



**VI Scuola Nazionale "Rivelatori ed Elettronica per Fisica delle  
Alte Energie, Astrofisica, Applicazioni Spaziali e Fisica Medica  
INFN Laboratori Nazionali di Legnaro, 23-27 Marzo 2015**

**Rivelatori di frammentazione di  
particelle: applicazioni nello Spazio  
e in terapia**

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# Outline

Bouncing from fundamental physics to applied physics and back...



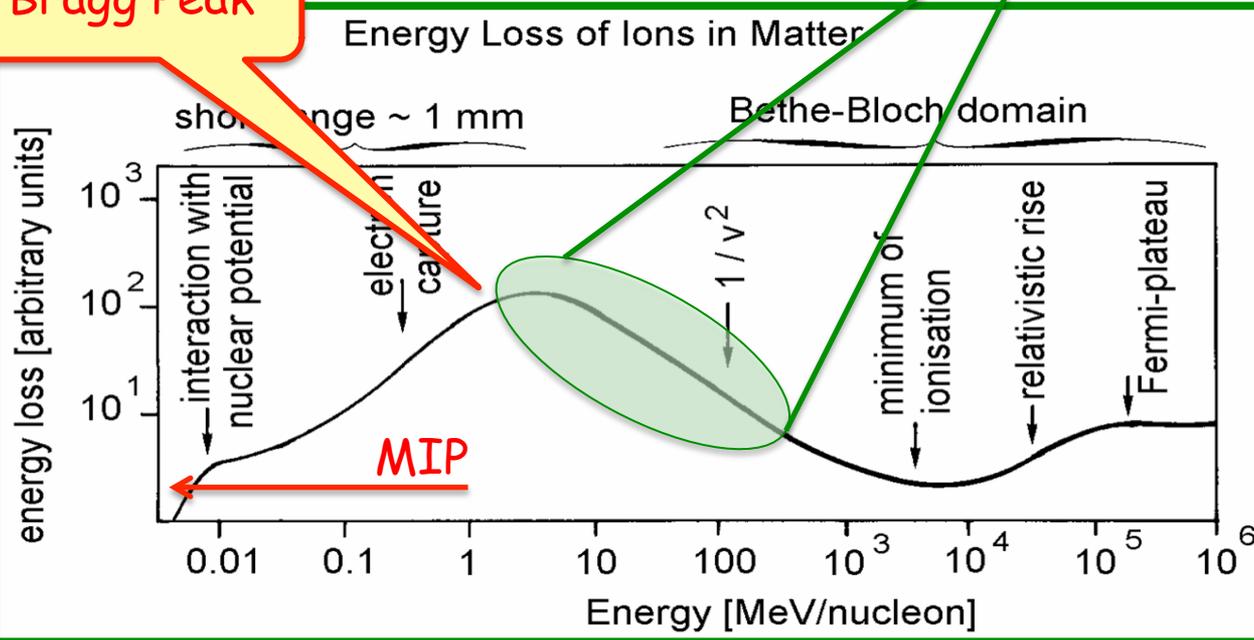
- Overview: fragmentation in PT and space
- Some recent fragmentation experiment
- Fragmentation & dose monitoring
- Summary and conclusions



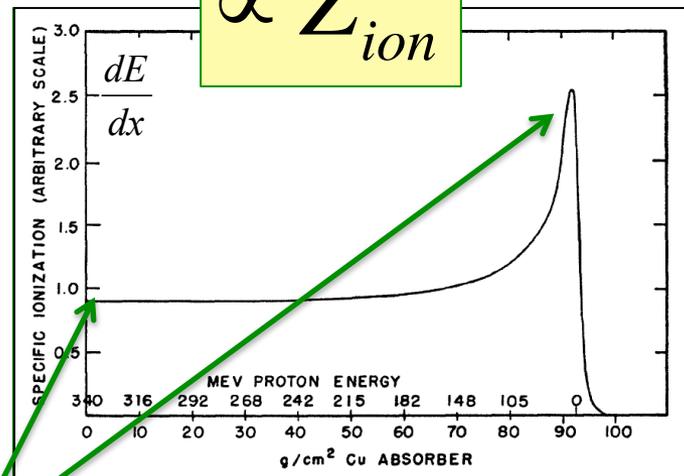
# Particle Therapy vs Particle Physics point of view

The release of energy by charge particles has very attractive features... why not to use them?

**Bragg Peak**



$$\propto Z_{ion}^2$$



lunghezza di penetrazione

Perfect to release energy (dose) in a tumor buried inside the patient, like a depth bomb..

Mostly proton, few  $^{12}\text{C}$  beams.

Future  $^4\text{He}$ ,  $^{16}\text{O}$ ?



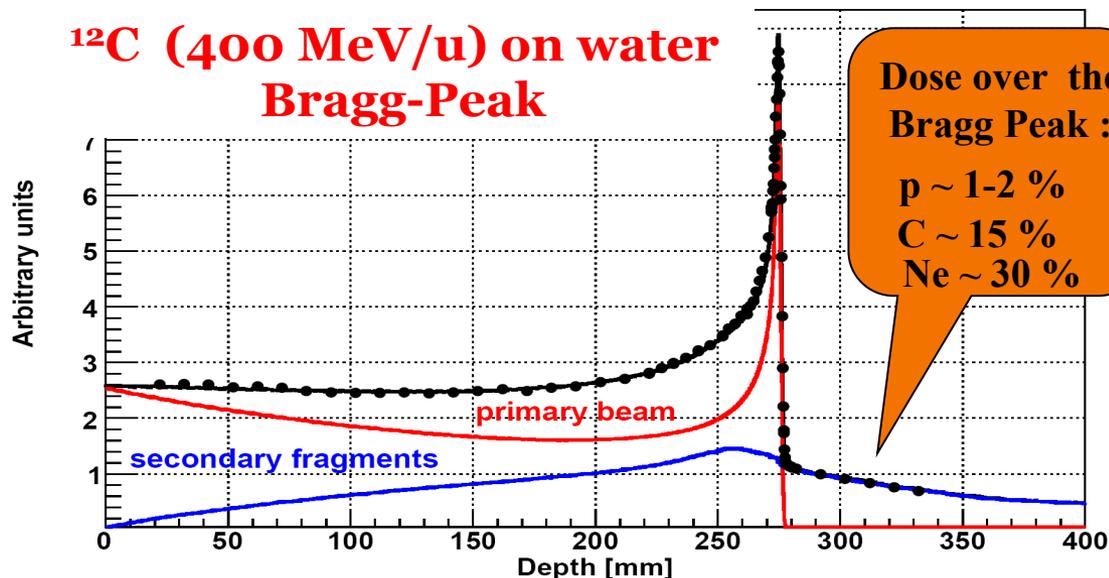
# Heavier is better? -> Fragmentation!

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*

**$^{12}\text{C}$  (400 MeV/u) on water Bragg-Peak**

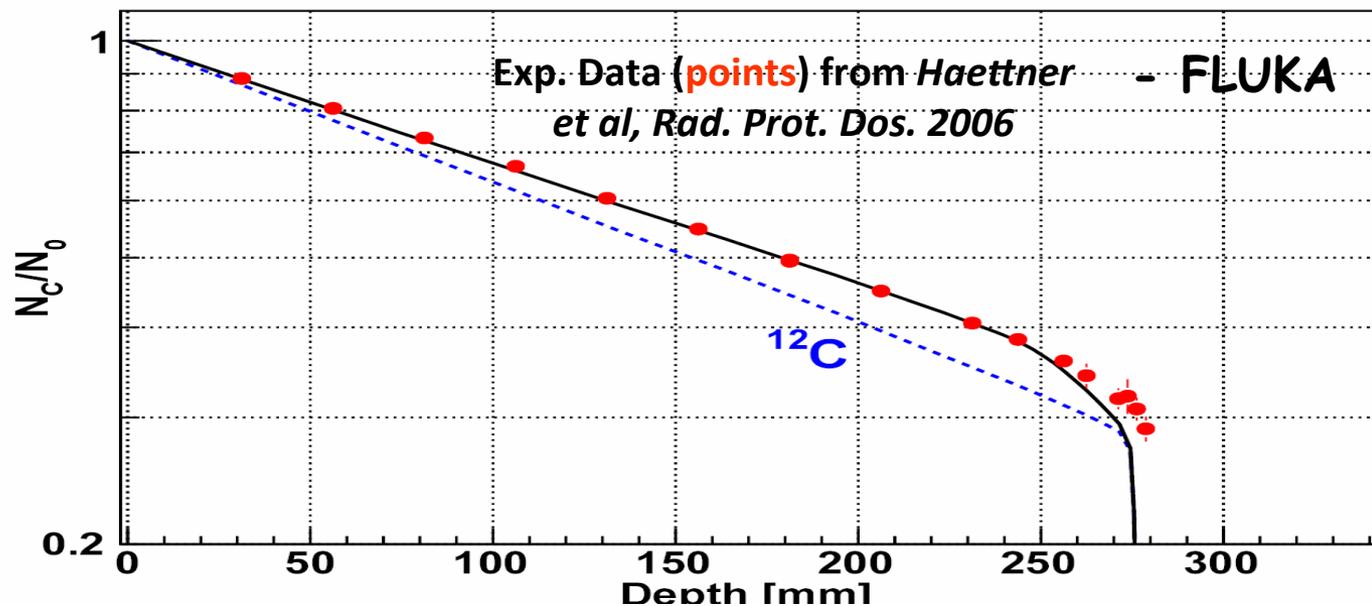


Exp. Data (points) from Haettner et al, Rad. Prot. Dos. 2006

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



# 400 MeV/n $^{12}\text{C}$ on water: Attenuation of the primary beams



The **70 %** of the carbon ions undergo nuclear reactions altering considerably the radiation field

Fragmentation rules out beams heavier than Oxygen and must be carefully taken into account in TPS even for  $^{12}\text{C}$



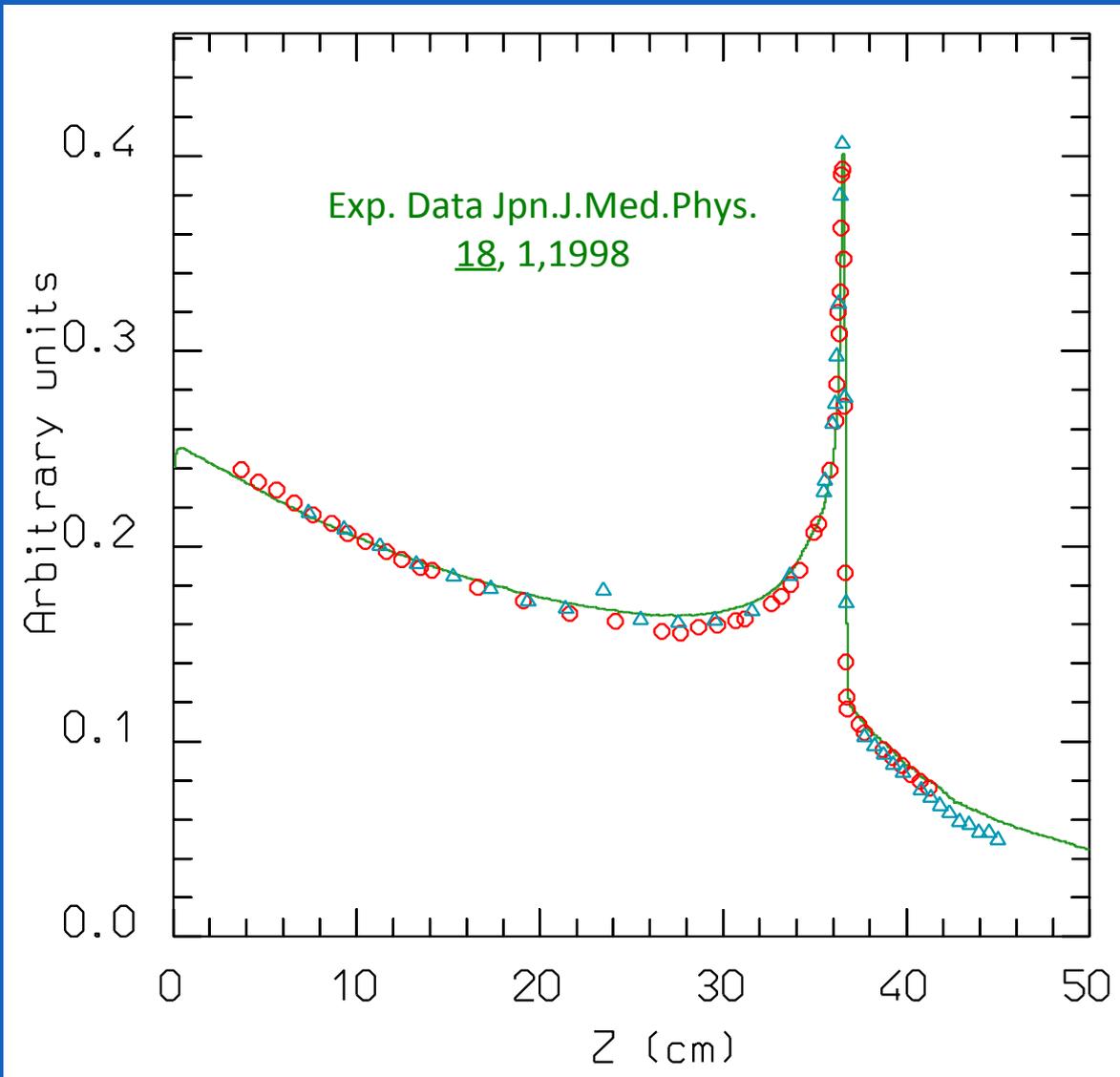
# Fragmentation of $^{20}\text{Ne}$ @ 670 MeV/n

Dose vs depth distribution for 670 MeV/n  $^{20}\text{Ne}$  ions on a water phantom.

The green line is the FLUKA MC prediction

The symbols are exp data from LBL and GSI

Huge dose contribution after the BP due to fragment



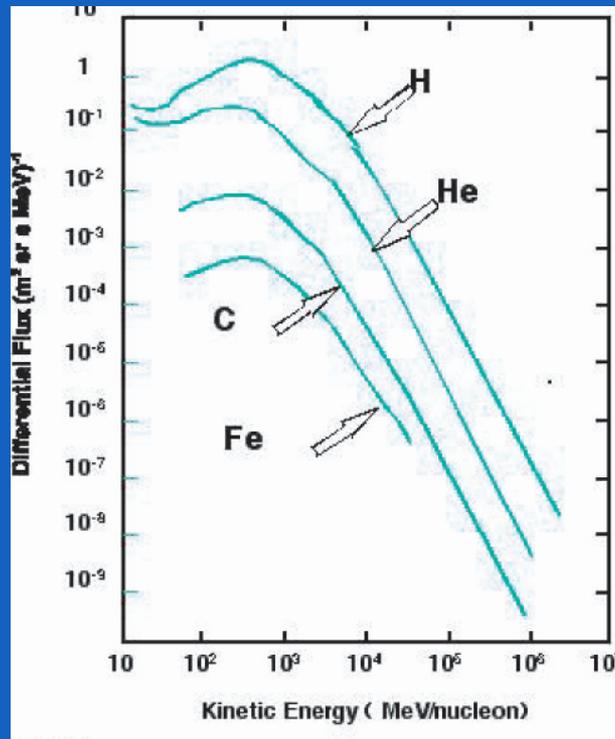


# Fragmentation in space

## Galactic Cosmic Rays

**spectrum:** 87% protons, 12% He ions and 1% heavier ions (in fluence) with peaks at 1 GeV/n

**flux:**  $\sim 4$  particles/(cm<sup>2</sup> s) at solar min.



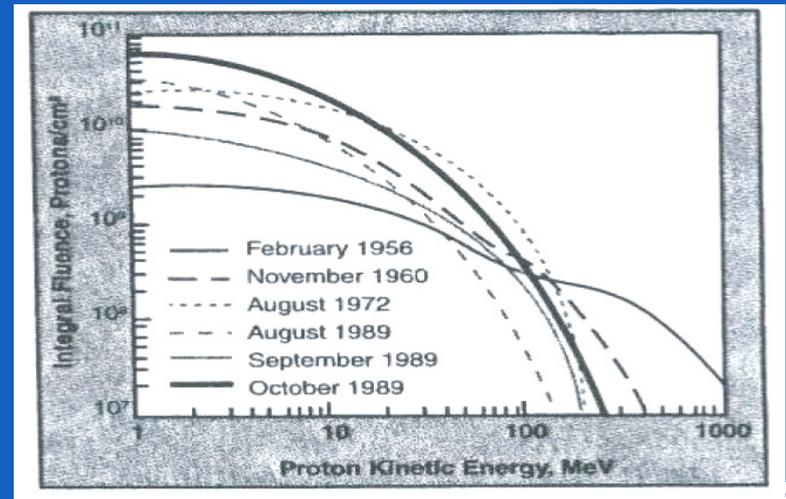
*NASA pub. 1998*

## Solar Particle Events

**spectrum:** 90% protons, 10% heavier ions with energy mainly below  $\sim 200$  MeV

**flux:** up to  $\sim 10^{10}$  particles/cm<sup>2</sup> in some hrs.

**dose:** order of Sv, strongly dependent on shielding and organ



Courtesy of Alfredo Ferrari

*NASA pub. 1998*



# Dose rates in space missions

*Shuttle*



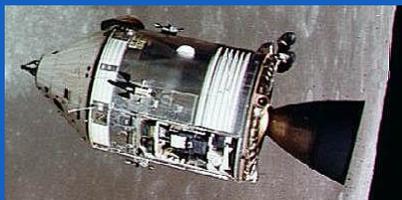
0.23 mSv/day

*ISS*



0.5-1 mSv/day

*Apollo*



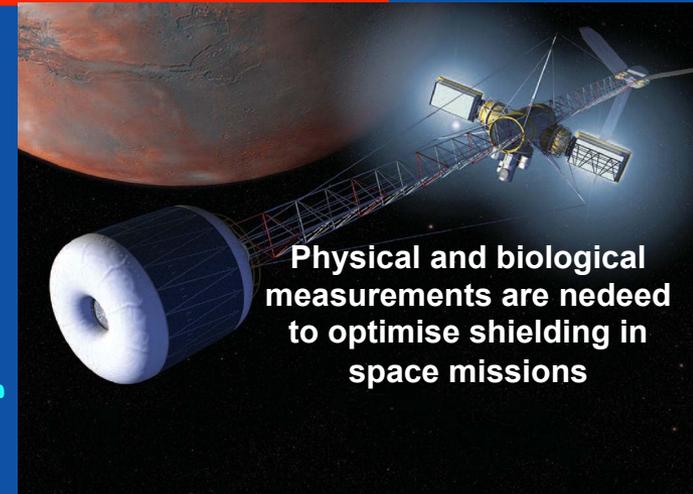
0.3 mSv/day

**by comparison:** an intercontinental flight rarely implies doses larger than 0.1 mSv; the radiation background on Earth is  $\approx$  mSv/year

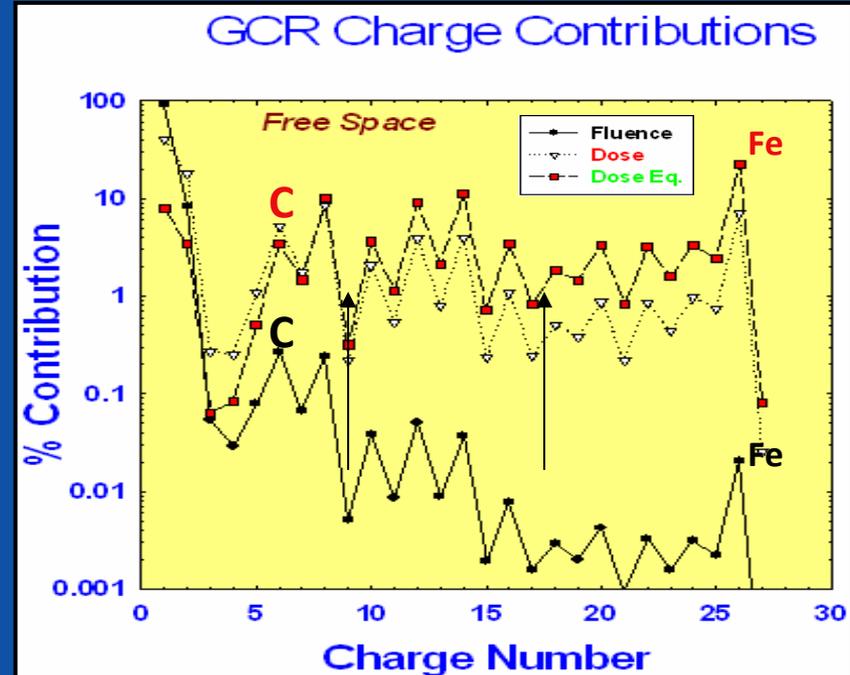
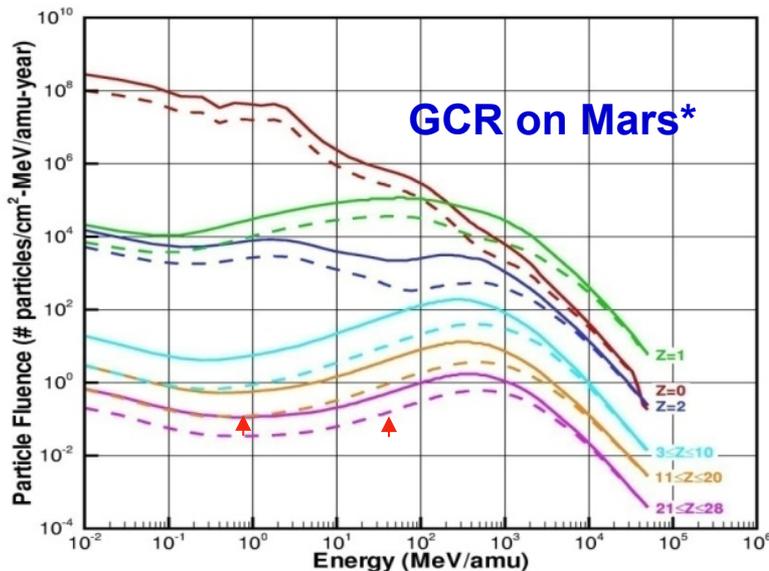


# Radioprotection & shielding

- Shielding are needed to have the possibility of long space missions.
- GCR fragmentation on the shielding must be carefully be taken into account, both for astronauts and for equipments



Physical and biological measurements are needed to optimise shielding in space missions

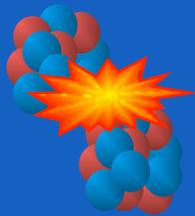




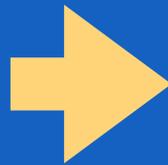
# Fragmentation features at 100-500 MeV/nucI

- Disclaimer.. Experimental point of view!!
- Standard ablation-abrasion process

Projectile (light ion)



Target (O,H,C.. Si,Al)



target fragment



projectile fragment



New mixed inner radiation field !

Interaction of the projectile with the patient body or the spacecraft hulls, etc..

## **Target Fragments**

- ... lower charge than target
- ... high LET
- ... short ranges

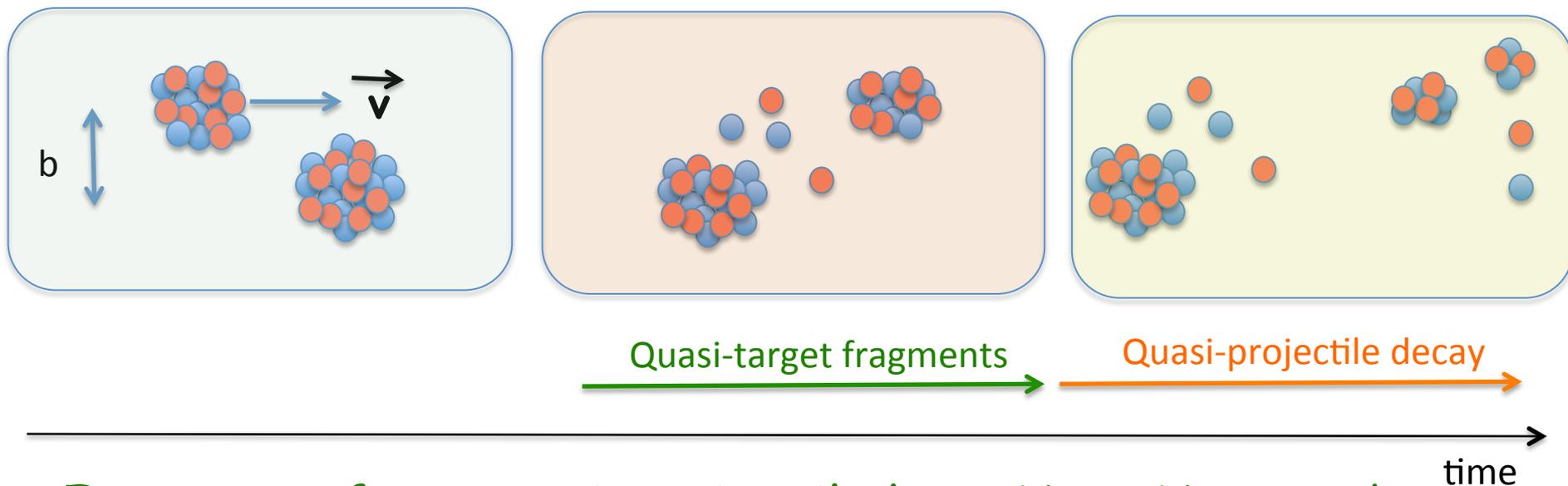
## **Projectile fragments**

- ... lower charge than primaries
- ... mixed LET
- ... long ranges

**NB !!: Only target fragmentation for proton beam/projectile !!!!**



# The ablation-ablation paradigm & PT



- Fragments from quasi-projectile have  $V_{\text{frag}} \sim V_{\text{beam}}$  and narrow emission angle. Longer range than beam
- The other fragments have wider angular distribution but lower energy. Usually light particles (p,d,He )
- The dose beyond the tumor distal part comes from the quasi projectile contribution. Wide angular halo from the rest of the process



# "Typical" modeling of nuclear interactions:

Target nucleus description (density, Fermi motion, etc)



Glauber-Gribov cascade with formation zone



(Generalized) IntraNuclear cascade



Preequilibrium stage with current exciton configuration and excitation energy  
(all non-nucleons emitted/decayed + all nucleons below 30-100 MeV)



Evaporation/Fragmentation/Fission model



$\gamma$  deexcitation

t (s)

$10^{-23}$

$10^{-22}$

$10^{-20}$

$10^{-16}$



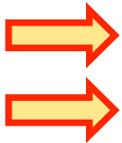
# "Typical" modeling of nuclear interactions:

Target nucleus description (density, Fermi motion, etc)



Glauber, Goldstone, ...

