Results of the INSIDE project

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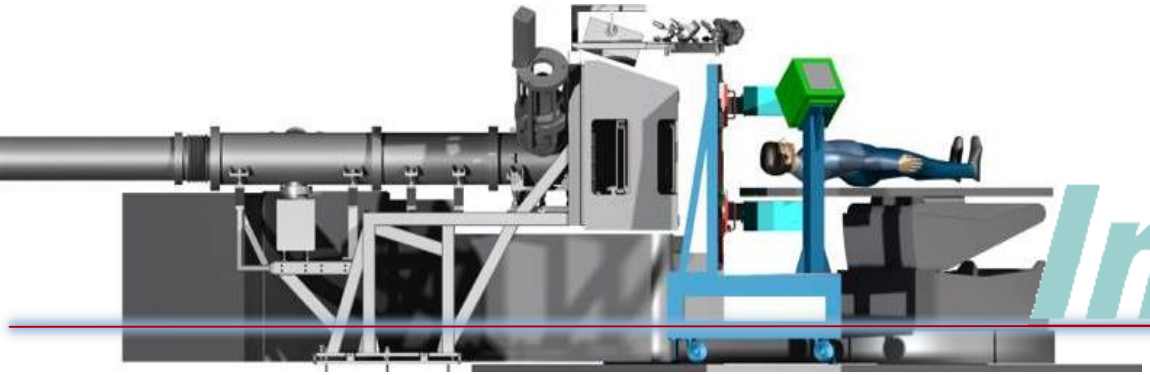
INFN Torino

Workshop on Innovative Delivery Systems in Particle Therapy, Torino, February 24th2017

Outline

- Range verification in hadrontherapy
- The INSIDE system
- Data monitoring and acquisition
- Monte Carlo simulations
- Test results with phantoms
- First in-vivo results



Range Verification in Hadrontherapy

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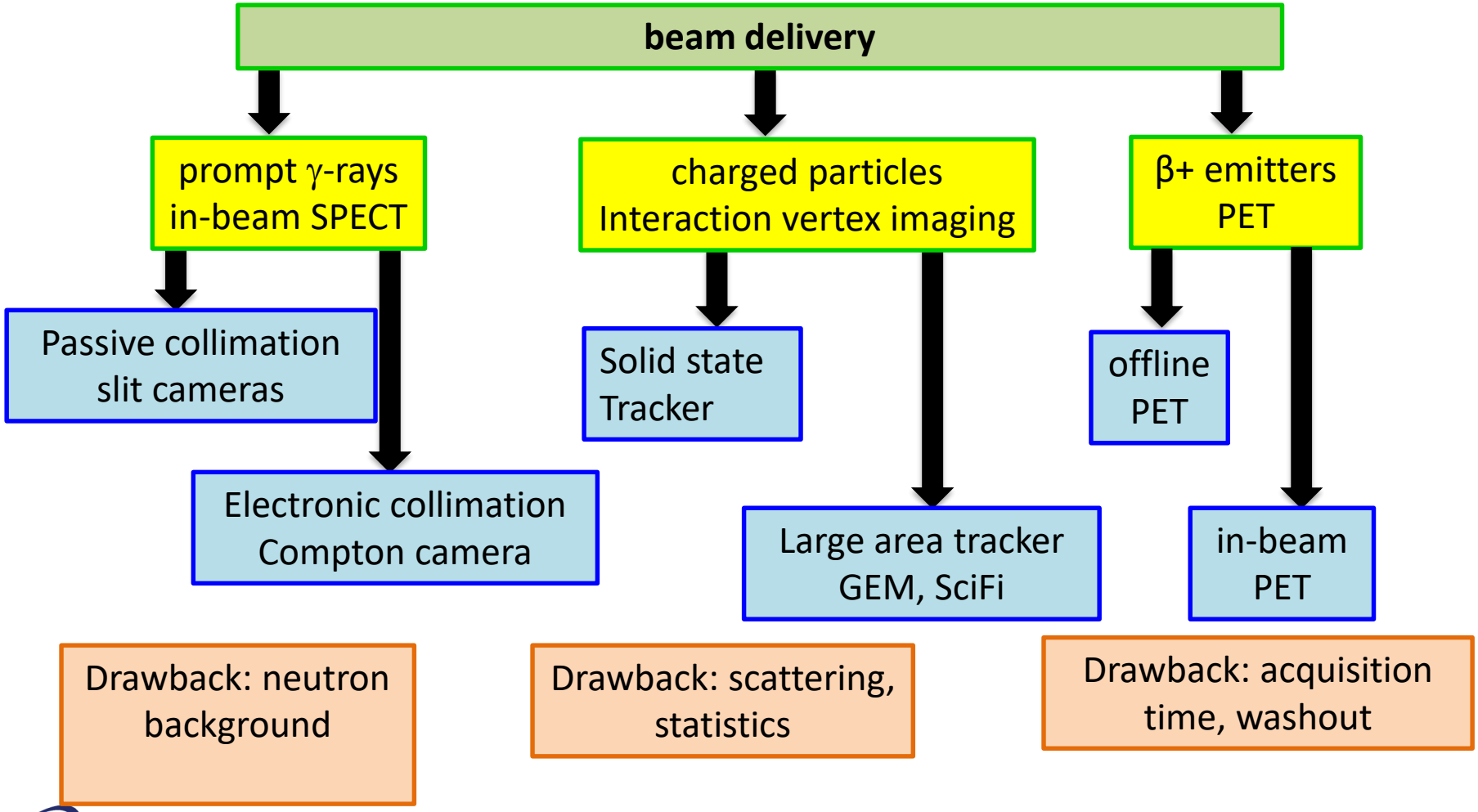
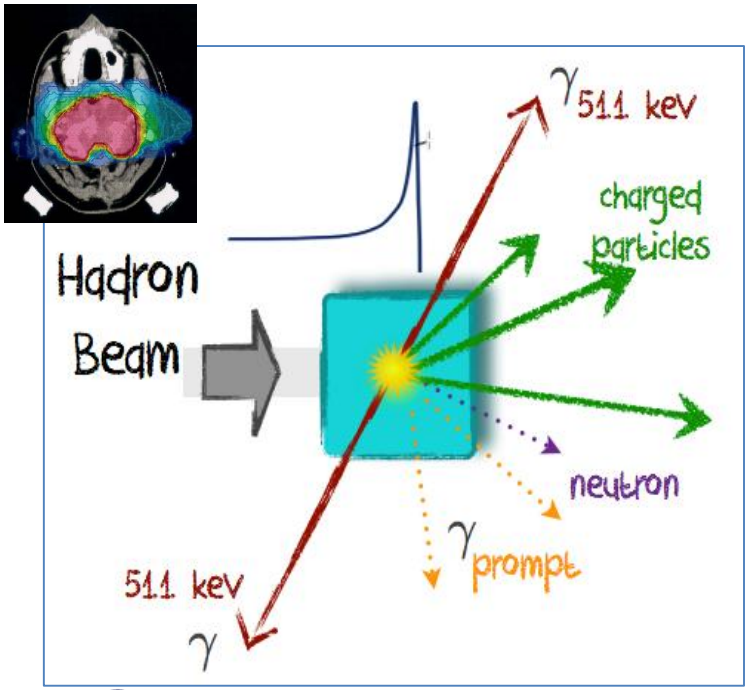
Particle Range Verification

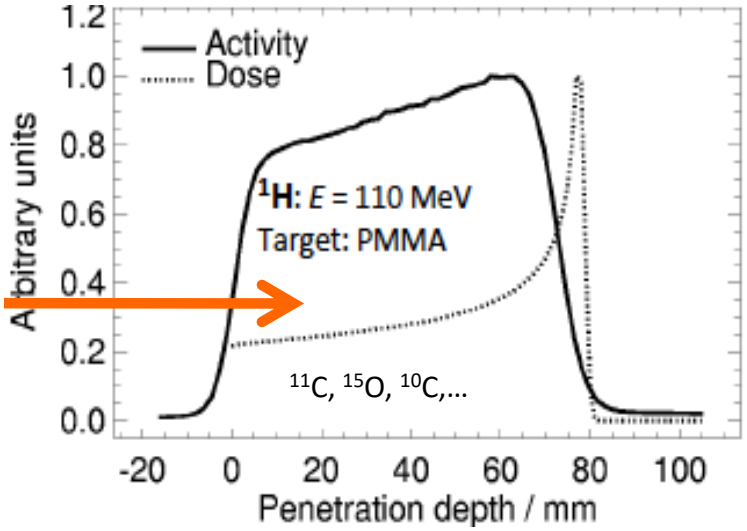


Particle Range Verification

Real time monitor of Bragg Peak depth with passive signals by secondary particles

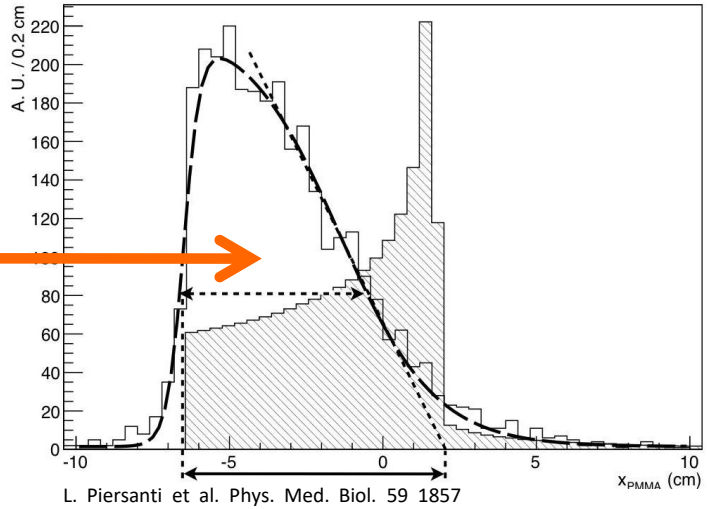


β⁺ activity distribution



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

prompt secondary particles emission



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

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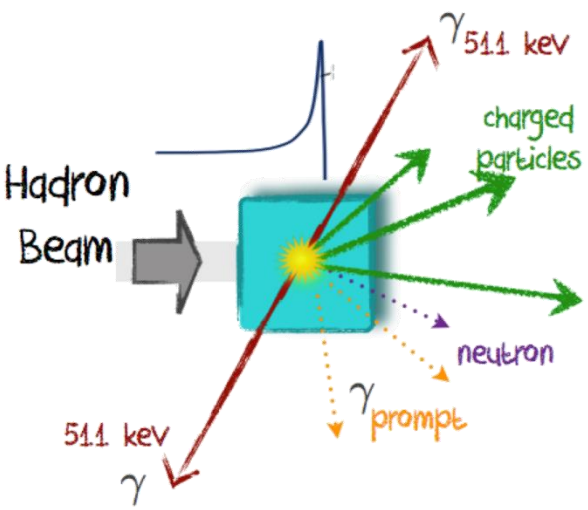
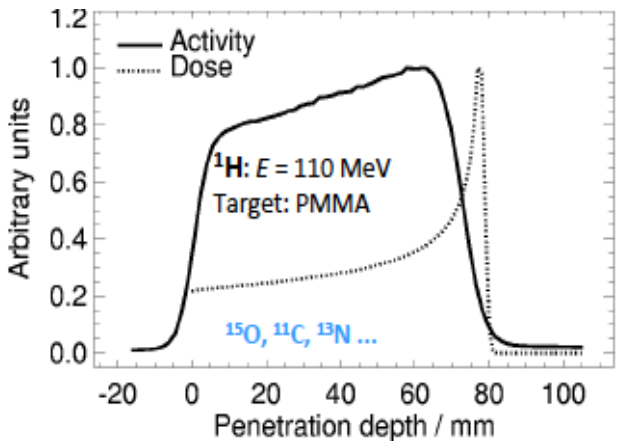
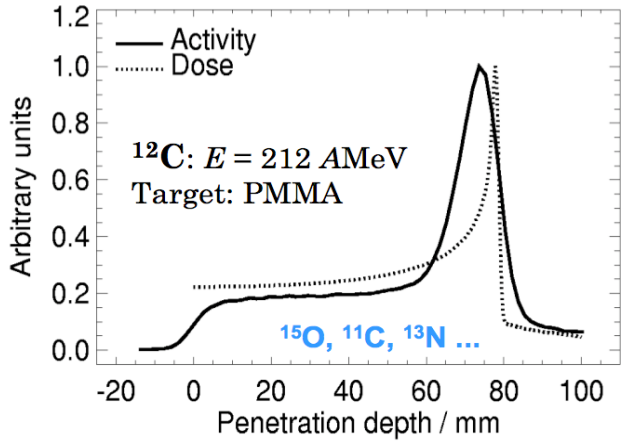
Particle Range Verification

