Dose profiling in Particle Therapy

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Radioguided Surgery and Particle Therapy Dose Profiling
mini workshop on Medical Physics
Roma, 21 March 2016

GSI Helmholtzzentrum für Schwerionenforschung GmbH

Outline

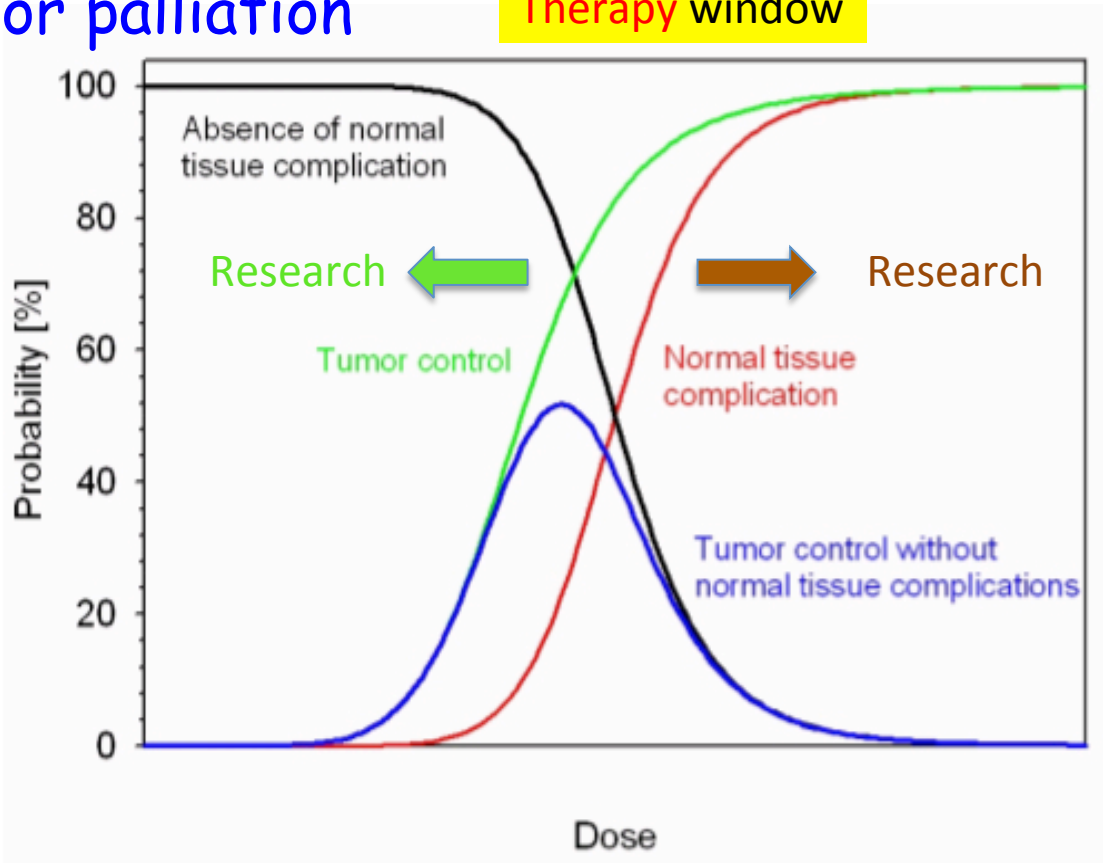
- Introduction to Particle Therapy
- The beam range monitor problem
- The INSIDE@CNAO solution
- Summary and conclusion

Tumor Control vs Tissue Complication

- Part of multi-disciplinary approach to cancer care
- Useful for 50-60% of all cancer patients (also together with surgery, chemotherapy)
- Can be given for cure or palliation

- Mainly used for loco-regional treatment
- Benefits and side-effects are usually limited to the area(s) being treated

$$Dose = \frac{dE_{abs}}{dm}(Gray)$$



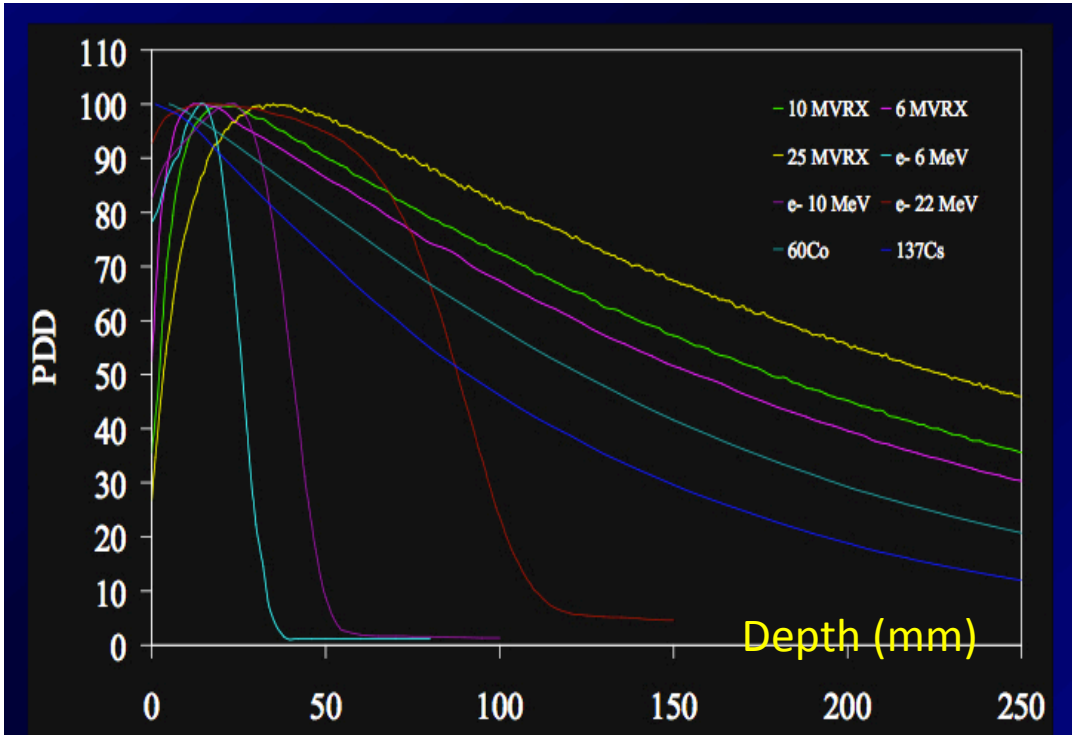
The conventional RT

The photon (and e^-) beams are the most common in RT. Cheap, small, and reliable.

The energy release is not suitable to release dose in a deep tumor.

But the use of sophisticated imaging (CT), superposition of several beams, computer optimization, multi-leaves collimators and >40 year of R&D make IMRT effective and widespread

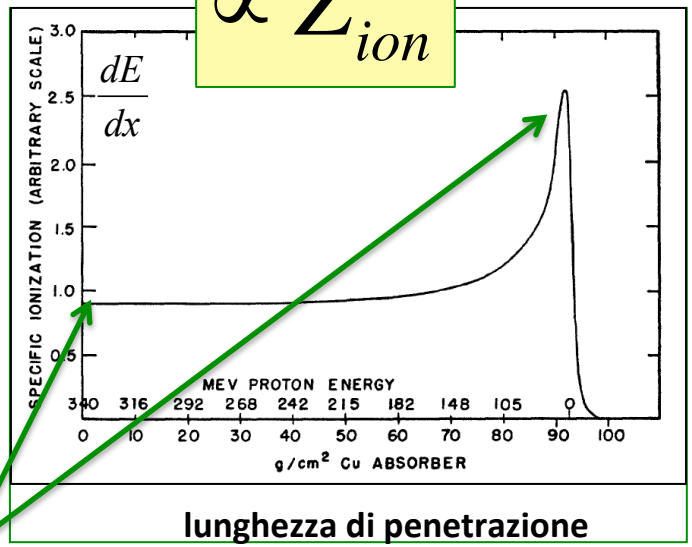
Dose-depth relation for γ and e^-



But physics can help…

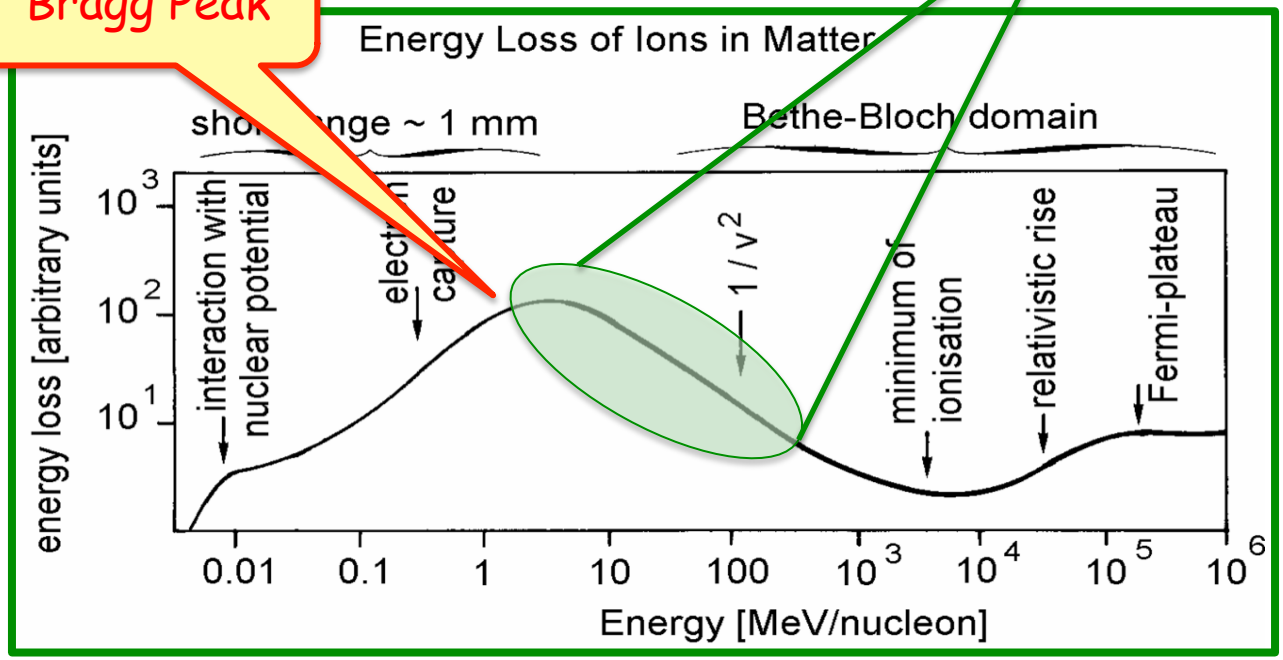
On the other hand, the release of energy by charge particles has very different, and attractive, features… why not to use them?

$\propto Z_{ion}^2$



lunghezza di penetrazione

Bragg Peak

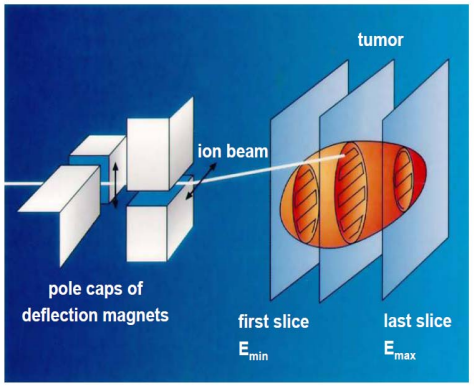


Perfect to release energy (dose) in a tumor buried inside the patient, like a depht bomb..

Mostly proton, few ^{12}C beams.

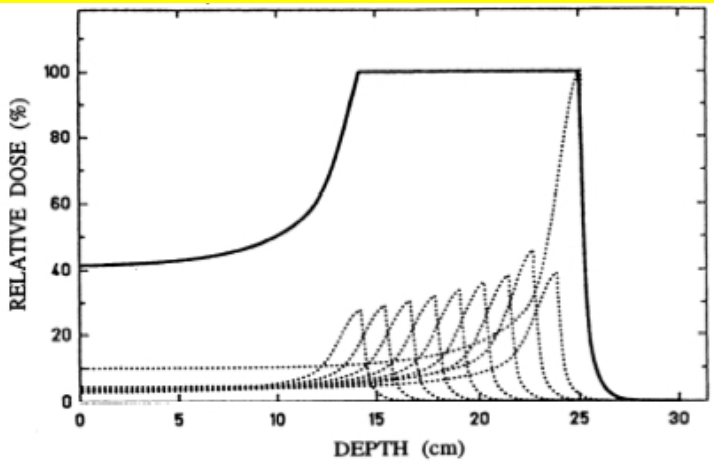
Future ^{4}He, ^{16}O ?

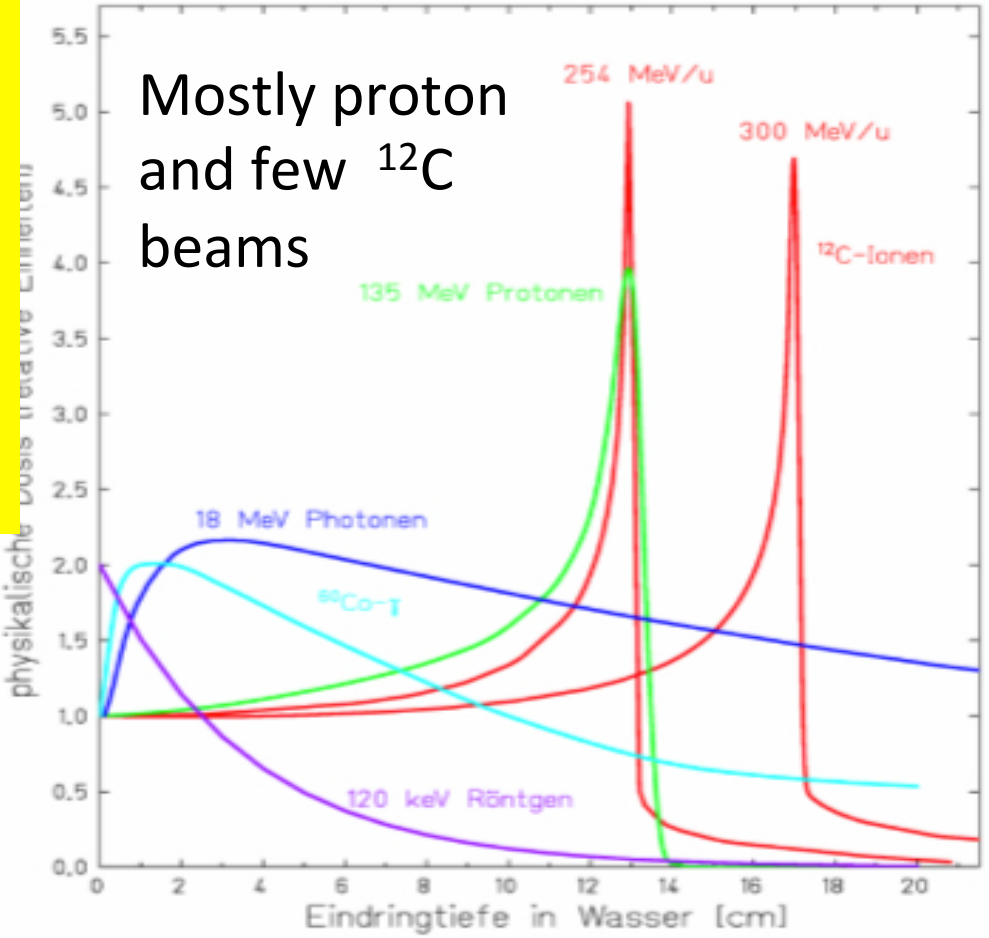
Particle therapy vs Photon RT



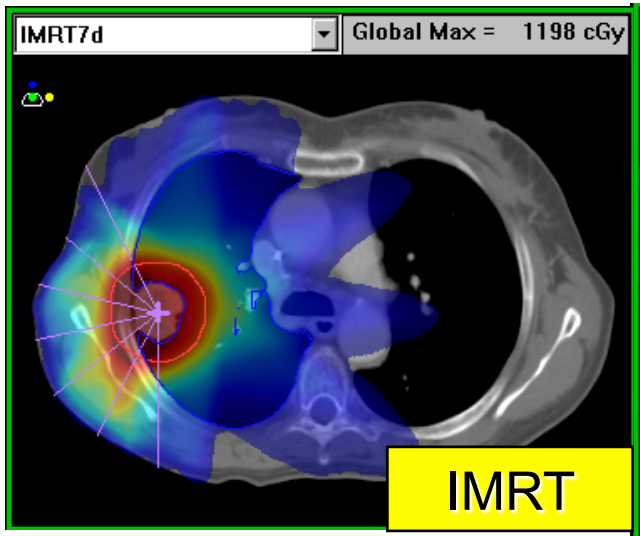
Photon beams are RT baseline. Hard competitors: small, reliable and not so expensive ->40 years R&D

