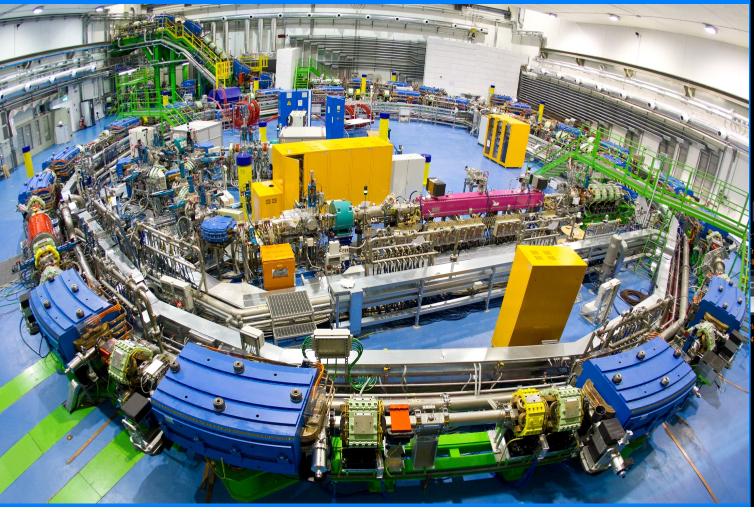
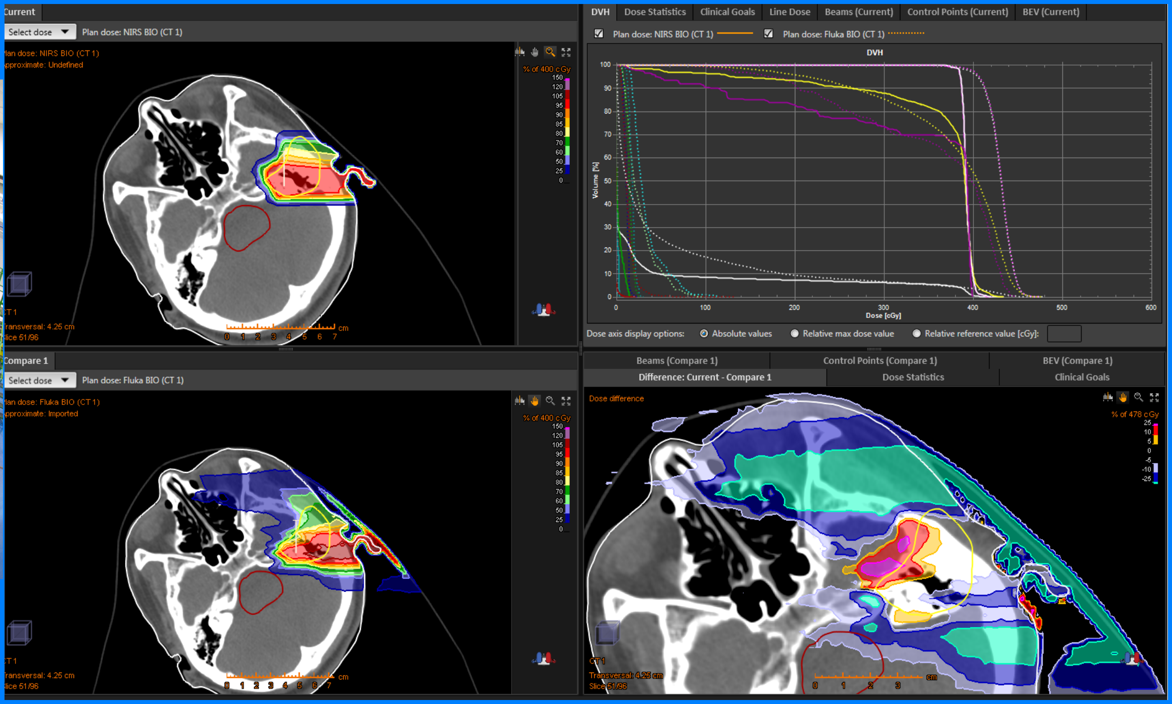




Nuclear Physics and Particle Therapy

Giuseppe Battistoni,
INFN, Milano, Italy

European Network for
Light Ion Hadron Therapy

Cancer and radiotherapy

Atunet al., Lancet Oncol16:1153-86, 2015

~50% of all cancer patients

Only 40-60% of patients with cancer have access to radiotherapy

- Highly individualized treatment
- 50% of cures -radiotherapy sole treatment or major component
- Organ-and function sparing, well tolerable
- More than 4m long term survivors in Europe
- Favorable cost/benefit

Benefits
2012:
1.5M pts. Local Control,
0.58M Survival

2035:
2.5M pts. Local Control,
0.95M Survival

	High-income countries	Upper-middle-income countries	Lower-middle-income countries	Low-income counties
Fractions	76 424 000	77 014 000	40 974 000	13 268 000
Radiotherapy departments	4600	3700	2000	600
Megavoltage machines	9200	7400	3900	1300
CT scanners	4600	3700	2000	600
Radiation oncologists to be trained	15 500	16 800	9900	3300
Medical physicists to be trained	17 200	12 500	7200	2400
Radiation technologists to be trained	51 900	45 300	24 900	8100

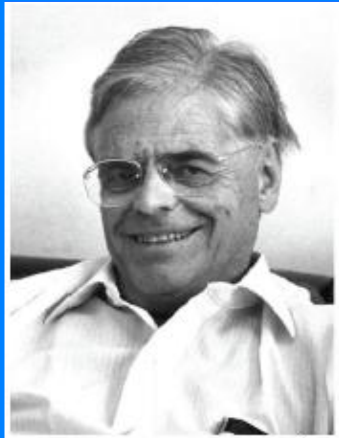
Data are n. The appendix contains more information about the CT scanner shared-use model.

Table 5: **Projected fractions and related resources needed in 2035**

A new approach for Radiotherapy using charged hadrons

Hadron RT was proposed by Robert Wilson in 1946

R.R. Wilson, "Foreword to the Second International Symposium on Hadrontherapy," in Advances in Hadrontherapy, (U. Amaldi, B. Larsson, Y. Lemoigne, Y., Eds.), Excerpta Medica, Elsevier, International Congress Series **1144**: ix-xiii (1997).



Radiological Use of Fast Protons

ROBERT R. WILSON

Research Laboratory of Physics, Harvard University

Cambridge, Massachusetts

EXCEPT FOR electrons, the particles which have been accelerated to high energies by machines such as cyclotrons or Van de Graaff generators have not been directly, used therapeutically. Rather, the neutrons, gamma rays, or artificial radioactivities produced in various reactions of the primary particles have been applied to medical problems. This has, in e part, been due to the very short ation in tissue of protons, deu particles from prese er-energy mach how

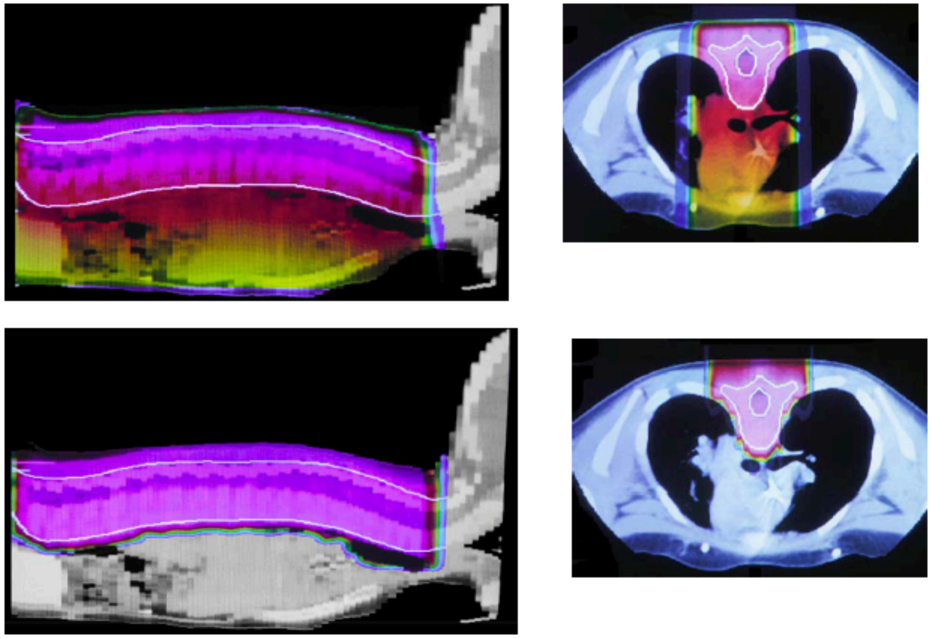
per centimeter of path, or specific ionization, and this varies almost inversely with the energy of the proton. Thus the specific ionization or dose is many times less where the proton enters the tissue at high energy than it is in the last centimeter of the path where the ion is brought to rest.

These properties make it possible to irradiate inter ly a strictly localized region

Radiology 47: 487-491, 1946

1954 - Berkeley treats the first patient and begins extensive studies with various ions
1957 - first patient treated with protons in Europe at Uppsala
1961 - collaboration between Harvard Cyclotron Lab. and Massachusetts General Hospital
1993 - patients treated at the first hospital-based facility at Loma Linda
1994 - first facility dedicated to carbon ions operational at HIMAC, Japan
2009 - first European proton-carbon ion facility starts treatment in Heidelberg

Rationale of Charged Particle Therapy



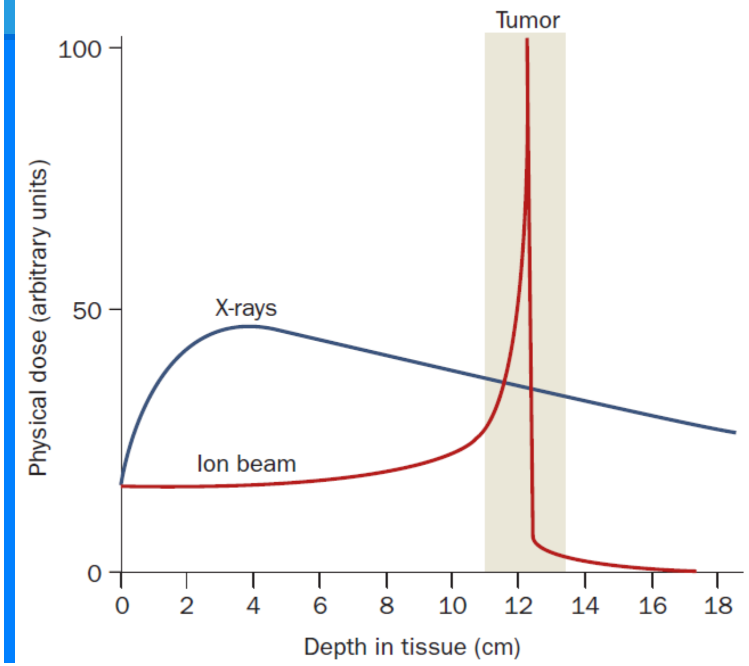
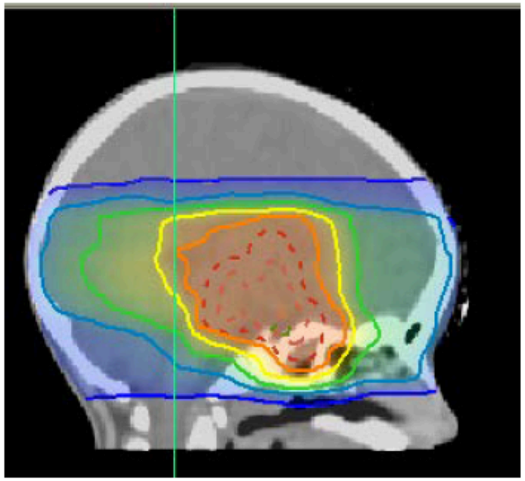


Image guided, conformal (IMRT), photon therapy

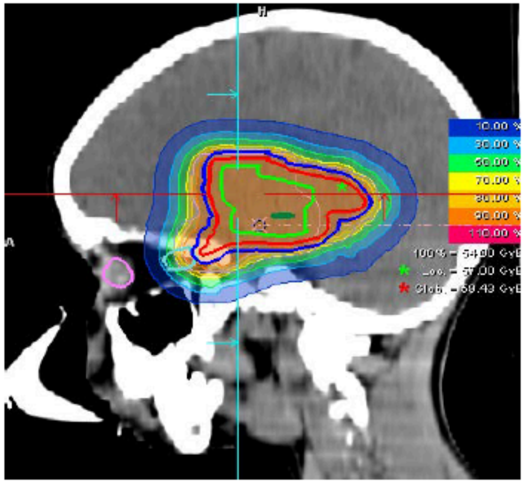
- 35% local recurrence
- Preventable distant metastases
- Large volumes irradiated
- Early, late and very late normal tissue damage

Photon-IMRT



Universitätsklinikum Dresden

Protons

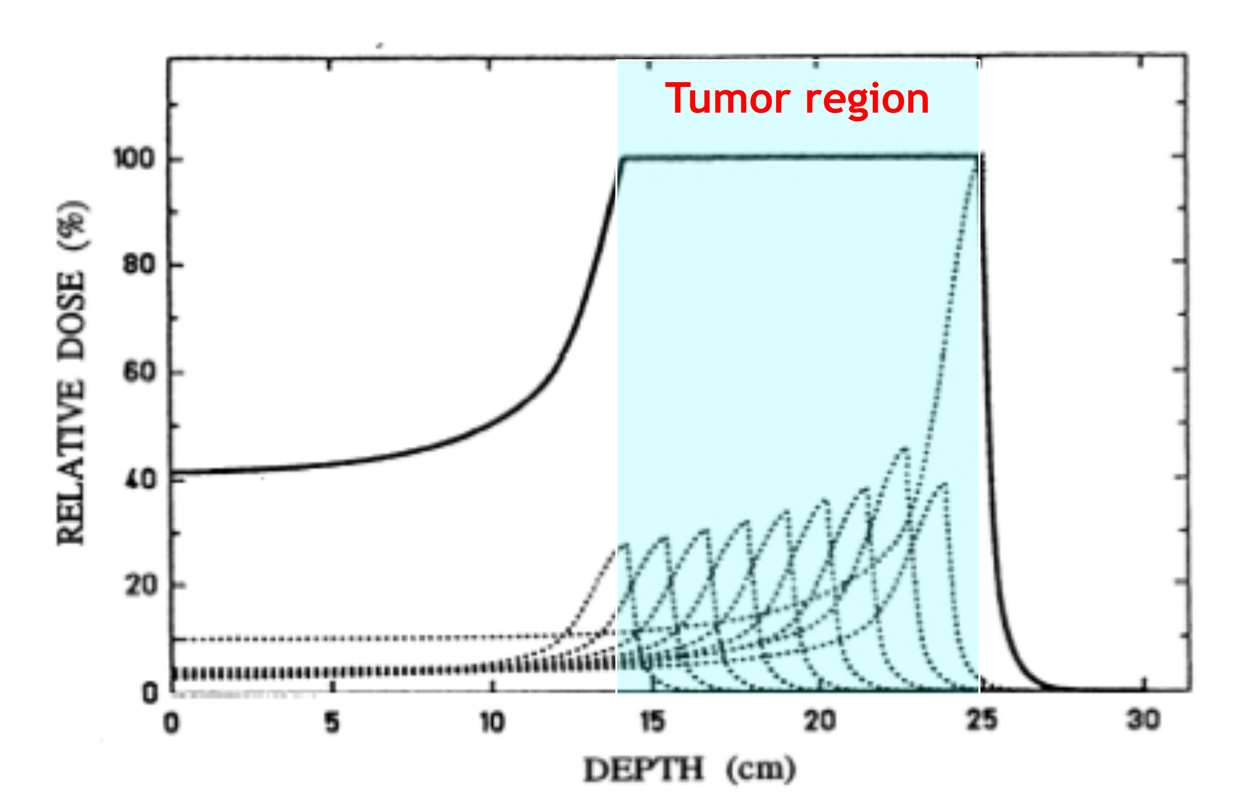


HIT, Heidelberg

The conformation capability

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

- Length of track function of the beam energy
- Dose decrease rapidly after the BP.
- Accurate conformal dose to tumour with **Spread Out Bragg Peak (SOBP)**

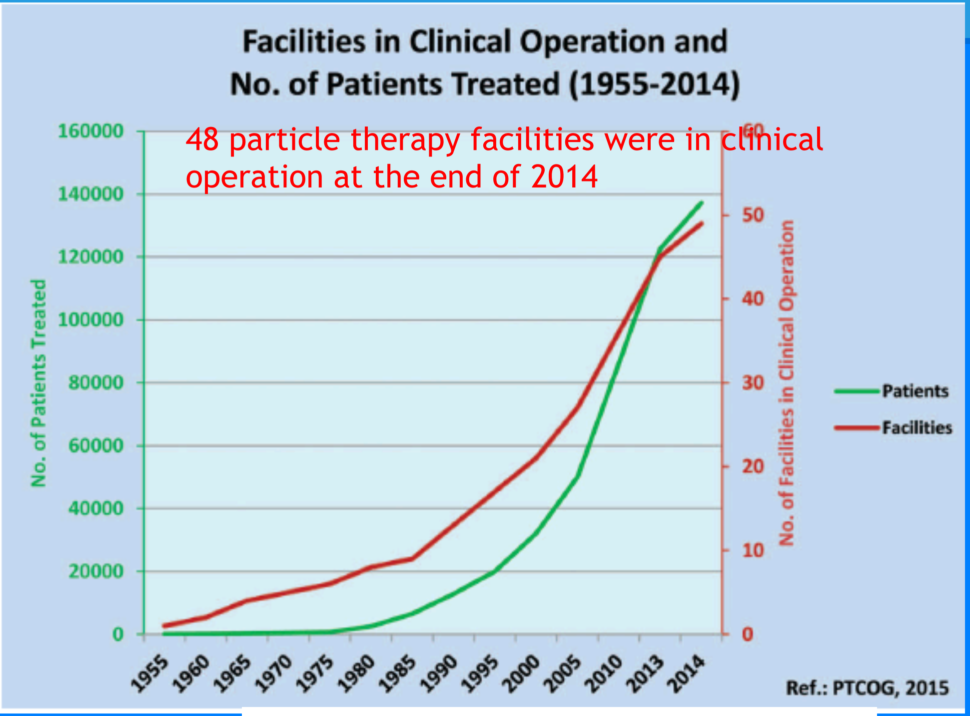


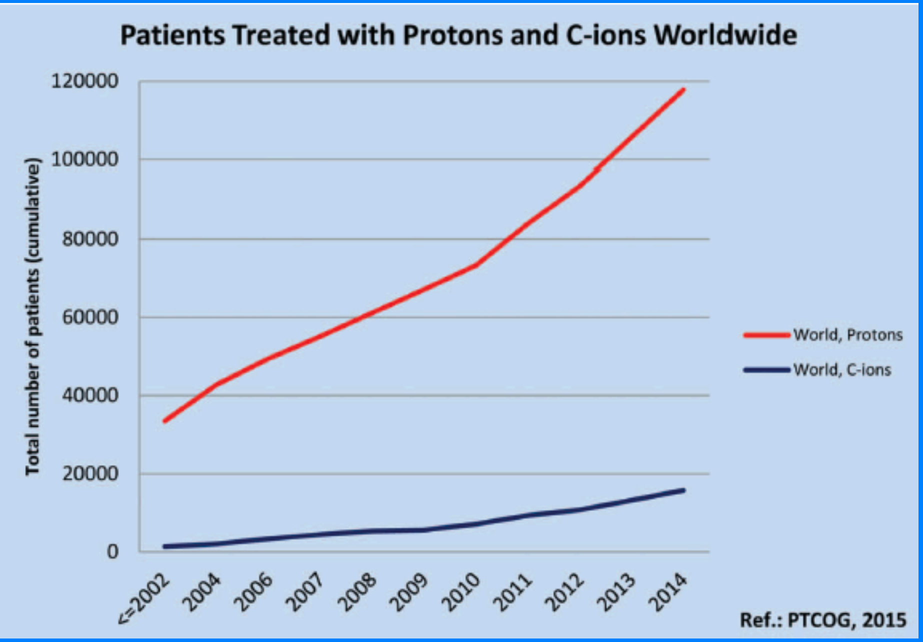
Charged particle therapy can be successfully applied to solid tumors.
For the moment primary tumors.
About 2% of all patients cured with radiotherapy

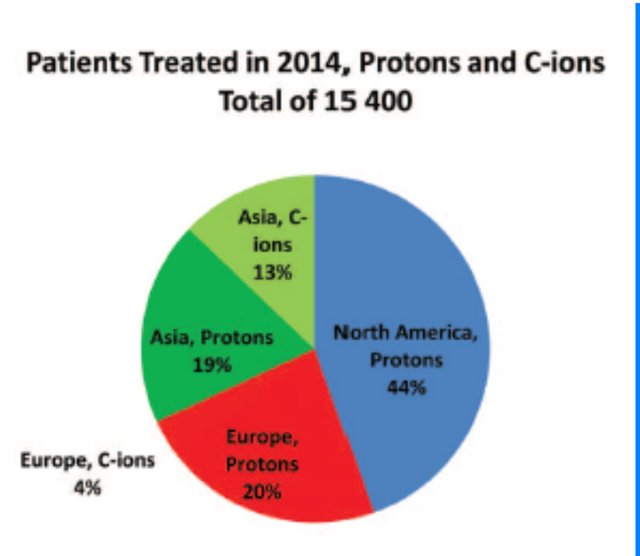
Patient Statistics 2014 (www.ptcog.ch)

Jermann M.. Int J Particle Ther. 2015;2(1):50-54.

He	2054	1957-1992
Pions	1100	1974-1994
C-ions	15736	1994-present
Other ions	433	1975-1992
Protons	118195	1954-present
Grand Total	**137179**	







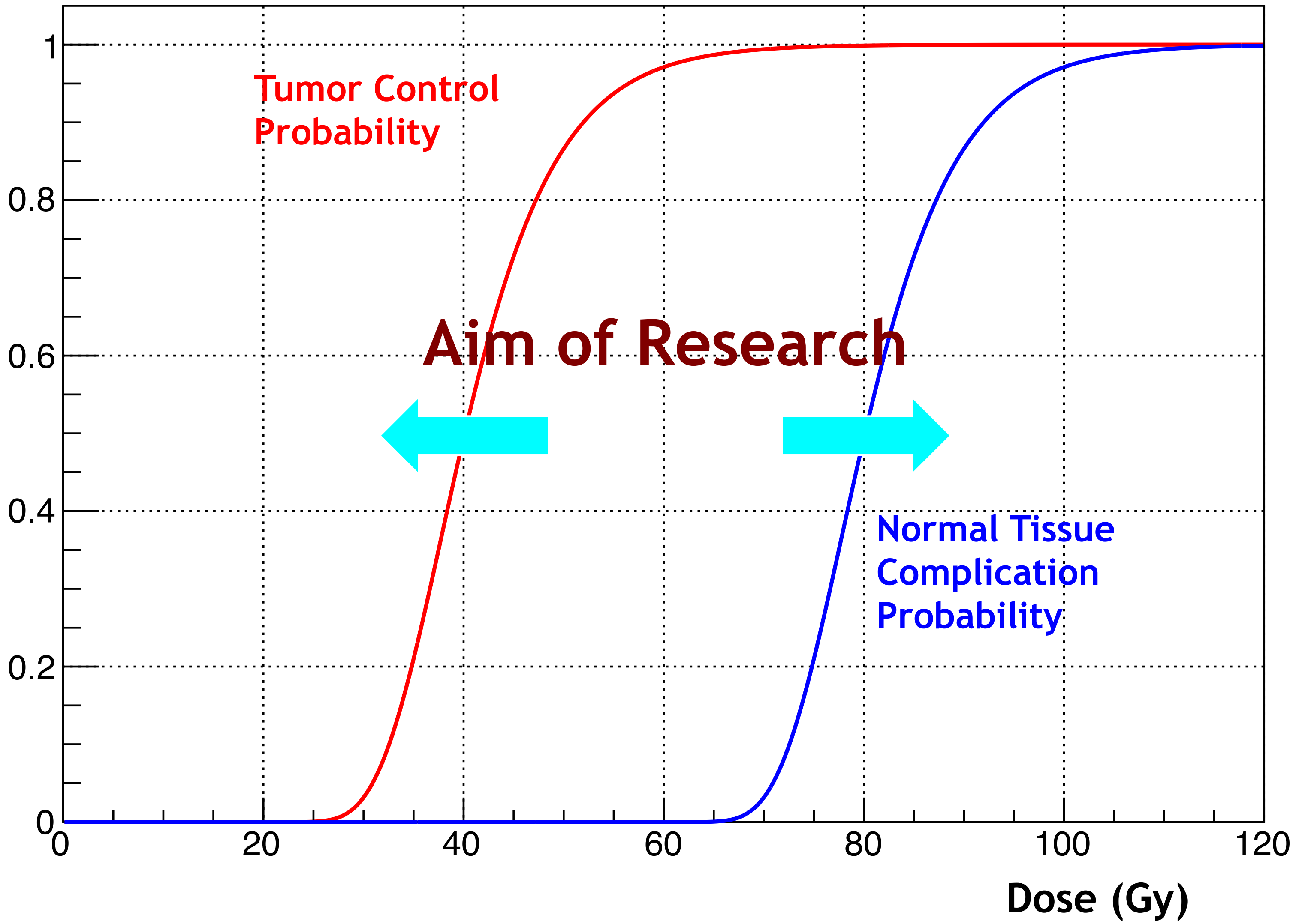
In 2014, about 10% of patients were pediatric and another 10% were treated for ocular melanomas.

At the beginning of 2015, more than 30 particle therapy centers, with a total of about 80 treatment rooms, were under construction worldwide.

~1/2 in the United States and ~1/3 in Asia.

About 15 centers expect to start technical and/or clinical commissioning in 2015 and about half of them should be ready for patient treatment before the end of 2015.

TCP vs NTCP


1
0.8
0.6
0.4
0.2
0
0
20
40
60
80
100
120
Tumor Control Probability
Aim of Research
Normal Tissue Complication Probability
Dose (Gy)

Interdisciplinary aspects: Physics and Biology

Ionisation tracks

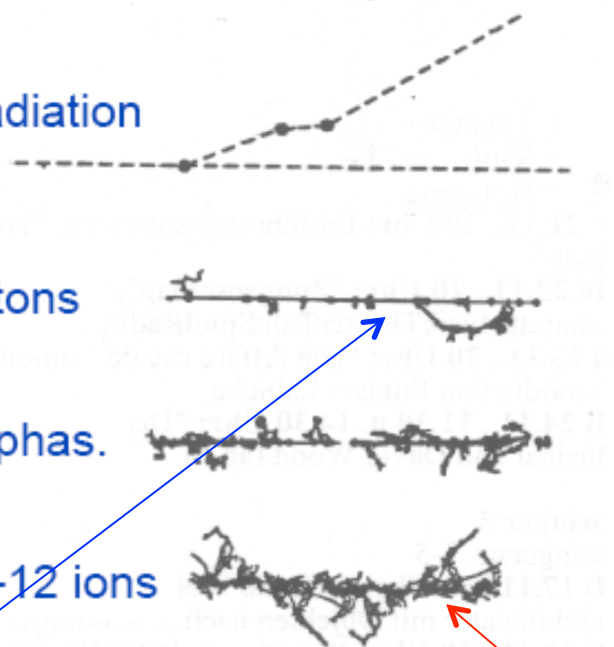
LET

Gamma radiation

1MeV Protons

1MeV/u alphas.

