Nuclear Fragmentation and Particle therapy

V. Patera
Universita' di Roma "La Sapienza" & INFN Roma1

Roma 21-25 Settembre 2015

Outline

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

- Overview: fragmentation in PT
  Projectile fragmentation: recent experiments
- The target fragmentation issue
- Fragmentation & dose monitoring
- Summary and conclusions

Outline

Bouncing from fundamental physics to applied physics and back…

- Overview: fragmentation in PT
  Projectile fragmentation: recent experiments
- The target fragmentation issue
- ~~Fragmentation & dose monitoring~~
- Summary and conclusions

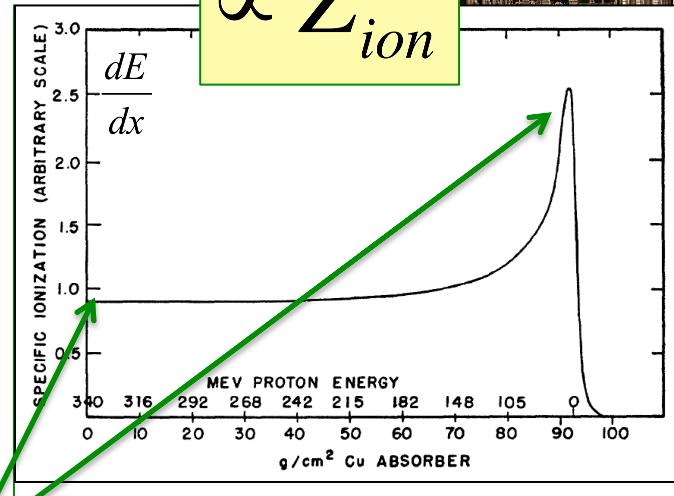
After previous talk by G.Battistoni !!!!

INFN Istituto di Fisica

Particle Therapy vs Particle Physics point of view

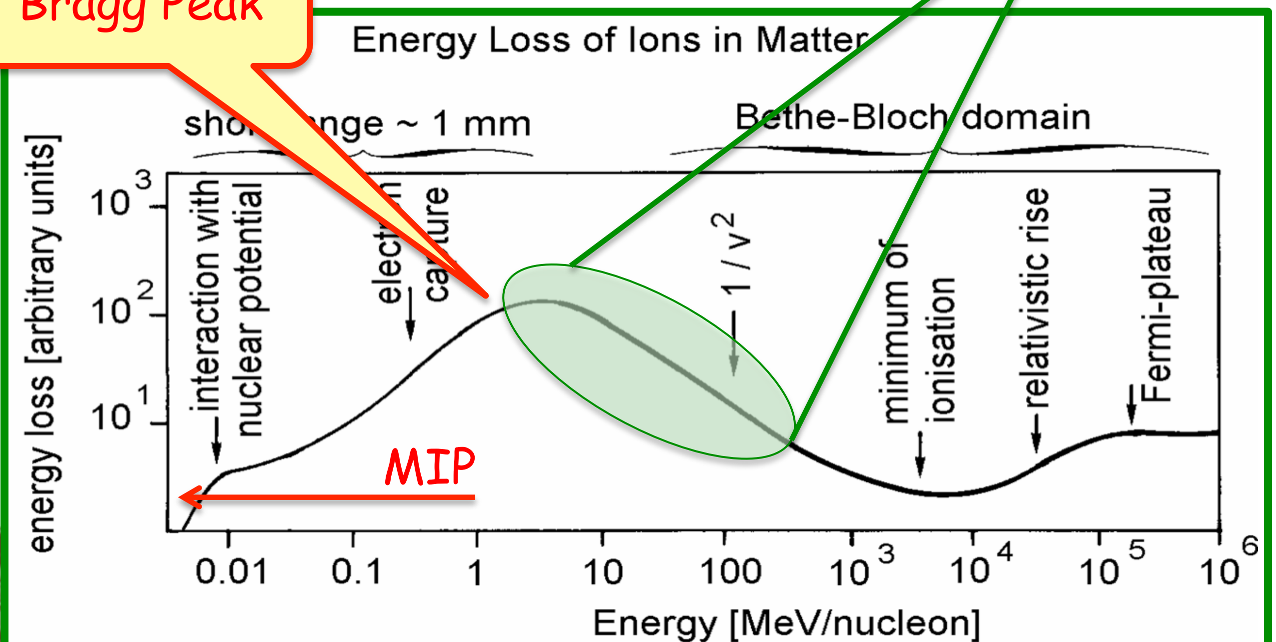
The release of energy by charge particles has very attractive, features… why not to use them?

$\propto Z_{ion}^2$



lunghezza di penetrazione

Bragg Peak



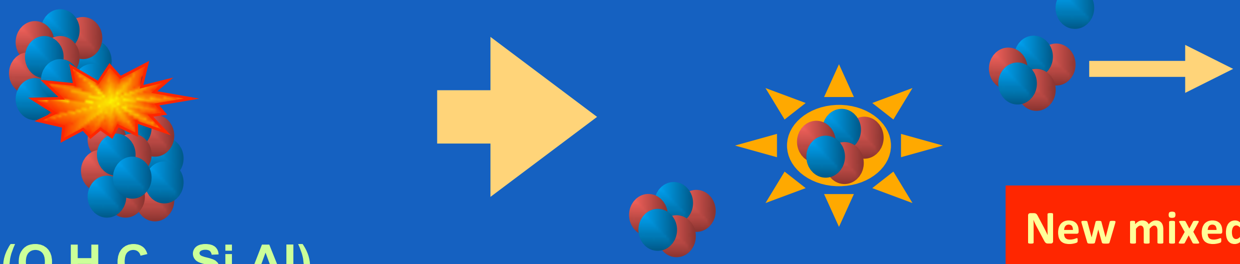
Perfect to release energy (dose) in a tumor buried inside the patient, like a depht bomb..

Mostly proton, few ^{12}C beams.

Future ^{4}He, ^{16}O ?

Fragmentation in PT : p,^{4}He,^{12}C,^{16}O fragmentation on CNO @100-500 MeV/nucl

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



Interaction of the projectile with the patient body

Target Fragments

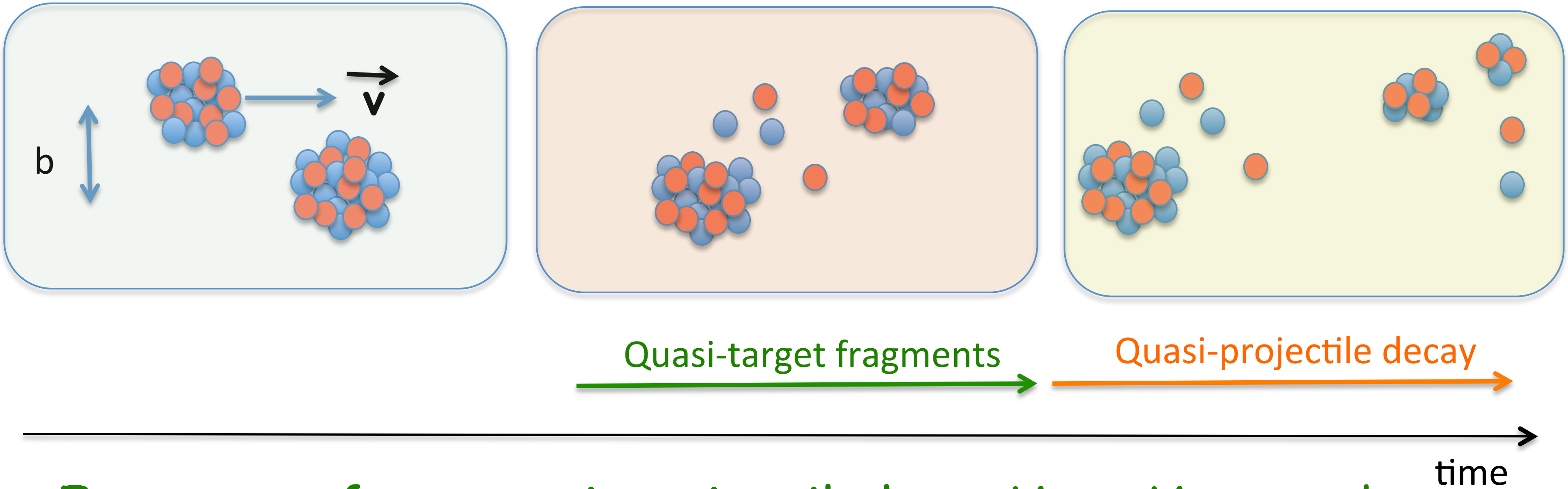
... lower charge than target
... high LET
... short ranges

Projectile fragments

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

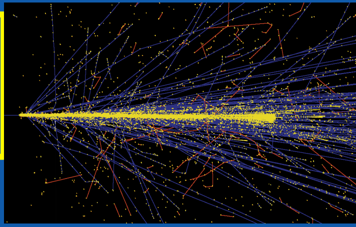
NB !!: Only target fragmentation for proton beam/projectile !!!!

The abration-ablation paradigm & PT



- Fragments from quasi-projectile have $V_{frag} \sim V_{beam}$ and narrow emission angle. Longer range then 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

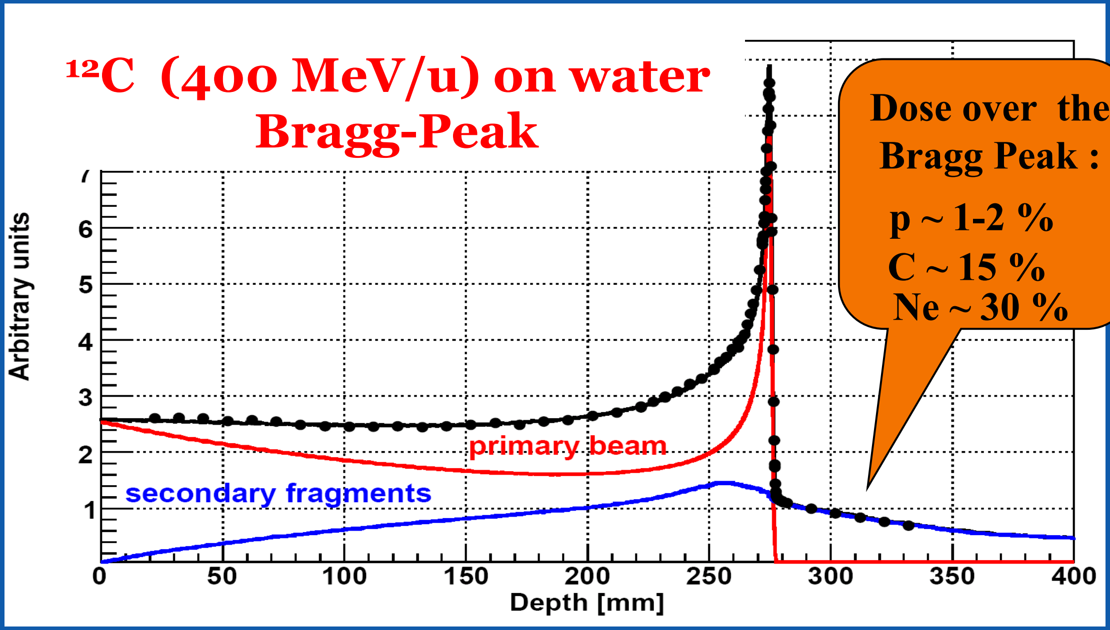
FRAGMENTATION OF ^{12}C in bio tissue



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

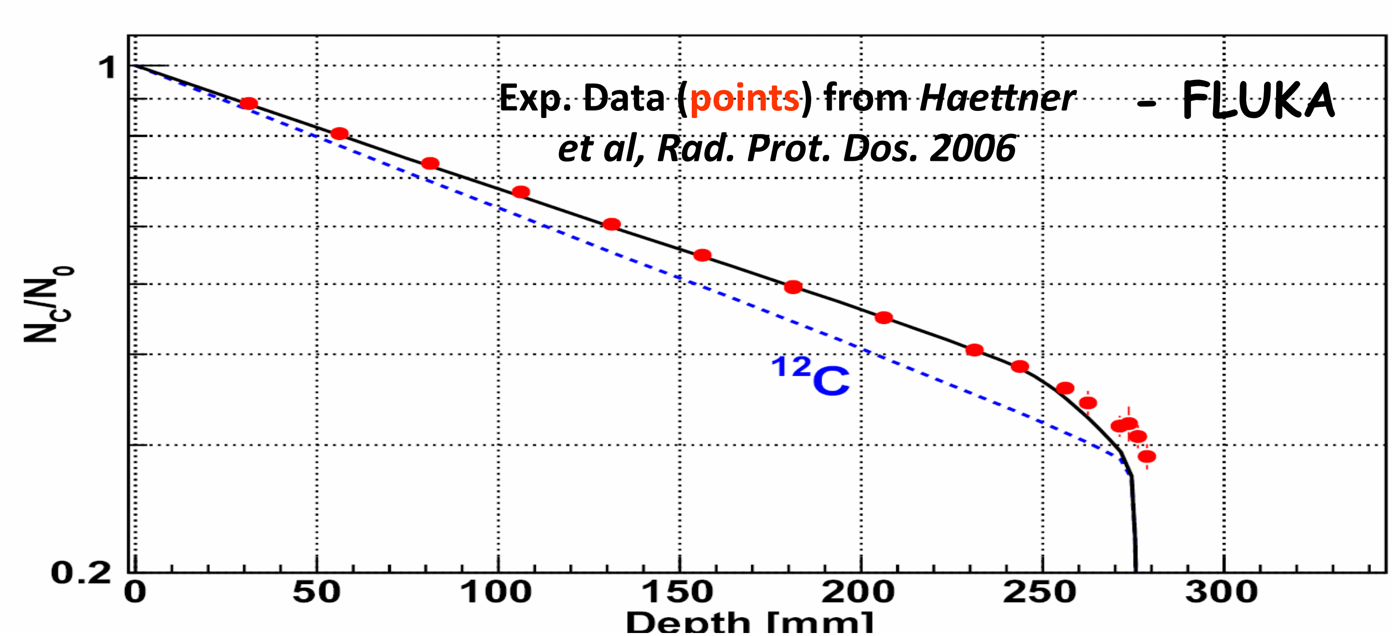
- ✓ *Mitigation and attenuation of the primary beam*
- ✓ *Different biological effectiveness of the fragments wrt ^{12}C*