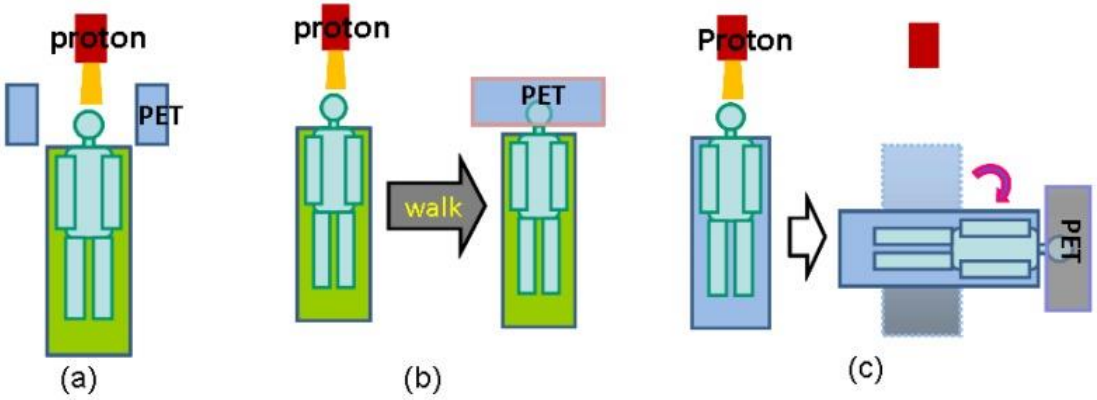


β+ isotopes





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.*

Main contribution:

^{11}C ($T_{1/2}$≈ 20.3 min)

^{10}C ($T_{1/2}$ ≈ 19.3 s)

^{15}O ($T_{1/2}$ ≈ 2.0 min)

^{13}N ($T_{1/2}$≈ 10.0 min)

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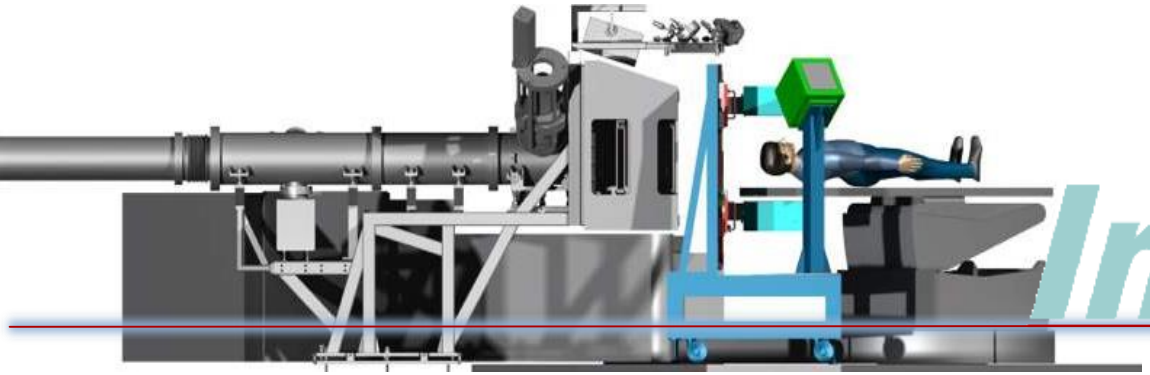

The INSIDE System

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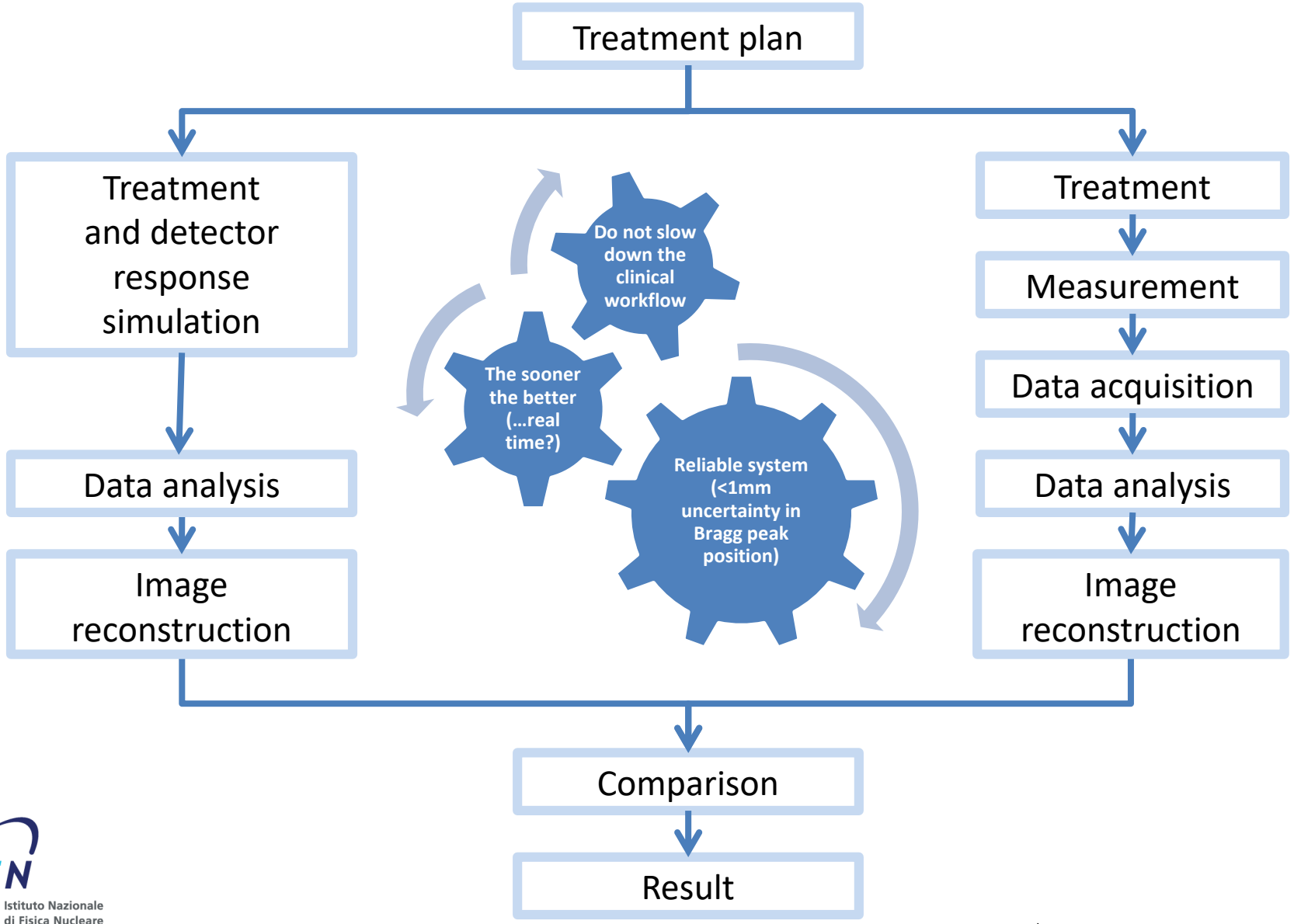
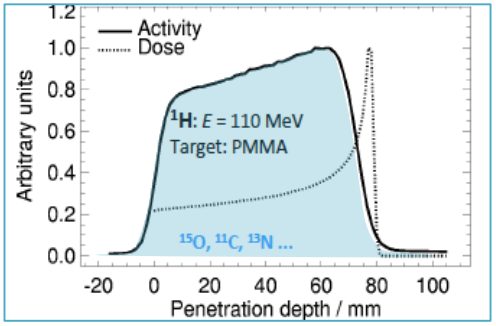
Operating Workflow

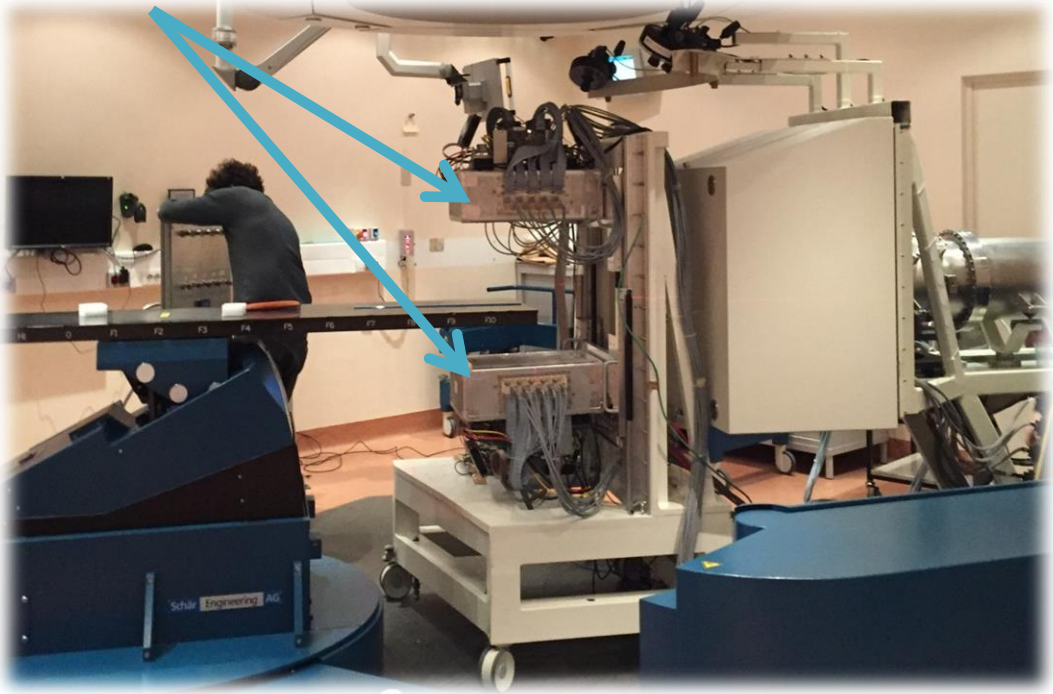


The INSIDE Project: in-beam PET



β⁺ activity distribution?

IN-BEAM PET PANELS



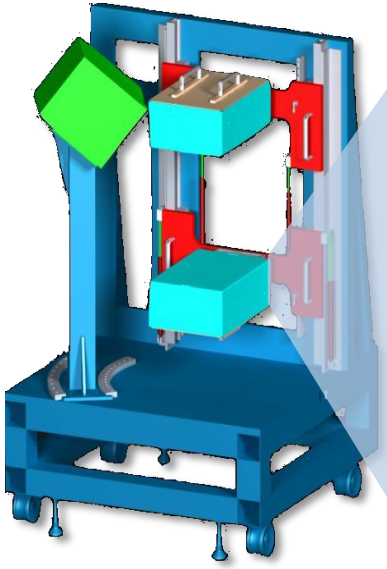
INnovative
Solutions for
In-beam
Dosim**E**try
in Hadrontherapy

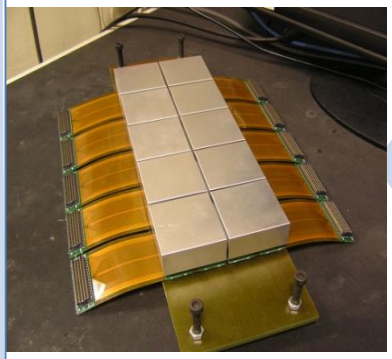
Funding by: PRIN + Centro Fermi + INFN (RM1-TO-MI-PI)

Designed to:

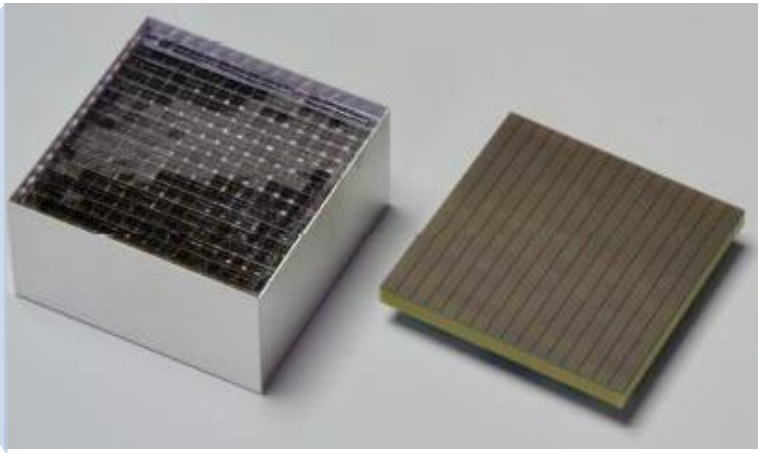
- operate in-beam
- **provide an IMMEDIATE feedback on the particle range**