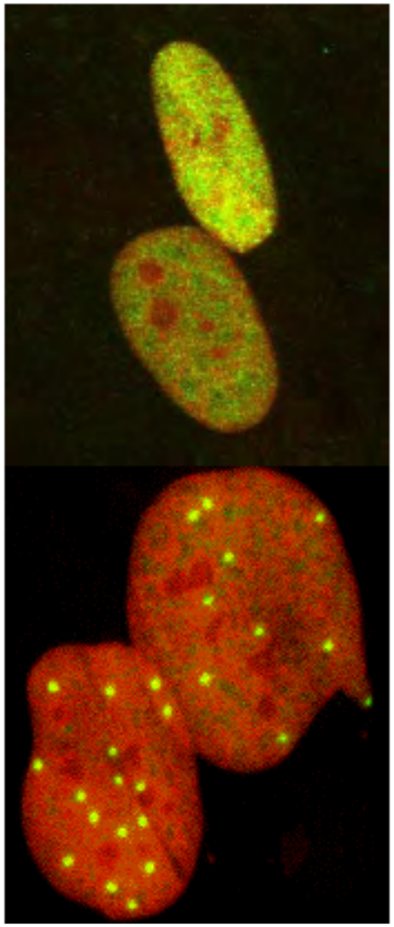
1MeV/u C-12 ions



p on the Bragg peak
when Rres ~ 0.2 mm
E ~ 4 MeV
LET ~ 10 keV/µm
<d> ~ 4 nm

^{12}C on the Bragg peak
when R_{res} ~ 1 mm
E ~ 17 MeV/u
LET ~ 140 kev/µm
<d> ~ 0.3 nm

Damage in nucleus



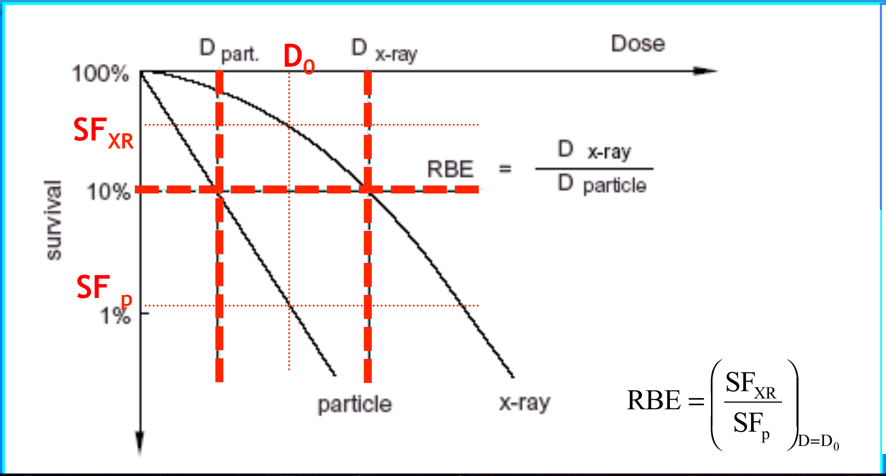
Low LET

Homogeneous deposition of dose

High LET

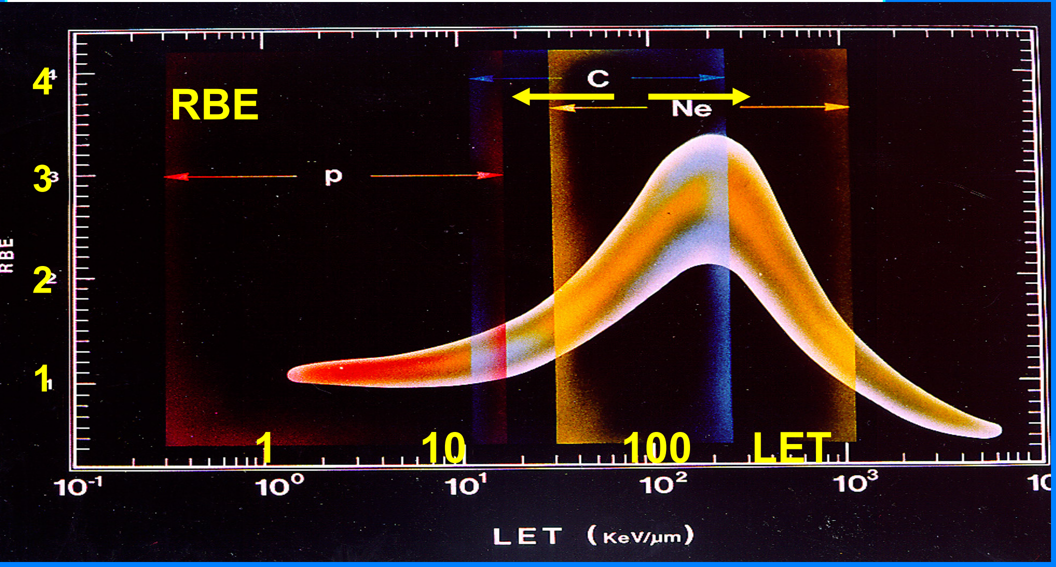
Local deposition of high doses

Radio Biological Effectiveness (RBE) and Oxygen Enhancement Ratio (OER)

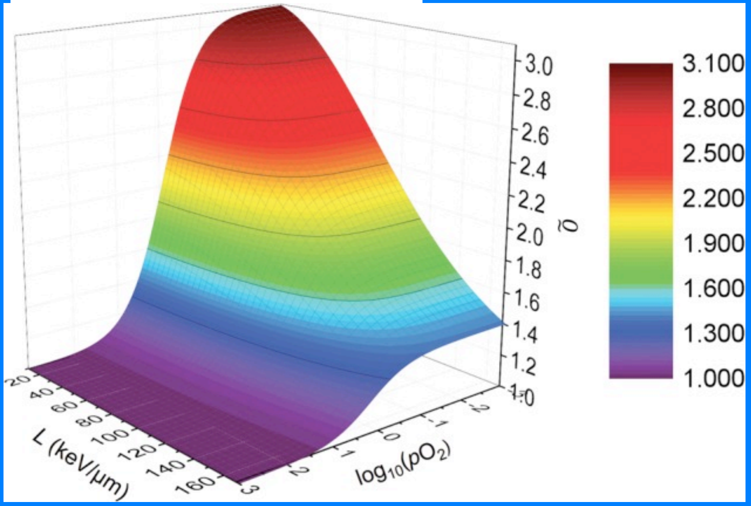


$$R.B.E. = \left(\frac{D_{RX}}{D_r}\right)_{SF=SF_0}$$

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



$$OER = \frac{D_{hypoxic}}{D_{oxigenated}}$$

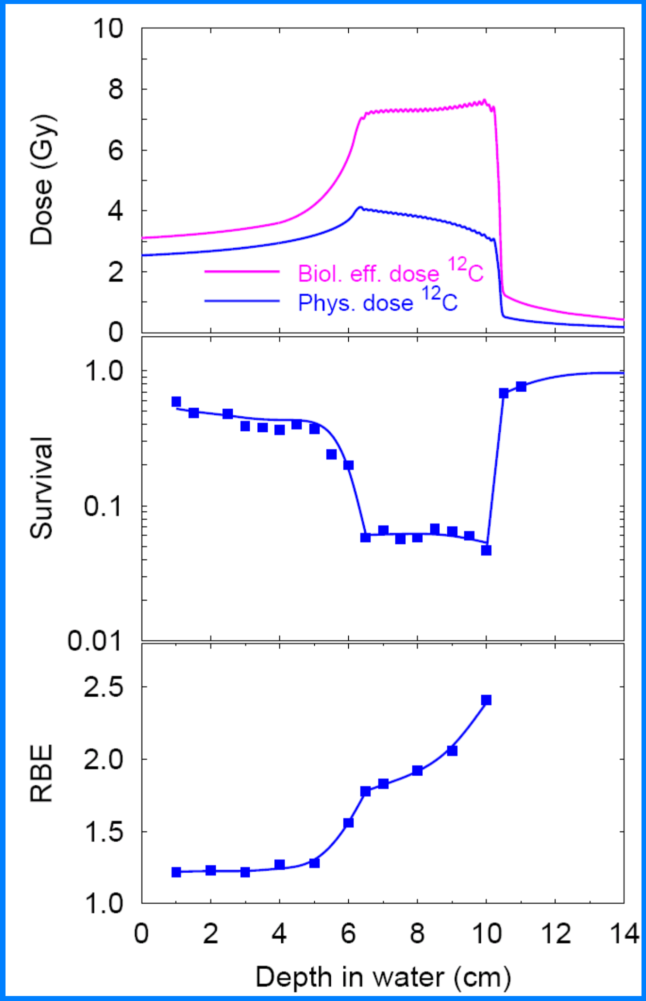


Laura Antonovic et al.
J Radiat Res. 2014 Sep; 55(5): 902-911.

Nuclear projectiles in Particle Therapy today

protons: 50-250 MeV

Relative Biological Effectiveness (RBE) ~ 1.1 *(under discussion…)*
accelerated by cyclotrons or synchrotrons



^{12}C: 60-400 MeV/u

Higher RBE → well suited for radio-resistant tumors
reduced no. of fractions
reduced lateral spread with respect to protons

However:
variable RBE vs energy, LET, …
accelerated by larger machines
Nuclear Fragmentation (➔complex RBE)
heavier gantries and magnets…

What clinicians ask today

- High quality clinical data for high level evidence
- Health economic assessments; global epidemiological assessments
- Improved clinical research structures, including IT
- Radiobiological core data (e.g. RBE)
- Integration into precision medicine era (e.g. biomarkers, combined modality effects)
- Range uncertainty reduced
- Control of organ motion, of anatomic changes during treatment, of biological changes during treatment
- Full image guided adaptive RT equipment
- Lower cost

M. Baumann

Taking full advantage of particle therapy in terms of physics requires:

- ✓ Full image guidance (real time)
- ✓ Reduced range uncertainties (real time beam imaging)
- ✓ In vivo dosimetry
- ✓ Highest level treatment planning
- ✓ Adaptive algorithms including all items above
- ✓ Very rapid and exact dose delivery (repainting, tracking)
- ✓ Reliable simulation tools (and fast !!)
- ✓ …

Hardware + Software

The contribue of physics to particle therapy development

There is still a significant fraction of people in the clinical community who consider hadrontherapy (ion therapy) too complicate, too expensive, not able to reach in practice the expected high level of precision, not yet in the realm of evidence-based medicine

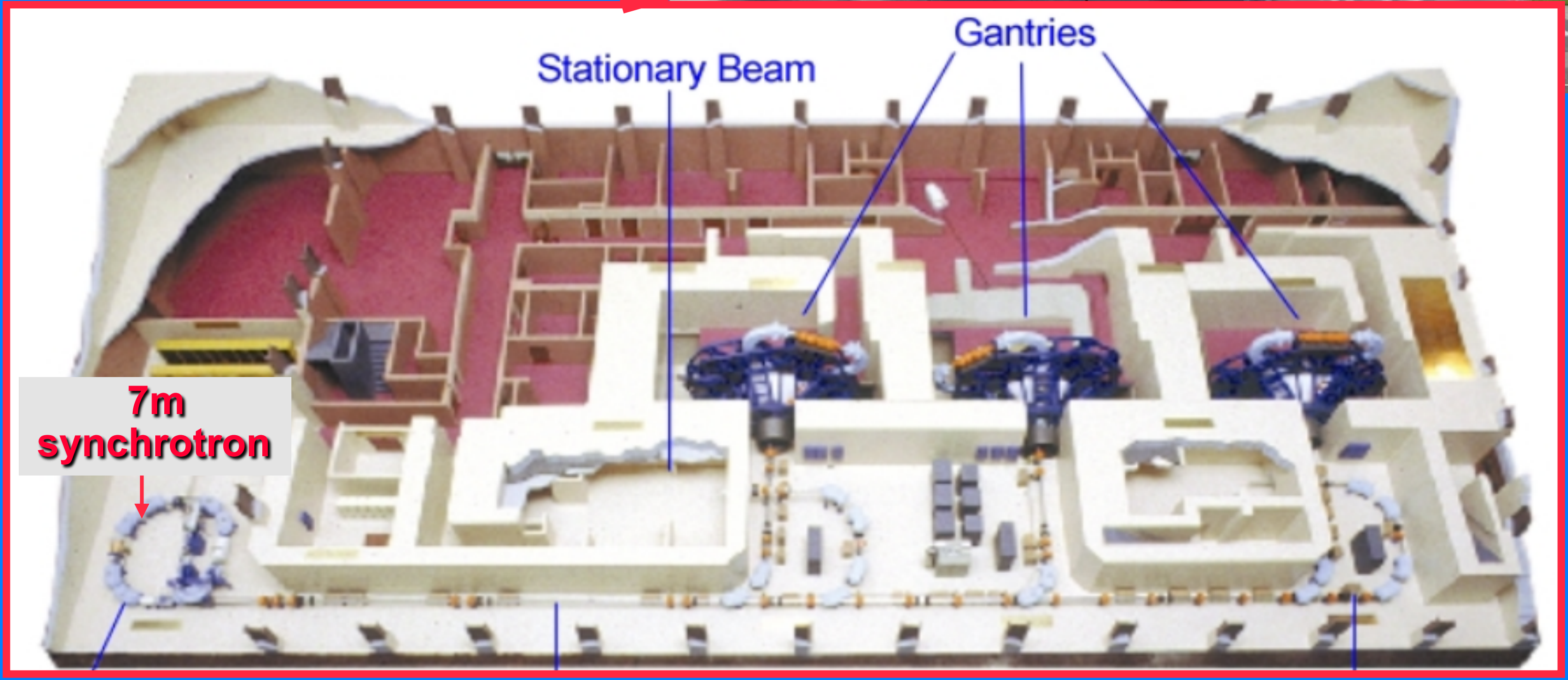
Nuclear Physics European Collaboration Committee (NuPECC)

Nuclear Physics for Medicine

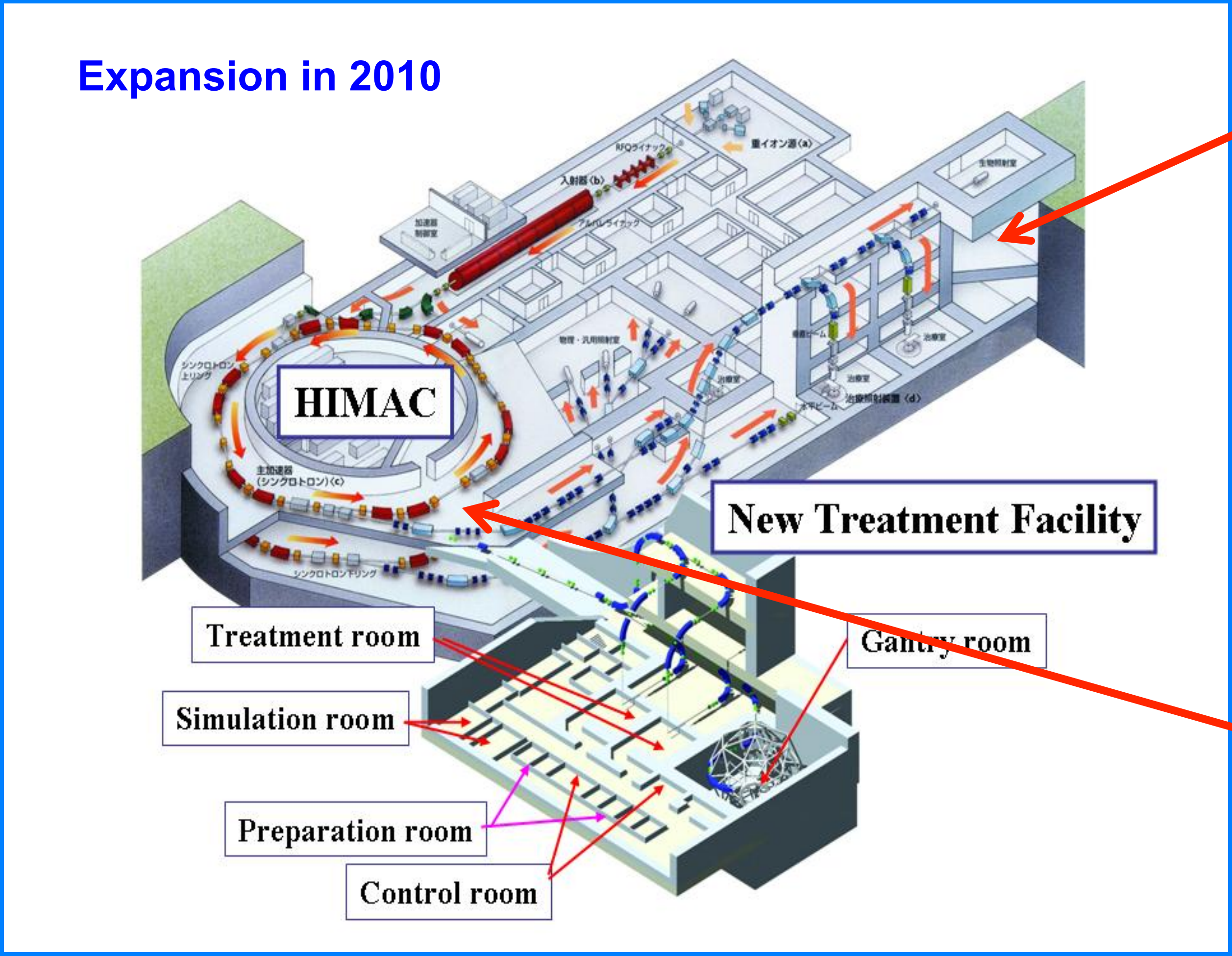
paradigmatic case of a topic in between research and actual clinical practice, where the contribution coming from physicists remains fundamental

Loma Linda University Medical Center

160 session/day



Carbon Ion facilities: HIMAC (Heavy Ion Medical Accelerator in Chiba)



3 treatment rooms
1 experimental room

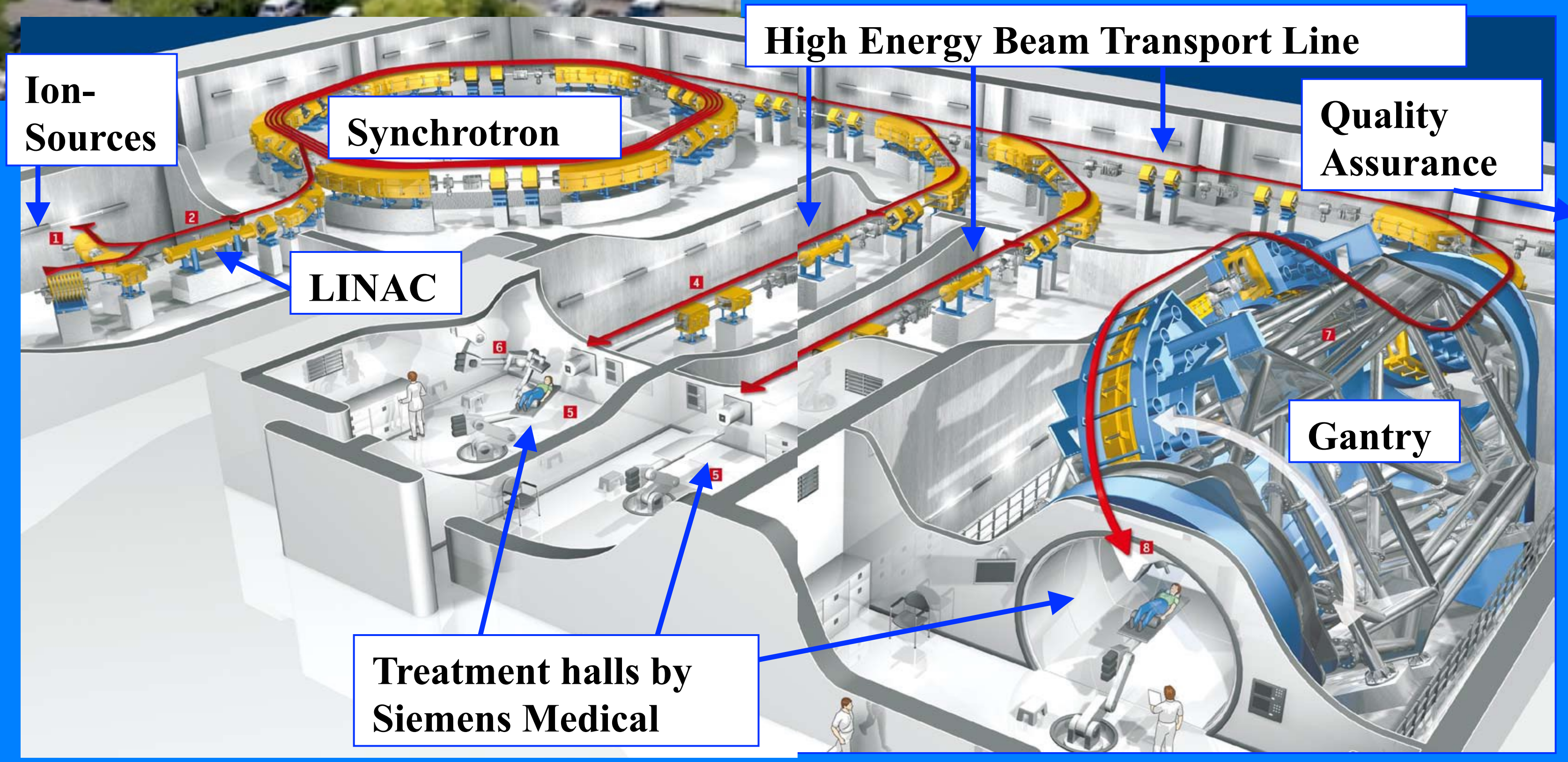
2 synchrotrons
800 MeV/u,
therapy and
nuclear physics

HIT - Heidelberg

HIT
Heidelberger Ionenstrahl-Therapiezentrum

First patient: end 2009

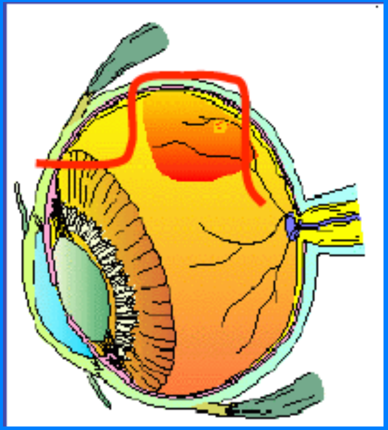
So far >2.000 patients



HadronTherapy in Italy

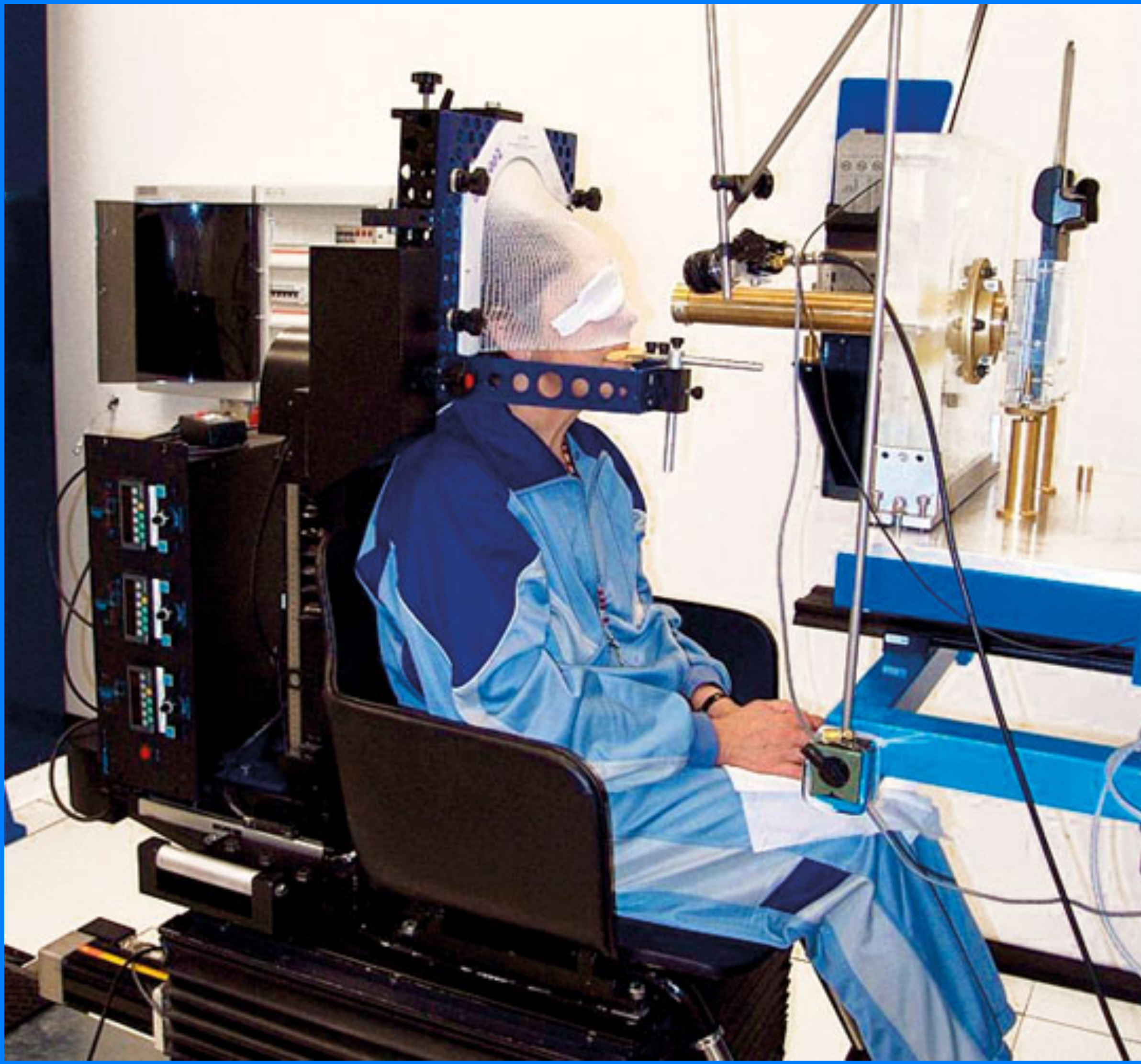
CATANA @INFN-LNS

- **>350 patients since 2002**



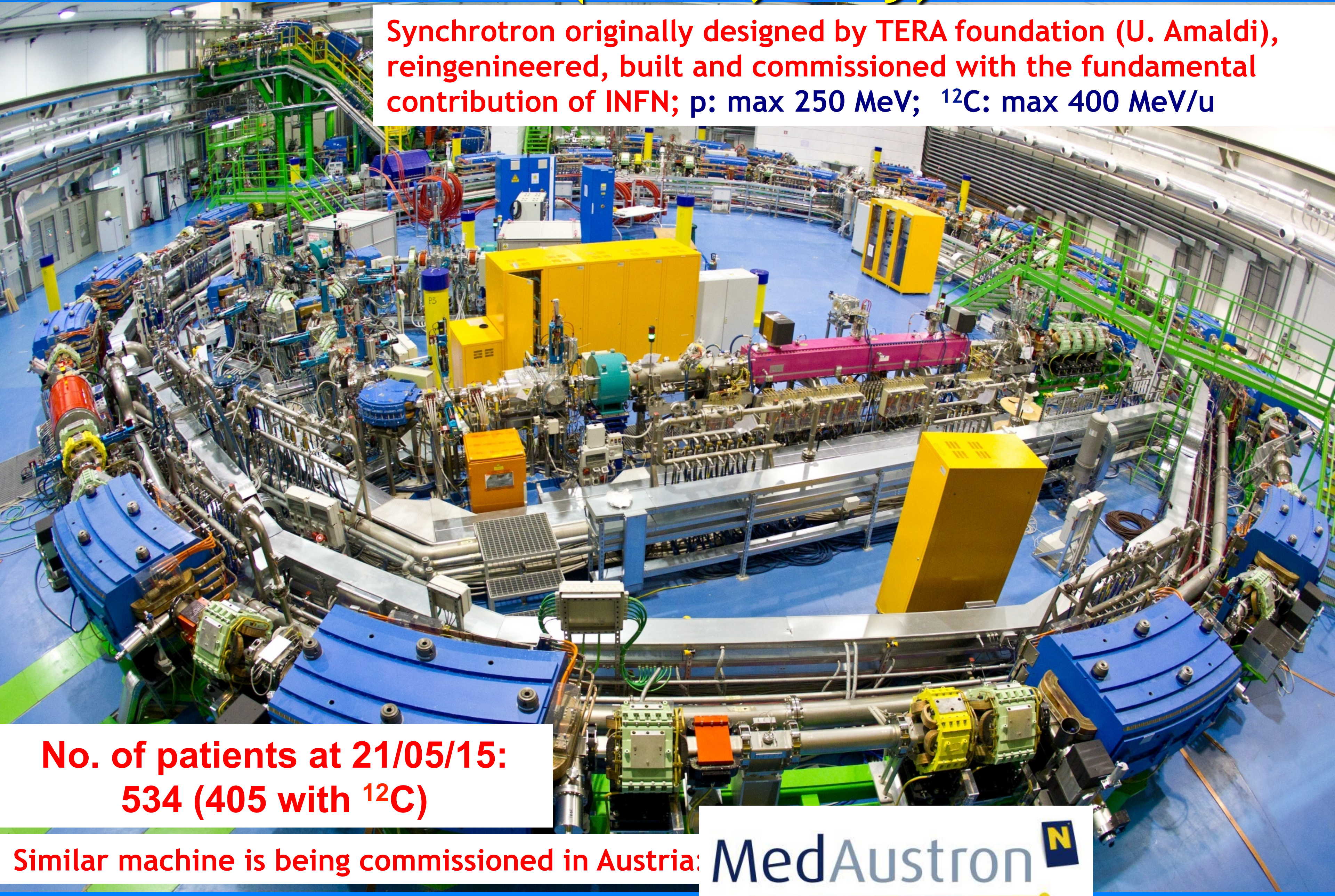
Treatment of thechoroidal and iris melanoma (In Italy about 300 new cases for year)

Eye retention rate 95 %
Survival 98 %
Local Control 95 %



CNAO (Pavia, Italy)

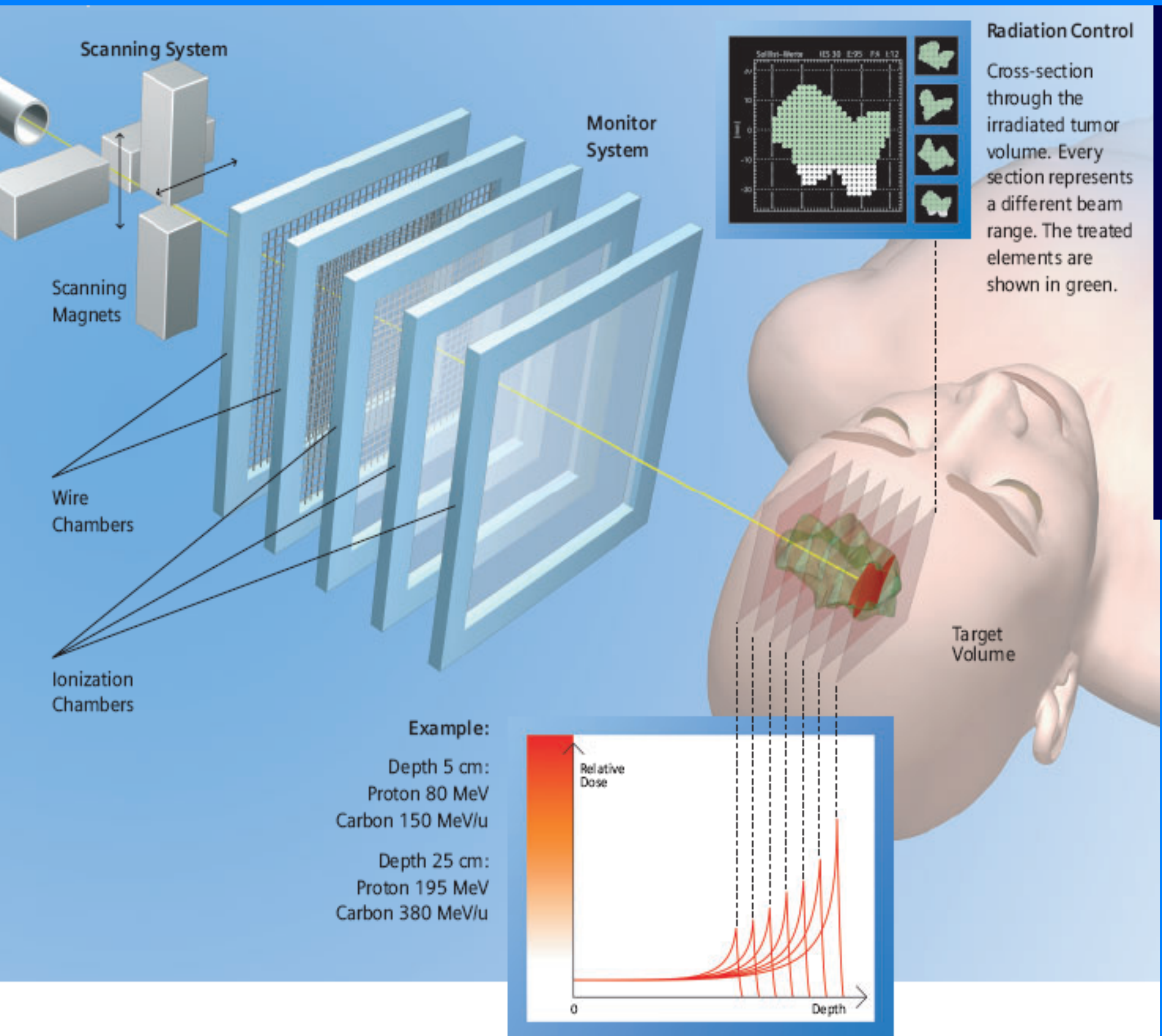
Synchrotron originally designed by TERA foundation (U. Amaldi), reingenineered, built and commissioned with the fundamental contribution of INFN; p: max 250 MeV; ^{12}C: max 400 MeV/u

