L'esperimento FIRST nell'ambito del progetto TPS dell'INFN

A.Sarti
LNF - INFN

Treatment Planning Systems

- The Treatment Planning System (TPS) is a tool (software) that is used to plan the irradiation of a patient in a Target Volume in order to kill tumors by means of radiation sparing the surrounding health tissues
- The TPS main inputs are:
  - The CT scan of the patient (Target volume AND surrounding tissues/organs)
  - The detailed description of the interaction of the Radiation Beam with the tumor and surrounding tissues/organs
  - The modeling of the Radio Biological Effectiveness (RBE) of the beam used as a function of the tissue/cancer to be treated
- The output should be:
  - **The fluence in the Target Volume**
- Monitoring of the TPS is mandatory in order to ensure that patient is treated properly / safely.

Areas of relevant competences within INFN

- The INFN can contribute with know-how in several different crucial steps in defining the TPS:
  - Nuclear / Radiation Physics: needed in the description of the beam interaction with the patient
  - MC simulation: needed for the treatment planning
  - Optimization algorithms: needed for 'online' TPS corrections, precise MC beam shaping
  - Experimental Radiobiology and Monitoring "in beam": needed in the RBE model validation and TPS monitoring

these are the 5 tasks of the INFN TPS project

- INFN participants: LNF, LNS, LNL + INFN Sez. Mi, Pi, To, Rm2, Rm3, (Ca?) + Università Roma 1, Roma 2, Roma3, Pisa, Torino

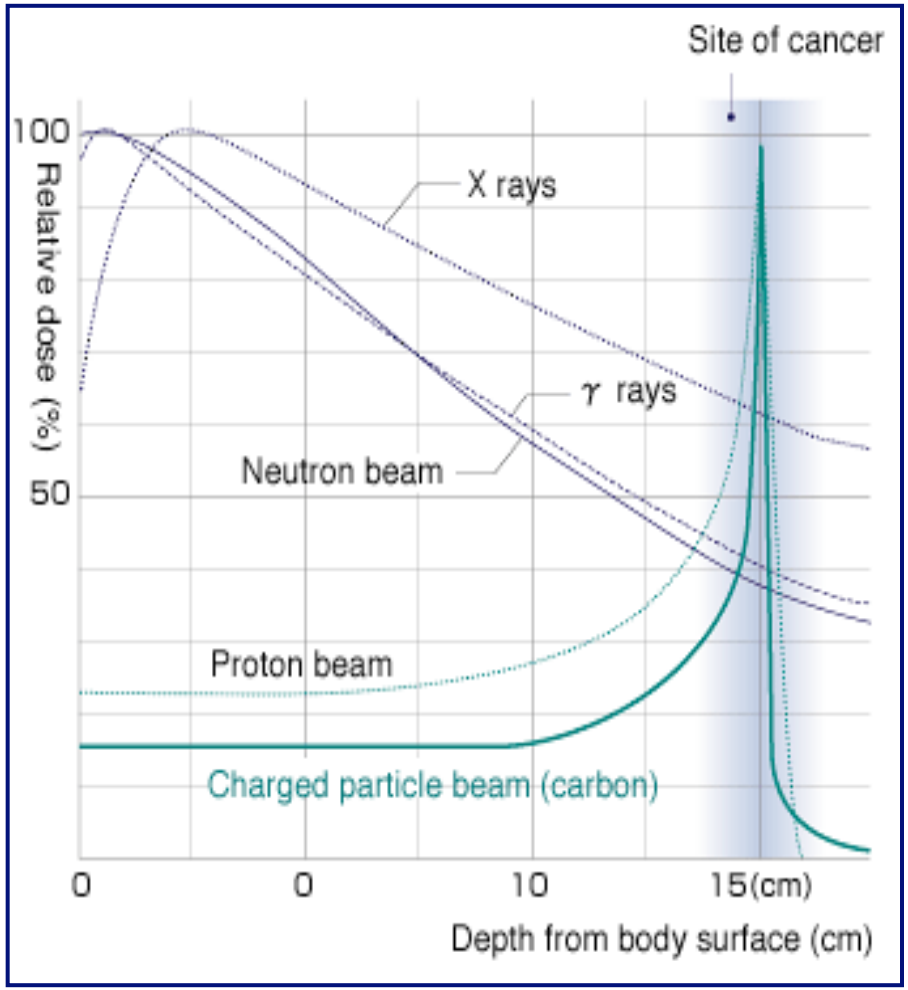
The TPS INFN project

- Currently working on Hadron Therapy TPS with 'active' voxel scanning and light ions [starting with ^{12}C] : reasons for those choices will follow shortly
- Contributing to
  - Management of TPS interfaces/corrections
  - **Description of nuclear interactions of the beam with target volume** and integration with local beam delivery systems
  - Implementation of "fast" calculation ➔ producing alternative plans in due time
  - Production of general and flexible analysis tools for the inspection of isodose curves on CT scans and Dose-Volume histograms (DHV), etc
  - Developing monitor using the Production of active nuclides, particle emission (in-beam monitoring and feed-back correction to planning)
- Project aim (developed for ^{12}C but extendable to other ions/protons):
  - Produce a well defined, certified and ready-to-use deliverable in collaboration with an industrial partner → IBA (through associated Elekta-CMS)
  - Collaboration with CNAO in Italy for testing and other European Institutes for aspects concerning nuclear physics and radiobiology

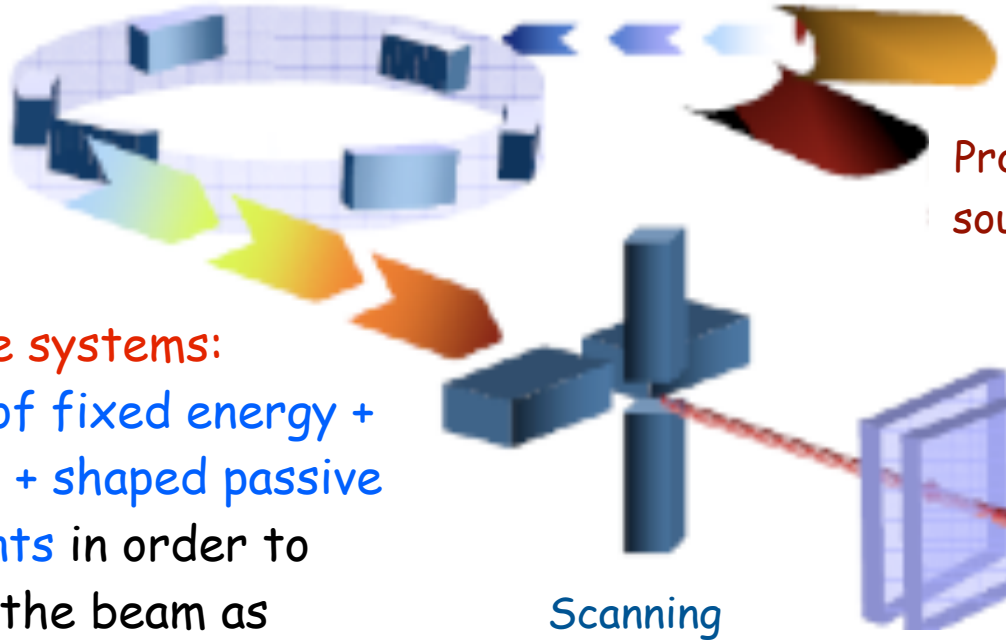
Hadron Therapy Motivation

- Light ions advantages in radiation treatments :
  - Better Spatial selectivity in dose deposition: Bragg Peak
  - Reduced lateral and longitudinal diffusion
  - High Conformal dose deposition
  - High Biological effectiveness

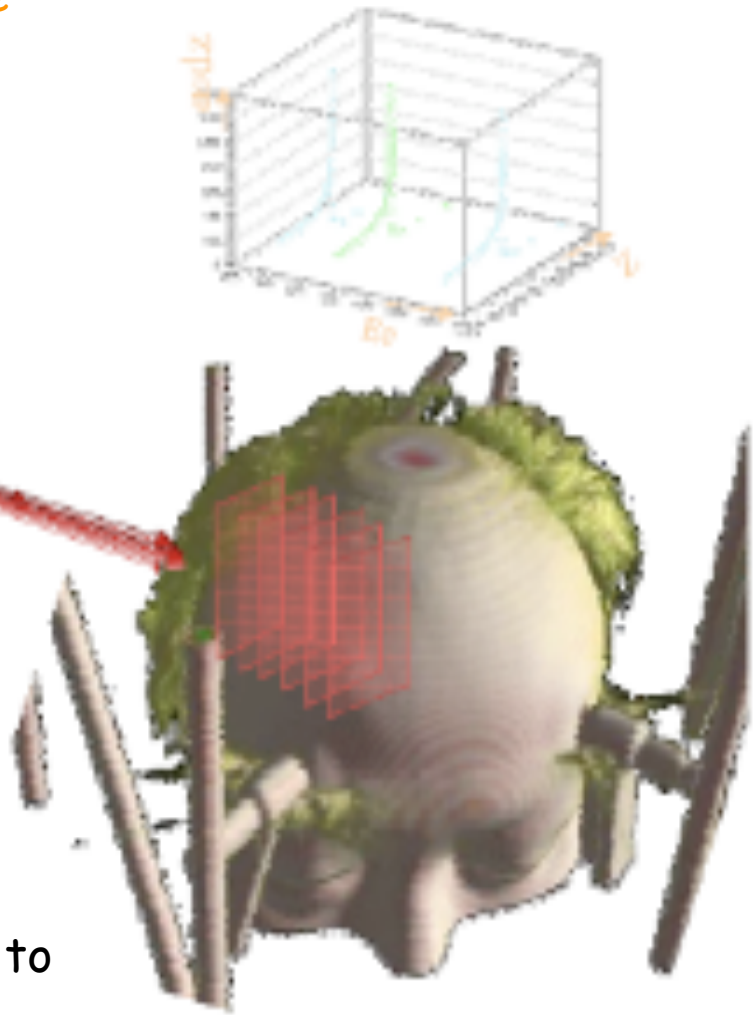
Treatment of highly radiation resistent tumours, sparing surrounding Organs At Risk (OAR)



Hadron Therapy with active scanning



Passive systems:
Beam of fixed energy + filters + shaped passive elements in order to model the beam as required by the TPS

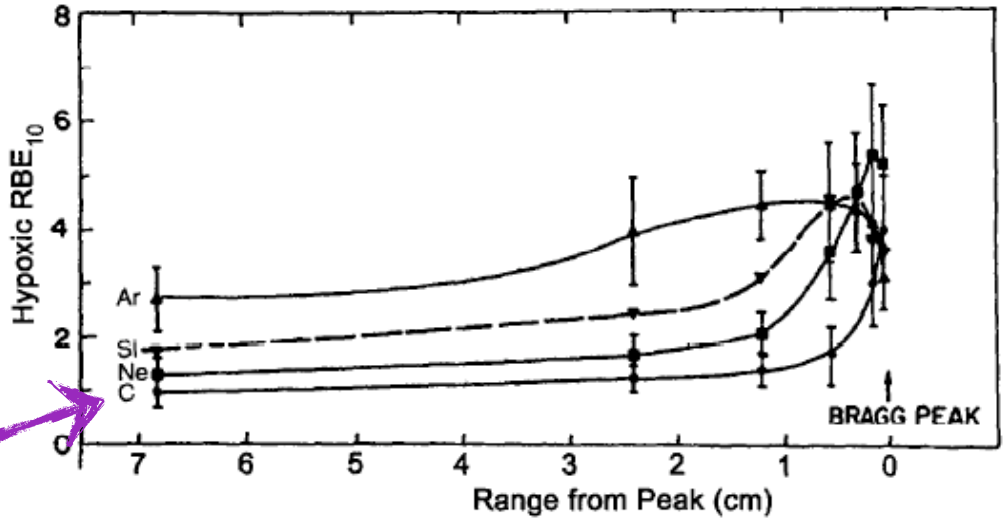


Active systems: Use the superposition of N (N≥100) elementary beams, with X,Y controlled by magnets and Z by the energy.

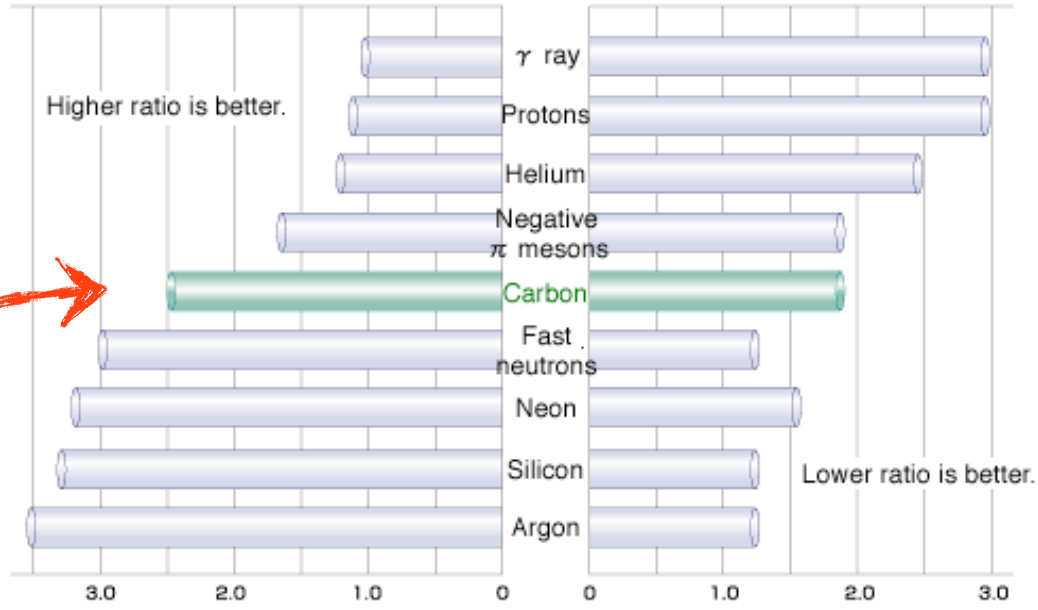
Mathematical determination of the weights of N beams so to achieve the required equivalent dose in the target region, minimizing the effects on surrounding regions and organs at risk

Hadrontherapy with ^{12}C ions

- The use of Carbon ions comes with several advantages:
  - Lower lateral and longitudinal diffusion vs. proton
  - More precise energy deposition
  - Optimal Radio Biological Effectiveness (RBE) profile vs penetration depth position.
  - Online PET for depth deposition monitoring
  - Good Compromise between RBE and (Oxygen Enhancement Ratio) OER. OER is defined as $D_{hypo}/D_{areated}$ to induce the same biological effect



Relative biological effectiveness (RBE) and oxygen enhancement ratio (OER) of various radiation types

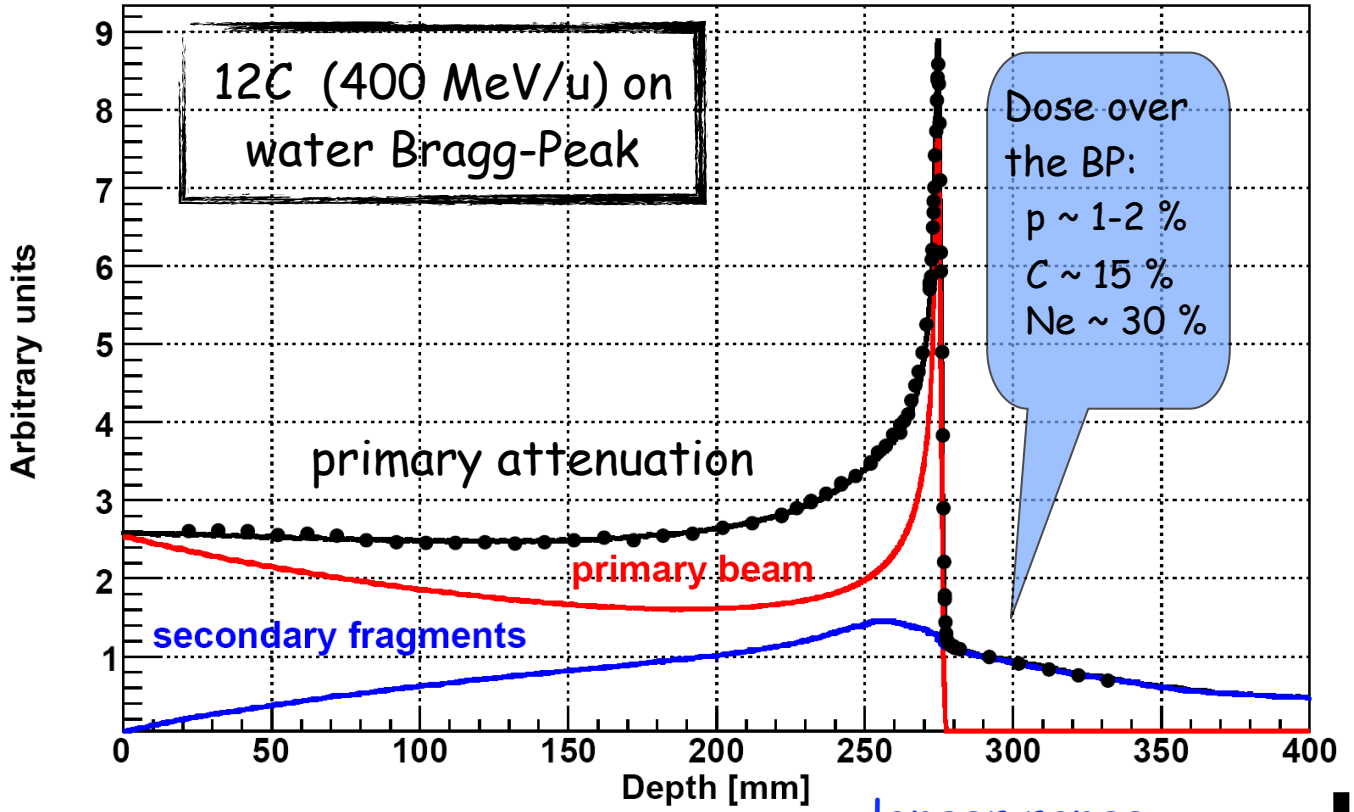


^{12}C ions: Fragmentation

- Nuclear Fragmentation of ^{12}C beam in the interaction with energy degraders and/or biological tissues
  - Attenuation of the primary beam
  - Different biological effectiveness of the fragments: RBE factor != for primary and fragments
  - Dosimetry, Planning: Mixed field complexity

Production of fragments with higher range vs primary ions
Production of fragments with different direction vs primary ions

Courtesy of Andrea Mairani



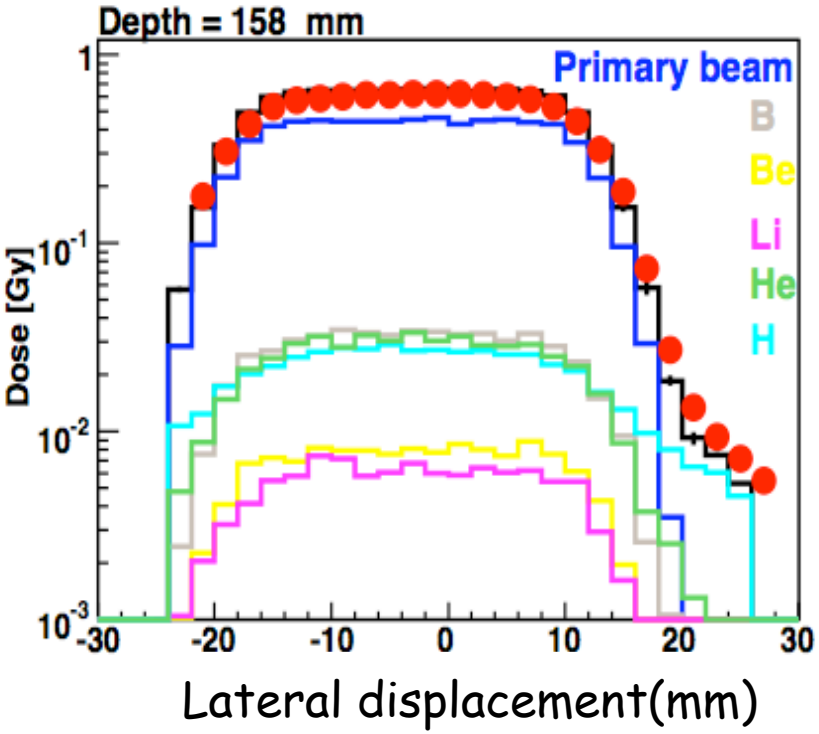
Exp. Data (points) from Haettner et al, Rad. Prot. Dos. 2006
Simulation: A. Mairani PhD Thesis, 2007, Nuovo Cimento C, 31, 2008

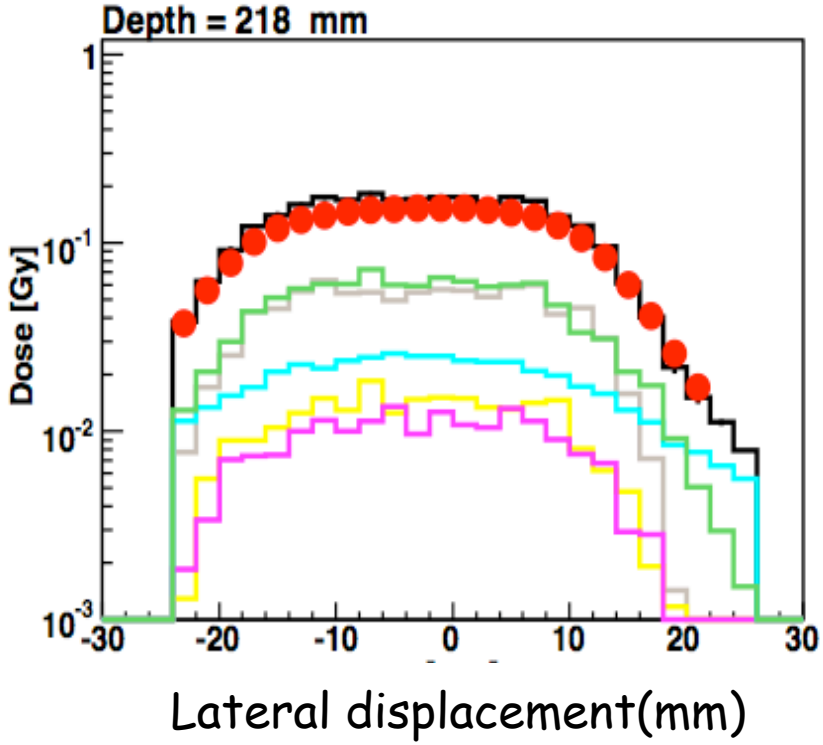
longer range lighter fragments

^{12}C ions: fragments lateral dose profile

- 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

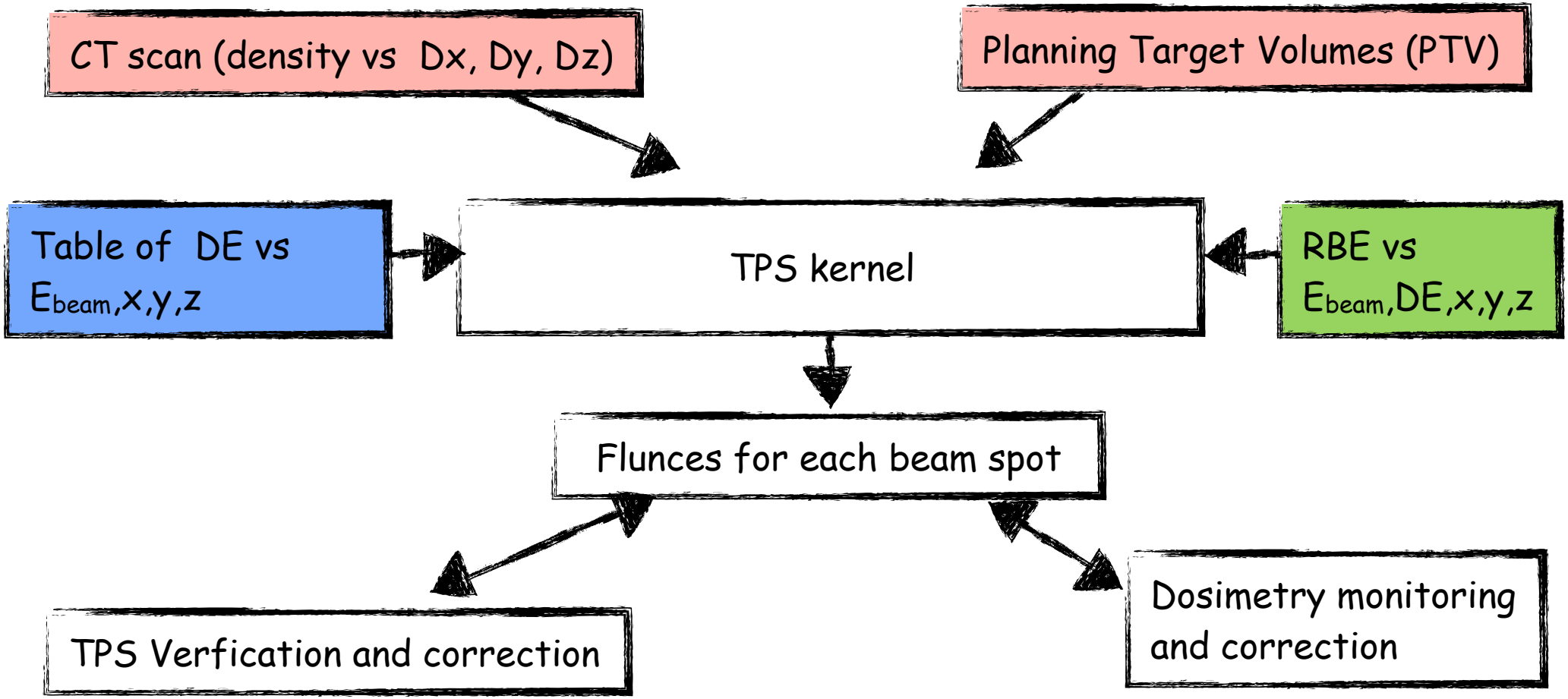
SOBP centered al 20 cm depth in water





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

A simplified scheme of the proposed TPS

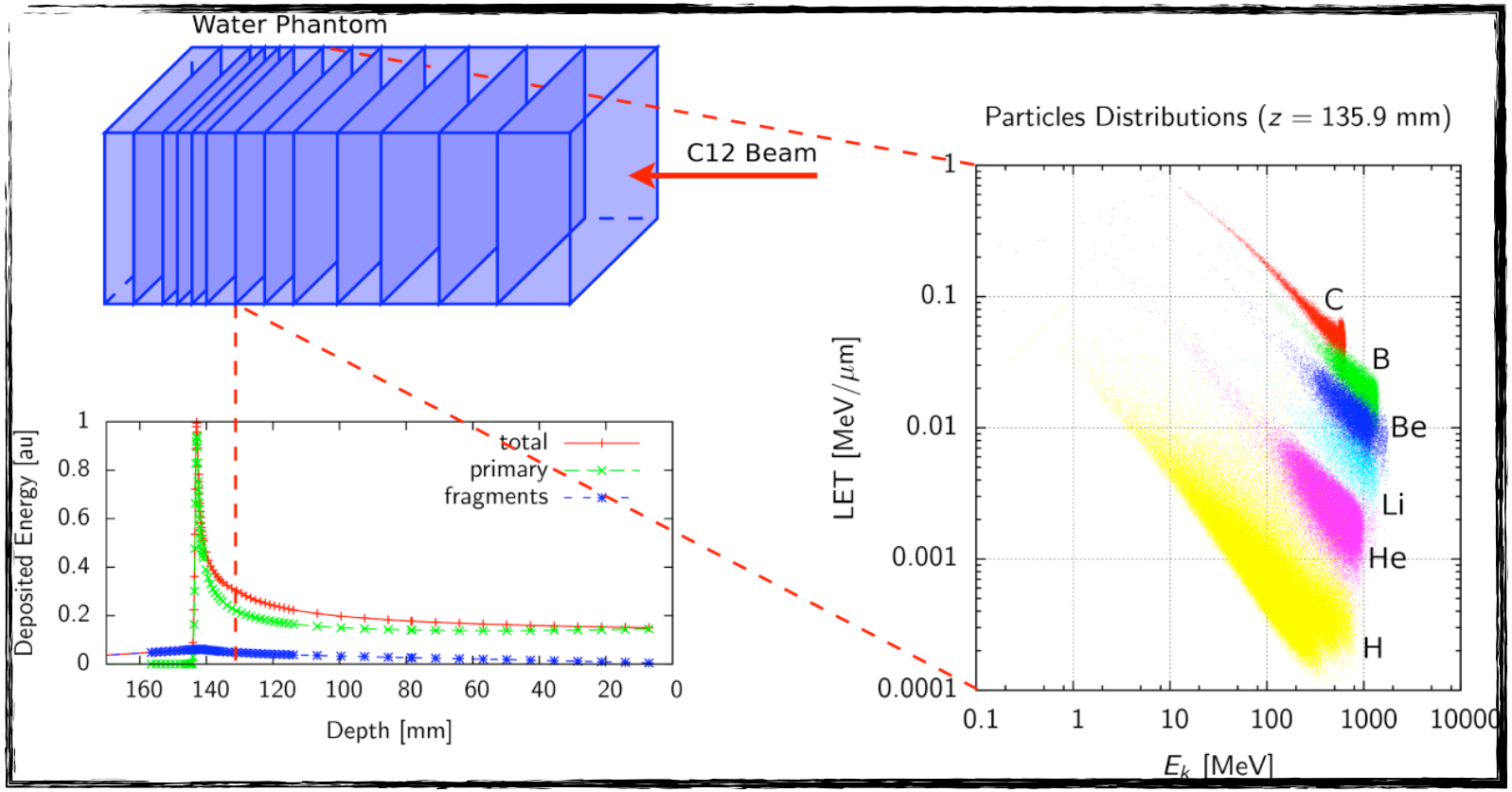


Choice of the RBE model

The choice of RBE model

- RBE: ratio of the dose from a reference radiation (D_{RX}) and the dose for the actual radiation (D_r) needed to achieve the same biological effect under consideration : $RBE = D_{RX}/D_r$
  - For a given radiation field, RBE depends on: The definition used in the calculus; The considered biological effect (survival, induction of mutations etc.); The cell type ....
- The heart of a TPS is the radiobiological model to calculate and take into account the RBE
  - Models generally used so far have limits and are not satisfactory from a conceptual point of view but are presently used in the clinic practice with satisfactory results: will be avoided when exp. data will cover the needs
  - The development of "microscopic" radiobiological models would be most appealing approach but requires a long time (years of work).
  - Decided to use the Local Effect Model (LEM) developed @ GSI

