GSI Helmholtzzentrum für Schwerionenforschung GmbH

INFN Istituto Nazionale di Fisica Nucleare

GSI Kolloquium

Nuclear aspects in hadrontherapy

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Universita' di Roma "La Sapienza" & INFN
GSI, Darmstadt, 24 nov 2015

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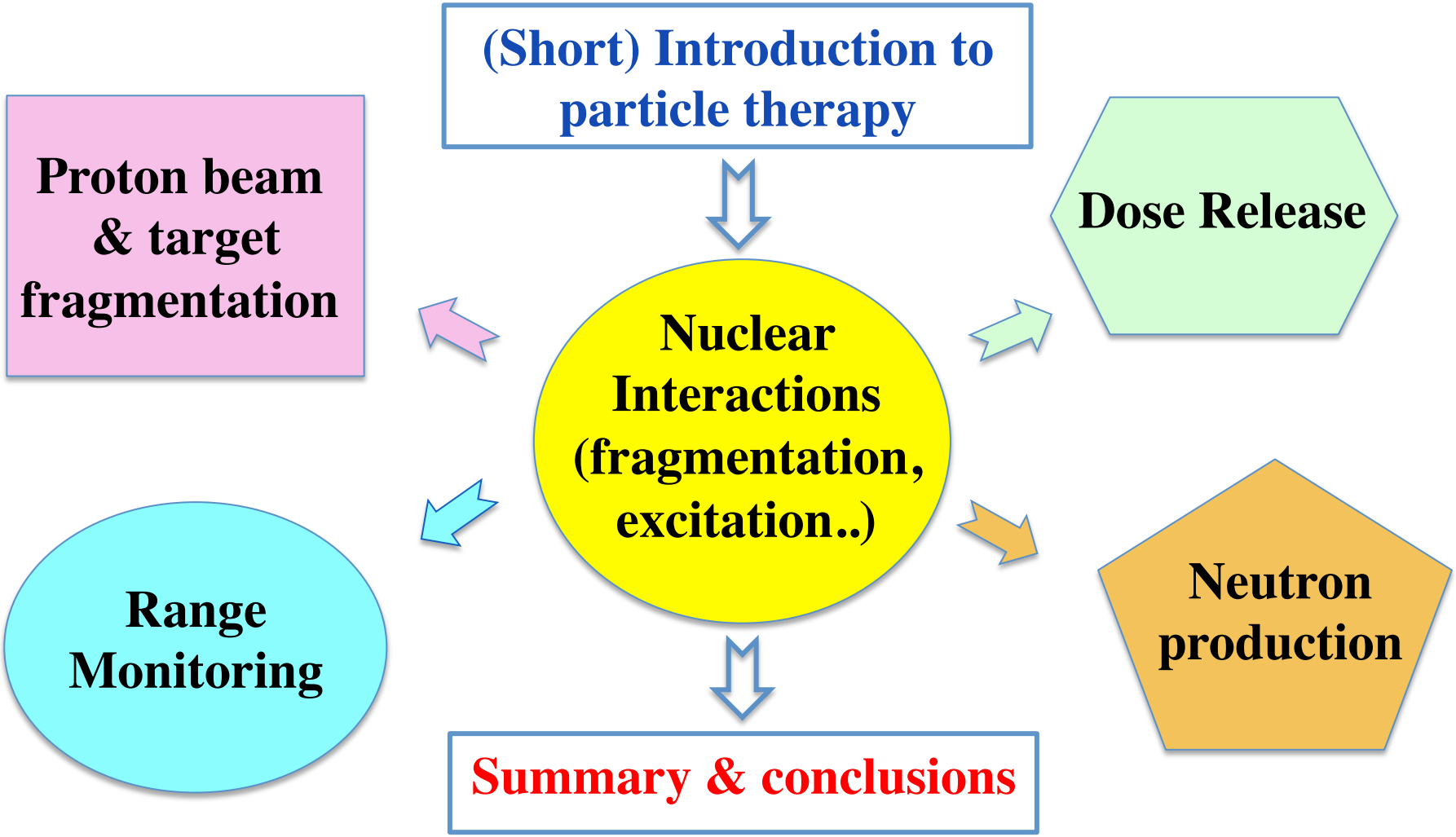
ARPG Applied Radiation Physics Group

Outline

Bouncing from fundamental physics to applied physics and back…
A spot-like, phenomenological, detector oriented view to the impact of nuclear interactions (fragmentation) on particle therapy



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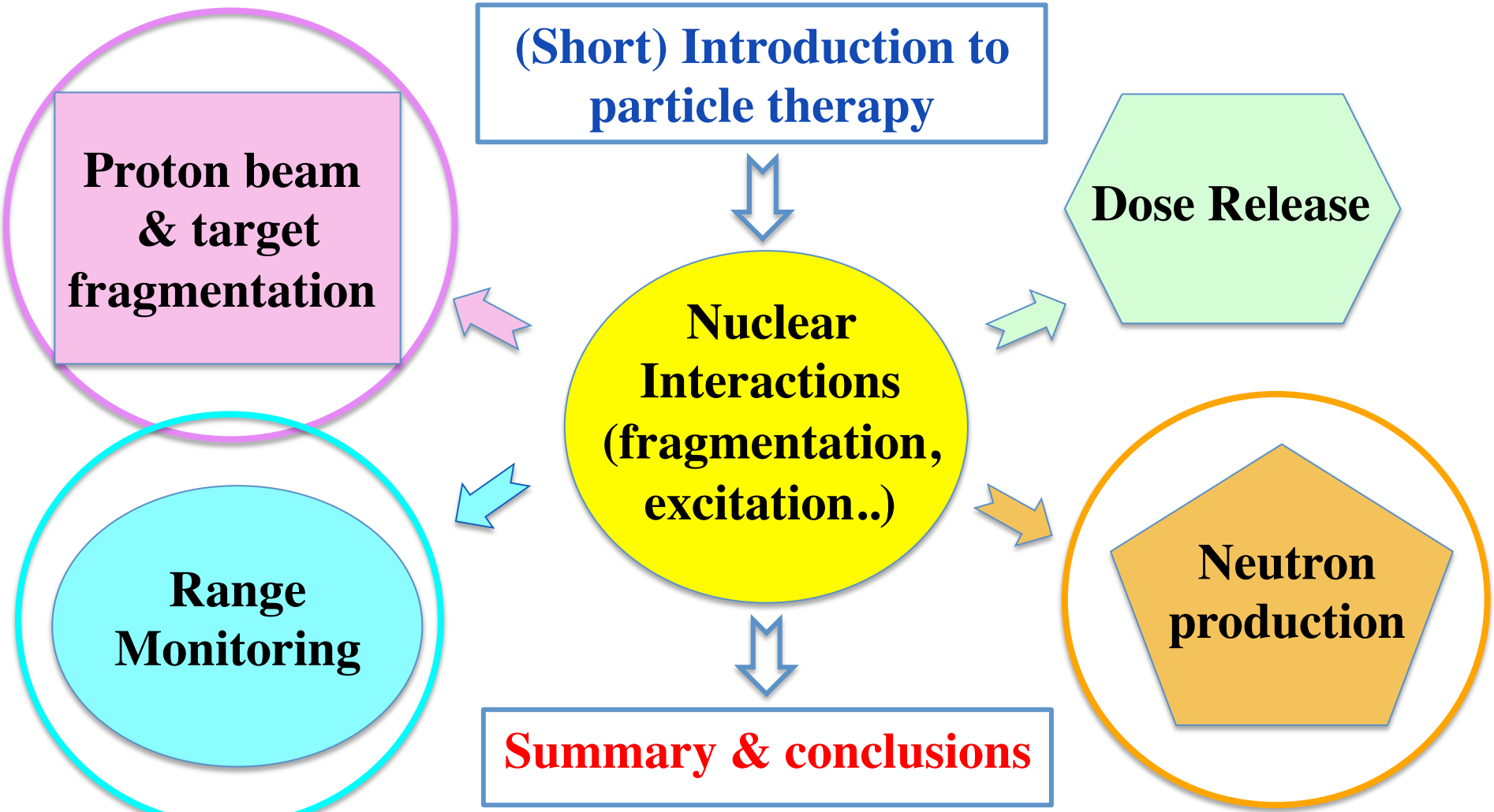


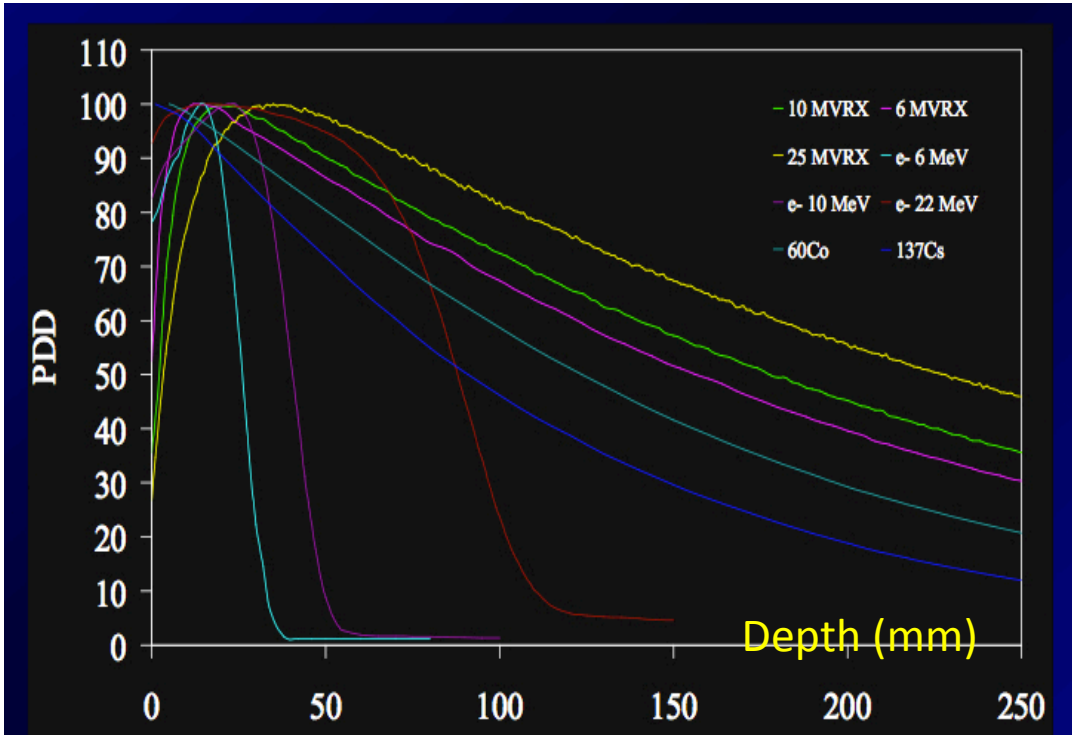
The conventional RT

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.

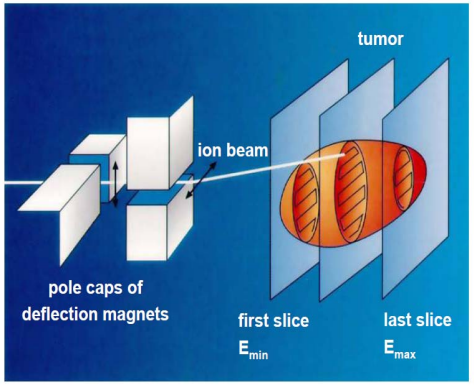
But the use of sophisticated imaging (CT), superposition of several beams, computed optimization, multi-leaves collimators and >40 year of R&D make IMRT effective and widespread

Dose-depth relation for γ and e^-

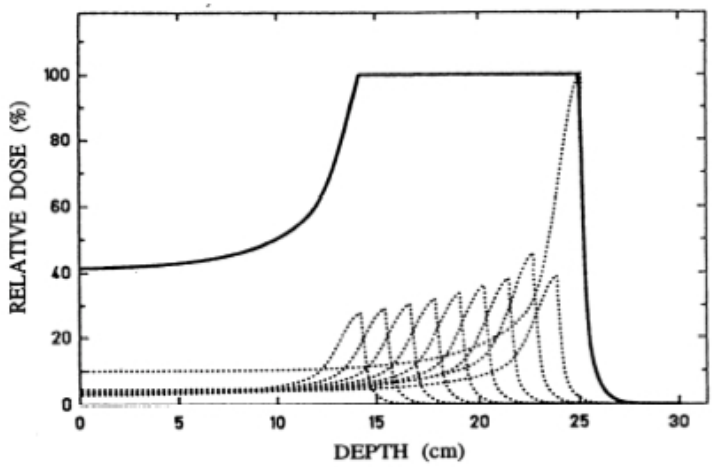


Particle therapy vs Photon RT

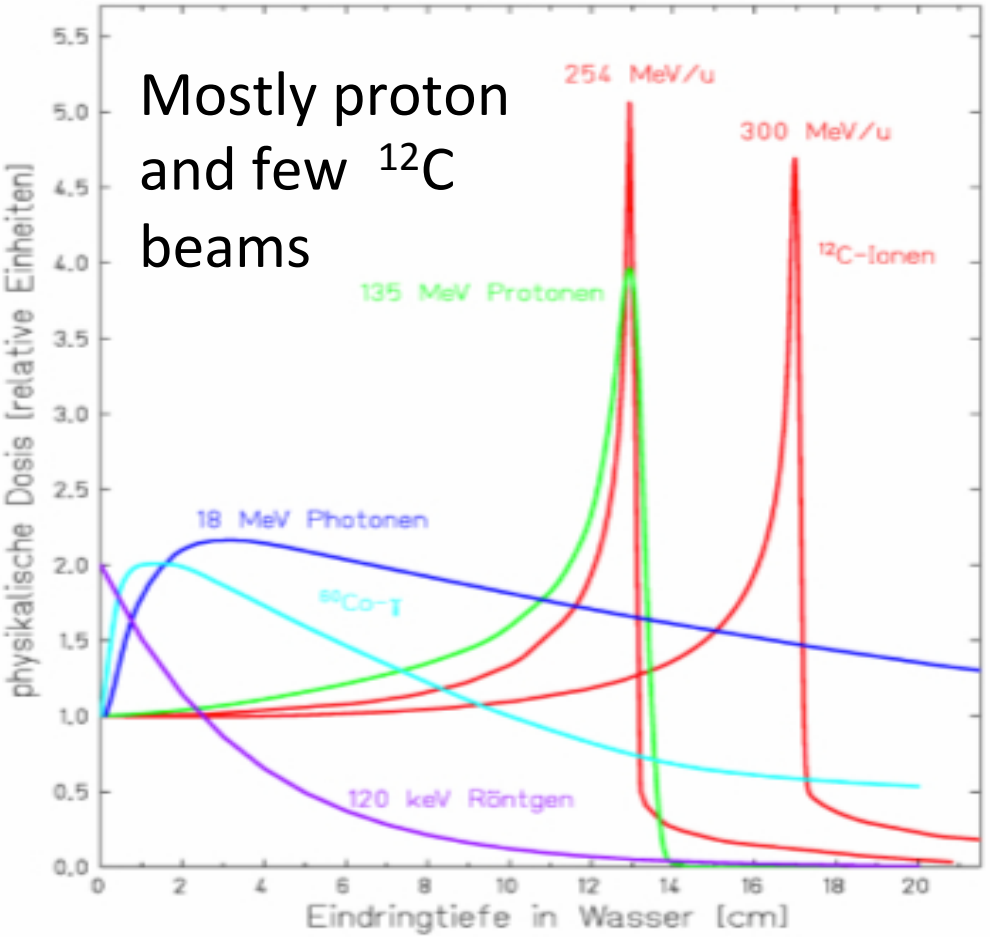
The highest dose released at the end of the track, sparing the normal tissue



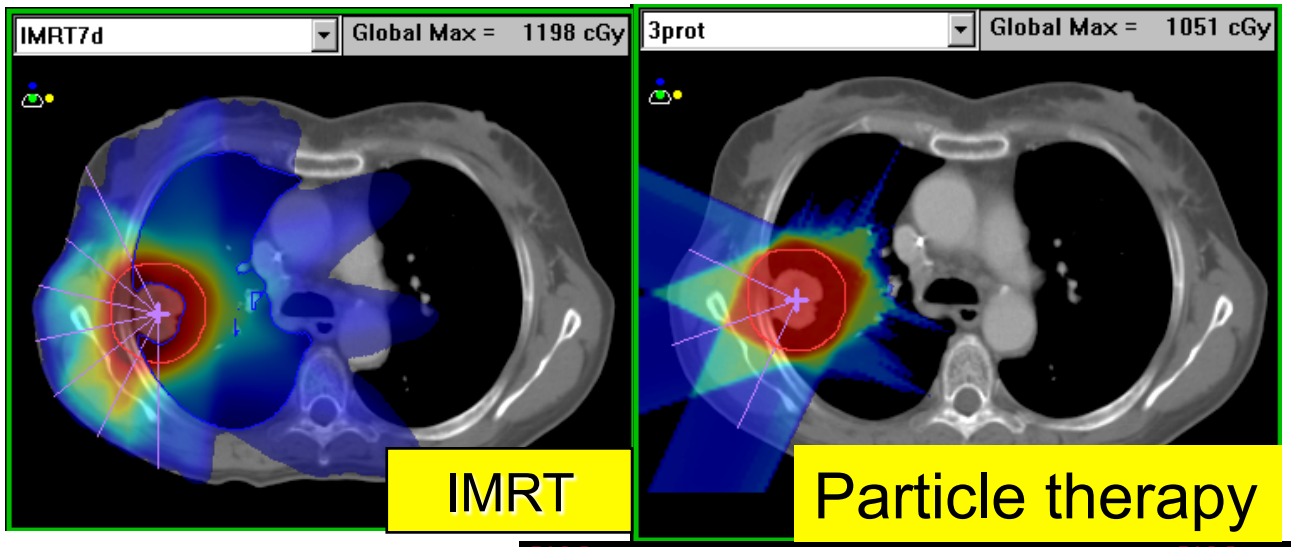
- Beam penetration in tissue function of the beam energy
- Dose decrease rapidly after the BP.
- Accurate conformal dose to tumor with Spread Out Bragg Peak (active scanning!)



Mostly proton and few ^{12}C beams

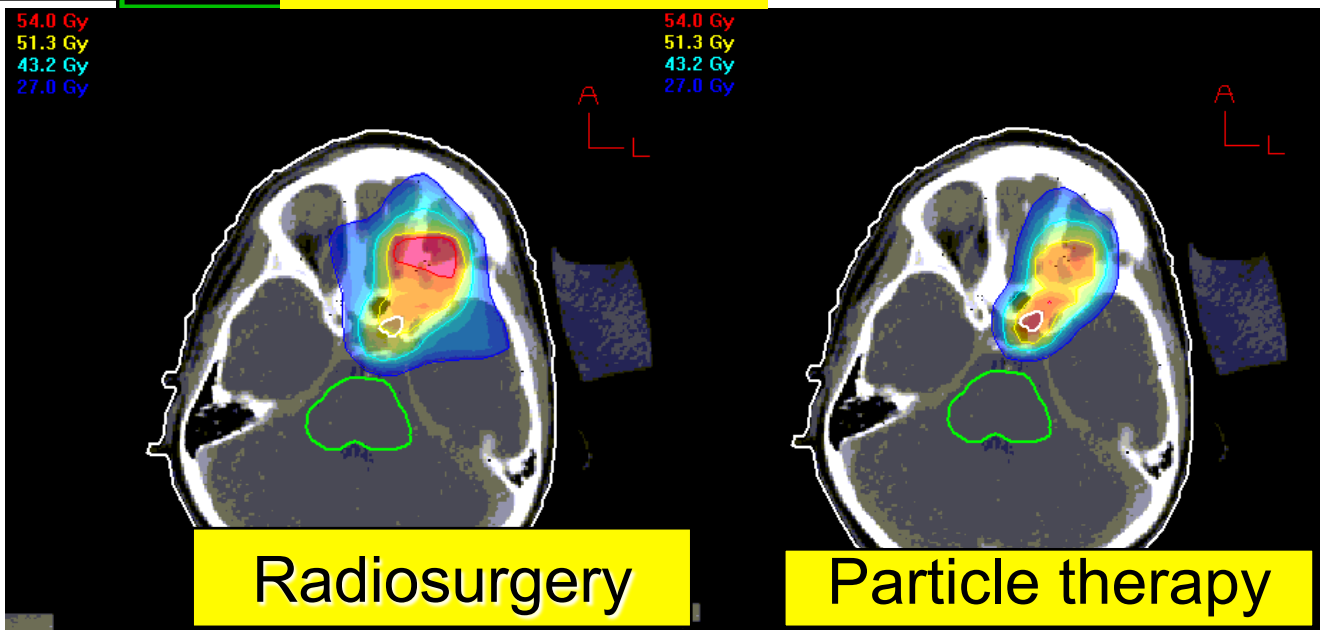


Photons vs Particle saga…

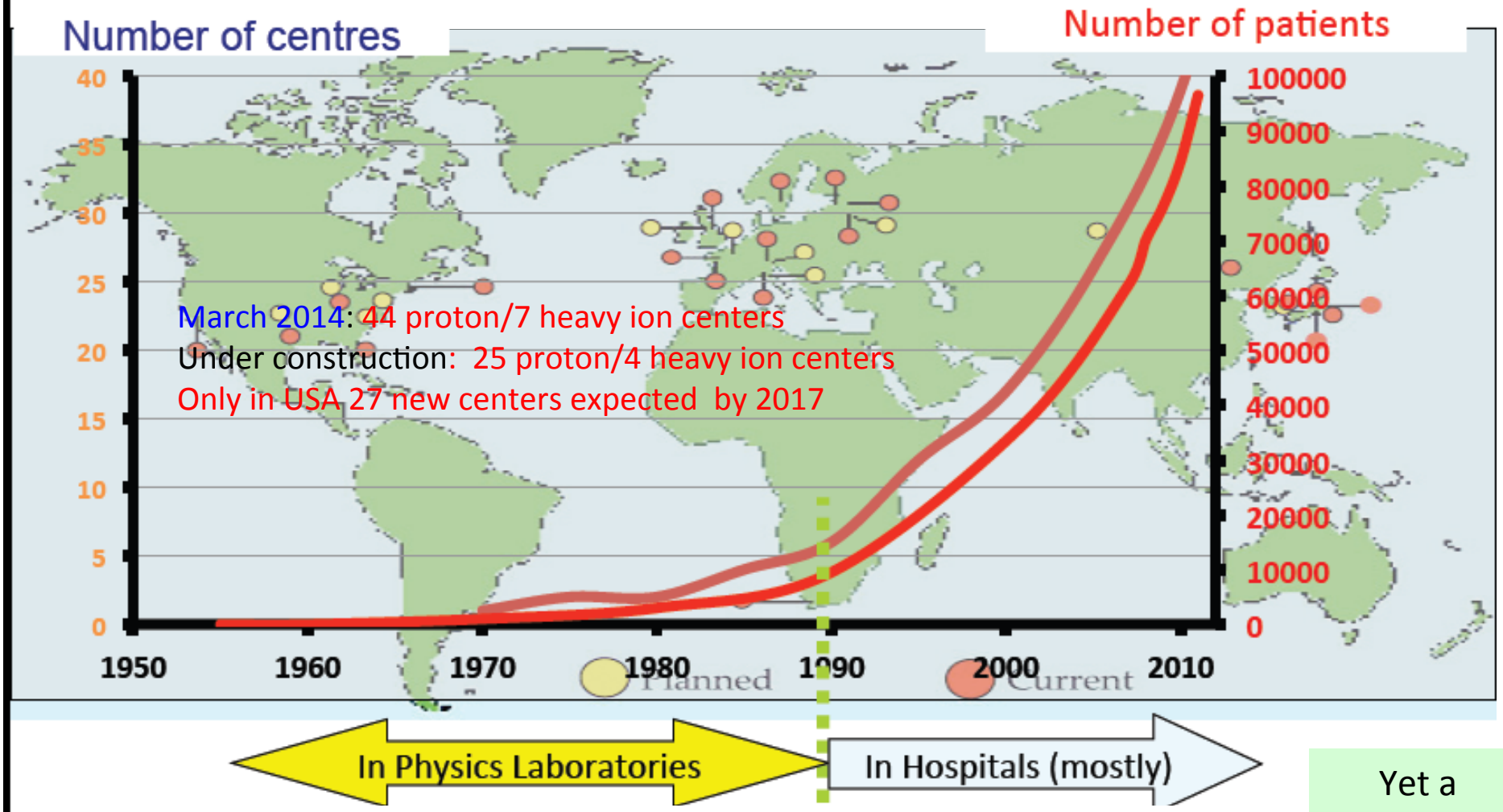


Particle therapy can easily show better selectivity wrt photon techniques…

Yet, randomized clinical trials seem the only commonly accepted method to assess eventual superiority of PT technique



Charged Particle Therapy in the world



~2014: 122499 treated patients: 105743 with p, mainly in USA, 53532

13119 with ^{12}C, mainly in Japan, 10993;

+ 46,000 in the past 5 years ≈ 10,000 patients per year

Yet a minimal fraction of photon RT

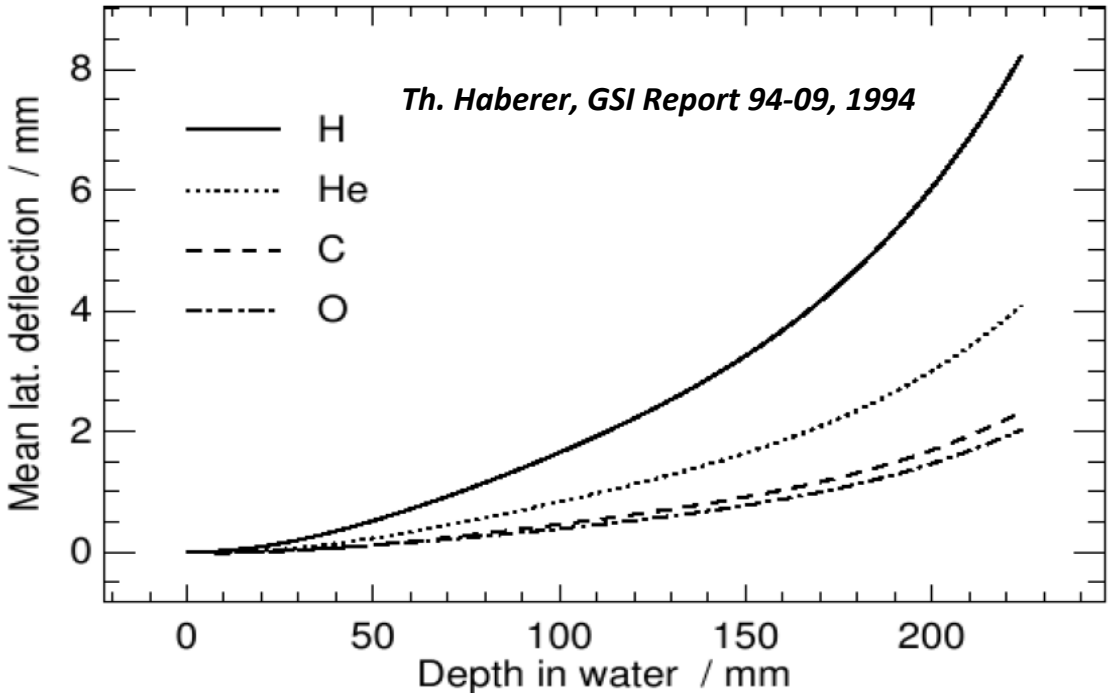
Which is the right beam for therapy?

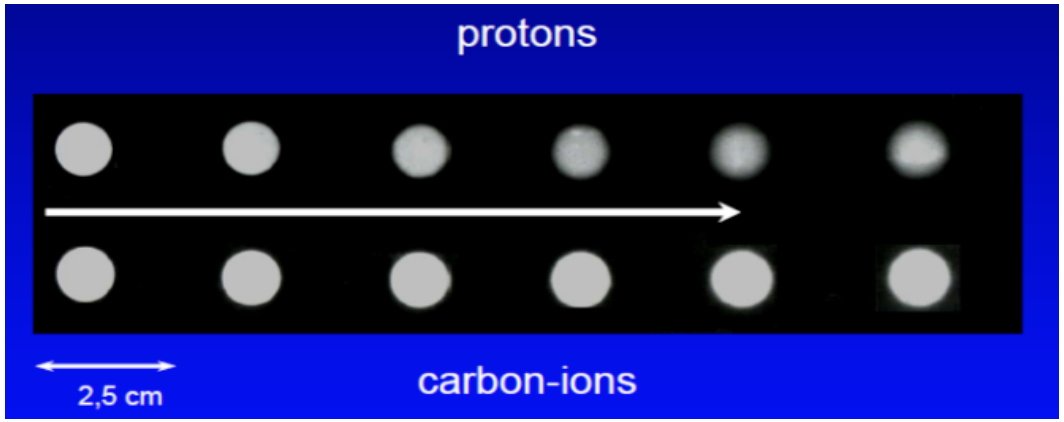
As far as money is the main concern.. protons win easily!

If we come to effectiveness, the landscape can change.

For instance, concerning the beam selectivity, comparing lateral deflection heavier ions have less multiple scattering

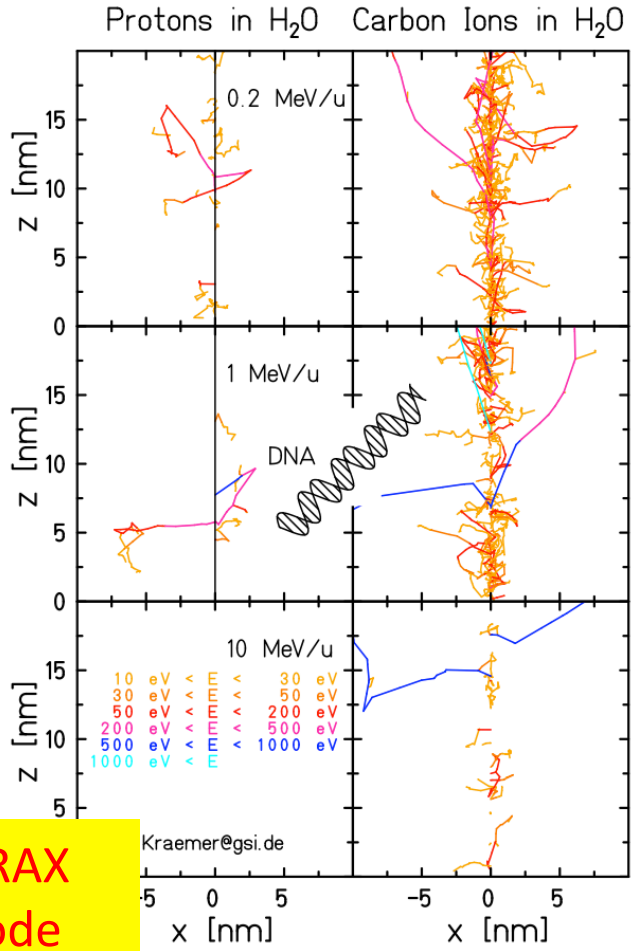
Beam lateral deflection





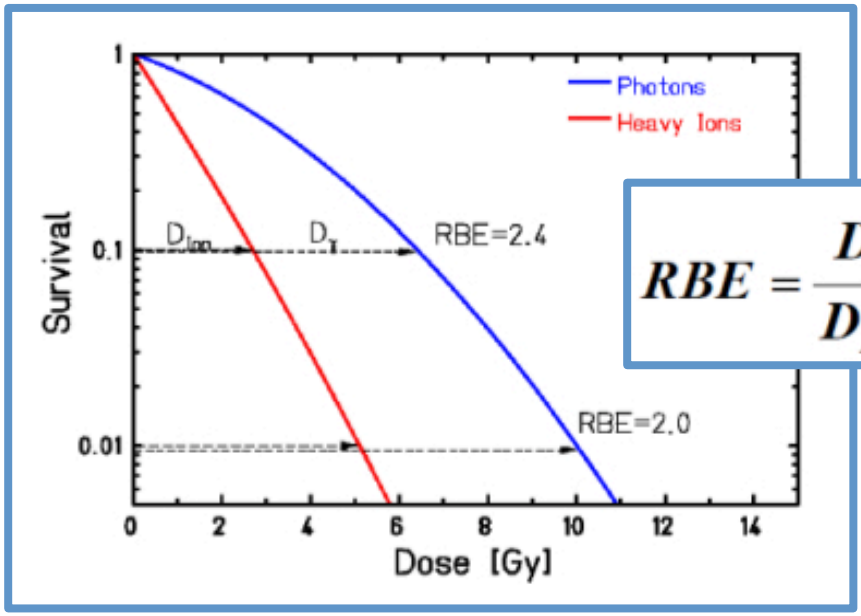
Heavier than proton? Maybe yes (RBE..)