- Cross sections: absorption/quasi-elastic
- Transition from single to multiple chains/collisions
- Onset of formation zone
- Fast light fragments
- (Pion interactions below 1 GeV)
- (In medium cross-sections)



Preequilibrium stage with current exciton configuration and excitation energy  
(all non-nucleons emitted/decayed + all nucleons below 30-100 MeV)



- Spin and parity...
- Statistical multi-fragmentation or binary emission?



$\gamma$  deexcitation



t (s)

$10^{-23}$

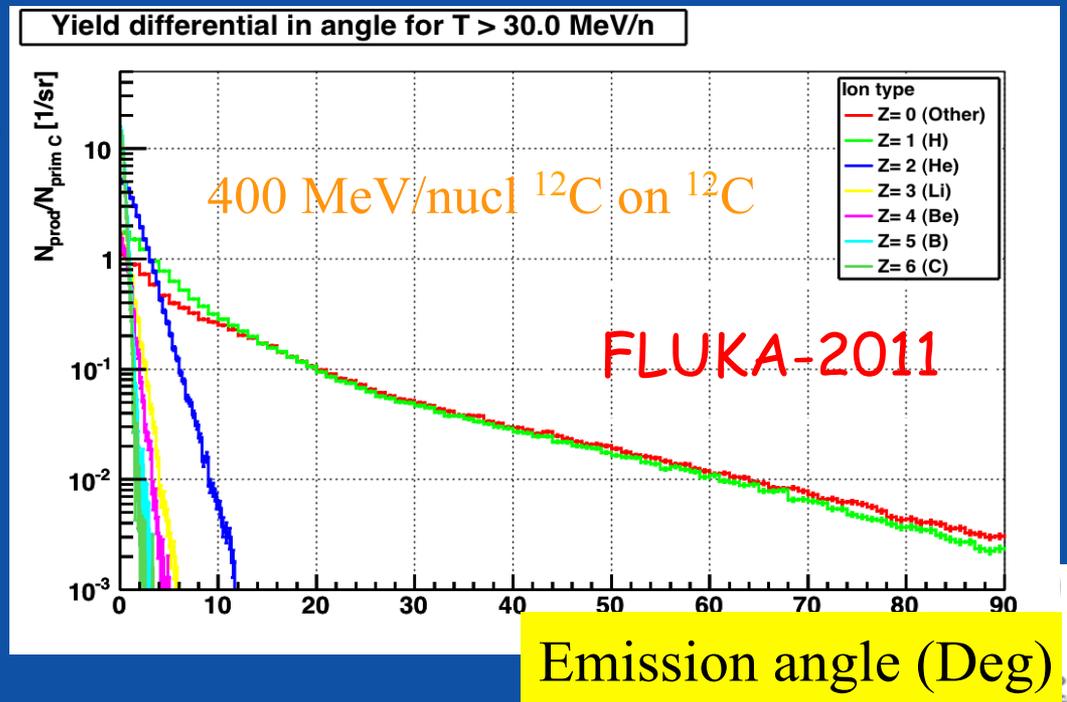
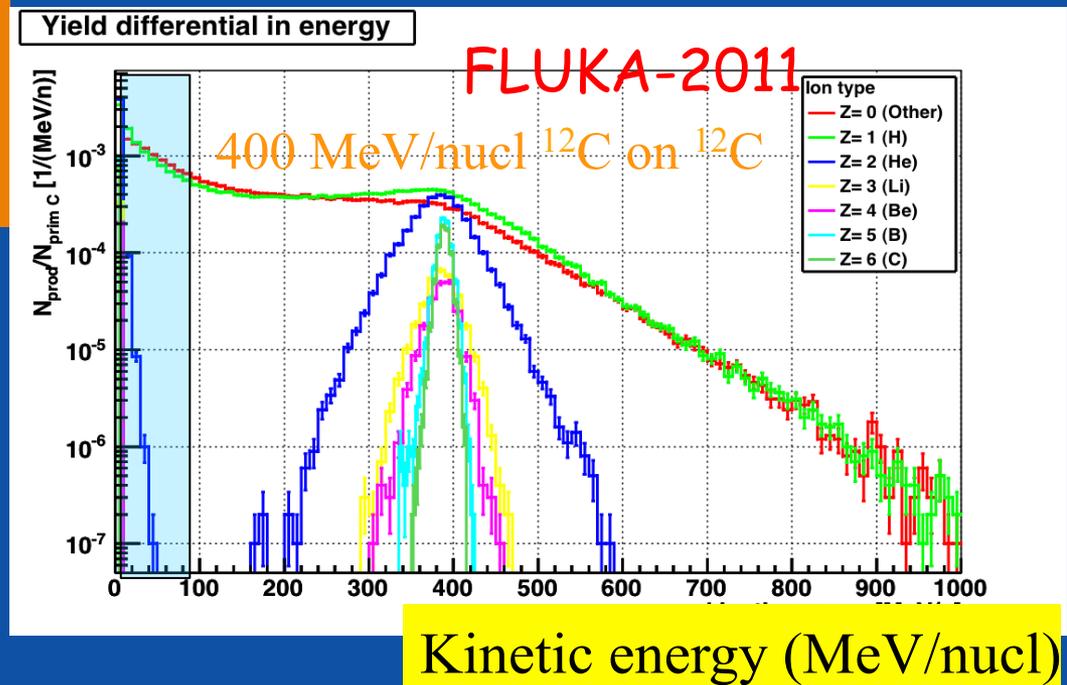
$10^{-22}$

$10^{-20}$

$10^{-16}$

# Typical example: $^{12}\text{C}$ beam on $^{12}\text{C}$ target

- The  $Z > 2$  produced fragments approximately have the same velocity of the  $^{12}\text{C}$  beam projectiles and are collimated in the forward direction
- The protons are by far the most abundant fragments with a wide  $b$  spectrum  $0 < \beta < 0.6$  and with a wide angular distribution with long tail
- The  $Z=2$  fragment are all emitted within  $20^\circ$  of angular aperture
- The  $DE/DX$  released by the fragment spans from  $\sim 2$  to  $\sim 100$  m.i.p.



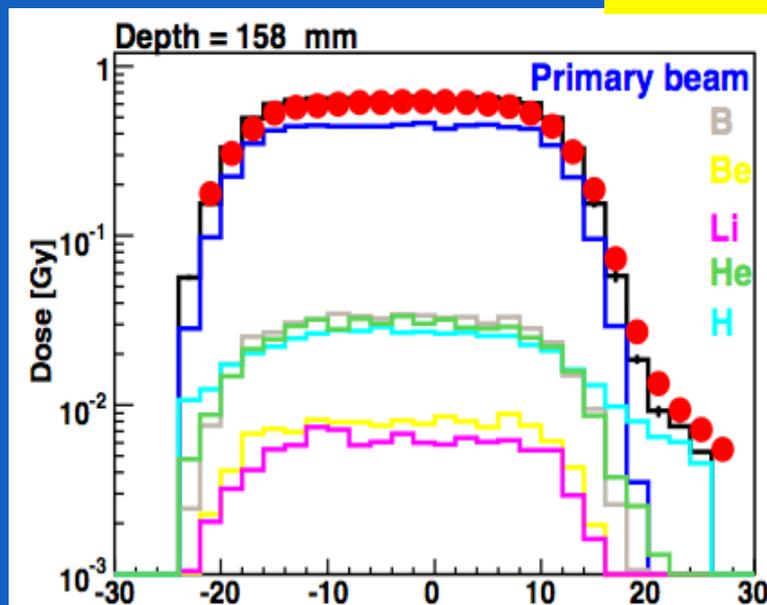


# Fragmentation & PT: Beam broadening

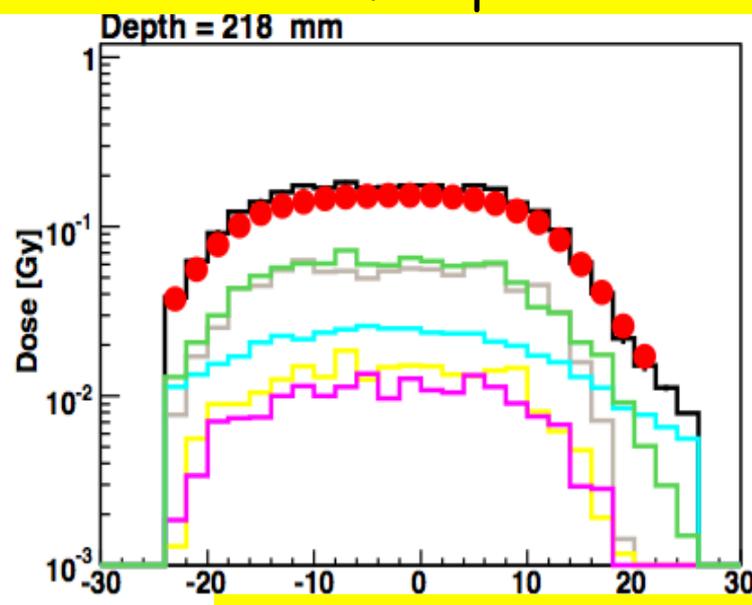
The secondary fragments, especially the lighter ones such H and He, broad the lateral dose profile.

Effect gets more and more important approaching, and going beyond, the Bragg Peak i.e. the tumor region

SOBP centered at 20 cm depth in water



Lateral displacement(mm)



Lateral displacement(mm)

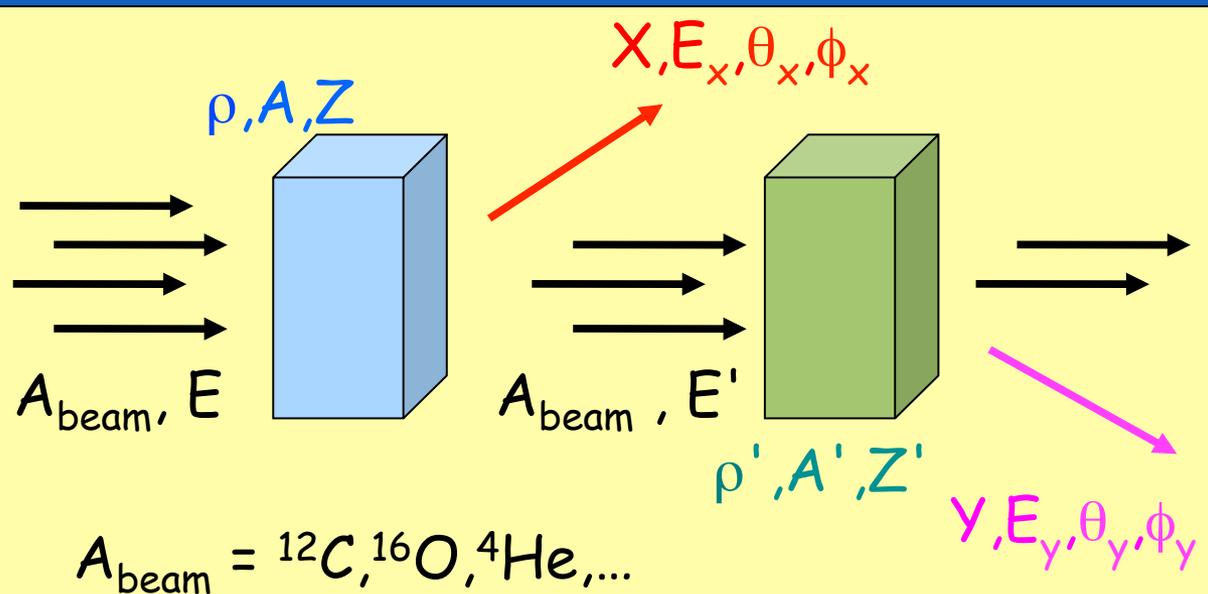
Data: S. Brons & K. Parodi (GSI)  
MC-FLUKA: A. Mairani PhD Thesis 2007 Pavia



# What we still miss to know about light ions fragmentation in 2015?

Data exist at  $0^\circ$  or on thick target. But we need to know, for any beam of interest and on thin target:

- Production yields of  $Z=0,1,2,3,4,5$  fragments
- ✗  $d^2\sigma/d\theta dE$  wrt angle and energy, with large angular acceptance
- ✗ For any beam energy of interest (100-500 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!!



# Fragmentation, TPS, MonteCarlo and all that..

- The nuclear interaction description are embedded in the **Treatment Planning System** through a "physical" DB generated on the basis of a **Interaction Model** (by analytical computation or MC code) where the energy releases and the fragment produced by the beam are stored. Thus the benchmarking of the MC with the measurements are getting more and more important due to:
  - ✓ Better representation of the nuclear interaction model wrt analytic calculation
  - ✓ Natural and easy 3D treatment of physics processes
  - ✓ More accurate patient representation wrt w.e. approach
  - ✓ Possibility of exploiting PET online
  - ✓ Easily taken into account the beam features

**KEY ISSUES: reliability of physics models -> must be tuned on data**



# MC for TPS: what is on the market?

The list is absolutely not exhaustive

- ◆ **EGS4, EGSnrc, ETRAN, PENELOPE**: electron and photon
- ◆ **MCNP** : only electron, photon and neutron
- ◆ **VMCpro, ISTAR, MCNPX**: only for proton. parametrised nuclear int
- ◆ **Geant4 , PHITS, FLUKA** : general purpose, transport any particle from photon to heavy ion → **suitable for  $^{12}\text{C}$  beam**
- ◆ **Geant4** : very large user community, optimised version for low energy, OO, flexible
- ◆ **We will use FLUKA as reference code: very accurate physics description, old style coding (FORTRAN).**

MC for physicist is like religion or favorite soccer team: you do not choose it , you are chosen by it, and once you are chosen, no way to change it !! ( see the G4 vs FLUKA religion war...)



# Data - MC comparison: $^{12}\text{C}$ ions

Build-up of charged fragments for  $^{12}\text{C}$  beam @400MeV/n in water

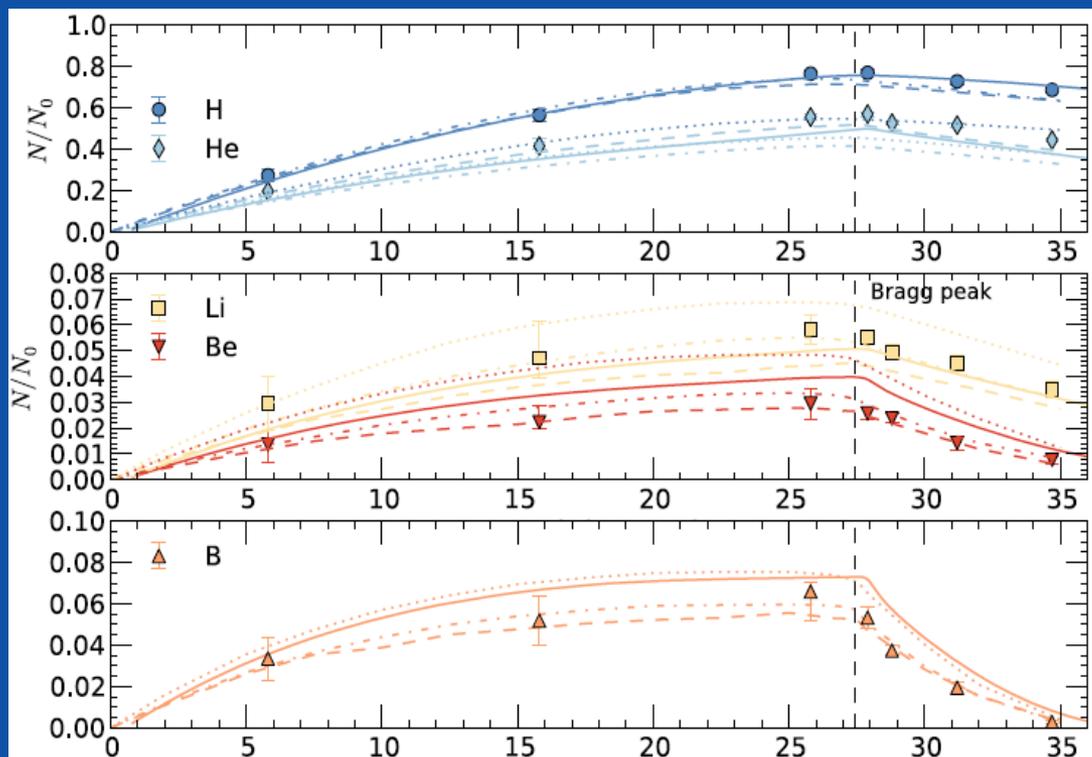
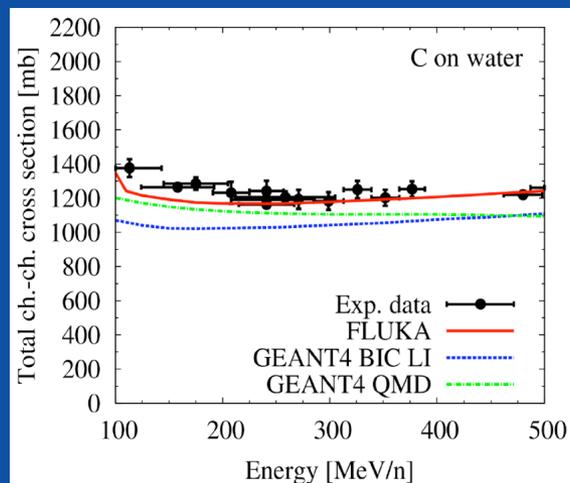


Figure 14. FLUKA, Geant4-QMD, Geant4-BIC LI (Böhlen *et al* 2010) and SHIELD-HIT10A simulations of the relative yield of fragments emitted within a  $10^\circ$  forward angle from a 400 MeV/u  $^{12}\text{C}$  beam in water, compared with experimental data (Haettner *et al* 2006). Dashed line: FLUKA simulation. Dashed-dotted line: Geant4-QMD simulation. Dotted line: Geant4-BIC simulation. Solid line: SHIELD-HIT10A simulation. The markers are experimental data. Where error bars are not visible, they are smaller than the markers.

• Integral quantities (fragment yields, charge changing cross sections) are generally within 10-20%

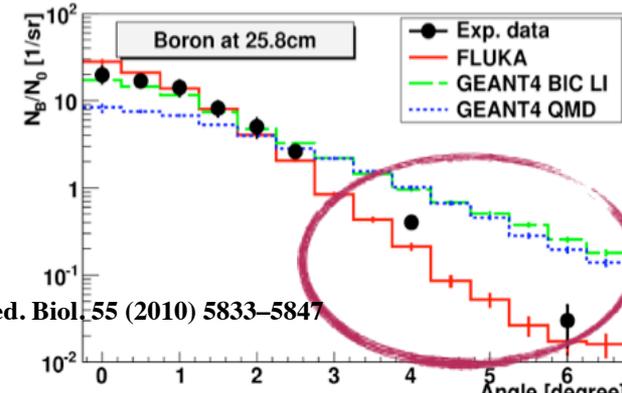
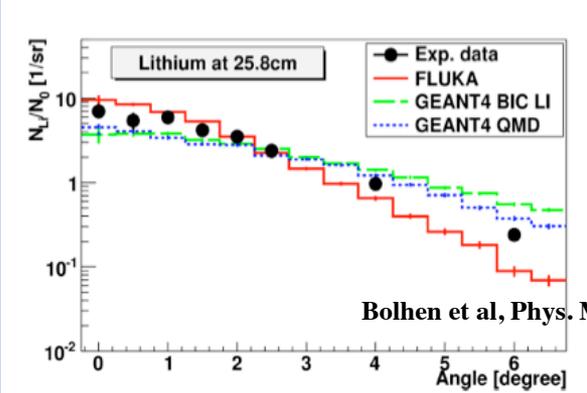
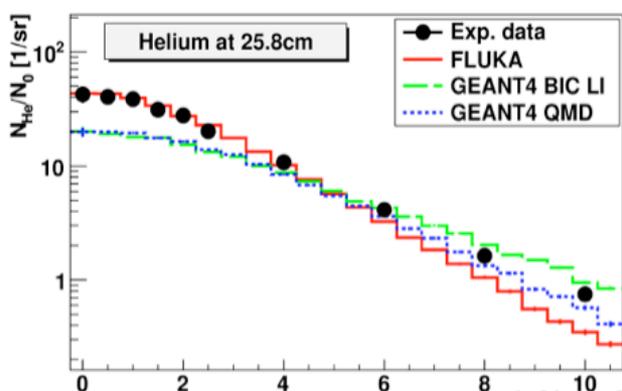
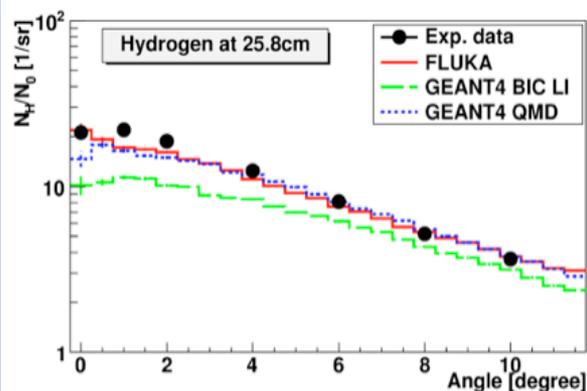
Bolhen *et al*, Phys. Med. Biol. 55 (2010) 5833–5847





# Data - MC comparison: $^{12}\text{C}$ ions

Differential/double- differential quantities (vs angle and/or energy)  $\rightarrow$  larger discrepancies found!



Bolhen et al, Phys. Med. Biol. 55 (2010) 5833–5847

**NB: the accuracy on delivered dose MUST be of the order of few %**

Some MC benchmarks:  
 Sommerer et al. 2006, PMB  
 Garzelli et al. 2006, ArXiv  
 Pshenichnov et al. 2005, 2009  
 Mairani et al. 2010, PMB  
 Böhlen et al. 2010, PMB  
 Hansen et al. 2012, PMB





# Outline

Bouncing from fundamental physics to applied physics and back...

- Overview: fragmentation in PT and space
- ➔ • Some recent fragmentation experiment
- Fragmentation & dose monitoring
- Summary and conclusions



# Frag meas: thick target

A lot of integral measurements are already around..

Projectile Energy[MeV/N] Target

$^4\text{He}$	100, 180	C, Al, Cu, Pb
$^{12}\text{C}$	100, 180, 400	C, Al, Cu, Pb
$^{20}\text{Ne}$	100, 180, 400	C, Al, Cu, Pb
$^{28}\text{Si}$	800	C, Al, Cu, Pb
$^{40}\text{Ar}$	400	C, Al, Cu, Pb
$^{56}\text{Fe}$	400	C, Al, Cu, Pb
$^{126}\text{Xe}$	400	C, Al, Cu, Pb

HIMAC by Kurosawa et al.

$^{20}\text{Ne}$	337	C, A, Cu and U
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BEVALAC by Schimmerling et al.

$^{93}\text{Nb}$	272	Al, Nb
------------------	-----	--------

BEVALAC by Heilbronn et al.

$^{93}\text{Nb}$	435	Nb
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$^4\text{He}$	155	Al
---------------	-----	----

NSRL by Heilbronn et al.

$^{12}\text{C}$	155	Nb
-----------------	-----	----

$^4\text{He}$	160	Pb
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SREL by Cecil

$^4\text{He}$	180	C, H <sub>2</sub> O, steel, Pb
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$^{12}\text{C}$	200	H <sub>2</sub> O
-----------------	-----	------------------

GSI by Günzert-Marx et al.

$^{12}\text{C}$	400	H <sub>2</sub> O
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GSI by Haettner et al.

Tentative & incomplete list at 2011

Courtesy of M. Durante





# Frag meas: thin target

A lot of measurements on thin target are already around.. but not wrt angle and energy

• Projectile Energy[MeV/N]Target

- $^4\text{He}$  135 C, Poly, Al, Cu, Pb
- $^{12}\text{C}$  135 C, Poly, Al, Cu, Pb
- $^{20}\text{Ne}$  135 C, Poly, Al, Cu, Pb
- $^{40}\text{Ar}$  95 C, Poly, Al, Cu, Pb

RIKEN by Sato et al.

- $^{12}\text{C}$  290, 400 C, Cu, Pb
- $^{20}\text{Ne}$  400, 600 C, Cu, Pb
- $^{40}\text{Ar}$  400, 560 C, Cu, Pb

HIMAC Iwata et al.

- $^4\text{He}$  230 Li, C,  $\text{CH}_2$ , Al, Cu, Pb
- $^{14}\text{N}$  400 Li, C,  $\text{CH}_2$ , Al, Cu, Pb
- $^{28}\text{Si}$  600 Li, C,  $\text{CH}_2$ , Al, Cu, Pb
- et al.
- $^{56}\text{Fe}$  500 Li, C,  $\text{CH}_2$ , Al, Cu, Pb
- $^{86}\text{Kr}$  400 Li, C,  $\text{CH}_2$ , Al, Cu, Pb
- $^{126}\text{Xe}$  400 Li, C,  $\text{CH}_2$ , Al, Cu, Pb

HIMAC Heilbronn

Tentative & incomplete list at 2011

Courtesy of M. Durante

only with detectors at 0°!





