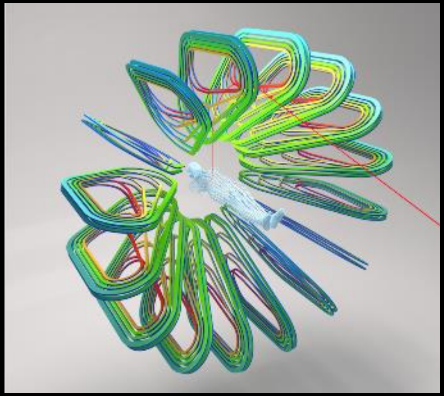
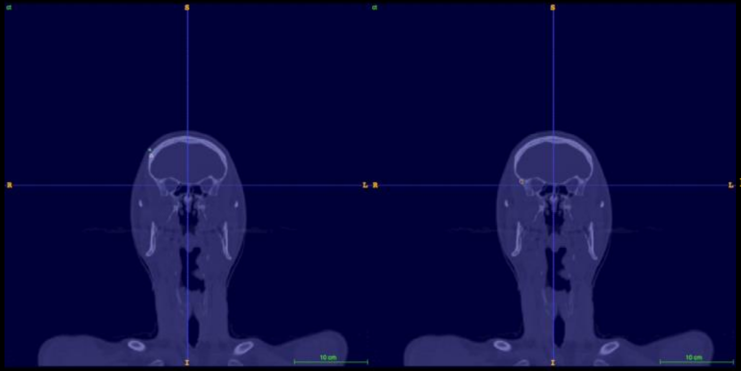
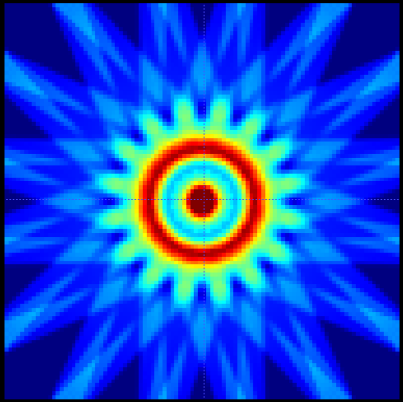




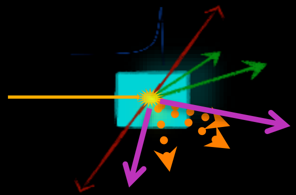


(Online) range monitoring in particle therapy: status and prospects

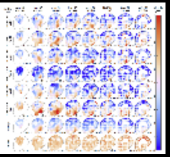
INFN Piergiorgio Cerello (cerello@to.infn.it)

Outline

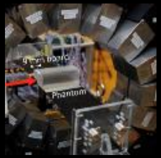
- Range monitoring: why and how?



- Prompt Photons

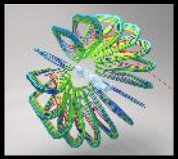


- PET

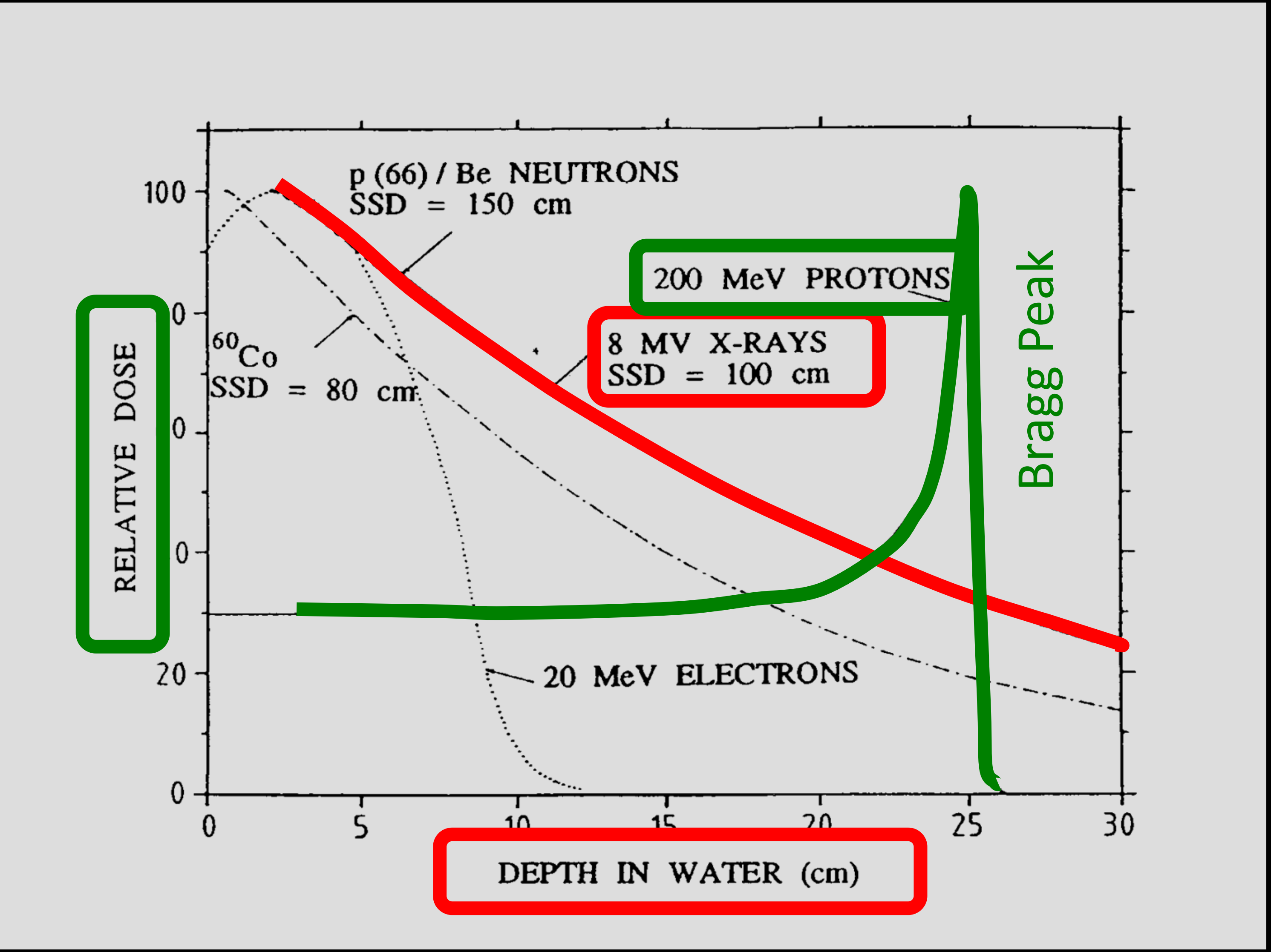


- INSIDE / I3PET

- GaToroid

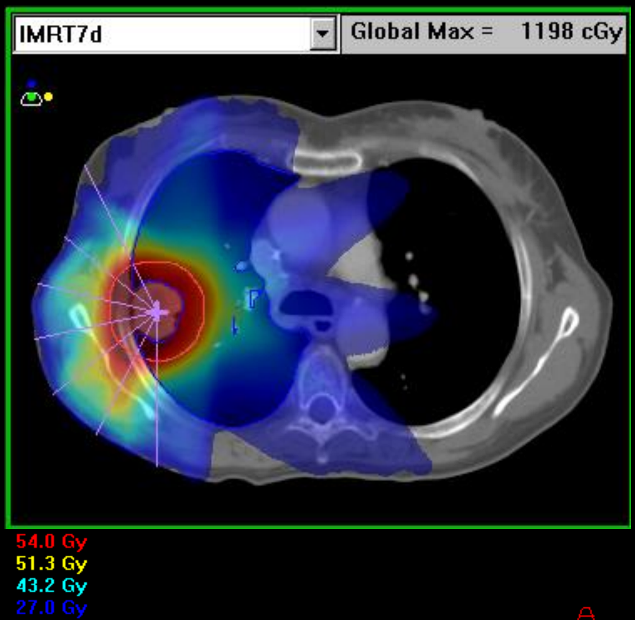


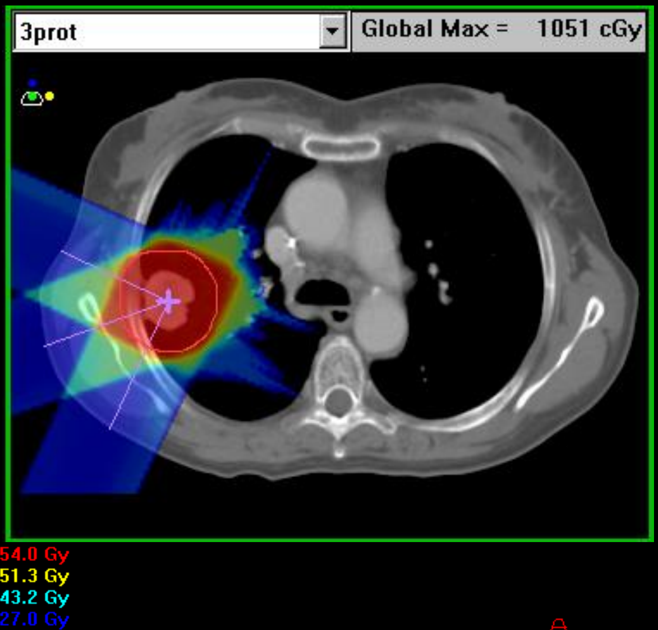
Radiotherapy vs. Particle Therapy



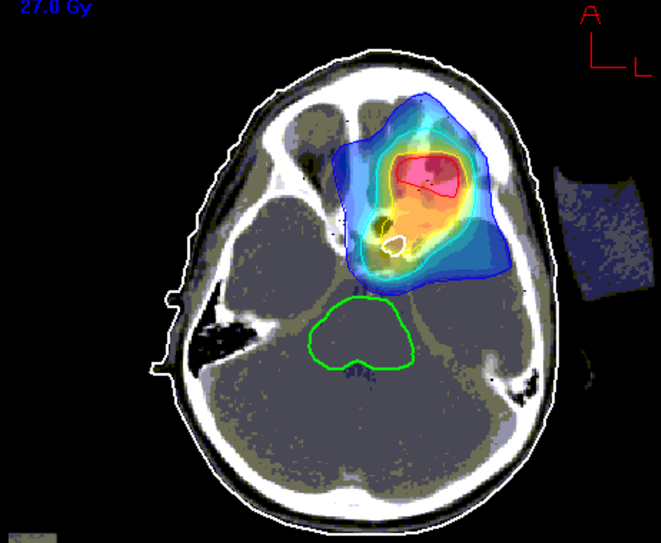
Radiotherapy vs. Particle Therapy

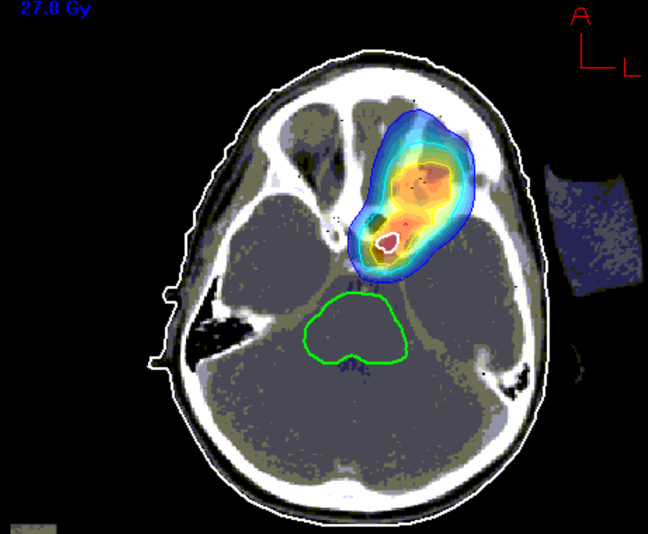
IMRT





Radiosurgery



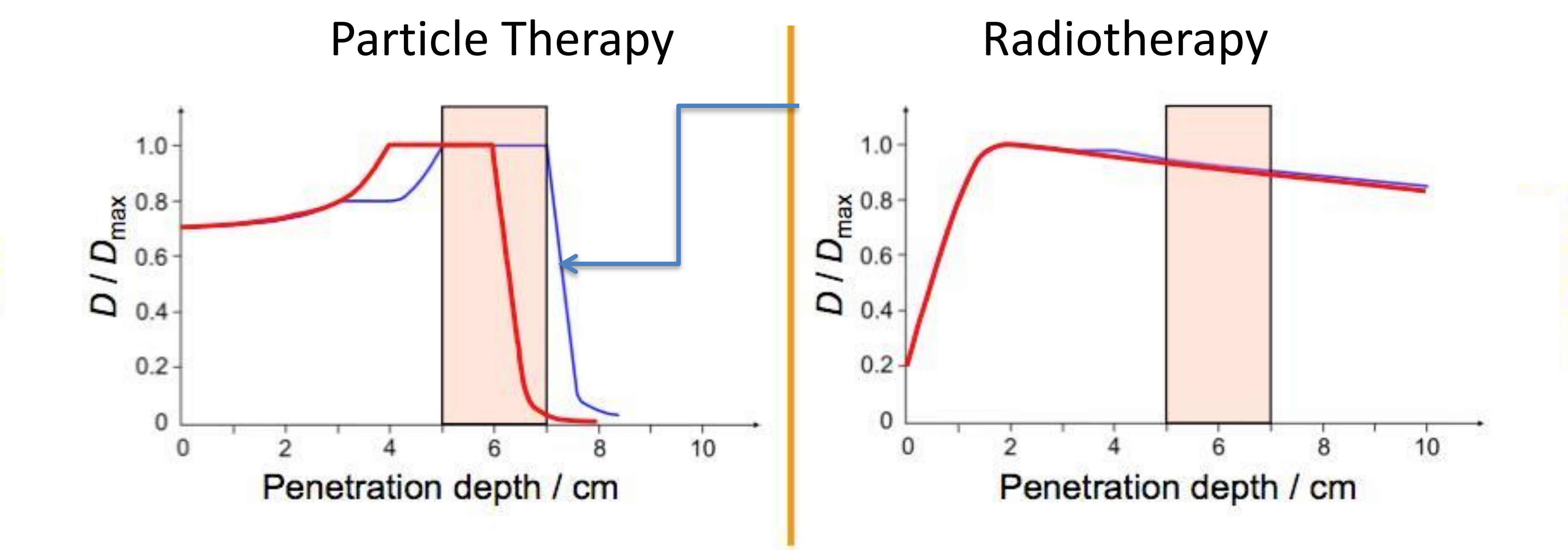


INFN

Range Uncertainties

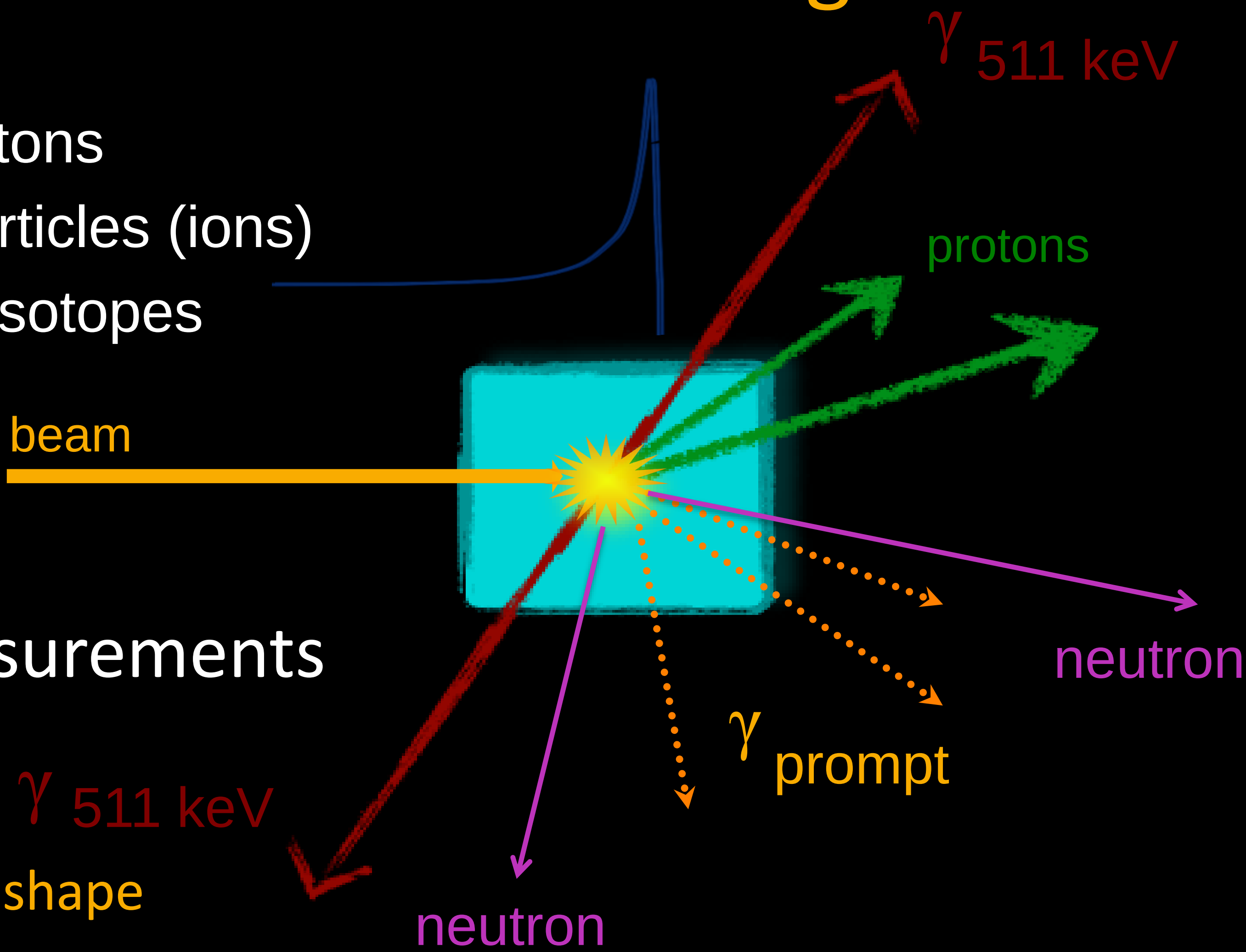
electron density (CT) vs. proton density (pCT)
patient positioning
morphological changes

➔ change in local dose release



How to measure the range?

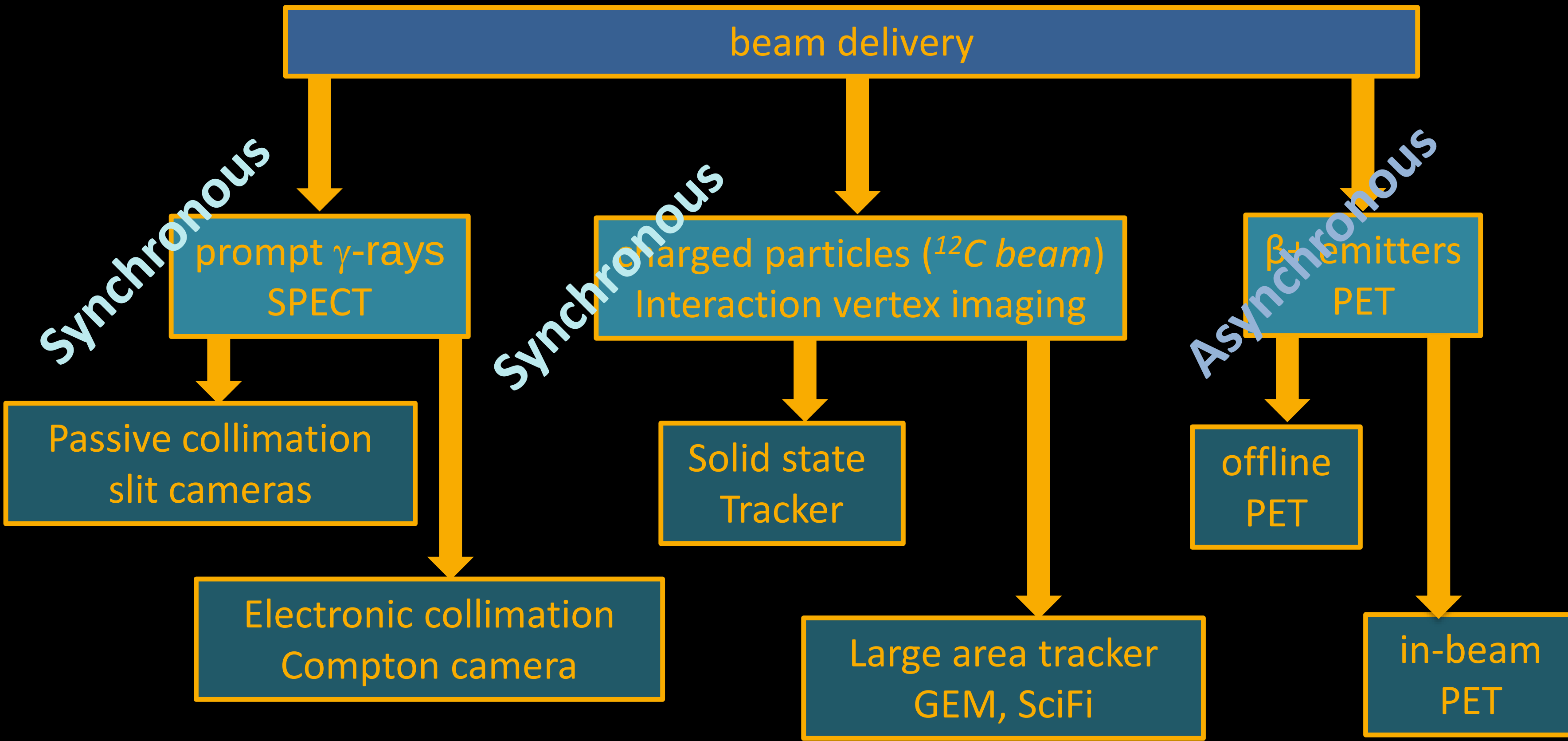
- Prompt photons
- Charged particles (ions)
- β^+ emitting isotopes



All passive,
indirect measurements

- dose release shape
- in-beam feedback
- integration in the treatment work-flow

Detection methods



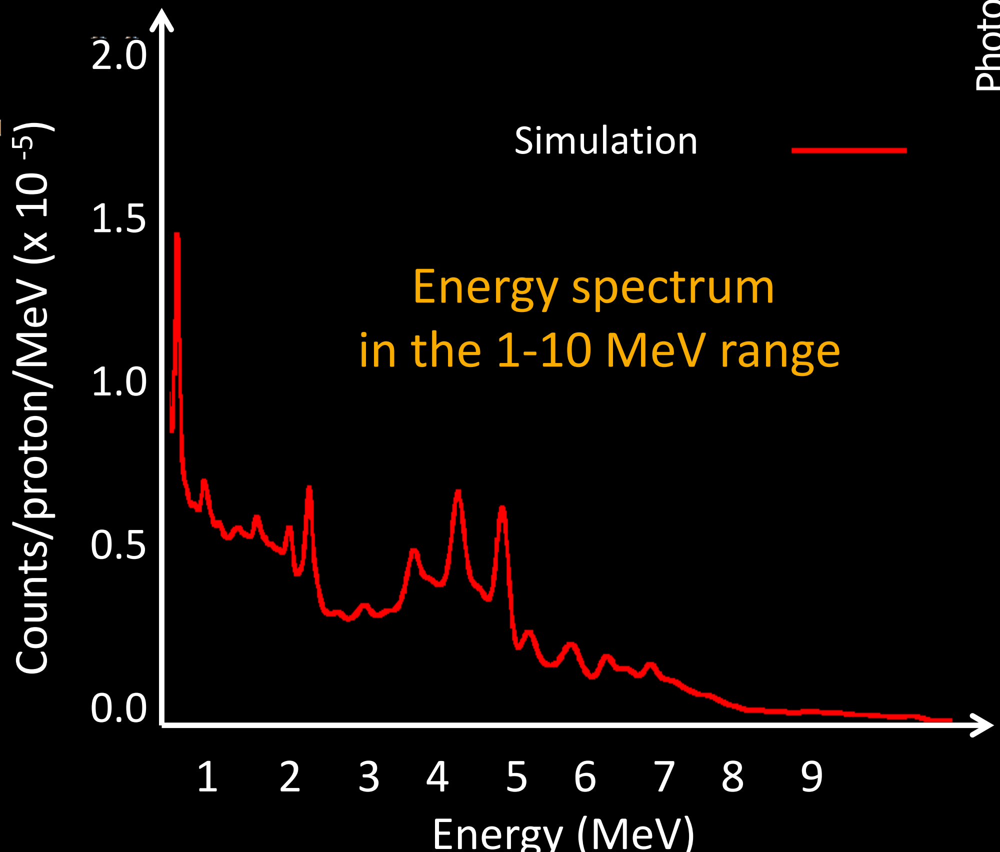
Goal: ~ **1 mm** precision on the Bragg peak depth