M.Kramer et al. JoP 373 (2012),



TRAX code

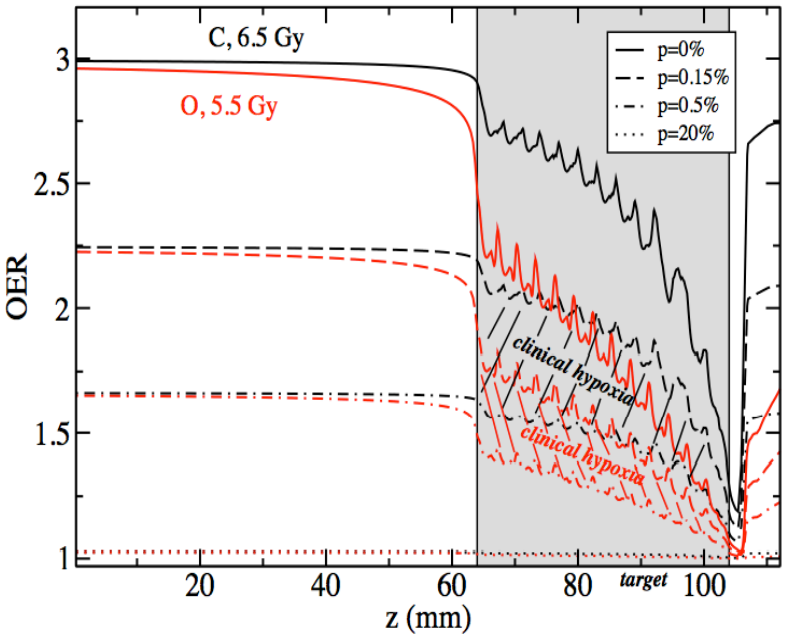
- The heavier ions are much better at killing the tumur cells with respect to the X rays (and p) for a given ➔high RBE
- Heavier ions have better plateau/peak ratio (less dose to the healthy tissue in a treatment) wrt to proton beams



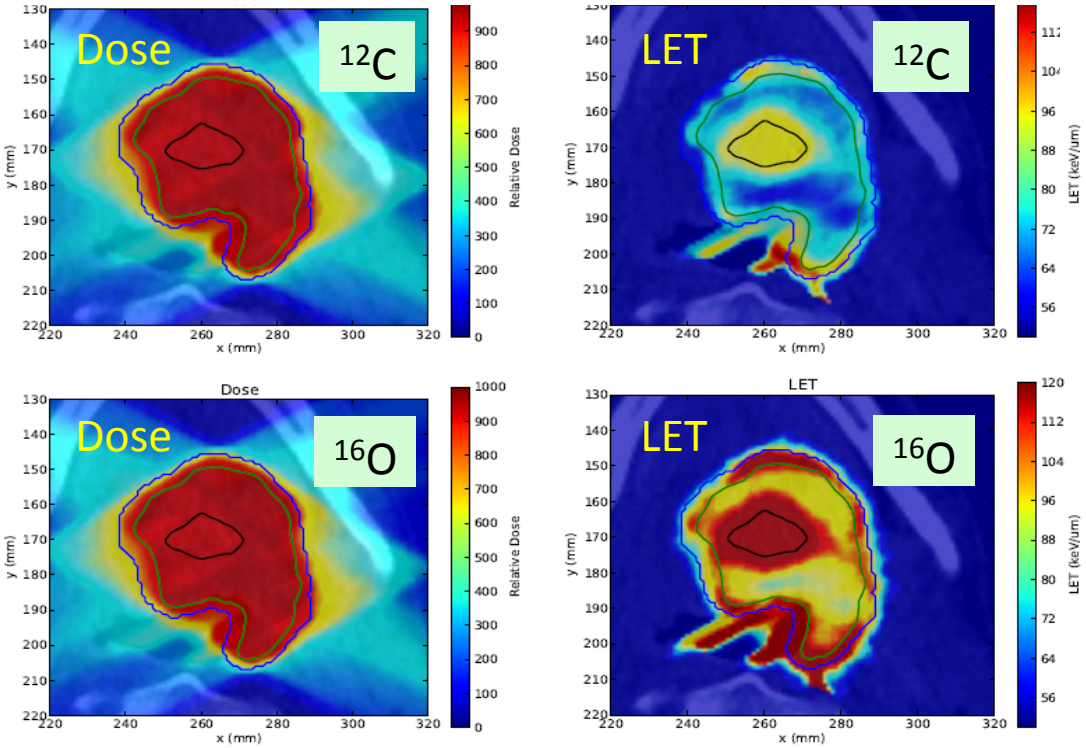
OER and ^{16}O beam

The high LET of the ^{16}O beam is effective against radio-resistant hypoxic tumors (low Oxygen Enhancement Ratio)

M.Kramer et al. JoP 373 (2012),



Bassler et al., Acta Oncol 2013



Full treatment or simple boost session with ^{16}O with hypoxic can be a clear improvement with respect to conventional Radiotherapy

Outline

Accuracy in the dose release, radio biological effectiveness and effectiveness on radio-resistant hypoxic tumors suggest an escalation to higher Z beam . But the nuclear interaction itself sets a limit …

(Short) Introduction to particle therapy

Proton beam & target fragmentation

Nuclear Interactions (fragmentation, excitation..)

Dose Release

Range Monitoring

Neutron production

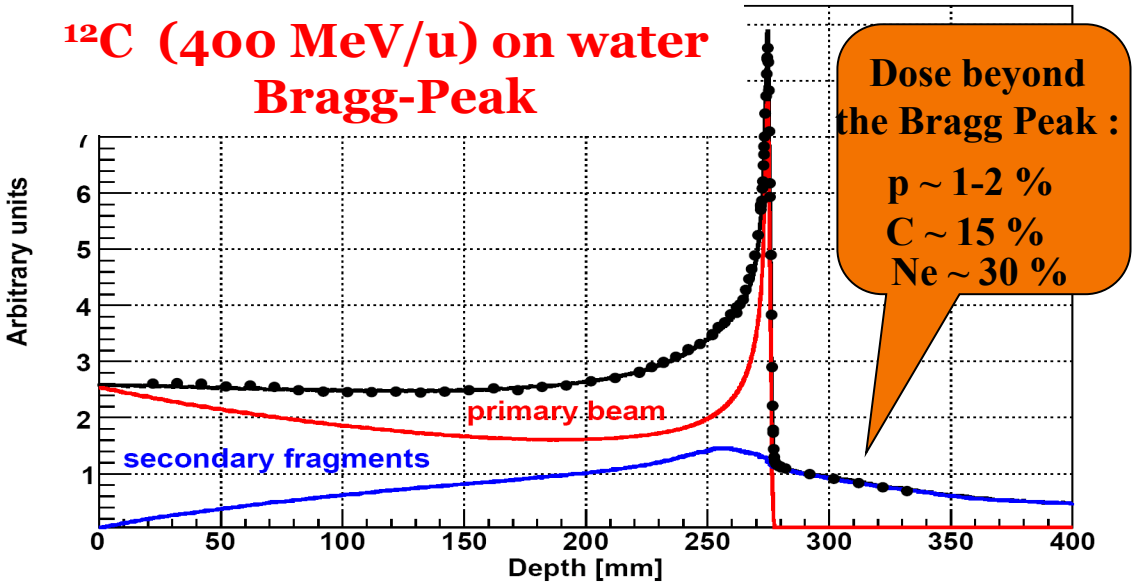
Summary & conclusions

Heavier is better?  Fragmentation!

Dose release in healthy tissues with possible long term side effects, in particular in treatment of young patients ➔must be carefully taken into account in the Treatment Planning System

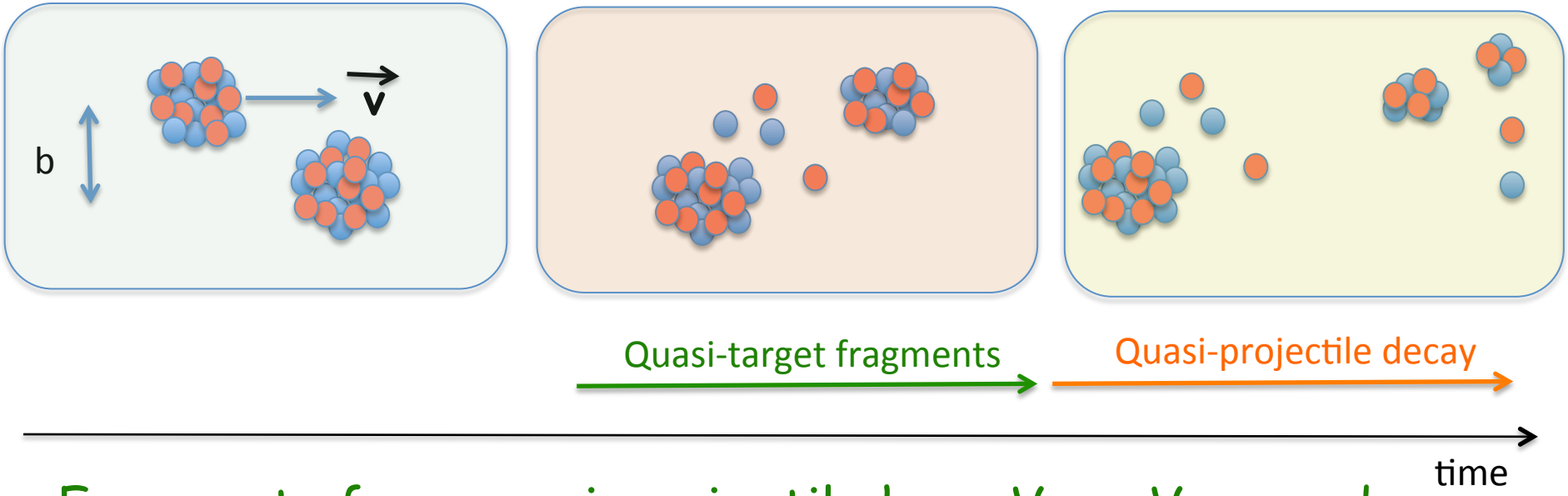
- ✓ Production of fragments with higher range vs primary ions
- ✓ Production of fragment with different direction vs primary ions

- ✓ *Mitigation and attenuation of the primary beam*
- ✓ *Different biological effectiveness of the fragments wrt the beam*



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

The abrasion-ablation paradigm



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

Fragments from ^{12}C beam (E_{kin}=400 AMeV) on ^{12}C

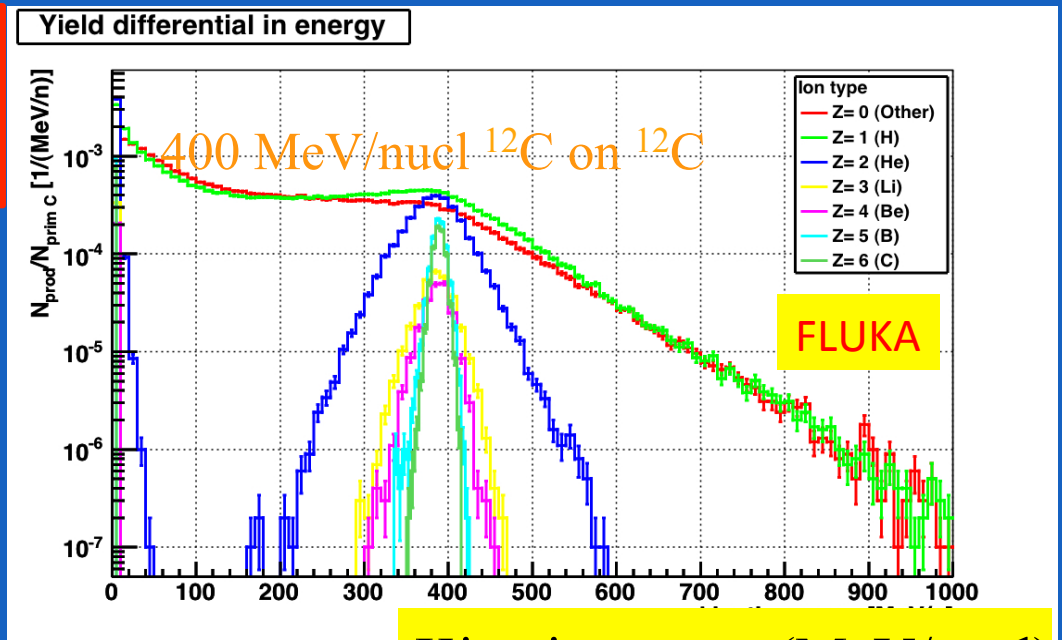
The Z>2 produced fragments approximately have the same velocity of the ^{12}C beam and are collimated in the forward direction

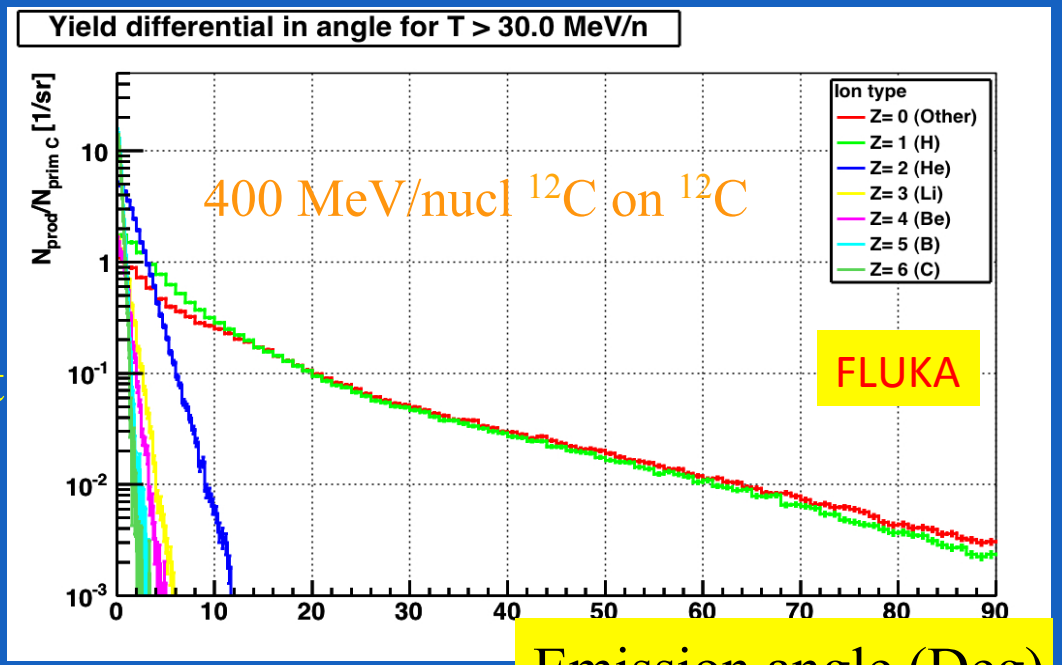
The protons are the most abundant fragments with a wide β spectrum $0<\beta<0.6$ and with a wide angular distribution with long tail

The Z=2 fragment are all emitted within 20^0 of angular aperture

The dE/dx released by the fragment spans from ~2 to ~100 m.i.p.

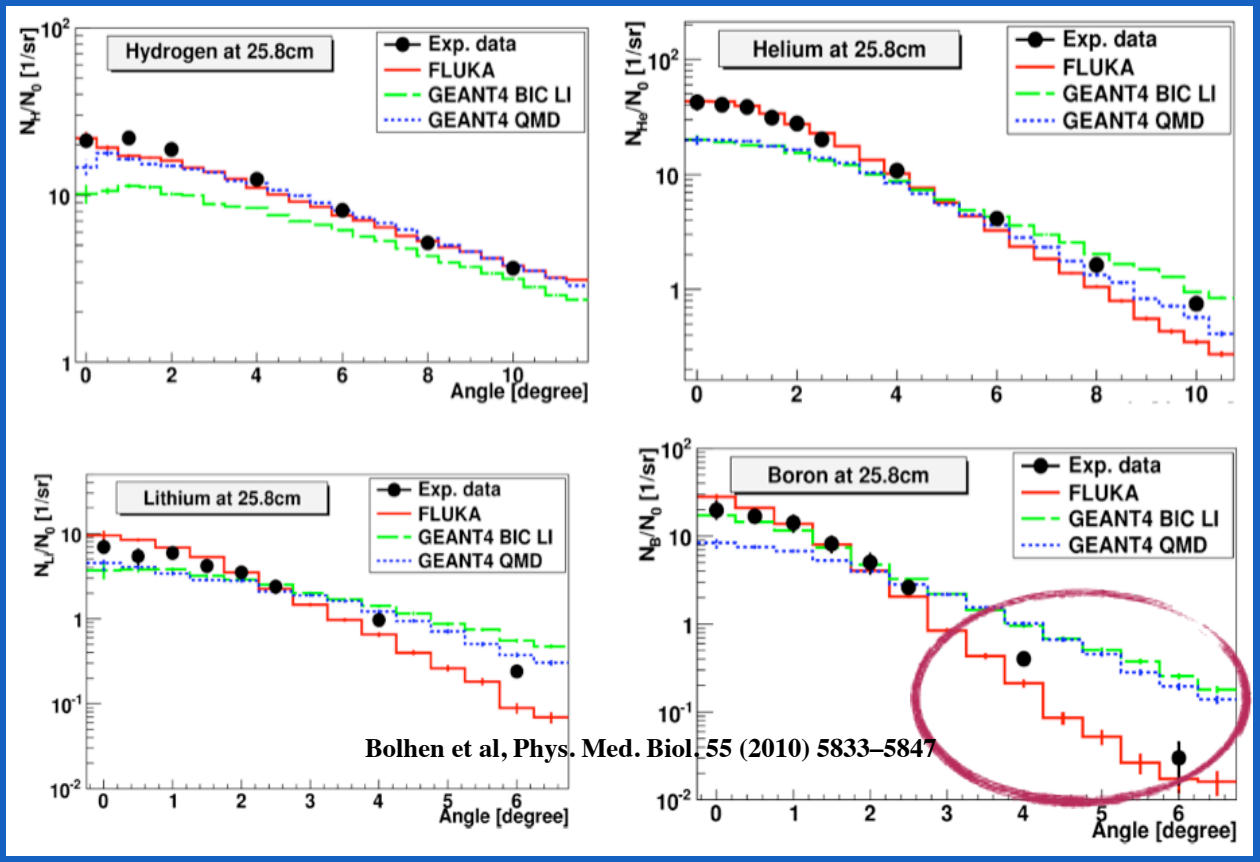
Do not trust MC too much!





Data - MC comparison: ^{12}C ions

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



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

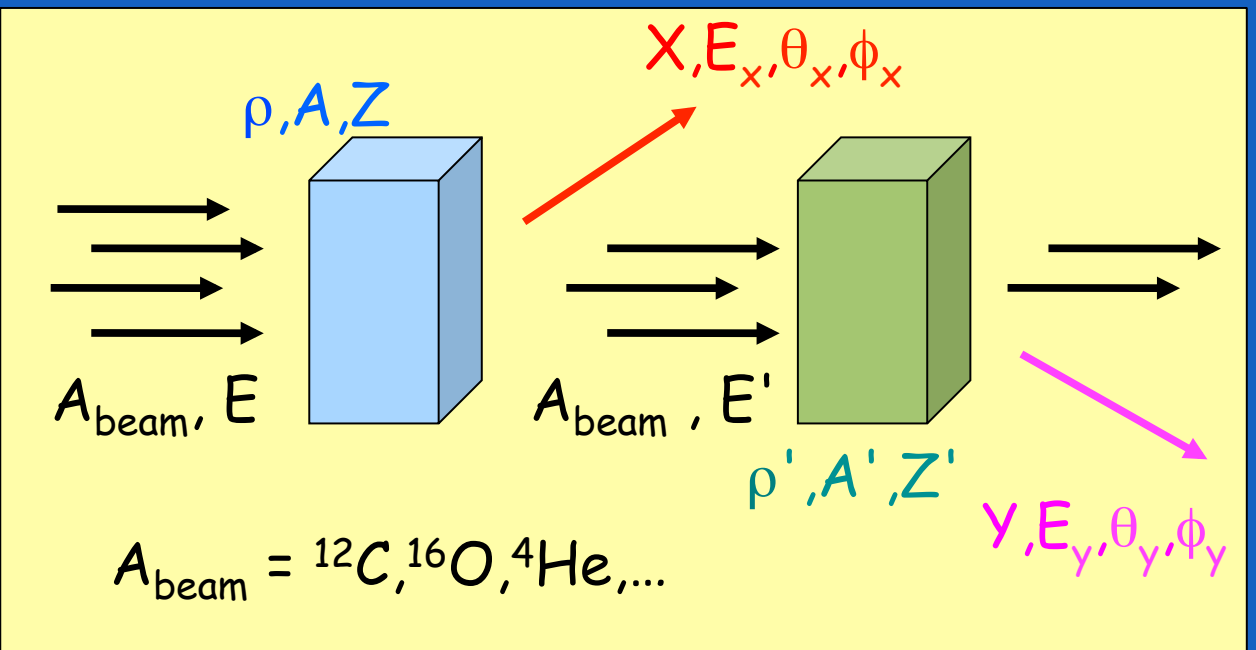
NB: the accuracy on delivered dose MUST be of the order of few %

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

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

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

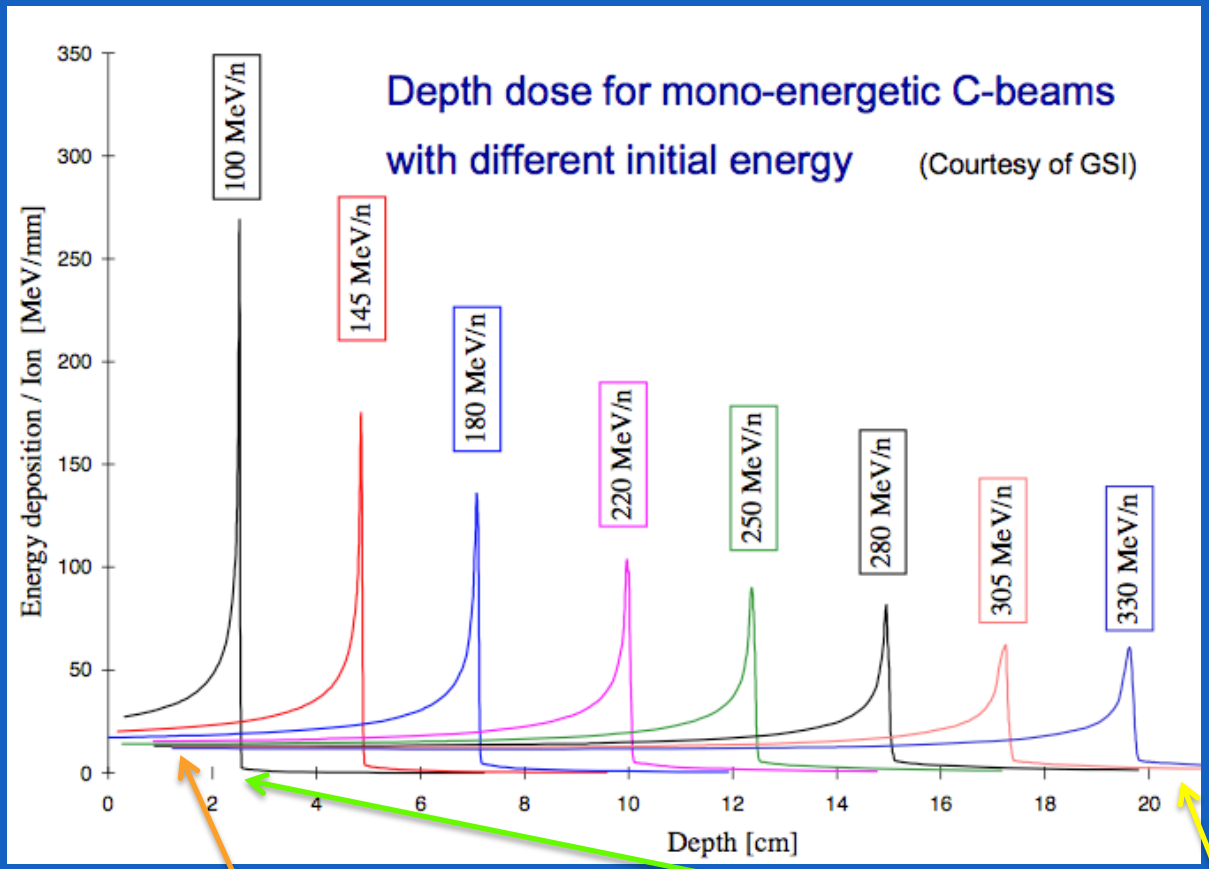
- Production yields of Z=0,1,2,3,4,5 fragments
- $d^2\sigma/d\theta dE$ wrt angle and energy, with large angular acceptance
- For any beam energy of interest (100-300 AMeV)
- Thin target measurement of all materials crossed by beam



Not possible a complete DB of measurements

We need to train a nuclear interaction model with the measurements!!

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



The community is exploring the interesting region for therapeutic application, in particular for the ^{12}C beam.
Yet there is a lot of energy range to explore in the range 150-350 AMeV (i.e. 5-17 cm of range…)

LNS 62AMev C beam See M. De Napoli talk in this session (2009)

GANIL 95AMev C beam - E600 collaboration (2011)

GSI 400Mev C beam FIRST experiment (2011->??)

FIRST setup @GSI

^{12}C beam
400 AMeV

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

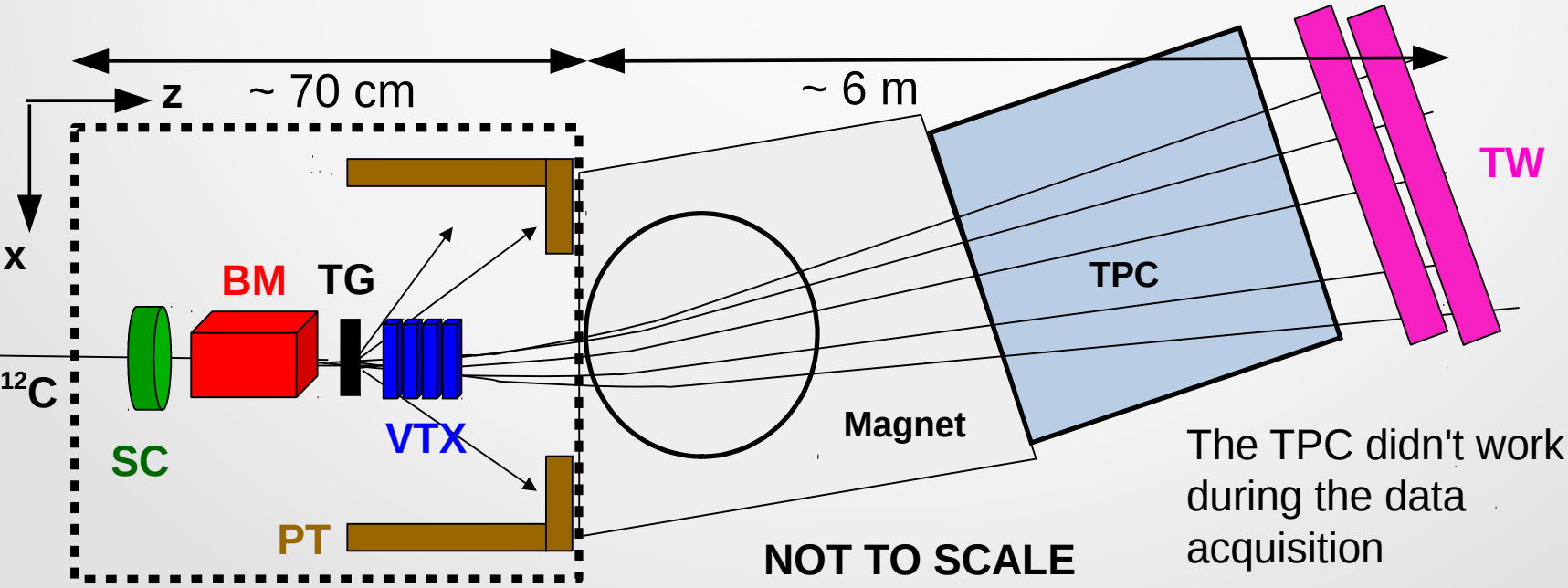
Beam Monitor (BM): drift chamber for beam direction and impact point measurements

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

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

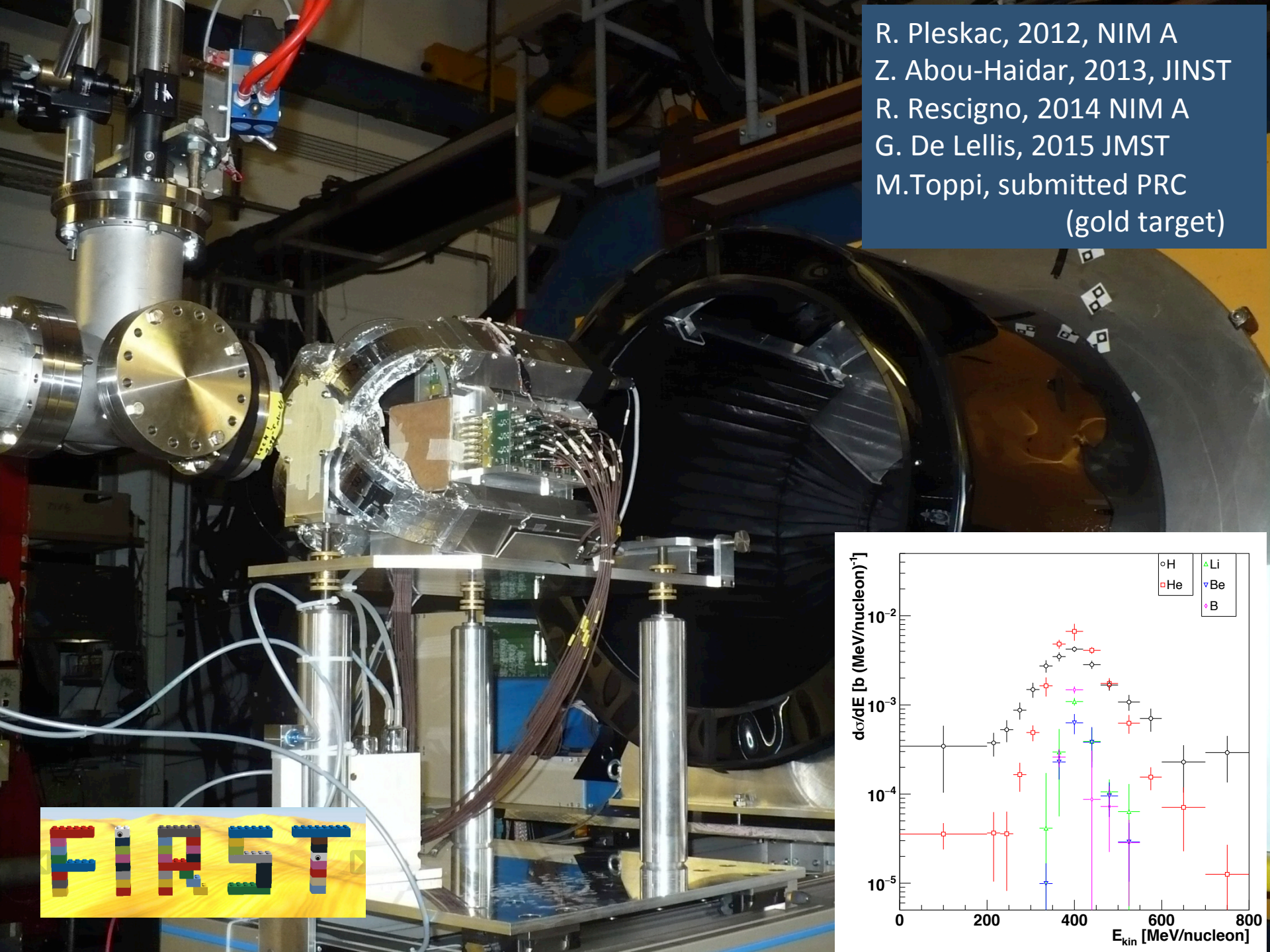
Proton Tagger (PT): plastic scint. and scint. fibers. Position, ToF, dE/dX for θ>5° H & He

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



The TPC didn't work during the data acquisition

R. Pleskac, 2012, NIM A
Z. Abou-Haidar, 2013, JINST
R. Rescigno, 2014 NIM A
G. De Lellis, 2015 JMST
M.Toppi, submitted PRC
(gold target)



Outline

The nuclear interaction of the beam prevents the use of beam heavier the Oxygen and must be taken into account in TPS.. But can be of help for another crucial aspect of particle therapy: range monitoring

(Short) Introduction to particle therapy

Proton beam & target fragmentation

Dose Release

Nuclear Interactions (fragmentation, excitation..)

