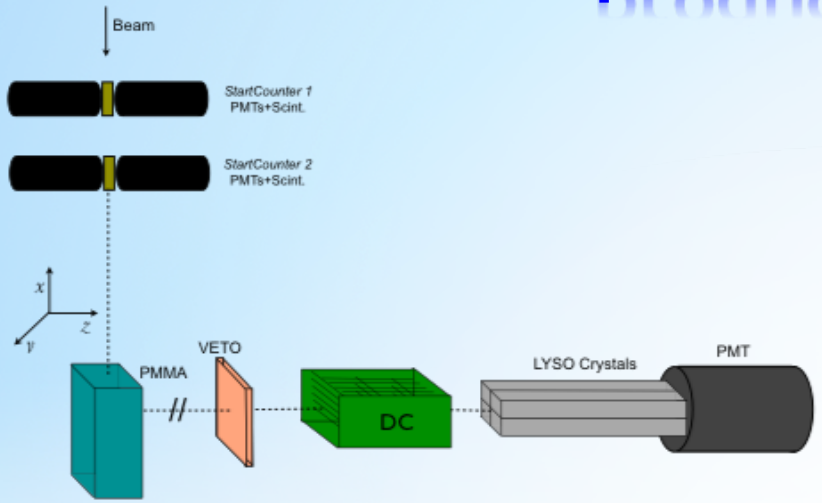


Space distribution of point of closest approach of the charged secondaries to the beam direction

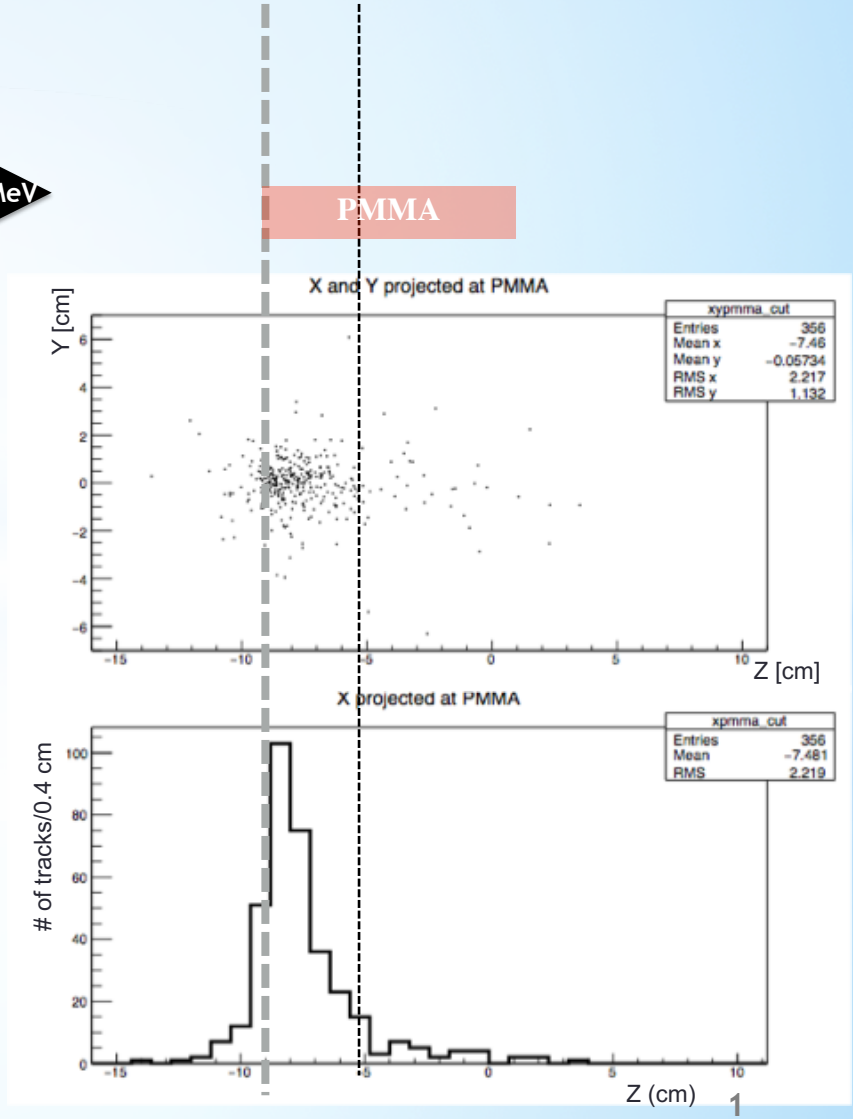
MC not too reliable, in particular at large emission angle wrt beam direction

K Gwosch et al Phys. Med. Biol. 58 3755

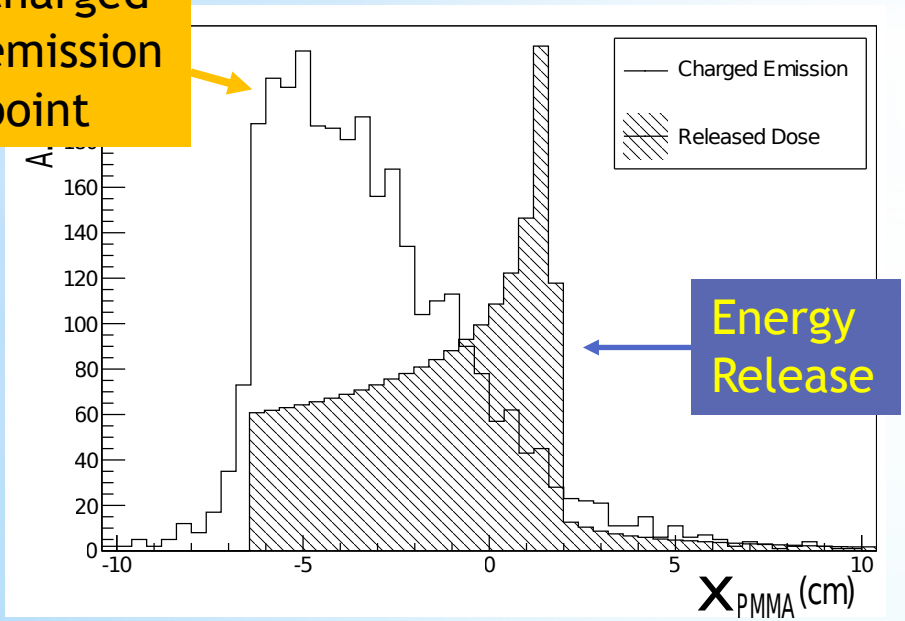
Large angle charged fragments production: C beam



C @120MeV beam



charged emission point



A Rucinski *et al* 2018 *Phys. Med. Biol.* **63** 055018

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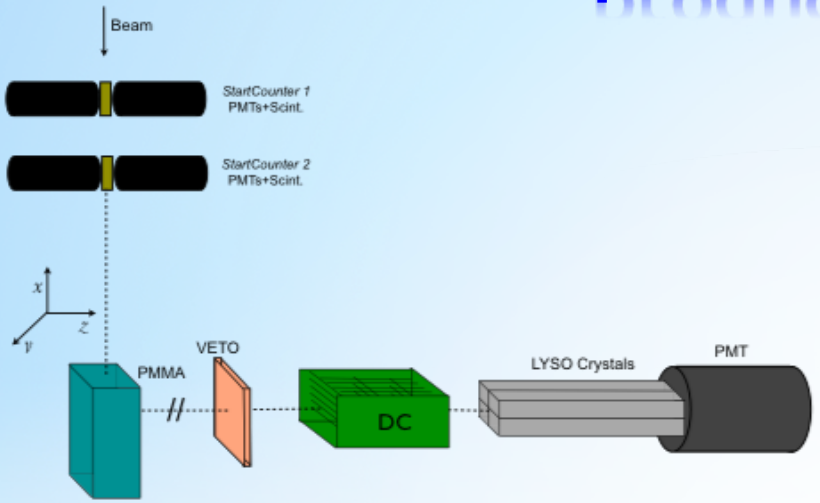
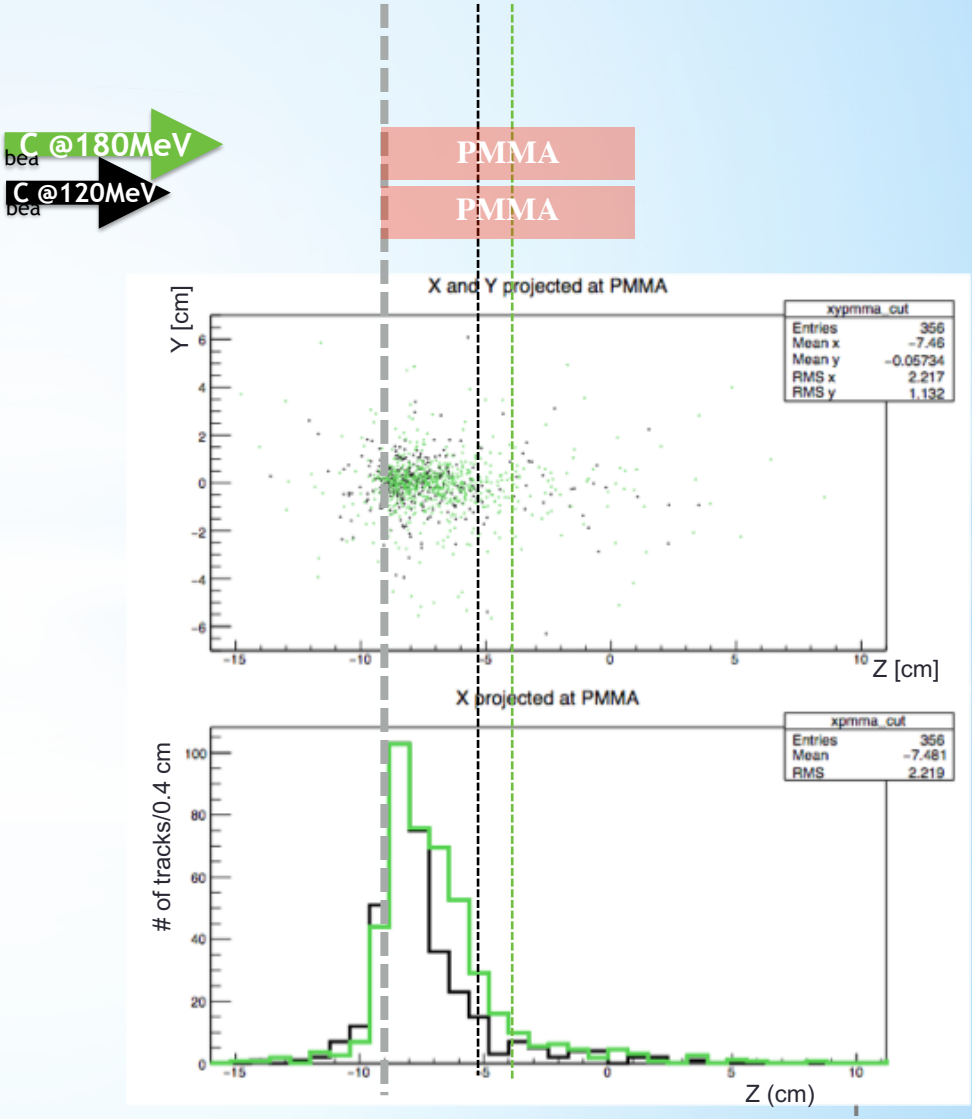
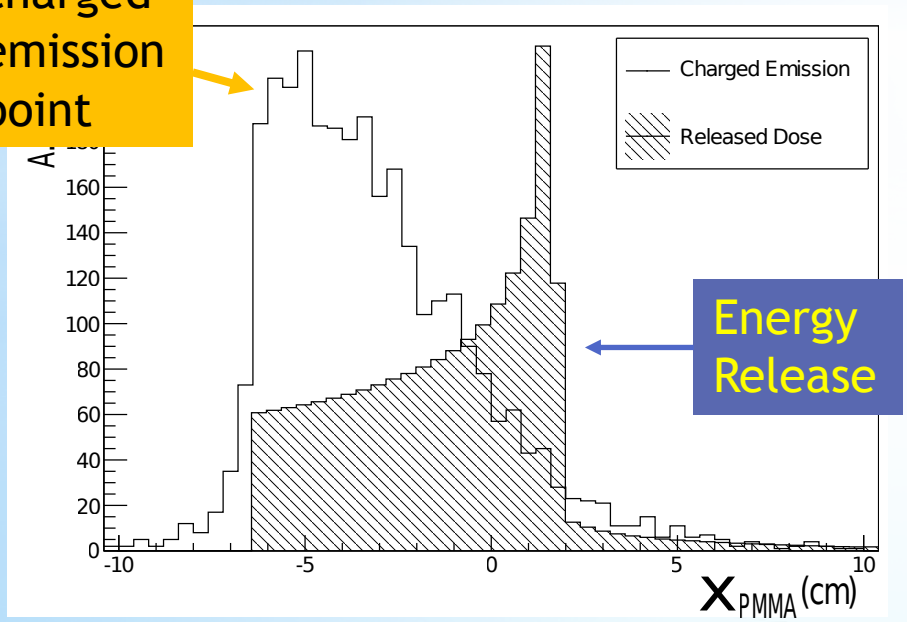




