FOOT

FragmentatiOn Of Target

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

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for the FOOT Collaboration

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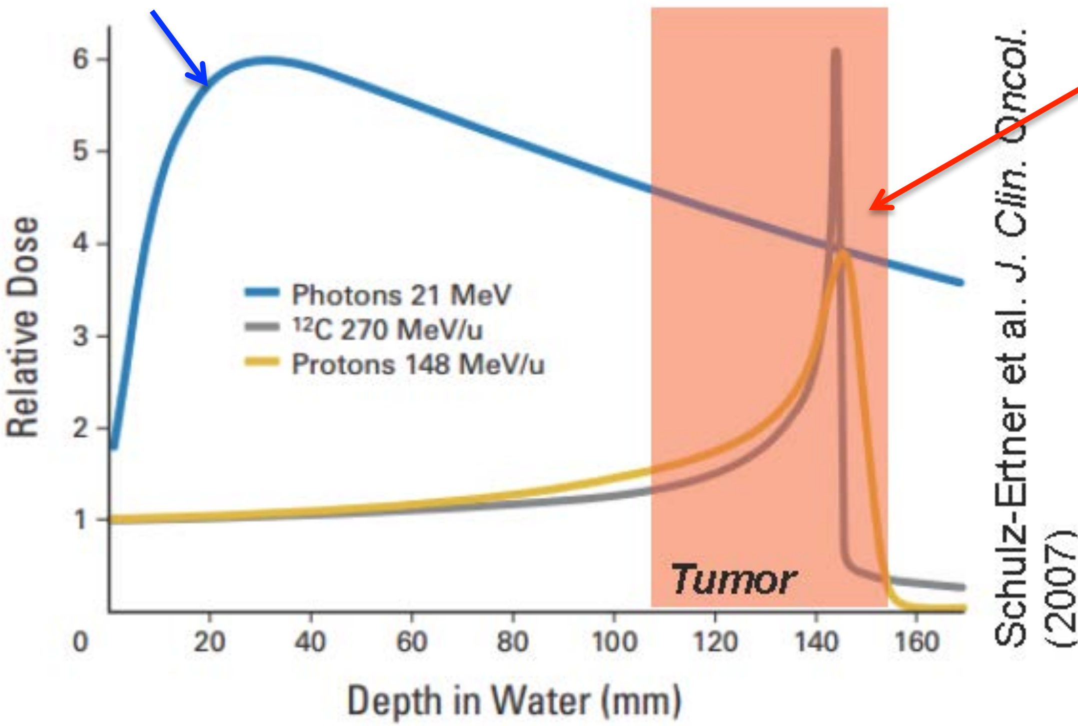
Rationale of Charged Particle Therapy

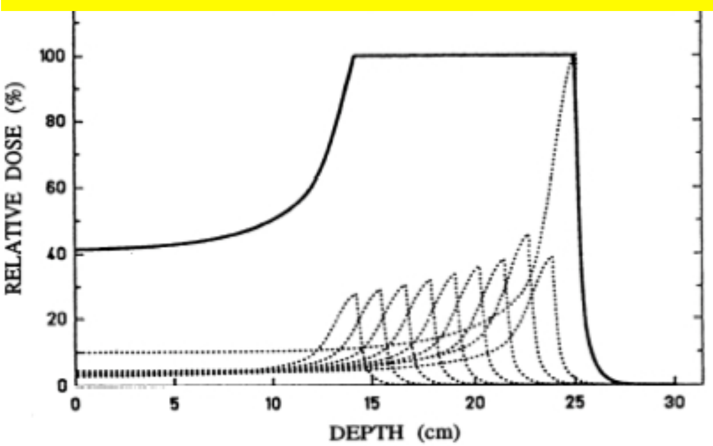
Radiotherapy concerns ~50% of all cancer patients. ~ 2M patients/year.

"Conventional" radiotherapy (photons)



Charged (hadron) particle therapy mostly protons; in few cases ^{12}C beams

- ✓ Advantageous for some kind of pathologies
- ✓ Peak of dose released at the end of the track, **better sparing the normal tissue**
- ✓ Beam penetration in tissue function of the beam energy
- ✓ Accurate conformal dose to tumor with Spread Out Bragg Peak

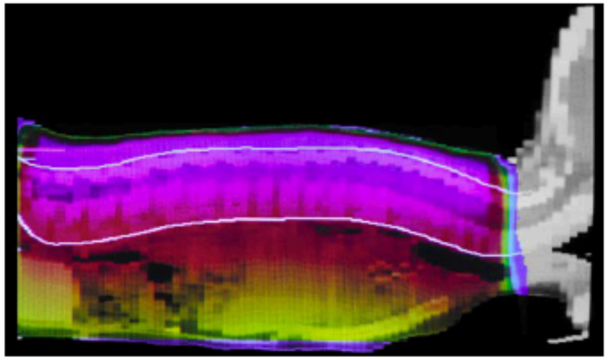


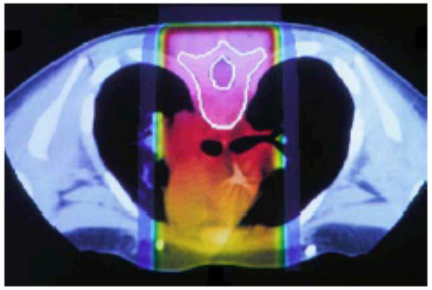
Nuclear physics is contributing to the development of hadrontherapy: Accelerator technology, Detectors, Monte Carlo codes and other software, study of contribution of nuclear reactions, ...

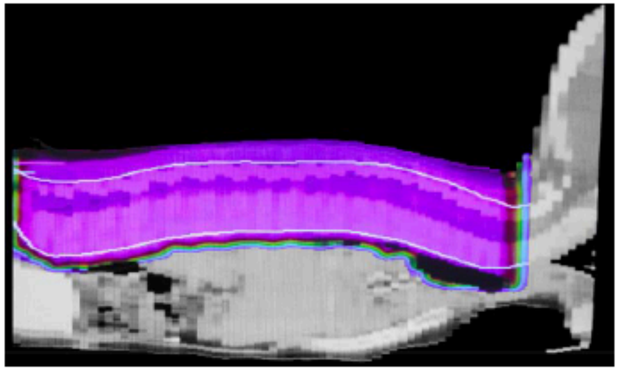
Typical example of advantages of Charged Particle Therapy

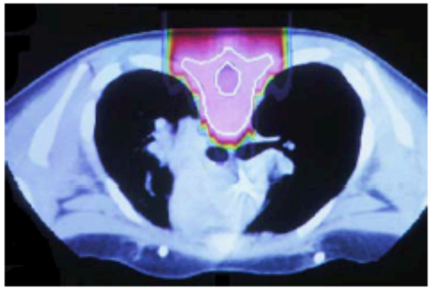
Image guided, conformal (IMRT), photon therapy

- 35% local recurrence
- Preventable distant metastases
- Large volumes irradiated
- Early, late and very late normal tissue damage





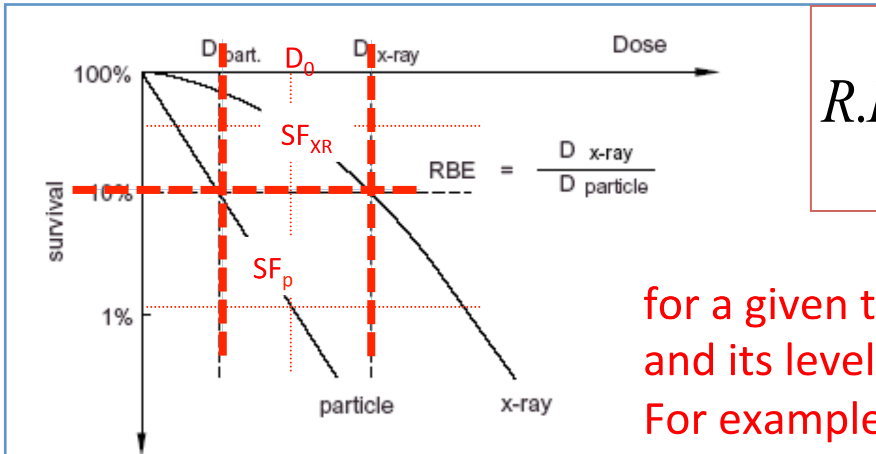




Conformal Proton therapy: higher selectivity!

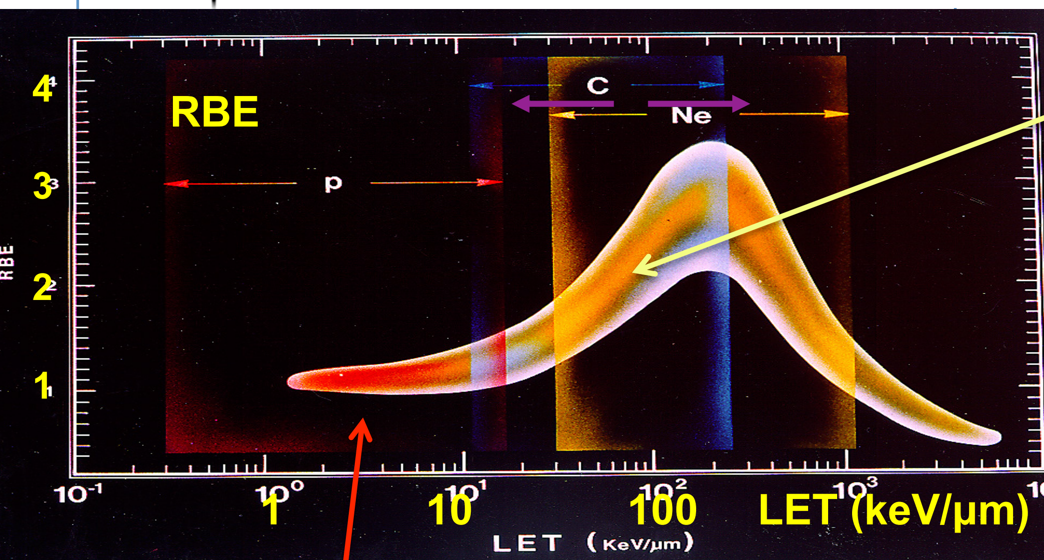
The future development of Charged Particle Therapy is strongly related to the possibility of demonstrating the effective reduction of complication probability in normal tissues for the same (or sometimes better) control of the tumoral region