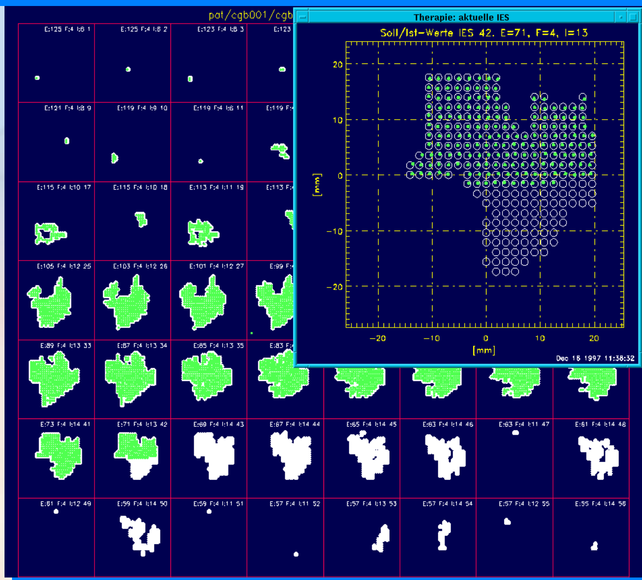


No. of patients at 21/05/15: 534 (405 with ^{12}C)

Similar machine is being commissioned in Austria: MedAustron

Dose delivery to tumor:
The Raster Scan method (“Active Scanning”)





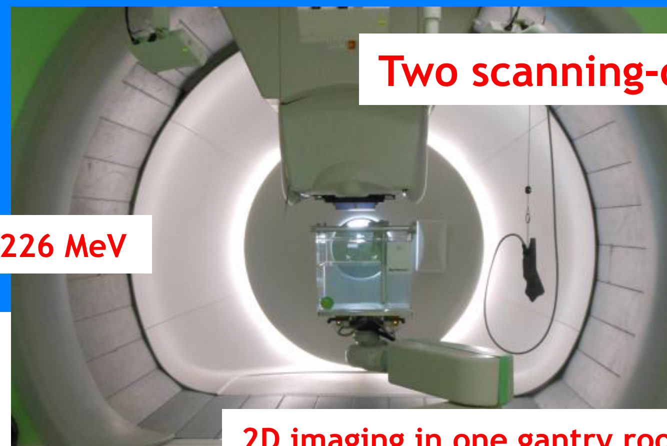
Typically:

p: ~10^9 p/s

^{12}C: ~ 10^8 p/s

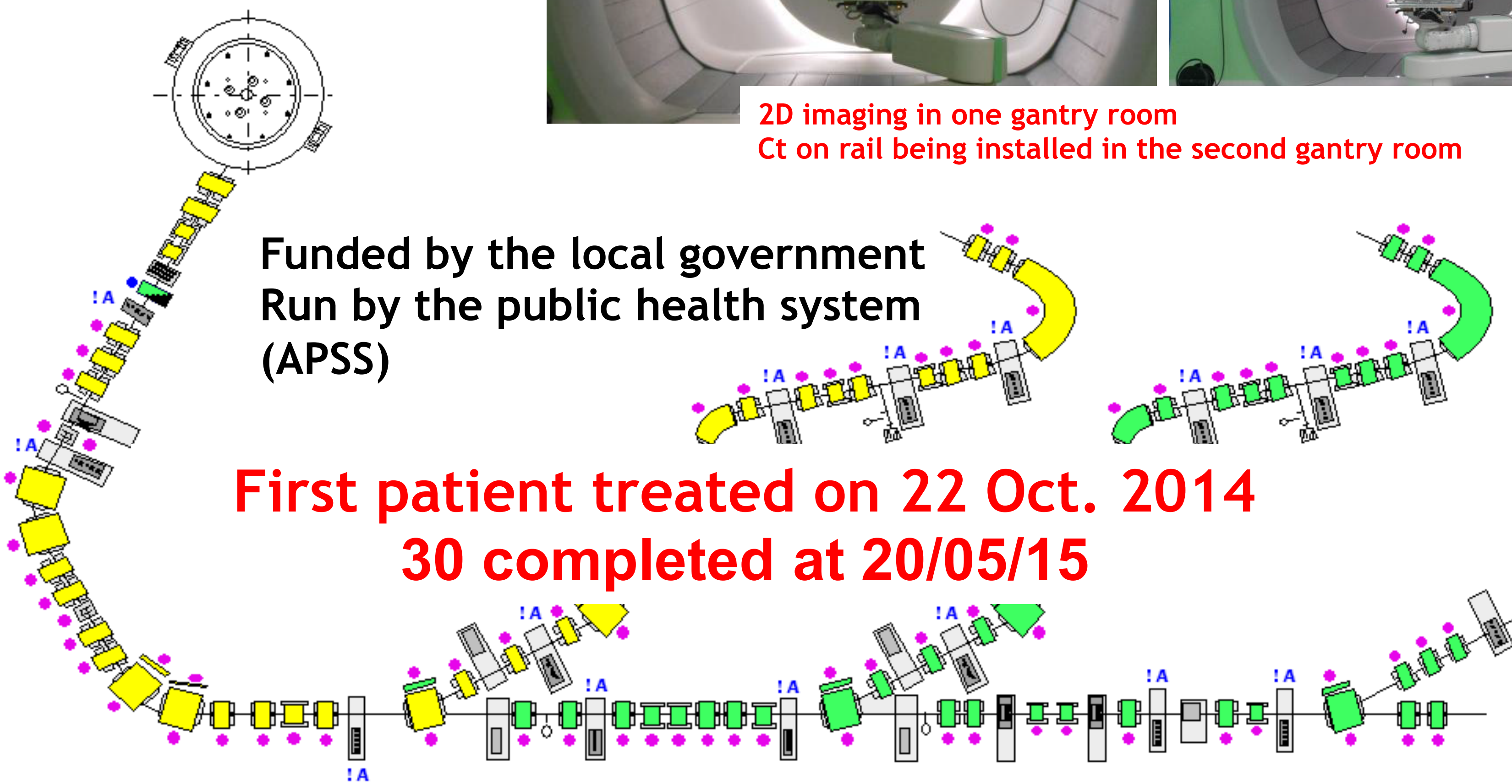
New Proton Therapy in Trento (Italy)

Energies at isocentre from 70 to 226 MeV



Two scanning-only 360°gantries

2D imaging in one gantry room
Ct on rail being installed in the second gantry room



Funded by the local government
Run by the public health system (APSS)

First patient treated on 22 Oct. 2014
30 completed at 20/05/15

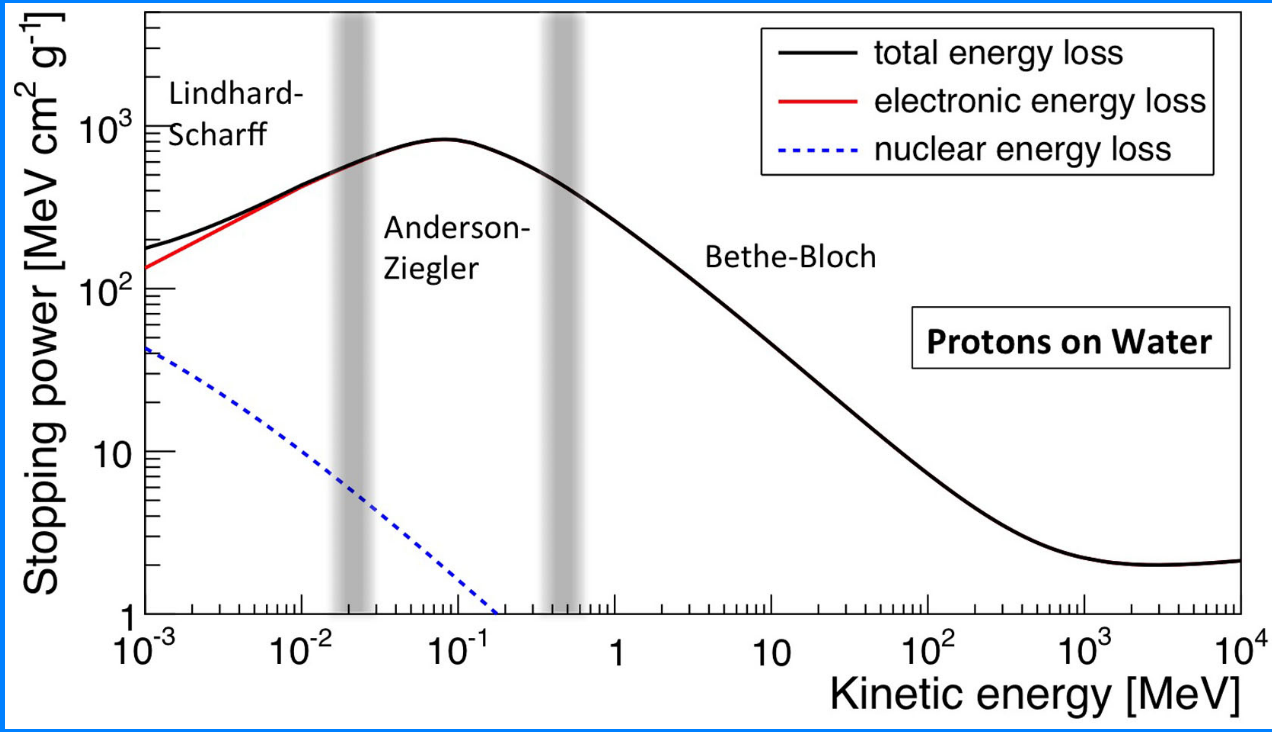
Physics of Bragg Peak

important at Low Energy dE/dx:

- Shell Corrections

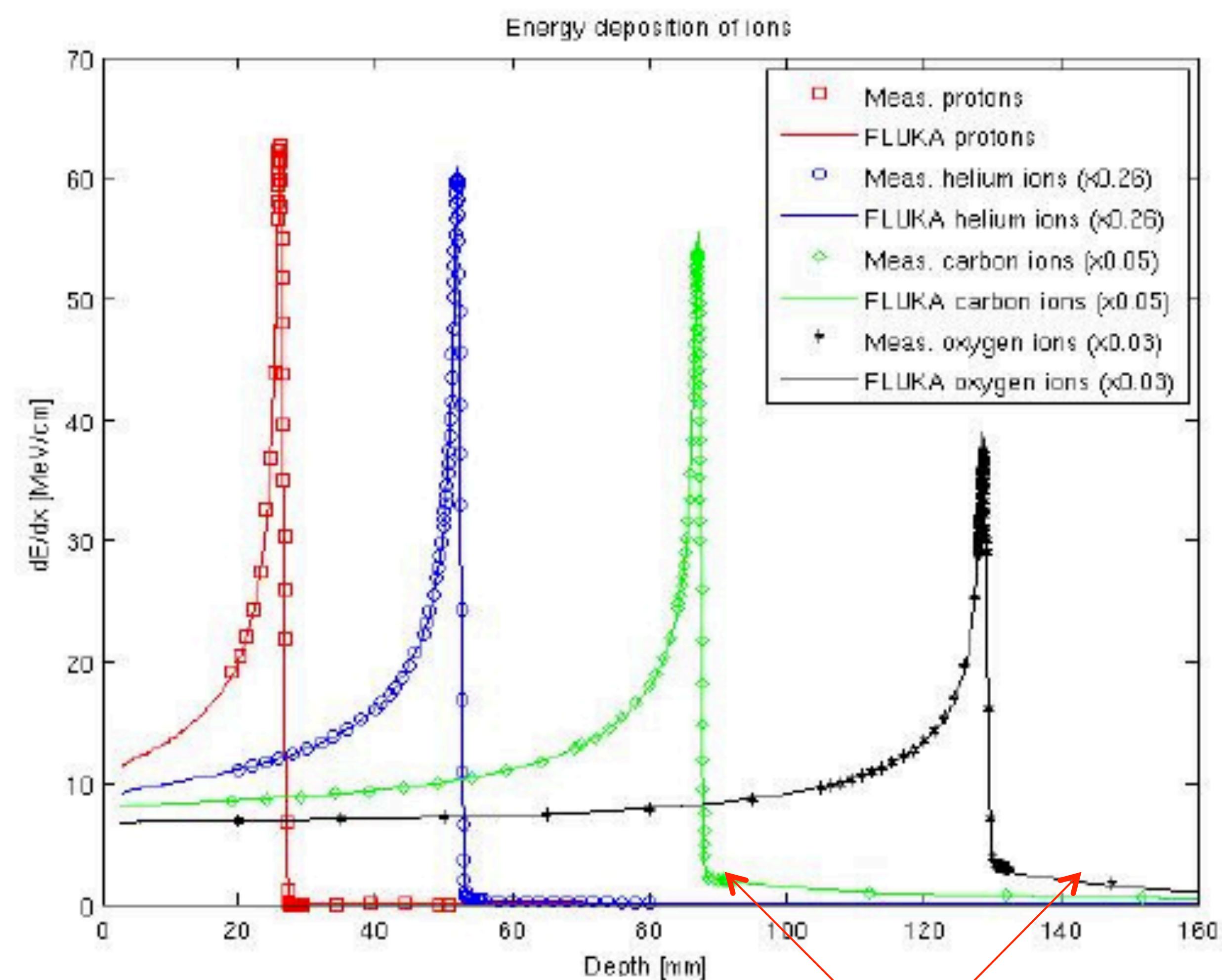
High order corrections

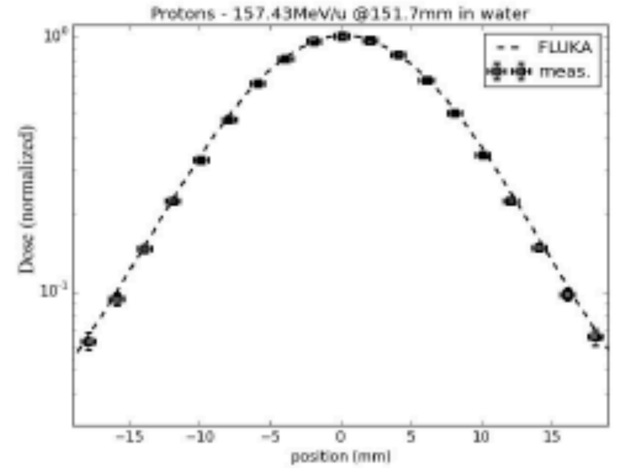
- Barkas correction ($\propto z^3$)
- Bloch correction ($\propto z^4$)
- Mott corrections

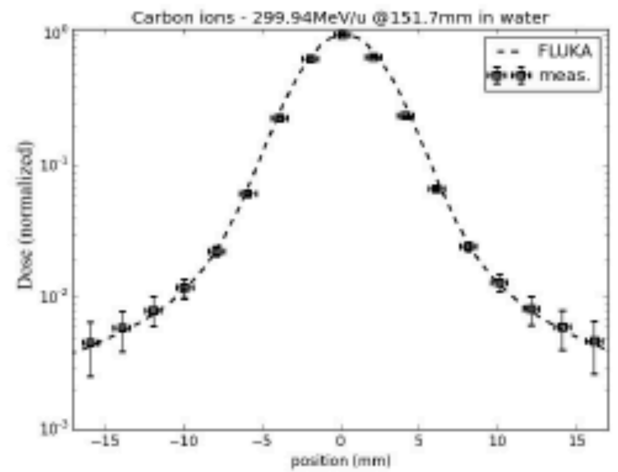


dominated by
interaction with electrons

MCS, Energy loss fluctuations
and <u>nuclear interactions</u>
<u>do affect the shape!</u>







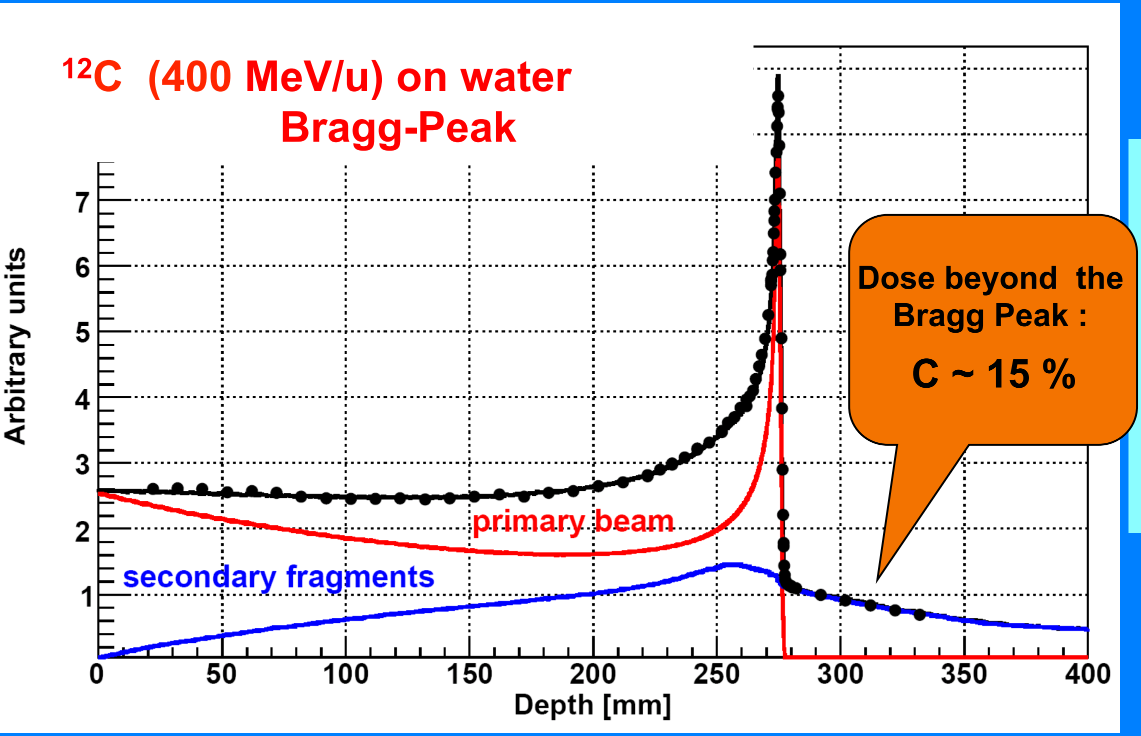
Some apparently trivial parameter is not well known. For example: <I>

Tail beyond the Peak due to nuclear fragmentation of Projectile

Nuclear Fragmentation and Particle Therapy

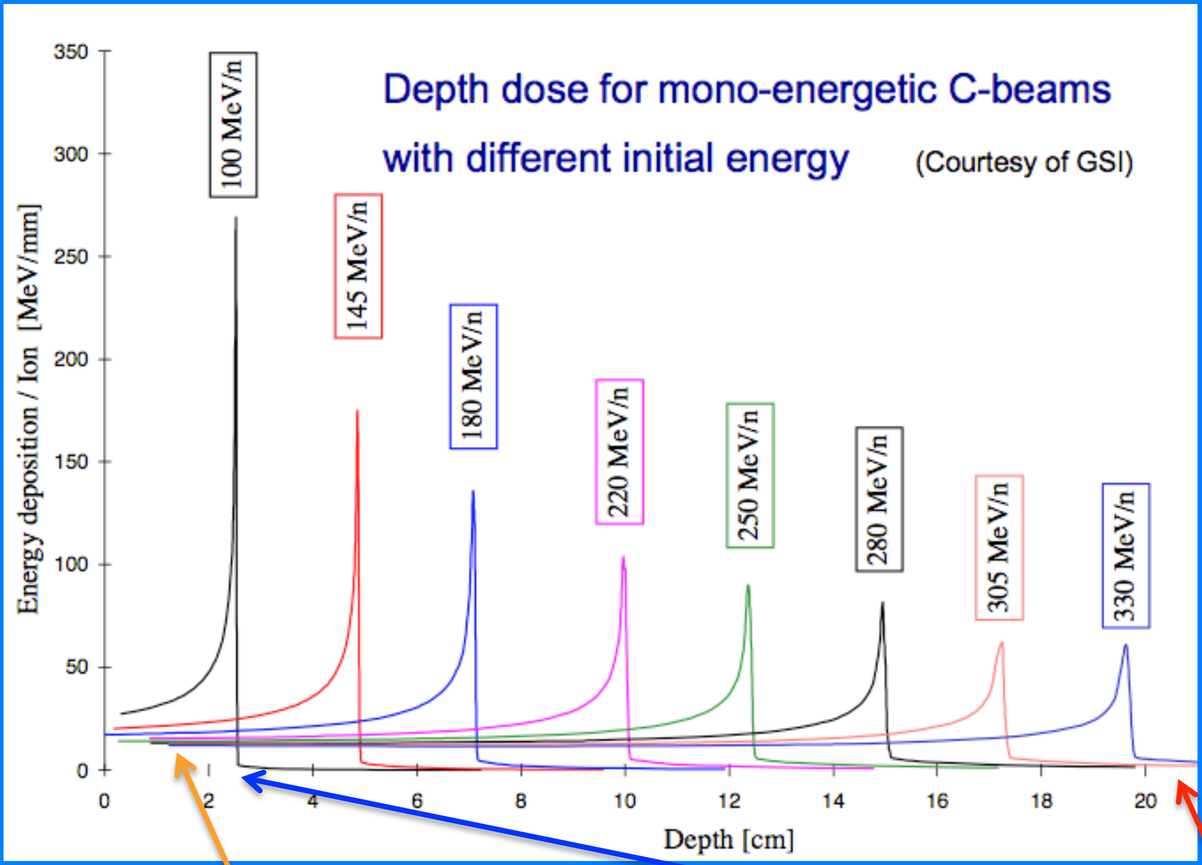
- Production of fragments with higher range vs primary ions
- Production of fragment with different direction vs primary ions:

Different biological effectiveness of the fragments wrt the beam



Dose release in healthy tissues with possible long term side effects ➔ must be carefully taken into account in the Treatment Planning System

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 (2009)

GANIL 95AMev C beam - E600 collaboration (2011)

GSI 400Mev C beam FIRST experiment (2011)

GANIL 50AMev C beam

Monte Carlo codes: the need for exp. data

MC are becoming more and more fundamental for:

- startup and commissioning of new facilities and beam line stuides
- database generation for Treatment Planning System commissioning
- Treatment Planning verification (and correction)
- Prediction and analysis of secondary production by hadron beams for monitoring purposes
- Study of detector response

Main important features

- Physics
- Overcaming Water Equivalent approximations
- Accurate 3D tracking
- Detailed description of actual patient geometry: → CT images directly read as input

Main Challenges: Nuclear physics models and exp cross sections for validation, Coupling with Radiobiological models, Computing time…

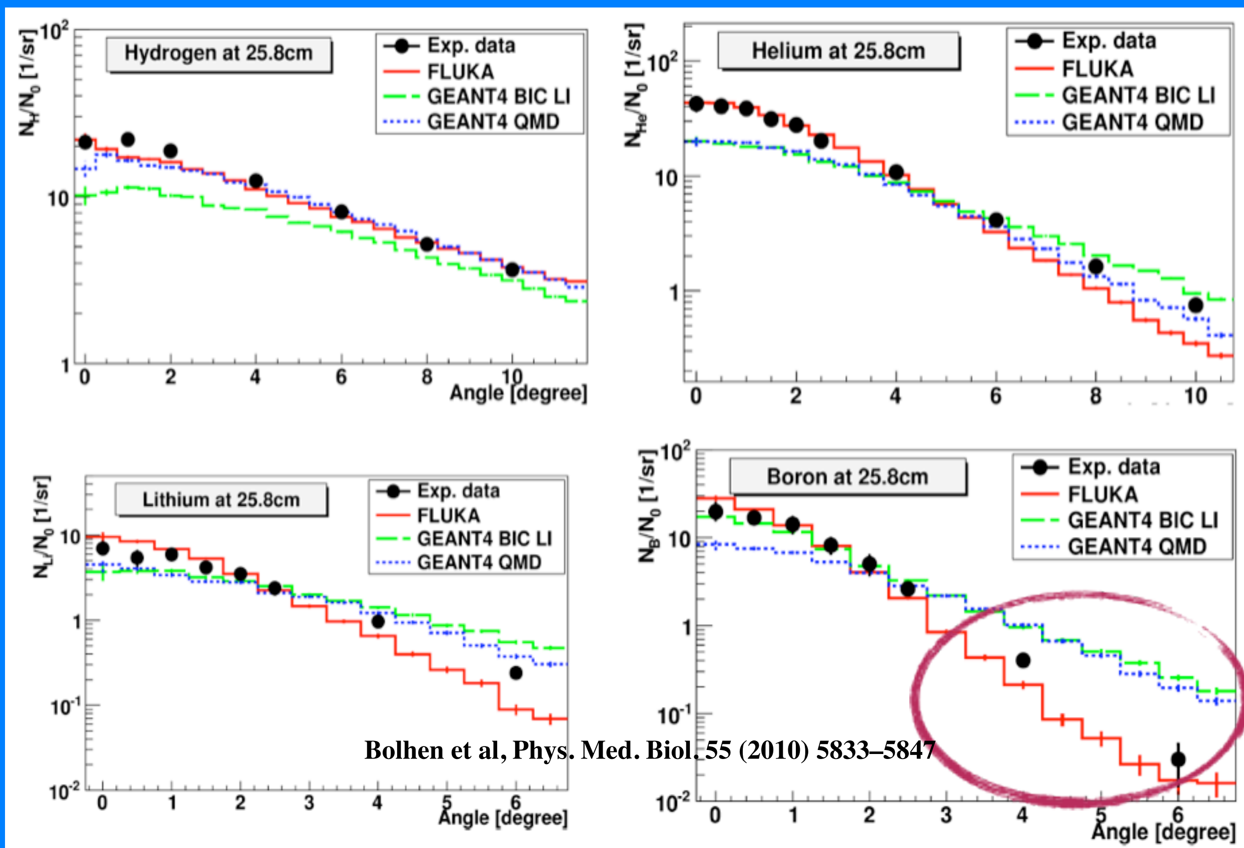
A few key issues in Monte Carlo physics

- Nuclear interaction models: phenomenological approaches to be tuned on the basis of experimental cross sections
  - Not enough data available for complete validation! (Fragmentation of C is still the example of open problem)
  - Interactions of very light nuclei (d, t, He, …)
- In general it is not possible to use the same model in the whole interesting energy range: great care to ensure continuity
- Quality of description of processes like pre-equilibrium, evaporation, break-up, de-excitation
- Extensive use of Evaluated Data bases is necessary

Huge progresses achieved in the last ~10 years.
Continous upgrade and development

Data - MC comparison: ^{12}C ions

Differential/double-differential quantities (vs angle and/or energy)