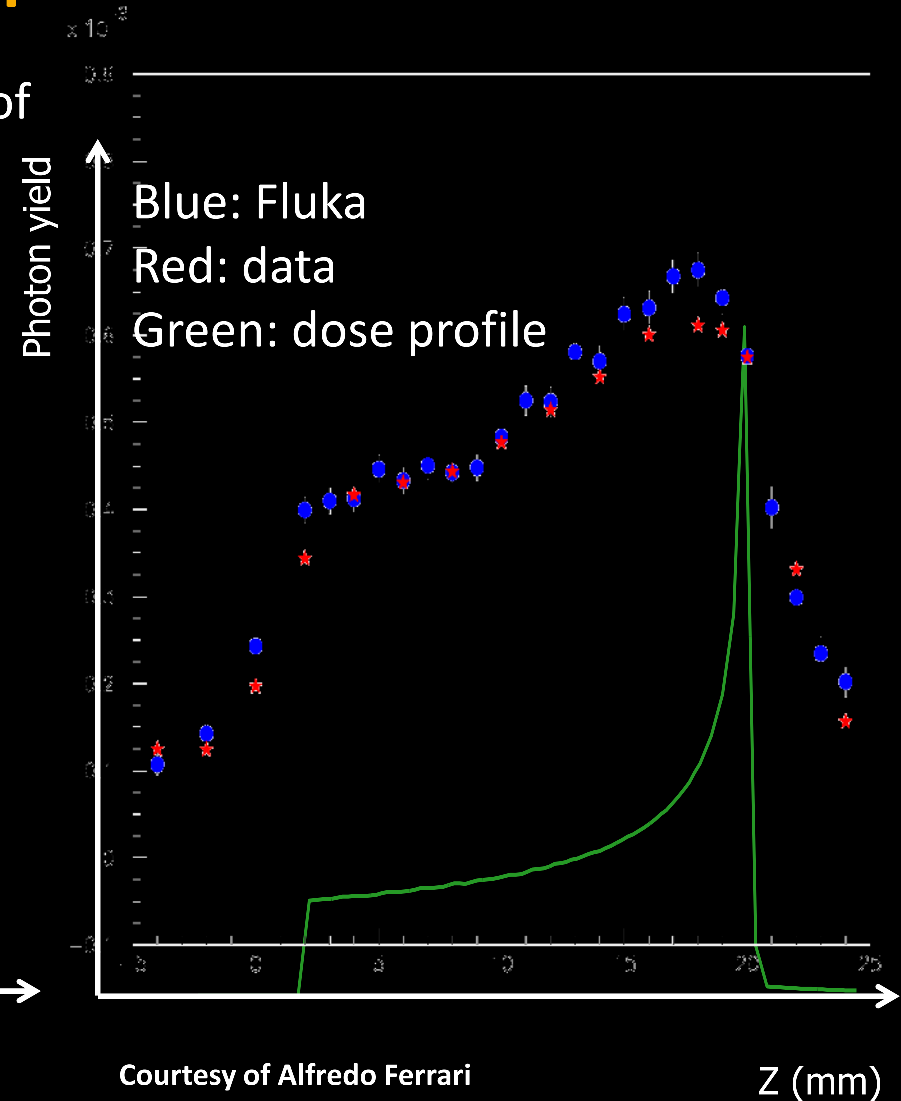
INFN

Prompt photons

Prompt photons

160 MeV proton beam Energy spectrum of prompt photons
(J.Smeets et al., IBA)

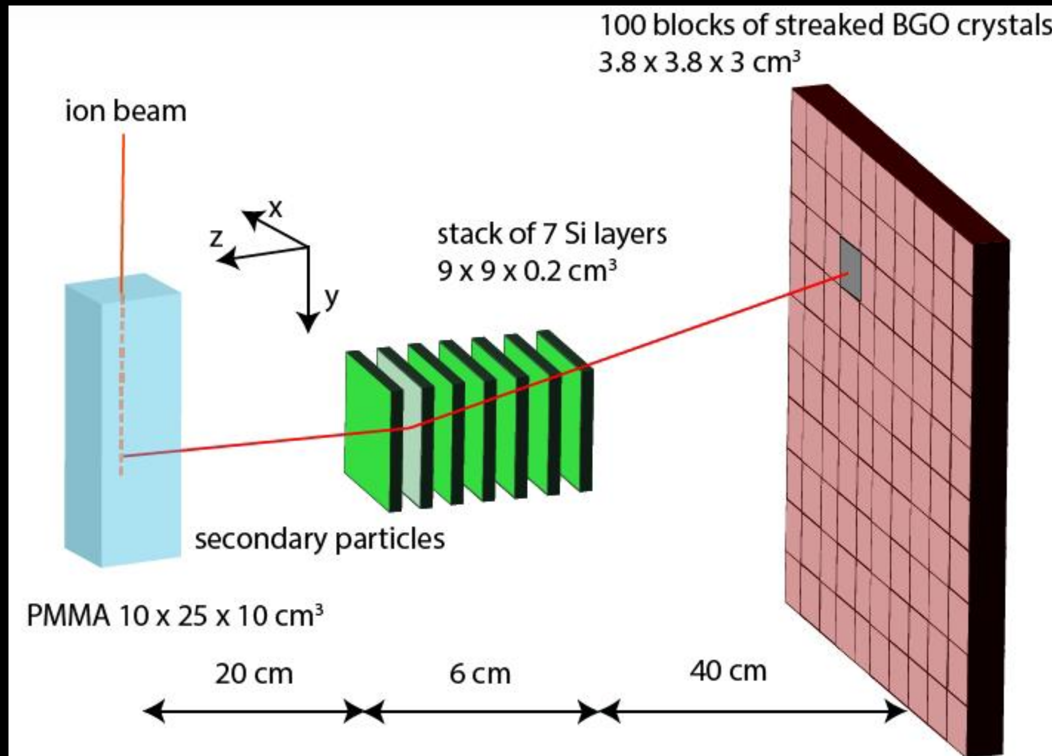




Courtesy of Alfredo Ferrari

Prompt photons: Compton camera

$$\cos\varphi = 1 - m_0 c^2 \left(\frac{1}{E_{\gamma'}} - \frac{1}{E_\gamma} \right)$$



CNRS,
UCB Lyon

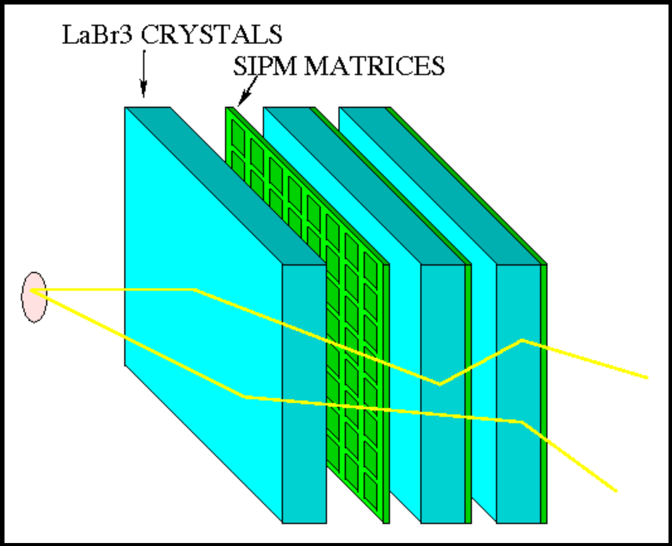
Absorber: Scintillator

- BGO 35 × 38 × 30 mm^3
- 4 PMT

Scatterer: Si strip detectors

- Large size detector bonded on PCB
- Dedicated low-noise ASIC

MACACO II: Compton telescope

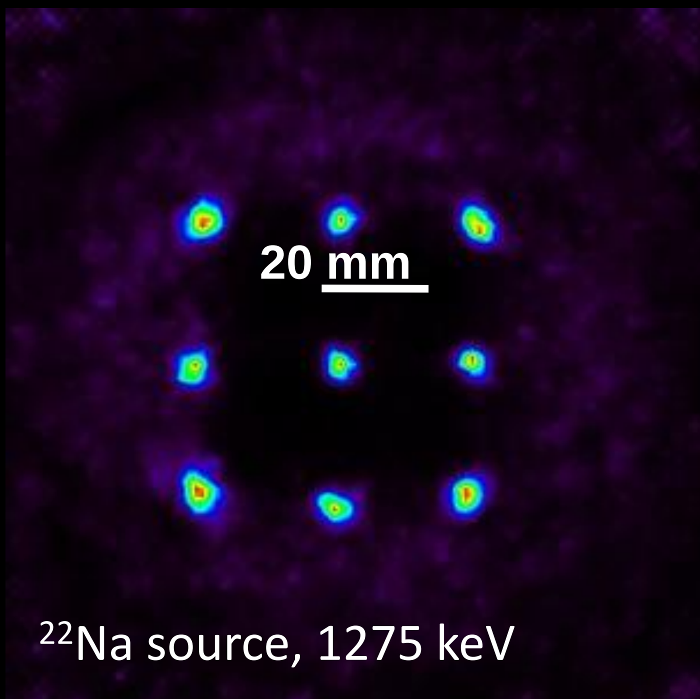


- Combination of :
  - 2 int events (high efficiency)
  - 3 int events (high resolution)

E. Muñoz et al., "Performance evaluation of MACACO: a multilayer Compton camera", Physics in Medicine & Biology, 62 (2017) 18

MACACO II: Compton telescope

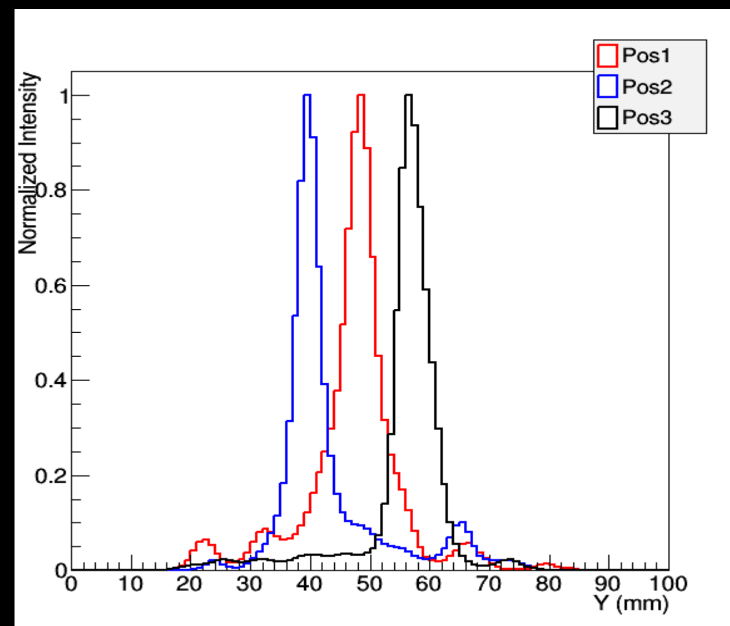
Laboratory tests



E. Muñoz et al., “Performance evaluation of MACACO: a multilayer Compton camera”, Phys. Med. Biol., 62 (2017) 18

Beam tests

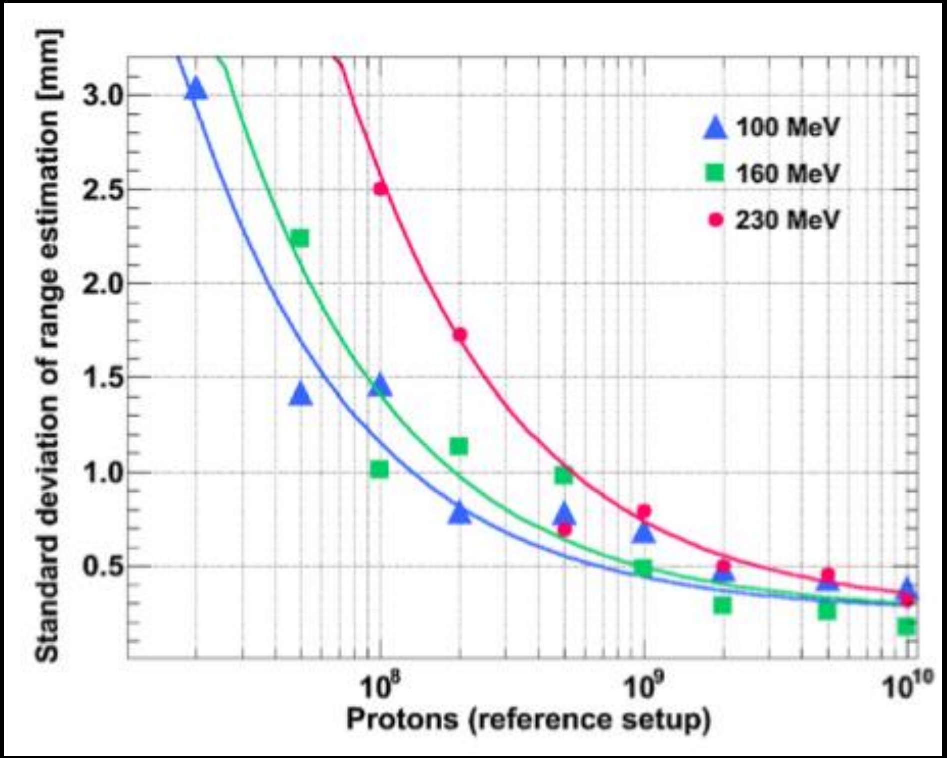
KVI, Groningen
HZDR, Dresden

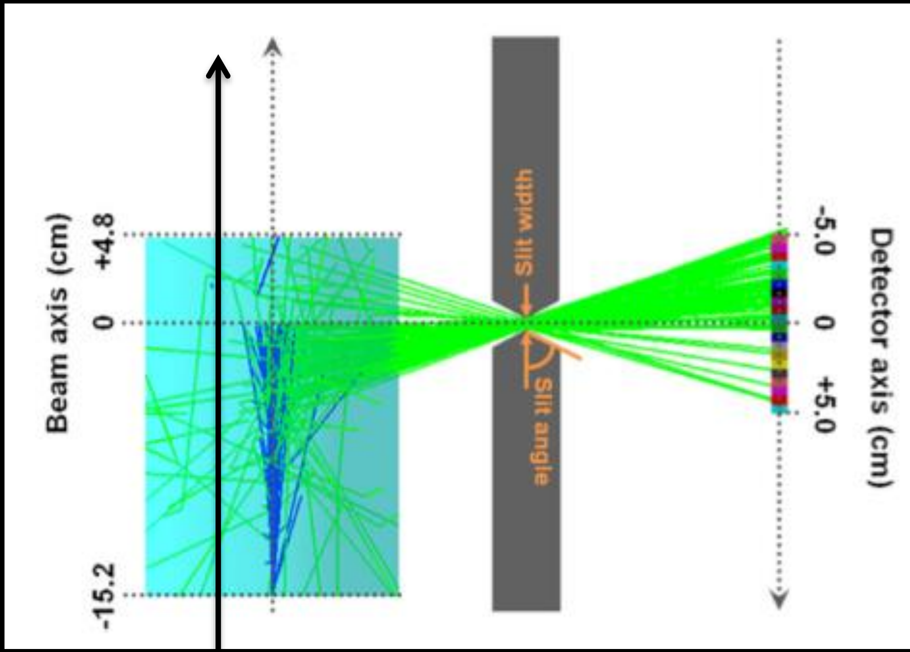


P. Solevi et al, “Performance of MACACO Compton telecope for ion-beam therapy monitoringL: first test with proton beams” Phys. Med. Biol., 61 (2016), 14, 5149-5165

Prompt photons: slit camera (IBA)

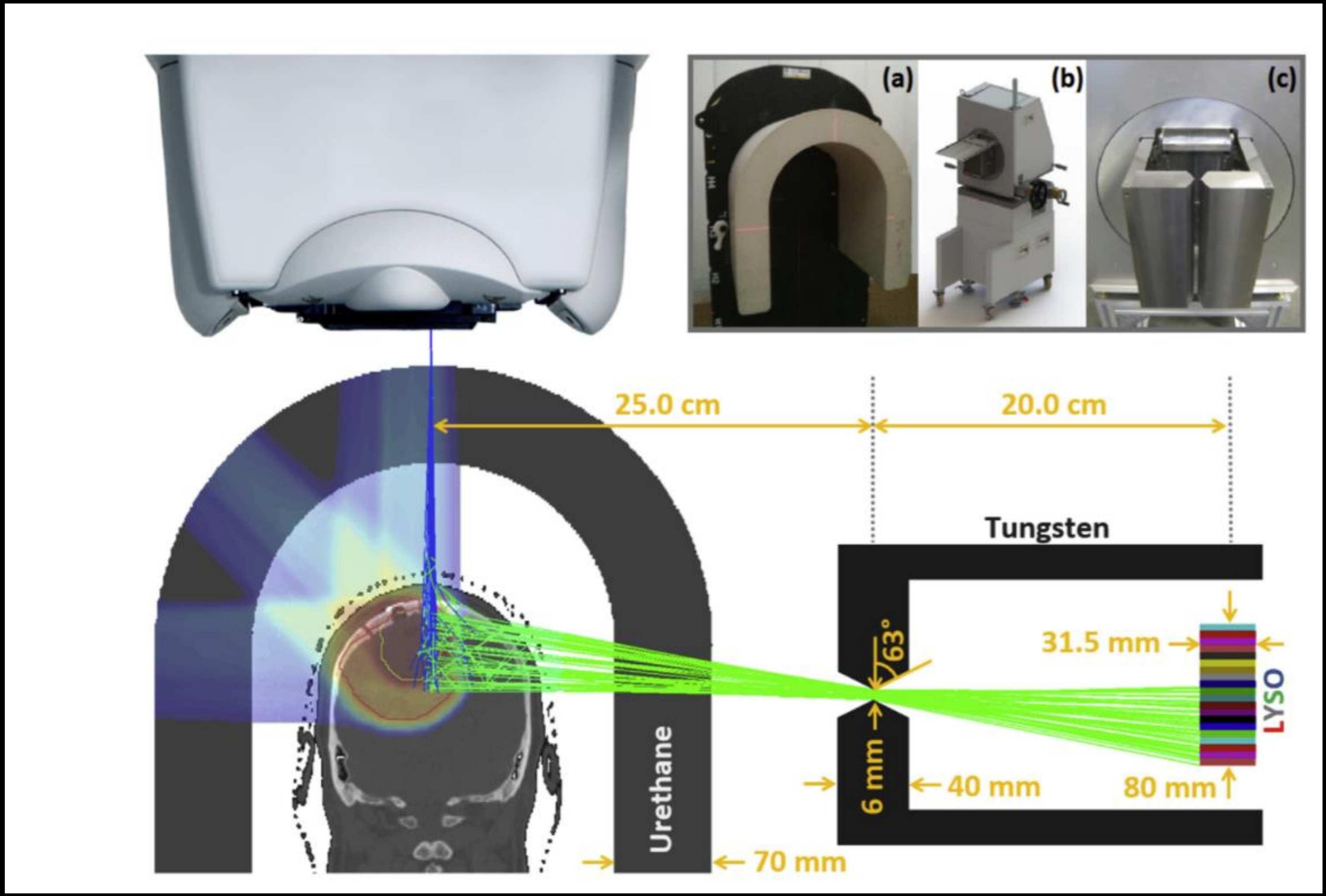
- Simple geometrical concept
- Optimized for range measurement on proton beams





J Smeets et al. Phys. Med. Biol. 57 (2012) 3371

Prompt photons: slit camera (IBA)

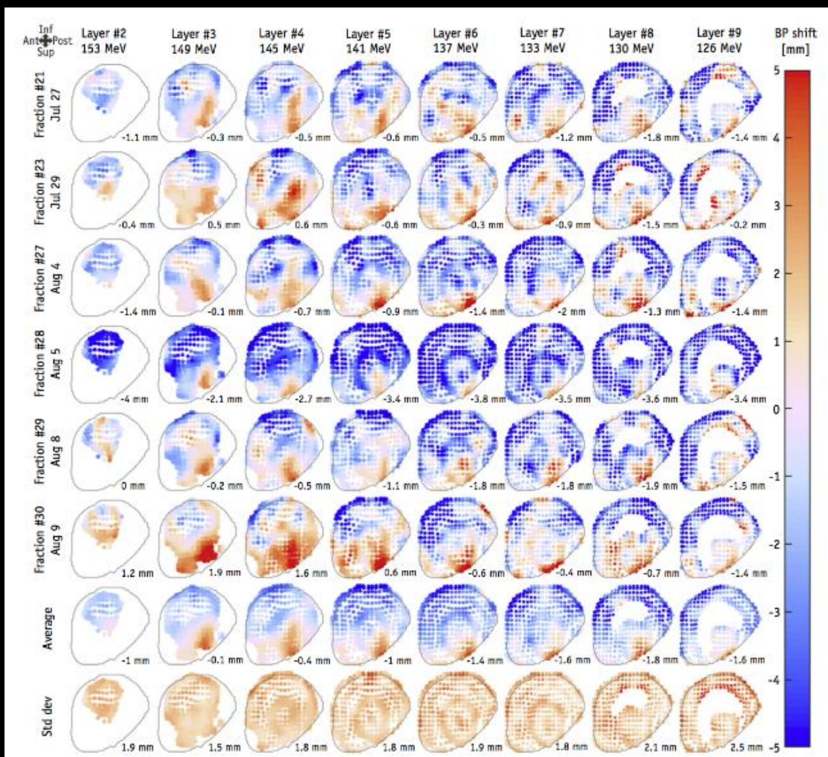


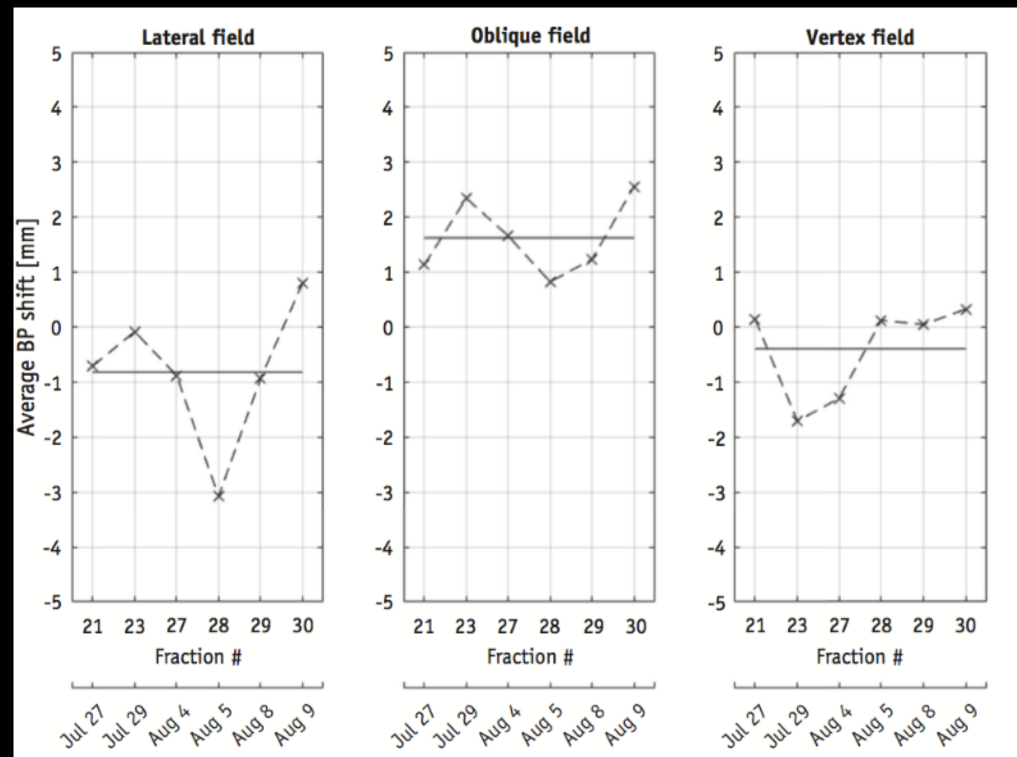
Y Xie et al. Int J Radiation Oncol Biol Phys, Vol. 99, No. 1, pp. 210e218, 2017

Prompt photons: slit camera (IBA)