charged emission point



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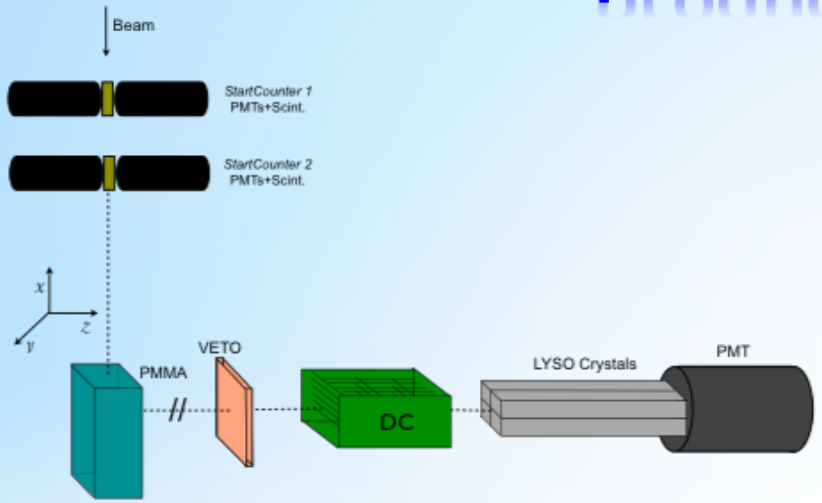
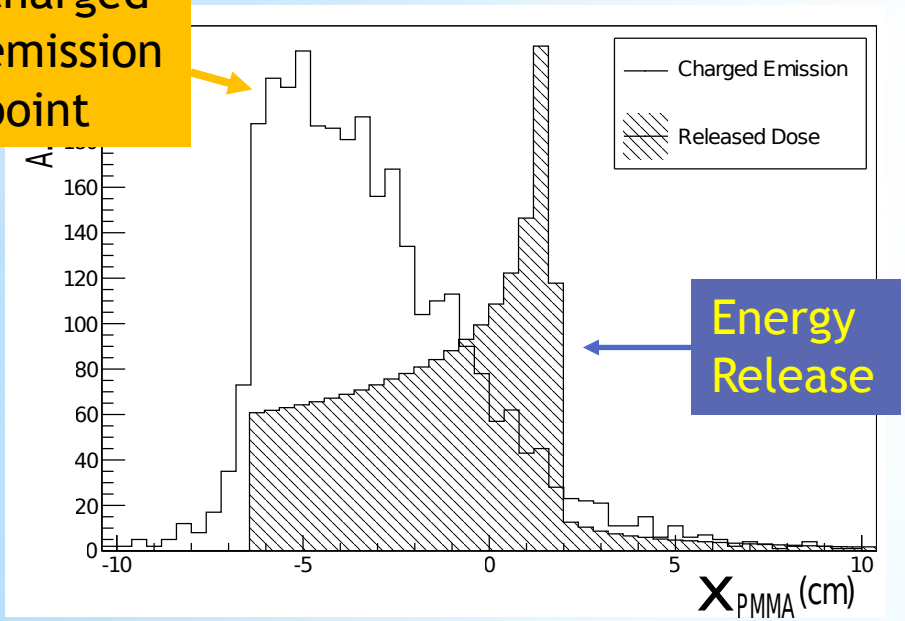
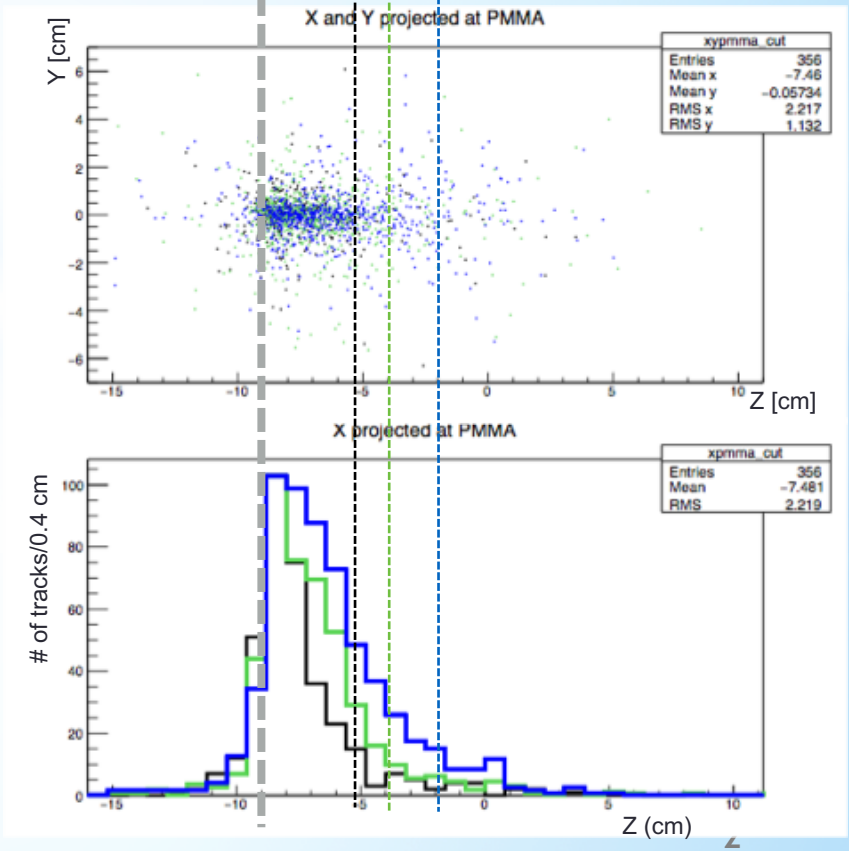


