IFD2015

INFN Workshop on Future Detectors

16-18 December 2015 - Torino - Italy

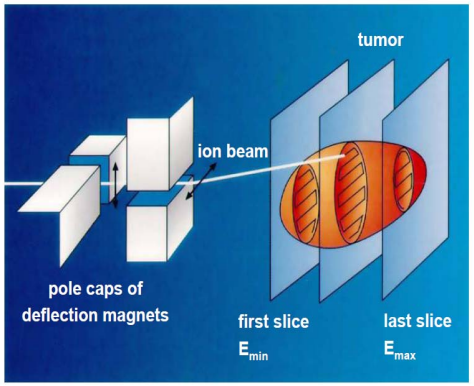
What are the new challenges in Particle Therapy?

V. Patera

Universita' di Roma "La Sapienza" & INFN Roma1

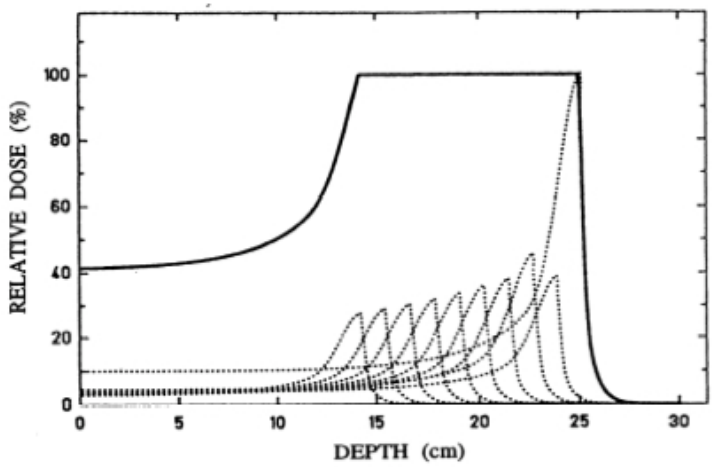
Torino 16-18 Dicembre 2015

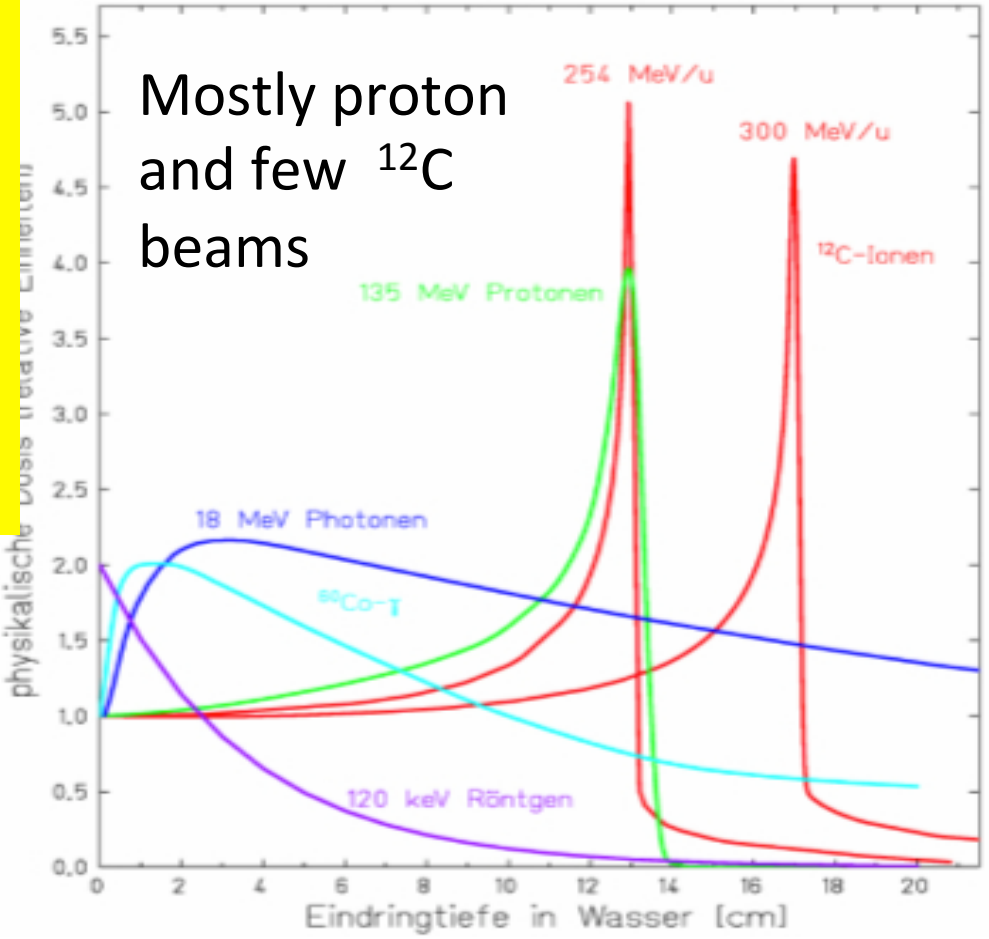
Particle therapy vs Photon RT



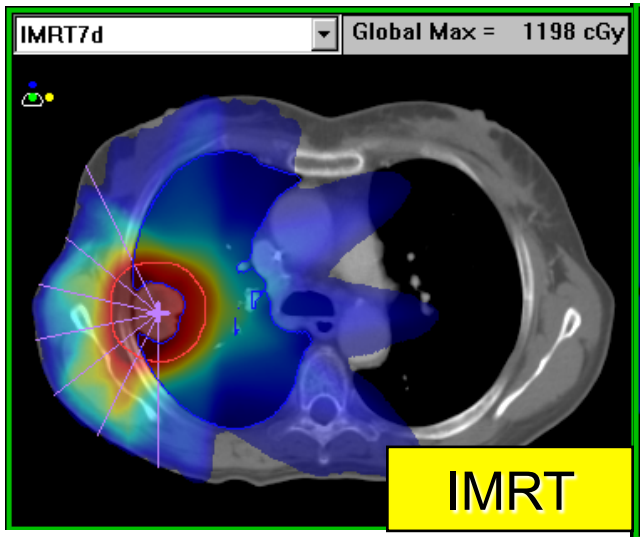
Photon beams are RT baseline. Hard competitors: small, reliable and not so expensive ->40 years R&D

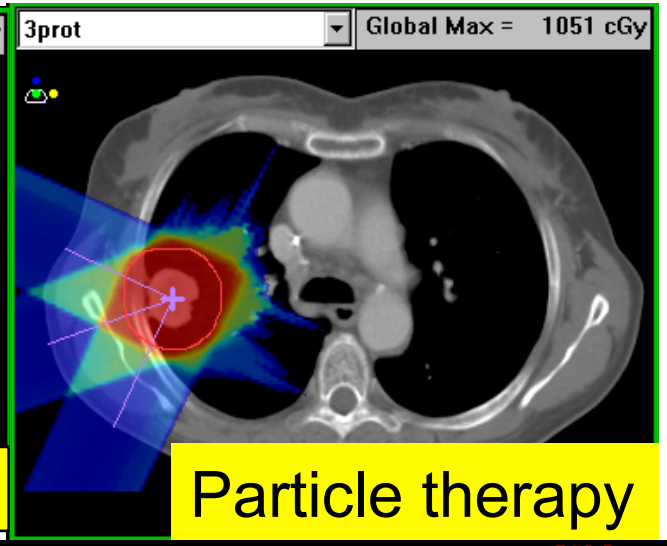
- Beam penetration in tissue function of the beam energy
- Peak of dose released at the end of the track, sparing the normal tissue
- Accurate conformal dose to tumor with Spread Out Bragg Peak





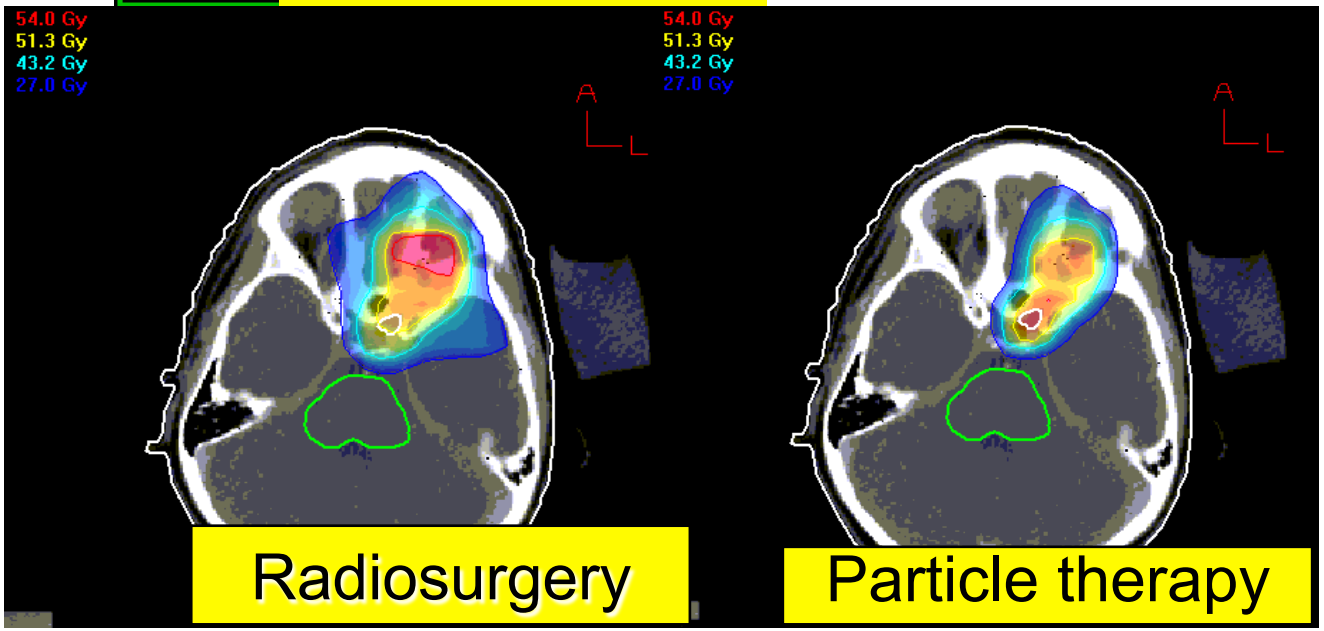
Examples of Photons vs Particle saga…



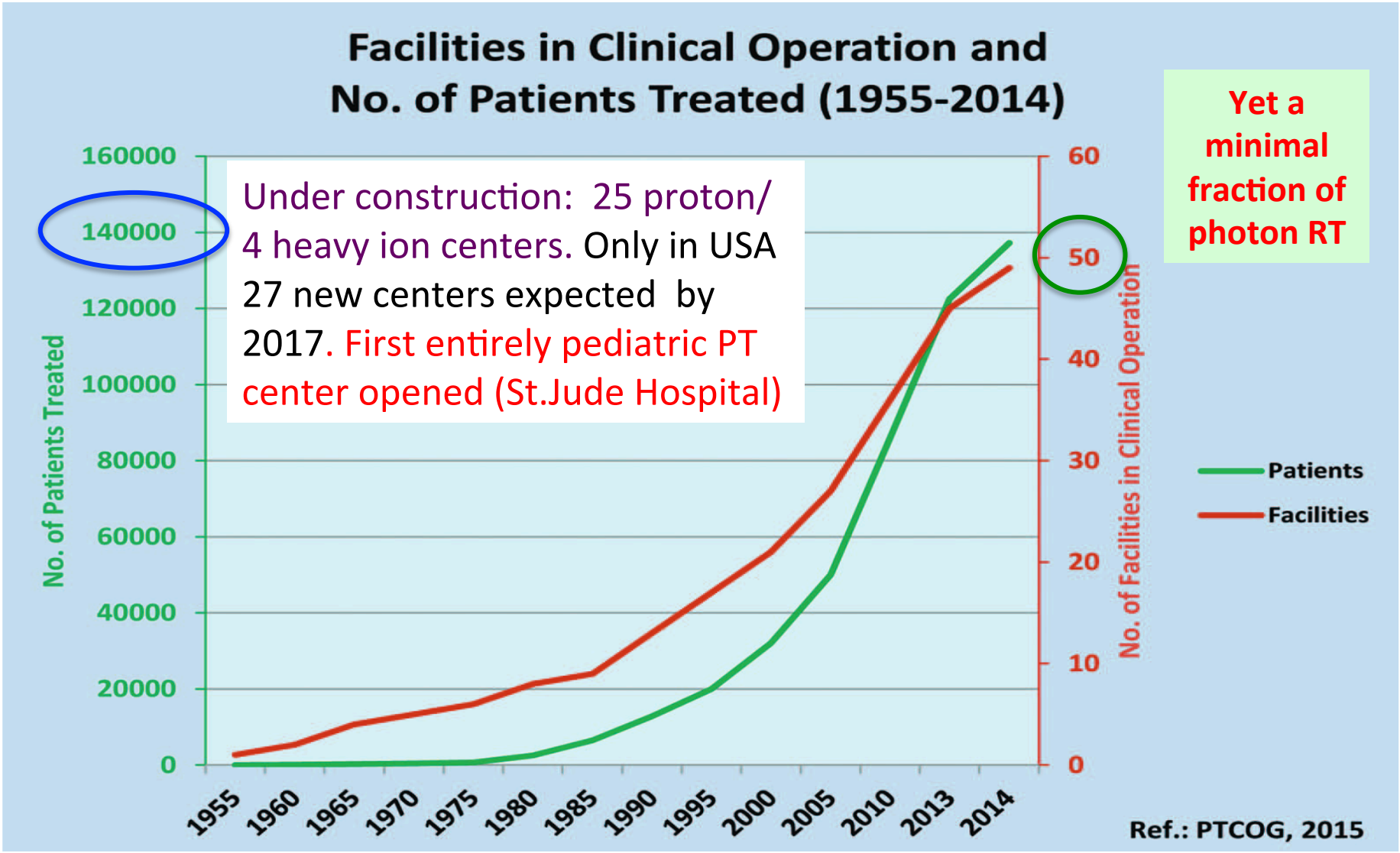


Particle therapy can easily show better selectivity with respect to photon techniques…

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



Charged Particle Therapy in the world



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

Typical Hype Cycle for Innovation Technology

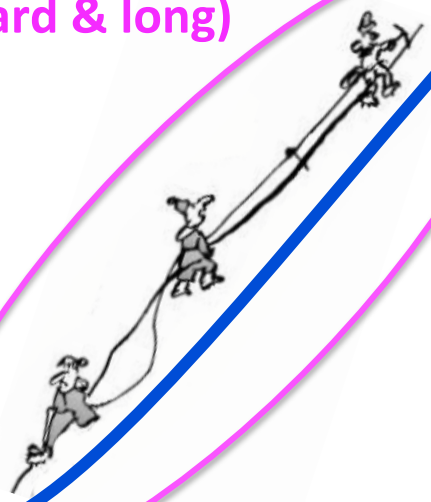
Peak of inflated Expectations (general interest)

Plateau of Productivity (general acceptance)

Visibility

Slope of Optimization (hard & long)

Trough of Disillusionment (system criticism)



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

Technology trigger

Maturity

adapted from Becker & Townsend

The INFN RDH project : R & D in Hadron Therapy

The INFN Research & Development effort in hadrontherapy is mainly coordinated within the RDH project. European (and beyond) netword of collaborations

1) Treatment Planning System
2) Proton Computed Tomography
3) Residual Range system
4) Dose Monitoring
5) Nuclear Fragmentation Studies
6) Radiobiology
7) Monitor for High Intensity Beam
8) Innovative Accelerators Components

GR5 & IRPT

ENVISION

ULICE
Union of Light Ion Centres in Europe

ENTERVISION

MAESTRO

+ MC_INFN project
(MC development)

Cagliari, Catania, Firenze, LNF, LNS, Milano, Pavia, Pisa, Roma1/2/3, Torino

The RDH project : R & D in Hadron Therapy

The INFN ...rch & Development effort in hadrontherapy is mainly coordinat... project. European (and beyond) networ... of collab...

1) Treat...
2) Prot...
3) Res...
4) Do...
5) N...
6) R...
7) Mon...
8) Innovative Accele...

Huge R&D activity lasting more then 15 years.

Personal and incomplete choice of the INFN (and non INFN) technology challenge of interest in Particle therapy.

Not treated the Accelerator Issues.

Apologize for mistakes and/or Omissions

GR5 & IRPT

+ MC_INFN project (MC development)

Cagliari, Catania, Firenze, LNF, LNS, Milano, Pavia, Pisa, Roma1/2/3, Torino

PT optimization & detector development

The main PT trends that ask for detector R&D are beam intensity escalation and QA of dose release.

- ✓ Detector working at high rate to monitor current and position of high intensity beam
- ✓ Detectors to monitor the dose profile along the beam path inside the patient
- ✓ Proton tracking and calorimeter system (software included) to improve patient imaging

The golden figure of this R&D activity is the accuracy on the released dose ~ few%

The developed devices are to be embedded in clinical environment: cost, reliability and "easy to use" features play a key role. Usually not bleeding edge, but wide spectrum

Beam Intensity & New Compact Accelerators

Each PT treatment is made of 20-30 fractions. Cost (and time) optimization asks for reduced treatment time and increased dose release in a single fraction. This will boost the beam intensity in future. Compact machine are likely to have high pulsed fluxes

Typical figures for future high flux pulsed charged particle beams	
Pulse frequency (kHz)	0.2 – 1
Pulse Length (μs)	5 – 20
Number of particles per pulse	10^7 -10^8
Instantaneous Intensity (prot/s)	10^{12} -10^{14} (1nA-20μA)

- Laser-driven acceleratos
- Cyclinac
- Synchrocyclotrons
- Fixed Field Alternating Gradient Accelerators

At high beam intensities the standard ionization chambers are no more reliable as intensity and position monitors

Approach to future beam intensity monitor

R&D spans from upgrade/modification of the standard devices to be immediately applied to next generation commercial accelerator to future single particle detector to be used at future machine.