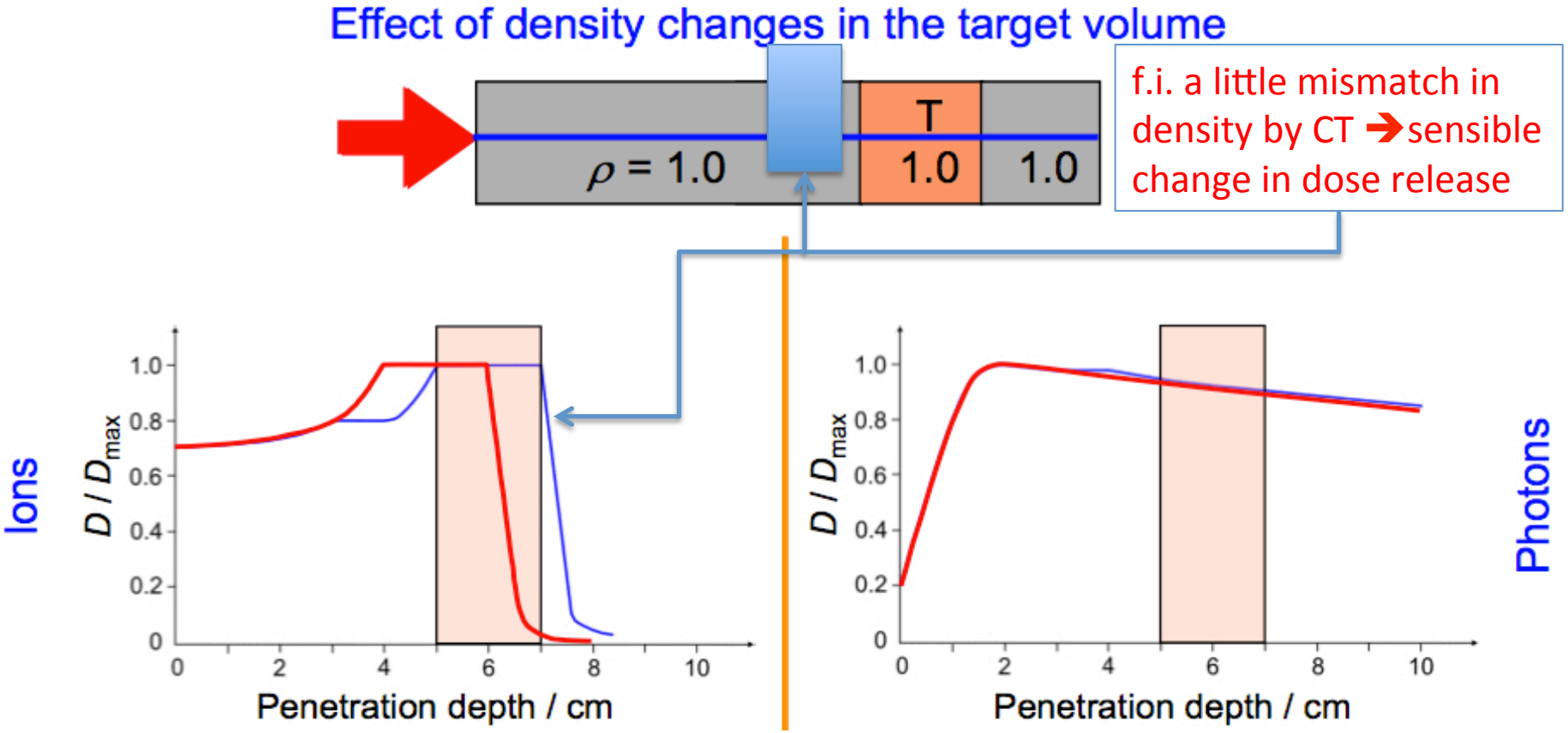
Range Monitoring

Neutron production

Summary & conclusions

Dose profile in PT

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



The range verification problem

AAPM, August 2012

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

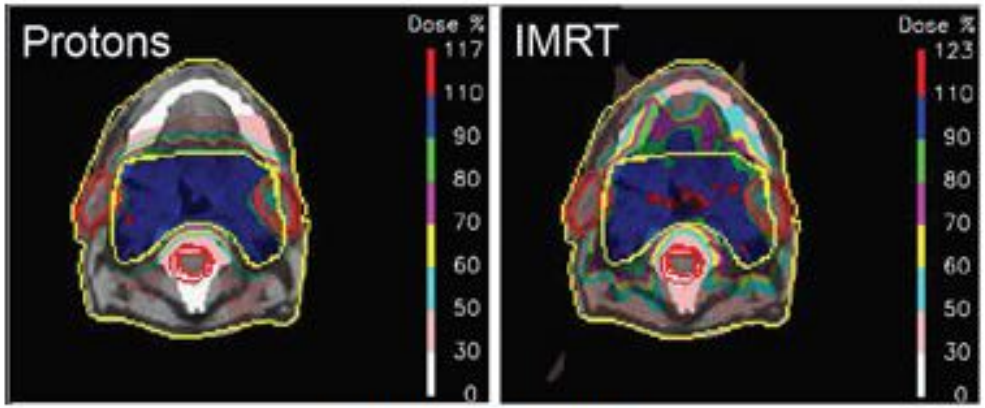
- 35 % unproven clinical advantage of lower integral dose
- 33 % range uncertainties
- 19 % never become a mainstream treatment option

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?



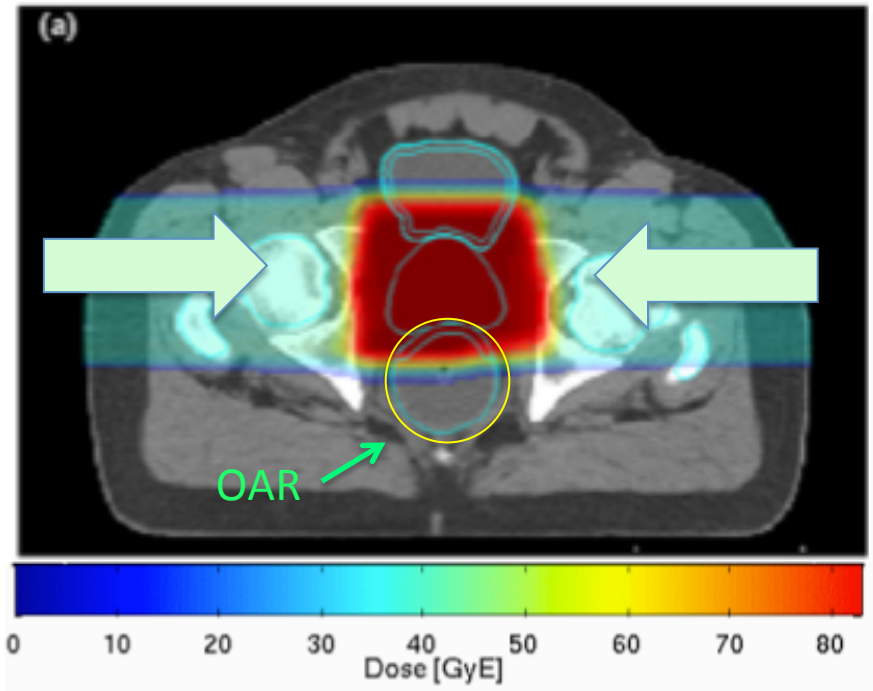
Protons versus IMRT

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

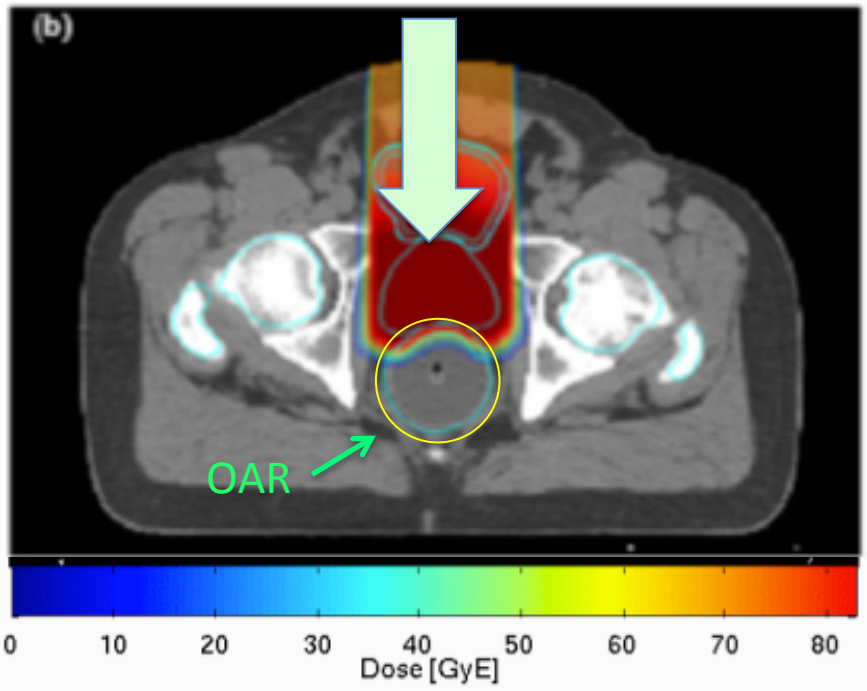
Accounting for uncertainties in the clinical practice

[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. An ideal PT monitor device should fulfill the following spec's:

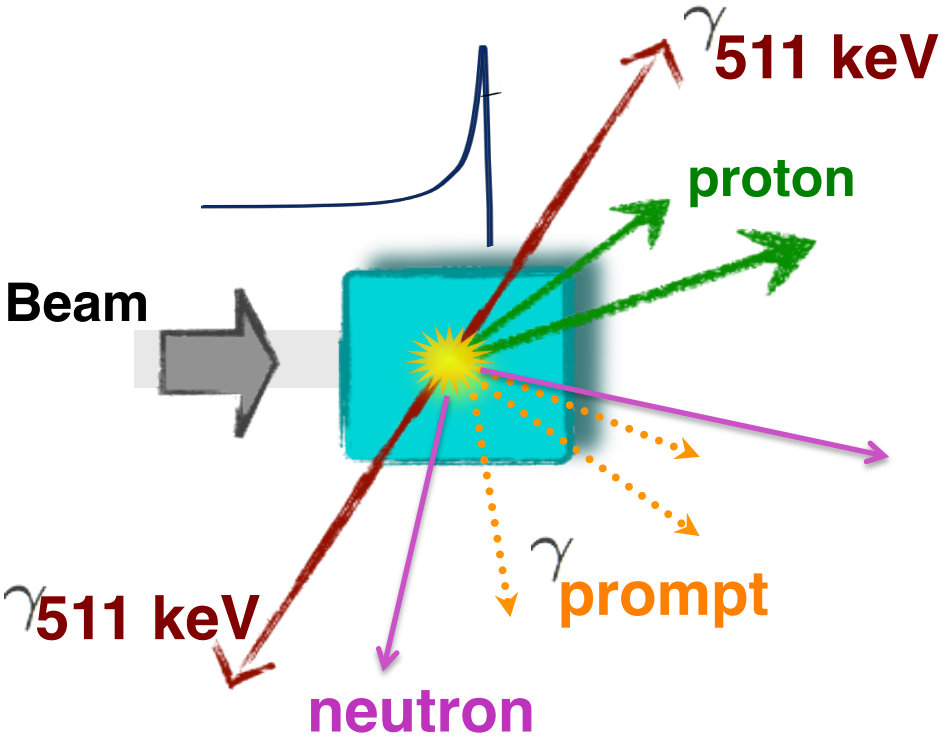
- Measure shape and (if possible) the absolute value of dose release to check the agreement between the planned target volume and the actually irradiated volume
- Measurements and feed-back should be provided during the treatment (in-beam). Even better if the monitor response can follow the irradiation scan on line
- Must 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

Help from Nuclear Physics: exploiting secondary products

The therapeutic beam is absorbed inside the patient: a monitor device can rely on secondaries, generated by the beam coming out from the patient. The p, ^{12}C beams generate a huge amount of secondaries: prompt γs, PET- γs, neutrons and charged particles/fragments

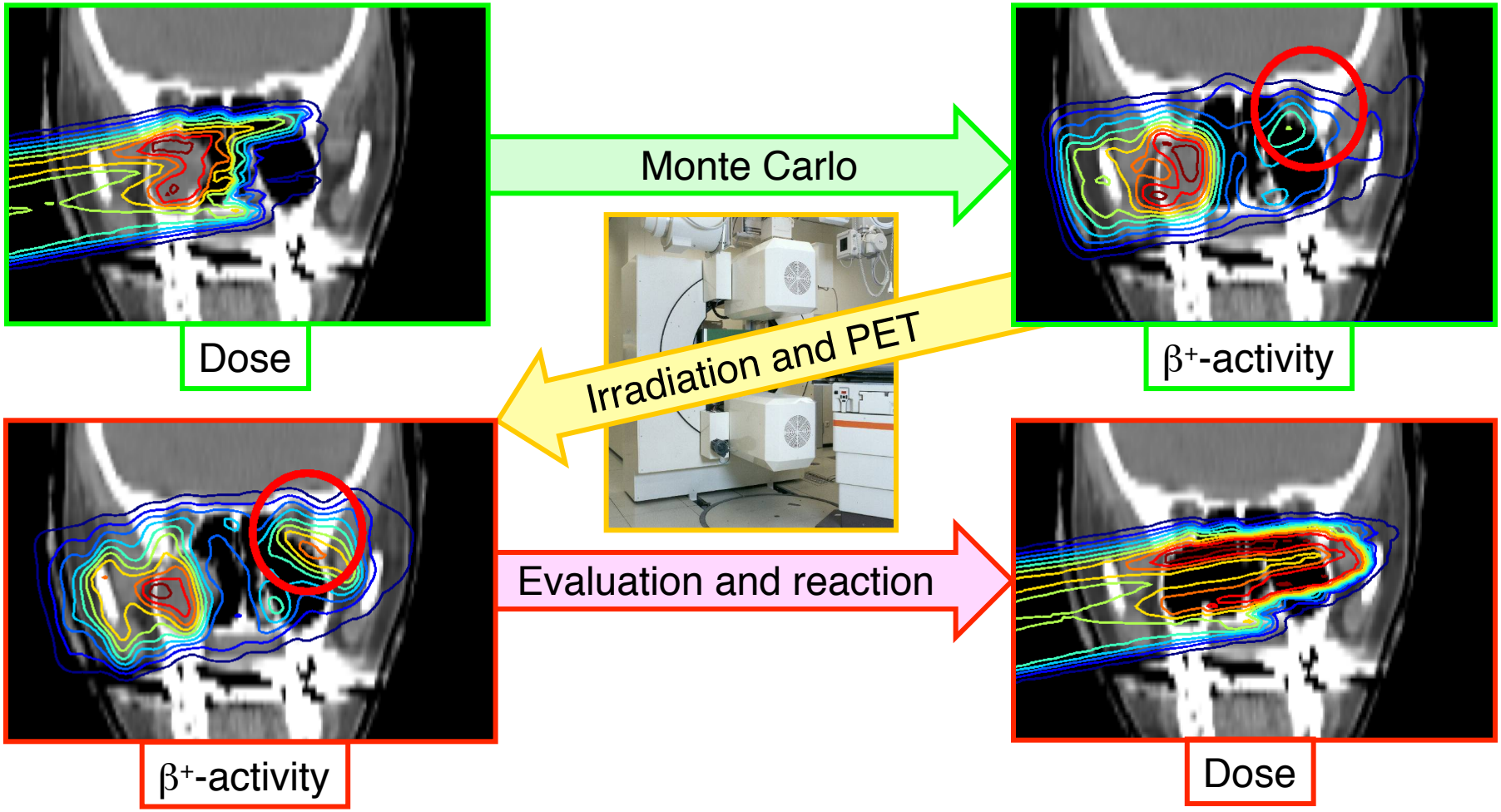
Activity of β^+ emitters is the baseline approach

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

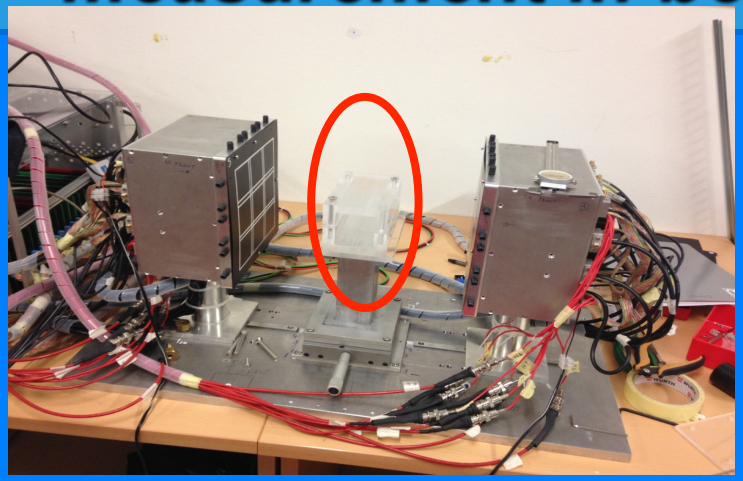


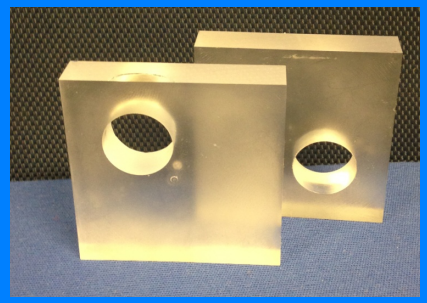
In-Vivo range measurement with PET: workflow and potential

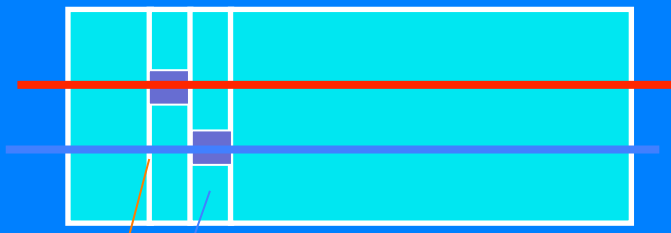
W. Enghardt et al.: Radiother. Oncol. 73 (2004) S96



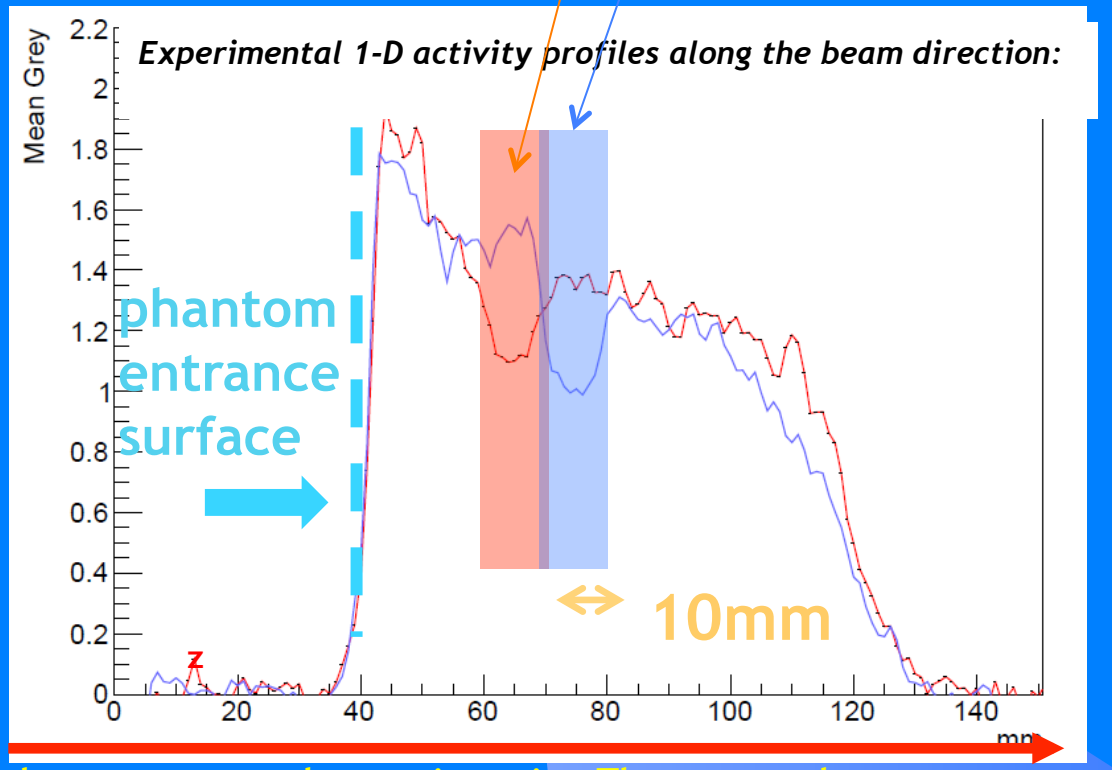
Spotting structures with β^+ activity measurement in-beam (proton beam at CNAO)







A PMMA phanton with air holes in two different positions was irradiated with protons.
A uniform 2 Gy dose was delivered to a 4x4x6 cm^3 PTV.
The proton TP is composed of 34 energy layers with energies ranging from 62 MeV up to 116 MeV/u.

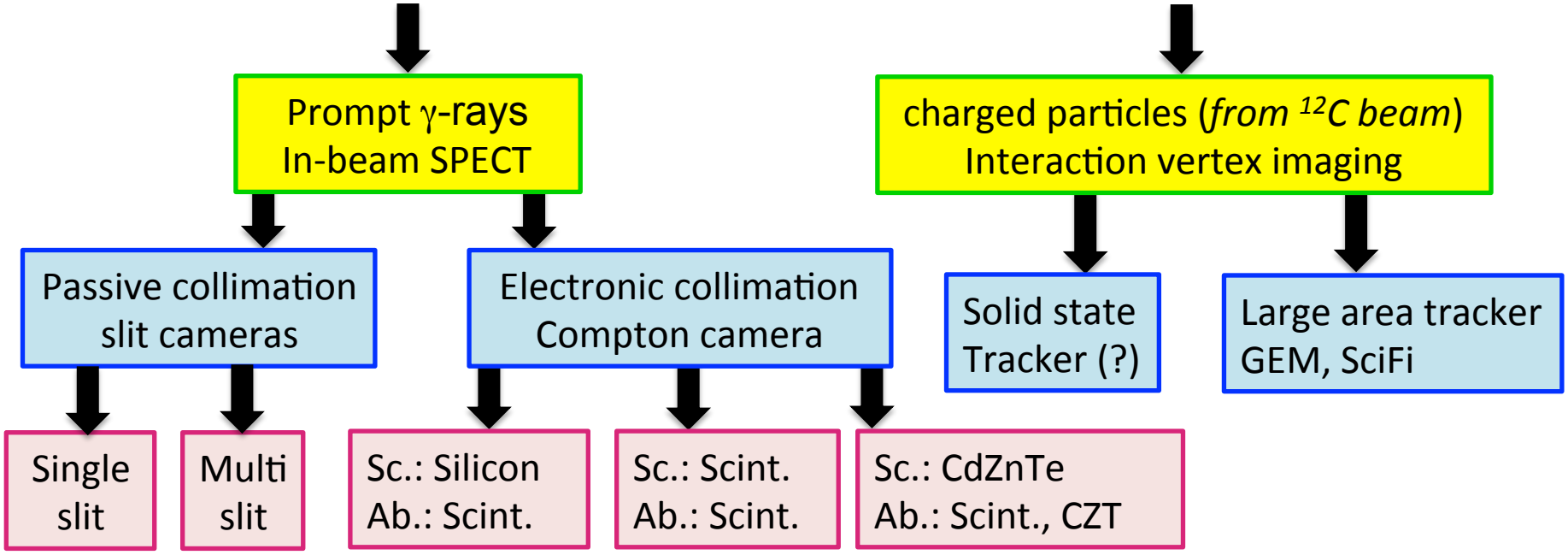


V. Rosso et al,
Submitted to Nucl. Instr. & Meth.

Each profile was calculated over a volume that passes trough one air cavity. The reported profiles correspond to 360 s data acquisition and the profiles were normalized to the same area.

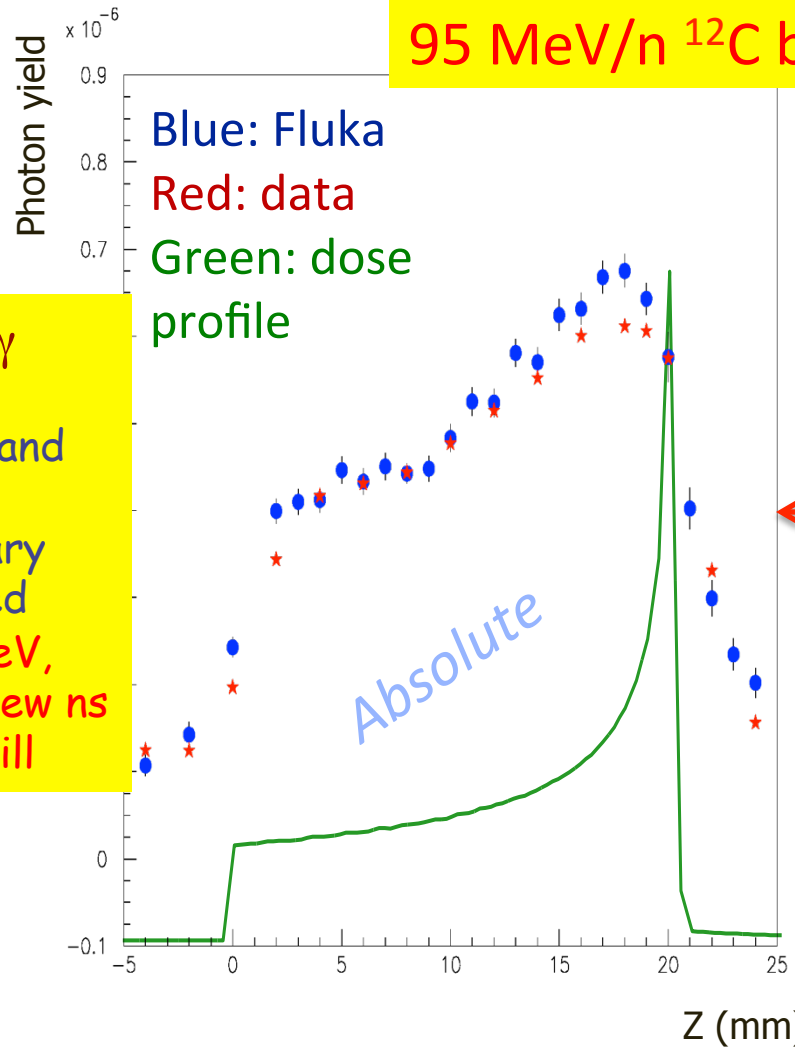
Non PET techniques: simplified overview

- Several different solutions under study
- Unique clinical solution not yet established
- Suitable detectors not commercially available
- Impressive number of physicists/institutions at work