The concept of **R**elative **B**iol. **E**ffectiveness

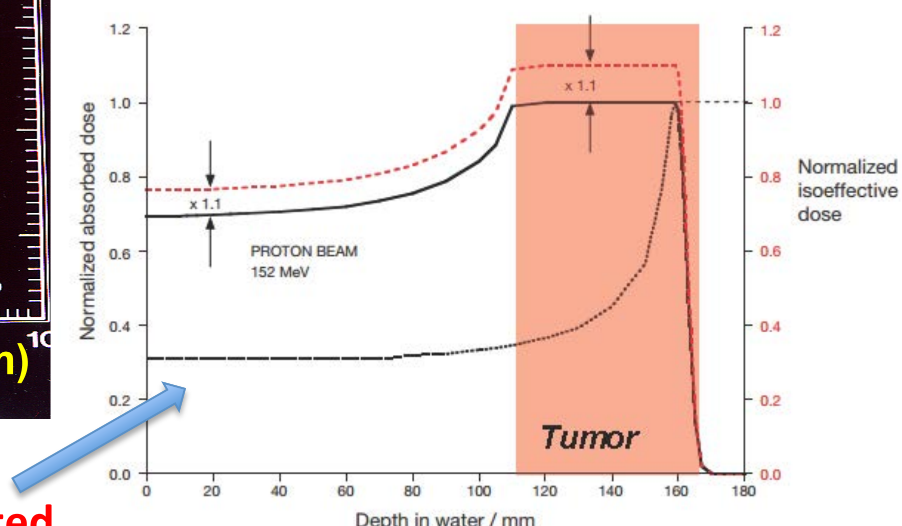


$$R.B.E. = \left(\frac{D_{RX}}{D_r} \right)_{SF=SF_0}$$

for a given type of biological end-point and its level of expression.
For example: Survival Fraction 10%



Ions with Z>1 can have RBE significantly >1

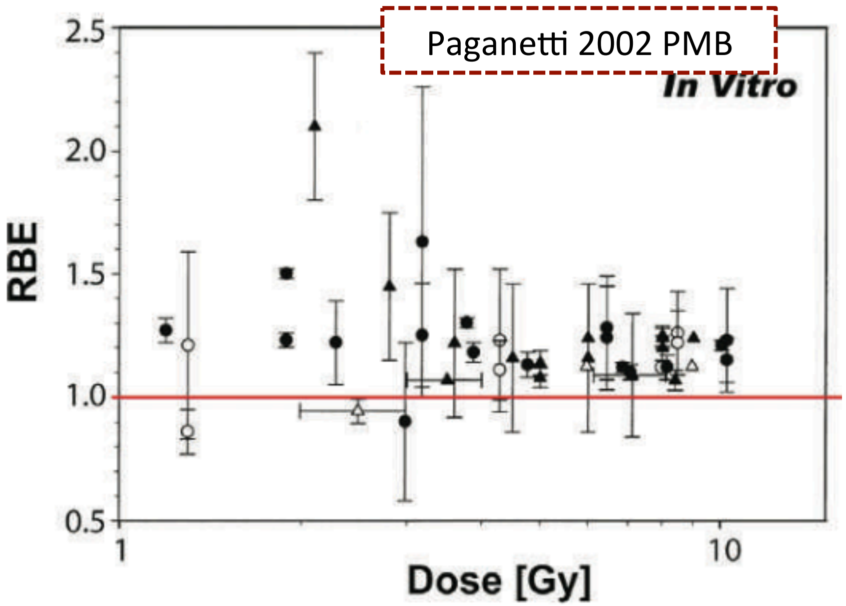


Protons: RBE slowly varying with LET, approximated constant 1.1 factor (→ 10% more effective than photons)

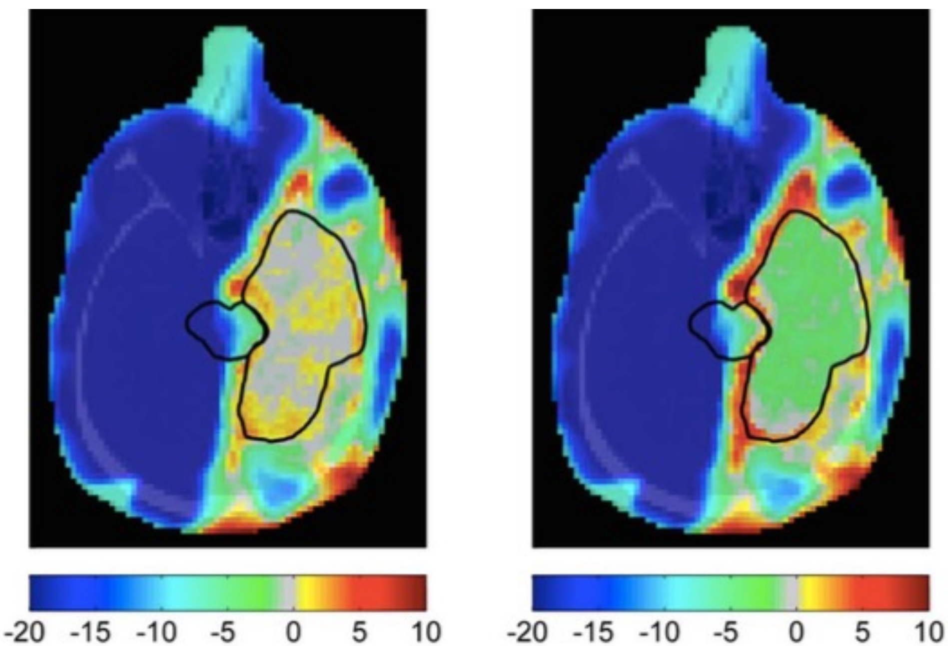
Protons are not simply like Photons*1.1

New Paradigm for Proton Radiobiology (Girdhani 2013 Radiat Res) →

Results point out that Protons and photons present distinct physics and biological properties at Sub-Cellular, Cellular and Tissue level



RBE=1.1 **Variable RBE**

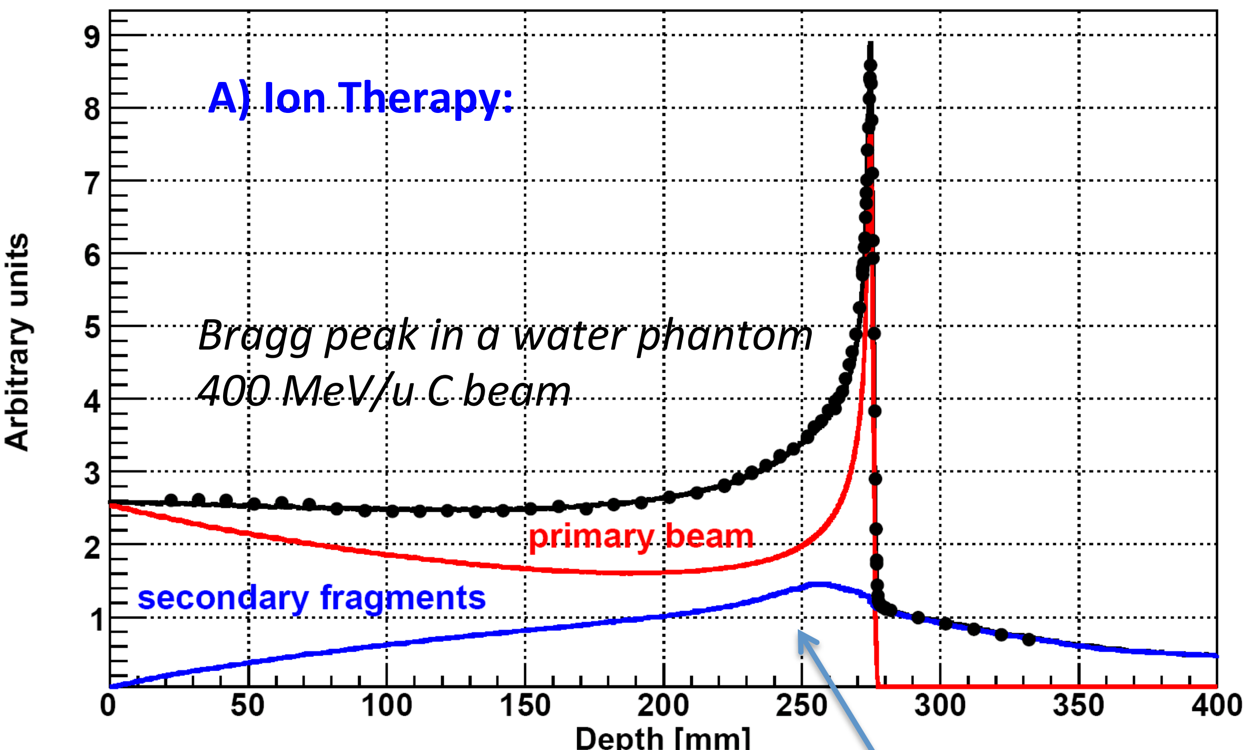


Experimental determinations of RBE exhibit large fluctuations. **RBE could be significantly >1.1**

Do nuclear interaction play a role?