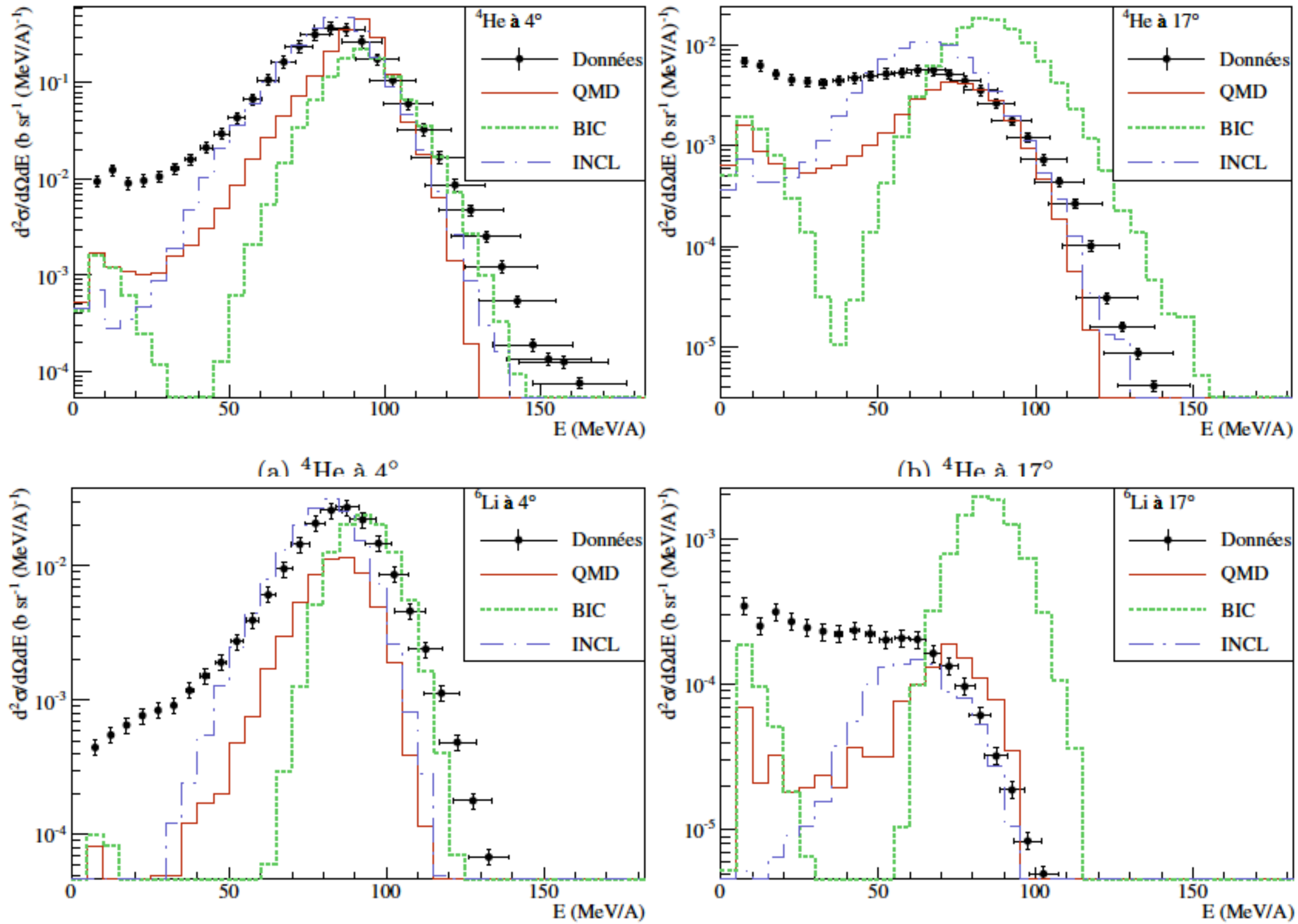


NB: the accuracy on delivered dose MUST be of the order of few %

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

Nuclear Fragmentation: C-C interactions at 95 MeV/u (Ganil) and comparison to MC

http://hadrontherapy-data.in2p3.fr/



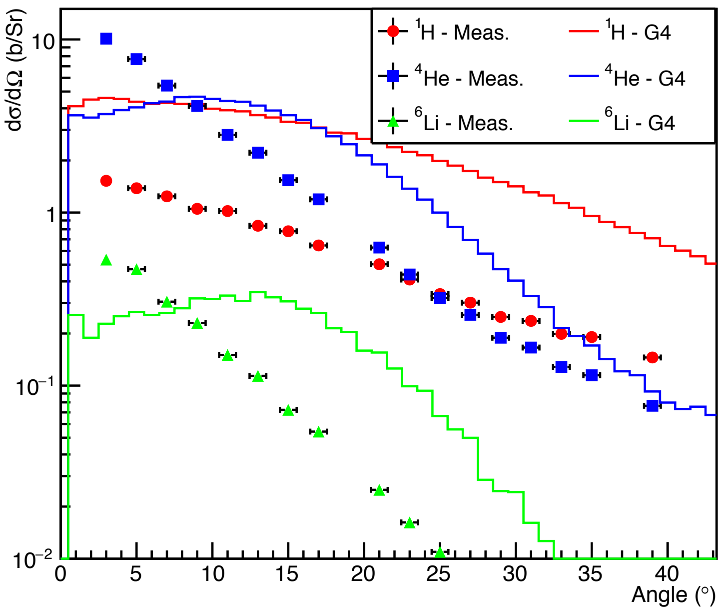
(a) ^{4}He à 4°

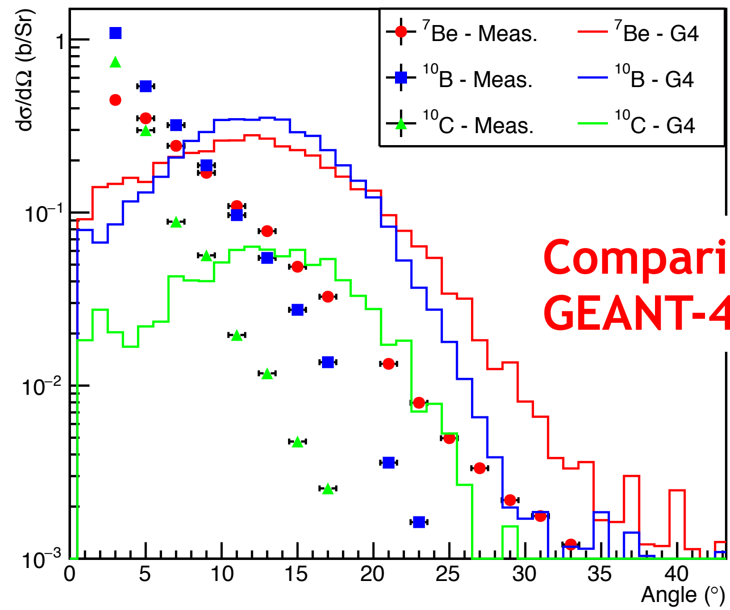
(b) ^{4}He à 17°

(c) ^{6}Li à 4°

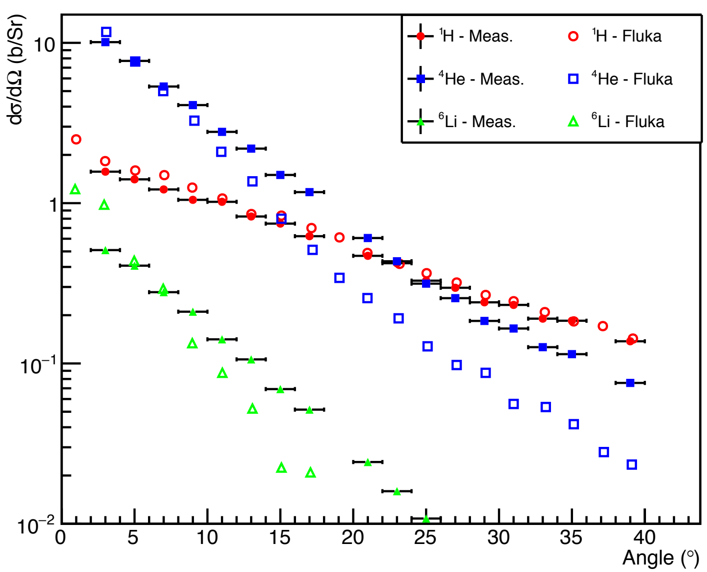
(d) ^{6}Li à 17°

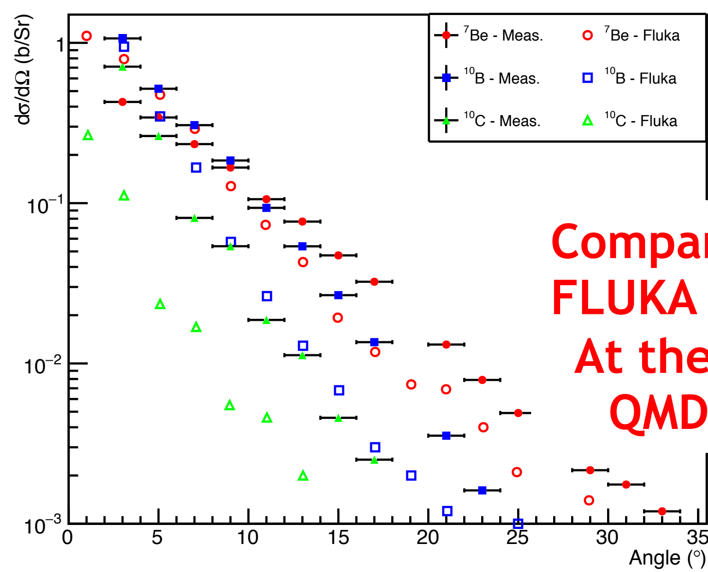
C-C @ 50 MeV/u (Ganil)





Comparison with GEANT-4 (QMD)

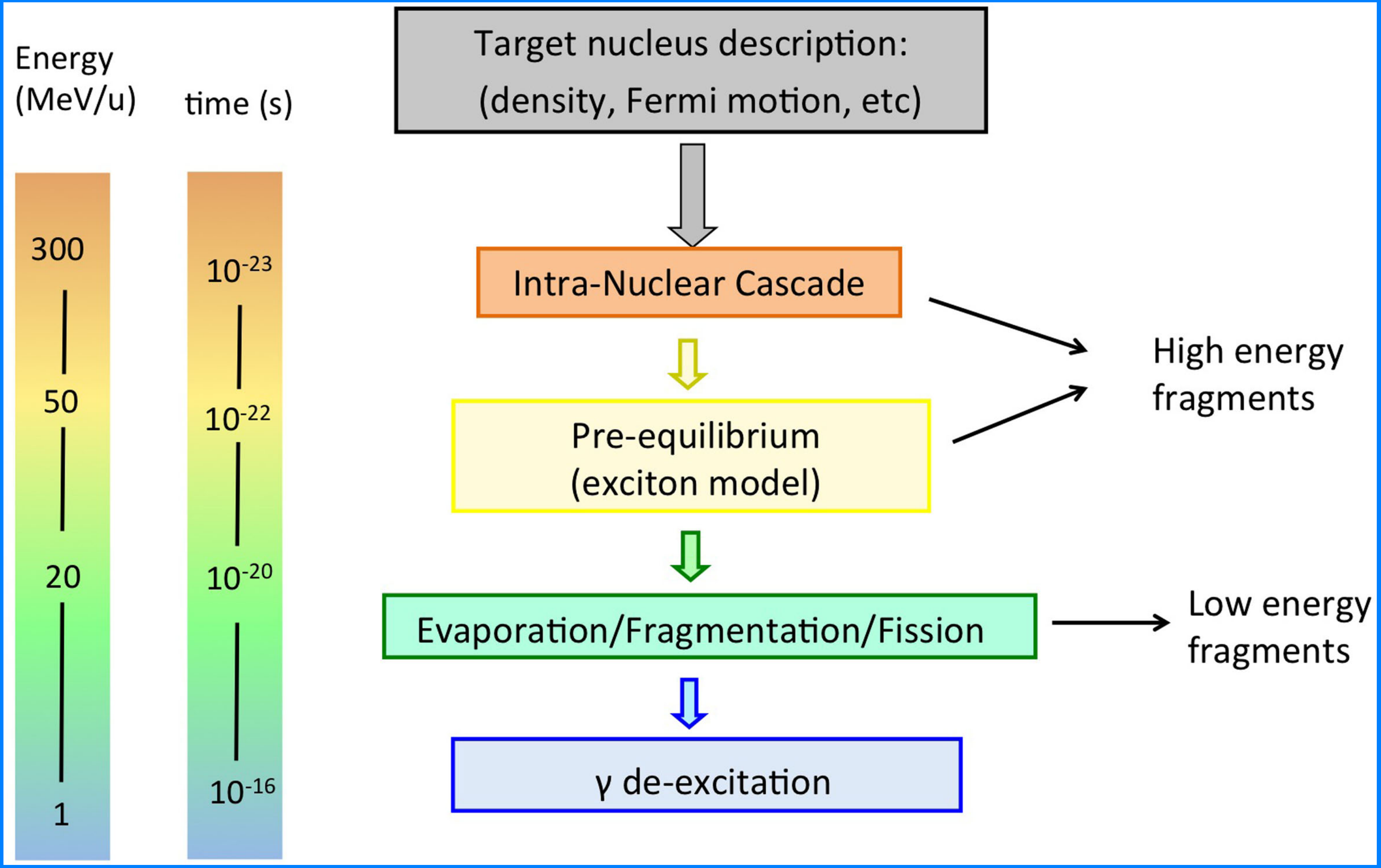




Comparison with FLUKA

At these energies QMD is not used

Some steps in hadron and nucleus interactions modelling



Nucleus-Nucleus interactions at energies useful for Particle Therapy

QMD (Quantum Molecular Dynamics) approach

Interaction of two nuclei starting from their initial state, modeled as a Fermi gas, following the propagation of each nucleon in the potential generated by all others nucleons. Described according to a quantum mechanical formalism. Dynamical evolution of particles, formation of heavy and light fragments and secondary nucleons is then predicted.

Different implementations exist

Invented to work down to ~ 1 GeV/u.
Sometimes difficult to extend it below

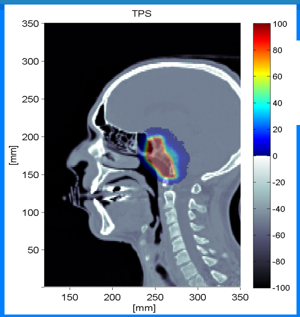
FLUKA MC code (reference at CNAO and Heidelberg):

0.12 GeV/u < E/A < 5 GeV/u: **rQMD** *H. Sorge, Phys. Rev. C 52, 3291 (1995)*

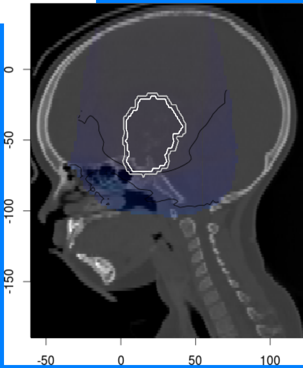
E/A < 0.12 GeV/u: **BME** *M. Cavinato et al., Nucl. Phys. A 679, 753 (2001)*

It describes the evolution of the de-excitation of the system of The two interacting nuclei during the pre-equilibrium phase. By solving a set of time-dependent transport equations, the model describes the evolution towards an equilibrium state through a sequence of two body reactions and ejection of unbound particles, whose multiplicity can be calculated

Software: Treatment Planning



(Effective) Dose Optimization

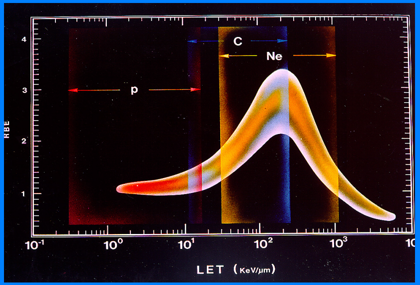


Imaging:
CT scan
and/or PET-CT)

Electron density

Radiotherapist:
identification of Target Volume
and of Organs at Risk

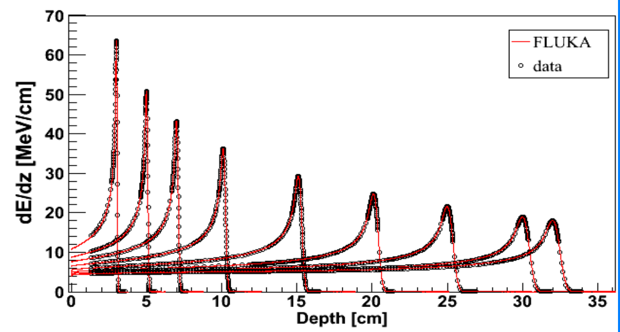
Radiobiology:
RBE parameters
OER (not yet…)



Nuclear Physics:
Dose vs Depth
hadrone/nucleus scattering:
fragments etc.

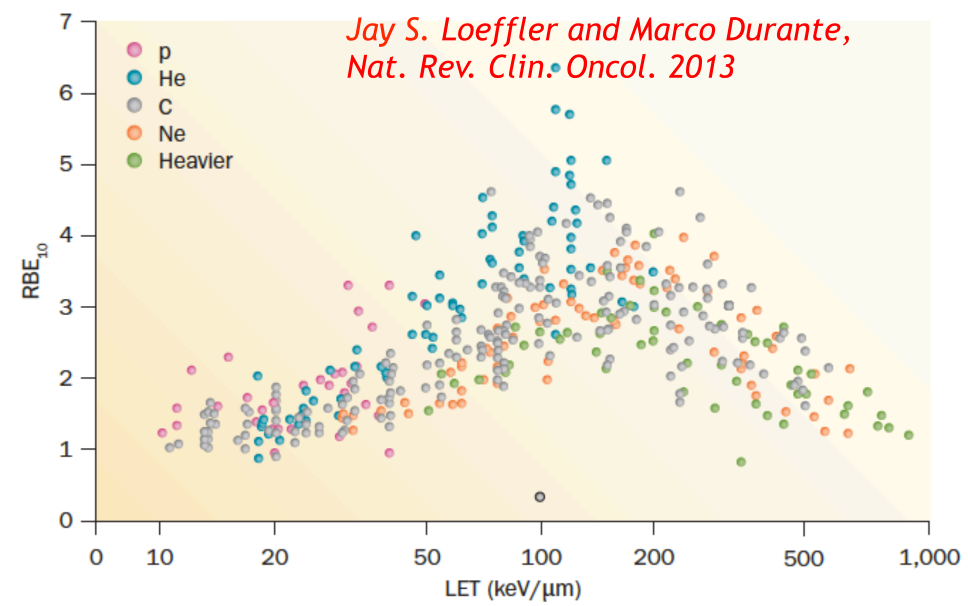
Treatment Planning System

Intensity, position and energies to be delivered to patient

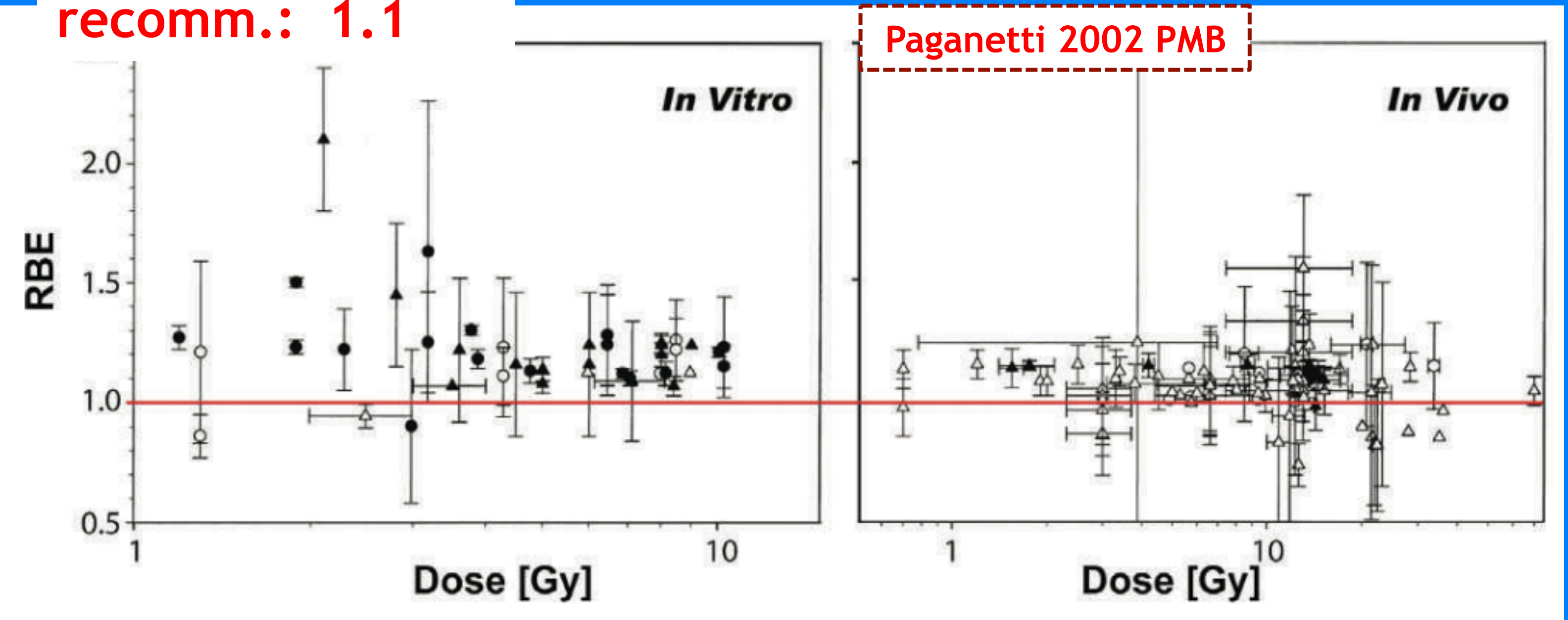


Radiobiology and its uncertainties

RBE versus LET from published experiments on *in vitro* cell lines. RBE is calculated at 10% survival.



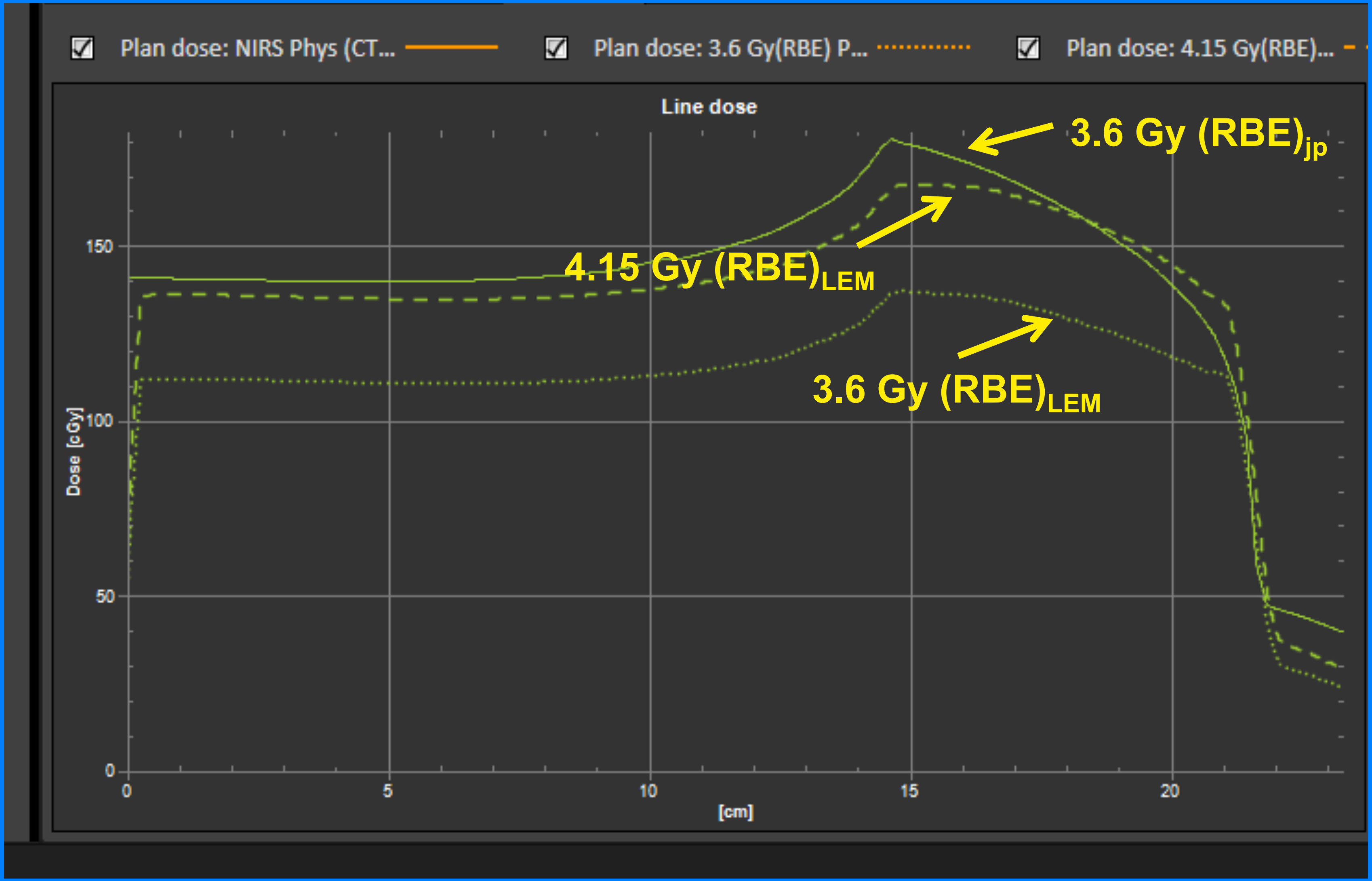
RBE of protons recomm.: 1.1



New Paradigm for Proton Radiobiology (Girdhani 2013 Radiat Res) → **Protons and photons present distinct physics and biological properties at Sub-Cellular, Cellular and Tissue level**

Prostate Pt – BHC 400MeV/u - 3.6 Gy (RBE)$_{jp}$

NIRS vs CNAO prescription Dose – Absorbed Dose comparison



Uncertainties related to particle range

The error intrinsic in this conversion (due to $\mu(\eta_e,Z)$ dependency on atomic number and electron density) is the principal cause of proton range indetermination (3%, up to 10 mm in the head)

[Schneider U. (1994), Med Phys. 22, 353]

AAPM 2012: **main obstacle to proton therapy becoming mainstream:**

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

proton based imaging system (pCT):

Conventional X ray tomographies taken before the proton treatment session and in a different setup. Precision improvement if positioning and treatment could be done in one go

Treatment planning is defined using X-CT *but* protons and photons interact differently with matter. Direct measure of the stopping power maps with same particles used to irradiate

The method

$$\int_L \eta_e(\vec{r})\, d\vec{r} = K \int_{E_{out}}^{E_{in}} \frac{dE}{S(E)}$$

E_{in} is the incident proton energy and E_{out} is the proton energy after traversing through the object, $S(E)$ is the proton stopping power, and K is a constant.