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

400 MeV/n ^{12}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}C

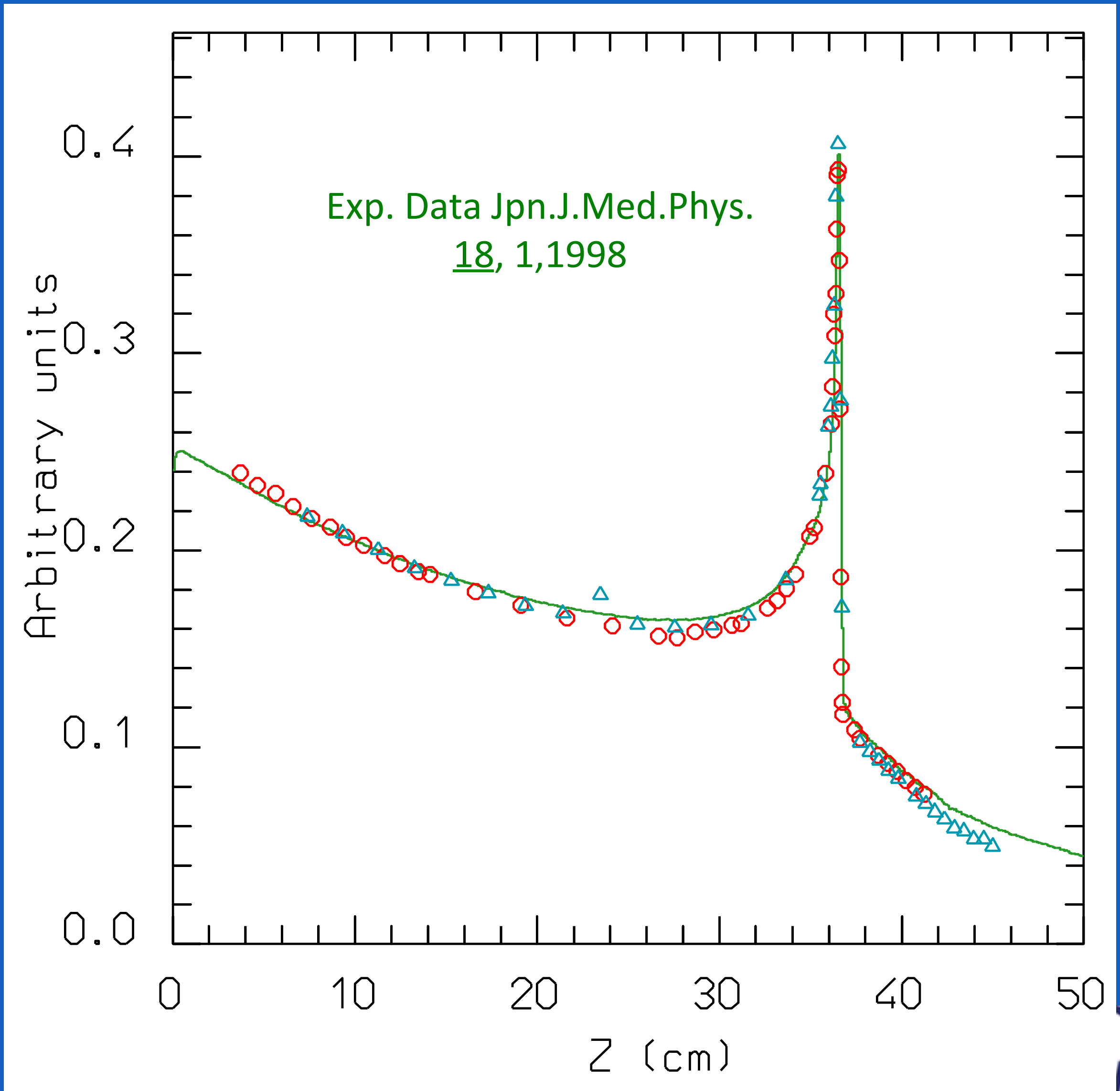
Fragmentation of ^{20}Ne @ 670 MeV/n

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

The green line is the FLUKA MC prediction

The symbols are exp data from LBL and GSI

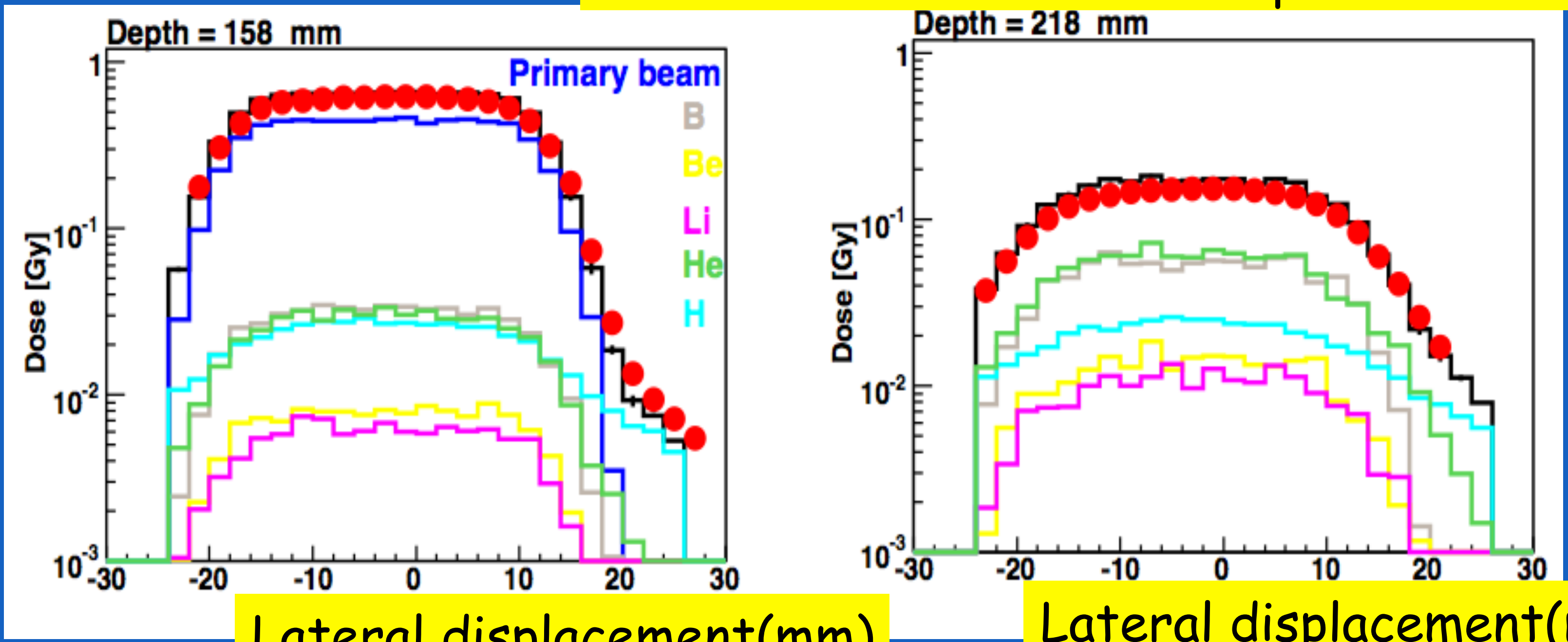
Huge dose contribution after the BP due to fragment



Fragmentation & 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 depht in water



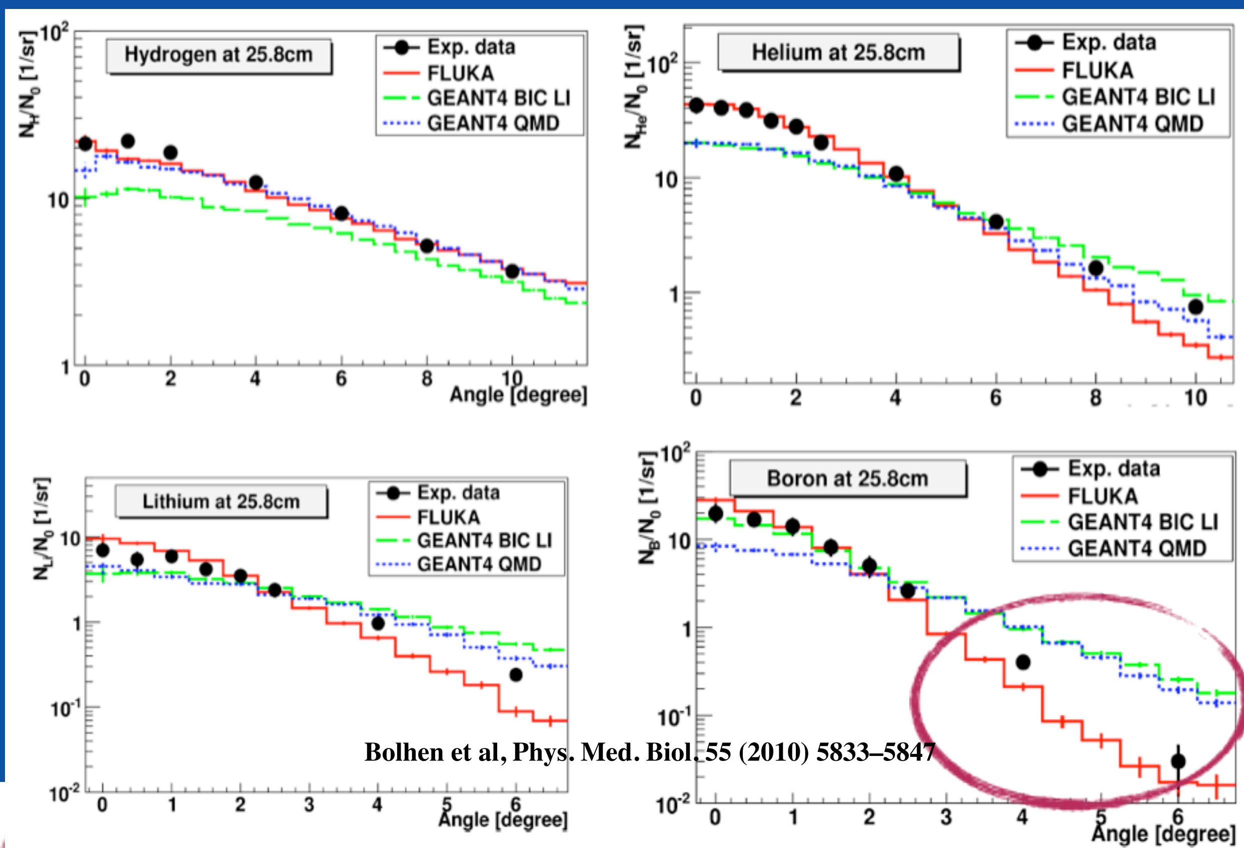
Lateral displacement(mm)

Lateral displacement(mm)

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

Data - MC comparison: ^{12}C ions

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



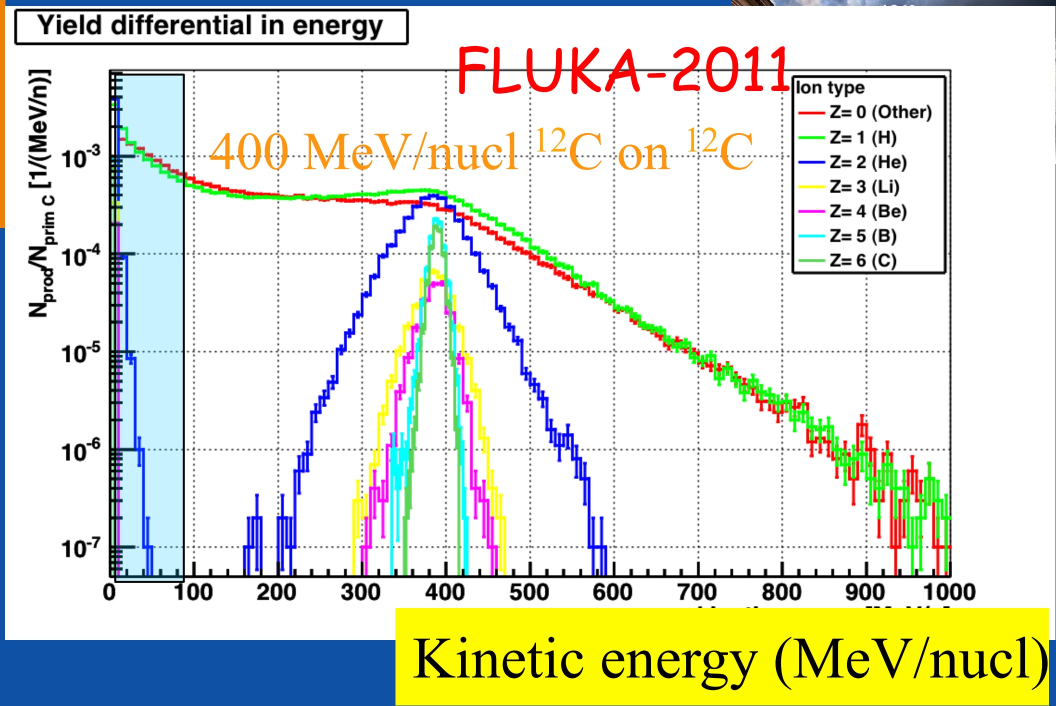
Bolhen et al, Phys. Med. Biol. 55 (2010) 5833–5847