It has been pointed out a possible impact of variable proton RBE on Normal Tissue Complication Prob. values. **Present Treatment Planning does not take this into account**

The two sides of the problem



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

B) Proton Therapy:
Nuclear Fragmentation of Target

Possible contribution to biological effect

Not considererd in treatment plannig so far

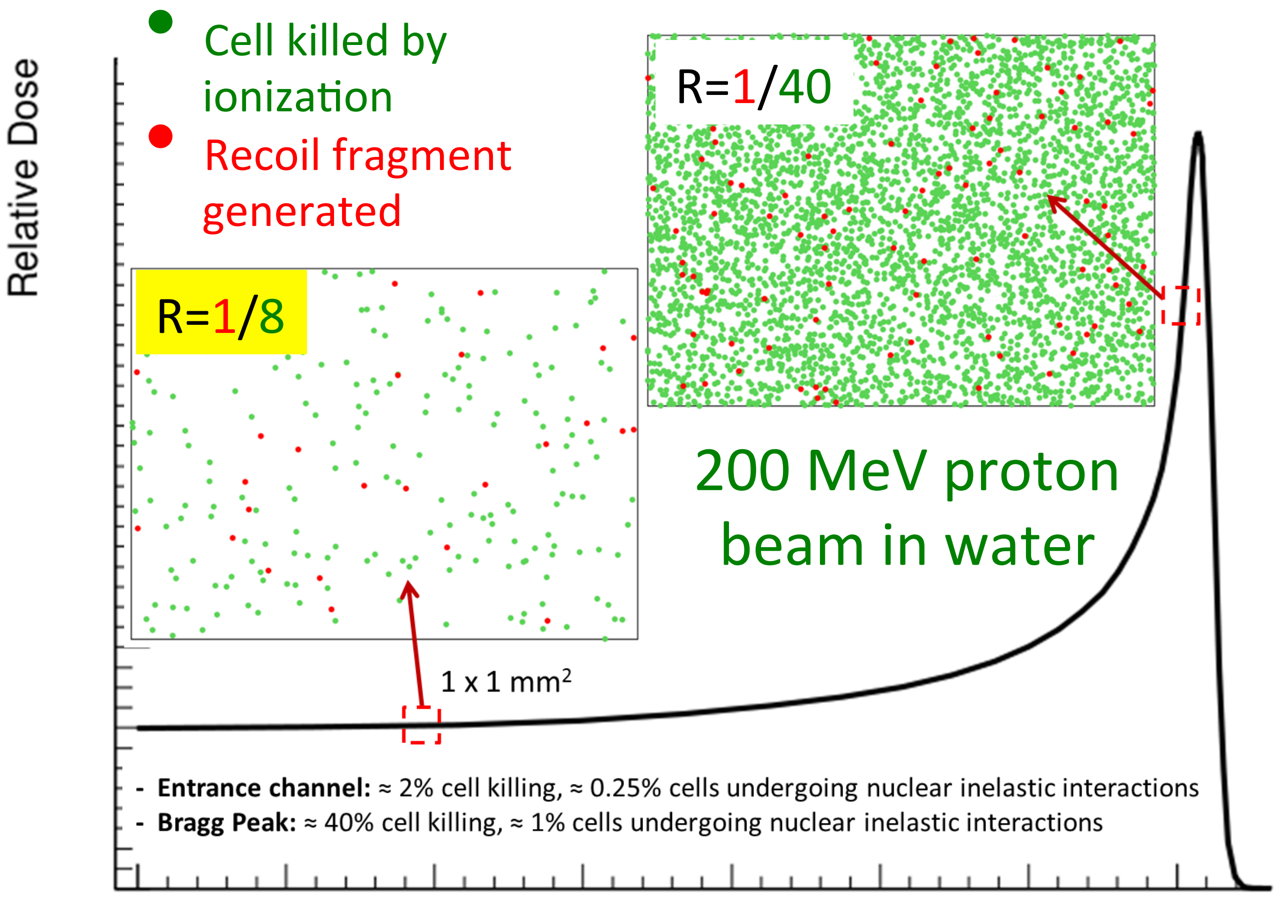
Data exisiting only for production of very light fragments (nucleons)

New

Known effect of **Nuclear Fragmentation of Projectile**:
mixed contribution of different RBE/LET
Considered in treatment, but still scarce validation data!

Target fragmentation & healthy tissue

Target fragmentation in proton therapy gives higher contribution in healthy tissue, where beam is still energetic (~200MeV) !!



Cancers 2015,7 Tommasino & Durante

About 10% of biological effect in the entrance channel due to secondary fragments (Grun 2013)

Largest contributions of recoil fragments expected from

He, C, Be, O, N

In particular on Normal Tissue Complication Probability

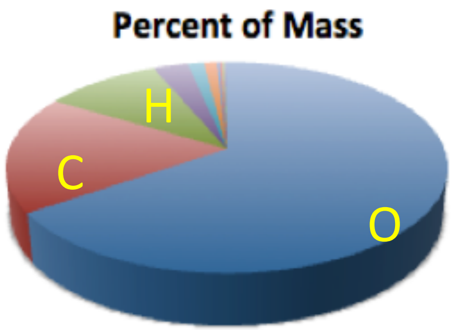
See also :

- Paganetti 2002 PMB
- Grassberger 2011 PMB

p+C, p+O scattering @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 heavy fragments.

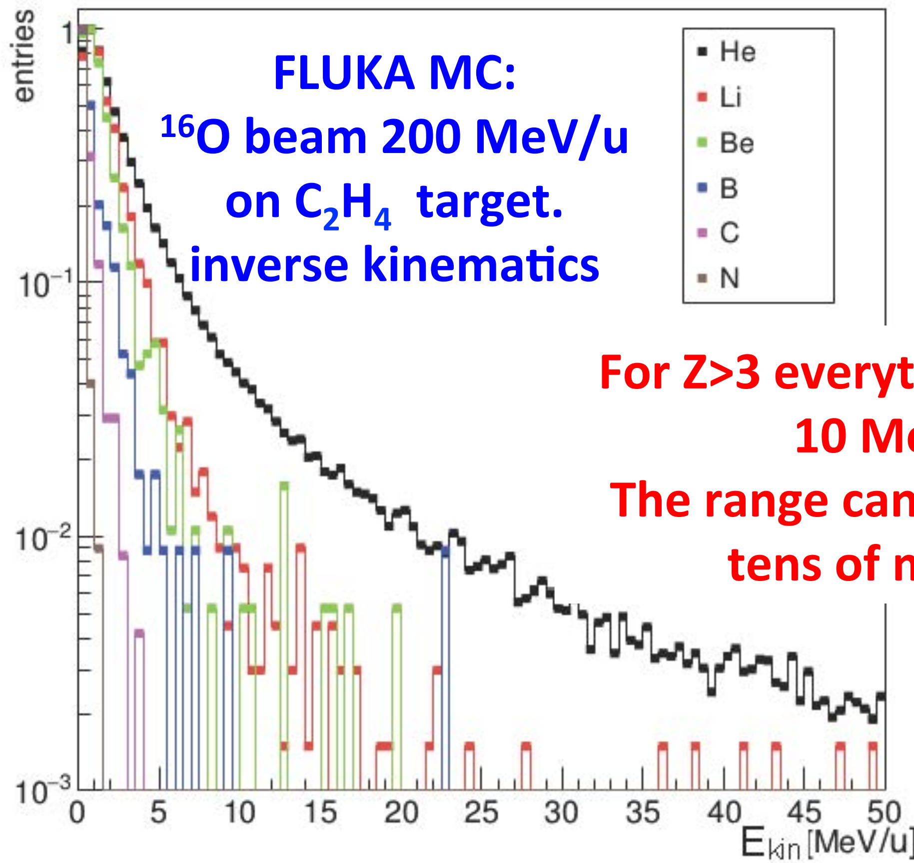


Very low energy-short range fragments, almost isotropic.

MCs confirm this picture but…..

Nuclear model & MC not yet reliable or benchmarked at the needed level

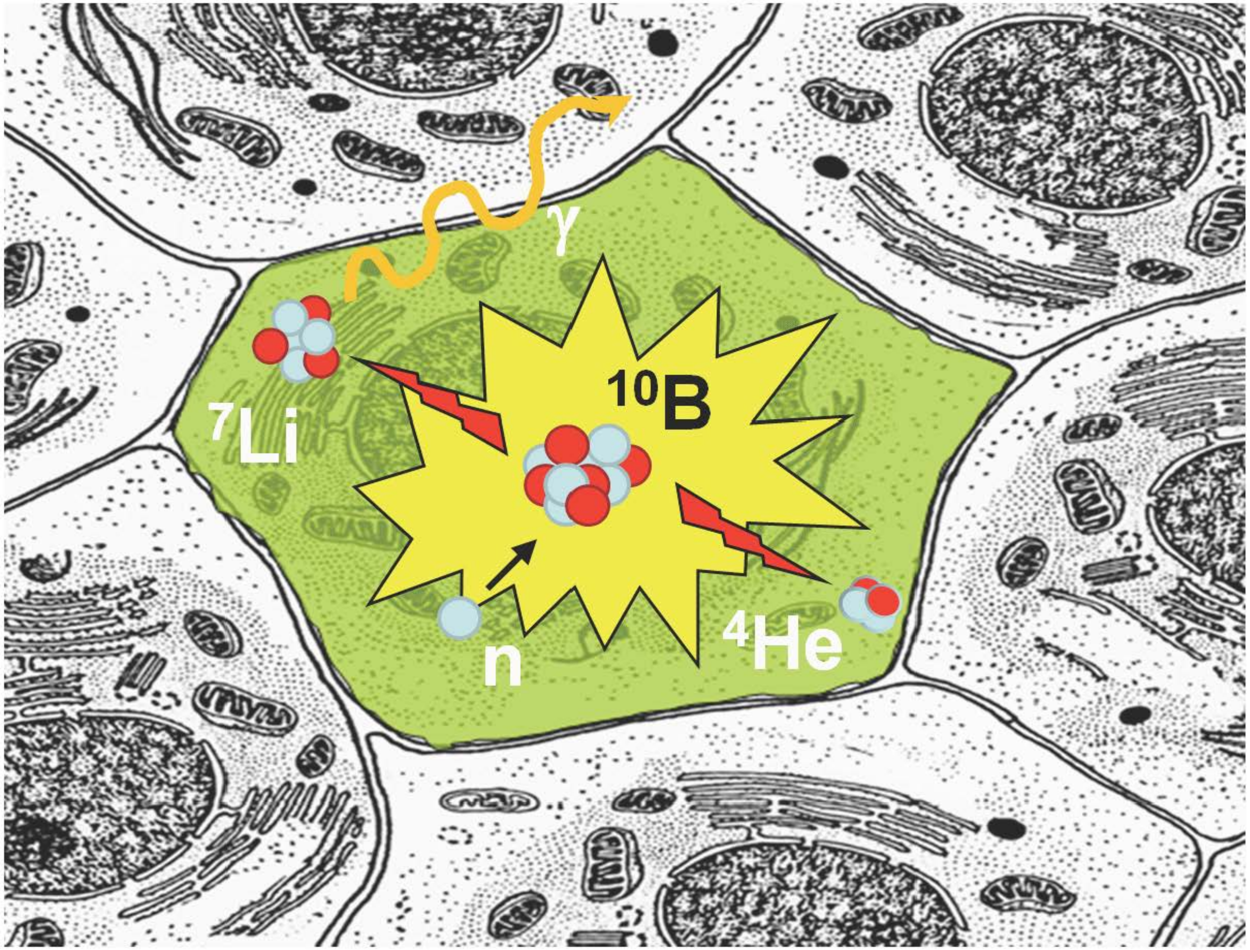
Needed Z>2 fragment yields and emission energy



For Z>3 everything is within 10 MeV/u

The range can be as low as tens of micron!!