charged emission point





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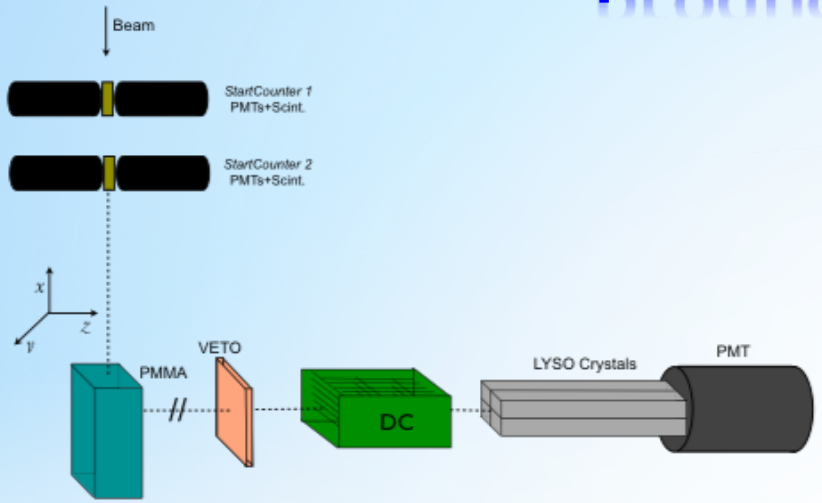
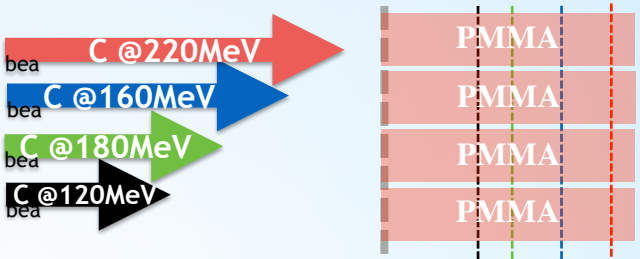
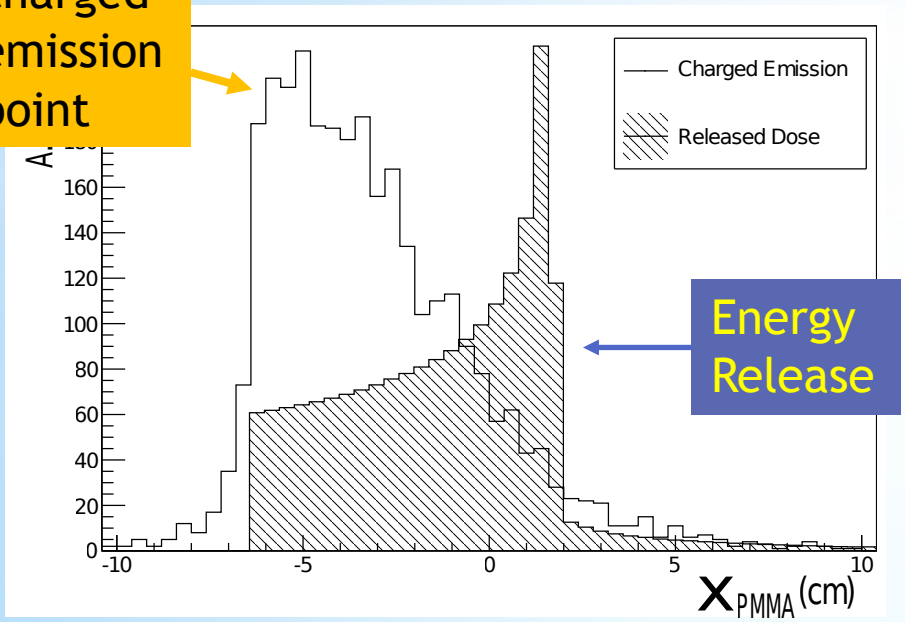
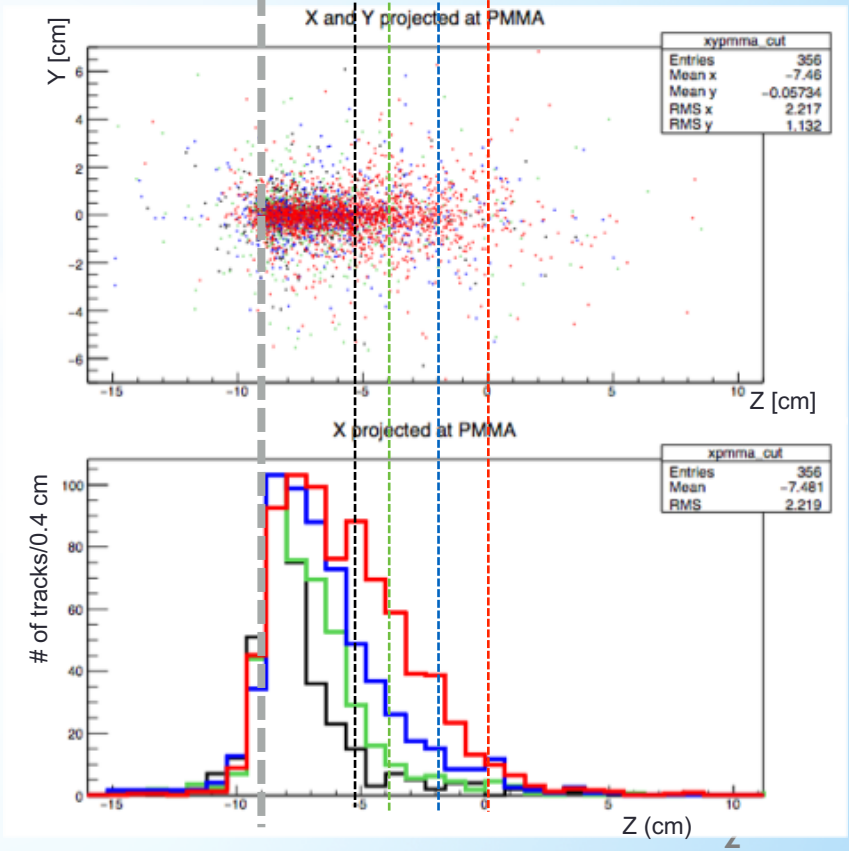




charged emission point





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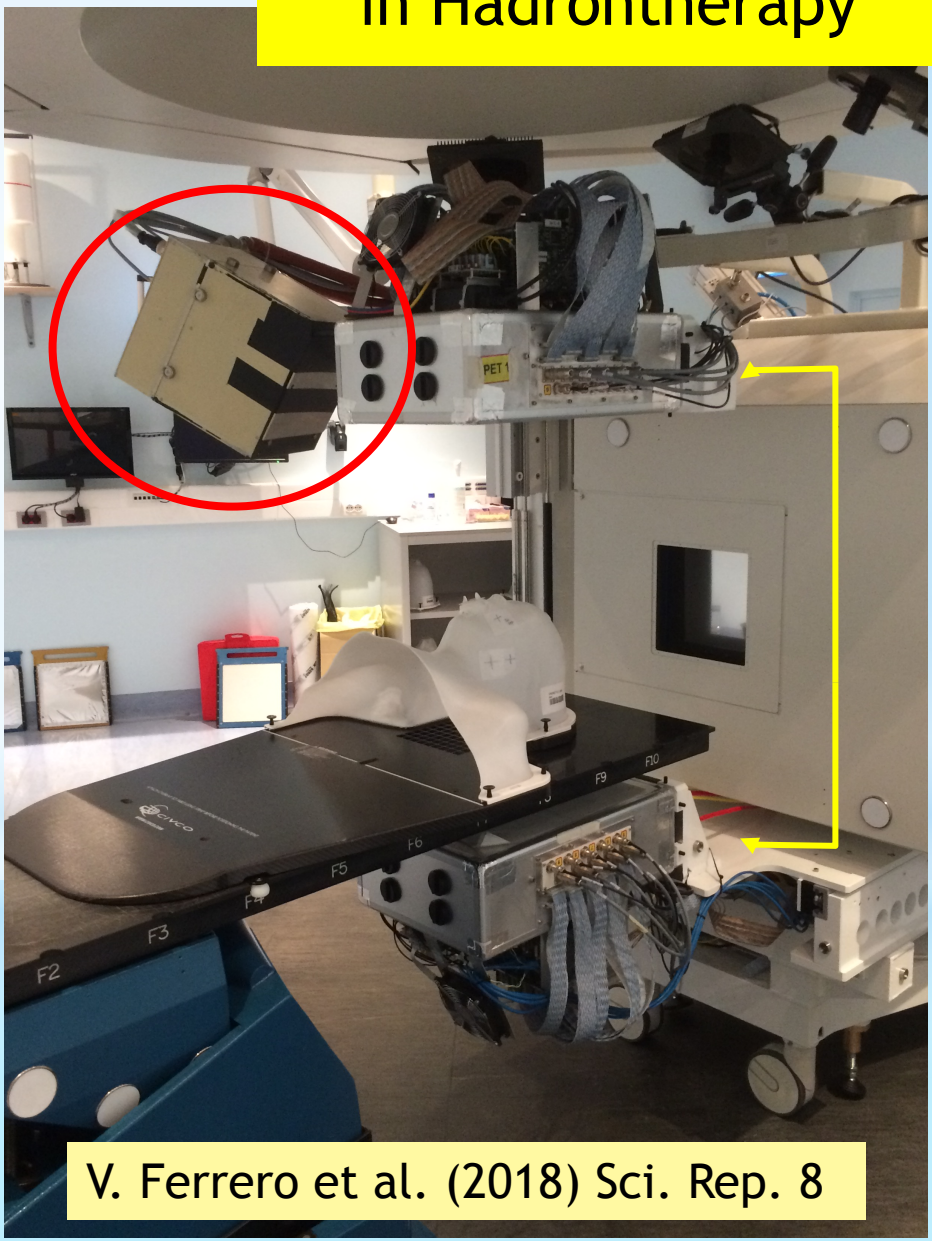
The InSIDE Project

INnovative **S**olutions for In-beam **D**osim**E**try in Hadrontherapy

- In september 2018 a Dose profiler (fragment tracker) has been installed in Room 1 at CNAO. A clinical test with ~10 patients will start in 2019
- The DP will be operated together two PET heads developed by Pisa and Torino INFN sections
- The first aim of the test is to monitor the physiology change in the patient between the series (~30) of irradiation sessions
- Crucial the knowledge of the fragment production features