# The IDEAL detector

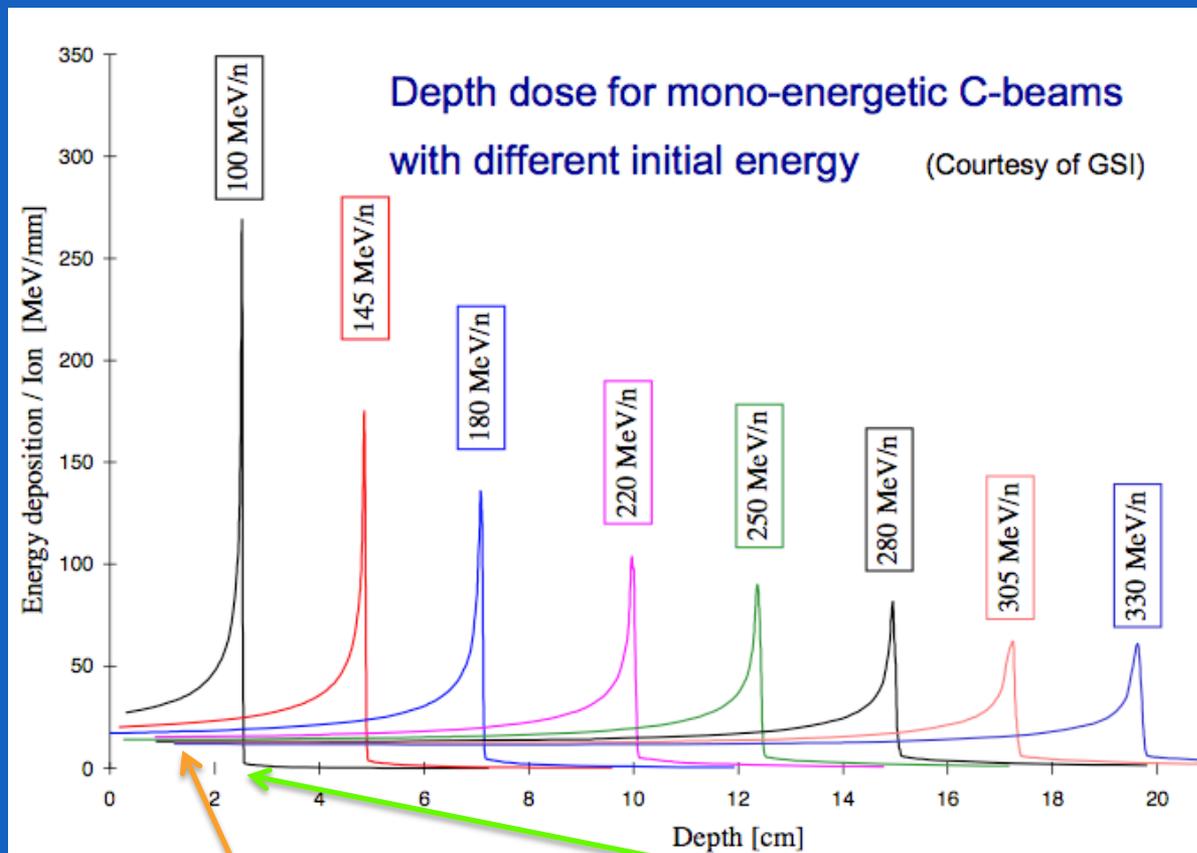
On an event by event basis, the ideal detector should:

- Identify **all** the fragment produced, i.e. detect charge , with  $0 < Z < 6$  and detect **mass**, on all **the solid angle**
- Detect the **energy** of the fragments ( from 0 to 700 MeV p)
- Measure the **emission angle** of the fragments (0-90 deg)
- Detect all the **correlations**, with **systematic below few %** (rescattering in TG, out of TG fragmentation, etc..)

**Starting from scratch**, such a detector would be **VERY expensive** , would take **LONG time** and a **LARGE group** to be designed and built.



# Recent thin target, Double Diff Cross Section C-X measurements



The community is exploring the interesting region for therapeutical application.

GSI 400 A MeV C beam  
FIRST experiment

LNS 62 A MeV C beam  
FRAG experiment

GANIL 95 A MeV C  
beam - E600  
collaboration (2011)



# Fragments detection techniques

Standard techniques exploit the  $dE/dx$  measurement ( $\Delta E$ ), calorimetric  $E$  measurement, Time of Flight ( $\beta$ ) measurement

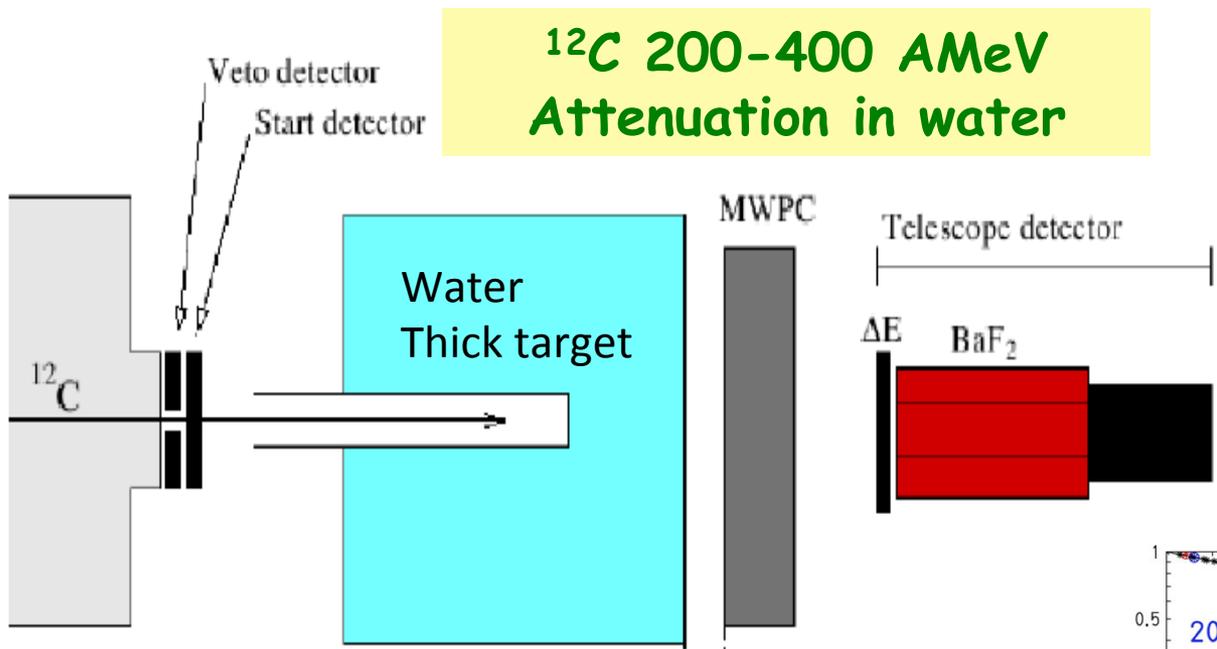
All this measurement are closely related with the particle identification (PID)

- $\Delta E$  vs  $E \rightarrow$  PID
- $\Delta E$  measurement provided PID  $\rightarrow E$
- ToF ( $\beta$ ) measurement provided PID  $\rightarrow E$

particle	$E_{kin}/nucl$ (MeV)	$dE/dx$ (MeV/cm)	Range (cm)
proton	10	42.6	0.1
proton	100	7.4	7.6
He	10	186	0.1
He	100	29	7.6
Be	10	78	0.06
Be	100	114	4.4
Carbon	100	259	2.5
Carbon	400	108	26.3



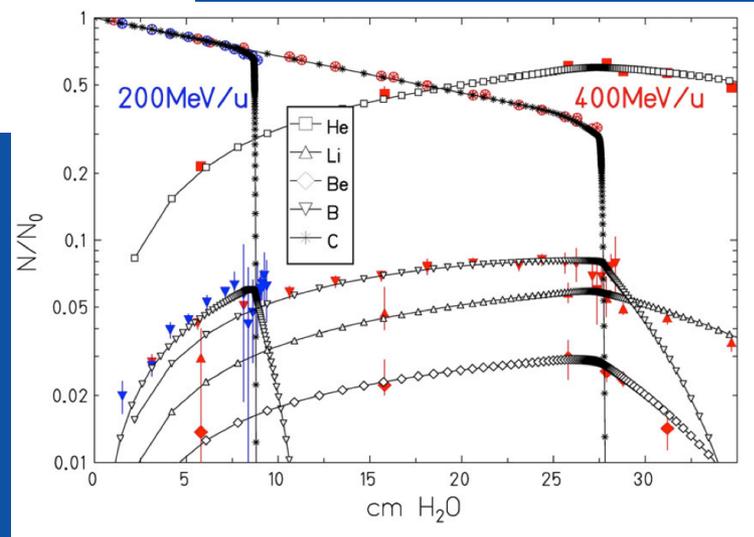
# Typical PT fragmentation setup



$\Delta E$ - $\text{BaF}_2$ : energy loss and total energy

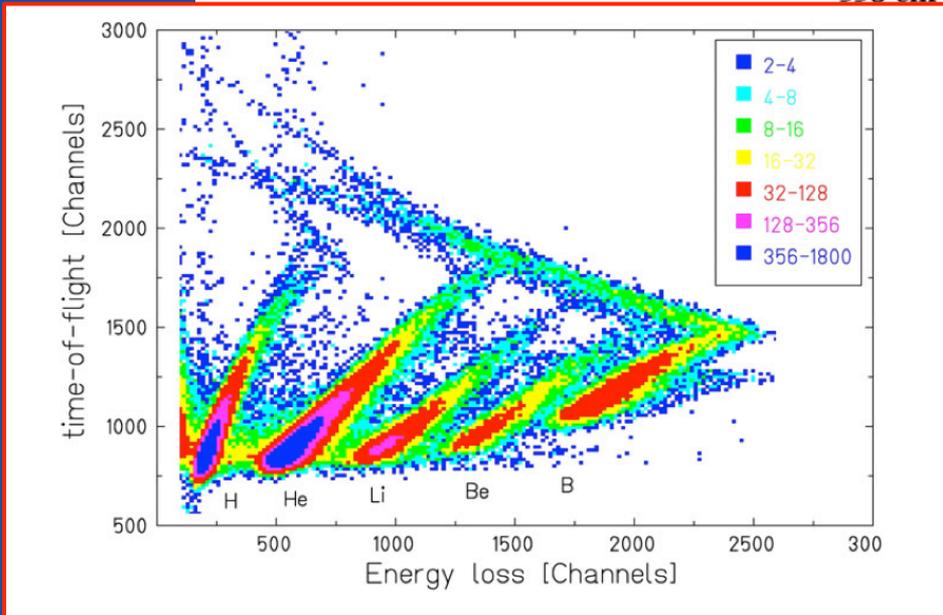
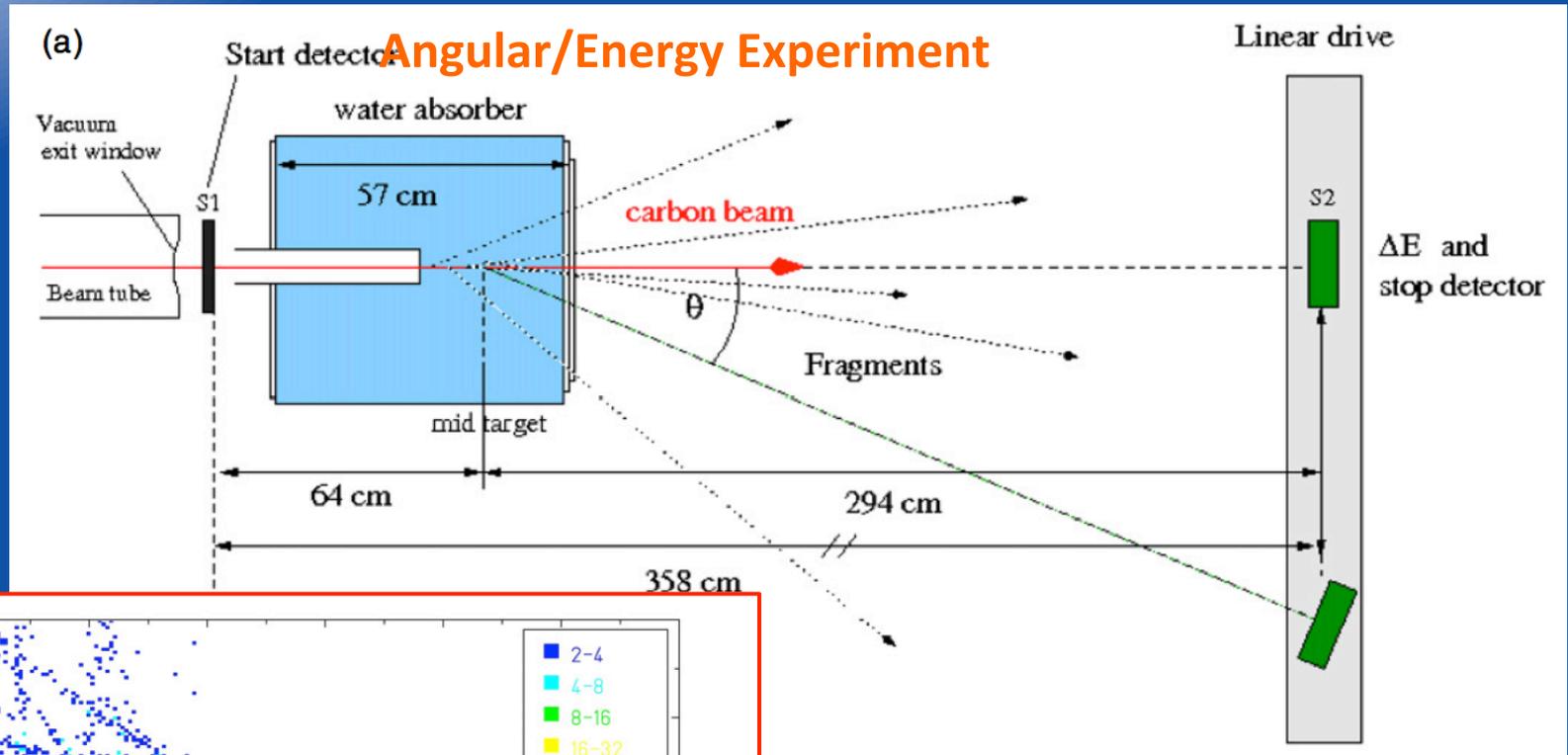
ToF: total energy

provide the number of surviving C ions leaving the water phantom as a function of its thickness.





# Typical PT fragmentation setup



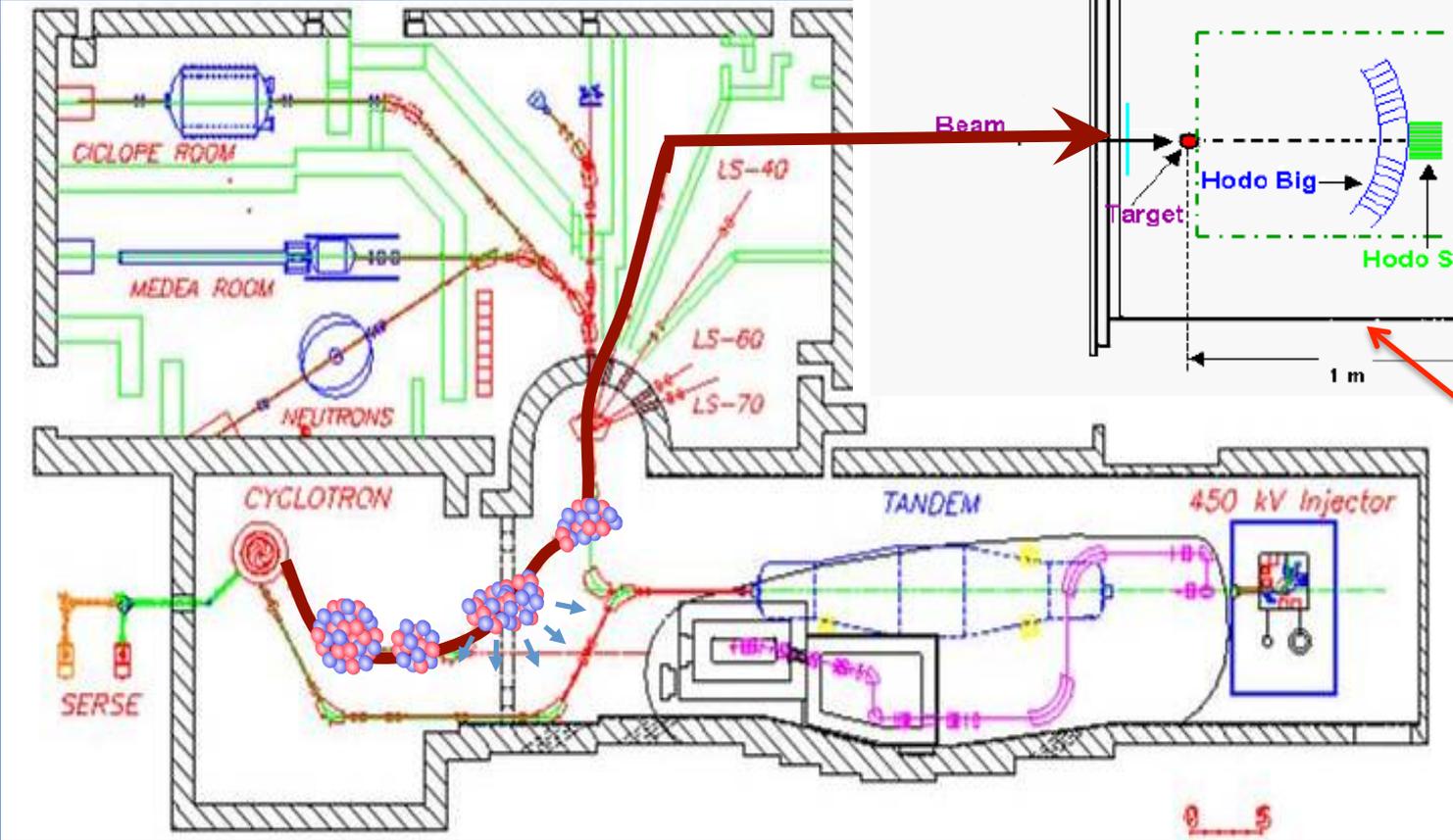
measure the angular & energy distributions of secondary fragments

H1: energy loss

ToF: total energy



# Frag Experiment at LNS



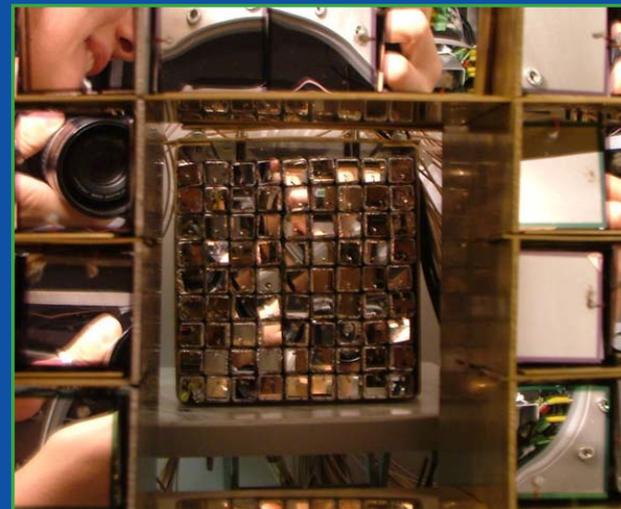
Target chamber in vacuum

:  $^{12}\text{C}$  63 A MeV beam on  $^{12}\text{C}$

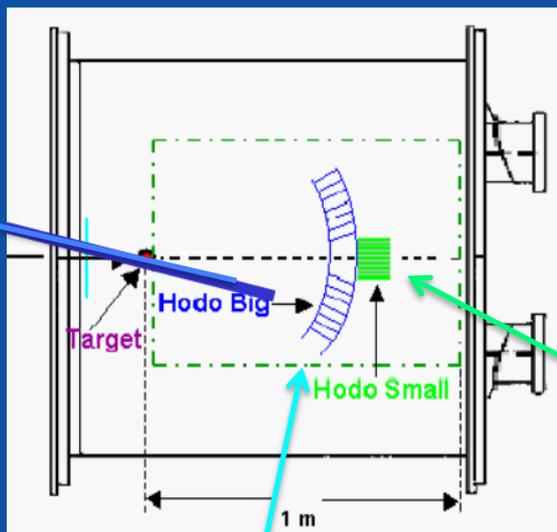




# Frag Experiment at LNS



The **Hodo-small**, set up at a distance of 80 cm from the target consisted of 81 two-fold telescopes:  $300 \mu\text{m}$  Silicon detectors  $1 \times 1 \text{ cm}^2$  of active area followed by a  $1 \times 1 \text{ cm}^2$  and 10 cm long CsI(Tl) and covered the angular range  $\theta_{lab} = \pm 4.5^\circ$ .



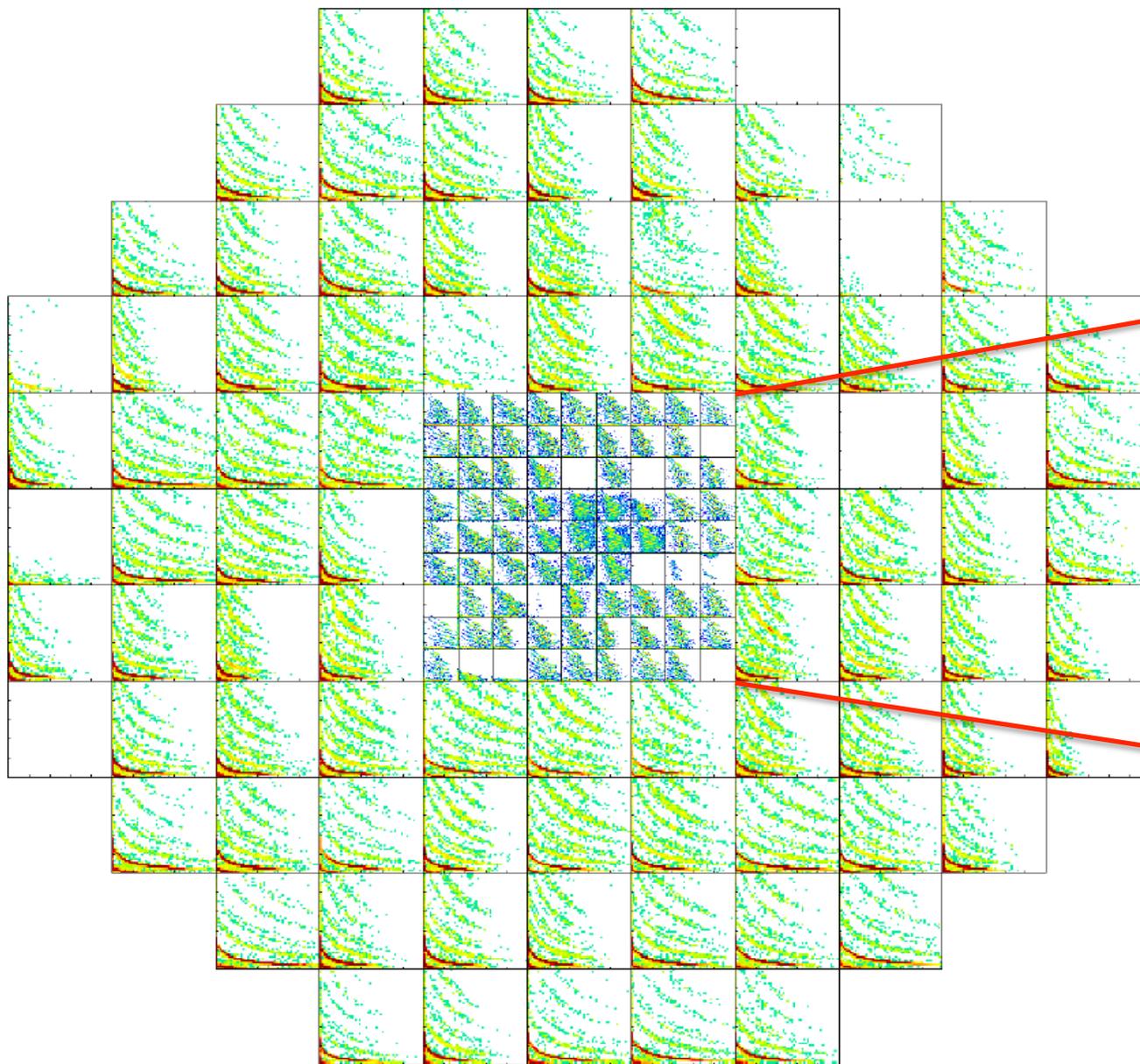
The **Hodo-big**, set up at a distance of 0.6 m from the target, consisted of 89 three-fold telescopes  $50 \mu\text{m} + 300 \mu\text{m}$  Silicon detectors both having  $3 \times 3 \text{ cm}^2$  surface followed by a 6 cm long CsI(Tl) of the same surface. It covered the angular range  $\theta_{lab}$  between  $\pm 4.5^\circ$  and  $\pm 20^\circ$



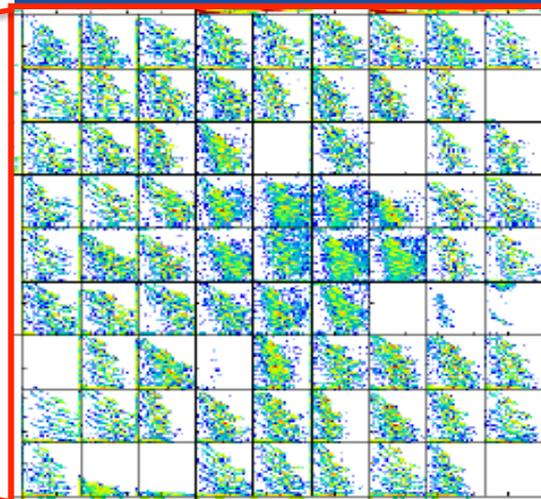
E  $\rightarrow$  CsI(Tl)



# Frag @LNS : Fragment ID by $\Delta E$ vs $E$



Intercalibration  
is an issue!!