An example of target fragmentation at work: BNCT



Inverse kinematic strategy

Shooting a proton (for instance E_{kin}=200 MeV → β~0.6) on a "patient" (i.e. at 98% a C,O,H nucleus) could not be the right choice. In particular large systematic on the fragment yields and energies can be due to the non zero target thickness.

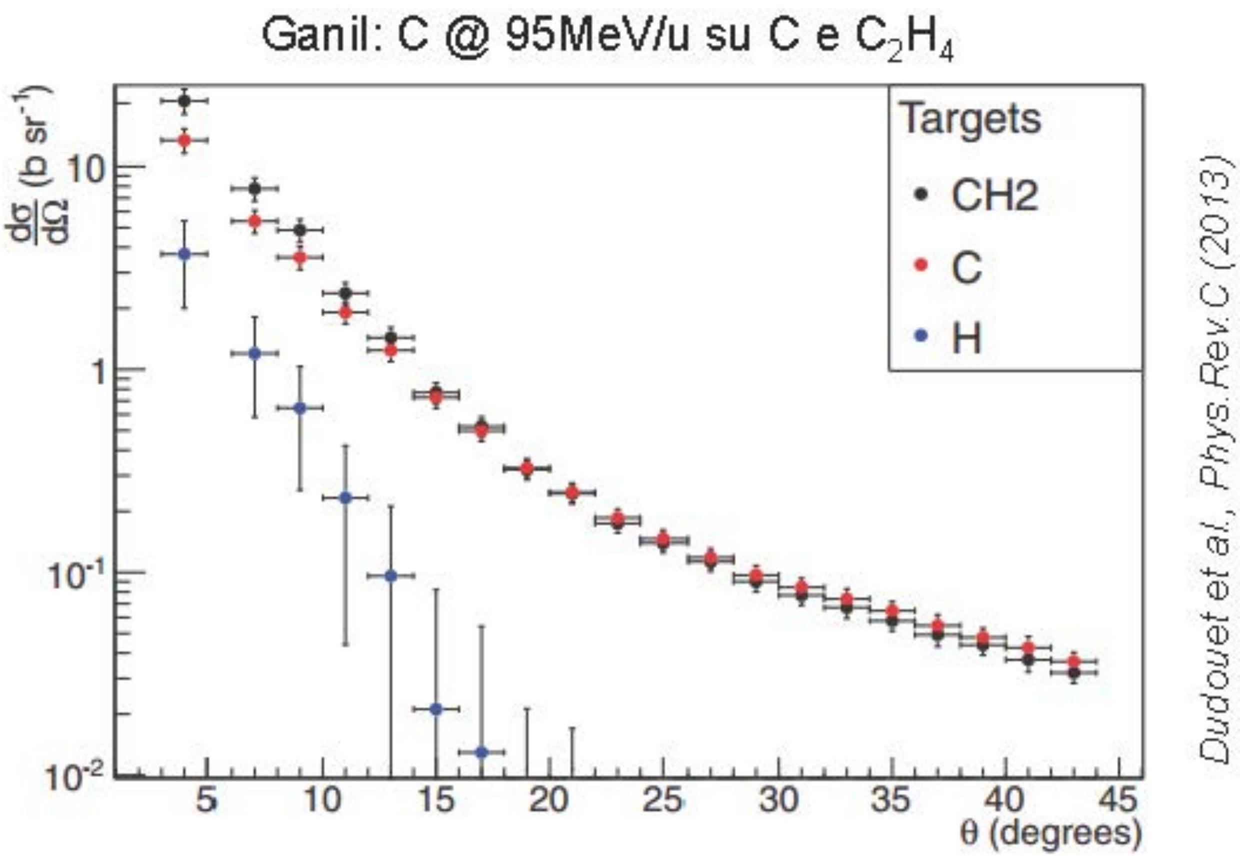
A possible work around is to shoot a β=0.6 patient (i.e. O,C beam) on a target made of protons and measure the fragments..

- Use as beams the ions that are the constituents of the patient (mainly ^{16}O, ^{12}C) with E_{kin}/nucl ~ 200MeV/u.
- Use twin targets made of C and polyethylene $(C_2H_4)_n$ and obtain the fragmentation results on H target from the difference
- Apply the reverse boost with the well known β of the beam

CAVEAT!: The fragment direction must be well measured in the Lab frame to obtain the correct energy in the patient frame

Experience at GANIL

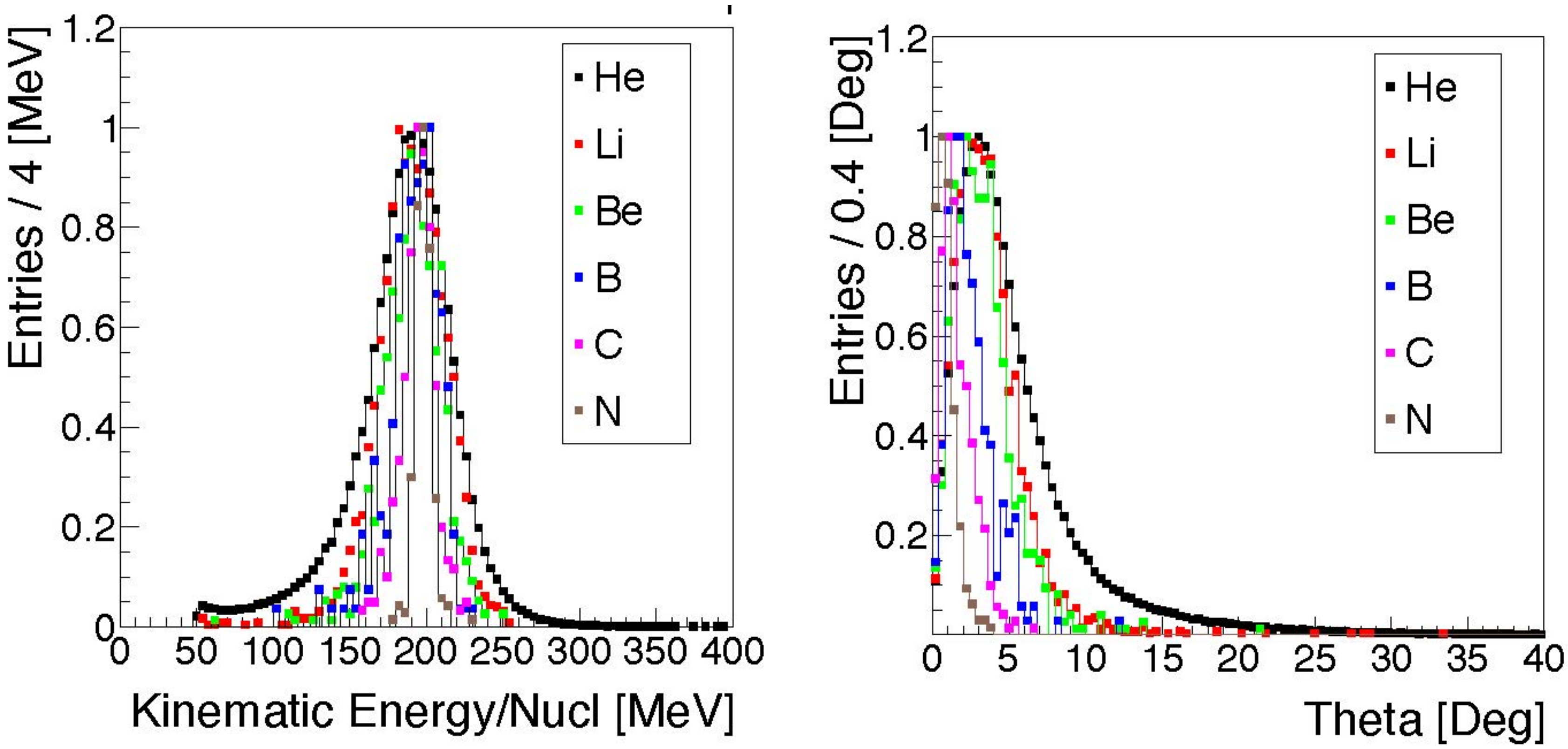
$$\sigma(H) = (\sigma(C_2H_4) - 2\sigma(C))/4$$



Monte Carlo Predictions: example

Direct kinematics: ^{16}O beam 200 MeV/u on C_2H_4 target

FLUKA MC code



Fragment production spectra

Normalized at the same peak value

Radiobiology requests & detector constraints

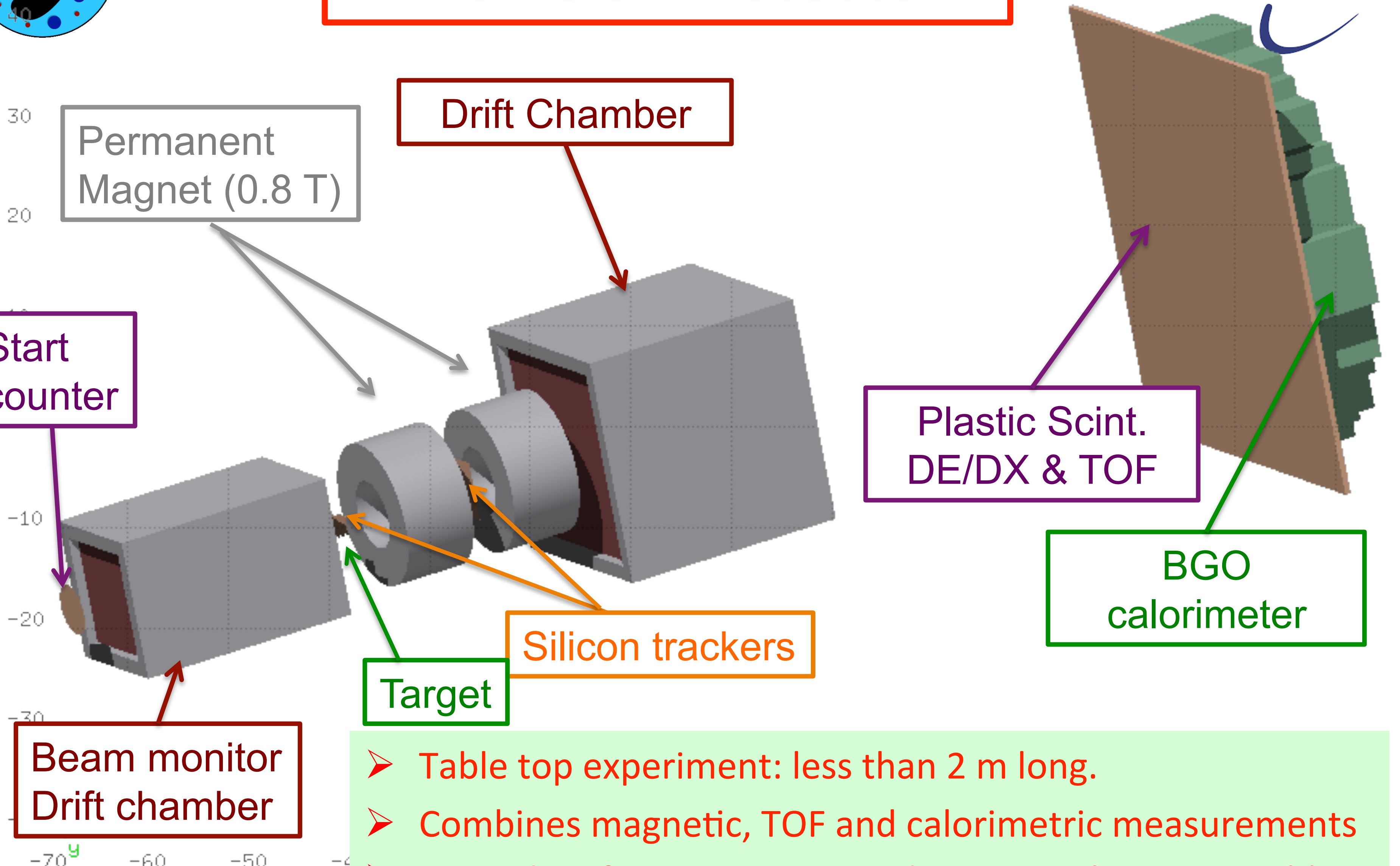
To implement sound NTCP models the requirements on the knowledge of the p+C,O interaction @200 MeV are very strict:

- Heavy fragment (Z>2) production cross section with uncertainty of 5%
- Fragment energy spectrum (i.e. $d\sigma/dE$) with 1-2 MeV/u accuracy
- Capability of resolving Z of fragment
- Capability of resolving isotopes, at least for lower Z nuclei.
- Study light ions production at large angle
- Angular resolution in "patient frame" is instead not relevant. Fragments have a very short range

Guide lines for the detector

- Main focus on Z>2 fragment yields & emission energy. **Precise angle measurement are also needed to apply correct inverse boost transformation**
- The fragment charge ID is the basis of the measurement.
- The fragment mass ID is a challenge and can be performed after a Z ID. An eventual wrong A assignment has an effect on the range evaluation-> **less severe at high A**
- PID achieved due to combinaton of measurements of energy, momentum and TOF measurement of fragments
- The fragmentation contribution due to detector material MUST be kept as low as possible and eventually subtracted
- **Detector portability to different beams is an absolute need: size of the detector should be in the 2 meters range**

The FOOT Detector



- Table top experiment: less than 2 m long.
- Combines magnetic, TOF and calorimetric measurements
- Secondary fragmentation on detector as low as possible

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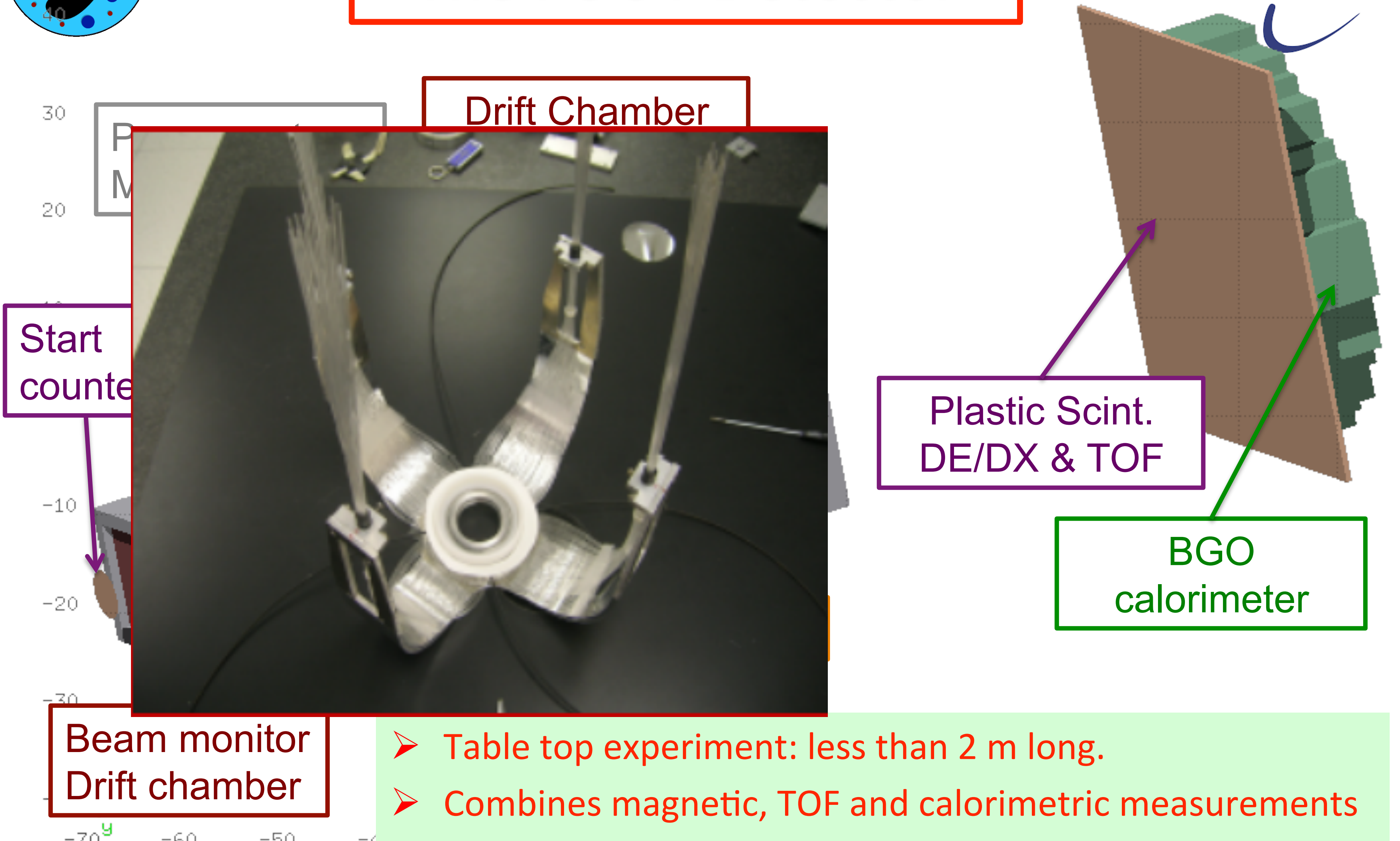

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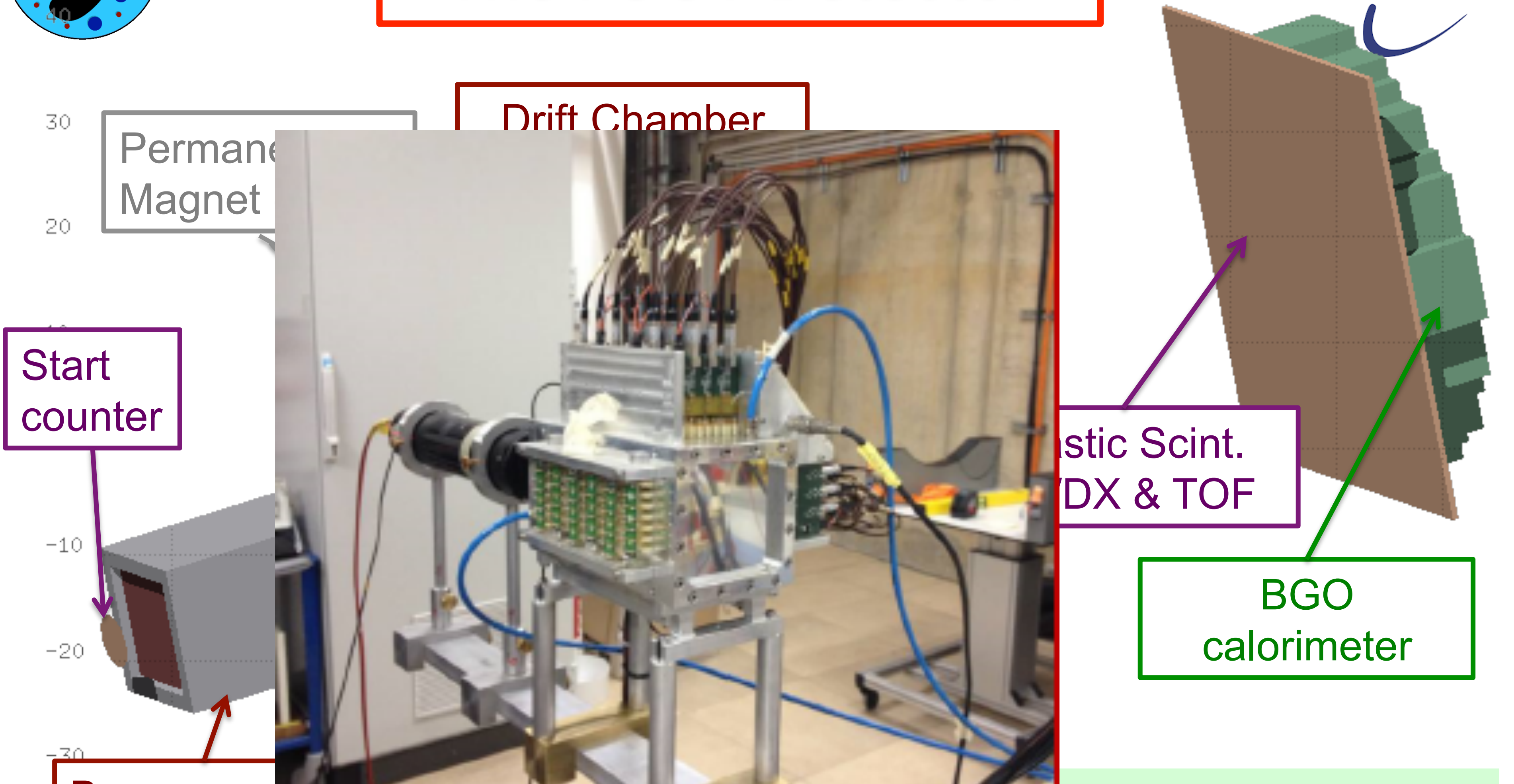