V. Ferrero et al. (2018) Sci. Rep. 8

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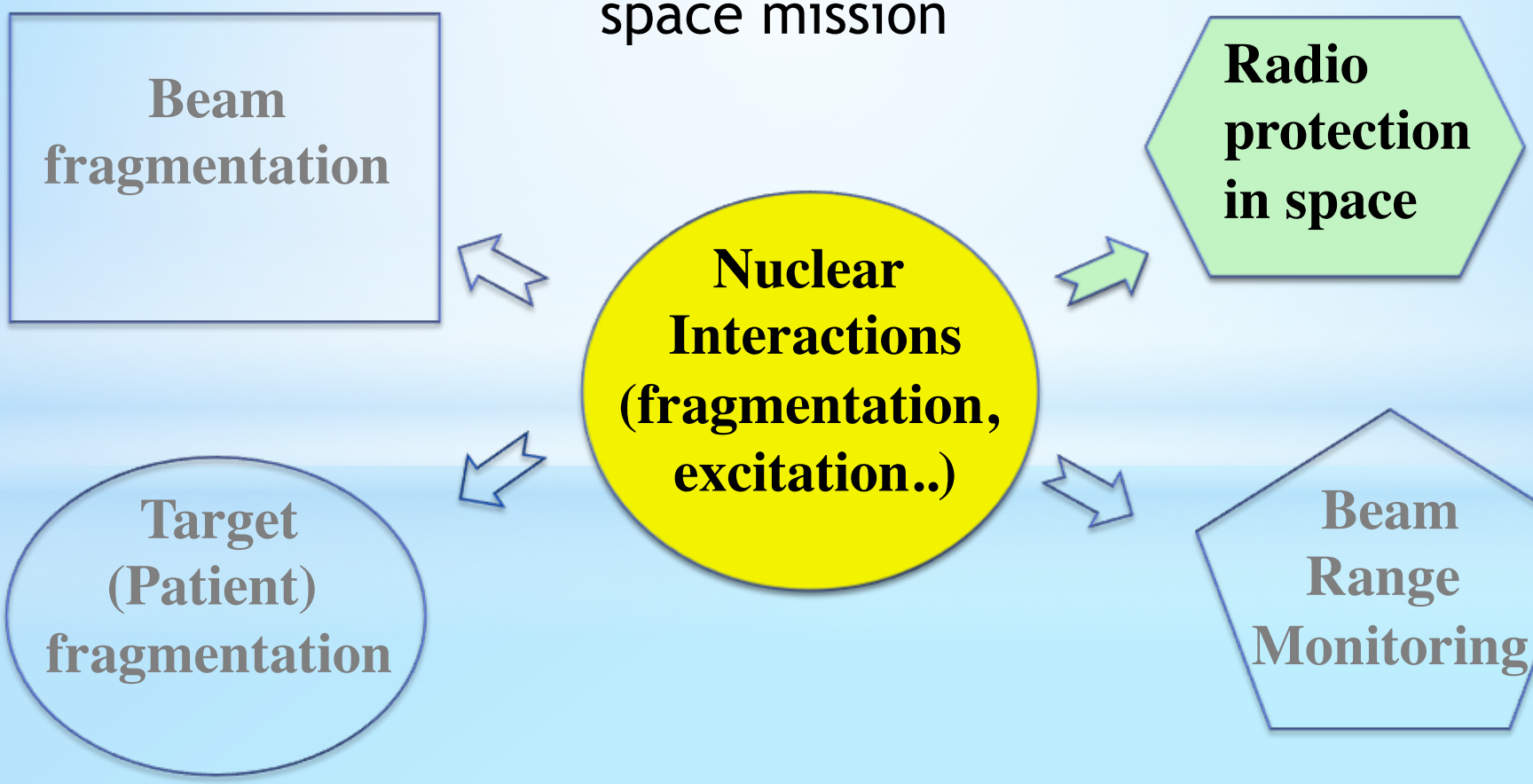
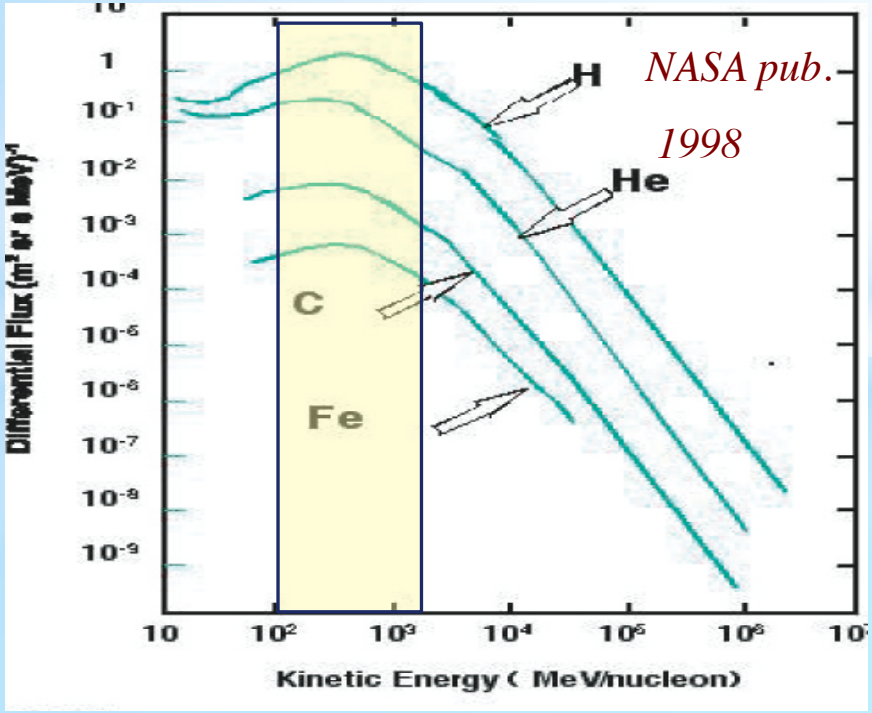


From treatment room to space

Long term mission ()Mars) : the astronauths will be exposed to Galactic Cosmi 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

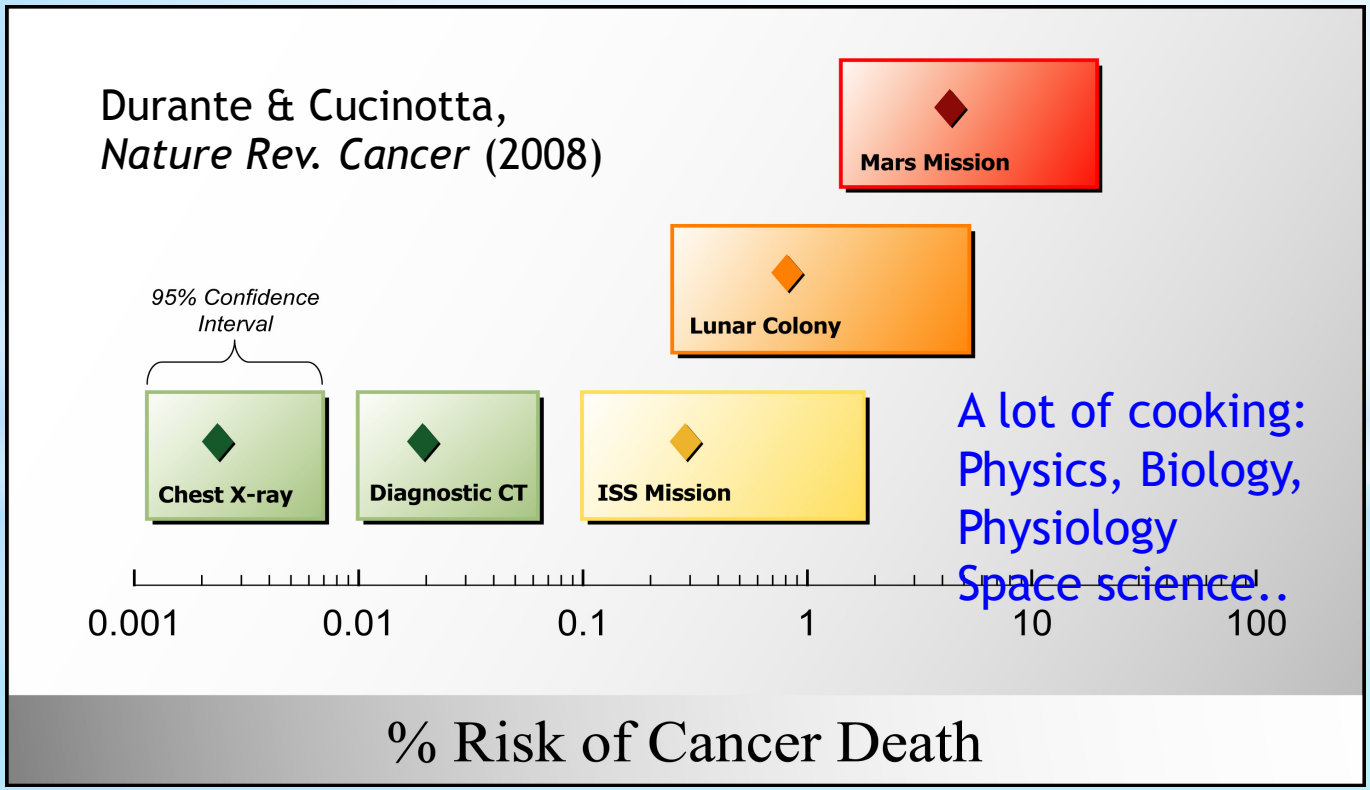


spectrum: 87% protons, 12% He ions and 1% heavier ions (mainly O,C,N) with peaks at 0,7- 1 GeV/n

flux: ~4 particles/(cm^2 s) at solar min.

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



A lot of cooking: Physics, Biology, Physiology Space science..

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

“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 or hydride/polymer composites

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

The best shield material is the same of 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 (below 1 GeV/nucl)

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

Nagoya University (Japan), GSI (Germany)

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

10 INFN sections/labs & most of the funding

More than 80 researchers, 60% permanent, 40 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:

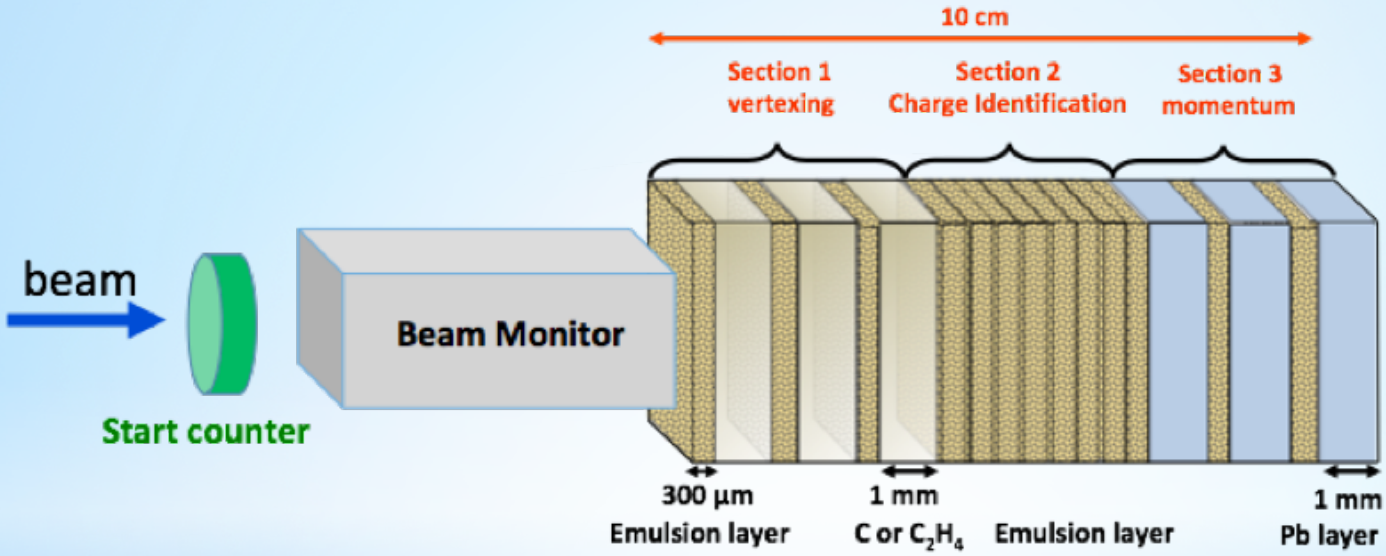
- Using C, C_2H_4 ➔ cross sections on C and H
- Using C, C_2H_4, PMMA ➔ cross sections on C, O and H

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 suggestions!!!