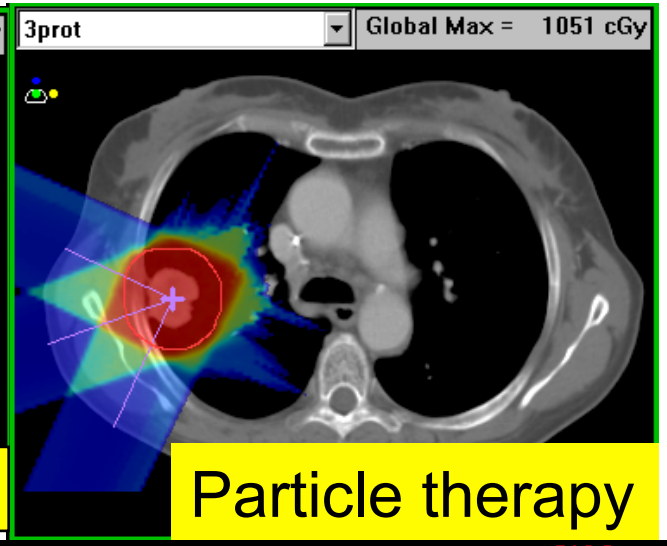
- Beam penetration in tissue function of the beam energy
- Peak of dose released at the end of the track, sparing the normal tissue
- Accurate conformal dose to tumor with Spread Out Bragg Peak





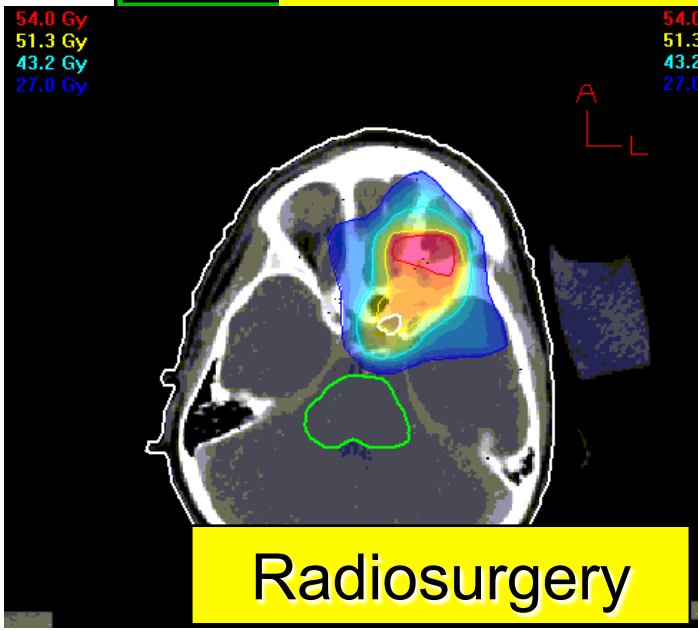
Examples of Photons vs Particle saga…

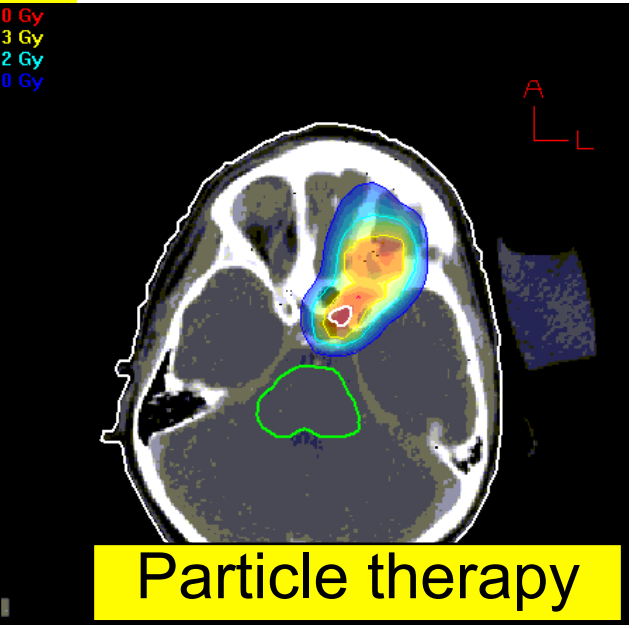




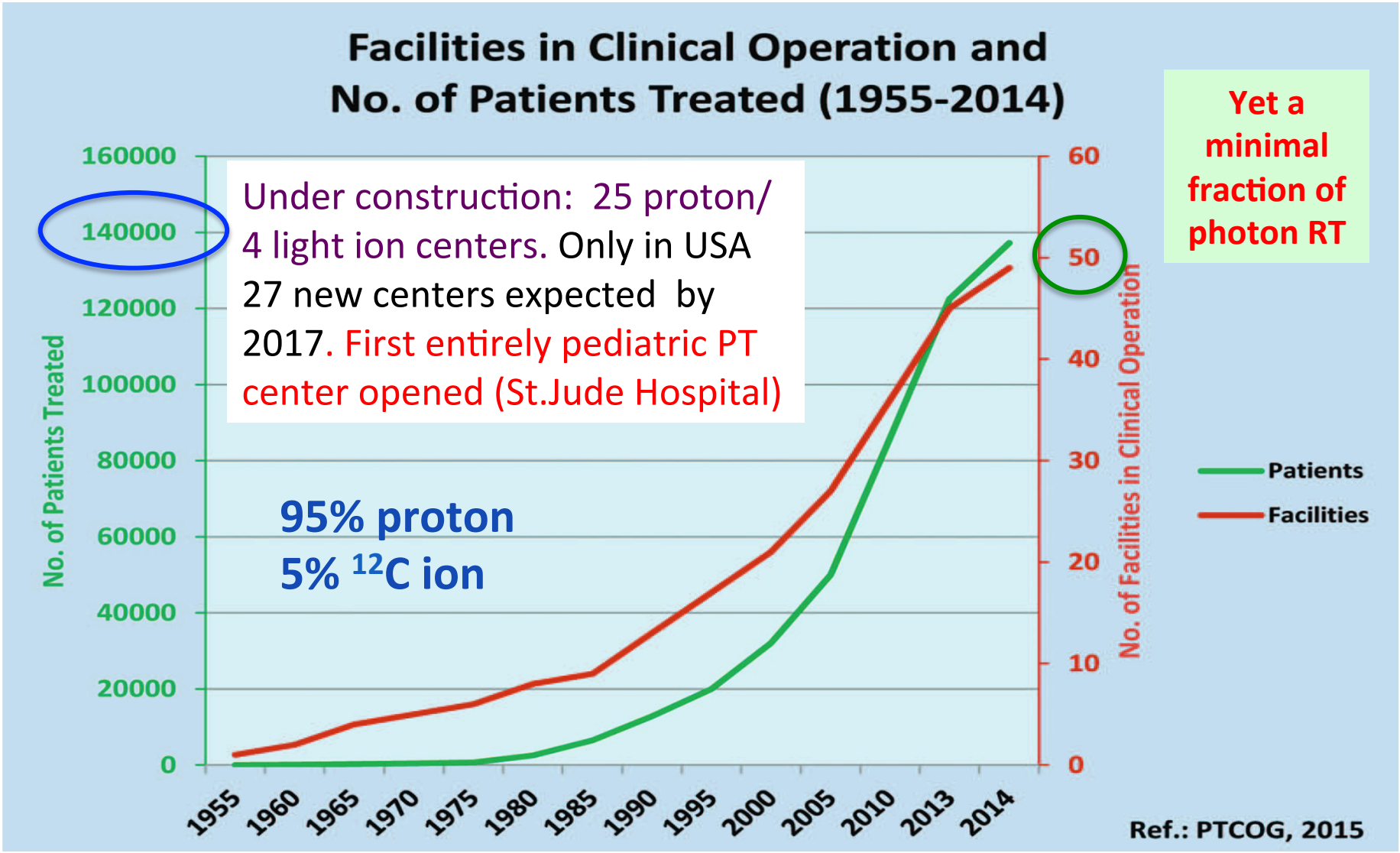
Particle therapy can easily show better selectivity with respect to photon techniques…

Yet, extensive randomized clinical trials (the only accepted method to assess eventual superiority of PT technique in EVM) are still missing





Charged Particle Therapy in the world



Community looking at ^{4}He – ^{16}O beams: begin to be tested at clinical center

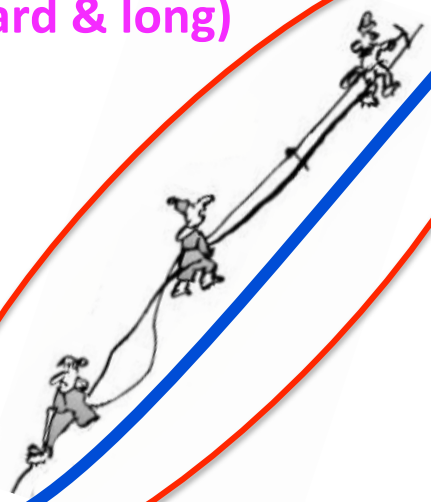
Typical Hype Cycle for Innovation Technology

Peak of inflated Expectations (general interest)

Plateau of Productivity (general acceptance)

Slope of Optimization (hard & long)

Trough of Disillusionment (system criticism)



If you are optimistic Particle Therapy is now in the Optimization Stage: plenty of space for R&D

Visibility

Technology trigger

Maturity

adapted from Becker & Townsend

The range verification problem

AAPM, August 2012

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

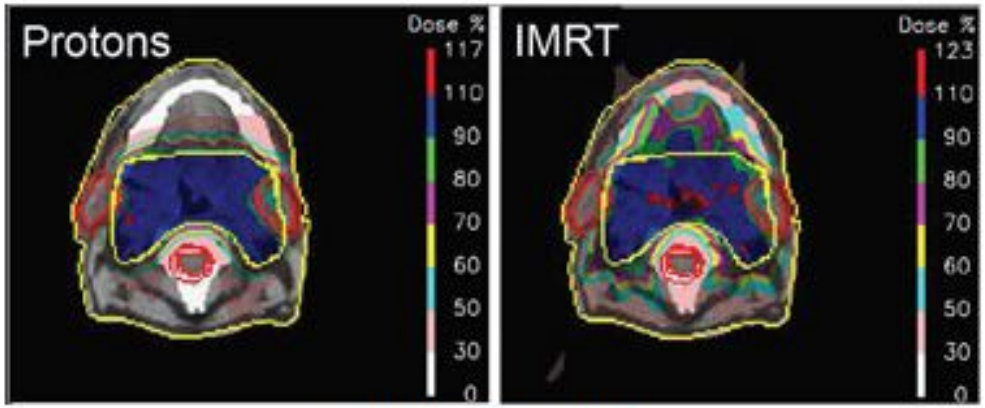
- 35 % unproven clinical advantage of lower integral dose
- 33 % range uncertainties
- 19 % never become a mainstream treatment option

RESEARCH

Aug 22, 2012

Will protons gradually replace photons?

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

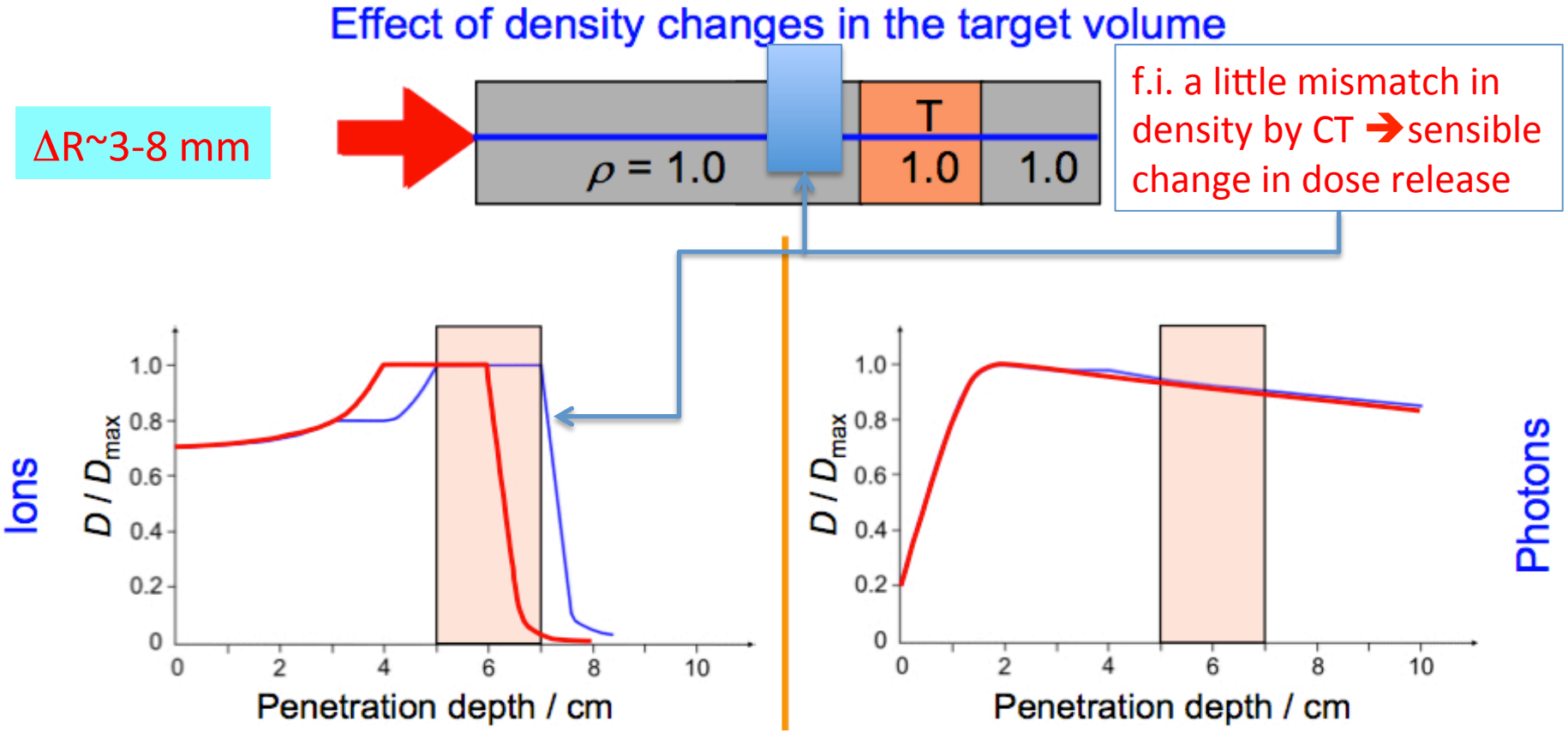


Protons versus IMRT

http://medicalphysicsweb.org/cws/article/research/50584

Dose profiling in Particle Therapy

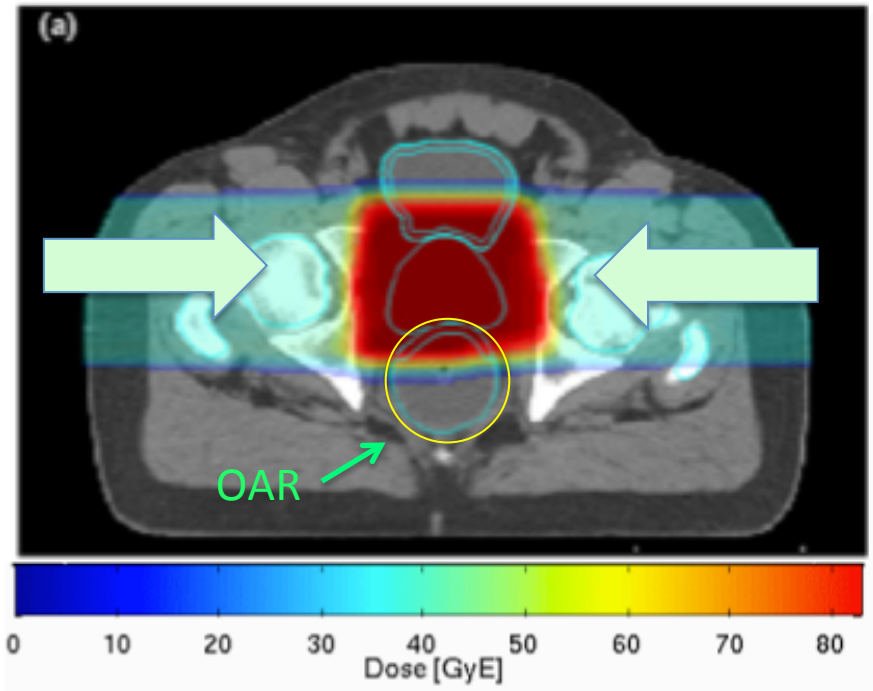
Why is so crucial to monitor the dose in particle therapy with respect to photon RT? It is like firing with machine-gun or using a precision rifle..
Inhomogeneities, metallic implants, CT artifact, HU conversion, inter session anatomical/physiological changes-> range variations



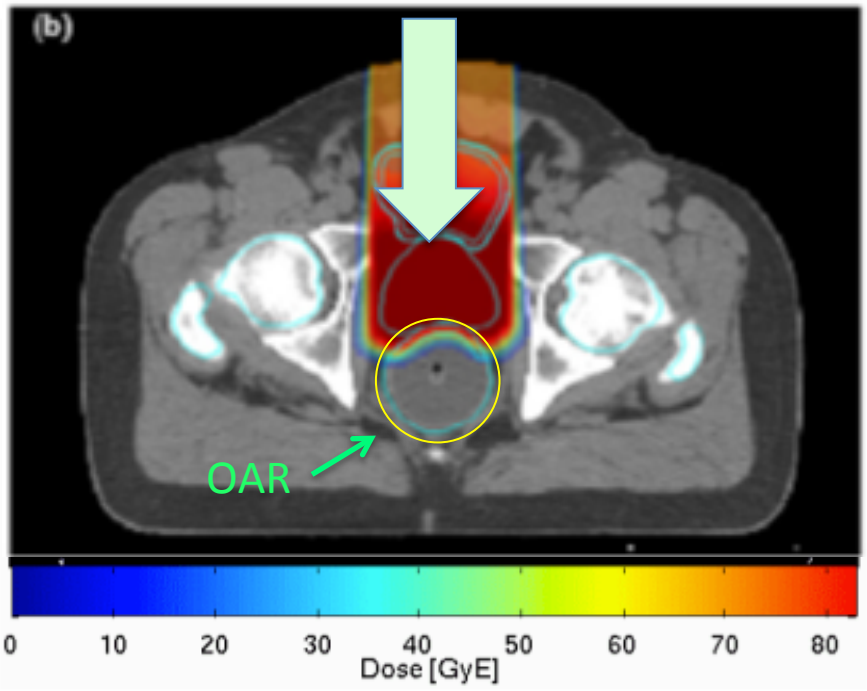
Accounting for uncertainties in the clinical practice

[Tang et al. 2012]

Current approach:
Opposed fields, overshooting



Desirable approach:
Different beam angles and no overshooting



Protons

Spec's of particle therapy monitor

In PT the beam is easily monitored in the transverse direction but longitudinally stops inside the patient.