Range variation maps

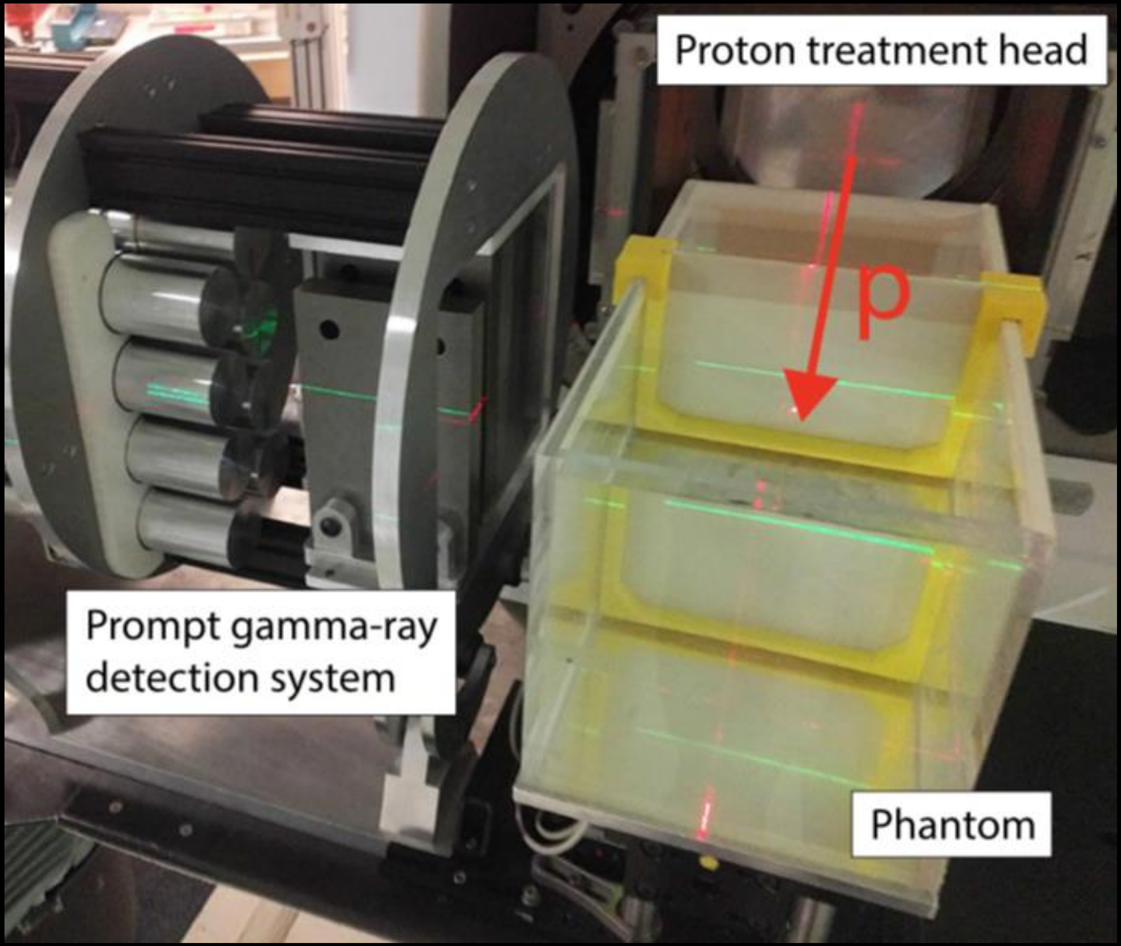
Range variation as a function of time





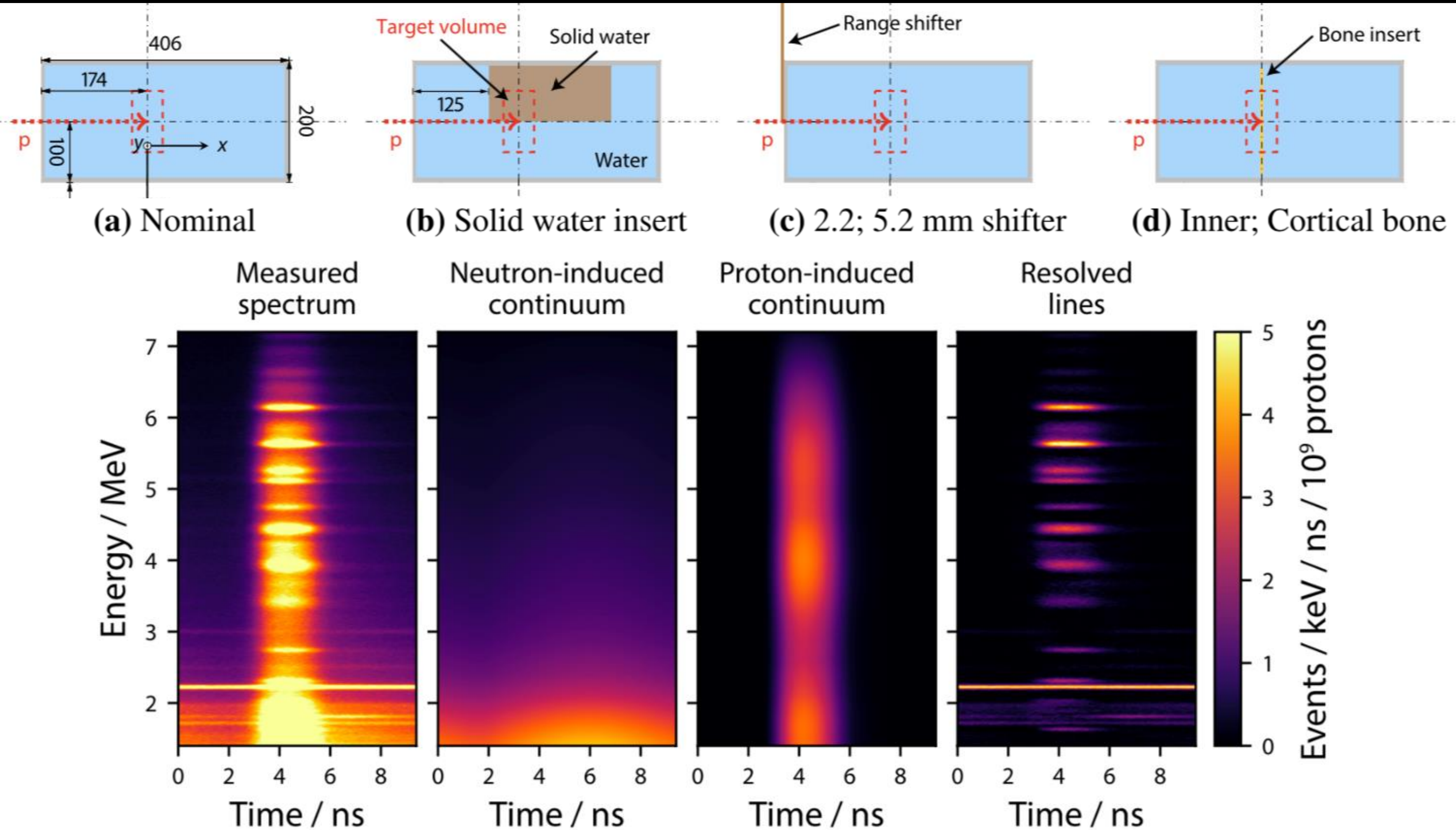
Y Xie et al. Int J Radiation Oncol Biol Phys, Vol. 99, No. 1, pp. 210e218, 2017

Prompt photons: spectroscopy



F. Hueso-González et al., “A full-scale clinical prototype for proton range verification using prompt gamma-ray spectroscopy”, 2018 Phys. Med. Biol. 63 185019

Prompt photons: spectroscopy



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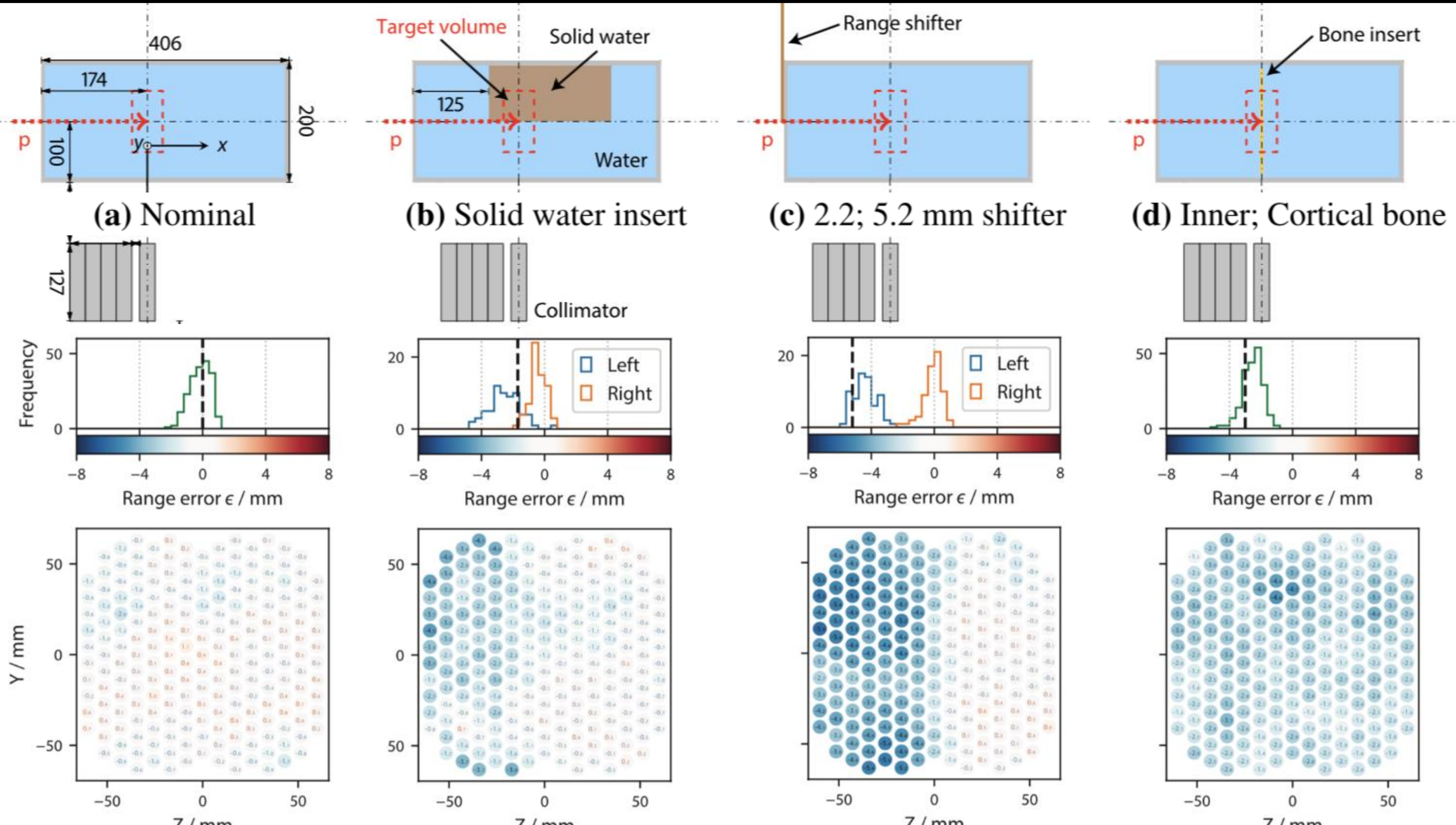
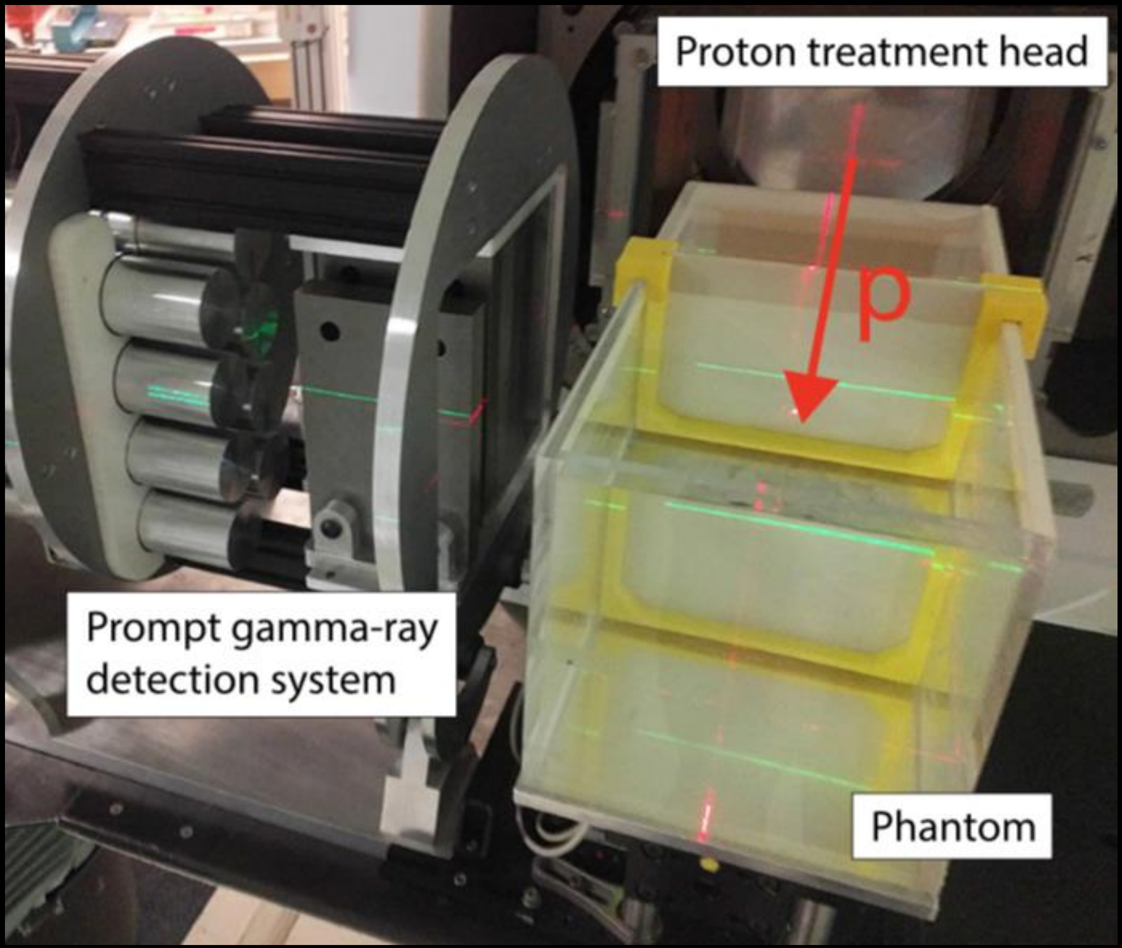
Prompt photons: spectroscopy



F. Hueso-González et al., "A full-scale clinical prototype for proton range verification using prompt gamma-ray spectroscopy", 2018 Phys. Med. Biol. 63 185019

Prompt photons: spectroscopy



- 1.1 mm at a 95% confidence level
- 0.5 mm mean absolute deviation
- for a 0.9 Gy delivered dose*

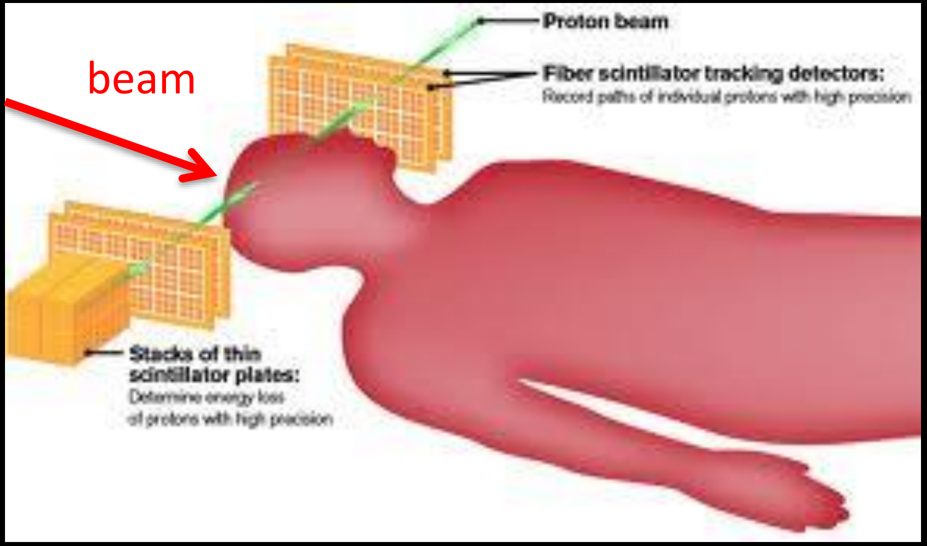
*aggregating pencil-beam spots within a cylindrical region of 10 mm radius and 10 mm depth

F. Hueso-González et al., “A full-scale clinical prototype for proton range verification using prompt gamma-ray spectroscopy”, 2018 Phys. Med. Biol. 63 185019

Charged particle

Charged Particles

- detection efficiency ~ 100%
- easily back-tracked to the emission point
  - correlation to the beam profile
- low rate
- energy threshold ~ 50-100 MeV
- multiple scattering inside the patient (6-8 mm single track resolution)
- only for ion-based treatments



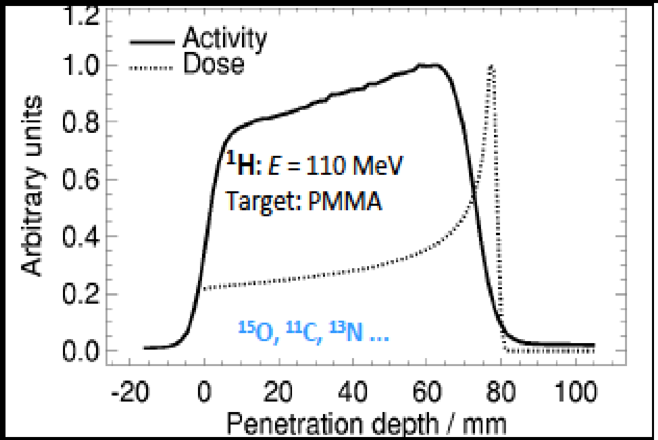
~ 10^3 events required to achieve desired accuracy on the emission point distribution

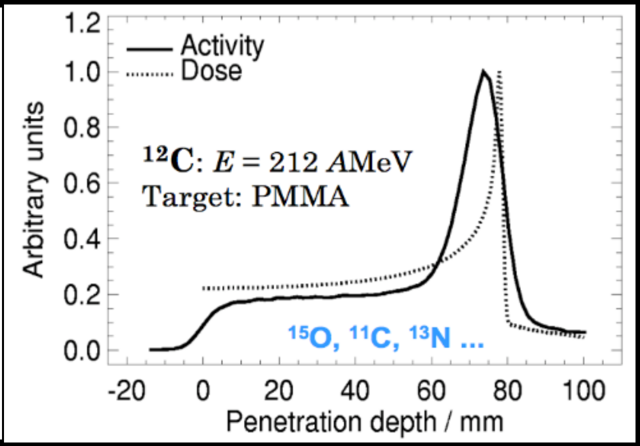
PET

Range Verification with PET

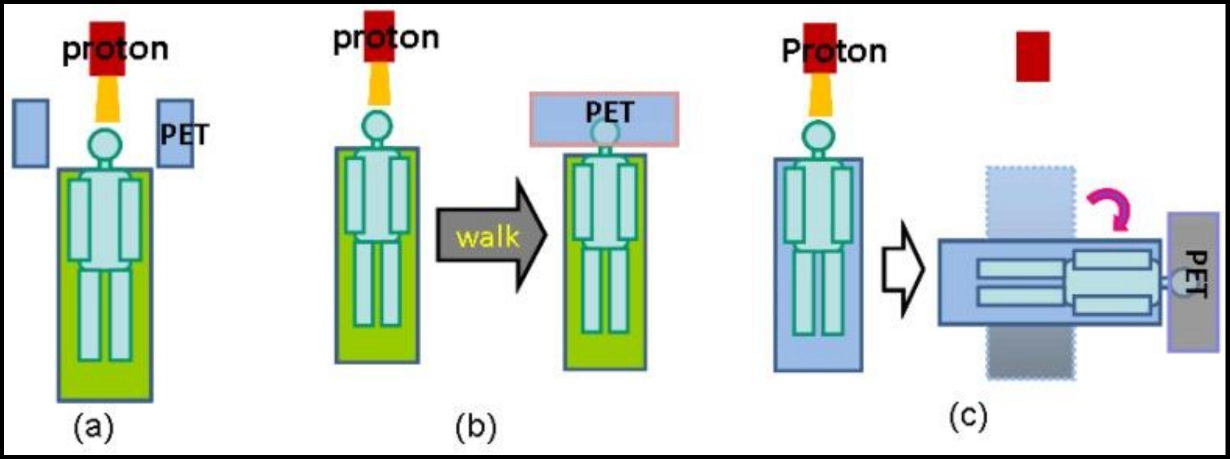
β^+ isotopes

Proton beam | Carbon beam





J Pawelke et al., Proceedings IBIBAM, 26.-29.09.2007, Heidelberg



(a) in-beam PET (b) off-room PET (c) in-room PET

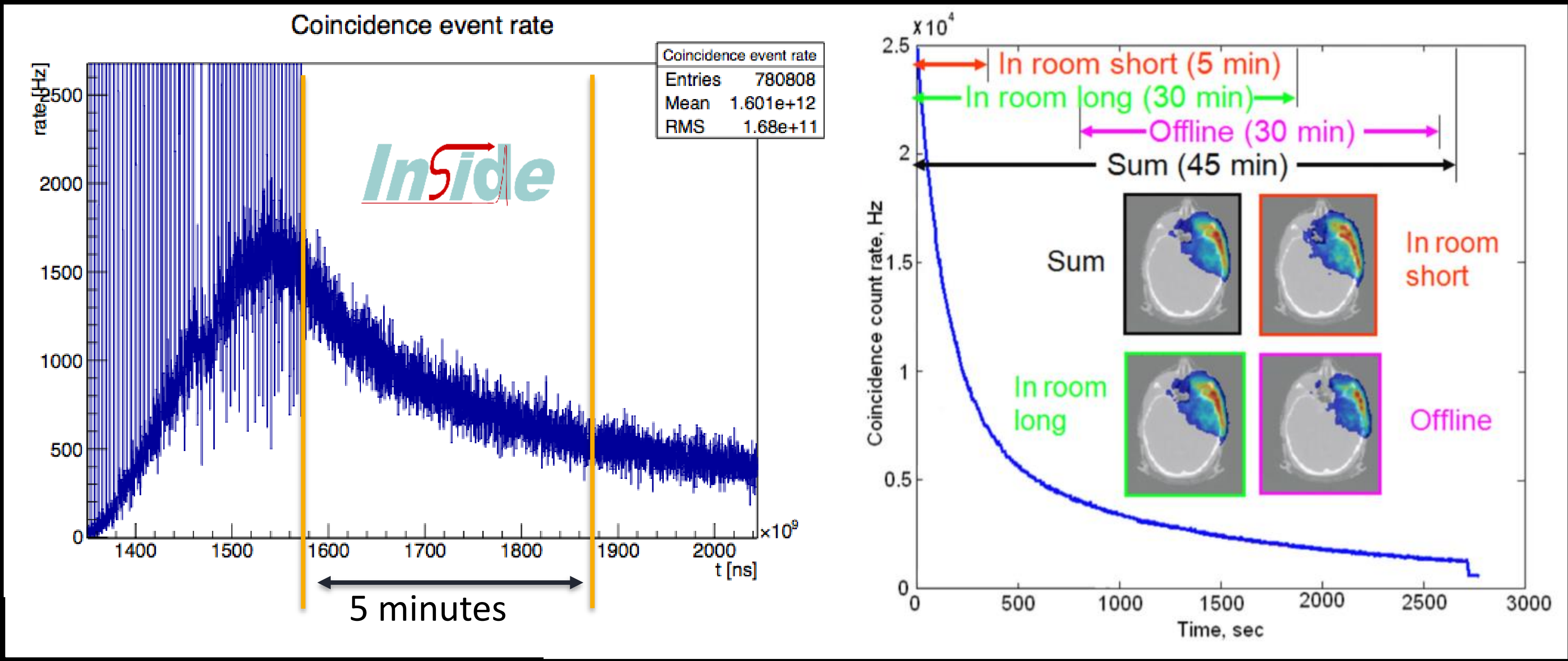
Zhu X, Fakhri GE. *Theranostics. 2013;3(10):731-740*

Isotope	Half-life (s)	Activity (Bq cm^{-3} Gy^{-1})
^{11}C	1223	1600
^{10}C	19.3	
^{15}O	122	1030
^{13}N	598	
^{8}B	0.77	*projectile

in-room PET

@MGH, Boston

- mobile PET scanner in the proton therapy treatment room
- in-room PET has a higher sensitivity compared to the off-line modality

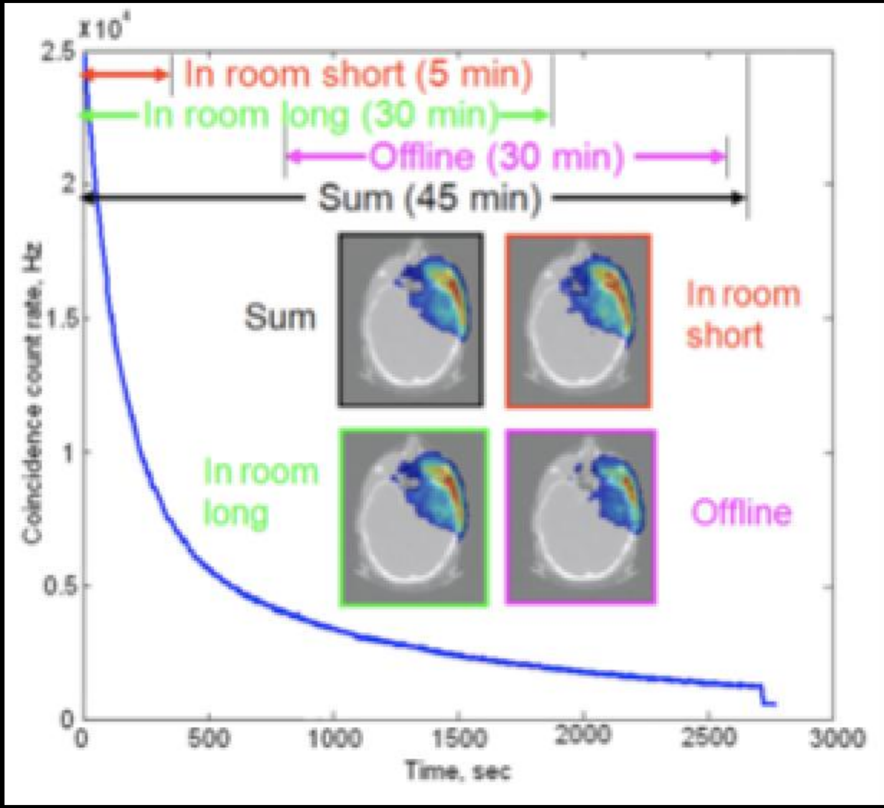


Treatment ends

Monitoring proton radiation therapy with in-room PET imaging, Phys Med Biol. 2011 July 7; 56(13): 4041–4057

@MGH, Boston

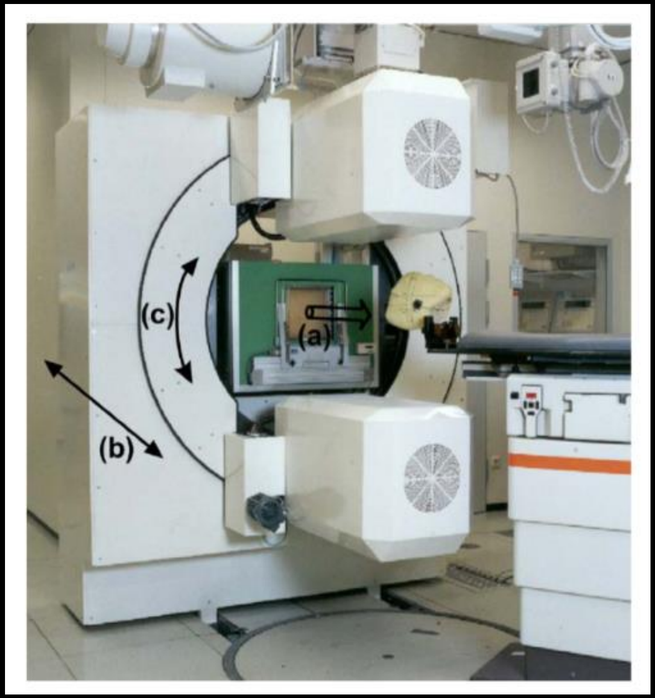
- **in-room PET**: low cost, high sensitivity modality for in vivo verification of proton therapy
- acquisition time from 30 min (offline PET) to 5 min (in-room scanner)
- better accuracy in Monte Carlo predictions, especially for biological decay modeling, is necessary