Delivered energy and Biological Effect

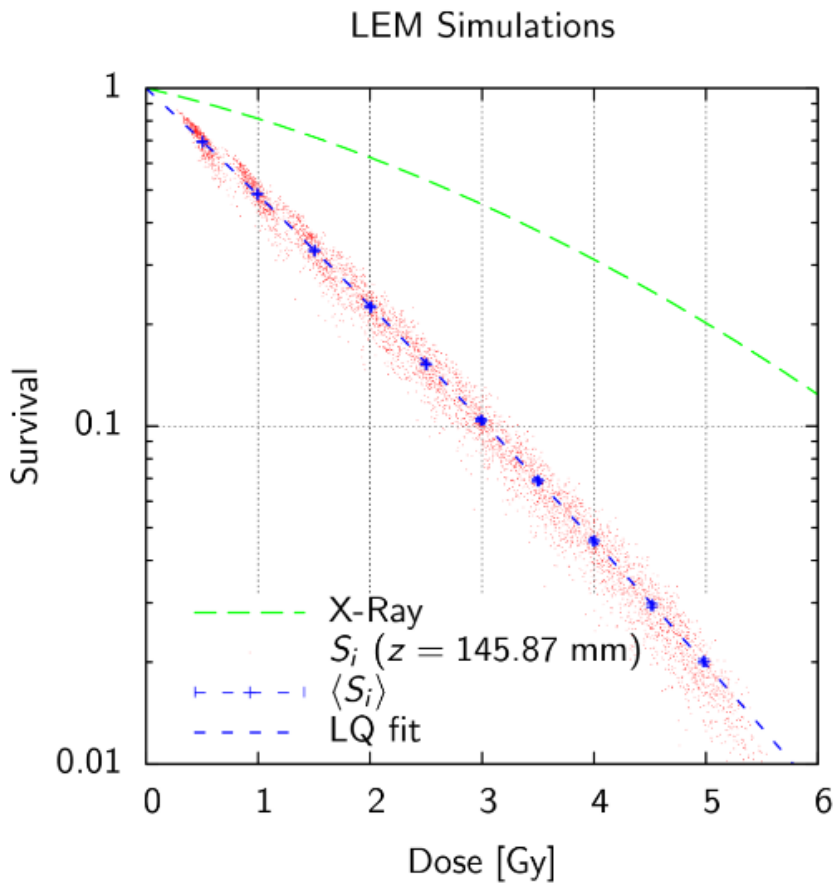


Experimental / MC input

- Once you know the Energy transferred to each voxel as a function of the Beam conditions, the Biological Effectiveness (Survival probability) must be used for the Plan optimization
- The RBE is used to convert the 'Delivered dose' into a 'Survival Probability' for the cells under treatment

RBE with LEM

- LEM model:
  - It is used to convert Dose information into Survival Probability [parameter used in the TPS cost function minimization]
  - Assumes that: BE is entirely determined by Dose distribution inside cell nucleus
  - The only relevant parameter is the released dose: all the radiation types are treated in the same manner
  - The cell nucleus is assumed to be homogeneus
- The survival probability S is then computed as
  - $S = \exp(-\alpha\ D - \beta D^2)$
  - a Linear-Quadratic (LQ) approximation with D = delivered dose, and α,β depend on the cell line [are taken from measurements/ literature]



Treatment planning: cost function

- Once the volume to be treated (m_T), the dose to be delivered (D_T), the maximal dose (D_{OAR}) and prescriptions about organs-at-risk (OAR) are defined (physician input!).. The cost-function to be minimized can be written as:

$$X^2 = \sum_{i \in m_T} [D_i^b - D_T]^2 + \sum_{i \in OAR} [D_i^b - D_{OAR}]^2$$

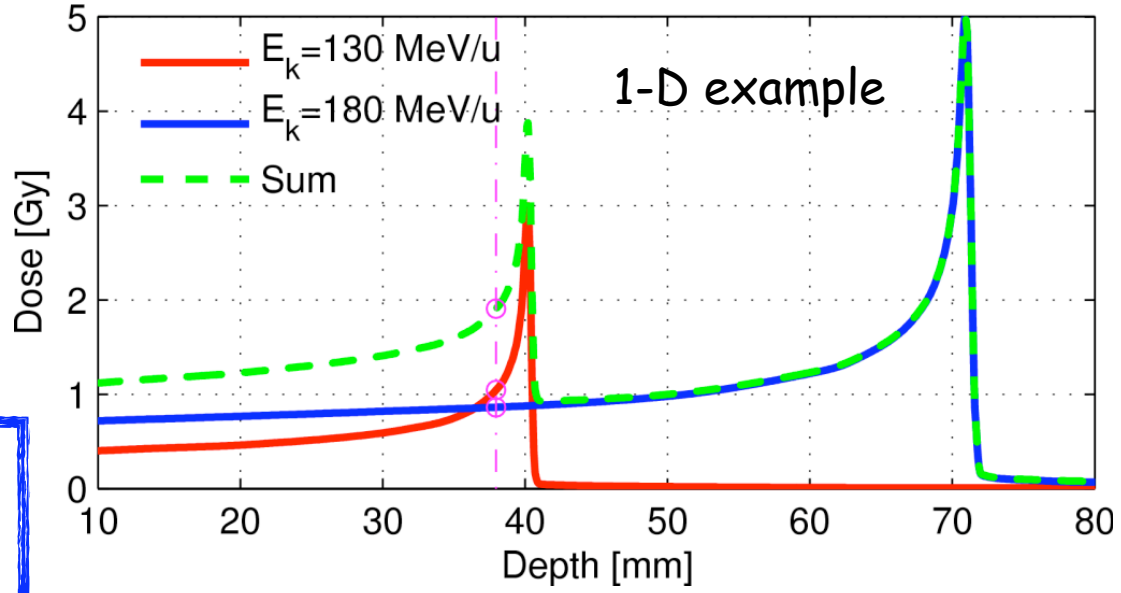
sum is extended to all interested voxels (m_T e OAR) and D_i^b represents the biological dose given to voxel i-th

Several beams contribute to the same voxel:

$$X^2 = \sum_{i \in V}^{cond} [RBE_i * \sum_l (d_i^l * f_l) - D_T]^2$$

- d_i^l is the dose released from l-th beam
- f_l is the fluence (to be determined) of the l-th beam
- RBE_i is the radiobiological effectiveness on the i-th voxel averaged on all the beams delivering dose on the i-th voxel

Dose Cost function is converted into Survival Cost function using LEM

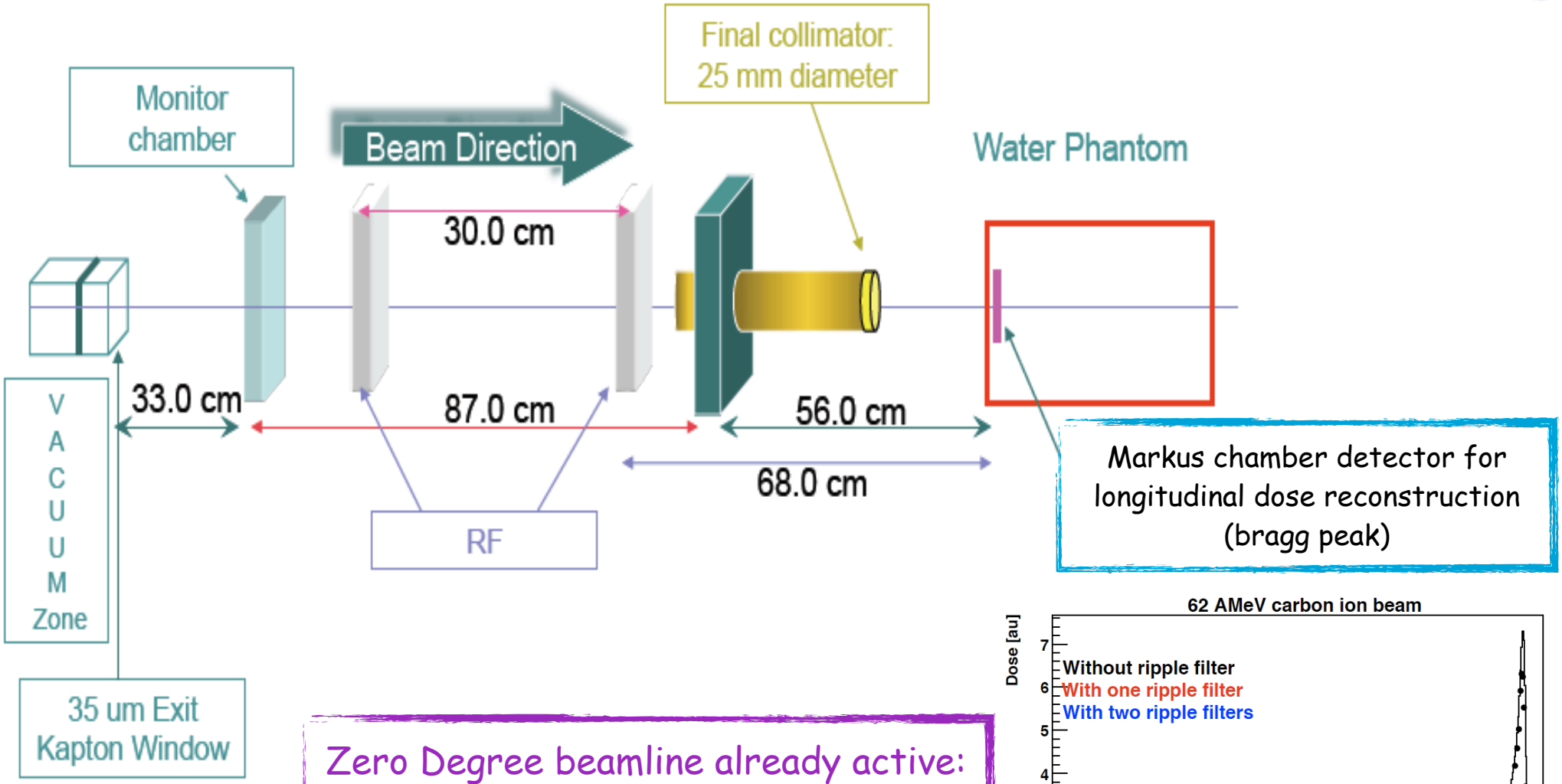


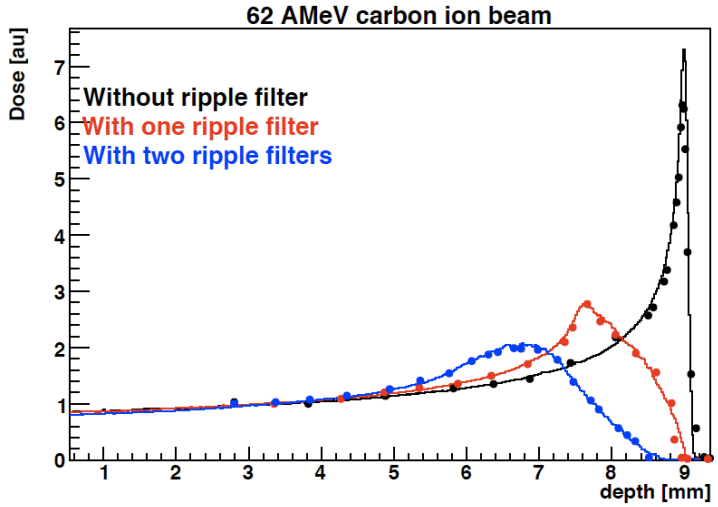
The Experimental Radiobiology Task

2 main directions:

- Characterization of therapeutic beams:
  - Study of Survival-Dose correlation in water phantoms
  - Definition of RBE = RBE(x,y) i.e. lateral distr. of RBE
  - Measurement using tissue-like phantoms
  - …
- Production of data for TPS validation and to produce the RBE database to build the TPS itself (for instance the set of α and β which are used as parameters in LEM)
  - LEM validation and integration by means of the widest possible set of experimental data: survival curves for different tissues and cellular lines (both normal and tumoral ones)
  - Use of human cells together with a cellular type considered as a reference biological system.
  - Comparison with results from other hadron therapy centers in the world
  - Study of different end-points such as chromosomic alteration, apoptosis induction, etc.
  - Integration of studies of short and long term effects on non-tumoral tissues
  - ….

LNS "Zero-Degree" beamline





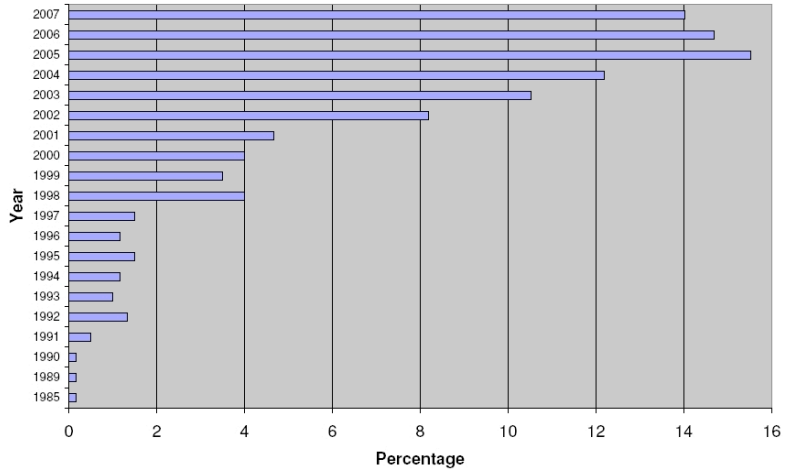
Zero Degree beamline already active:
Bragg peaks for 62 MeV/u Carbon ion beam in different conditions

The MC task

The Monte Carlo task

- MC can be used to
  - Take into account the real composition of human body, going beyond the "water equivalent" approximation
  - Automatically describe the complexity of mixed radiation field
  - Account for 3-Dim spread
  - Treat Complex/Difficult geometries
  - Follow in detail all physics interactions
  - Provide the basic transport and fragmentation data for treatment optimization

In the period 2000-2007 there has been an exponential growth of the MCTP related papers (source: ISI Web Science)

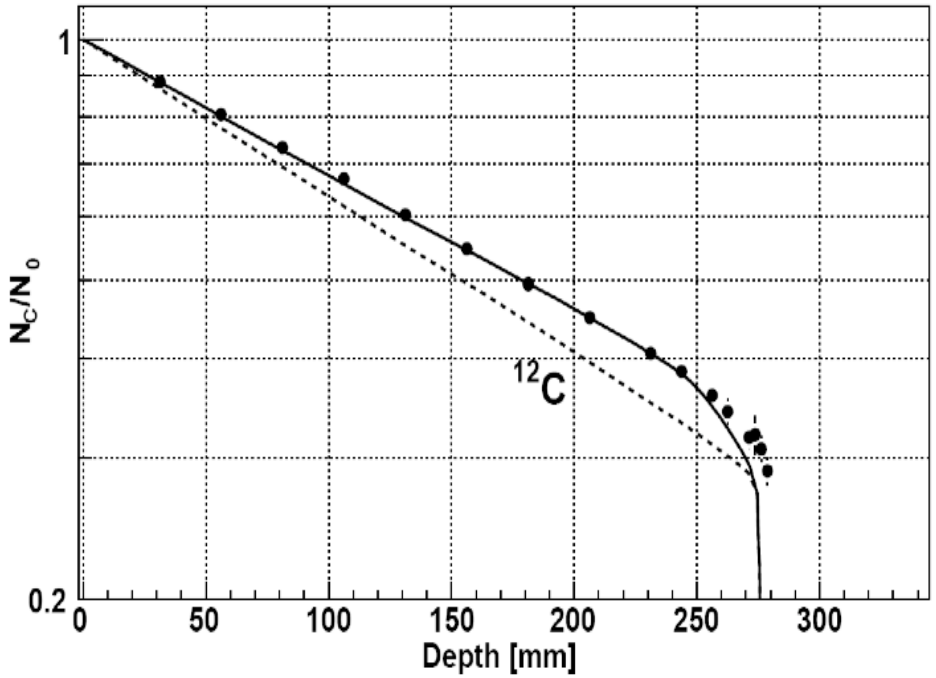


- Lot of products on the market:
  - EGS4, EGSnrc, ETRAN, PENELOPE, MCNP, VMCpro, ISTAR, MCNPX
  - Geant4 , PHITS, FLUKA : general purpose, transport any particle from photon to heavy ion ➔ suitable for ^{12}C beam
- FLUKA (INFN-CERN property) is the baseline choice for this project (http://www.fluka.org)

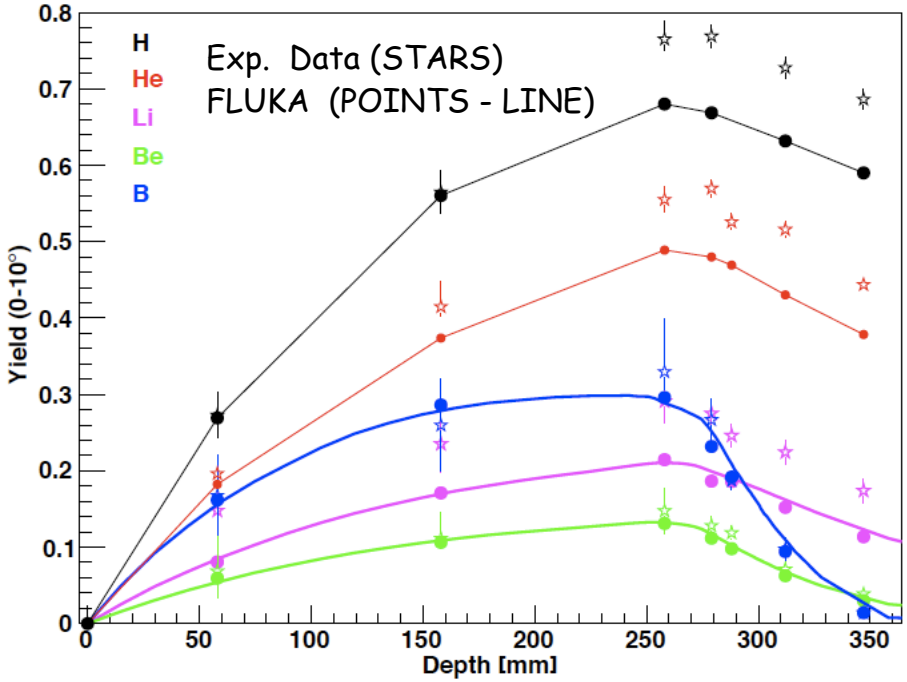
Mixed Radiation Field in ^{12}C Ion Therapy

- FLUKA benchmark against thick target experimental data

Attenuation of primary beam



Build-up of secondary fragments



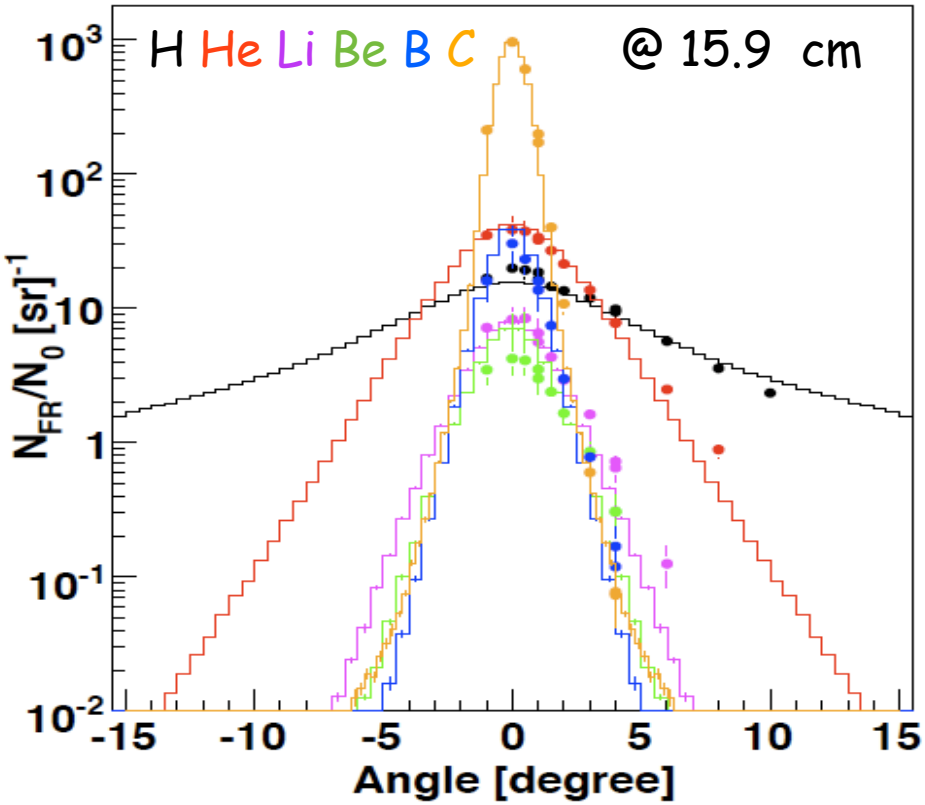
^{12}C (400 MeV/u) on water

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

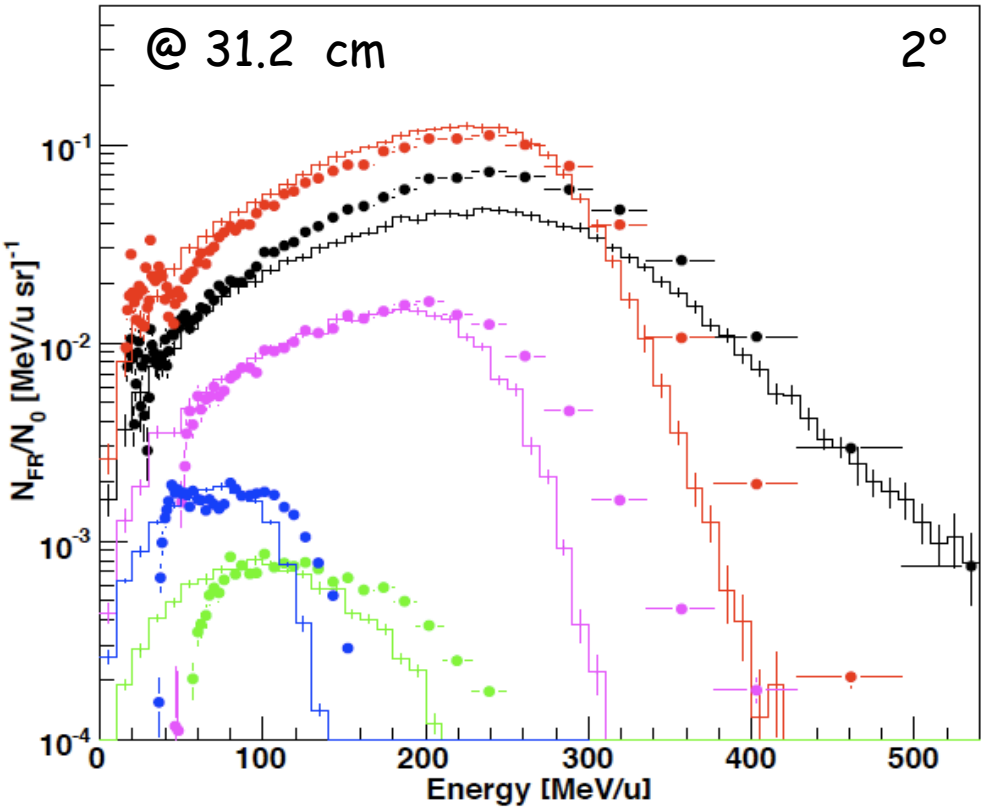
Mixed Radiation Field in ^{12}C Ion Therapy