A PT range monitor should measure the shape and (possibly) the absolute value of dose release with the following spec's:

- ✓ Must relay on the signal by secondary particles, generated by the beam, that comes out from the patient
- ✓ Must deal with the background of the "non signal" secondaries that come out
- ✓ Measurements and feed-back should be provided during the treatment (in-beam). Even better if the monitor response can follow the irradiation scan on line
- ✓ Must be embedded in a treatment room: space, reliability and "easy to run" issues are crucial

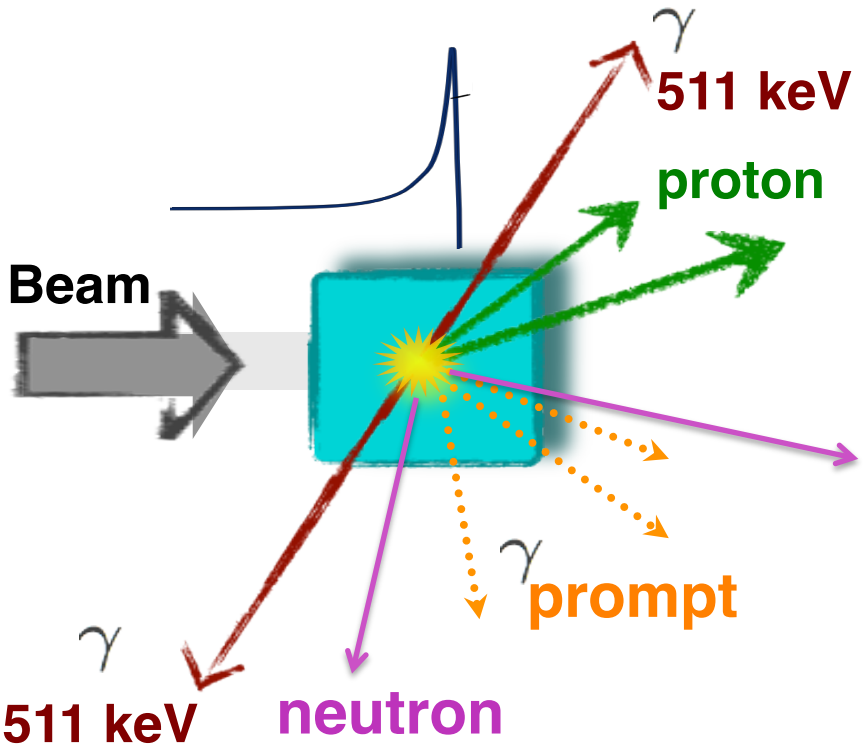
Beam secondaries.. Background or Signal?

Indicative secondary flux emitted on full solid angle by ~ 150 MeV p beam

Incident protons:	1.0
Photons	0.3
Neutrons	0.15
Protons	0.005

G4 simulation

How much are the nuclear models reliable? Huge experimental and theoretical development effort ongoing to improve model and update MC



The p, ^{12}C beams generate a huge amount of secondaries: prompt γs, PET- γs, neutrons and charged particles (in particular ^{12}C beam)

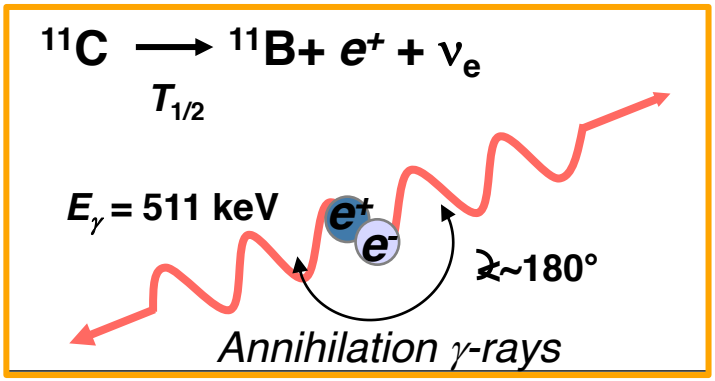
Can be used to track the tumor path inside the patient

baseline dose monitoring in PT : PET

Baseline for monitor in PT is PET : autoactivation by hadron beam that creates β^+ emitters.

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

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



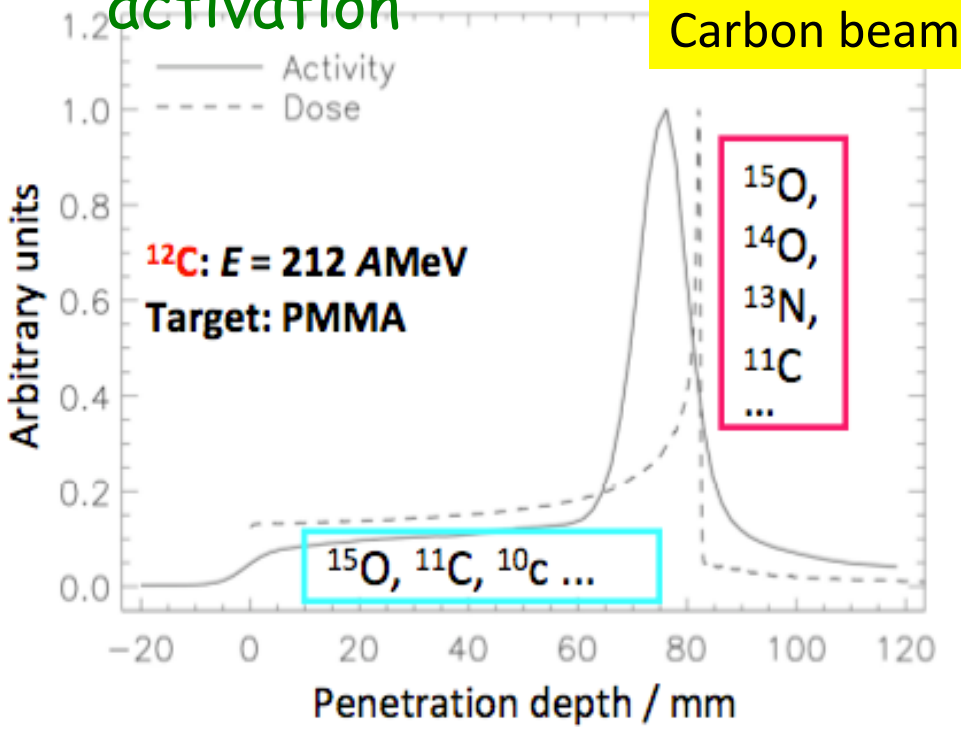
Correlation between β^+ activity and dose

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

p treatment uses more particles than ^{12}C treatment(dose ~ Z^2)

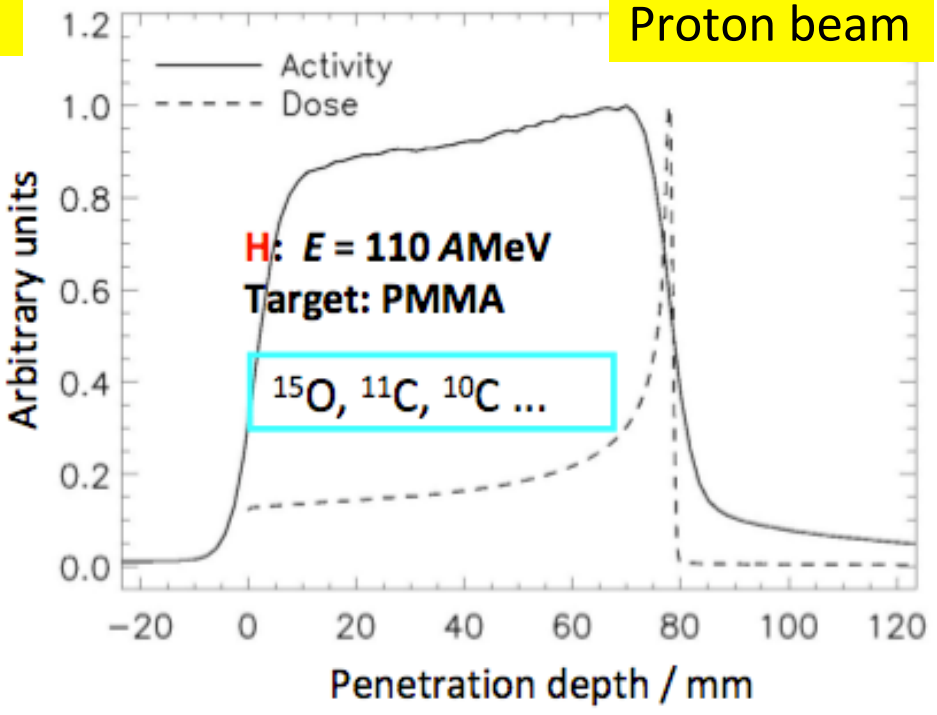
beam & target activation

Carbon beam



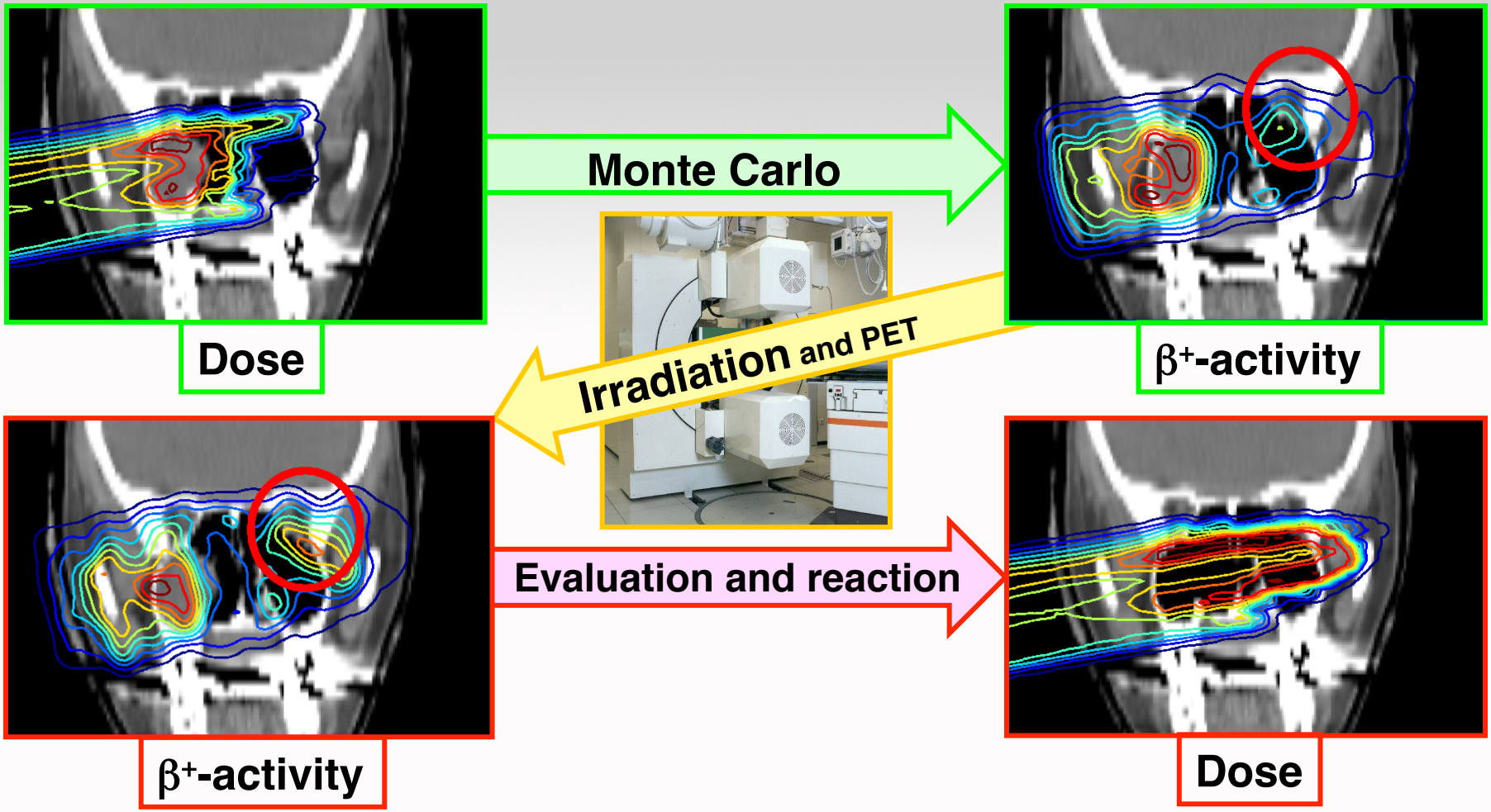
Target activation

Proton beam



In-Vivo range measurement with PET: workflow and potential

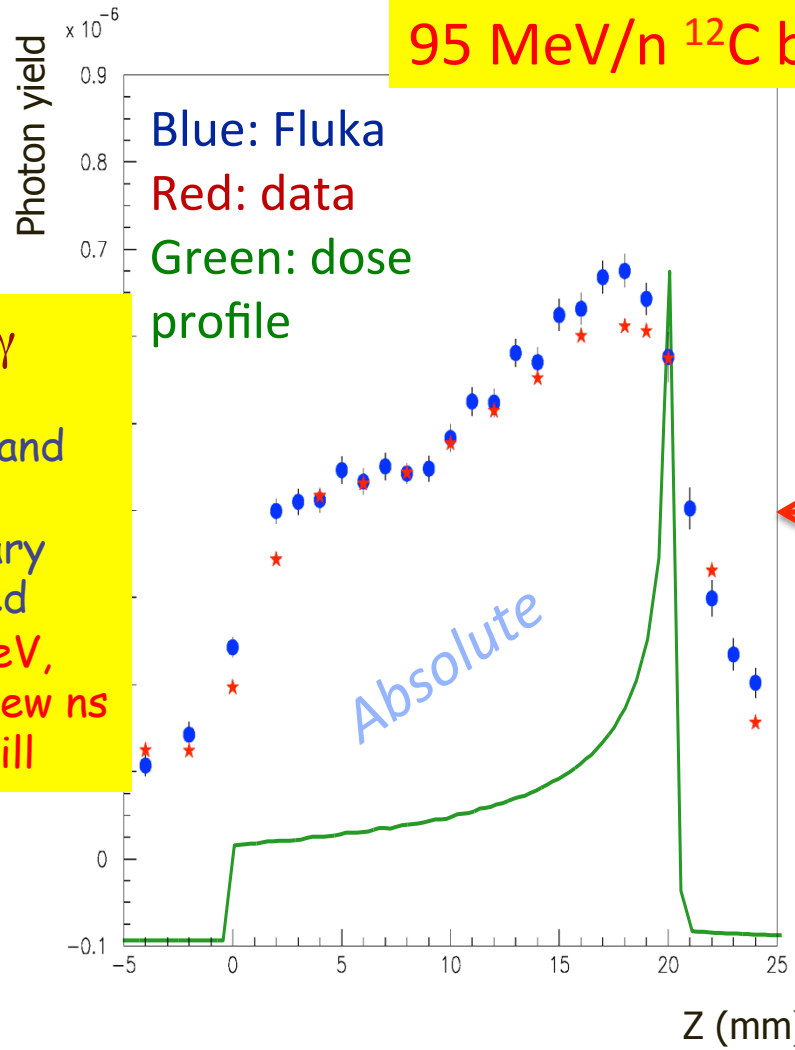
W. Enghardt et al.: Radiother. Oncol. 73 (2004) S96