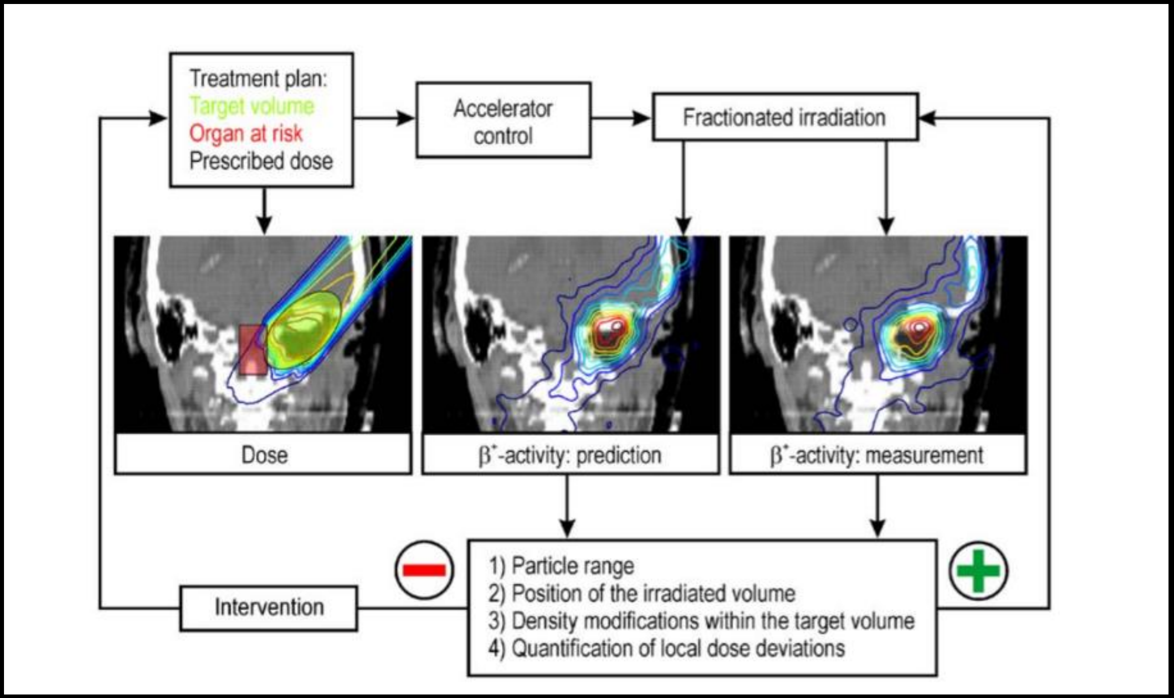


Monitoring proton radiation therapy with in-room PET imaging,
Phys Med Biol. 2011 July 7; 56(13): 4041–4057

in-beam PET

@GSI, Darmstadt



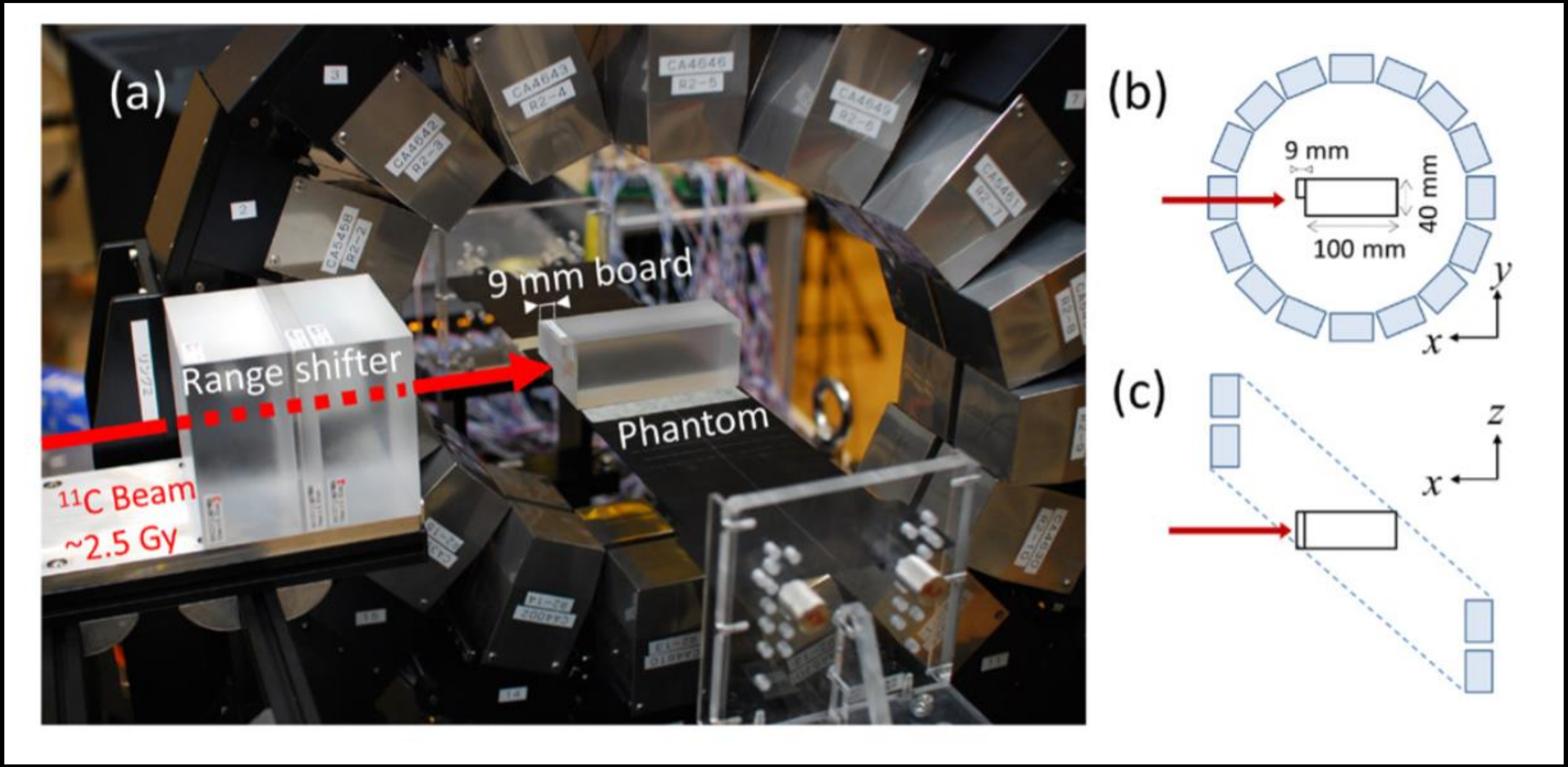


Quality assurance of **carbon ion therapy**

- particle range in tissue
- position of the irradiated volume with respect to anatomical landmarks
- local deviations between the planned and delivered dose distributions

Charged hadron tumour therapy monitoring by means of PET,
Nuclear Instruments and Methods in Physics Research A 525 (2004) 284–288

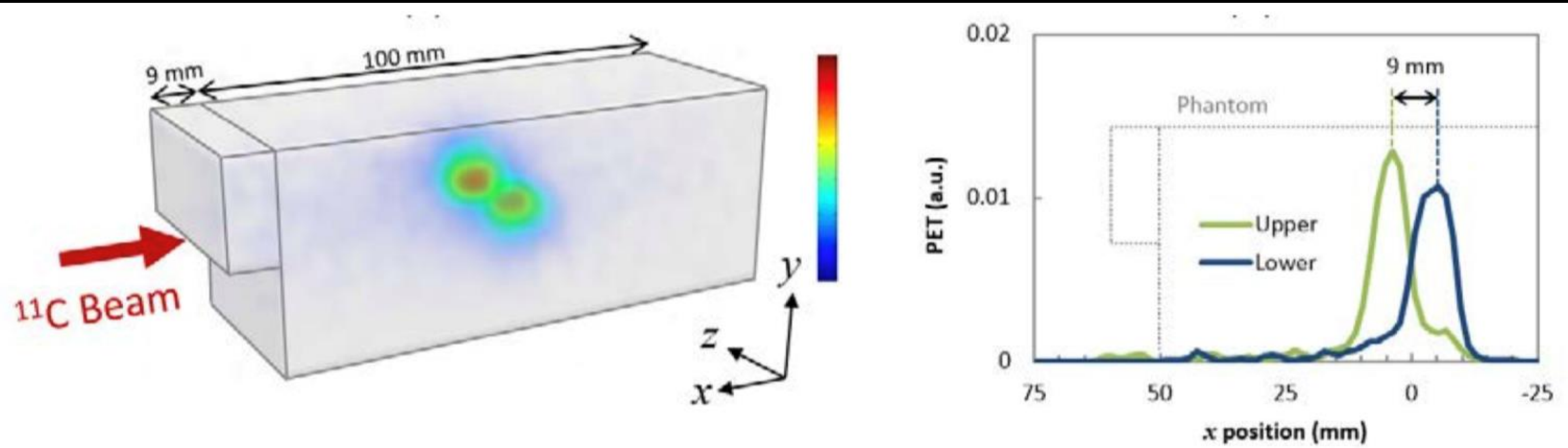
OpenPET (@HIMAC)



Development of a small single-ring OpenPET prototype with a novel transformable architecture,
Phys. Med. Biol. 61 (2016) 1795–1809

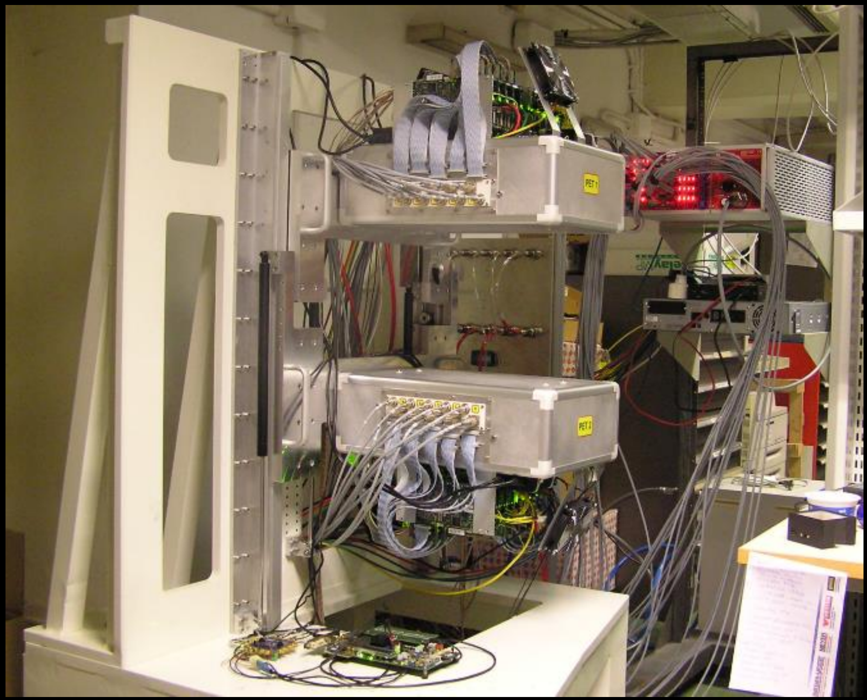
OpenPET (@HIMAC)

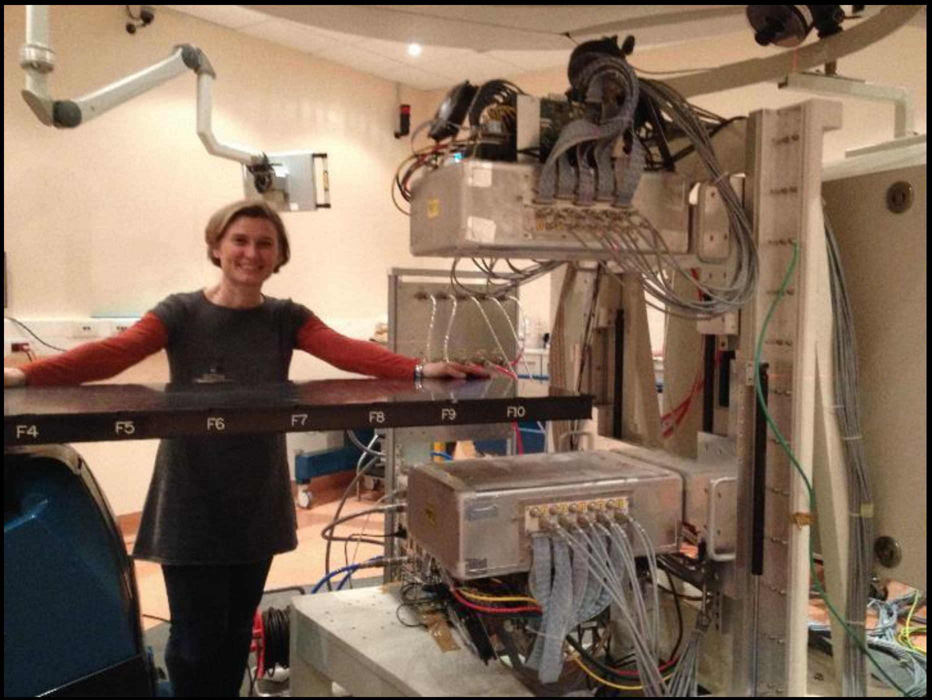
- in-beam imaging with the ^{11}C beam irradiation of about 2.5 Gy
- potential reduction of patient time for PET measurements < 1 min
- potential direct conversion to the range information



OpenPET: a novel open-type PET system for 3D dose verification in particle therapy,
T Yamaya 2017, J. Phys.: Conf. Ser. 777 012023

Range Monitoring / INSIDE



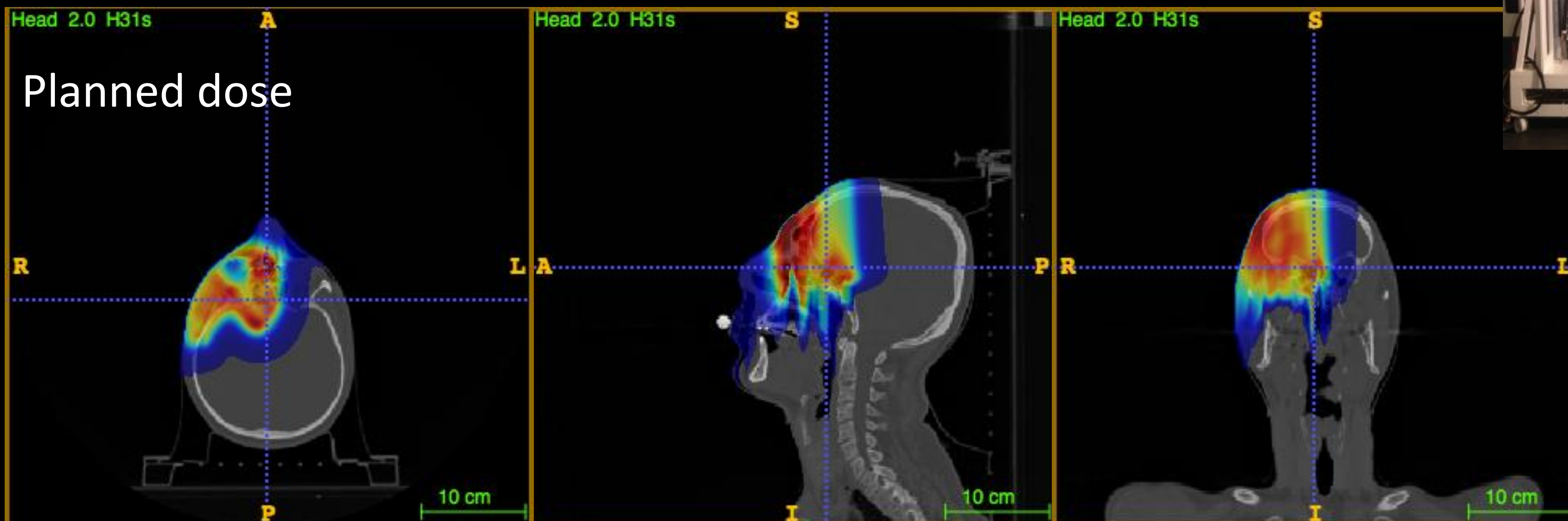


PET built @ INFN–Torino in January 2016

First test @ CNAO on February, 7th, 2016

Range Monitoring / INSIDE

First clinical test @CNAO, 1-2 Dec. 2016



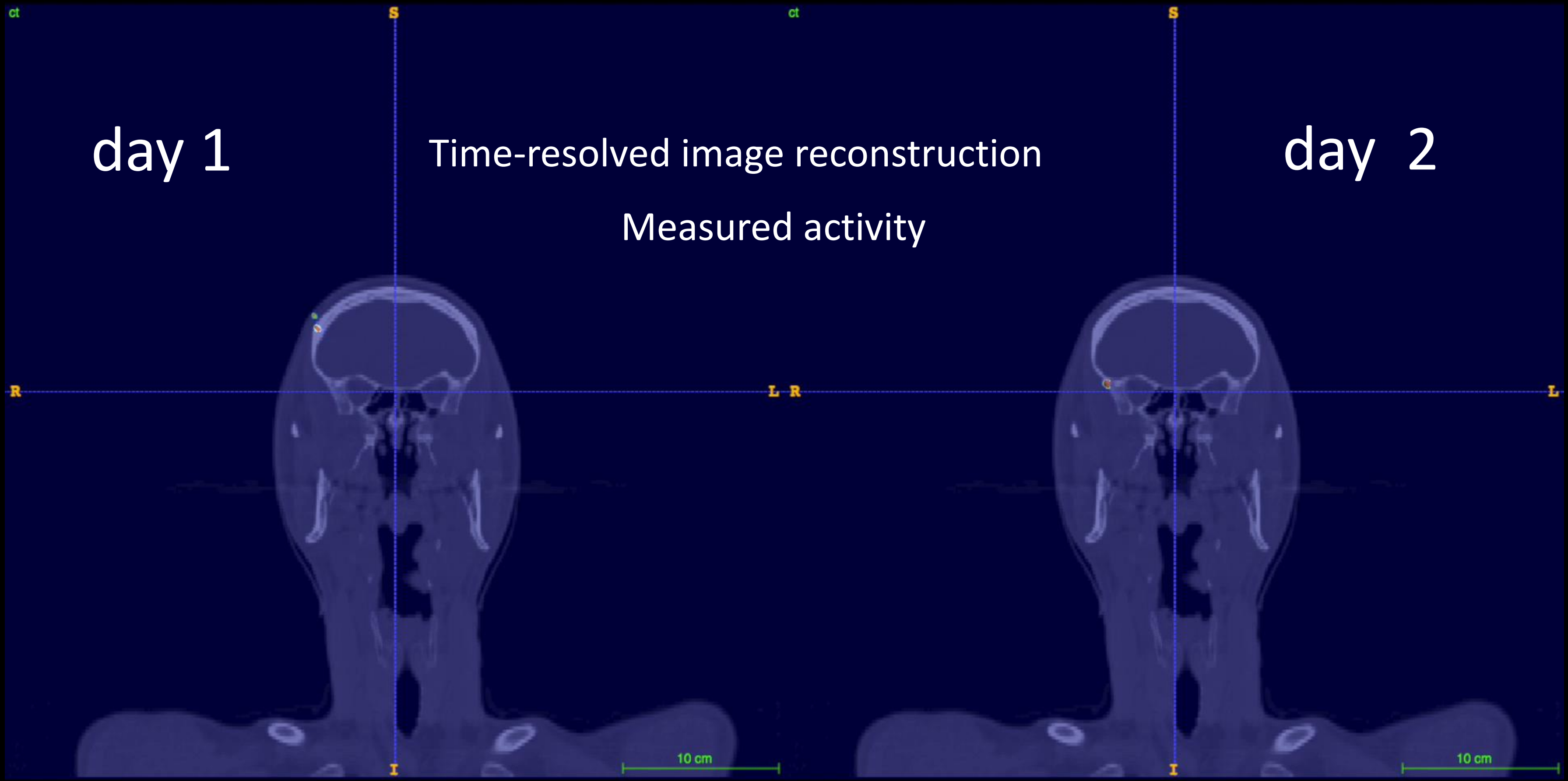
Carcinoma of the lacrimal gland
3.7 10^{10} protons, [66.3, 144.4] MeV/u
Vertex field, (28-29)/30 fractions, 2.2 GyE

Inside

V. Ferrero et al., "Online proton therapy monitoring: clinical test of a Silicon-photodetector-based in-beam PET"
Scientific Reports, *(2018) 8:4100*

INFN

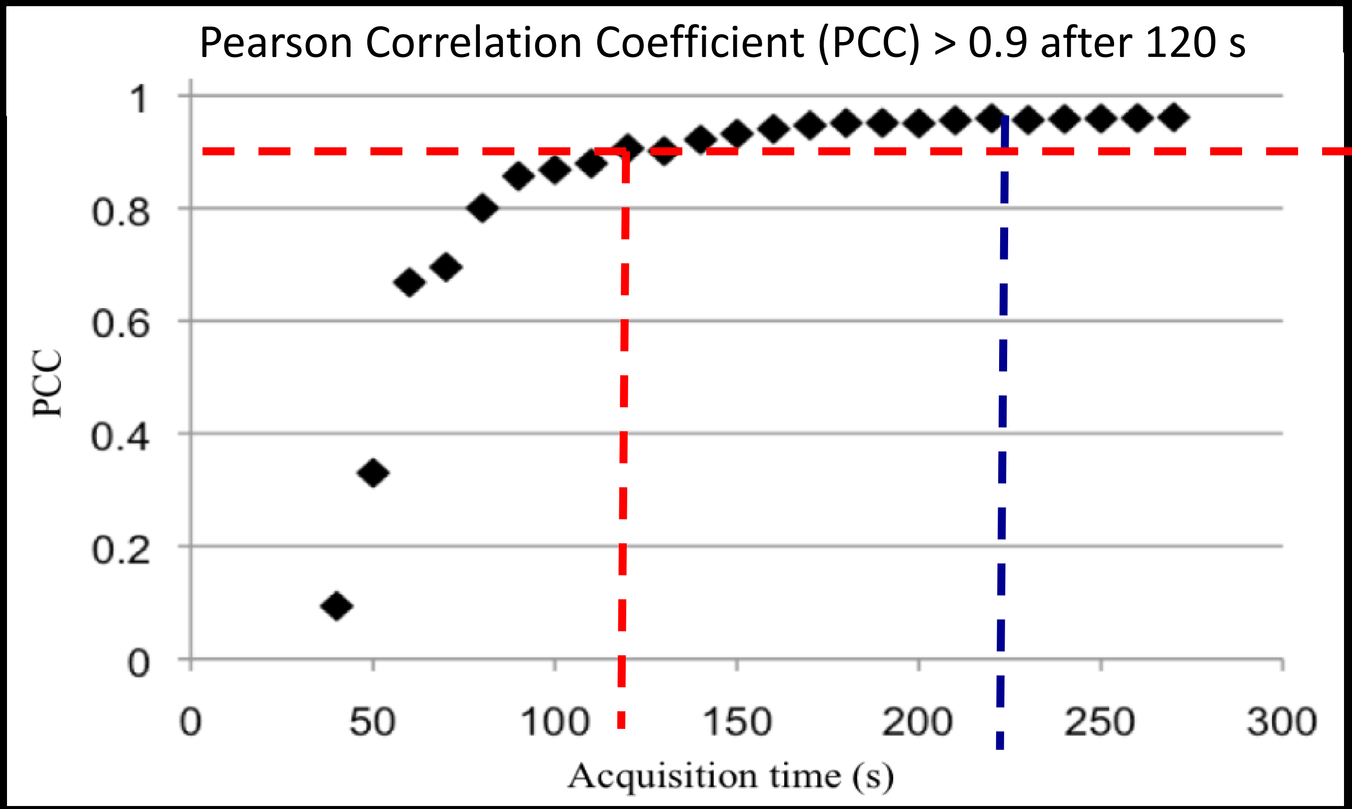
Range Monitoring / INSIDE



V. Ferrero et al., “Online proton therapy monitoring: clinical test of a Silicon-photodetector-based in-beam PET”
Scientific Reports, *(2018) 8:4100*

Range Monitoring / INSIDE

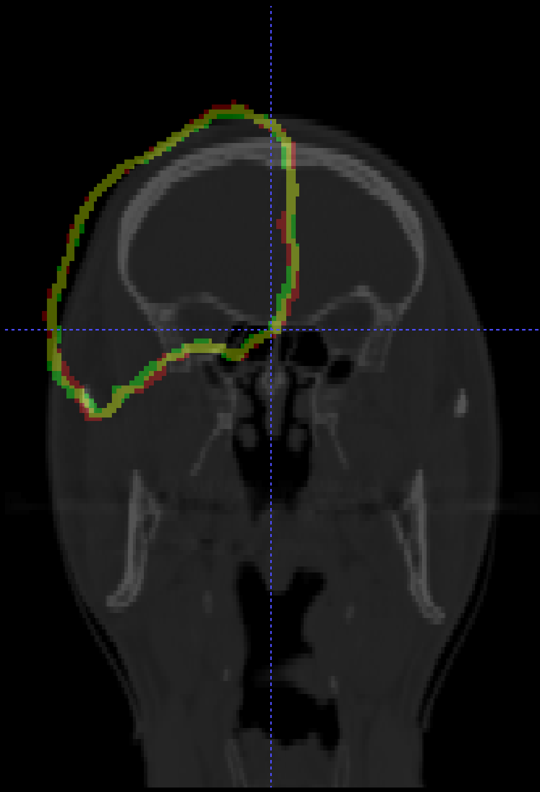
Quantitative Comparison: PCC

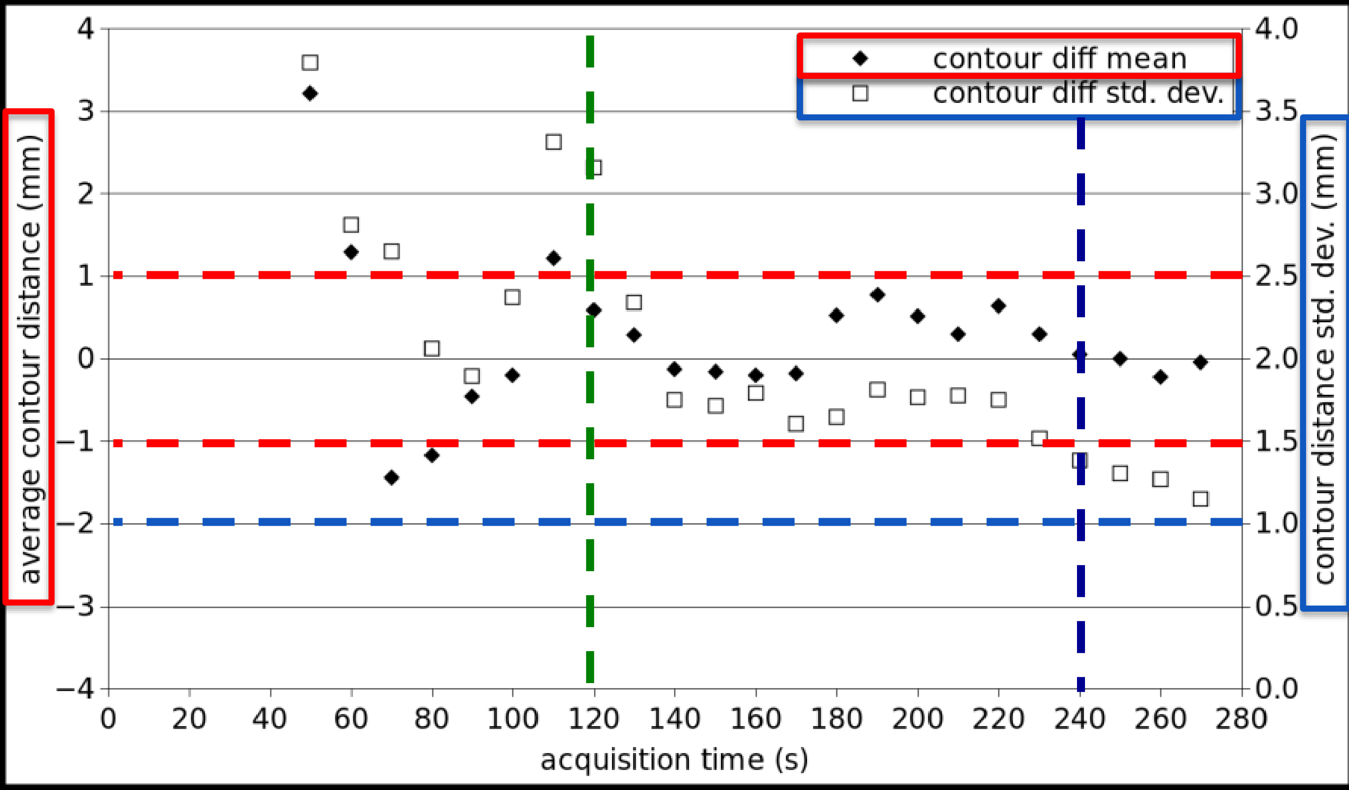


V. Ferrero et al., “Online proton therapy monitoring: clinical test of a Silicon-photodetector-based in-beam PET”
Scientific Reports, *(2018) 8:4100*