C+C  
C+Au  
C+CH



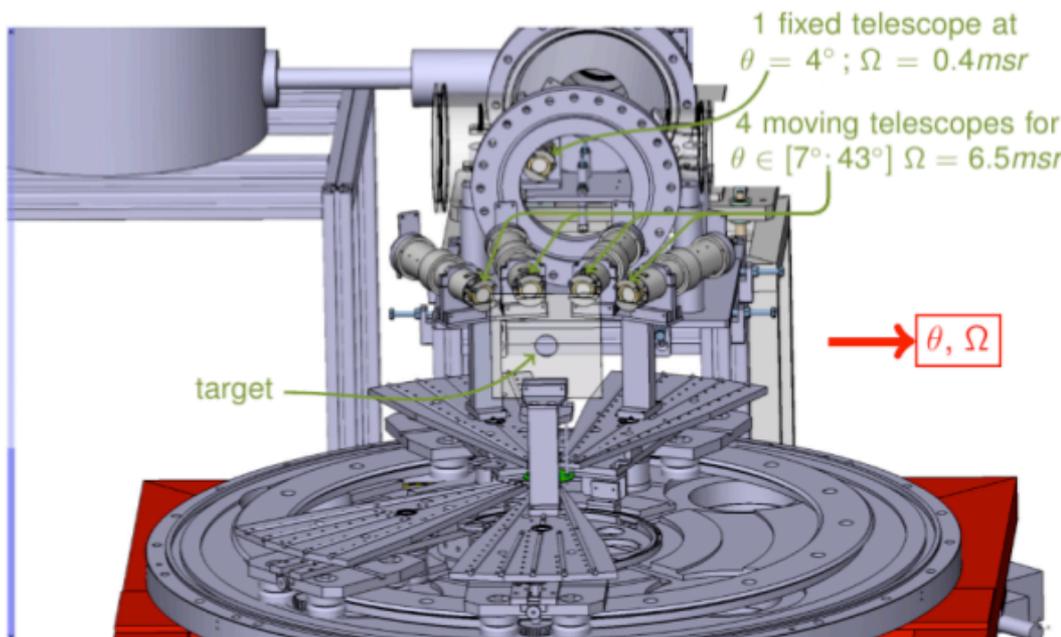
# Measurement @95AMeV : $^{12}\text{C}$ beam

E600 experiment at GANIL (Caen ; may 2011)

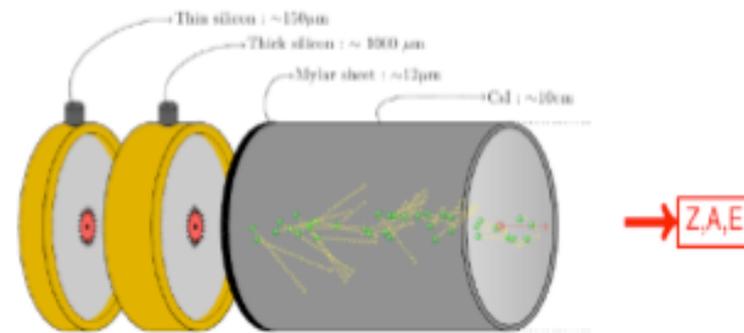
Courtesy of M. Labalme

- Projectiles : 94.6 MeV/u  $^{12}\text{C}$
- Thin Targets ( $\sim 50\text{mg}/\text{cm}^{-2}$ ) : C,  $\text{CH}_2$ , Al,  $\text{Al}_2\text{O}_3$ , Ti

$\Rightarrow \frac{\delta^2\sigma}{\delta E \cdot \delta\Omega}$  fragmentation measurements of  $^{12}\text{C}$  on C, H, O, Ca ( $A_{\text{Ti}} \sim A_{\text{Ca}}$ )  
 $\approx 95\%$  of a human body composition



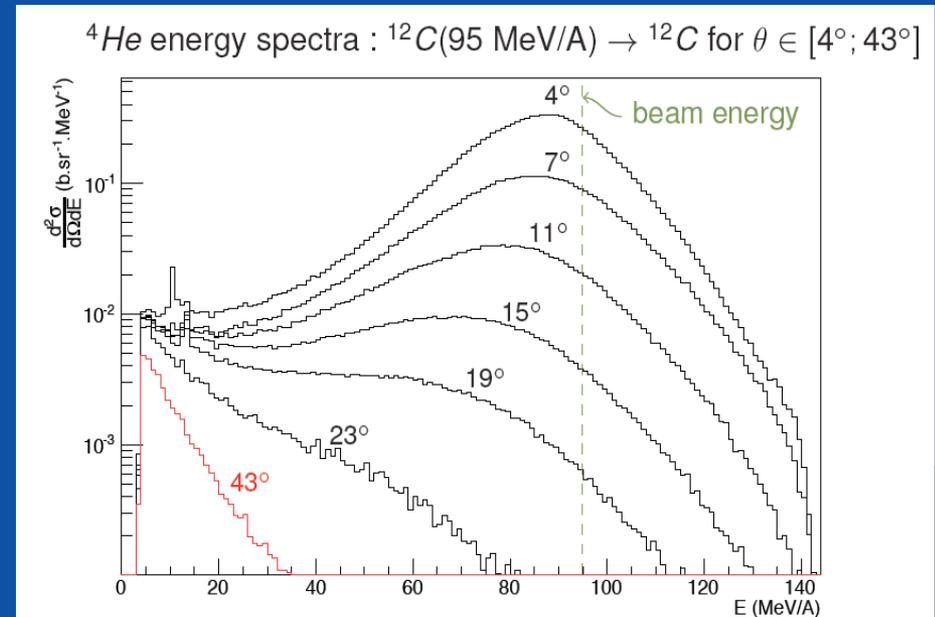
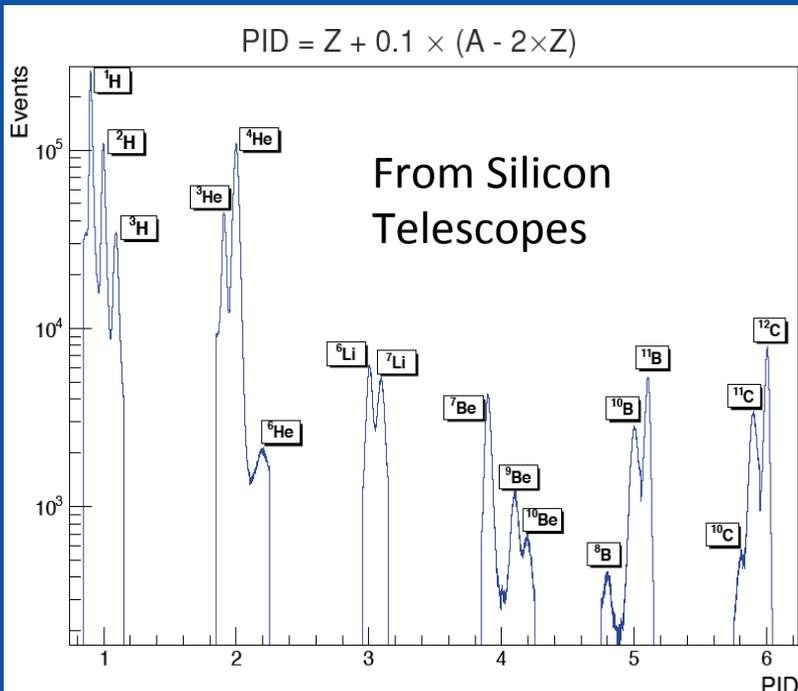
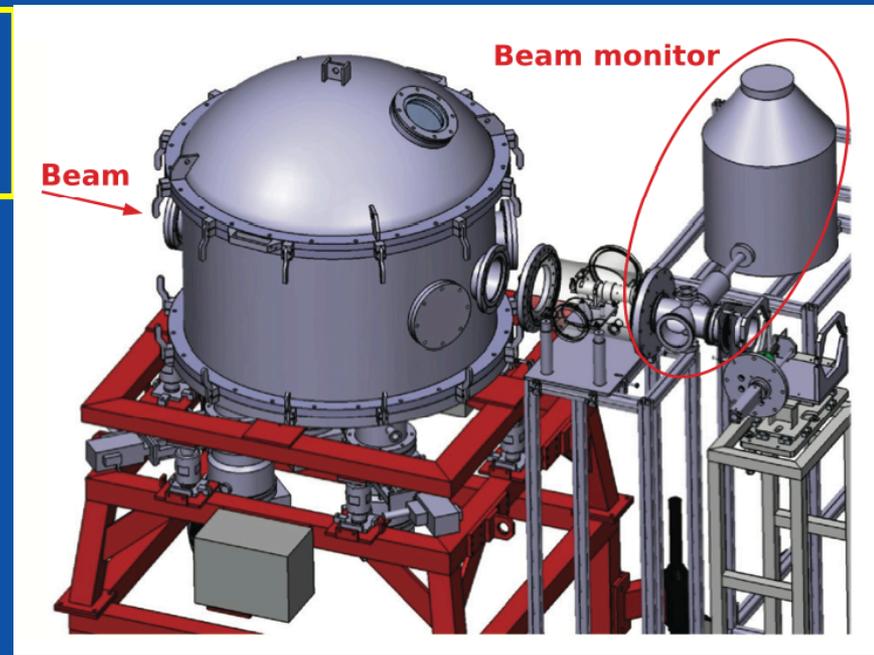
Array of 5 SI + CsI telescopes





# E600 (Ganil)

- Very good particle identification
- Currently focusing on: assessing systematics and comparing with MC to benchmark difference nuclear MC models

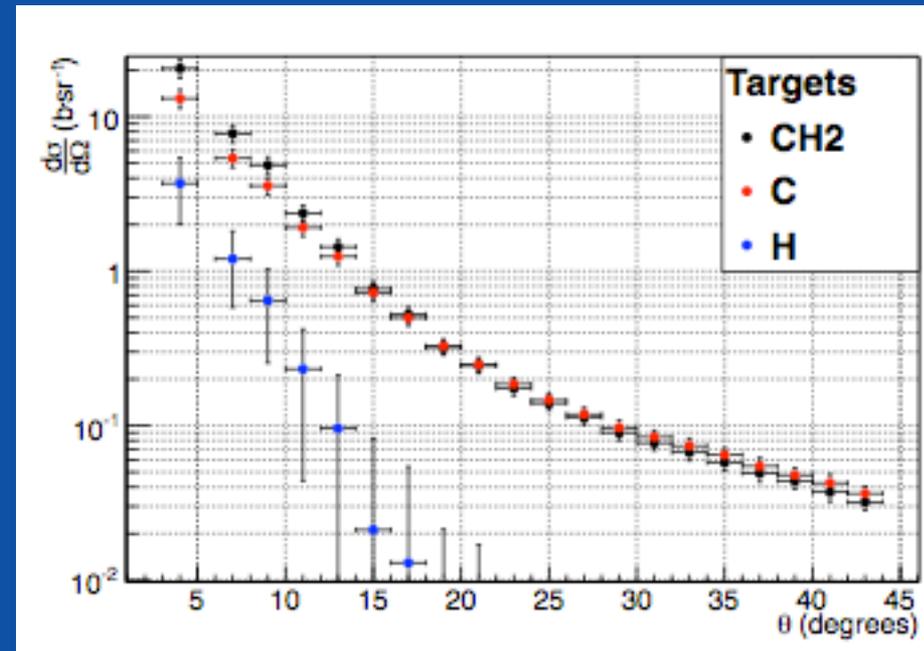
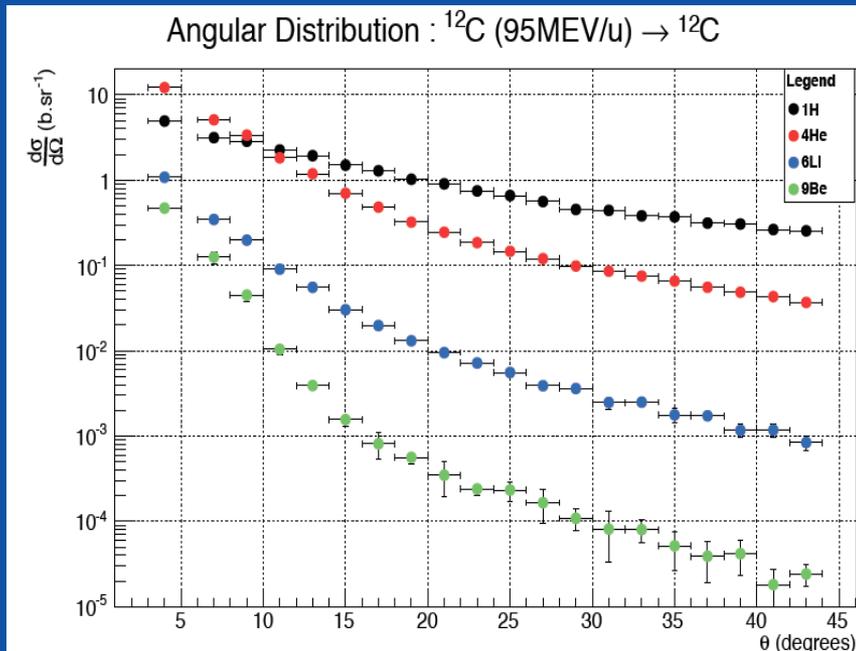




# Measurement @95AMeV : $^{12}\text{C}$ beam

Courtesy of M. Labalme

- Obtained results for Single and Double Diff. X Section.
  - one interesting conclusion: Composite targets can be deduced from the cross sections of elemental targets (-> organic tissues)

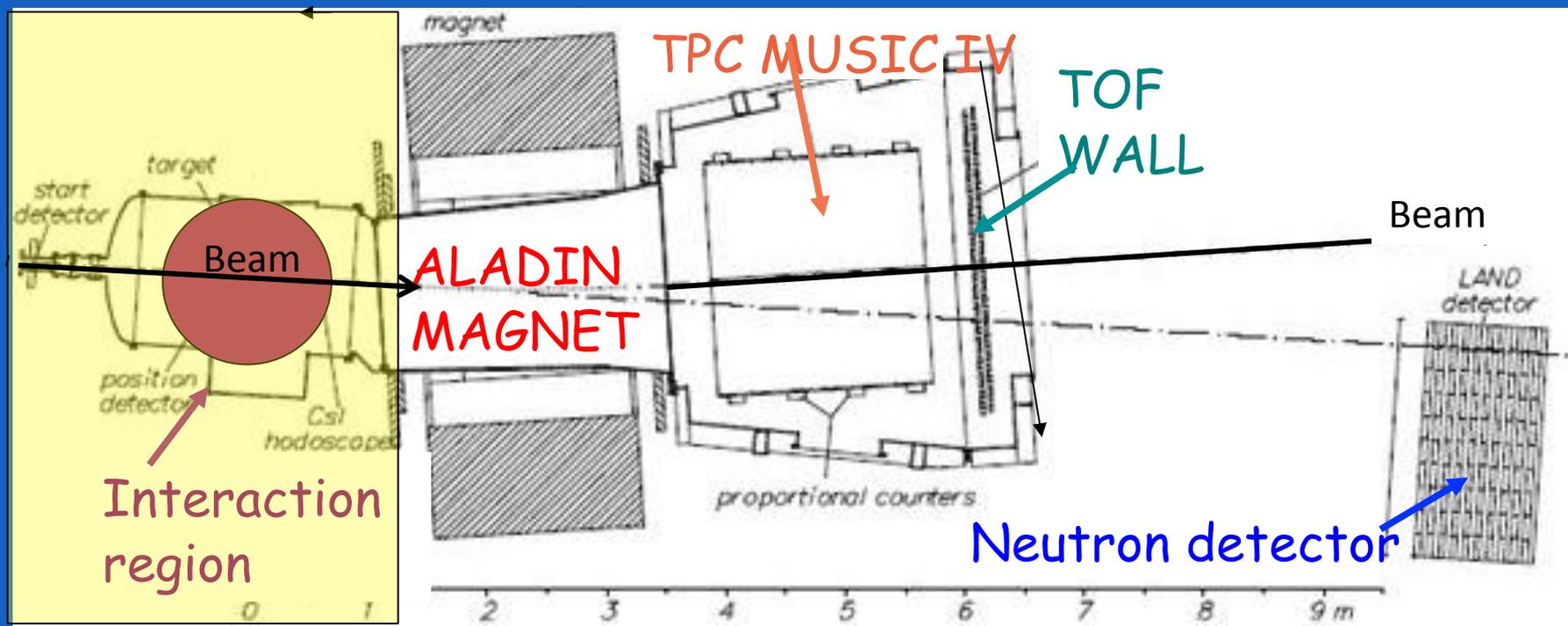




# Higher energy $\rightarrow$ FIRST exp. @GSI

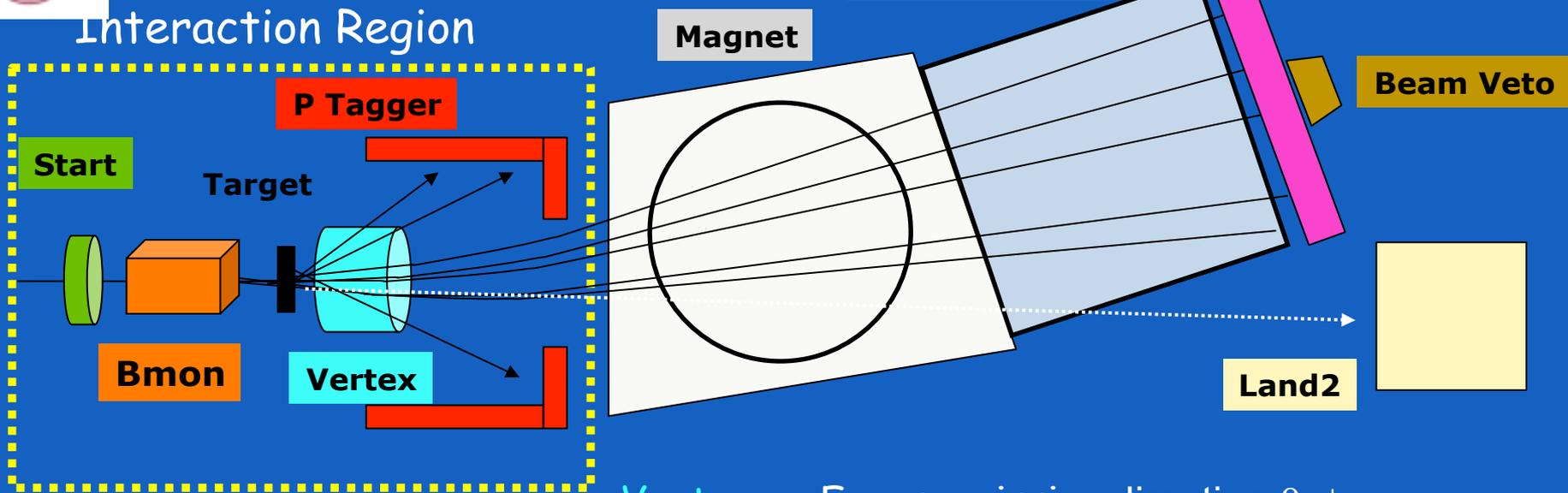
Experimental setup of dimensions, complexity and cost typical of medium size nuclear physics experiment.

- Existing setup designed for higher E and Z fragments: Dipole magnet, Large Volume TPC, TOF Wall, low angle Neutron detector.
- Added Vertex Tracker, Start Counter scintillator counter, Beam Monitor drift chamber, scintillator Proton Tagger/Calorimeter





# Who measures what...?



Setup redundancy → allows calibration and systematic checks of the reconstructed fragment features:  $Z, A, \theta, E$ .

- Vertex** → Frags emission direction  $\theta, \phi$
- Start** → start TOF and trigger
- TOF WALL** → frags position & TOF, trigger
- Beam mon** → Beam direction & impact point
- Tagger** → Large  $\theta$  frags: position, TOF,  $dE/dX$
- TPC MUSIC** →  $\theta, \phi, dE/dx$  after bending
- LAND2** → low angle neutron

**Beam Veto** → Veto of the non interacting beam



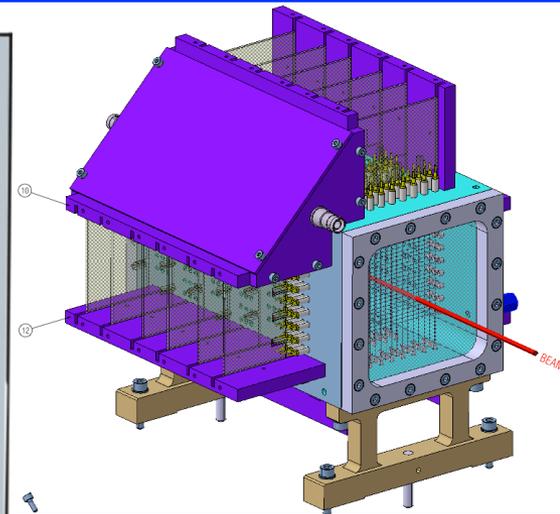
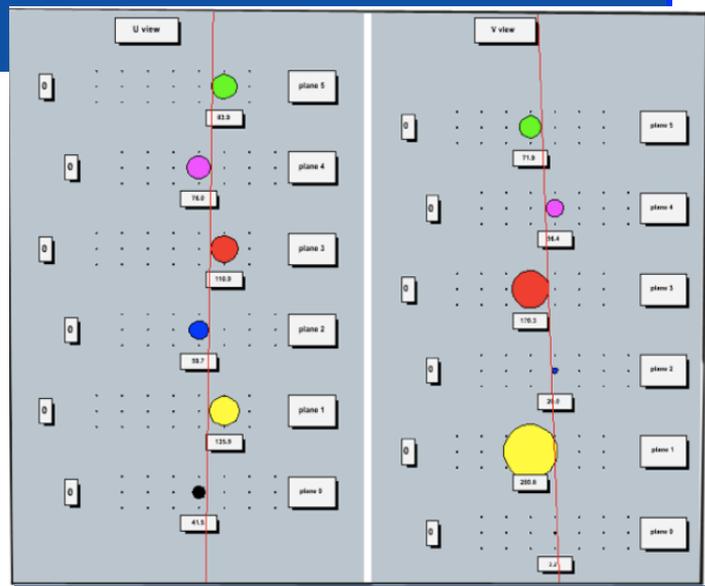
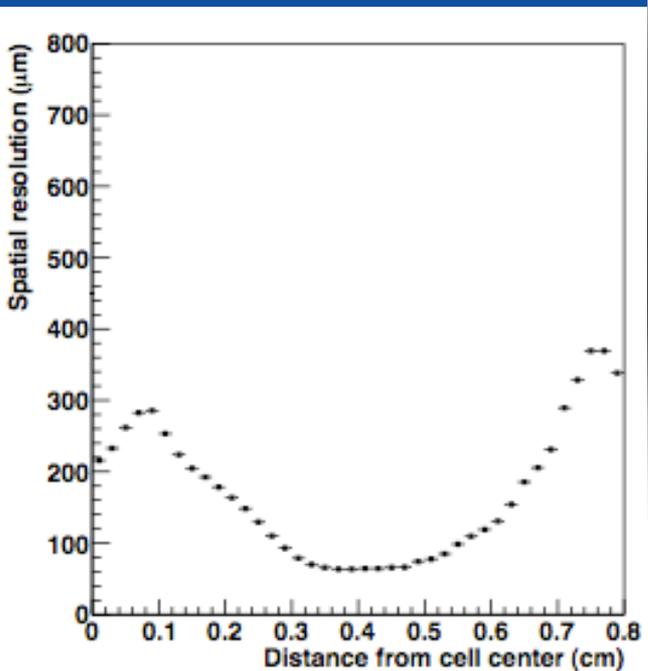
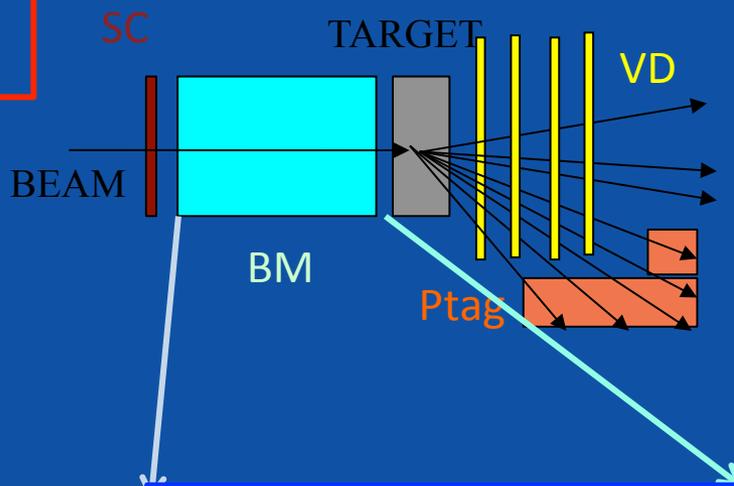
# Beam Monitor

Drift chamber: measures the direction and the impact point of the beam on the target

3 rectangular cell/plane (8x5 mm<sup>2</sup>)

6 planes for each U-V views

Ar-CO<sub>2</sub> 80/20 gas mixture @ 2.2 kV@v



Correct matching of the correct carbon track among possible pile-up beam track in the “slow” vertex detector

Input position and direction of the 12C projectile (beam spot ~ 6mm FWHM)

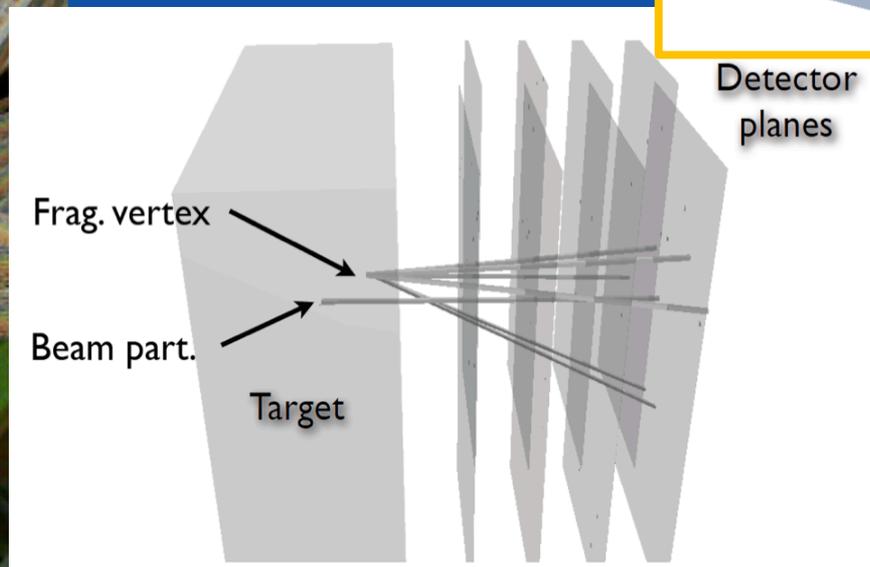
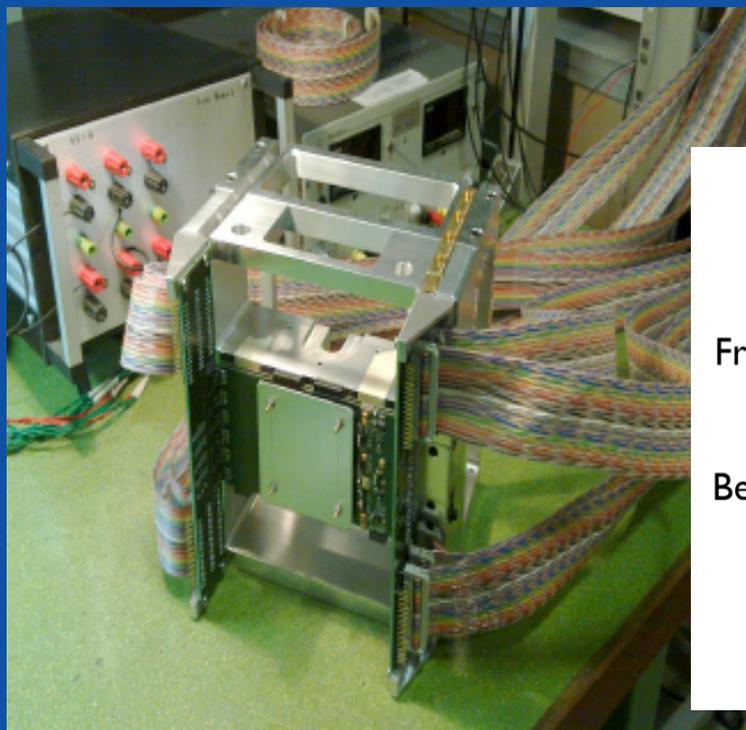
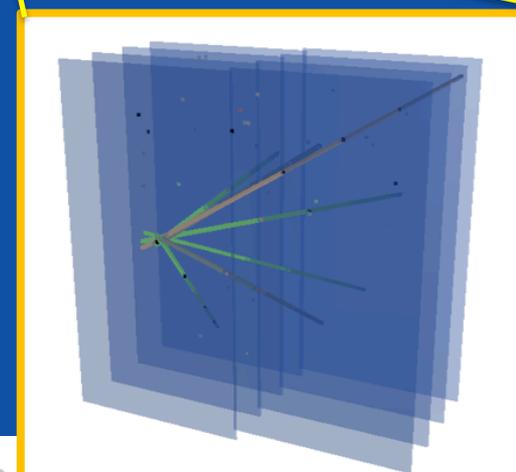
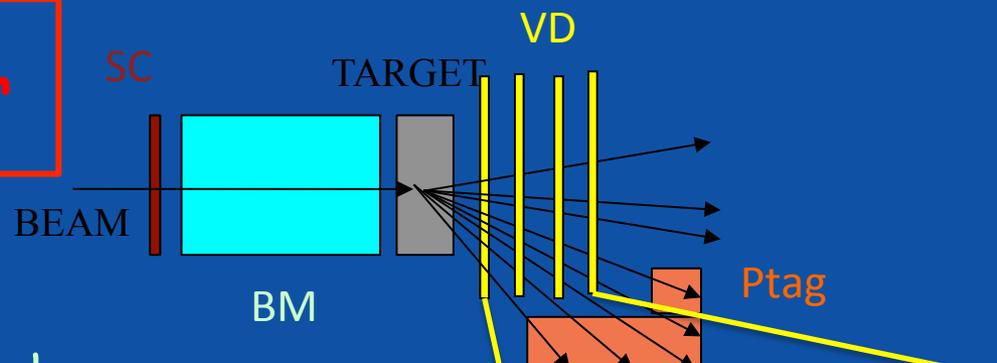