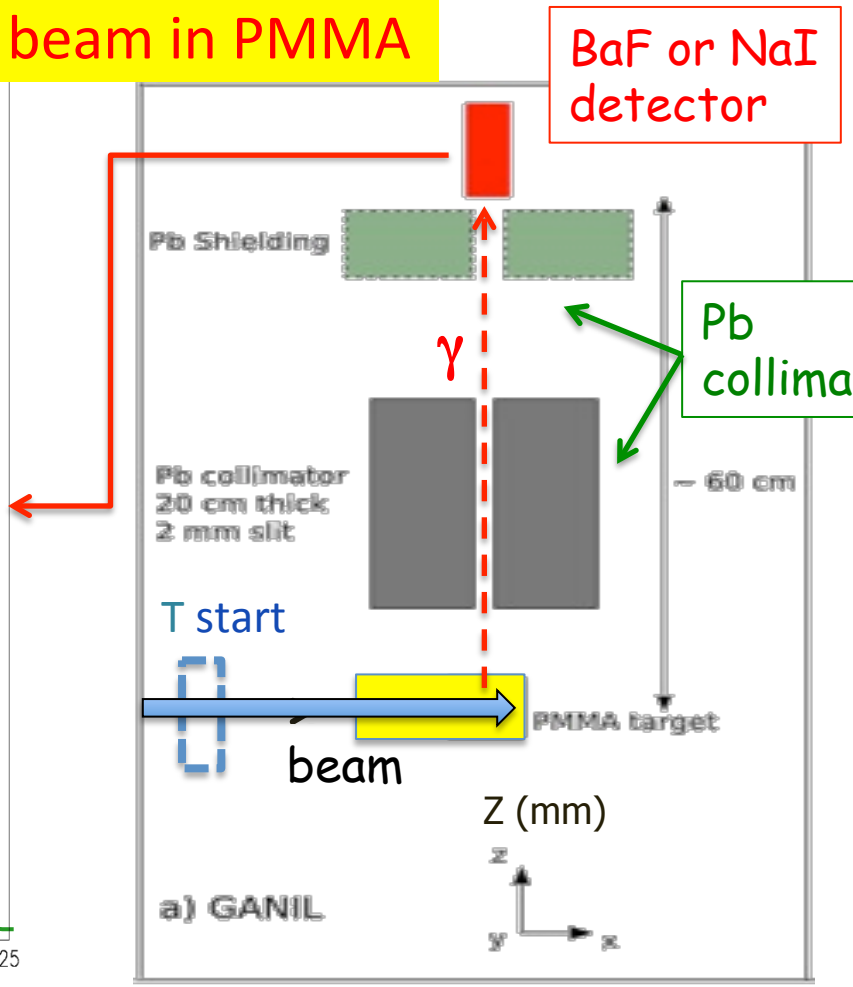
Problem to solve: Metabolic Washout! In-beam measurement is really necessary, but difficult. Trade-off: in-room or off-room measurement after irradiation (Heidelberg for example)

The prompt photons solution

95 MeV/n ^{12}C beam in PMMA



90 deg γ signal
Energy and ToF of secondary recorded
E_γ > 2 MeV, within few ns from spill

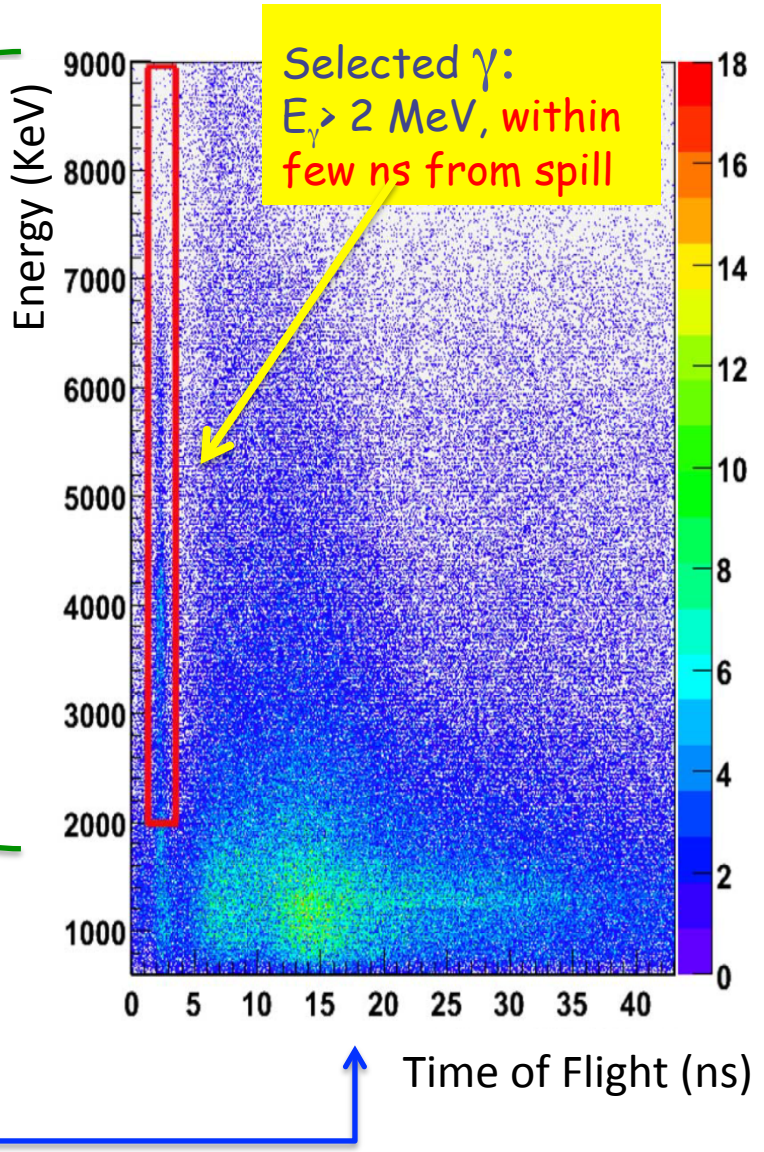


Courtesy of Alfredo Ferrari

[sketch and exp. data taken from F. Le Foulher et al IEEE TNS 57 (2009), E. Testa et al, NIMB 267 (2009) 993. exp. Data reevaluated in 2012 with substantial corrections

The prompt γ emission: summary

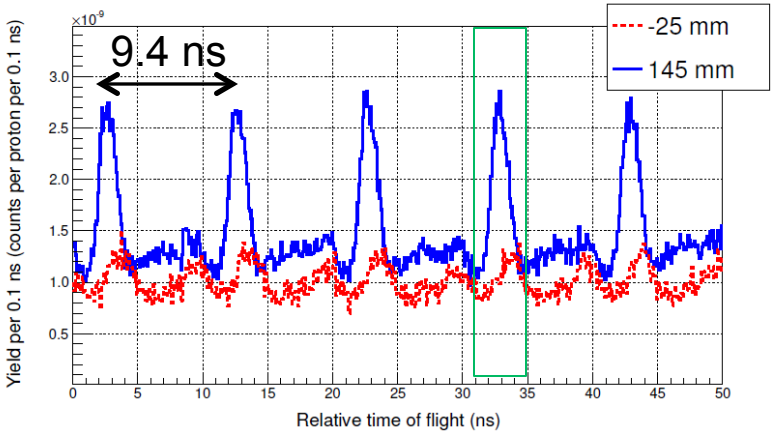
- The gamma are quite copiously produced by proton and ^{12}C beam by nuclear excitation.
- The emission region stretches along all the beam path but has been shown to ends near the Bragg peak for both beams.
- It's not simple backpointing the γ direction: the γ energy is in the 1-10 MeV range-> much more difficult to stop and collimate with respect to ^{99}Tc 144 KeV γ in standard SPECT imaging
- Huge background (beam, energy and site specific) due to neutrons & uncorrelated γs produced by neutrons. TOF not easy to exploit in clinical practice

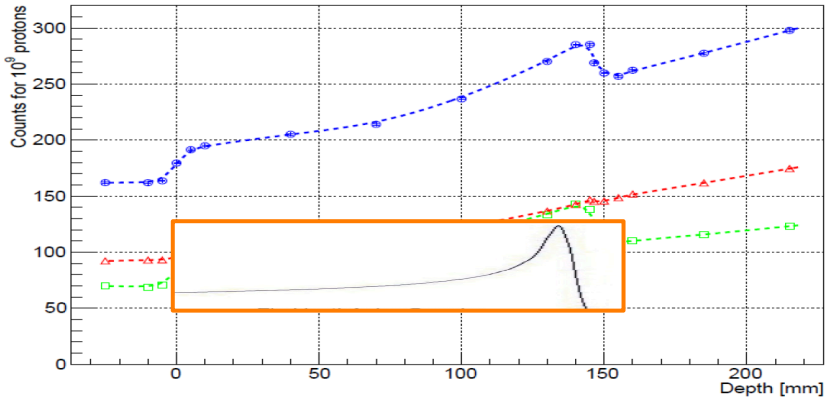


TOF & Pγ profiles in collimated cameras

160 MeV protons in PMMA

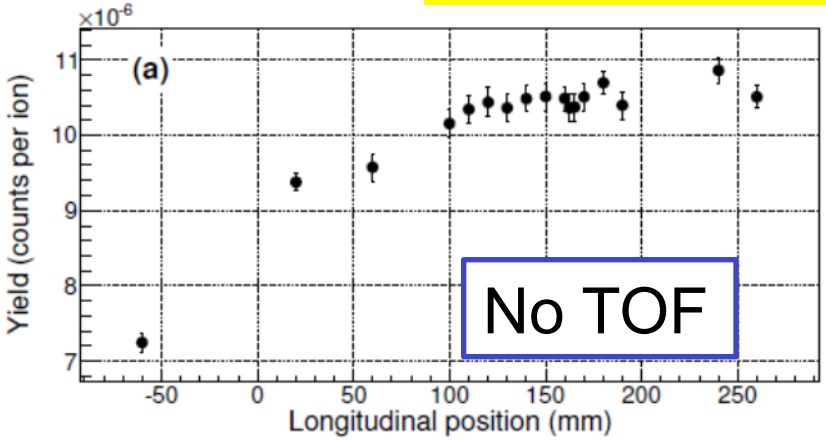
Roellinghoff PMB 2014

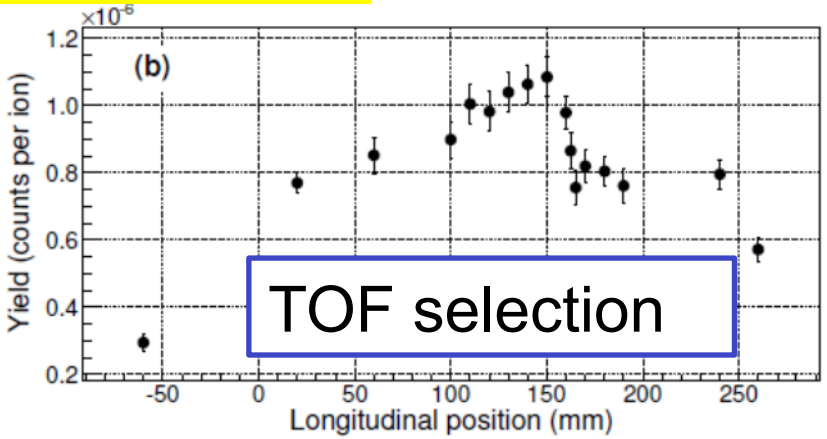




310 *A*MeV carbon ions in PMMA

M. Pinto, New J Phys



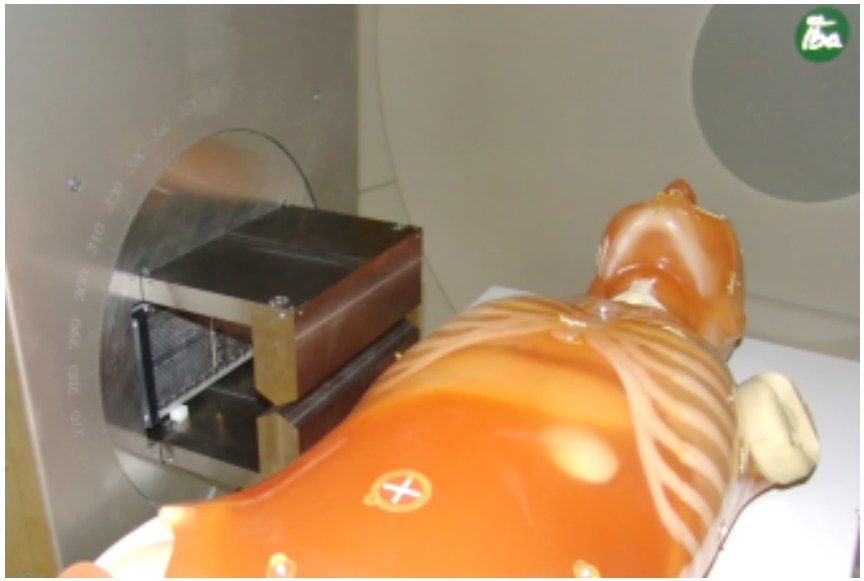


TOF : mandatory for carbon ions

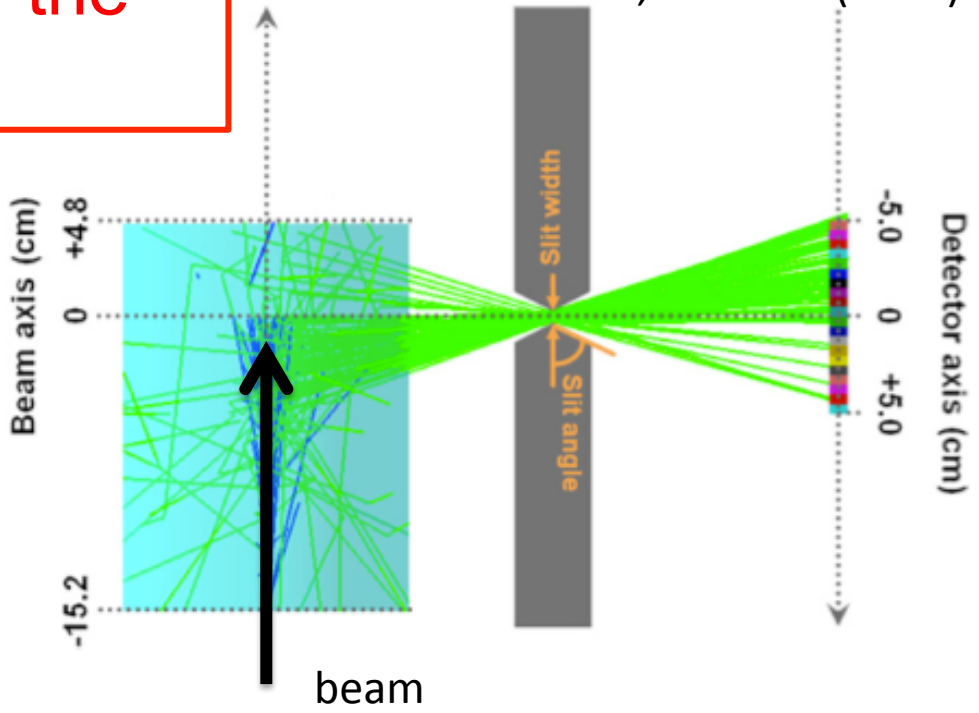
Not easy with clinical beam!!!

Courtesy of D. Dauvergne

The simpler, the better: the IBA slit camera



J Smeets, PMB. **57** (2012)



Designed and assembled by IBA, in collaboration with Politechnic Milano.

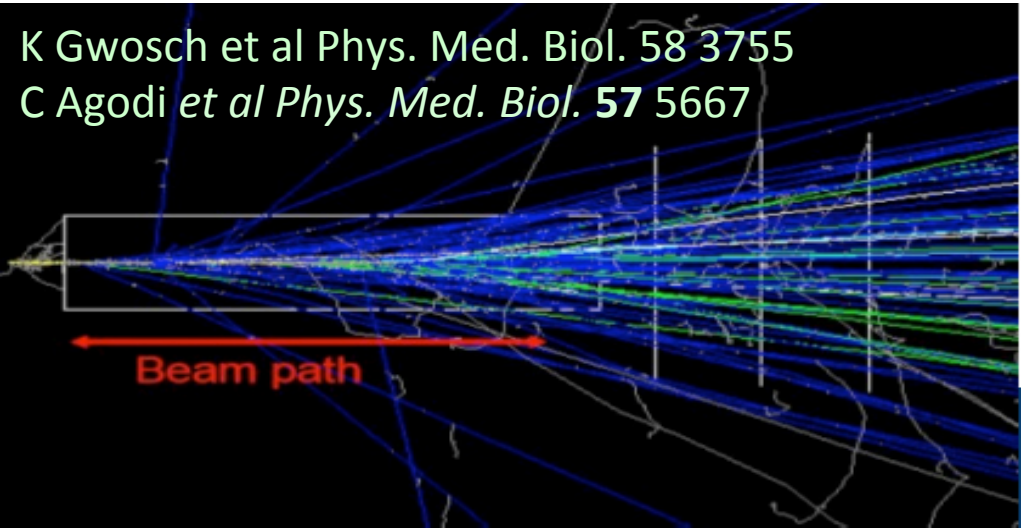
Benchmarking against alternative detection methods (multi-slit) with U. Lyon and Oncoray-Dresden

Close to clinical use, few mm accuracy

What about heavier beam (^{12}C) ? LET grows as Z^2 and the nuclear interaction increase with A. Thus, for the given dose, ^{12}C gives:

- less prompt γ than proton
- more background than proton

Non proton beams : something else useful? Charged fragments (protons)



Charged secondaries have several nice features as

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

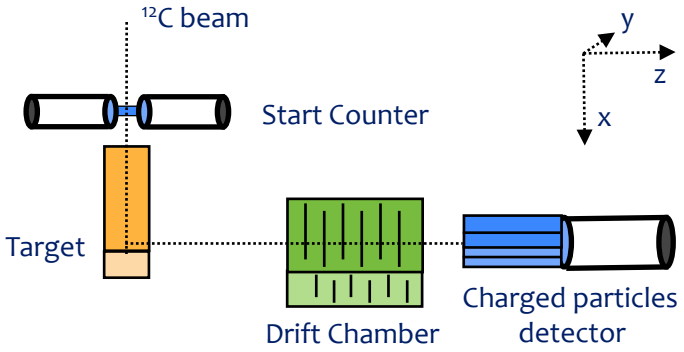
BUT…

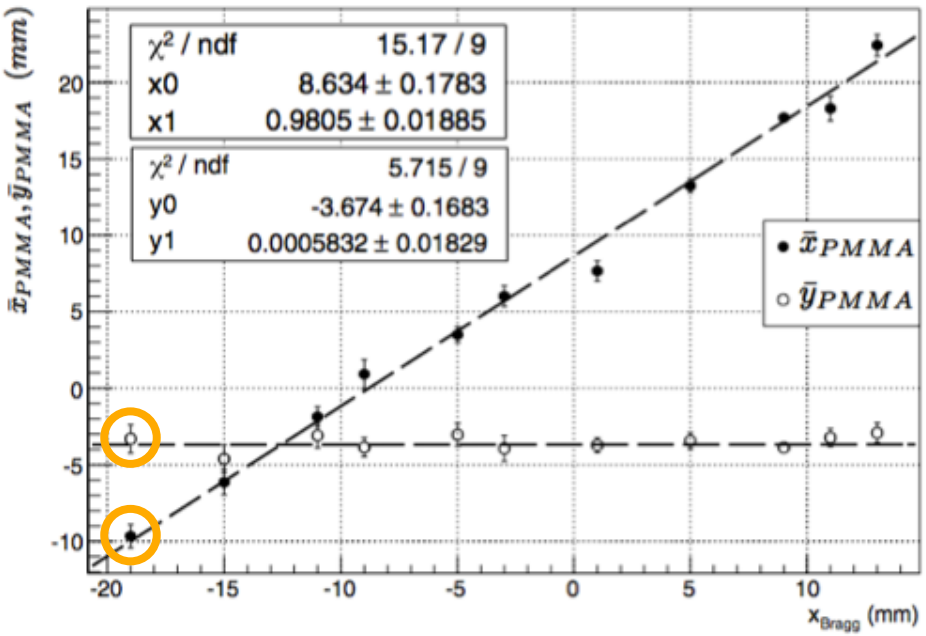
- They are forward peaked
- Energy threshold to escape the patient ~ 80-90 MeV
- They suffer multiple scattering inside the patient -> worsen the back-pointing resolution

MC highly unreliable, probing the very tail of the angular distribution of secondary

Charged secondary emitted from BP ?