- FLUKA benchmark against thick target experimental data

Angular distribution



Energy distribution



^{12}C (400 MeV/u) on water

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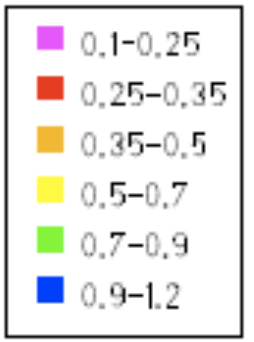
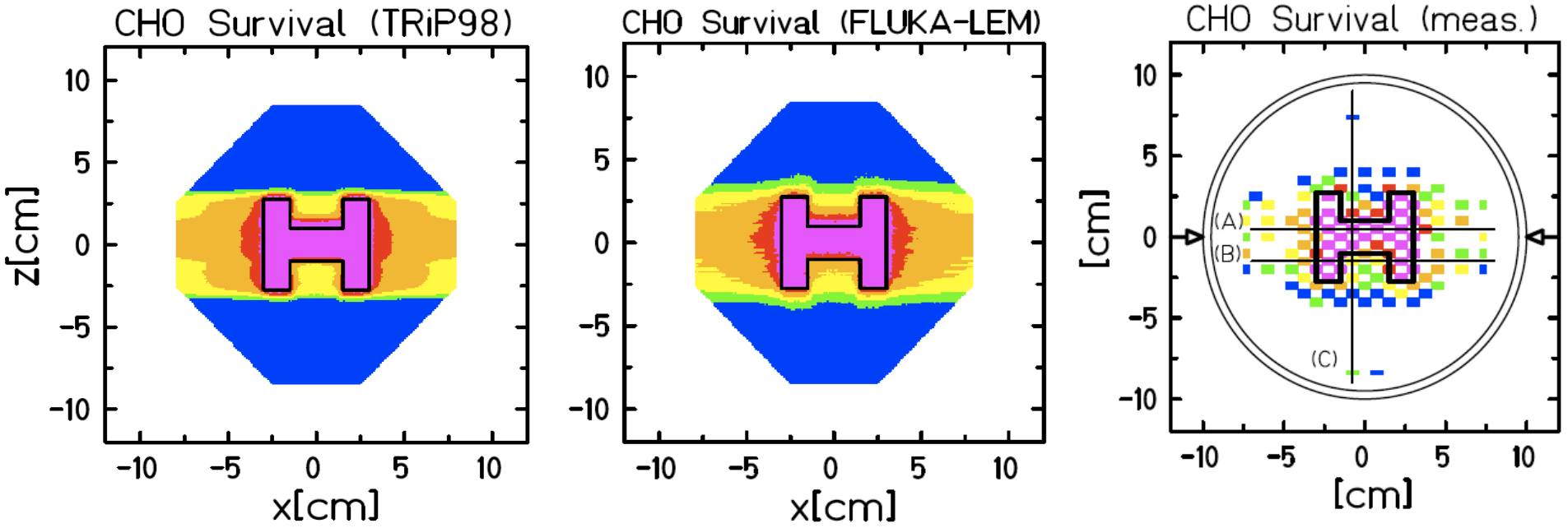
LEM FLUKA interface

Comparison with analytical calculations and exp data

- Two opposing dose ramps with tissue sparing (as brain-stem)
- TRiP98 Analytical calculations: biological planning and optimization for CHO cells
- FLUKA-LEM: forward calculation of the optimized plan



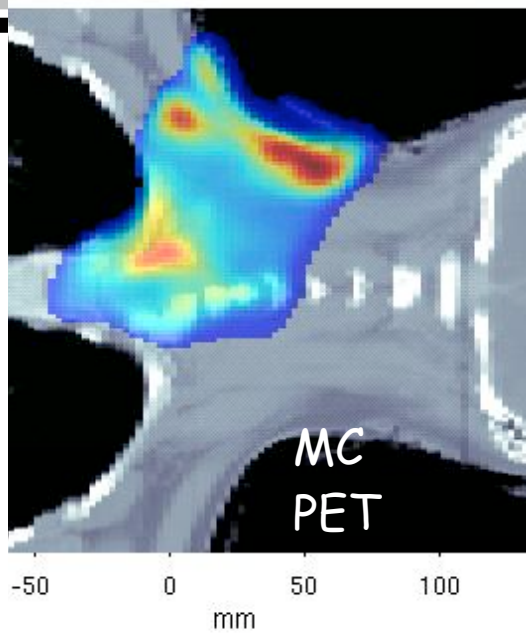


Exp. Data and analytical calculations: Krämer et al, PMB 48 (2003) 2063

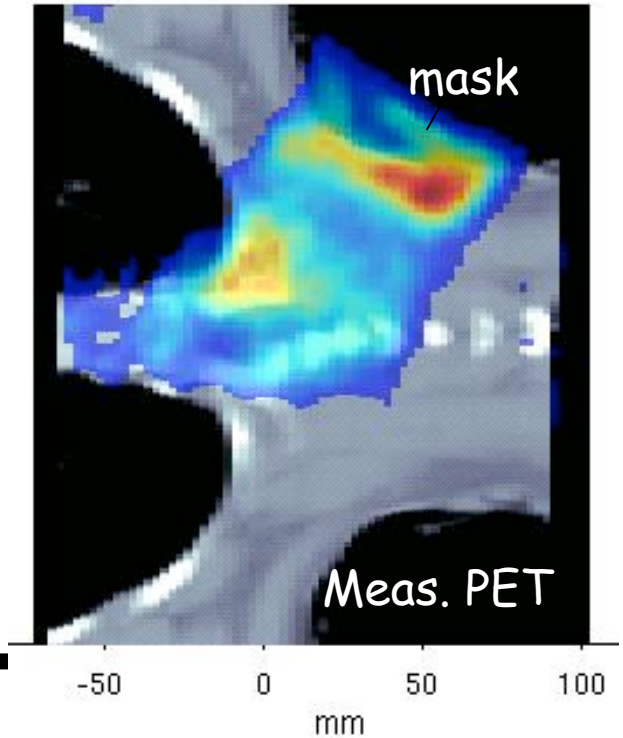
Activity prediction and PET monitoring

T-spine Chondrosarcoma proton therapy
K. Parodi et al., PMB52, 3368 (2007)

Predict the distribution of β^+ emitters for on line PET tomography



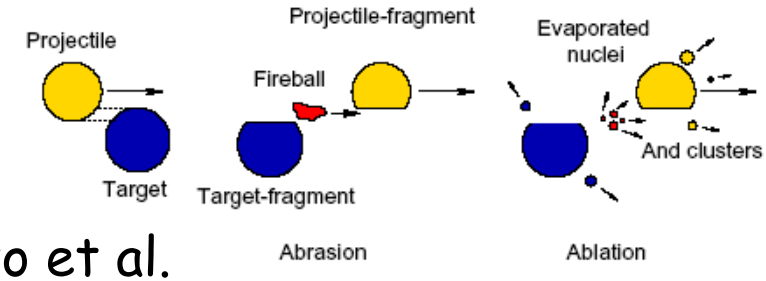
- The distribution of β^+ emitters can be predicted by FLUKA and used for online PET development
- PET in beam is an almost unique tool to verify on line ("in vivo") the release of dose.
  - Protons:
    - $p + {}^{16}O$, $(p,n) + {}^{15}O$ [$\tau^{15}O$=121.8 s]; $p + {}^{12}C$, $(p,n) + {}^{11}C$ [$\tau^{11}C$ =1222.8 s]
  - Carbon:
    - ${}^{12}C + p$, ${}^{11}C + (p,n)$; ${}^{12}C + p$, ${}^{10}C + (p,2n)$ [$\tau^{10}C$ =19.3 s]
- The difference in β^+-activation processes and the dominant mechanism of energy deposition, the activity registered by the PET image is not directly proportional to the delivered dose. A proper unfolding algorithm (from exp. data) must be used.



The nuclear physiscs task

Fragmentation: exp. status

- Carbon ions in radiation therapy undergo fragmentations inside the patient body
- Thick target
  - HIMAC by Kurosawa et al.
  - BEVALAC by Schimmerling et al.
  - BEVALAC by Heilbronn et al.
  - etc etc
- Thin target
  - RIKEN by Sato et al.
  - HIMAC Iwata et al.
  - HIMAC Heilbronn et al.



A lot of integral measurements measurements are already around..

but not wrt angle and energy: only with detectors at 0°!

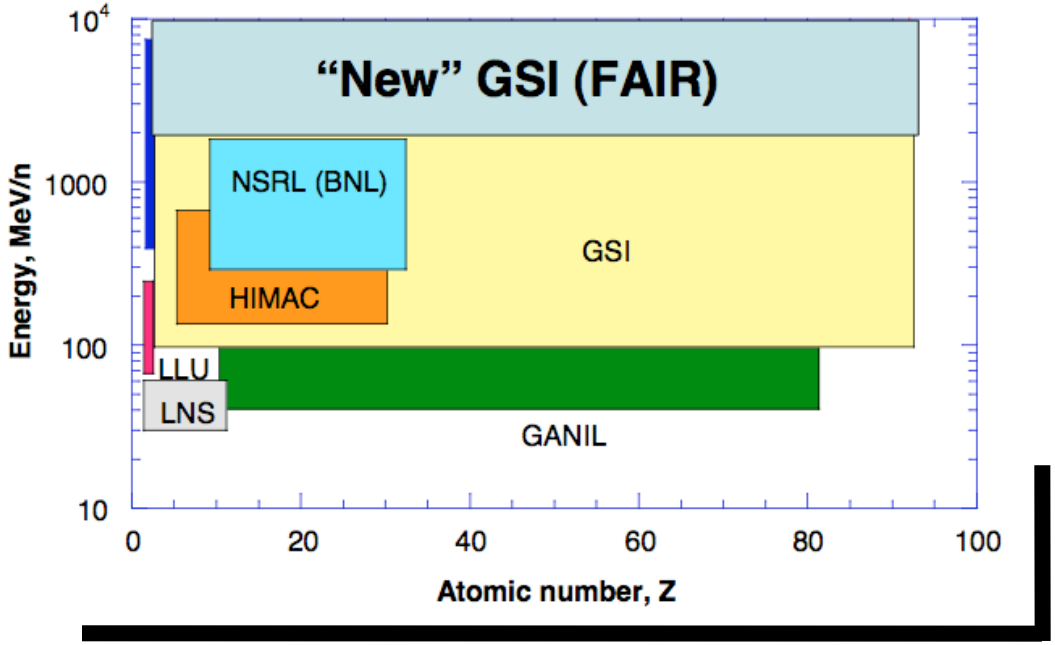
- Ion fragmentation measurements (mainly ^{12}C):
  - Up to now there is a lack of data systematic in literature of ^{12}C projectile fragmentation cross sections measurements **at intermediate energies**, that is around **20 MeV/A ≤ E/A ≤ 250 MeV/A, range of high interest for hadrontherapy**. ➔ Decided to go for a new experiment: FIRST

The FIRST experiment

- Target: Double differential cross section (with respect to the emission q and E) for each of the produced fragments in C-C, C-Au (Fe-C, Fe-Si, O-C) interaction, with 3% accuracy.
- At GSI there are the proper beam and a previous setup that has been designed for a similar (but not the same) physics. We will improve, adapt and optimize the ALADIN experimental setup for our goal
- 27 Feb. 2009: approval by G-PAC for C-C: beam in early 2011, 33 shifts

Requested Beam Time

Control of setup: 1 day per period of beam	
C+C @ 0.2, 0.4 and 1.0 AGeV	6 days
C+Au @ 0.2, 0.4	4 days
O+C @ 0.2, 0.4	4 days
Fe+Si @ 0.5 and 1.0 AGeV	4 days
Fe+C @ 1.0 AGeV	2 days
Calibration	2 days



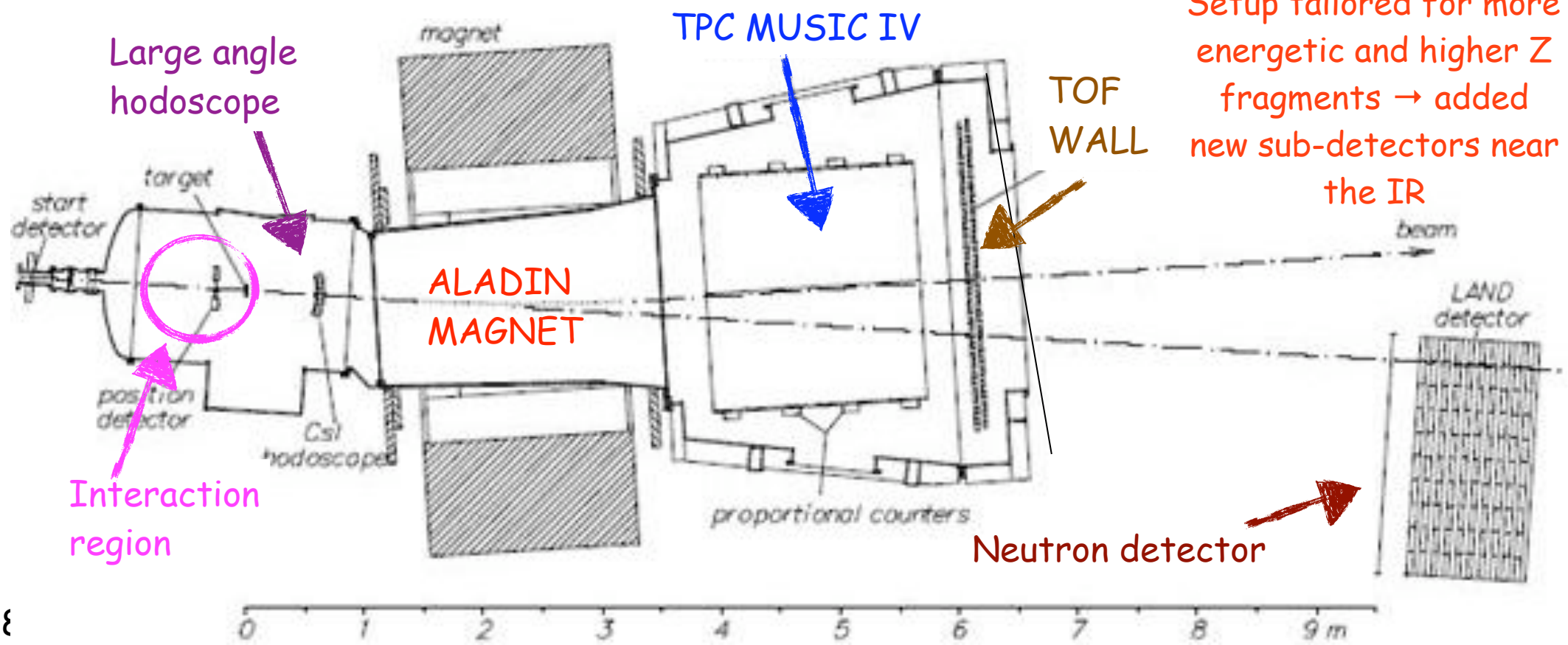
The FIRST collaboration

FIRST stands for: Fragmentation of Ions Relevants for Space and Therapy S371 is the GSI label for us

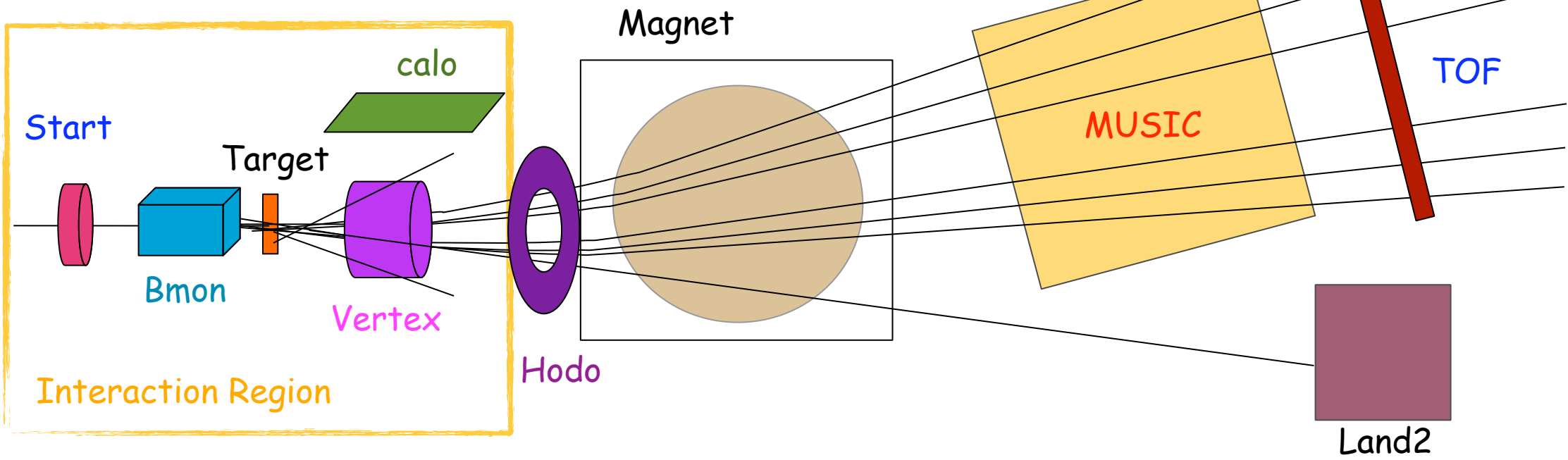
- INFN: (Cagliari?), LNF, LNS, Milano, Roma2, Torino: G.Cuttone, C.Agodi, G.Battistoni, G.A.P.Cirrone, M.De Napoli, E.Iarocci, A.Mairani, V.Monaco, M.C.Morone, A.Paoloni, V.Patera, G.Raciti, E.Rapisarda, F.Romano, R.Sacchi, P.Sala, A.Sarti, A.Sciubba, C.Sfienti, E. Spiriti
- DSM/IRFU/SPhN CEA Saclay, IN2P3 Caen, Strasbourg, Lyon: S.Leray, M.D.Salsac, A.Boudard, J.E. Ducret, M. Labalme, F. Haas, C.Ray
- GSI: M.Durante, D.Schardt, R.Pleskac, T.Aumann, C.Scheidenberger, A.Kelic,M.V.Ricciardi, K.Boretzky,M.Heil,H.Simon, M.Winkler
- ESA: P.Nieminem, G.Santin
- T.Bohlen

Detector requirements

- On an event by event basis, the FIRST experiment 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
- Starting from scratch: VERY expensive (several M€), LONG time and a VERY LARGE group to design and build it.



Who measures what...?



- MUSIC → Z/p, Θ, ϕ after bending
- MUSIC → Energy loss $\mu (Z/\beta)^2$
- Hodo → Large angle fragment E, Θ, ϕ
- Vertex → Fragments emission Θ, ϕ
- Start, TOF wall → TOF= L(p,Z,Θ,ϕ)/β
- Bmon → Beam impact point

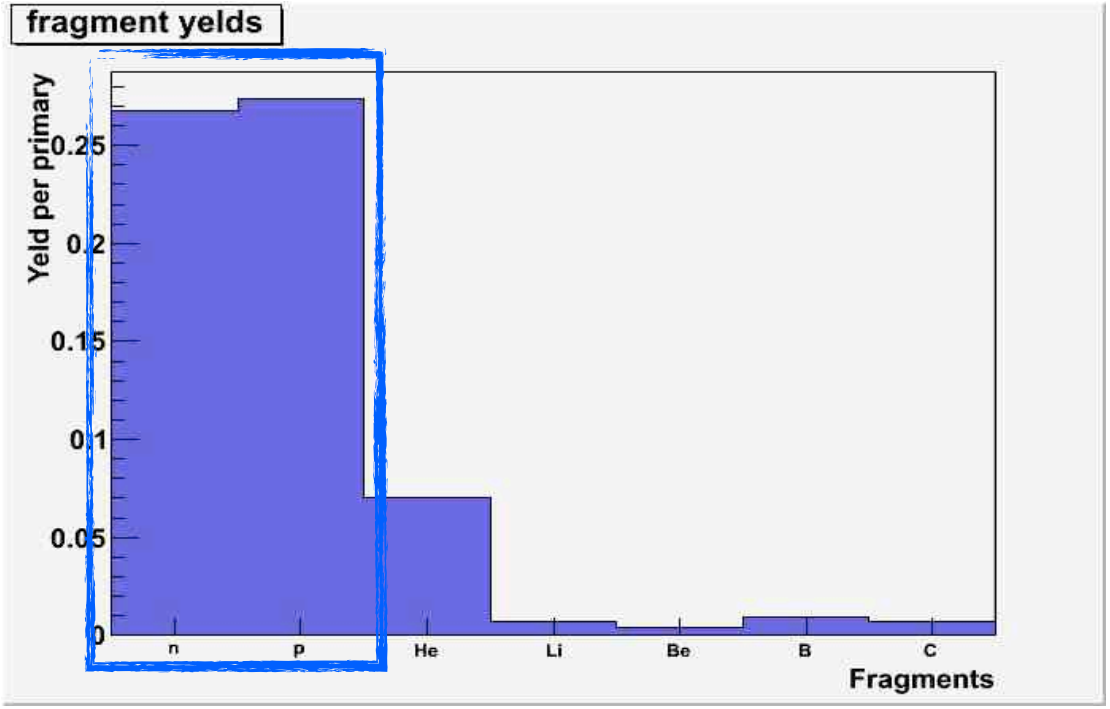
To extract Z, A, Θ_{emiss}, p_{emiss} the reconstruction must exploit all the setup information

CALO → Large angle p

LAND2 → neutron flux

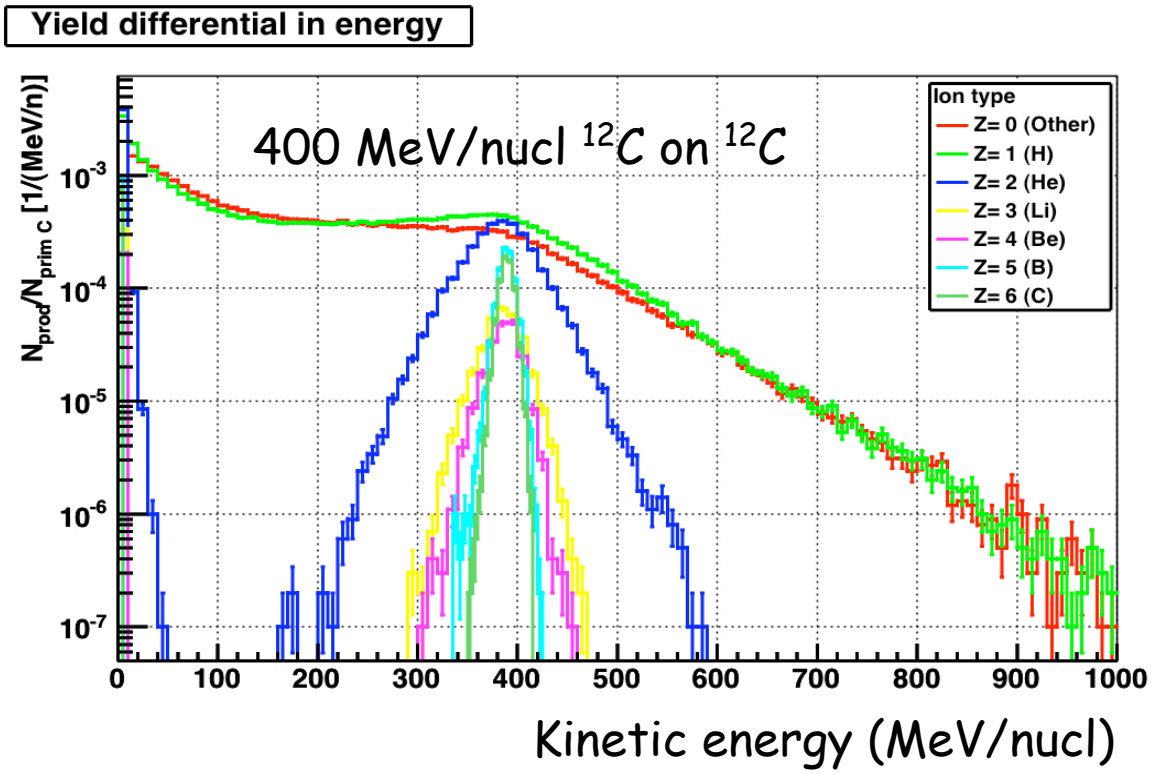
What we expect: MC studies

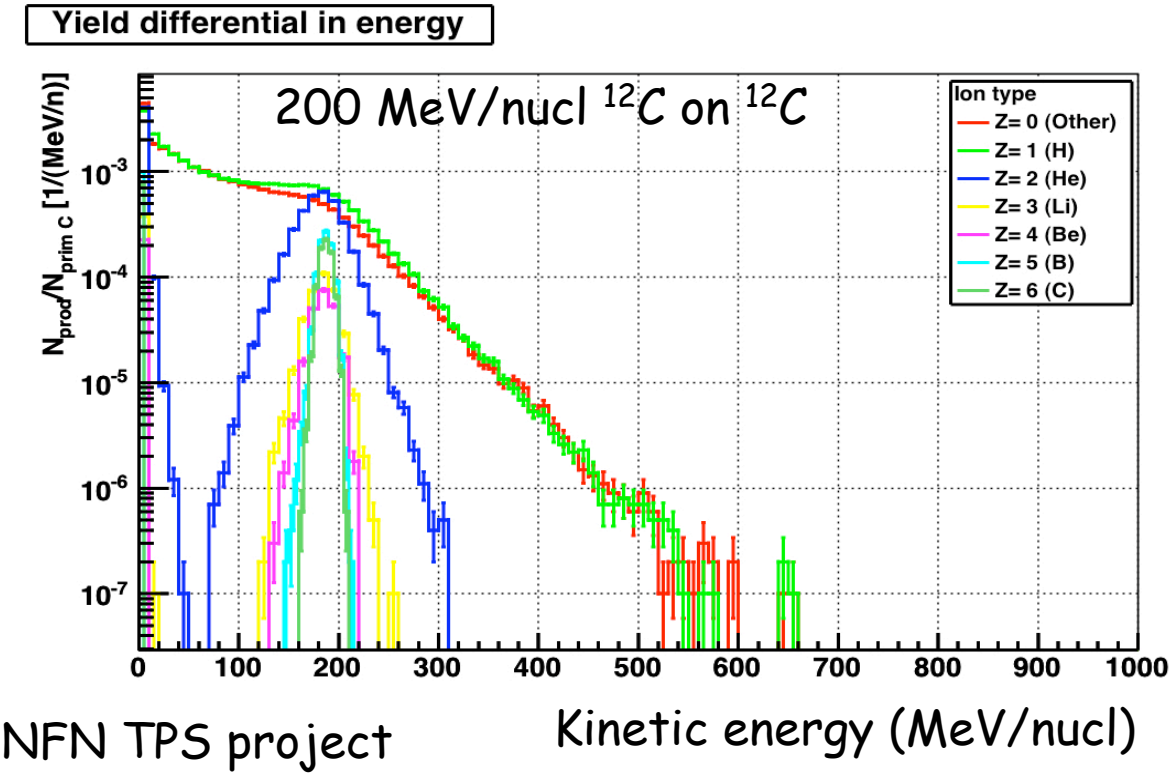
- FLUKA used as benchmark MC for our studies. The MC distribution can be used as "rule of thumb" indicator useful mostly to optimize the detector for critical items
- Simulated the interaction of a 400 MeV/nucl Carbon ion on a 5mm thick Carbon target. 5% of the primary carbons interact in the target
- The fragment production are dominated by Protons and Neutrons. They are 1 order of magnitude more than the other fragments!!
- The events have small multiplicity (total ~ 13, charged ~ 8)



MC: fragment energy

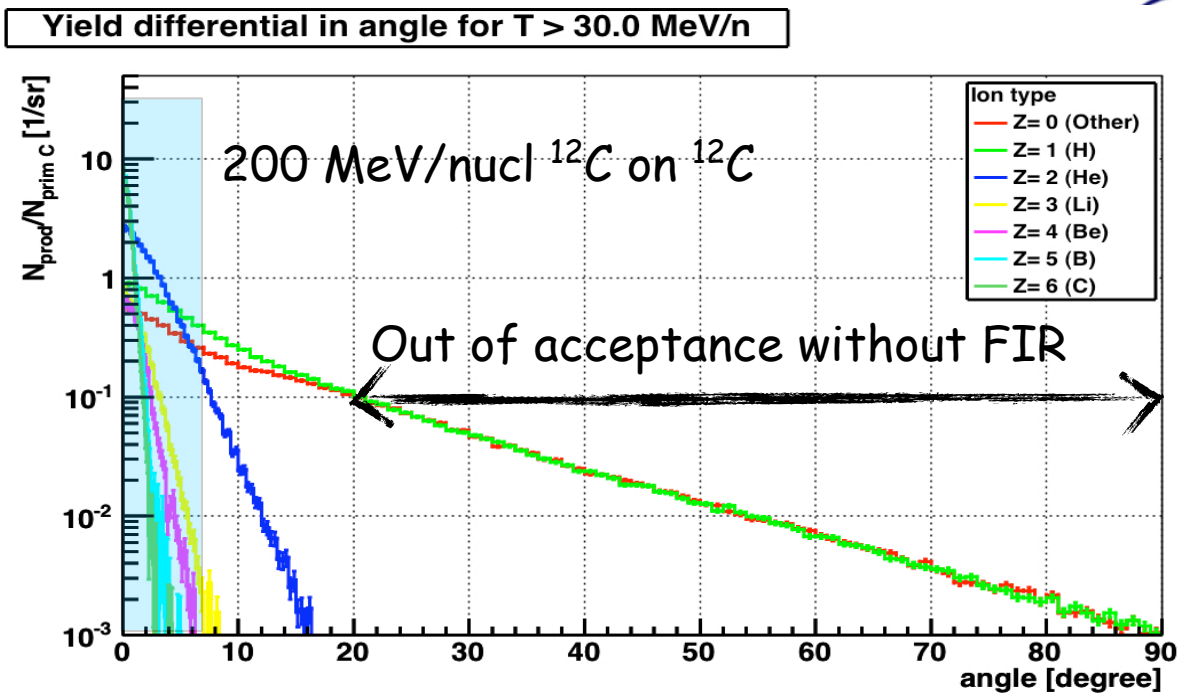
- The Z>2 produced fragments approximately have the same velocity of the C ion projectiles
- The proton have a very wide spectrum with 0<β<0.6
- The DE/DX released by the fragment spans from ~2 to ~100 m.i.p.