In-beam PET Panels



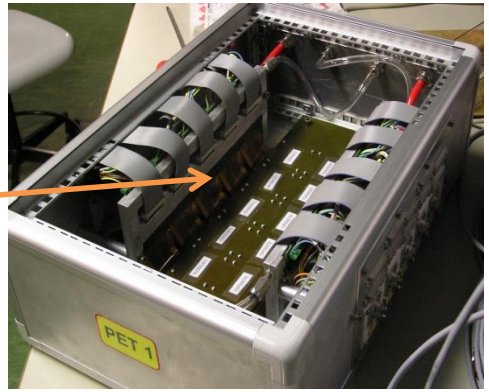


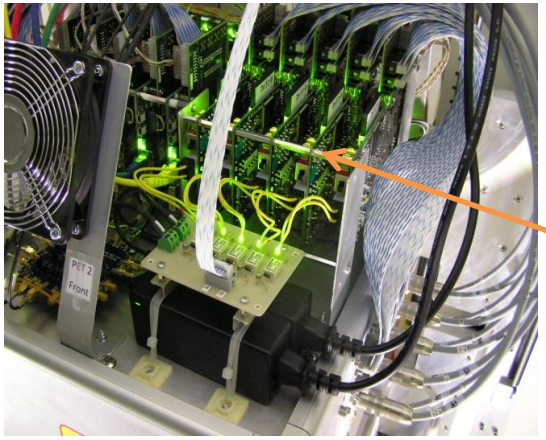
10 x 25 x 5 cm^3
Distance from the isocenter=30 cm



256 LFS pixel crystals (3x3x20mm^3) coupled one to one to MPPCs (Multi Pixel Photon Counters, SiPMs).

20xFE board (4 Tofpet ASIC[1] each)

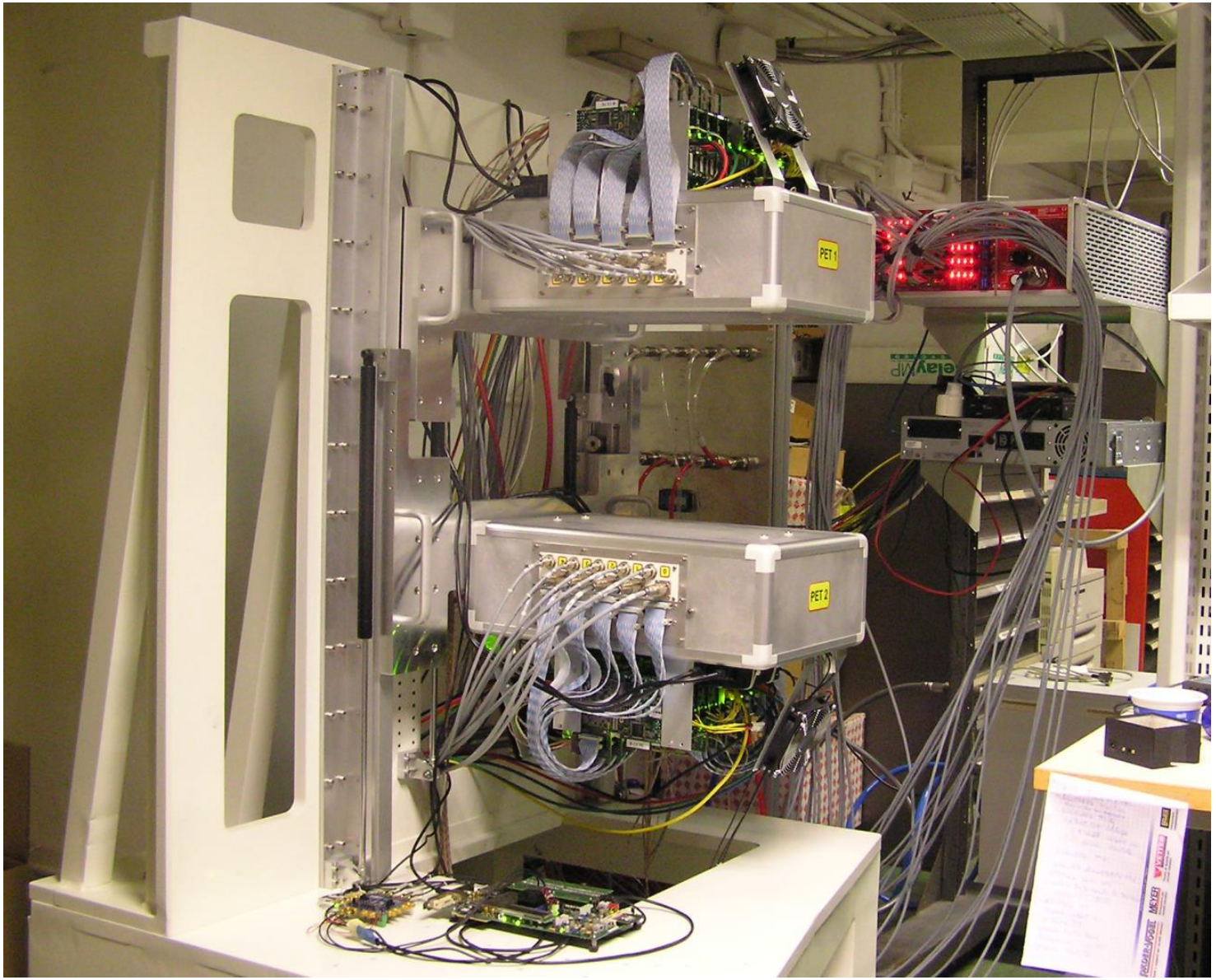




20xFPGA Xilinx Spartan6-SP605

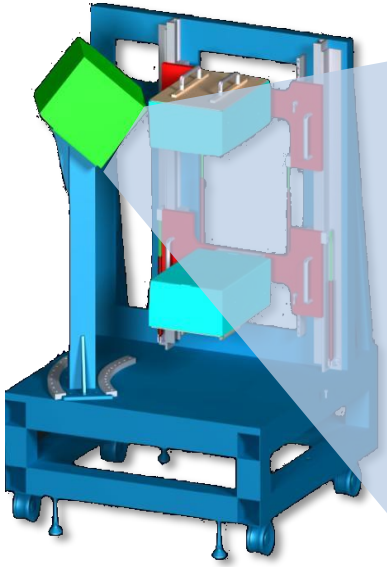
[1] Work partly funded by the European Union 7th Framework Program (FP7/ 2007-2013) under Grant Agreement No. 256984 EndoTOFPET-US and supported by a Marie Curie Early Initial Training Network Fellowship of the European Union 7th Framework Program (PITN-GA-2011-289355-PicoSEC-MCNet).

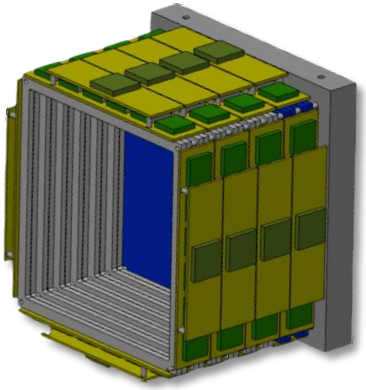
January 2016



Completed in-beam PET detector (running) @ INFN Torino

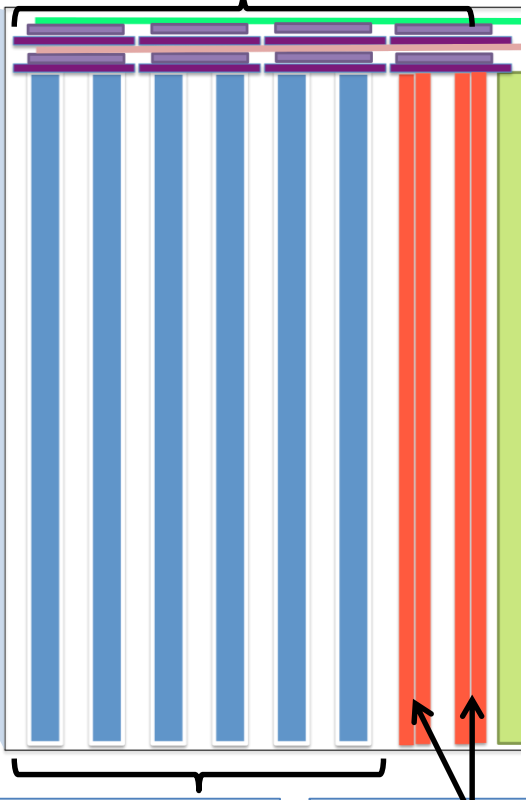
The INSIDE Project: dose profiler

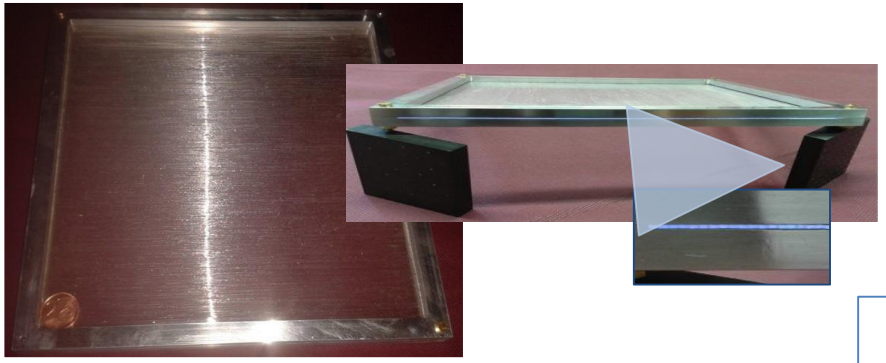




28 x 28 x 35 cm^3

Elettronics: BASIC32, FPGA



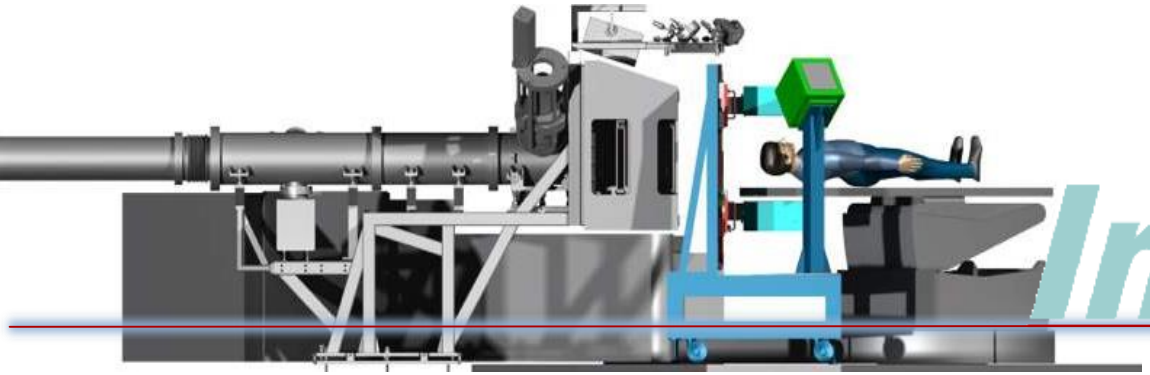


6 fibre planes planes of orthogonal squared scintillating fibers coupled to SiPMs

plastic scintillator

The INSIDE Project: dose profiler

Assembled dose profiler @ INFN Roma - SBAI
Courtesy of G. Traini, V. Patera and G. Battistoni



Data Acquisition & Monitoring

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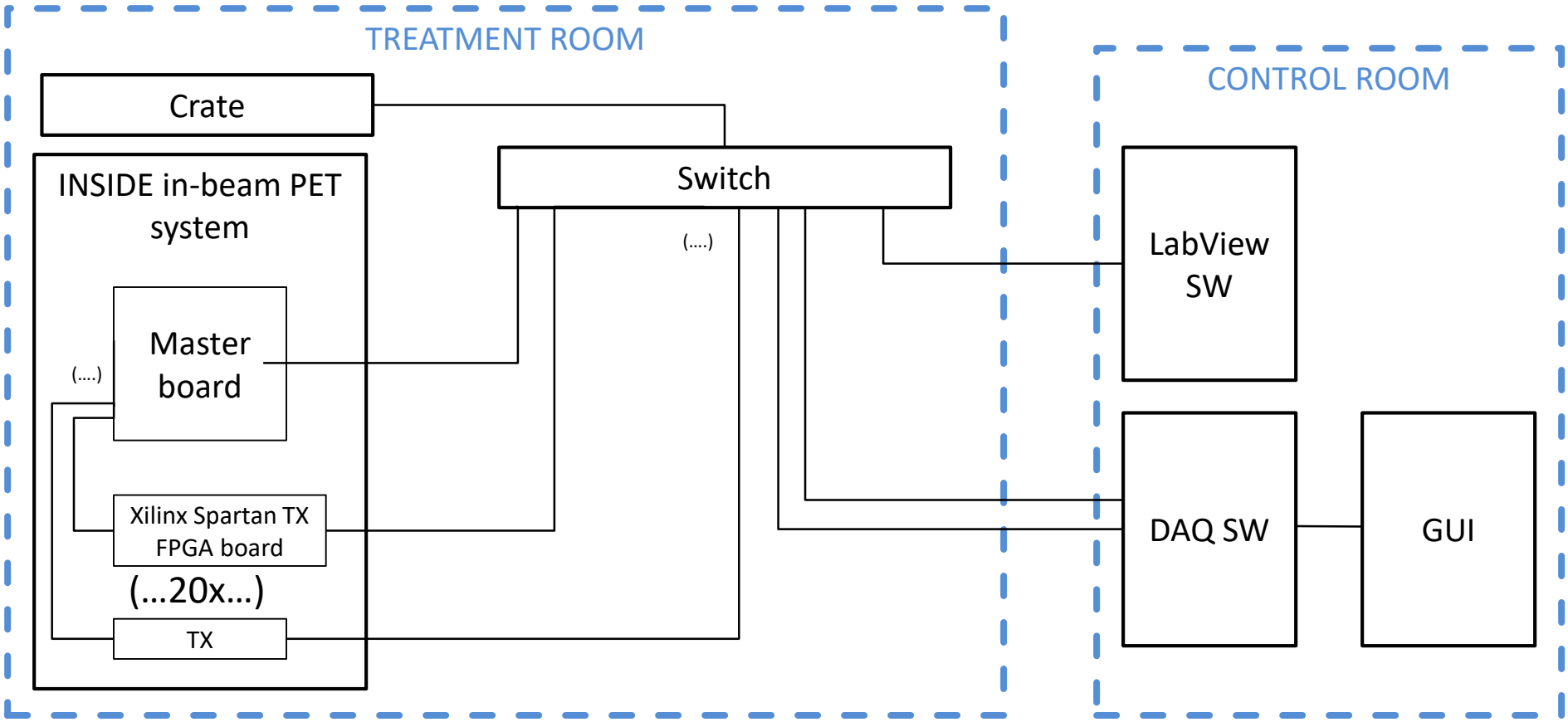
DAQ & Monitoring Chain