- Measurements at LNS (Catania) ^{12}C beam @ 80 MeV/ nucleon. Range in PMMA phantom ~ 1 cm.
- Corresponds to the last part of the path in the patient of higher energy, longer range pencil beam -> signal from BP region
- Moving the target the charged signal follows





Agodi et al. PMB 2012

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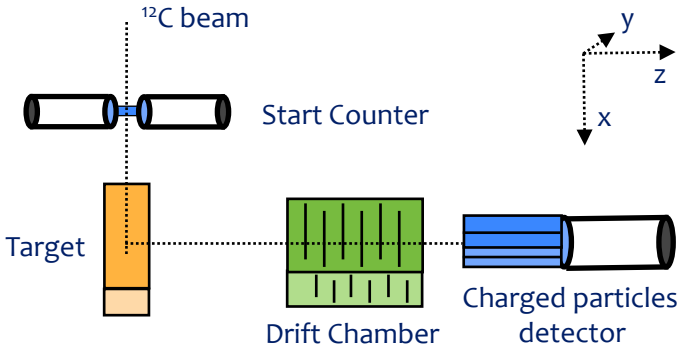

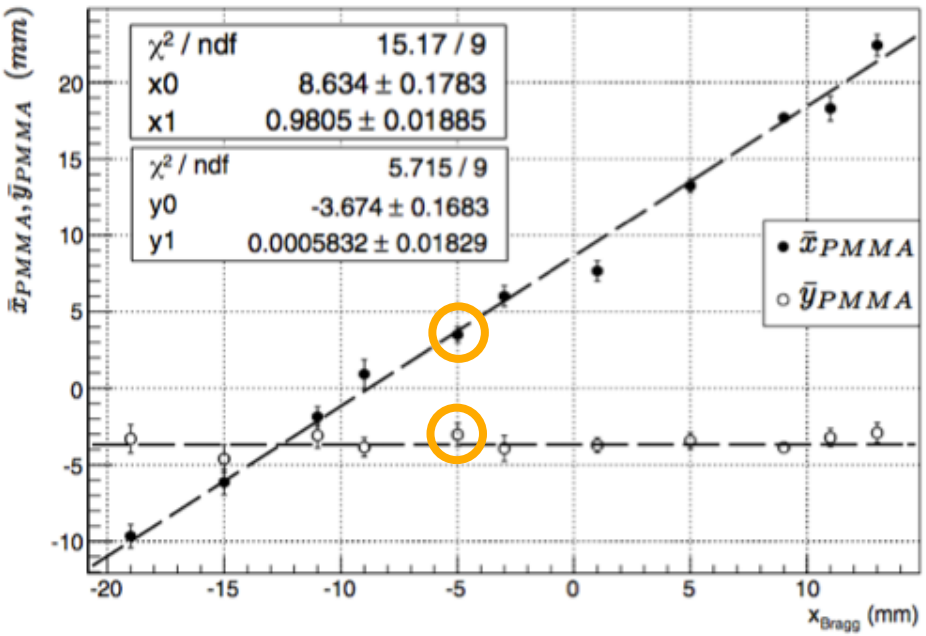

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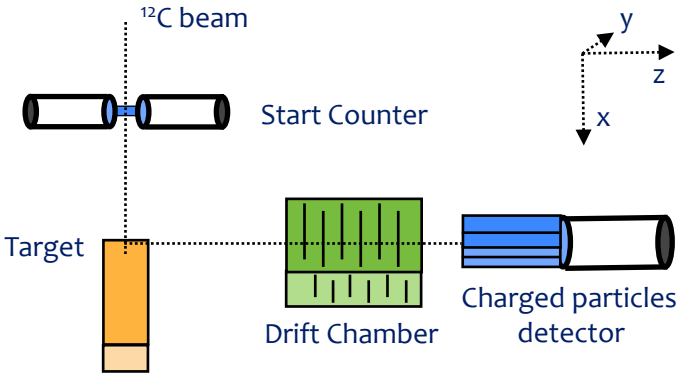
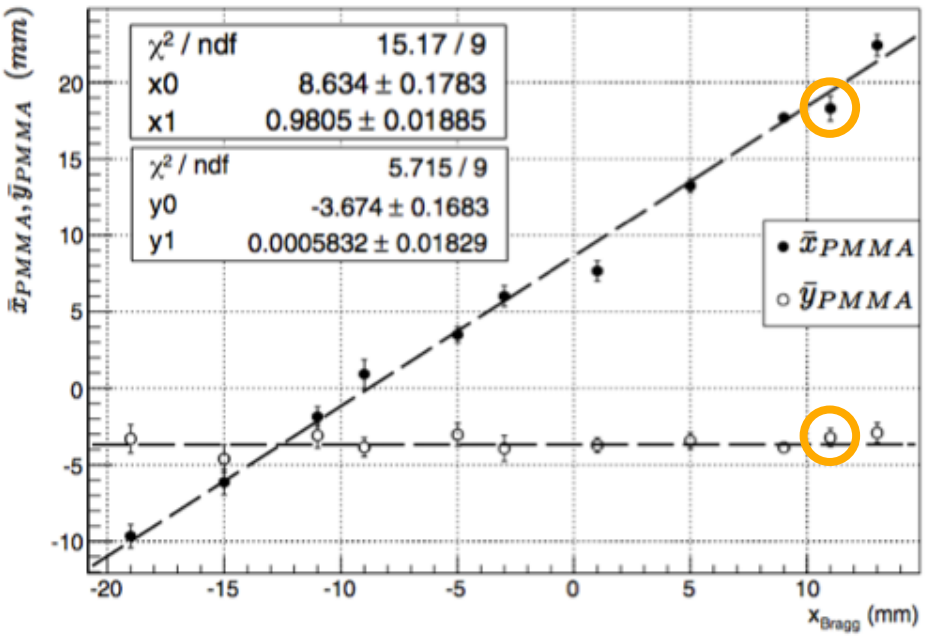


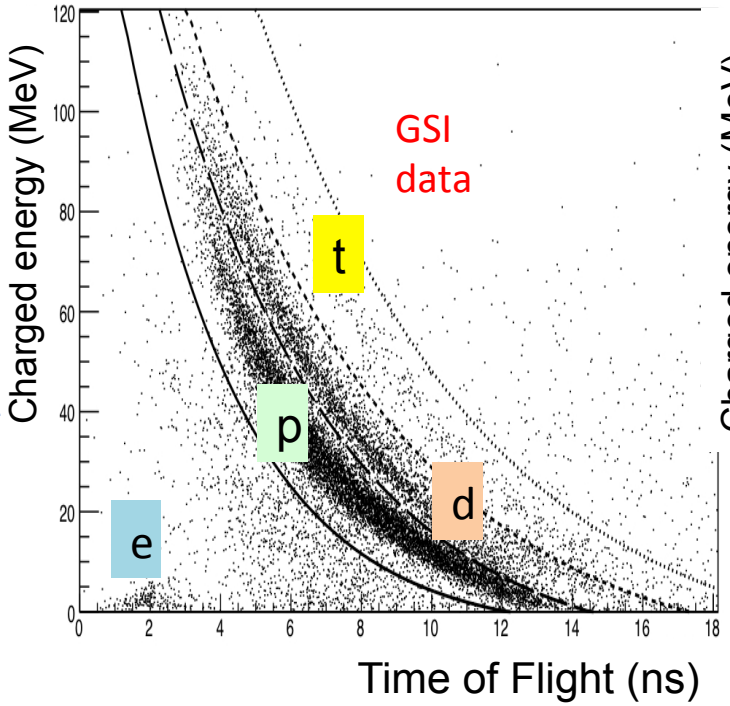


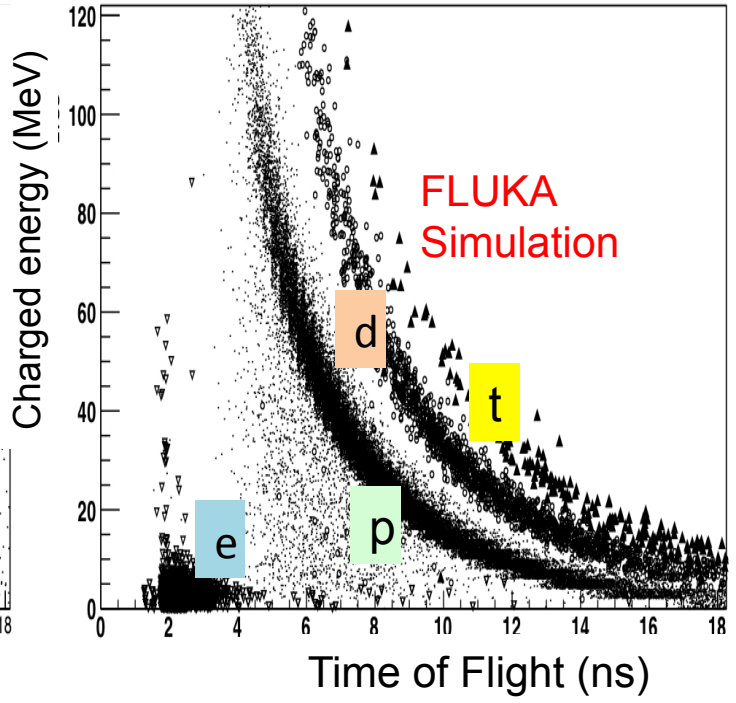
Agodi et al. PMB 2012

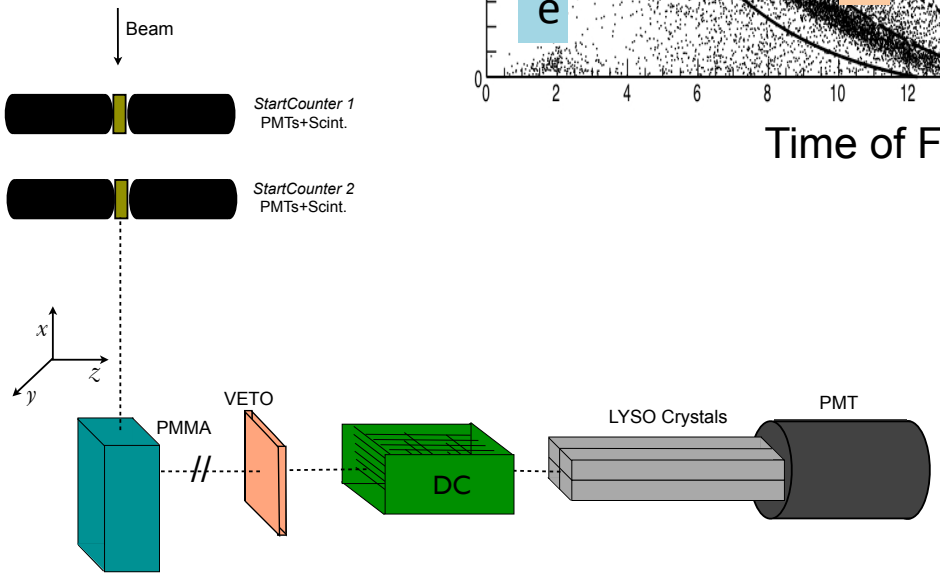
charged secondaries & ^{12}C beam radiography

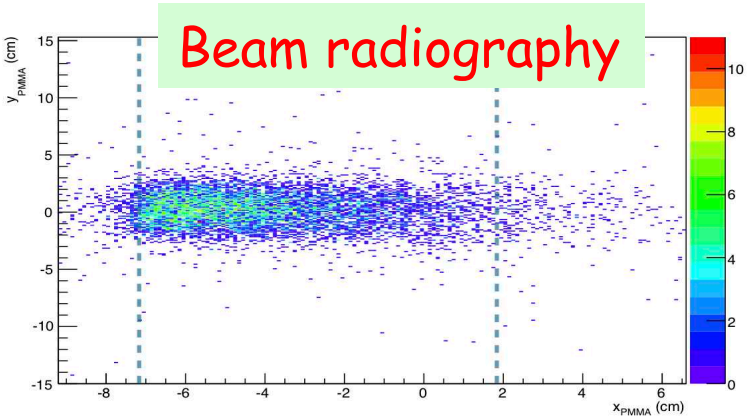
L.Piersanti et al. PMB, 2014

Charged secondaries produced at 90^0 wrt the beam from PMMA target on 220 AMeV. ^{12}C beam at GSI







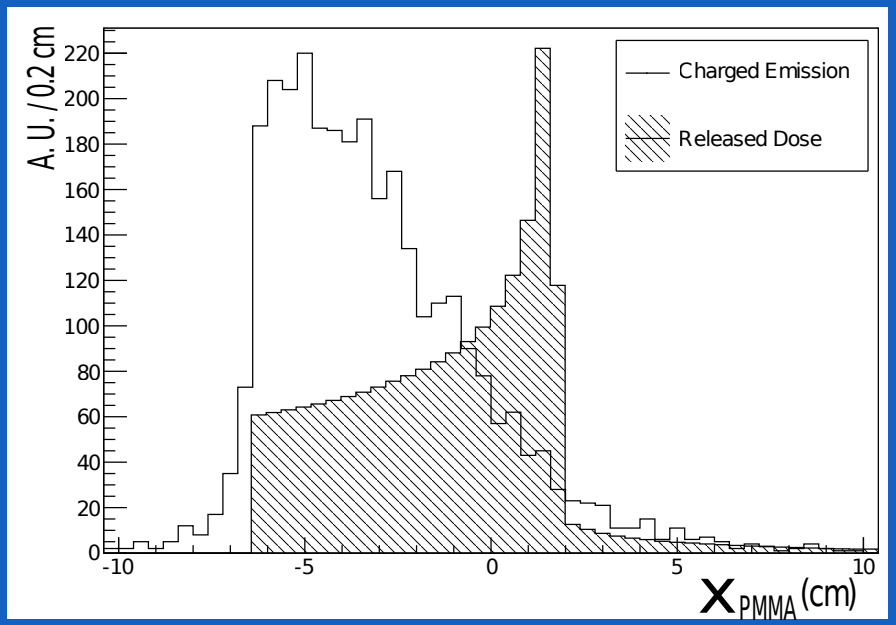


Secondary emission point, BP and the patient

The materials crossed to exit from the patient modifies the detected distribution (absorption & MS). Similar approach of PCT needed: exploiting the knowledge of the pencil beam transverse position and the CT deconvolute the emission shape