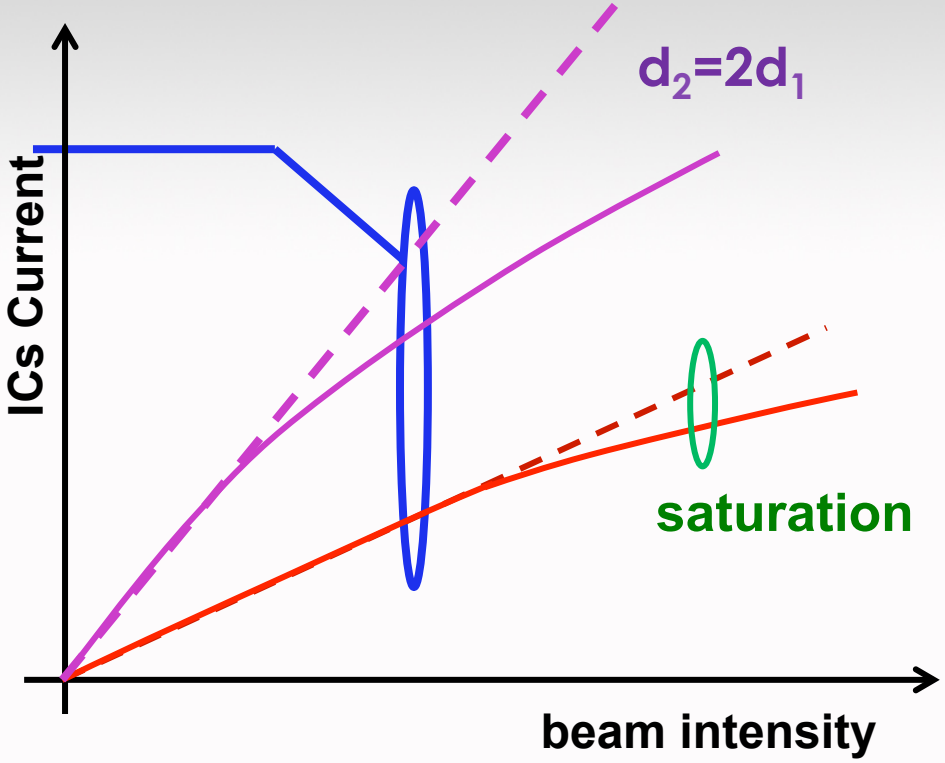
- ✓ Multigap Ionization chamber (RDH-TO)
- ✓ Low material tracker based on thin SciFi planes coupled with SiPM (RDH-LNS)
- ✓ GemPix detector (mutant device from GEM+ MediPix, CERN-LNF)
- ✓ Single particle devices: Si solid state detector (RDH-TO,ELI-NP)

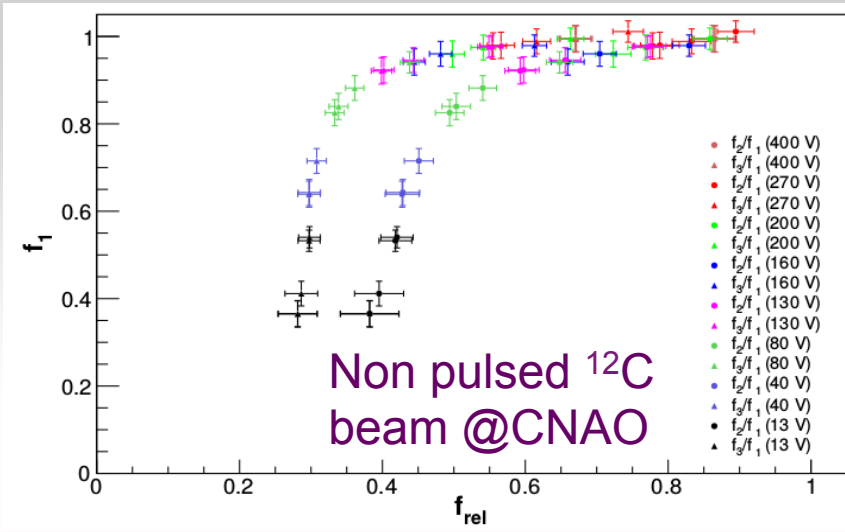
now

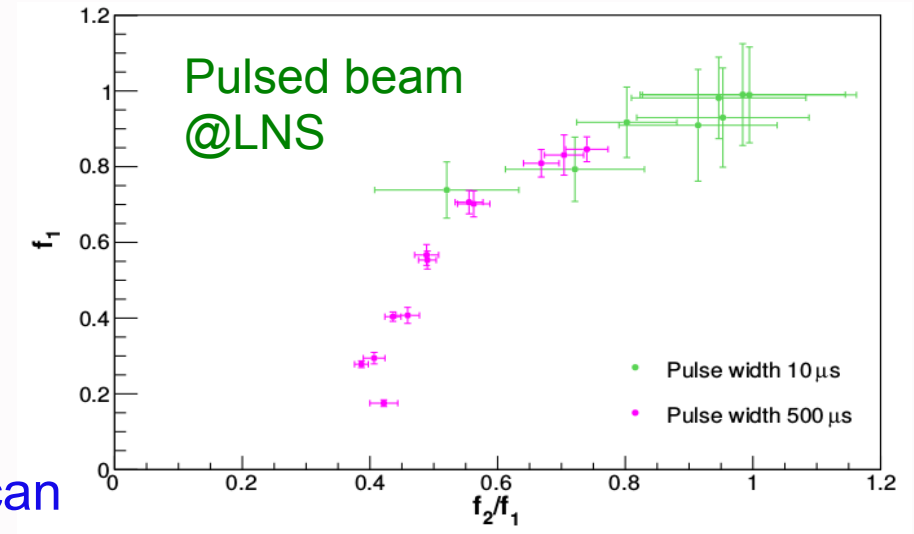
202??

"Ready to go" solution : multigap IC

Multi-gap chamber solution fully characterized at continuous and pulsed beams





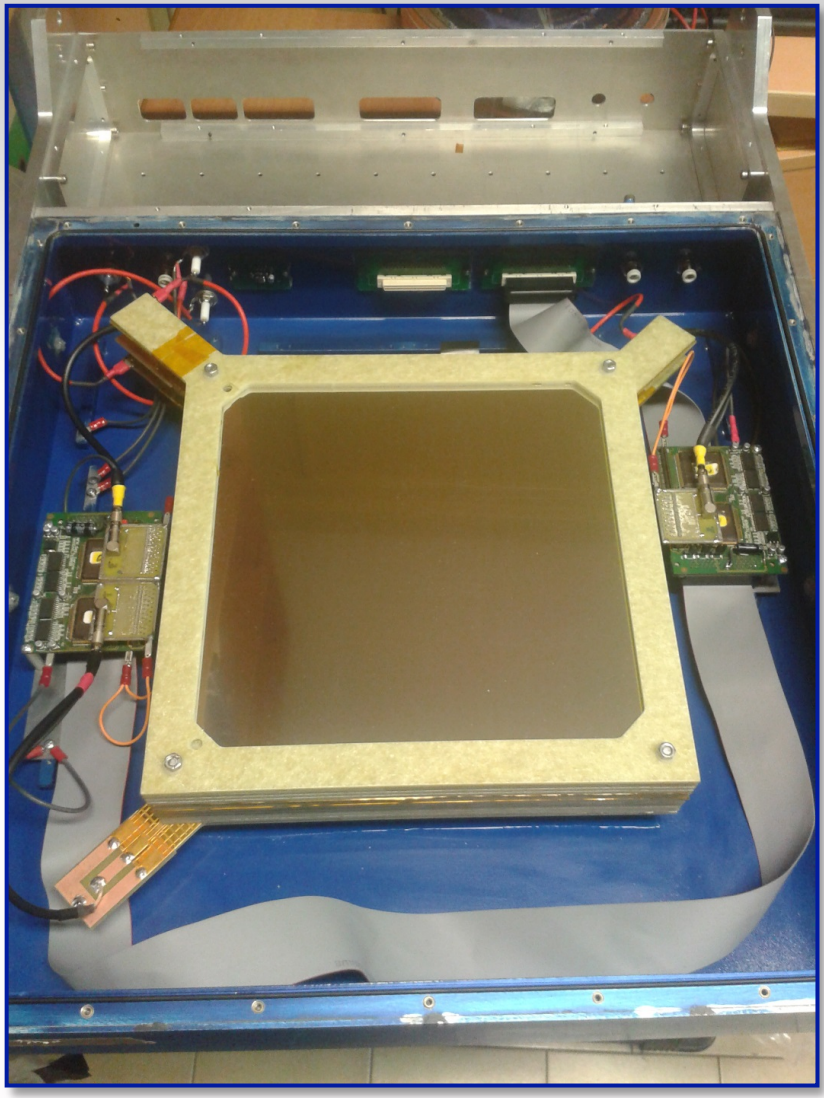


If V/d^2 is fixed, the ratio between the currents in the two ICs only depends on ionization density n_0 -> beam intensity can be extracted

Multigap IC

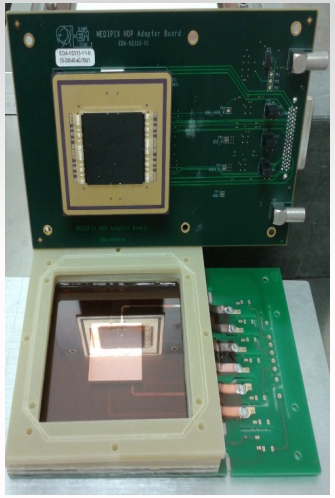
- New double-gap chamber under construction for dosimetry at ELIMED beamline (Prague)

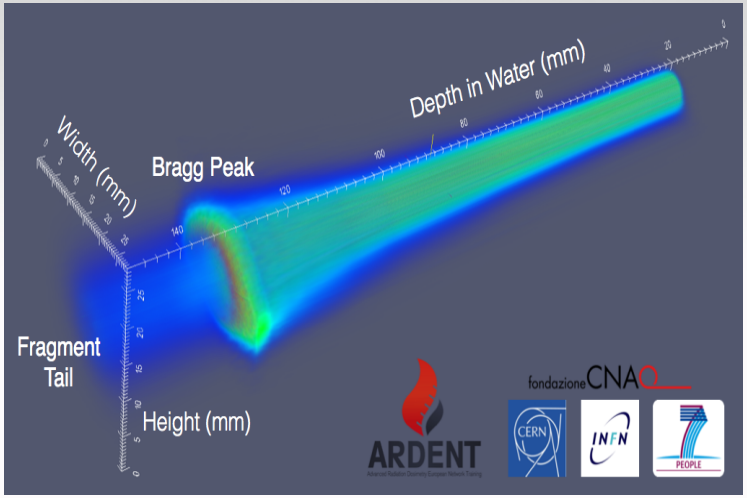
- New readout chip **TERA09** has been designed
  - extends by > 10^2 the dynamic range of TERA08 (used at CNAO, MedAustron, ...)
  - fully compatible with TERA08 current applications
  - prototype under test @ INFN-Torino
  - development under cooperation agreement with De.Tec.Tor company
  - joint INFN-De.Tec.Tor patent request has been submitted

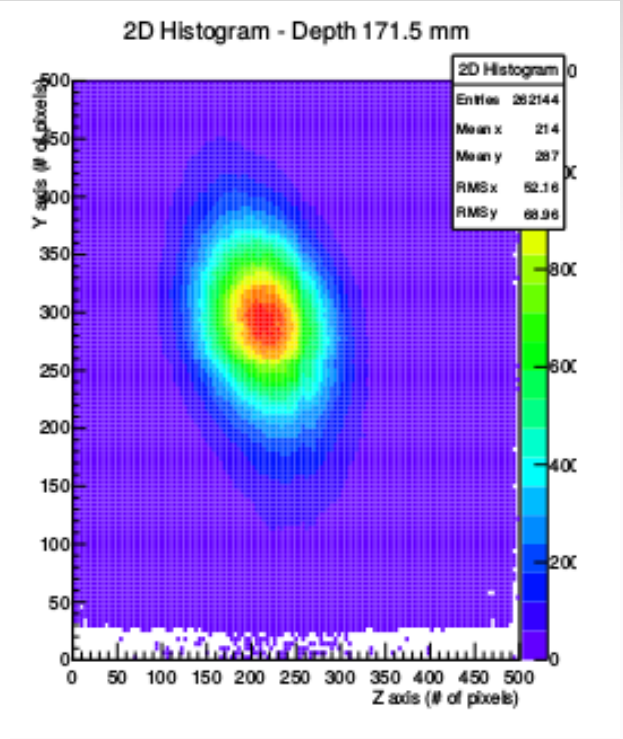


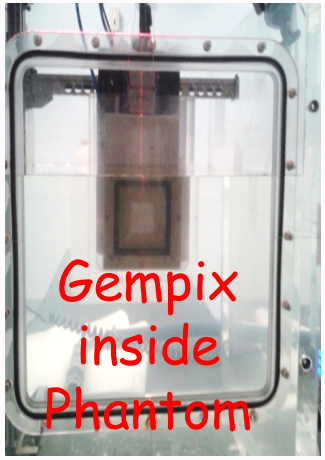
GEMPIX for Hadrotherapy

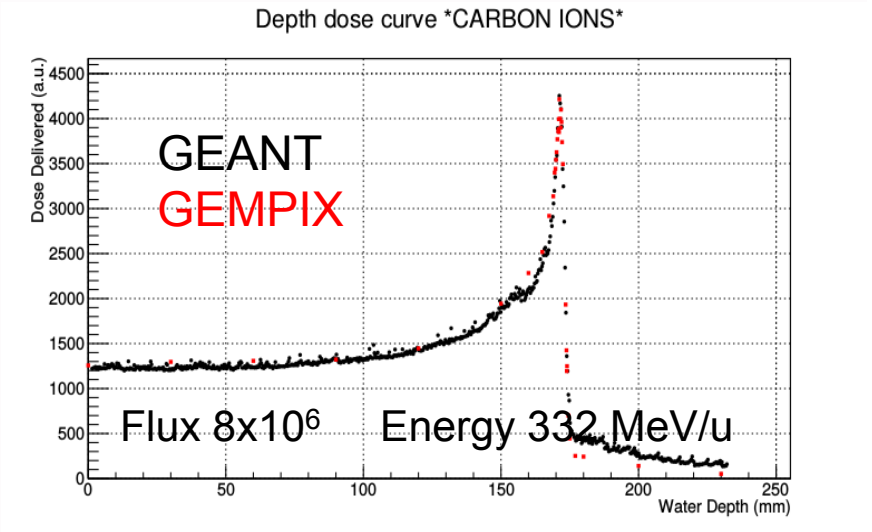
Gempix Detector (10 cm^2 GEM detector read by 55x55μm pixels)
- 3D measurements of energy released in water phantom @CNAO Pavia











F.Murtas , M. Silari, G. Stuart
A.Rimoldi, A.Tamborini,
M.Ciocca and A.Mirandola
CERN, INFN, UNIPV, CNAO

Courtesy of F.Murtas

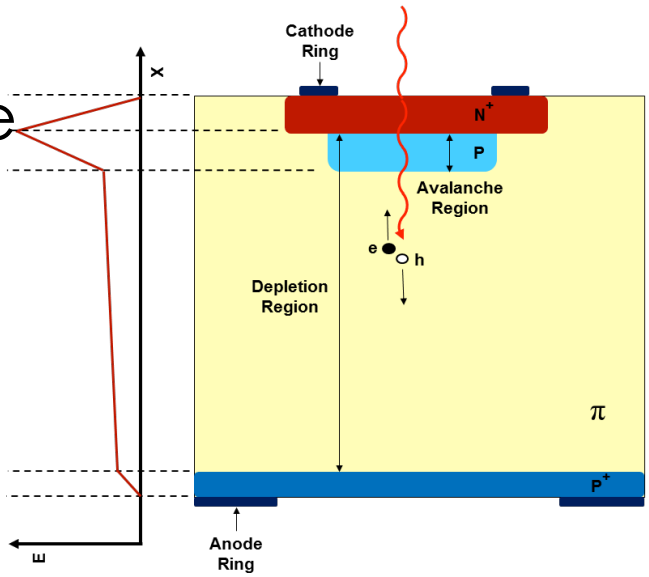
Si-detectors as counting devices (RDH-TO)

The performance required are **extremely challenging:**

- **very fast collection time (< 1 ns) for GHz counting capability, limited multiple scattering -> thin sensor (< 50 um)**
- **finely segmented (>10^4 pixels for 10 GHz counting with pile-up probability < 0,1 %, beam transversal shape could be monitored)**
- **hybrid electronic chip with independent readout of single channels**
- **radiation tollerant**

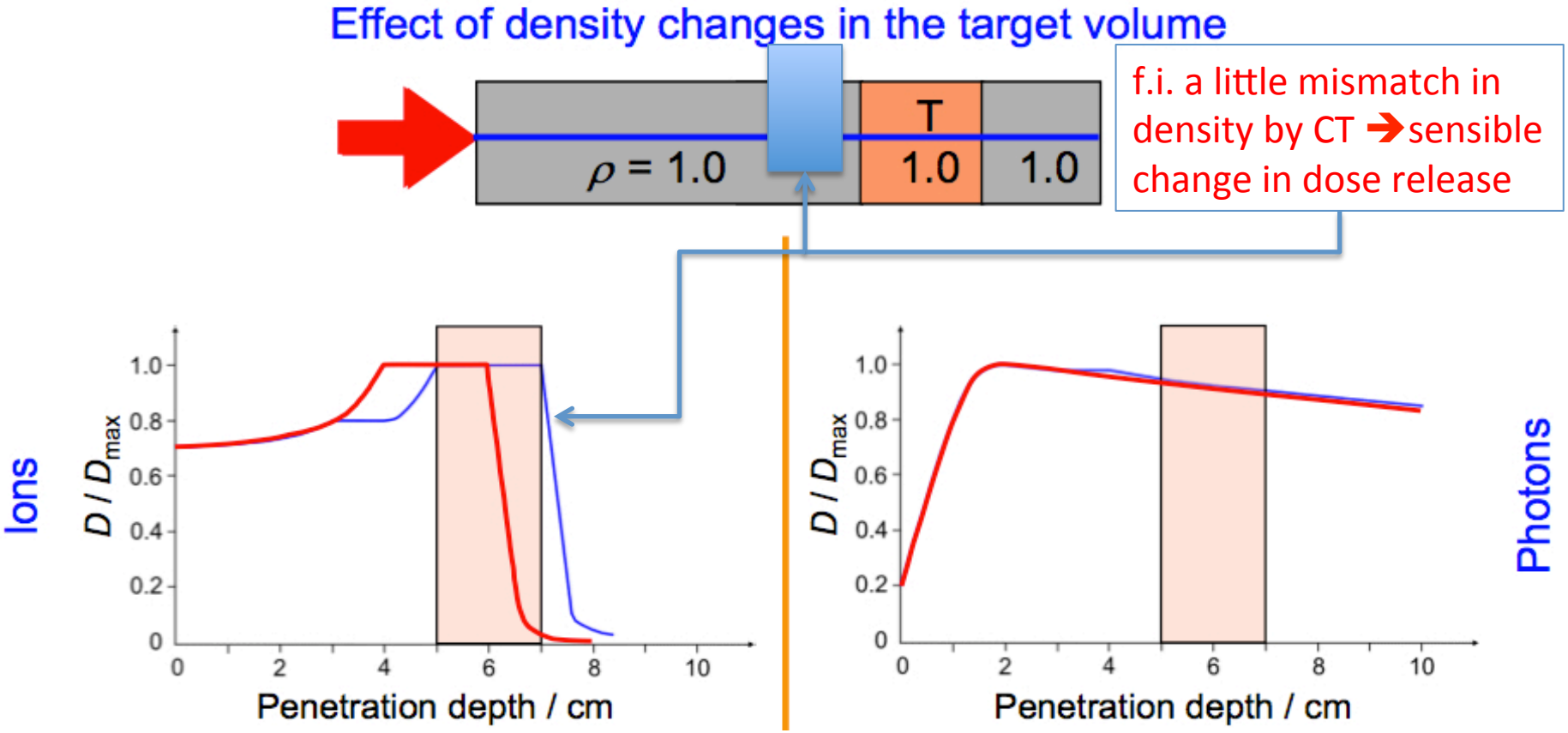
Investigated the possibility to use **thin silicon detectors.** The low signal to noise ratio of thin sensors can be compensated with an **internal gain**.