# vertex detector

Tracks all the charged fragments downstream the target (<60 deg)

4 planes of  $2 \times 2 \text{ cm}^2$  active area, each made of two MIMOSA 26 silicon pixel detectors (MAPS), 3 mm spaced,  $18.4 \mu\text{m}$  pitch,  $60 \mu\text{m}$  thick,  $10^6$  pixel/layer



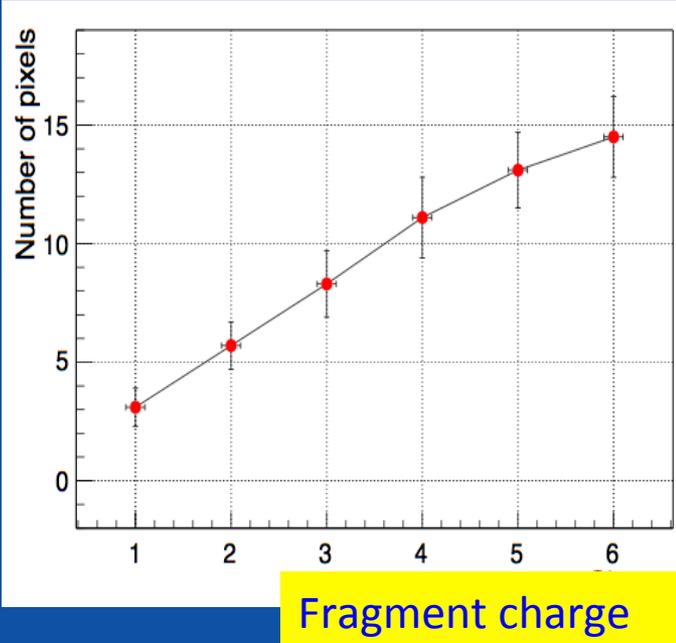
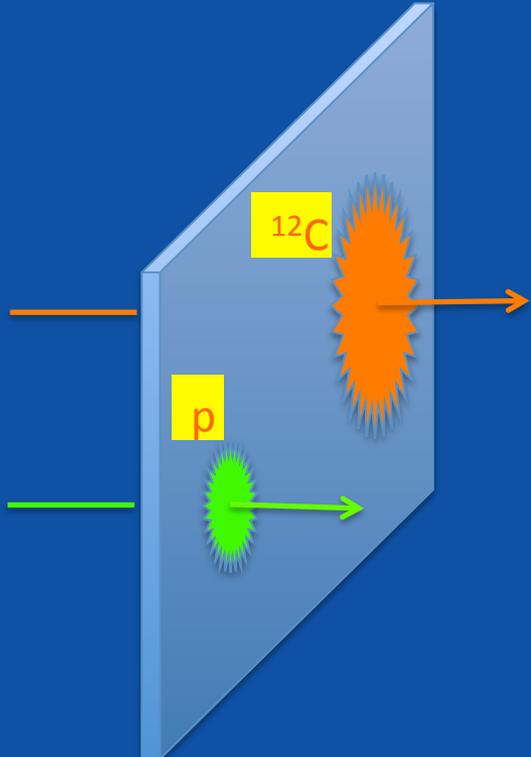
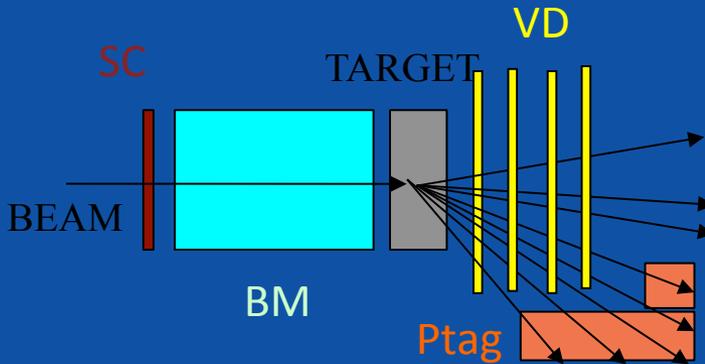


# Vertex Detector

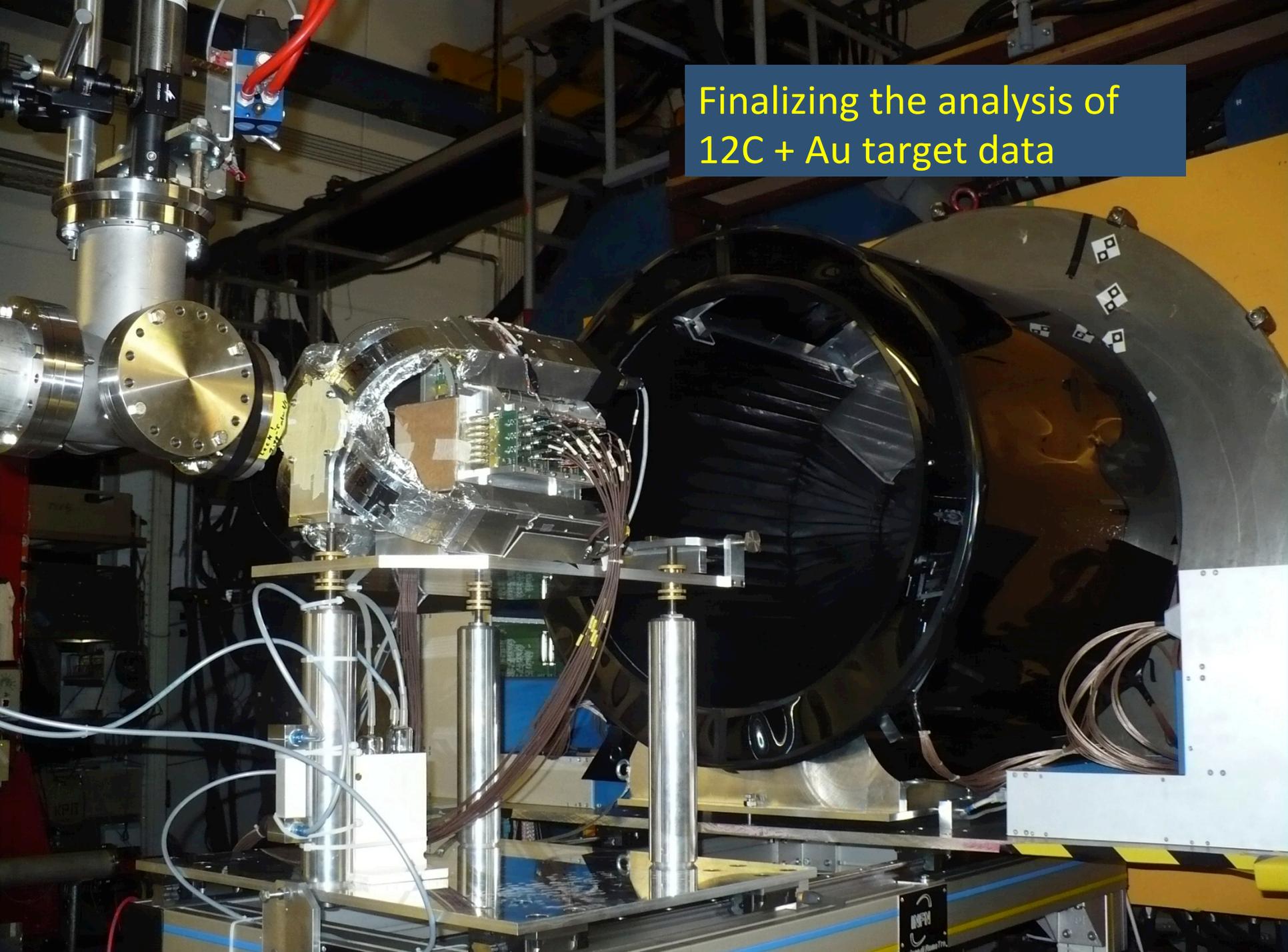
Tracking resolution  $\sim 10 \mu\text{m}$  (x,y) and  $60 \mu\text{m}$  (z) is fundamental to correctly extrapolate the fragment track along  $\sim 6\text{m}$  to the TOF wall

Tracking efficiency for fragments  $\sim 99\%$

The vertex provides also information on the fragment charge looking at the number of fired pixels



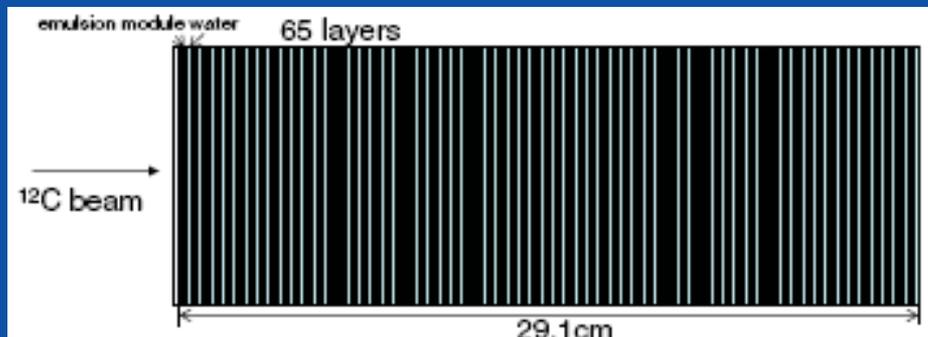
Finalizing the analysis of  $^{12}\text{C} + \text{Au}$  target data



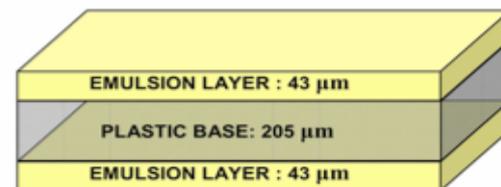


# A "new" approach: Emulsion Chamber

Density grain is proportional to energy loss



Chamber unit layer



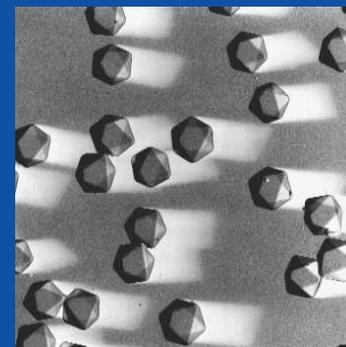
PROs

- ✓ High spatial resolution ( $\sim\mu\text{m}$ )
- ✓ High angular resolution ( $\sim 0.5$  mrad)
- ✓ Multiparticle separation

CONs:

- ✓ No event by event informations
- ✓ No correlation info
- ✓ Limited flux integrated

**AgBr crystal**  
( 0.2  $\mu\text{m}$ ) is  
the unit active  
detector

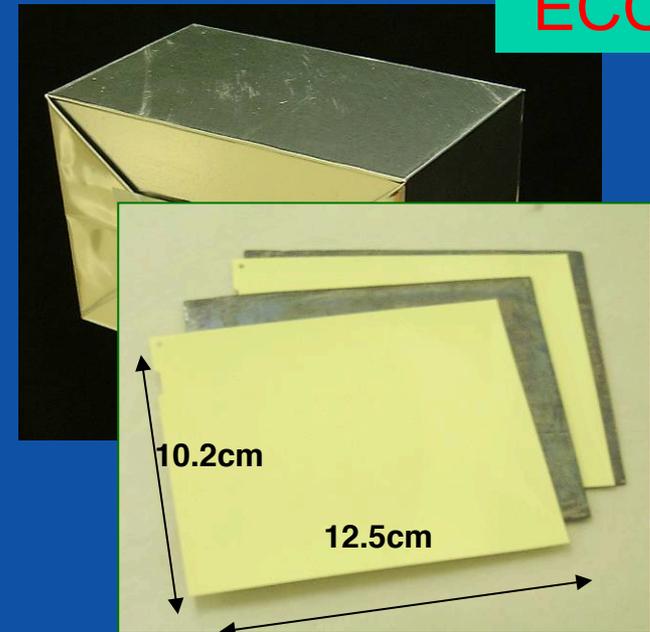
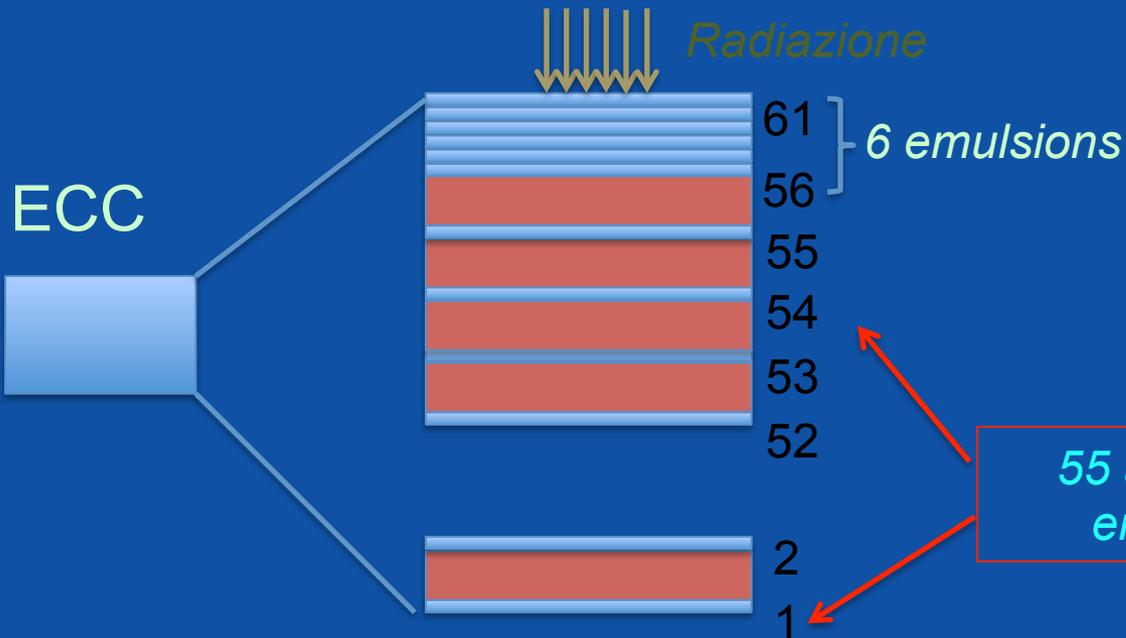


Toshito. et al., *Phys. Rev. C.*, 2008



# Emulsion Cloud Chamber (ECC) for fragmentation measurement

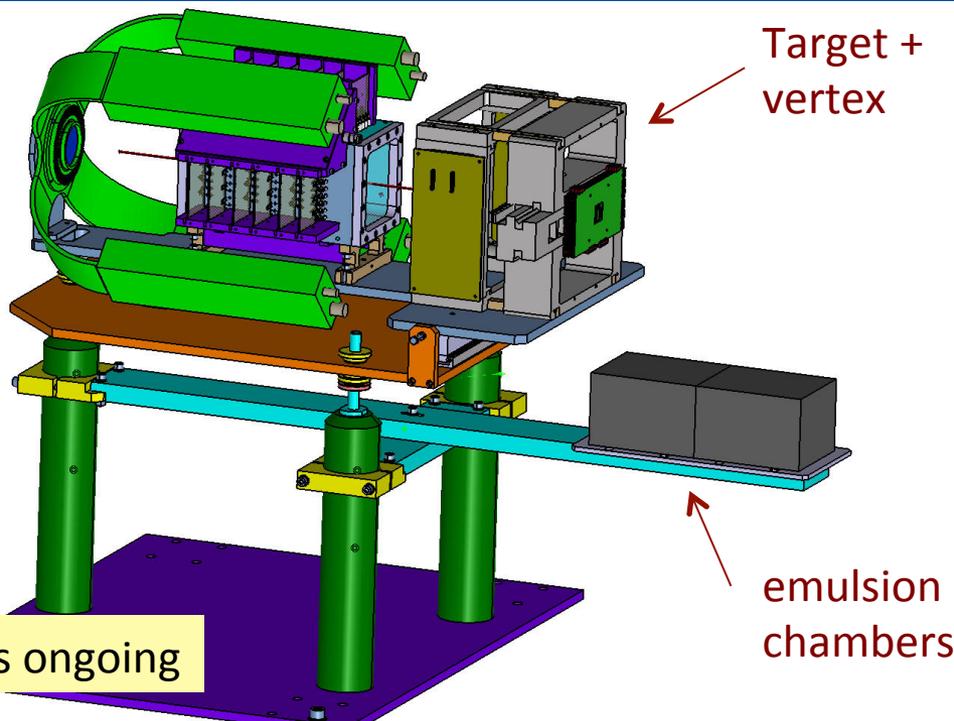
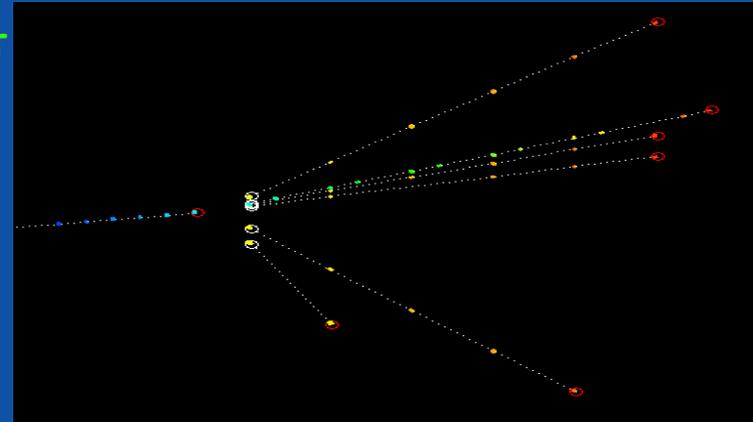
Emulsion Cloud Chamber (ECC) (10.2 x 12.5 x 7.5 cm) for frag. measurement is made alternating 1mm lead layer and (300  $\mu\text{m}$ ) emulsion layer.



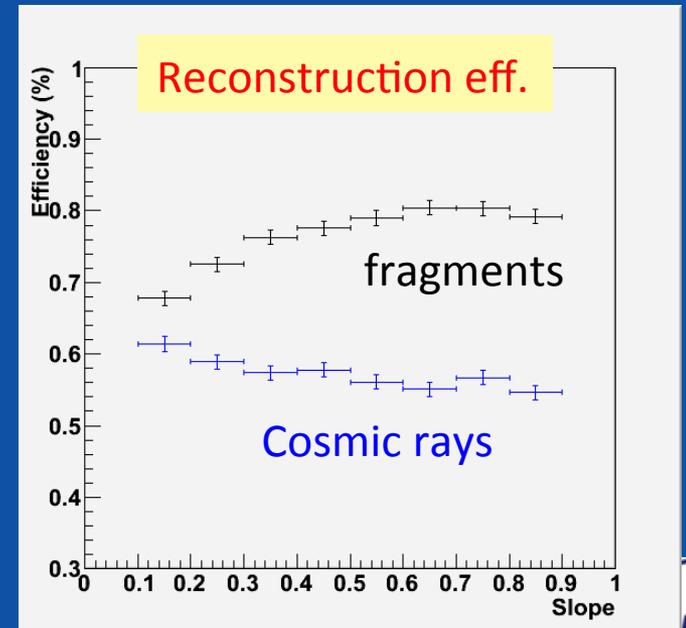


# Emulsion Chambers @ FIRST

2 cloud emulsion chambers by OPERA experiment have been exposed to fragments (2 hours) by G. De Lellis and coworkers from Napoli University  
Detect fragments at large angle, mainly He and protons,  $30^\circ < \theta < 75^\circ$   
Comparison on going with the proton tagger distributions



Analysis ongoing





# Outline

Bouncing from fundamental physics to applied physics and back...

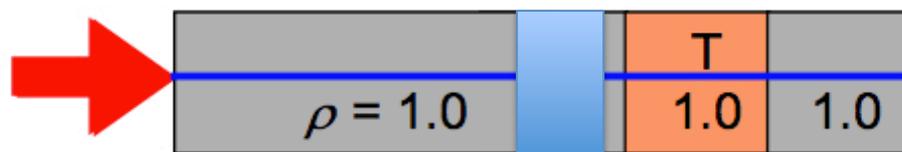
- Overview: fragmentation in PT and space
- Some recent fragmentation experiment
- ➔ • Fragmentation & dose monitoring
- Summary and conclusions



# Monitoring the dose in HT

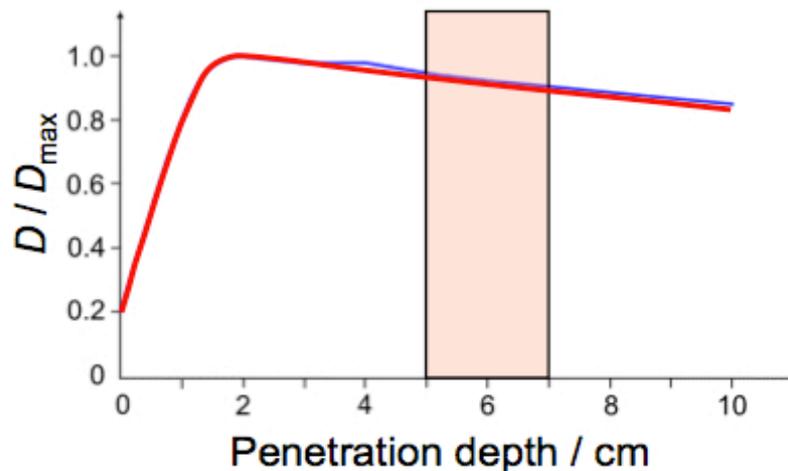
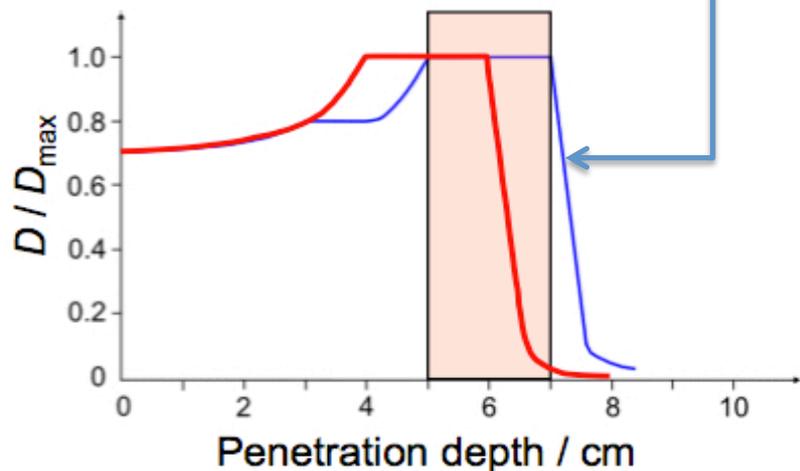
- Why is so crucial to monitor the dose in hadrontherapy with respect to conventional (photon) RT? Is like firing with machine-gun or using a precision rifle..

Effect of density changes in the target volume



A little mismatch in density by CT → sensible change in dose release

Ions



Photons



# The range verification problem

AAPM, August 2012

Delegates were asked what they considered as the main obstacle to proton therapy becoming mainstream:

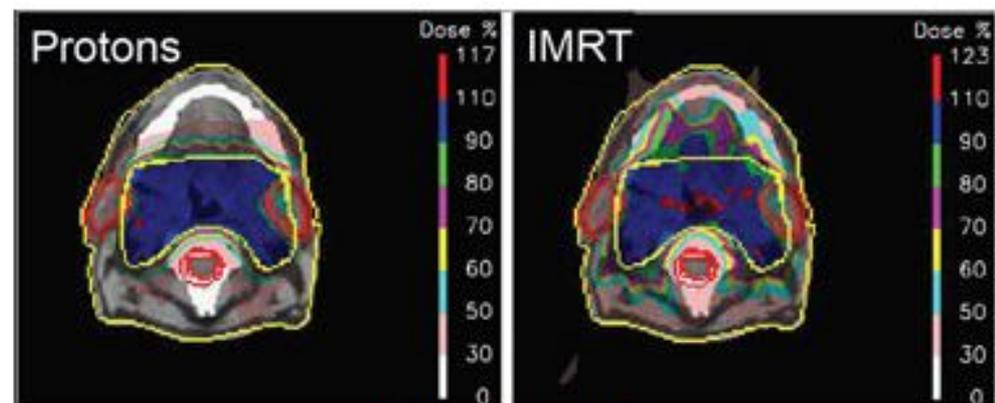
- 35 % unproven clinical advantage of lower integral dose
- 33 % range uncertainties
- 19 % never become a mainstream treatment option

## RESEARCH

Aug 22, 2012

### Will protons gradually replace photons?

The dose distribution advantages offered by proton therapy, particularly with the introduction of pencil-beam scanning, have stimulated increasing interest in this modality. But is the large capital expenditure required to build a proton therapy facility hindering the widespread implementation of this technique? And how big a problem is range uncertainty, which can prevent proton therapy from meeting its full potential?