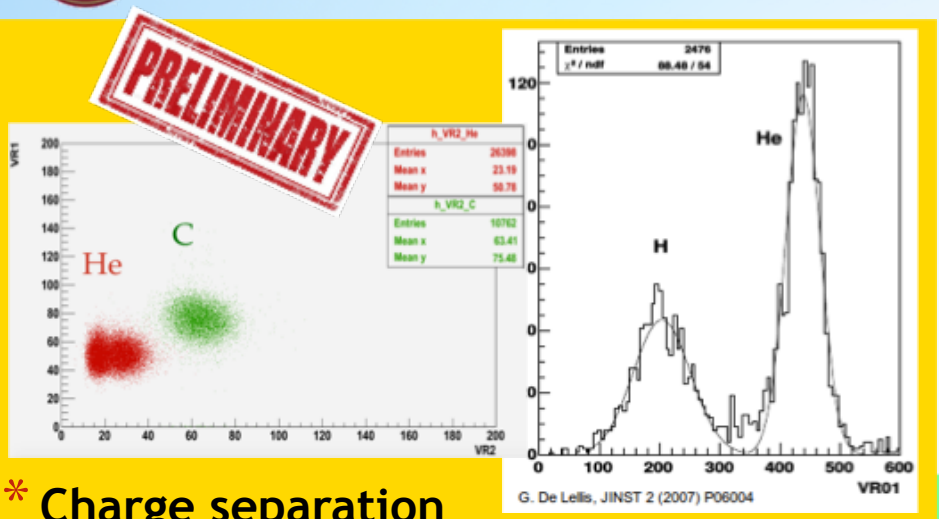
Light fragments:emulsion setup

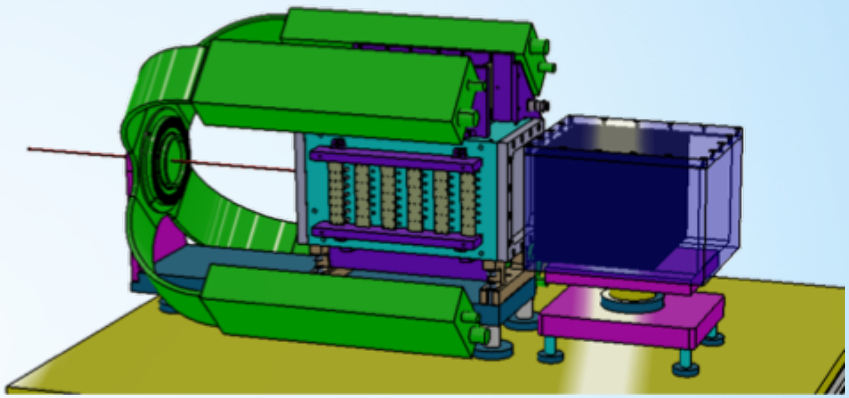


- ✓ Both target and detector integrated in a very compact setup
- ✓ Accurate reconstruction of the interactions inside the target (sub-micrometric resolution)
- ✓ Fragment charge detection eff > 99%
- ✓ Automated scanning system : very fast and with wide angular acceptances

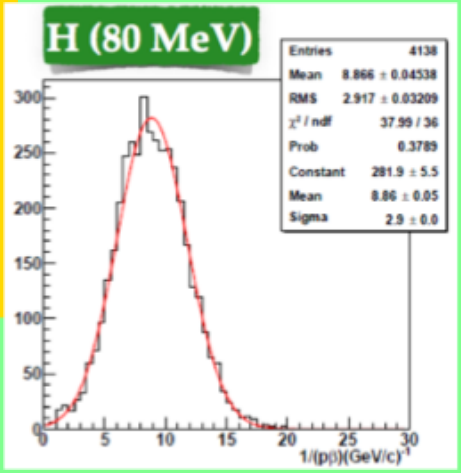
- optimised for light (Z≤3) fragments
- less than 1m: can be easily movable to fit the space limitations from experimental and treatment rooms
- angle setup: ±75°

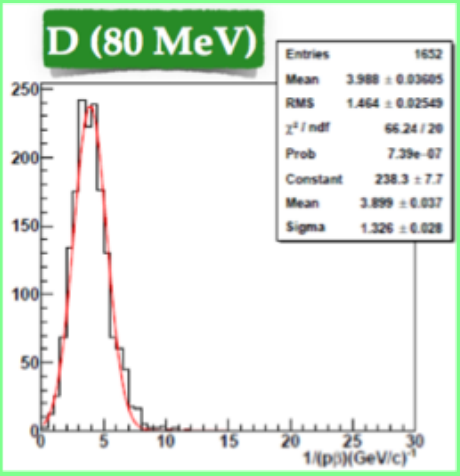
ECC performances





* **Charge separation**
  - Z ∝dE/dx ∝ grain density ∝ track volume
  - **Charge identification efficiency ~ 99%**



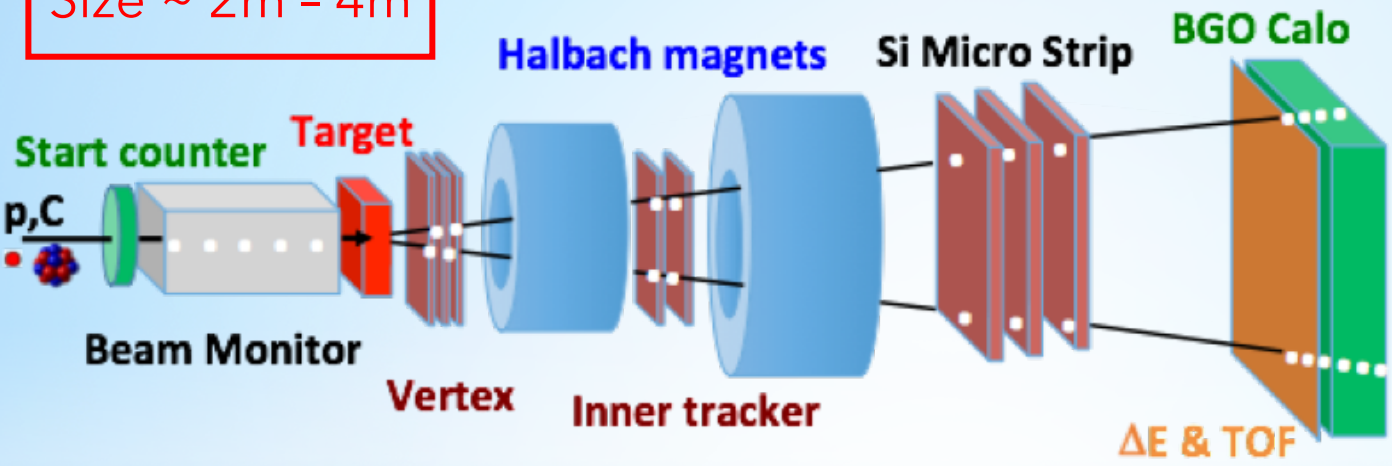


Test performed at LNS p, ^{4}He and ^{12}C beams

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

The FOOT electronic setup

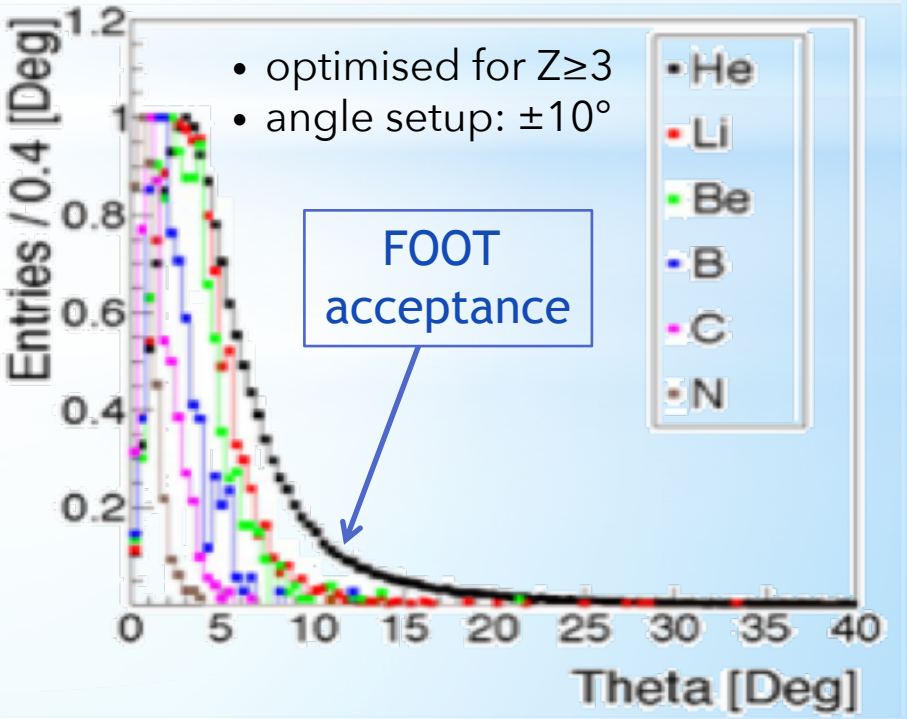
Size ~ 2m – 4m



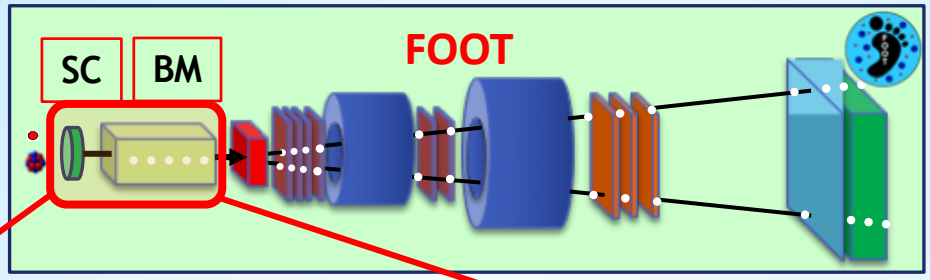
Target performances

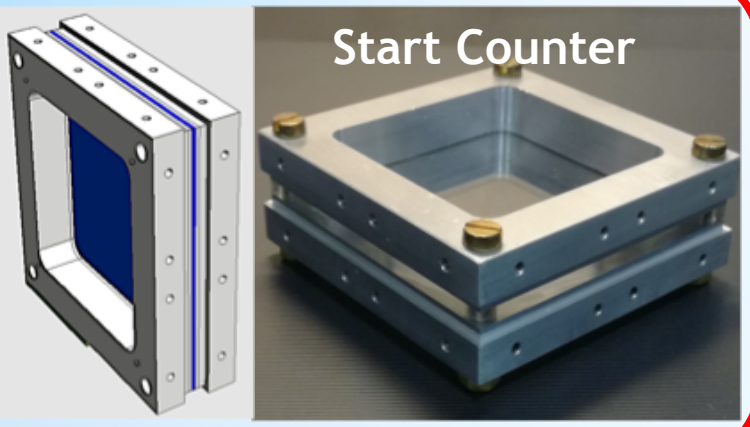
- $\Delta p/p$ <3.5%
- Δ_{TOF} <70ps
- $\Delta E_{kin}/E_{kin}$ <2%
- $\Delta(dE)/dE$ ~3%

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)