Synergy with the UFSD (Ultra Fast Silicon Detectors) project of CSN5



Quality Assurance & Dose profiling in PT

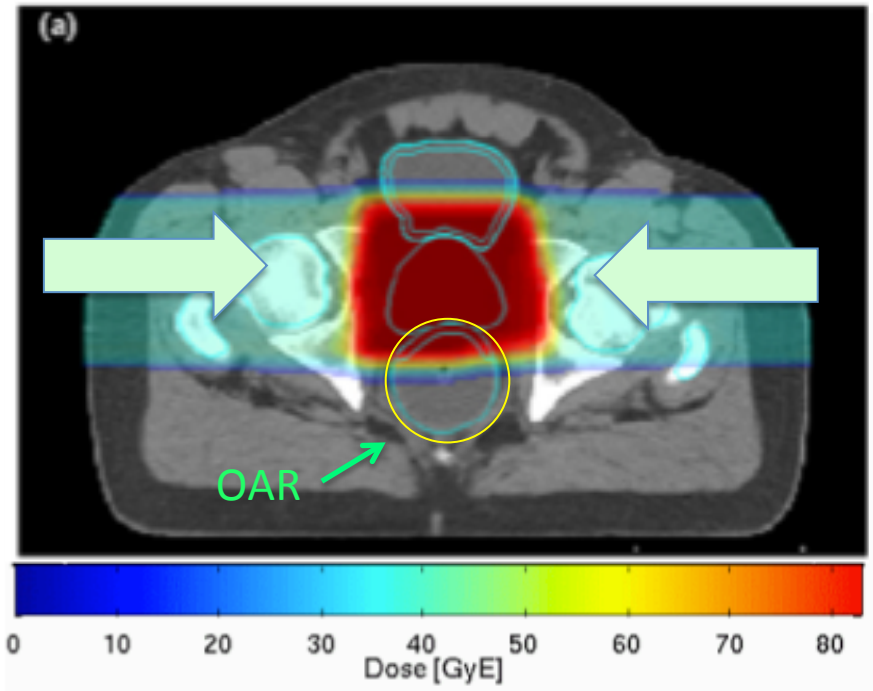
Why is so crucial to monitor the dose in particle therapy with respect to photon RT? It is like firing with machine-gun or using a precision rifle..
Inhomogeneities, metallic implants, CT artifact, HU conversion, inter session anatomical/physiological changes-> range variations



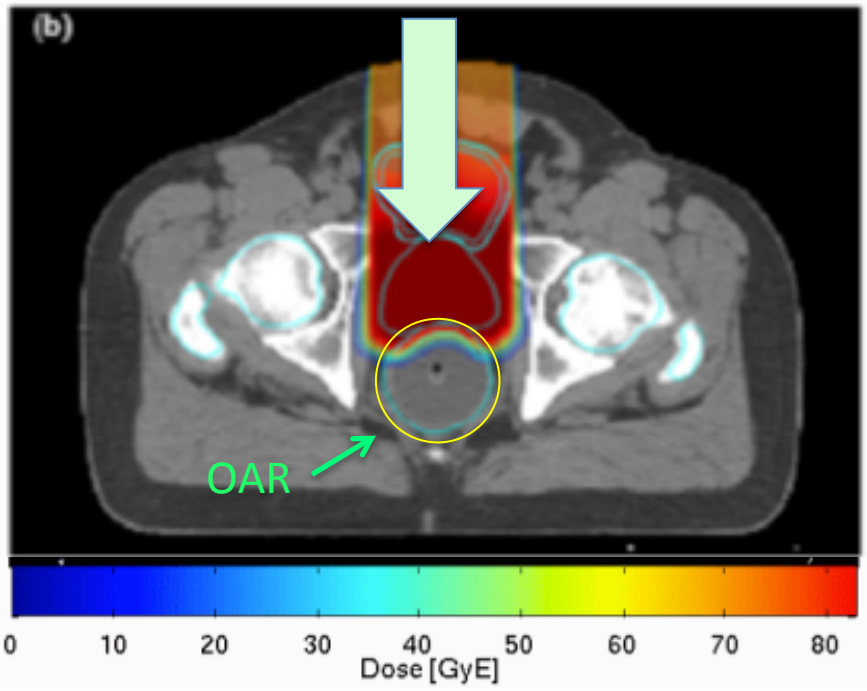
Accounting for uncertainties in the clinical practice

[Tang et al. 2012]

Current approach:
Opposed fields, overshooting



Desirable approach:
Different beam angles and no overshooting



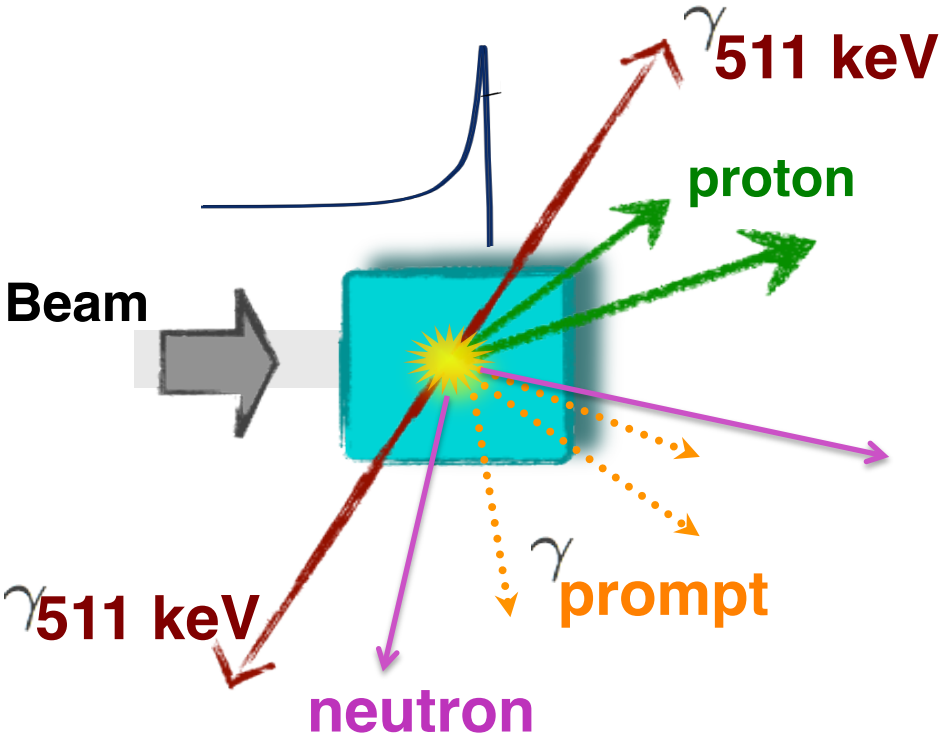
Protons

Beam range & secondary products

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

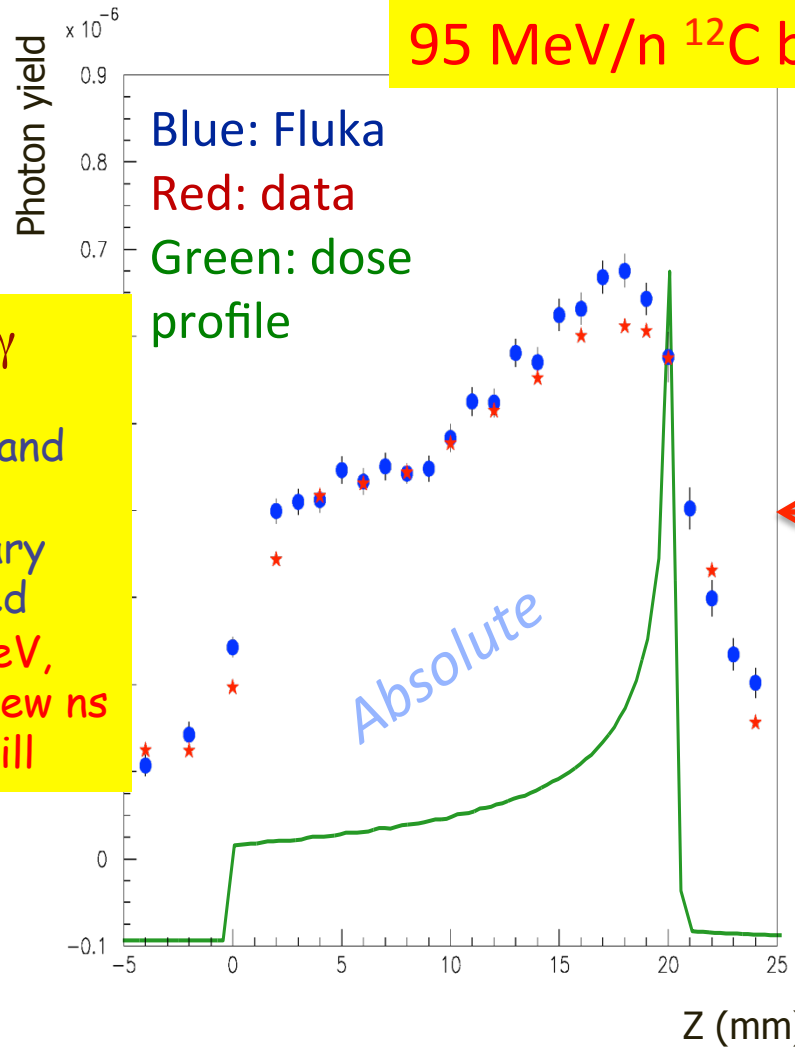
Activity of β^+ emitters is the baseline approach

- 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

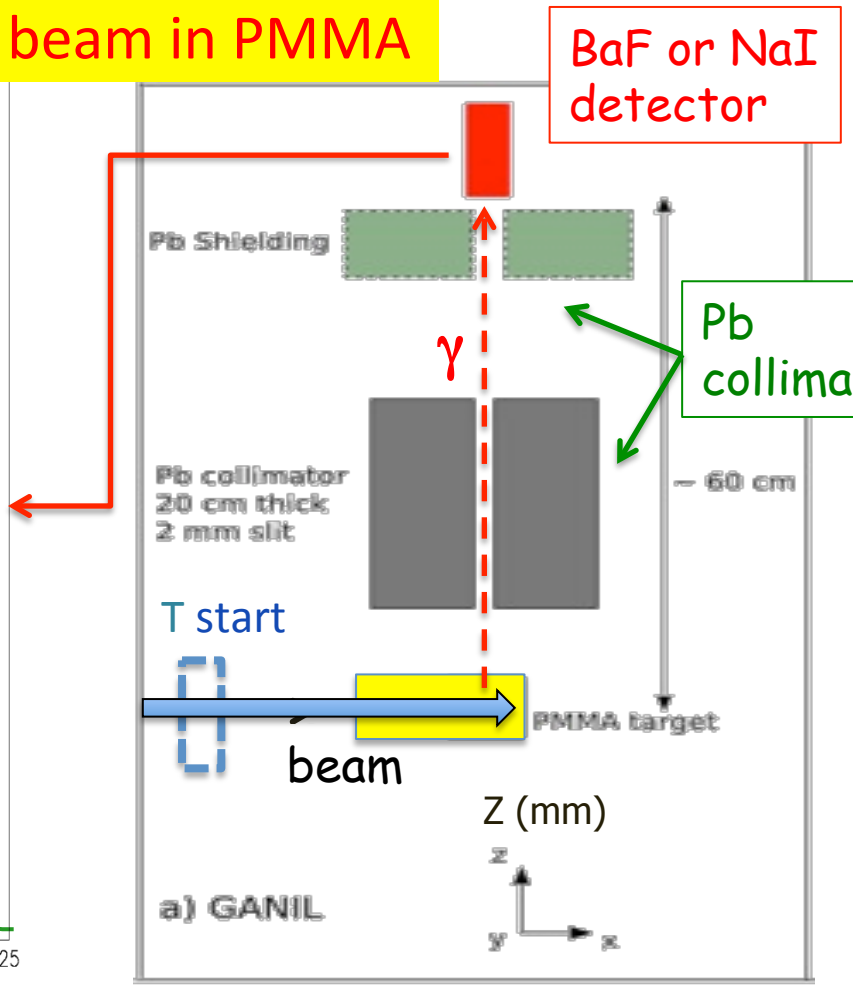


The prompt photons solution

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

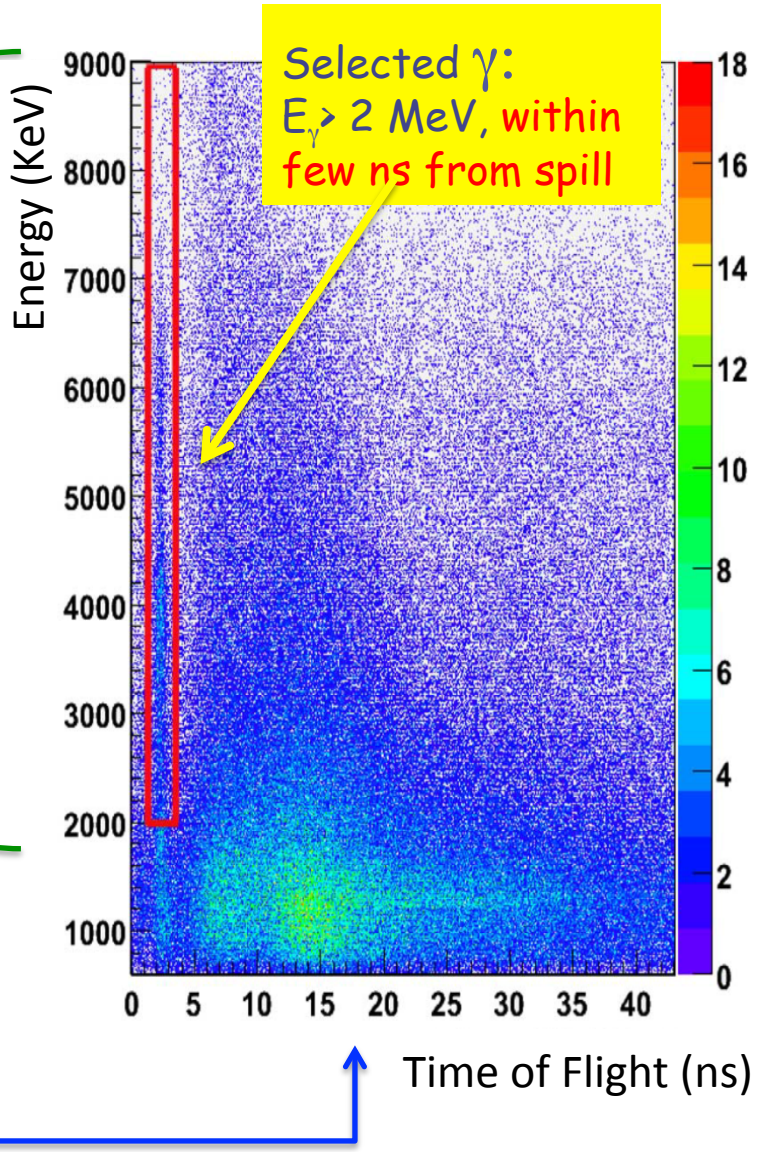


Courtesy of Alfredo Ferrari

[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

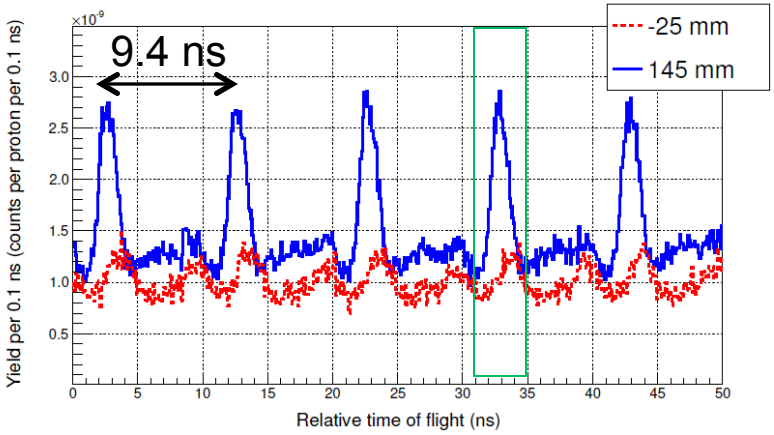
The prompt γ emission: summary

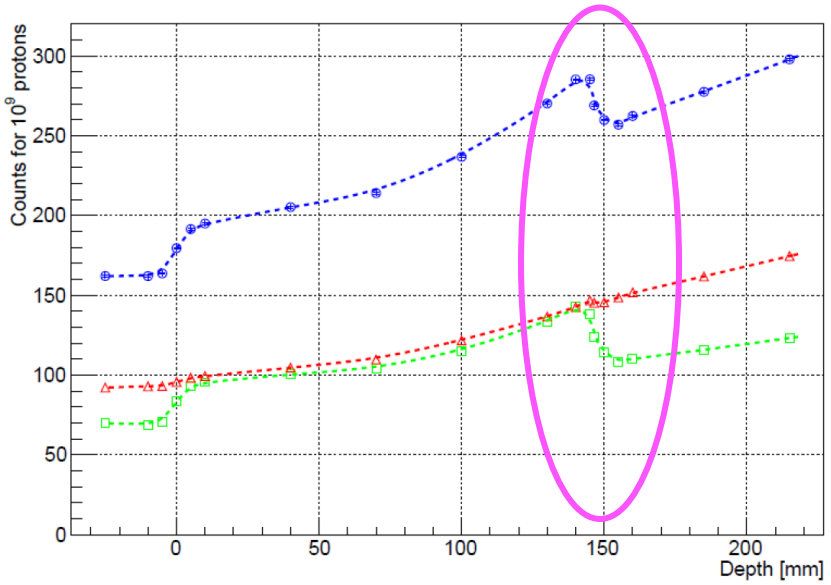
- The gamma are quite copiously produced by proton and ^{12}C beam by nuclear excitation.
- The emission region stretches along all the beam path but has been shown to ends near the Bragg peak for both beams.
- It's not simple backpointing the γ direction: the γ energy is in the 1-10 MeV range-> much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