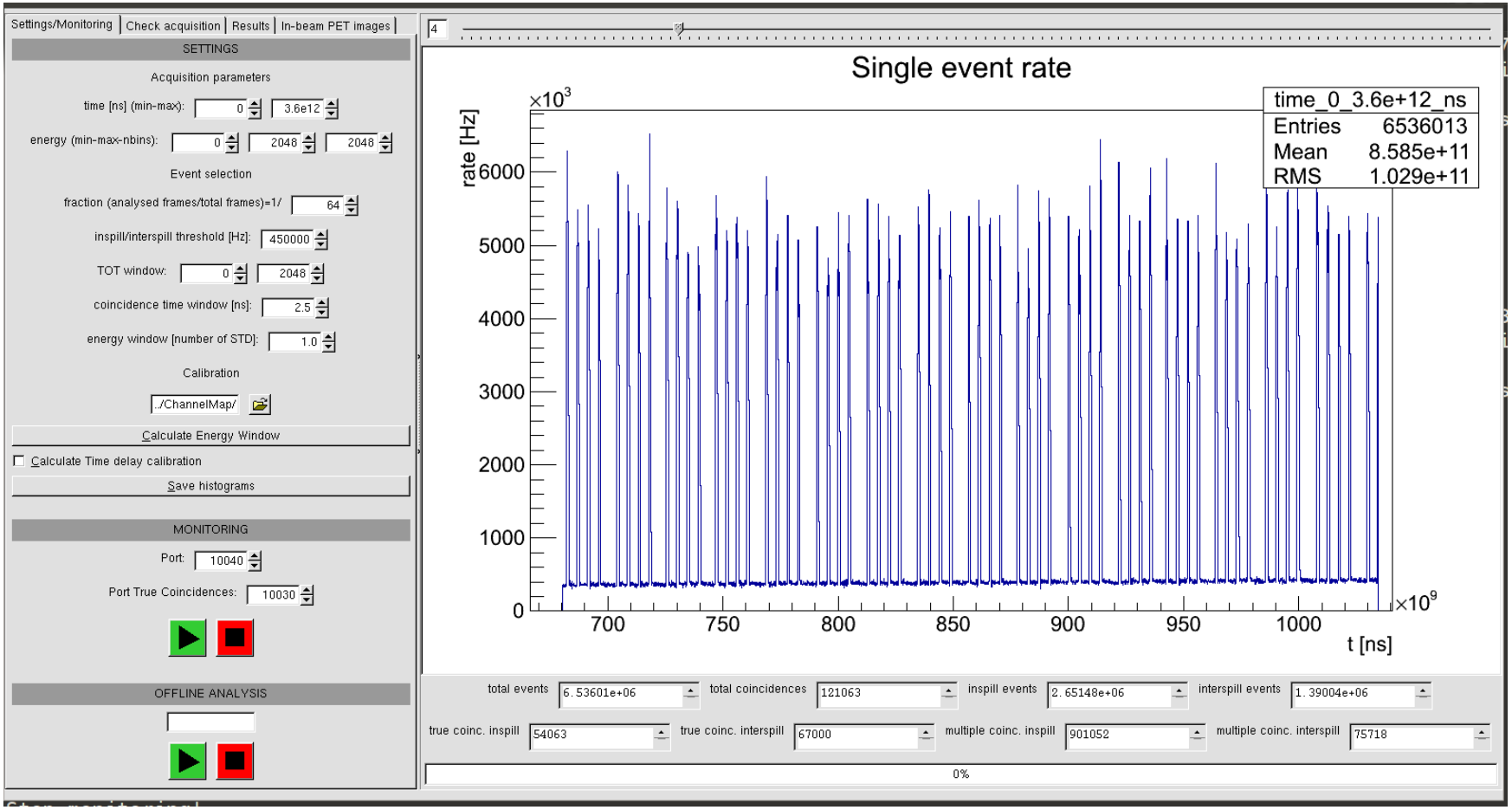
Switch: 24-port Gigabit + 8 port Gigabit
Control PC (desktop)
DAQ Server: 32 cores HT, 128 GB RAM
Monitoring PC: 4 cores, 6 Gb RAM (desktop)

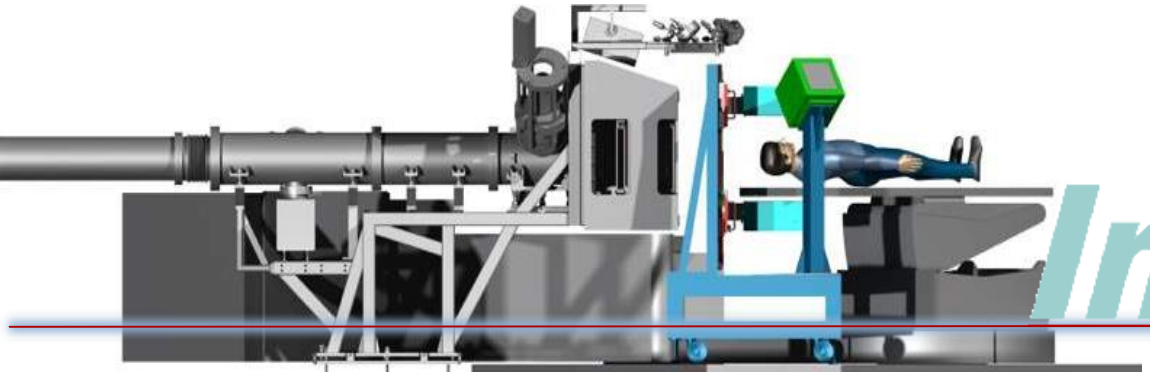
Data Processing

Tasks to be performed online:

- Data quality monitoring (GUI)
- Energy threshold and **coincidences finding** (dedicated high-performance machine and code)
- In-spill and inter-spill discrimination
- Fast MLEM 3D image reconstruction (reconstruction time ~ 2-5 s) – as soon as enough data is collected
- On-line comparison with expected image

On-line data analysis





FLUKA
Monte Carlo Simulations

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In-beam PET Simulation

Isotopes production is a poor signal →all the statistics must be simulated.

STEP 1:
Beam simulation

FLUKA

- **Input: patient CT and RTplan (DICOM) or DDS** measurements
- About 1/1000 of primary hadrons

Time-tagged activity scoring

- Annihilation time and position
- Isotope production map:
  ^{11}C ($t_{1/2}$=1220.04s)
  ^{15}O ($t_{1/2}$=122.4s)
  ^{10}C ($t_{1/2}$=19.290s)
  …

1000x

STEP 2:
PET simulation

FLUKA

All positrons are simulated.
Detector simulation.

digitization

Data analysis & image reconstruction

Same as real data:

- Line Of Response (LOR) list extraction
- Image reconstruction (MLEM algorithm, 5 iterations)

Total simulation time ~ 10 h

The temporal structure of the beam delivery is simulated.

Isotope decays are simulated.

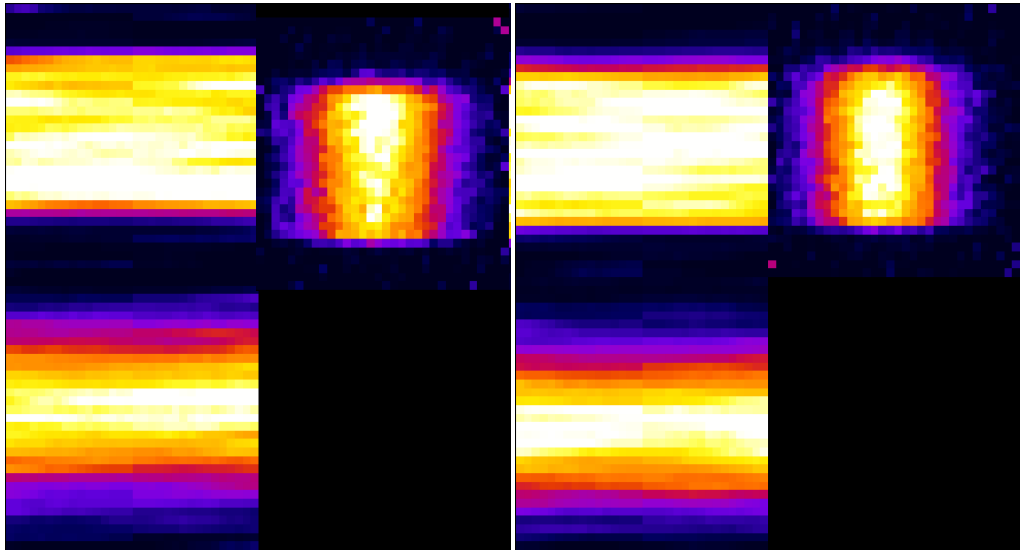
The 4D reconstructed image depends on the acquisition time.

Why detector simulation?

Dual-head scanner -> LORs have only limited angular distribution

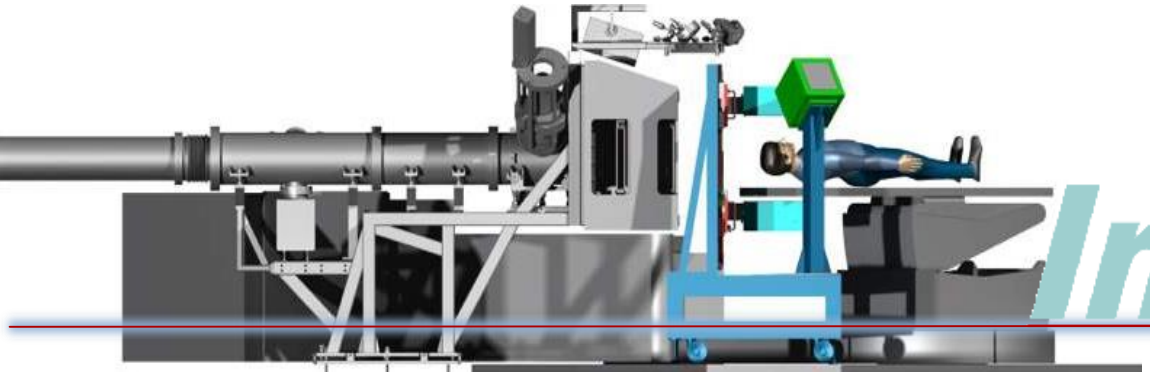
- Severe artifacts in reconstructed image along the vertical coordinate
- … good resolution on the horizontal plane

- Simulate PET detectors and digitization
- Look for coincidences
- Reconstruct the simulated image with the same algorithm used for data!



simulation data

Artifacts due to missing projections are reproduced



Beam Test Set Up and Simulation Validation

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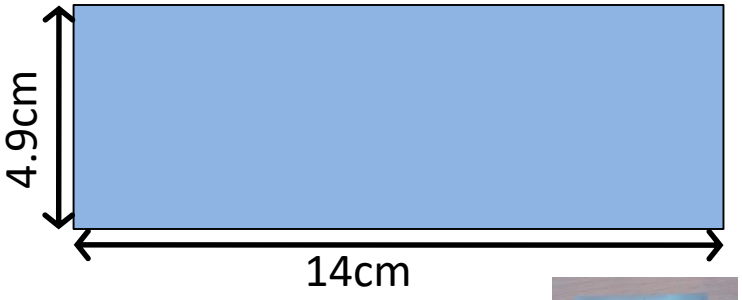
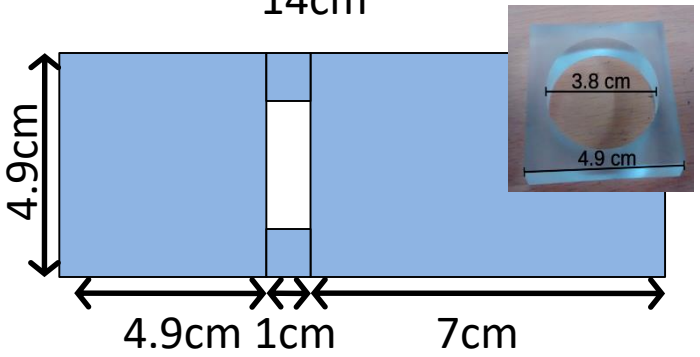
Profile Analysis