Range Monitoring / INSIDE

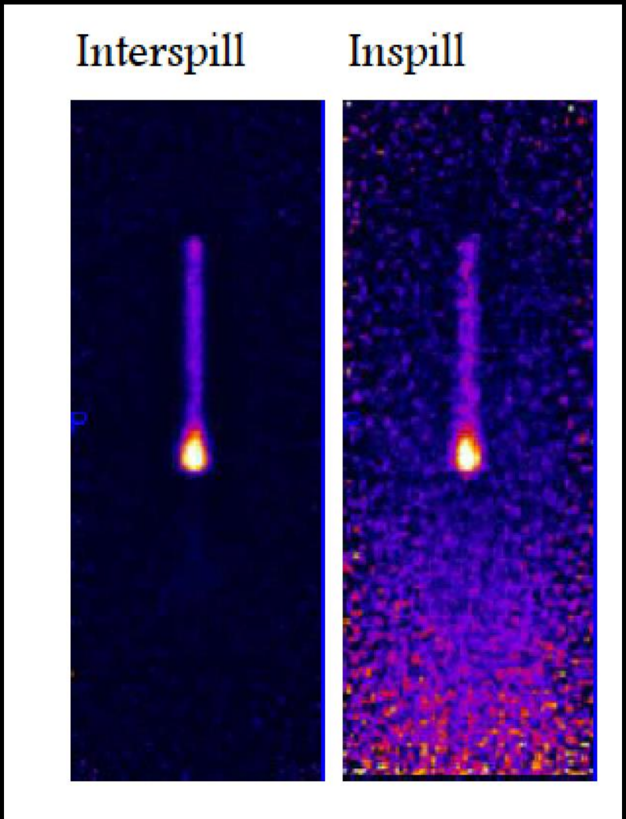
Quantitative Comparison: overall view

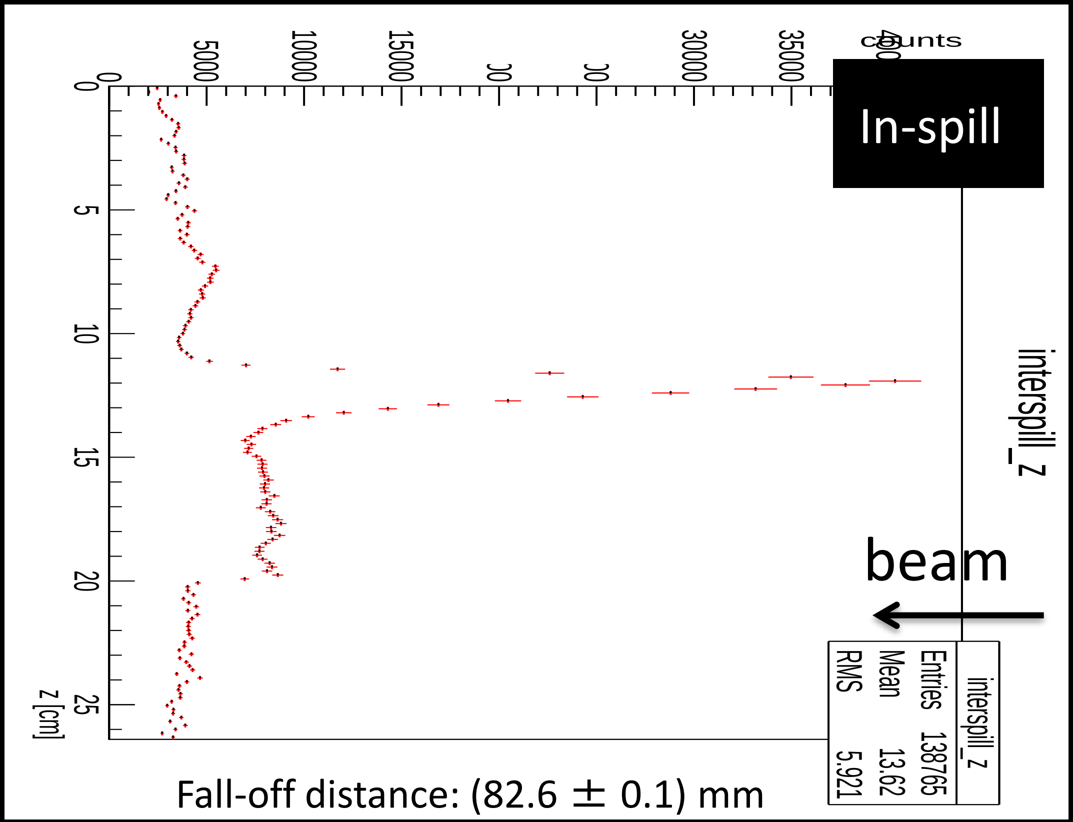




V. Ferrero et al., "Online proton therapy monitoring: clinical test of a Silicon-photodetector-based in-beam PET"
Scientific Reports, *(2018) 8:4100*

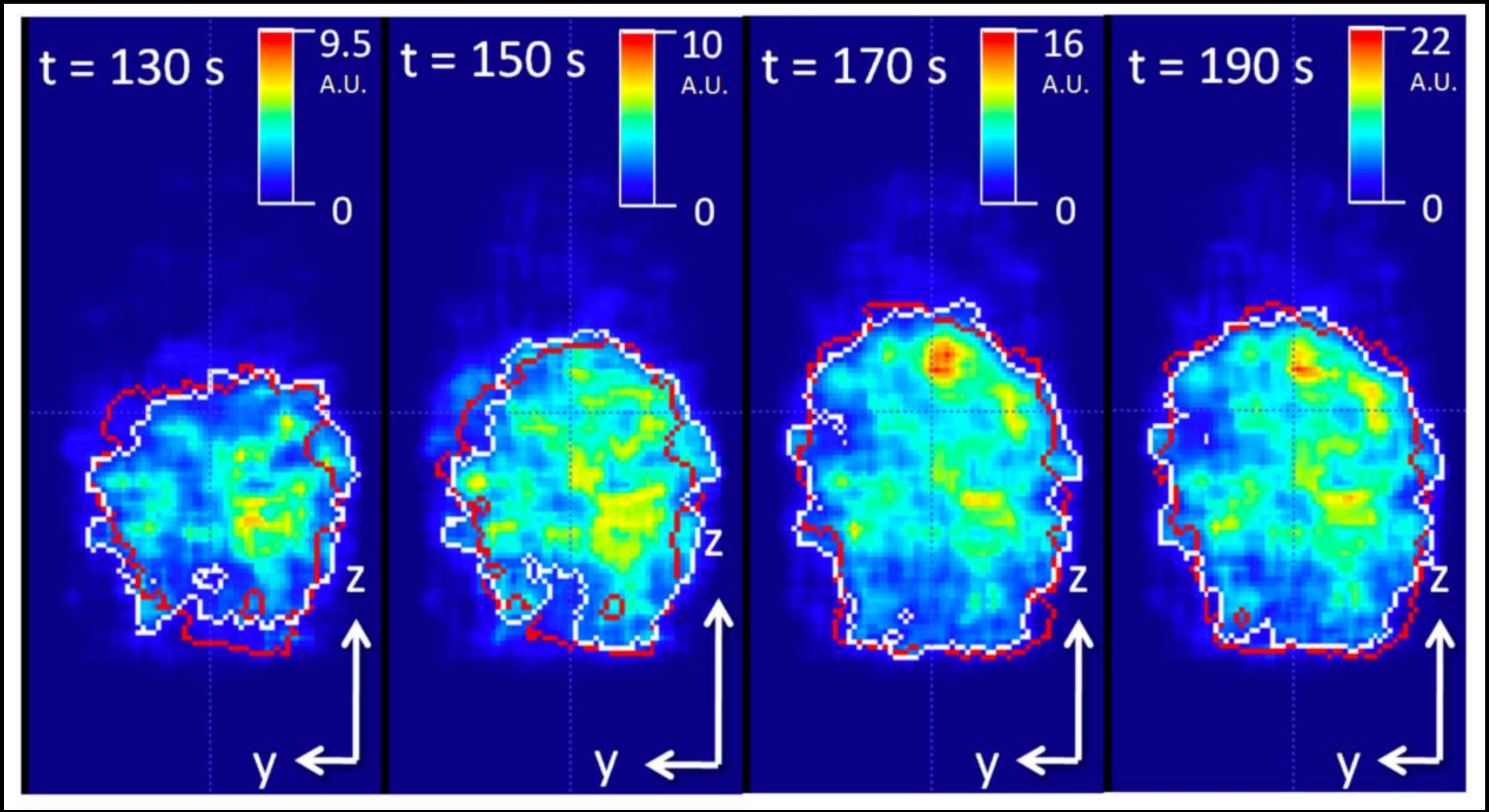
Range Monitoring / INSIDE





F. Pennazio et al., "**Carbon ions beam therapy monitoring with the INSIDE in-beam PET**", Phys. Med. Biol. 2018 Jul 17;63 (14) :145018

Range Monitoring / INSIDE



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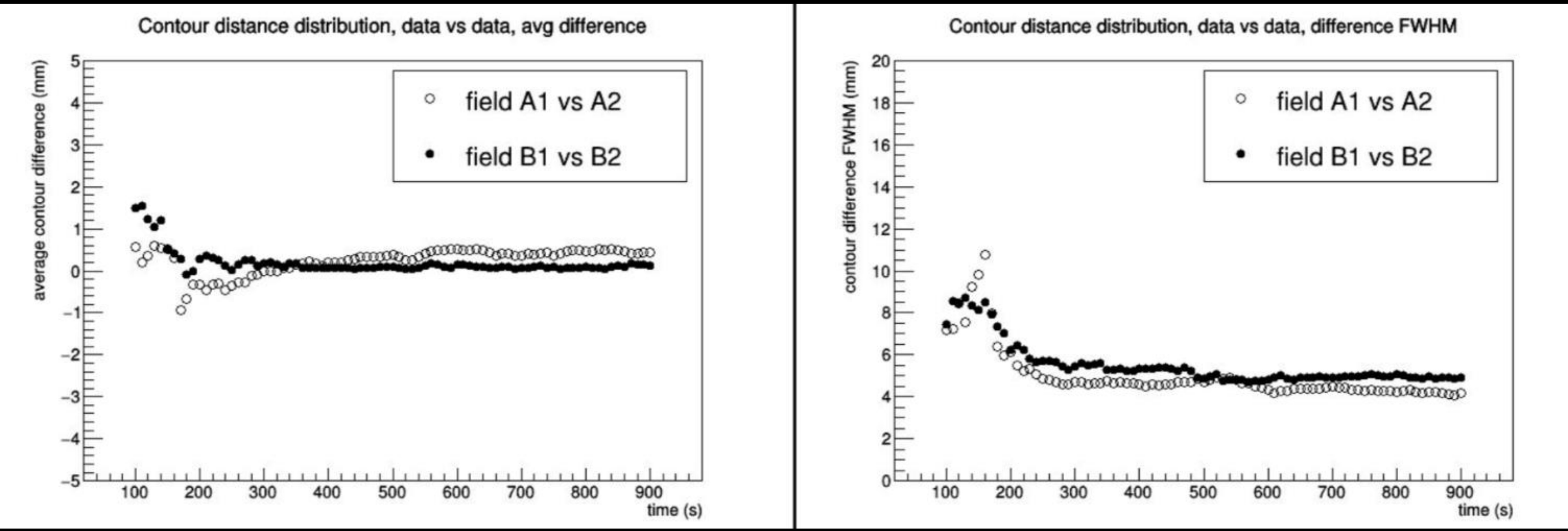
Range Monitoring / INSIDE

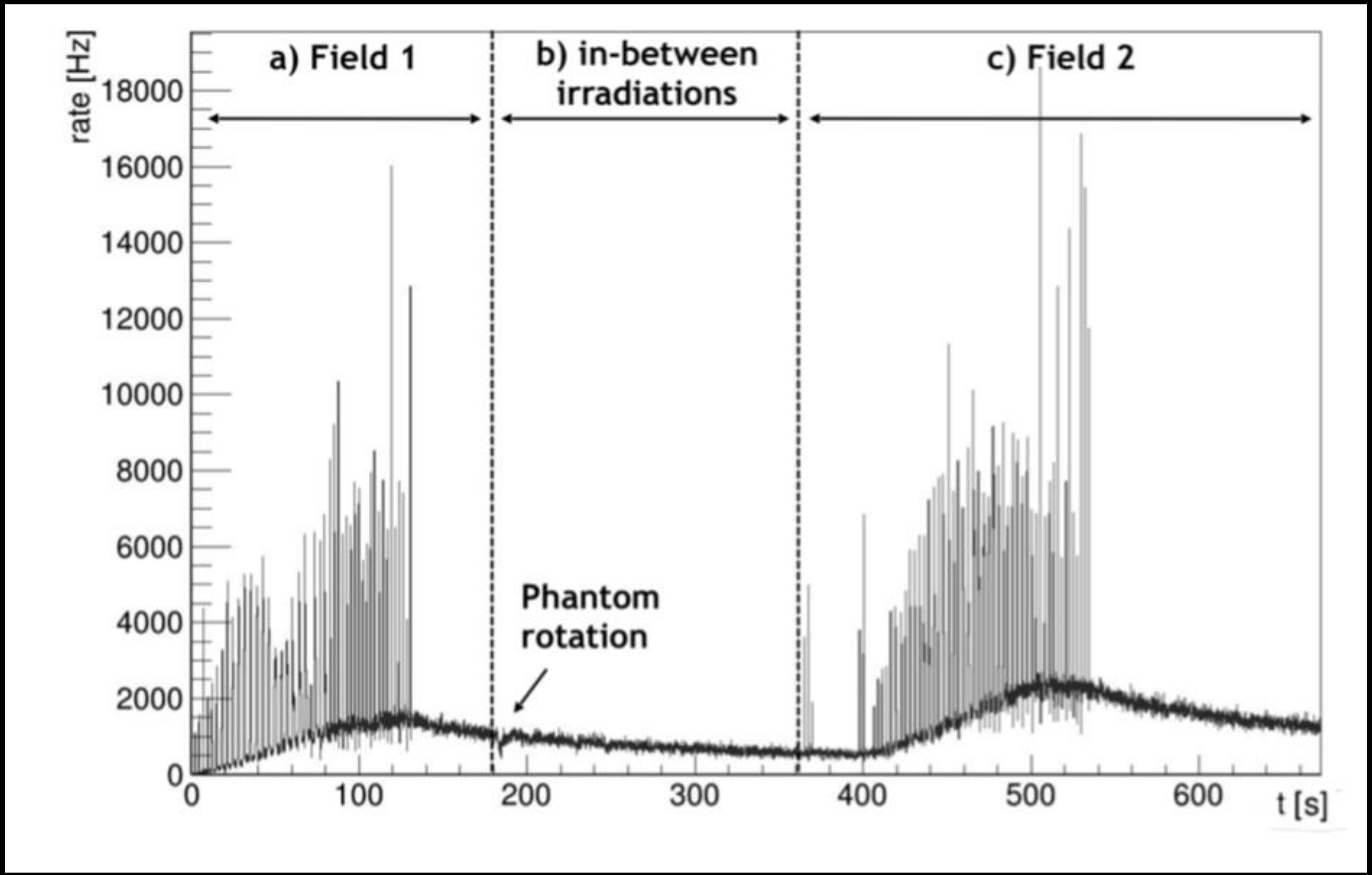


InSide

F. Pennazio et al., "**Carbon ions beam therapy monitoring with the INSIDE in-beam PET**", Phys. Med. Biol. 2018 Jul 17;63 (14) :145018

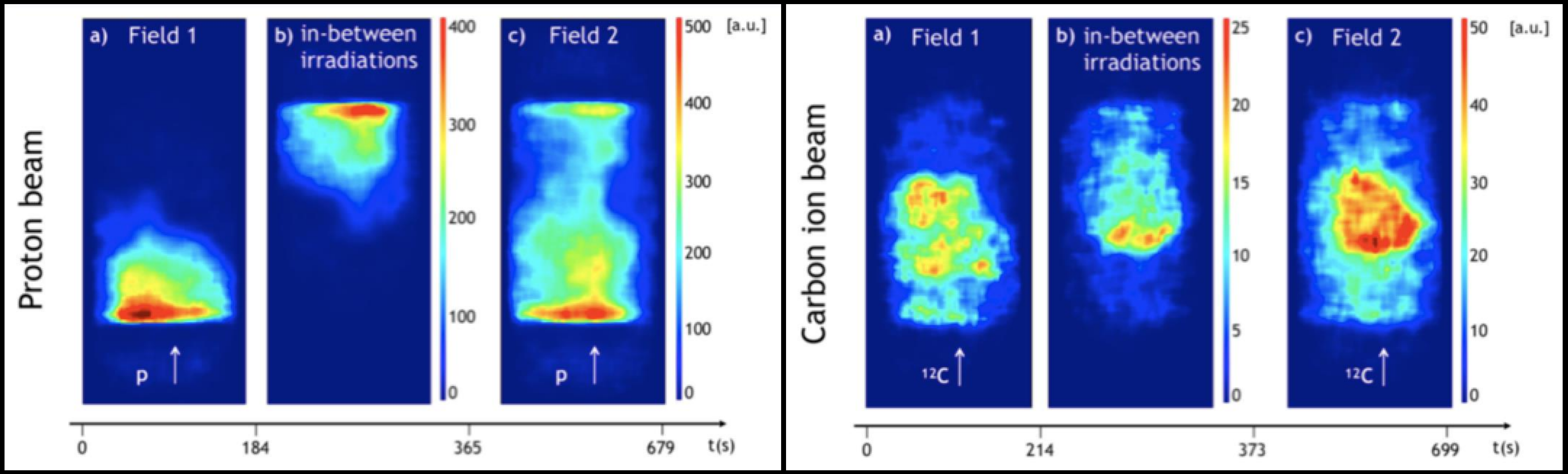
INFN

Range Monitoring / INSIDE



V. Ferrero et al., "**Double-Field Hadrontherapy Treatment Monitoring with the INSIDE In-Beam PET Scanner: Proof of Concept**", IEEE TRPMS 2;6; Nov 18, 588-593

Range Monitoring / INSIDE



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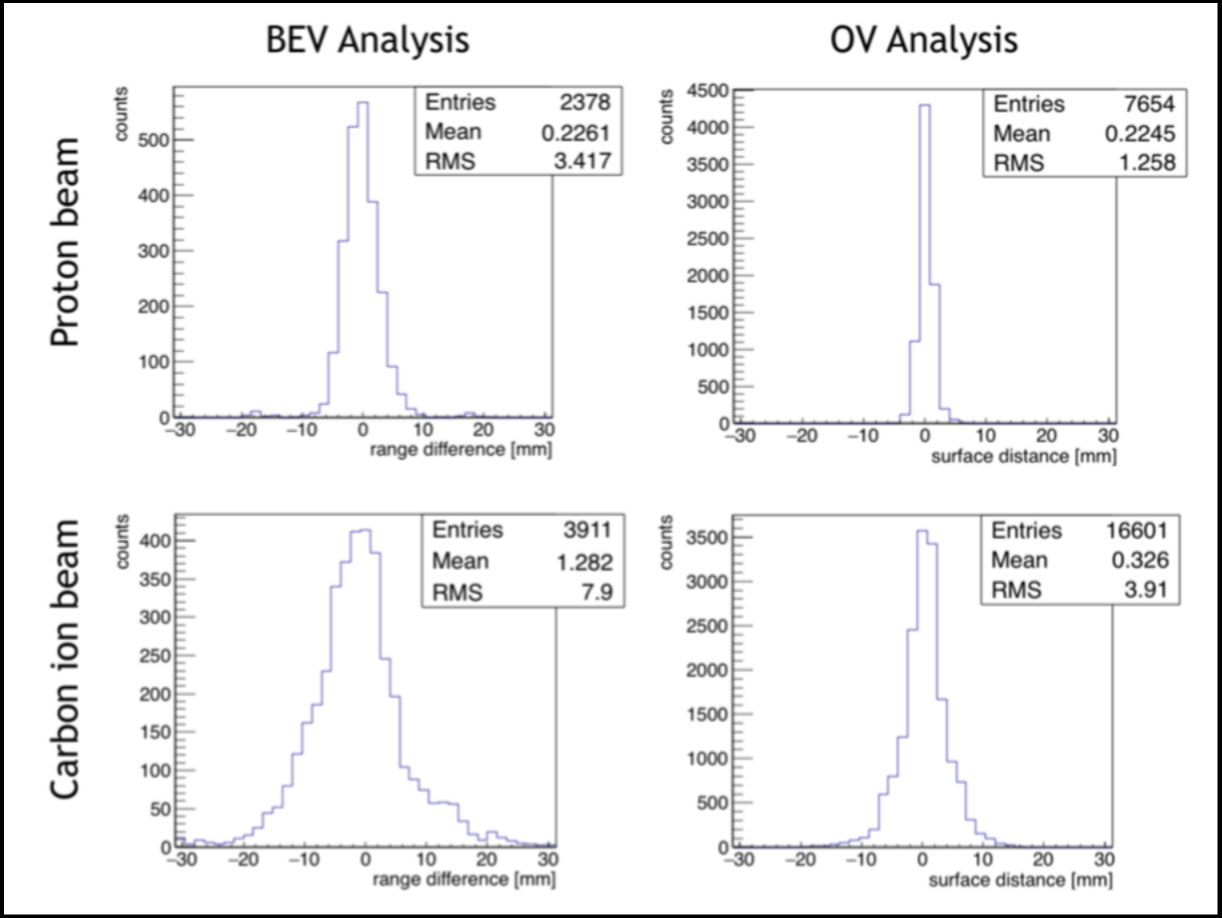
Range Monitoring / INSIDE



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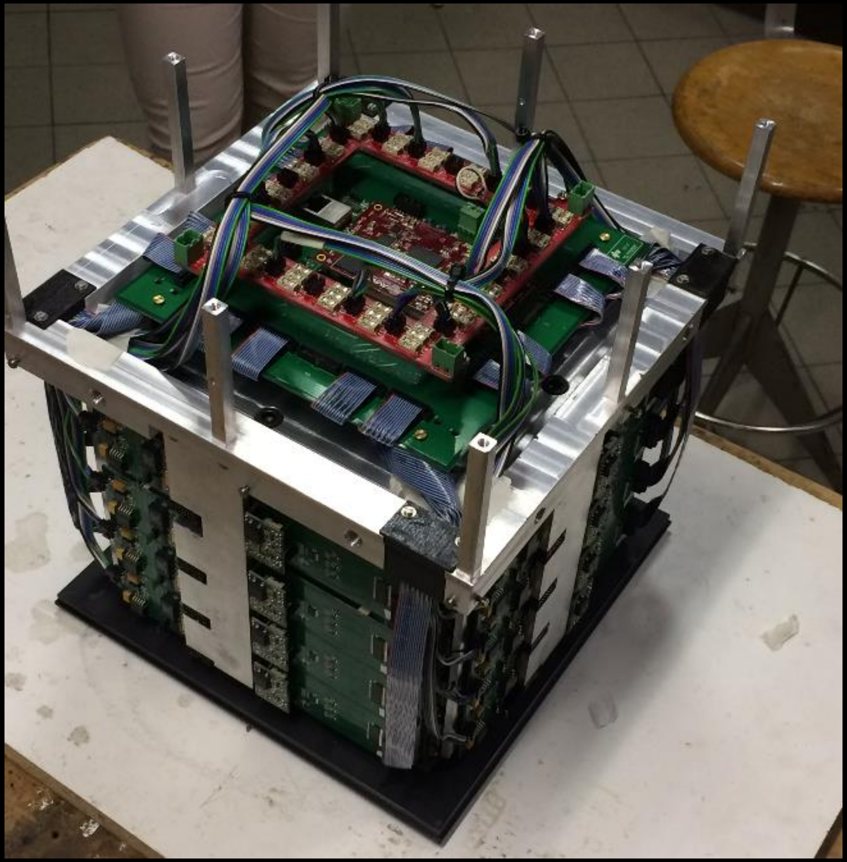
Range Monitoring / INSIDE