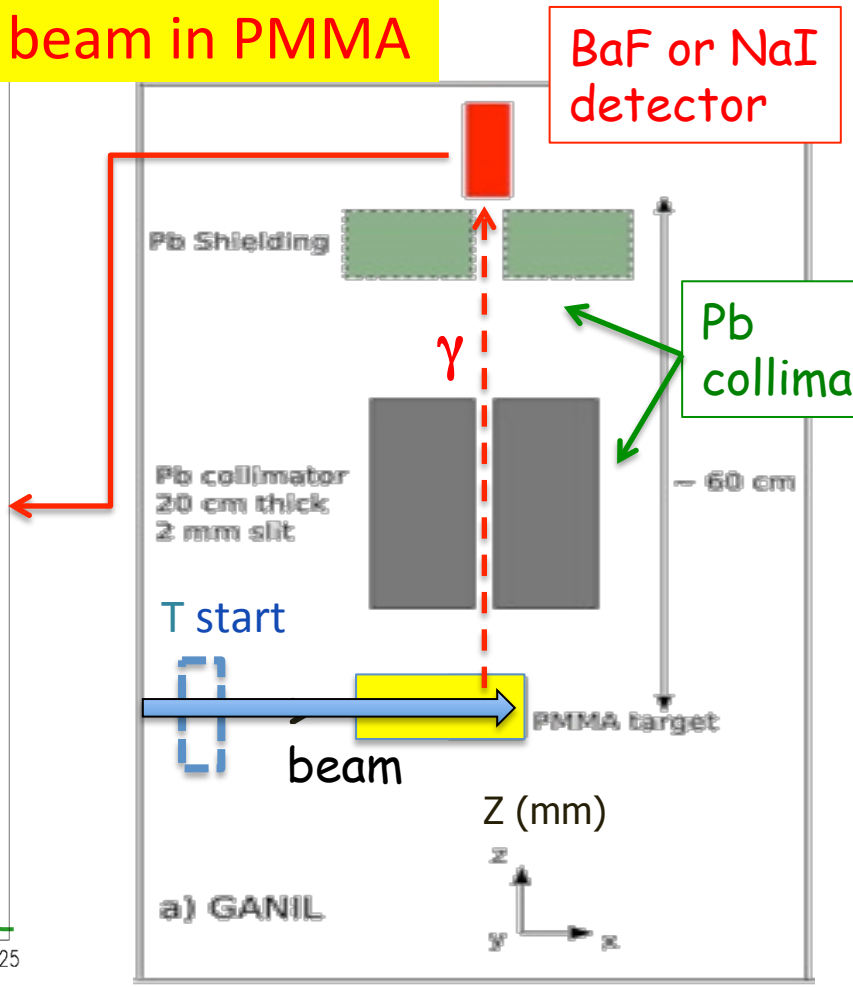


The prompt photons solution

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

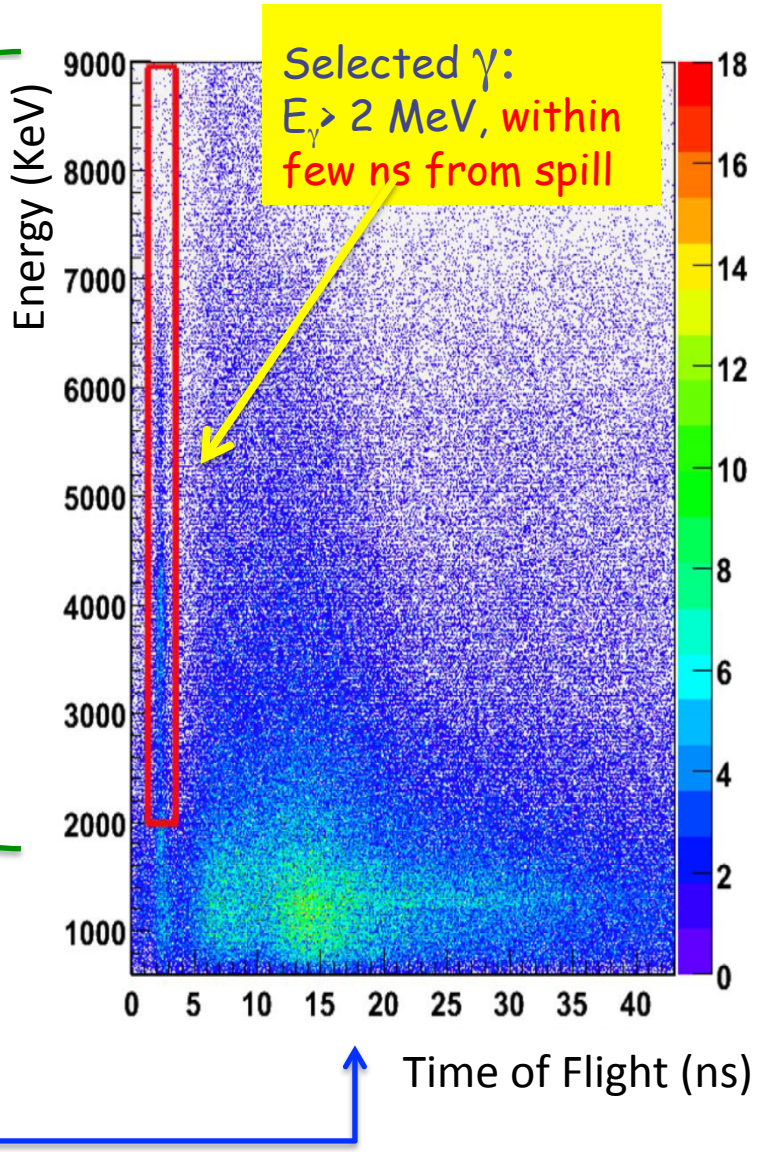


Courtesy of Alfredo Ferrari

[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

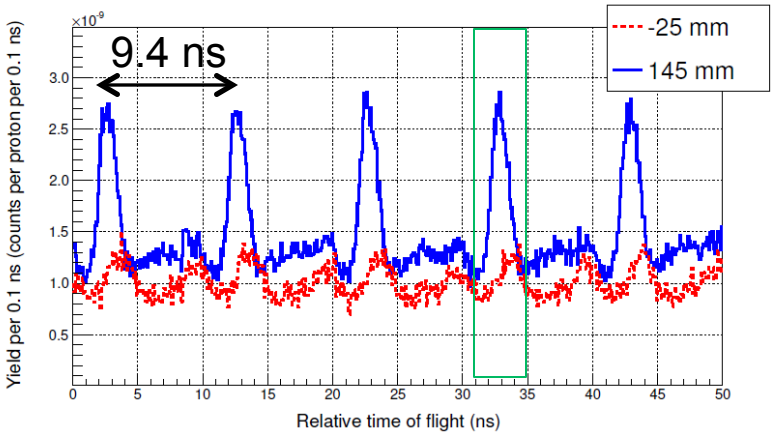
The prompt γ emission: summary

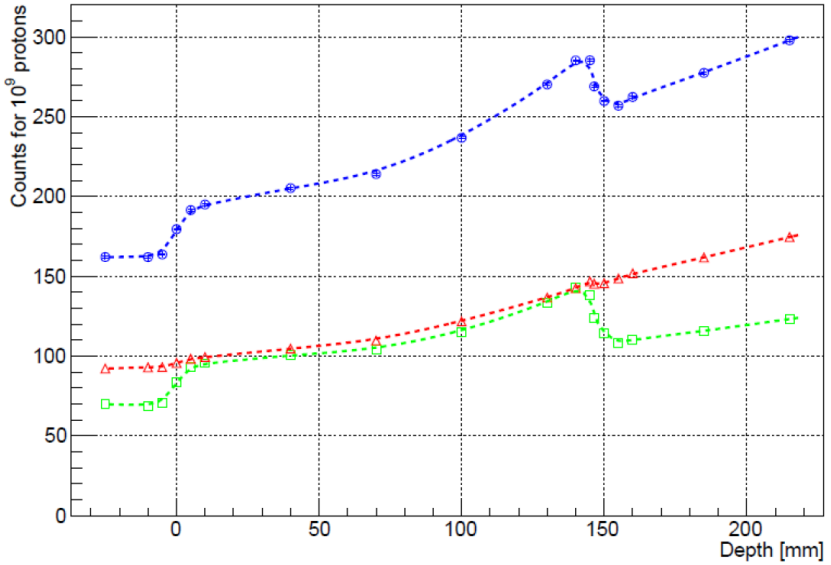
- The gamma are quite copiously produced by proton and ^{12}C beam by nuclear excitation.
- The emission region stretches along all the beam path but has been shown to ends near the Bragg peak for both beams.
- It's not simple backpointing the γ direction: the γ energy is in the 1-10 MeV range-> much 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



Influence of TOF on PG profiles (collimated cameras)

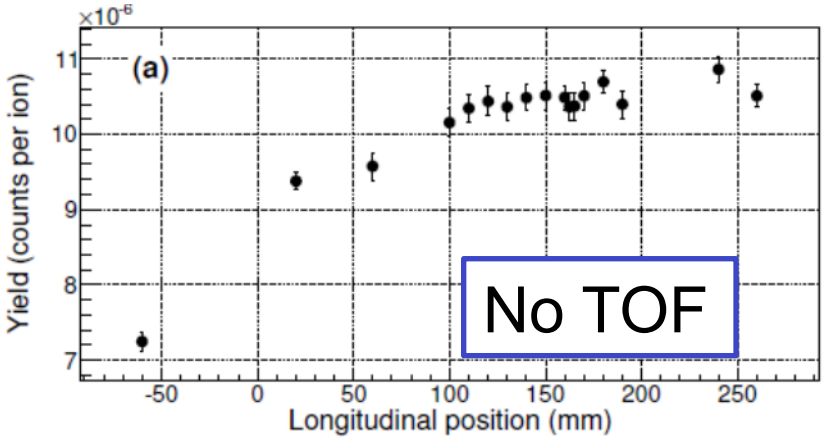
160 MeV protons in PMMA
IBA C230 cyclotron

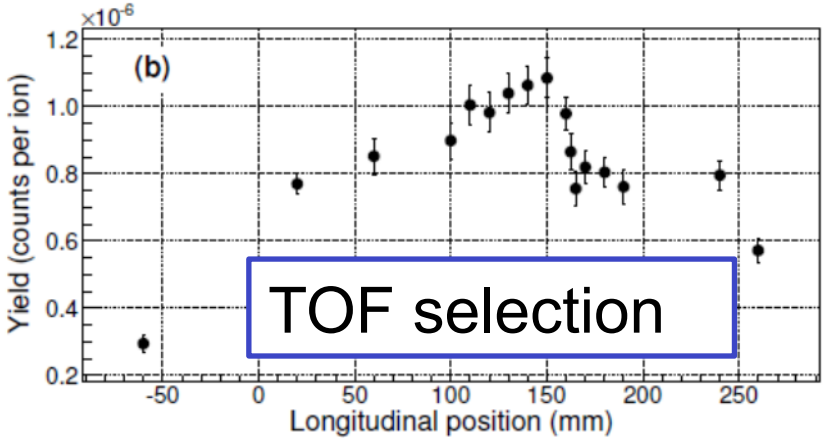




Roellinghoff PMB 2014

310 *A*MeV carbon ions in PMMA





TOF : mandatory for carbon ions

M. Pinto, submitted New J Phys

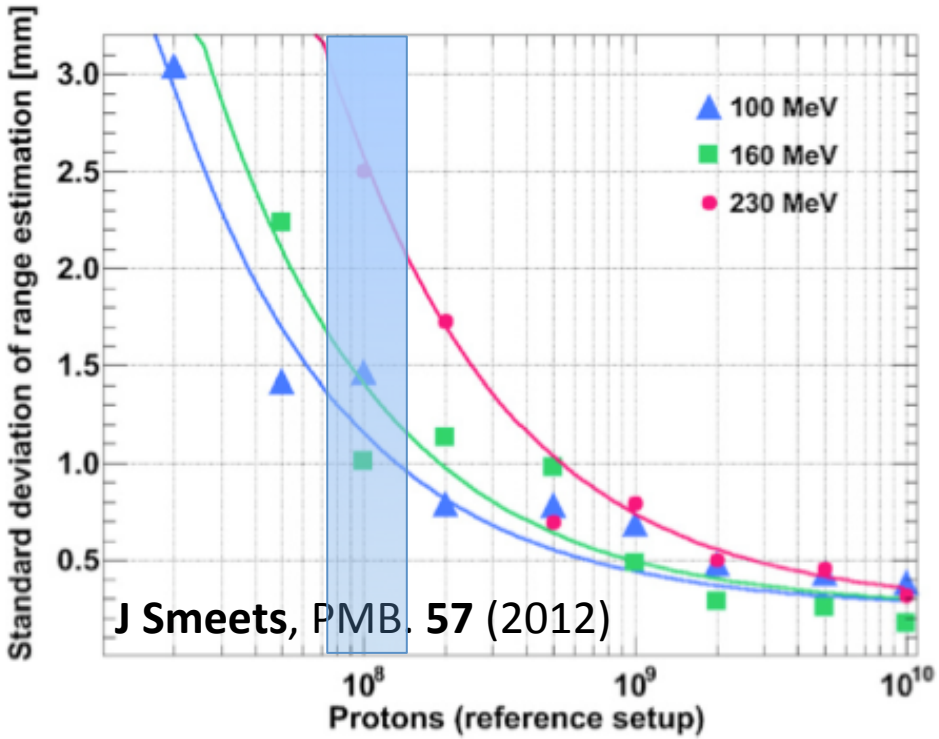
Courtesy of D. Dauvergne

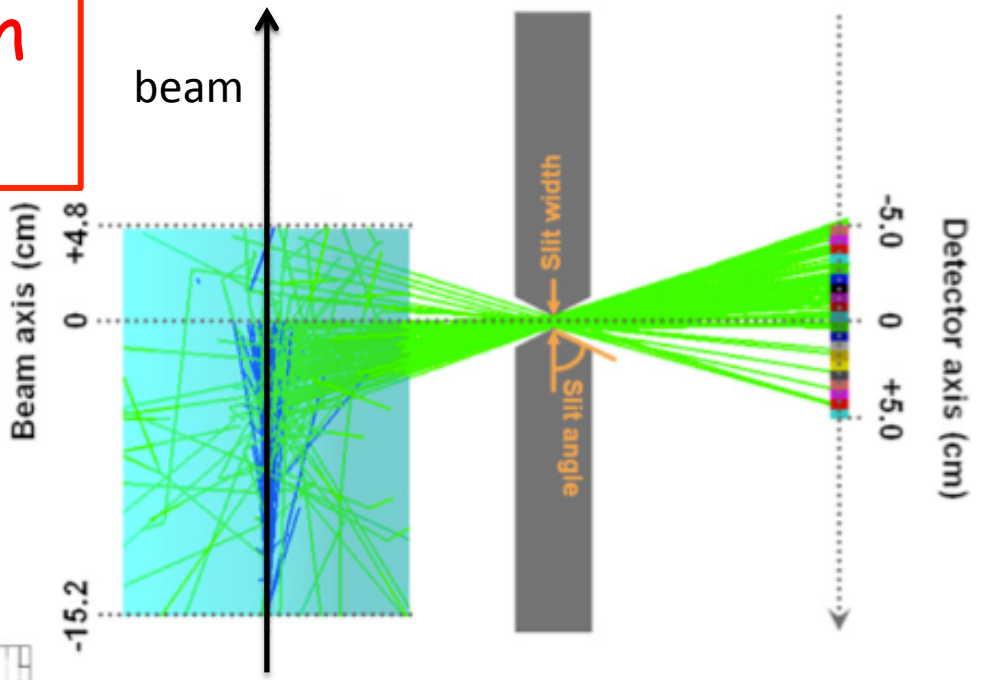
Range monitor for proton beam: the slit camera

Optimized on proton beam

Several groups working also on:

- electronic collimated (Compton) camera
- Multi-slit collimated camera



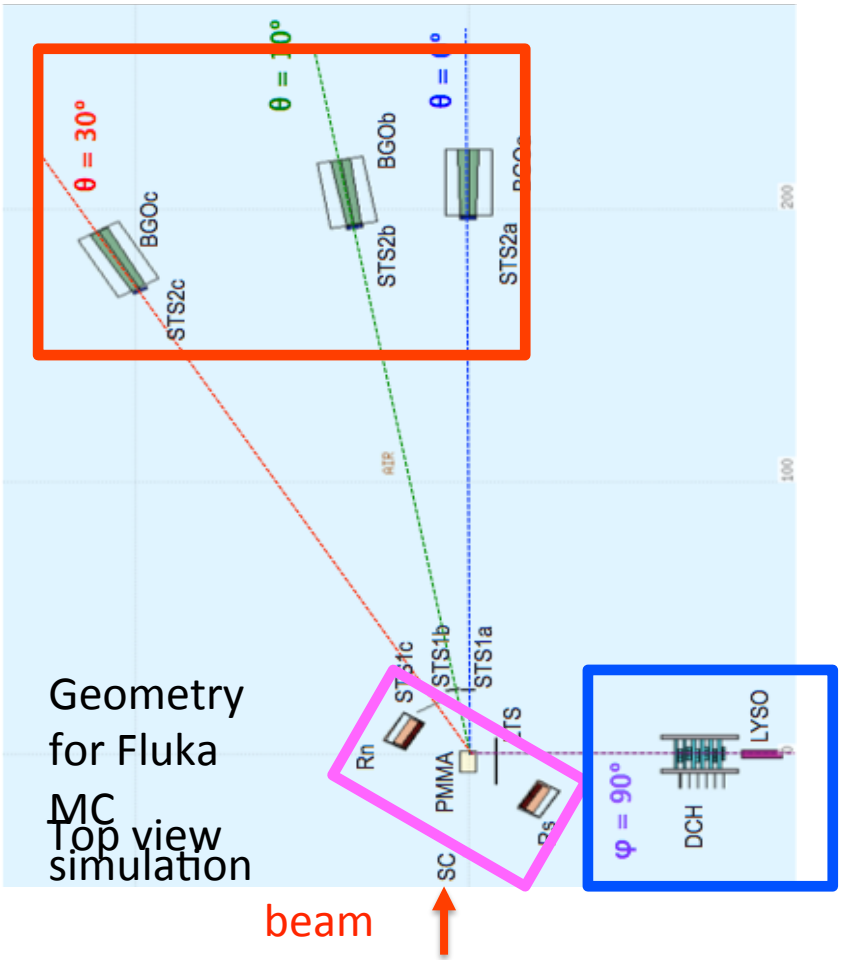


Possible clinical solution envisaged for proton beam, but what about heavier beam (^{12}C) ? LET grows as Z^2 and the nuclear interaction increase with A. Thus, for the given dose, ^{12}C gives:

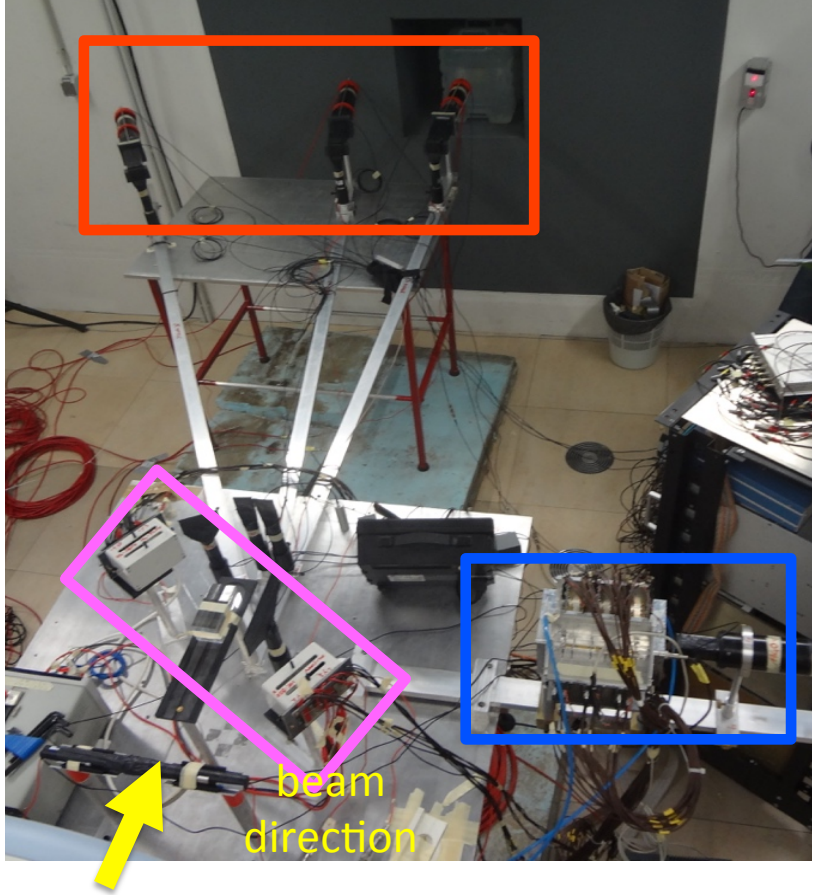
- less prompt γ than proton
- more background than proton

Secondary @ HIT from ^{4}He, ^{12}C, ^{16}O beams

- He, C , O beams with therapeutical energy
- thick PMMA target with **fixed** distance between BP and PMMA exit window



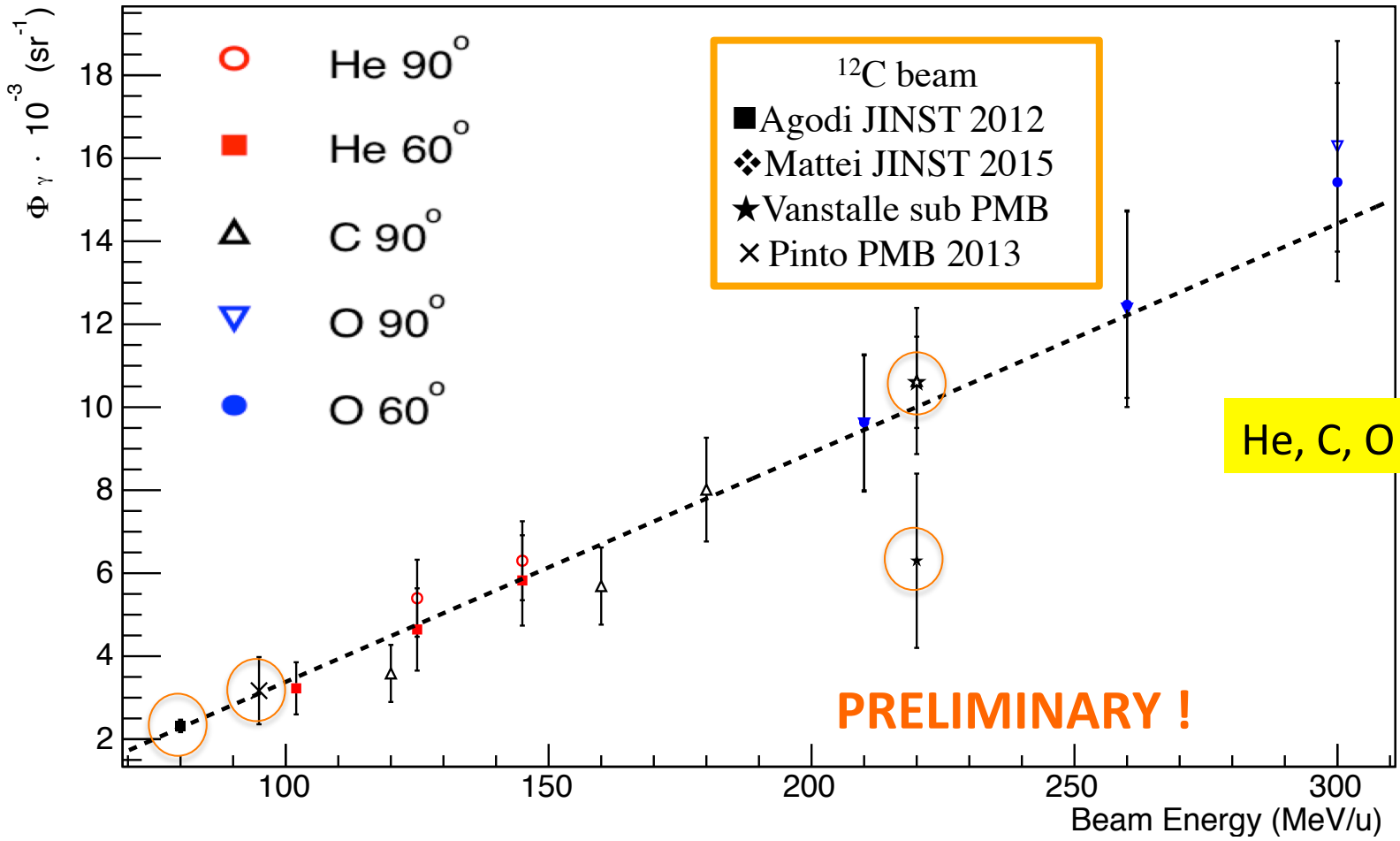
Geometry for Fluka MC simulation



- ✓ BGO detectors for forward [0° - 30°] fragmentation studies
- ✓ pixelated LYSO detectors for PET monitoring
- ✓ {DCH} + {LYSO} setup for prompt-γ and charged particles studies
- ✓ Thin plastic scintillators have been used for ToF and dE measurements.

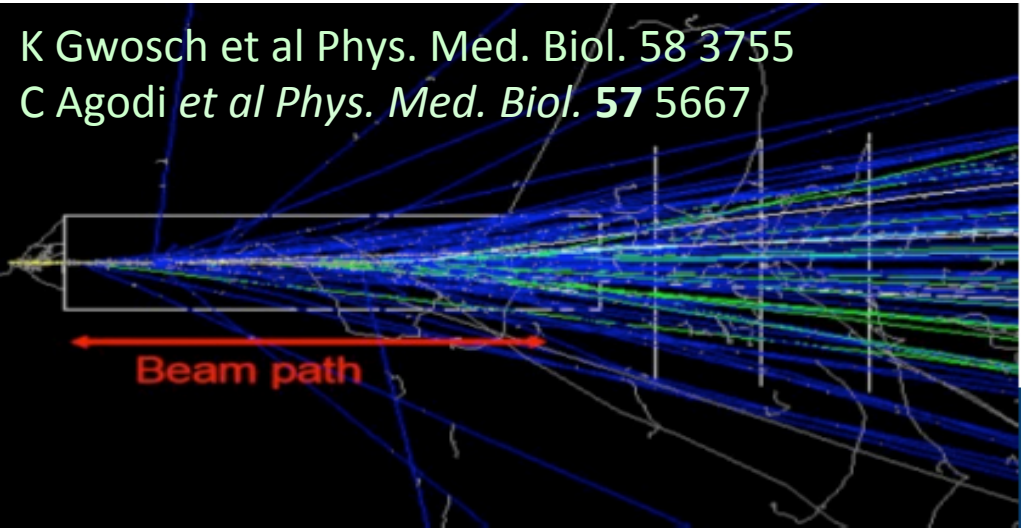
Non proton beams: Prompt γ vs E_{kin}

- Approximate linear scaling with E_{kin}/nucleon irrespectively of *A*
- Is the number of the de-excitation γ proportional to the nuclear collisions of the beam?



He, C, O beam @ HIT

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

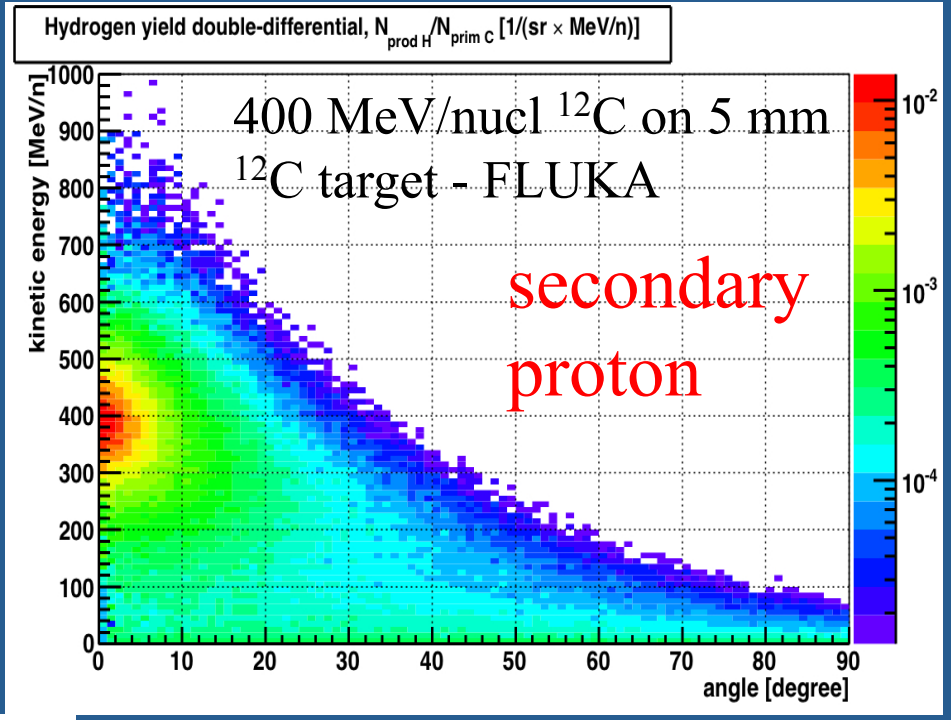
BUT…

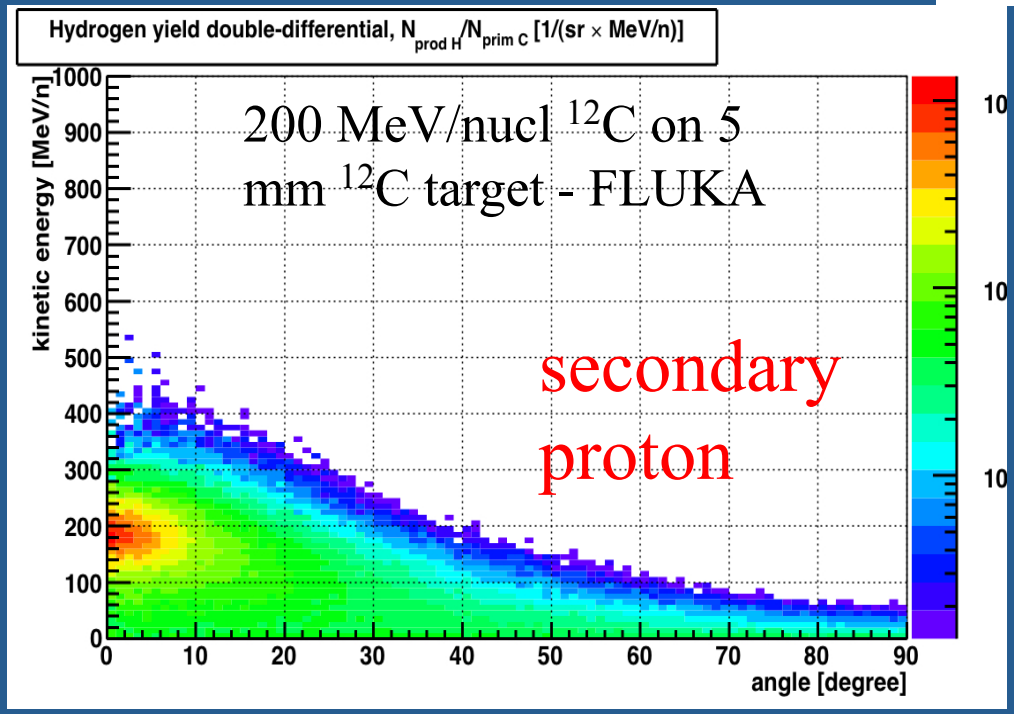
- They are forward peaked
- Energy threshold to escape the patient ~ 80-90 MeV
- They suffer multiple scattering inside the patient -> worsen the back-pointing resolution

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

Secondary proton: angle vs energy

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



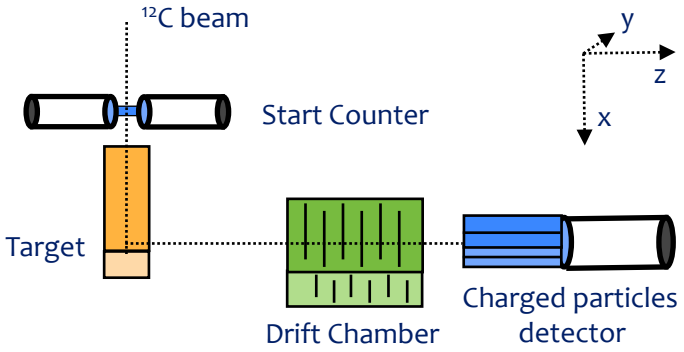


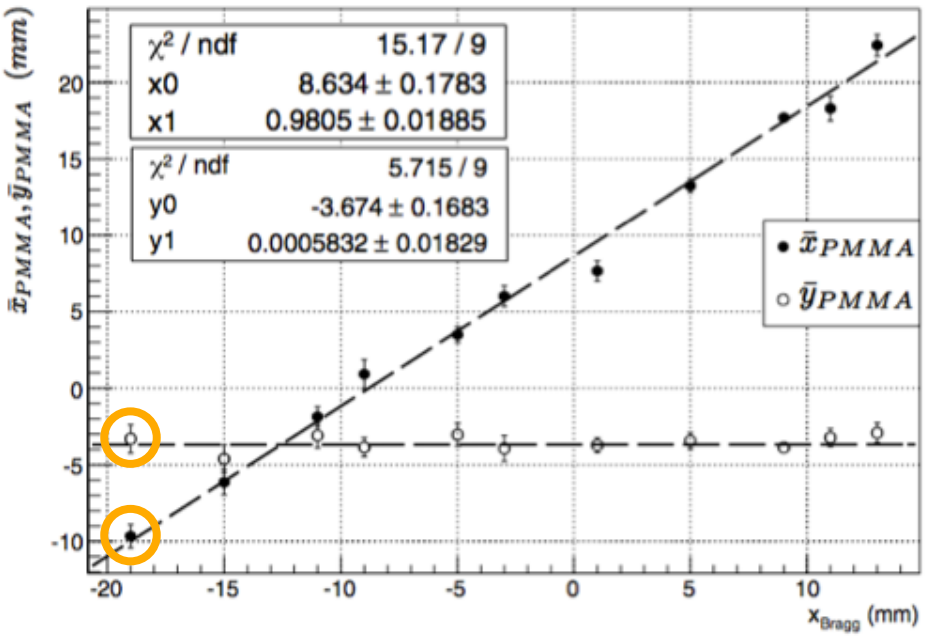
The proton flux at large angle is mainly made by low energy particles.. Can be of any use for monitoring???