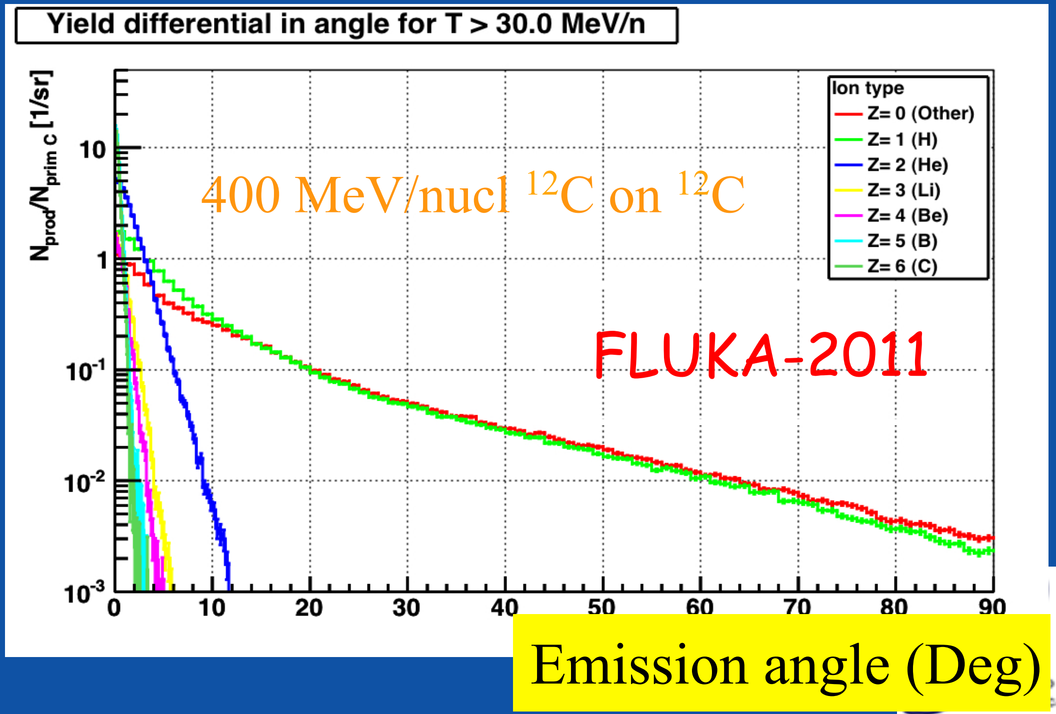
NB: the accuracy on delivered dose MUST be of the order of few %

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

Typical example: ^{12}C beam on ^{12}C target

- The Z>2 produced fragments approximately have the same velocity of the ^{12}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<β<0.6 and with a wide angular distribution with long tail
- The Z=2 fragment are all emitted within 20⁰ of angular aperture
- The DE/DX released by the fragment spans from ~2 to ~100 m.i.p.

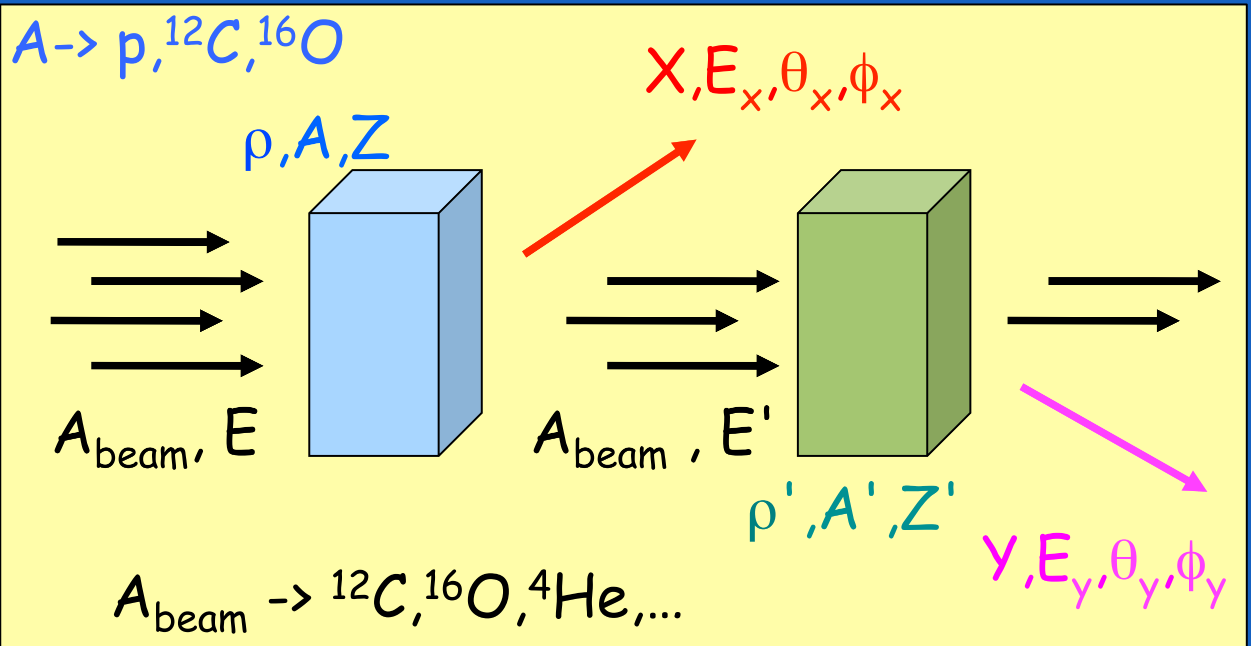




What we still miss to know about light ions fragmentation in 2015?

Data exist at 0^0 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!!

Outline

Bouncing from fundamental physics to applied physics and back…

- Overview: fragmentation in PT
- Projectile fragmentation : recent experiments
- The target fragmentation issue
- Summary and conclusions

The IDEAL detector for projectile fragmentation measurement

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

- ➔ Identify all the fragment produced, i.e. detect charge , with $0 < Z < Z_{beam}$ (≤8) and detect mass, on all the solid angle
- ➔ Detect the energy of the fragments (included from 0 to 700 MeV protons)
- ➔ 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.

Fragments Charge ID techniques

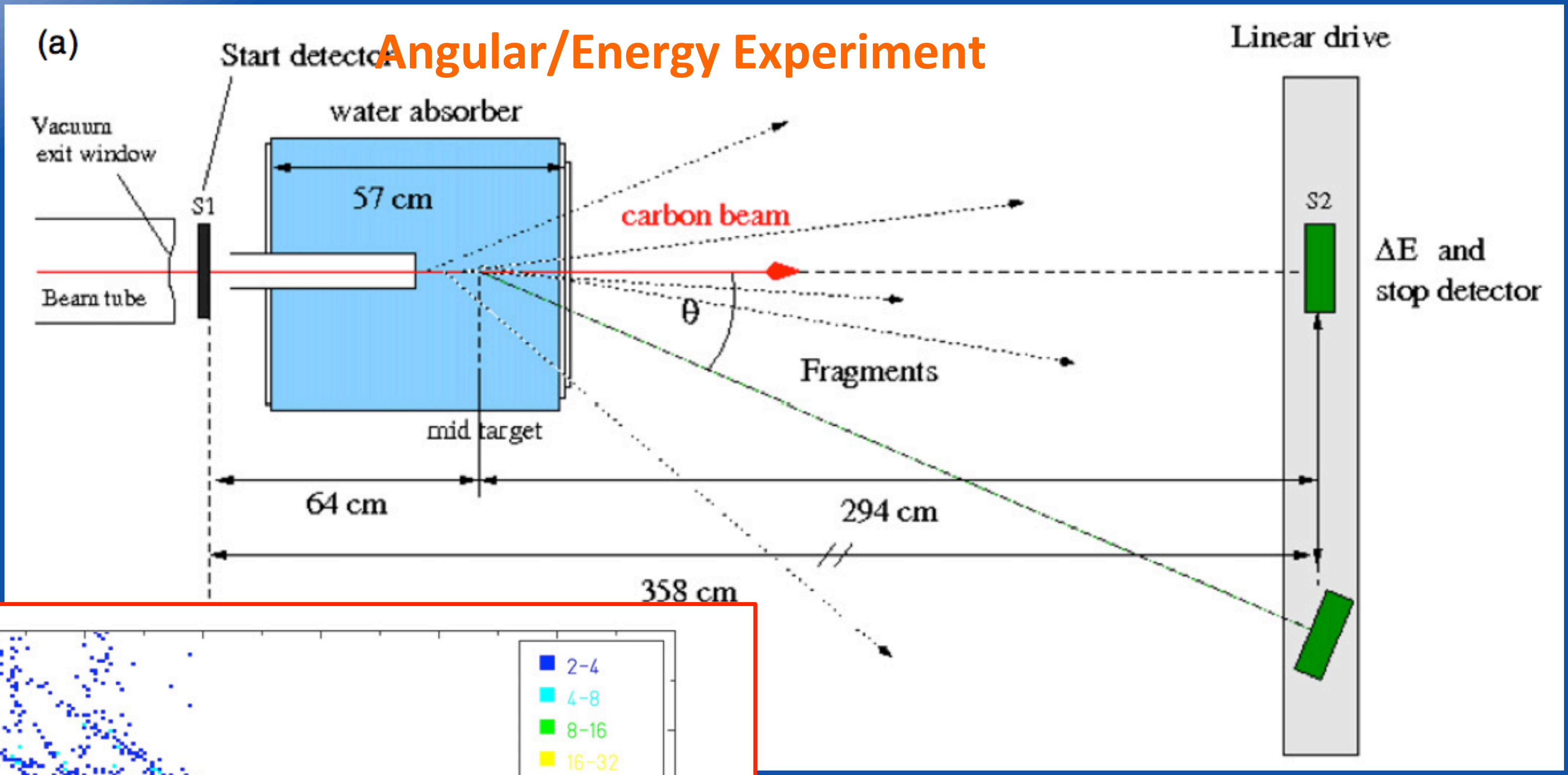
Standard techniques exploit the de/dx measurement (ΔE), calorimetric E measurement, Time of Flight (β) measurement, magnetic momentum (p) measurement

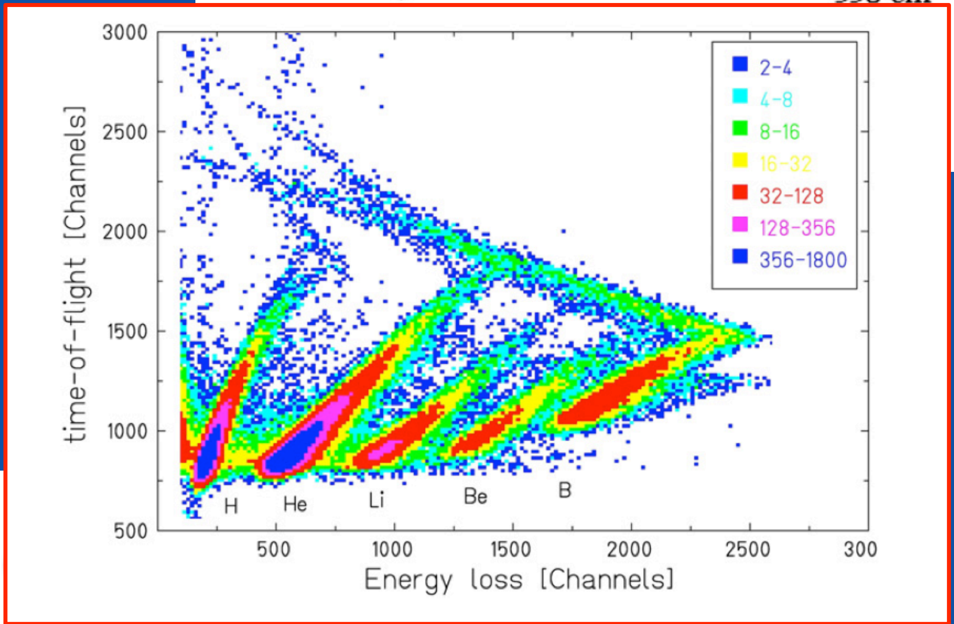
All this measurement are closely related with the particle identification (PID)

- ΔE vs E -> PID
- ΔE measurement provided PID -> E
- ToF (β) measurement provided PID -> E
- Very different De/Dx !! Need for large dynamic range detectors

particle	Ekin/nucl (MeV)	De/dx in H2O (MeV/cm)	Range (cm)
proton	200	4.6	25.9
proton	100	7.4	7.6
He	200	18	25.6
He	100	29	7.6
Be	200	70	13.5
Be	100	114	4.4
Carbon	200	155	9.4
Carbon	100	259	2.5