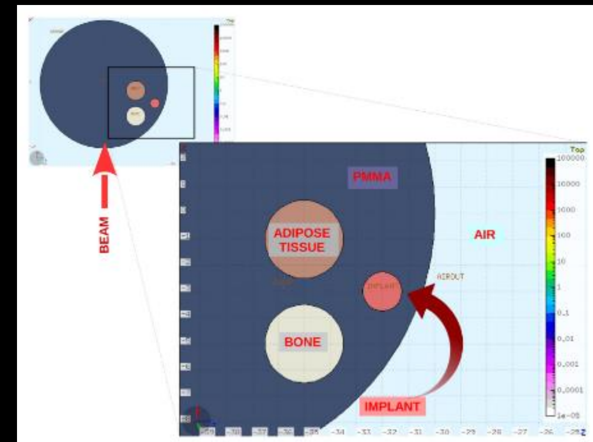


Dose Profiler

- 6 xy fiber planes with 2 cm spacing
- for each plane: 2 stereo layers of 192 0.5x0.5 mm^2 square scintillating fibers
- Hamamatsu $1mm^2$ SiPM S12571-050P
- FPGA for data acquisition

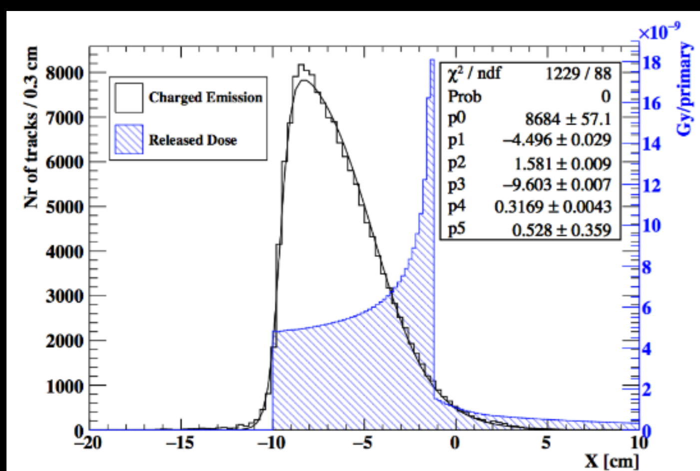
Design of a new tracking device for on-line beam range monitor in carbon therapy
Physica Medica 34 (2017) 18-27

Range Monitoring / INSIDE

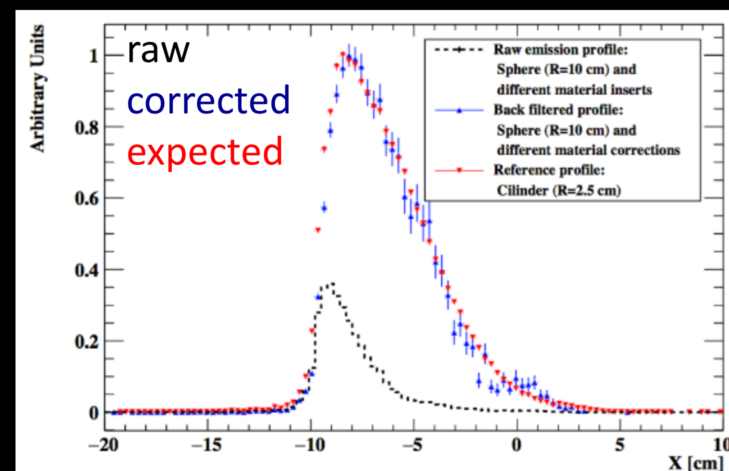


Dose vs. Charged Particle Emission Profiles

Simulated profiles



Measured profiles



InSide

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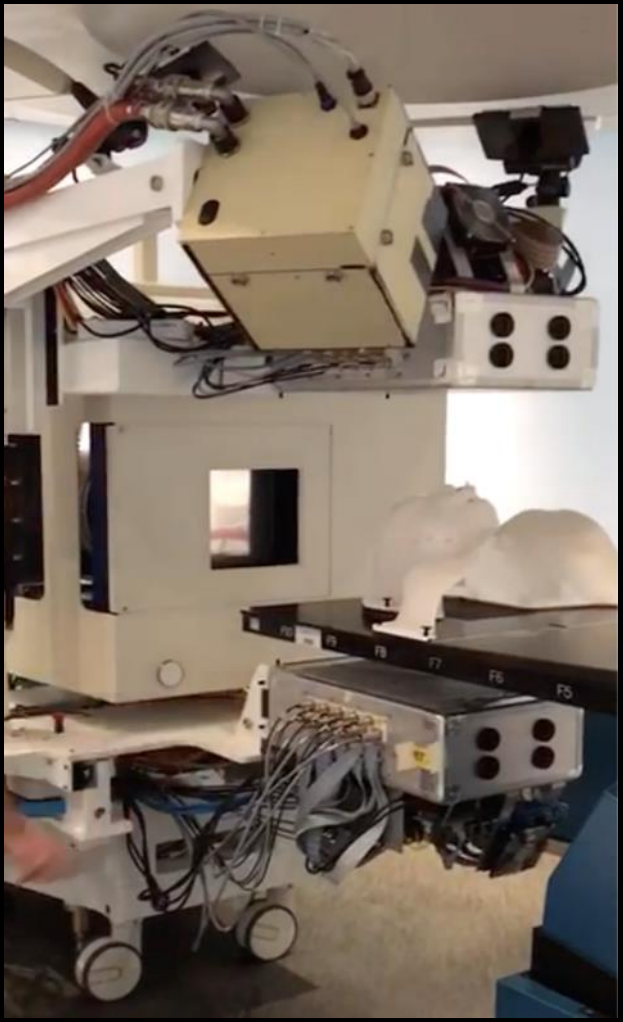
Range Monitoring / INSIDE



- Mechanical upgrade to minimise interference with patient movements
- Dose profiler integration
- Observational Clinical Trial soon starting at CNAO on 40 patients (p, C)
- https://clinicaltrials.gov/ct2/show/NCT03662373

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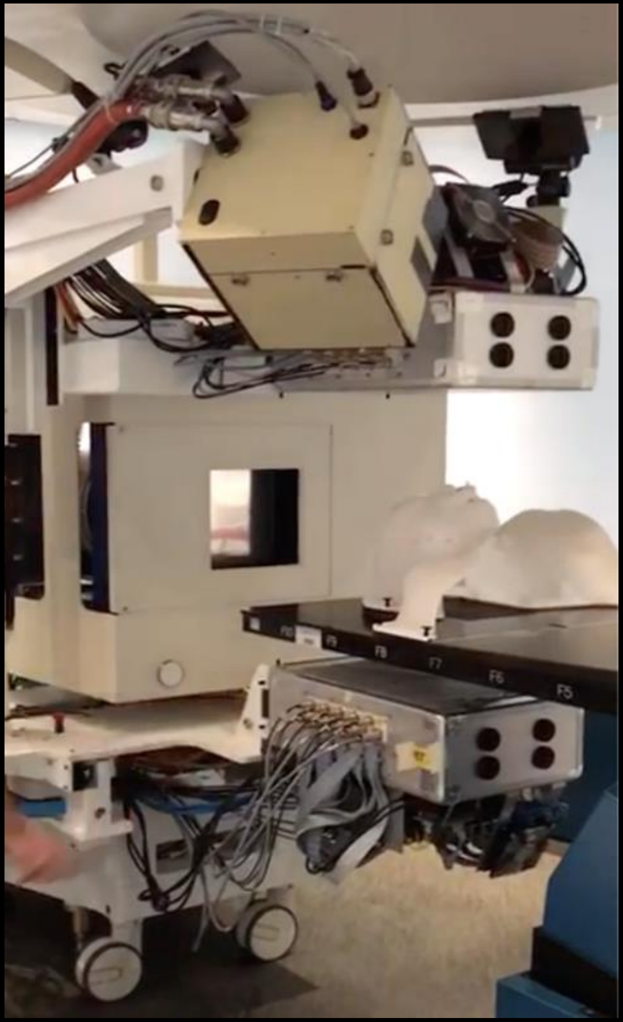
Range Monitoring / INSIDE



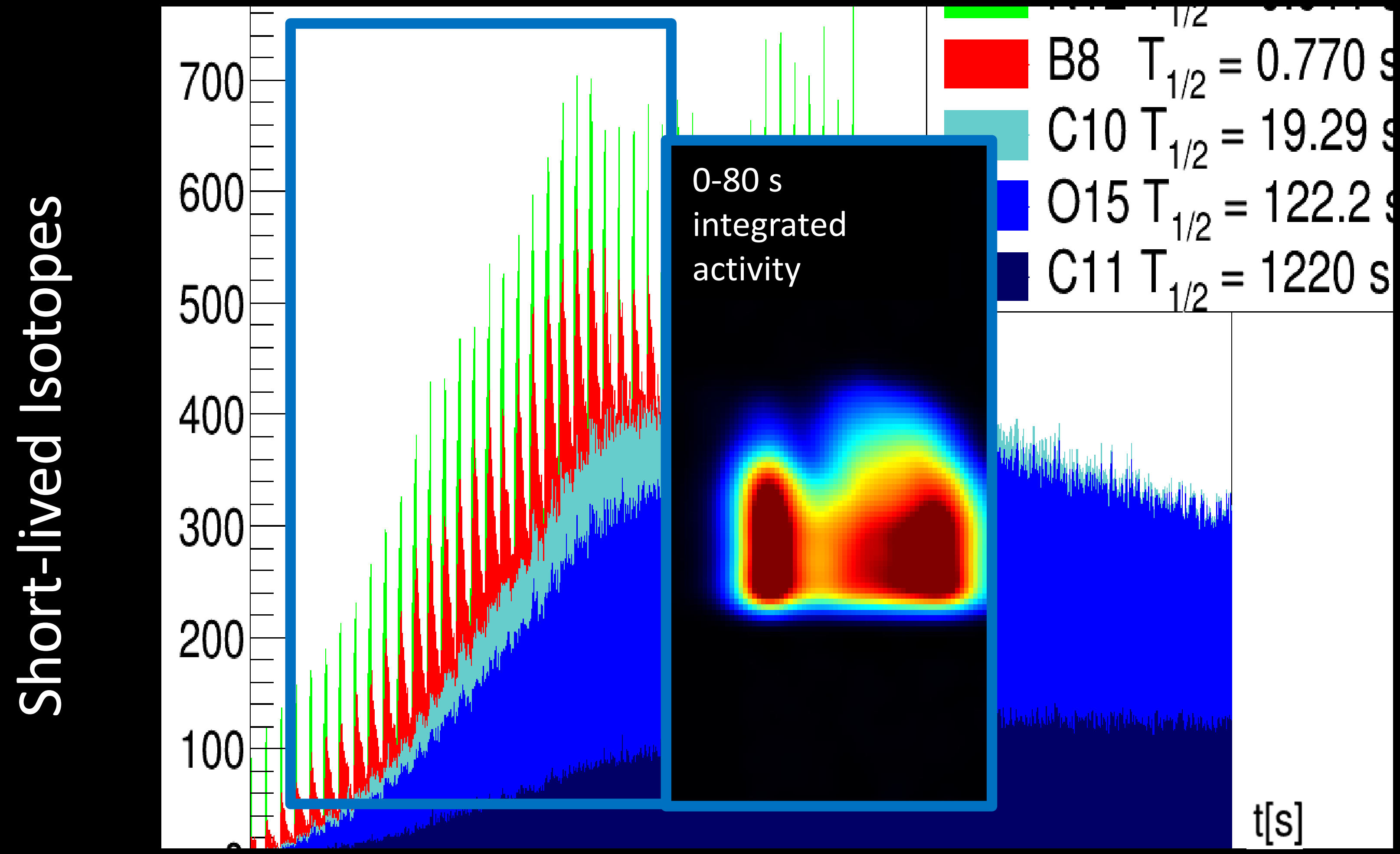
in beam-PET

metabolic wash-out minimized
quick(er), very accurate response
3D activity in real-time

limited acceptance,
bad measurement of vertical coordinate,
no time of flight (yet)

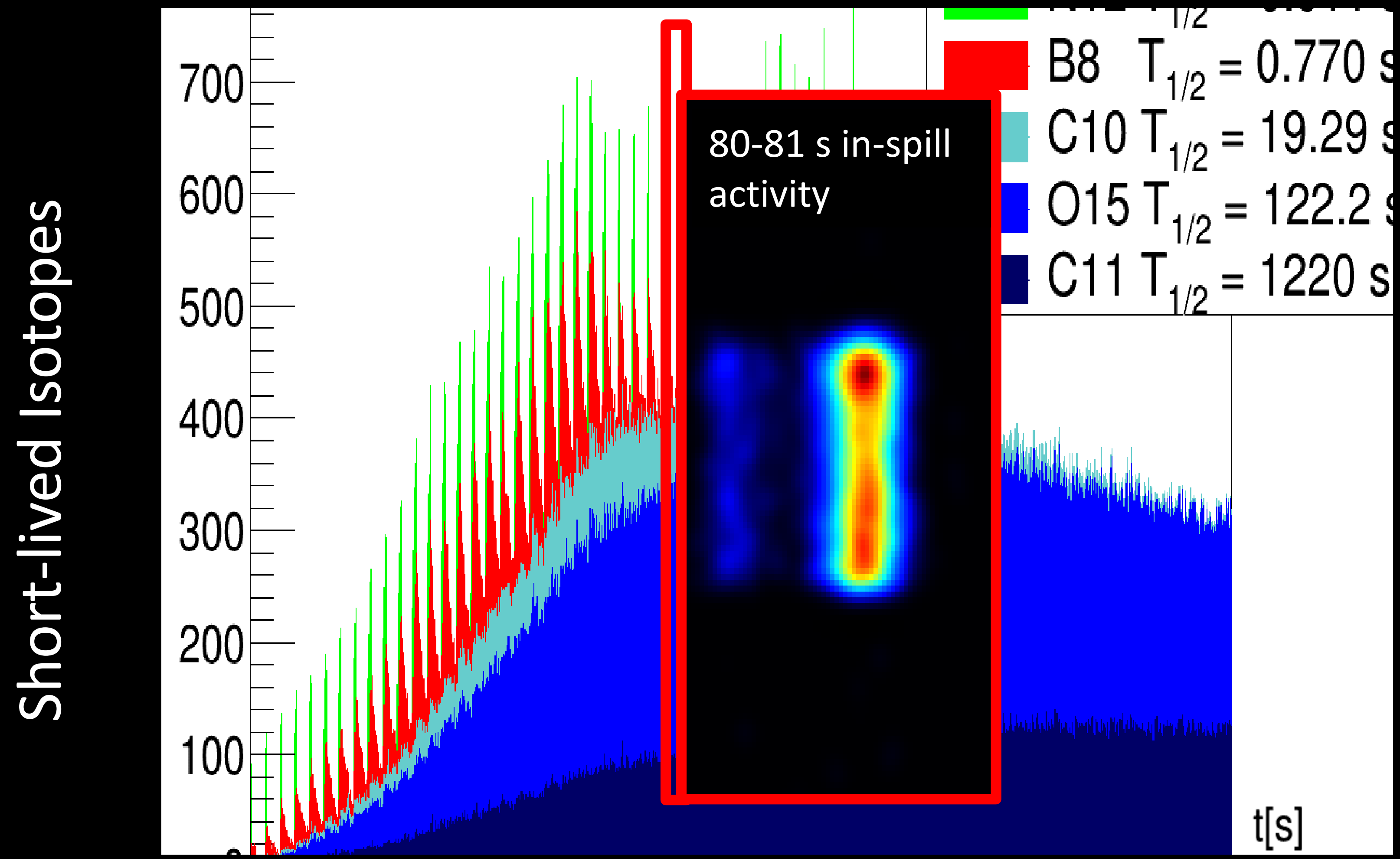
how to exploit
in-spill data (i.e., short lived isotopes)?
prompt photons?

Range Monitoring / I3-PET*



*INFN CSN5 Young Researchers Grant (F. Pennazio)

Range Monitoring / I3-PET*



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Beam Monitoring / MoVeIT*

MoVe IT

erc UFSD

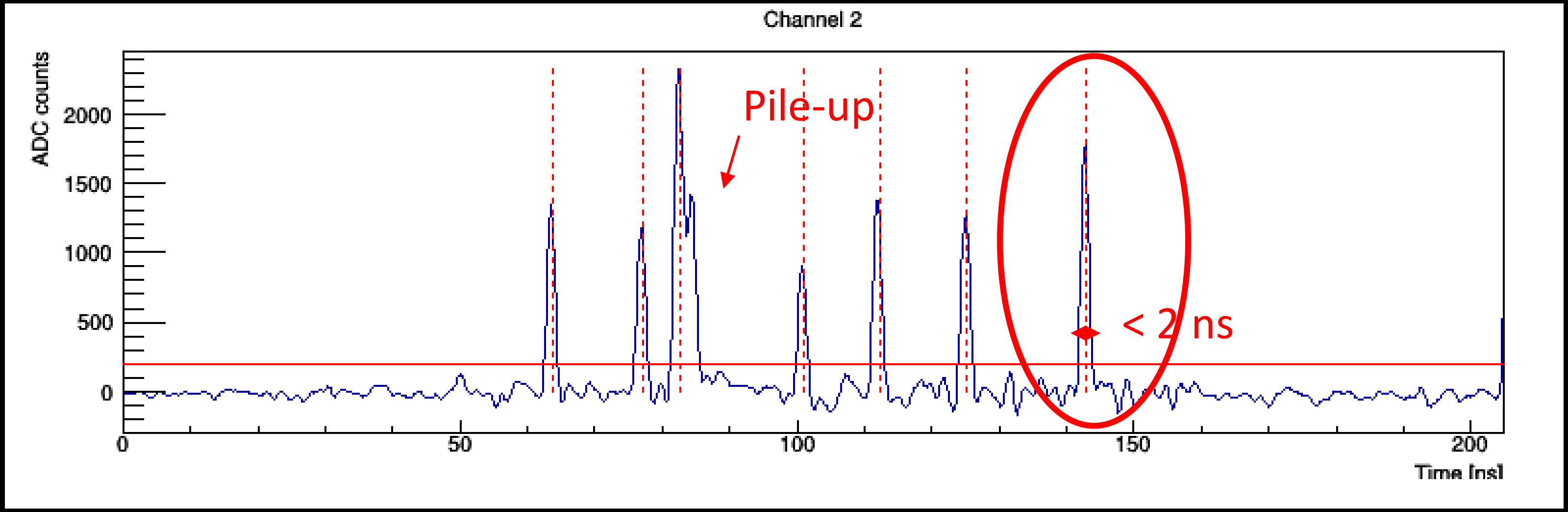
FONDAZIONE BRUNO KESSLER

INFN

Modeling and Verification for Ion beam Treatment planning

Development of dedicated strip silicon detectors based on LGAD/UFSD technology and of custom readout ASIC

Particle Counting



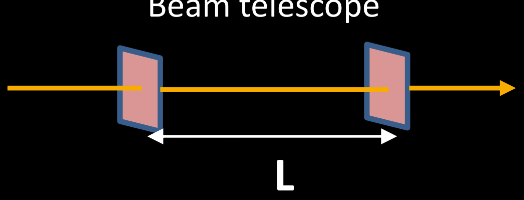
Data collected at CNAO

A. Vignati et al, “Innovative thin silicon detectors for monitoring of therapeutic proton beams: preliminary beam tests”, JINST 12 C12056 (2017)

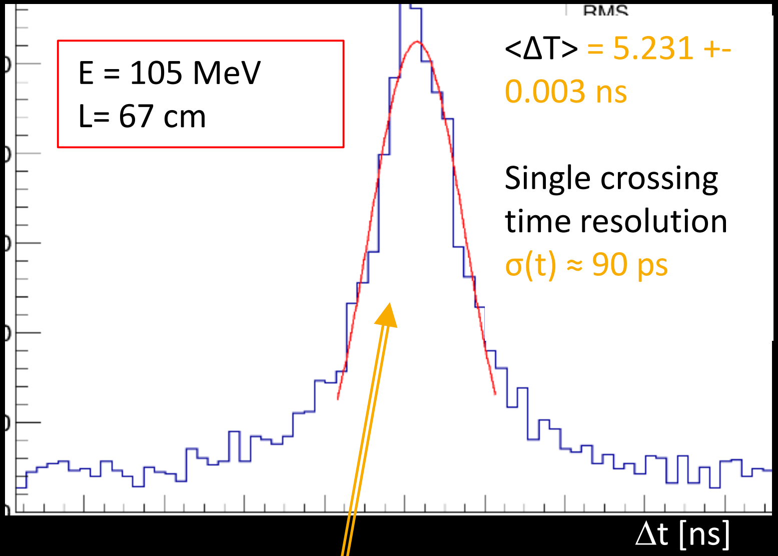
*INFN CSN5 Call 2017-2019

Beam Monitoring / MoVeIT*

Beam Energy
from Time-of-Flight

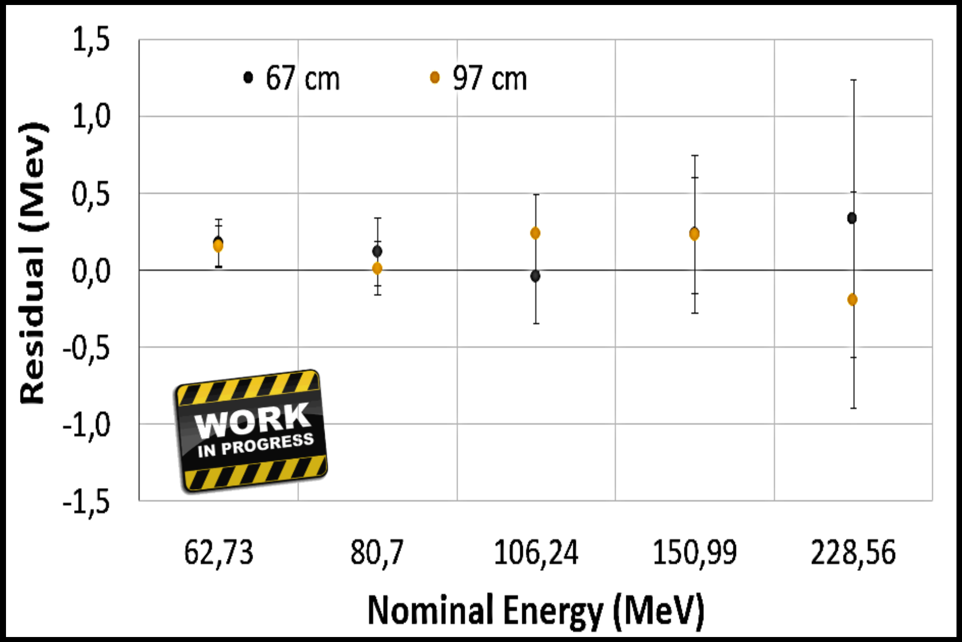


Data collected with a digitizer (5 Gs/s)
Constant Fraction algorithm applied off-line



Correlated pulses in the peak

Residual = Nominal E – Measured E



*INFN CSN5 Call 2017-2019

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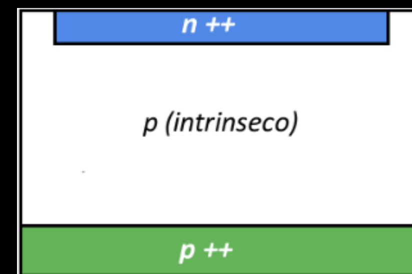
Beam Monitoring / MoVeIT*

Ionization chambers		Silicon detectors	

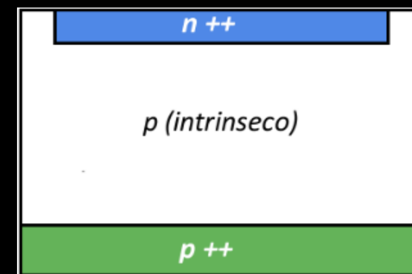


	Ionization chambers		Silicon detectors	
Charge collection time:	~ 100 μs	→	~ 1 ns	fast response time, single particle detection
Sensitivity:	~ 10^4 protons	→	single particle	
Spatial resolution:	~ 100 μm	→	~ 10-100 μm	
Time resolution:	poor	→	~ 100 ps	(30 ps with UFSD)
# of particles:	indirect	→	direct counting	(single particle detection)
Magnetic field:	sensitive	→	insensitive	

Beam Monitoring / MoVeIT*

Ionization chambers

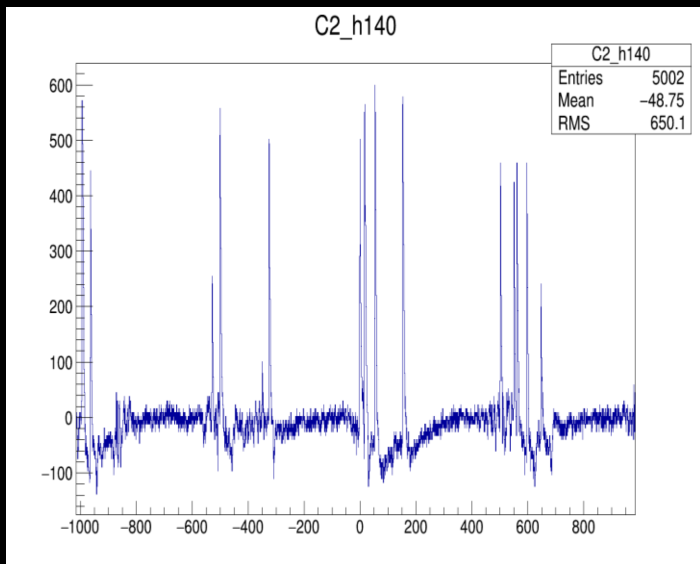
Silicon detectors



Ionization chambers		Silicon detectors
Saturation effects at very high currents	→	signal pile-up (depending on the segmentation)
radiation resistant	→	prone to radiation damage
Simple, reliable, stable, cheap	→	more complex architecture, readout and operation
Large size	→	Small size