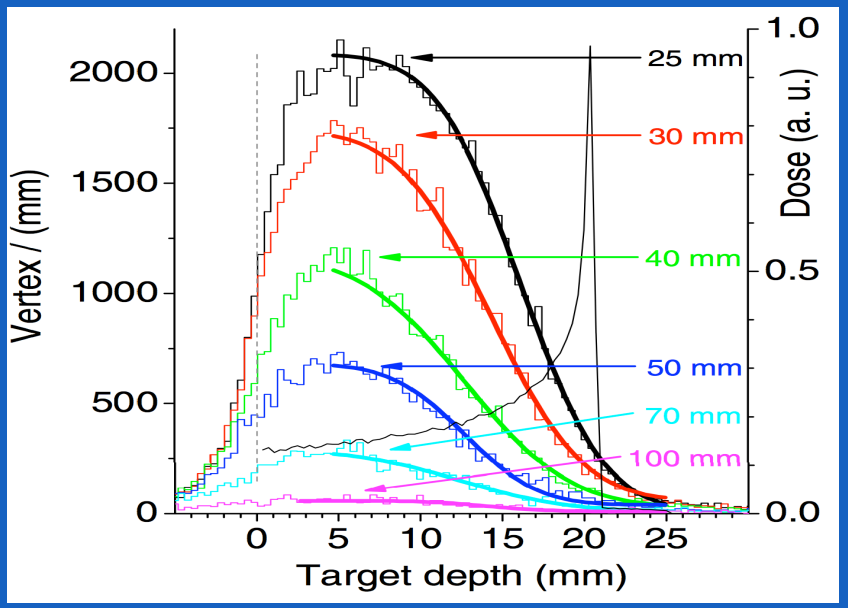
Measured emission shape of protons outside a 5 cm thick PMMA at 90^0 wrt the direction of 220 AMeV ^{12}C beam

L.Piersanti et al. PMB, 2014



Simulated emission distribution shape of protons as detected outside different PMMA thickness at 30^0 wrt the direction of 95 AMeV ^{12}C beam

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



Carbon beam @90° (reference runs)

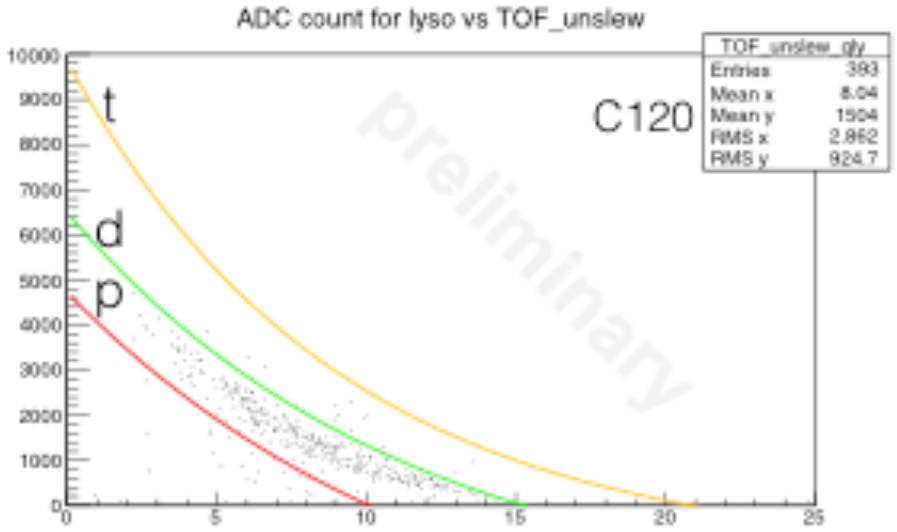
Charged secondaries monitoring

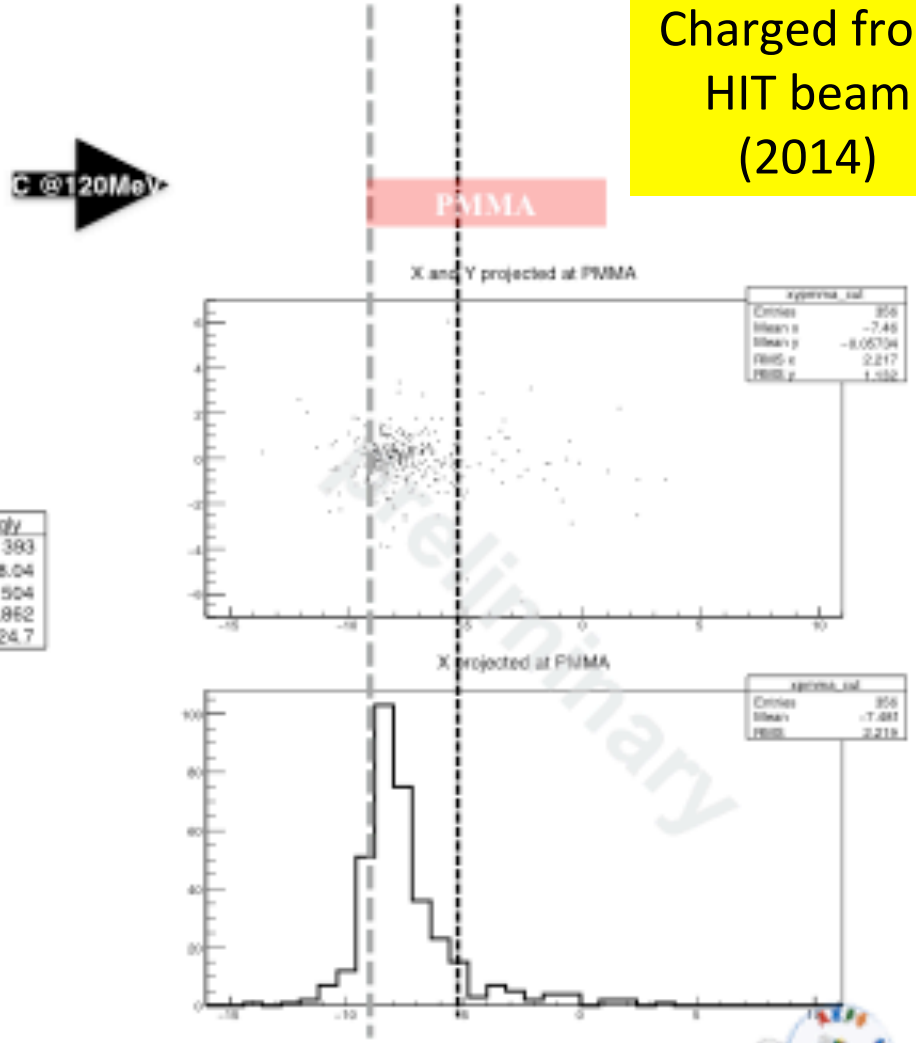
A non negligible production of charged particles at large angles is observed for all beam types.

The emission shape is correlated to the beam entrance face and BP position as already measured with ^{12}C at GSI.

[Piersanti et al. PMB, 59 (2014)]

Charged from HIT beam (2014)





To be submitted to PMB

preliminary

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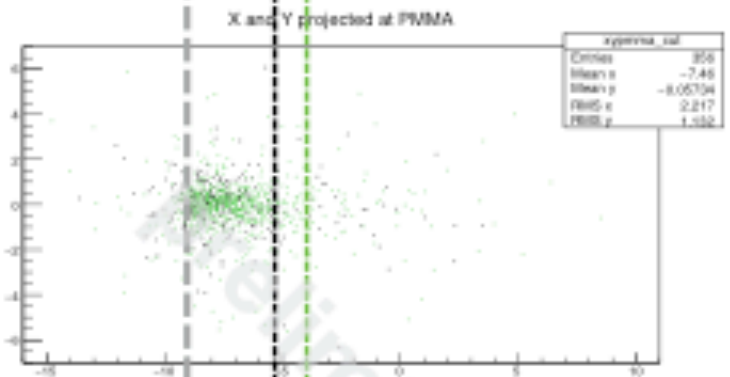

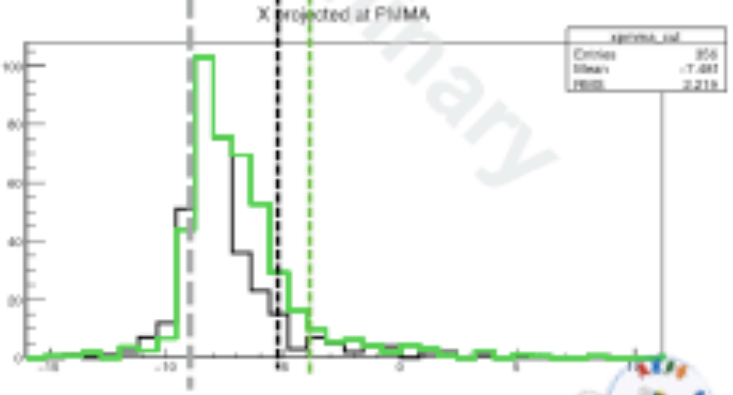

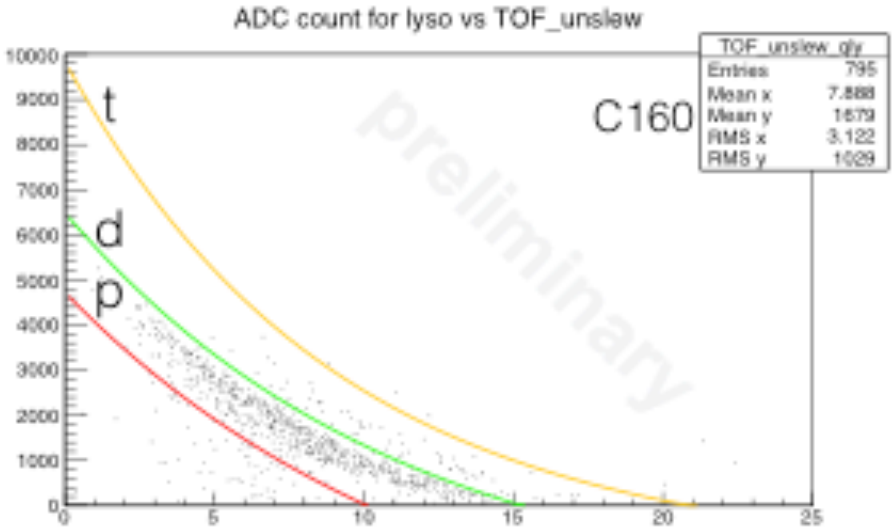

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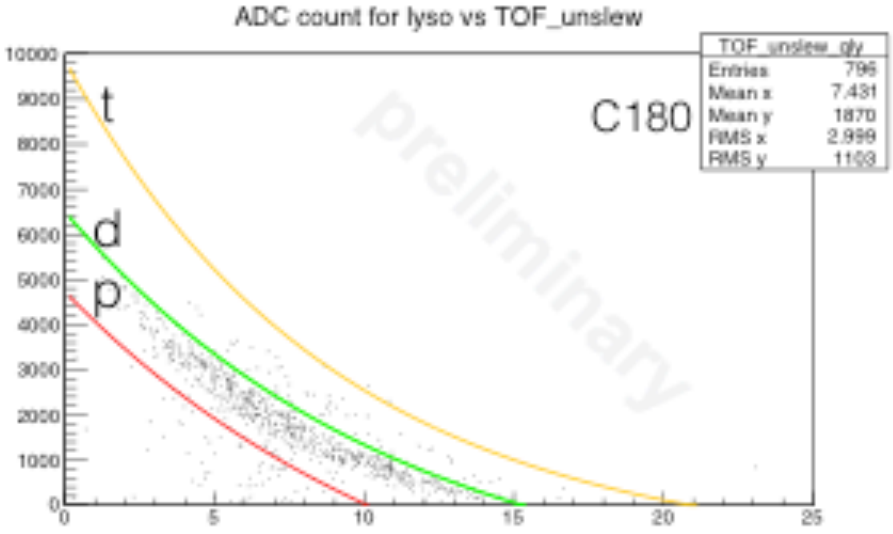

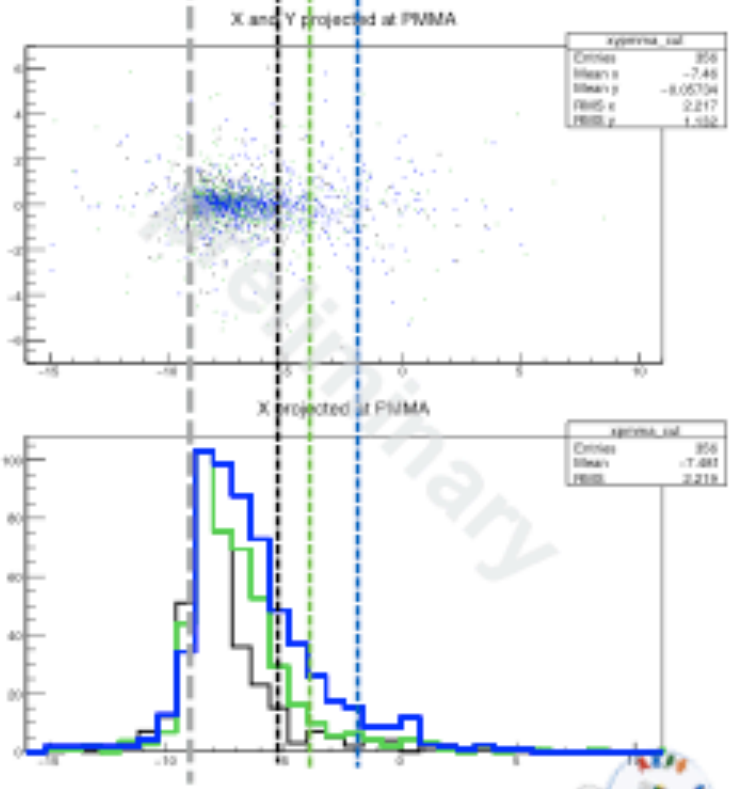

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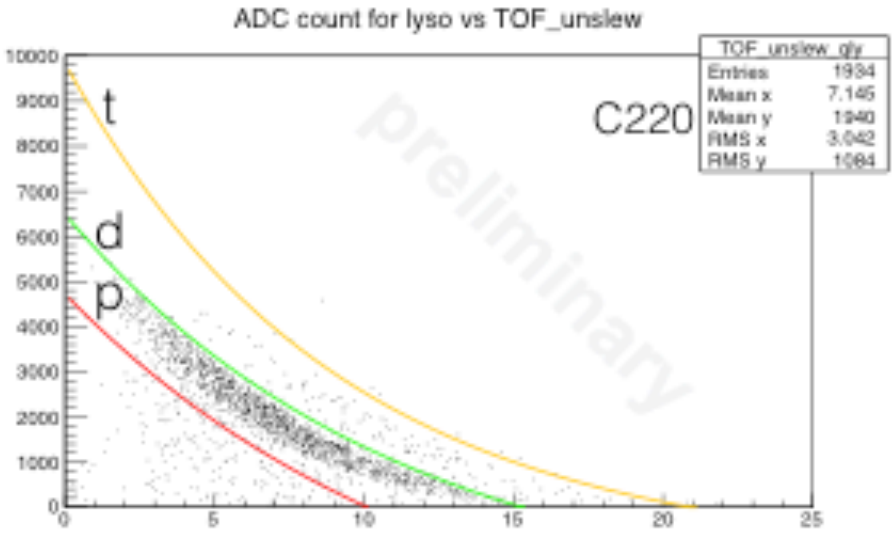
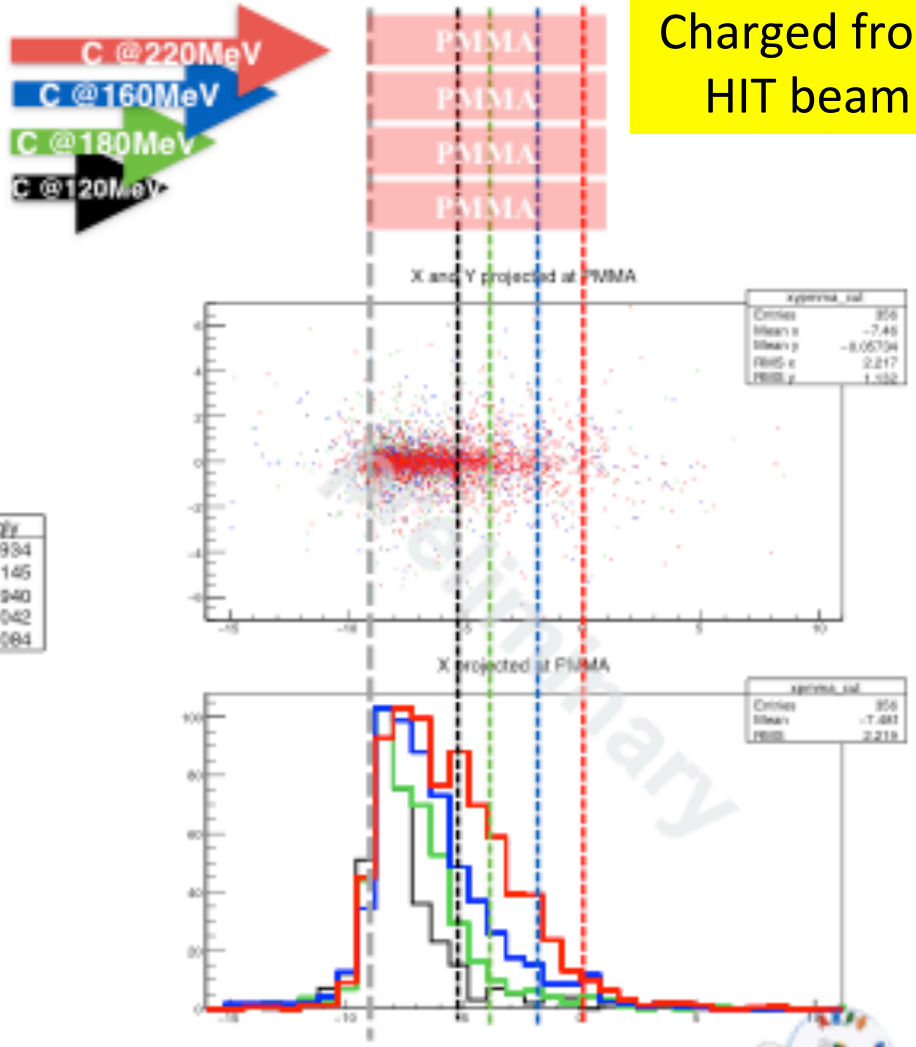