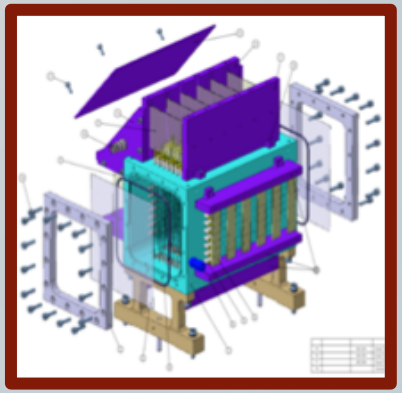


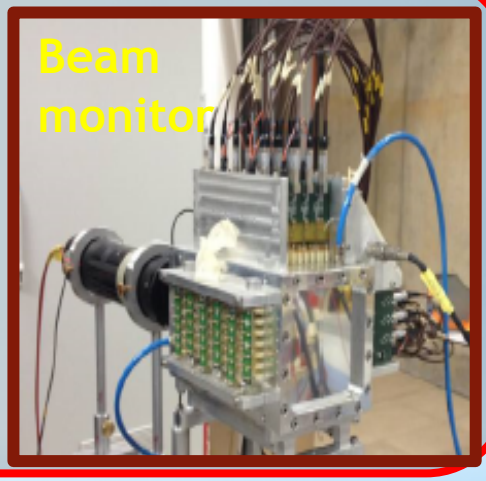
FOOT interaction region





Trigger and ToF start



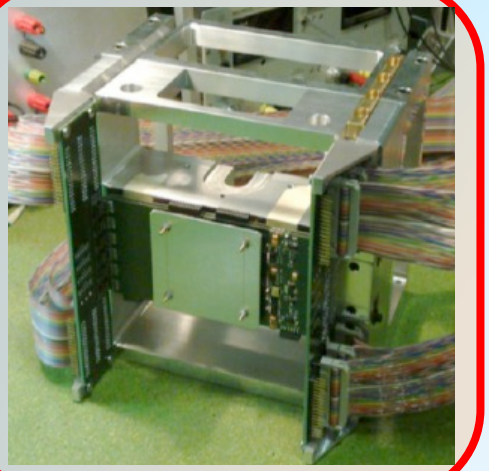


Beam position and direction

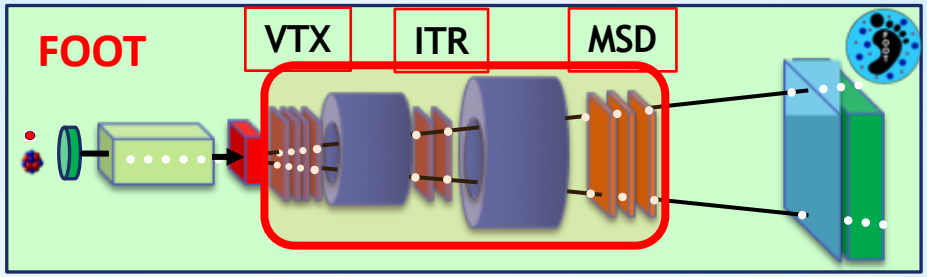
- 250 μm plastic scintillator read out by 48 SiPM (12/side)
- Readout by WFD at 5 Gsample/s.
- Time resolution: 65 ps for ^{12}C @ 200 MeV/nucl (CNAO beam)

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

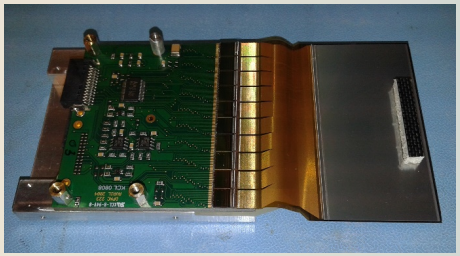
Tracking region



Vertex & Inner Tracker

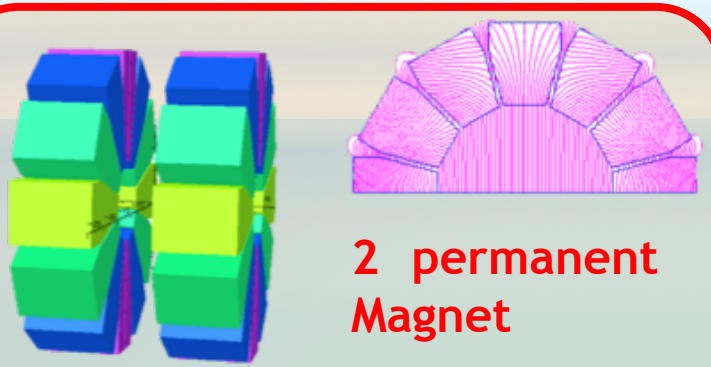


2 permanent magnets
Hallbach geometry
B field in y direction (max 1.1 T)



Micro Strip Detector

VTX: 4 layers of Si pixel (20 x 20 μm)
ITR: 2 layers of Si pixel (20 x 20 μm)

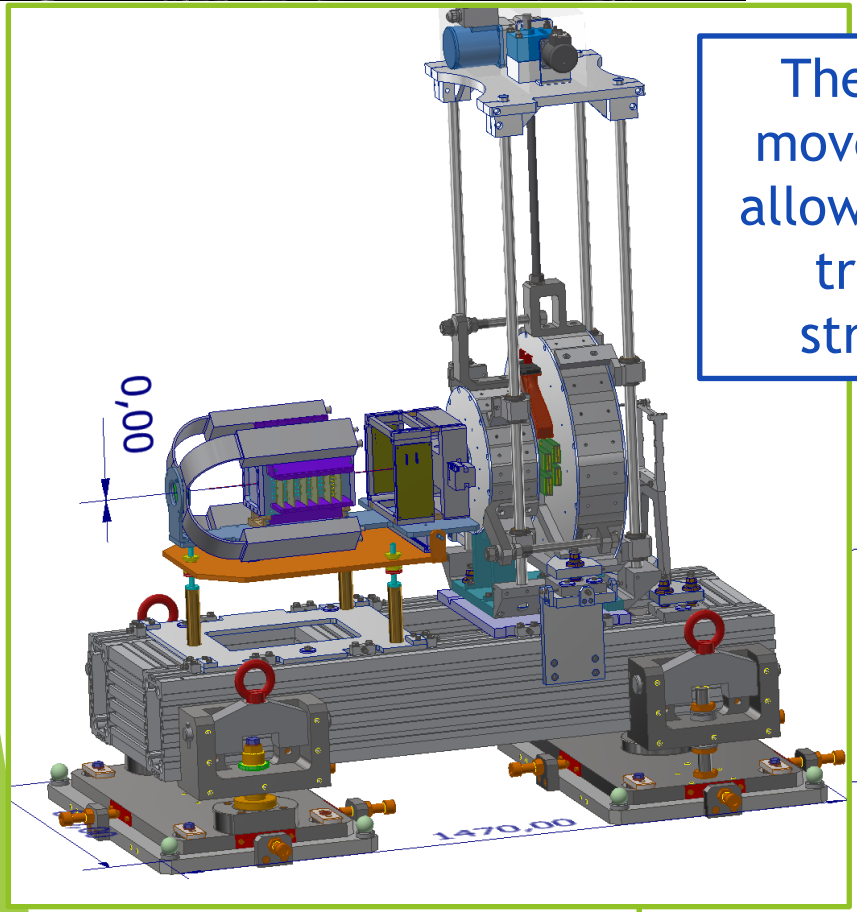


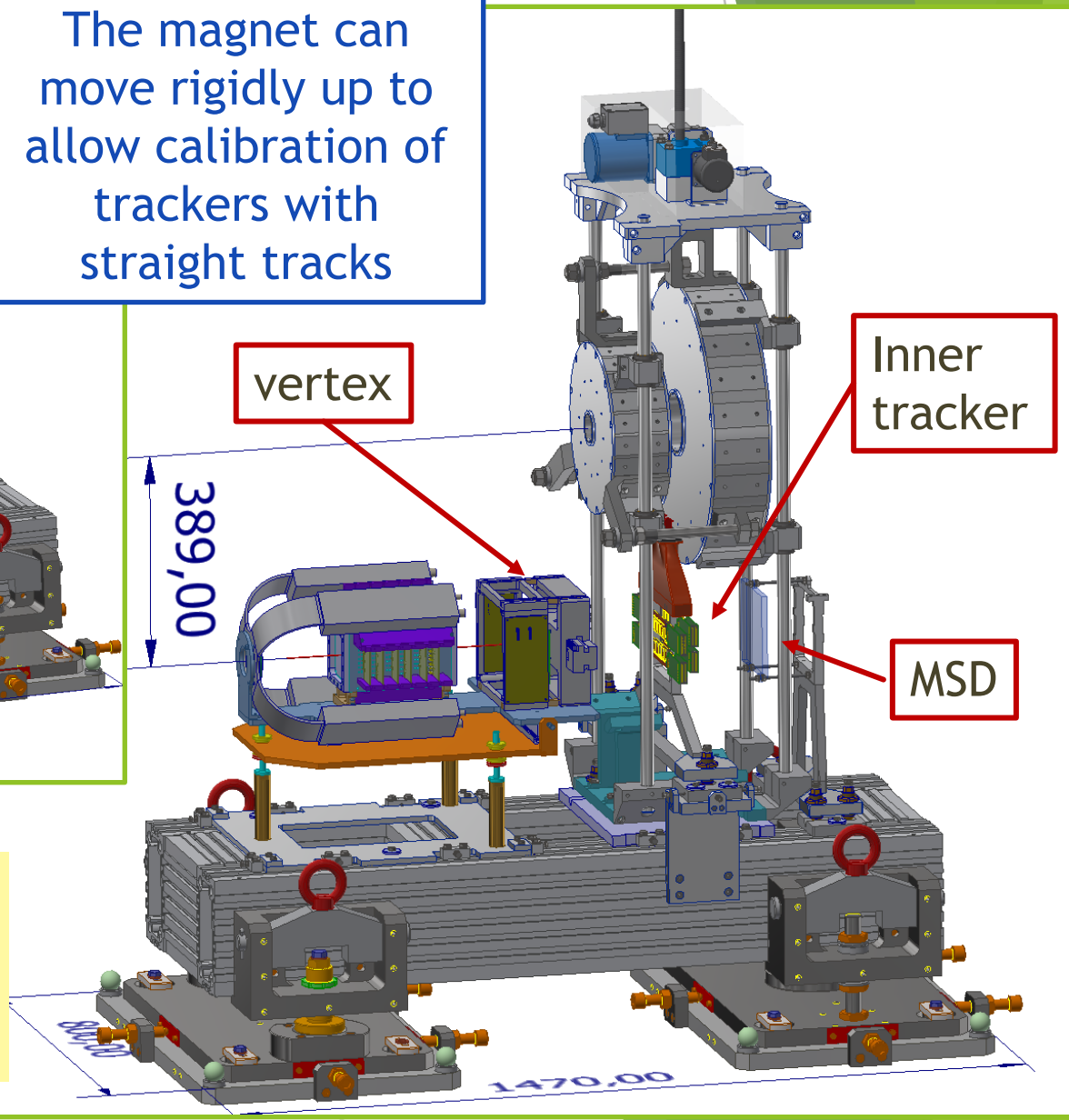
2 permanent Magnet

MSD:
3 layers of Si strips (120 μm x 9 cm)