"old" style frag. Exp for PT TPS





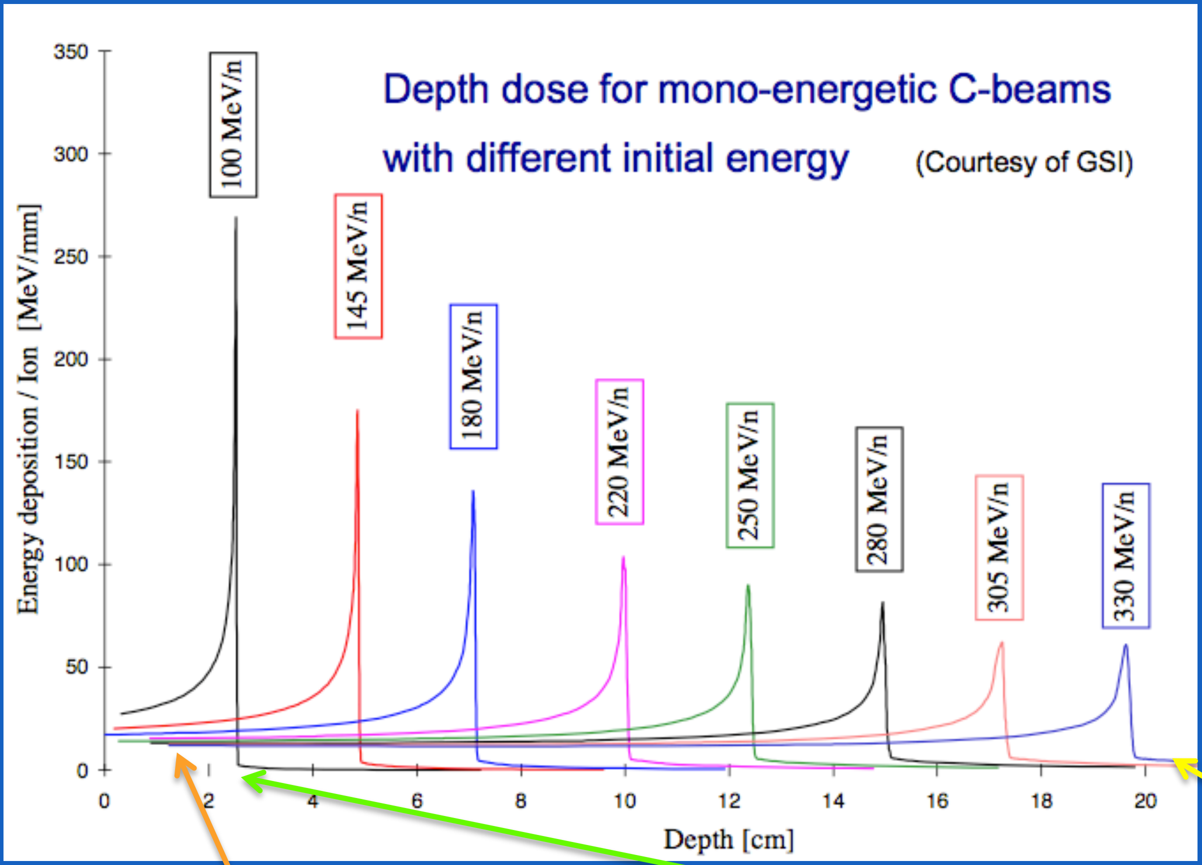
E Haettner Phys. Med. Biol. 58 (2013)

measure the angular & energy distributions of secondary fragments

H1: energy loss

ToF: total energy

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



The community is rapidly exploring the interesting region for terapeutical applications.

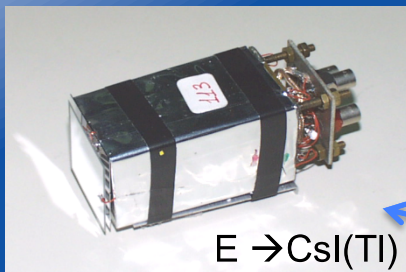
The experiments complexity (and cost) increase with the energy

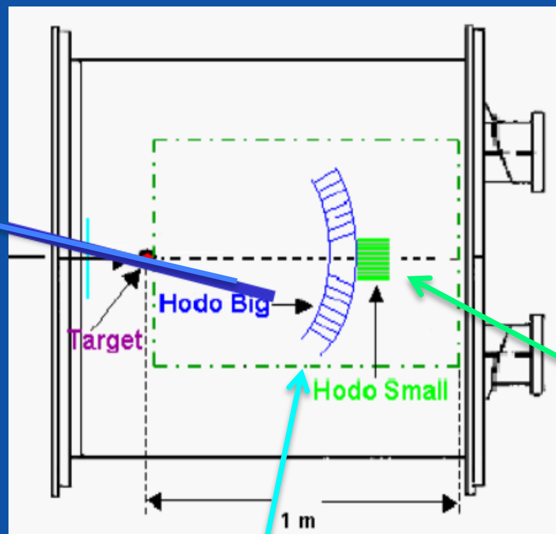
LNS 62AMev C beam FRAG experiment

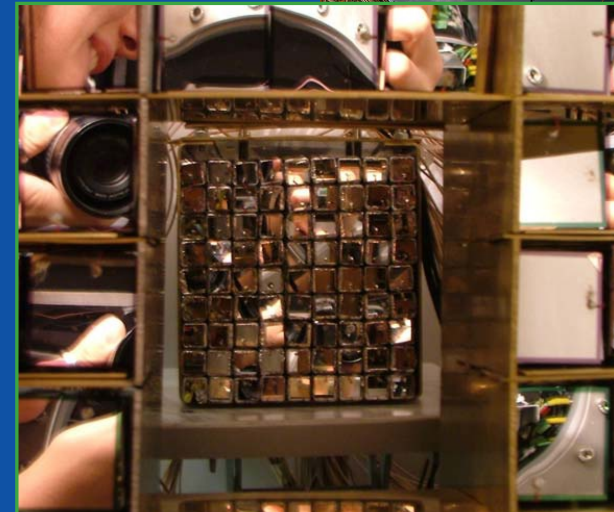
GANIL 95AMev C beam - E600 collaboration (2011)

GSI 400 AMev C beam FIRST experiment

Frag Experiment at LNS



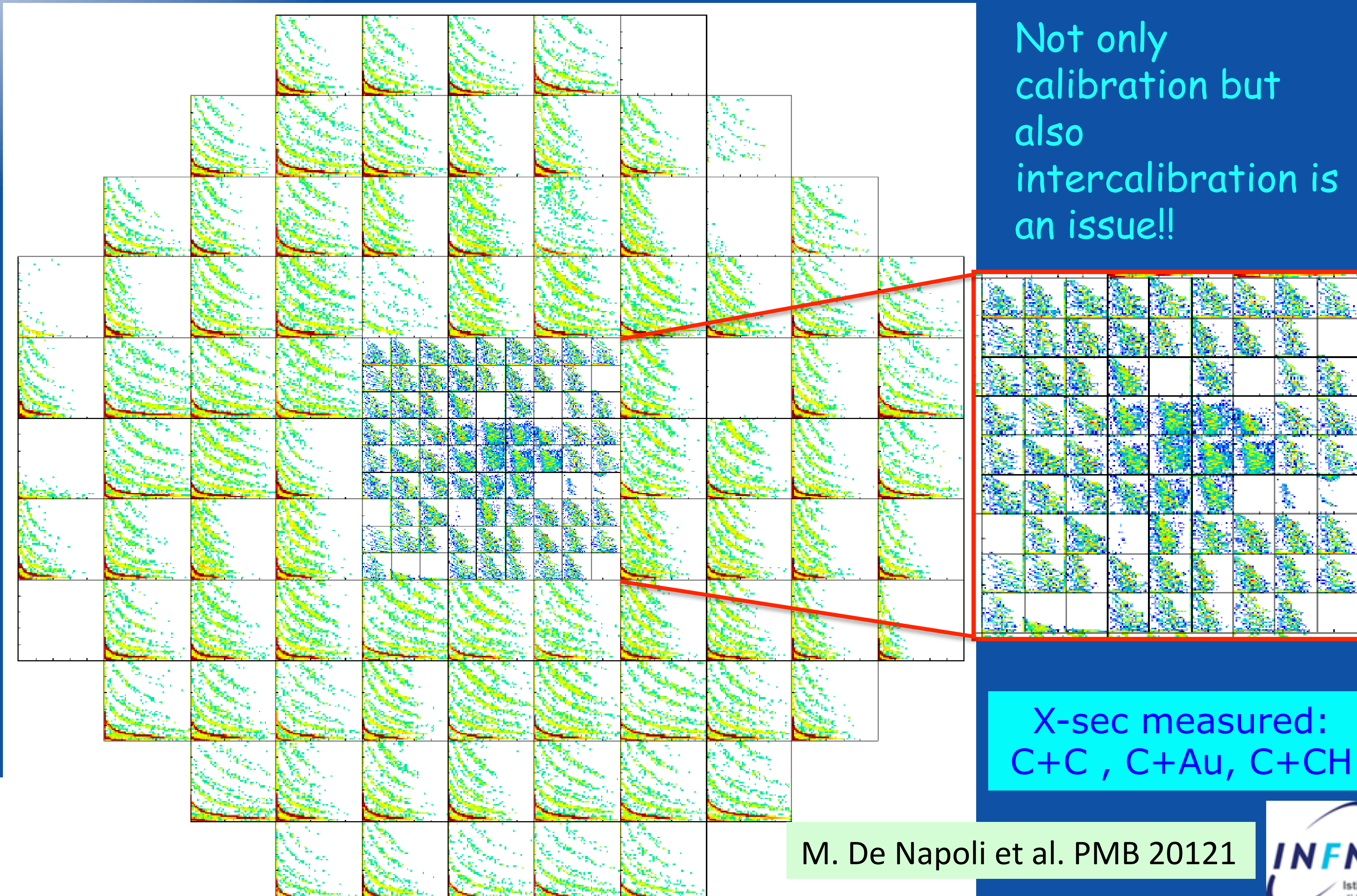




The **Hodo-small**, set up at a distance of 80 cm from the target consisted of 81 two-fold telescopes: 300 μm Silicon detectors 1x1 cm^2 of active area followed by a 1x1 cm^2 and 10 cm long CsI(Tl) and covered the angular range θ_{lab}=±4.5°.

The **Hodo-big**, set up at a distance of 0.6 m from the target, consisted of 89 three-fold telescopes 50 μm + 300 μm Silicon detectors both having 3x3 cm^2 surface followed by a 6 cm long CsI(Tl)of the same surface. It covered the angular range θ_{lab} between ±4.5° and ±20°

Frag @LNS :Fragment ID by ΔE vs E



Not only calibration but also intercalibration is an issue!!

X-sec measured:
C+C , C+Au, C+CH

M. De Napoli et al. PMB 20121

Measurement @95AMeV : ^{12}C beam

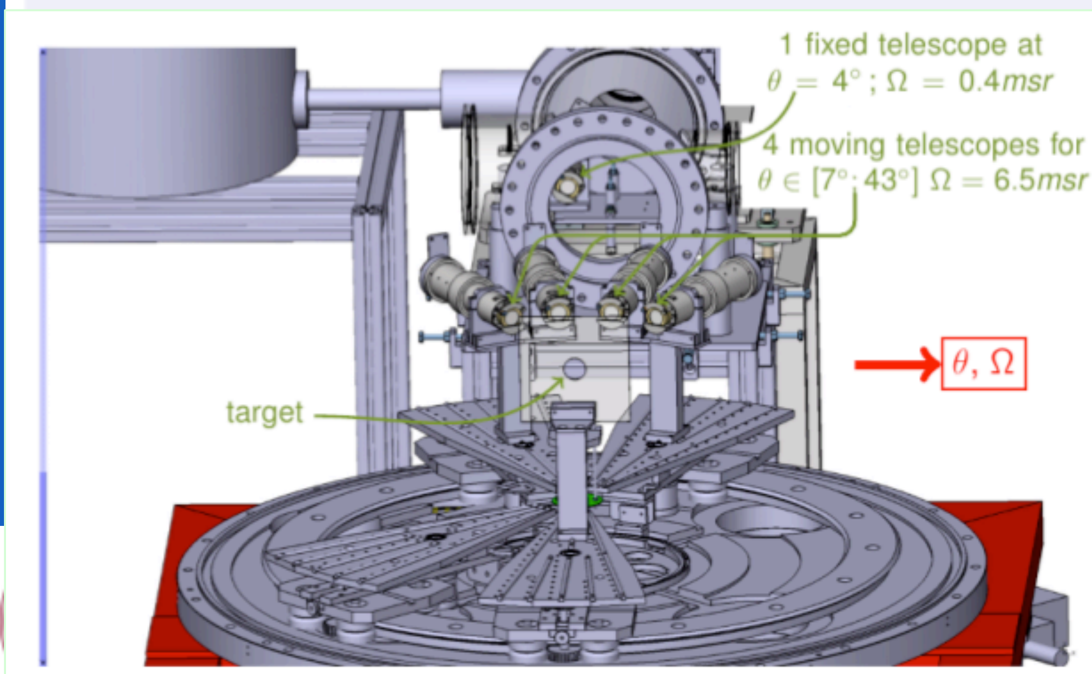
E600 experiment at GANIL (Caen ; may 2011)