Projectile: proton
Two 2.7x2.7 cm^2 slices
at 77 MeV/u and 105 MeV/u
10x10 spots
5.E7 protons per spot

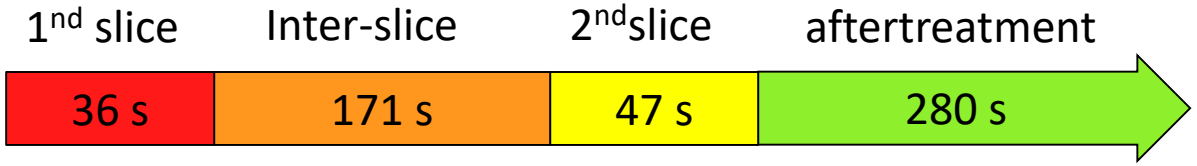
A) PMMA homogeneous phantom



B) PMMA + air gap inhomogeneous phantom



A) PMMA homogeneous phantom



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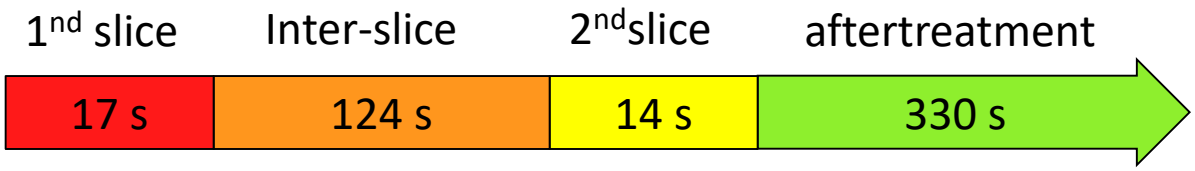
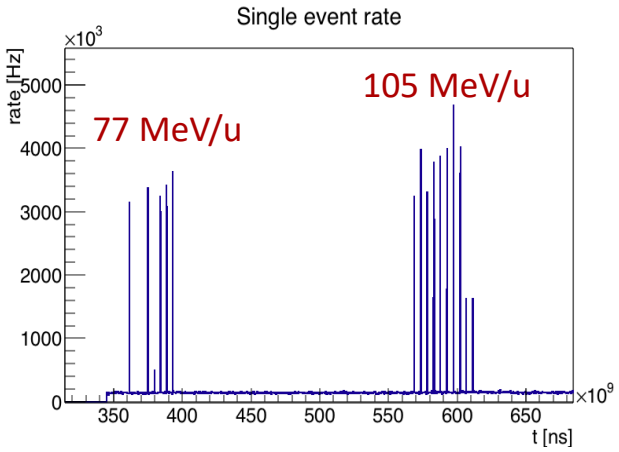
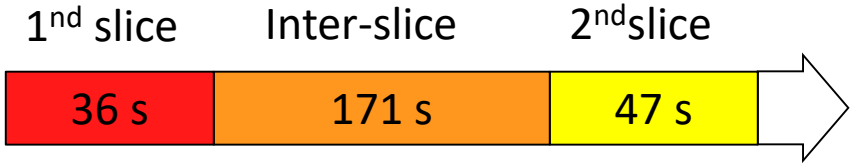
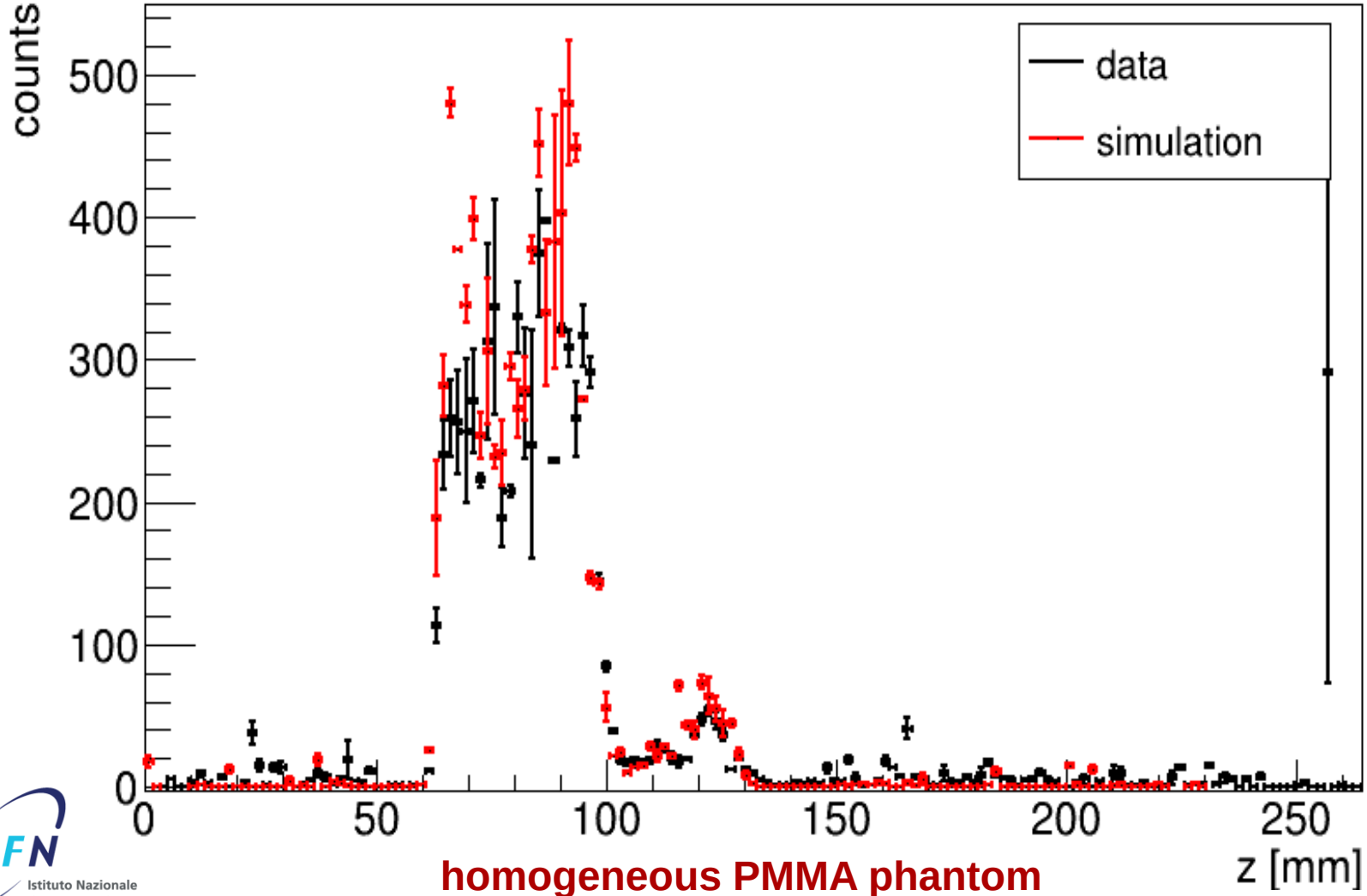