WATCH OUT!! How much are MC reliable at the moment? They are rapidly improving, but…

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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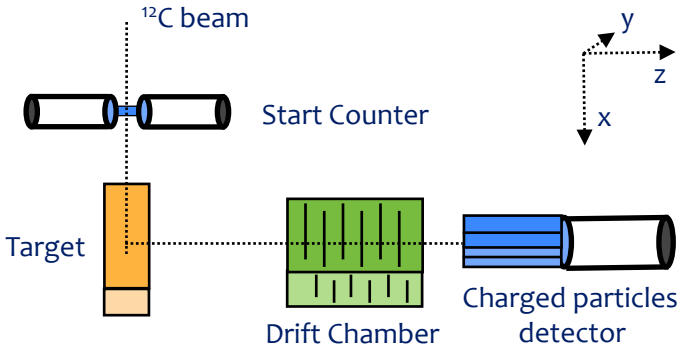

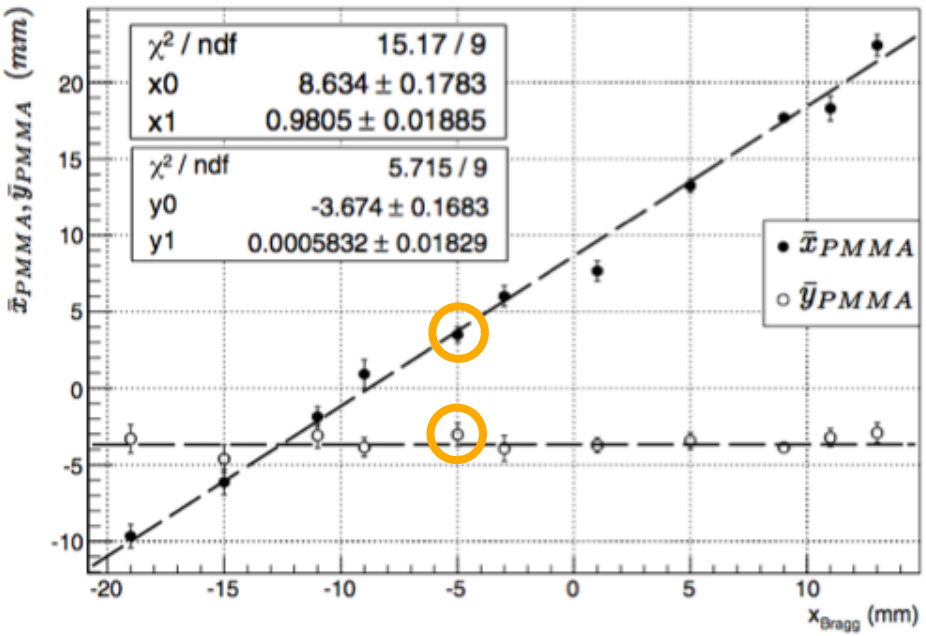

Agodi et al. PMB 2012

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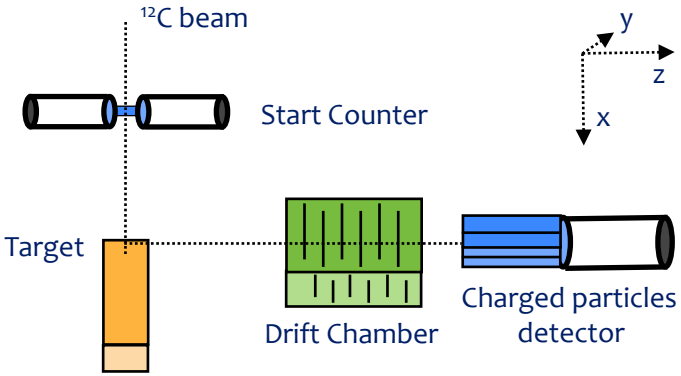
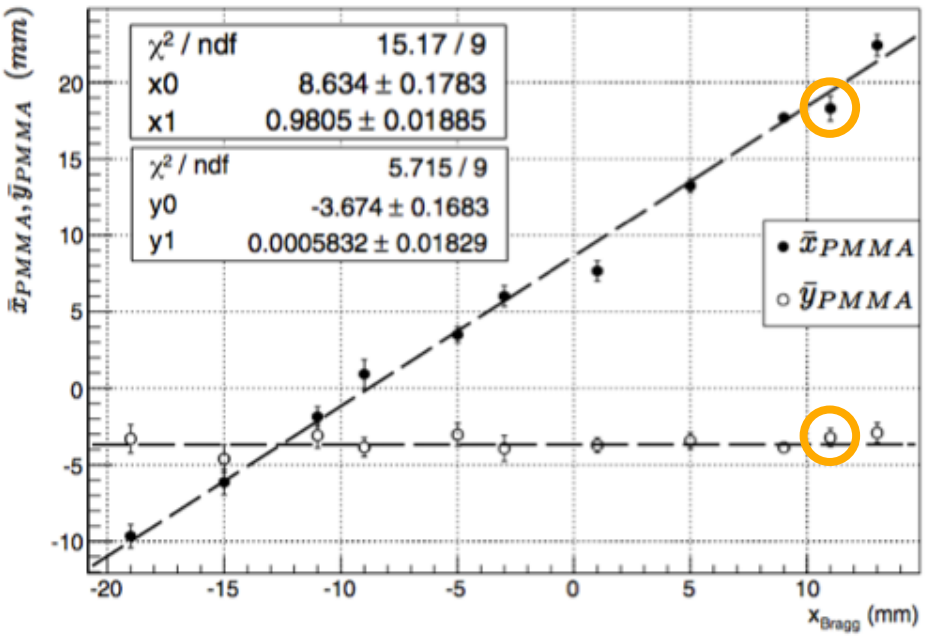


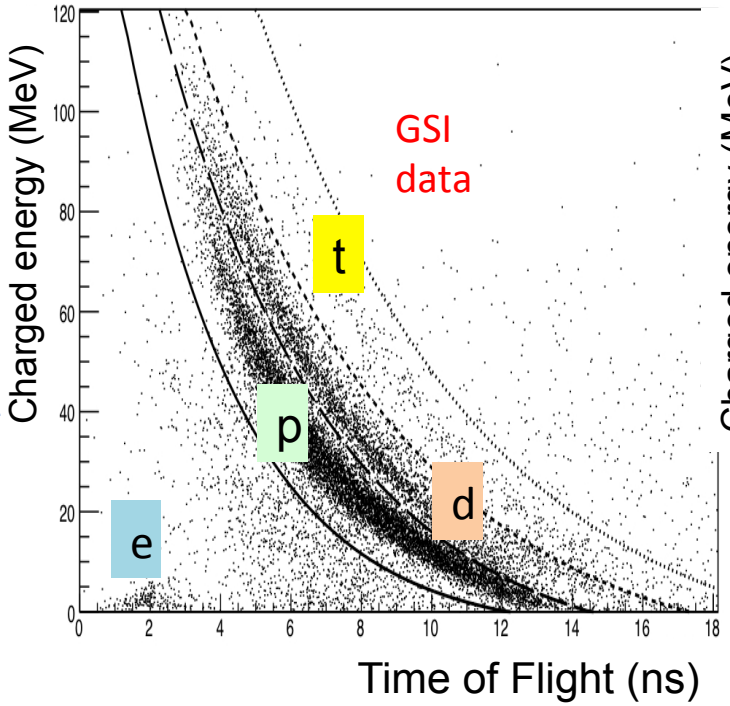


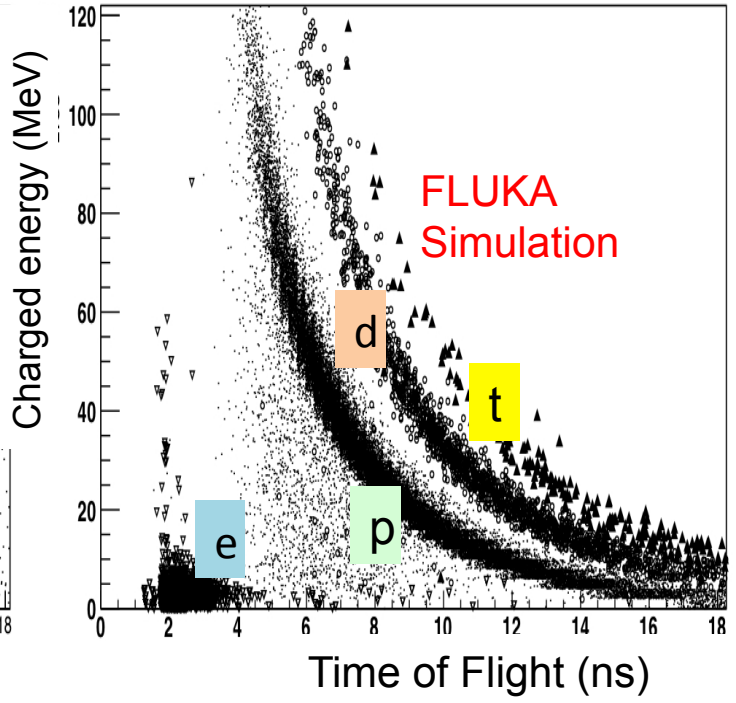
Agodi et al. PMB 2012

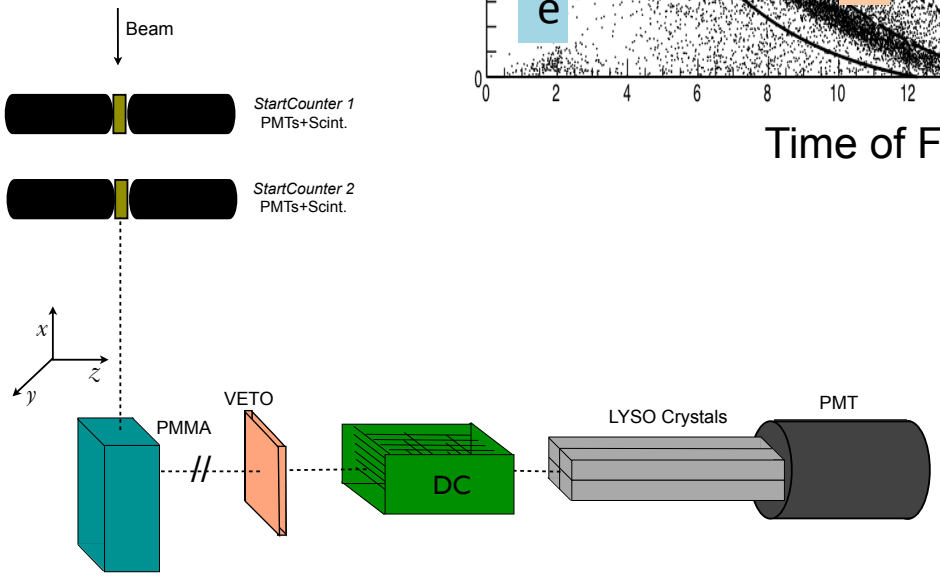
charged secondaries & ^{12}C beam radiography

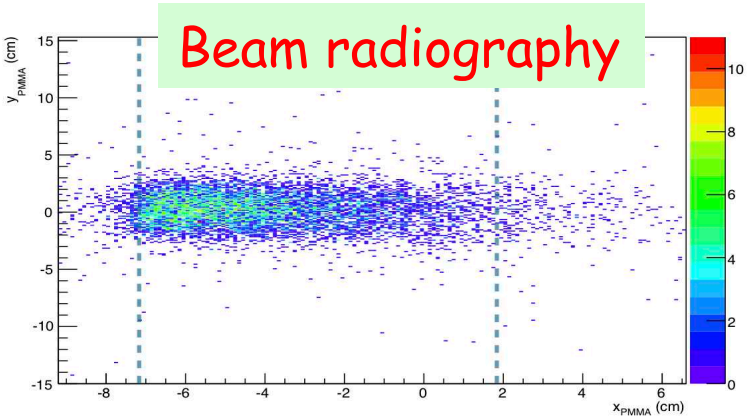
L.Piersanti et al. PMB, 2014

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









Carbon beam @90° (reference runs)

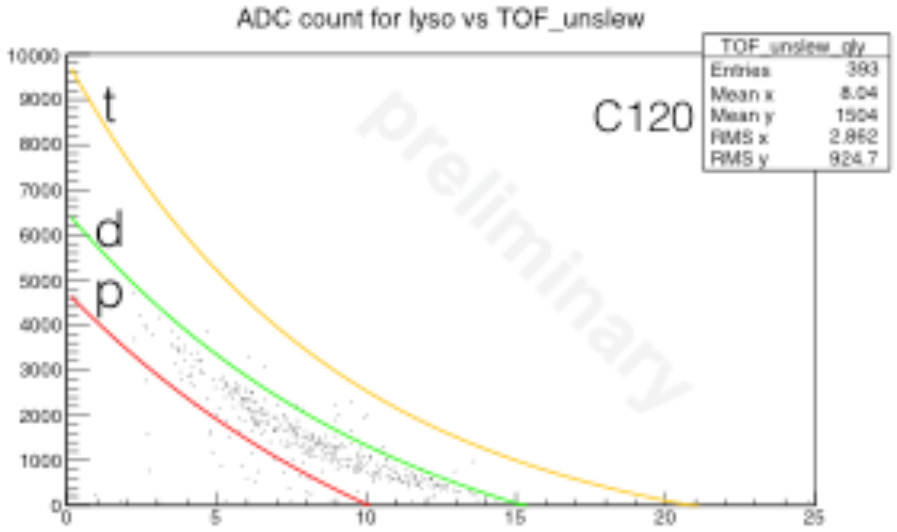
Charged secondaries monitoring

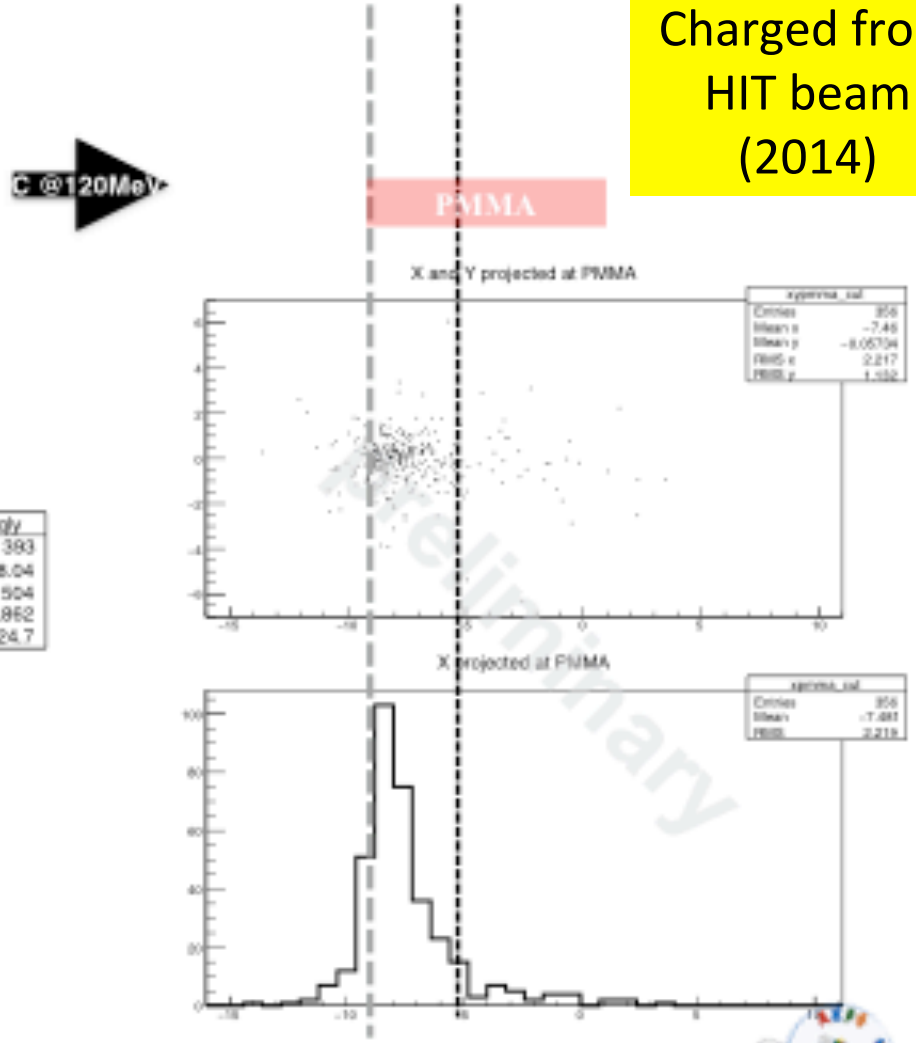
A non negligible production of charged particles at large angles is observed for all beam types.

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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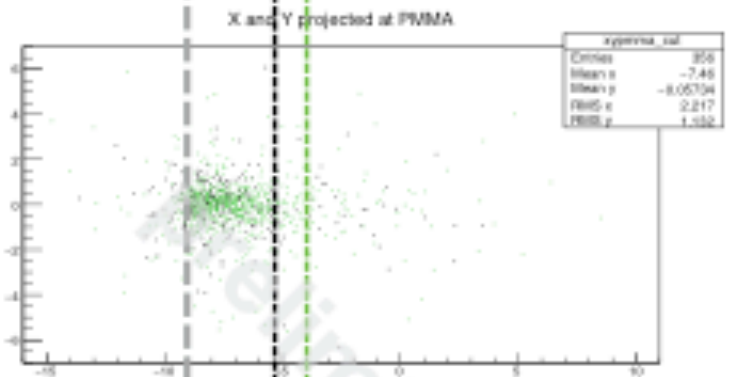

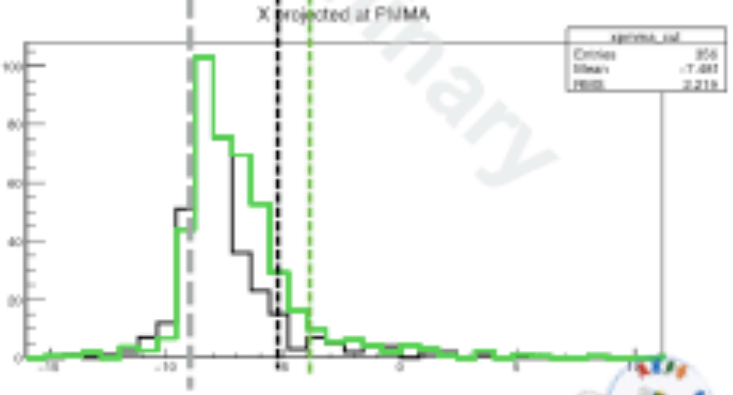

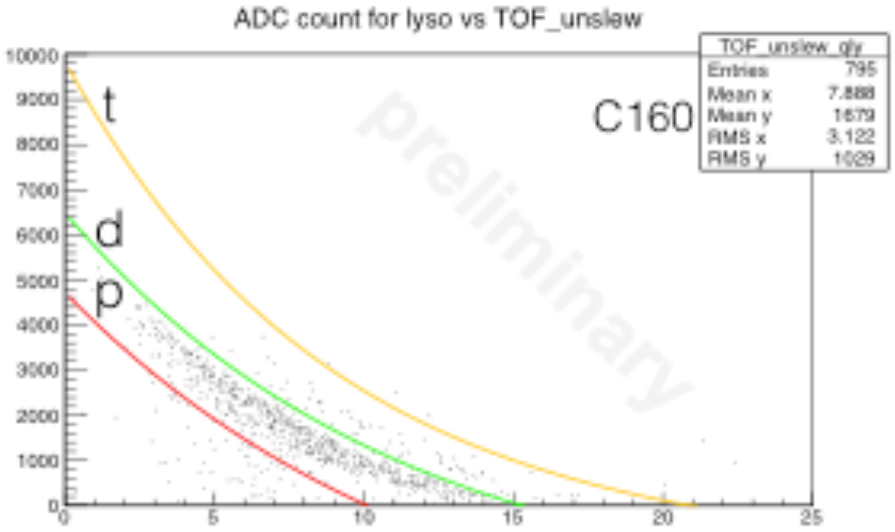

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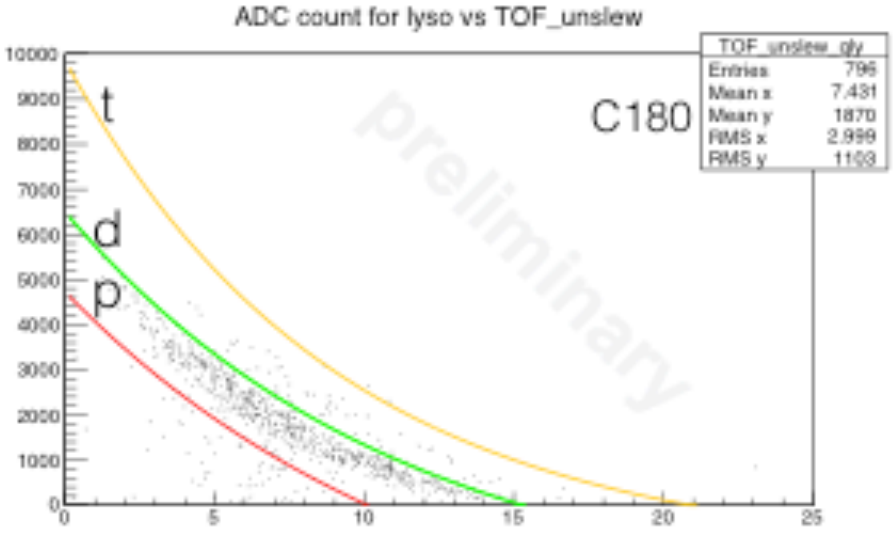

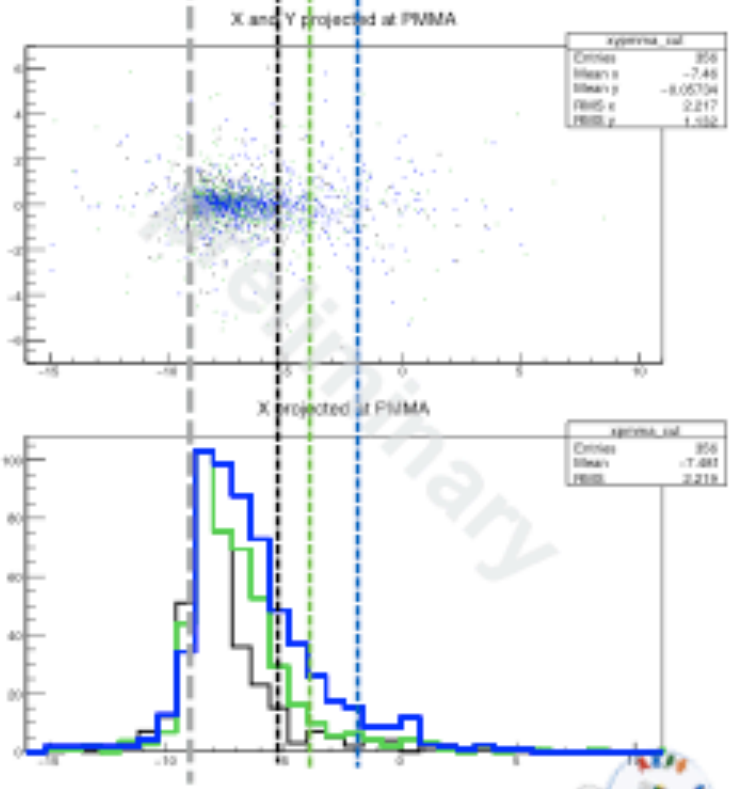

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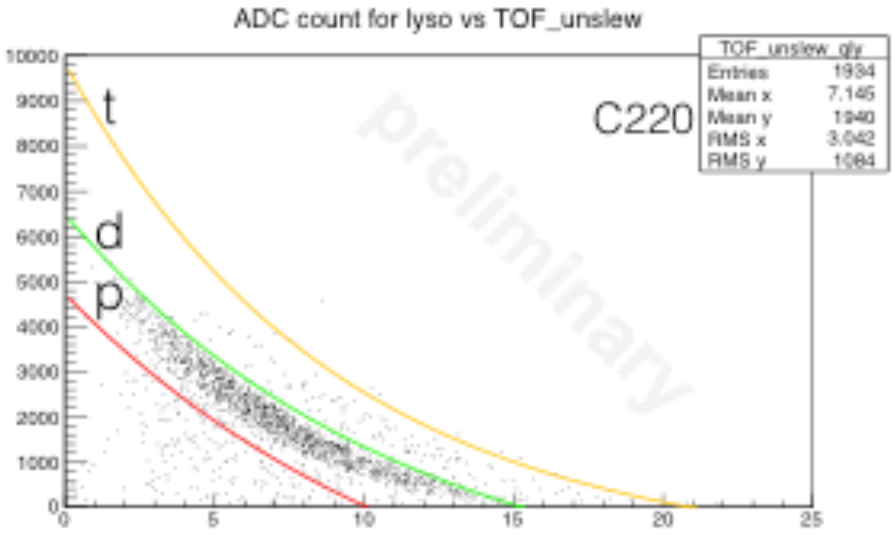

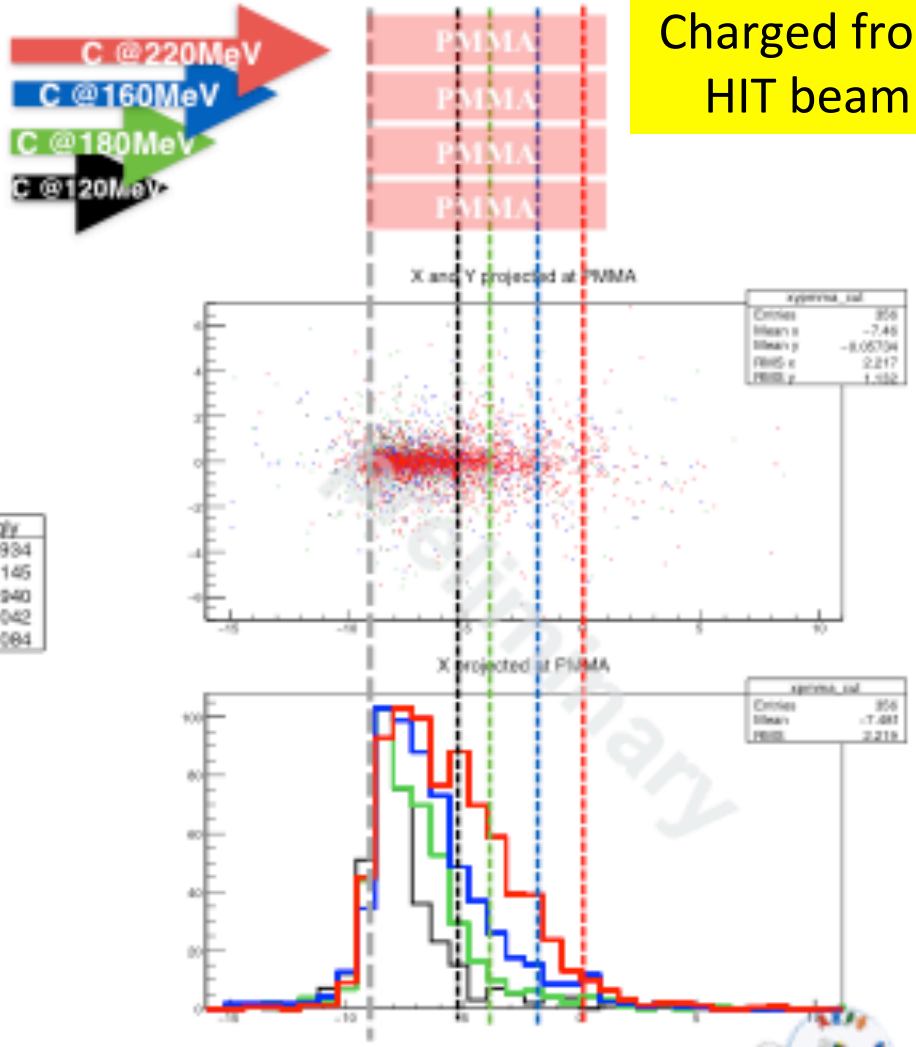

Charged from HIT beam

To be submitted to PMB

preliminary

Helium beam @90°

Charged secondaries monitoring

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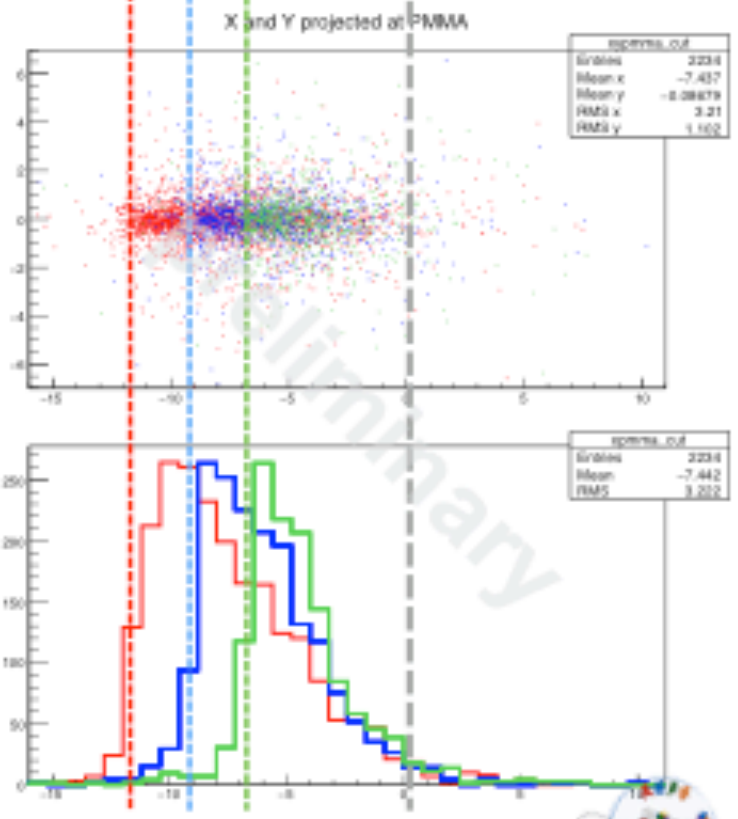
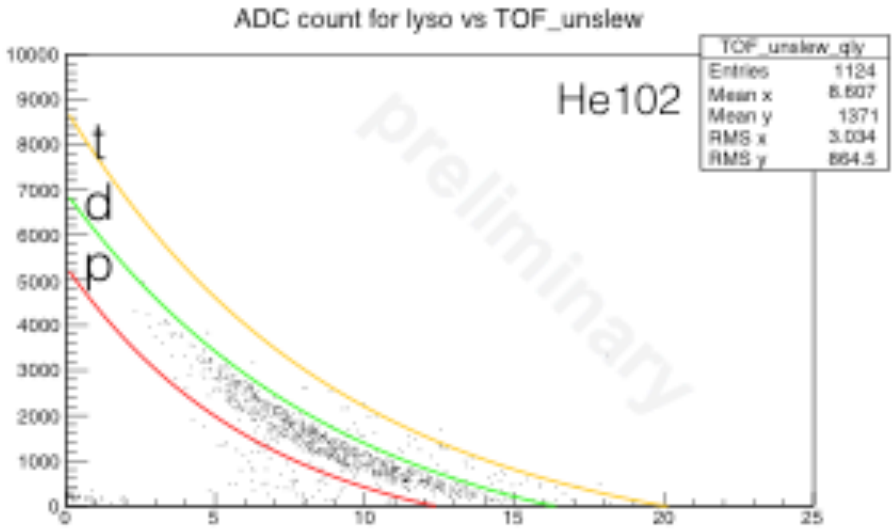