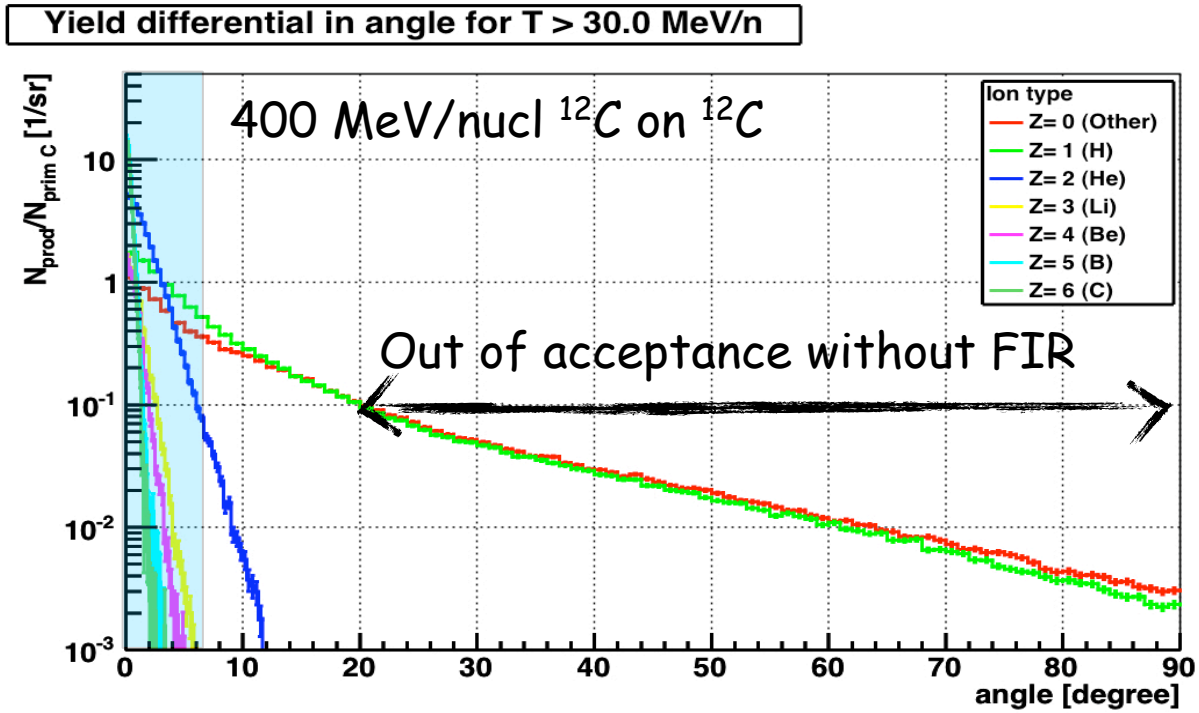




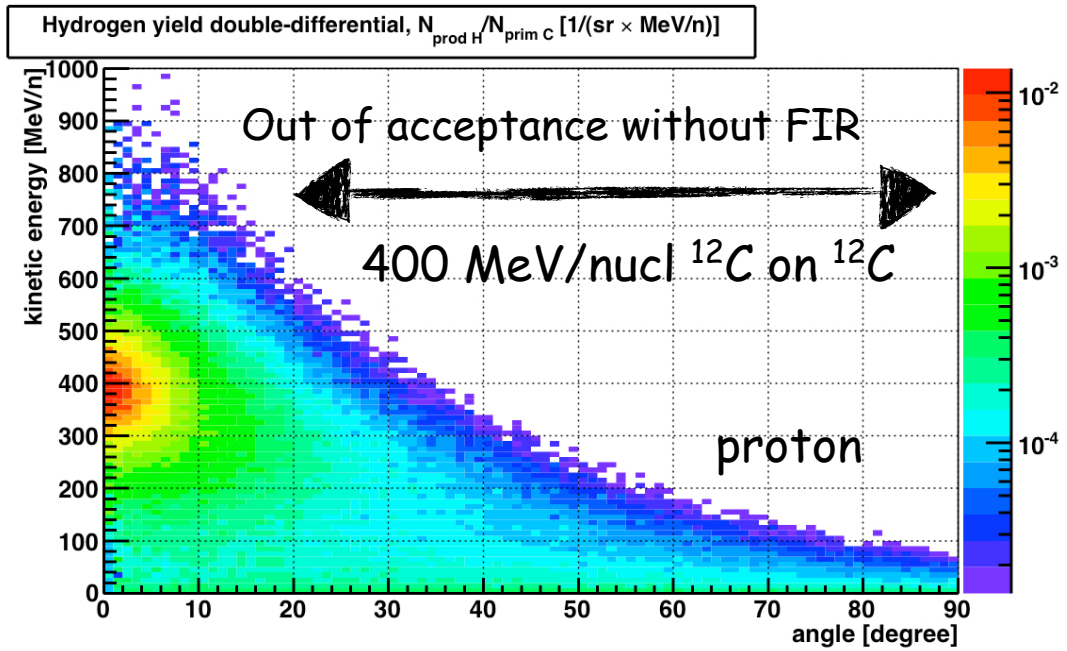
MC: Angular distributions

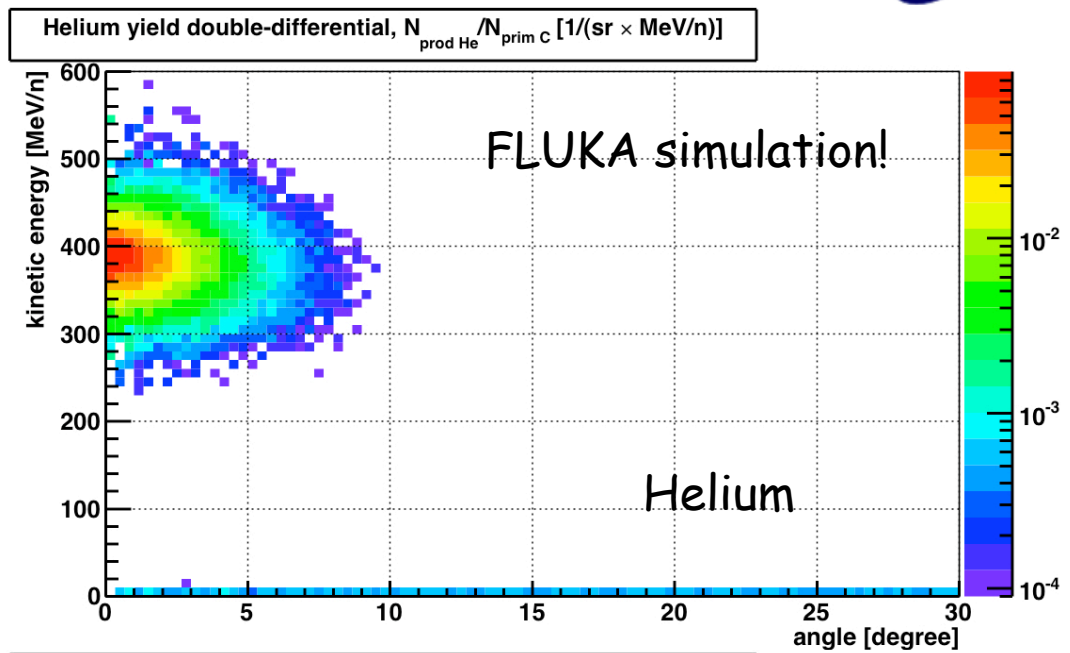
- The Z>2 fragment are well collimated in the angular acceptance of the ALADIN magnet
- The Z=2 fragment can be recovered by the Si Hodoscope
- The protons are emitted mostly at large angle, out of the acceptance of the existing setup → must be recovered by FIRST IR (FIR)

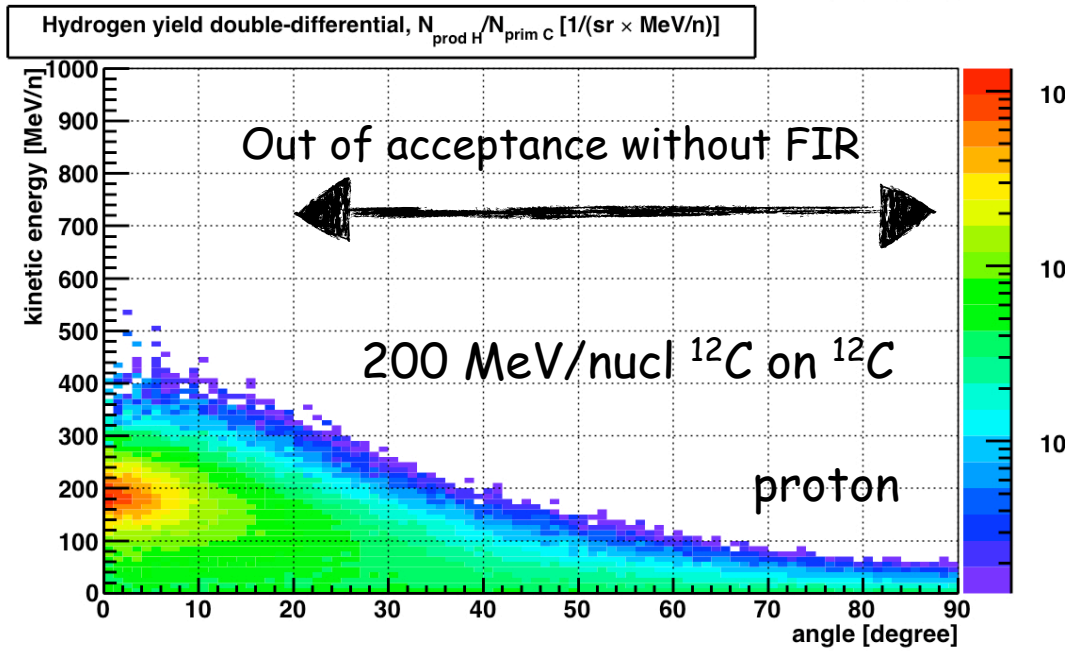


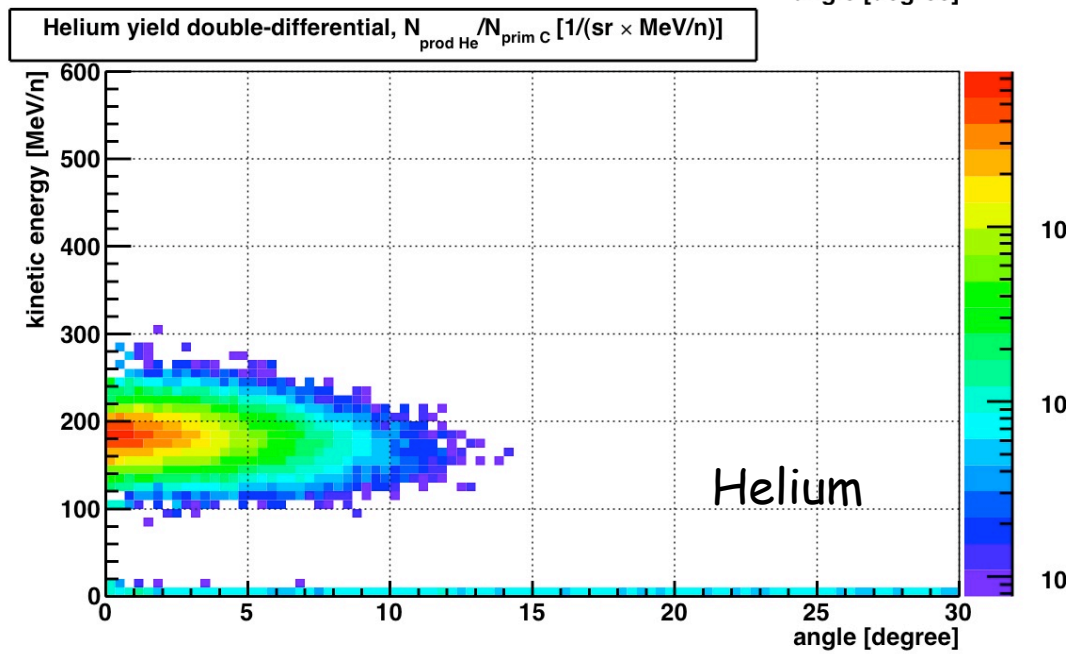


Produced p and He: angle vs energy

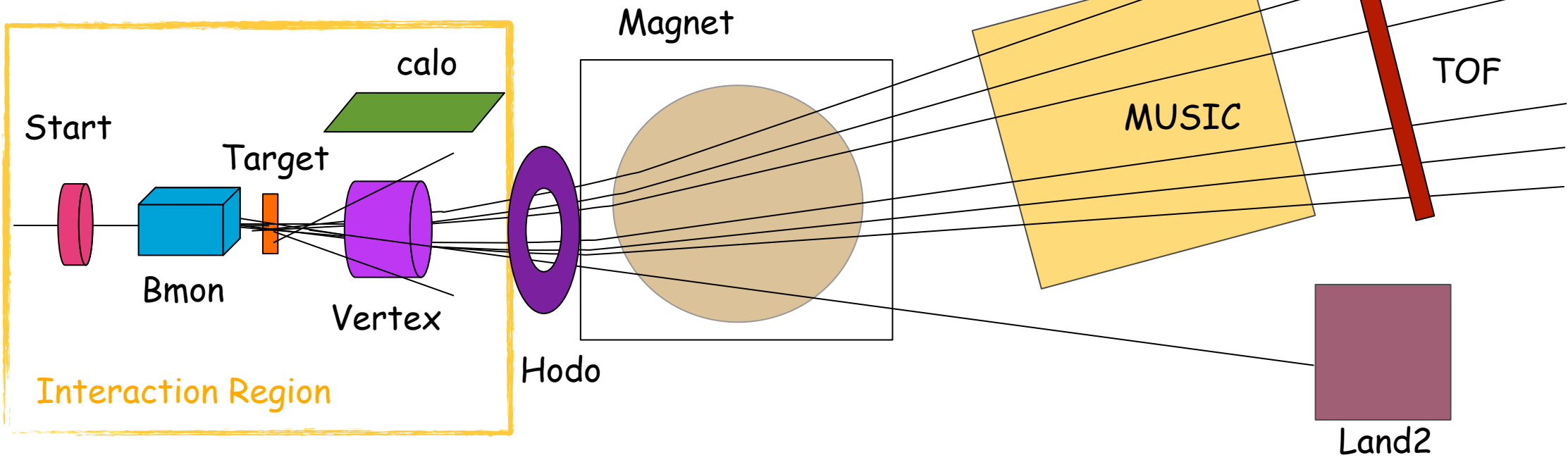








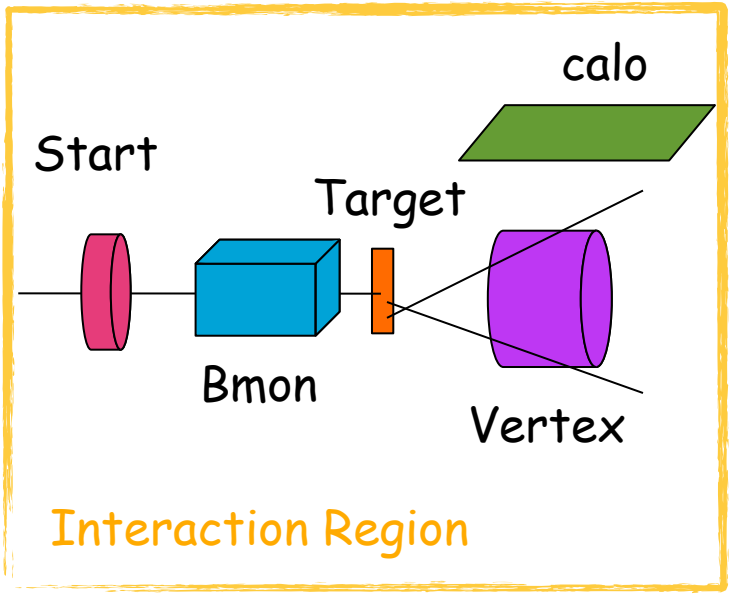
Some other boundary conditions



- Out of target interactions must be kept below % level wrt on target interactions.
- Trigger rate ≤ kHz due to pile-up in the MUSIC TPC (10% pile-up @4kHz)
- Maximum target thickness of 10 mm → maximum ~10% of interaction probability.
- The beam spot for Carbon projectiles can be ~ 3mm FWHM
- The geometric acceptance of the ALADIN magnet for the produced fragments is ~4° in Θ and ~9° in ϕ

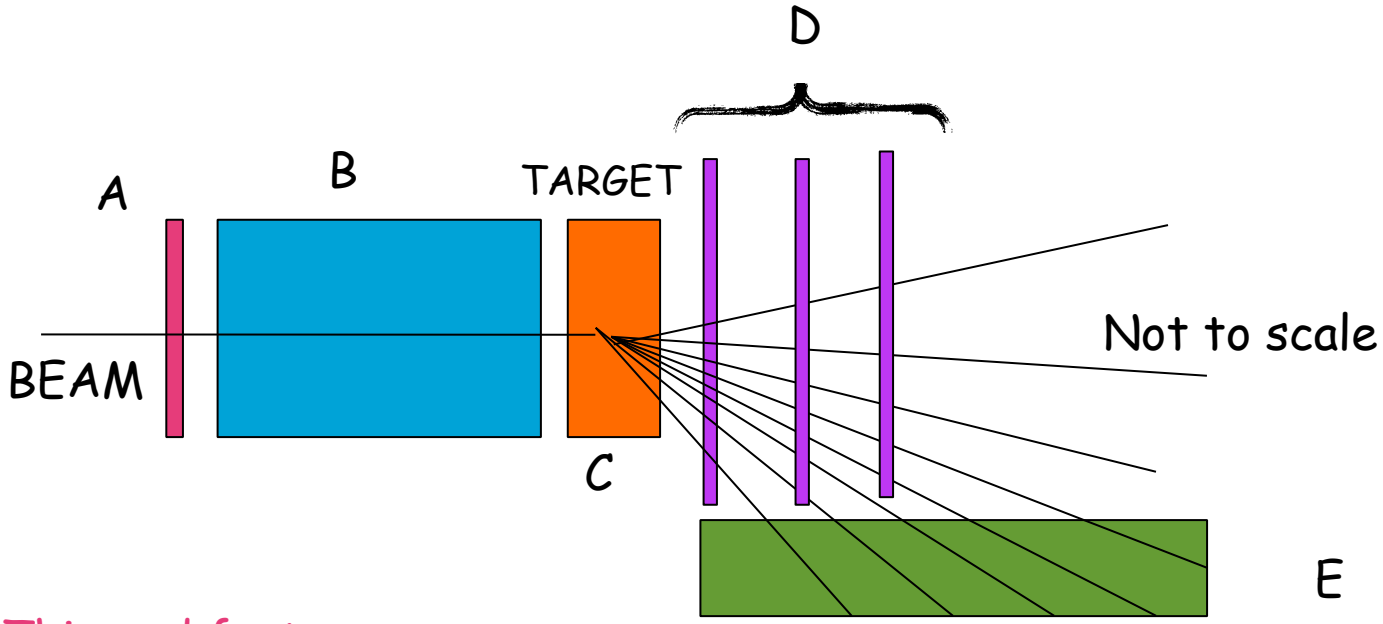
The Interaction Region

- Brand new component. All components must operate in vacuum and must have very limited material budget to reduce as much as possible the out of target interactions
- Gives the start to Time Of Flight measurement. Should match the stop (TOF WALL) time resolution (~200ps)



- Measures the beam direction & impact point on target event by event.
- House the target system. Remotely controlled system that embed different thin (~few mm) targets
- Tracks the fragments just downstream of the target.
- Detects the particle escaping from the magnet acceptance

FIRST target region



A) Start counter. Thin and fast scintillation detector. Gives the start to TOF measurement.

B) Beam monitor. Drift chamber that measures the beam impact point on target.

C) Target system. Remotely controlled system that embed different thin (~few mm) targets

D) Vertex Si telescope: tracks the fragments just downstream of the target. Measures the emission angle with the requested precision and detects out of target interactions

E) One arm Lead-fiber calorimeter covering wide θ angular region in a narrow φ range (yet to be approved)

The start counter

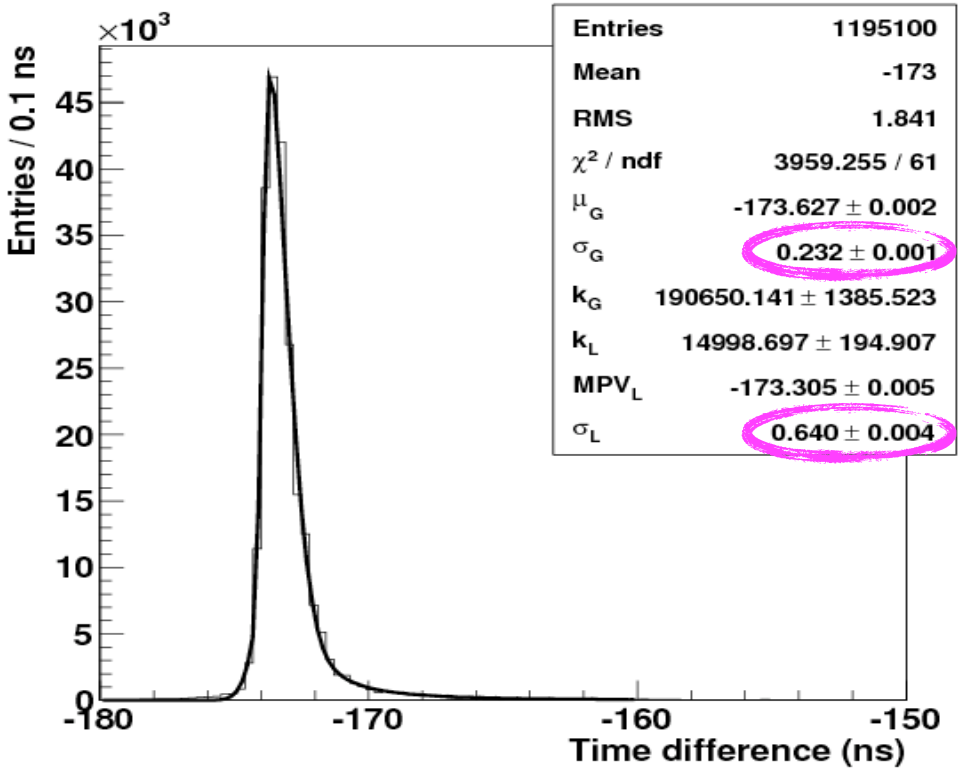
- Provides the START to the TOF measurement and to the TRIGGER. Plastic scintillator [100 μm EJ228 (Pilot U) 390 nm Scintillator] with peculiar features to fulfill the TOF requirements:
  - At most 200 μm thickness to avoid interactions (2-3% of the target thickness)
  - Must integrate enough light to have O(200-300ps) of time resolution. A ^{12}C @300 MeV releases in 200 μm as much as one mip in 5 mm, Birks saturation included.