Protons versus IMRT

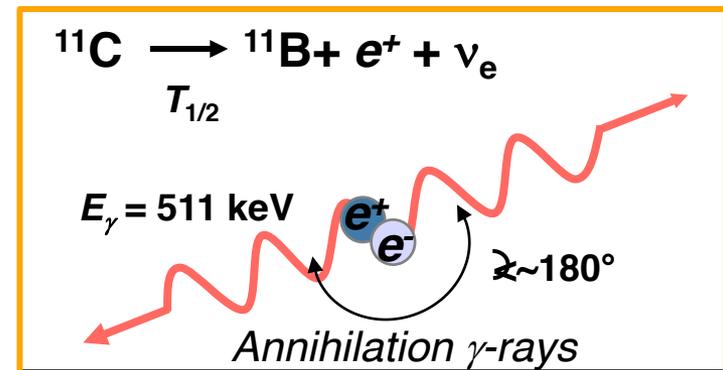


# baseline dose monitoring in PT : PET

Baseline for monitor in PT is PET : fragmentation by hadron beam creates  $\beta^+$  emitters.

- Isotopes of short lifetime  $^{11}\text{C}$  (20 min),  $^{15}\text{O}$  (2 min),  $^{10}\text{C}$  (20 s) with respect to conventional PET (hours)
- Low activity in comparison to conventional PET need quite long acquisition time (some minutes at minimum)
- Metabolic wash-out, the  $\beta^+$  emitters are blurred by the patient metabolism

No direct space correlation between  $\beta^+$  activity and dose release ( but can be reliable computed by MC)



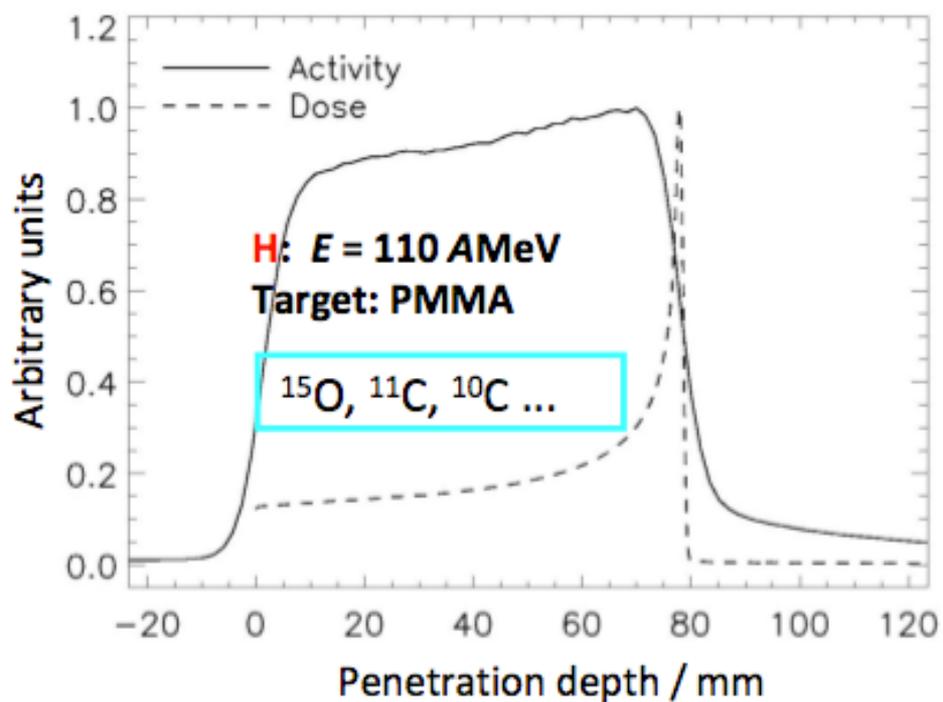
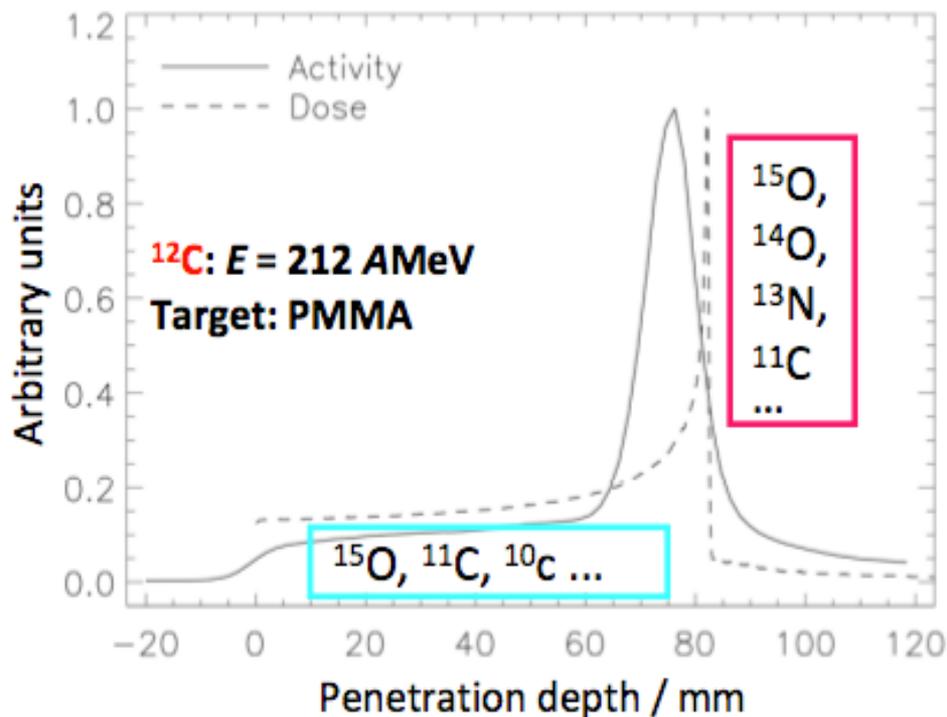


# Correlation between $\beta^+$ activity and dose

Therapy beam	$^1\text{H}$	$^3\text{He}$	$^7\text{Li}$	$^{12}\text{C}$	$^{16}\text{O}$	Nuclear medicine
Activity density / $\text{Bq cm}^{-3} \text{ Gy}^{-1}$	6600	5300	3060	1600	1030	$10^4 - 10^5 \text{ Bq cm}^{-3}$

## Projectiles & target fragmentation

## Target fragmentation



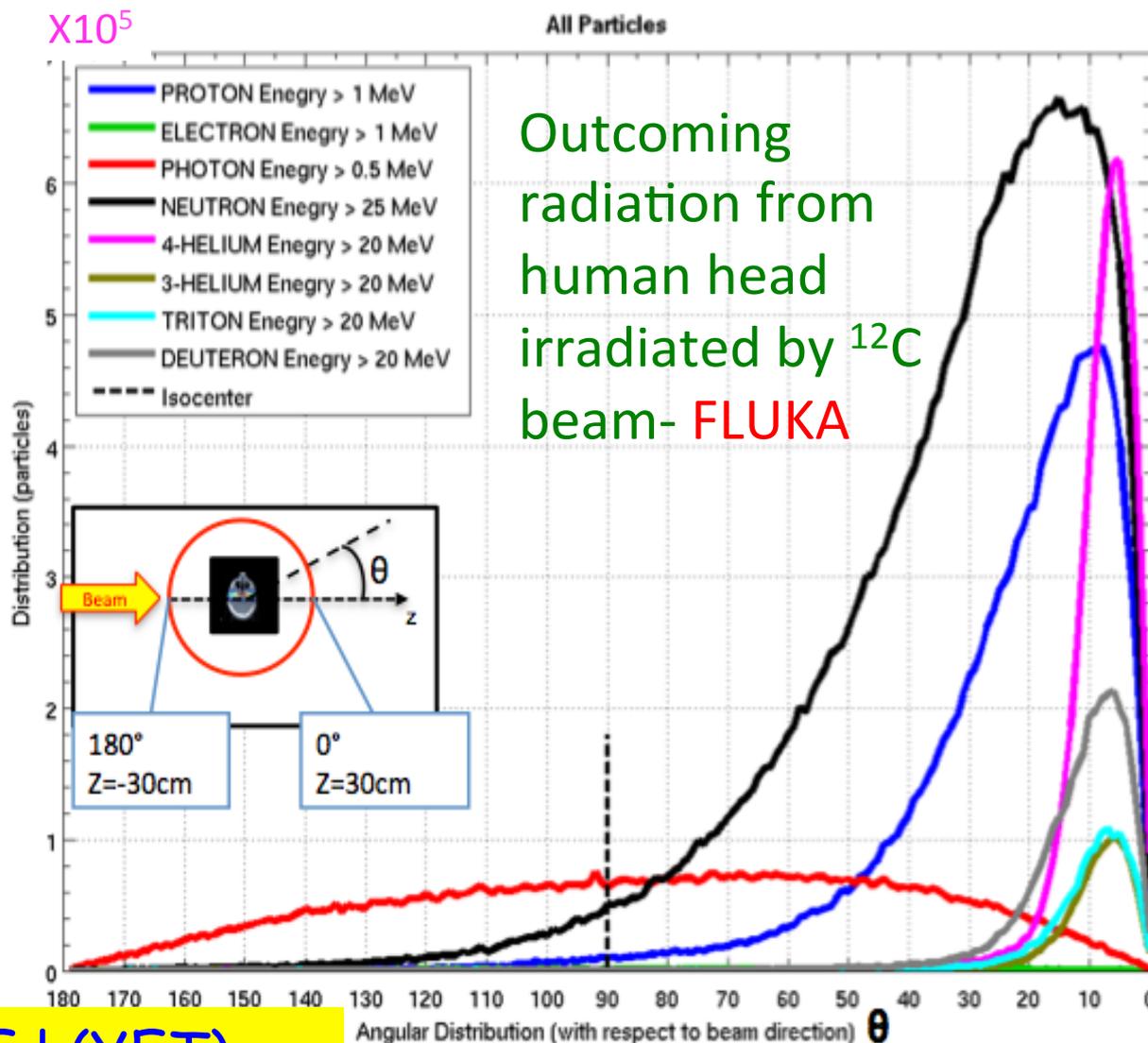


# Fragmentation, nuclear excitation, $\beta^+$ emitter production... Background or signal?

The p,  $^{12}\text{C}$  beams generate a huge amount of secondaries..

In particular prompt single  $\gamma$ s, PET  $\gamma$ s, protons and neutrons.

Can be used to track the beam inside the patient



MC NOT RELIABLE! (YET)



## The prompt gamma saga...

- The gamma are quite copiously produced by proton and  $^{12}\text{C}$  beam by nuclear excitation.
- The emission region stretches along all the beam path but has been shown to ends near the Bragg peak for both beams.
- There is a huge background due to neutrons & uncorrelated gamma produced by neutrons. This background is beam, energy and site specific
- It's not simple backpointing the  $\gamma$  direction: take profit by the SPECT technique... but the energy of these  $\gamma$  is in the 1-10 MeV range-> much more difficult to stop and collimate!!



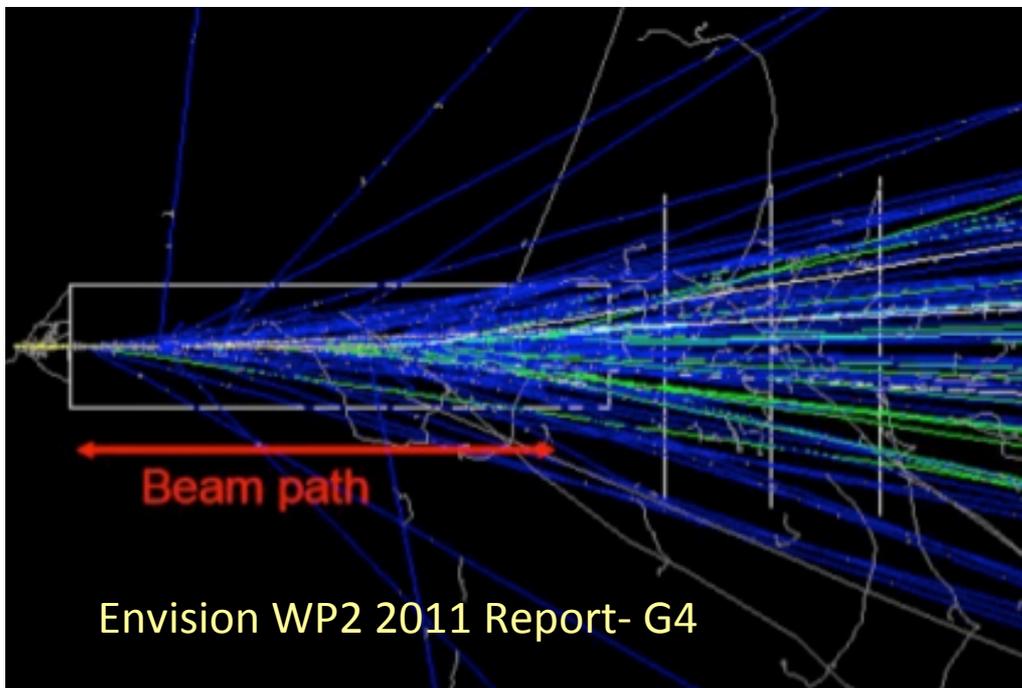
# Something else useful?...the fragments!

Low energy protons are surely emitted by hadron beam. Also from region near BP? And with enough energy to exit from the patient body and be detected?

And for a proton beam also?

K Gwosch et al *Phys. Med. Biol.* **58** 3755  
C Agodi et al *Phys. Med. Biol.* **57** 5667

- Best space resolution for large angle emission → low statistics
- MC highly unreliable, probing the very tail of the angular distribution of secondary



Envision WP2 2011 Report- G4



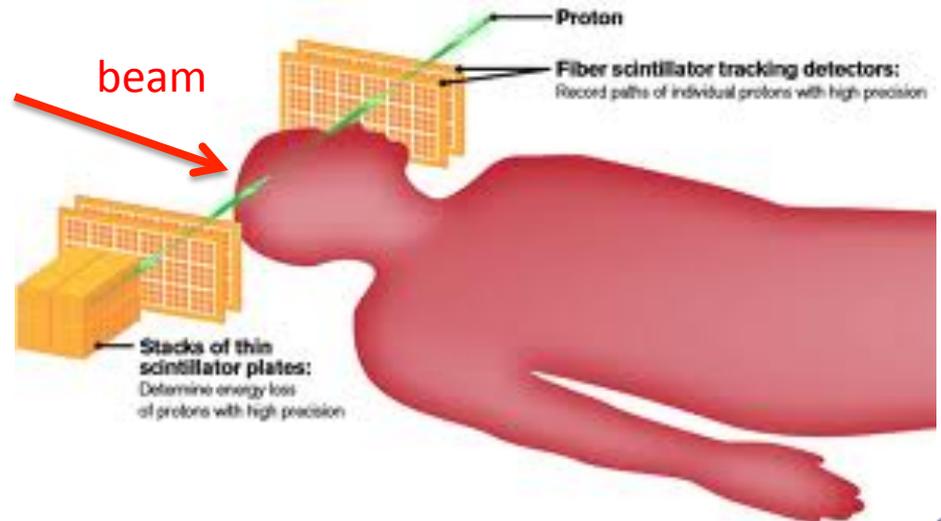
# Why so excited about charged particles emitted by the beam??

Charged particles 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 & BP

BUT...

- They are not so many
- Energy threshold to escape  $\sim 100$  MeV
- They suffer multiple scattering inside the patient → worsen the back-pointing resolution

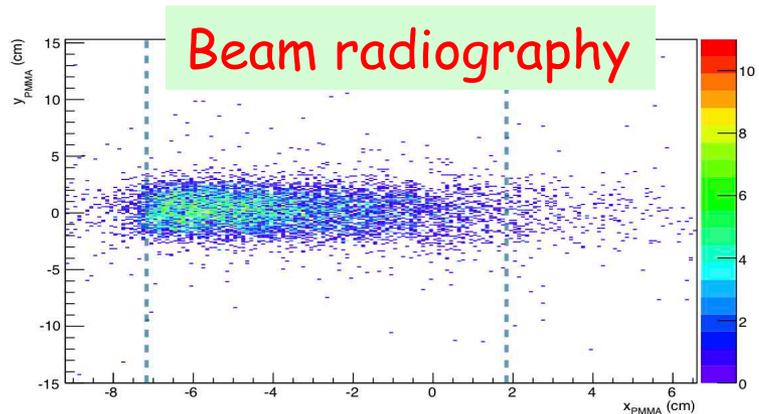
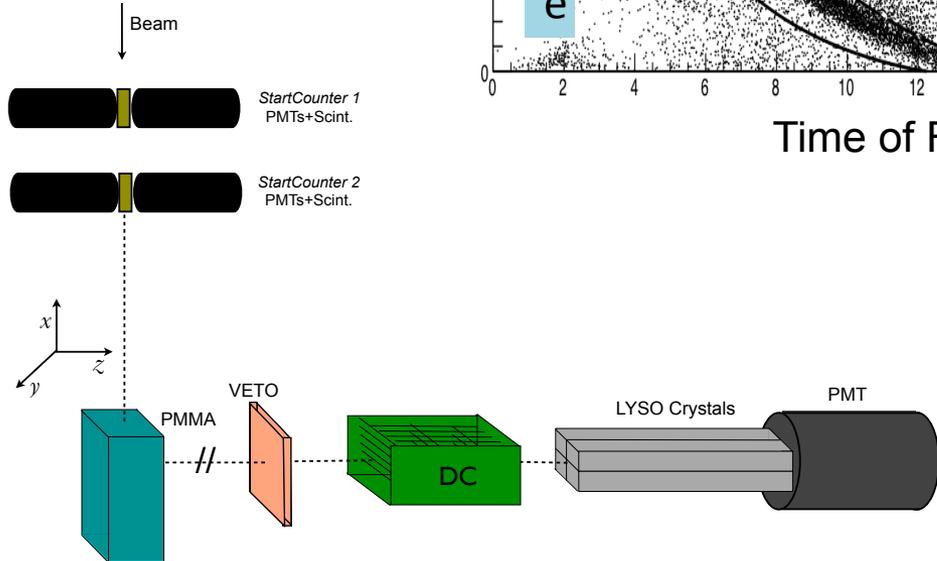
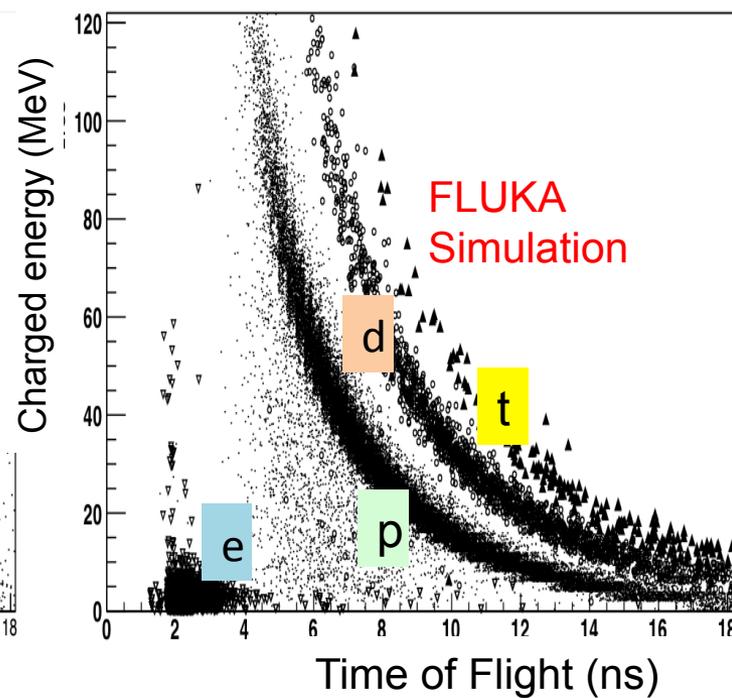
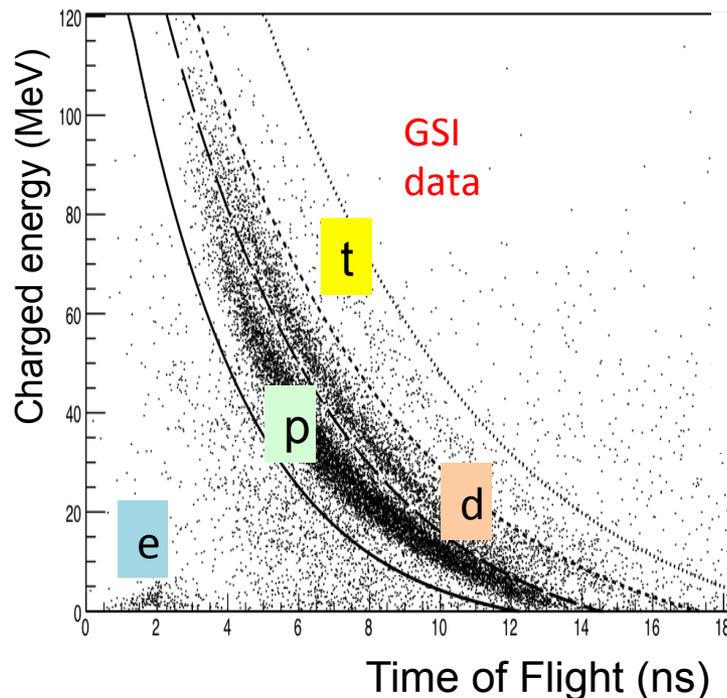




# Searching for charged secondaries...

L. Piersanti et al. PMB 2014

Charged secondaries produced at  $90^\circ$  wrt the beam from PMMA target on 220 AMeV  $^{12}\text{C}$  beam at GSI



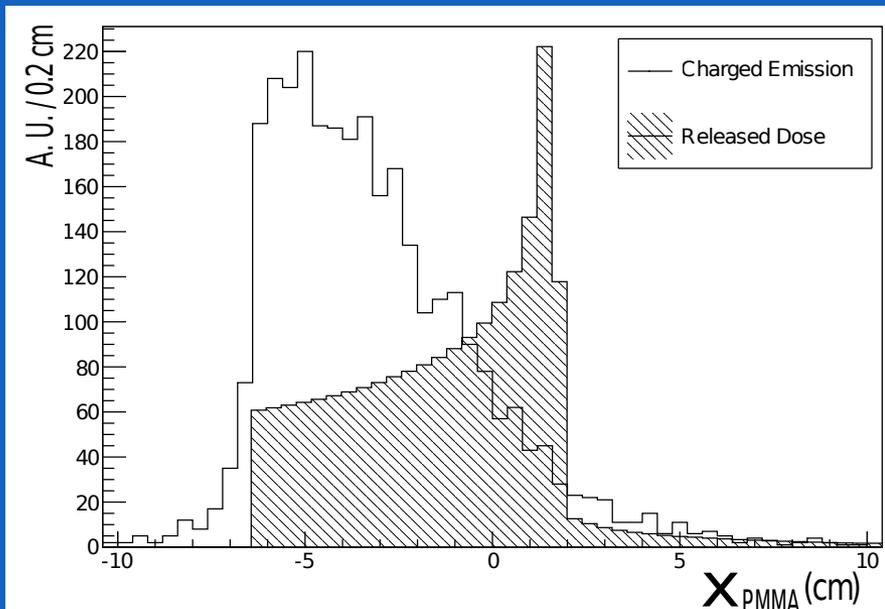


# Fragmentation & dose monitoring

There are indications that emission point distribution of 100-150 MeV secondary protons provides info on the BP position

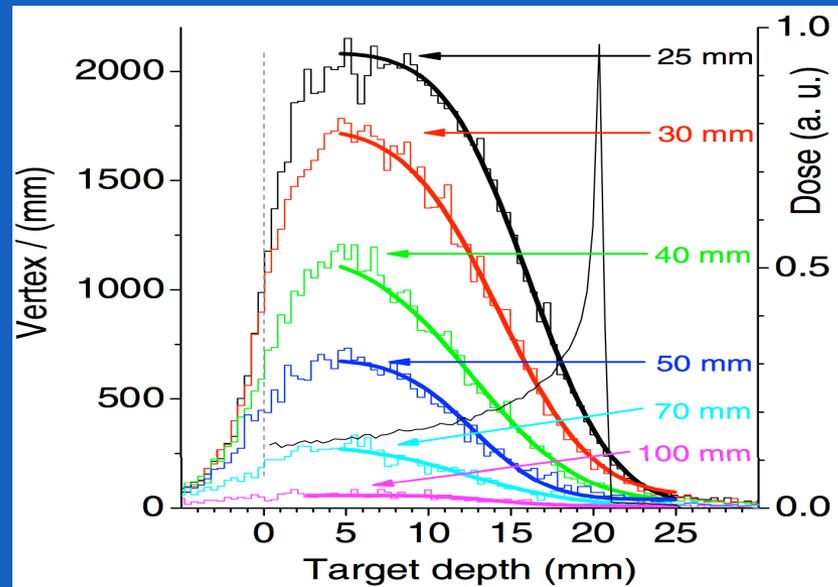
Measured emission distribution shape of protons as detected outside a 5 cm thick PMMA at 90° wrt the direction of 220 AMeV <sup>12</sup>C beam

L. Piersanti et al Phys. Med. Biol 2014



Simulated emission distribution shape of protons as detected outside different PMMA thickness at 30° wrt the direction of 95 AMeV <sup>12</sup>C beam

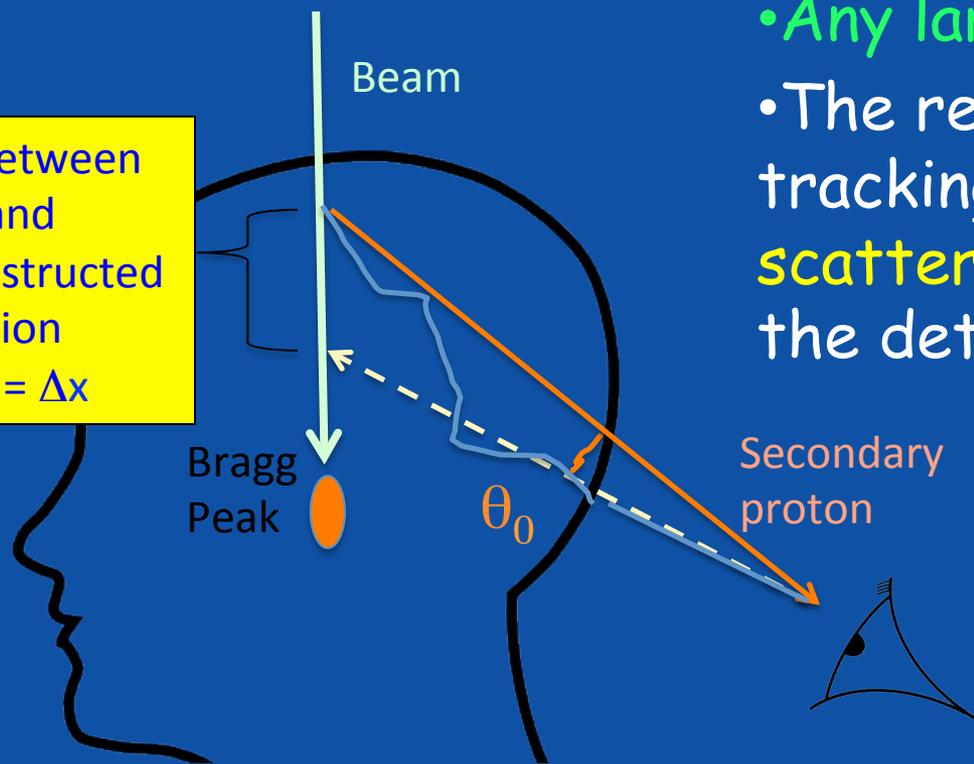
E. Testa et al Phys. Med. Biol. 57 4655





# Which detector should be used?

Diff between true and reconstructed emission point =  $\Delta x$

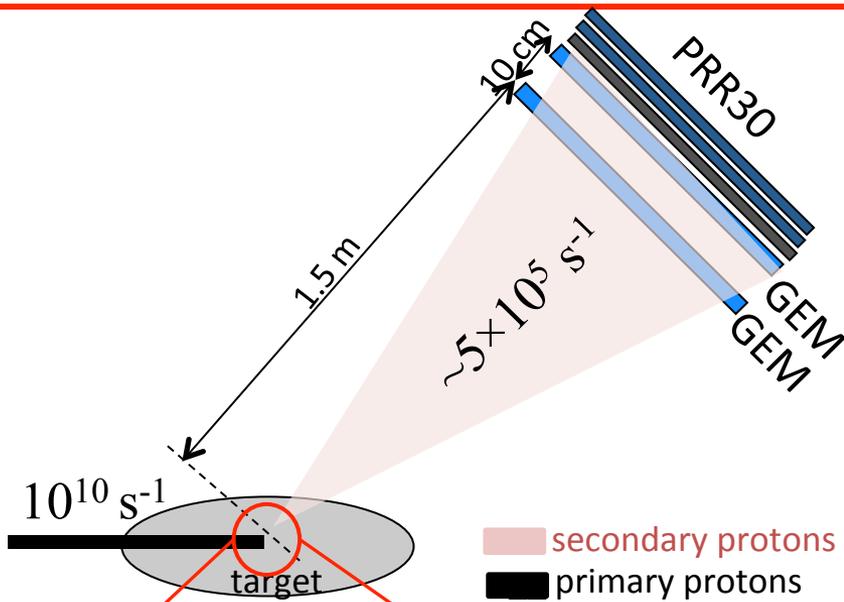


- Any large tracking detector!!
- The resolution of the back-tracking is limited by the **multiple scattering in the patient**, not by the detector resolution..