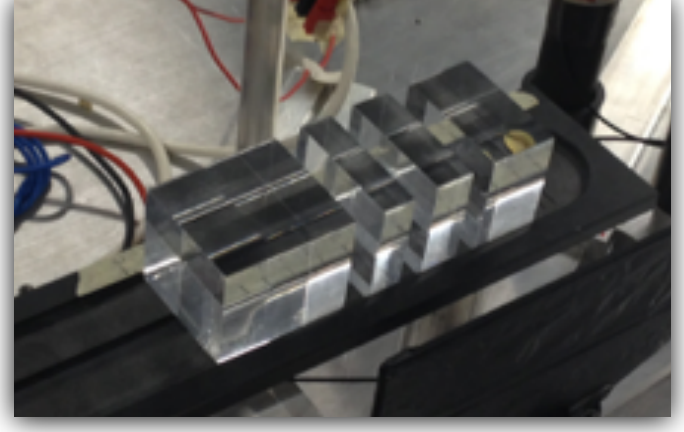


Charged from HIT beam

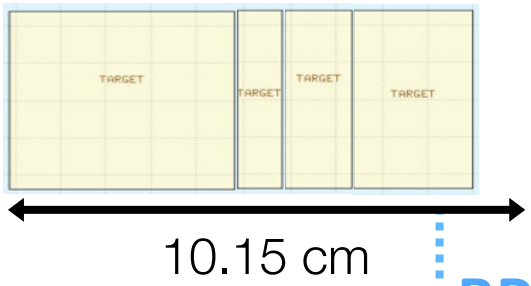
To be submitted to PMB

preliminary

Detecting inhomogeneities



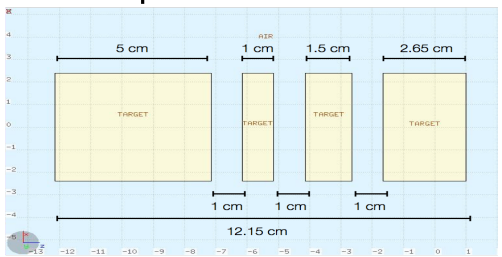
Reference Target: no AIR spaces

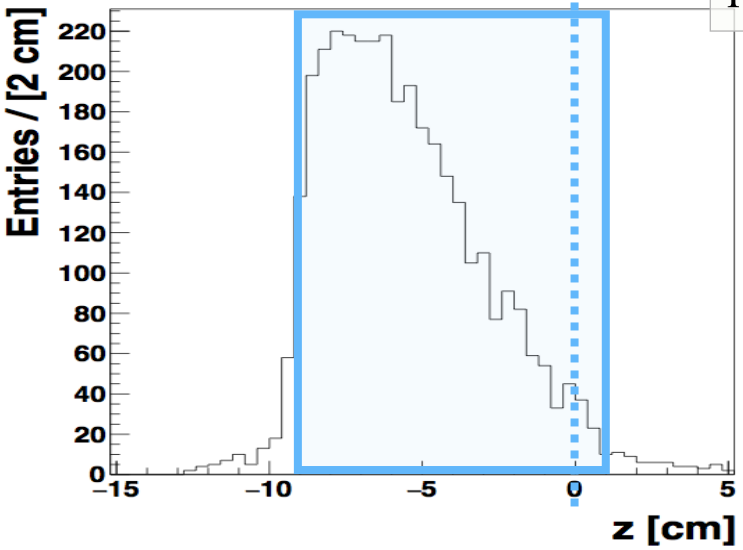


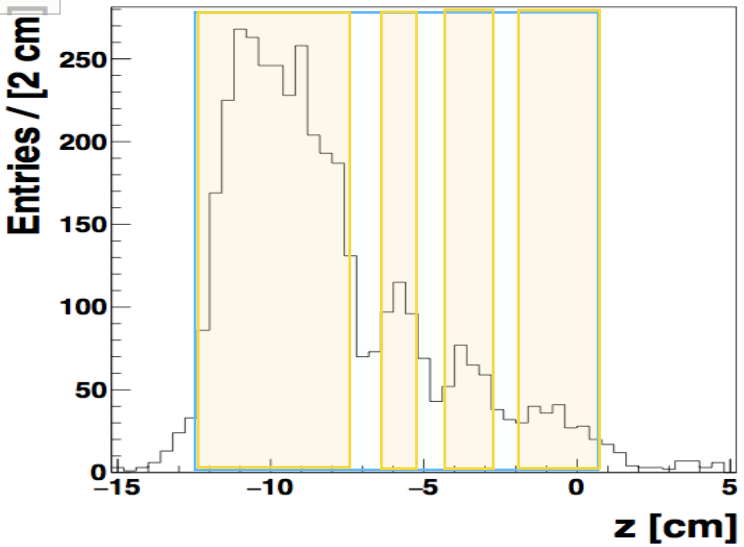
preliminary

~4k tracks;
#^{16}O ions: 8 10^8

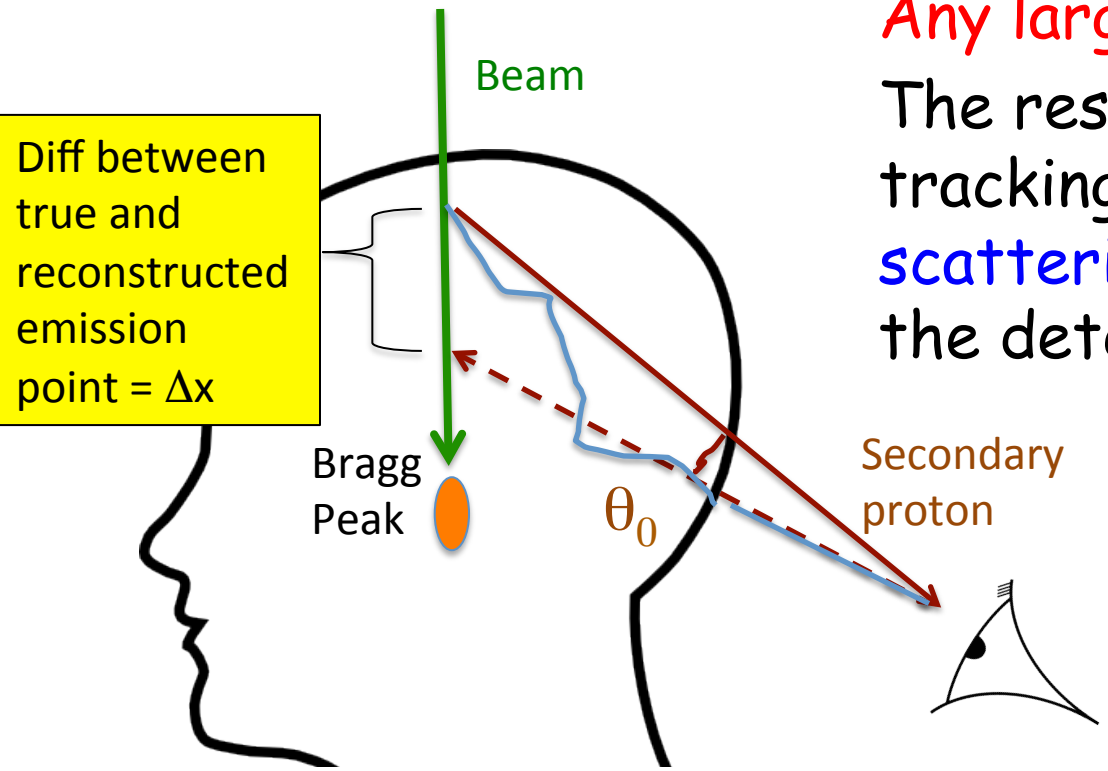
Segmented 12.15 cm Target: with AIR spaces







Which detector should be used?



Any large tracking detector!!

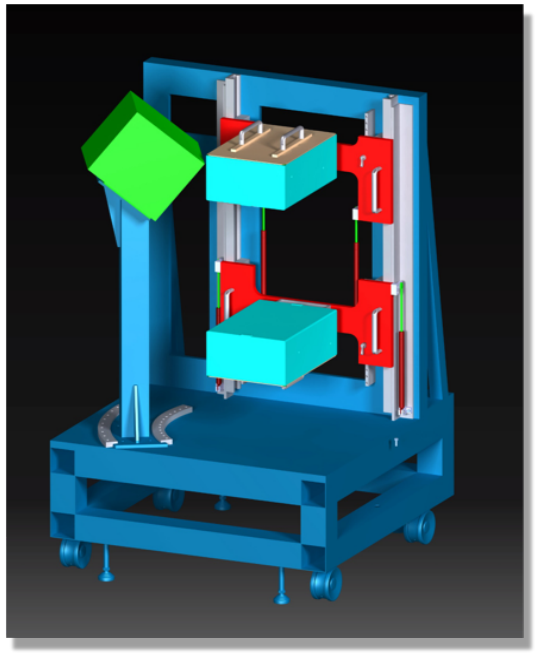
The resolution of the back-tracking is limited by the multiple scattering in the patient, not by the detector resolution..

Typical resolution on Δx is of the order of 6-8 mm

Integrating enough statistic (~ 10^3 events) helps to lower the accuracy on the emission point distribution (and then on the beam profile) to mm level ➔ detector size

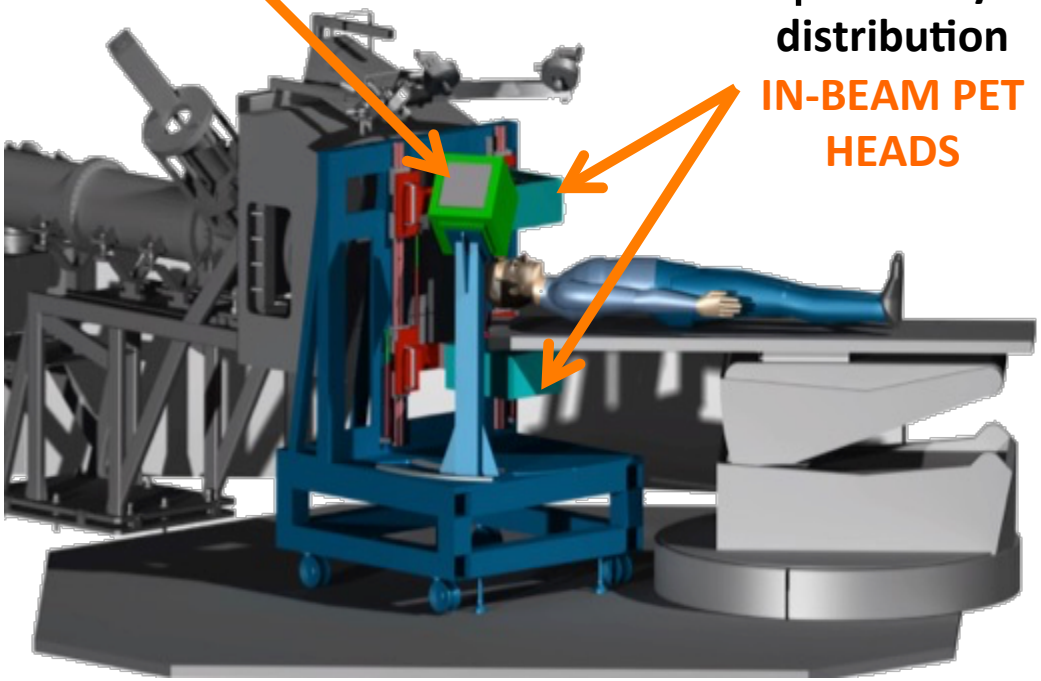
The InSide Project @ CNAO

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



proton emission
Tracker + Calorimeter = DOSE PROFILER

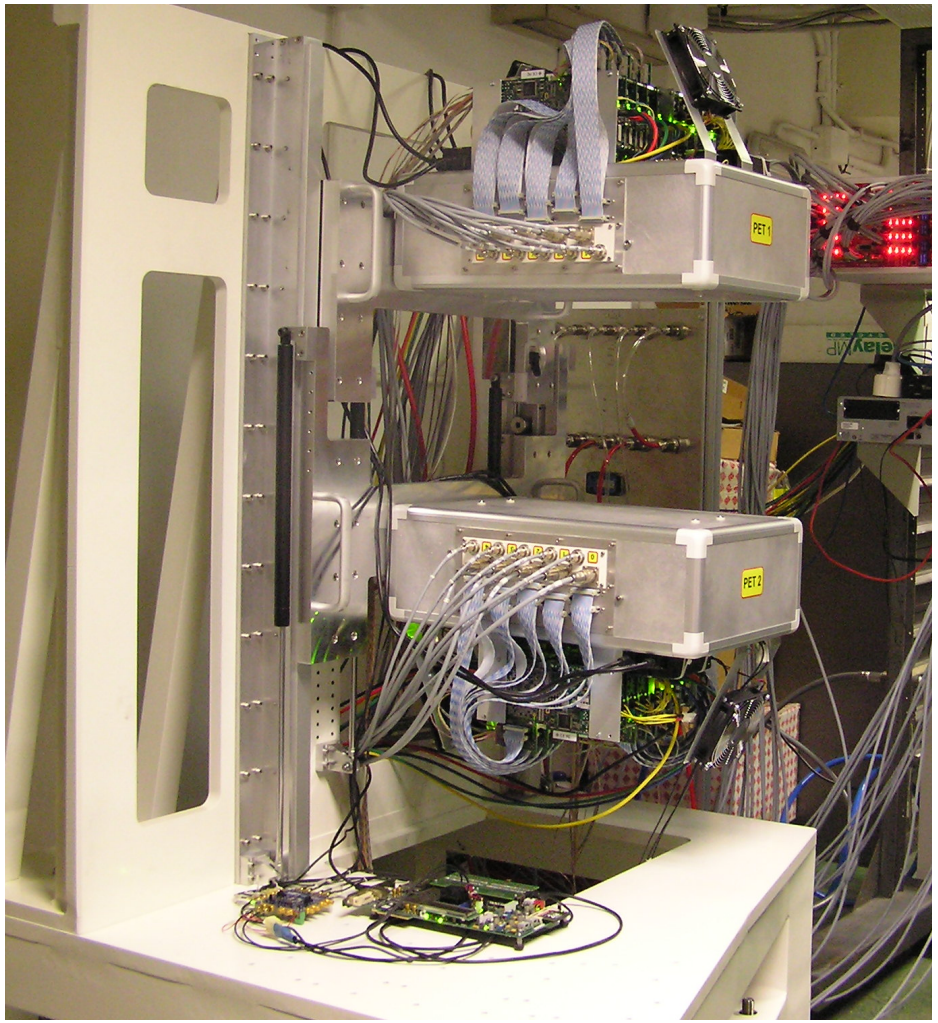
β^+ activity distribution
IN-BEAM PET HEADS



- ✓ integrated in treatment room of Centro Nazionale di Adroterapia Oncologica (CNAO)
- ✓ operated in-beam
- ✓ IMMEDIATE feedback on the particle range
- ✓ Effective both on proton and ^{12}C beam

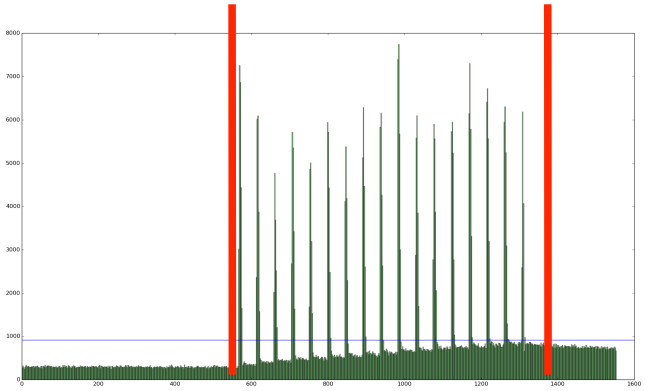
The INSIDE PET system

- DAQ sustains annihilation and prompt photon rates during the beam irradiation
- Two planar panels each 10 cm x 20 cm wide. Each panel will be made by 2 x 4 detection modules
- Each module is composed of a pixelated LYSO scintillator matrix 16 x 16 pixels, 3x3 mm^2 crystals, 3.1 mm pitch, for a total sensitive area of 5x5 cm^2
- One SiPM array (16x16 pixels) is coupled to each LYSO matrix. 200 ps FWHM TOF capability