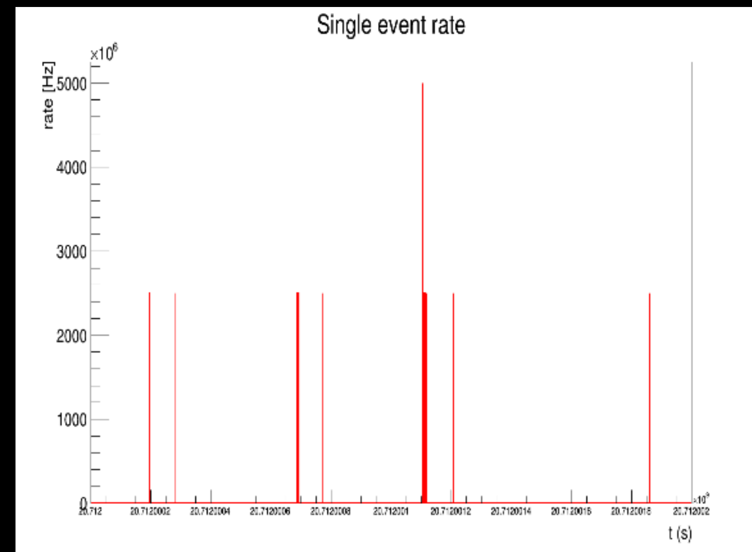
Range Monitoring / I3-PET*

UFSD primaries



2 µs snapshot of UFSD strip @ CNAO, 151 MeV proton beam (preliminary results)

INSIDE secondary events



2 µs snapshot of INSIDE @ CNAO, 151 MeV proton beam (preliminary results)

Same structure -> UFSD are suitable for bunch discrimination

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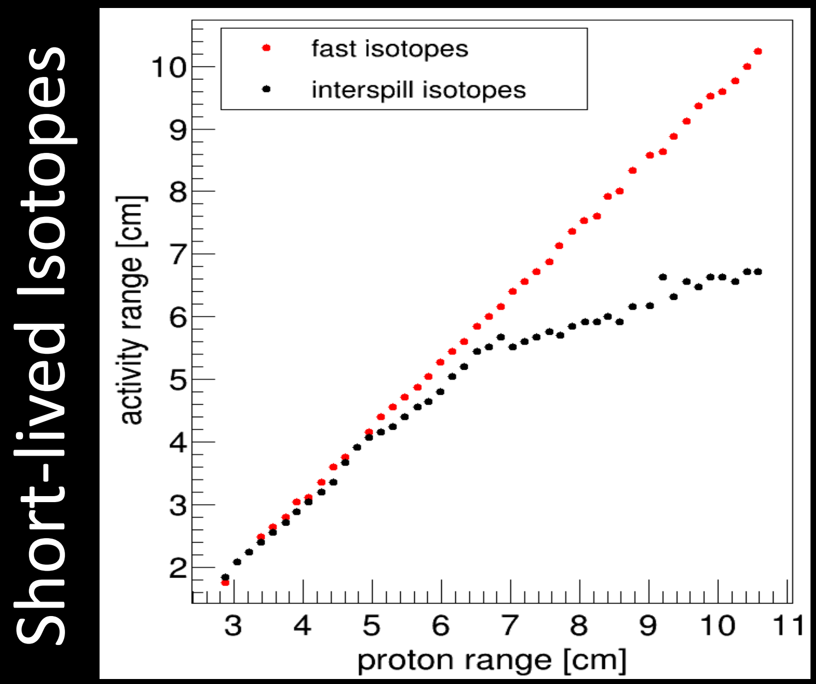
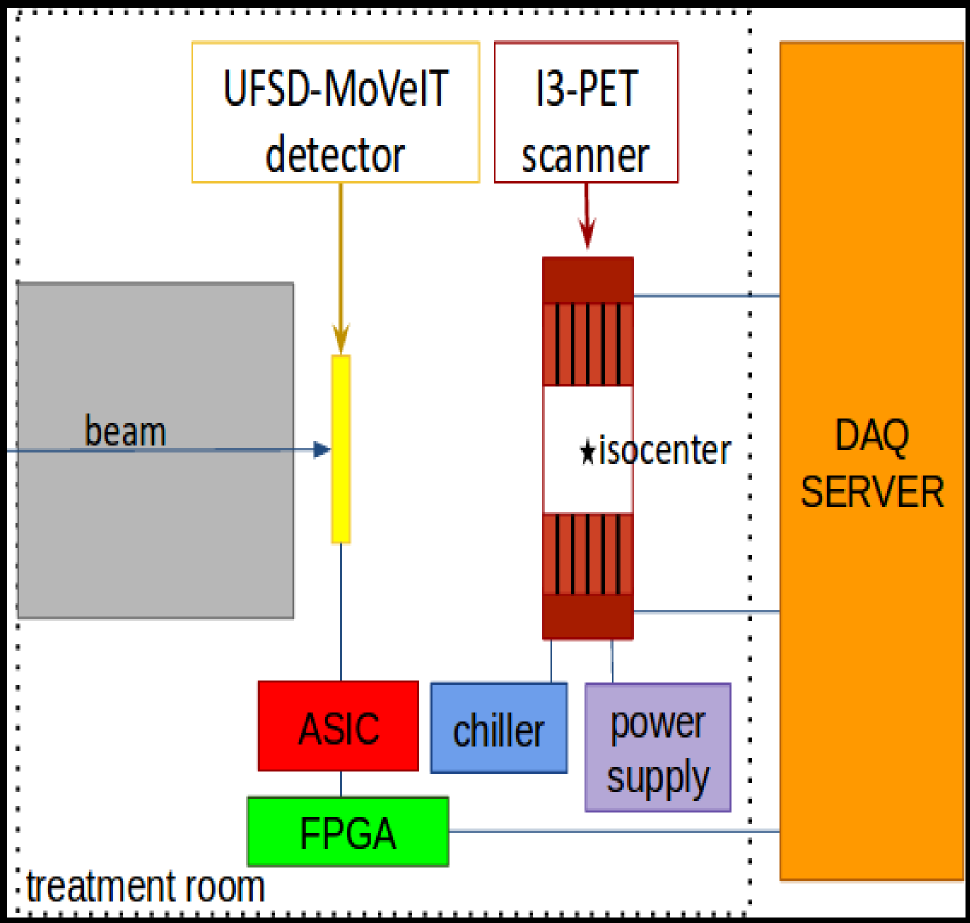
Range Monitoring / I3-PET*





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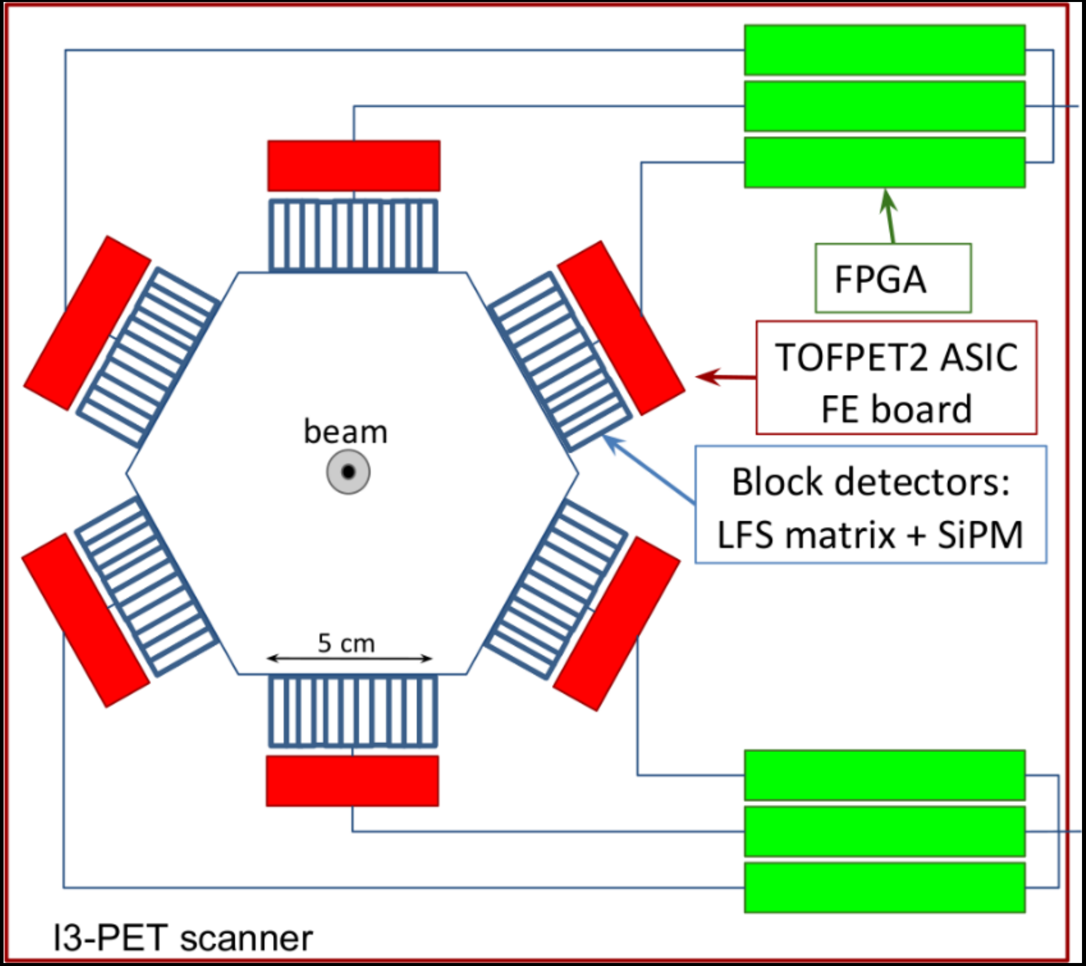
Range Monitoring / I3-PET*

Small diameter scanner

LFS+SiPM detectors

TOFPET2 ASICS (50 ps LSB, 480 kHz/channel event rate)

Readout & DAQ with Xilinx FPGA



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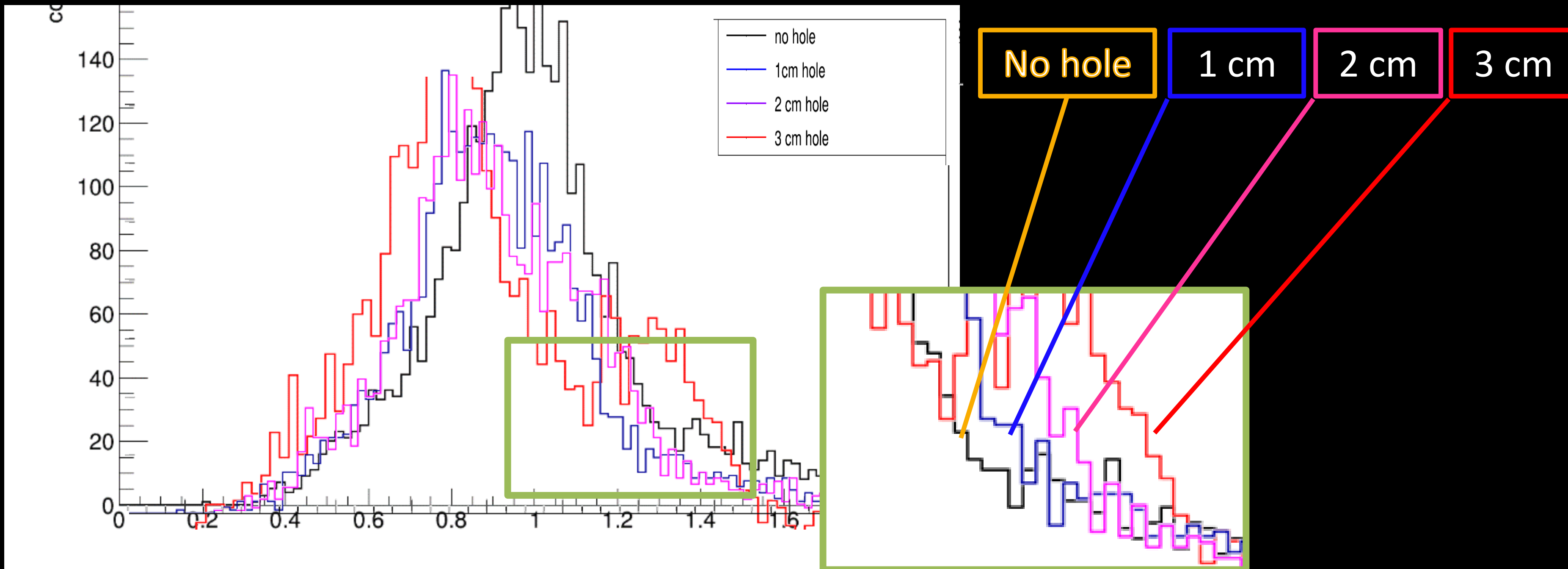
Range Monitoring / I3-PET*



FLUKA simulation of CNAO pencil beam impinging on PMMA phantom

- UFSD 3x3 cm^2 detector, 30 ps time resolution
- PET block detector, 215 ps CTR
- Preliminary hits digitization & coincidence finding
- $2.5 \cdot 10^6$ protons (< typical spot), 125 MeV

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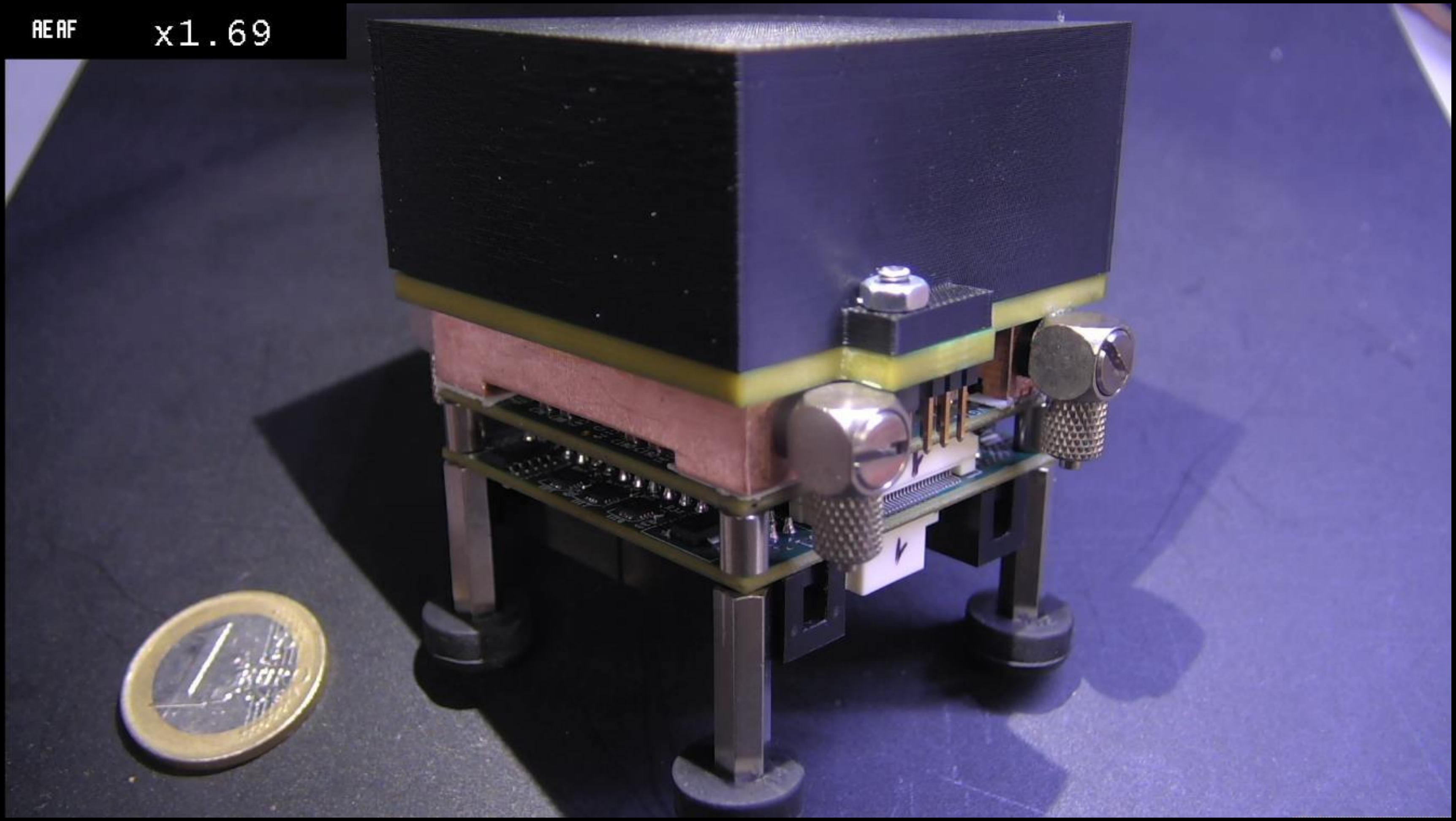
Range Monitoring / I3-PET*



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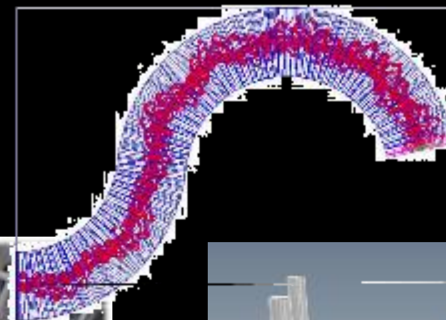
Ga-Toroid

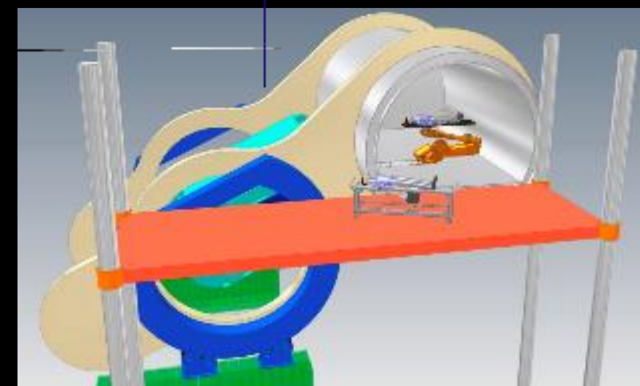
Ion Gantries

HIT
Heidelberger Ionenstrahl-Therapiezentrum

NIRS
HIMAC



BROOKHAVEN
NATIONAL LABORATORY



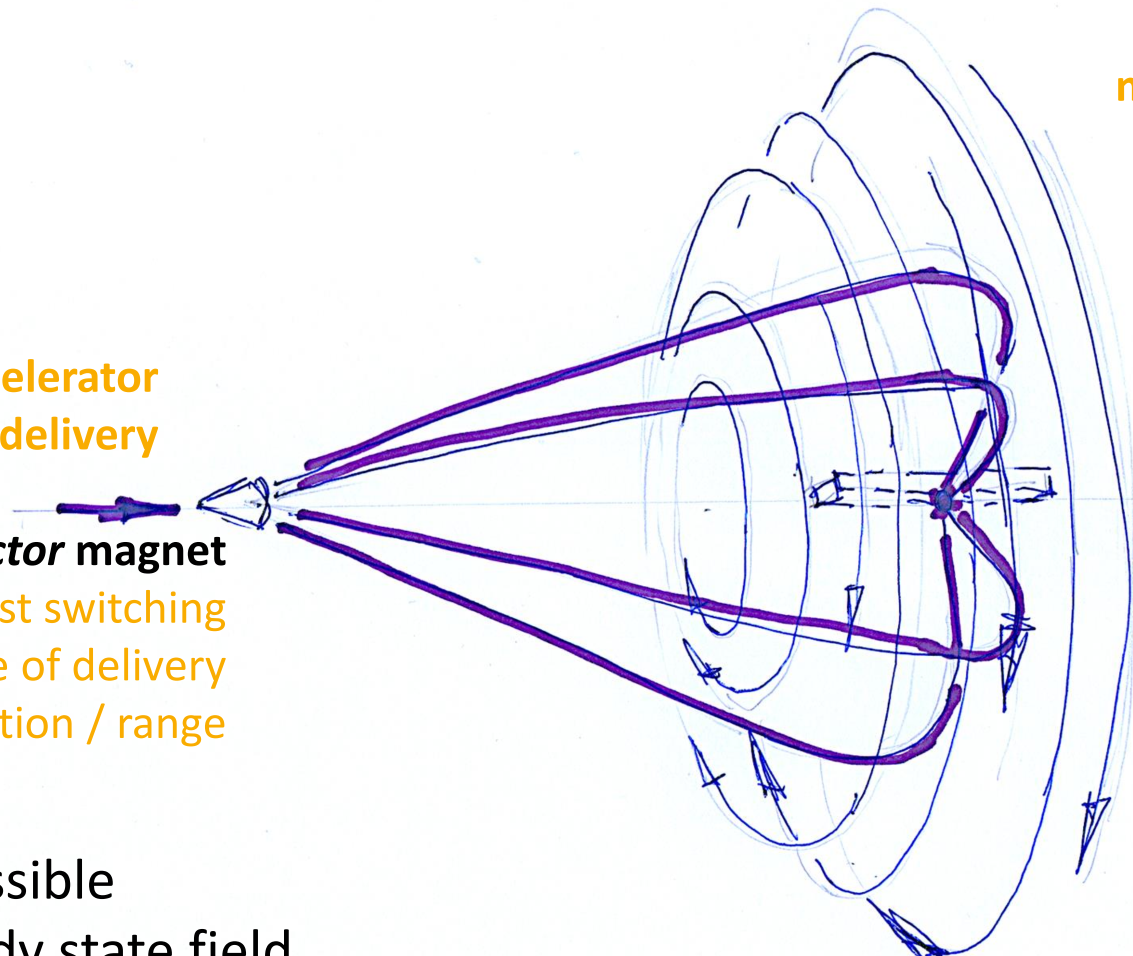
ULICE

Parameter		HIT	HIMAC	FFAG	Riesen-rad
Radius	[m]	6.5	5.5	4.2	8.5
Length	[m]	25	13	8	16
Weight	**[tons]**	**670**	**350**		**350**
Rot. angle	[deg]	360	360	360	360

GaToroid

Toroidal magnetic field operated in **steady-state**

Accelerator beam delivery



Patient

***Vector* magnet**
X-Y kicker with fast switching capability for change of delivery direction / range

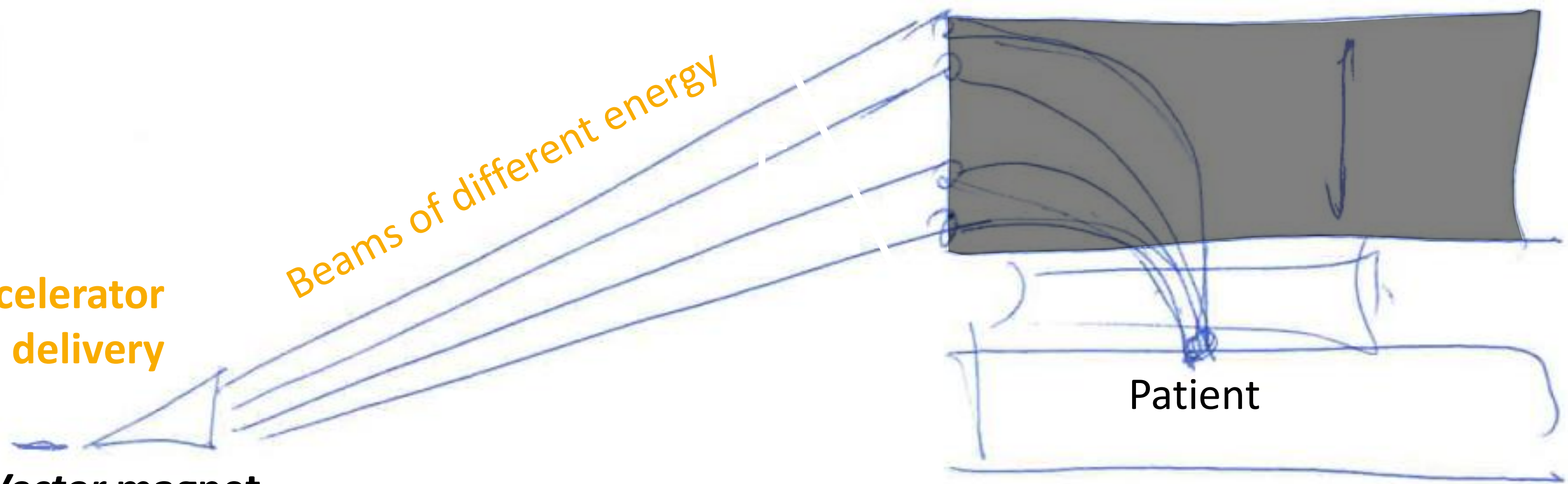
Fast switching is possible because of the steady state field

A Gantry and Apparatus for Focusing Beams of Charged Particles.
L. Bottura, European Patent Application EP 18173426.0, May 2018

GaToroid

Large acceptance superconducting magnet with **toroidal periodicity** operated in **steady-state**