Calibration with straight tracks

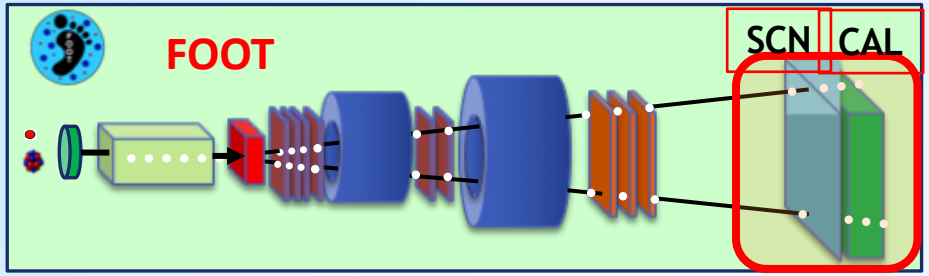
The magnet can move rigidly up to allow calibration of trackers with straight tracks

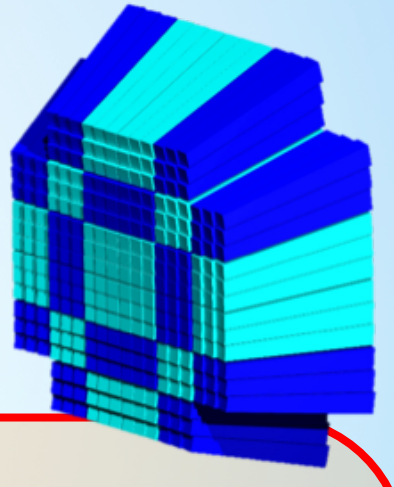




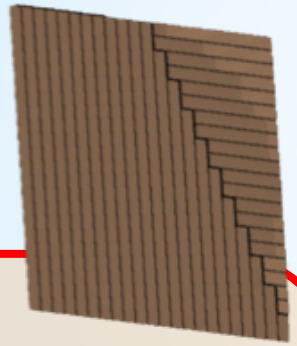
Mechanical structure derived from the ELI mechanics!!

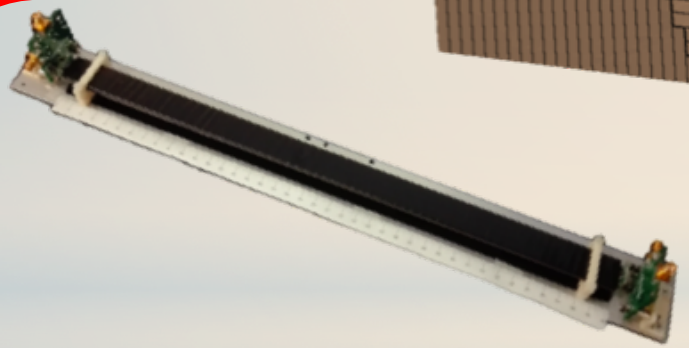
Downstream region





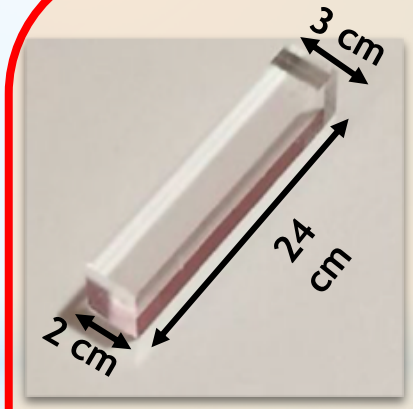
Plastic Scintillator ΔE/TOF measurement





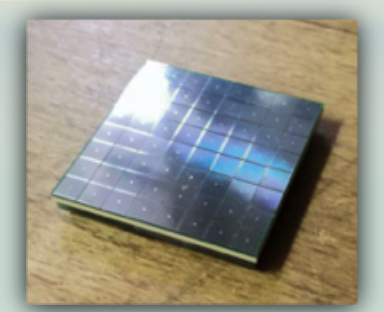
40 x 2 x 0,3 cm3 plastic scintillator bars
2 XY layers of 20 bars
Readout: 4 x 3mm^2 SiPM/bar
35 ps resolution @ 12C at 200 MeV/nucl (CNAO)

BGO Calorimeter



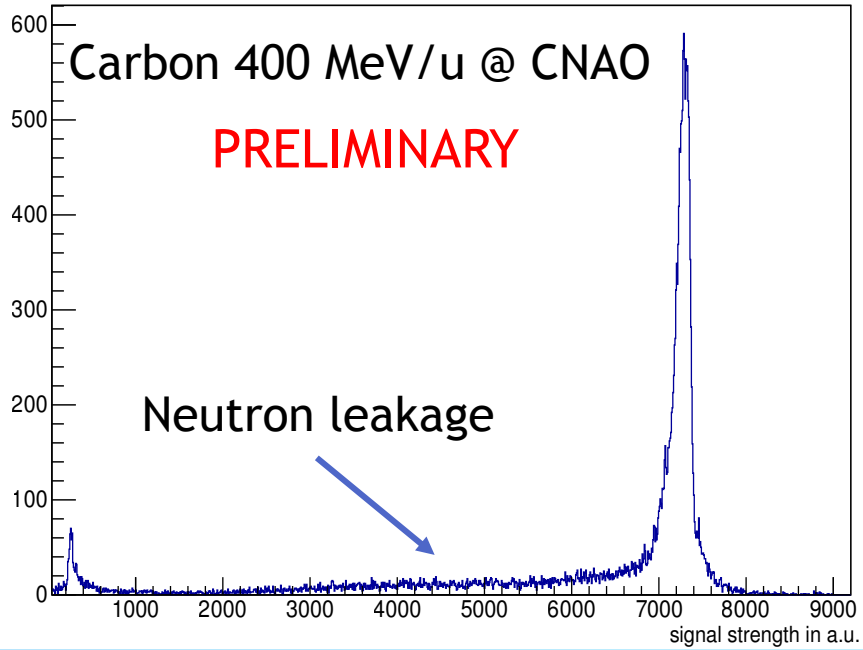
400 BGO crystals
Z_{eff} = 74
P_{BGO} = 7.13 *g/cm^3*
Weight = 1.027 kg
Total weight 330 Kg

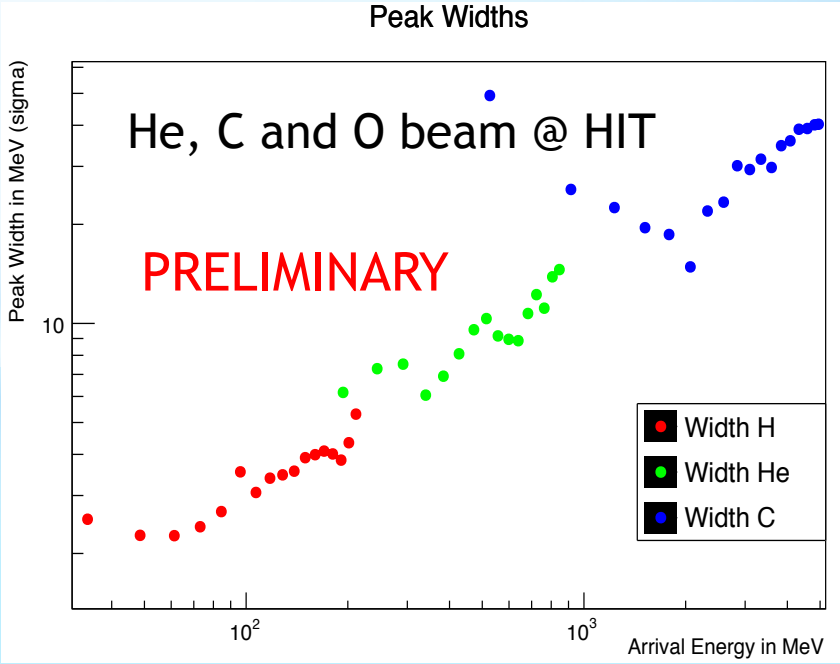
Readout:
SiPM 8x8 mm^2
cell 20 μm
Voltage breakdown 53 V



Calo test beam @ 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 fragmemnts)





Estimated performances: charge Z reconstruction

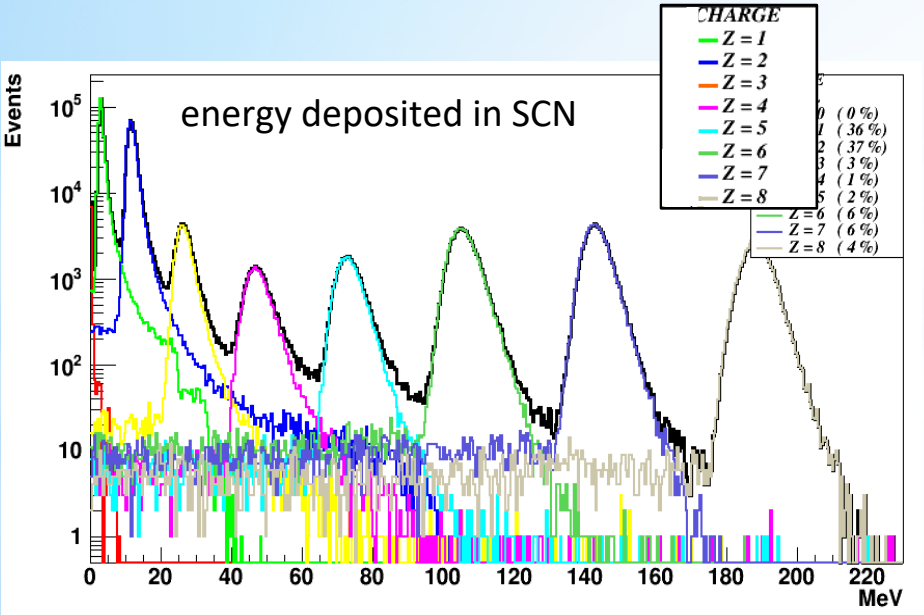
FLUKA simulation : ^{16}O (200 MeV/u)→ C_2H_4