S(E,x,y) is obtained by solving the tomographic equation *(Wang, Med.Phys. 37(8), 2010: 4138)*

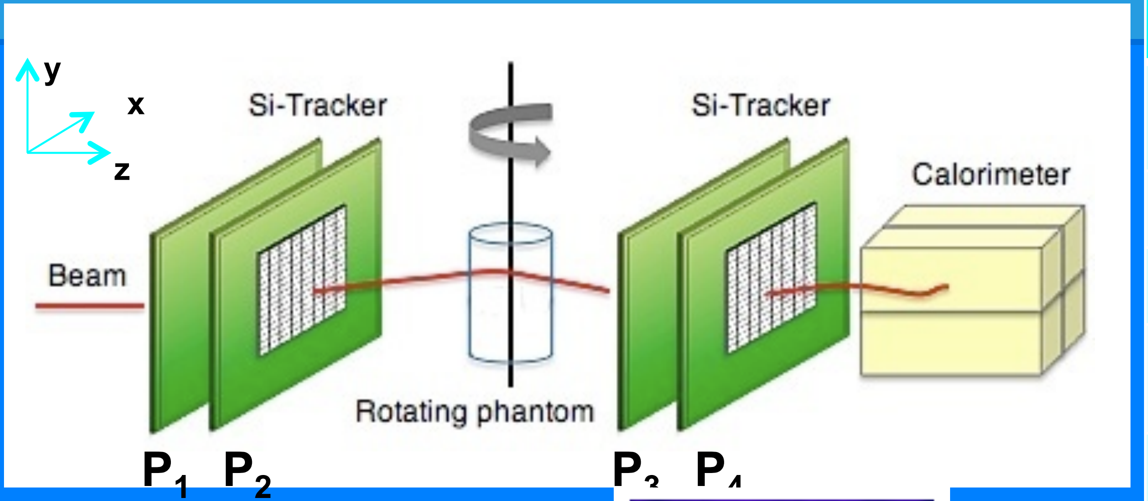
$$\int_{Path} S(x,y,E_0)\, dl = \int_{E_{res}}^{E_0} \left[\frac{S}{\rho}(H_2O,E_0) \Big/ \frac{S}{\rho}(H_2O,E) \right] dE$$

«projection»

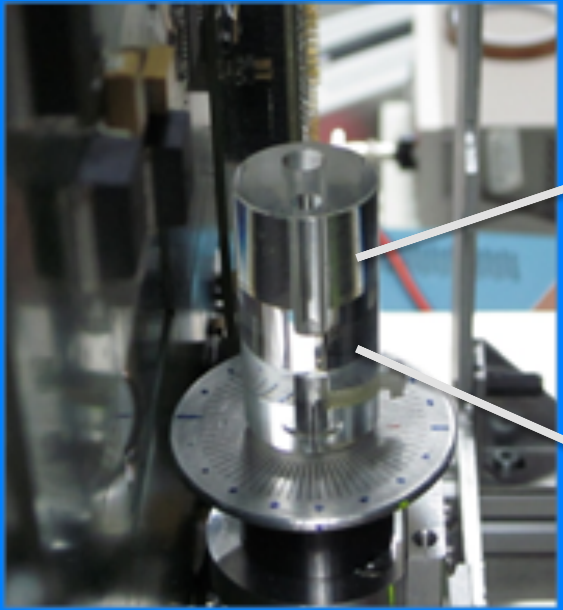
Unknown stopping power distribution (at E_0)

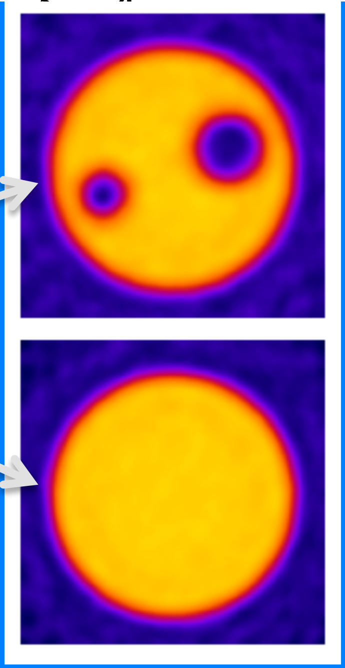
Evaluation of the "projection" term (through numerical integration starting from tables (ex. NIST) in H_2O and using the measured E_{res}

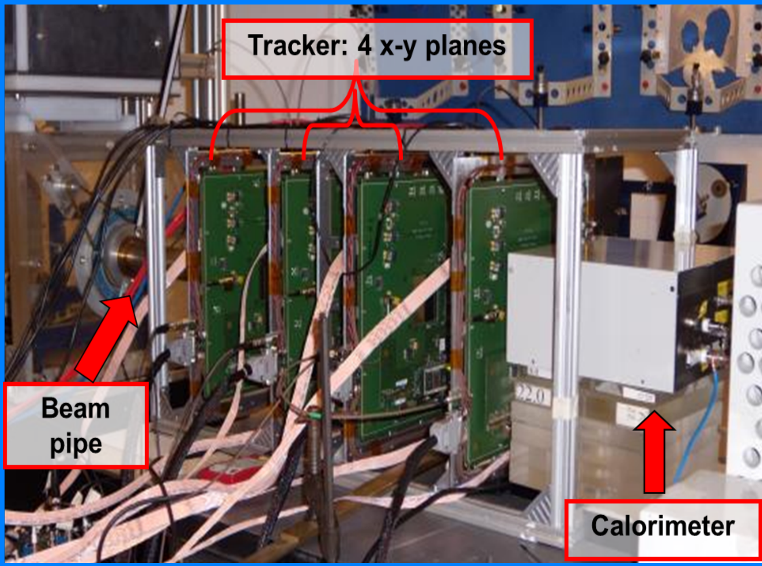
Proton CT: the INFN approach (Fi-LNS-Ct-Ca)



PARAMETER	VALUE
Proton beam kinetic energy	~300 MeV
Proton beam rate	1 MHz
Spatial resolution	< 1 mm
Electronic density resolution	<1%
Detector radiation hardness	>1000 Gy
Dose per scan	< 5 cGy







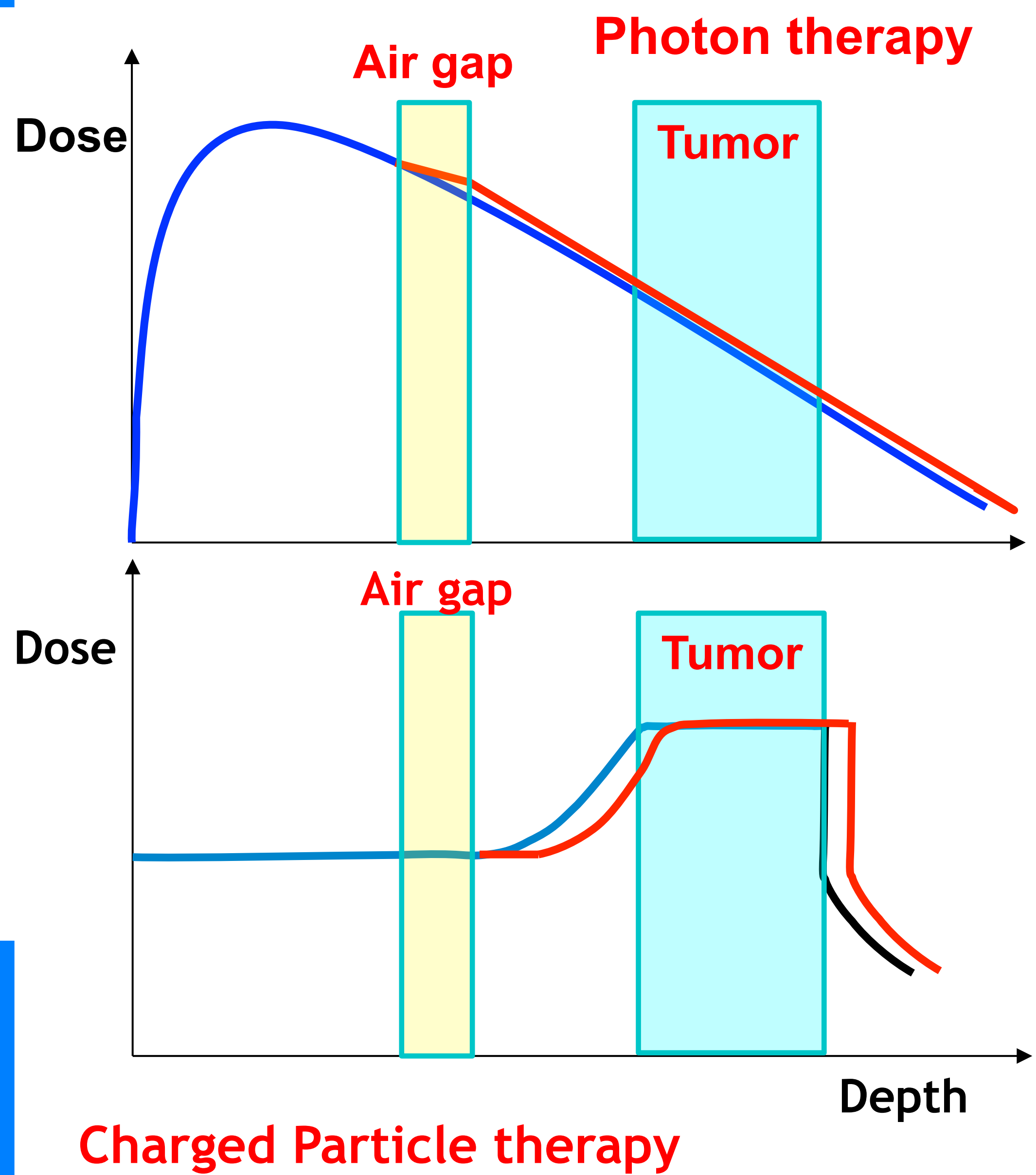
Proof of principle at 60 MeV LNS p beam

The need for in-vivo monitoring of particle therapy

Again uncertainties:

- Limitations of CT data (beam hardening, noise, resolution etc)
- **Uncertainty in energy dependent RBE**
- **Calibration of CT to stopping power**
- CT artifacts
- **Variations in patient anatomy**
- **In-homogeneity along the beam path**
- Variations in ion beam energy
- Variations in patient positioning

Planning uncertainty > 5 mm
(margin of 3.5% + 2 mm)

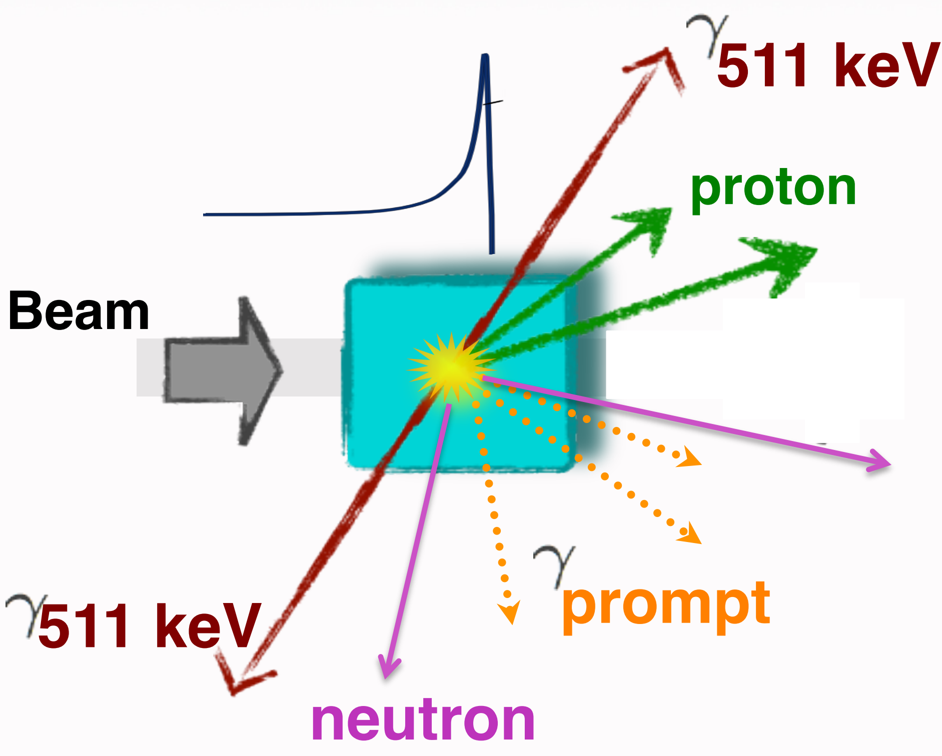


Help from Nuclear Physics: exploiting secondary products

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

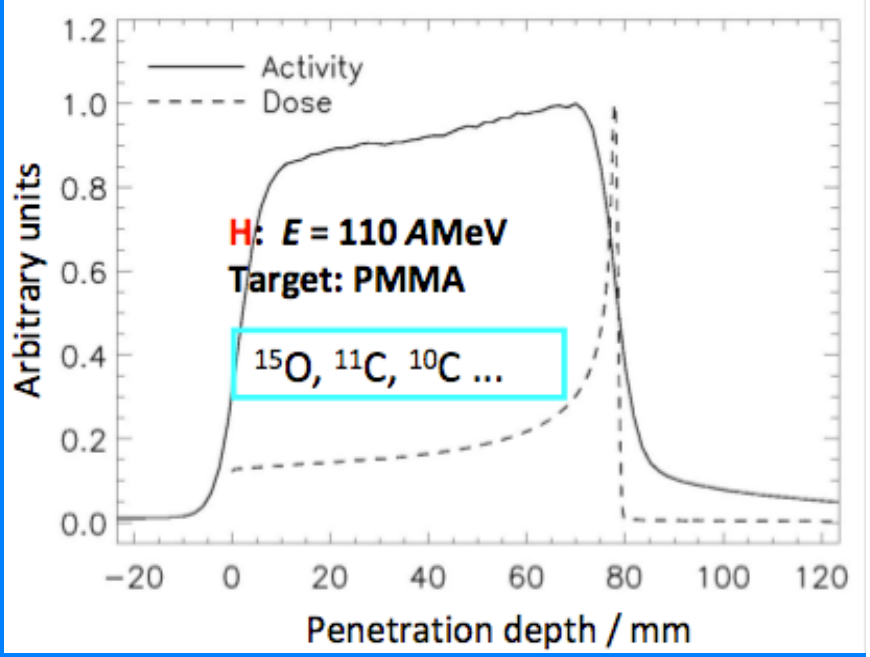
- Isotopes of short lifetime ^{11}C (20 min), ^{15}O (2 min), ^{10}C (20 s) with respect to conventional PET (hours)
- Low activity asks for quite a long acquisition time (some minutes at minimum) with difficult in-beam feedback
- Metabolic wash-out, the β^+ emitters are blurred by the patient metabolism



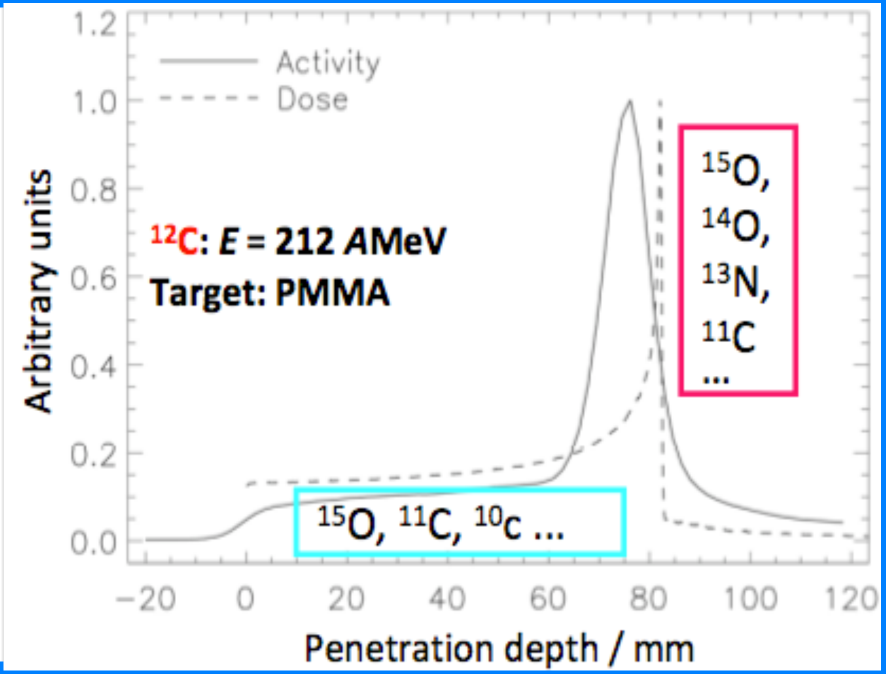
Correlation between β⁺ activity and dose

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}

Target fragmentation

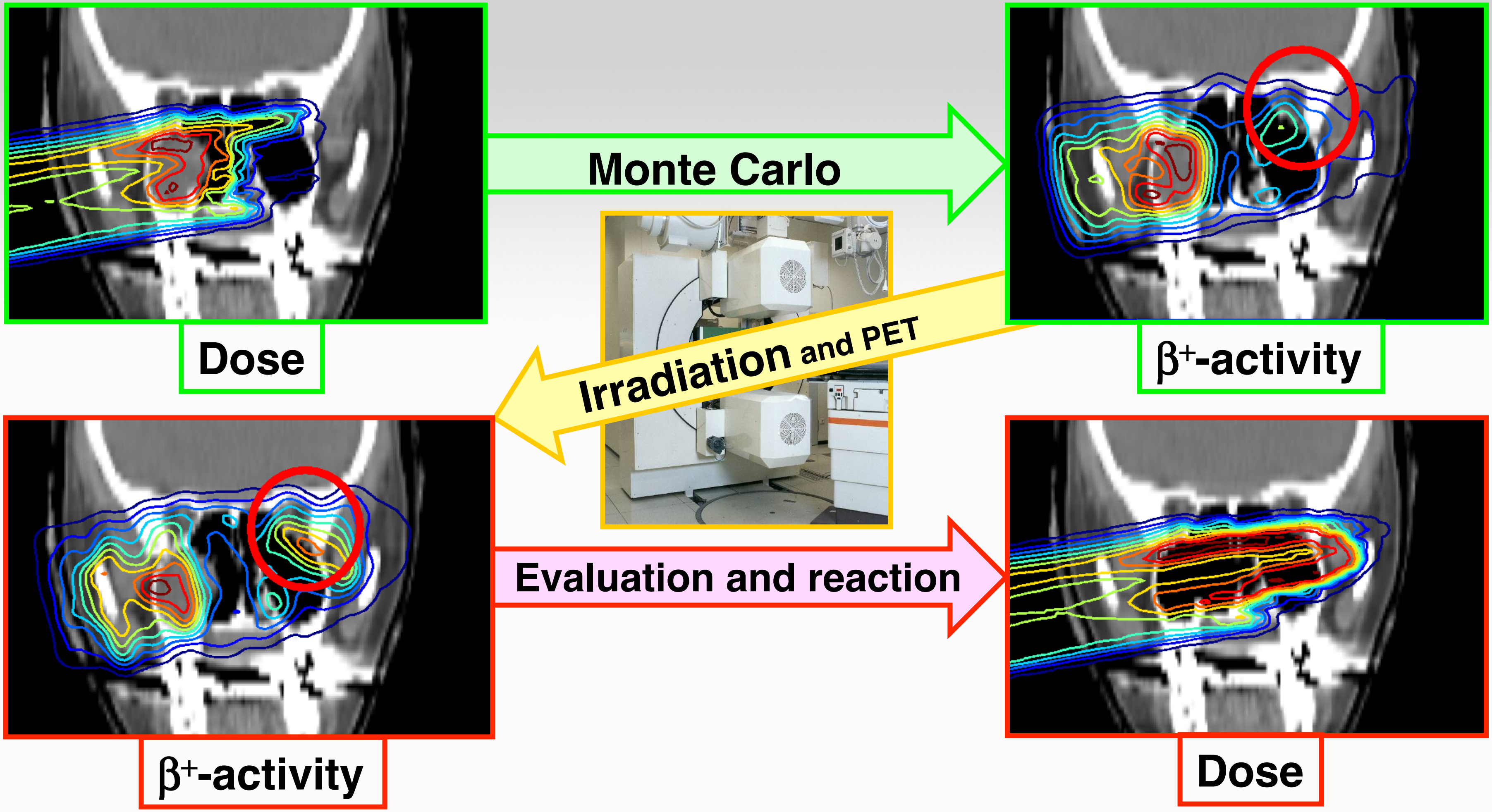


Projectiles & target fragmentation



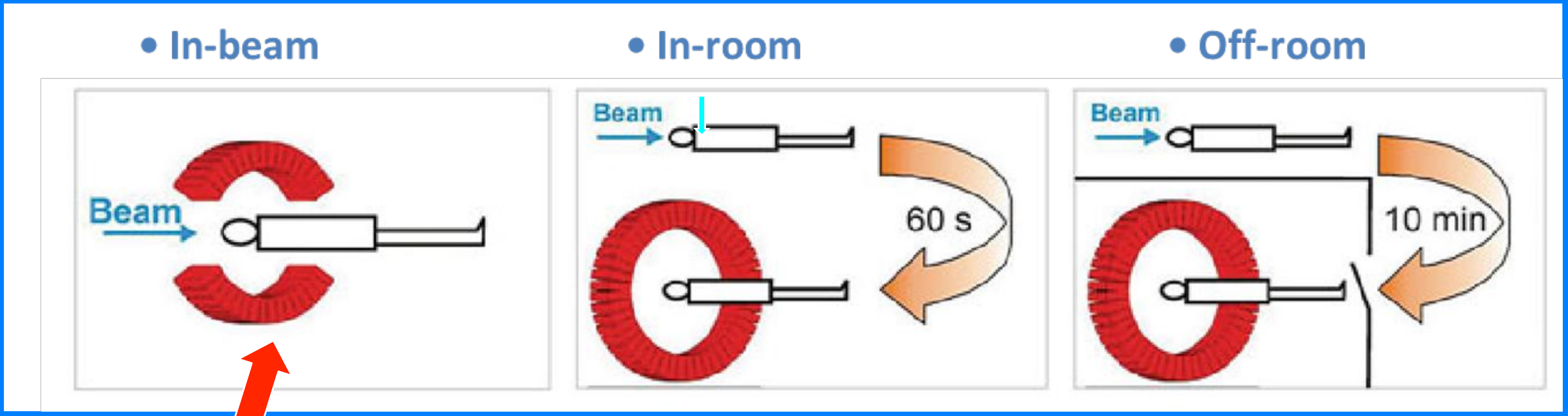
In-Vivo range measurement with PET: workflow and potential

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)

Towards real in-beam measurement

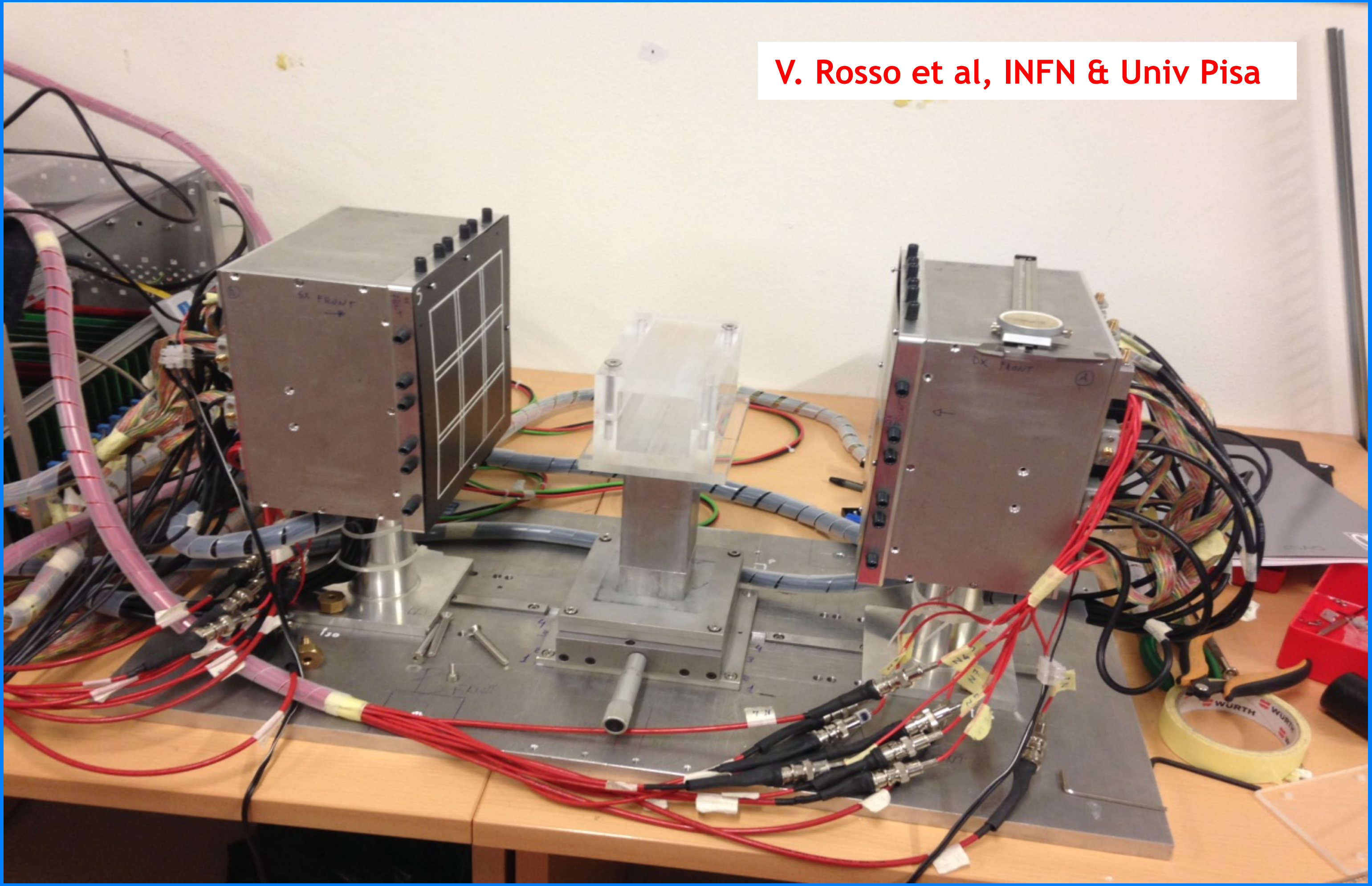


Ambition

practice @Heidelberg

Towards real in-beam measurement

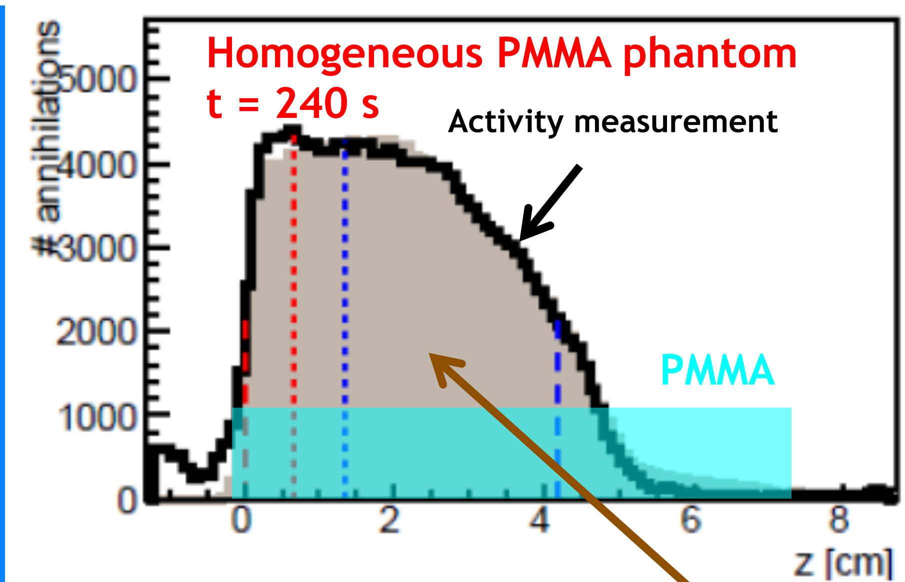
First INFN approaches

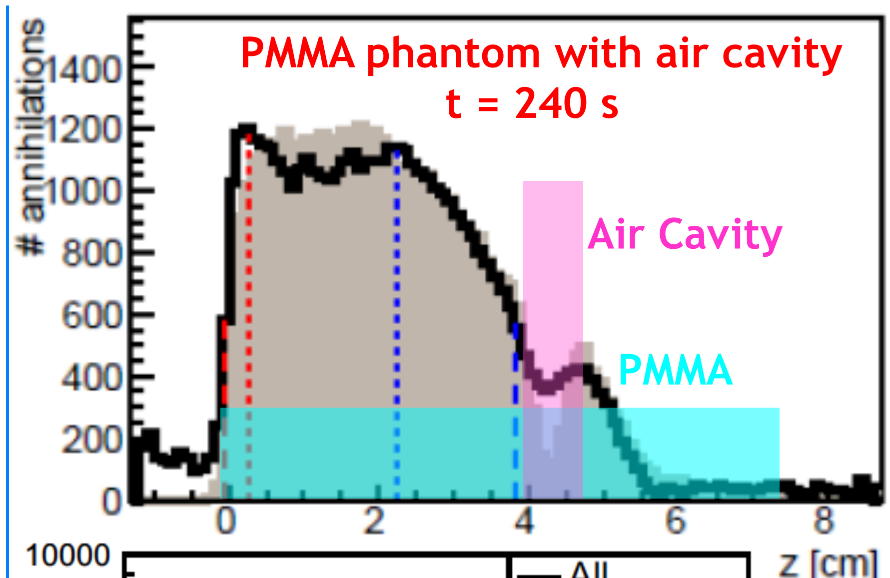


Spotting structures with β^+ activity measurement in-beam (proton beam at CNAO)

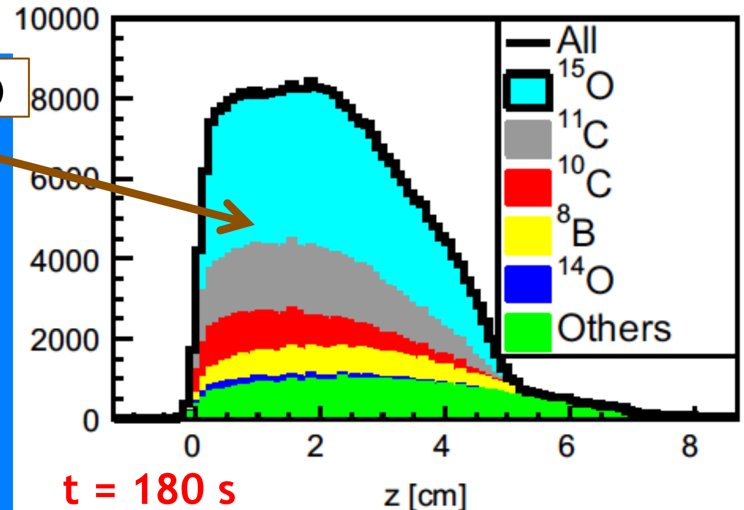
A.C. Kraan, G. Battistoni, N. Belcari, N. Camarlinghi, M. Ciocca, A. Ferrari, S. Ferretti, A. Mairani, S. Molinelli, M. Pullia, P. Sala, G. Sportelli, A. Del Guerra, V. Rosso, NIM A *786, (2015) 120-126*

2 Gy uniform dose in 3x3x3 cm^3
17 energies: 62.3 - 90.8 MeV
146 s



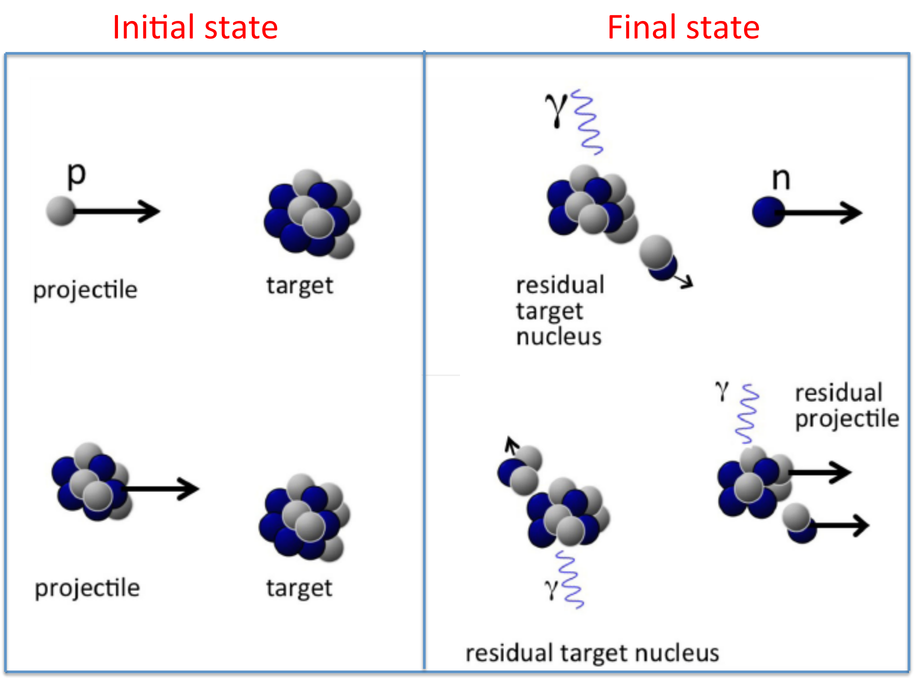


Mont Carlo prediction (FLUKA)