Prototype with fiber readout built and tested @ 62MeV/nucl carbon beam in LNS. No cosmic, β sources or X sources can be used to test it in lab, only a particle

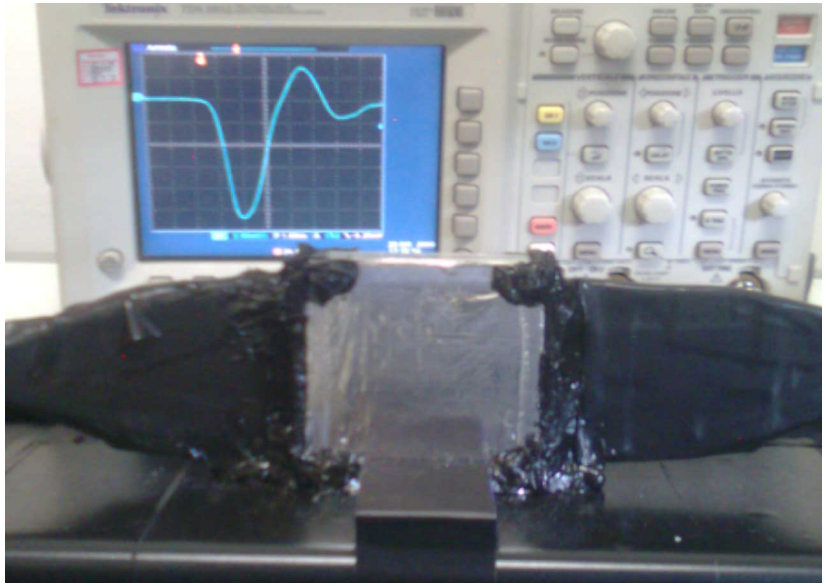
Readout using fast (~ 250ps/√(p.e.)) and high q.e. (~40%) brand new Hamamatsu photomultipliers H10721-210

Timing performances

- ~300 ps sigma with large tails → bad S/N (10 mV/5 mV r.m.s) due to grounding and small amplitude



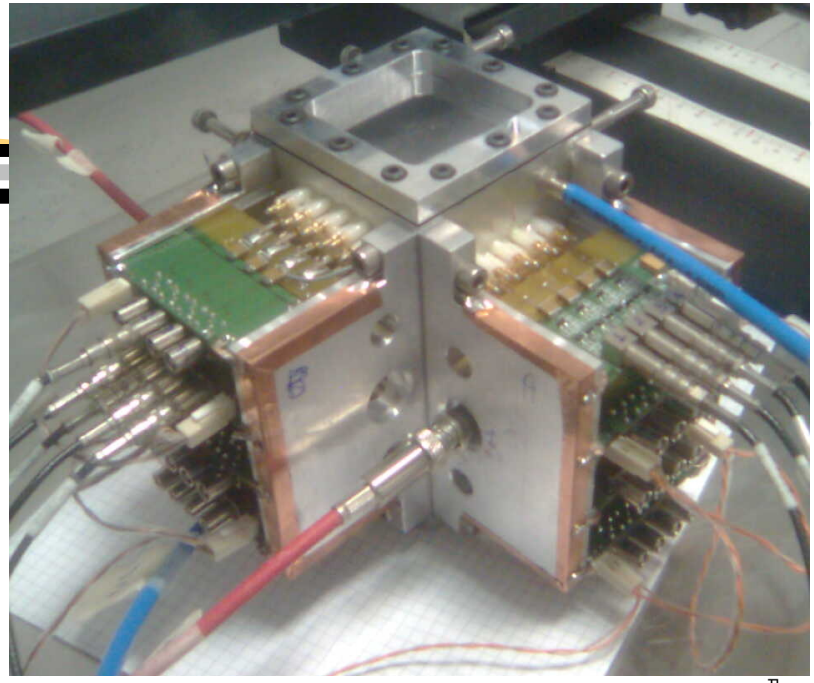
short signals: 5 mV vs 1 ns



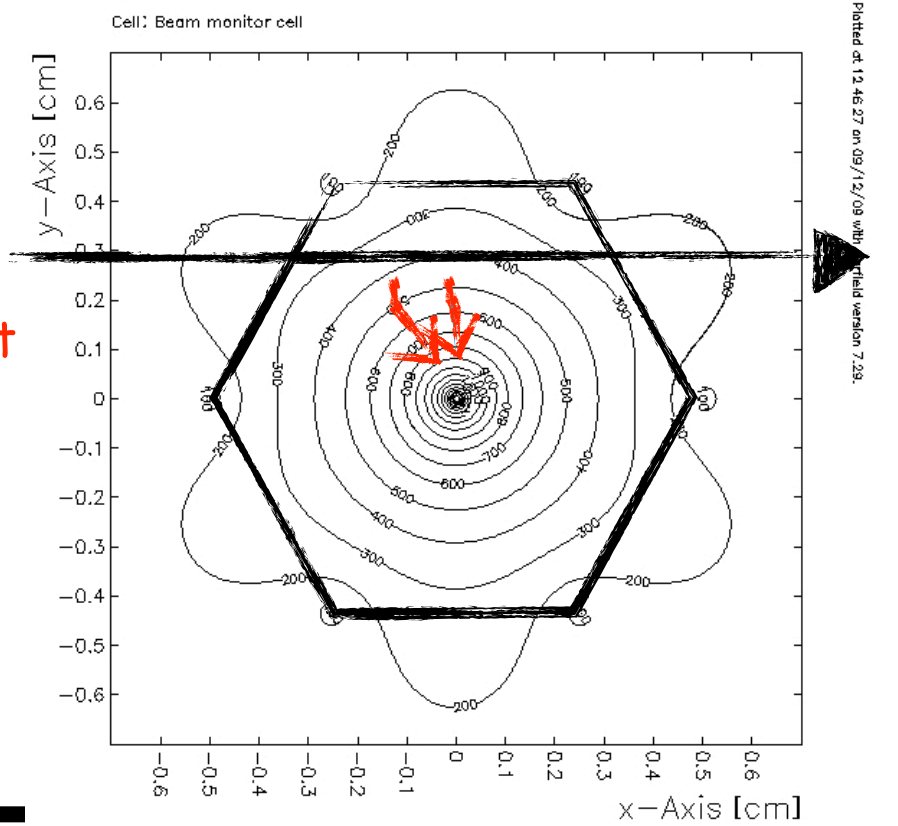
Ready for vacuum operation

Wrapped with thin aluminum-mylar envelope → 2 x 2,1μm aluminized mylar windows

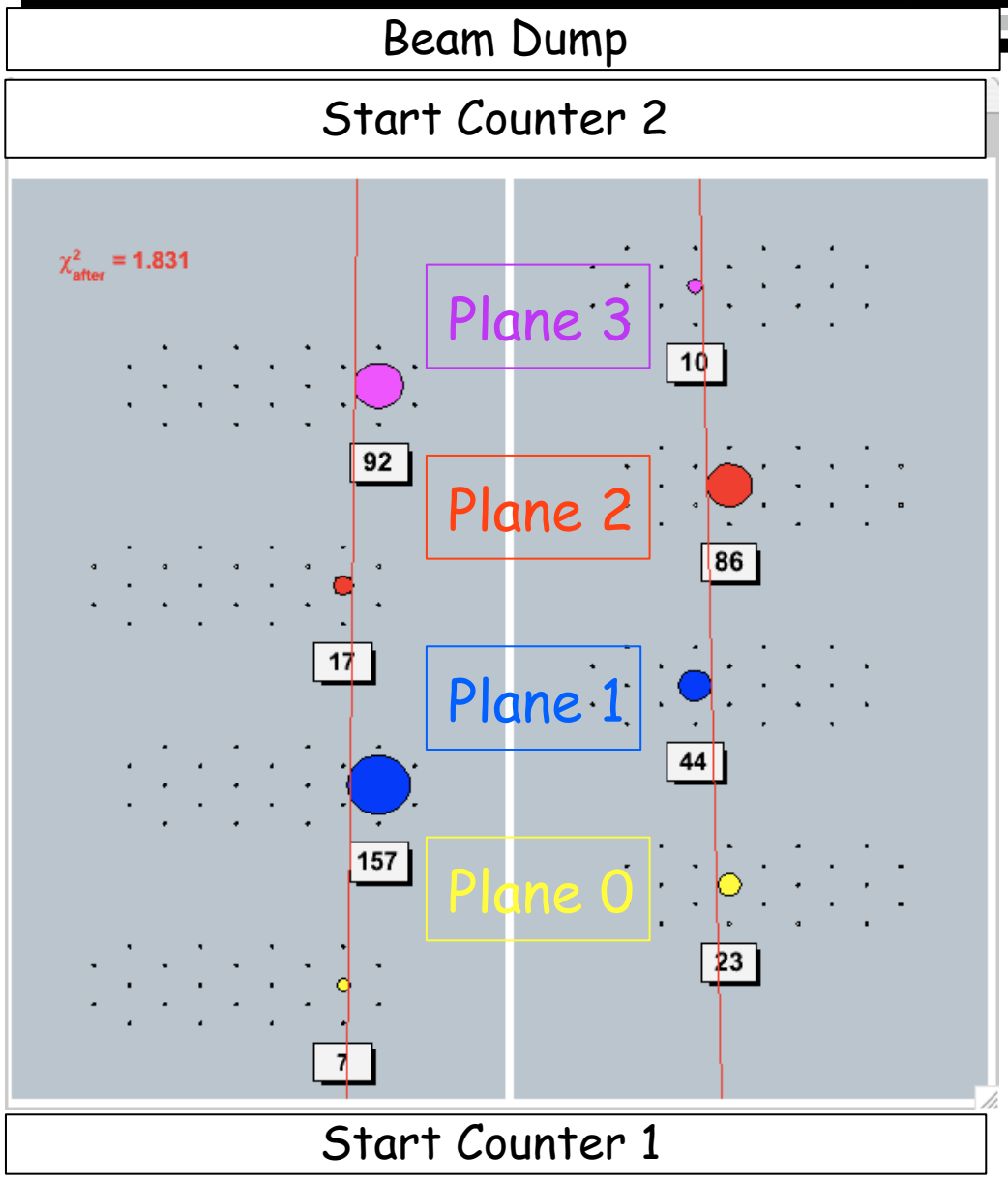
The Beam Monitor

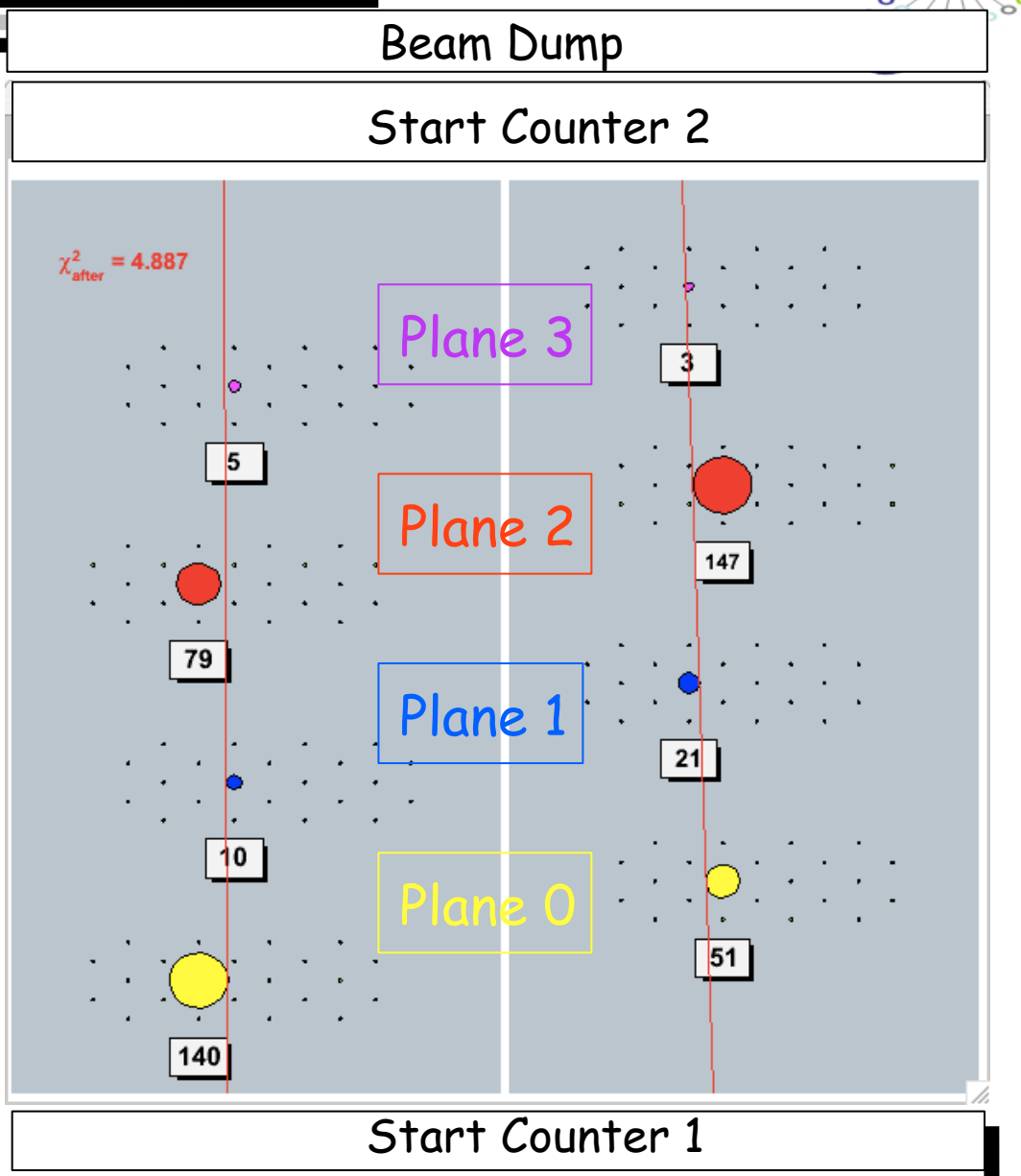


- Tracks the carbon beam. Gives the impact point on target and the primary carbon direction: crucial to spot out of target interaction and to recover events with double primary carbons.
- Tested at LNS 62MeV/nucl ^{12}C beam
  - Drift chamber with exgonal shape cells
  - 4 planes in the y and x direction
  - Wire thickeness: 90 μm field – 30 μm sense
  - O(100 μm) single hit resolution with mip ➔ O(100-50 μm) impact point resolution on target with ^{12}C
- Operation with carbon @ 300MeV/nucl ? Proportional vs quasi-proportional?
- Target mixture: P10 (AR-Ethane) but can operate both with Ar-CO_2 (safety!)



Beam Monitor @ 62MeV/nucl ^{12}C beam

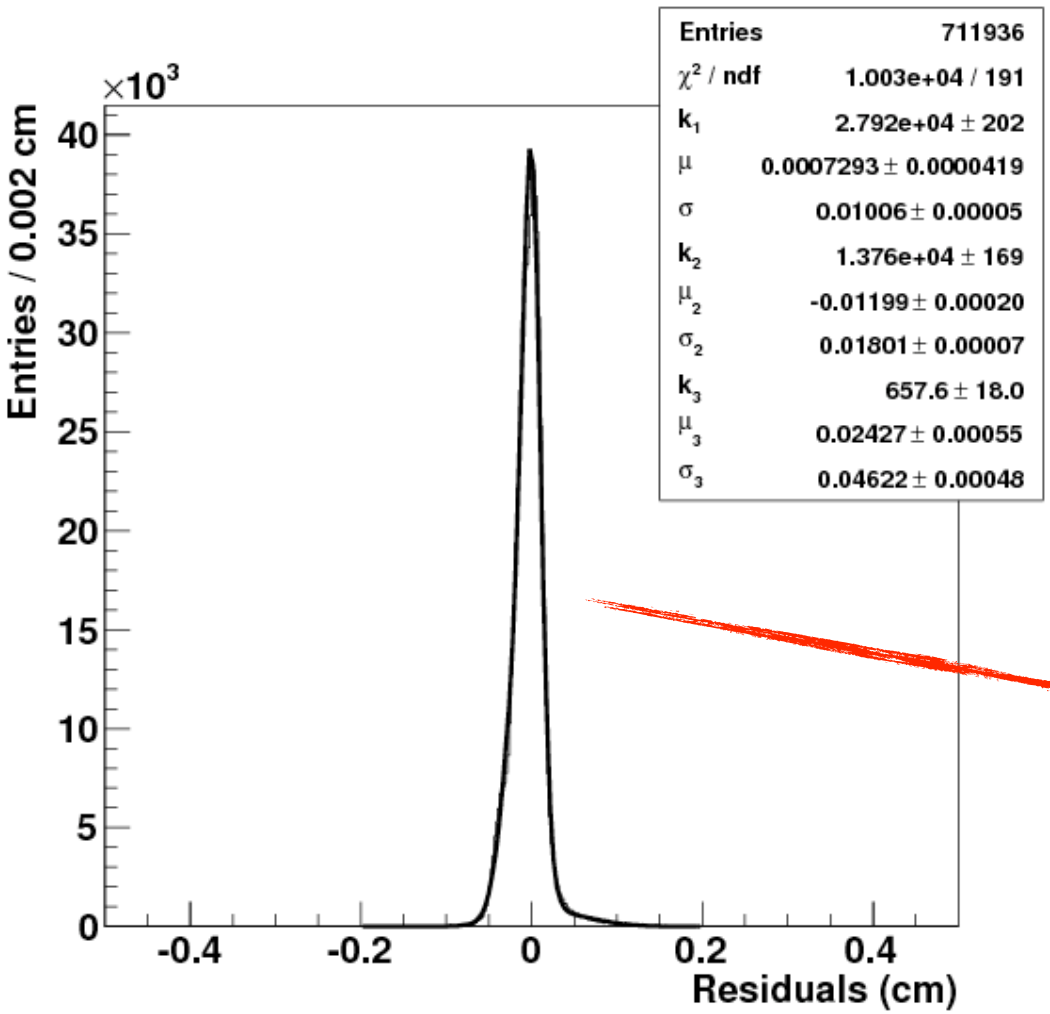


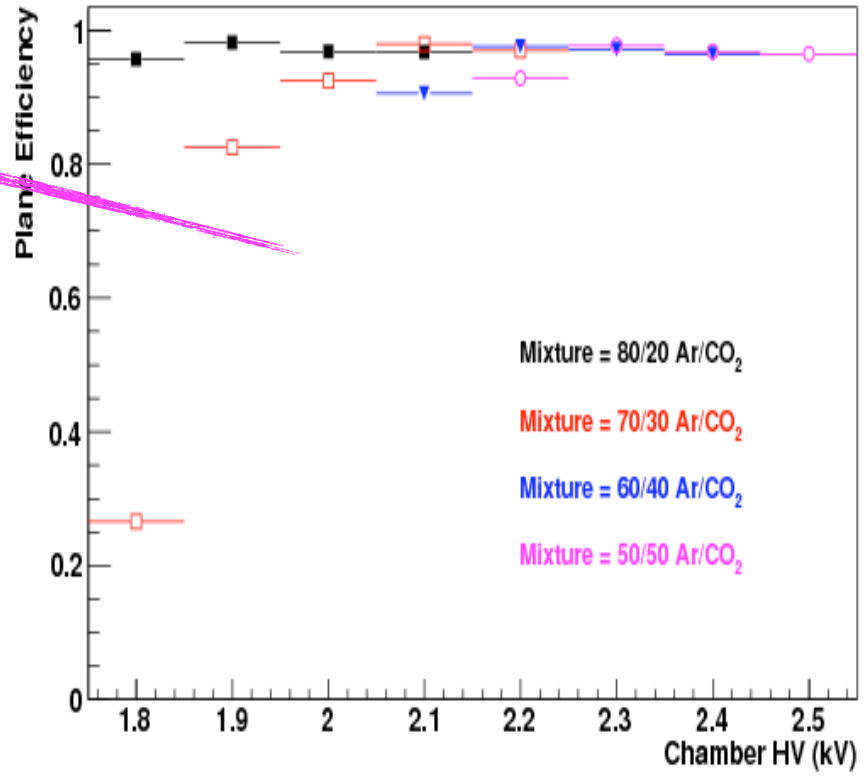


B.M. Resolution & Efficiency

preliminary

Fair efficiency (~ 95-96%) obtained with A CO_2 mixture. P10 mixture (default for exp.) should be even better





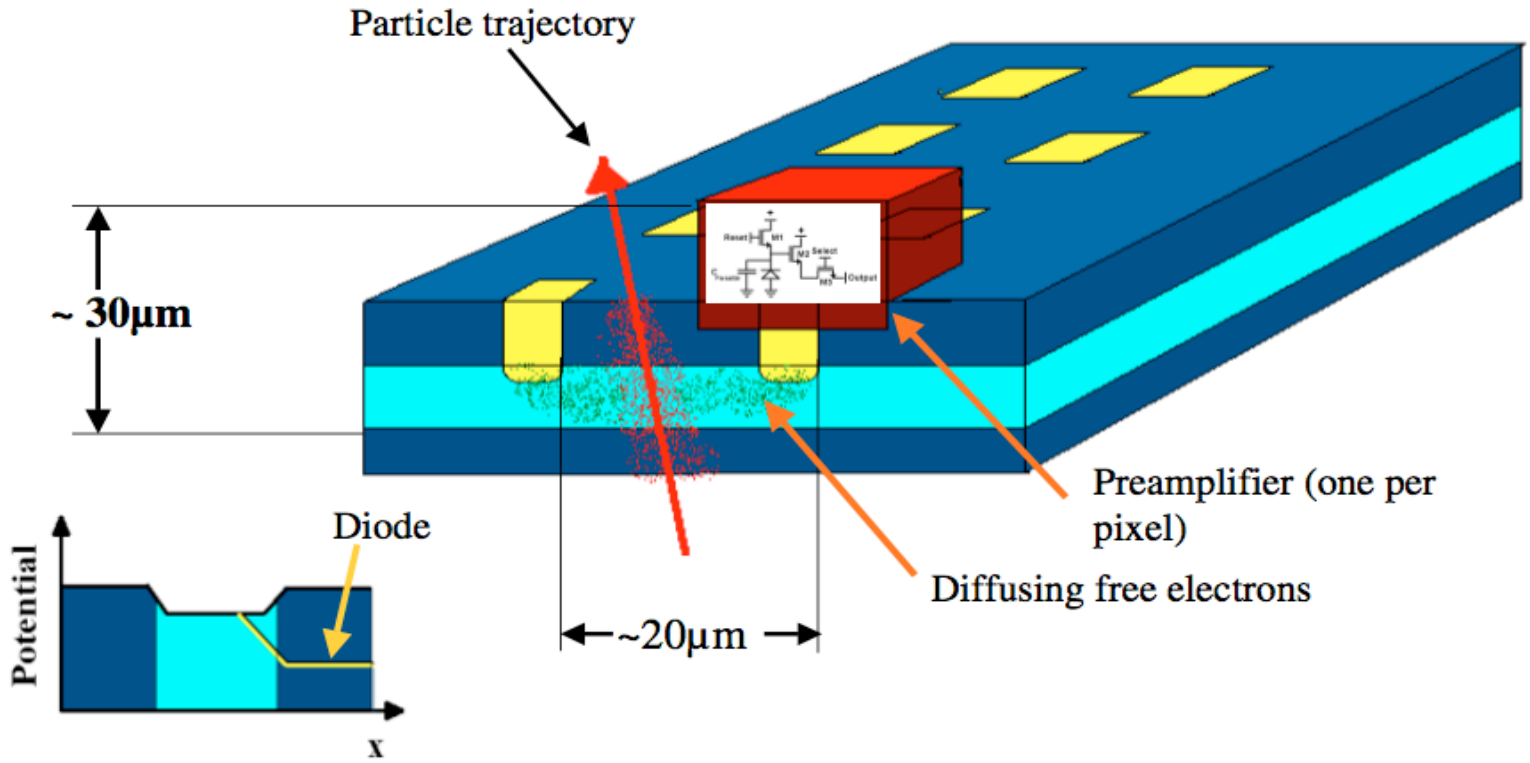
Spatial resolution of right order of magnitude **O(100-200) μm** is obtained (no R-T correction, no precise wire positioning, poor gas mixture knowledge)

Constraints on vertex detector

- The Carbon beam spot has a FWHM = 3mm → The active size must be at least in the range of cm^2
- The angular acceptance must be as large as possible to track the protons emitted at large angles (>40^0)
- The angular resolution on track must be ~ 0.3 deg to match the requirement for the therapy (1 CT voxel resolution after 15 cm of path) and to spot if the fragmentation vertex is outside the target
- Dynamic range should deal with signals ranging from 2 to 100 m.i.p. with good efficiency (>98-97%)
- If we consider 3 station then thickness must be less than 100 μm for each station, accounting for some % of the target thickness (N.B. Carbon interaction in vertex cannot be detected → directly contribute to systematic!!)

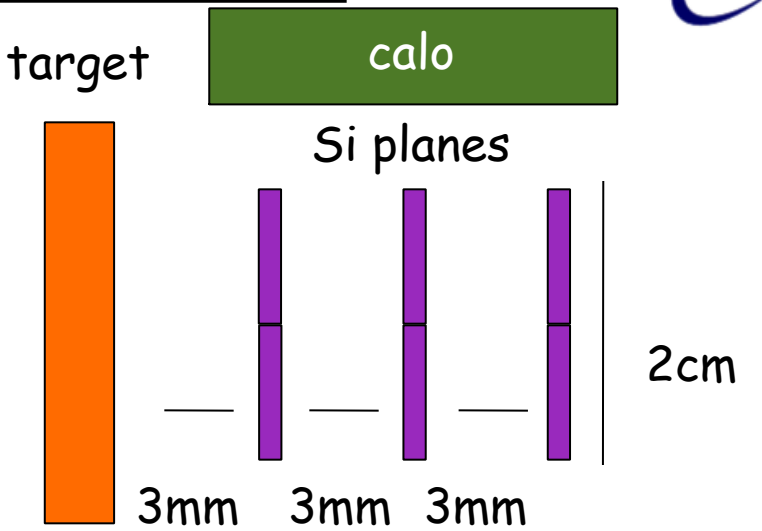
The MIMOSA26 detector

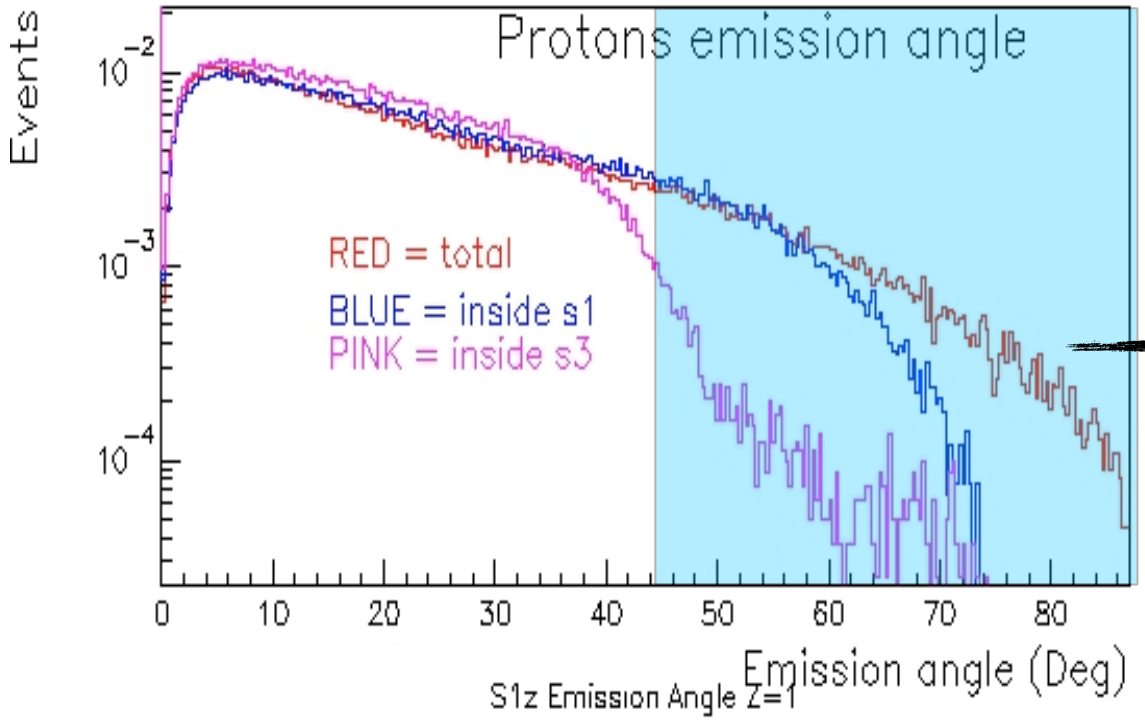
- Active surface :1152 columns of 576 pixels (21.2x10.6mm^2)
- **Pitch: 18.4 µm →0.7 Mpixel → σ_{sp}~5µm**
- Digital readout at 10 Khz rate
- On chip electronic to process the signal in few µm layer
- Zero suppression on board
- Can be thinned at 50-60 µm



Vertex detector : setup geometry

- The shown setup, (6 MAPS in 3 planes) could give large angular acceptance and 0.4^0 angular resolution even with clusters of pixels detected with 50 μm spatial resolution
- The MIMOSA chip shows a correlation between the energy deposit and the cluster size: can improve ion identification.