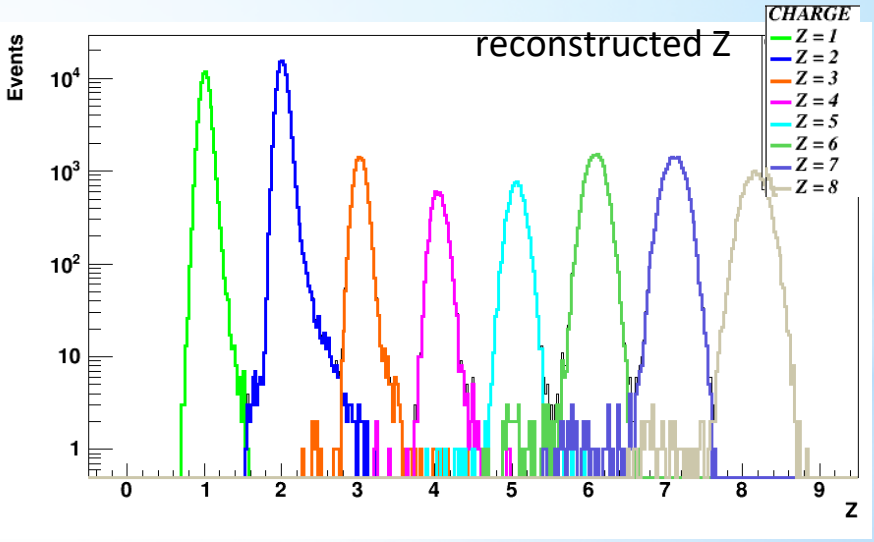
Fragment charge are derived from energy release in DE/TOF scintillator and from the fragment velocity

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

SCN

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

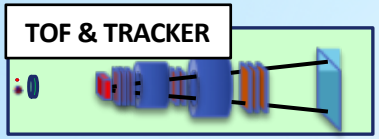
Estimated wrong charge assignment < 1%

Fragment Mass identification

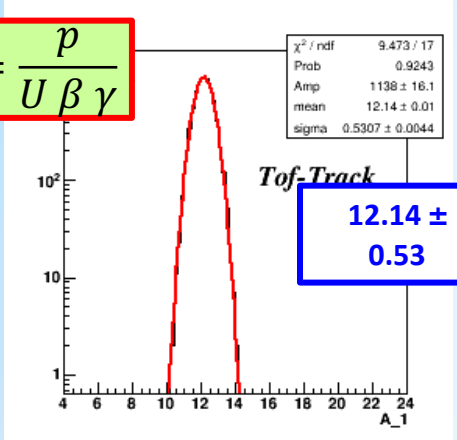
REDUNDANT Detector → 3 different ways to determine A

Fluka simul ^{16}O (200 MeV/u)→ C_2H_4

TOF & TRACKER

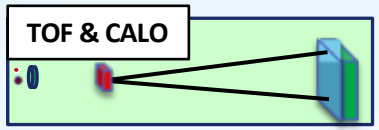


$$A_1 = \frac{p}{U\,\beta\,\gamma}$$

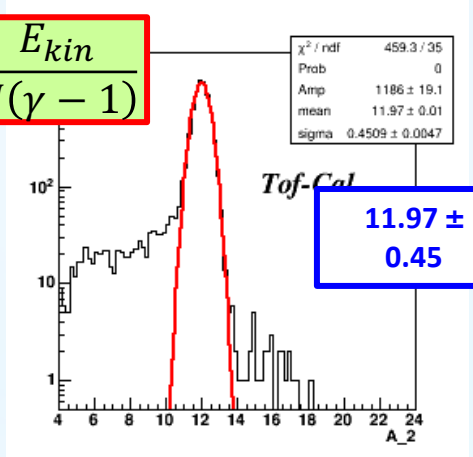


12.14 ± 0.53

TOF & CALO

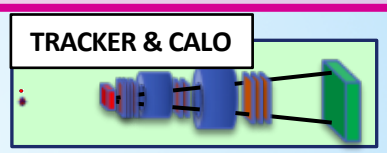


$$A_2 = \frac{E_{kin}}{U(\gamma - 1)}$$

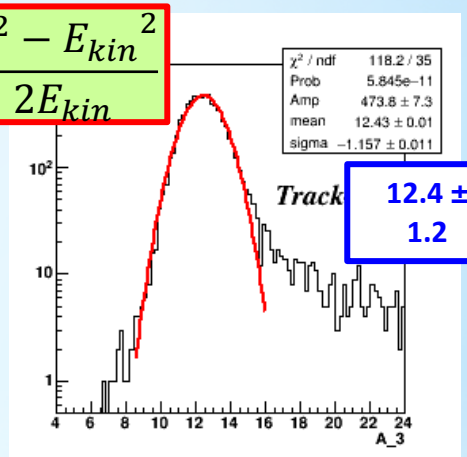


11.97 ± 0.45

TRACKER & CALO



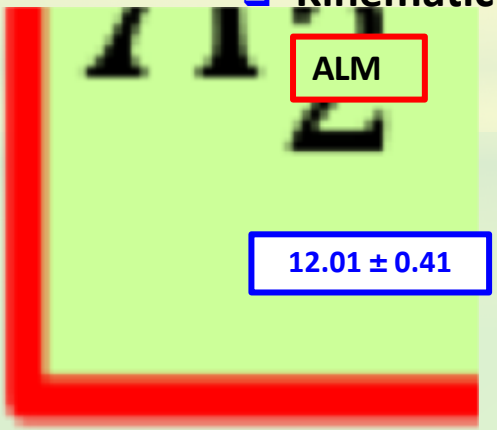
$$A_3 = \frac{p^2 - {E_{kin}}^2}{2E_{kin}}$$



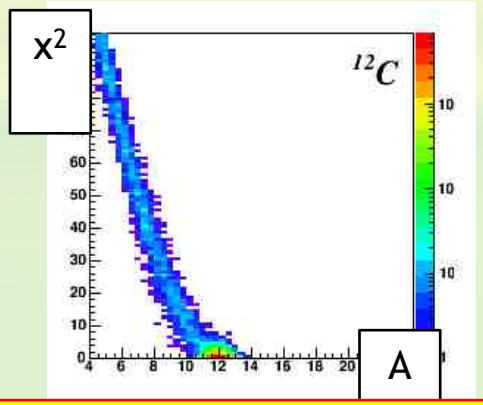
12.4 ± 1.2

- **Kinematic fit by Augmented Lagrangian (ALM)**

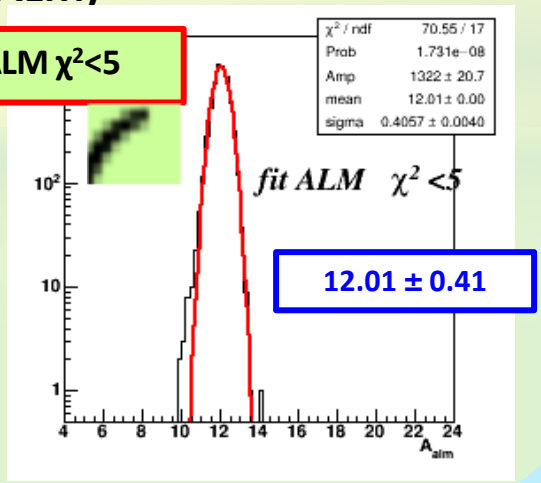
ALM



12.01 ± 0.41



ALM χ²<5



12.01 ± 0.41

Fit cut the wrong reconstructed fragments

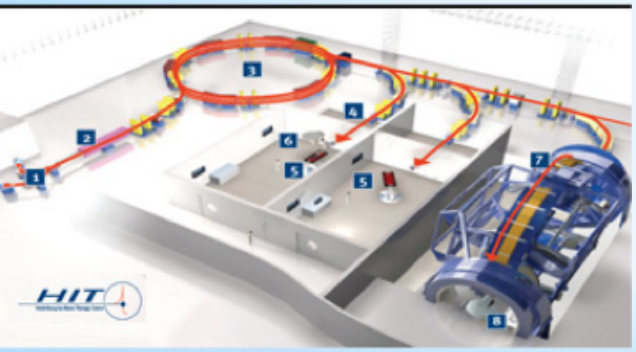
Future: bams, data taking & schedule

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

GSI : all beams

HIT : only up to 400 MeV/nucl

CNAO : only ^{12}C up to 400 MeV/nucl (since late 2019)



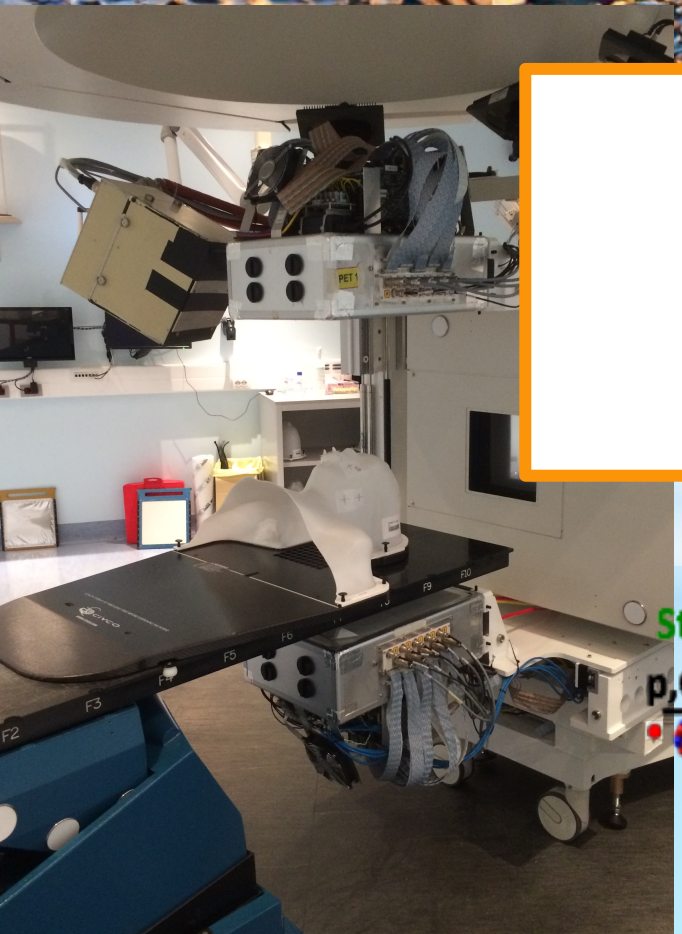
FOOT detector can be moved !!!

- First data taking at GSI in April 2019 with ^{16}O beam 200-700 MeV/nucl focused on emulsion (setup ready)
- The electronic setup will be completed mid 2020. (first engineering run in April 2019)
- Data taking campaign next year

Summary & conclusions

* Nuclear fragmentation has multiple impacts on Particle therapy : it can play a role in target fragmentation in proton therapy , beam fragmentation and possibly beam monitoring 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 old style nuclear physics whose physics program, devoted to the measurement of the relevant fragmentation cross section, can directly address these PT and RPS related issues

SPES
exotic beams for science



Thanks...