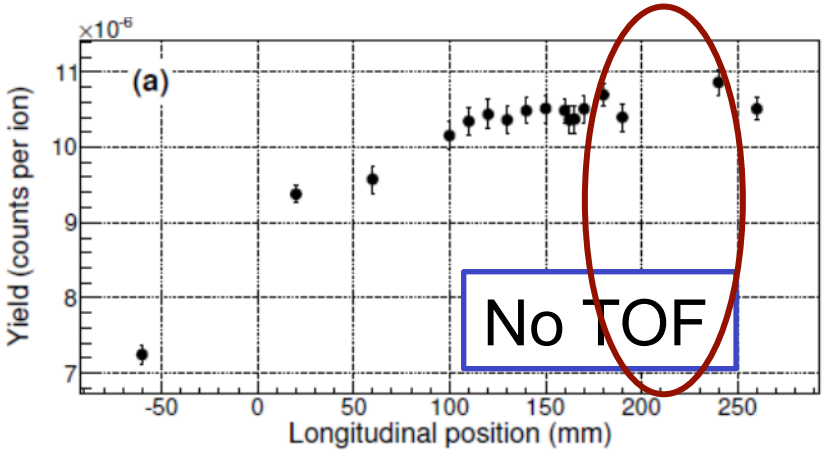
160 MeV protons in PMMA
IBA C230 cyclotron

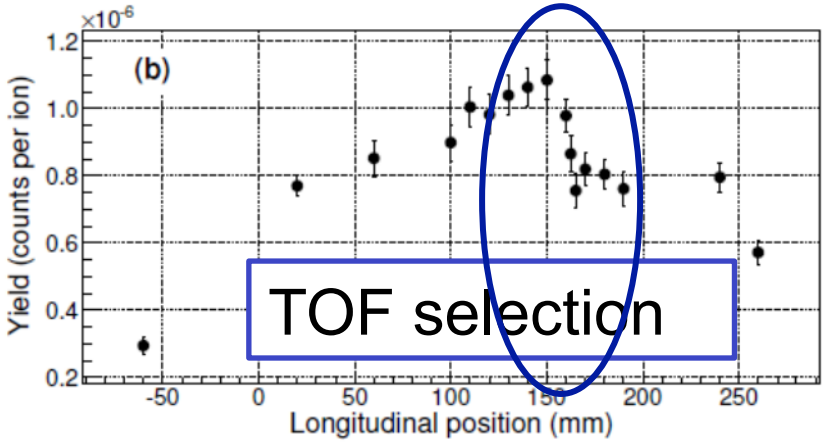




Roellinghoff PMB 2014

310 *A*MeV carbon ions in PMMA





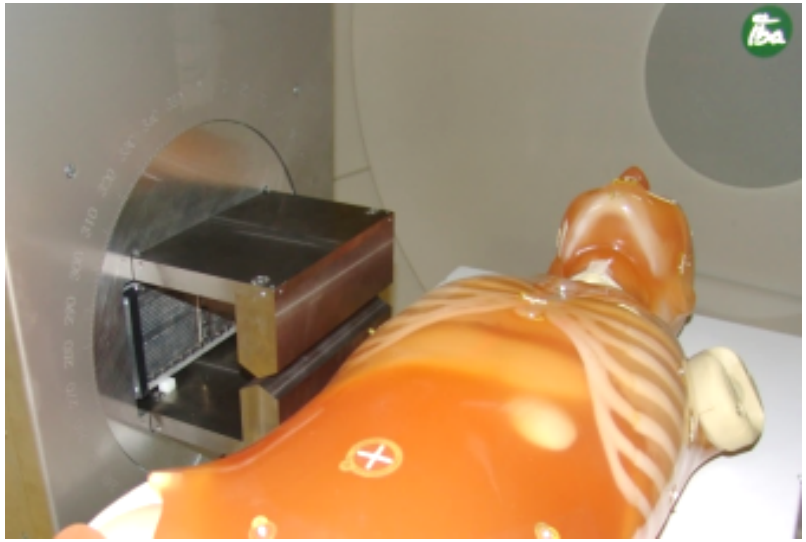
TOF : mandatory for carbon ions (?)
Single part. beam monitor needed

M. Pinto, submitted New J Phys

Courtesy of D. Dauvergne

Range monitor for proton beam: the slit camera

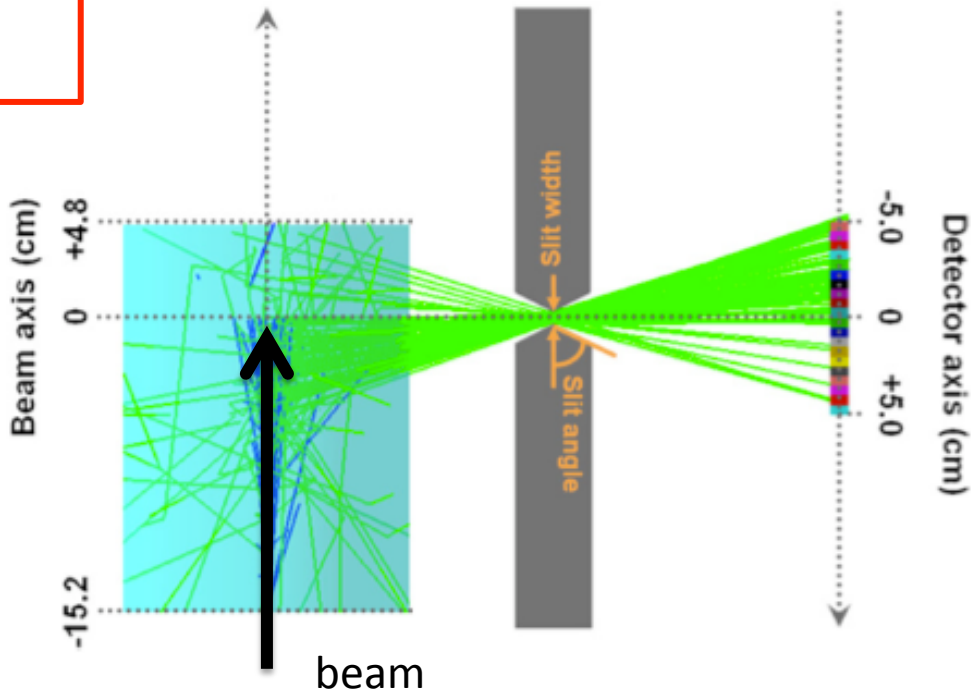
Near to clinically practice: IBA, Politecnico & Xglab spinoff from Milano



Many groups working also on:

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

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



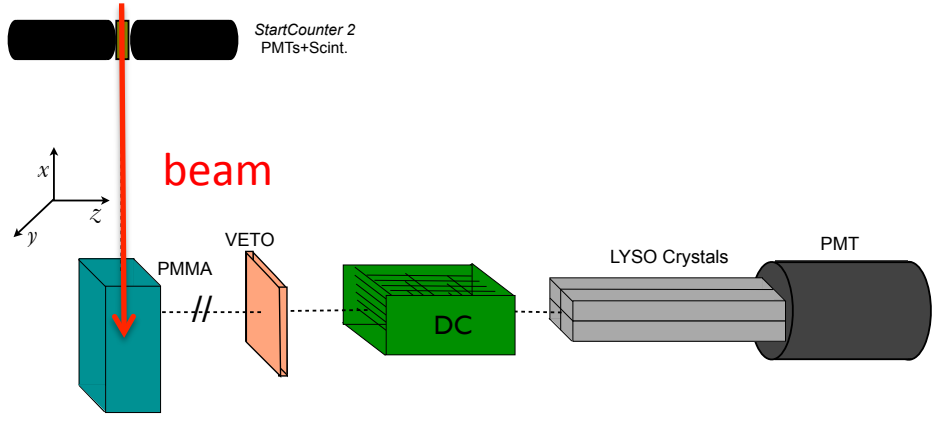
What about heavier beam (^{12}C) ?
LET grows as Z^2 and the nuclear interaction increase with A. Thus, for the given dose, ^{12}C gives:

- less prompt γ than proton
- more background than proton

^{12}C (^{16}O) beams : something else useful? Secondary protons

Charged secondaries have several nice features

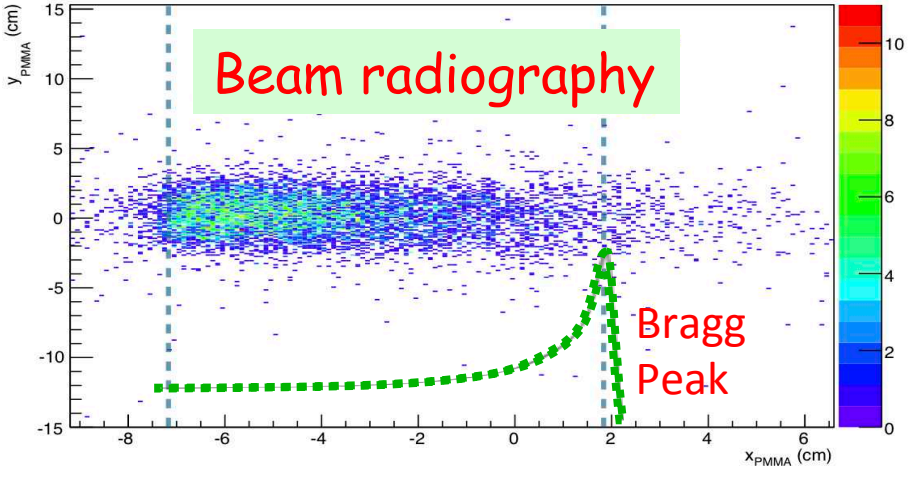
- The detection efficiency is almost one
- Can be easily back-tracked to the emission point-> can be correlated to the beam profile & BP



- 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



K Gwosch et al PMB 58 3755

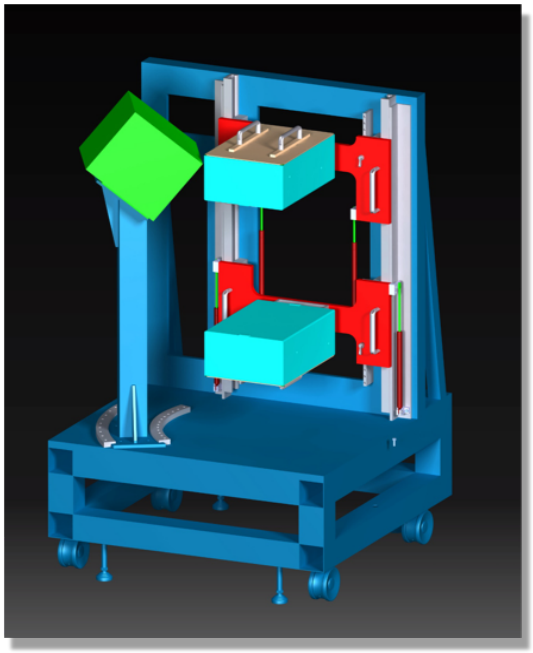
C Agodi *et al PMB* **57** 5667

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

The InSIDE Project @ CNAO

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

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

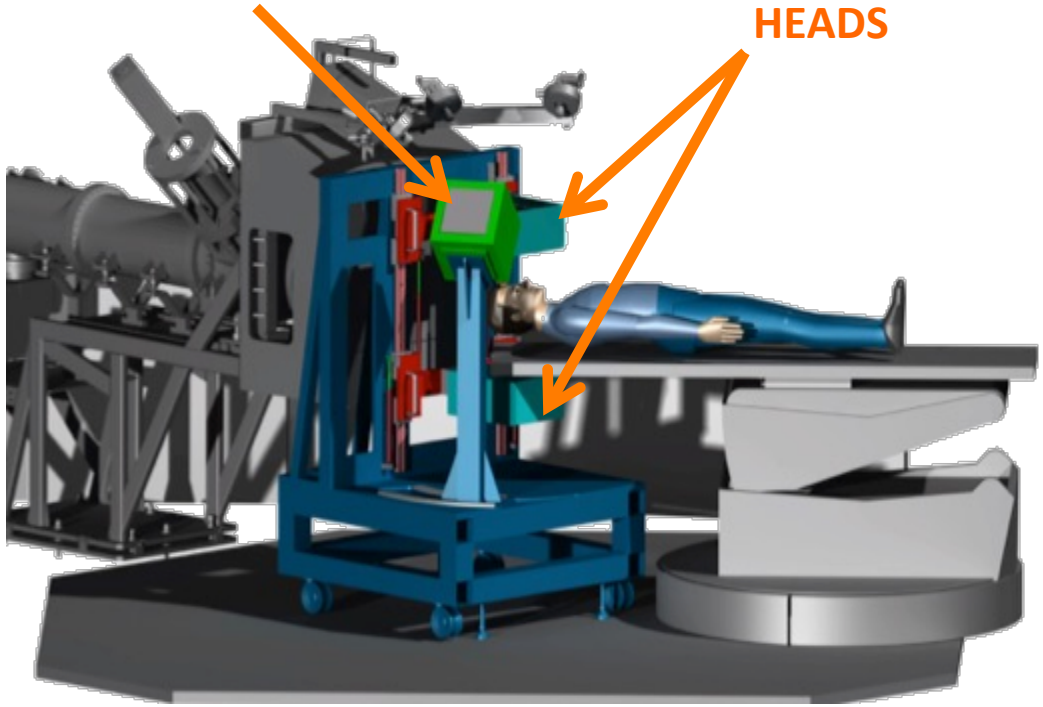


proton emission

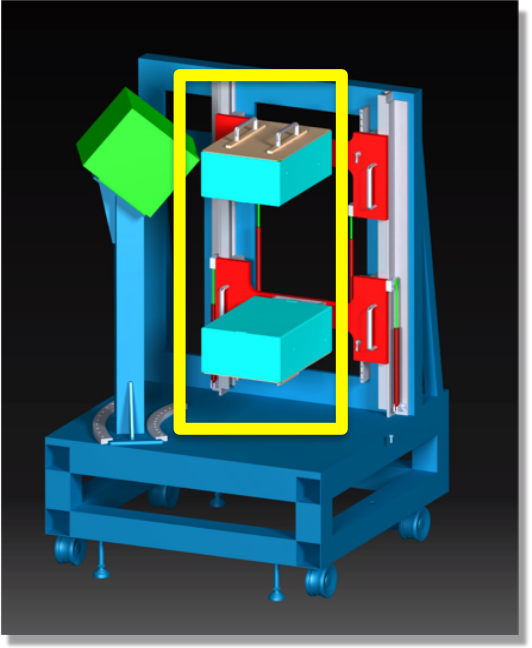
Tracker + Calorimeter = DOSE PROFILER

β^+ activity distribution

IN-BEAM PET HEADS

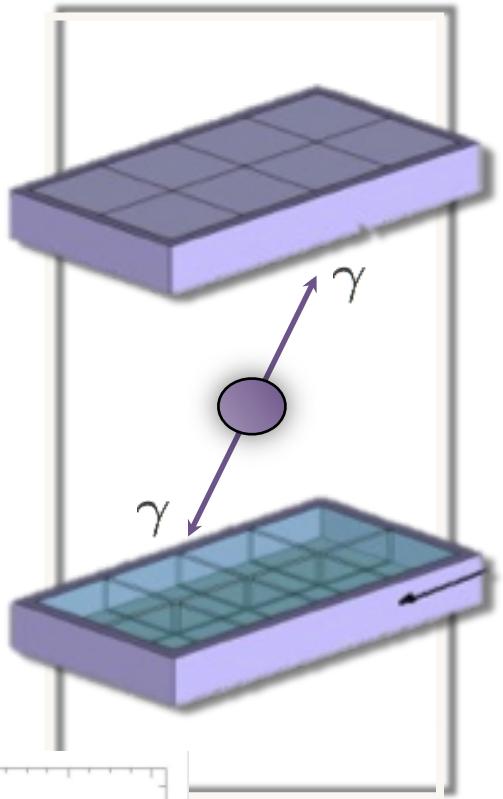


- Dual signal operation
- integrated in treatment room
- Provide in-beam feedback on beam range
- Challenge: fusion of charged and PET information