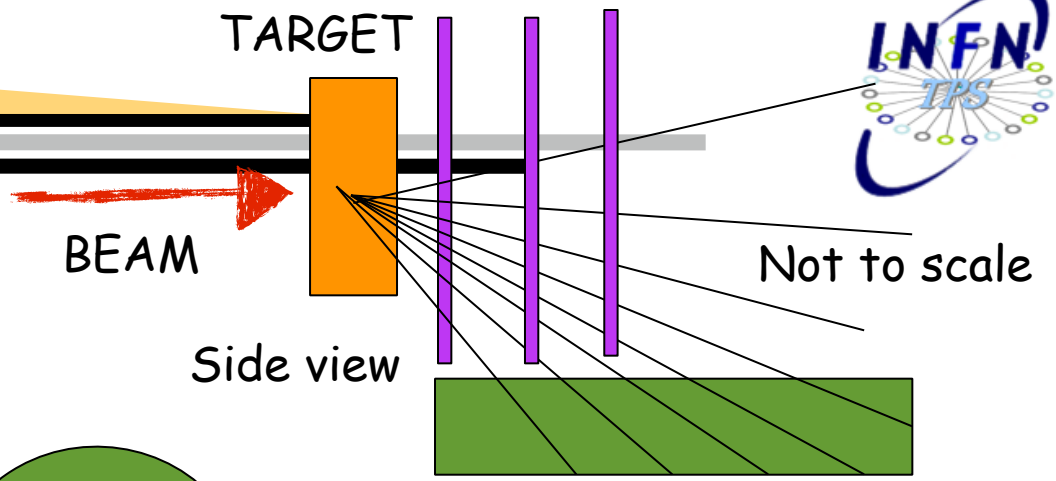


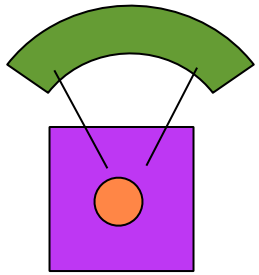


Only ~15% of the proton angular distribution is out of acceptance of the Vertex (3 planes).
Only few % asking 1 plane + calorimeter
Proton energy coarsely measured by the lead-fiber calorimeter

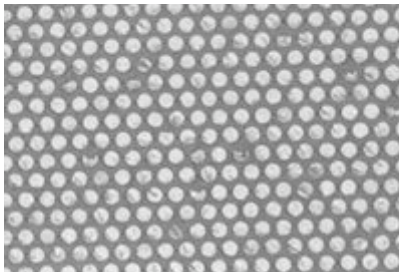
I.R. Calorimeter

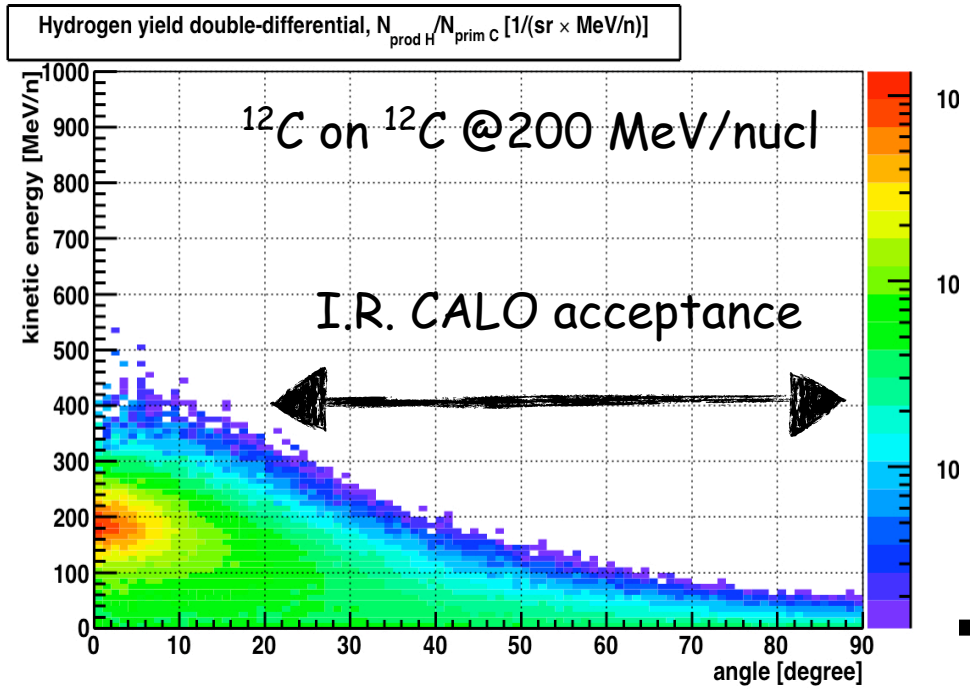
- Needed to detect the large angle fragment escaping from the HODO and ALADIN acceptance (mainly protons)
  - Yet to be approved, but INFN institution already at work
- A possibility would be a lead-fiber calorimeter with reduced aperture in φ to save FEE (and MONEY!)
  - Proton-deuteron-tritium ID possible by TOF
  - Coarse tracking and sufficient Energy resolution for low energy proton





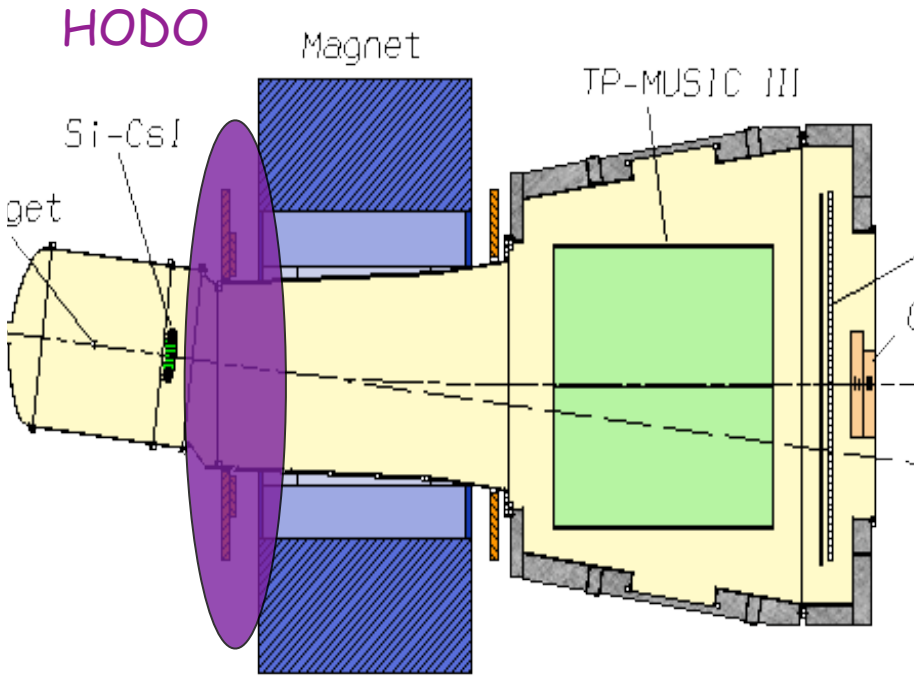
Front view

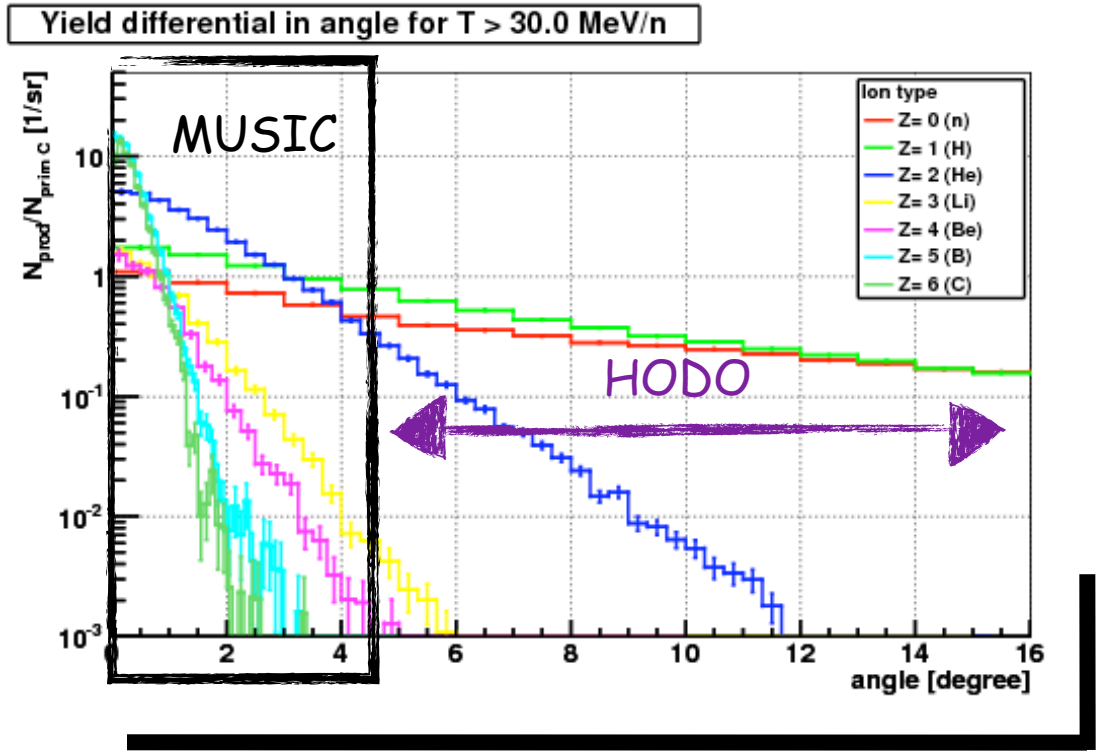




The Large angle Hodoscope

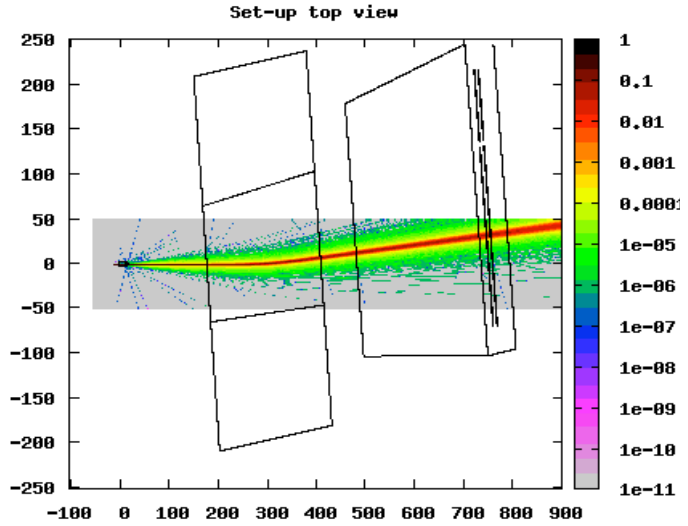
- 89 three-fold telescopes 50 μm + 300 μm Silicon detectors both having 3x3 cm^2 surface followed by a 6 cm long CsI(Tl) of the same surface.
- Acceptance θ_{lab} between ±4.5° and ±20°, tracks not entering in MUSIC, mainly p & He
- Measure dE/dx, E, Θ, ϕ

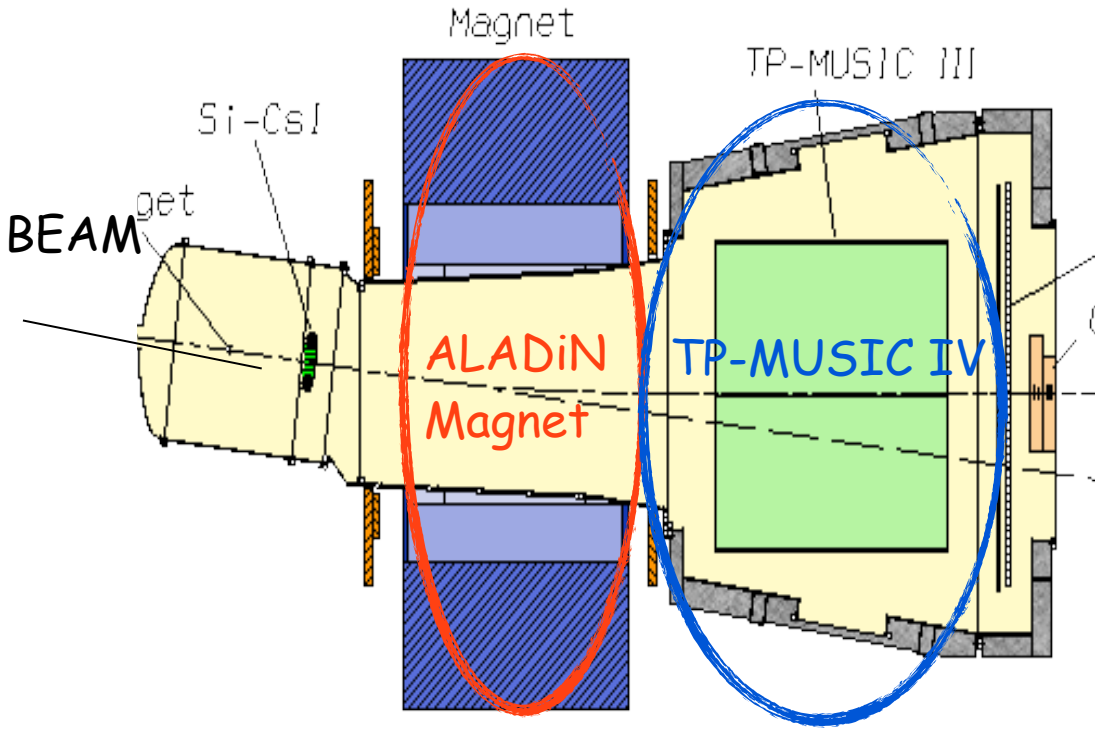




The Downstream Tracking: Aladin + Music

- Downstream the IR we have Aladin, a large area dipole magnet, coupled with the large volume MUSIC IV TPC. The combination provides info on:
  - Fragment tracks after bending → R=p/(ZeB)
  - Fragment DE/Dx → $(Z/\beta)^2$





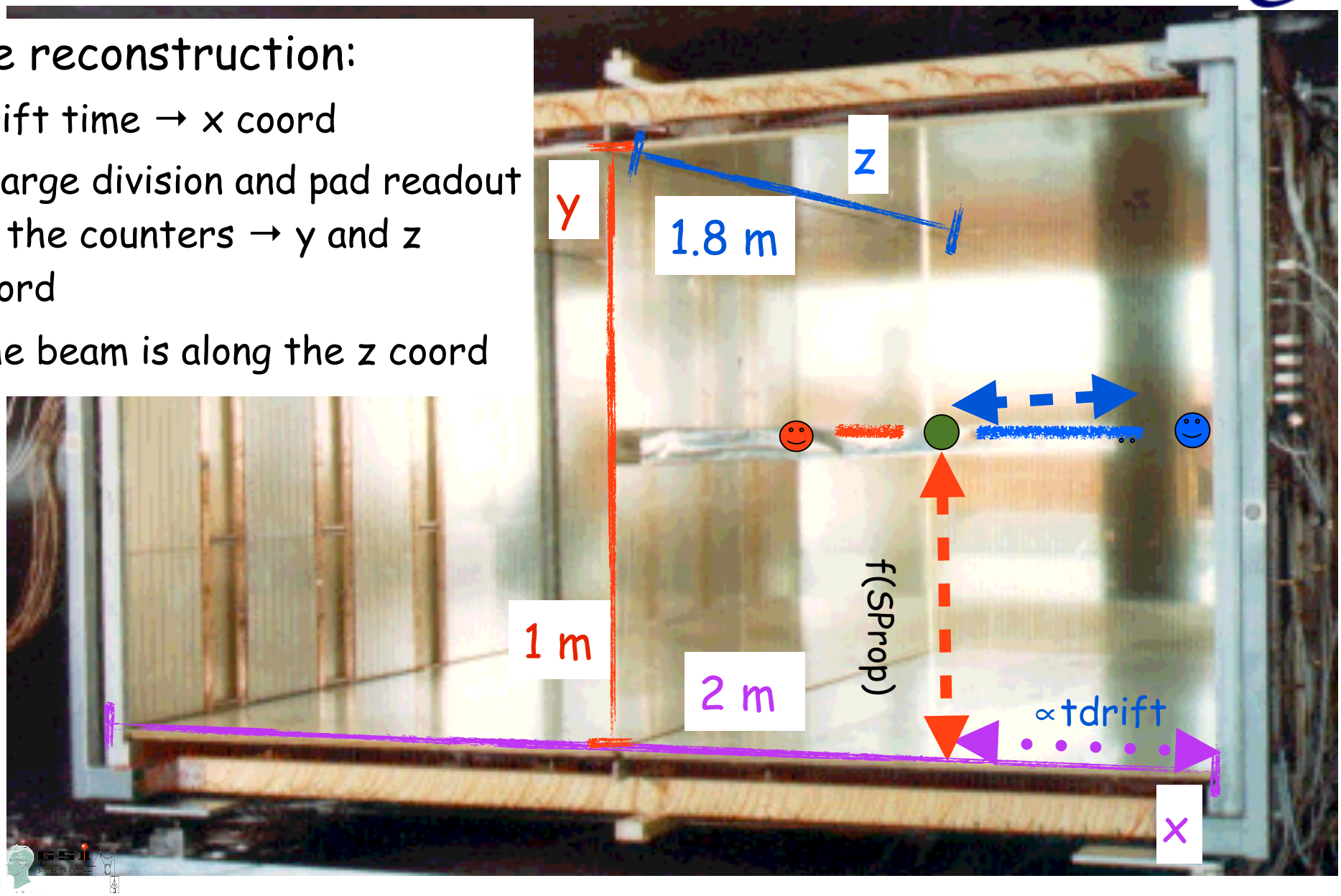
Large dinamic range needed (2-100 m.i.p signal)

Maximum track rate due to long drift time (~100 μs) of ionization electrons: O(1-2 KHz)

Full geometrical acceptance for frags Z>2, fair for He, poor for p

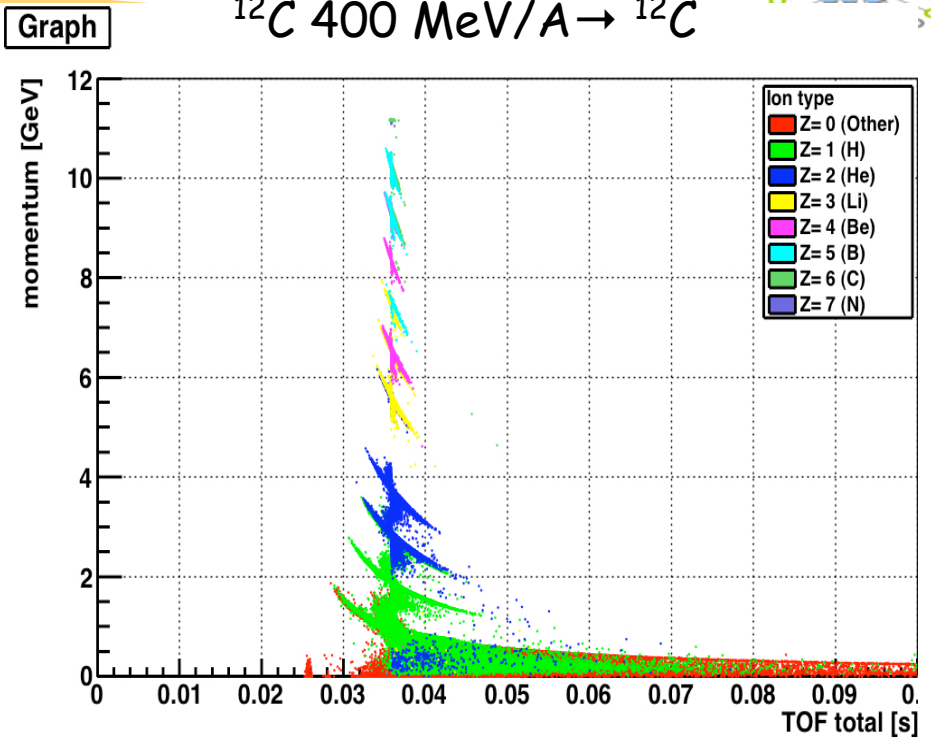
The TPC-MUSIC IV

- Space reconstruction:
  - Drift time → x coord
  - Charge division and pad readout of the counters → y and z coord
  - The beam is along the z coord



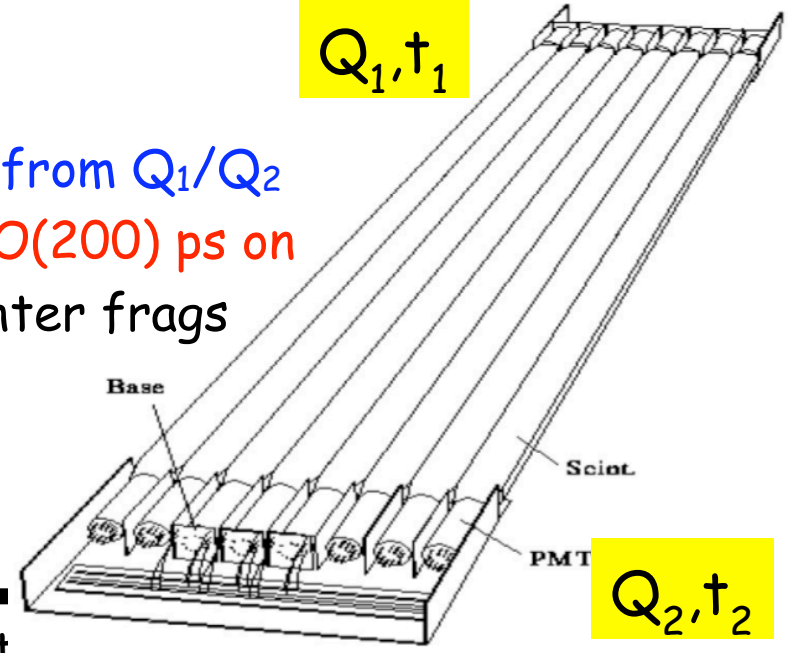
The TOF WALL

- Gives arrival time and impinging position of the fragments
  - Time resolution be matched by resolution of start counter
  - β = L(p,Z,Θ,ϕ)/TOF The time performance must be matched by the tracking capabilities of the setup



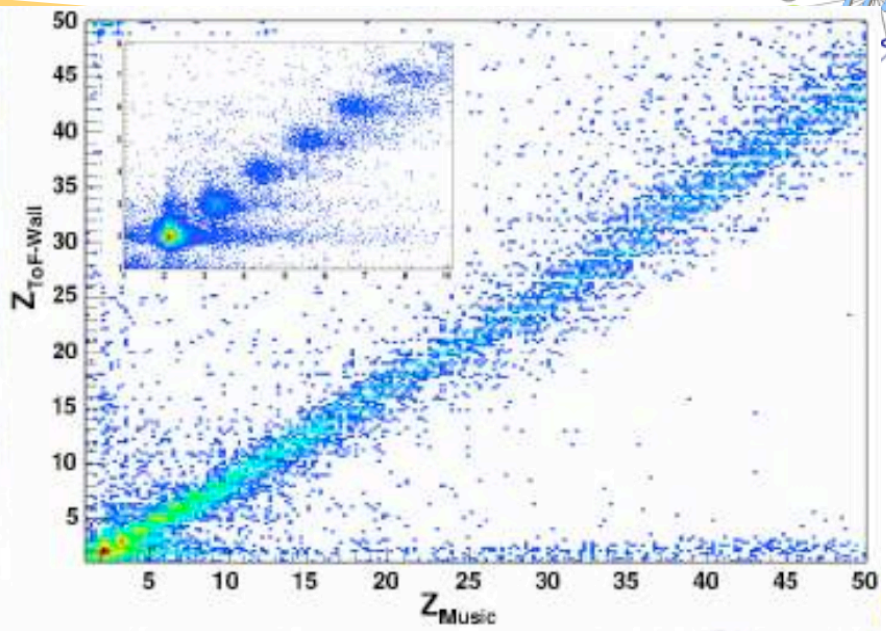
- Two detector layers (front and back), each made of 12 modules
- Each module made of 8 plastic scintillators (BC408), 1.10 m long, 2.5cm wide and 1 cm thick

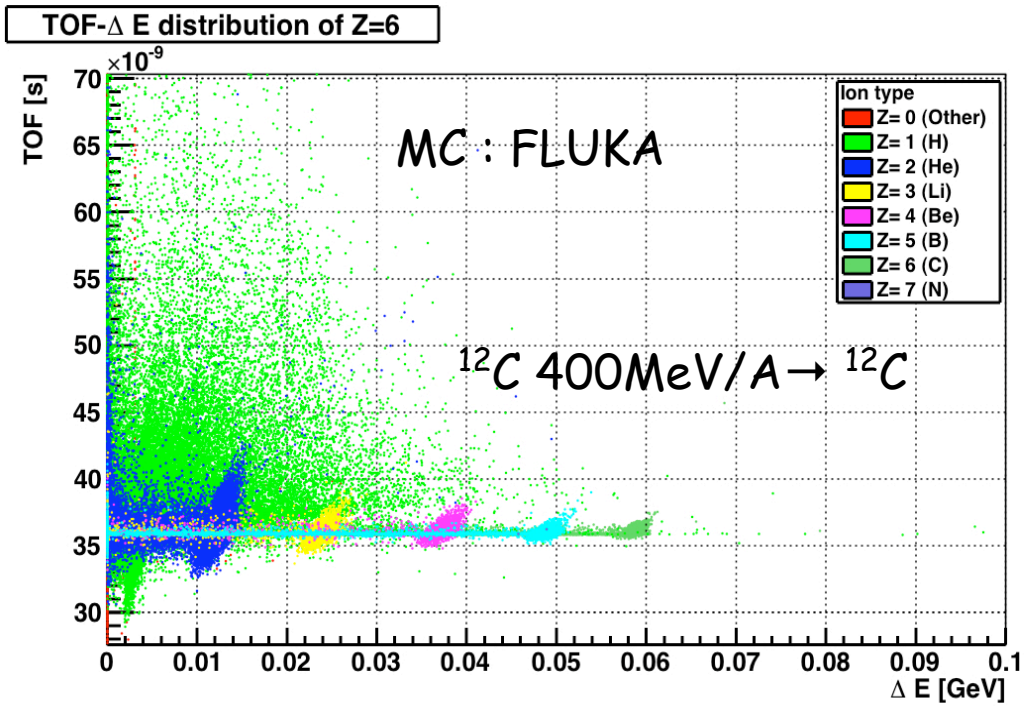
Coord along slat from Q_1/Q_2
Time resolution O(200) ps on ^{12}C, worse on lighter frags

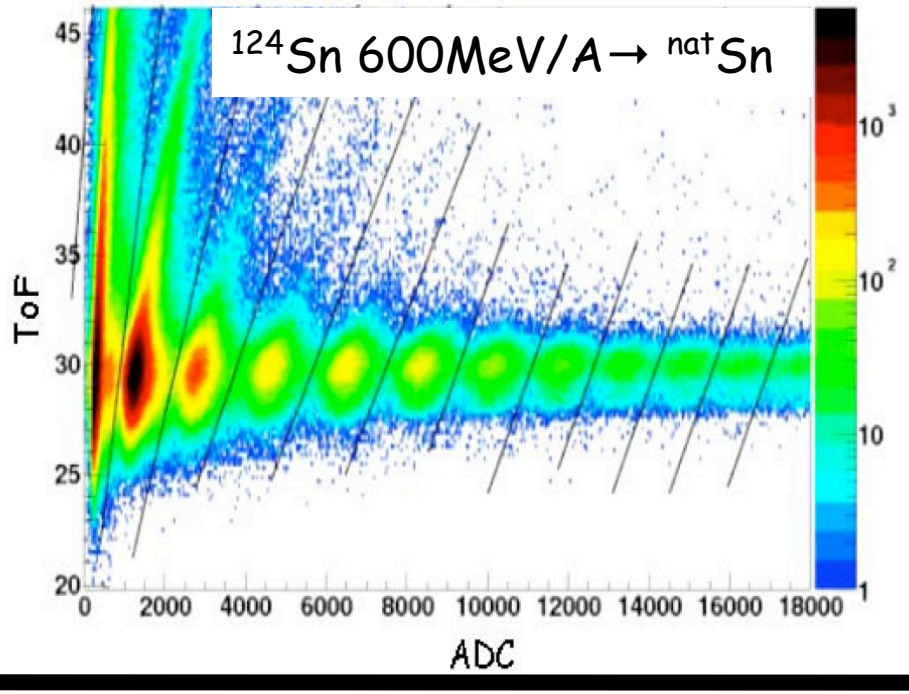


TOF-WALL performances

- TOF vs Q analysis provides standalone Z separation power
- Fragments ID power fully exploited with MUSIC info
- Dinamic range to be optimized for low Z fragments