Courtesy of M. Labalme

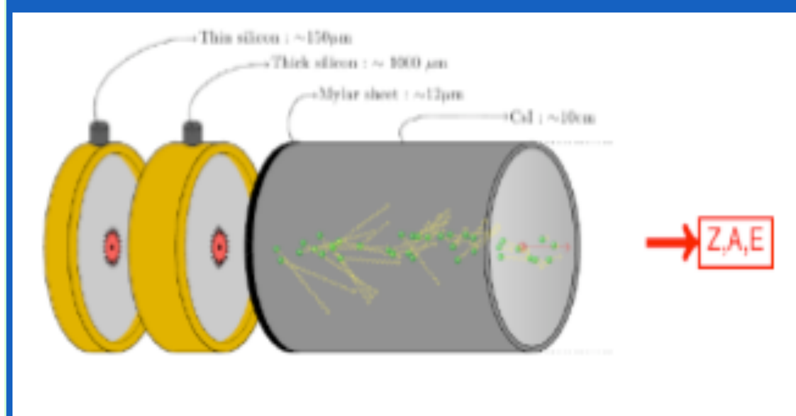
- Projectiles : 94.6 MeV/u ^{12}C
- Thin Targets (~50mg/cm^{-2}) : C, CH_2, Al, Al_2O_3, Ti

$\Rightarrow \frac{\delta^2\sigma}{\delta E \cdot \delta\Omega}$ fragmentation measurements of ^{12}C on C, H, O, Ca ($A_{Ti} \sim A_{Ca}$)

≈ 95% of a human body composition

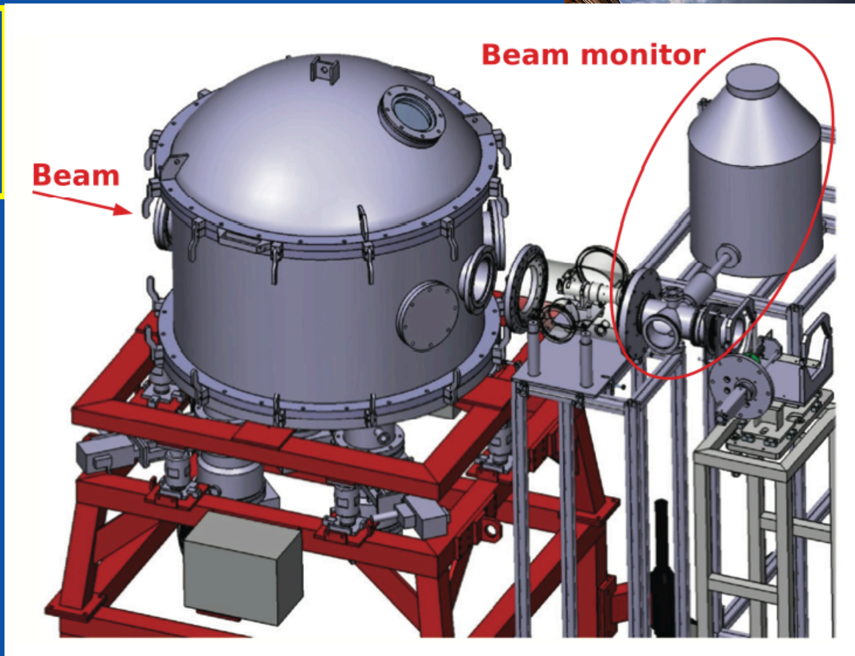


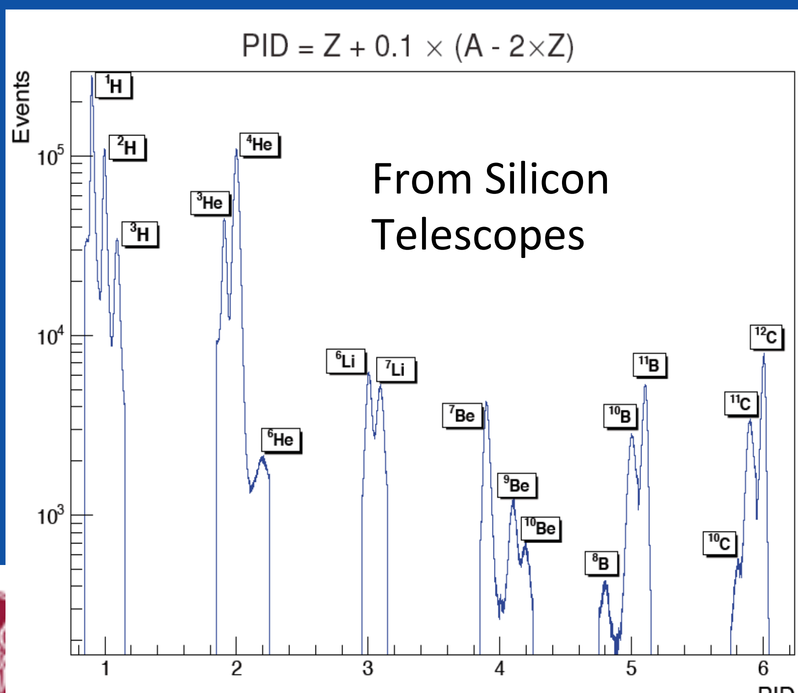
Array of 5 SI + CsI telescopes

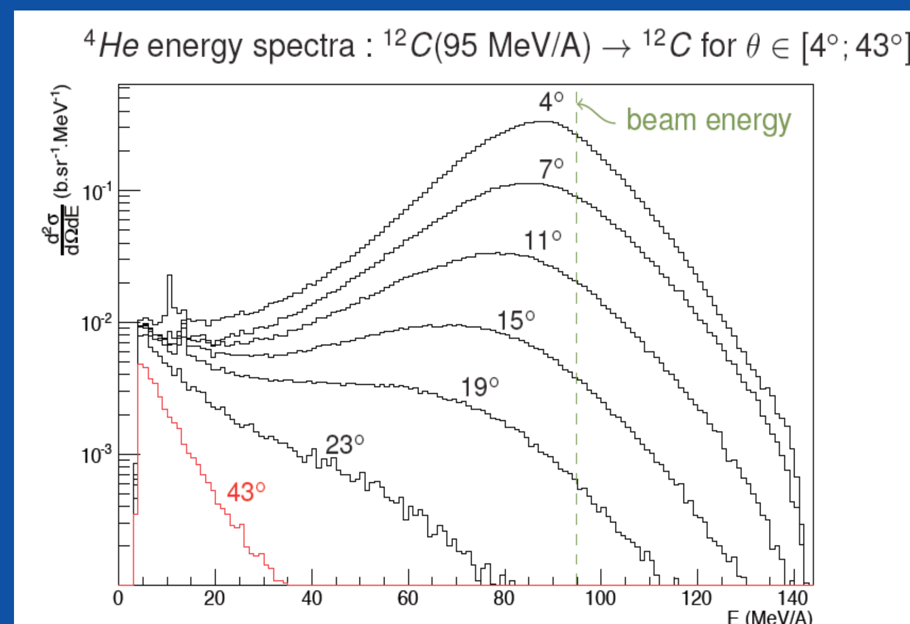


E600 (Ganil)

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

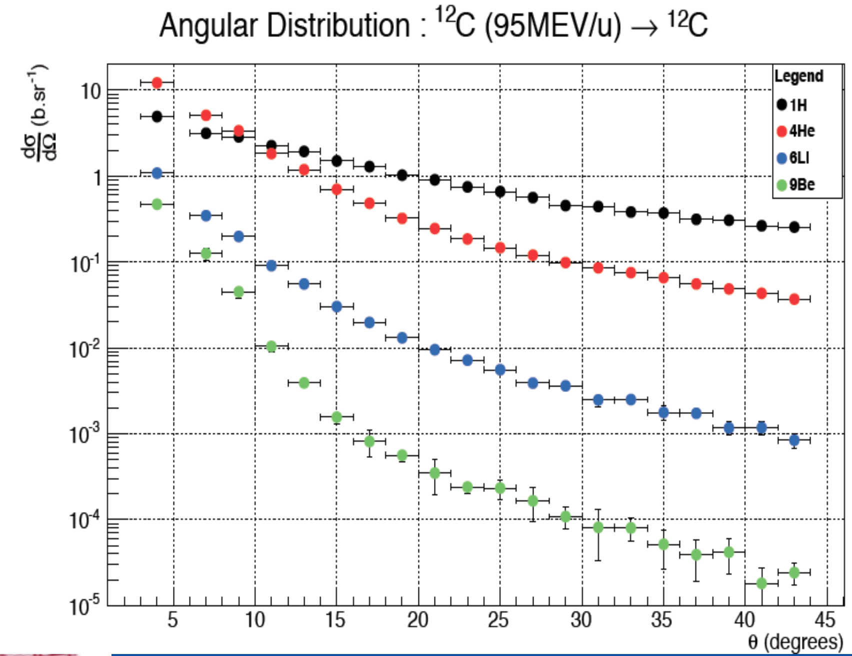


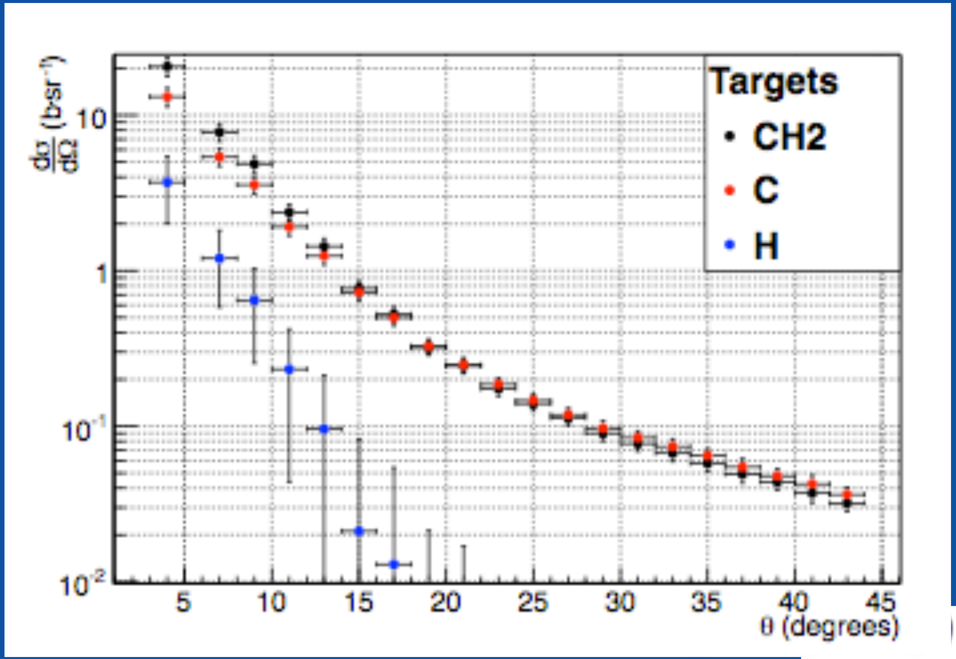




Measurement @95AMeV : ^{12}C beam

- 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)





Courtesy of M. Labalme

Higher energy-> FIRST exp. @GSI

^{12}C beam
400 AMeV

Start Counter (SC): thin scintillator. N_C, start of ToF and trigger

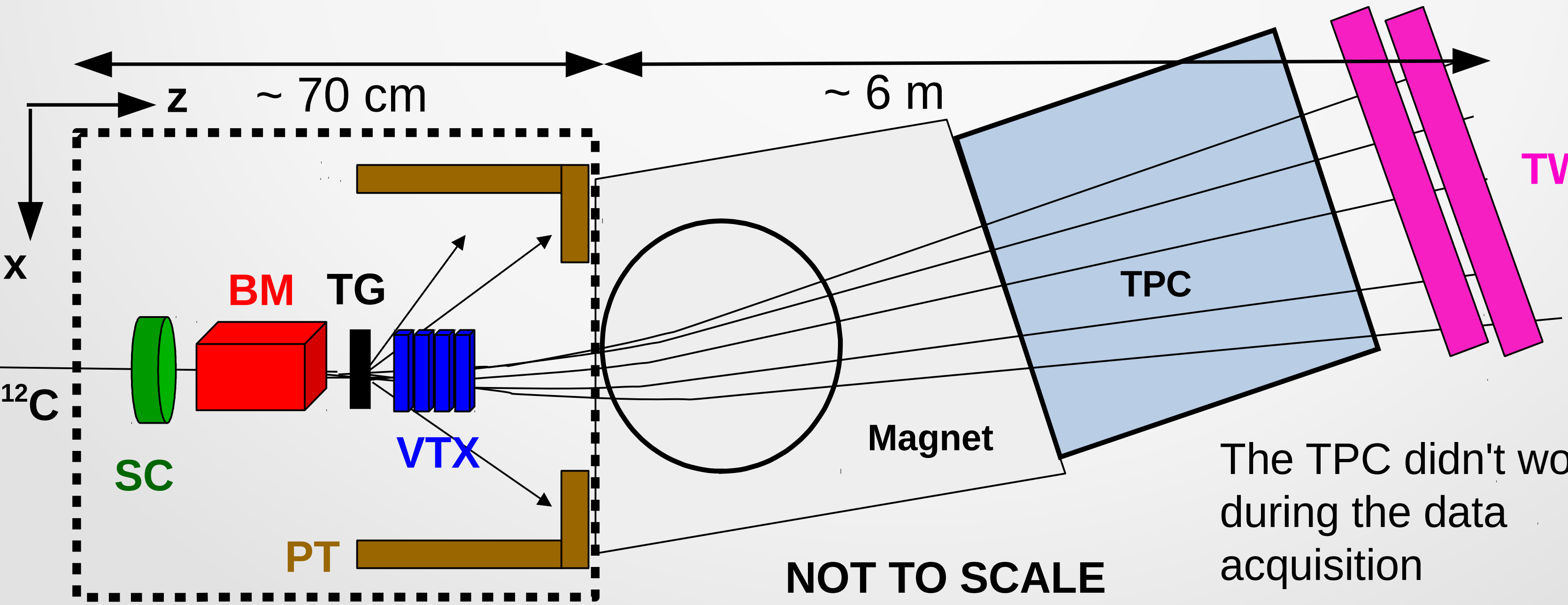
Beam Monitor (BM): drift chamber for beam direction and impact point measurements