The INSIDE PET system

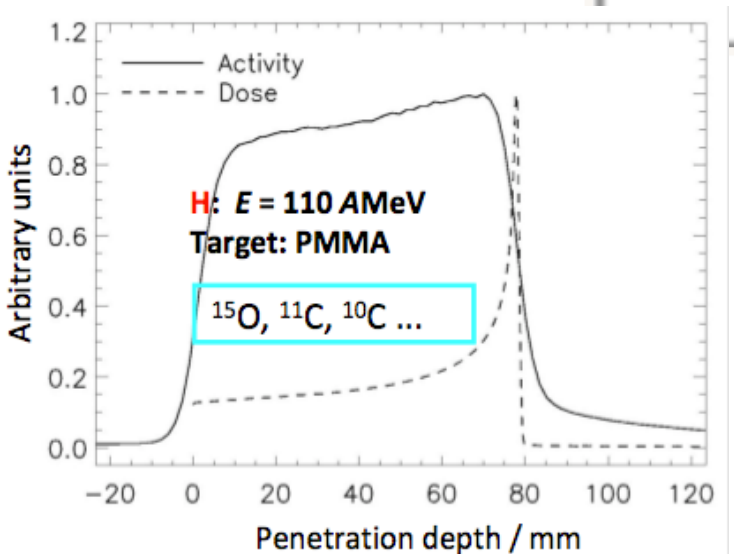
- Detectors to measure the 511 keV back-to-back photons in order to reconstruct the β^+ activity map.
- Two planar panels: 10 cm x 20 cm wide => 2 x 4 detection modules;
- 1-2 mm resolution expected along the beam path



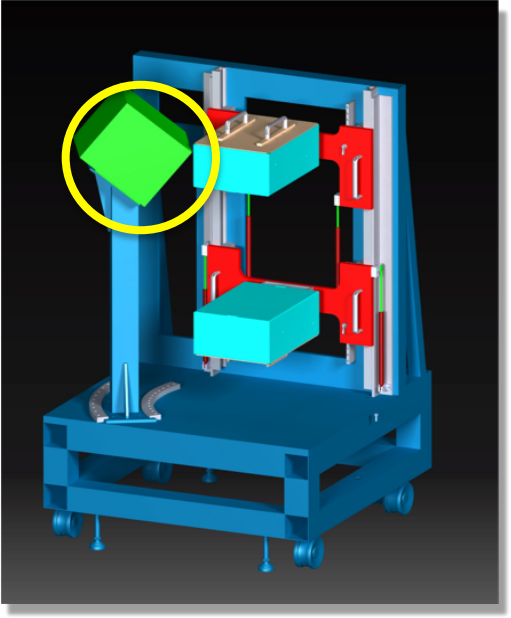
Each module = pixelated LSO matrix 16 x 16 pixels, 3 mm x 3 mm crystals (pitch 3.1mm)

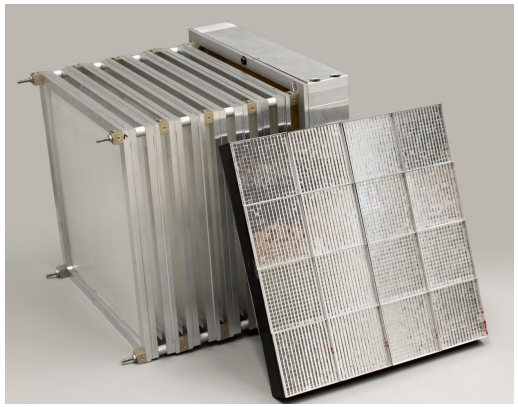
LYSO matrix readout: array of SiPM (16x16 pixels) coupled one-to-one.

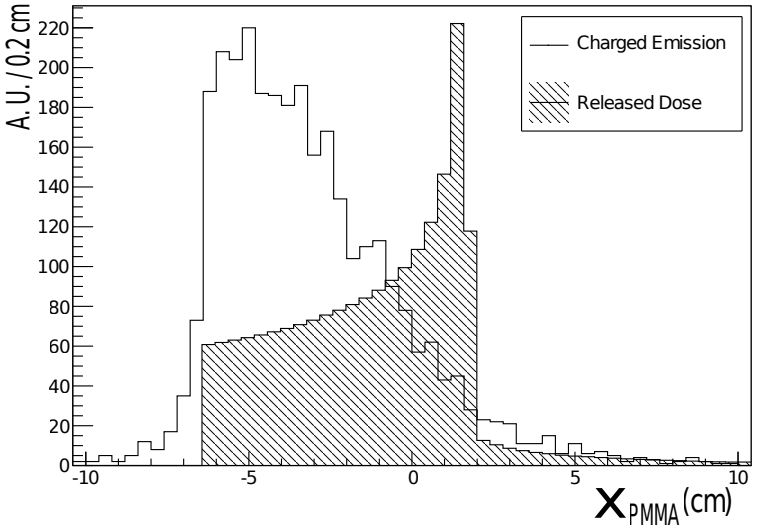
Custom TOF-PET asic
(Courtesy of M. Rolo, LIP and ENDOTOFPET EU project)



The INSIDE charge Profiler





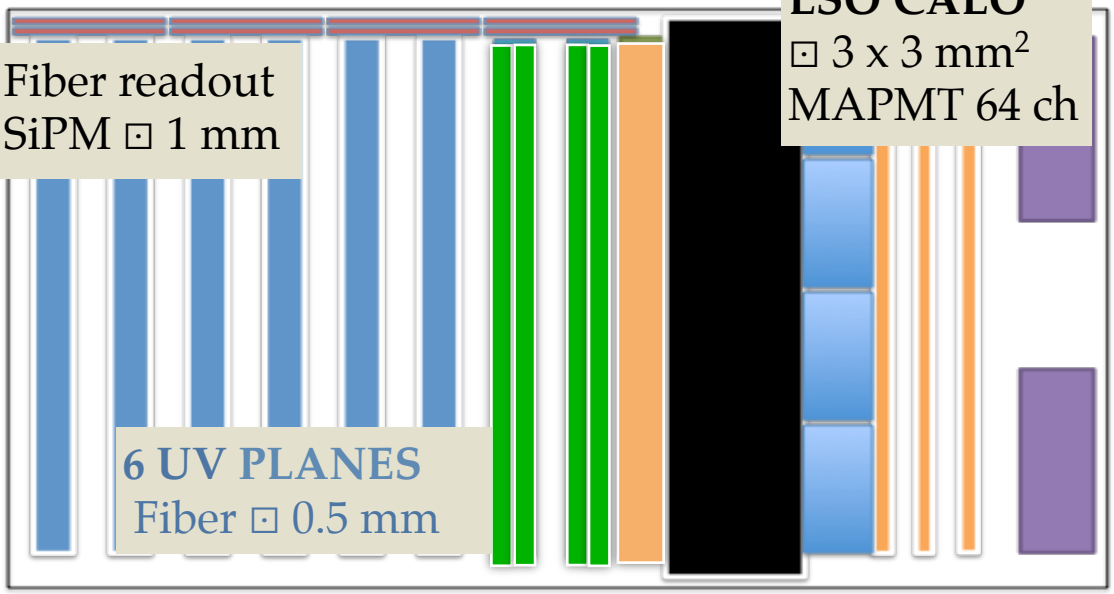


Tracker: back-tracking of secondary protons to the beam line

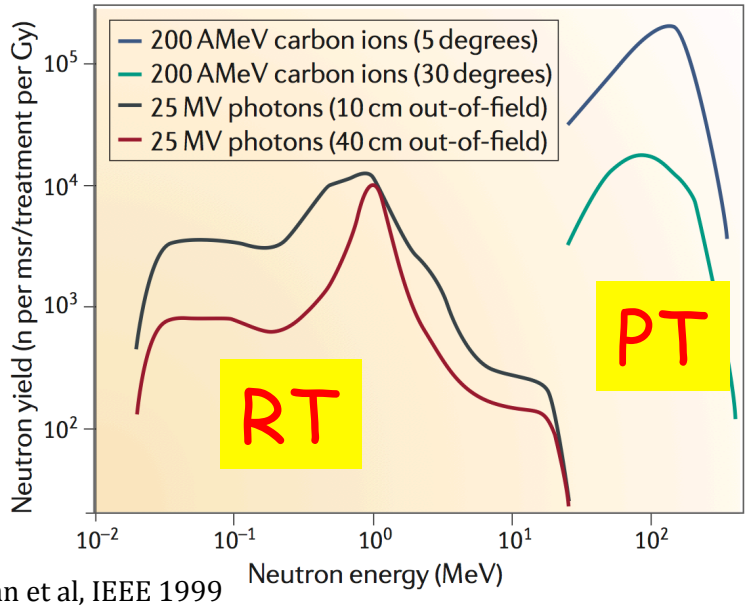
Calo: select higher energy protons to minimize MS in the patient.

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

Calibration: BP position vs Emission shape parameters



Neutrons in RT & PT



Ryan et al, IEEE 1999

The neutron flux dominates, by orders of magnitude, the total secondary flux. Neutrons directly produced by the beam in PT are mainly ultra fast neutrons [20-200 MeV]

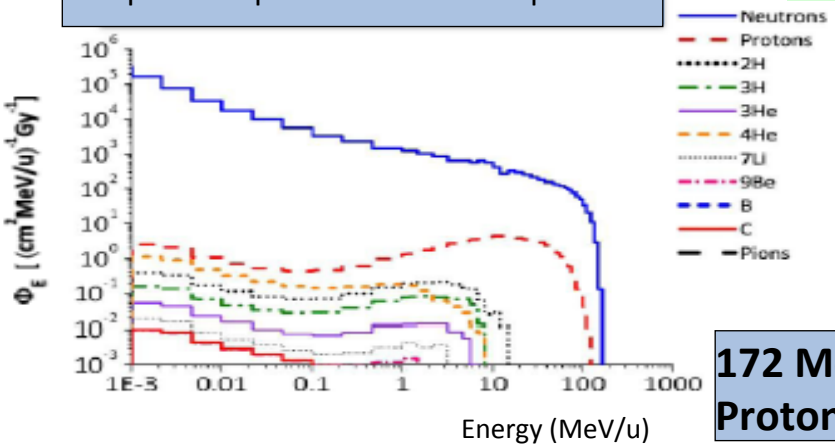
Accurate n production X-section by p,^{12}C beam on (O,C), with angle and energy distribution, are still missing.

Neutron monitoring during PT is particularly difficult, (no directionality, scattering from environment, probabilistic release of energy, PID?, etc..)

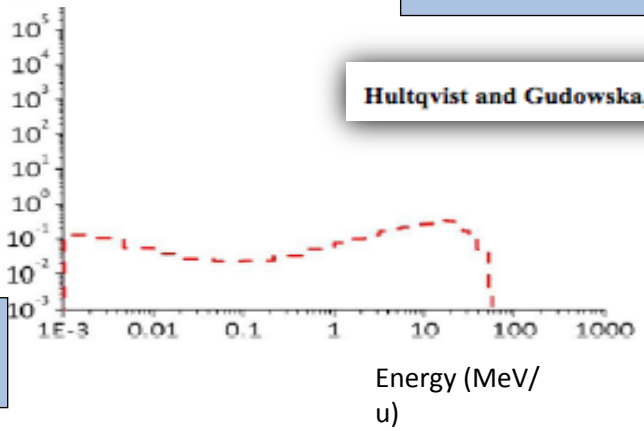
All particles produced and transported

Gonads ~12 cm from target
Particles flux

All particles produced but no neutron transported

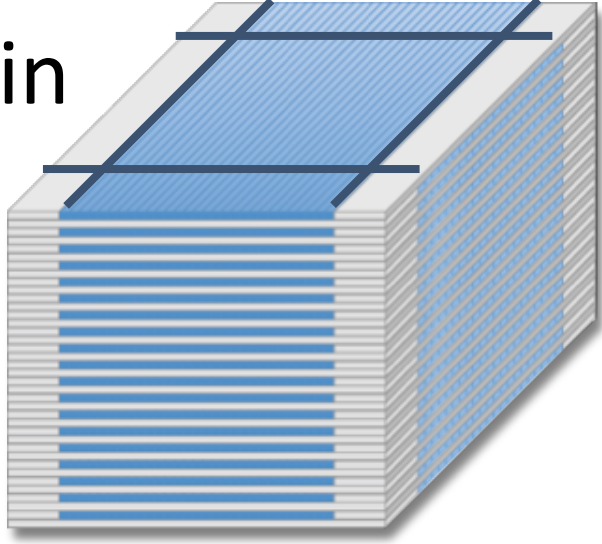


172 MeV Proton beam



Hultqvist and Gudowska, PMB 55,2010

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 layers;

Image Intensifier
- Triple GEM

Read Out
- CMOS

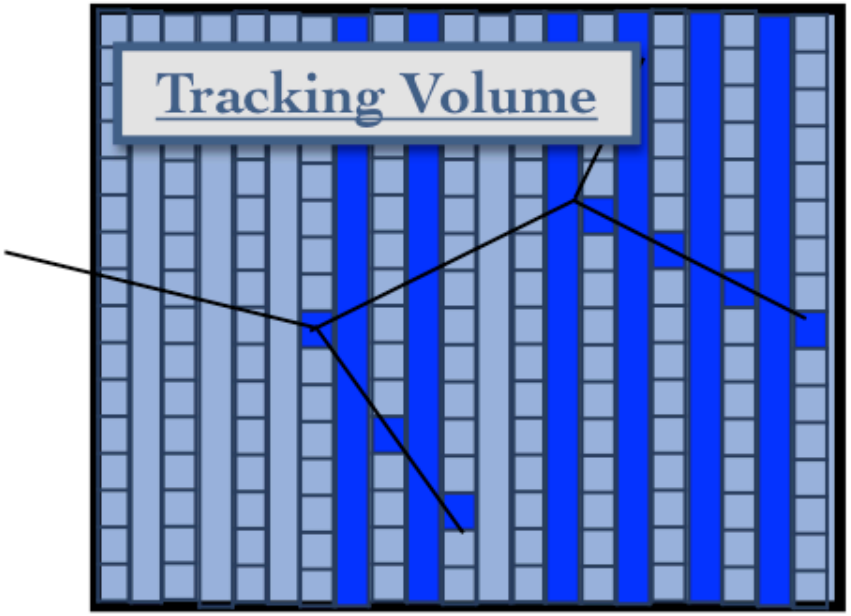
TRACKING the neutron !!

- ✧ Neutron tracking device efficient in the 20:300 MeV range
- ✧ Efficiency in 10^{-2} – 10^{-3} range
- ✧ Funded by SIR 2014+INFN Young Grant 2015

MOnitor for Neutron Dose for hadrOntherapy

JINST M.Marafini et al 2015

Tracking Detector



Plastic Scintillator

- 20 x 20 x 20 cm^3;
- scintillating fibres 250 μm;
- 800 squared fibres per layer;
- x-y layer orientation;

Neutron

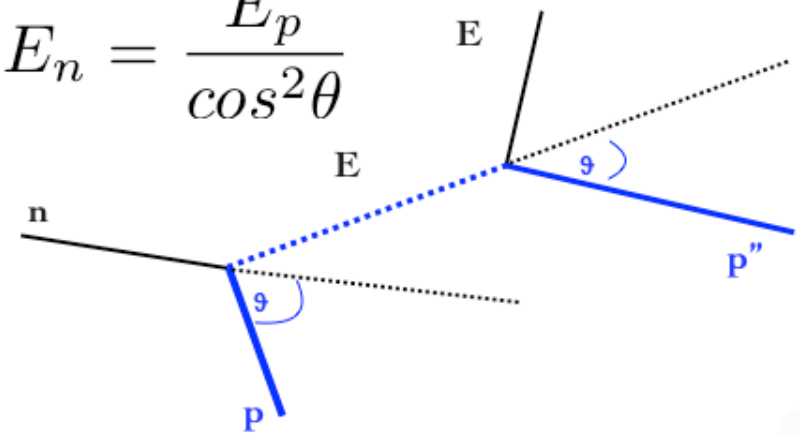
- E_{kin}=[20-200] MeV
- Inter. length. ~ 1m

Proton mean path

- E_{kin} = 100 MeV=> 8 cm
- E_{kin} = 10 MeV=> 0.1 cm

Double elastic scattering interaction

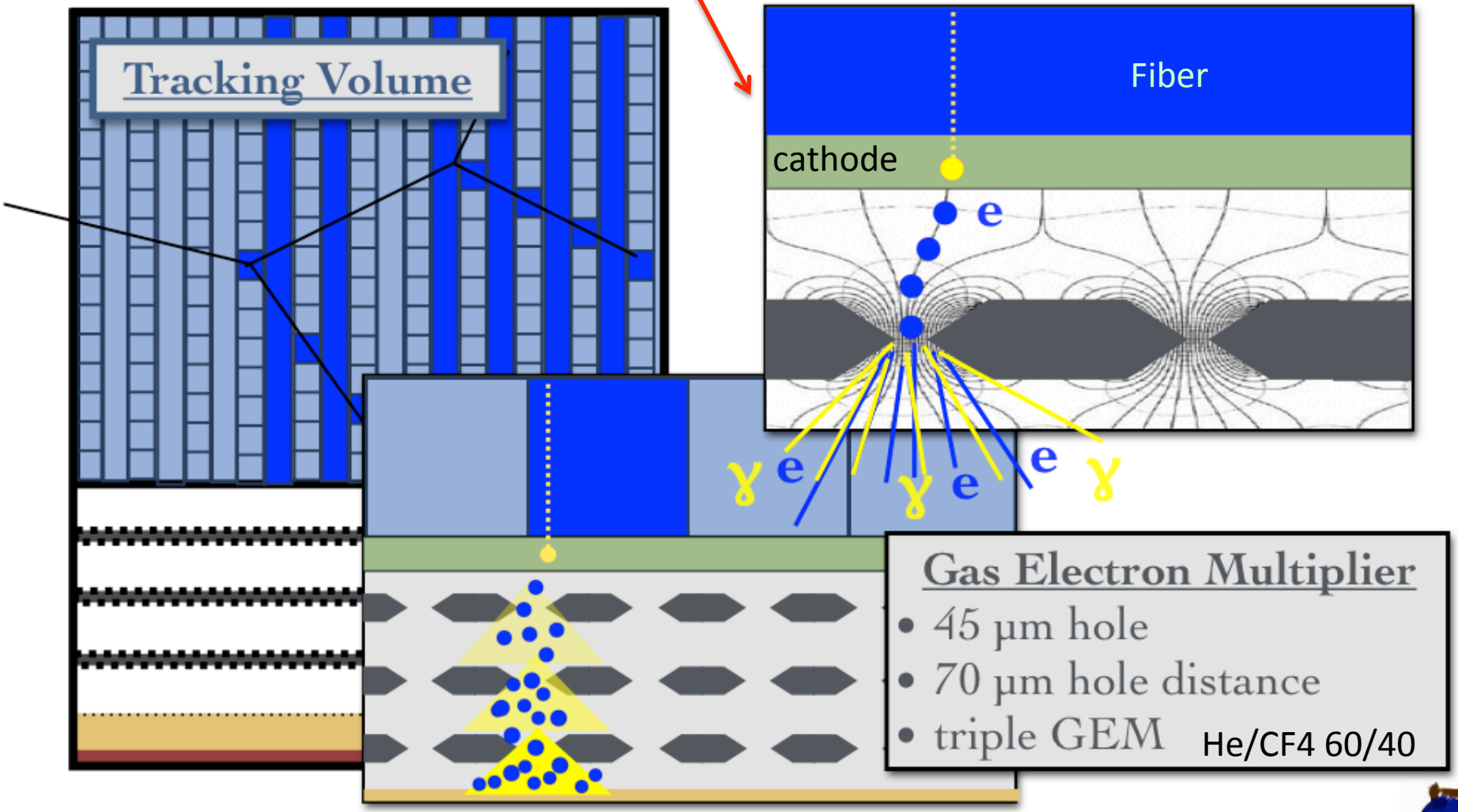
$$E_n = \frac{E_p}{cos^2\theta}$$



MOnitor for Neutron Dose for hadrOntherapy

Cathode on first GEM layer in trasmission/reflection geometry: collaboration with RD51 group of CERN