Profile Analysis

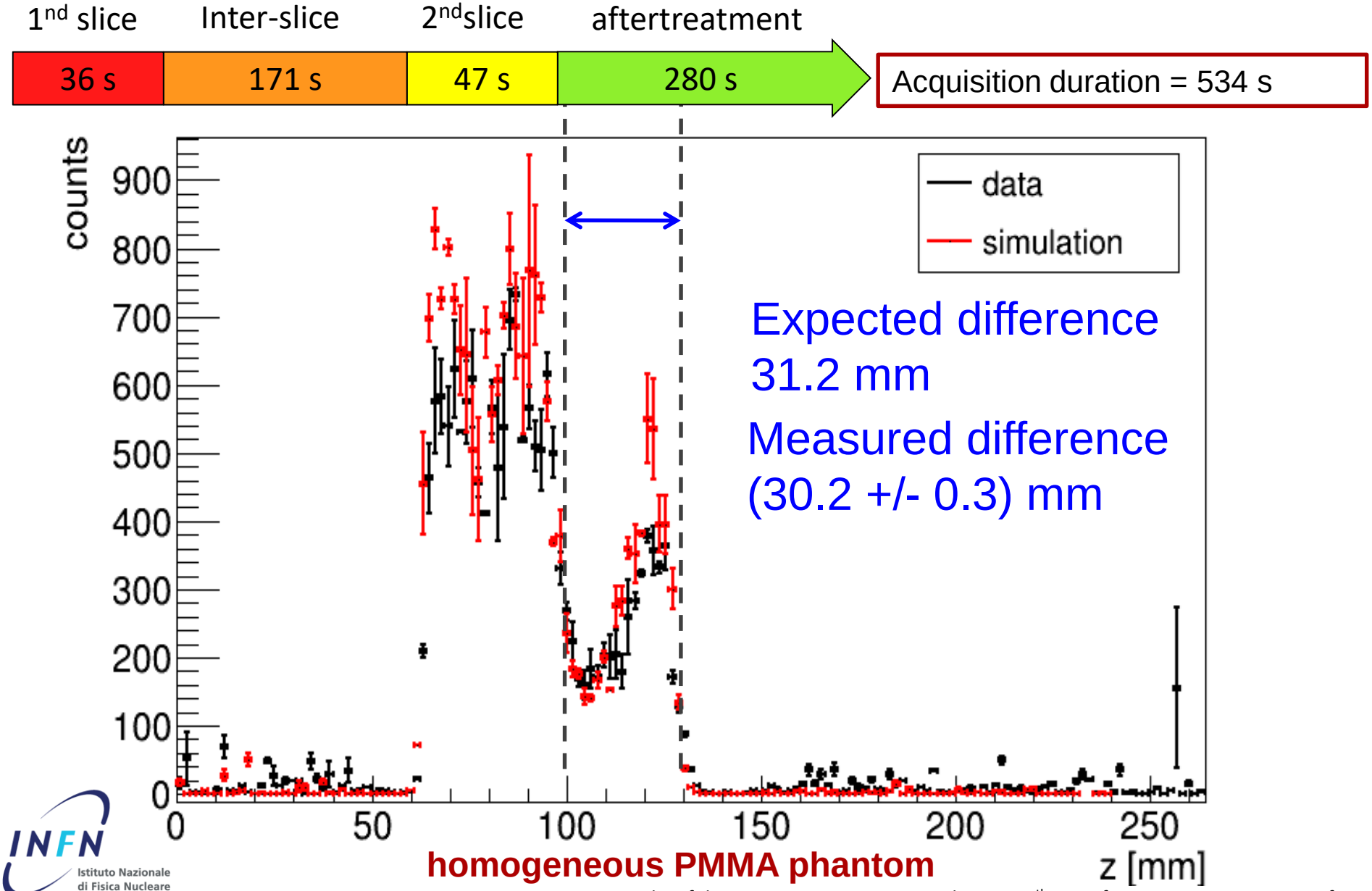


Acquisition duration = 254 s



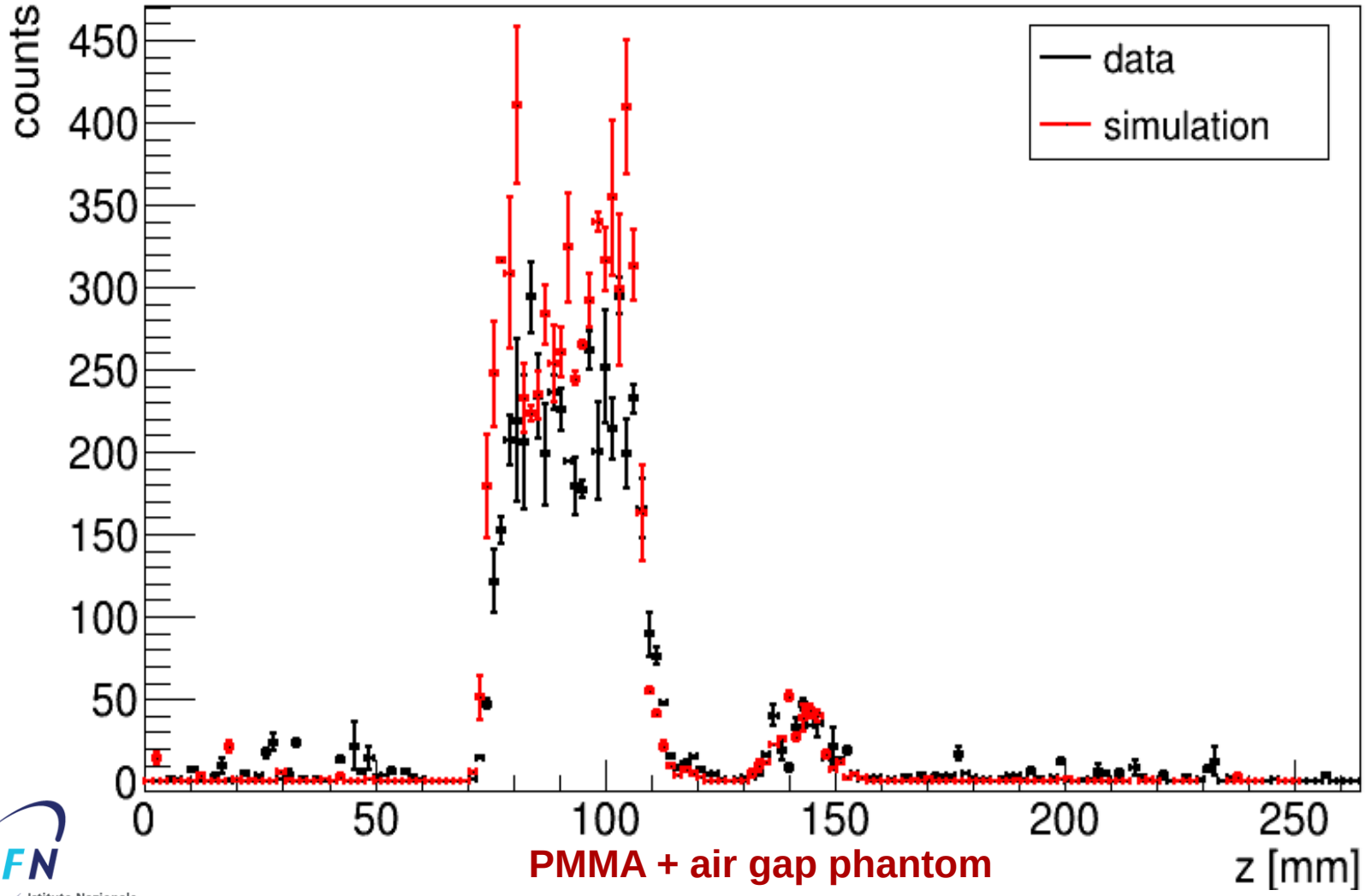
homogeneous PMMA phantom

Profile Analysis



Profile Analysis

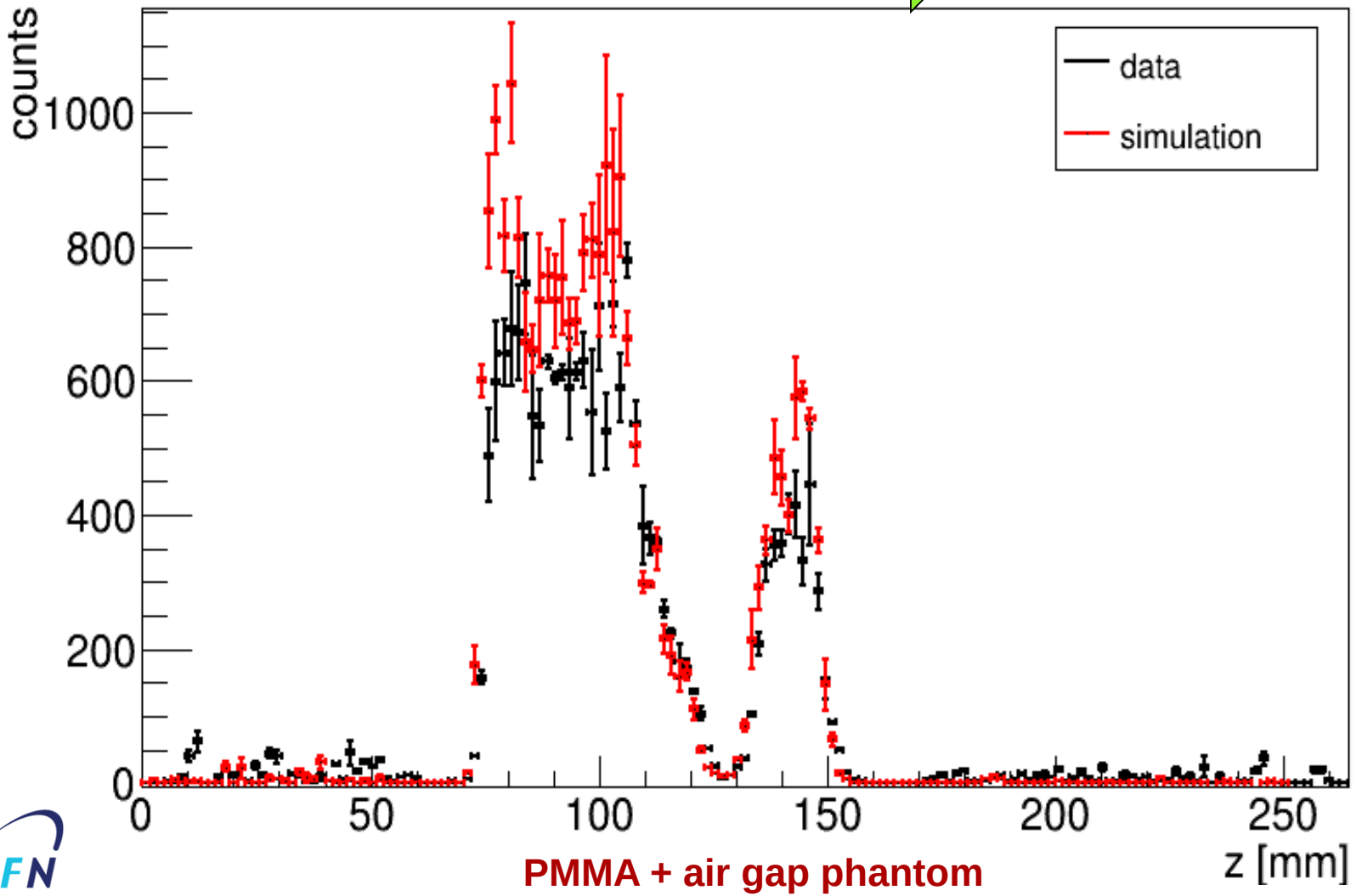
Acquisition duration = 155 s



Profile Analysis

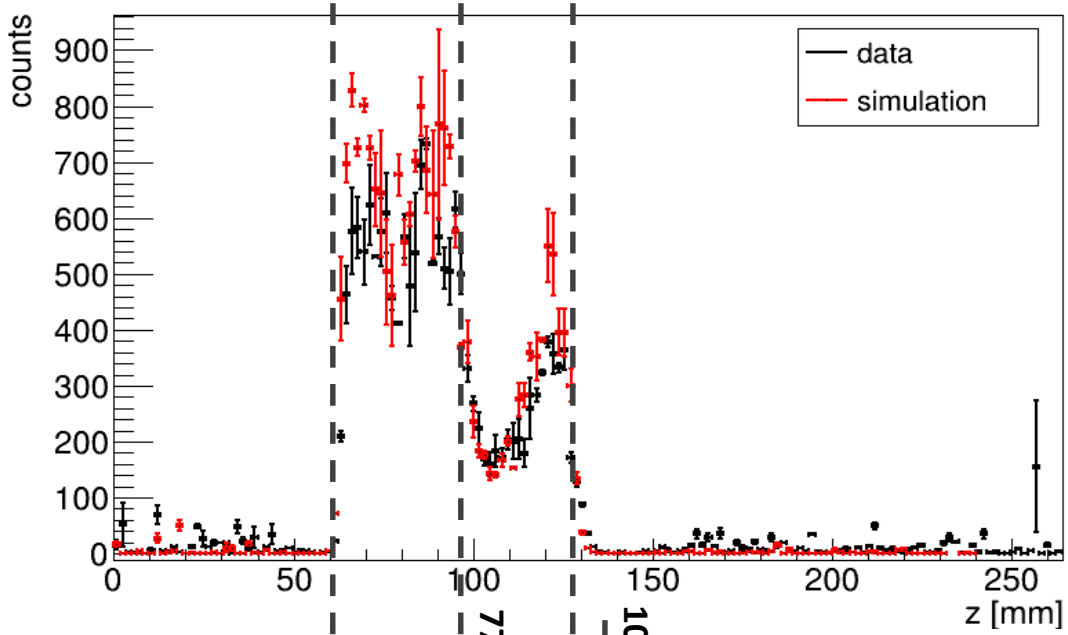
1nd slice	Inter-slice	2ndslice	aftertreatment
17 s	124 s	14 s	330 s

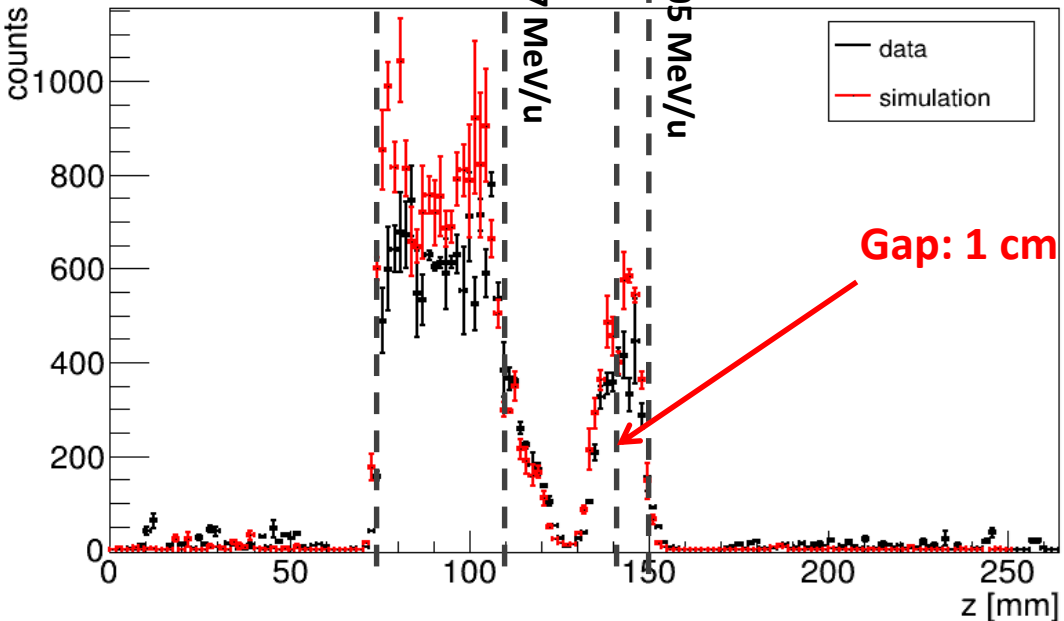
Acquisition duration = 485 s



PMMA + air gap phantom

Profile Analysis





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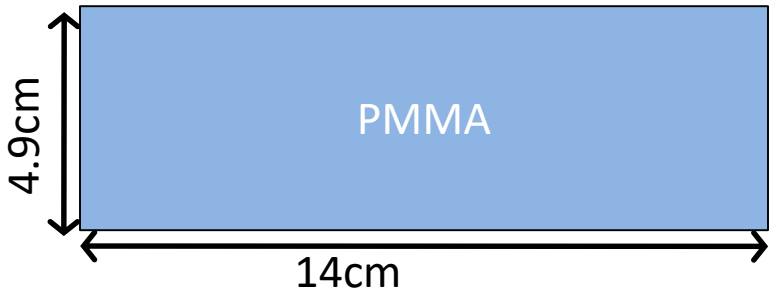
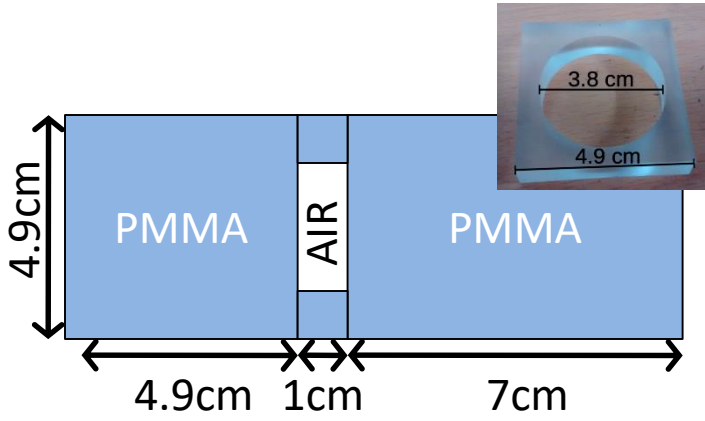
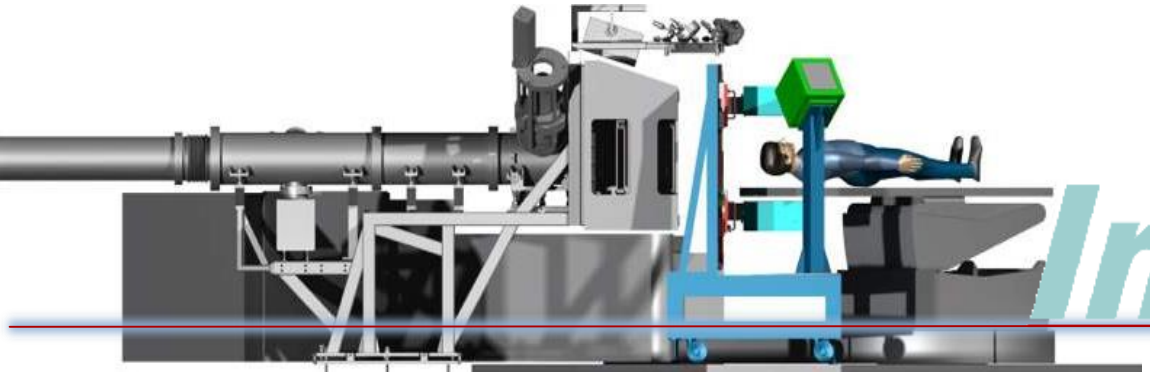
10x10 spots
5.E7 protons per spot