Conclusions

- The TPS INFN project is 'up and running'
  - Basic ingredients have been identified: FLUKA + LEM + FIRST will be used to gather all the needed information to feed the TPS Kernel algorithms
- MC and LEM models are under development:
  - Improvement in the current Data-MC comparisons as well as improvement in the data sample collection for benchmarking in nuclear interactions and Biological Effects is ongoing
- The FIRST experiment @ GSI has been approved: data taking foreseen in 2011, to study in ^{12}C interactions with several targets
  - A 'new' IR has been designed, in order to fulfill all the requirements for low energy, large angle fragments study
  - Most of the hardware is already available / under test, with performances in agreement with expectations
  - Vertex and Calo detectors are under developement: firs Test Beam expected for this summer

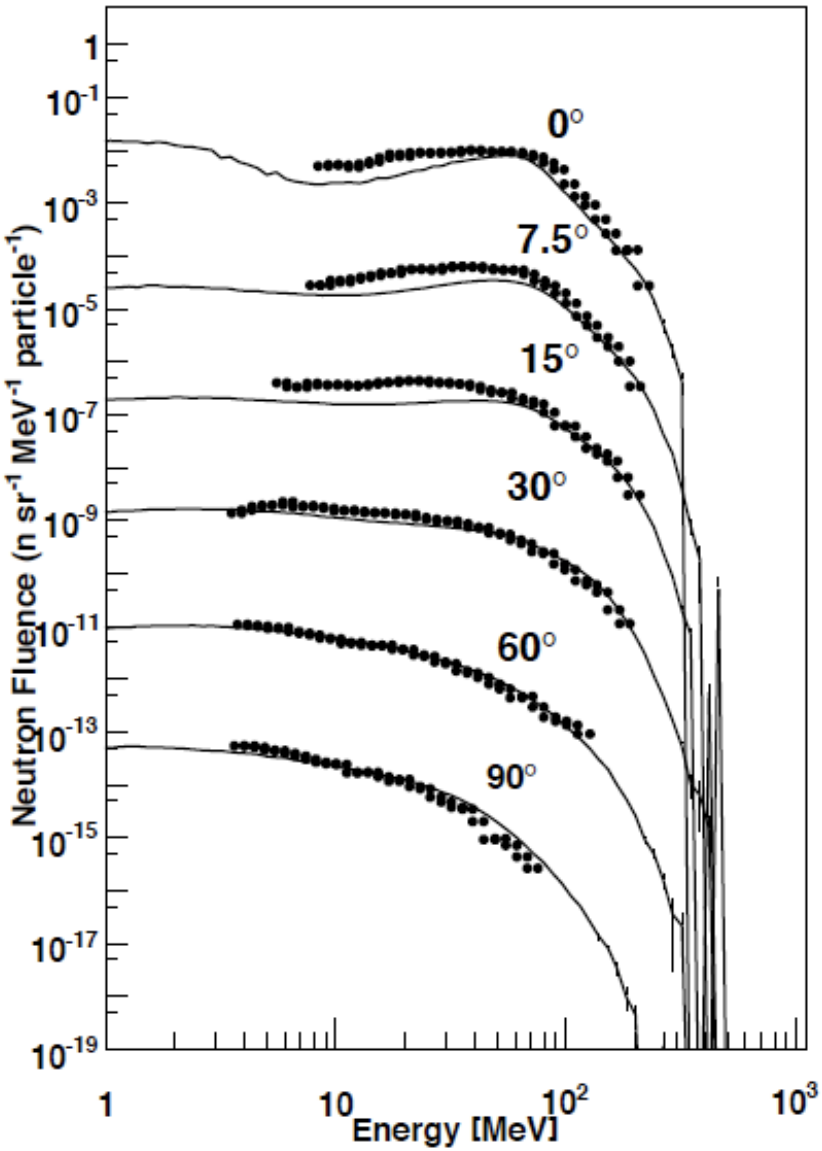
Spares

FLUKA developments for nucleus-nucleus interactions: BME

- BME is the nucleus-nucleus interaction generator for E < 100 AMeV
  - fusion to preequilibrium +
  - 2 body for large impact parameters
  - 3 body for small b + preeq
  - FLUKA evaporation/fragmentation
- Work in progress: refinement of the treatment of peripheral interactions : 2-body and 3-body channels
- Benchmarks: "high" energy (almost no fusion) neutron spectra, neutron angular distributions and fragment yields

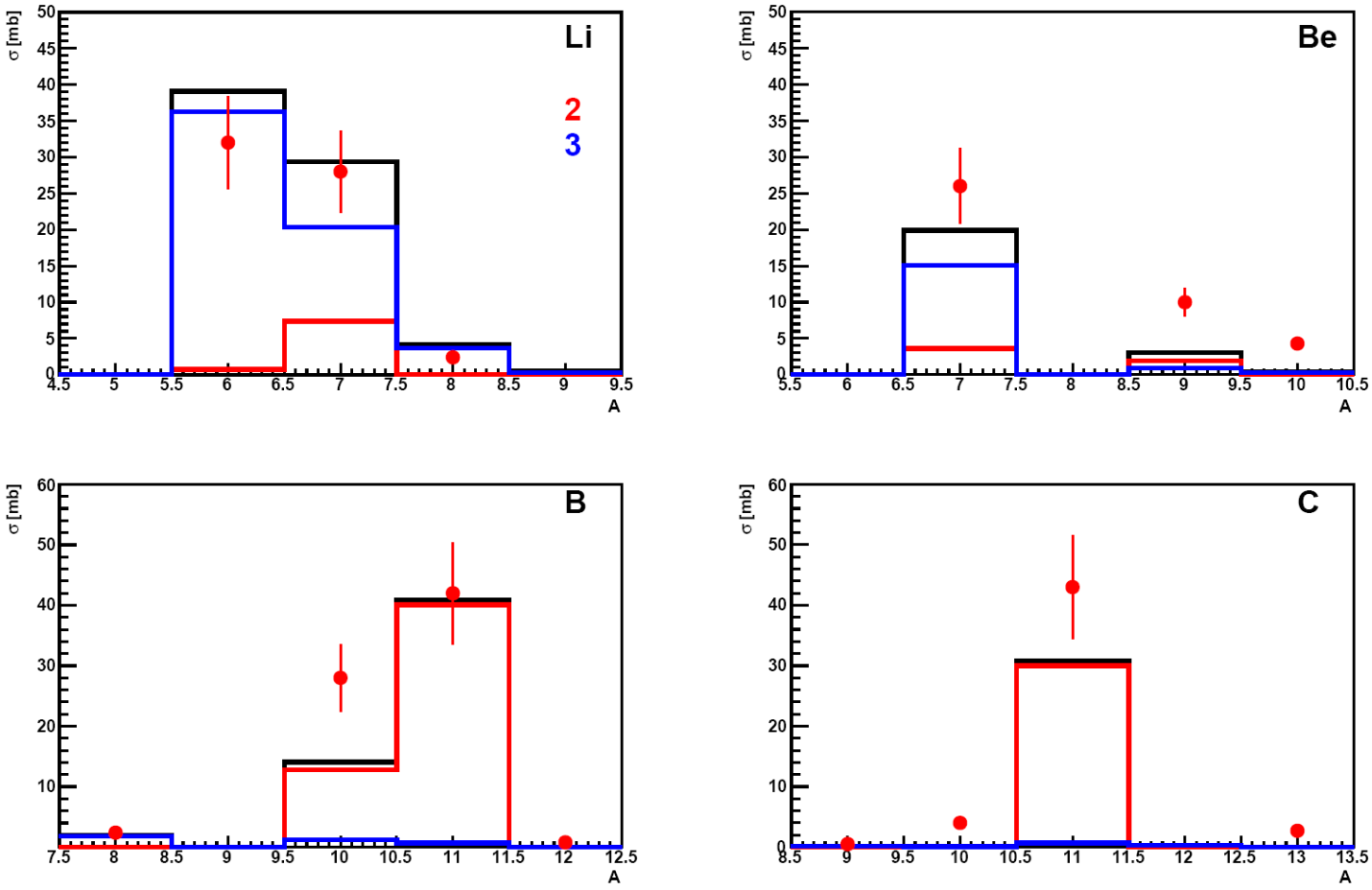
^{12}C (100MeV/n) +^{12}C – double differential neutron spectra , thick target

Exp. Data (points): T.Kurosawa,N.Nakao ,T.Nakamura et al.,Nucl. Sci. Eng. 132,30-57(1999)



Fragment production

exp. data from H. Ryde, Physica Scripta **T5**, 114-117 (1983)



86 MeV/n ^{12}C ions on ^{12}C

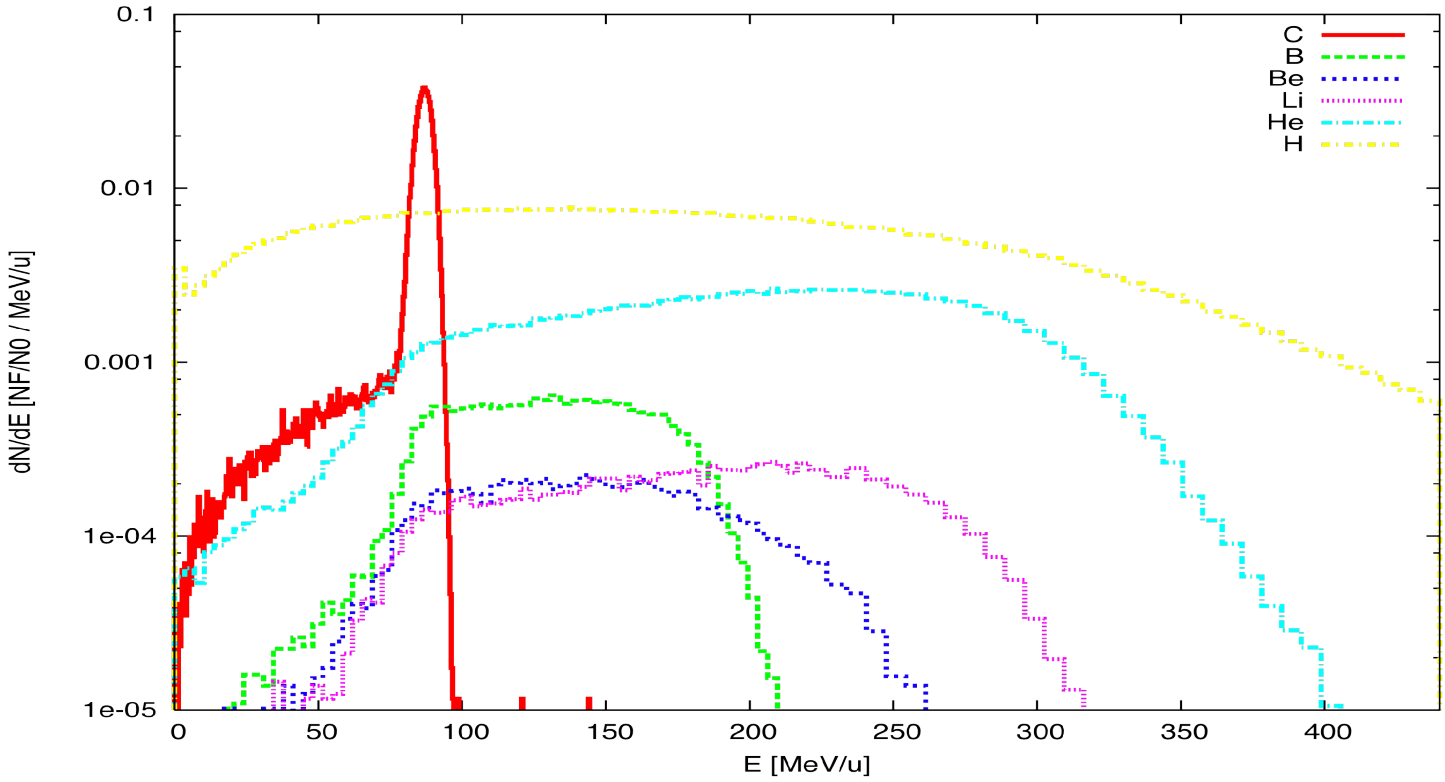
$2^o < \theta_{LAB} < 22^o \qquad T_{LAB} > 10 MeV/n$

Fluka spectra database for analytical tPS@ HIT

^{12}C ions (400 MeV/u) in Water

Fragment spectra $dN(E_{beam},z,T,E)/dE$ at 25.4 cm

Preliminary



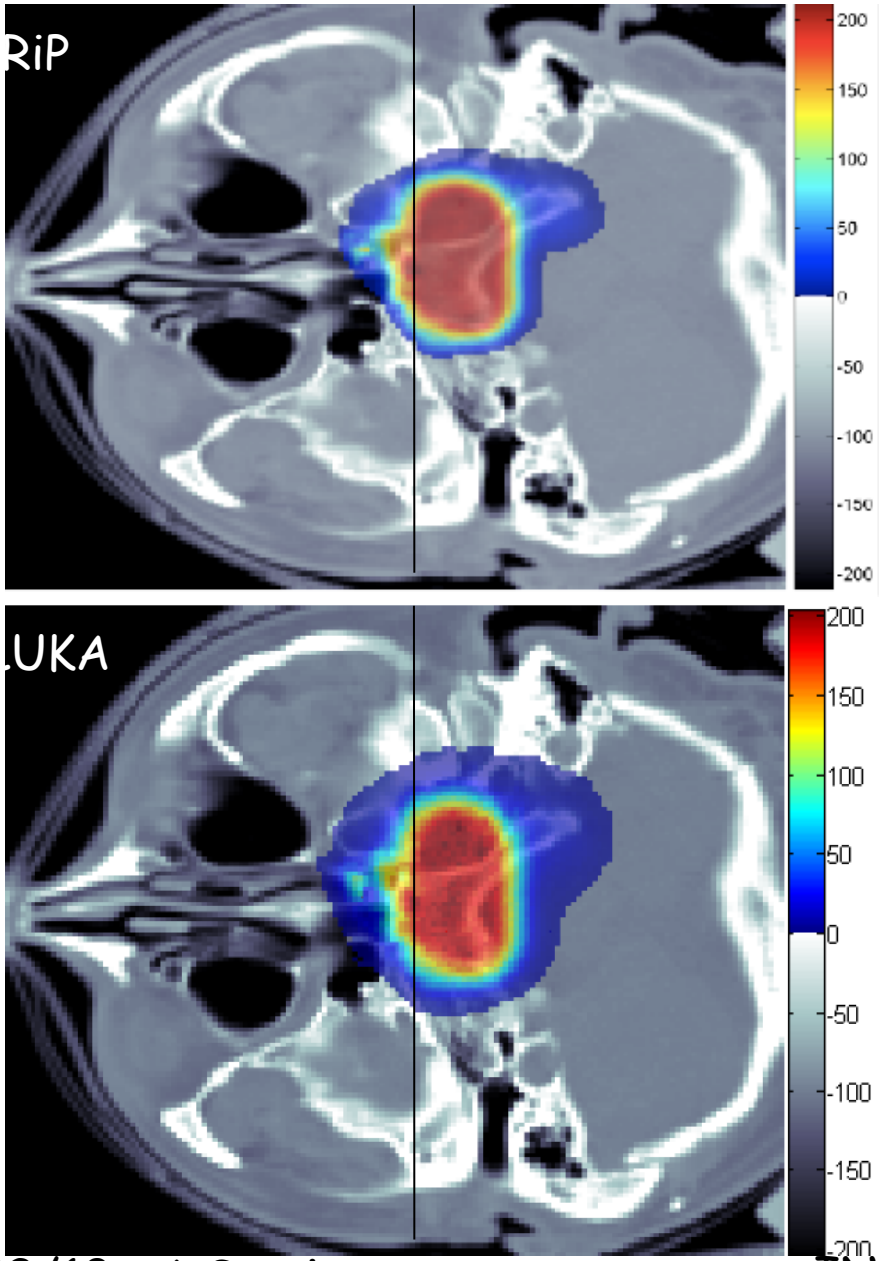
A. Mairani and K. Parodi (HIT)

FLUKA for hadrontherapy

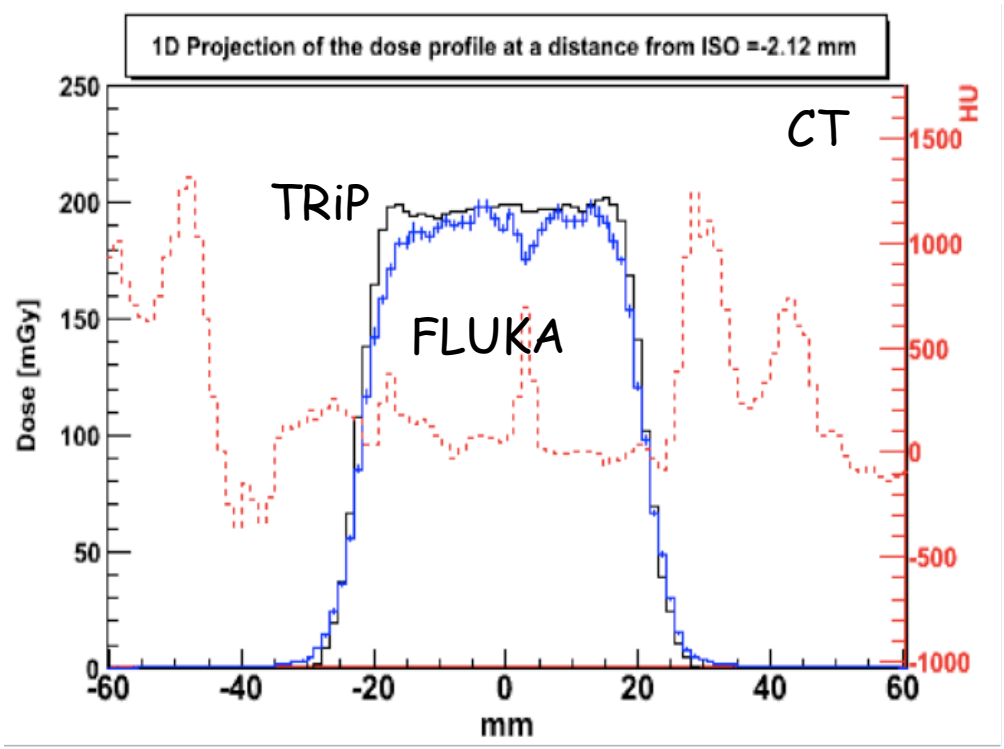
- Reliable nuclear models. Recent developments:
  - BME event generator to treat low energy nucleus-nucleus reactions (Cerutti et al, Ric. Scient. ed Educ. Perm. S126, Univ. degli Studi di Milano, 2006, 507)
- Already applied to proton therapy:
  - Dosimetric/radiobiological studies (Biaggi et al NIM B 159, 1999)
  - Import of raw CT scans with optimized algorithms for efficient transport in voxel geometries (Andersen et al Radiat. Prot. Dosimetry 116, 2005)
- Enormous work in the recent years to include Nucleus-Nucleus interactions
- Very promising results in the initial studies of nuclear fragmentation in water (Sommerer et al PMB 51, 2006, Mairani PhD Thesis, Pavia, 2007)
- First important results in the comparison with analytical TPS for different clinical cases with both protons and C ions (K. Parodi et al JPCS 74, 2007, Mairani PhD Thesis, Pavia, 2007)
- Recent results obtained for the interface of LEM model (GSI) to calculate biological effects (Mairani PhD Thesis, Pavia, 2007)

MC vs Trip for Clivus Chordoma @ GSI

Absorbed dose distributions mGy



Prescribed physical dose 0.47 Gy
Comparisons performed at ~0.25 Gy

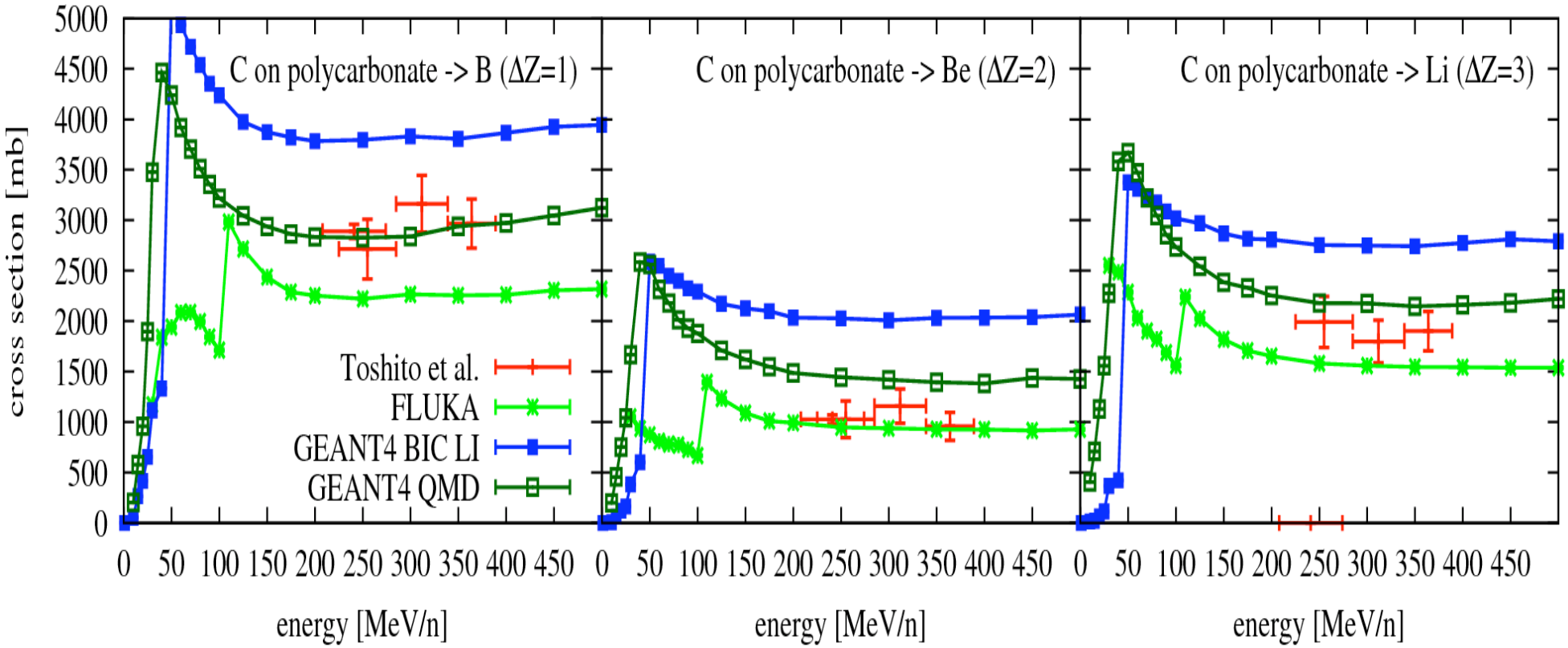


A. Mairani PhD thesis 2007, Pavia

MC nuclear interaction model

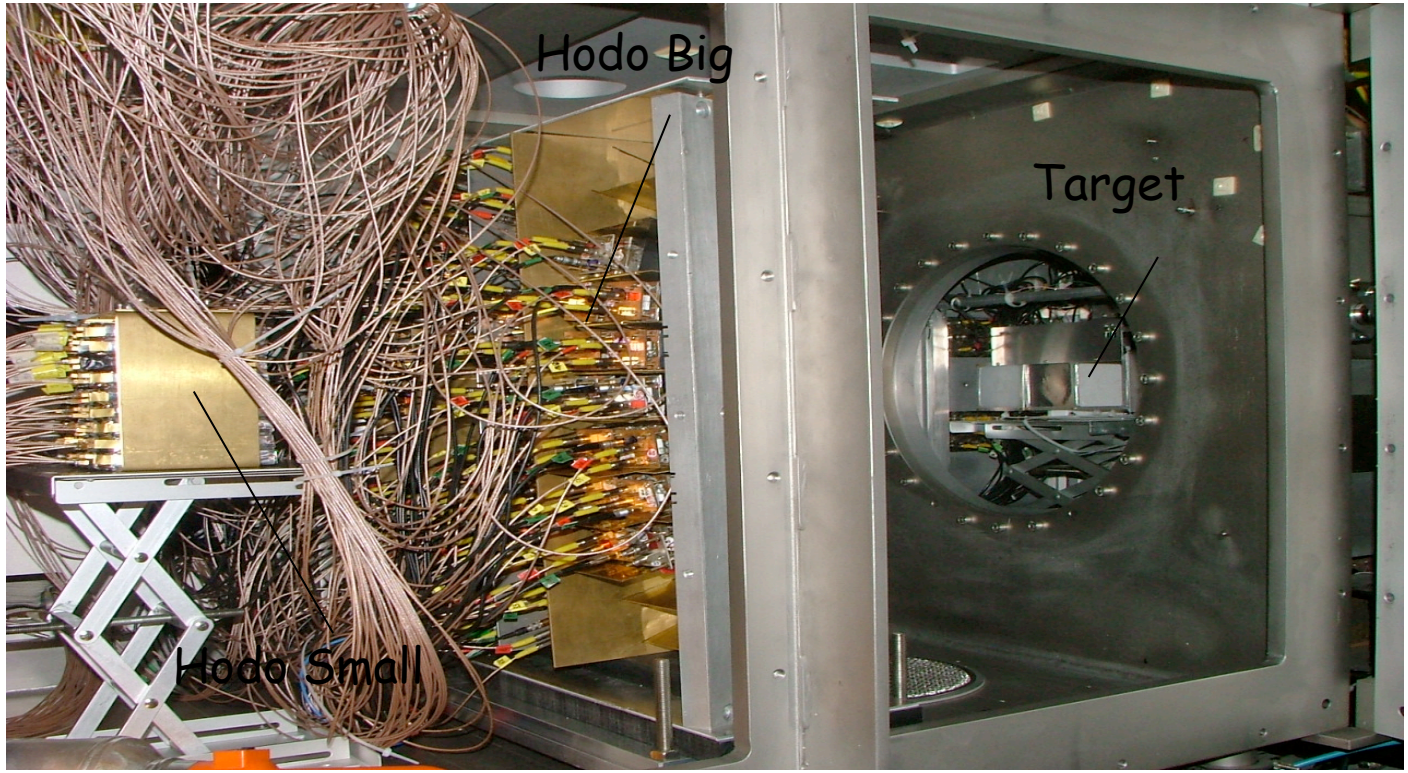
- Charge-changing X-sections for C on polycarbonate

exp. data: Toshito et al. 2006



activity at INFN-LNS

First phase: systematic study of fragmentation cross section of ^{12}C on Au and plastic targets at 60 and 80 MeV/A, @ LNS using the Superconducting Cyclotron.



Hodo-big: 89 three-fold telescopes 50 μm + 300 μm Silicon detectors 3x3 cm^2 surface followed by a 6 cm long CsI(Tl) θ_{lab} between ±4.5° and ±16.5°.

Hodo-small: 81 two-fold telescopes: 300 μm Silicon detectors 1x1 cm^2 of active area followed by a 10 cm long CsI(Tl) θ_{lab}=±4.5°.