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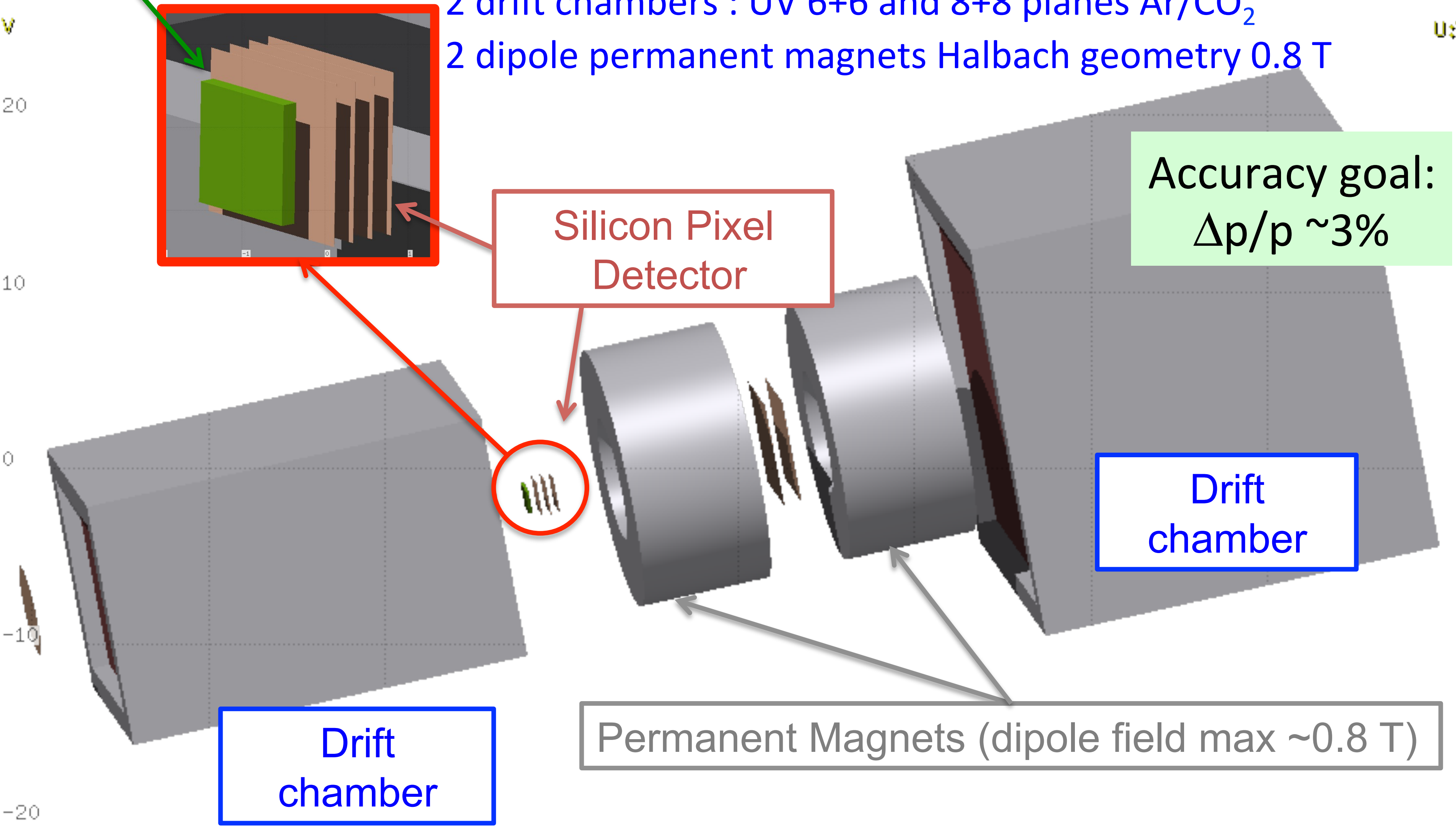
FOOT : momentum measurement

1 vertex + 1 tracking silicon pixel detector: MAPS MIMOSA 28 silicon pixel (20x20 mm)