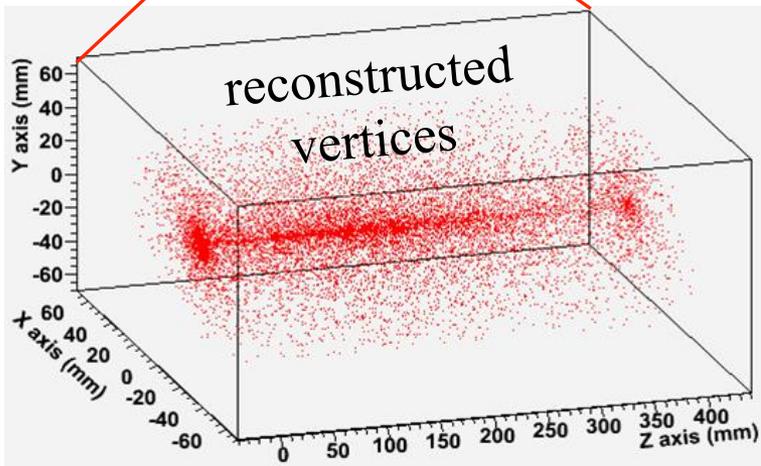
Typical resolution on  $\Delta x$  is of the order of 6-8 mm

Integrating enough statistic ( $\sim 10^3$  events) helps to lower the accuracy on the emission point distribution ( and then on the beam profile) to mm level  $\rightarrow$  **detector size**

# Vertex imaging...some Results



- $\sigma_{GEM\text{-spatial}} \cong 400\mu\text{m}$
- $\rightarrow \sigma_{\theta} \cong 6\text{mrad}$  Angular resolution
- $\rightarrow \Omega \sim 0.3\%$  (0.04 sr) Solid angle



- Large-angles beam diagnostics is feasible
- at an acquisition rate of 10<sup>6</sup> tracks/s

Courtesy of  
**TERA**



# PRR30

In collaboration with: AGH University, PSI

## Scintillators stack: Range/Energy loss

- Plastic scintillators (3mm):
  - 2 modules in coincidence for trigger
  - 48 modules (~15 cm water equivalent)
  - density ~1 (almost tissue equivalent)
- Wavelength shifter fibers
- Silicon Photomultipliers Readout

High intrinsic rate capability (>1 MHz)

***30 MeV < RESIDUAL RANGE < 190 MeV***



## GEMs: Tracker

- 30x30 cm<sup>2</sup> Gas Electron Multiplier (GEM)
- Gas: Ar-CO<sub>2</sub> (70:30)
- HV: 3.9-4.2 kV
- 2D strip readout

High rate (~1 MHz)

Radiation resistant



Courtesy of Martina Bucciantonio - TERA Foundation

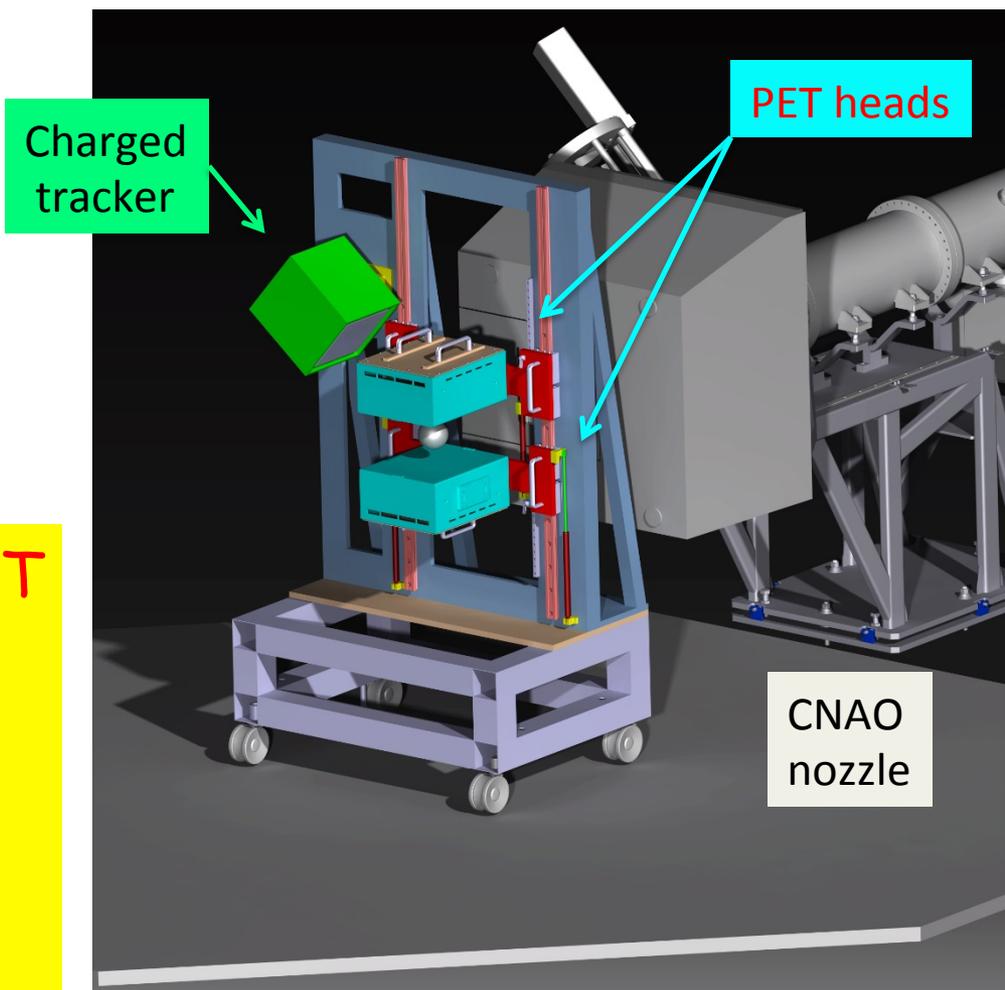


# Multimodal approach: The INSIDE project @CNAO

•INSIDE (Innovative Solutions for In-beam Dosimetry in Hadrontherapy) is a joint project MIUR-INFN-Centro Fermi-CNAO. 40 researchers.

In-beam dose profiling by PET activities and charged secondaries detection.

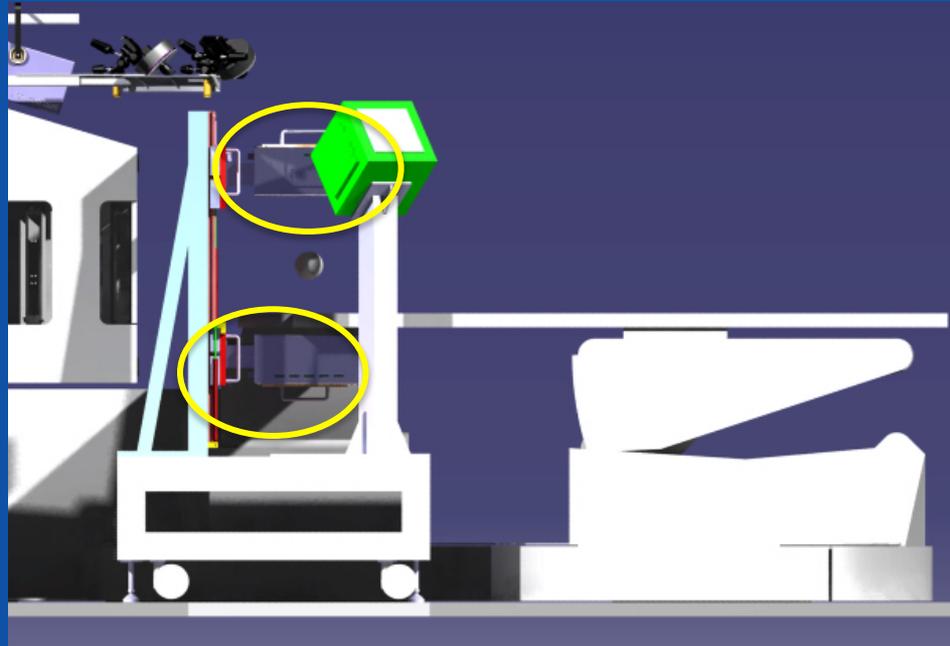
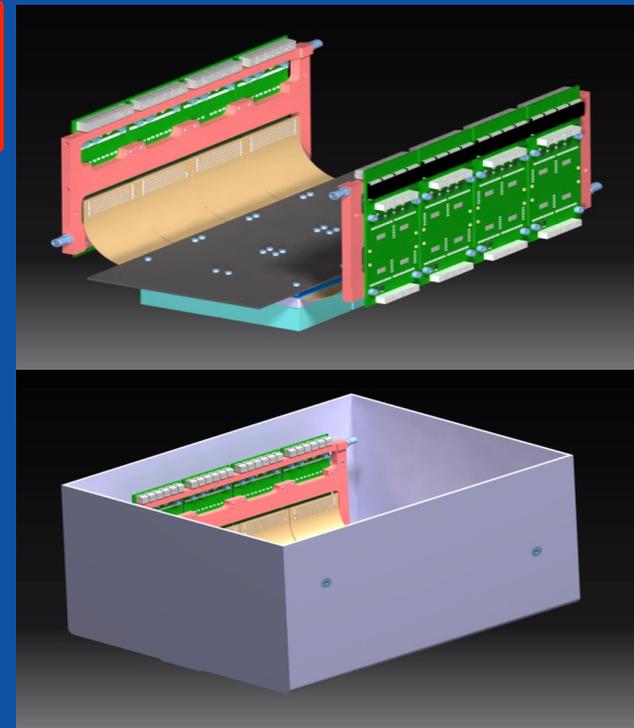
Mechanics and operation optimized to be inserted in the CNAO work-flow





# The INSIDE PET system

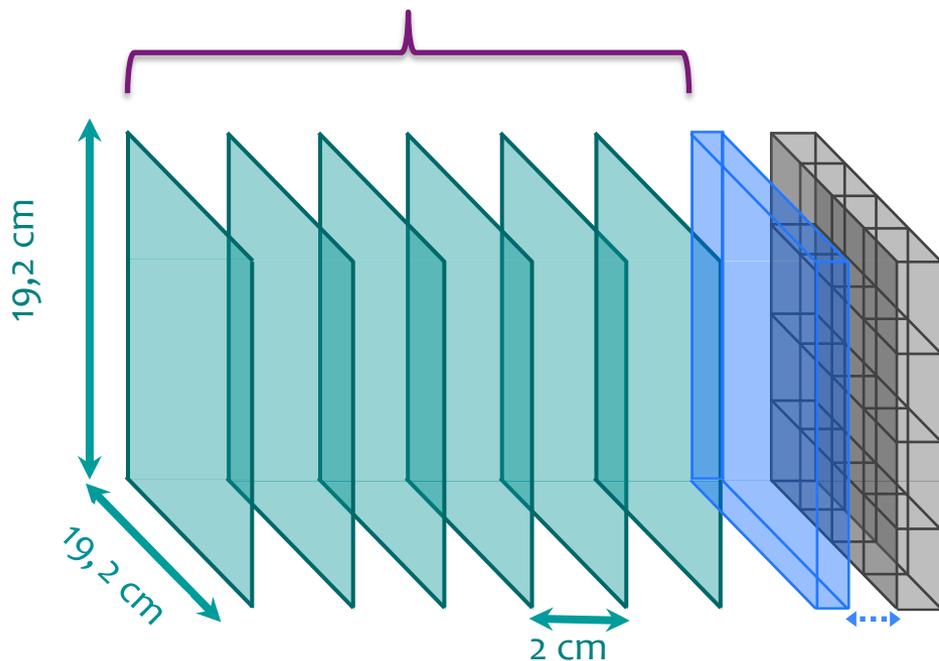
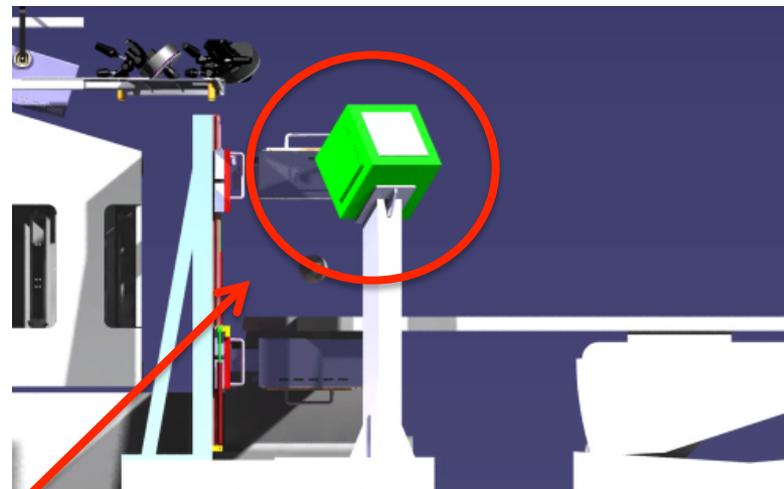
- DAQ sustains annihilation and prompt photon rates during the beam irradiation
- Two planar panels each 10 cm x 20 cm wide. Each panel will be made by 2 x 4 detection modules
- Each module is composed of a pixelated LYSO scintillator matrix 16 x 16 pixels, 3x3 mm<sup>2</sup> crystals, 3.1 mm pitch, for a total sensitive area of 5x5 cm<sup>2</sup>
- One SiPM array ( 16x16 pixels) is coupled one-to-one to each LYSO matrix





# INSIDE: charged tracker

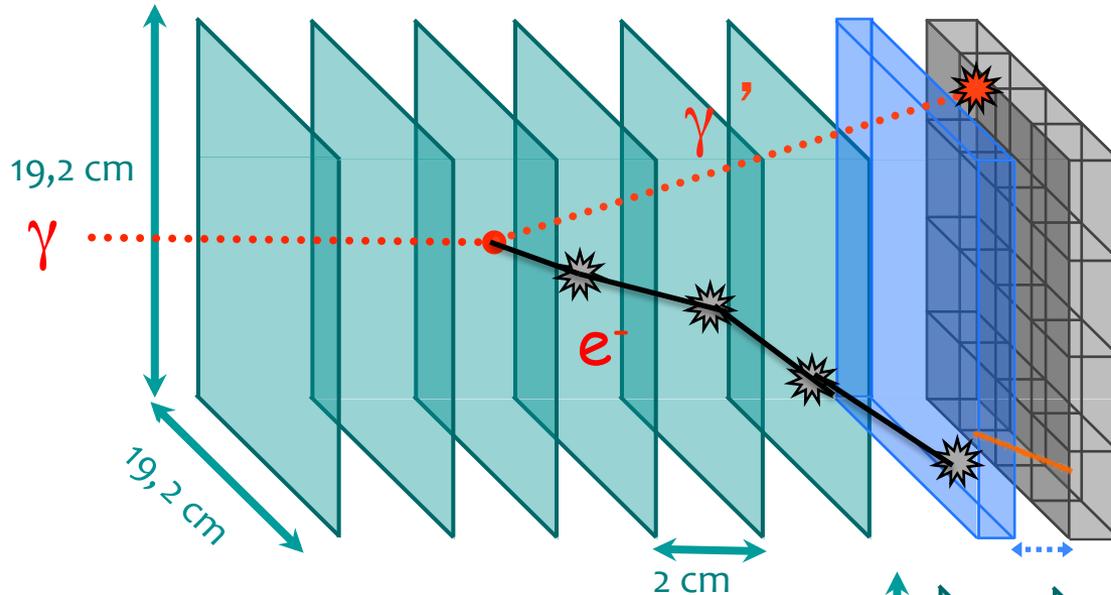
- 6 XY planes with 2 cm spacing. Each plane made of 2 stereo layers of 192  $0.5 \times 0.5 \text{ mm}^2$  square scintillating fibers
- 2x0.5 mm squared fibers read out by Hamamatsu  $1 \text{ mm}^2$  SiPM : S12571-050P
- 32 SiPM feed a 32 ch ASIC BASIC32



- 4x4 LYSO pixellated crystals tracking planes:  $50 \times 50 \times 16 \text{ mm}^3$
- Plastic absorber 1.5 cm thick in front of LYSO to screen electrons
- Crystals read out by 64 ch Hamamatsu MultiAnode



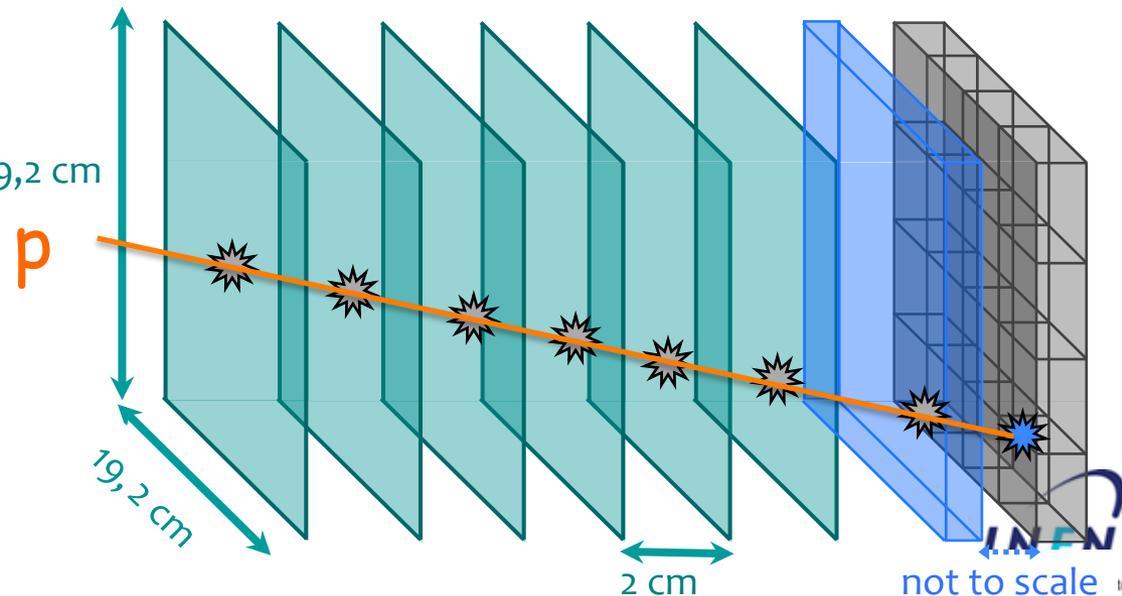
# INSIDE Profiler: prompt secondaries



“dual mode” detector

- Compton camera for prompt photons ( $E_\gamma \sim 1-10$  MeV)
- Tracking device for charged secondaries ( $E_{kin} \sim 30-130$  MeV)

- Heavy charged secondary cross all TRK planes up to LYSO crystals
- Electrons from Compton event have winding tracks (mul. scatt.) and are not detected in the LYSO





## Summary & conclusions (I)

- Nuclear fragmentation prevents the use of ions heavier than Oxygen and must be taken into account in the Treatment Planning System for PT and in shielding calculation in Space Radioprotection
- The nuclear measurements go directly in the clinical practice or spacecraft design
- The experiments seem to evolve towards more and more complexity and dimensions
- No mention has been done in this talk of neutrons production due to nuclear fragmentation and their measurement



## Summary & conclusions (II)

- The nuclear interaction of the beam with the patient in PT provide also the only method to monitor the released dose, backtracing the produced secondaries from the beam path to the BP:  $\gamma$  from  $\beta^+$  emitters, prompt photons from nuclear excitation and light charged fragments
- Huge experimental activity that has direct application in the clinical practice



# CREDITS

I have been given a lot of slides, plots, comments by many colleagues...

- M.Durante
- G.Battistoni
- K.Parodi
- E.Testa
- A.Ferrari
- + others...

Thanks!!



spares



# Simplified scheme of a Treatment Planning System

CT scan (density vs  $D_x, D_y, D_z$ )

PTV

Table of  
DE vs  
 $E_{\text{beam}}, x, y, z$

TPS kernel  
optimisation

RBE vs  
 $E_{\text{beam}}, DE, x,$   
 $y, z$

Fluences for each beam  
spot

Pink = fragmentation  
related

TPS Verification and  
correction

Dosimetry monitoring  
and correction (PET)

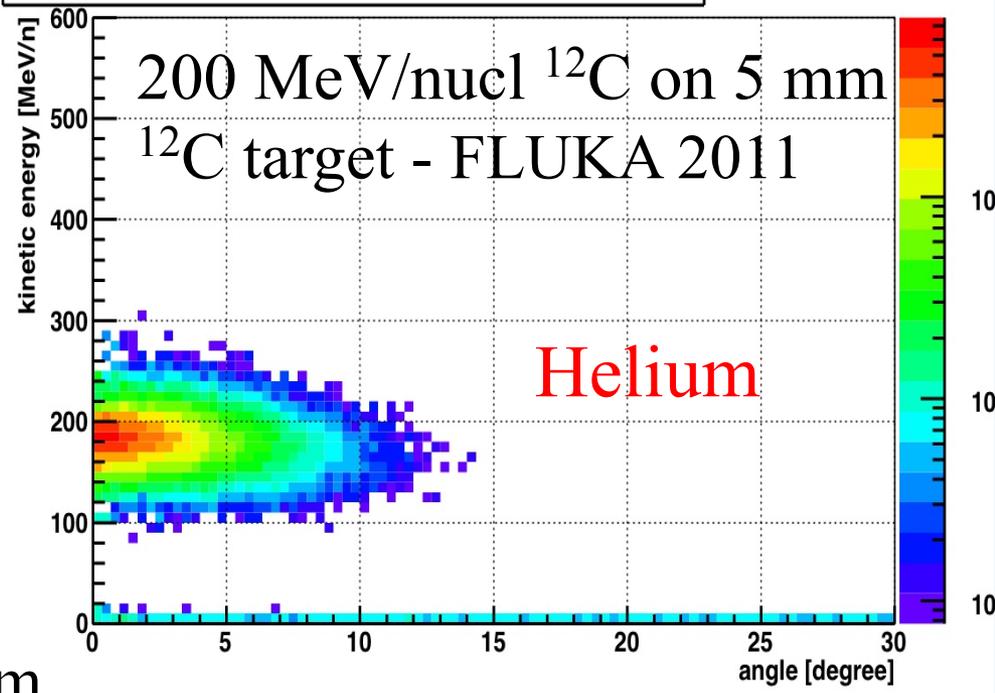
Yellow = (can be) MC based



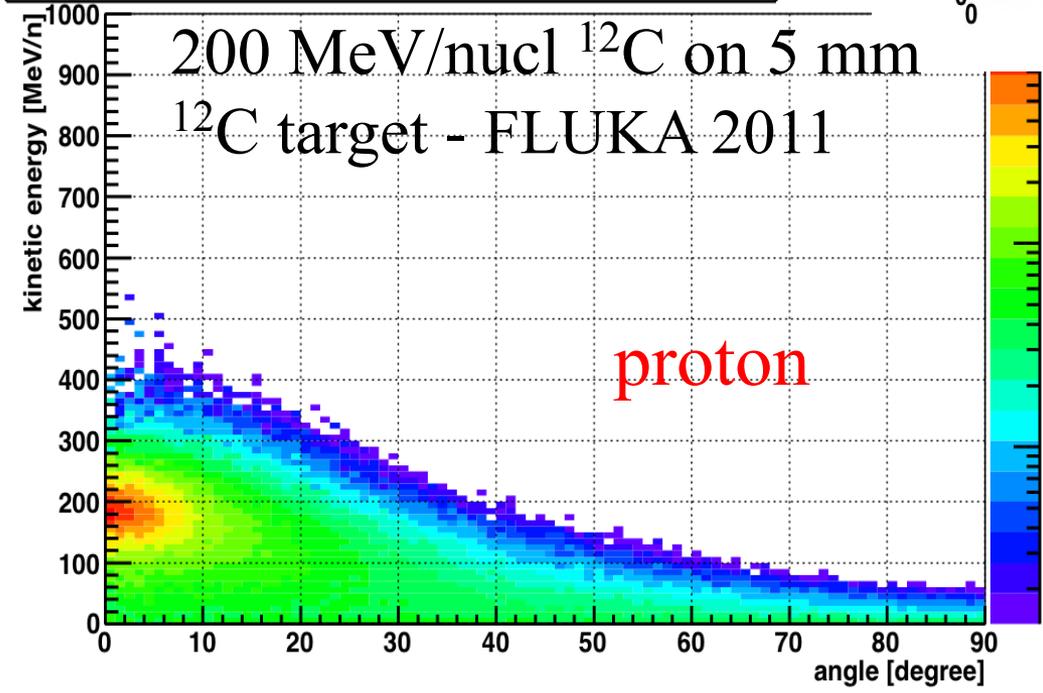
# Produced p and He: angle vs energy

The protons could be a possible candidate for beam imaging... if they can escape the patient!! ( $E_{kin} > 100$  MeV)

Helium yield double-differential,  $N_{prod He} / N_{prim C} [1/(sr \times MeV/n)]$



Hydrogen yield double-differential,  $N_{prod H} / N_{prim C} [1/(sr \times MeV/n)]$



- The proton flux at large angle is mainly made by low energy particles
- WATCH OUT!! How much are MC reliable?