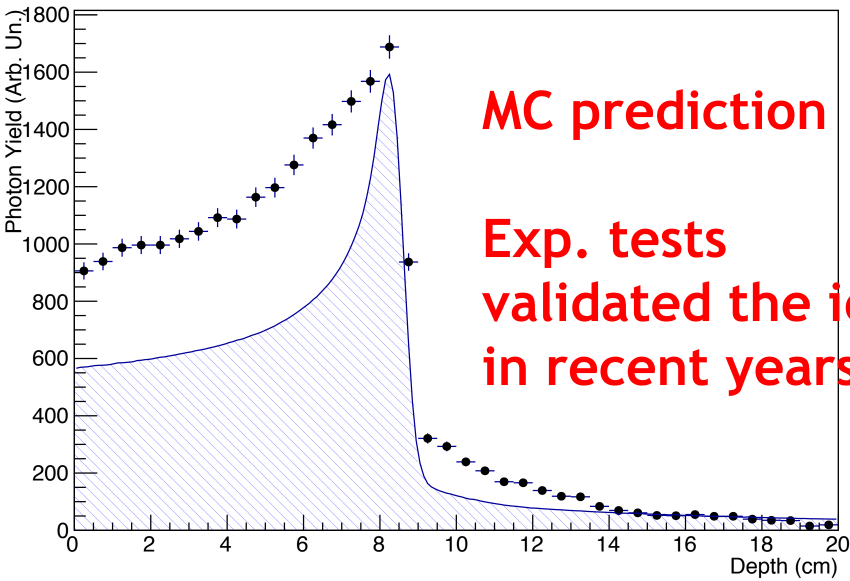
In-beam PET is a base-line solution but:
➡ Hard to go really "online" which is necessary to avoid "metabolic washout"
must sustain high rates (PET + prompt γ + n)

“prompt” de-excitation γ’s



- $4 \cdot 10^9$ /fraction (2 Gy)
- γ-energy: 0… ~8 MeV

not suited for standard gamma-imaging devices of nuclear medicine



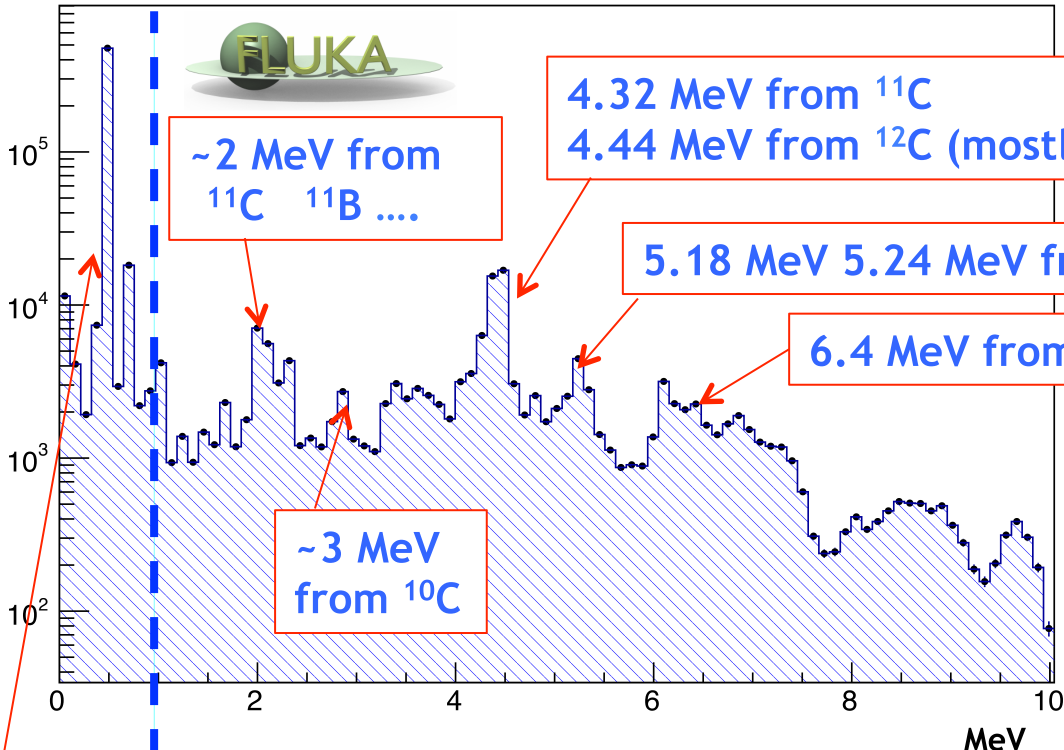
MC prediction

Exp. tests validated the idea in recent years

Huge background from neutrons and γ’s produced by neutrons.
TOF: not easy to implement in clinical practice

MC prediction of de-excitation γ's

MC: γ Energy spectrum produced by p impinging on a PMMA target



~2 MeV from ^{11}C ^{11}B ....

4.32 MeV from ^{11}C
4.44 MeV from ^{12}C (mostly from O fragmentation)

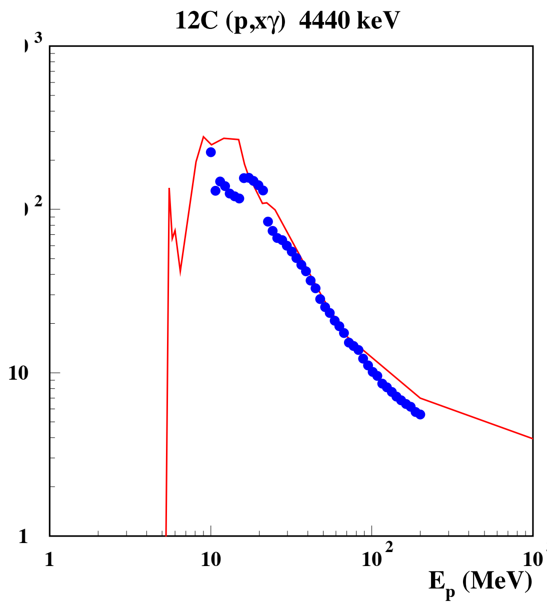
5.18 MeV 5.24 MeV from ^{15}O

6.4 MeV from ^{16}O

~3 MeV from ^{10}C

Broadening: nuclear recoil

0.511 MeV from e^+ annihilation



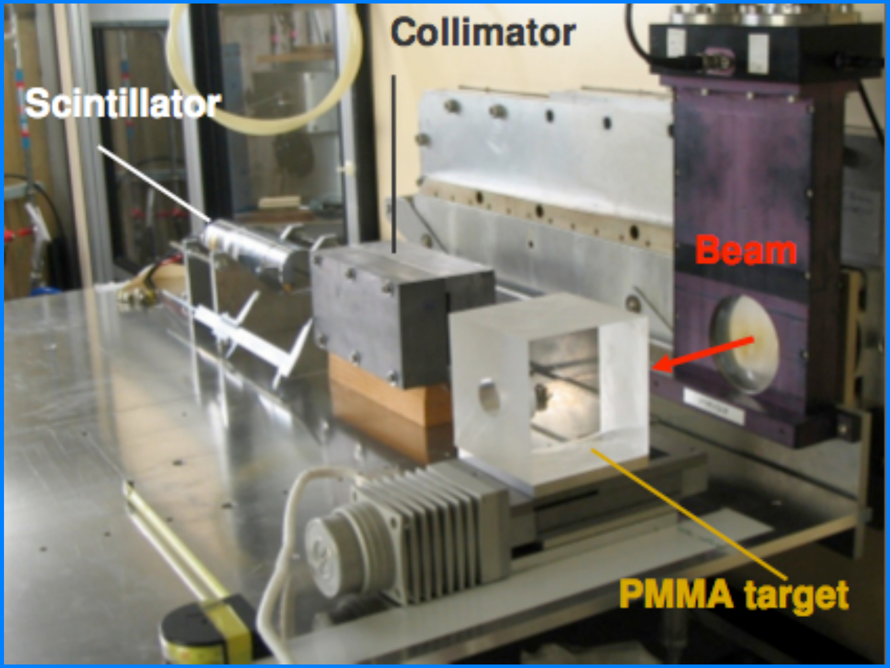
Prompt γs @GANIL

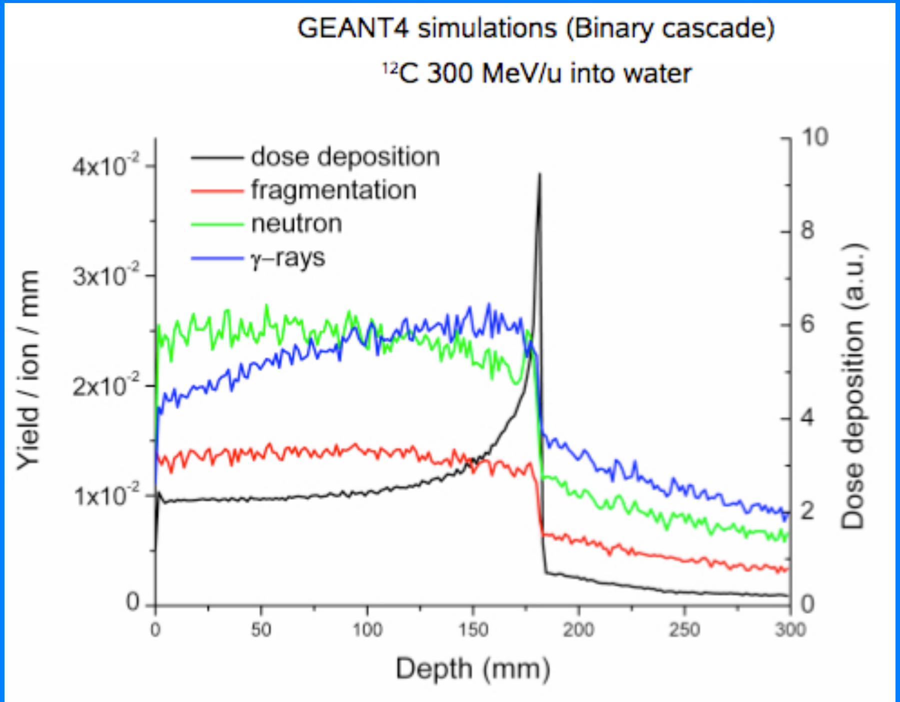
73 AMeV carbon beam

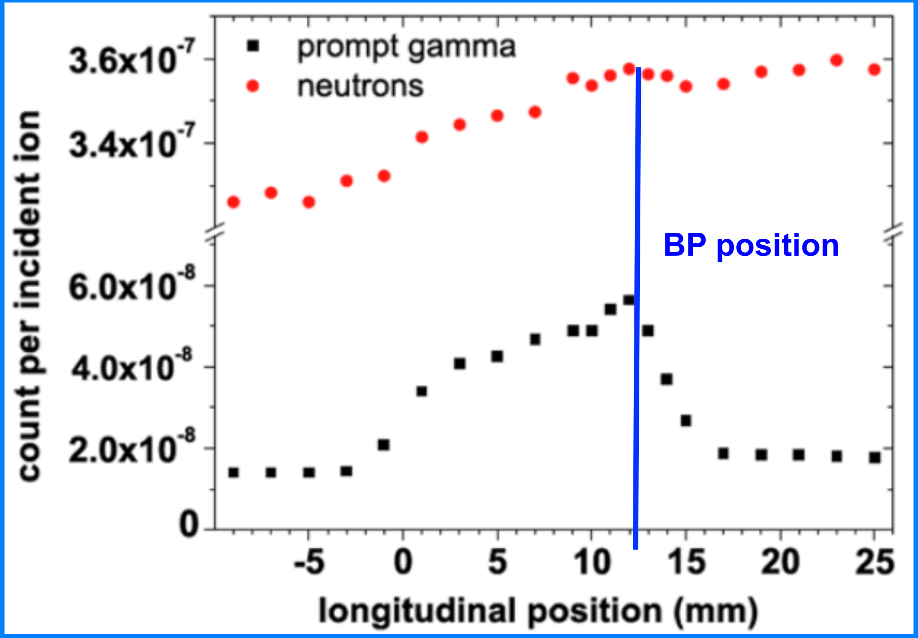
γ peak correlated with BP

MC one order of magnitude off (more..)

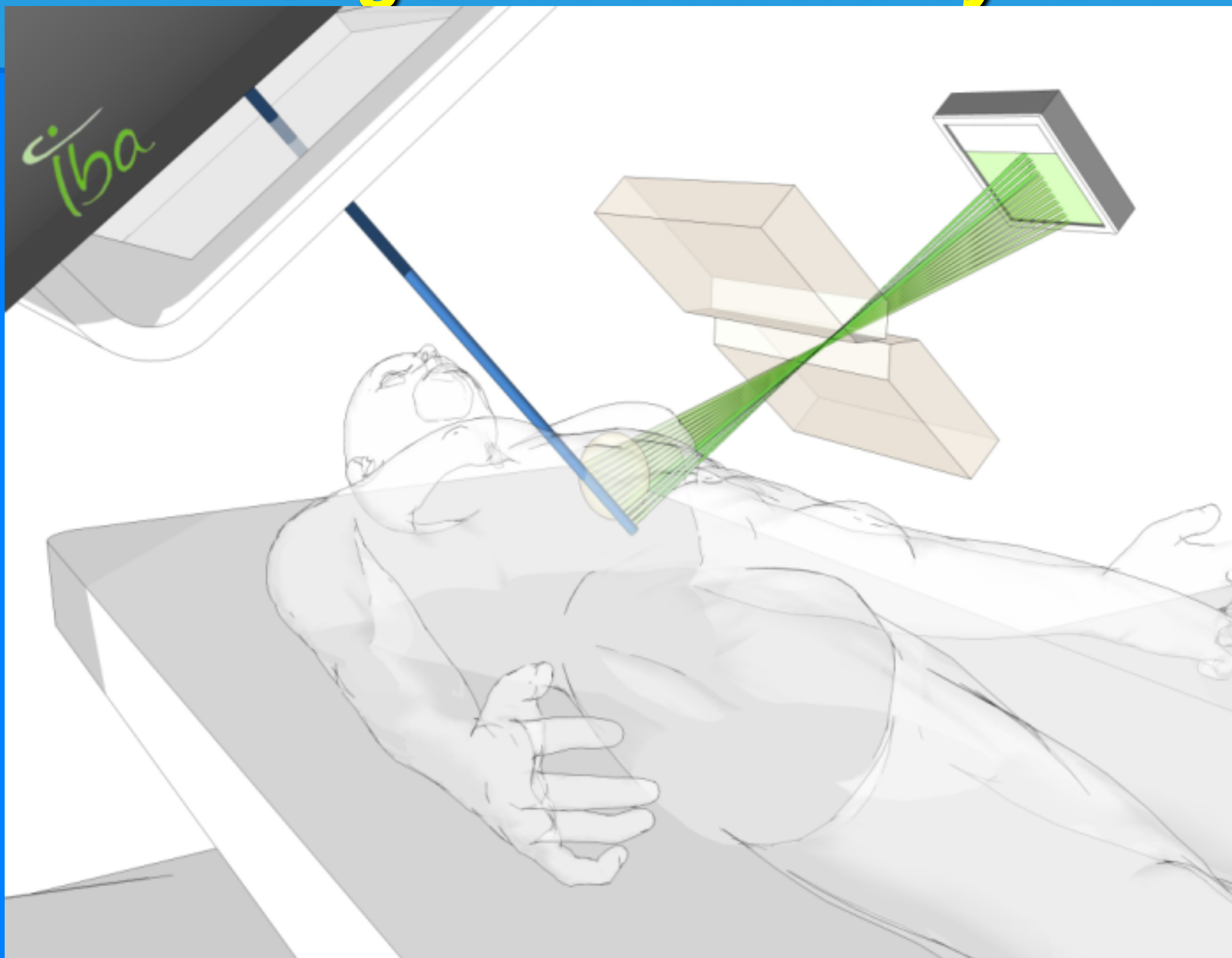
Neutrons background (TOF rejection ?)

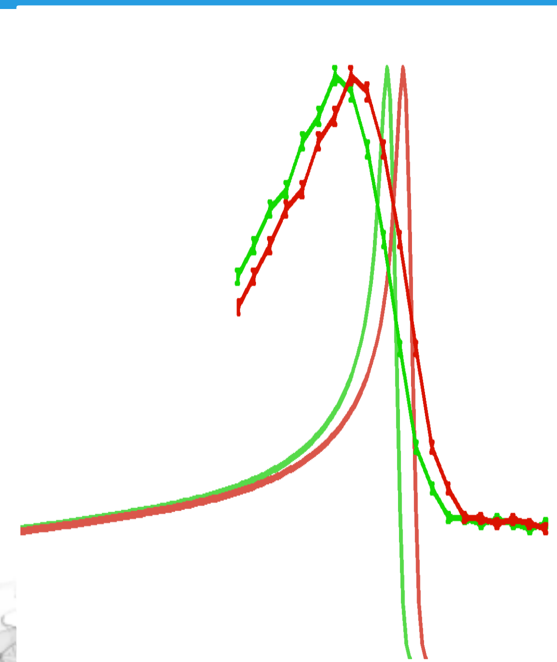






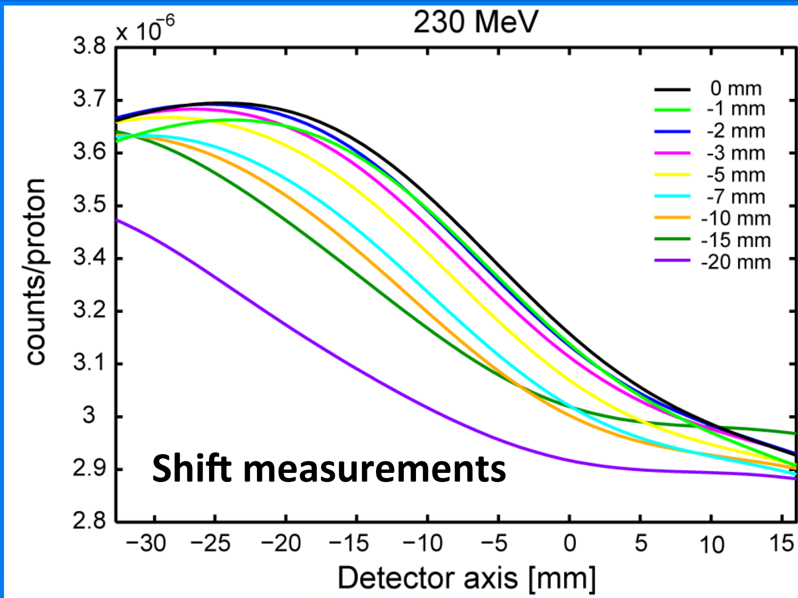
Knife-edge-slit camera by IBA





Collimator, software and project PI

Experimental Validation



Clinical partner

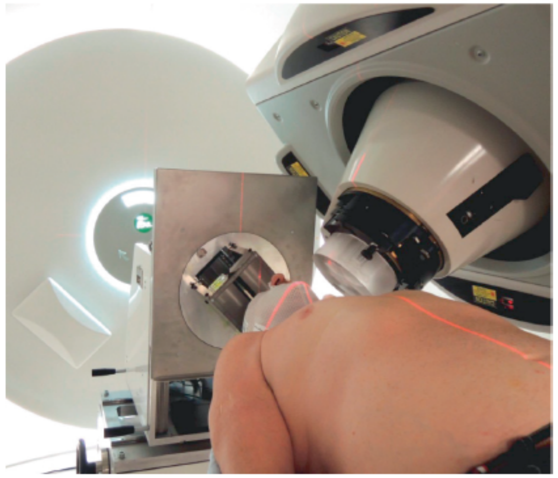


Fig. 1. PGI slit camera trolley (upper row) and its application during patient treatment (lower row).

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Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original article

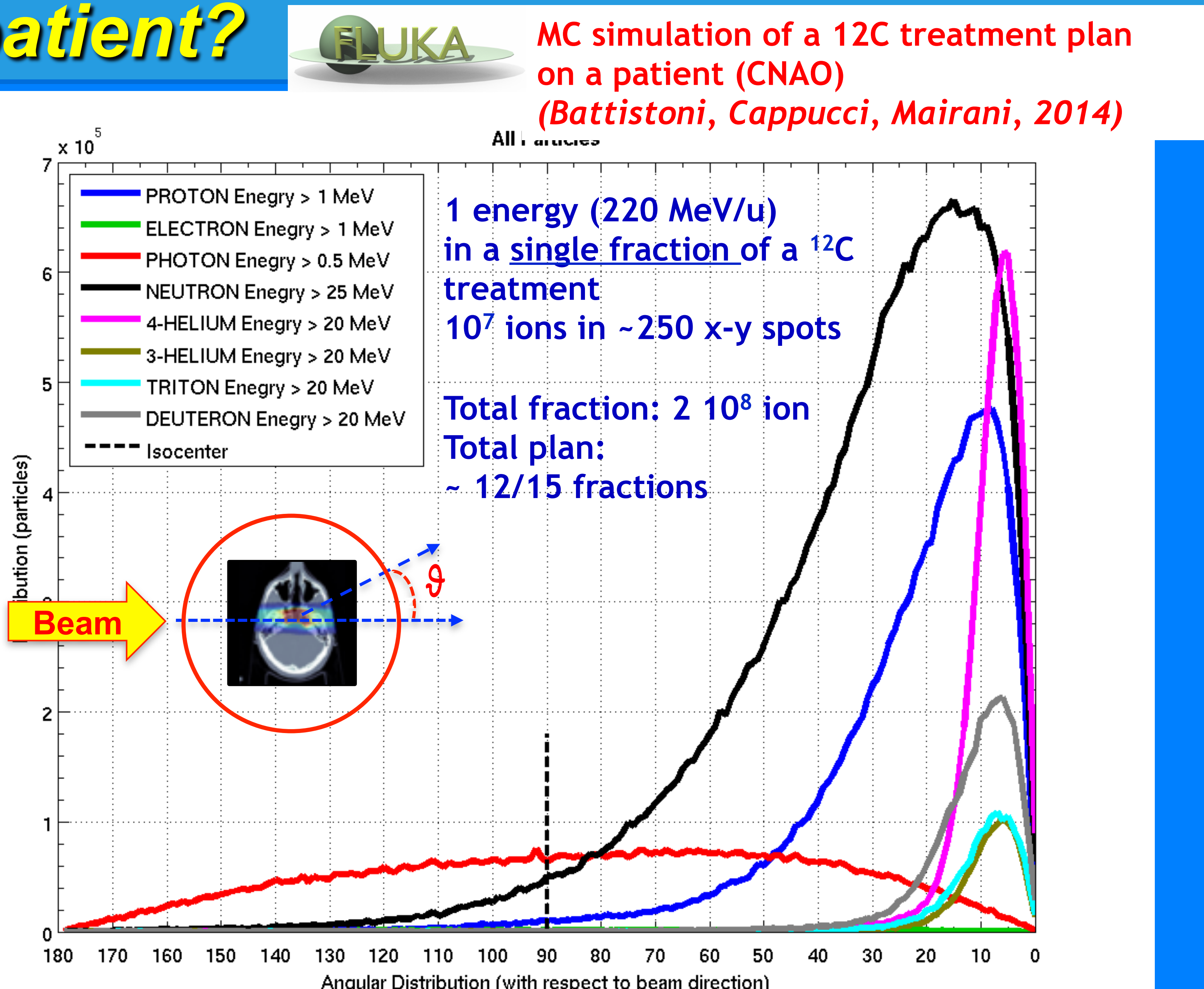
First clinical application of a prompt gamma based *in vivo* proton range verification system

Christian Richter [a,b,c,d,e,*], Guntram Pausch [a,b,c], Steffen Barczyk [a,b], Marlen Priegnitz [c], Isabell Keitz [a], Julia Thiele [b], Julien Smeets [f], Francois Vander Stappen [f], Luca Bombelli [g], Carlo Fiorini [h], Lucian Hotoiu [f], Irene Perali [h], Damien Prieels [f], Wolfgang Enghardt [a,b,c,d,e], Michael Baumann [a,b,c,d,e]

[a] *OncoRay – National Center for Radiation Research in Oncology, Faculty of Medicine and University Hospital Carl Gustav Carus, Technische Universität Dresden, Helmholtz-Zentrum Dresden – Rossendorf;* [b] *Department of Radiation Oncology, Faculty of Medicine and University Hospital Carl Gustav Carus, Technische Universität Dresden;* [c] *Helmholtz-Zentrum Dresden – Rossendorf;* [d] *German Cancer Research Center (DKFZ), Heidelberg;* [e] *German Cancer Consortium (DKTK), Dresden, Germany;* [f] *Ion Beam Applications SA, Louvain-la-Neuve, Belgium;* [g] *XGLab S.R.L., Milano; and* [h] *Politecnico di Milano, Dipartimento di Elettronica, Informazione e Bioingegneria, Italy*

How many particles/fragments out of a patient?

MC simulation of a 12C treatment plan on a patient (CNAO)
(Battistoni, Cappucci, Mairani, 2014)

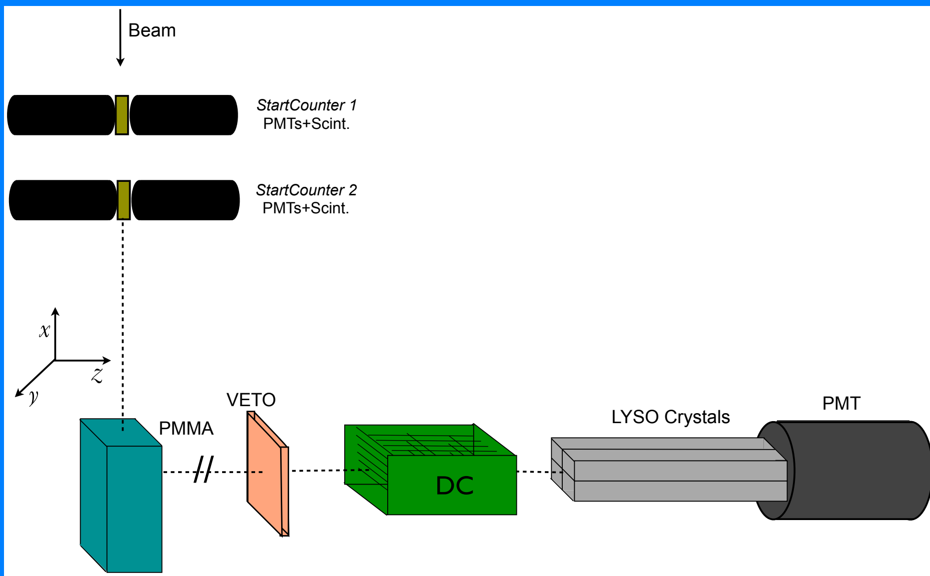


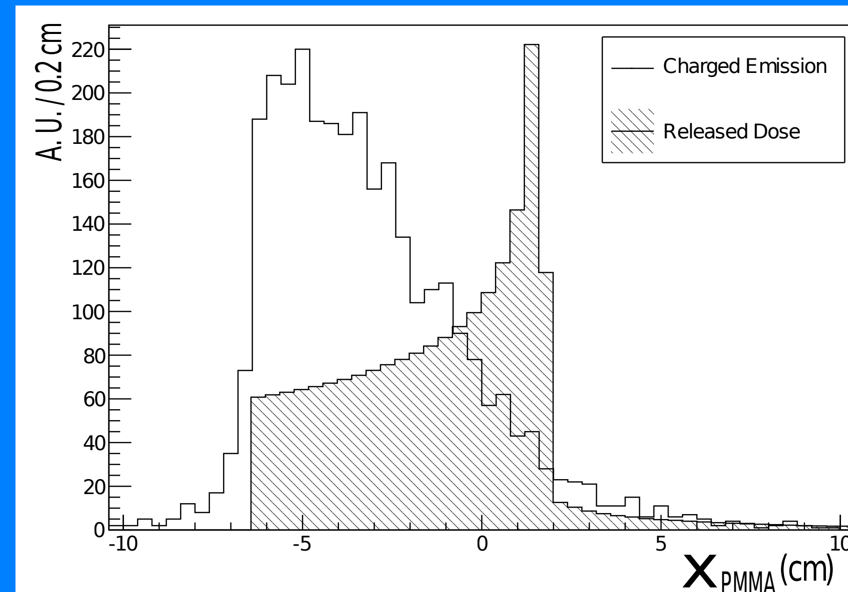
To be validated by experiment

First Exp. Test at large angle with ^{12}C ions

L. Piersanti et al. 2014 *Phys. Med. Biol.* 59 1857

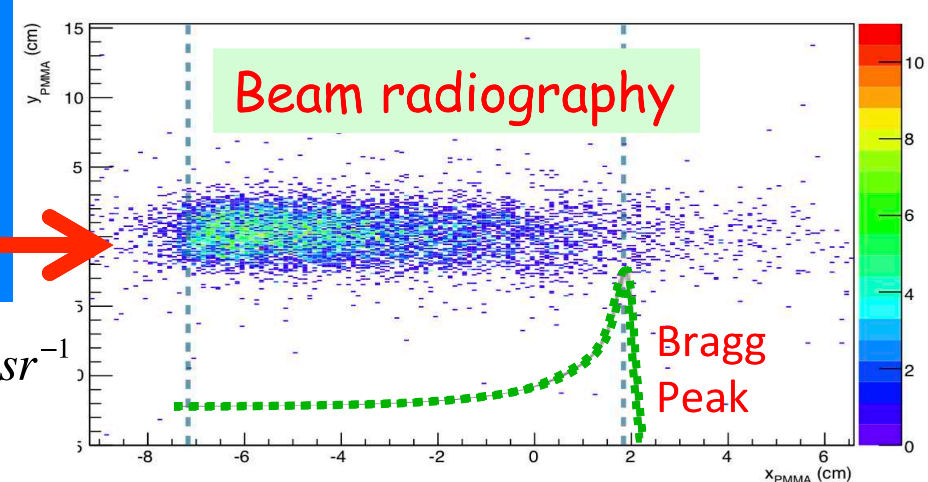
Charged secondary produced at 90^0 by ^{12}C 220 MeV/u at GSI