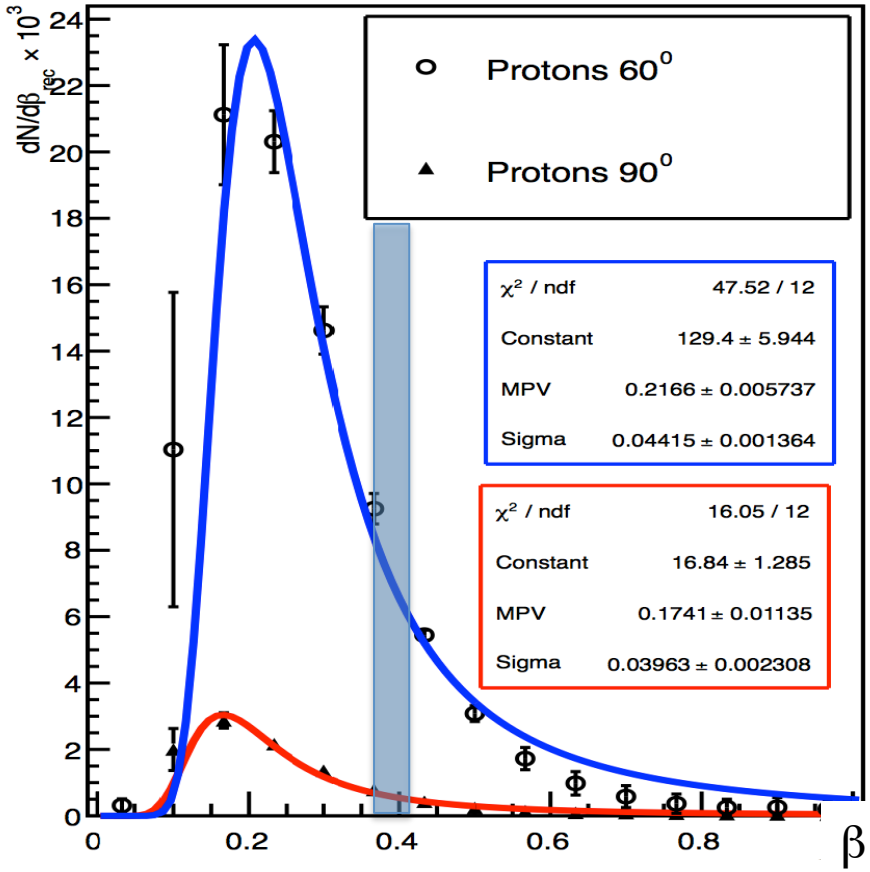
To be submitted to PMB

preliminary

Secondary proton: energy distribution

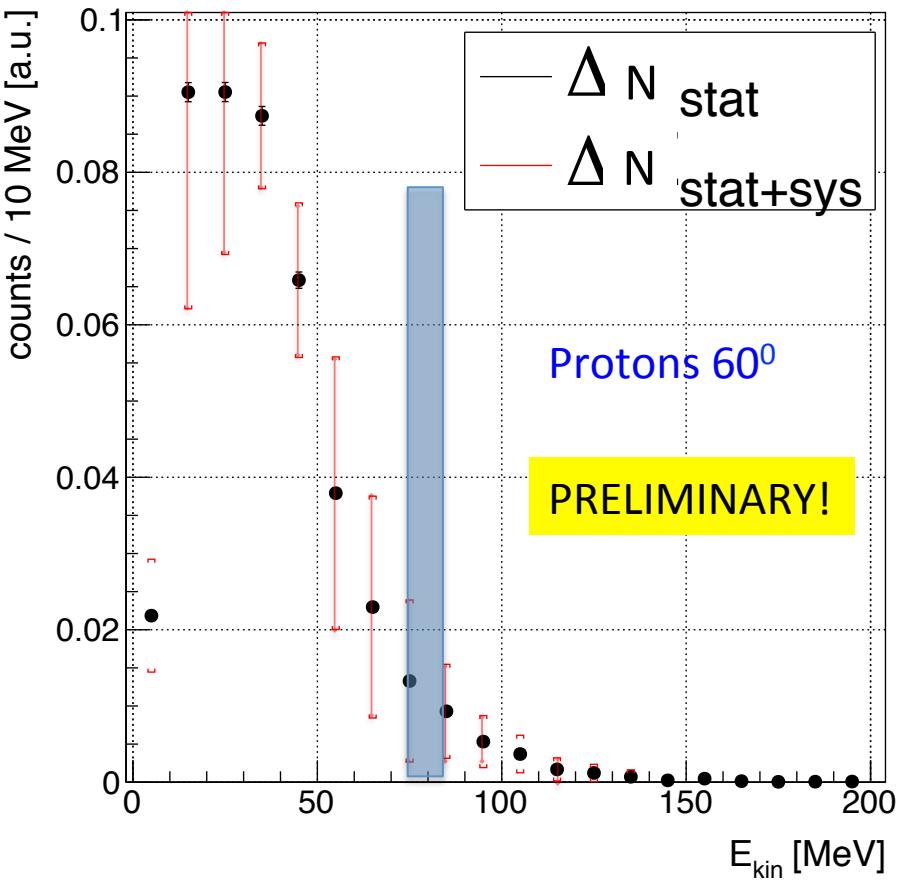
Only a fraction of the p flux can exit the patient.. 80-90 MeV are needed in the worst case (deep tumor at 8-9 cm from skin)

^{12}C @220 AMeV *L.Piersanti et al. PMB, 2014*



0 20 80 180 320 E_{kin}(MeV,

^{4}He @145 AMeV (HIT) to be sub. to PMB

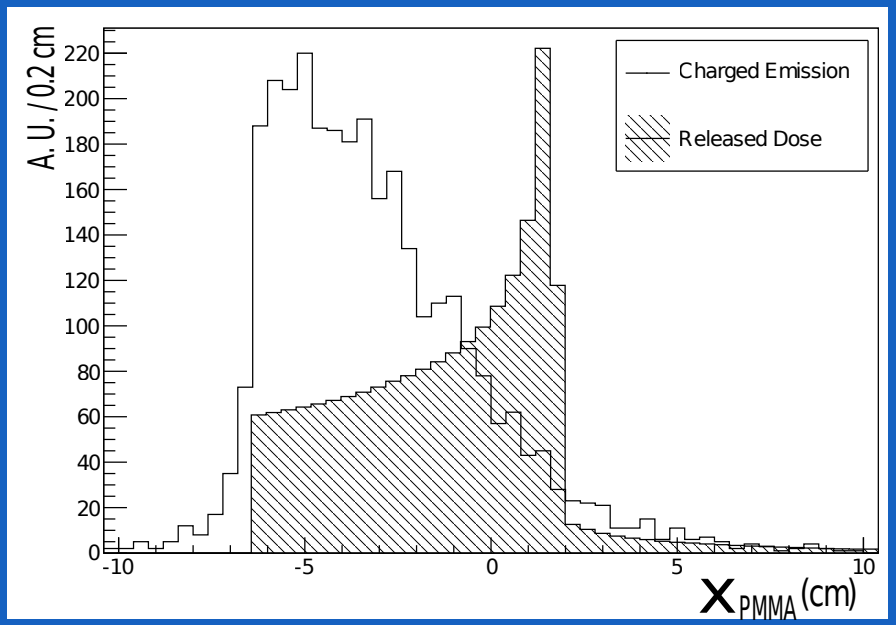


Secondary emission point, BP and the patient

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

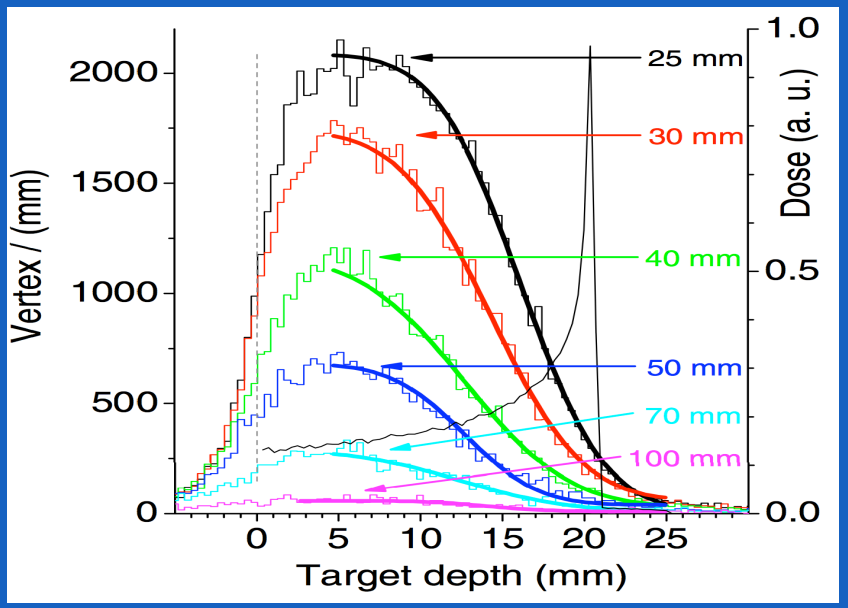
Measured emission shape of protons outside a 5 cm thick PMMA at 90^0 wrt the direction of 220 AMeV ^{12}C beam

L.Piersanti et al. PMB, 2014



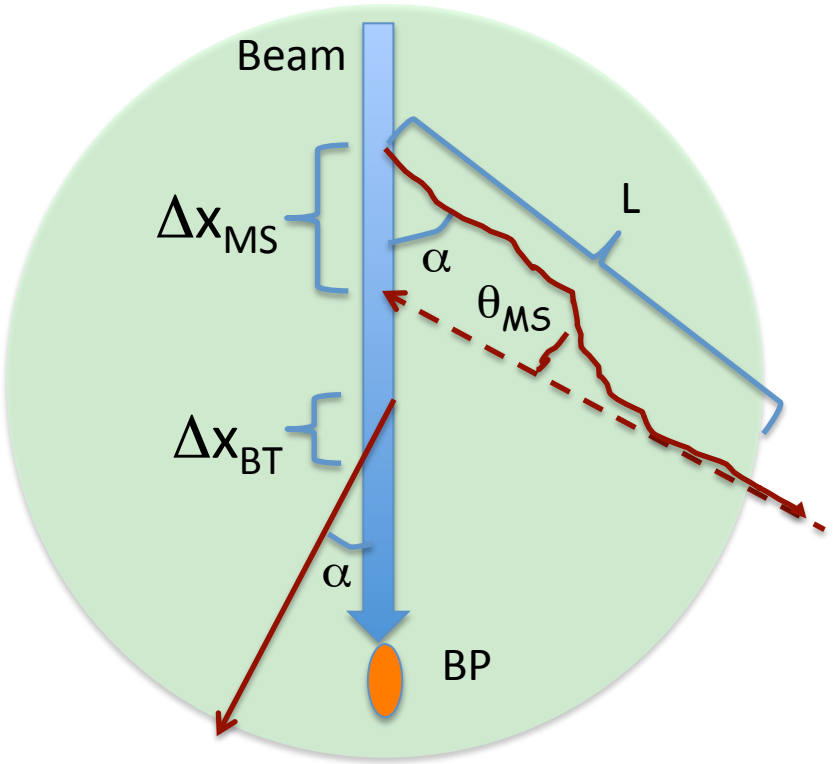
Simulated emission distribution shape of protons as detected outside different PMMA thickness at 30^0 wrt the direction of 95 AMeV ^{12}C beam

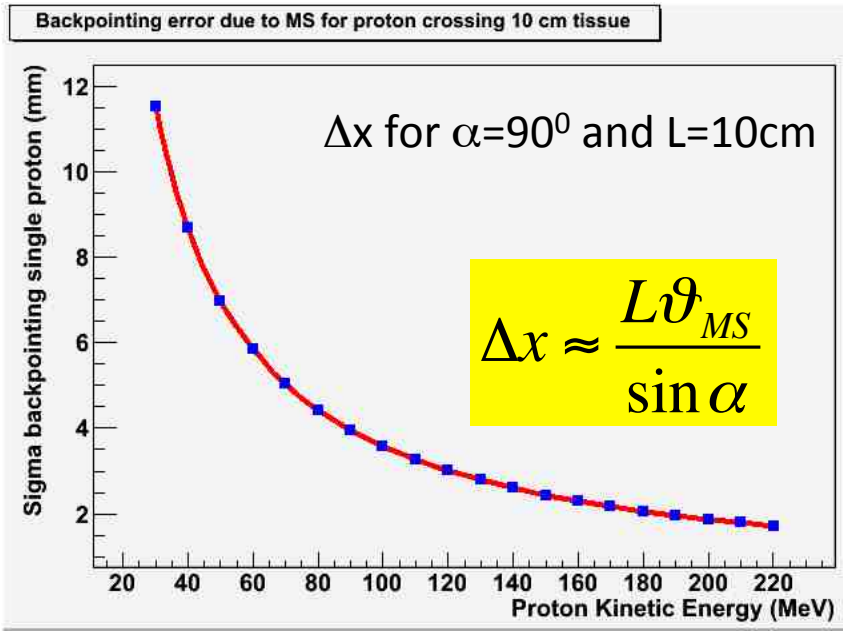
E. Testa et al Phys. Med. Biol. 57 4655



detector: which & where?

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





Small angle	Large angle
• higher momentum -> less MS • Higher statistic • Back-tracking is much worse	• Optimal back-tracking • lower momentum -> more MS • Less statistics

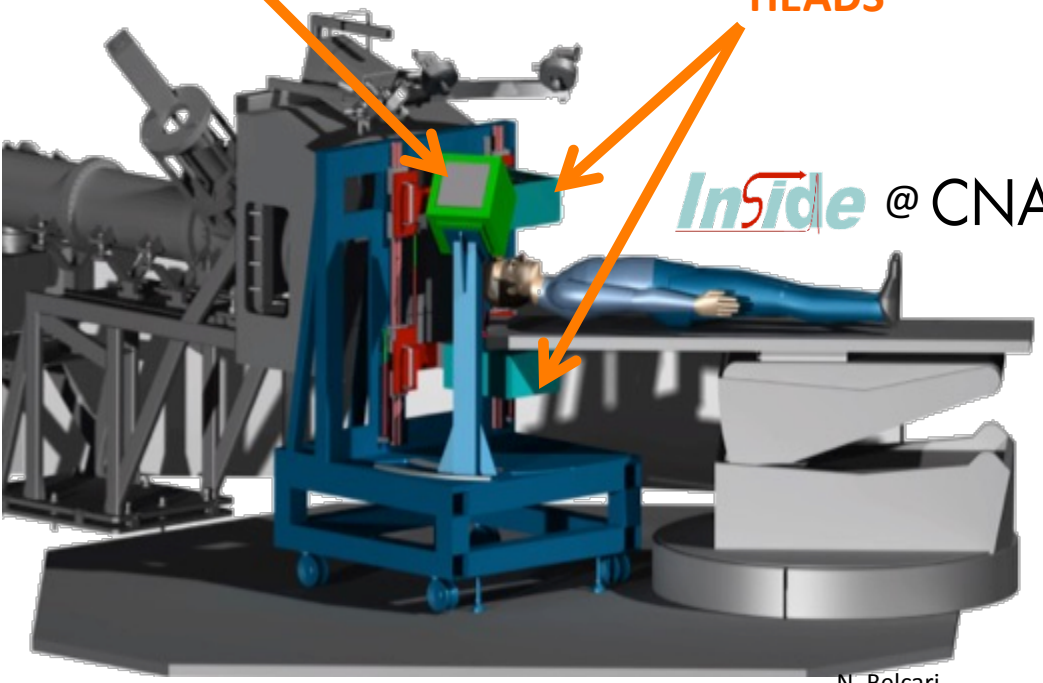
The InSide Project

Prompt secondary particles emission

Tracker + Calorimeter = DOSE PROFILER

β^+ activity distribution

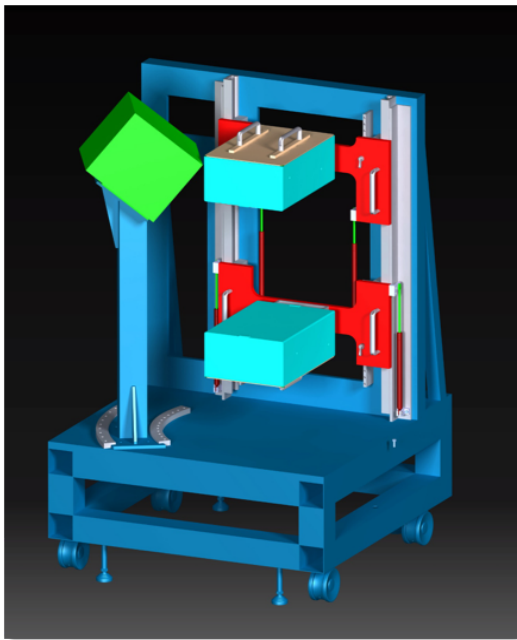
IN-BEAM PET HEADS



InSide @ CNAO

INnovative Solutions for In-beam DosimEtry in Hadrontherapy

- integrated in treatment room
- operated in-beam
- **provide an IMMEDIATE feedback on the particle range**



PRIN + Centro Fermi + INFN project

P. Cerello
S. Coli
E. Fiorina
G. Giraudo
F. Pennazio

N. Belcari
G. Bisogni
N. Camarlinghi
A. Del Guerra
S. Ferretti
E. Kostara
A. Kraaan

N. Marino
M. Morrocchi
M.A. Piliero
G. Pirrone
V. Rosso
G. Sportelli

C. Peroni
A. Rivetti
R. Wheadon
A. Attili,
S. Giordanengo

E. De Lucia
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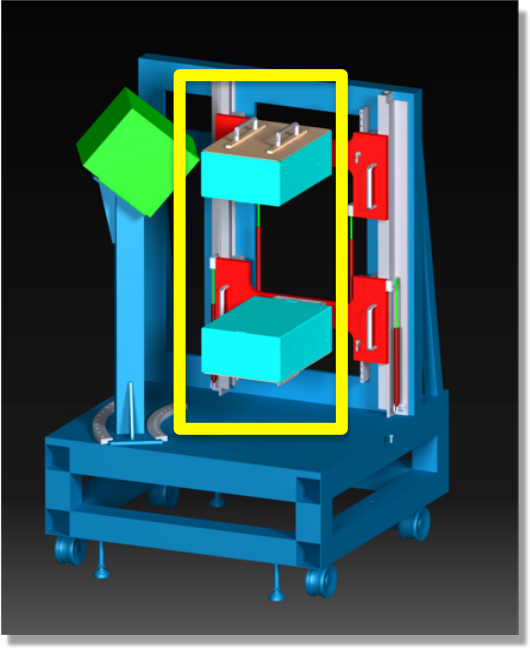
C. Morone

V. Patera
L. Piersanti
A. Sarti
A. Sciubba
C. Voena

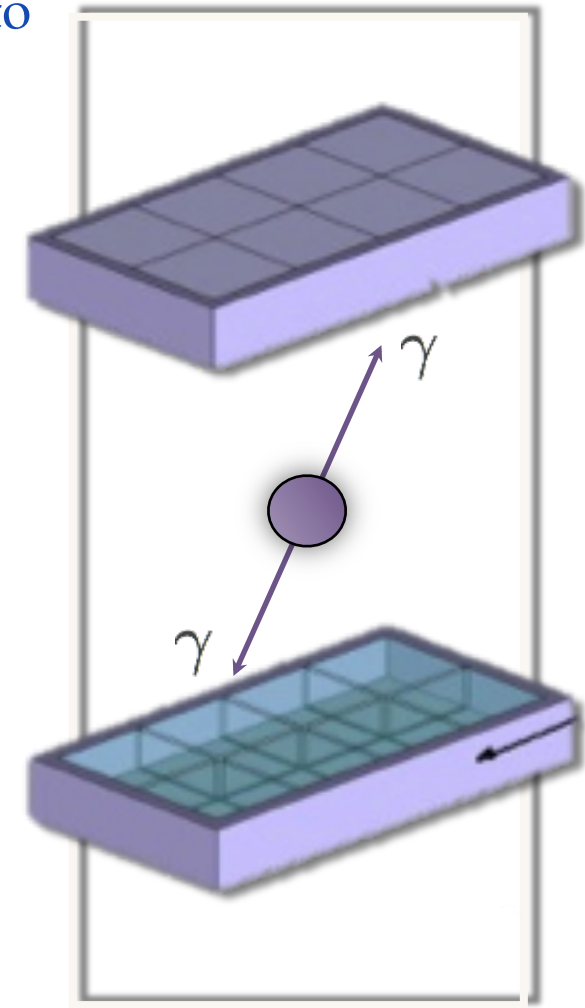
F. Ciciriello
F. Corsi
F. Licciulli
C. Marzocca
G. Matarrese

G. Battiston
S. Muraro
P. Sala



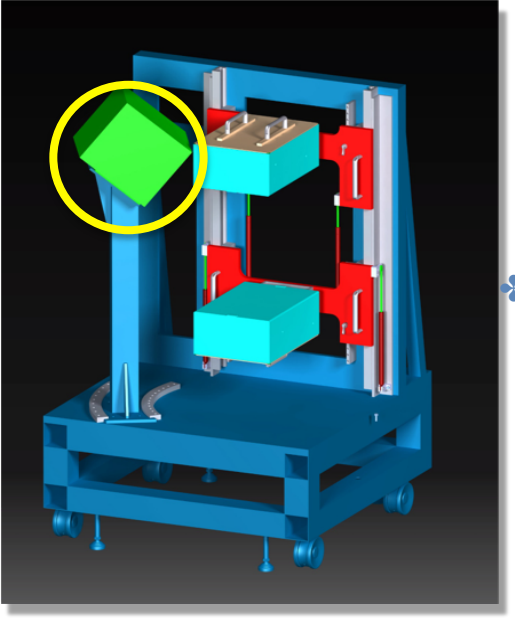
The INSIDE Project: PET system

- Detectors to measure the 511 keV back-to-back photons in order to reconstruct the β^+ activity map;
- Two planar panels: 10 cm x 20 cm wide => 2 x 4 detection modules;



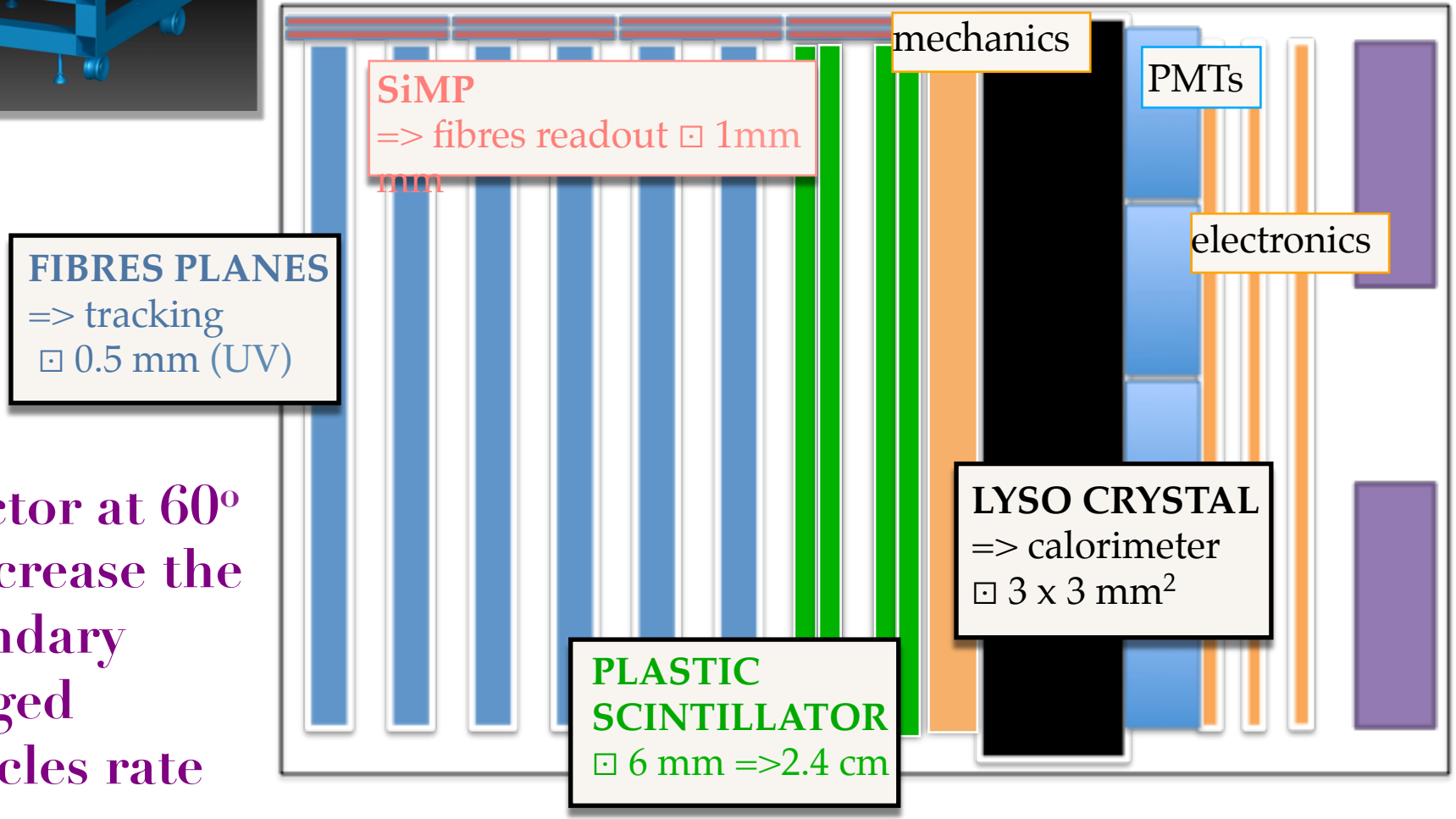
- Each module is composed of a pixelated LYSO matrix 16 x 16 pixels, 3 mm x 3 mm crystals (pitch 3.1mm);
- LYSO matrix readout: array of SiPM (16x16 pixels) coupled one-to-one.

The **resolution** of the two PET heads system in the β^+ activity reconstruction map is expected to be between 1 and **2 mm (FWHM)** in beam direction.



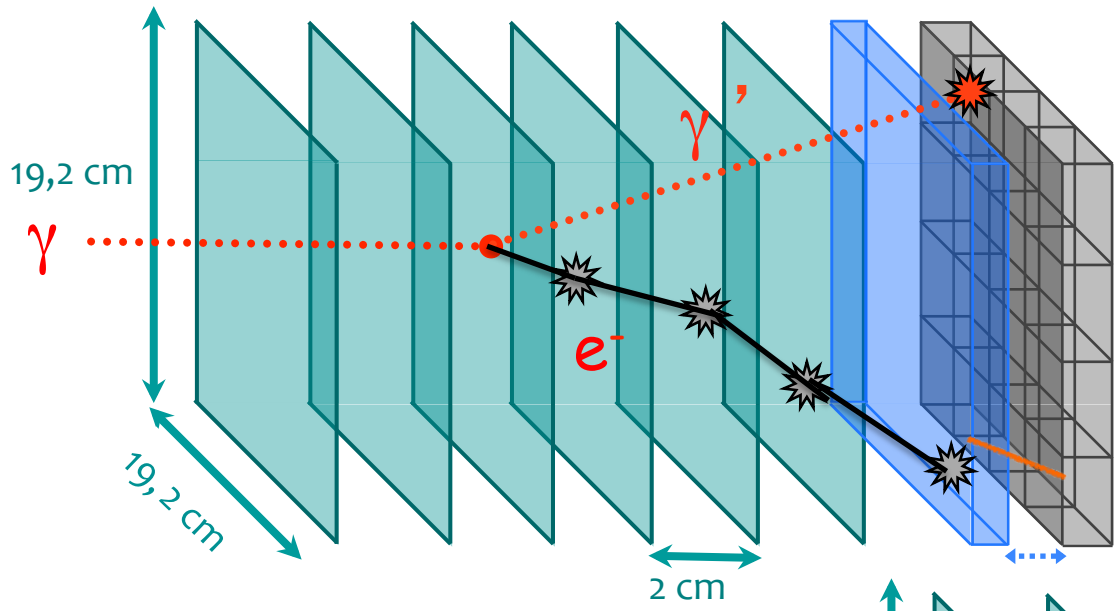
The INSIDE Project: Dose Profiler

- The Dose Profiler aim is to back tracks the secondary particles (p,d,t and prompt photons) and reconstruct their emission point together with their flux.