Target (TG): A 0.5 mm gold target (4,5 M events) and a 8 mm composite target (C/O/Cr/La/P/Ca) = (35/47/8/7/2/1)% (24 M events)

Vertex Detector (VTX): pixel silicon detector. Tracks direction θ (±40°), φ (2π)

Proton Tagger (PT): plastic scint. and scint. fibers. Position, ToF, dE/dX for θ>5° H & He

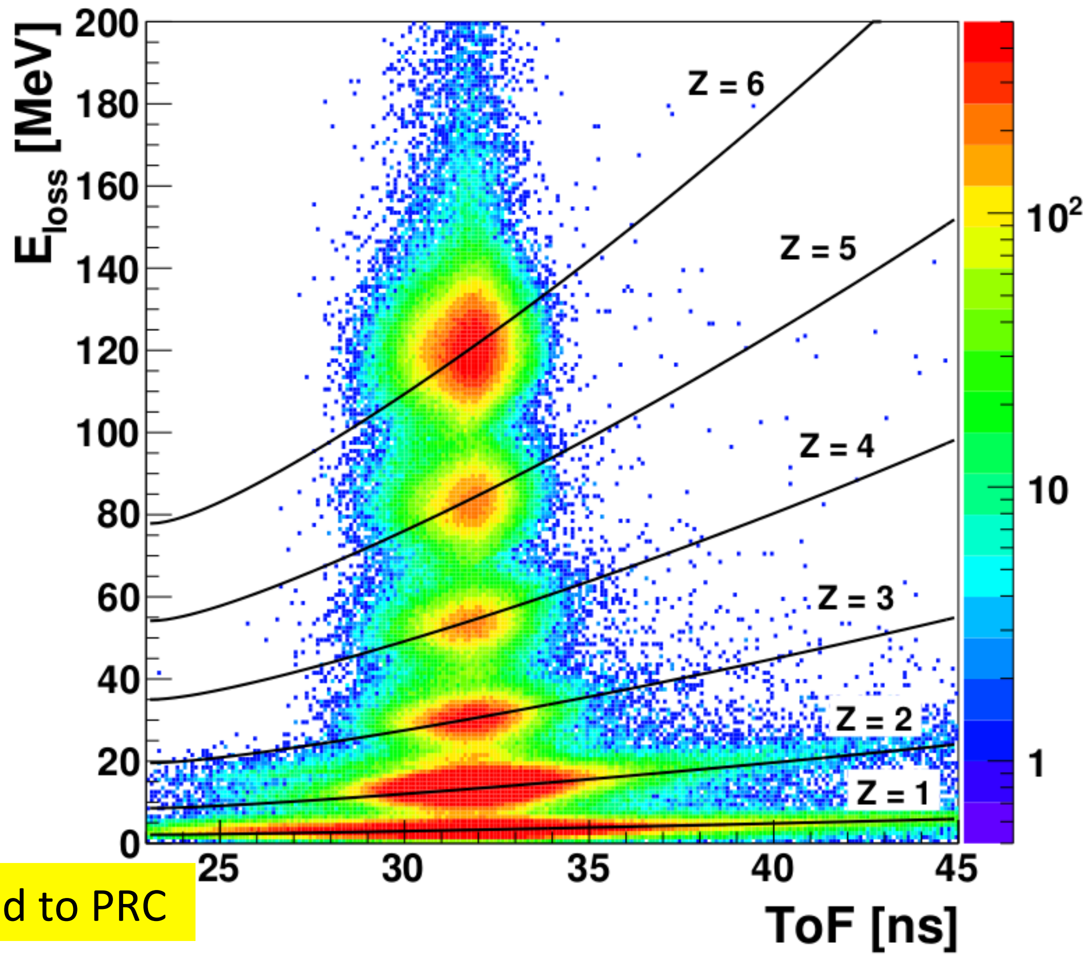
ToF Wall (TW): two layers of plastic scint. Impact position (x, y, z), Z_ID, ToF for trks θ < 5°



The TPC didn't work during the data acquisition

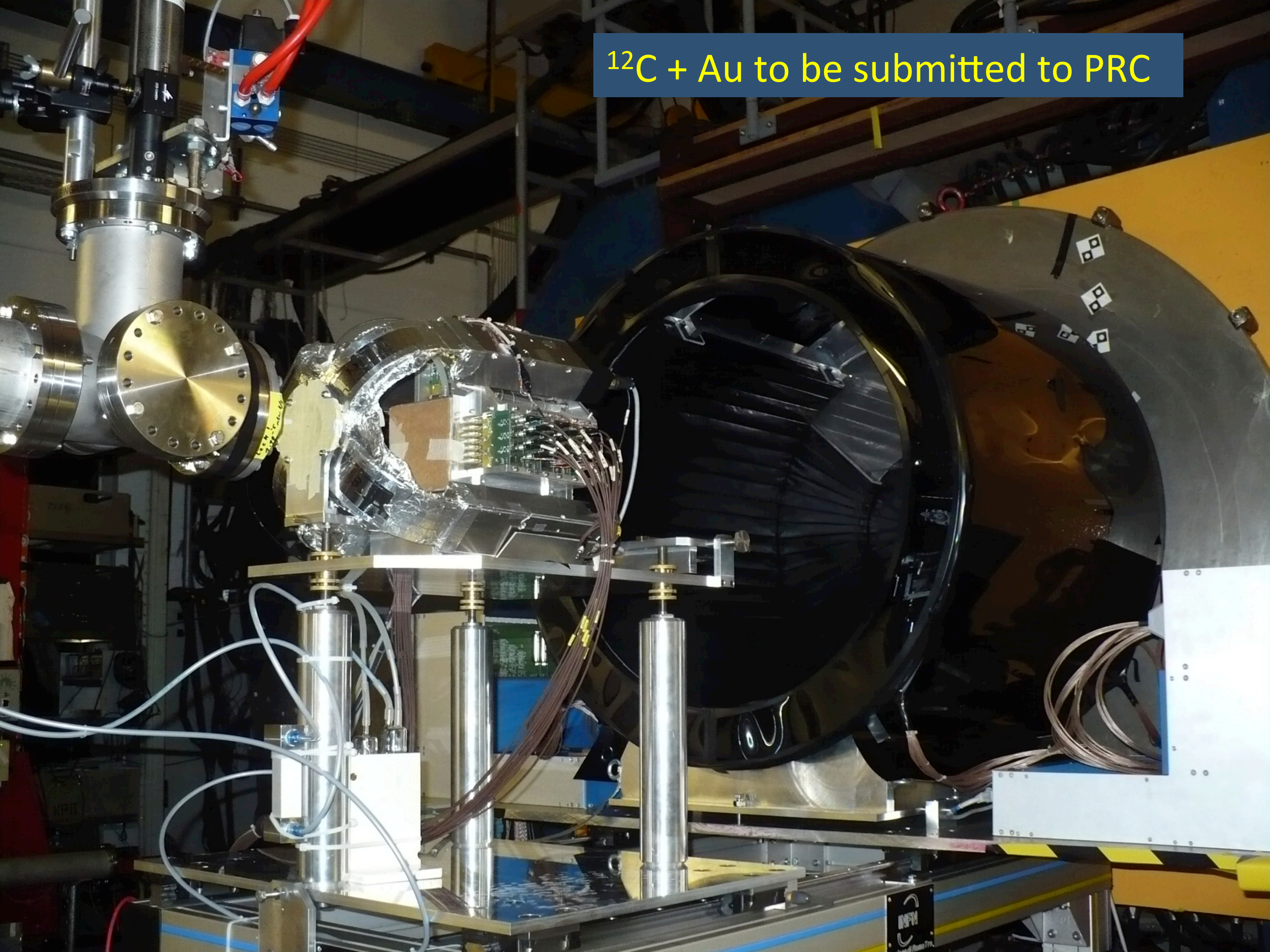
Charge identification (ZID) algorithm

- **Fragment charge ID is performed using a 2D algorithm based on detected dE/dX in the TW vs Tof**
- **The ZID algorithm assigns to a TW hit the charge that minimize its distance wrt the different Bethe-Bloch curves relative to different Z hypothesis**



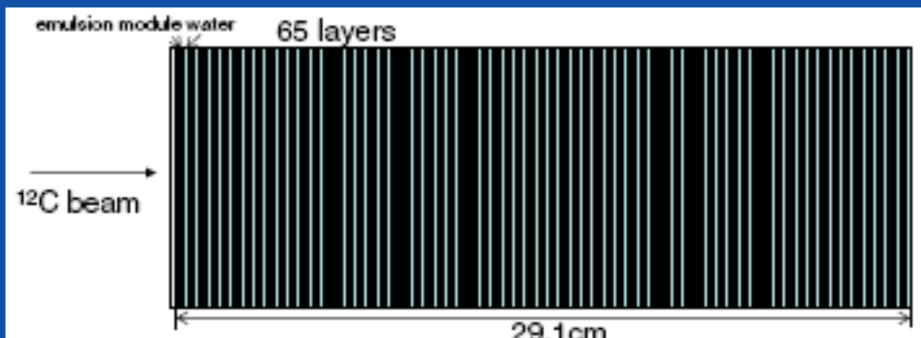
C+Au results to be submitted to PRC

^{12}C + Au to be submitted to PRC

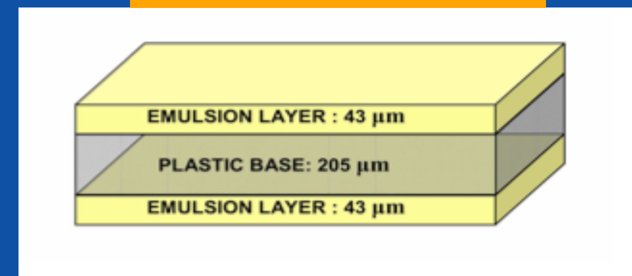


A “new” approach: Emulsion Chamber

Density grain is proportional to energy loss



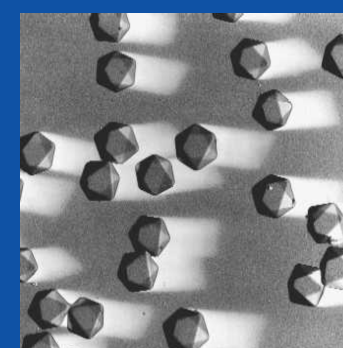
Chamber unit layer



PROs

- ✓ High spatial resolution (~μm)
- ✓ High angular resolution (~0.5 mrad)
- ✓ Multiparticle separation

AgBr crystal (0.2 μm) is the unit active detector



CONs:

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

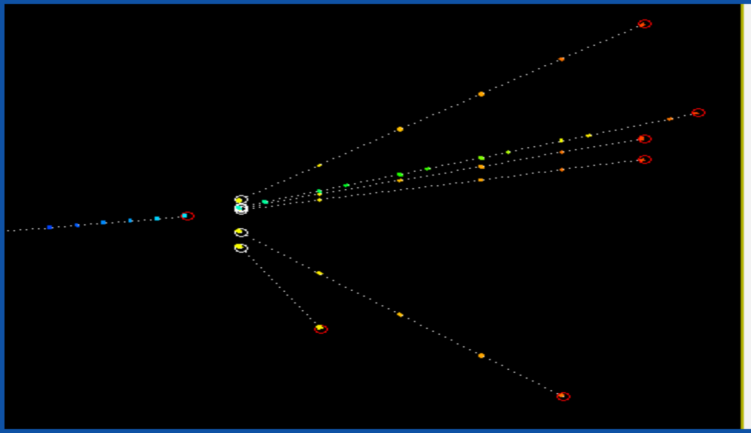
Toshito. et al., *Phys. Rev. C.,* 2008

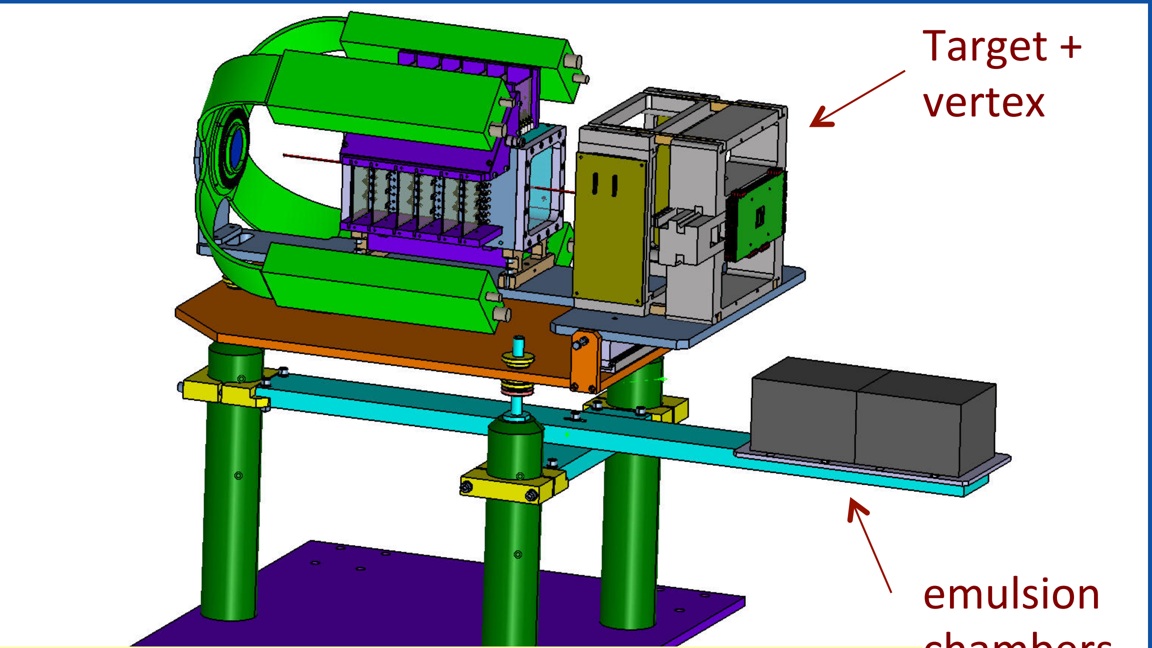
Emulsion Chambers @ FIRST

2 cloud emulsion chambers by OPERA experiment have been exposed to fragments (2 hours) by G. De Lellis and coworkers from Napoli University