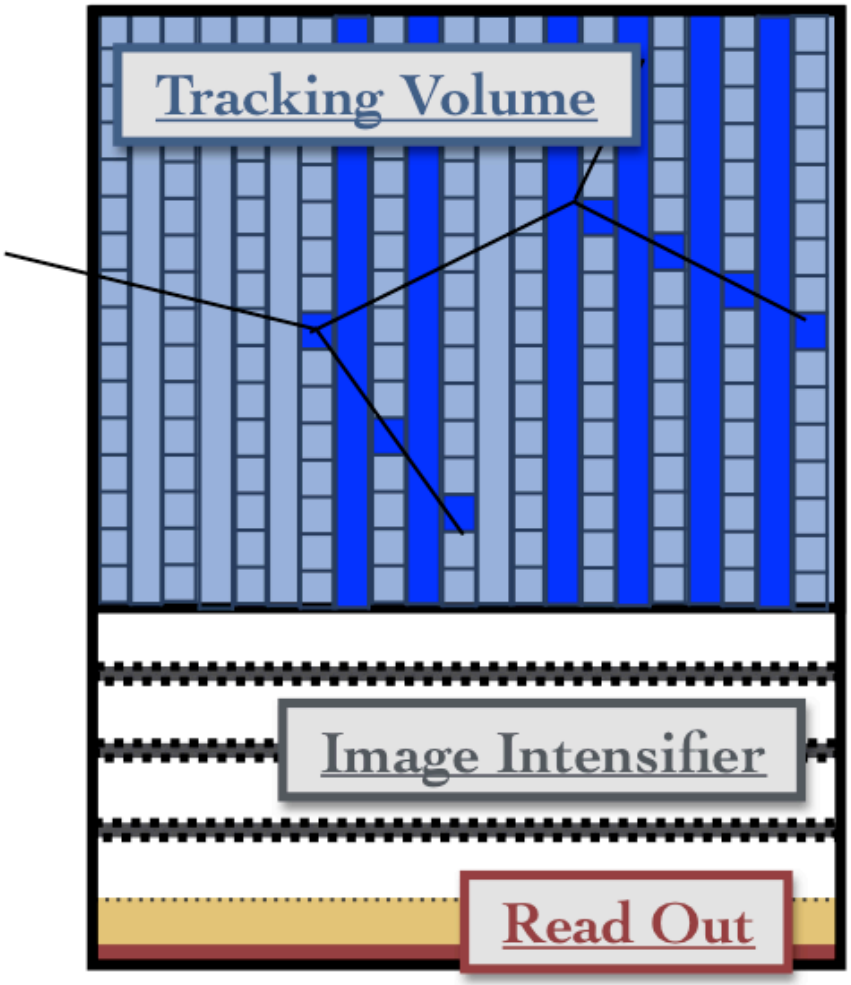
Image Intensifier

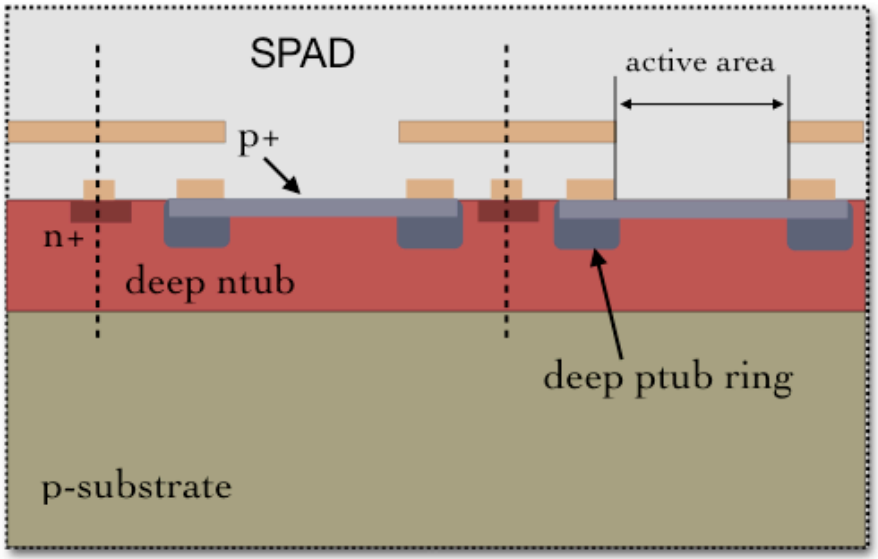


MOnitor for Neutron Dose for hadrOntherapy

The photon produced by the GEM avalanche are transmitted to a CMOS light sensor

Photon ReadOut





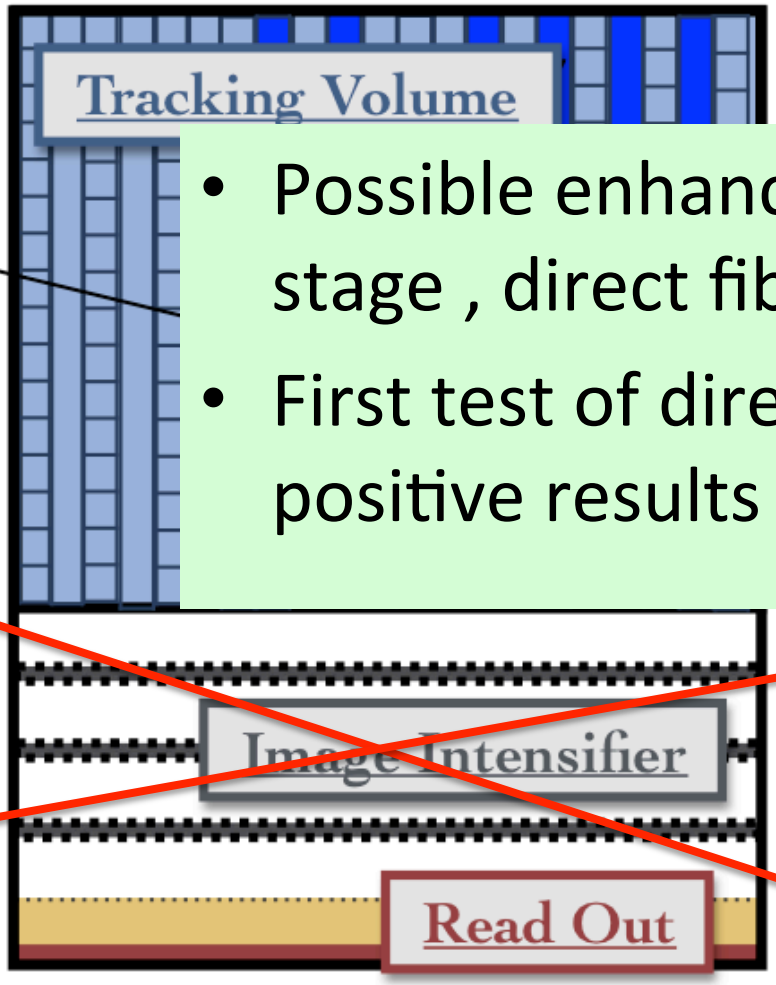
CMOS Single Photon Avalanche Diode (SPAD) array

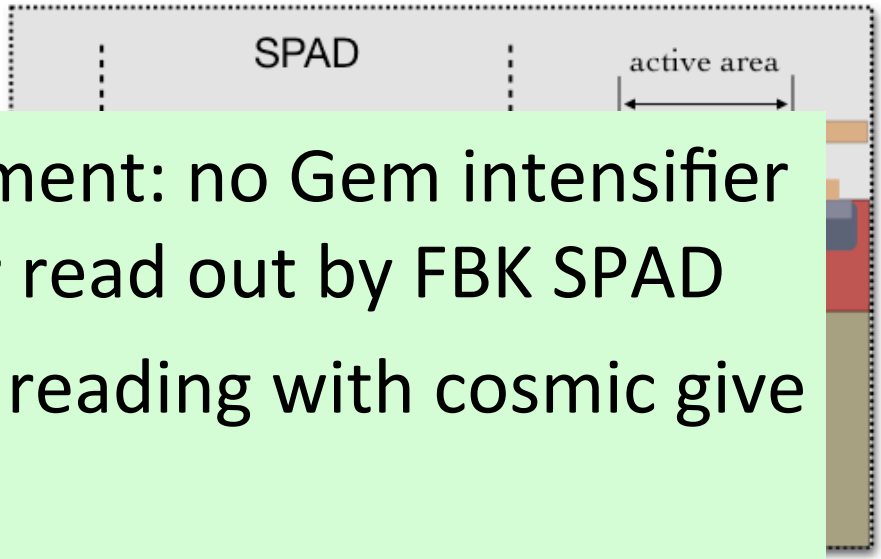
Developments with FBK

* Fondazione Bruno Kessler
http://www.spadnet.eu/

MOnitor for Neutron Dose for hadrOntherapy

Photon ReadOut





- Possible enhancement: no Gem intensifier stage , direct fiber read out by FBK SPAD
- First test of direct reading with cosmic give positive results

CMOS Single Photon Avalanche Diode (SPAD) array

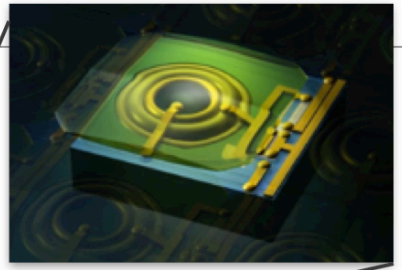
Developments with FBK

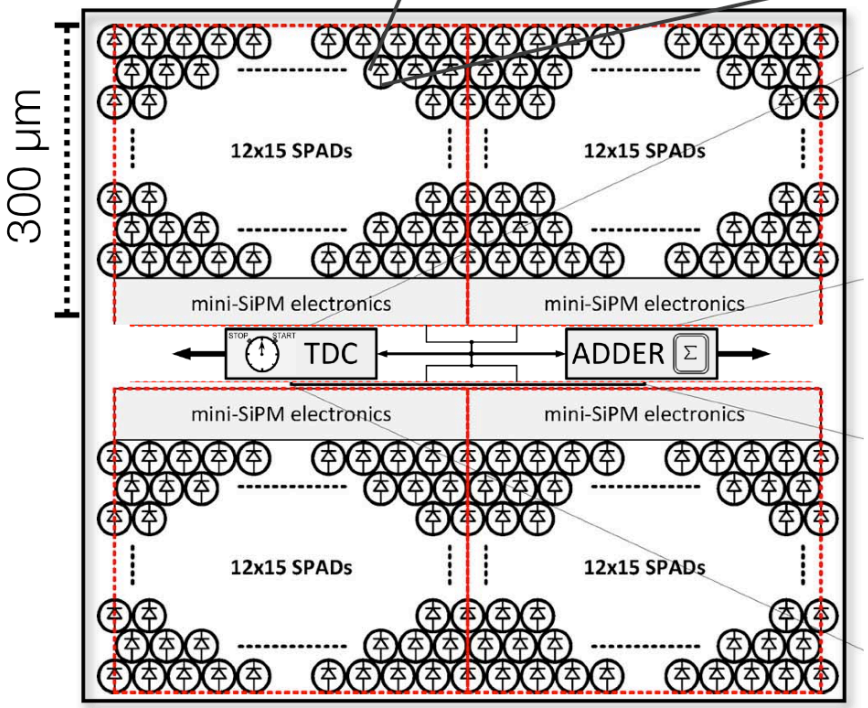
* Fondazione Bruno Kessler
http://www.spadnet.eu/

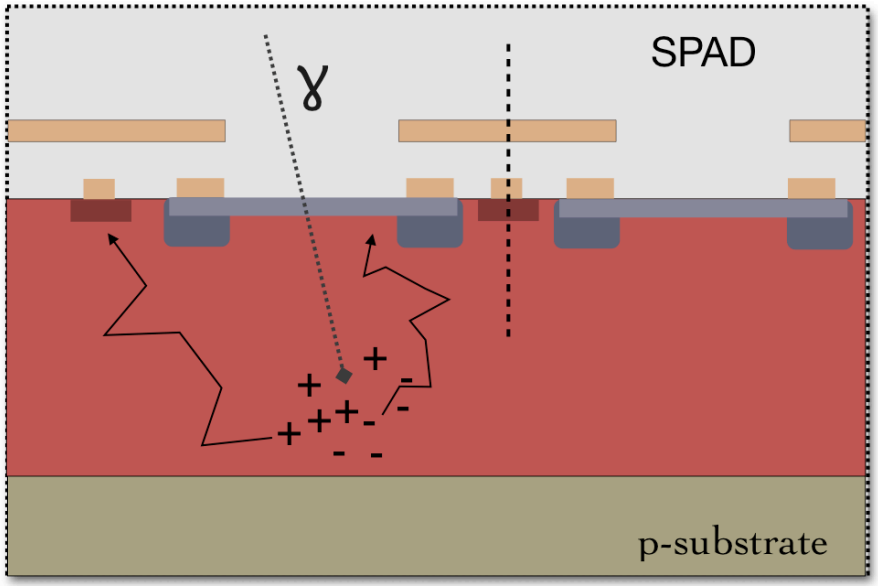
MOnitor for Neutron Dose for hadrOntherapy

Photon ReadOut

SPAD Matrix prototype







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

Sampling of the number of µSPAD fired at 10 ns frequency

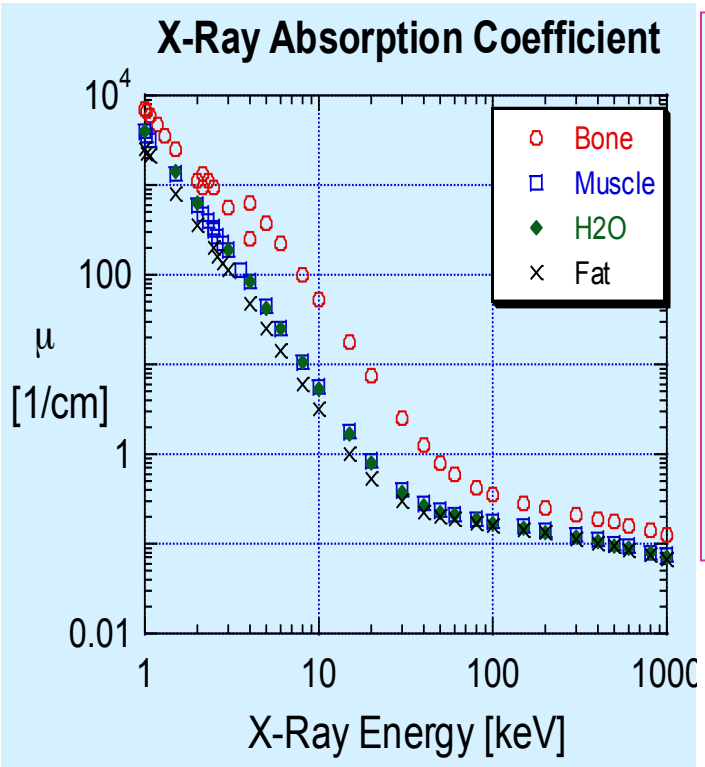
Optimized for LYSO signal, to be adapted to the plastic scintillator signal time

The Read out pixel will match the fiber section

proton based imaging system (pCT)

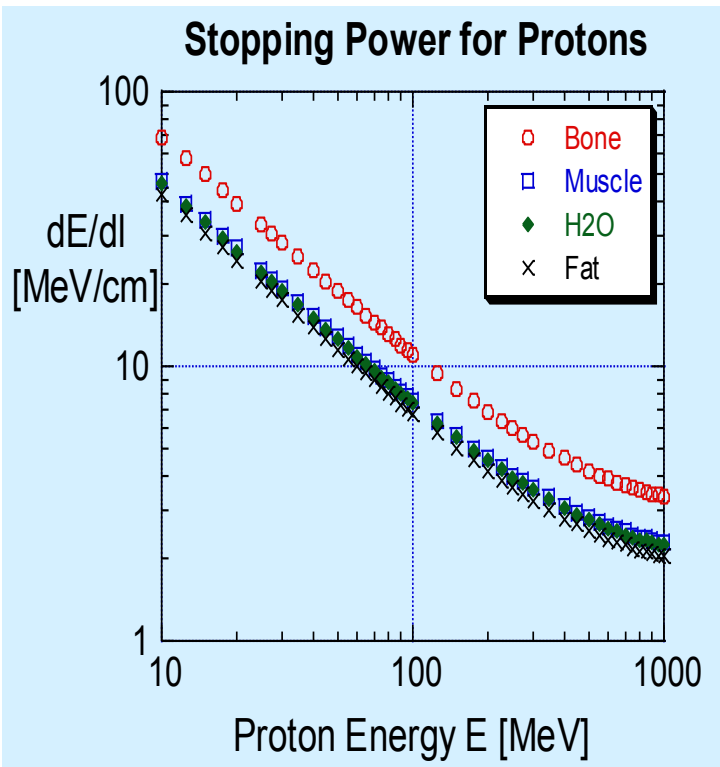
Conventional X ray tomographies taken before the proton treatment session and in a different setup. Precision improvement if positioning and treatment could be done in one go