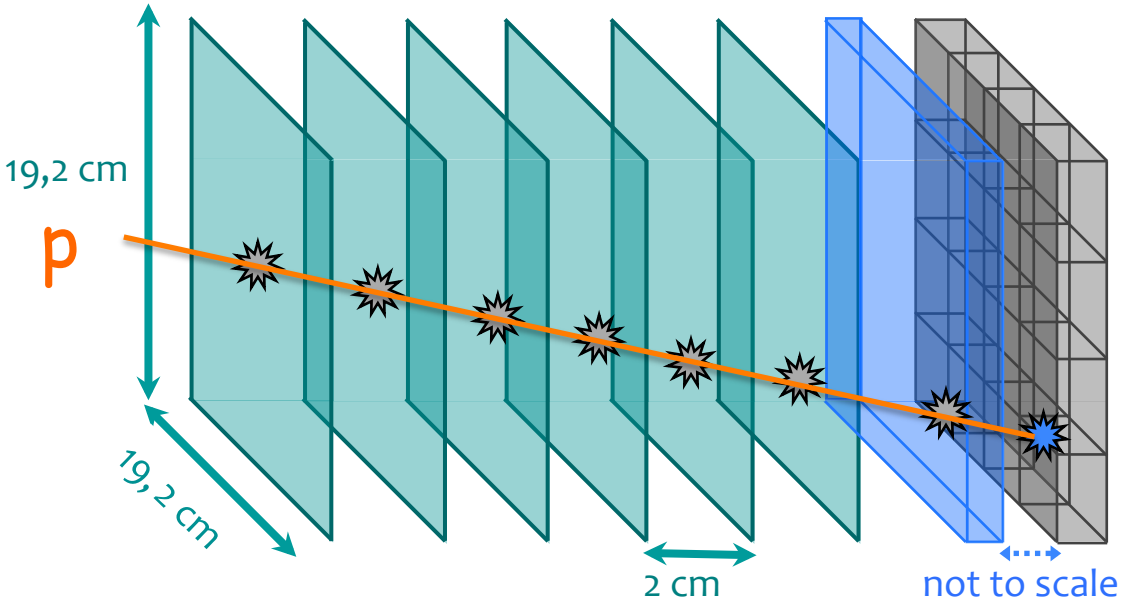
detector at 60° to increase the secondary charged particles rate

INSIDE Profiler: dual mode detector



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

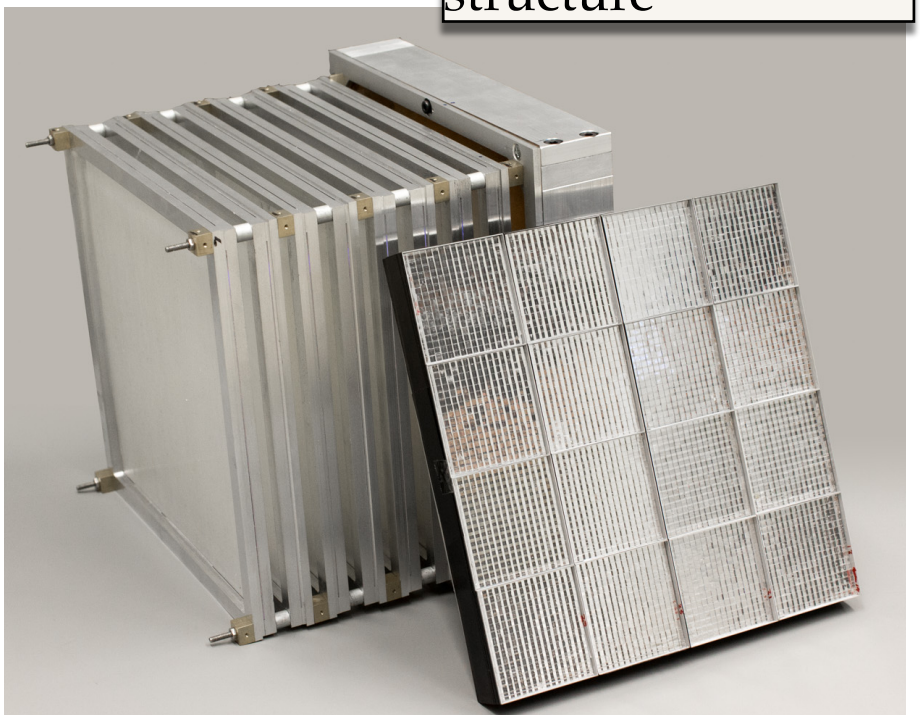
- Heavy charged secondary cross all TRK planes up to LYSO crystals
- Electrons from Compton event have winding tracks (mul. scatt.) and are not detected in the LYSO

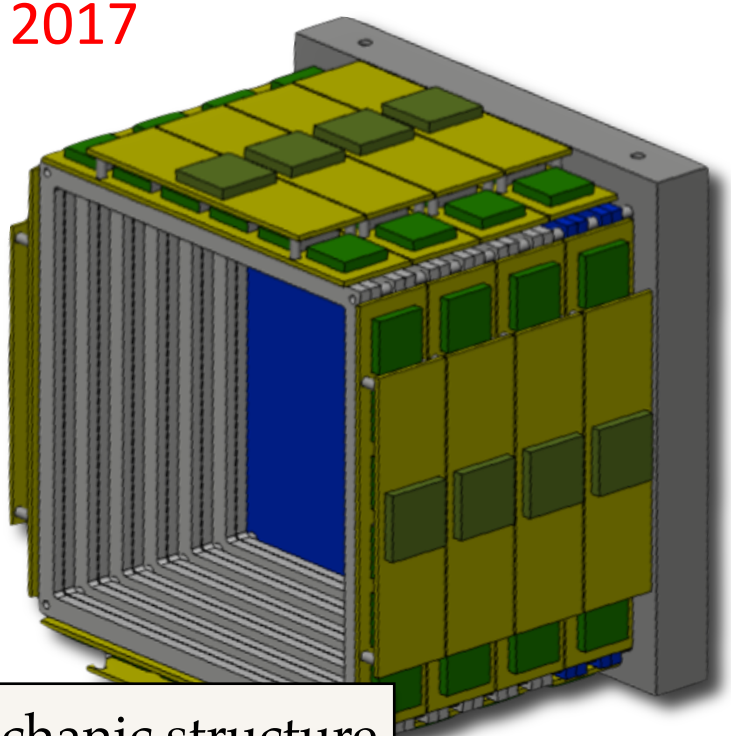


The INSIDE Project: Dose Profiler

- ✓ Expected 3mm accuracy on a slice on ^{12}C beam
- ✓ Calibration at Trento proton beam during 2016
- ✓ Test at CNAO with phantom end 2016- first 2017

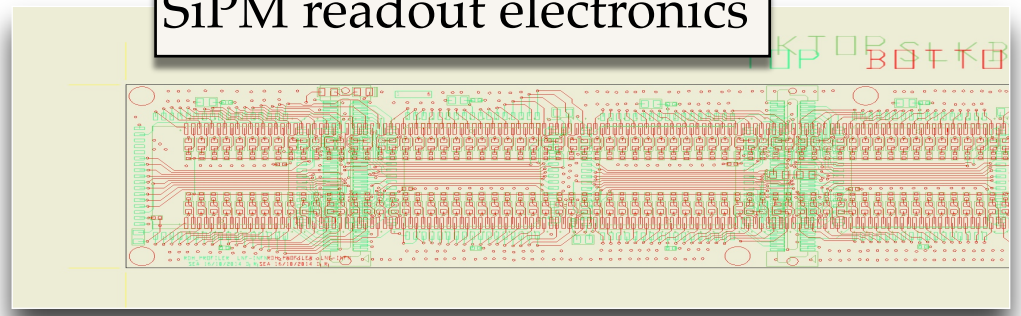
Fiber + calorimeter structure





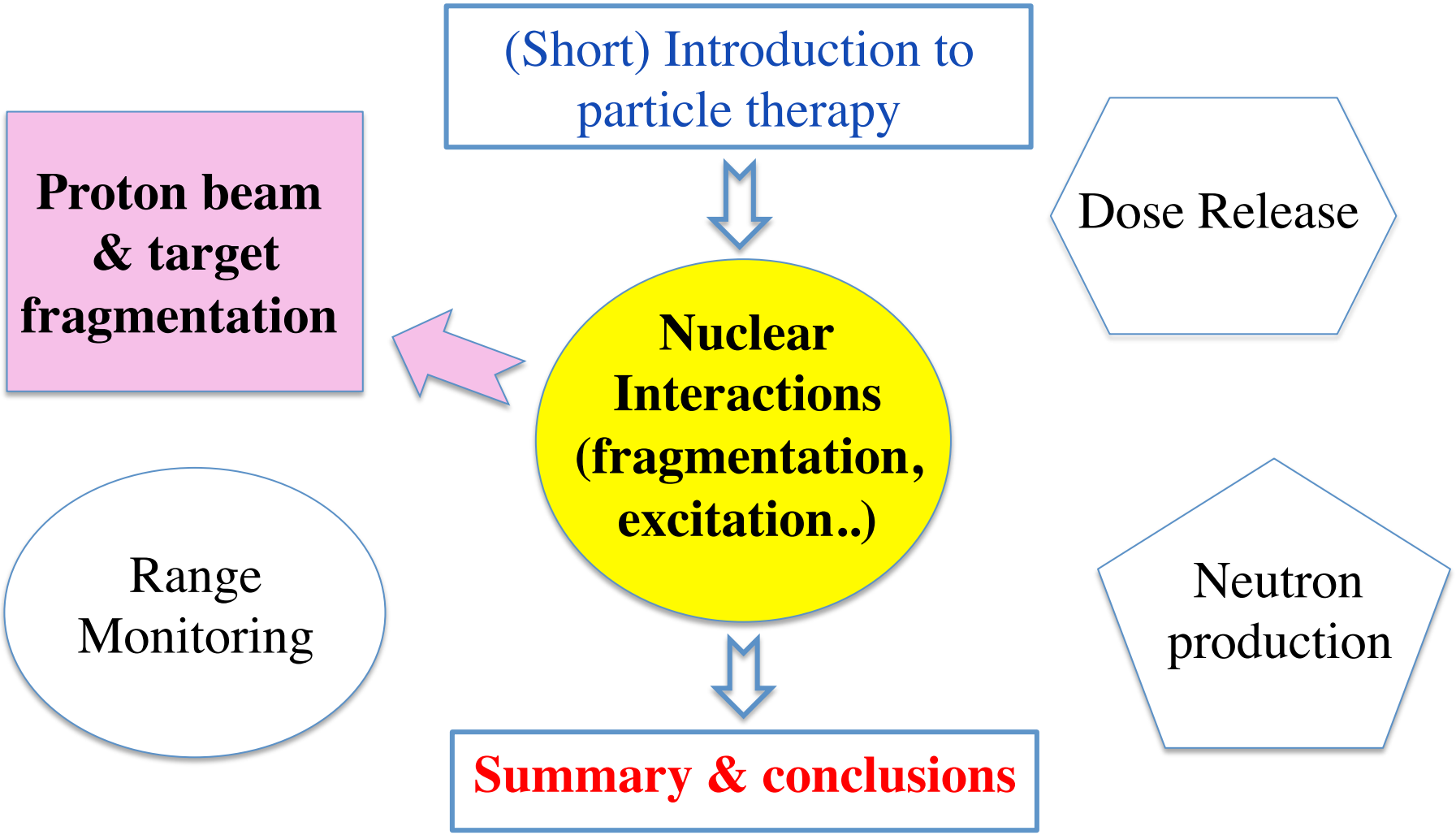
Mechanic structure

SiPM readout electronics



Outline

In clinical practice the proton beam is handled qualitatively as the photon beam (RBE=1.1). But the protons DO HAVE nuclear interaction with the patient that could have clinical impact

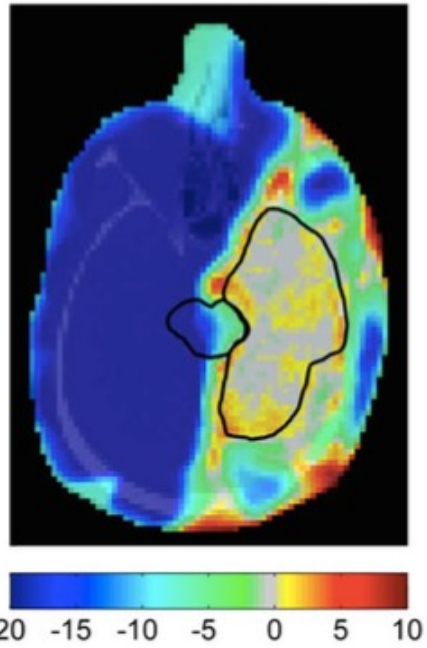


Target fragmentation & proton RBE

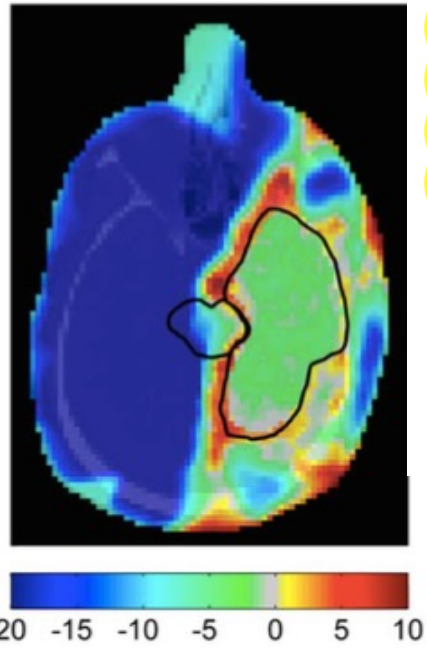
Currently the contribution of target fragments and of the increasing RBE near the PB is implicit (ICRU reccommendation RBE=1.1)

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

RBE=1.1



Variable RBE



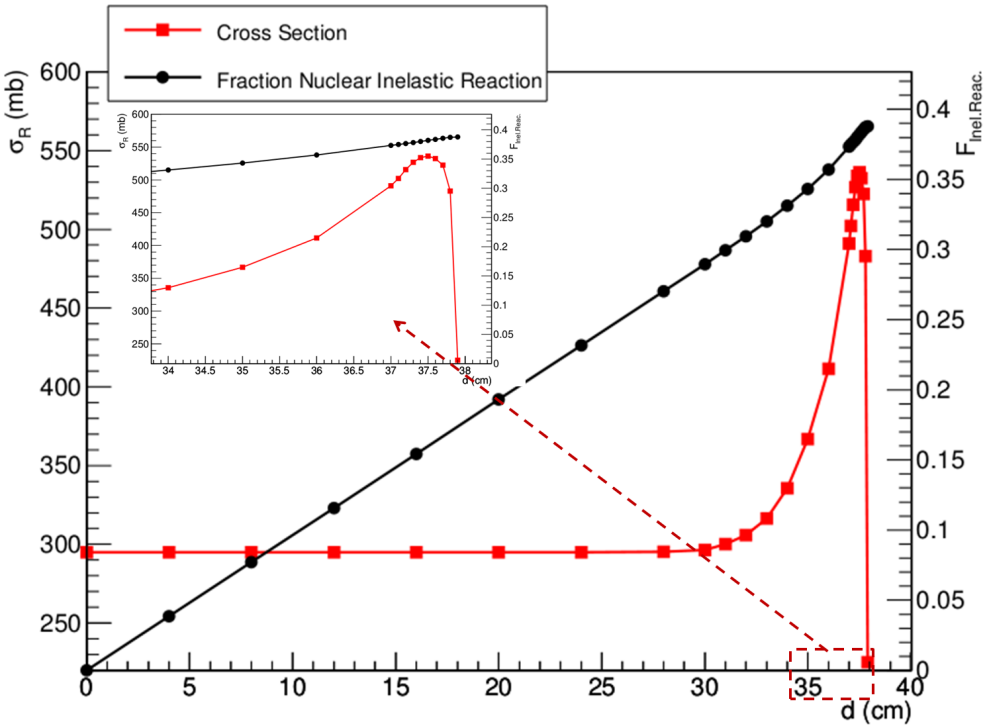
The differences in DVHs and dose distributions are also translated into different NTCP values, shown in Table III. As an example, the probability of necrosis in the brain stem is estimated in case1 to 0.84% for the IMRT plan and 0.57% for the proton plan when assuming a RBE equal to 1.1. However, when assuming a variable RBE the probability increases to 2.13%. Equivalently, the probability for blindness increases from 1.13% (RBE = 1.1) to 4.21% (variable RBE) for protons compared to 1.21% for photons for the optic nerve. The same tendency of estimating a lower NTCP for protons compared to photons when having RBE equal to 1.1, but obtaining a higher NTCP compared to photons when assuming a RBE distribution is also observed for the chiasm and for the other brain cases (see Table III).

Wedenberg 2014 Med Phys

Target fragmentation & PT: is an issue at all?

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

Example : analytic approximation of p -> H_2O @250 MeV



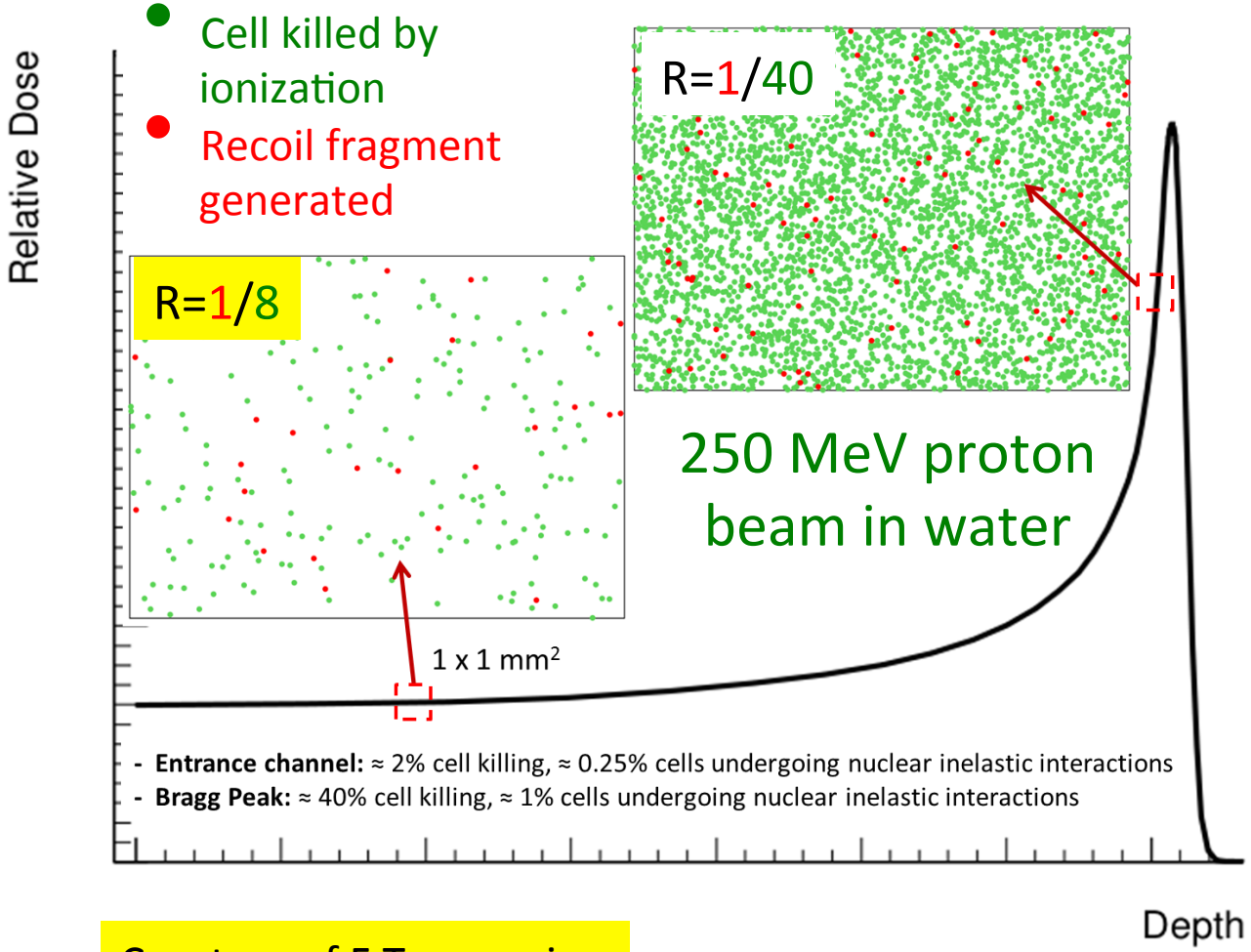
Bradt-Peters formula (Sihver 2009 Radiat Meas)

- In water, **about 1% cm-1** of protons undergo inelastic nuclear interactions
- In a typical treatment, this corresponds to **about 20% of the primary beam**
- 60% of the energy deposited by recoil in charged fragments
- 40% in neutrons and photons out of the field

Courtesy of F.Tommasino

Target fragmentation & PT: where is an issue?

Target fragmentation in proton therapy: gives contribution also outside the tumor region!



About 10% of biological effect in the entrance channel due to secondary fragments

Largest contributions of recoil fragments expected from
He, C, Be, O, N

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

Courtesy of F.Tommasino

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

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

P->H_2O @ 200 MeV

BUT.....

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

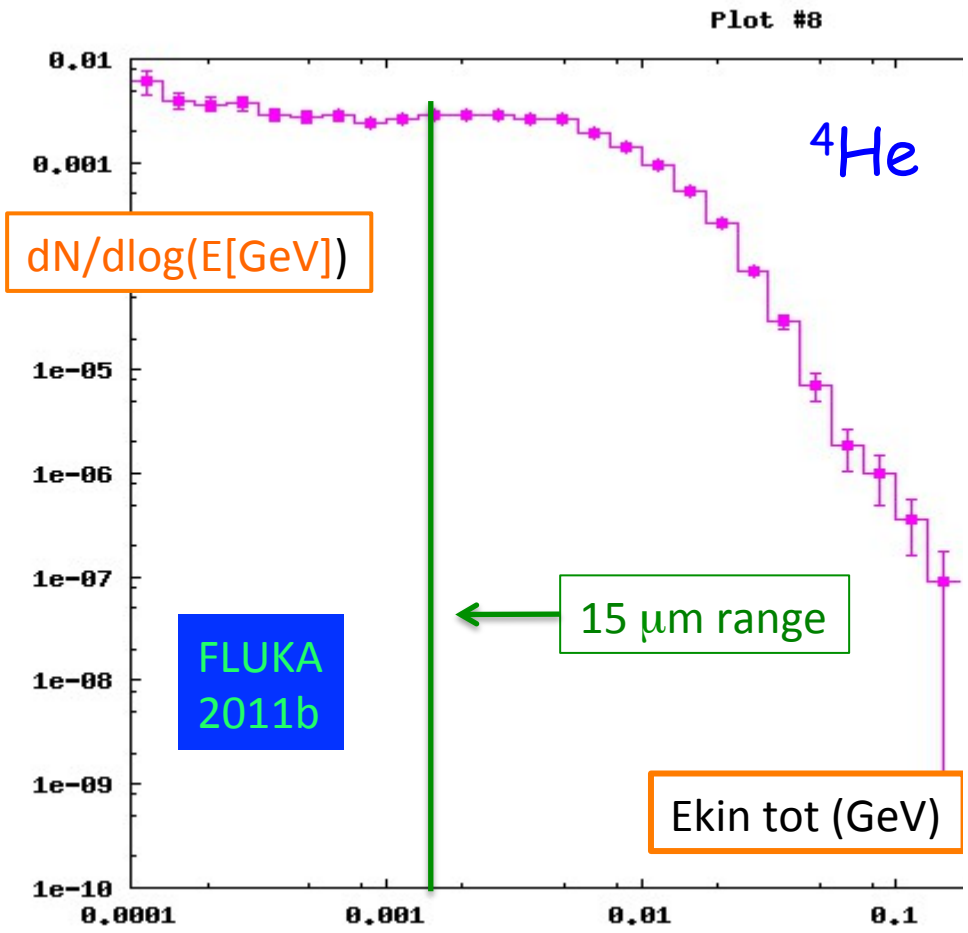
Very low energy-short range fragments.

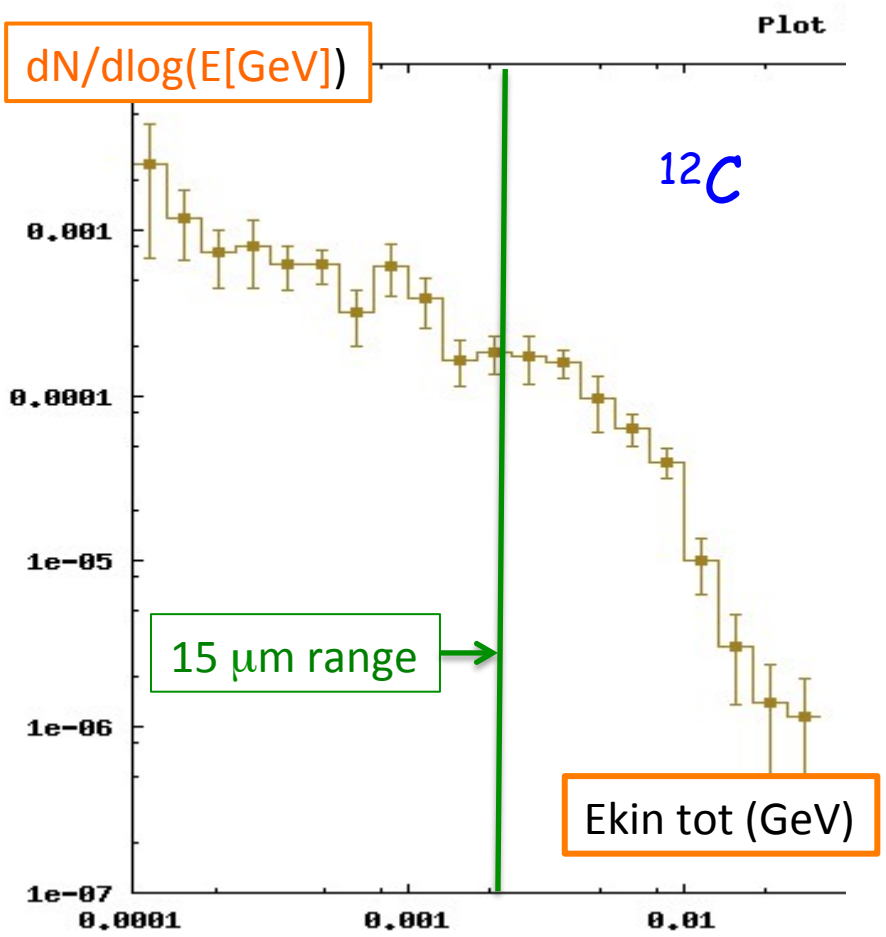
Fragment	E (MeV)	LET (keV/µm)	Range (µm)
^{15}O	1.0	983	2.3
^{15}N	1.0	925	2.5
^{14}N	2.0	1137	3.6
^{13}C	3.0	951	5.4
^{12}C	3.8	912	6.2
^{11}C	4.6	878	7.0
^{10}B	5.4	643	9.9
^{8}Be	6.4	400	15.7
^{6}Li	6.8	215	26.7
^{4}He	6.0	77	48.5
^{3}He	4.7	89	38.8
^{2}H	2.5	14	68.9

Cancers 2015,7 Tommasino & Durante

p-> Brain scattering @200 MeV

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





Direct measurements strategy

For RBE exploitation $d\sigma/dE$ is compulsory !!

- The fragments travel few μm in the target-> difficult to directly detect them, even for very thin target (10 μm?)
- The energy loss of the fragment in the target would be substantial and would be a severe systematic to be evaluated
- Such a very thin target produces very few events -> very careful control of the background.
- Possible solution from JET target techniques, where the target is a focused flux of gas crossing the beam in vacuum: difficult and expensive

Inverse kinematic strategy

Since shooting a proton with a given β (Ekin=200 MeV ➔ β=0.6) on a patient (C,O,N nuclei) at rest gives no detection opportunity… let's shoot a β=0.6 patient (C,O,N nuclei) on a proton at rest and measure how it fragments!!

Then if we measure the X-section, provide we apply an inverse velocity transformation, the result should be the same.

- Use (as patient) beams N, O, C ions with β= 0.6 ➔ Ekin/nucl=200MeV.
- Use a target made of H… but this is difficult! (I will come to this…)

The heavy fragment (all but p,d,t,He) has ~200MeV/nucleon kinetic energy and are forward peaked

Inverse kinematics and the target

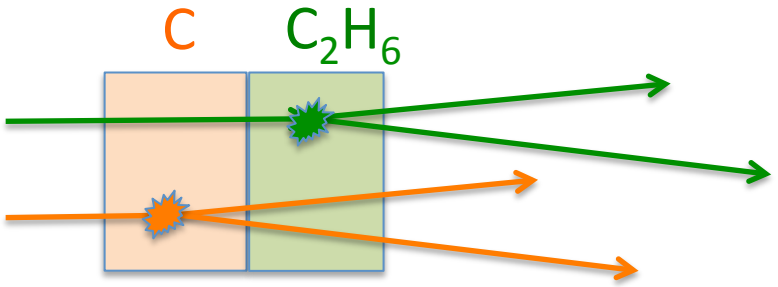
The target can be thick as few mm, since the fragment range is larger than several cm.

The H target could be a Liquid Hydrogen, but with little non H material on the beam path➔criogenics?

A possible solution is to use twin targets: C and hydrocarbons. The fragmentation cross section can be obtained by subtraction.

Simultaneous double target data taking can to minimize systematic, if the setup has good vertexing capability along beam line

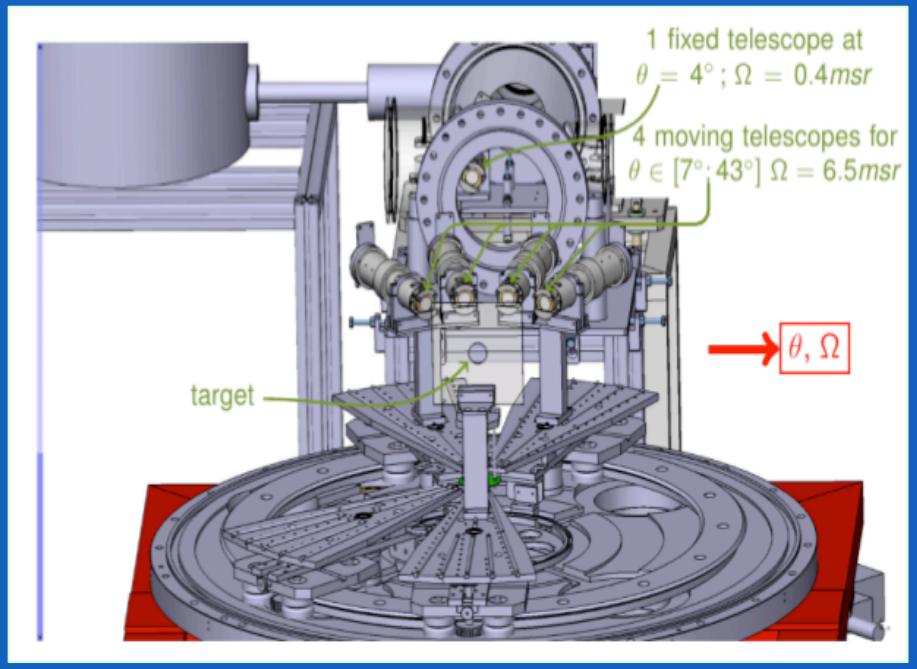
Heavy fragment are forward peaked, must be separated by the beam: very good PID capability

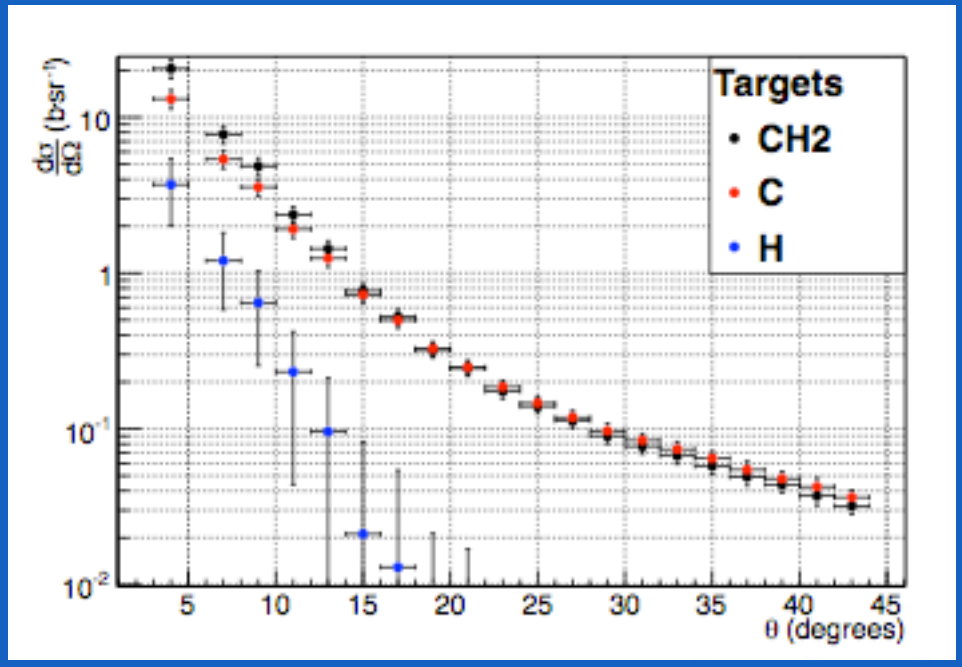


C-H X-section extraction: ^{12}C beam on C,CH_2 target @ 95AMeV

GANIL experiment of C-C fragmentation. Obtained results for Single and Double Diff. X Section.

- interesting conclusion: X-sections for composite targets can be deduced from the cross sections of elemental targets (-> organic tissues)
- Systematics???





Courtesy of M. Labalme

Physicists & the Lord of the Ring…

A lot of colleagues are fan of the Tolkien masterpiece (myself included), but a particular scene from "The return of the King" explains very well the physics attitude community toward a difficult (or impossible) enterprise…

Certainty of death..
Small chance of success..

WHAT ARE WE WAITING FOR???

New target fragmentation Experiment?

The community is starting to think at target fragmentation experiment: newcomers are welcome !

- Challenging measurement: support by Nuclear Physics Commission of INFN
- A first meeting dedicated to this opportunity/challenge held in Villa Tambosi (TN) in July 2015 , near TIFPA
- Beam available in Europe: HIT, CNAO, GSI(?)