First in-vivo measurements
1-2 December 2016

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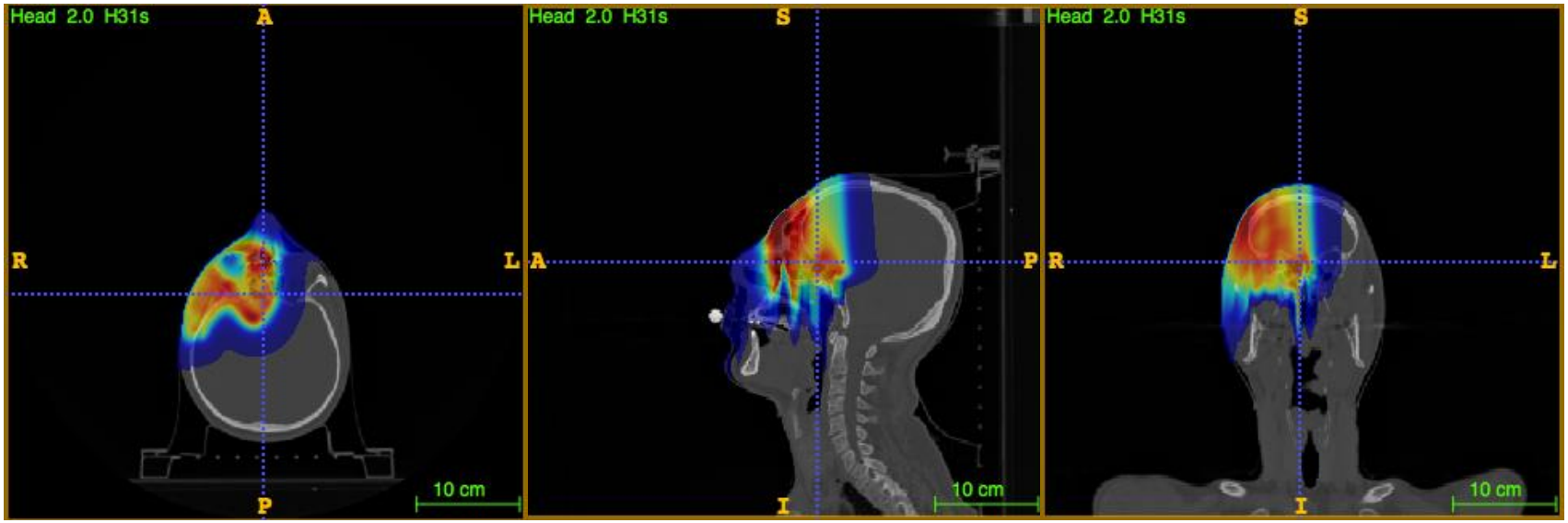
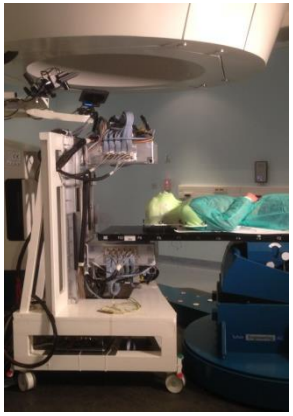
First clinical test @CNAO, 1-2 Dec. 2016

Planned dose



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

240 s treatment + 30 s after-treatment of data acquisition



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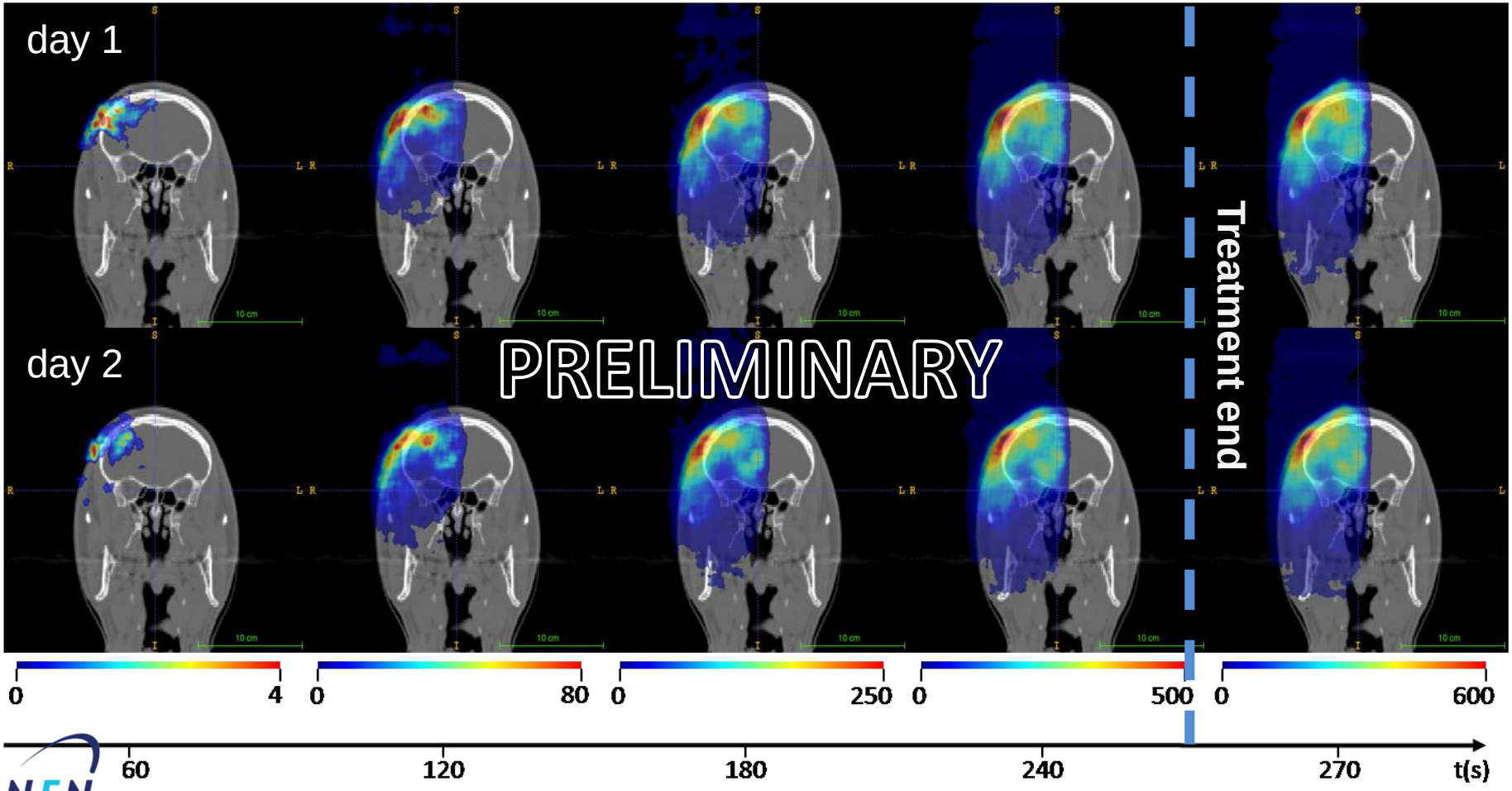
First clinical test @CNAO, 1-2 Dec. 2016