The monitoring task

The task about PET on line/Monitoring Tool

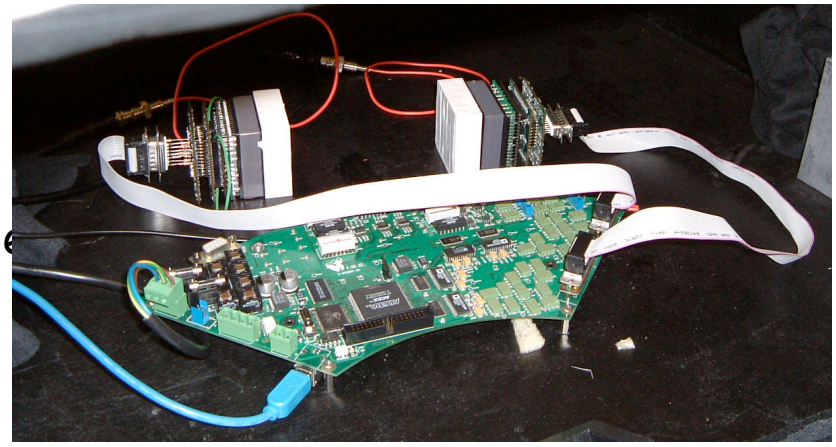
- We have a specific competence on PET in beam (DOPET exp. in Gr.5)
- It is an almost unique tool to verify on line the release of dose.
  - Protons:
    - $p + {}^{16}O, (p,n) + {}^{15}O$ $\quad$ $p + {}^{12}C, (p,n) + {}^{11}C$
    - $\tau_{15\text{-}O}=121.8$ s $\quad$ $\tau_{11\text{-}C}=1222.8$ s
  - Carbon:
    - $^{12}C + p, {}^{11}C + (p,n)$ $\quad$ $^{12}C + p, {}^{10}C + (p,2n)$ $\quad \tau_{10\text{-}C}=19.3$ s
- The difference in β+-activation processes and the dominant mechanism of energy deposition, the activity registered by the PET image is not directly proportional to the delivered dose. A proper unfolding algorithm must be used.
- Therapy with ions requires the best possible accuracy in the monitoring of the applied treatment: for this reason the "in vivo" information is extremely useful.
- It is however an indirect method which requires unfolding starting from experimental data
- The work requires the development of a specific hardware integrated to a software tool for prediction and comparison (integration with the MC task)

Software goals

- Improvement of the algorithm for the 3D reconstruction of the activity distribution to achieve a better image quality
- Improvement of the system model
- Realization of an unfolding filter to extract the Dose
- Inverse filter to achieve dose localization:
- InvFilt * Att = Dose.

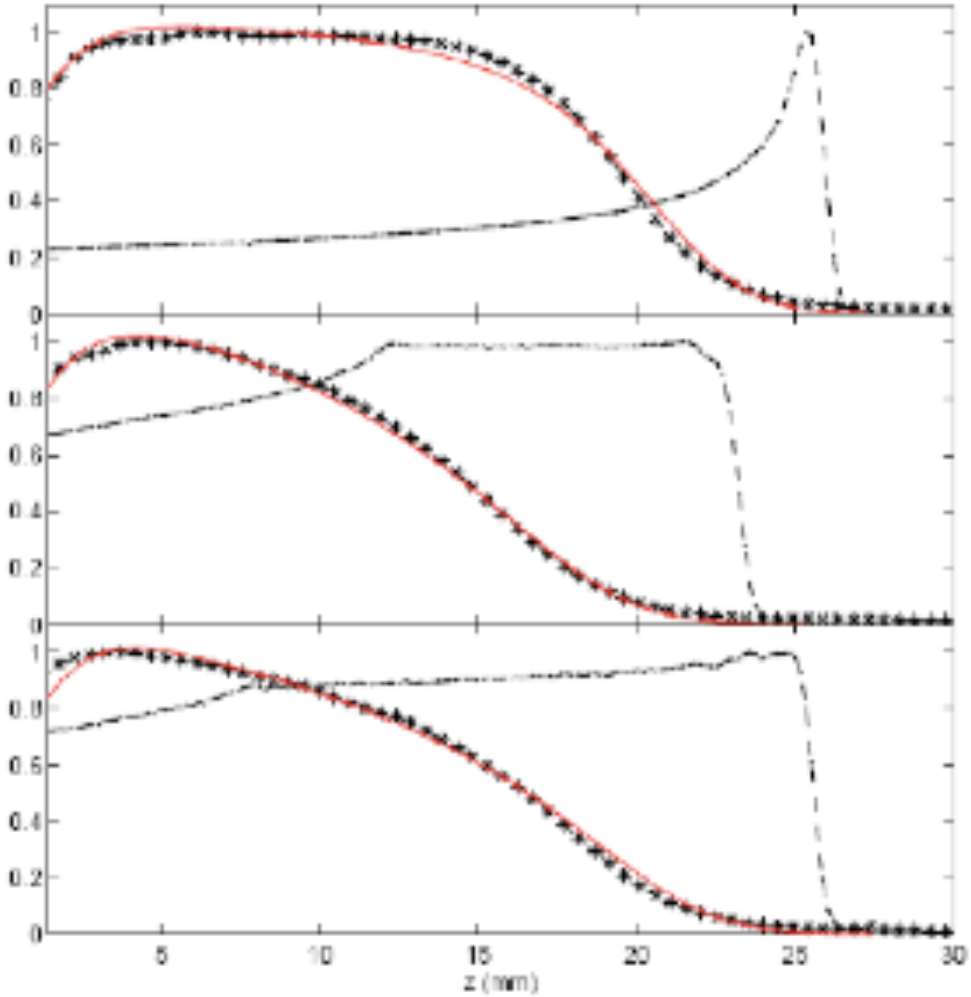
Hardware goals

Design, assembly and test of improved detection module and readout



Unfolding

DoPET results
F. Attanasi et al.



Fe (62 MeV)

12 mm SOBP

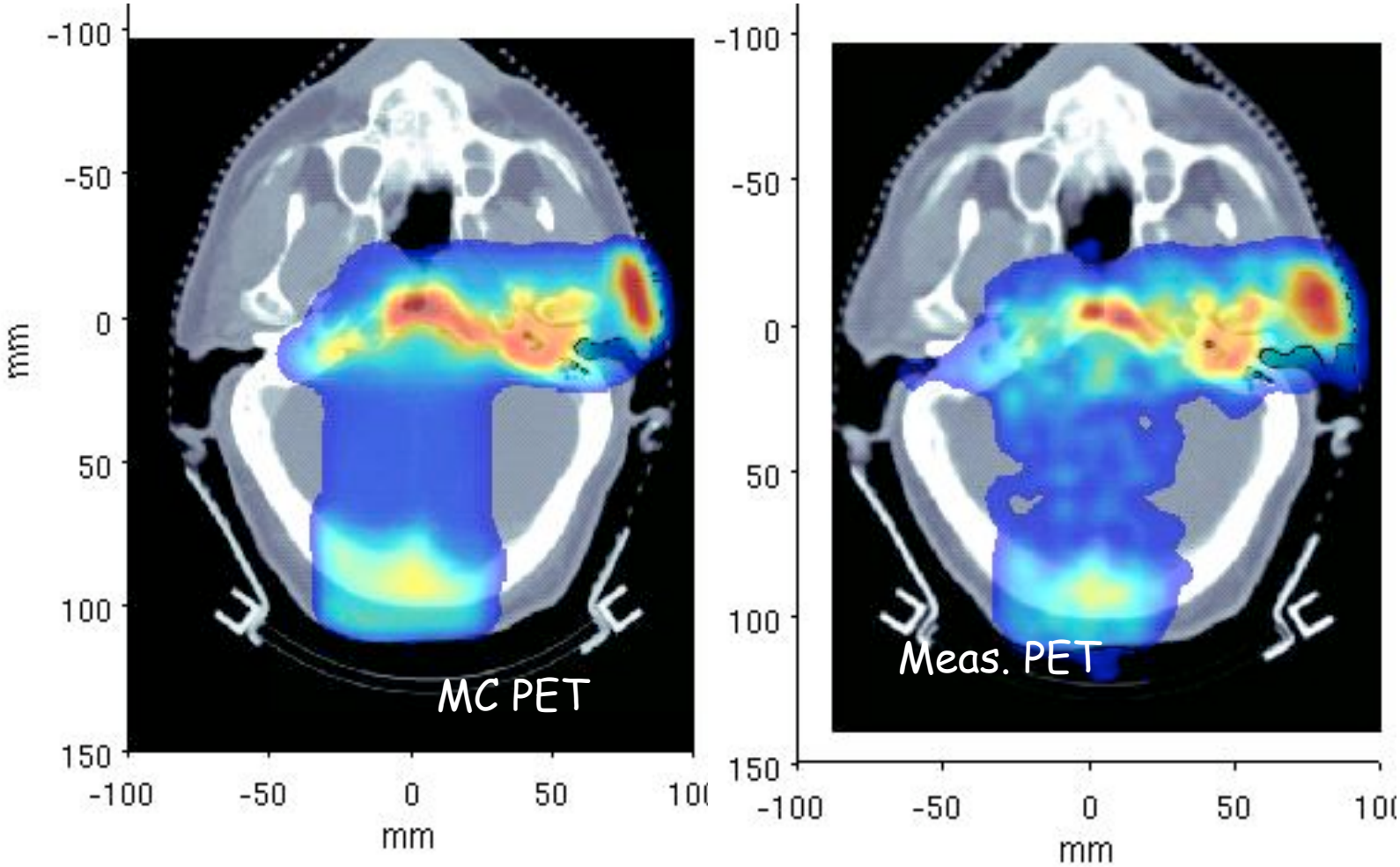
20 mm SOBP

Reconstructed activity (*) in comparison with the dose (dash-dot line) and the filtered dose (solid red line)

Experience at MGH with protons:

K. Parodi et al., IJROBP 68 (2007)

Clival Chordoma,
0.96 GyE / field,



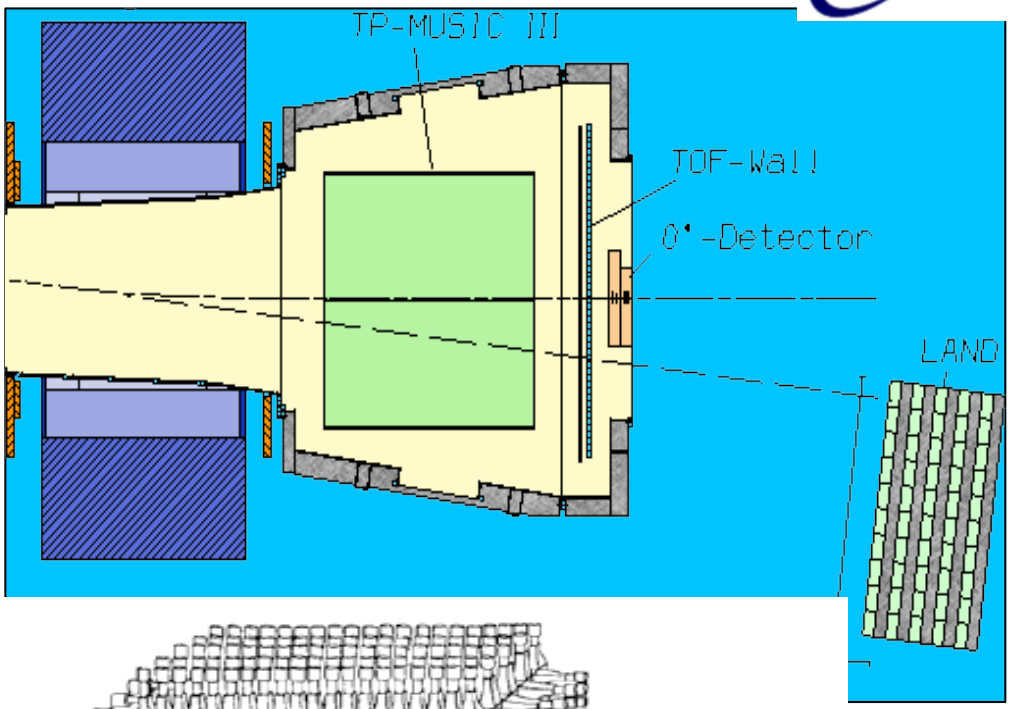
In the case of protons the calculation was performed by folding FLUKA with tabulated cross sections for β+ emitter production (fast) For C beams: in general cross section not known: full calculation needed

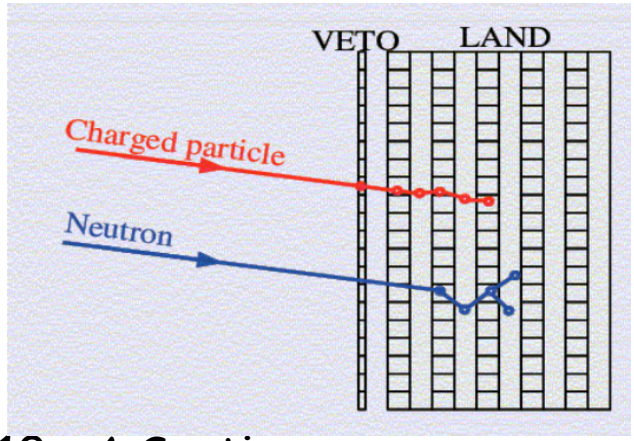
Time schedule: the principal milestones

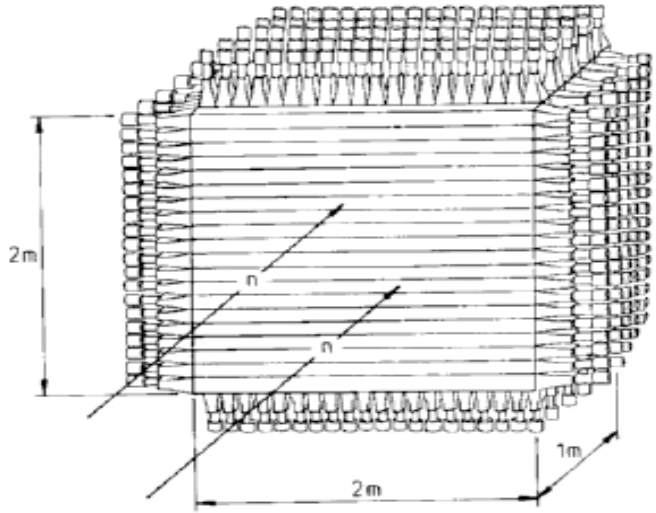
	First year	Second year	Third year
Nuclear Physics	Measurement of 12C fragmentation at 40-80 MeV	Setup of detector and measurements in the range 80-400 MeV	
Radiobiology	Measurement with 12C beam up to 80 MeV (LNS)	Measurement with 12C beam up to 400 MeV	
Optimization	Implementation of LEM Multifield optimization	Prod. of radiob. database for specific cless of a given clinical case	Data for several tumors 4D optimization Simulation tools
Monte Carlo	Interface with LEM Study of nuclear models Interface with CT	First prototype of validation tool Validation with full MC + LEM simulation	Production of validation tool Benchmarking activity
PET Monitoring	Start of inverse filter calculation Proc. of components for hardware developments	Assembling of new detector Data taking and inverse filter optimization	Characterization of the complete in-bema PET monitoring and integration with TPS

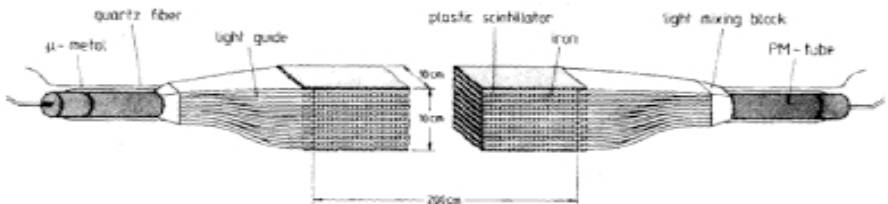
LAND, the neutron detector

- Active volume: 2x2x1 m^3
- Divided in 200 paddles 200x10x10 cm^3.
- Each paddle made of 11 sheet of iron ad 10 sheet of scintillator 5 mm thick
- Veto in front of the detector for charged particle





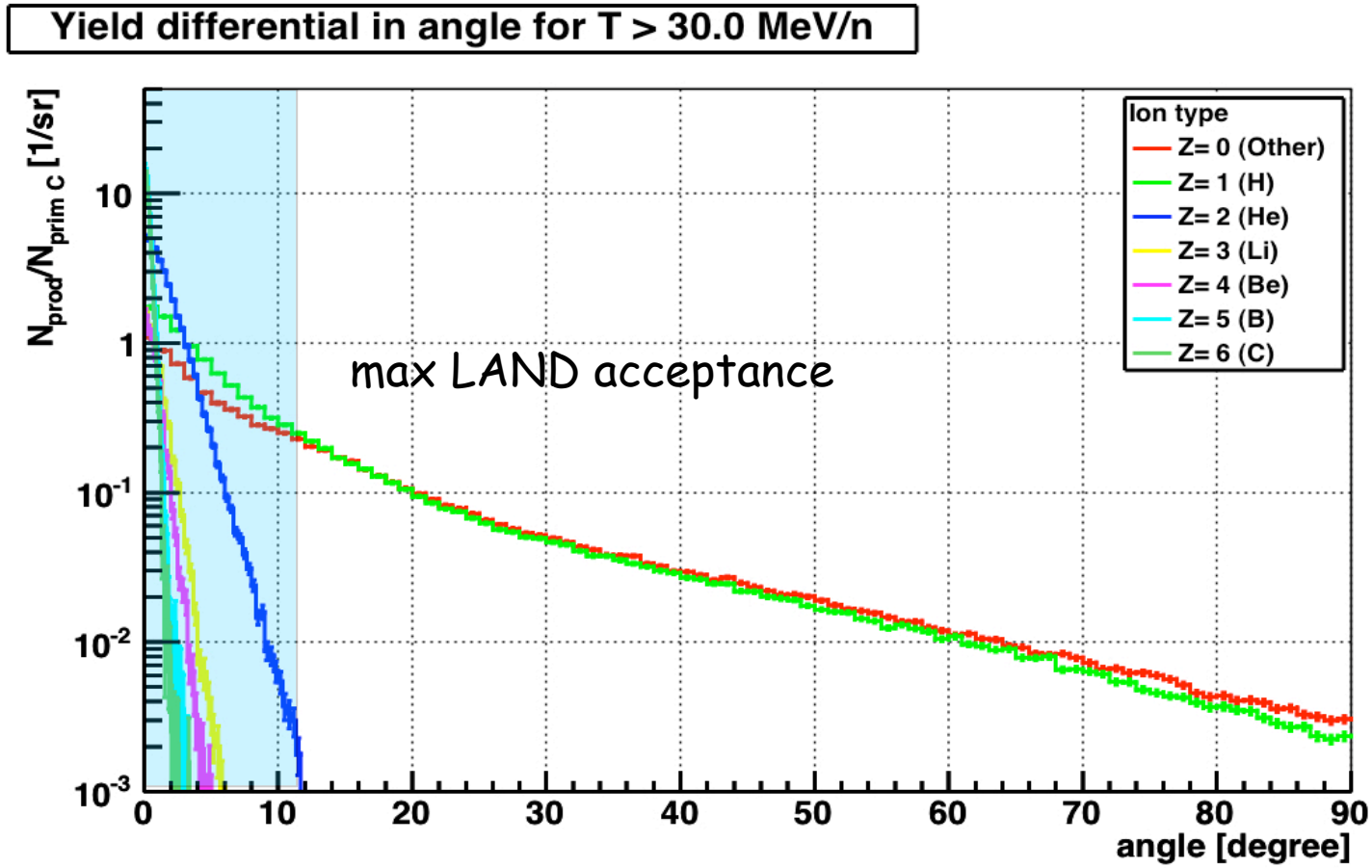




LAND, the neutron detector

- Reduced angular acceptance: is it enough to test the model?
- The IR calo could help the neutron flux measurement

Eff ~ 90% for 300 MeV neutron
Time res ~ 500 ps



MIMOSA26: response to light ions

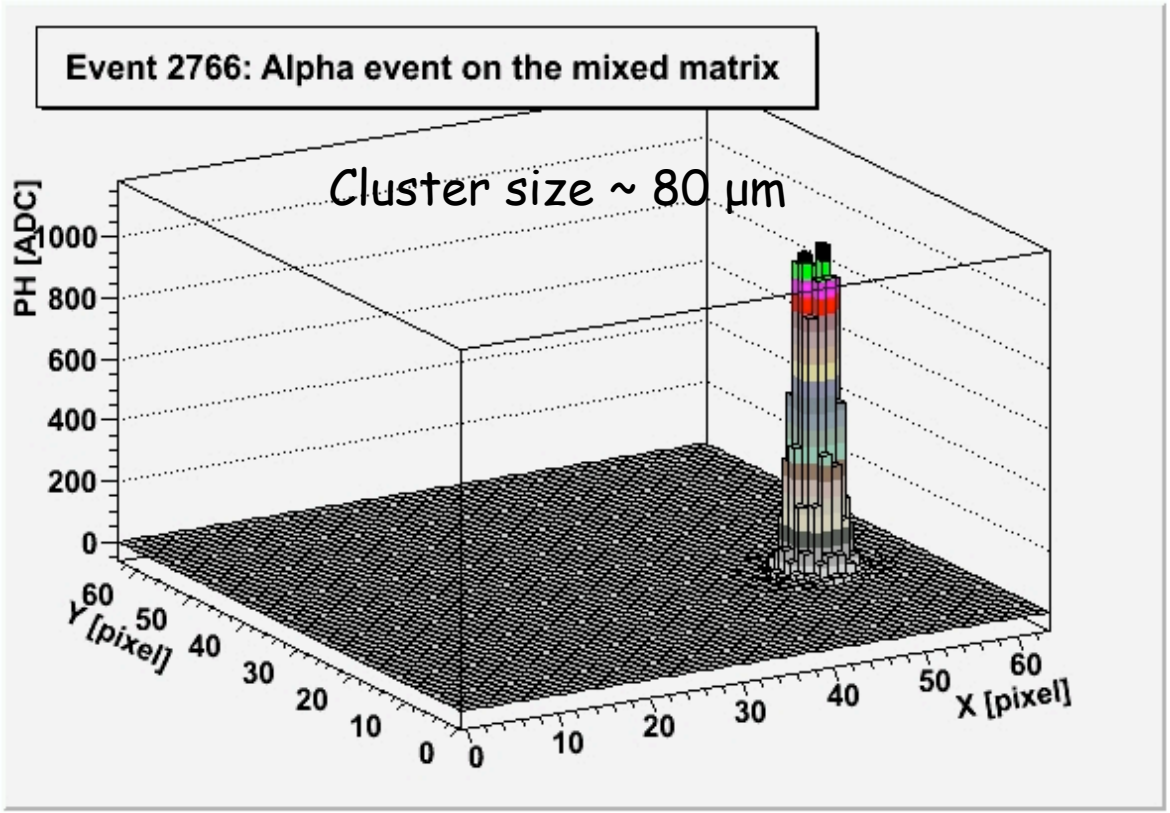
The MIMOSA chip shows a correlation between the energy deposit and the cluster size: can improve ion identification.

Am241 event in MIMOROMA, same MAPS technology of MIMOSA26

Response to light ions (cluster size, eff,..) foreseen to be studied at LNS ^{12}C beam

Can be tested also with a from Am241 source but...

Energy release by Am241 is larger than by 200 MeV/nucl carbon → carbon has smaller cluster size



The TP-MUSIC IV

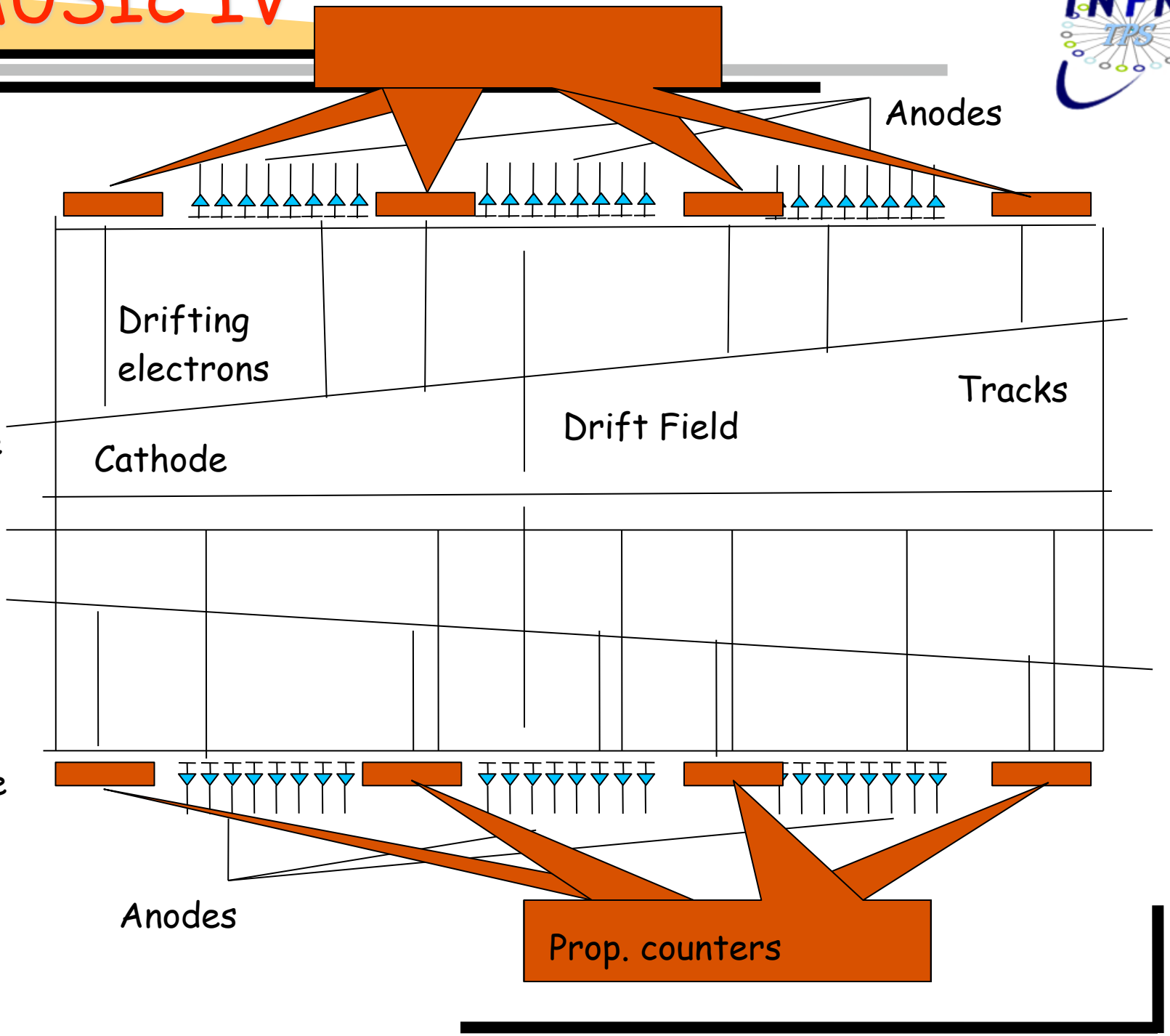
48 Ionization chamber layers

8 proportional chamber layers

Time and charges of the counters registered

Prop counters read by pads to detect transverse position

Digital processing of the signal



The MUSIC IV - TPC

- Must be tuned for low Z fragments
  →reduce the dinamic range
- Fragment directions measured must be bactraced along some meters to IP