FramentatiOnOf Target

A possible setup (FLUKA Simulation)

Scint. Fiber Tracker (INSIDE)

20 cm

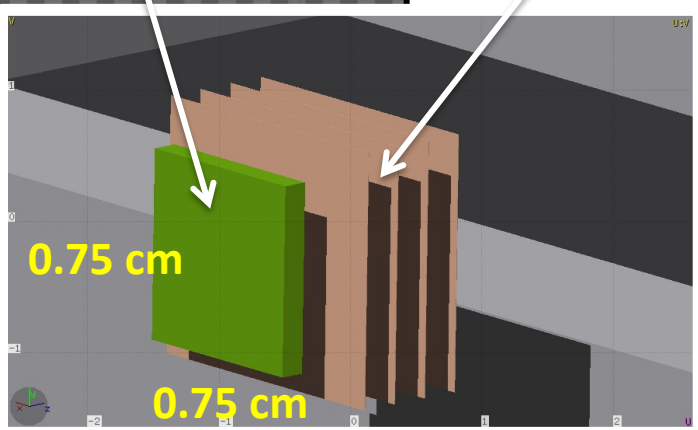
20 cm

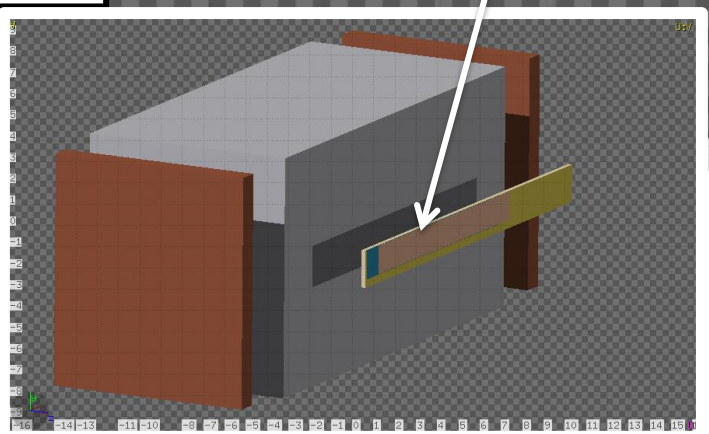
Permanent Magnet (0.5 T)

C or CH_2 Target

Silicon Pixel (20 µm) Front Tracker

Silicon Pixel Back Tracker ("Plume")





Outline

Neutron production in PT and long term effect of the dose induced by neutrons on patient has been a long standing "hot" item in the querelle RT vs PT

(Short) Introduction to particle therapy

Proton beam & target fragmentation

Dose Release

Nuclear Interactions (fragmentation, excitation..)

Range Monitoring

Neutron production

Summary & conclusions

Radiotherapy and secondary cancers

Cancer survivors represent about 3.5% of US population

Second primary malignancies in this high-risk group accounts for about 16% of all cancers

Three possible causes:

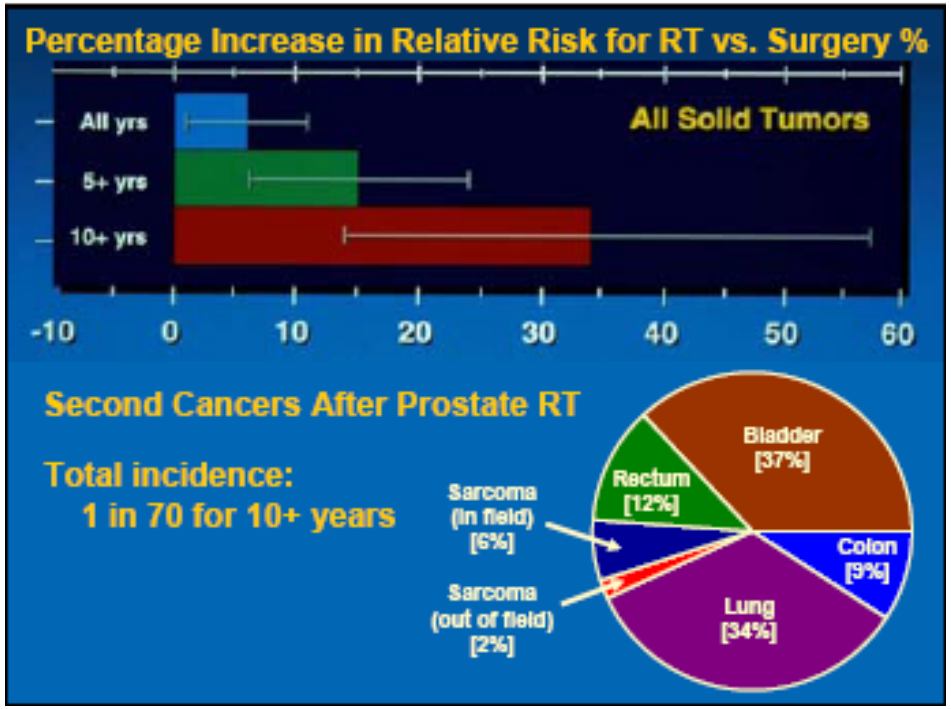
- Continuing lifestyle
- Genetic predisposition
- Treatment of the primary cancer

Assessment is difficult because of lack of controls

Prostate and cervix cancer: surgery is an alternative

Hodgkin's lymphoma: risk of breast cancer very high

Radiation-induced secondary cancers are mostly carcinomas, but a sarcomas in heavily irradiated sites are also observed



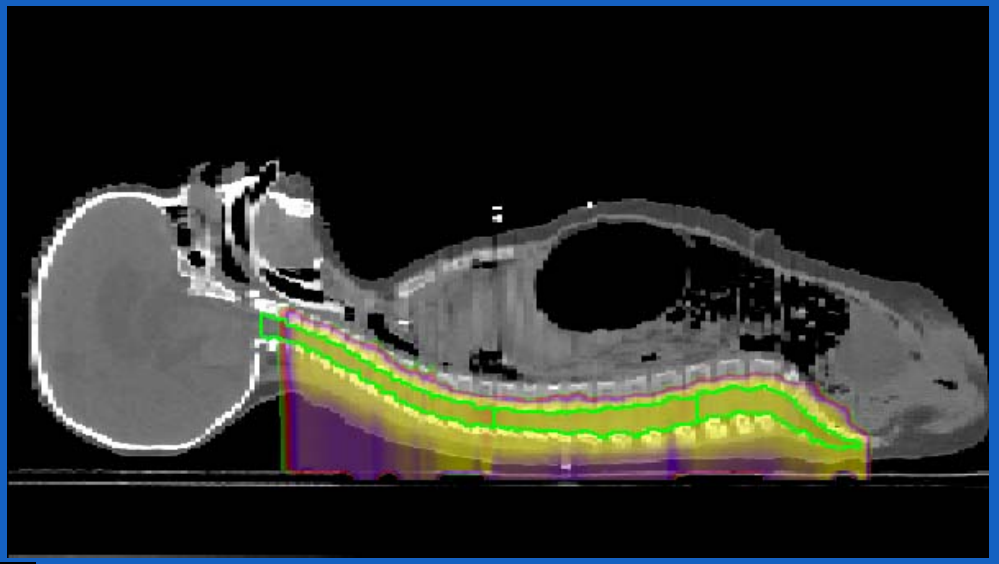
Brenner *et al., Cancer* (2000)

Courtesy M.Durante

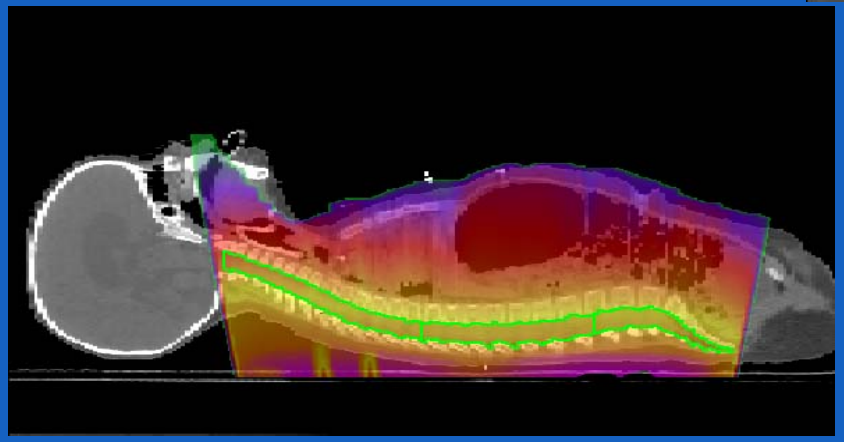
PT and pediatric tumors

Eventual secondary effect of diffuse dose are very relevant for pediatric tumor, where the expected life span is longer.

The neutron contribution is particularly difficult to model and to be taken into account in TPS (environment, reflection, beam halo, etc..



Protons

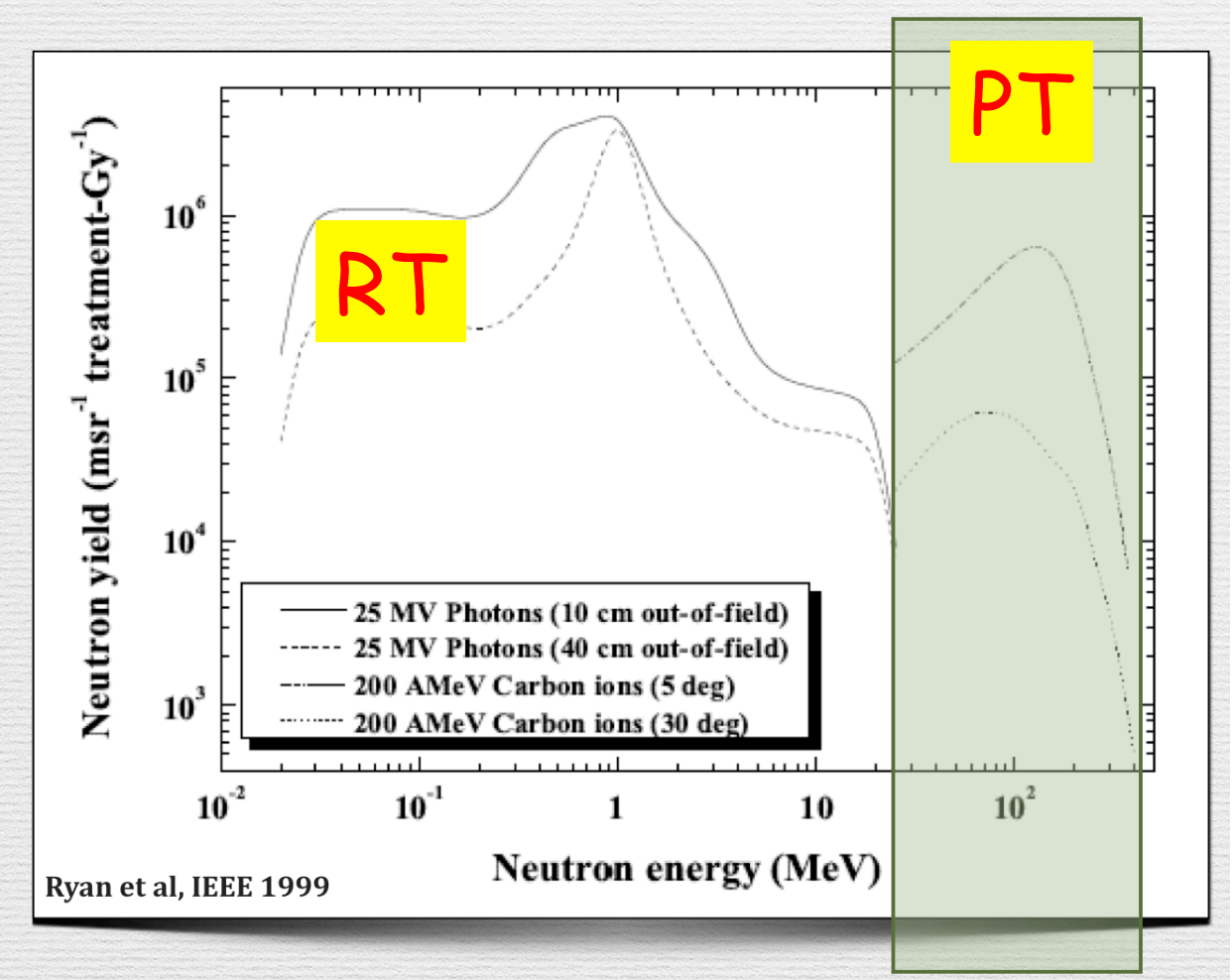


Photons

Courtesy of R.Orecchia

	X-ray	IMRT	Proton
CTV	90%	90%	90%
Heart	18.2	17.4	0.1
Right lung	3.5	21.9	0.1
Esophagous	11.9	32.1	10.2
Stomach	3.7	20.6	0.1
Right kidney	3.3	29.8	0.1
Transvers colon	2.6	18.0	0.1

Neutrons & Radio/Proton/Carbon therapy



The expected neutron flux dominates, by orders of magnitude, the total secondary flux nearly at all energies.

Neutrons produced by the beam in PT treatments are mainly fast neutrons [20-200 MeV]

Degradation by scattering with patient/materials produces large flux of slow neutrons.

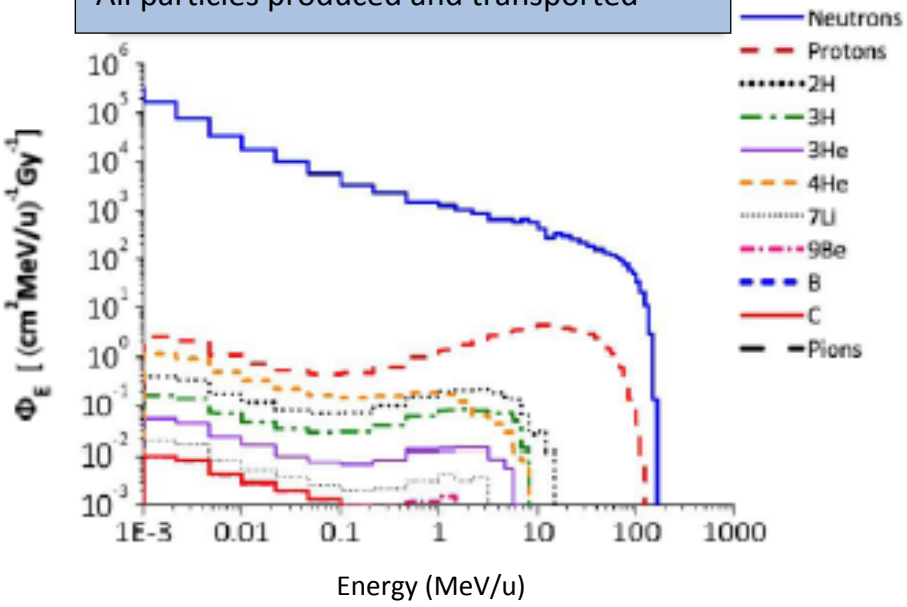
Neutron quest… old saga!

- ✓ Accurate measures of n production X-section by p,^{12}C beam on needed materials (O,C), with angle and energy distribution, is still missing.
- ✓ Due to their intrinsic detection efficiency, neutron on line monitoring during PT is particularly difficult, (no directionality, scattering from environment, probabilistic releas of energy, PID?, etc..)

172 MeV Proton beam

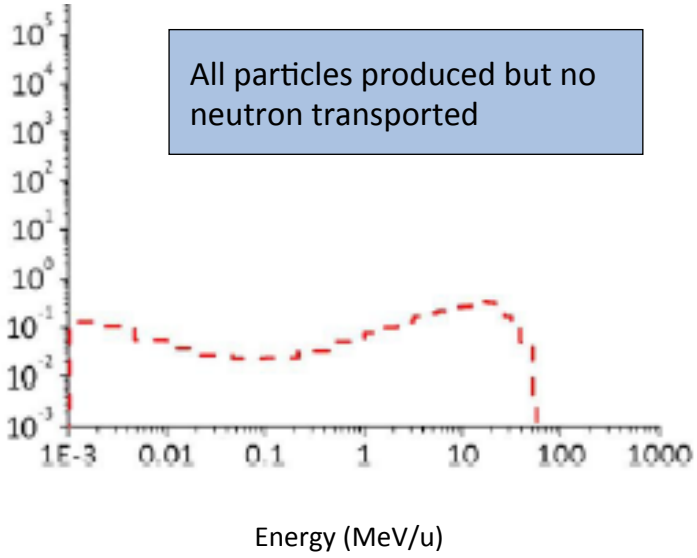
Hultqvist and Gudowska, PMB 55,2010

All particles produced and transported

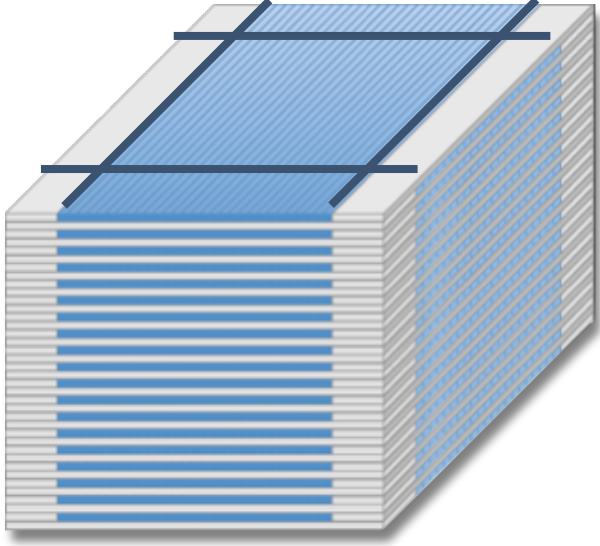


Gonads ~12 cm from target
Particles flux

All particles produced but no neutron transported



MOnitor for Neutron Dose in hadrOntherapy



Plastic Scintillator
- 4 x 4 x 8 cm^3;
- scintillating fibres 250 µm;
- 160 squared fibres per layer;
- 320 U-V layers;

Image Intensifier
- Triple GEM

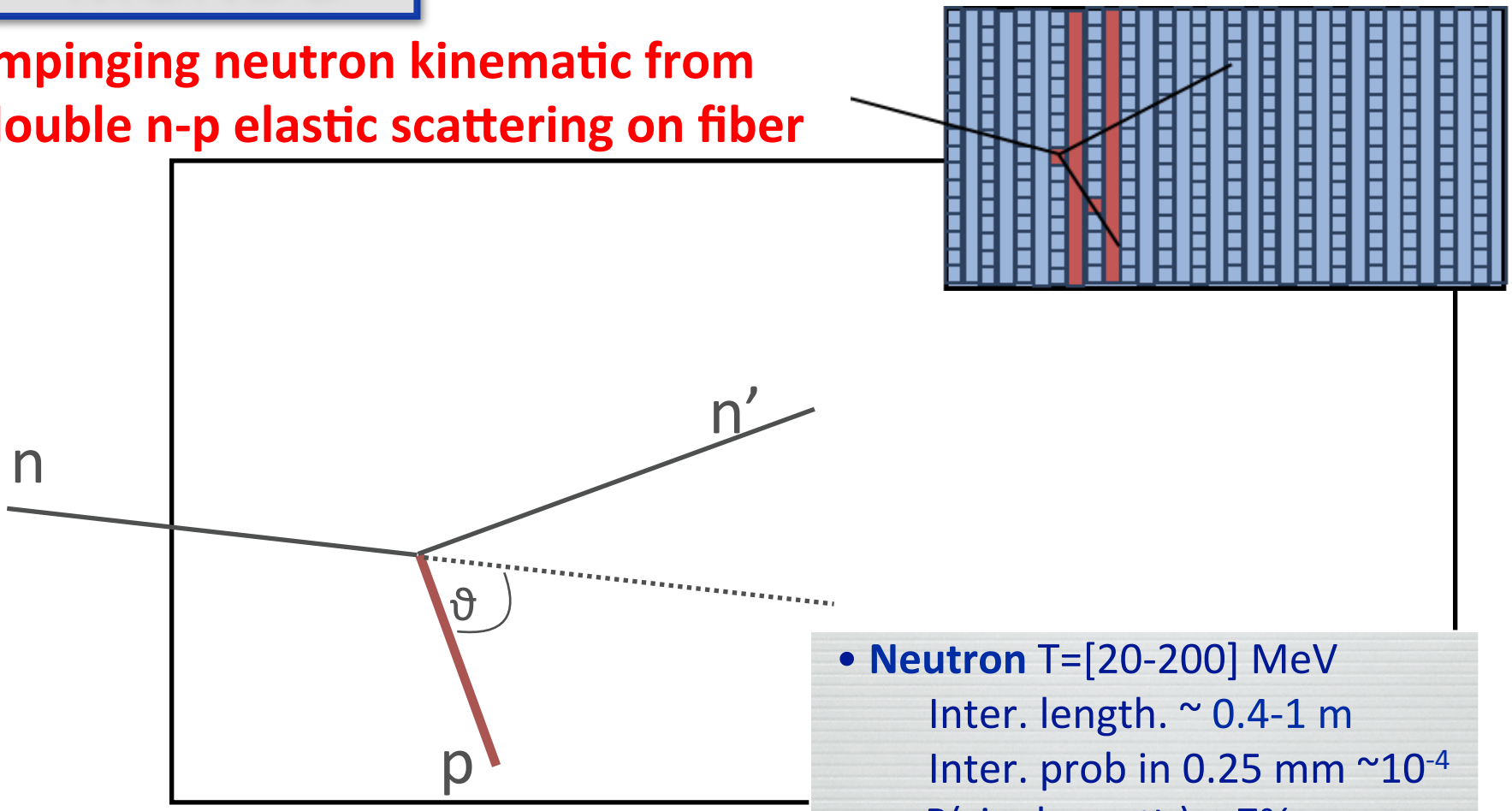
Read Out
- CMOS

TRACKING the neutron !!

- ✧ Tracking device for 20:300 MeV neutrons
- ✧ Efficiency in 10^{-2} - 10^{-3} range
- ✧ Funded by MIUR (PRIN) +INFN Young Grant (2016-2018)

MONDO

Impinging neutron kinematic from double n-p elastic scattering on fiber

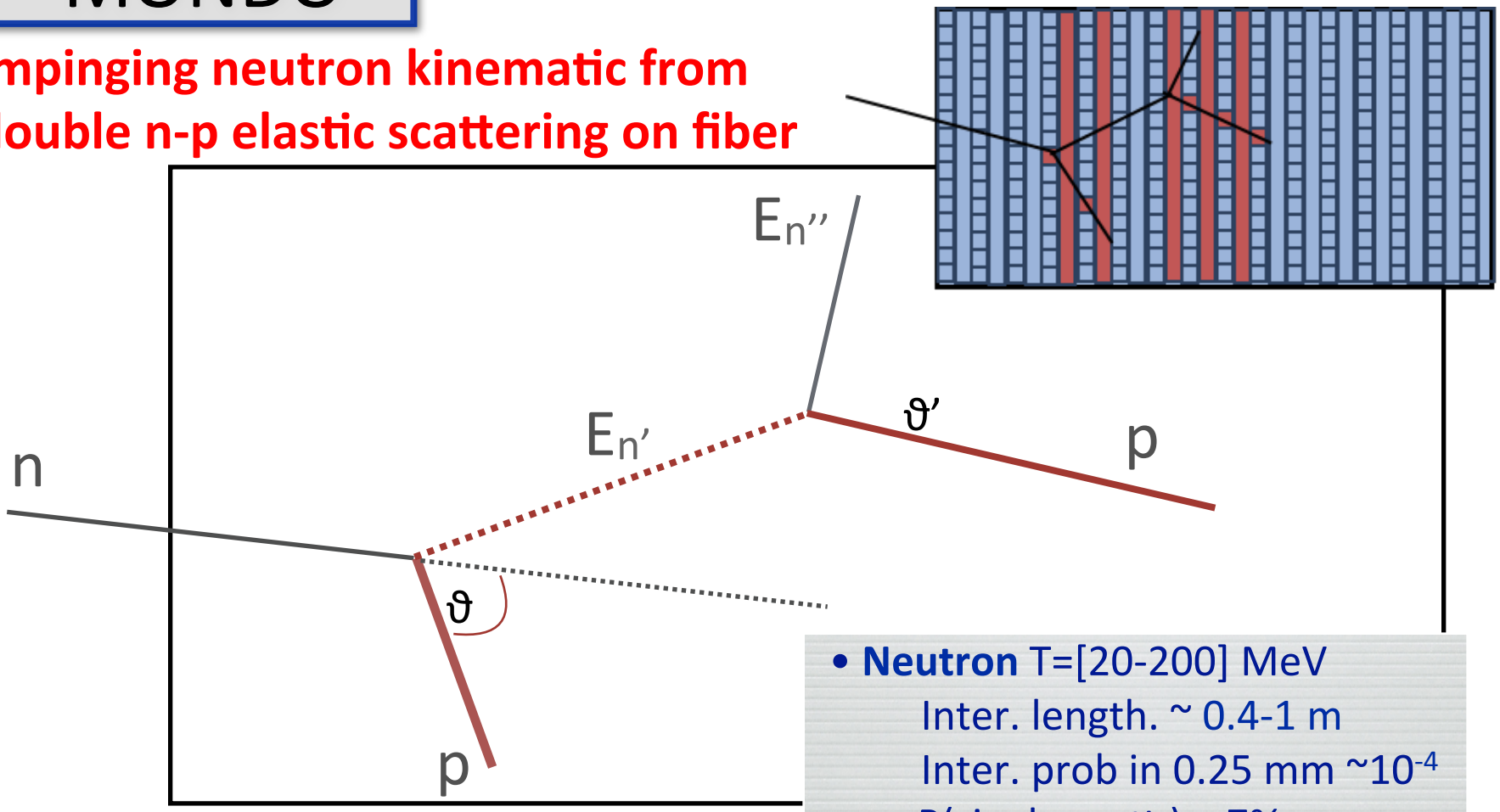


- **Neutron** T=[20-200] MeV
  - Inter. length. ~ 0.4-1 m
  - Inter. prob in 0.25 mm ~10^{-4}
  - P(single scatt.) ~ 7%
- **Proton range**
  - T = 100 MeV=> 8 cm
  - T = 50 MeV=> 2 cm
  - T = 30 MeV=> 1 cm
  - T = 10 MeV=> 0.1 cm

Single hit resolution:
E_{kin} = 10 -100 MeV => 7-20 %
40 hit/cm sampling
Read out by SPAD (digital SiPM)

MONDO

Impinging neutron kinematic from double n-p elastic scattering on fiber



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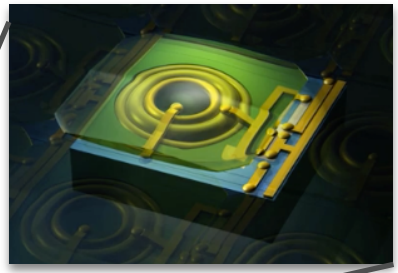
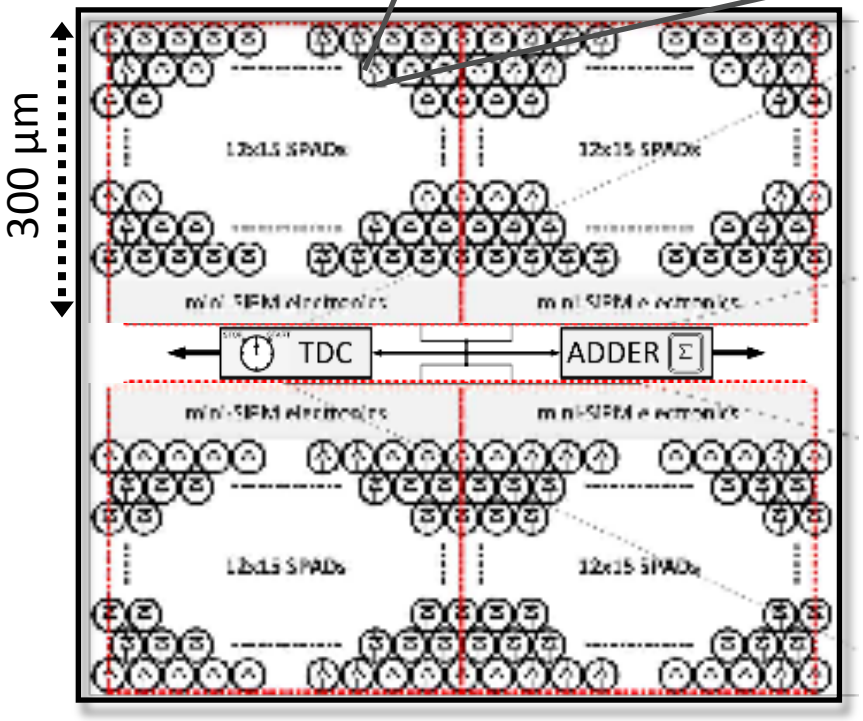
Single hit resolution:
E_{kin} = 10 -100 MeV => 7-20 %
40 hit/cm sampling
Read out by SPAD (digital SiPM)

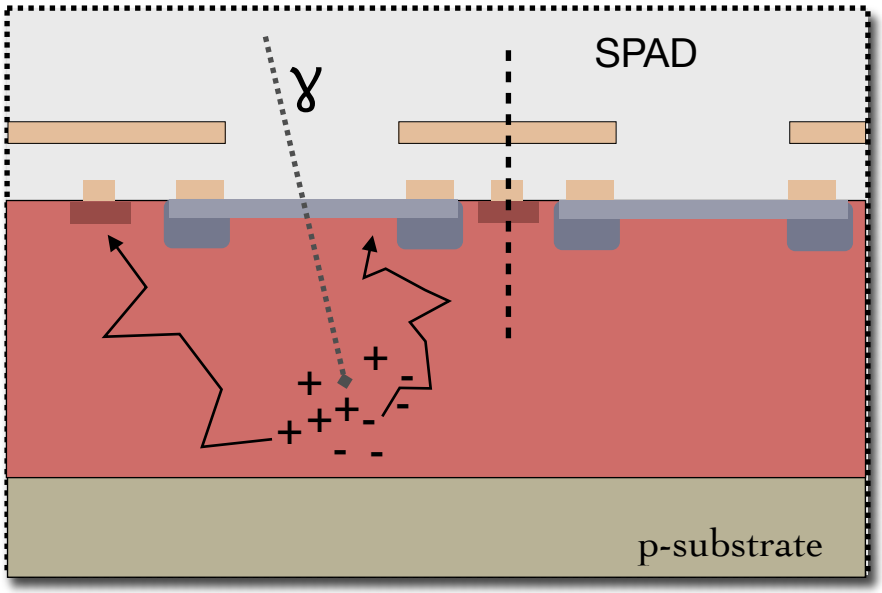
MOnitor for Neutron Dose for hadrOntherapy

SPAD Matrix prototype: digital output of the # of SiPM fired in 10 ns





Photon ReadOut



- integrated TDC (resolution ~65 ps)
- self triggered sensor
- pixel 600 µm (-> 300 µm)

Development of the sensor in collaboration with FBK (Trento)

Summary & conclusions

- Particle therapy is becoming a new tool to help oncologist in the multi-approach war to cancer.
- The higly conformal dose release (all hadron) and the high biological efficency in killing tumor (light ions) gives new treatment possibilities for radio-resistant tumor or seated near organ at risk
- Nuclear fragmentation of the beam prevents the use of ions heavier then Oxygen and must be taken into account in the Treatment Planning System: the nuclear measurements go directly in the clinical practice
- Nuclear fragmentation of target can have an impact on the proton therapy: new measurement/experiment?

Summary & conclusions II

- The nuclear interactions of the beam provide also a method to monitor the released dose, back-tracking the produced secondaries : γ from β^+ emitters, prompt photons from nuclear excitation and light charged fragments
- The neutron production must be carefully measured and taken into account, in particular for pediatric patients: challenge for the detector development

I did not discuss here:

- R&D in the accelerator technologies: very lively field, can chance the landscape of the beam that can be embedded in an Hospital, and that an hospital can afford
- The economic part of the story: PT is more expensive than conventional RT, and needs more space (i.e. dedicated centers…). This can change in future but must be taken into account

Applied Radiation Physics Group

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V. Patera[2,4,5], D. Pinci[2], L. Recchia[2], A, Rucinski[2], A. Russomando[1,2,6],
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Oncological application:

- CHIRONE: Probes for radio-guided surgery

Particle therapy activities:

- ✓ Fragmentation measurements (FIRST);
- ✓ Prompt secondaries measurements;
- ✓ INSIDE: dose profiler@CNAO;
- ✓ MONDO: neutron dose measurements;
- ✓ FOOT experiment (??)

GSI Helmholtzzentrum für Schwerionenforschung GmbH

INFN Istituto Nazionale di Fisica Nucleare

Thanks….

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