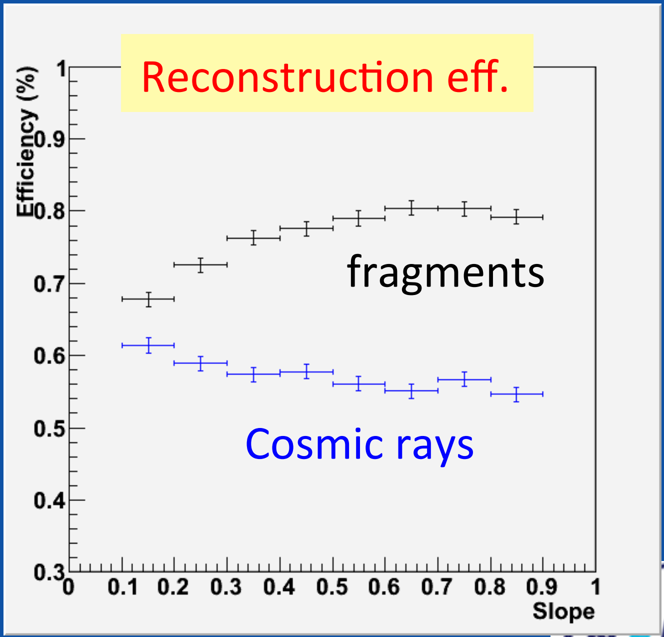
Detect fragments at large angle, mainly He and protons, $30^0 < \theta < 75^0$

Comparison on going with the proton tagger distributions





G. De Lellis et al Meas. Sci. Technol. 26 (2015)



Outline

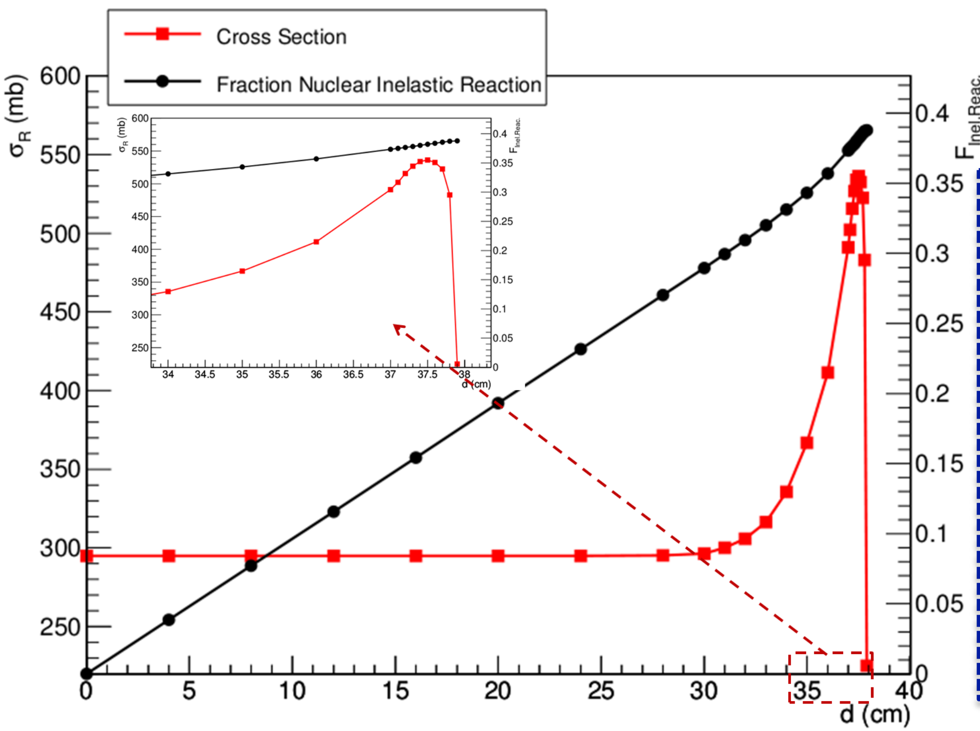
Bouncing from fundamental physics to applied physics and back…

- Overview: fragmentation in PT
- Projectile fragmentation : recent experiments
- The target fragmentation issue
- Summary and conclusions

Target fragmentation & PT: is an issue at all?

The target fragmentation could relevant (only?) for proton beam treatment. The proton inelastic scattering on patient nuclei (C,O,N) produces Z≤8 fragments with low energy -> very high LET and very good at cell killing (very high RBE)

Example: analytical approximation to p -> H2O scattering @250 MeV



$$N(x) = N_0 \cdot e^{-x/\lambda} \qquad \lambda = \frac{M_{mol}}{N_A \rho \sigma_R}$$

Bradt-Peters formula (Sihver 2009 Radiat Meas):

$$\sigma^r(p, N, E_p) = \sigma_0^r(p, N) \cdot f(E_p, Z_T)$$

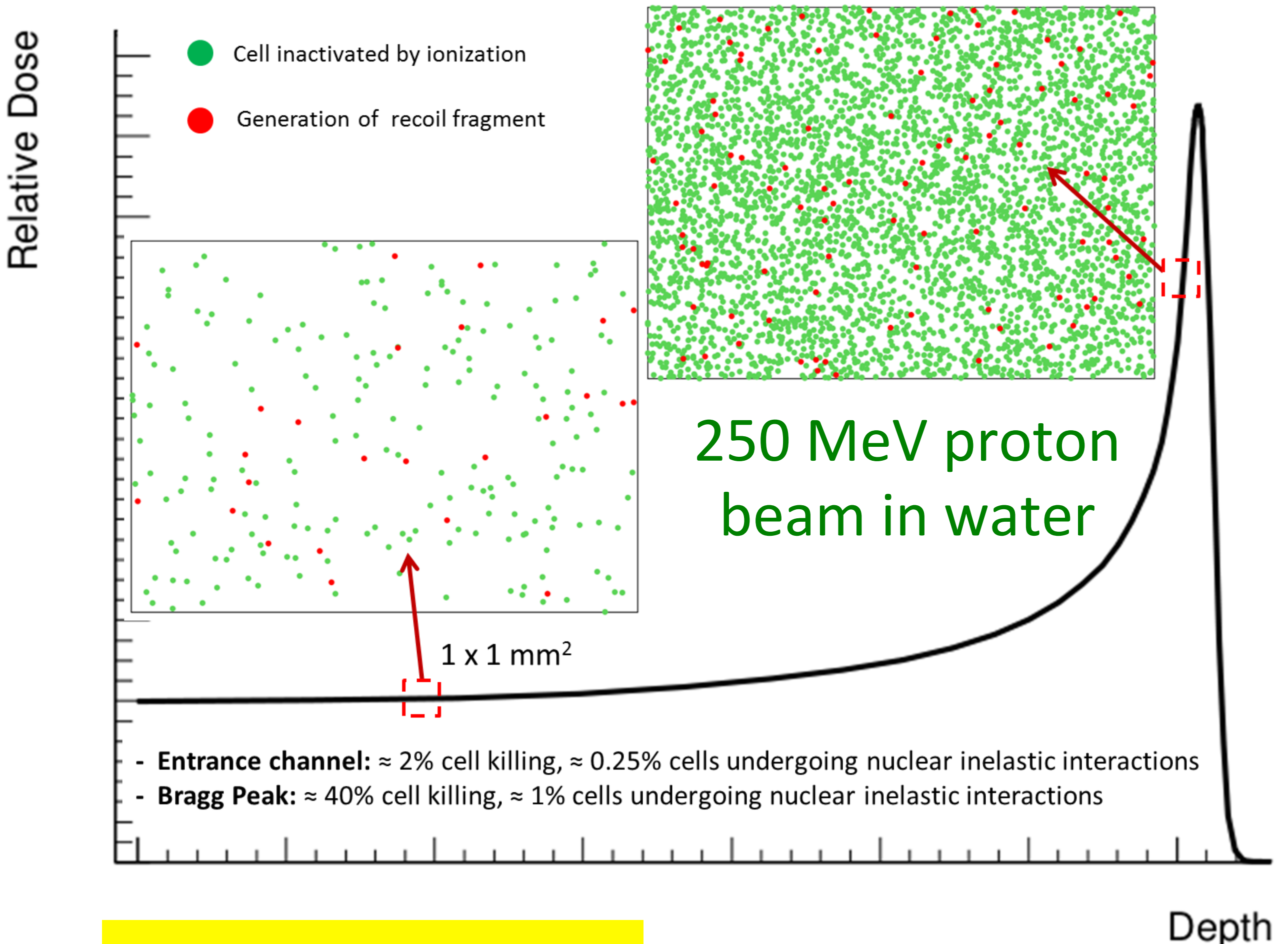
$$\sigma_0^r(p, N) = \pi r_0^2 \left[1 + A_T^{1/3} - b_0(A_T)(1 + A_T^{-1/3})\right]^2$$

$$b_0(A_T) = 2.247 - 0.915\left(1 + A_T^{-1/3}\right)$$

$f(E_p, Z_t)$ depending on E_p and Z_t range

Courtesy of F.Tommasino

Target fragmentation in proton therapy: gives contribution 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**

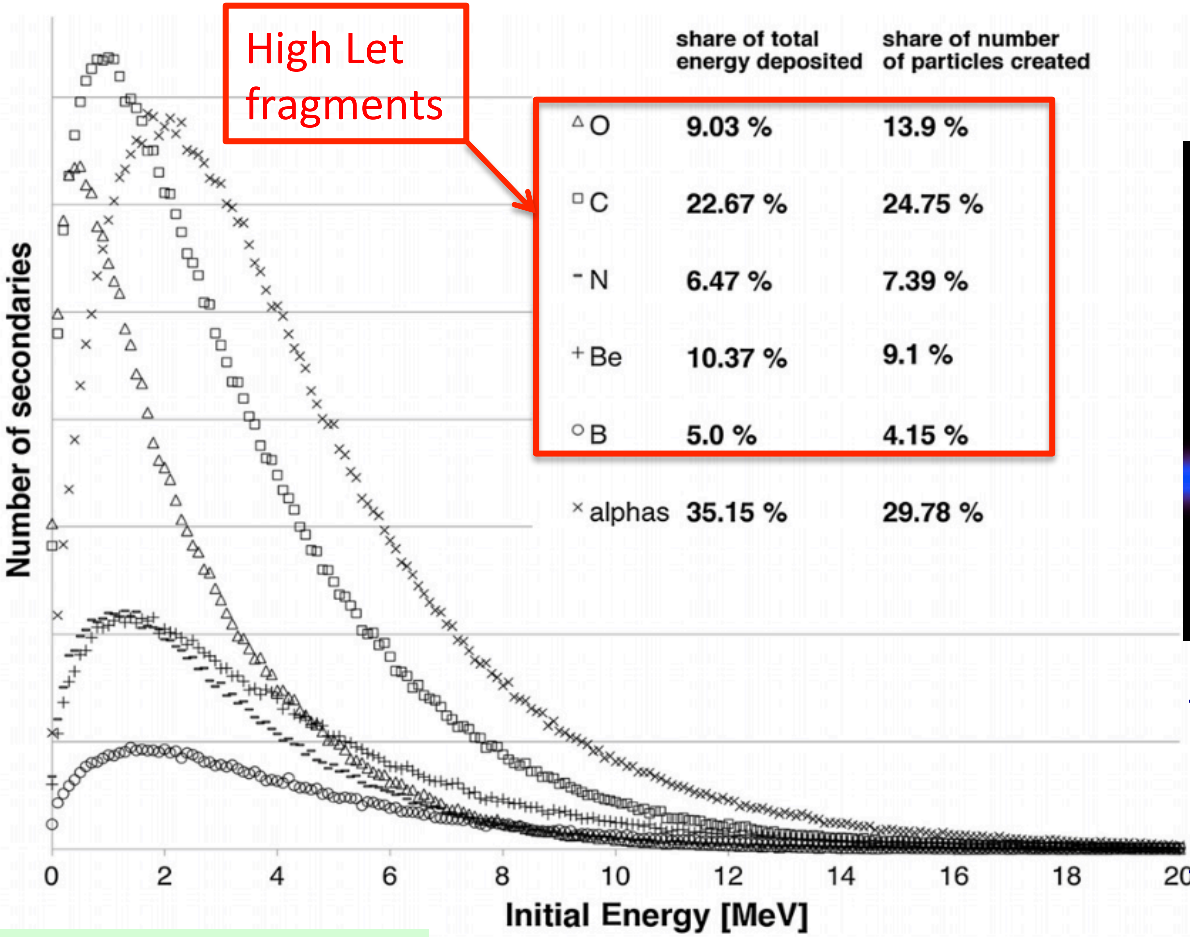
See also dedicated MC studies:
- Paganetti 2002 PMB
- Grassberger 2011 PMB