Accelerator beam delivery



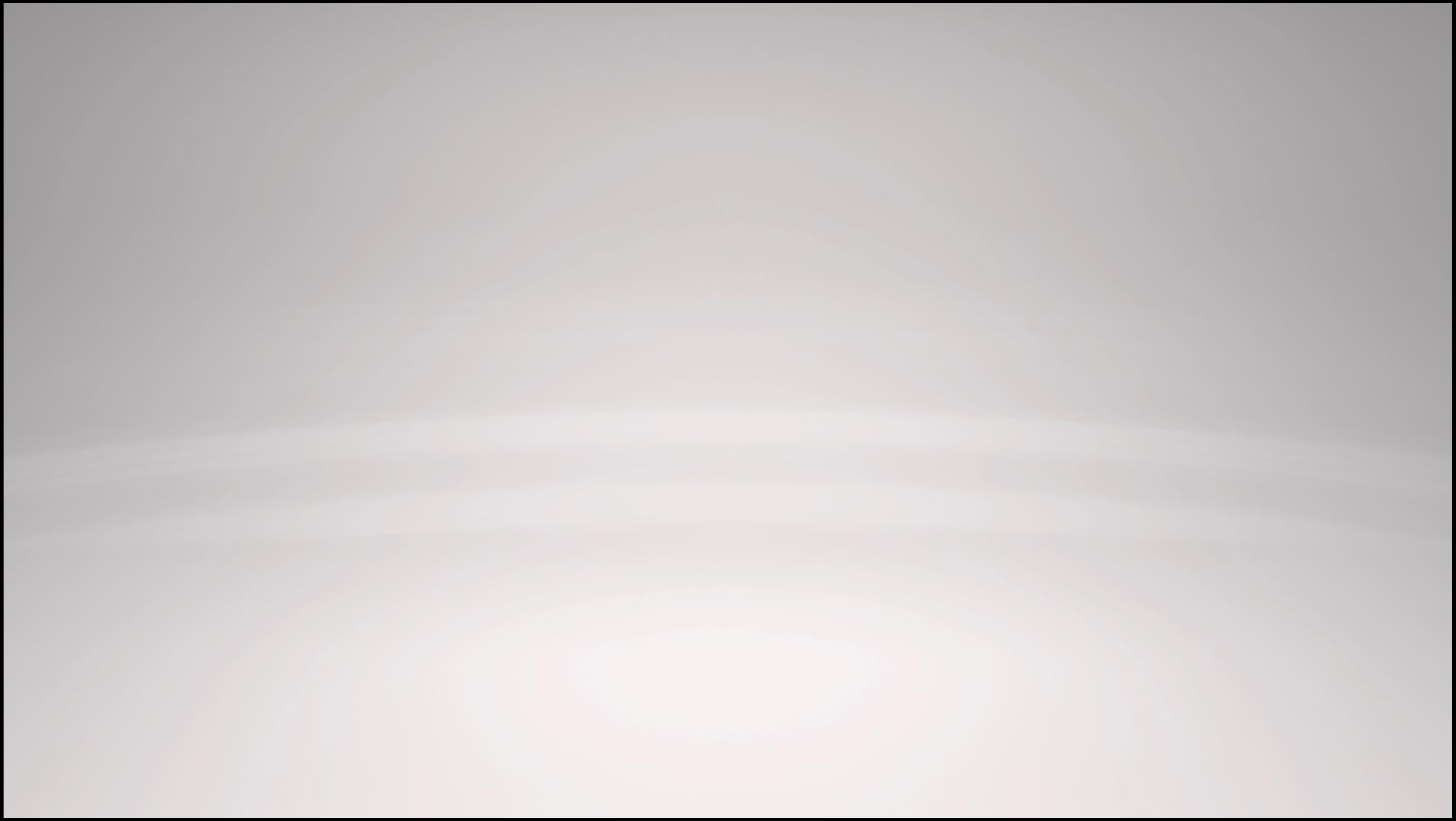
***Vector* magnet**

X-Y kicker with fast switching capability for fast beam energy switching

Fast energy switching is possible because of the steady state field and the large acceptance

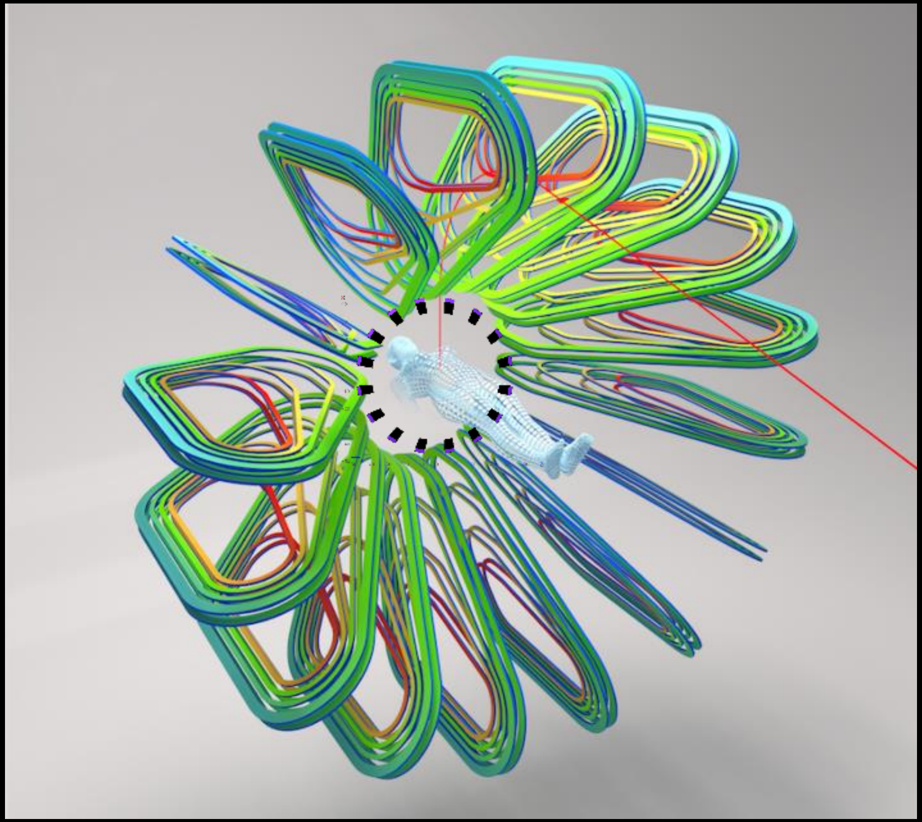
A Gantry and Apparatus for Focusing Beams of Charged Particles.
L. Bottura, European Patent Application EP 18173426.0, May 2018

GaToroid – typical session



A Gantry and Apparatus for Focusing Beams of Charged Particles.
L. Bottura, European Patent Application EP 18173426.0, May 2018

Beam and Range Monitoring in GaToroid



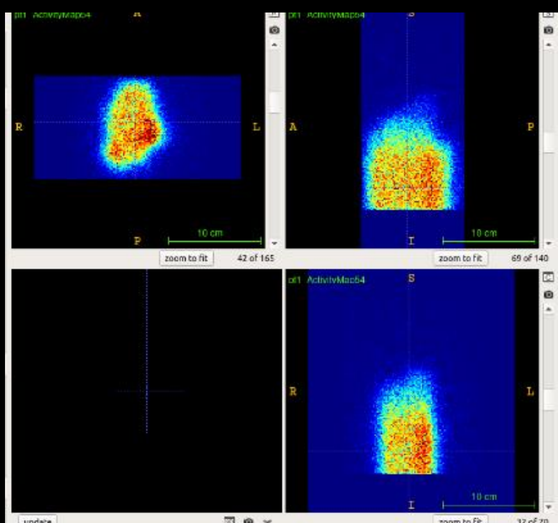
- **Beam Monitoring**
  - UFSD detectors on the beam entrance windows
    - size limitation overcome
- **Online Range Monitoring**
  - PET modules below the coils
    - good angular coverage
    - large field of view
    - improved statistics & image quality
    - in-spill data exploitation

Beam and Range Monitoring in GaToroid

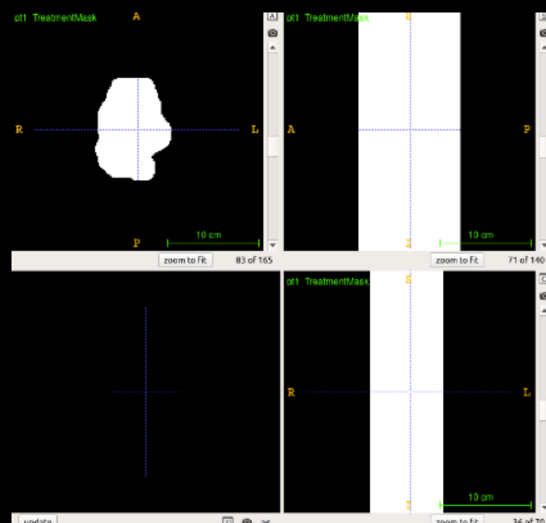
Treatment Plan Simulation

- 10^{10} protons
- E = 83-150 MeV

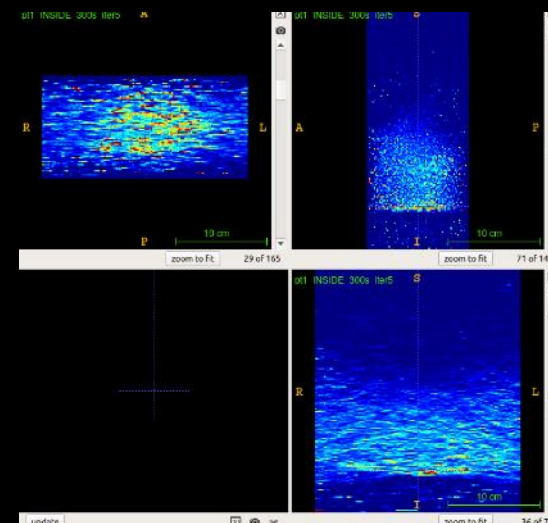
Monte Carlo (step1)



Treatment plan mask



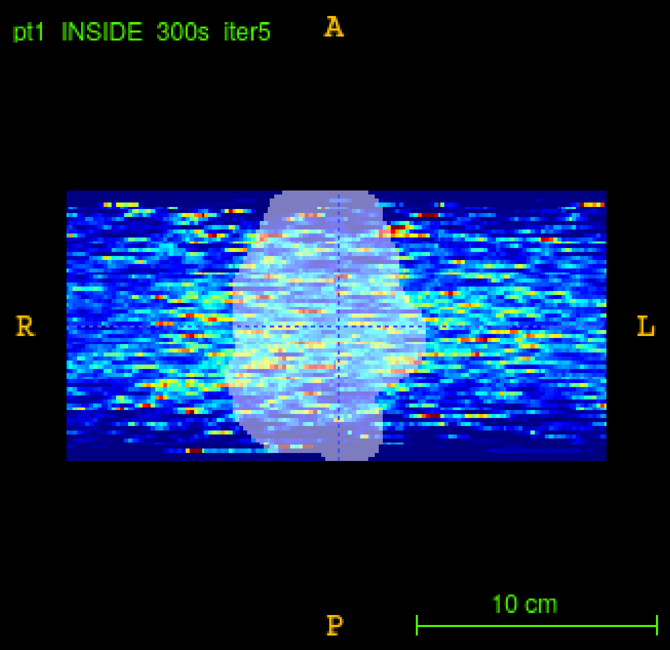
INSIDE reconstruction



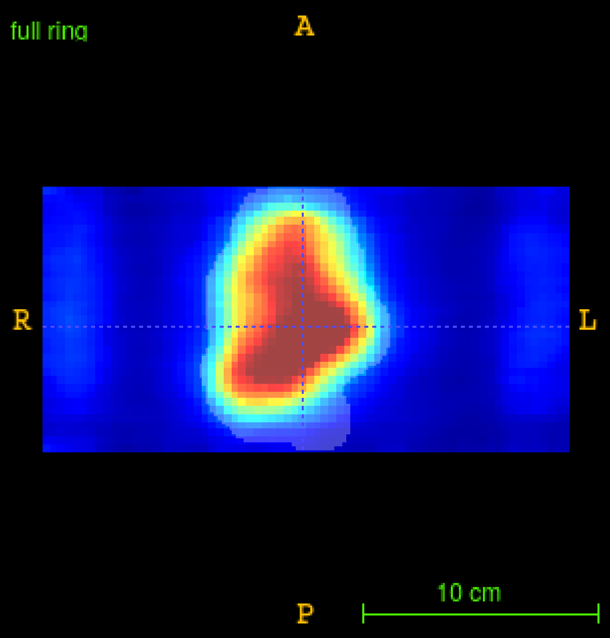
Beam and Range Monitoring in GaToroid

CNAO Treatment Plan Simulation

INSIDE reconstruction



GaToroid reconstruction

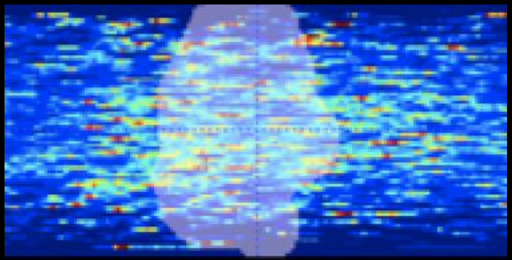


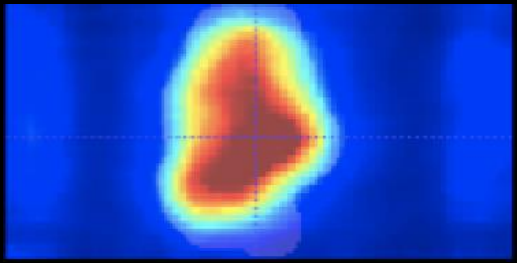
Summary

- (Online) Range Monitoring crucial for the treatment assessment in particle therapy

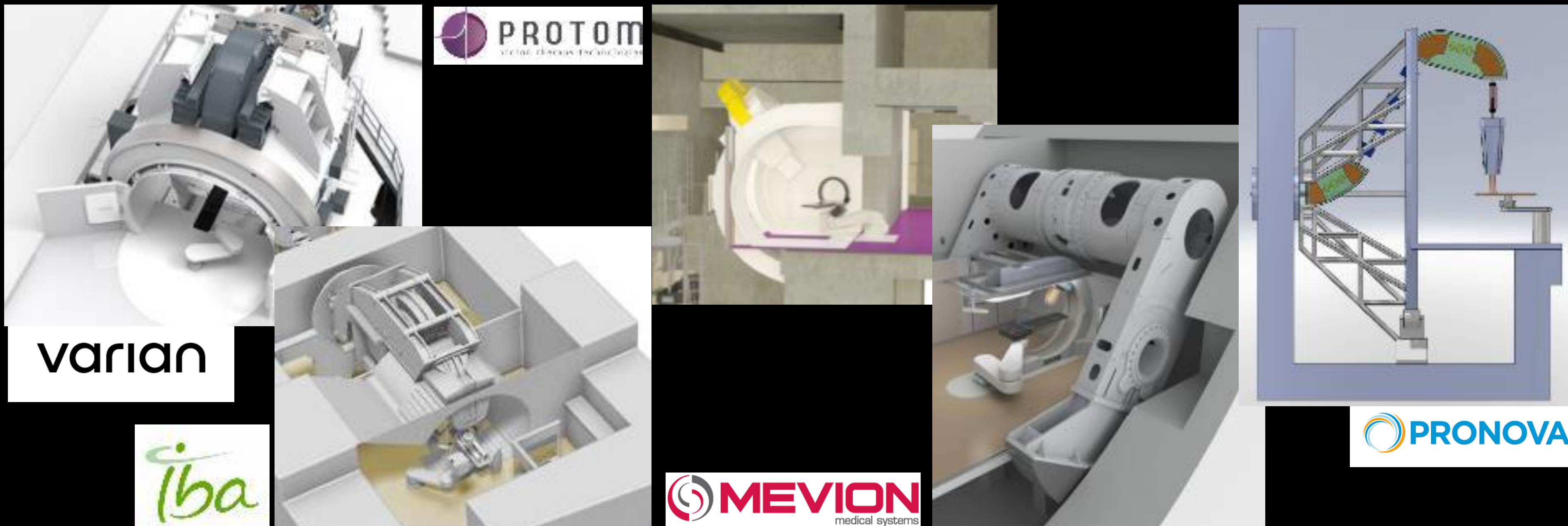
- Most promising modalities
  - Prompt gamma with passive collimation
  - In-beam PET
  - Hybrid systems

- Prospects: integrated design with gantries



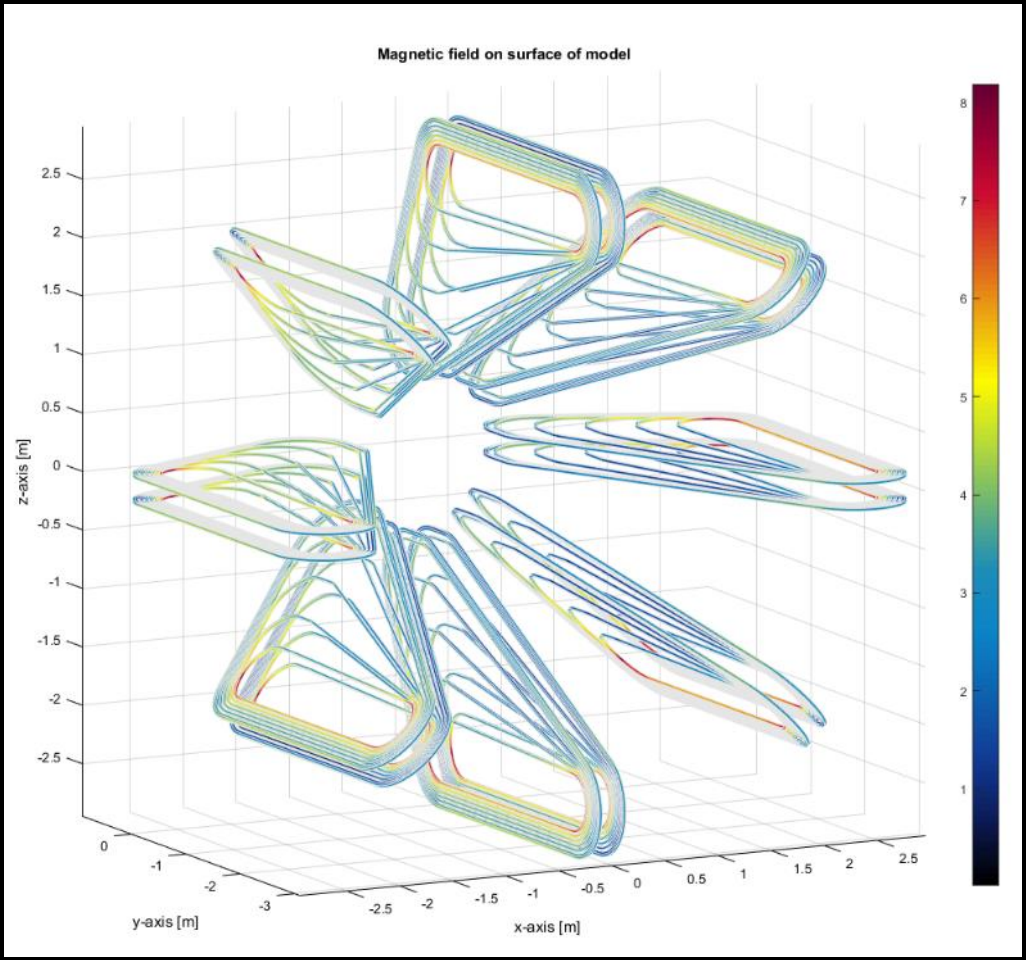


Proton Gantries



Parameter		Pro Beam	Proteus One	R330	S250i	Hitachi	SC360
Radius	[m]	5.5	3.6	≈ 4	4.3	4	4
Length	[m]	≈ 9.5	9.5	≈ 10	4.3	≈ 8	≈ 8
Weight	[tons]	270	110		17	125	25
Rot. angle	[deg]	360	220	180	190	360	360

GaToroid for carbon ions



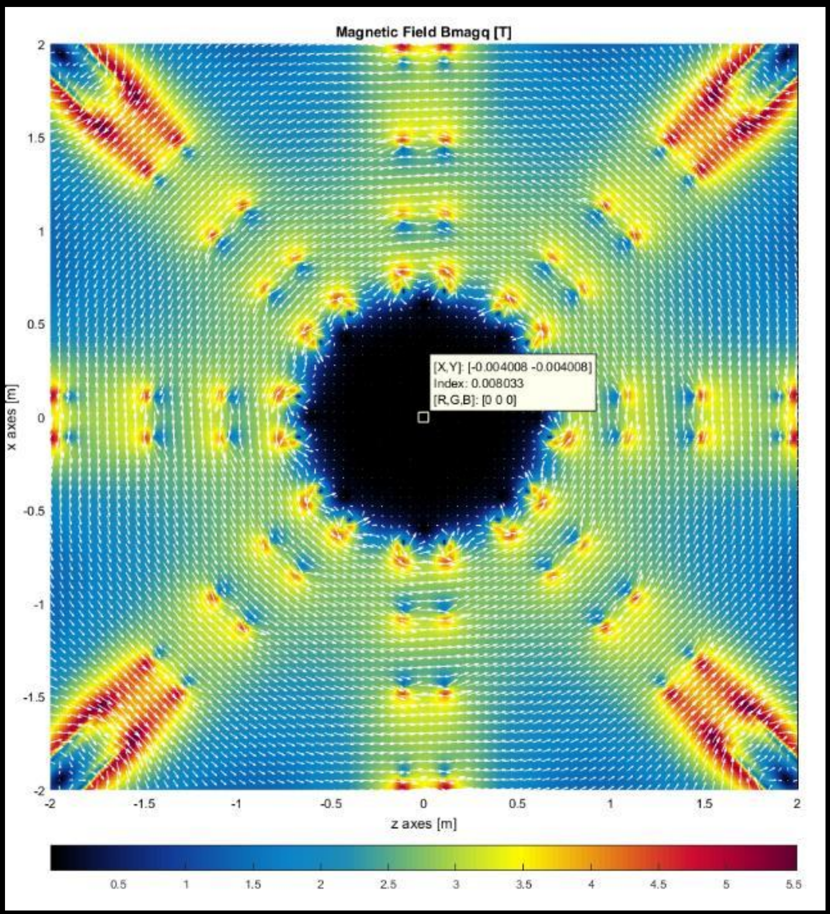
Parallel Channel

- 8 coils
- 8T peak field
- Bore: 130 cm

- Cost reduction
- Assembly simplification
- Inductance and stored ener gy reduction

- Force imbalance

GaToroid for carbon ions



Field lines are a bit distorted, but the Field at Isocenter is ~ mT

B ~ 0.1T at radius of 50cm

Field lines between 2 coils are basically parallel
→ dipole

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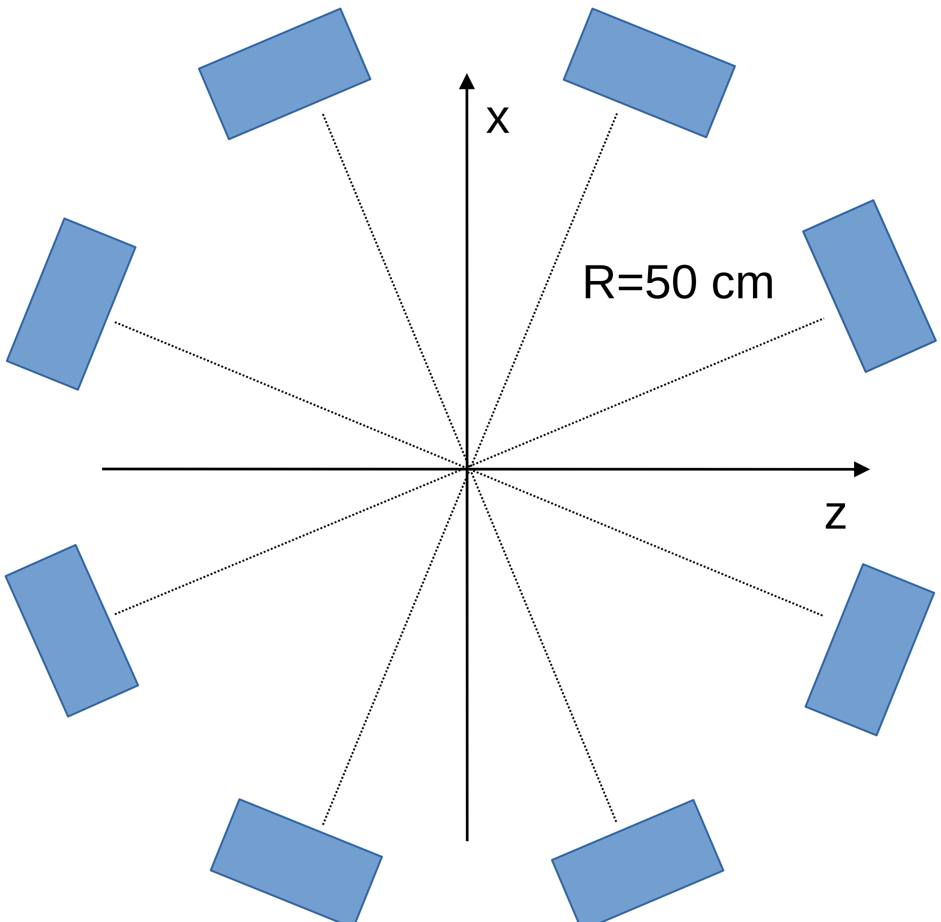
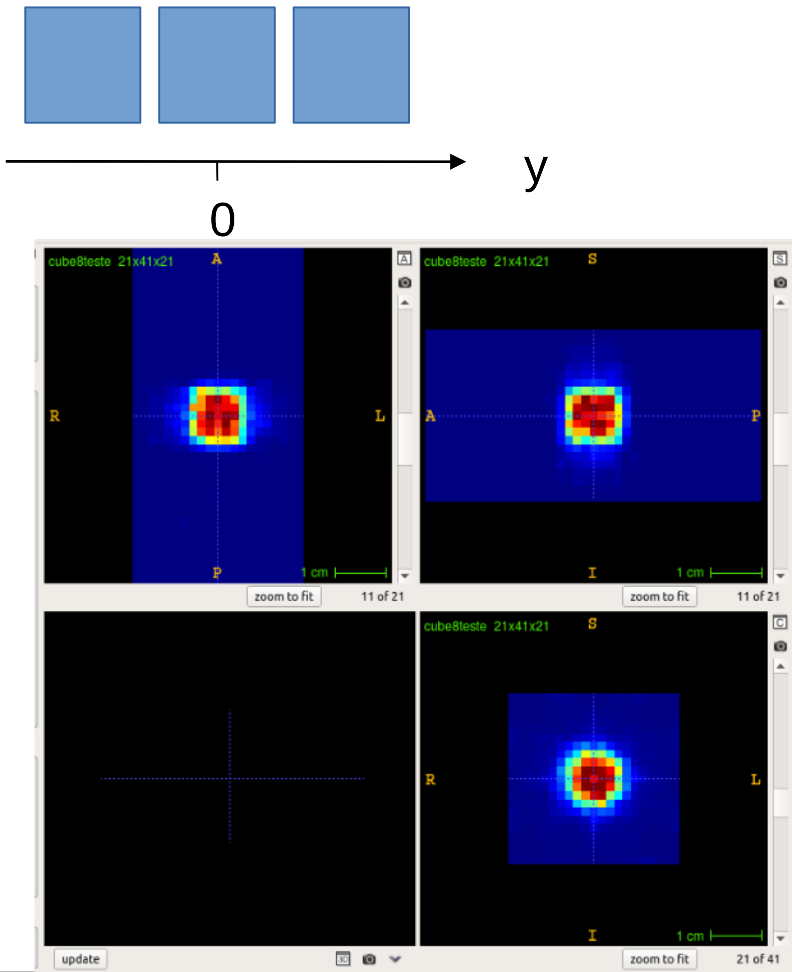
Beam and Range Monitoring in GaToroid





8 PET heads, 3 modules each, 5x15 cm^2