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



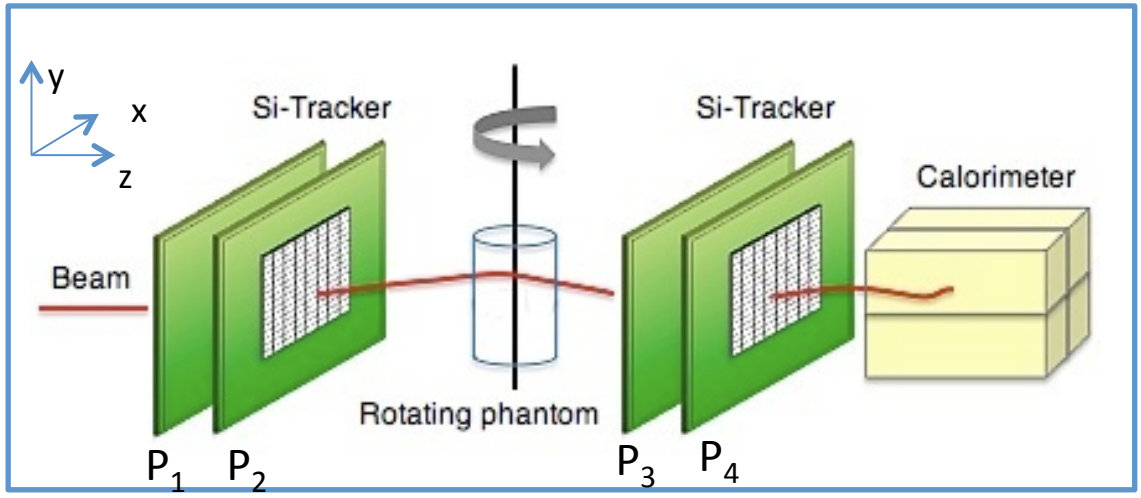
Proton CT:

- replaces X-ray absorption with proton energy loss
- reconstruct mass density (ρ) distribution instead of electron distribution



PCT principle and setup

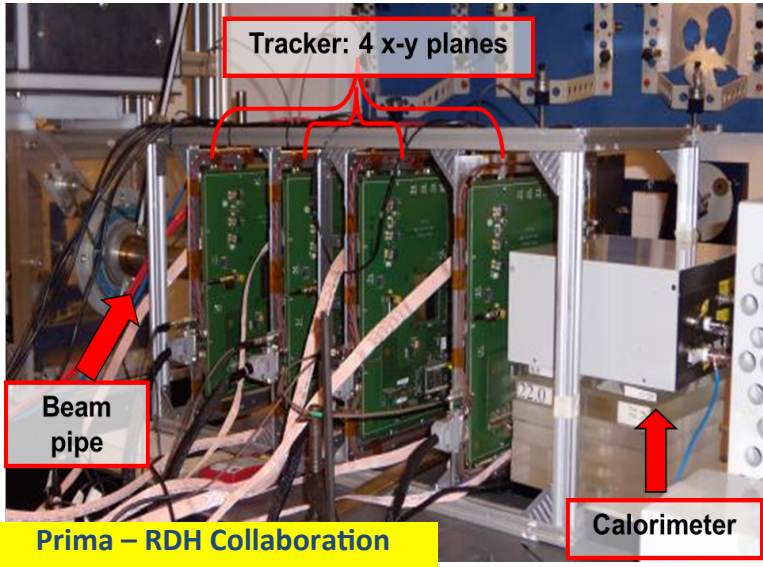
- Single particle proton tracking: **silicon strip detectors** → MLP
- Residual energy measurement: **crystal calorimeter** → energy loss



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

A set of single event information can be processed by appropriate reconstruction algorithms (FBP, ART) to produce tomographic images.

No particular request on track or calo system…

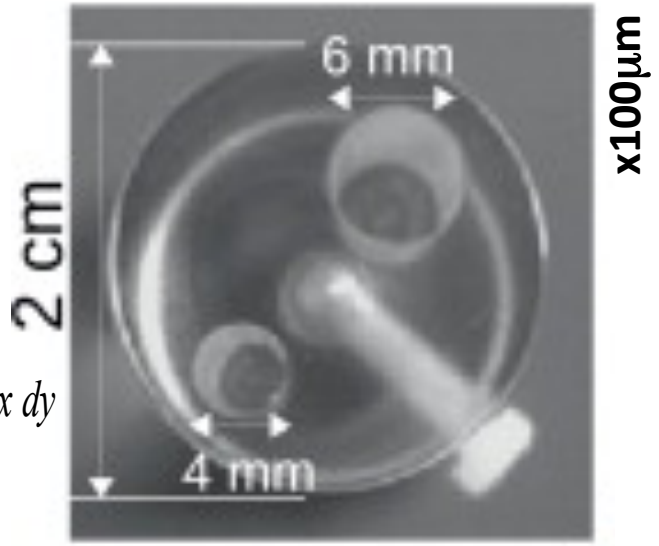


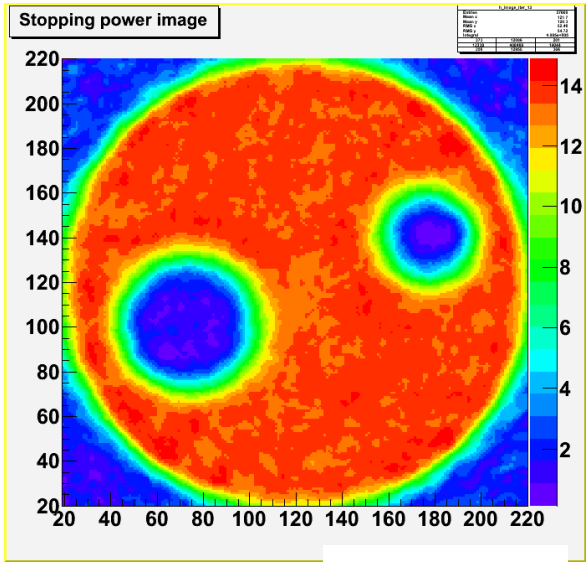
Proof of principle at 60 MeV LNS p beam

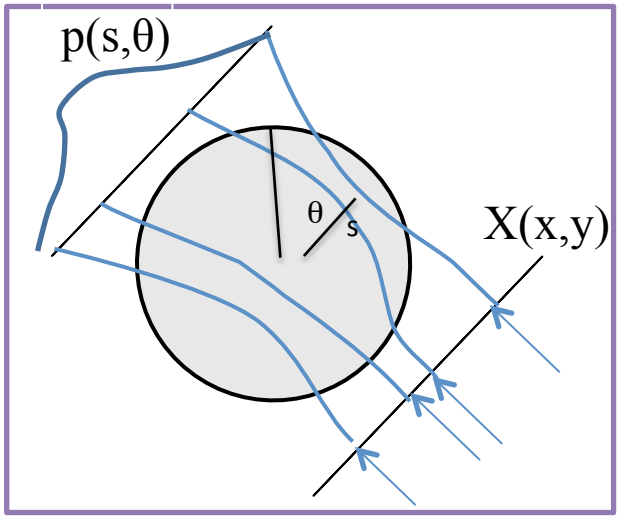
Reconstruction of PMMA phantom with Filtered Back Projection as seed for Algebraic Reconstruction Technique. Using Modified Radon Transform:

$$p(s,\theta) = \int_{-\infty}^{+\infty}\int X(x,y)\, F(s + x\,sen\theta - y\cos\theta)\, dx\, dy$$

Vanzi E. *et al.,* Nucl. Instr. and Meth. **A 730** (2013)







pCT reconstruction after patient positioning for treatment and Treatment Planning System recalculation with pCT data need massive CPU power -> real challenge of pCT on the fly

GPU technology needed (INFN-RIDOS-FRED)

Conclusions

- ✓ Particle Therapy needs a wide spectrum, (somewhat incoherent) R&D activity to survive the IMRT competition-> plenty of space for iniziative.
- ✓ Not straighforward need for bleeding edge technology -> different environment wrt INFN usual one , driving forse is clinical practice!!
- ✓ Software will play a equal (higher?) role in Particle Therapy R&D
- ✓ INFN has a world leading role in PT R&D, and a very active community, and such an investment should be preserved
- ✓ No time to mention machine development, possibility of 4D Treatment, Radiobiology studies, GPU software migrations, etc etc . It's my fault, sorry..

IFD2015

INFN Workshop on Future Detectors

16-18 December 2015 - Torino - Italy

Thanks

CREDITS

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

P.Cerello, G.Bisogni, G. Battistoni, R.Sacchi, M.Bruzzi, M.Marafini, M.Durante

& many others…

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:

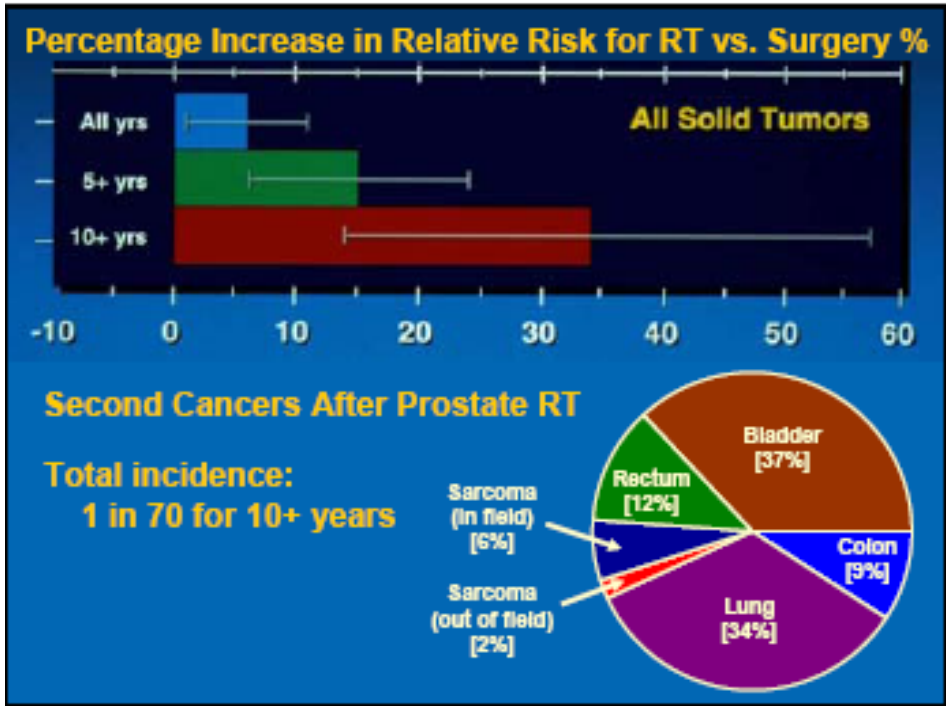
- Continuing lifestyle
- Genetic predisposition
- Treatment of the primary cancer

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

The range verification problem

AAPM, August 2012

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

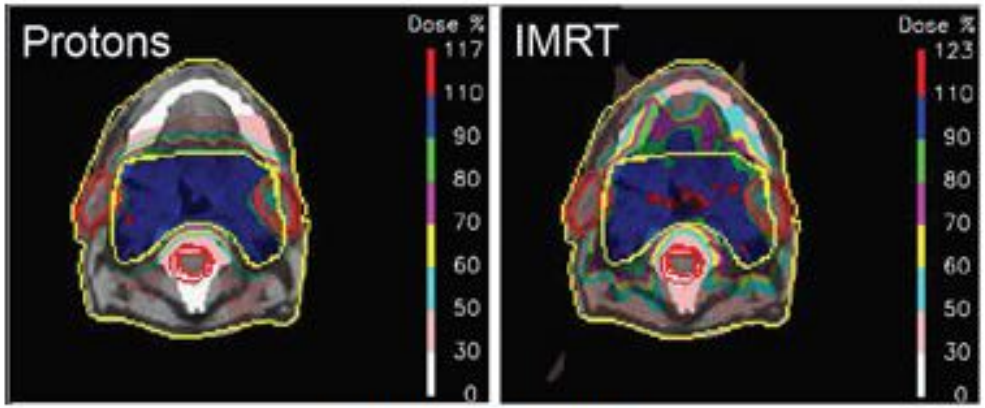
- 35 % unproven clinical advantage of lower integral dose
- 33 % range uncertainties
- 19 % never become a mainstream treatment option

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?

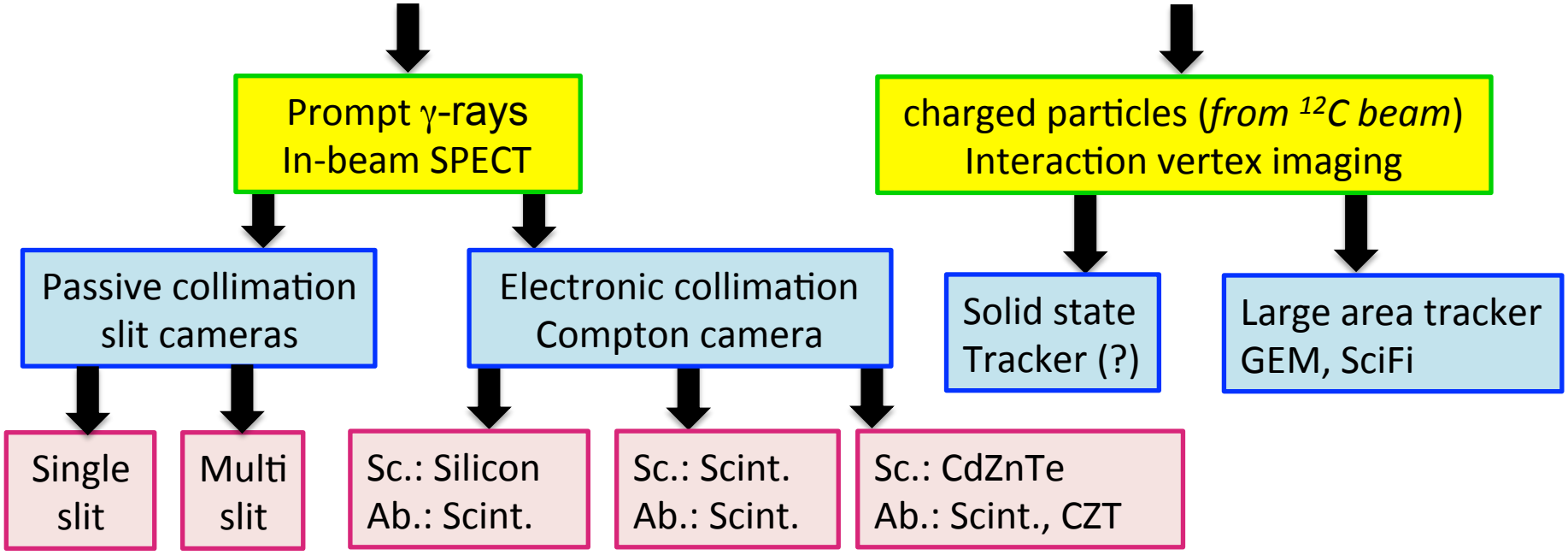


Protons versus IMRT

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

Non PET techniques: simplified overview

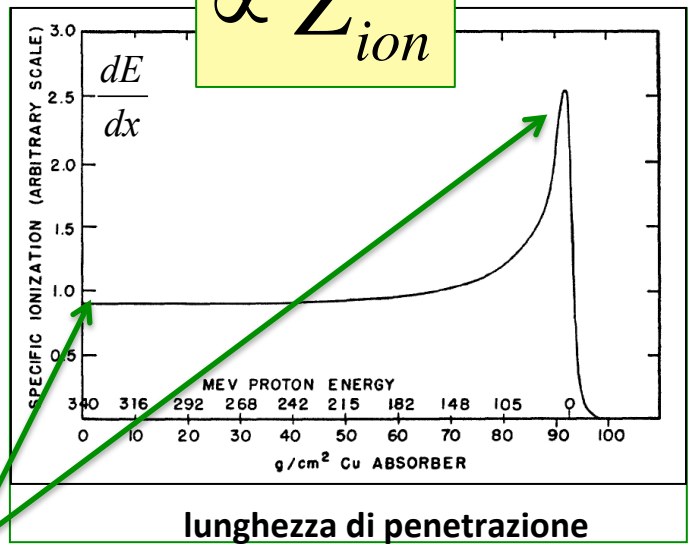
- Several different solutions under study
- Unique clinical solution not yet established
- Suitable detectors not commercially available
- Impressive number of physicists/institutions at work



Particle Therapy vs Particle Physics point of view

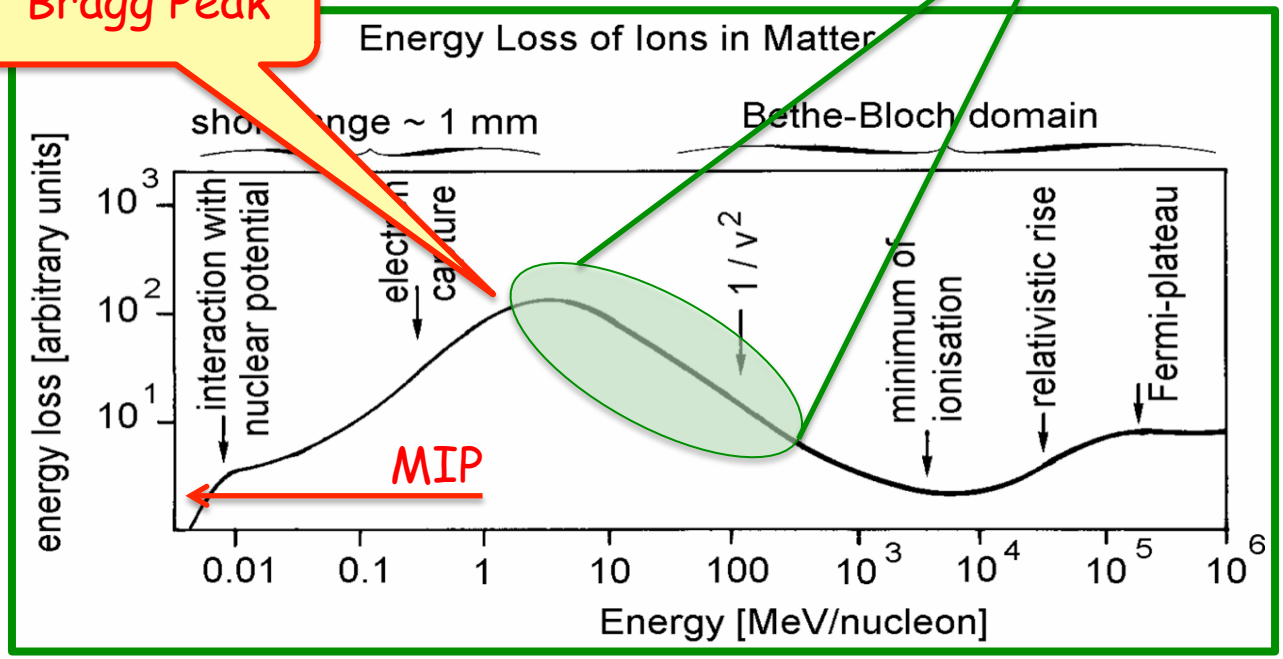
The release of energy by charge particles has very attractive, features… why not to use them?

$$\propto Z_{ion}^2$$



lunghezza di penetrazione

Bragg Peak



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

Mostly proton, few ^{12}C beams.