Courtesy of F.Tommasino

Trento Institute for
Fundamental Physics
and Applications

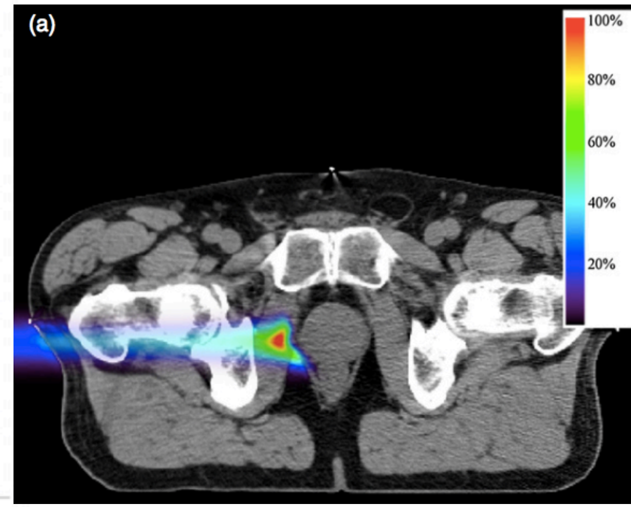
Grassberger & Paganetti 2011 PMB: Monte Carlo study (G4-based)

High Let fragments



	share of total energy deposited	share of number of particles created
△ O	9.03 %	13.9 %
□ C	22.67 %	24.75 %
- N	6.47 %	7.39 %
+ Be	10.37 %	9.1 %
○ B	5.0 %	4.15 %
× alphas	35.15 %	29.78 %

Prostate patient
160 MeV pencil beam



- **Strong contribution of secondary protons to lateral penumbra**
- **Expected high RBE associated to recoil nuclei**

CAVEAT: is the MC reliable???

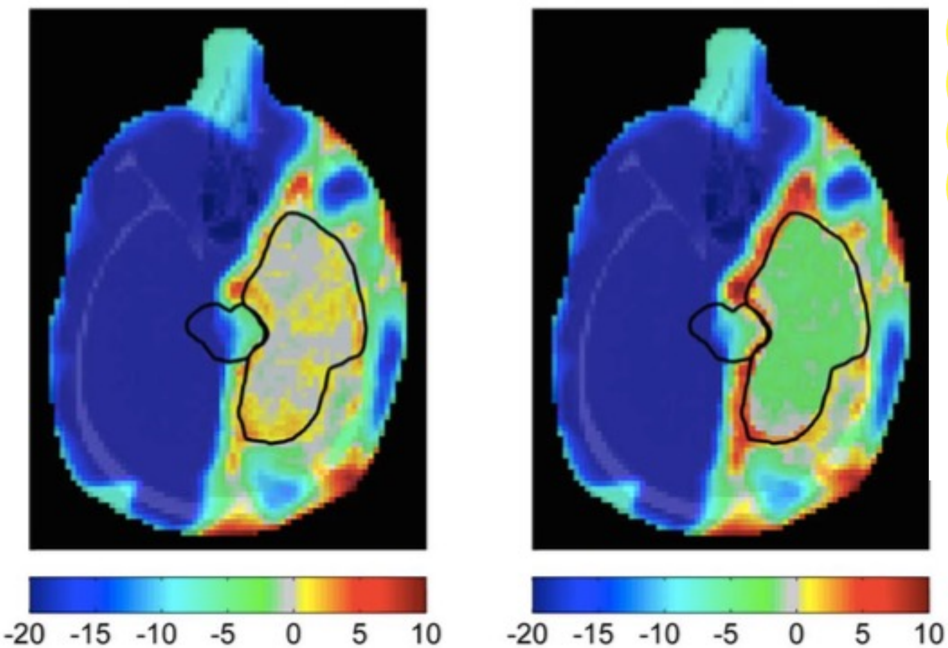
Courtesy of F.Tommasino

Target fragmentation & proton RBE

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

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

Courtesy of F.Tommasino

Focus on p-> X (C,O,N) scattering & heavy fragment production @100-250 MeV

The proton-nucleus elastic interaction and the light fragment production (p,d,t,He) are quite well known

Dedicated ICRU 63 publication available, reporting double differential X-sections on O, C, N, Ca,...

BUT.....

"Heavy" (A>4) fragment emission energy and angle largely unknown.

Very low energy-short range fragments.

Nuclear model (and MC) not reliable

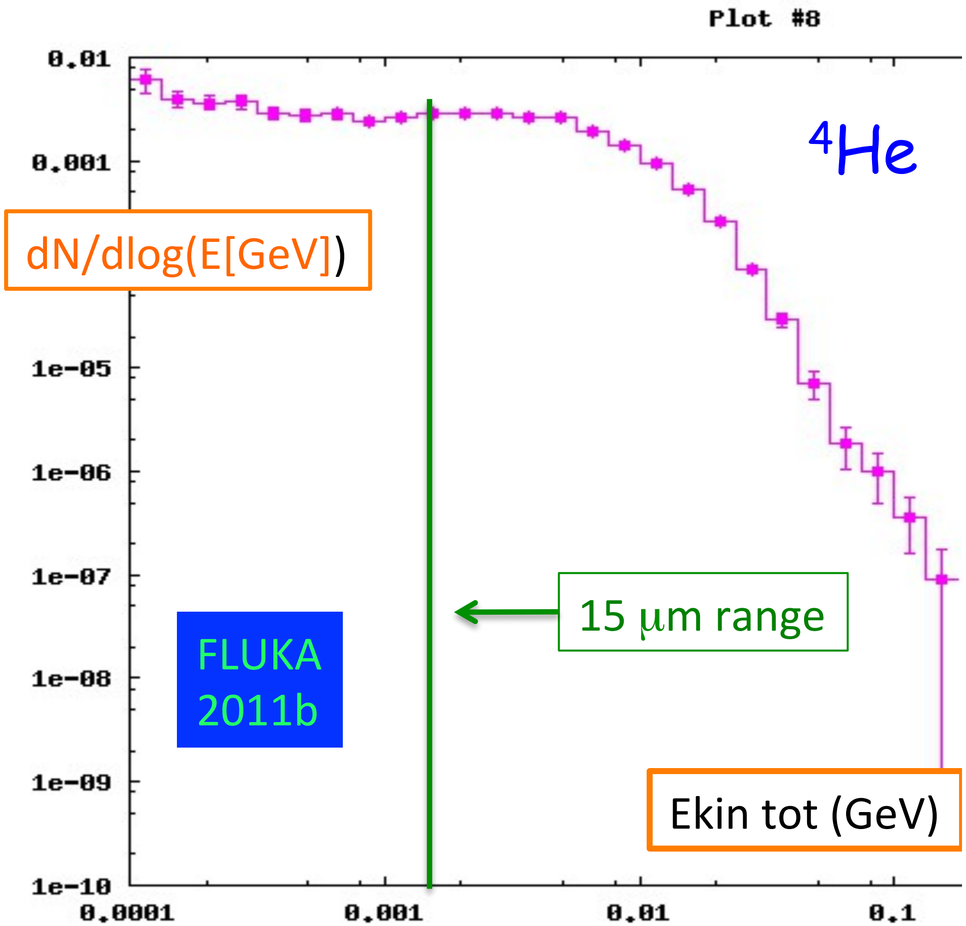
P->H2O @ 200 MeV

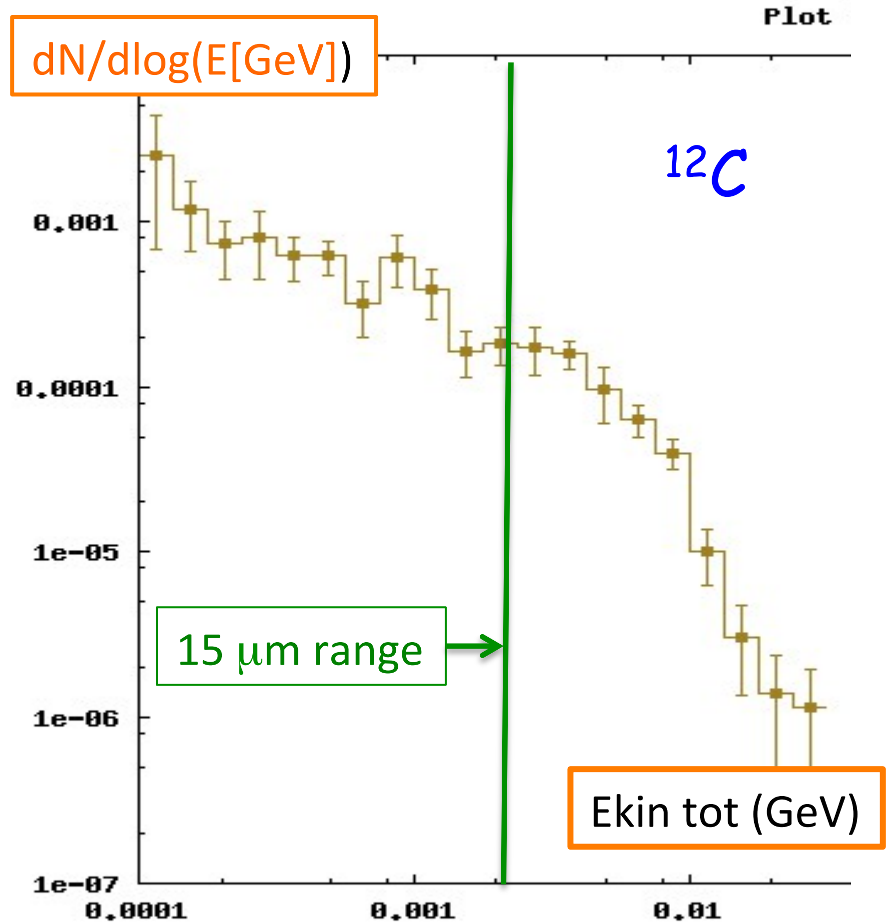
Fragment	E (MeV)	LET (keV/μm)	Range (μm)
^{15}O	1.0	983	2.3
^{15}N	1.0	925	2.5
^{14}N	2.0	1137	3.6
^{13}C	3.0	951	5.4
^{12}C	3.8	912	6.2
^{11}C	4.6	878	7.0
^{10}B	5.4	643	9.9
^{8}Be	6.4	400	15.7
^{6}Li	6.8	215	26.7
^{4}He	6.0	77	48.5
^{3}He	4.7	89	38.8
^{2}H	2.5	14	68.9

Cancers 2015,7 Tommasino & Durante

p-> Brain scattering @200 MeV

Also FLUKA MC suggest a low-energy, short range production of heavy frag: 200 MeV p on “BRAIN” : He vs C production





New target fragmentation Experiment?

The community is starting to think at target fragmentation experiment

FramentatiOnOf Target

FOOT

- Challenging measurement: large man power & funding needed
- A first meeting dedicated to this opportunity/challenge held in Villa Tambosi (TN) in July 2015 , near TIFPA
- Newcomers are welcome

How can we (reliably) detect these fragments? Direct scattering exp:

- 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 would produce very few events, with sizeable pollution even from beam fragmentation on air, beam window, etc.. -> forced to vacuum chamber setup with very low background
- Possible solution with a gaseus jet target (low density gas) shot against the terapeutical proton beam in vacuum

Very high tech (expensive) experiment!!

Let change point of view: Inverse kinematic strategy

Since shooting a proton with a given β (Ekin=200 MeV ➔ β=0.6) on a patient (C,O,N nuclei) at rest is a detection challenge… 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 measure the X-section, provide we apply an inverse velocity transformation, the result should be the same.

A possible procedure would be:

- Use (as patient) beams N, O, C ions with β= 0.6 ➔ Ekin/nucl=200MeV. High energy frag exp (large & expensive)
- Use a target made of H… but this is difficult! Needs for differential measurement with C & CH2 target-> systematics!!

Beams & Facilities

There is not a large availability of terabeutical-like beam in the word. An (almost) complete list includes:

- CNAO: time scale of experimental room uncertain (3 years?). Treatment rooms ok, but very busy
- GSI : uncertain beam availability
- HIT: ~ok, experimental room a bit small
- HIMAC, BNL: expensive (mission & beam time)
- LNS : perfect for measurement up to~80MeV nucl
- Trento: ok in few months, only proton
- CERN (future): starting to design a dedicated facility

Summary & conclusions (I)

- Nuclear fragmentation prevents the use of ions heavier then Oxygen and must be taken into account in the Treatment Planning System for PT
- The experiments seems to evolve towards more and more complexity and dimensions
- The target fragmentation could be an important issue to be accounted for in PT in next future
- No mention has been done in this talk of neutrons production due to nuclear fragmentation and their measurement

Thanks!!

spares