# Spec's of hadrontherapy monitor

In conventional RT ( i.e. with photons), the beam crosses the patient body and can be used for monitoring. In HT the beam is absorbed inside the patient.

An hadrontherapy monitor device, in principle, should:

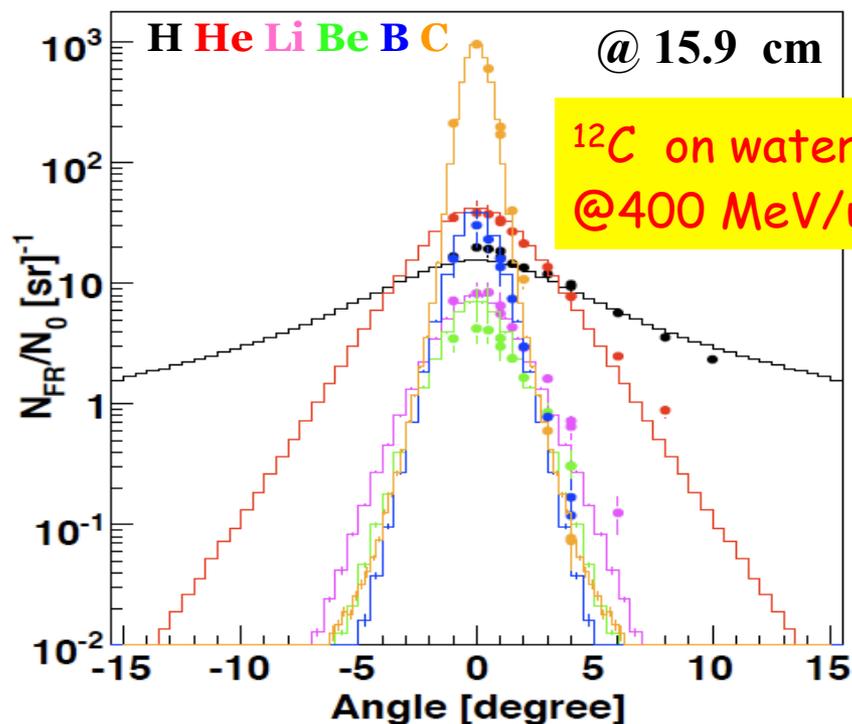
- Measure shape and absolute value of dose to check the agreement between the planned target volume and the actually irradiated volume
- The measurement should be done during the treatment (in-beam)
- Must rely on secondaries generated by the beam that comes out from the patient to spot the position of the dose release
- Must be able to deal with the other secondaries that come out that acts like background



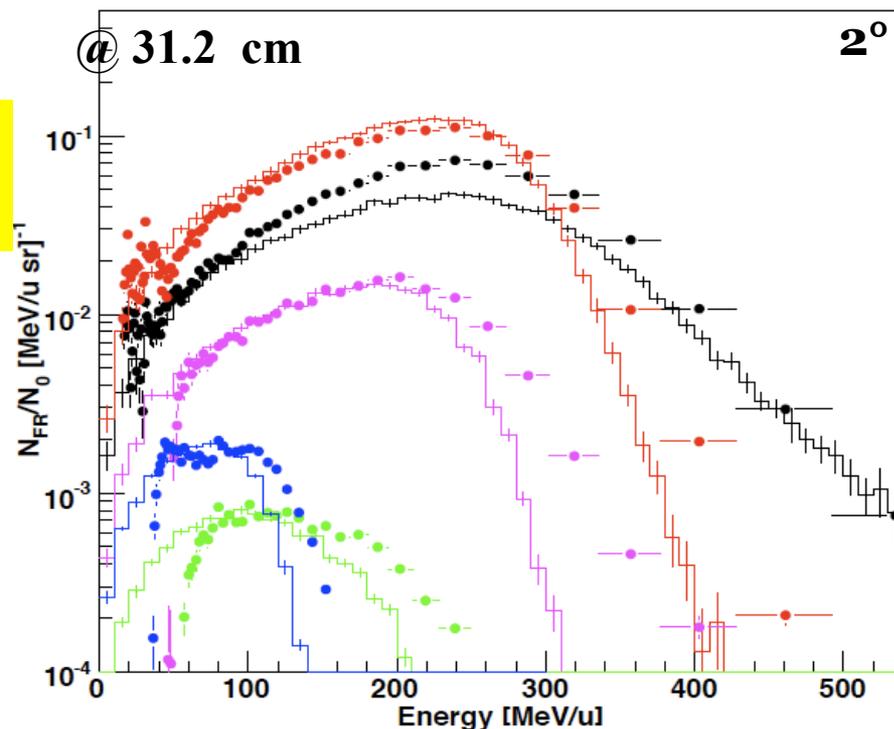
# Frag.s production by $^{12}\text{C}$ beam

The secondary fragments broaden the lateral dose profile and go beyond the tumor region.

## Angular distribution



## Energy distribution



FLUKA benchmark against thick target data

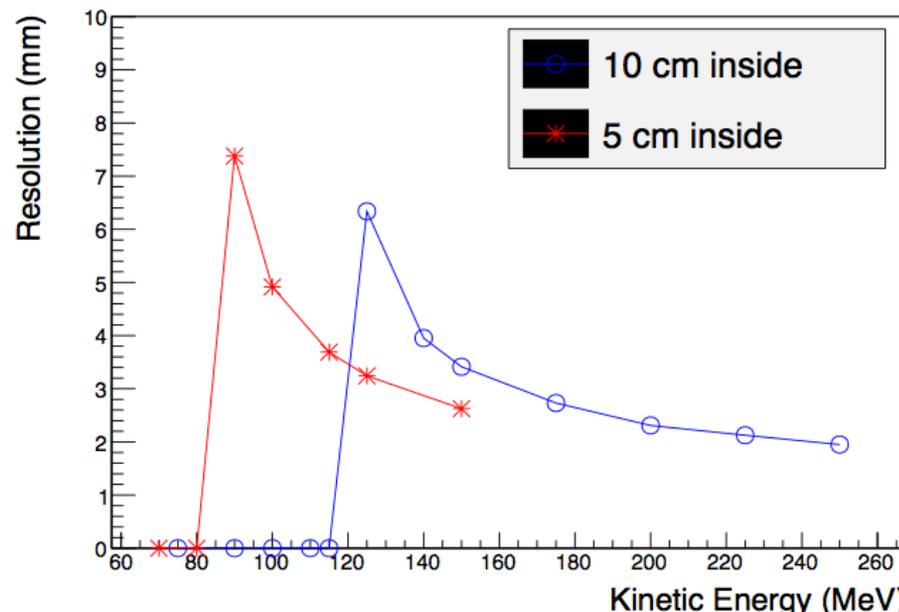
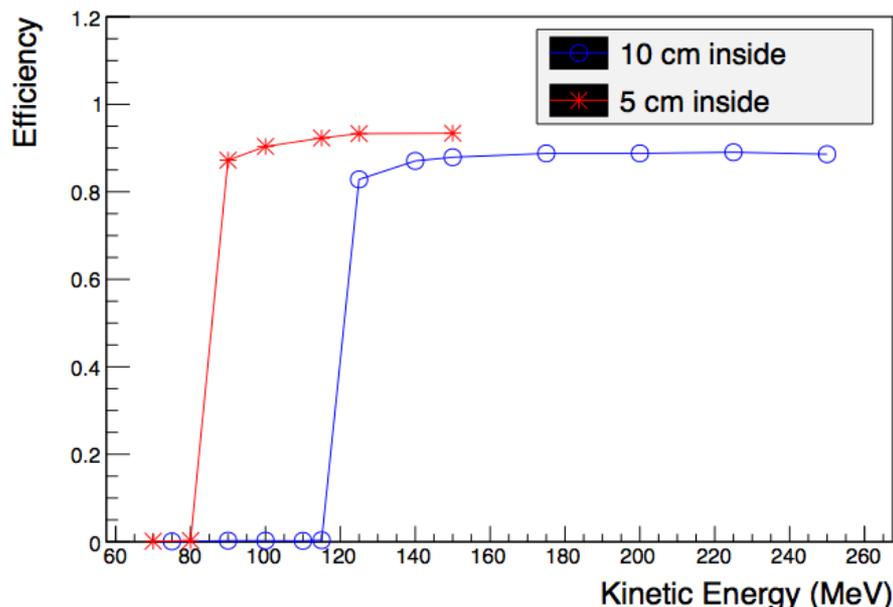
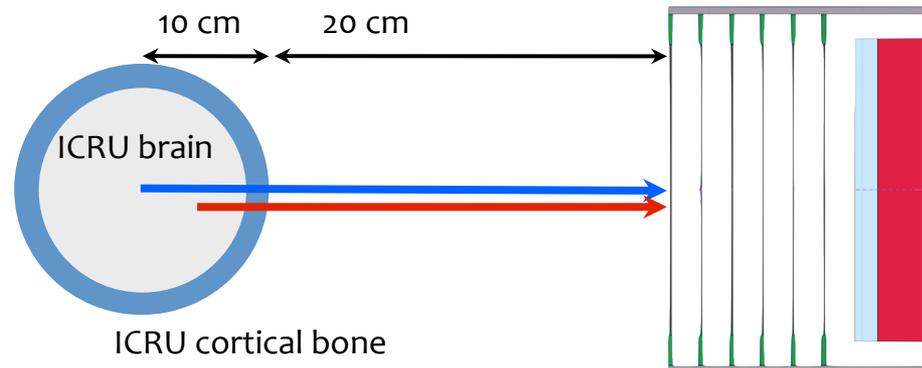
Exp. Data (points) from Haettner et al, Rad. Prot. Dos. 2006  
Simulation: A. Mairani PhD Thesis, 2007, PMB to be published



# Performance with emitted protons

Simulation of a “spherical patient” with ICRU materials, with proton source placed at different depths: 10 cm and 5 cm

Multiple scattering single track  
Spatial Resolution ~ few mm

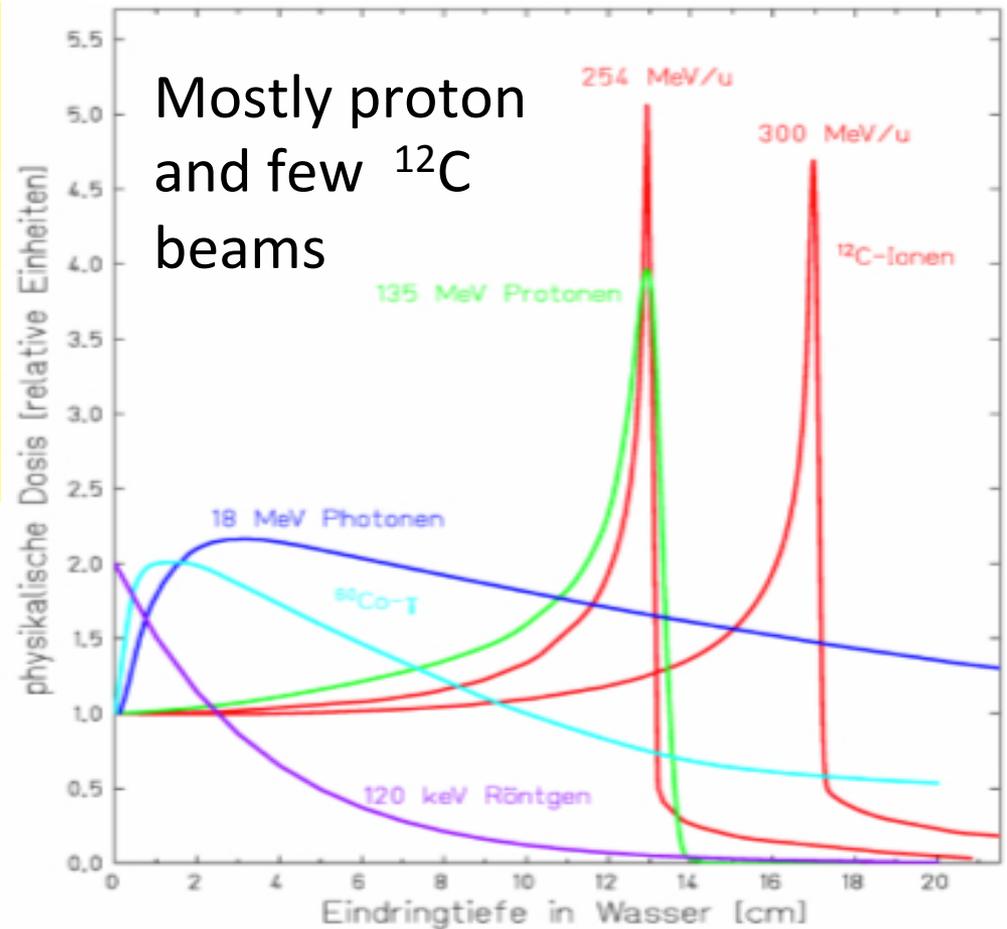
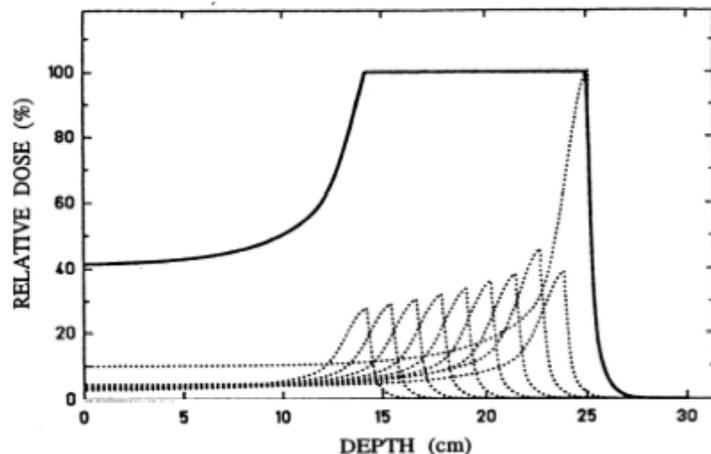




# Hadrontherapy vs Photon RT

The highest dose released at the end of the track, sparing the normal tissue

- Length of track function of the beam energy
- Dose decrease rapidly after the BP.
- Accurate conformal dose to tumour with Spread Out Bragg Peak



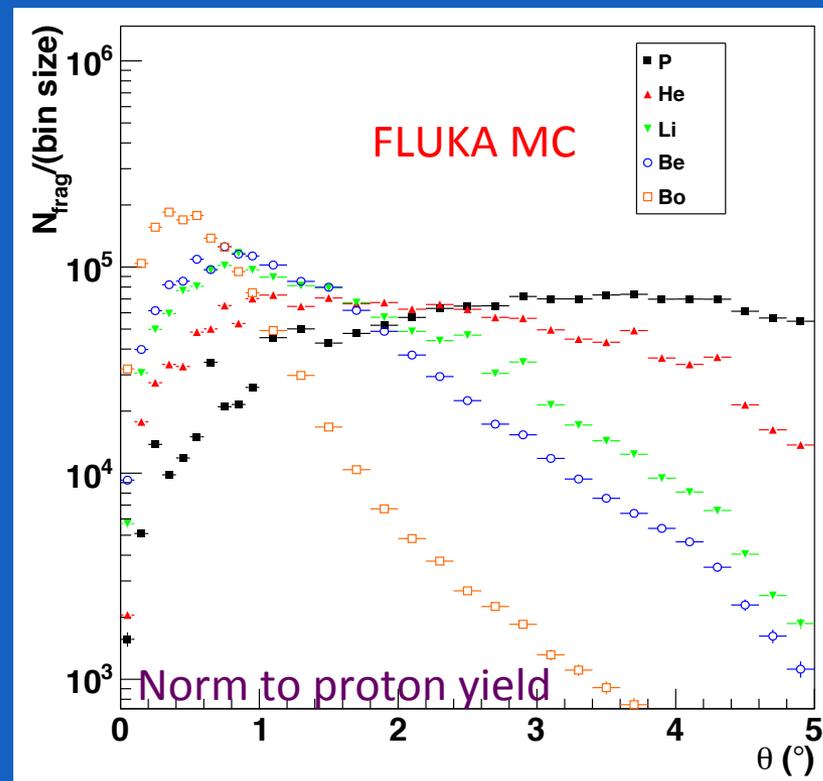
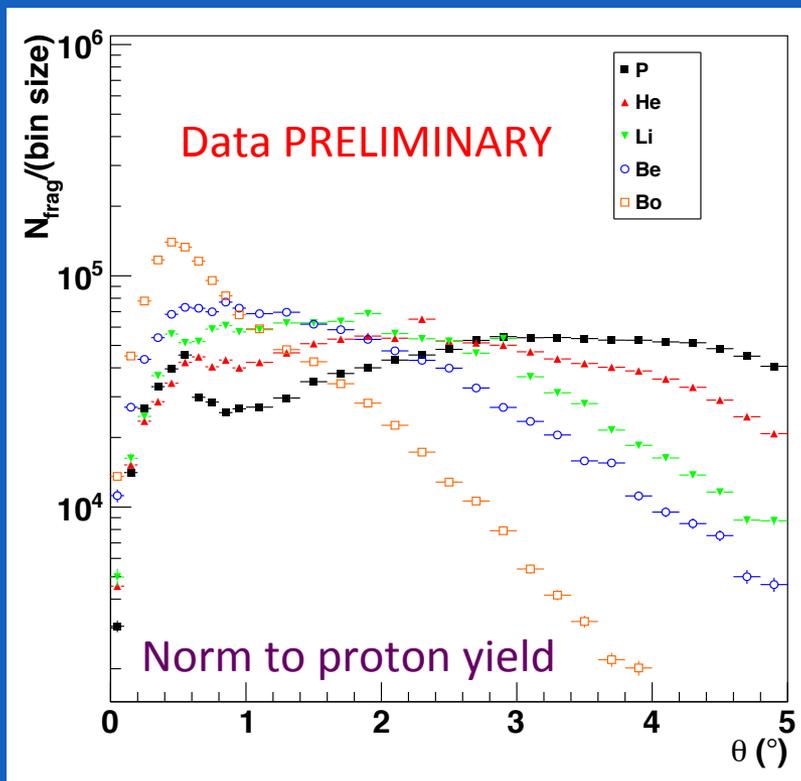


# Fragment yields of $^{12}\text{C}$ on composite target (O+C+BrLn) at small angles

First look at small angle  $\rightarrow$  corresponds to the region that induces the dose beyond the distal part of the treatment region

Reconstructed yields are distorted by the efficiencies (tracking/selection/etc..) and by acceptance... to be applied

The angle distributions seems to be wider in data than MC



# Treatment uncertainties in ion beam therapy

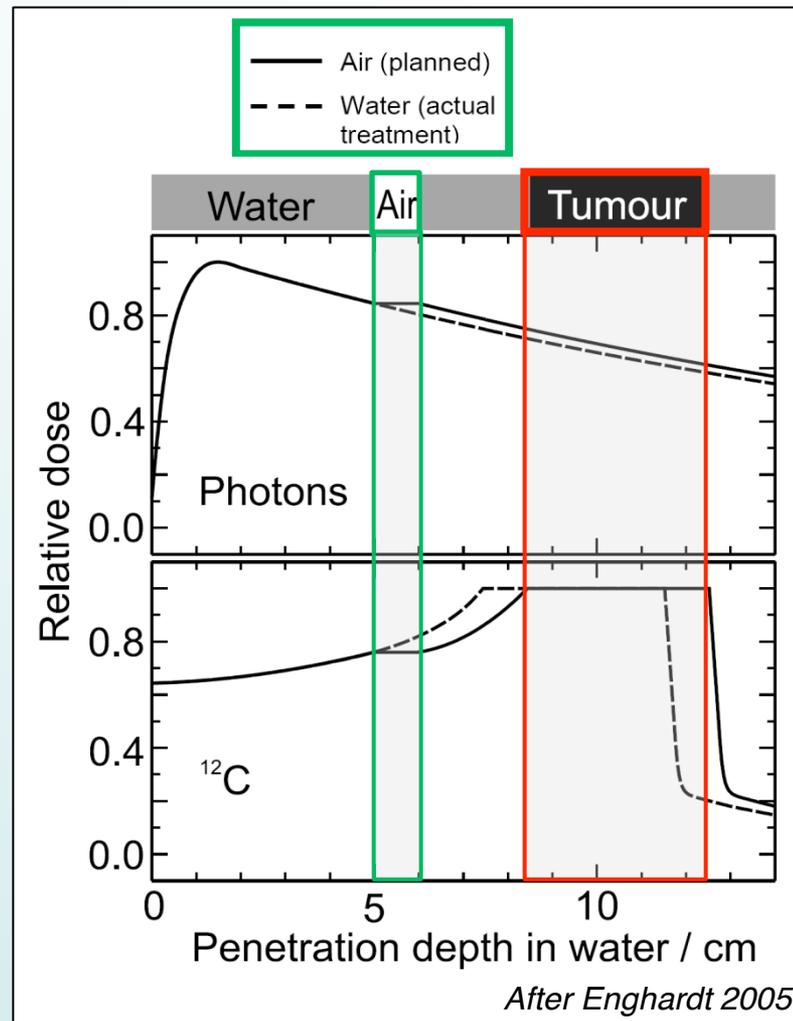
## ***TPS dose calculation errors***

- Inhomogeneities, metallic implants
- Conversion HU in ion range
- CT artifacts

## ***Difference TP / delivery***

- Daily setup variations
- Internal organ motion
- Anatomical / physiological changes

***Daily practice of compromising dose conformality for safe delivery***





# Emulsion scanning system

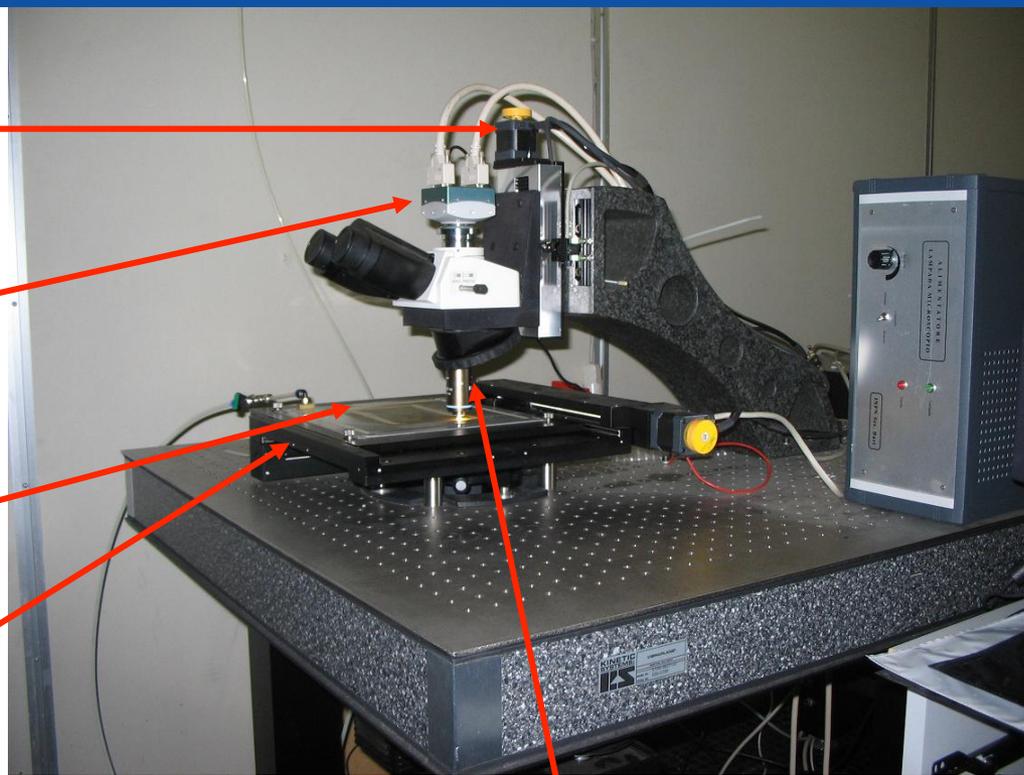
Z stage (Micos)  
0.05  $\mu\text{m}$  nominal  
precision

CMOS camera  
1280 $\times$ 1024 pixel  
256 gray levels  
376 frames/sec  
(Mikrotron MC1310)

Emulsion Plate

XY stage (Micos)  
0.1  $\mu\text{m}$  nominal  
precision

Illumination system, objective (Oil 50 $\times$  NA 0.85)  
and optical tube (Nikon)



- Scanning rate : 20cm<sup>2</sup>/h
- $\sim$ 2 mrad angular resolution
- $\sim$ 0.3  $\mu\text{m}$  spatial resolution
- $\sim$ 95% track detection efficiency

# FRAG (April 2009) $^{12}\text{C}+^{12}\text{C}, ^{197}\text{Au}, \text{CH}$ @62MeV

$\text{C} + \text{C} \longrightarrow N^\circ \approx 5 \cdot 10^{12}$

$I \sim 40 - 80 \text{ pA}$

$\text{C} + \text{CH}_2 \longrightarrow N^\circ \approx 1 \cdot 10^{12}$

$I \sim 40 - 60 \text{ pA}$

$\text{C} + \text{Au} \longrightarrow N^\circ \approx 11 \cdot 10^{12}$

$I \sim 180 - 230 \text{ pA}$