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

Charge Collection Efficiency in ICs

Inefficiency in charge collection originates from the charge recombination in the gas

Initial and columnar recombination

- recombination between charges generated along each track
- independent on dose rate
- can be corrected for by dosimetric calibration of the chambers
- described by Jaffe's theory

Volume recombination

- recombination between charges generated by neighbouring tracks
- depends on the dose rate, the quantity one wants to measure !
- several parametrizations, (Boag, Wilson, Townsend…)
- Typically
  - increases with the ionization density in the gas
  - decreases with the increase of the ratio **$E/d=V^2/d$**
    (d = distance between the electrodes, V= voltage)

→ serious issue for high intensity pulsed beams

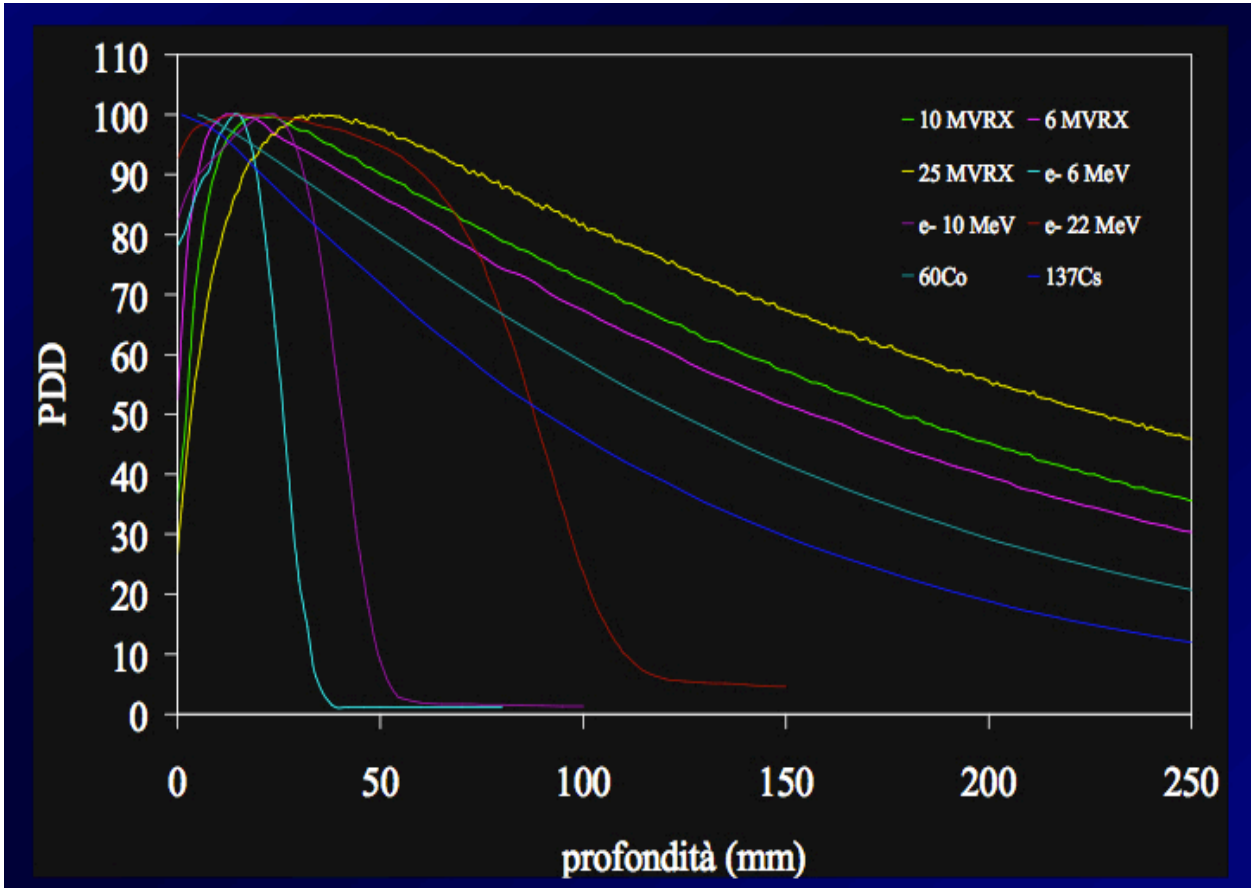
The conventional (photon based) RT

The photon (and e^-) beams are the most common in RT. They are not so expensive, small, and reliable.

It's a pity that the energy release shape is not so suitable to release dose in a deep tumor (remember the exponentian attenuation law..?).

But….

Dose-depth relation for different ionizing radiation: radiotherapy photon and electron beam, ^{60}Co source



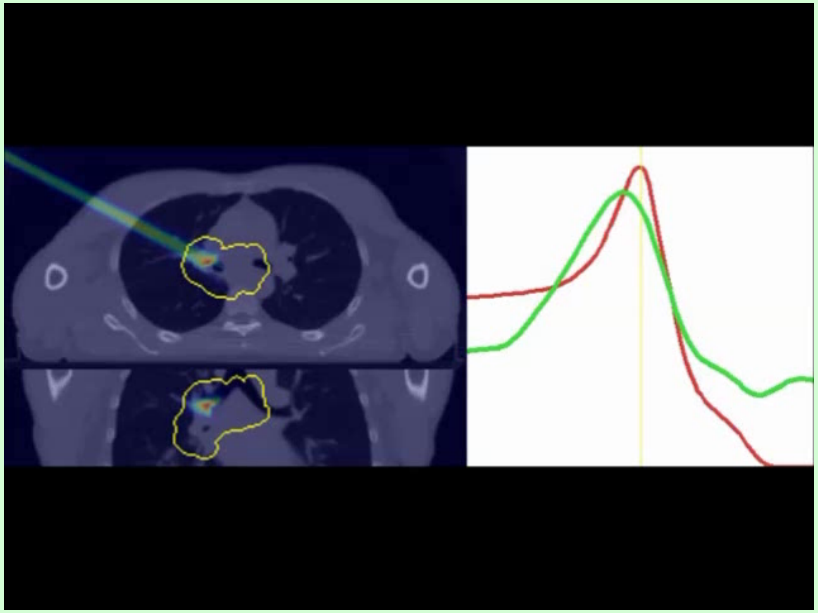
Spec's of particle therapy monitor

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:

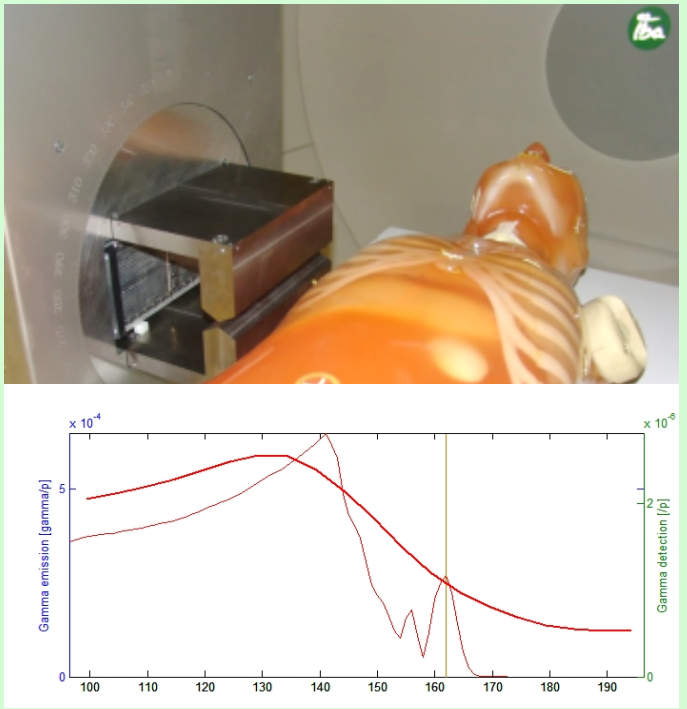
- Measure shape and (if possible) the absolute value of dose release to check the agreement between the planned target volume and the actually irradiated volume
- Measurements and feed-back should be provided during the treatment (in-beam). Even better if the monitor response can follow the irradiation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

In-vivo, real-time verification of effective proton range, by measuring the prompt gamma radiation emitted from the nuclear interactions of the protons with patient tissues.

Prompt gamma simulations in 4DCT



Prompt gamma camera prototype



Camera prototype designed and assembled by IBA, partly in the framework of EU projects, with contributions from Politecnico & Xglab spinoff from Milano.

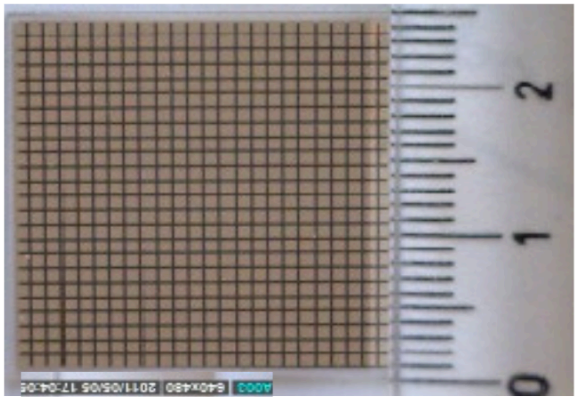
Collaborations and benchmarking against alternative detection methods with U. Lyon and Oncoray-Dresden.

Functional prototype now made available to clinical institutions in view of defining the use-case workflow.

Courtesy IBA

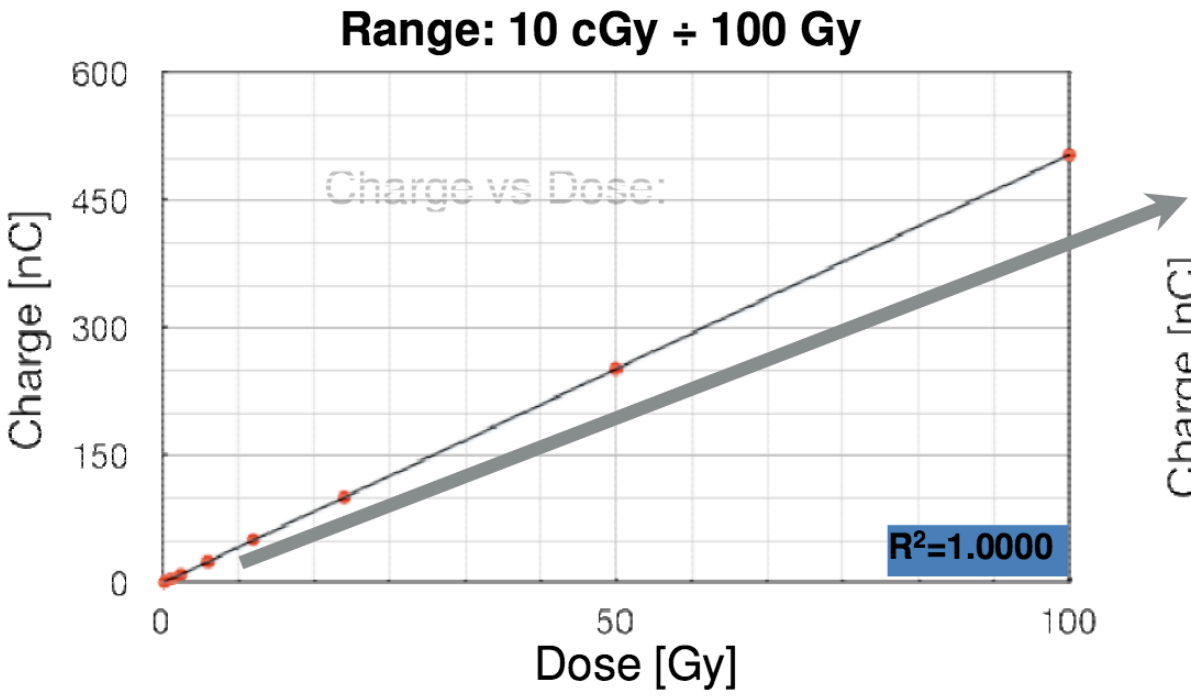
Diamond dosimeters:DiaPix experience

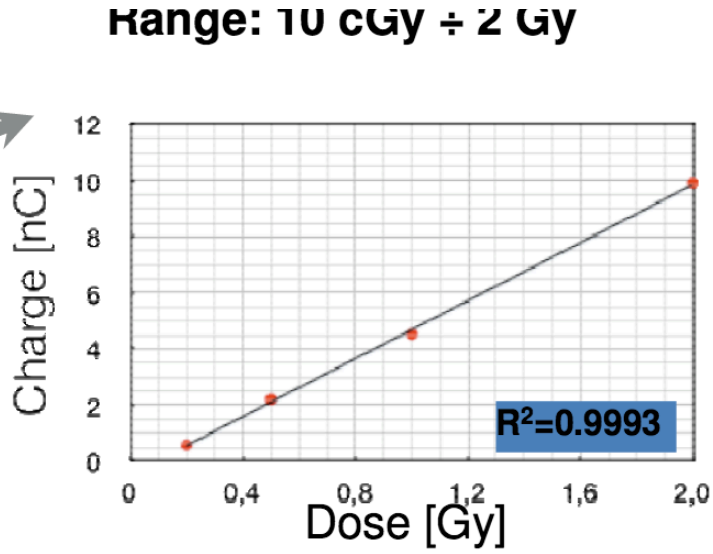
Premium Detector Grade (Diamond Detectors Ltd) polycrystalline diamond, 2.5x2.5cm^2 area, thickness = 300µm. 2D matrix of pixels produced in Florence, XUV lab with Cr/Au evaporation



24x24 matrix,
pixel area 0.8x0.8mm^2

M. Bruzzi et al. JINST 2012

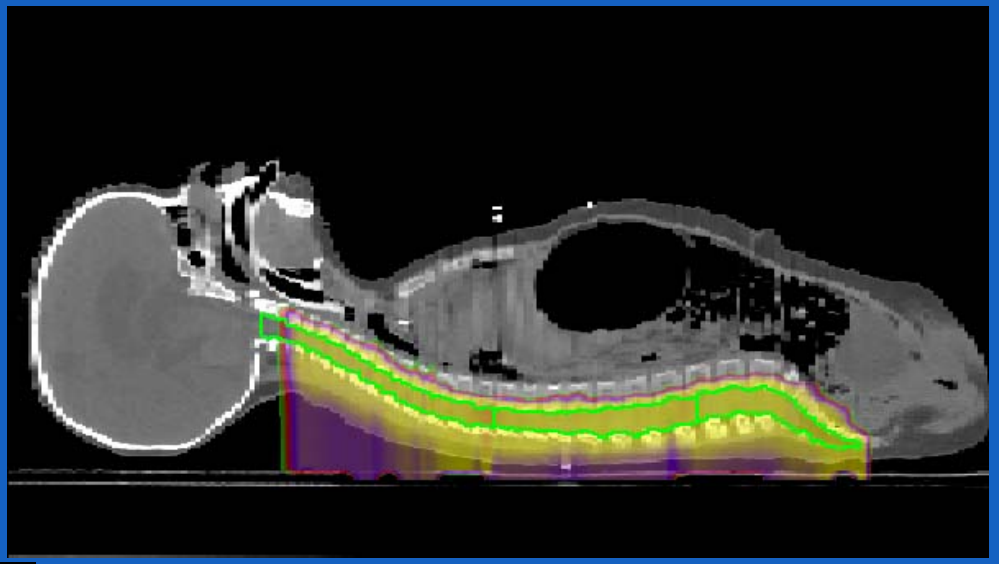




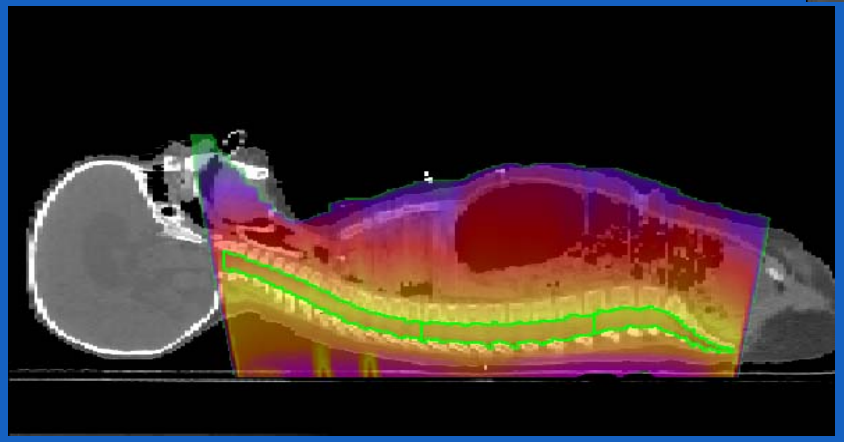
PT and pediatric tumors

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