2 drift chambers : UV 6+6 and 8+8 planes Ar/CO_2

2 dipole permanent magnets Halbach geometry 0.8 T



ΔE/TOF detector and Calorimeter

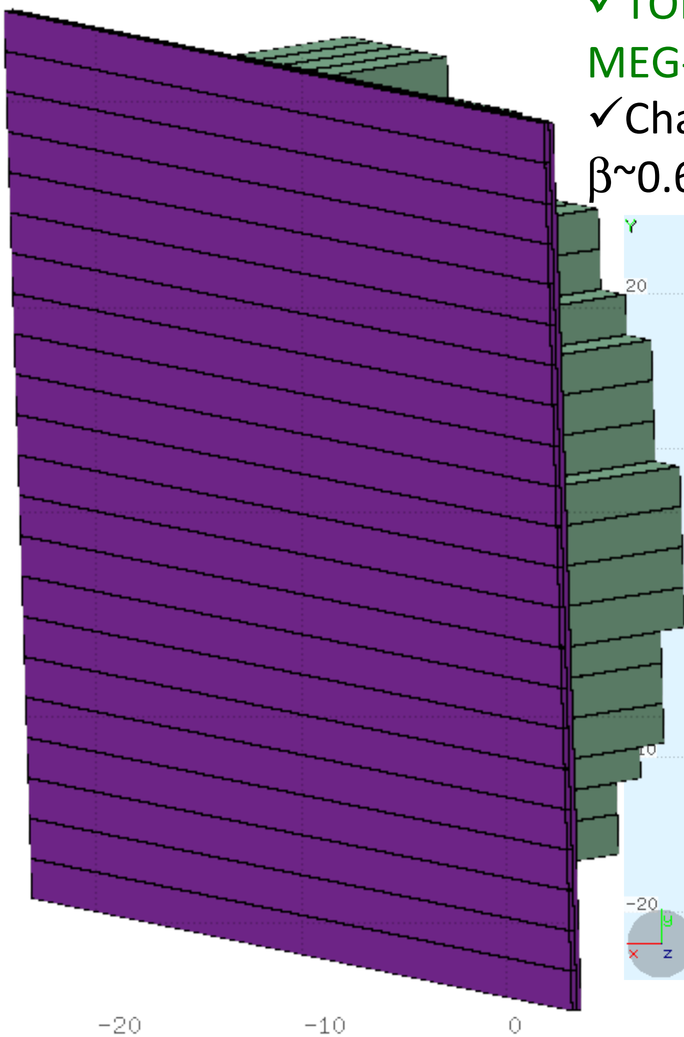
22 Y bars + 22 X bars

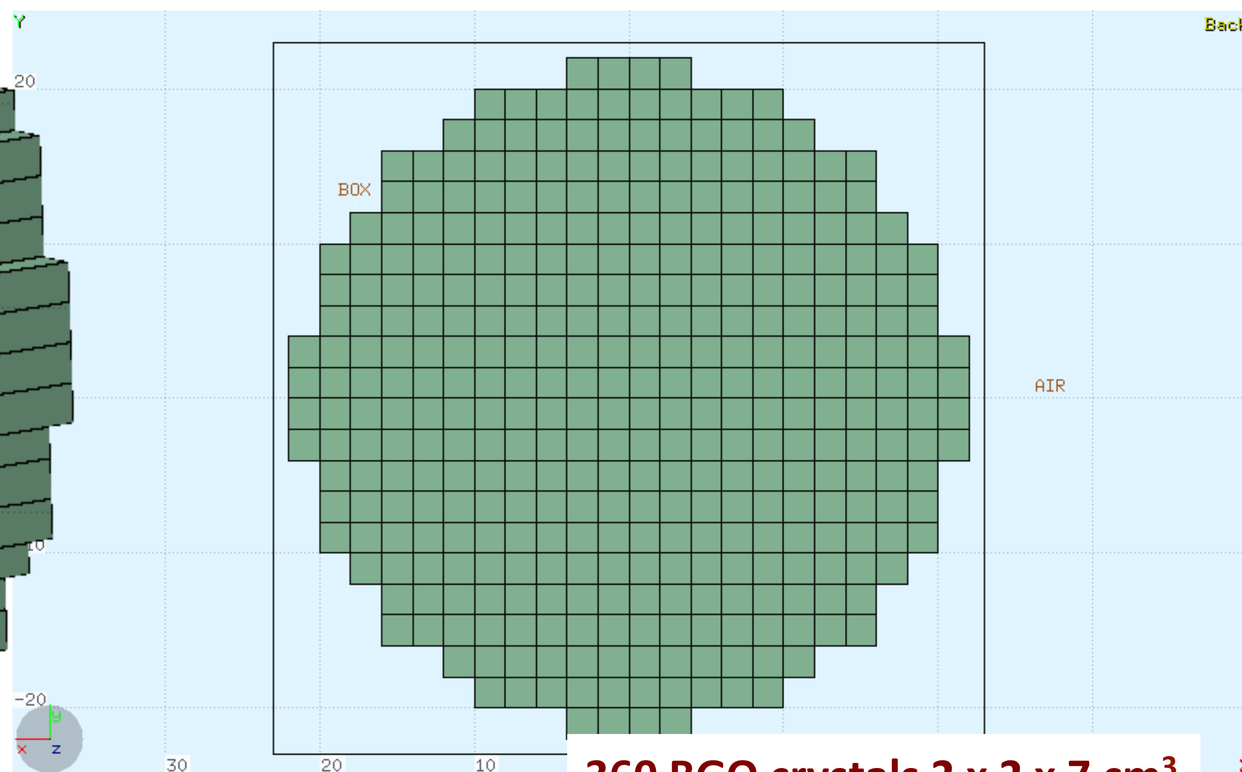
Scintillator type:
EJ-232

2 cm x 42 cm x 3 mm

✓TOF measurement below 100ps with heavy fragments: MEG-like digitizers

✓Charge mis-ID below the 2% level for Z=8 fragment at β~0.6





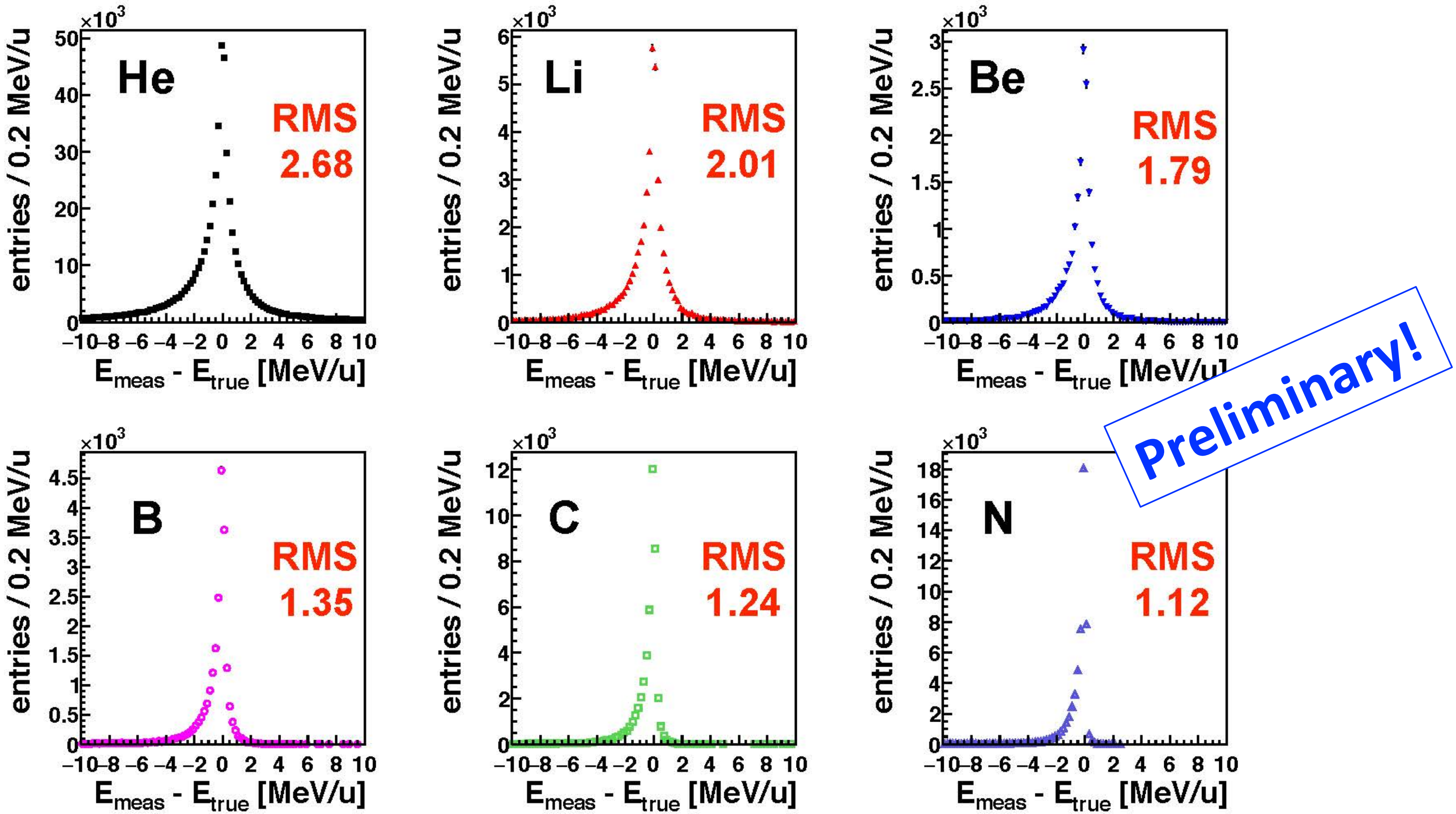
360 BGO crystals 2 x 2 x 7 cm^3

Resolution goals

σ_{TOF} ~ 100 ps
σ_p/p ~ 4 % for Ekin ~ 200 MeV/u
σ_E/E ~ 2- 3% for Ekin ~ 200 MeV/u
$\sigma_{\Delta E}/\Delta E$ ~ 3%

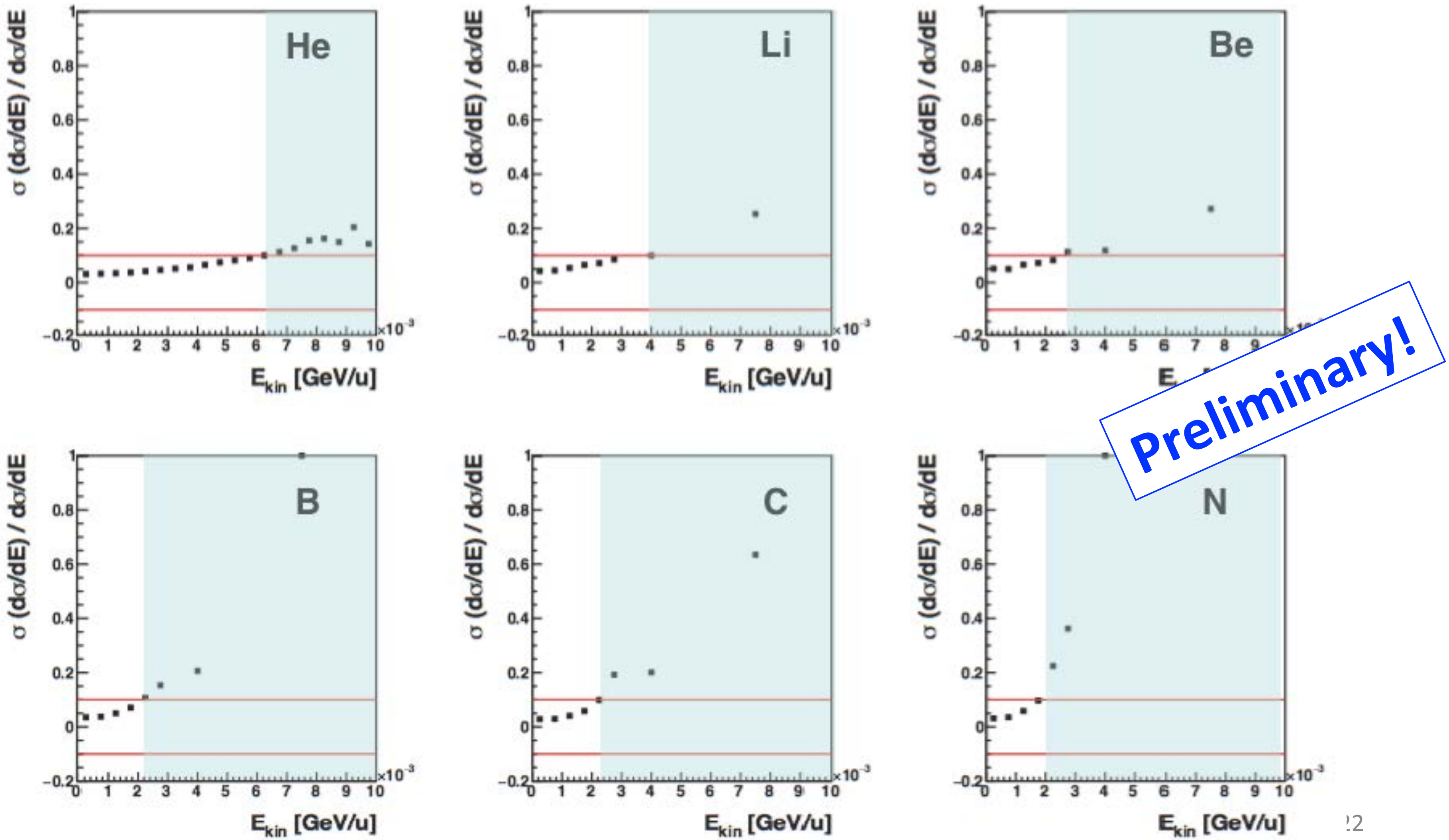
Evaluation of Energy Resolution in Inverse Kinematics (MC)

^{16}O beam 200 MeV/u on C target **assuming Δp/p ~ 4%**



Evaluation of Xsec Resolution in Inverse Kinematics (MC)

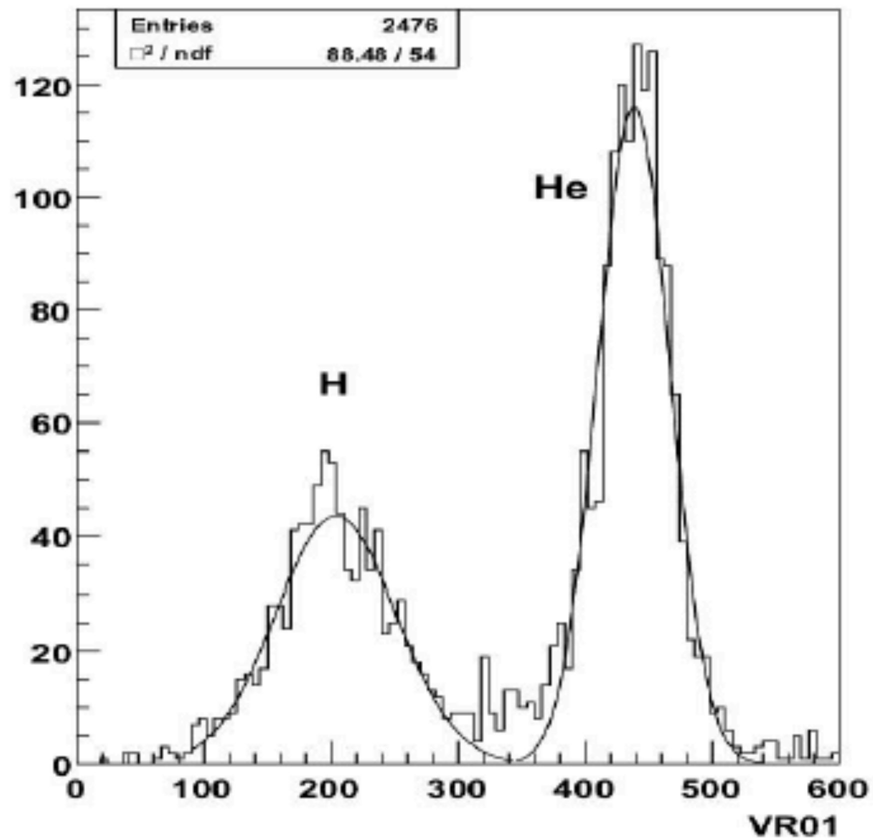
^{16}O beam 200 MeV/u on C target



light fragments (p, He): FOOT with emulsions

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

- Tracking procedure at large angle, up to 75^0 with respect to the beam direction, has been developed at Napoli (OPERA)
- The emulsion chamber must be exposed with a remotely controlled movement to avoid local pile-up
- Must be run inside FOOT with Start counter and Beam monitor for absolute flux normalization
- Particularly suited for radioprotection in space related measurement