Beam

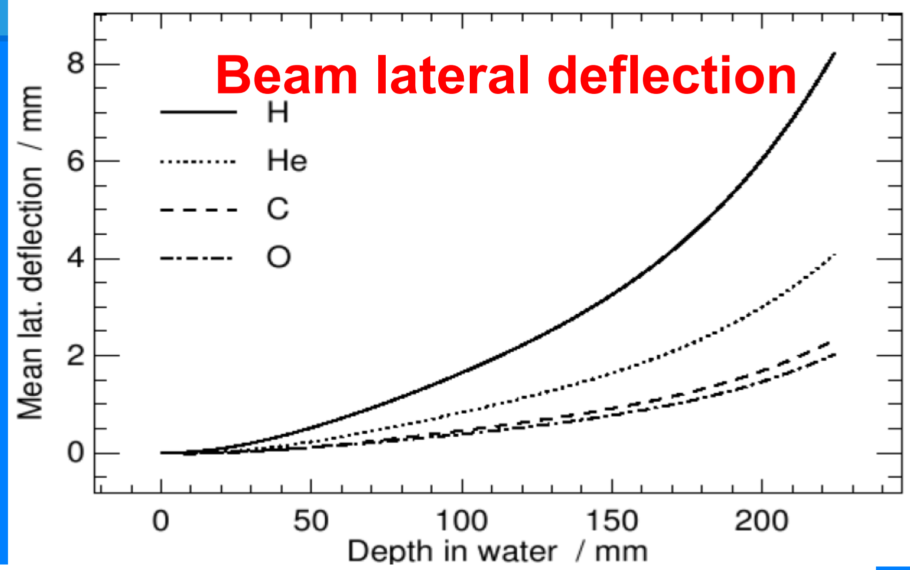
Beam



$$\frac{dN_{ch}}{N_{Prim}\,d\Omega}(60^o) \sim (13.40 \pm 0.08\,stat \pm 0.70\,sys)\cdot 10^{-3}\ sr^{-1}$$

$$\frac{dN_{ch}}{N_{Prim}\,d\Omega}(90^o) \sim (2.74 \pm 0.02\,stat \pm 0.17\,sys)\cdot 10^{-3}\ sr^{-1}$$

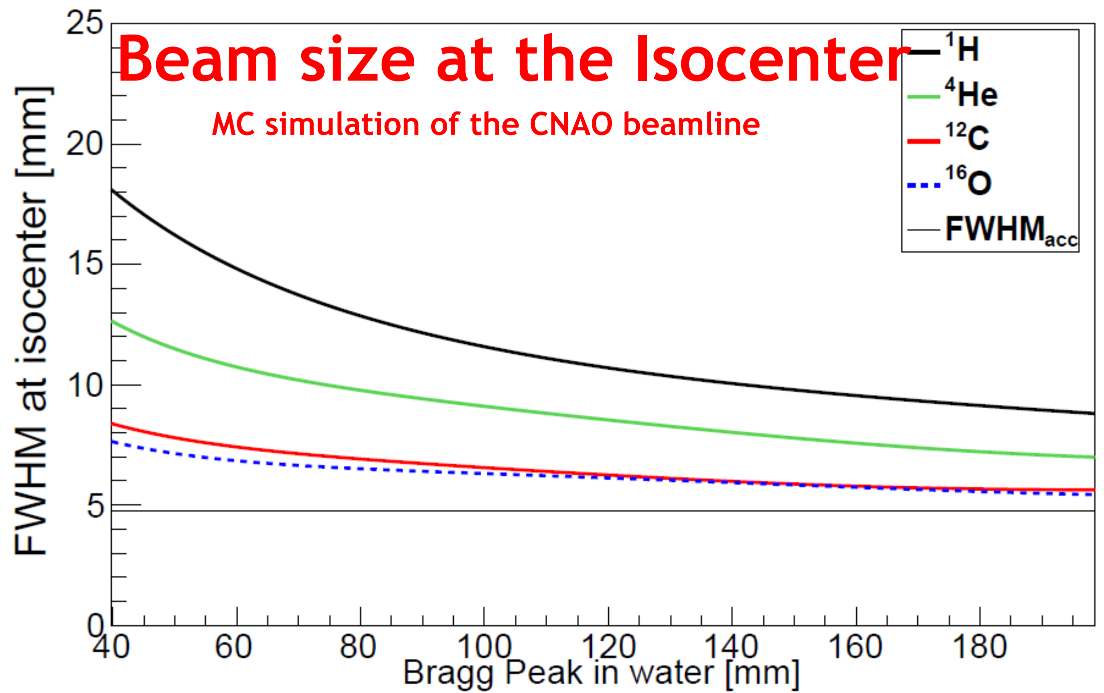
New ion beams proposed for therapy



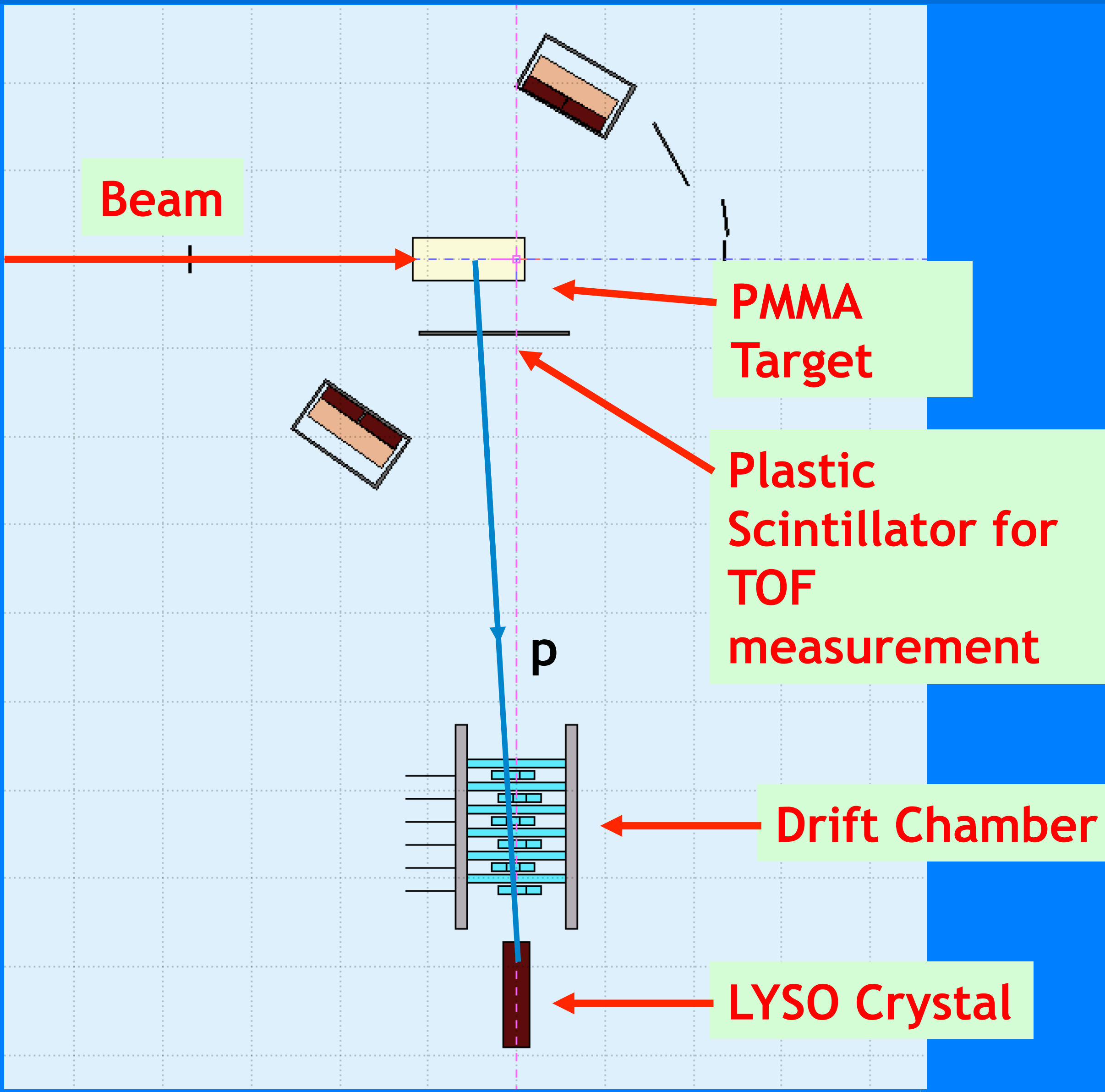
^{4}He (50-300 MeV/u):
negligible fragmentation, higher RBE than protons, but more limited lateral scattering

^{16}O (100-500 MeV/u):
to be used in particular case where high-LET is needed hypoxical tumors

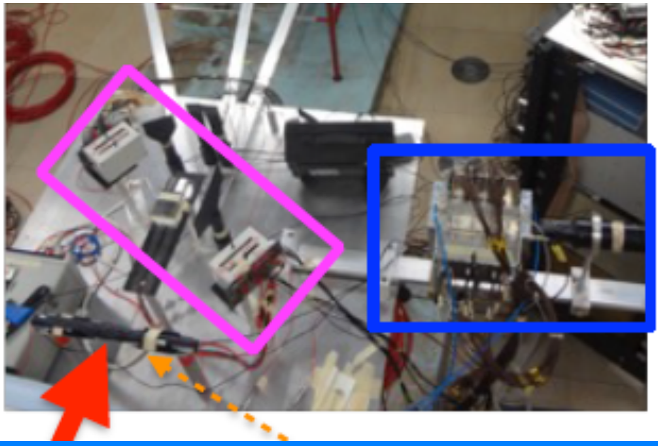
For a discussion of New Ions in therapy: F. Tommasino, E. Scifoni, and M. Durante, Int. J. Particle Ther. 2015 2:3, 428-438



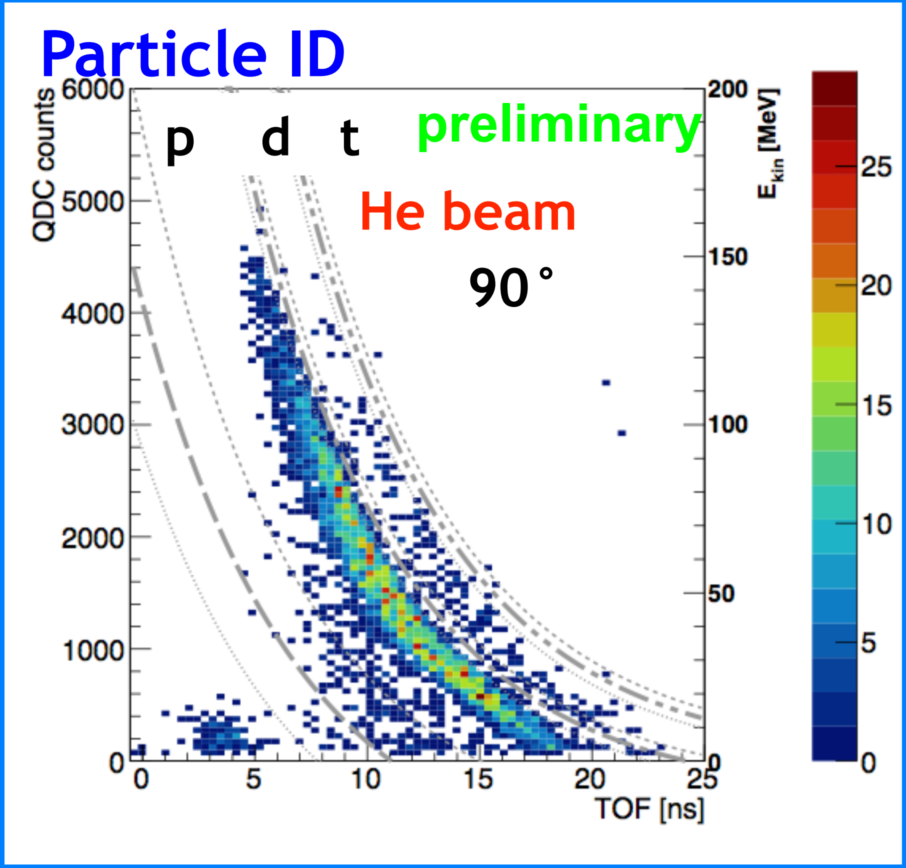
New test at Heidelberg with He, C and O beams: Prompt γ and Charged particles Detection

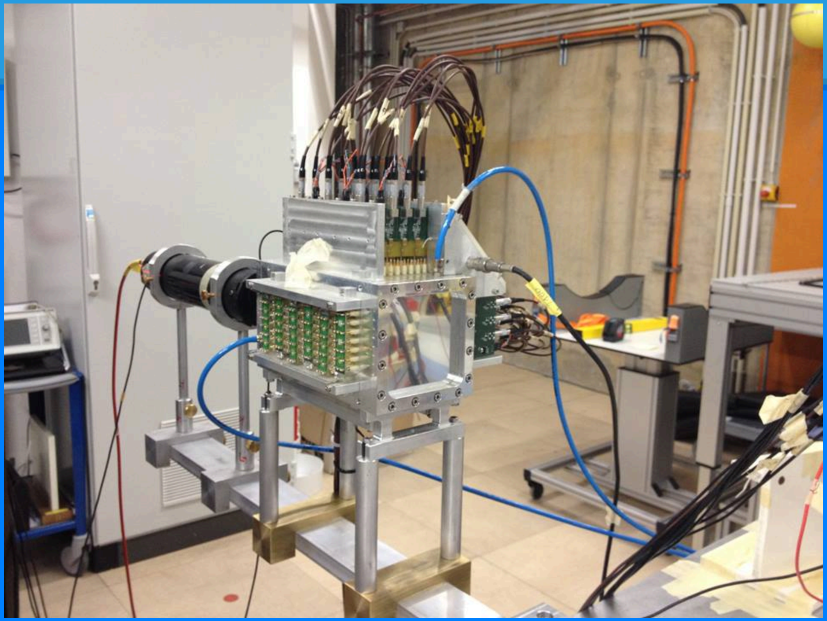


G. Battistoni, F. Bellini, F. Collamati, E. De Lucia, M. Durante, R.Faccini, M. Marafini, I. Mattei, S. Morganti, R. Paramatti, V. Patera, D. Pinci, A. Rucinski, A. Russomando, A. Sarti, A. Sciubba, M. Senzacqua, E. Solfaroli Camillocci, M. Toppi, G. Traini, C. Voena

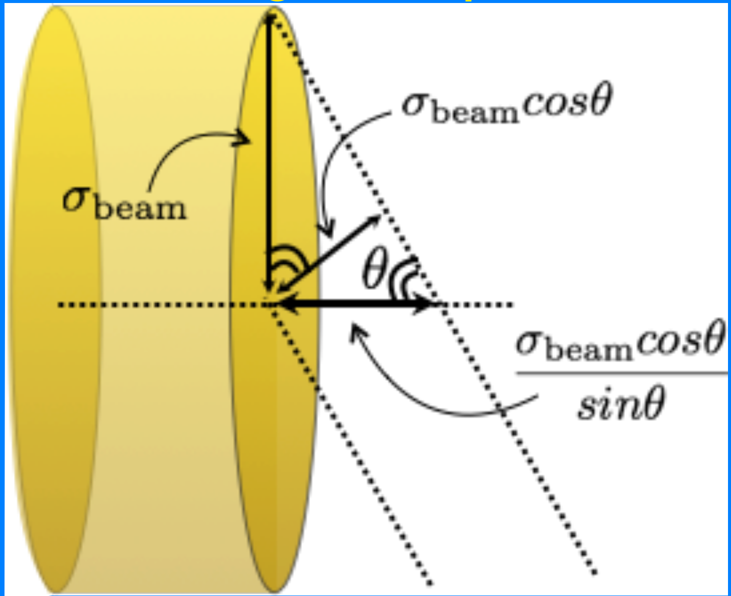


Charged particle production at large angle



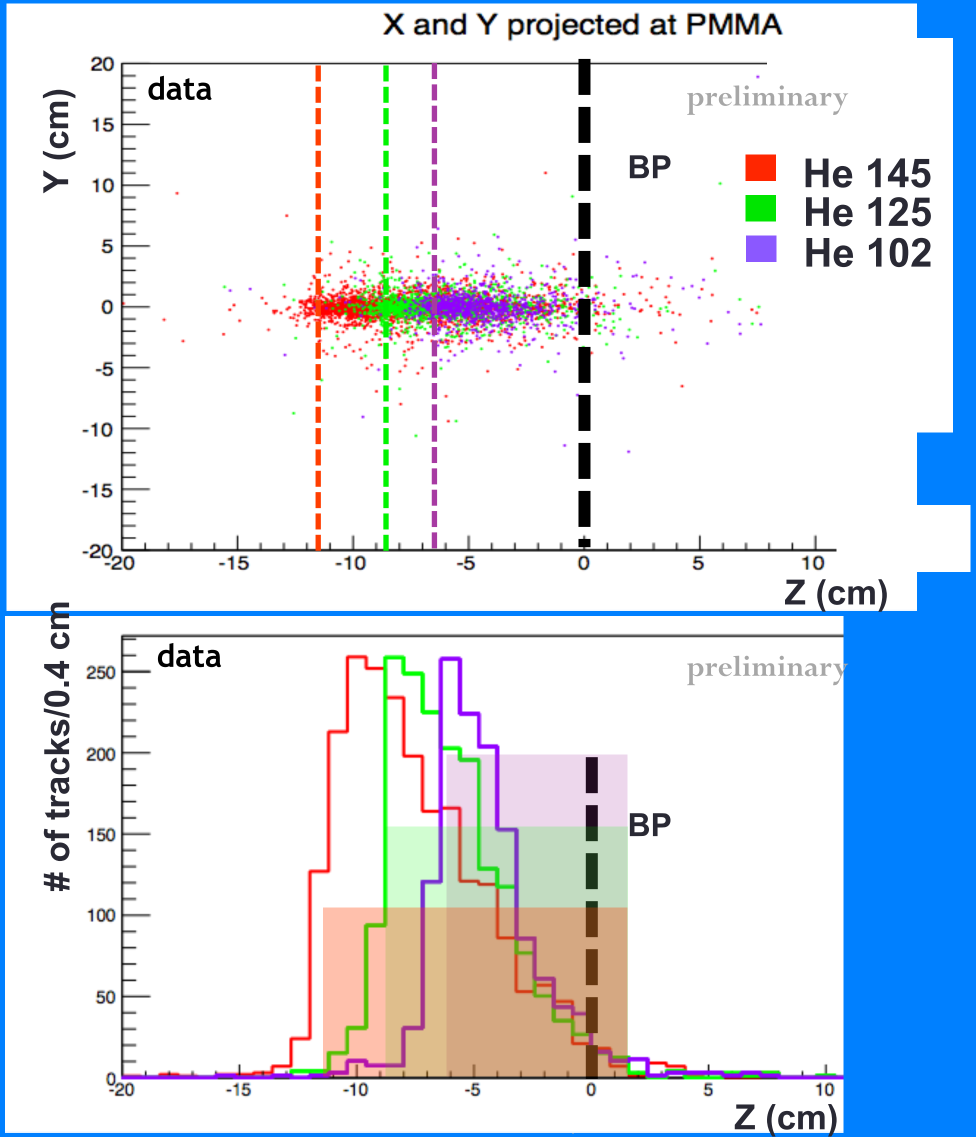


Detection angle and space resolution

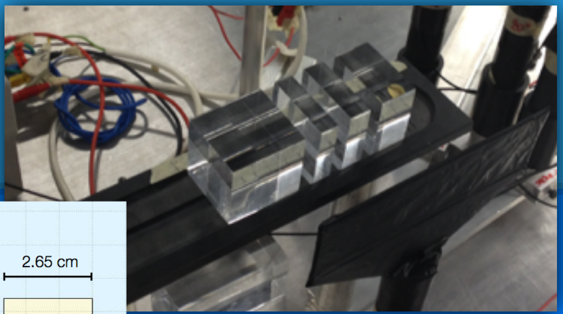


Typically, at HIT or CNAO, a ^{12}C Beam at 200 MeV/u has a FWHM ~ 0.8 cm at the isocenter

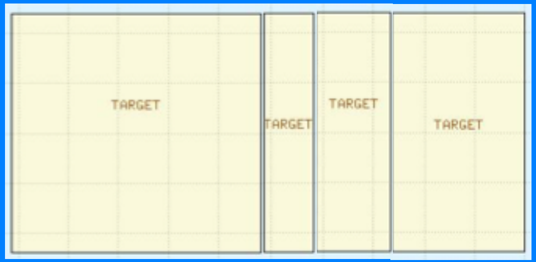
Charged Particle Production and BP monitoring



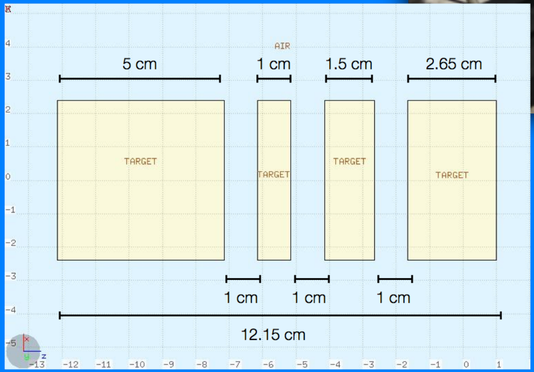
detecting inhomogeneities with charged particles



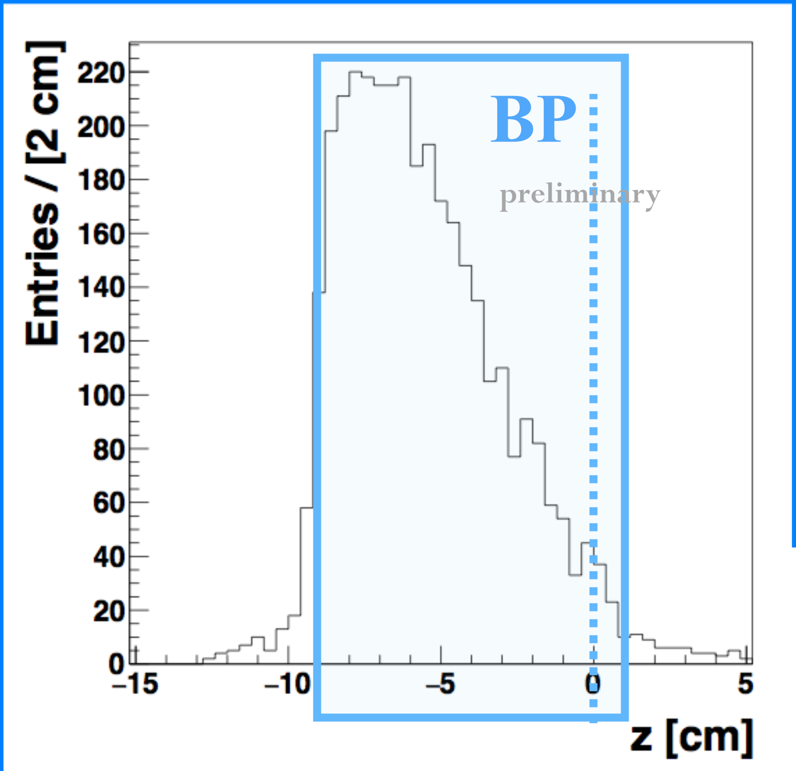
Reference Target: no AIR spaces

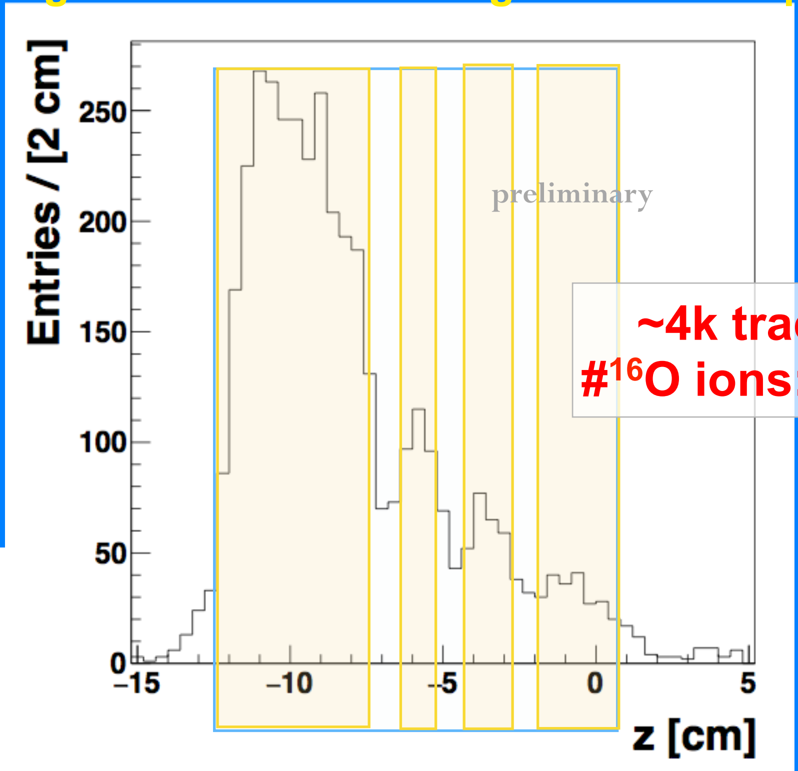


10.15 cm



Segmented 12.15 cm Target: with AIR spaces



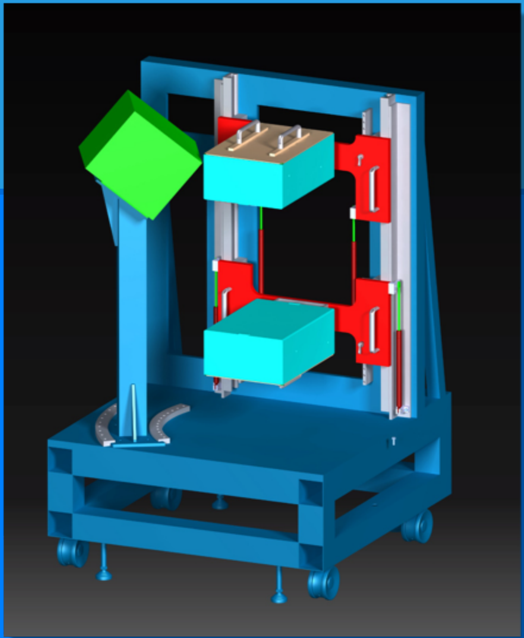


~4k tracks;
#^{16}O ions: 8 10^8

The InSide Project @ CNAO

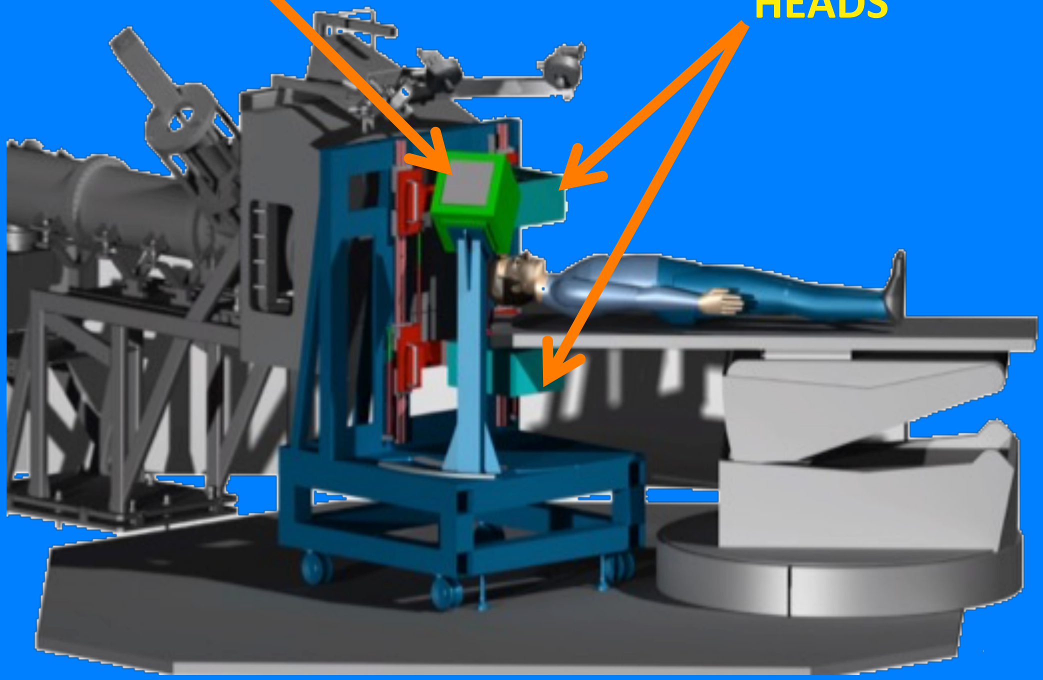
INnovative Solutions for In-beam DosimEtry in Hadrontherapy

Funds: PRIN + Centro Fermi + INFN (RM1-TO-MI-PI)



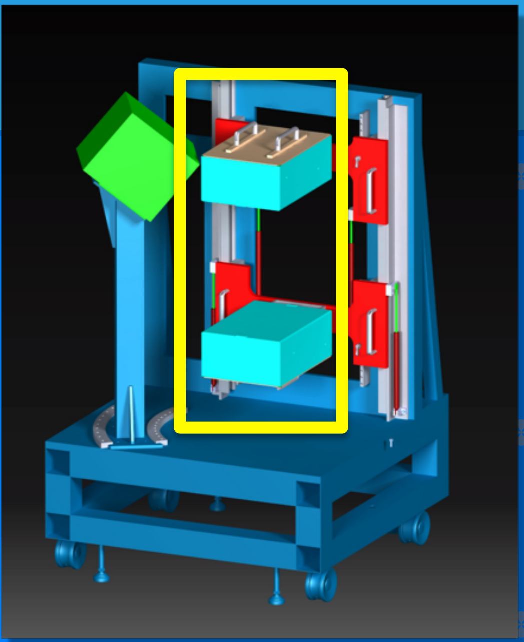
proton emission
Tracker + Calorimeter = DOSE PROFILER