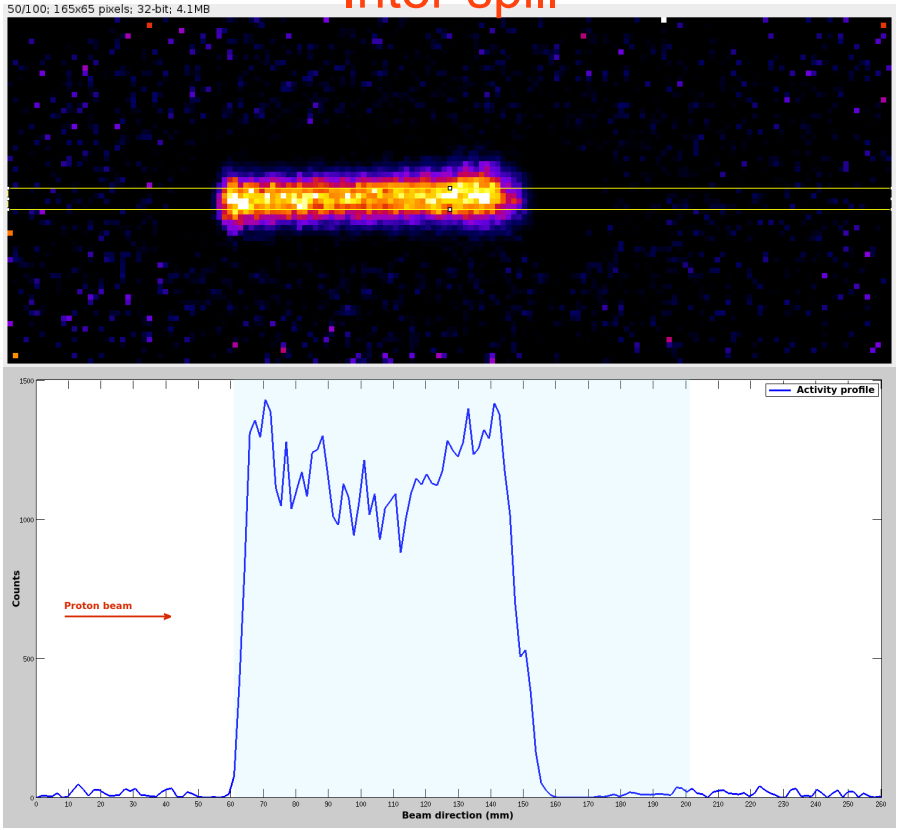


INSIDE- PET installed at CNAO 7/2/2016

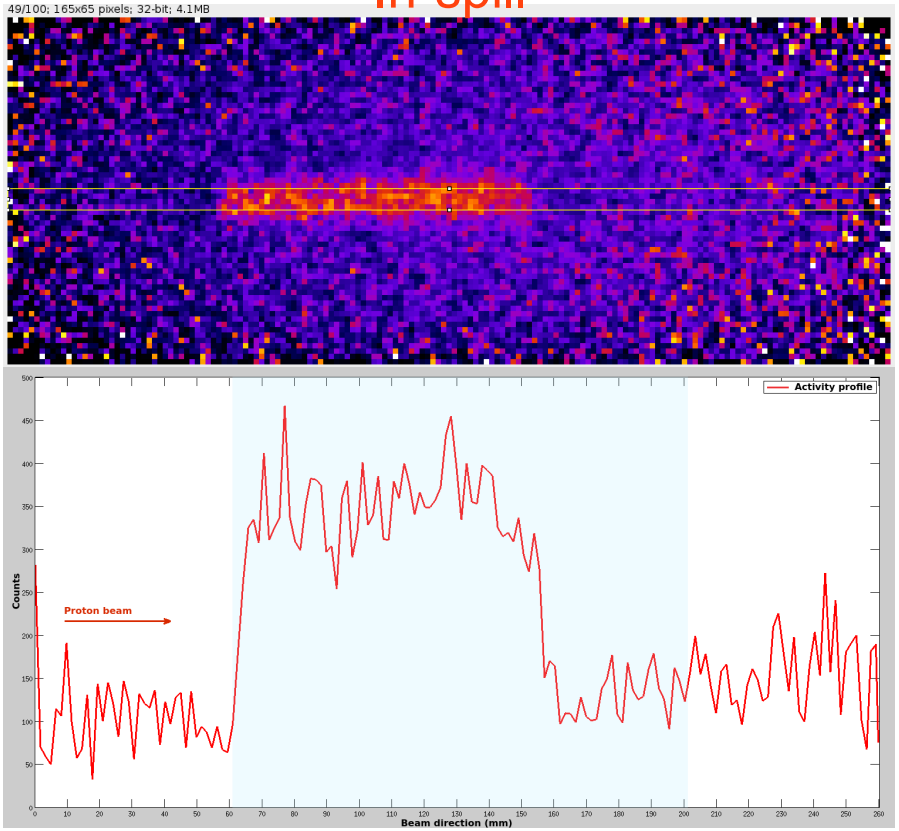
- Proton energy 124 MeV (111 mm in H2O)
- $2*10^{10}$ particles (~ 2 Gy)
- 50 x 50 x 140 mm3 homogeneous PMMA phantom
- 17 spills



Inter-spill

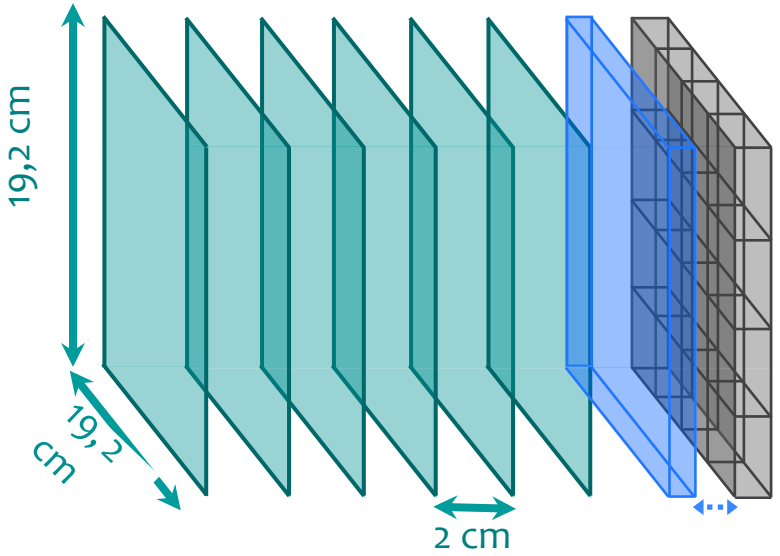


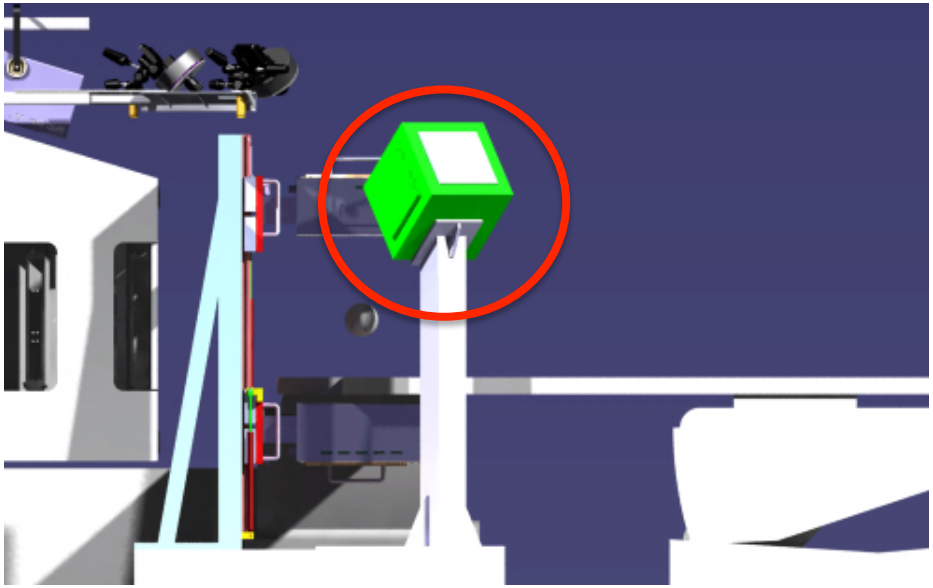
In-spill



INSIDE: charged tracker

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

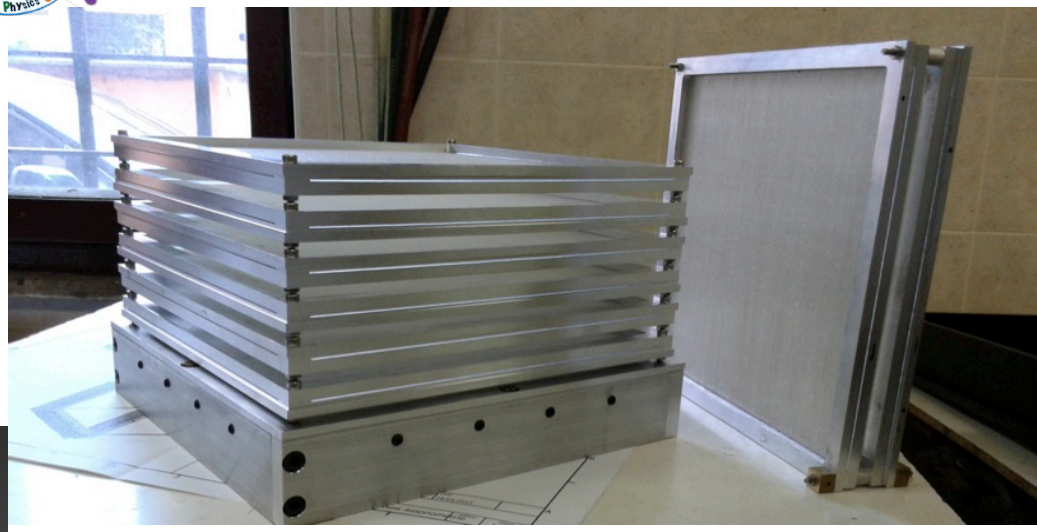


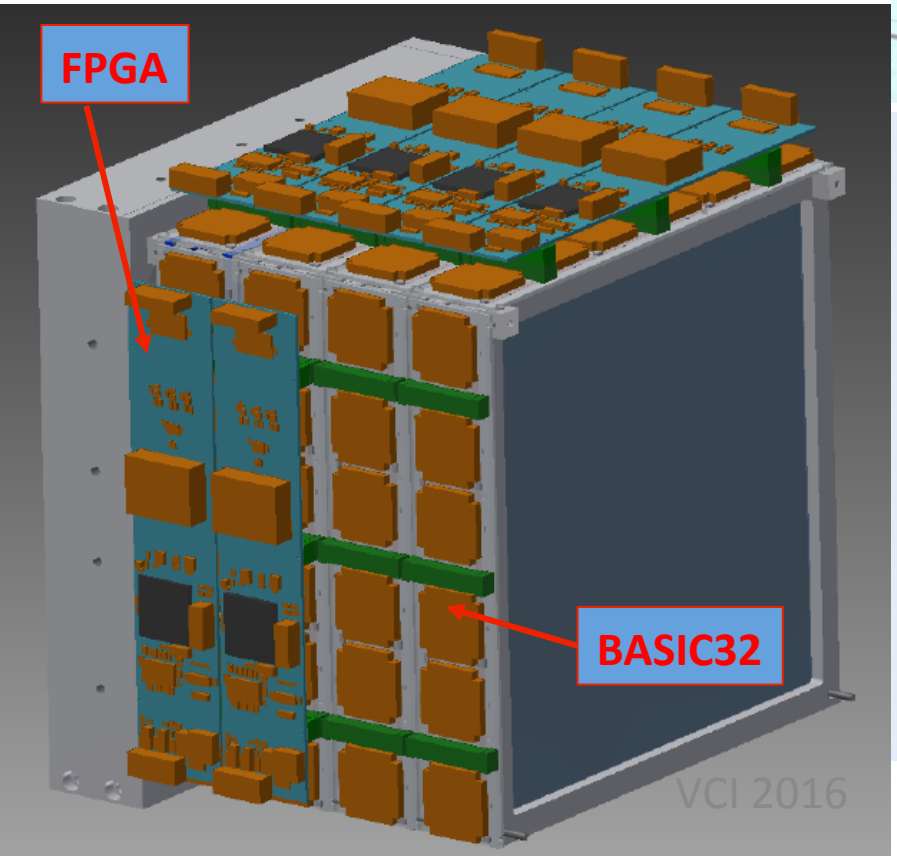


- ✓ 4x4 LYSO pixellated crystals tracking planes: 50 x 50 x 16 mm^3
- ✓ Plastic absorber 1.5 cm thick in front of LYSO to screen electrons
- ✓ Crystals read out by 64 ch Hamamatsu MultiAnode

Tracker

6 XY tracking planes: 384 scintillating fibers (0,5 mm) per side, with the minimal plane separation (2 cm) allowed by fibers front-end electronics readout in order to increase the geometrical acceptance and the compactness of the detector.





Readout:

- Hamamatsu 1mm SiPM.
- Each SiPM coupled with two adjacent fibers.
- In total the 19.2 x 19.2 cm^2 sensitive area is read by 192 channels per layer.
- 32 SiPM feed a 32 channels custom ASIC (BASIC32_ADC; F.Corsi, C.Marzocca et al. Politecnico and INFN Bari).
- Plane controller: one FPGA every 6 BASICS32

Calorimeter

The role of the high density compact crystal scintillator placed behind the tracker is to measure the protons energy helping in track reconstruction (trigger and event selection).

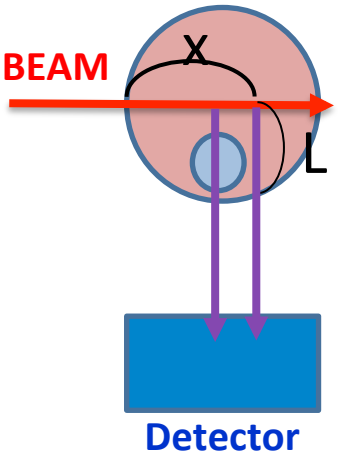
- 64 x 64 matrix of pixelated **LFS** (**L**utetium **F**ine **S**ilicate) **crystals** arranged in 4 x 4 blocks (16 x 16 matrices 5 cm x 5 cm x 2 cm from Hamamatsu).
- The crystal **readout** will be performed by means of Multi Anode Photo-Multiplier (MAPMT H8500 from Hamamatsu).
- On the back, the MAPMT (MultiAnode PhotoMultiplier Tubes), the **acquisition board** (based on BASIC32_ADC) and the data concentrator.

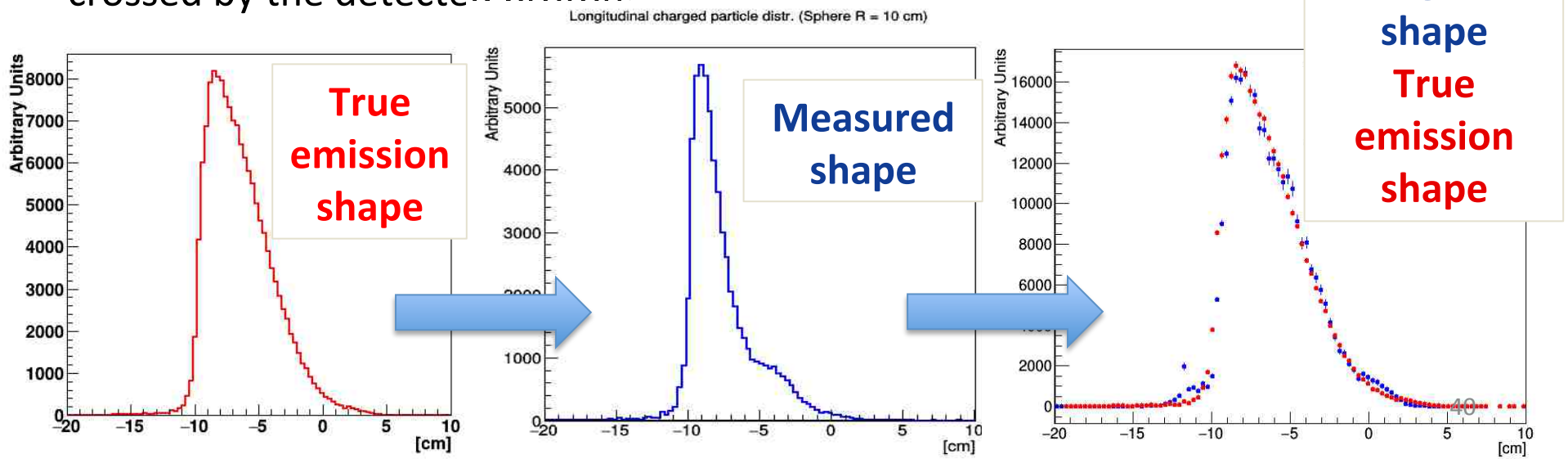
Proton emission shape attenuation inside the patient

By means of the **attenuation study** of the proton emission shape for different material thickness, we get a method to correlate the shape detected by the profiler coming out from the patient with the **B**ragg **P**eak position.

We apply to each reconstructed track a weight which takes into account the thickness and density of the material crossed by the detected proton

Example: inhomgeneous PMMA sphere containing a smaller sphere of lighter material





Summary & conclusions

- Particle therapy is becoming a new tool to help oncologist in the multi-approach war to cancer.
- Monitoring the beam range is a necessary step to meet the quality standard of a mature clinical technique
- The nuclear interactions of the beam provide the signal to monitor the released dose: PET-γ from β^+ emitters, prompt γ from nuclear excitation and light charged fragments from fragmentation
- Very fast R&D: solutions close to clinical practice for proton, yet on the way for ^{12}C: multimodal approach
- I apologize since I neglected a lot of interesting items/work/R&D as Compton chambers, ionoacustic devices, etc etc …

Thanks….

CREDITS

I am in debt for a lot of slides, plots, comments, discussions and with many collegues…

M.Durante, G.Battistoni, A.Sarti, A.Sciubba, M.Marafini, K.Parodi, D. Dauvergne & many others…