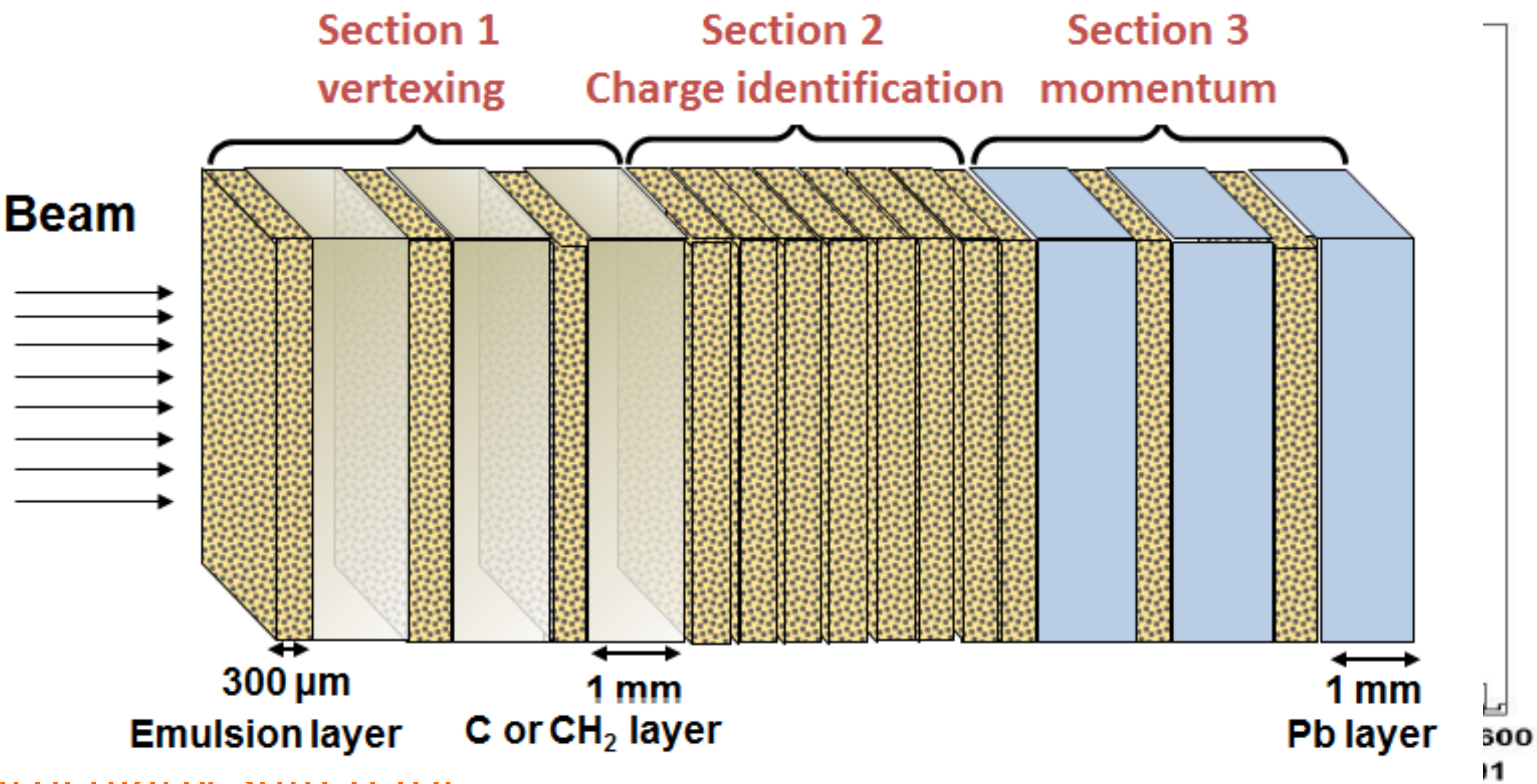


Emulsion run could be the first data taking of FOOT in 2018

Emulsions and light fragments

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

- Tracking procedure at large angle,



- Particularly suited for radioprotection in space related measurement

Emulsion run could be the first data taking of FOOT in 2018

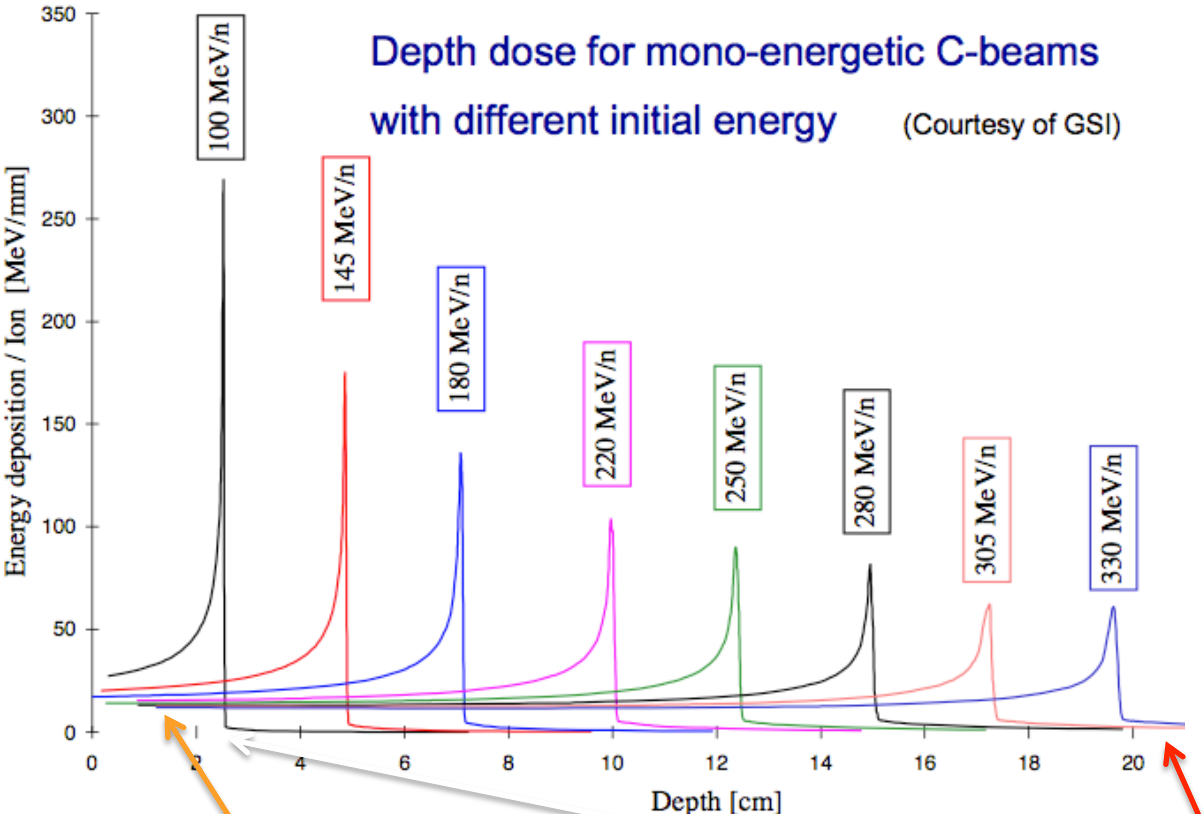
Where can we lay down FOOT?

Wish-list for an experimental facility:

- C,O (N) beams in the 100-350 MeV/u energy range availability
- Possibility to mount and calibrate the experimental setup before data taking for “long” time (1-2 week)
- Beam time availability in the week time range -> dedicated experimental hall
- Several data taking period possible, with safe time schedule to be known in advance

- CNAO Experimental room is our choice. Explicit interest and participation in the FOOT project. Exp. Hall ready by 2019
- HIT: possible B plan, experimental room a bit small
- GSI ?
- Trento proton beam and LNS ion beams are fundamental for calibration purpose

Projectile Fragmentation. Existing thin target, Double Diff Cross Section C-C measurements



The community is interested for the ^{12}C beam therapy, to explore the region 150-350 AMeV (i.e. 5-17 cm of range in tissue…)

LNS 62AMeV C beam (2009)

GANIL 95AMeV C beam - E600 exp. (2011)

GANIL 50AMeV C beam

GSI 400MeV C beam (2011): **to be repeated**

Timeline & measurements program

Experimental program of FOOT:

- ✓ Target fragmentation of p on O,C @100-200 MeV/u
- ✓ Projectile fragmentation of O on C @200-400 MeV/u
- ✓ Projectile fragmentation of C on C @200-350 MeV/u
- ✓ Evaluation of production of some β^+ emitters production (for example ^{8}B) from C,O on C @200-400 MeV/u: *useful for range monitoring of Particle Therapy*
- ✓ Fragmentation measurement of several beam on $(C_2H_4)_n$ of interest for radioprotection in space

In a realistic (moderately optimistic) schedule at least the a),b) measurements should start by 2019-2020

FOOT collaboration in pills

Starting collaboration, funded by INFN for 2017, with contribution of Centro Fermi Institute

- INFN Sections/Labs: Bologna, Frascati, Milano, Napoli, Perugia, Pisa, Roma1, Roma2, Torino, Trento
- CNAO Collaboration
- People: ~50 researcher
- DATA taking foreseen @ CNAO/Heidelberg/GSI in 2020
- International collaborations: Nagoya Univ.; GSI under discussion; **open to other groups and institutions**

Parallel NCTP modeling radiobiology activity within INFN: MoVE-IT (**Mo**deling and **Ve**rification for **I**on beam **T**reatment planning)

Conclusions

- ✓ The issue of the proton RBE (and of the target fragmentation) is under the spot in the Particle Therapy community
- ✓ The FOOT collaboration is designing a detector to measure both target fragmentation in proton therapy and projectile fragmentation in carbon therapy
- ✓ The R&D for experiment during 2017 has been approved and funded by INFN, with contribution by Centro Fermi Institute. Final approval for the 2018-2021 period expected in june 2017
- ✓ Initiative in the starting phase and open to collaborations
- ✓ Datat taking foreseen in late 2019 - 2020

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Thanks for your attention

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