β^+ activity distribution IN-BEAM PET HEADS

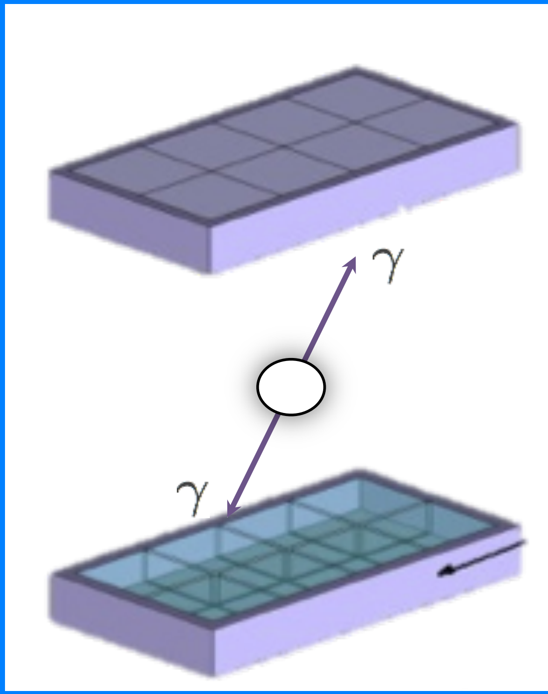


- Dual signal operation
- integrated in treatment room
- Provide in-beam feedback on beam range
- Challenge: fusion of charged and PET information

The INSIDE PET System



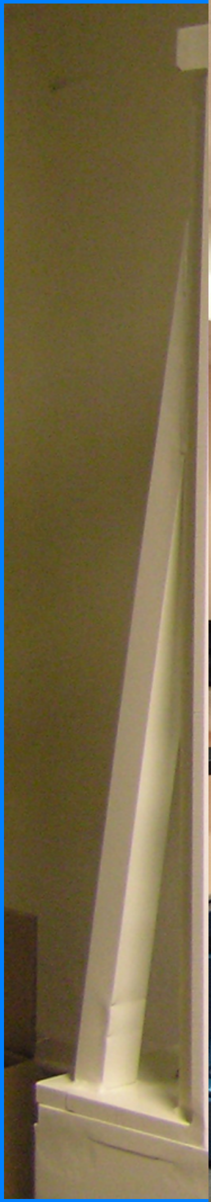
- Detectors to measure the 511 keV back-to-back photons in order to reconstruct the β^+ activity map.
- Two planar panels: 10 cm x 20 cm wide => 2 x 4 detection modules;
- 1-2 mm resolution expected along the beam path

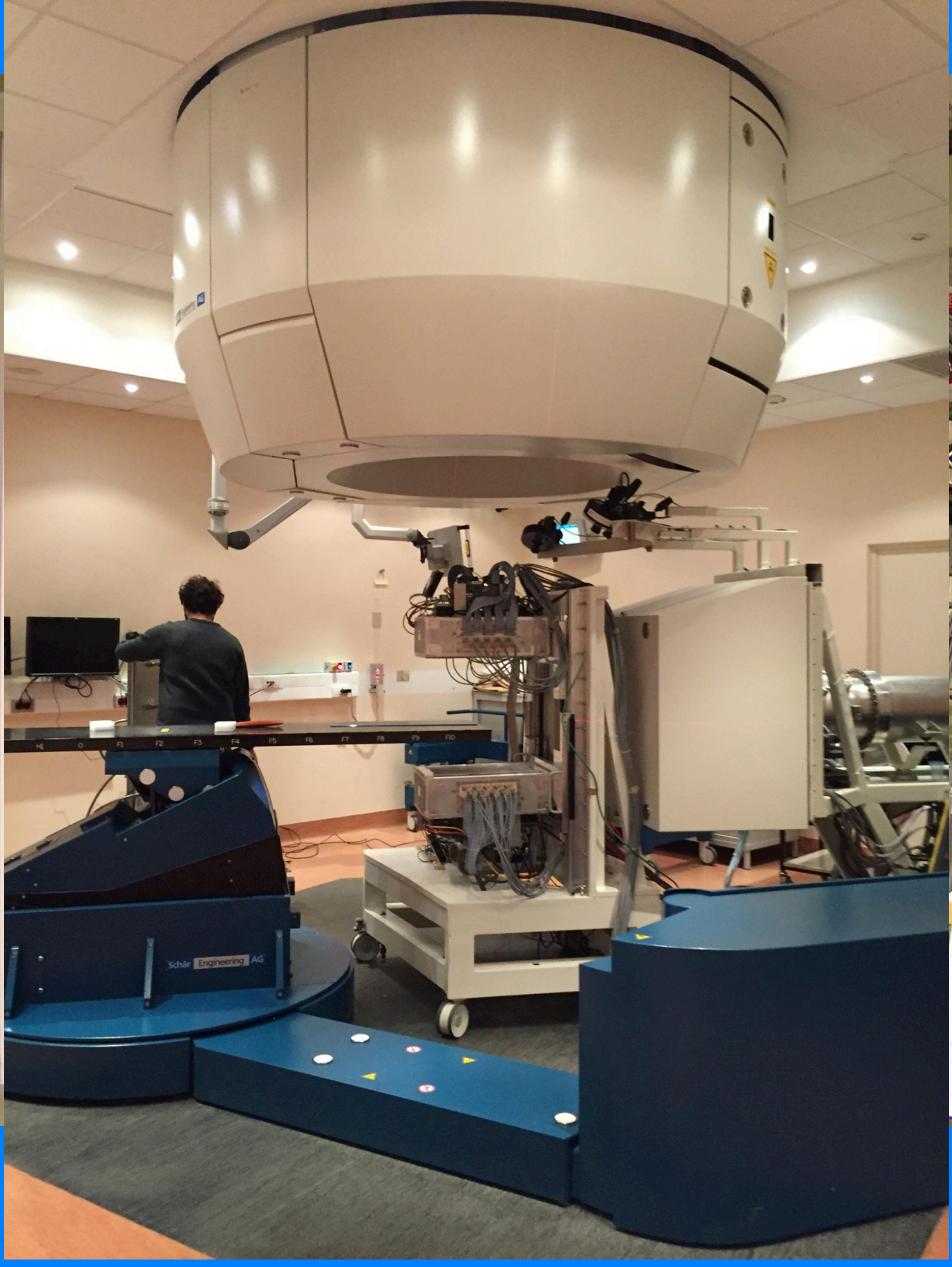


Each module = pixelated LSO matrix 16 x 16 pixels, 3 mm x 3 mm crystals (pitch 3.1mm)

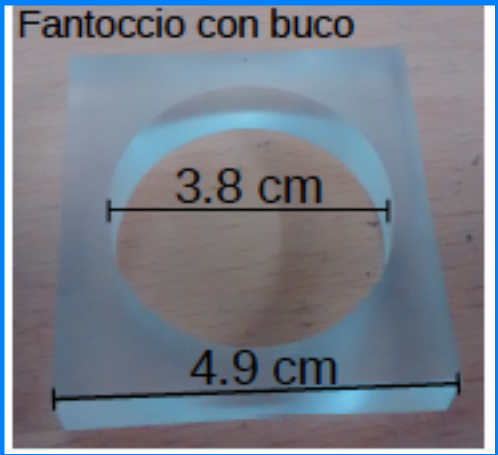
LYSO matrix readout: array of SiPM (16x16 pixels) coupled one-to-one.

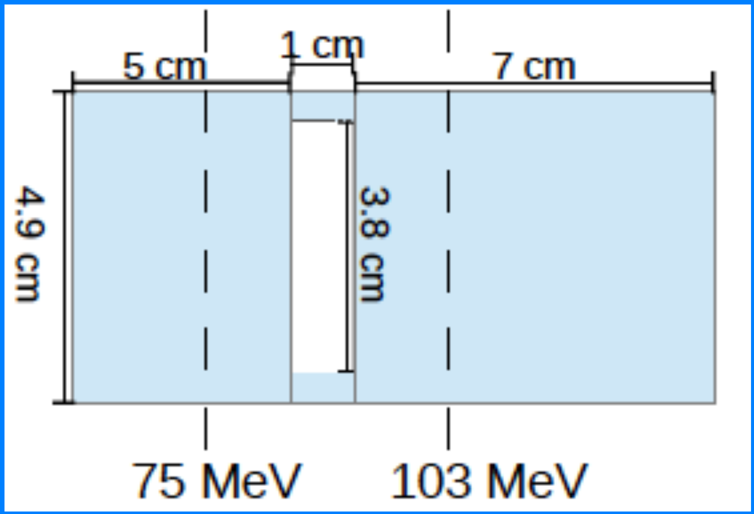
Custom TOF-PET asic (Courtesy of M. Rolo, LIP and ENDOTOFPET EU project)

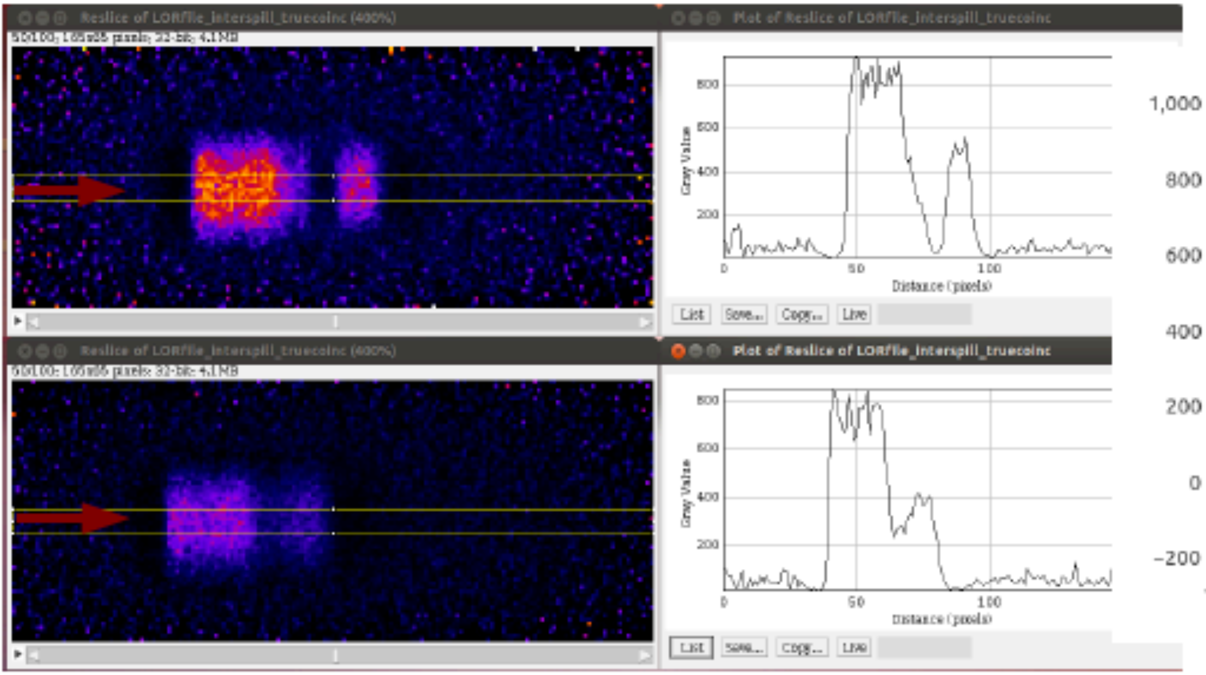


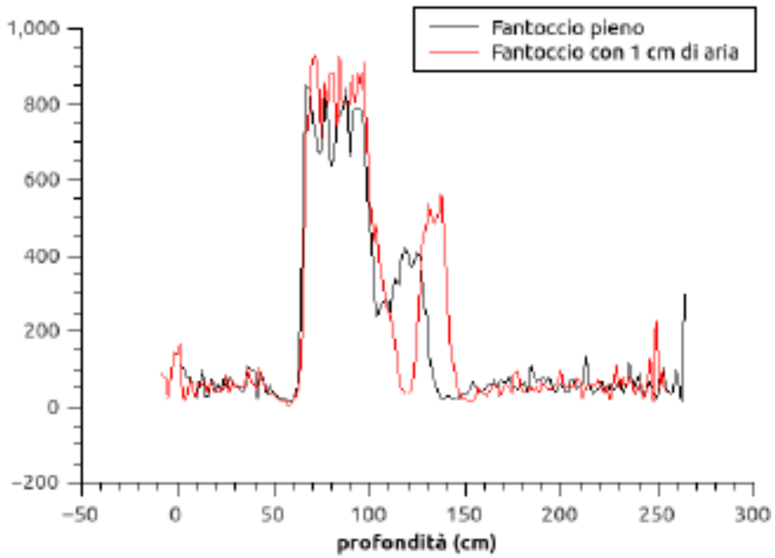

Schär Engineering AG

Proton beam on a 3 cm x 3 cm surface
Two "slices" at different energies: 75 MeV and 103 MeV
2 cases: - PMMA phantom
- PMMA phantom with 1 cm air gap

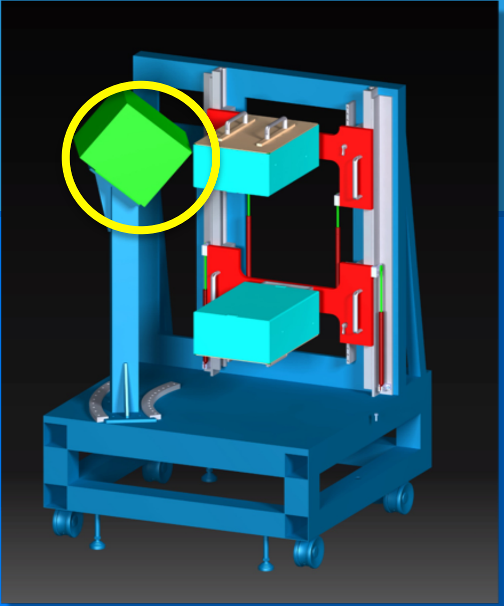


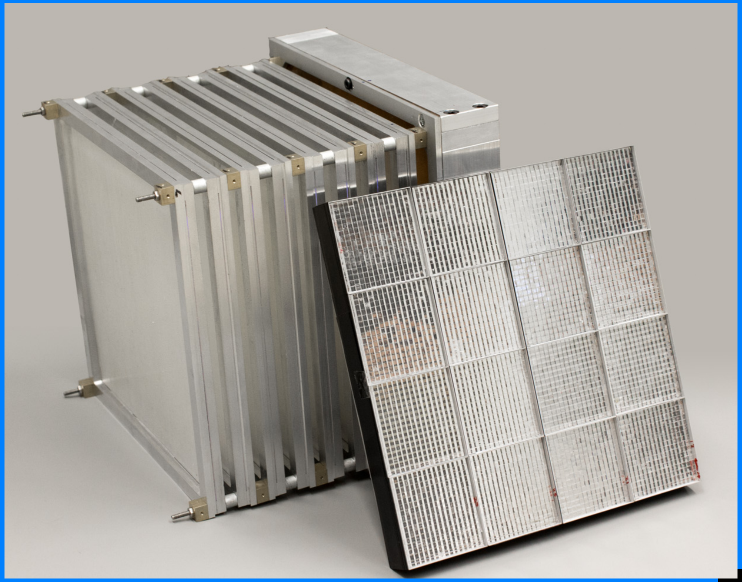






The INSIDE charge Profiler



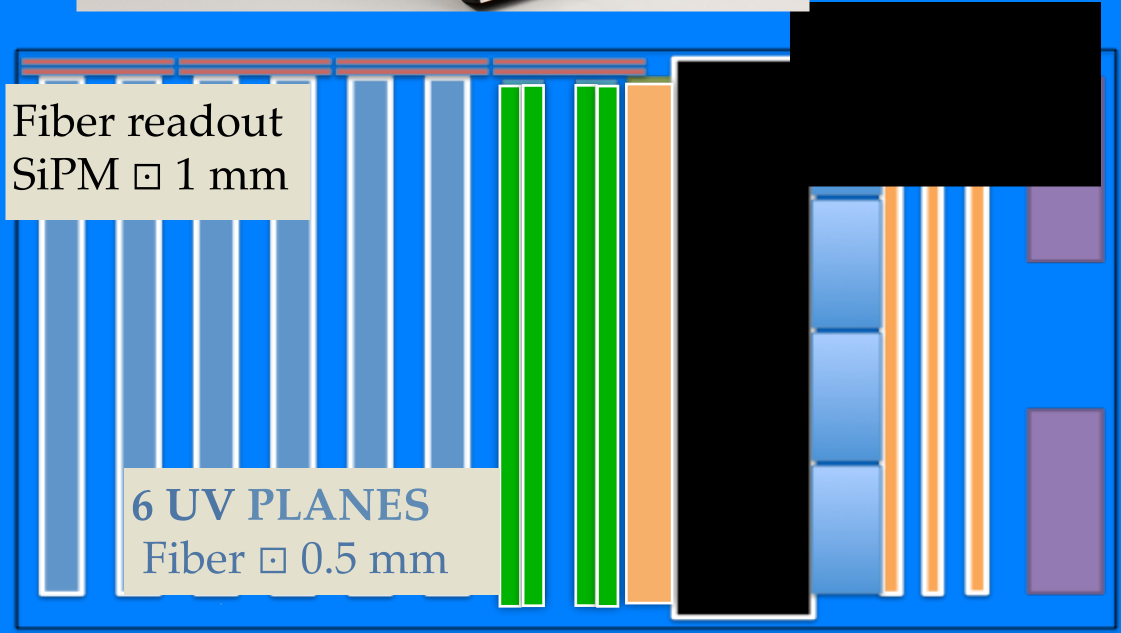


Tracker: back-tracking of secondary protons to the beam line

Calo: select higher energy protons to minimize MS in the patient.

Reconstruction: deconvolution of absorption inside the patient from the emission shape

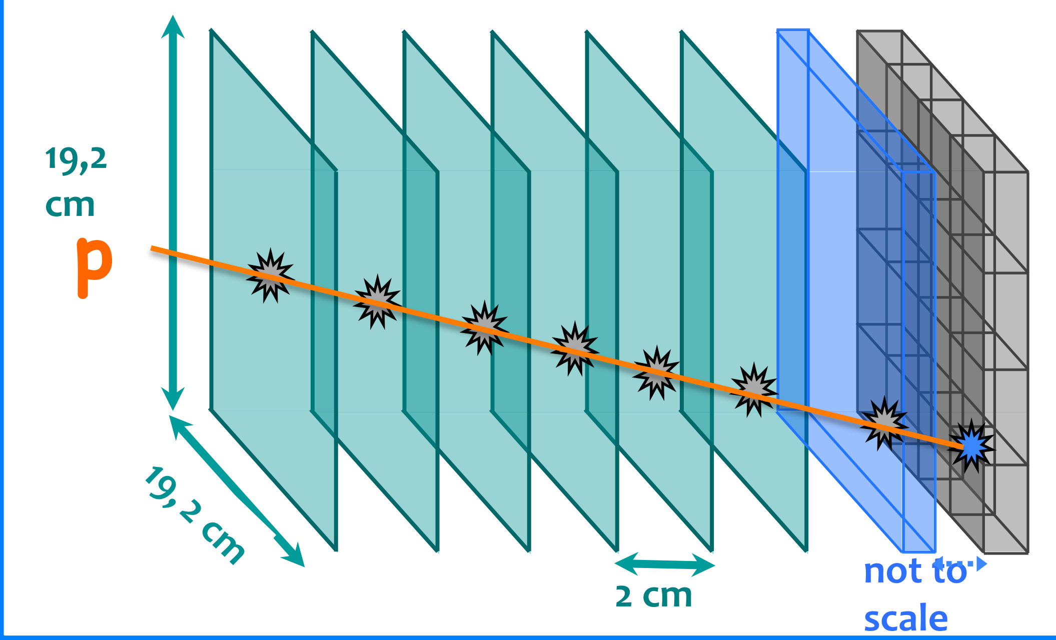
Calibration: BP position vs Emission shape parameters

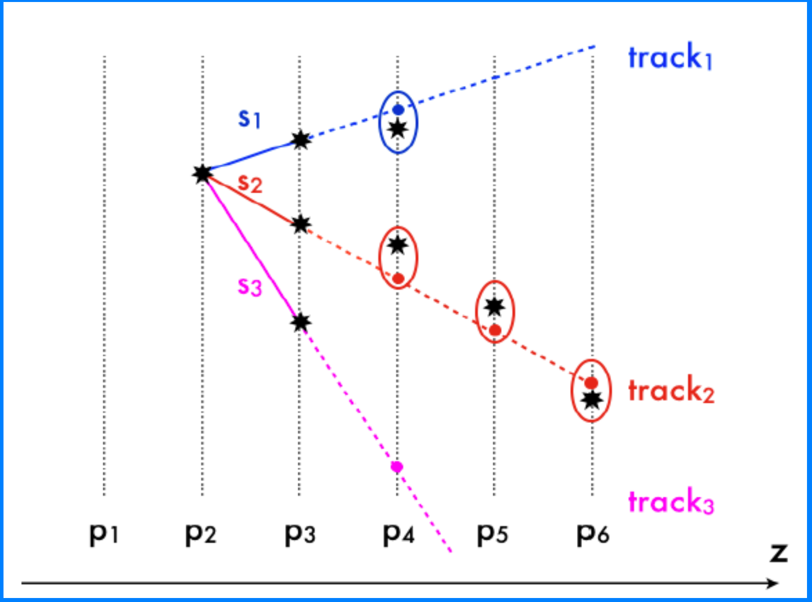


INSIDE Dose Profiler

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 calorimeter





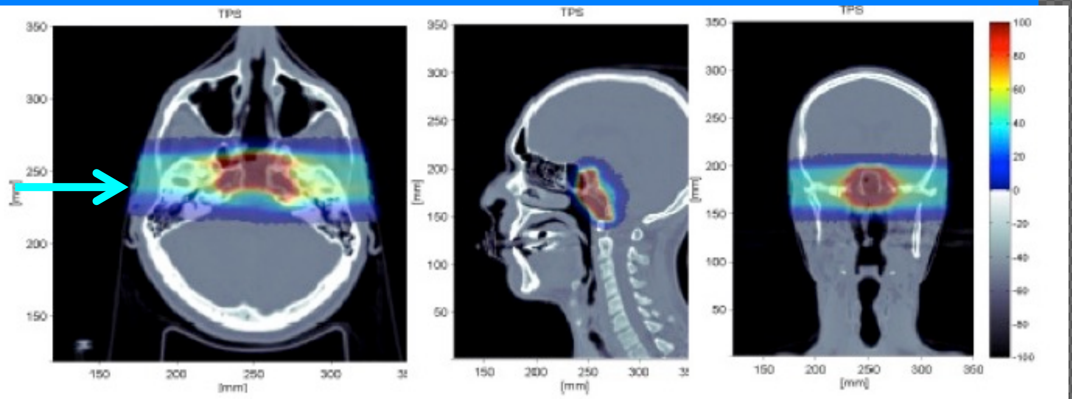
Particles are reconstructed with a track finding algorithm that starts from deposits in the fibers grouped together to form 3D clusters.

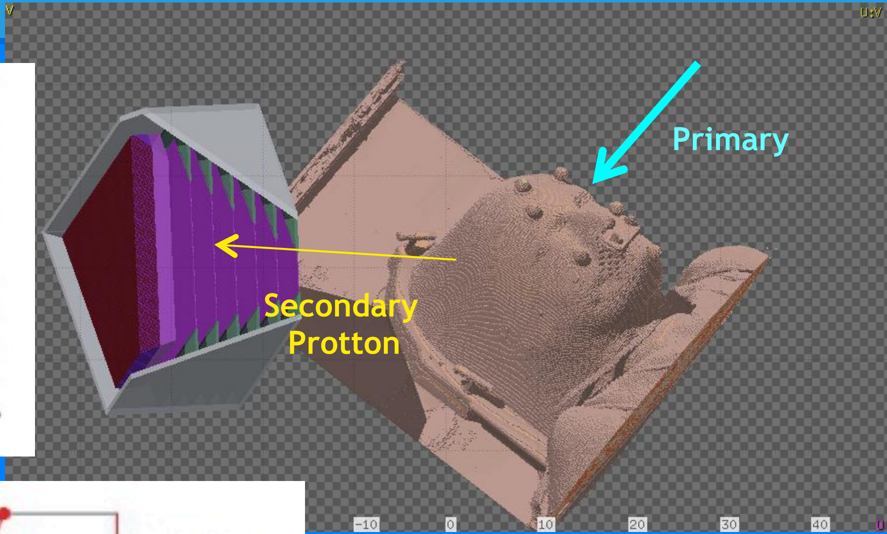
Protons detected at 90º

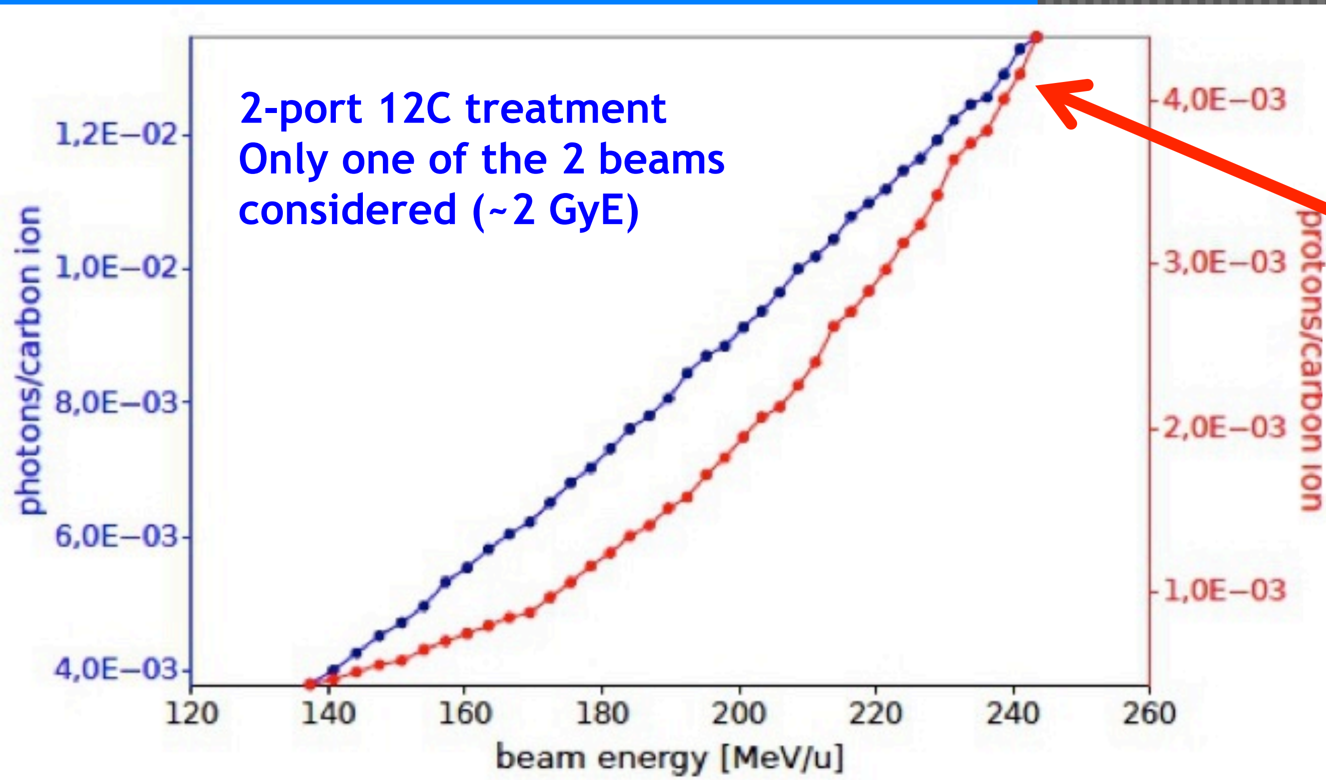
Average resolution on the single proton emission point along the primary beam direction σ ~ 0.4 cm

(Dominated by MCS in the patient)

Estimated no. of protons detected at ~60º as a function of energy in a single fraction







~2.3 10^5 primaries/spot
~1000 protons/spot
➜2-3 mm resolution on the distal slices

Conclusions: Open Problems to be addressed with the help of Physicists

- Fragmentation studies are still an open issue. This will become more important when entering the precision era of Particle Therapy.
- Not only ^{12}C: the possible next use of ^{4}He and ^{16}O beams requires specific studies.
- The importance of MC in particle therapy is increasing. Models are improving but there are not enough valuable data for benchmarking
- Real Time Monitoring in Particle Therapy is still an open issue.
  - In-beam PET is not yet established. ^{11}C beams?
  - The exploitation of prompt photons in clinics (protontherapy) is starting.
  - Charged Particles seem to be an interesting alternative, to be explored in the next two years.
  - Fancy alternatives are now proposed (acoustic waves)
- The evaluation of (low) neutron dose in patients is now starting to be considered, mainly in view of long term effects

Conclusions: Open Problems to be addressed with the help of Physicists

- MC treatment planning
- Ultrafast treatments -> Higher intensity beams
- Treatment of moving organs
- Hypofractionation, Radiosurgery (single fractions for cancer and non-cancer diseases) ⇒ Range check mandatory
- Personalized treatments:
  - LET or RBE "painting" (aiming at hypoxical/radioresistant regions) ⇒ Efficient "in-beam" imaging. Modelling, Fast computing
  - Image guided hadron-therapy
- Accelerator developments and cost reduction
  - New components
  - Compact acceleration systems
  - Future: new acceleration techniques towards more compact structures

⇒ Laser driven Plasma acceleration ?

Thank you for the attention

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