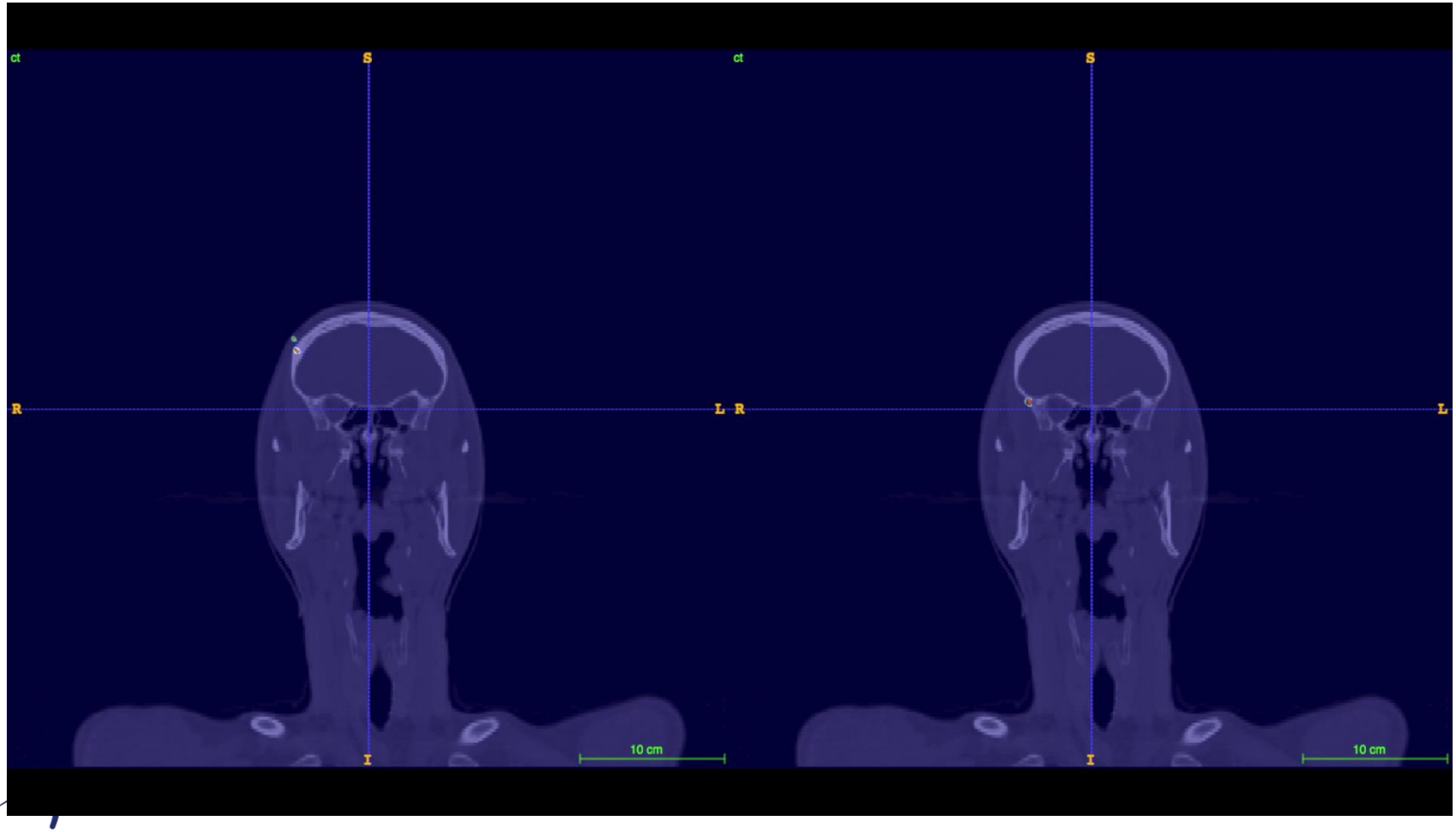
Time-resolved image reconstruction

Measured activity

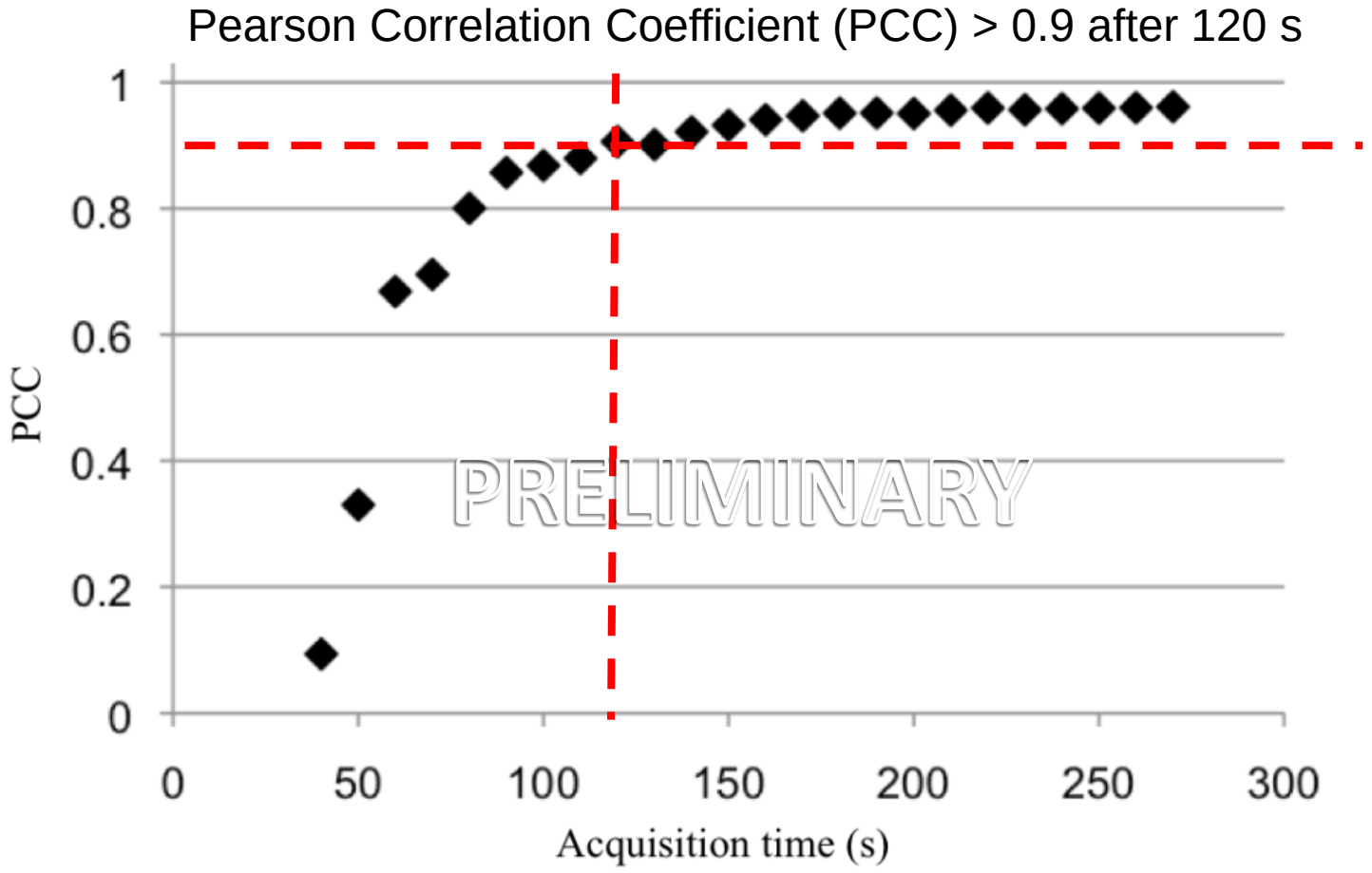


First clinical test @CNAO, 1-2 Dec. 2016

Time-resolved image reconstruction

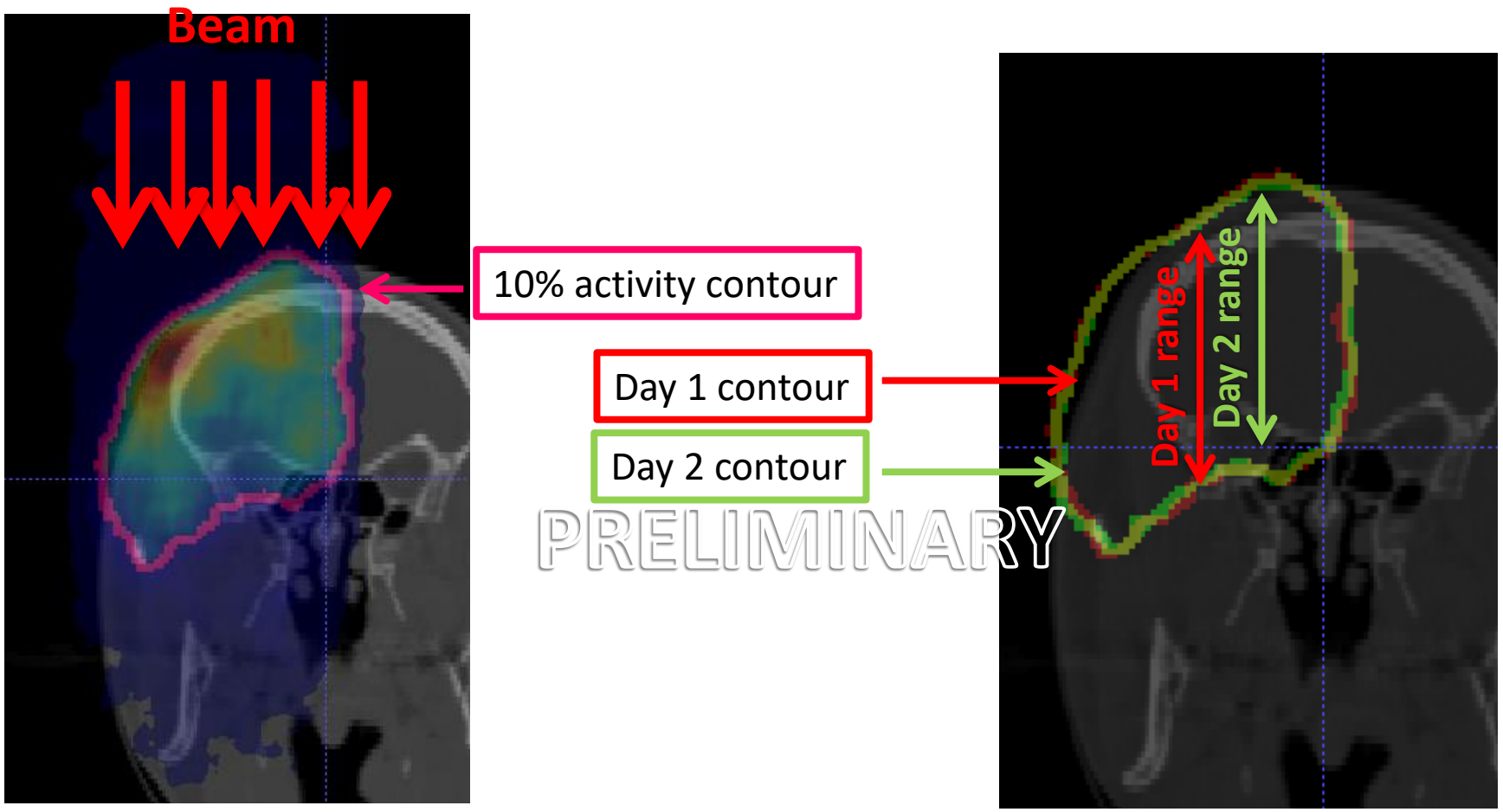


Quantitative comparison 1: PCC

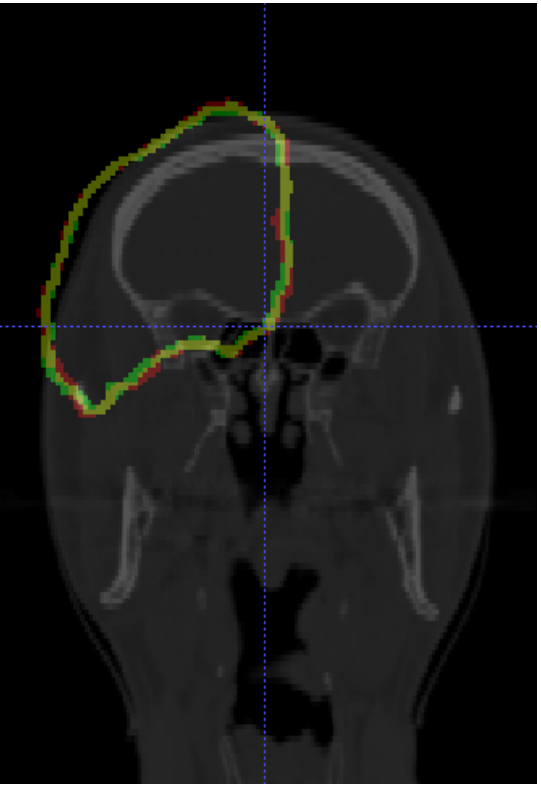


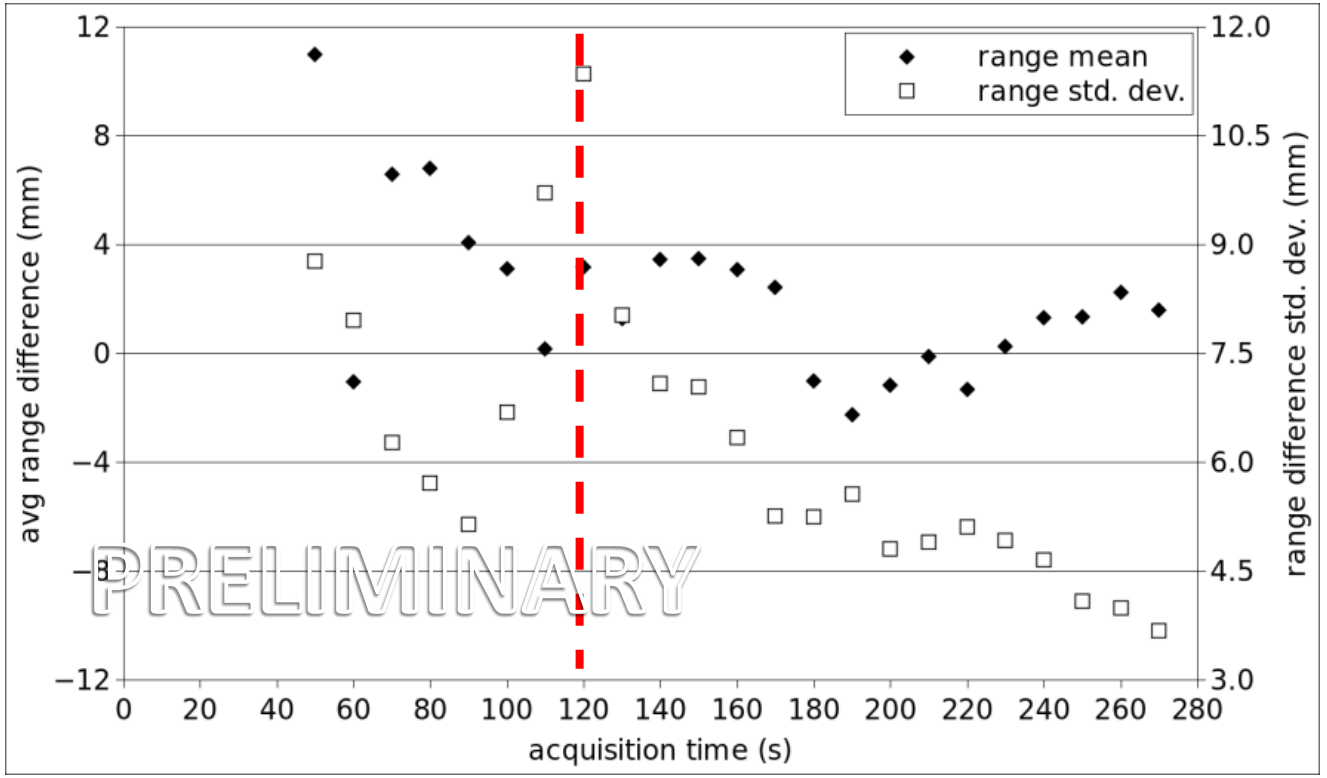
Kuess P, Birkfellner W, Enghardt W, Helmbrecht S, Fiedler F, Georg D. Using statistical measures for automated comparison of in-beam PET data. Med Phys. 2012 Oct;39(10):5874-81.

Quantitative comparison 2: beam's eye view



Quantitative comparison 2: beam's eye view

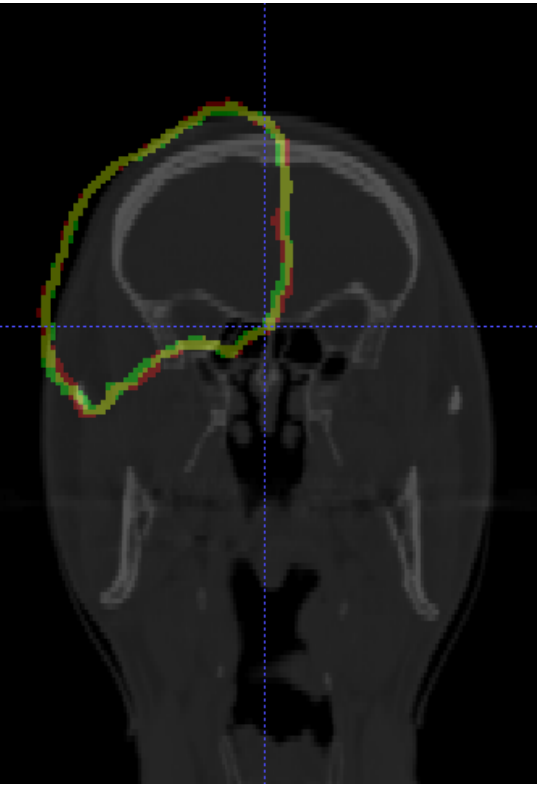


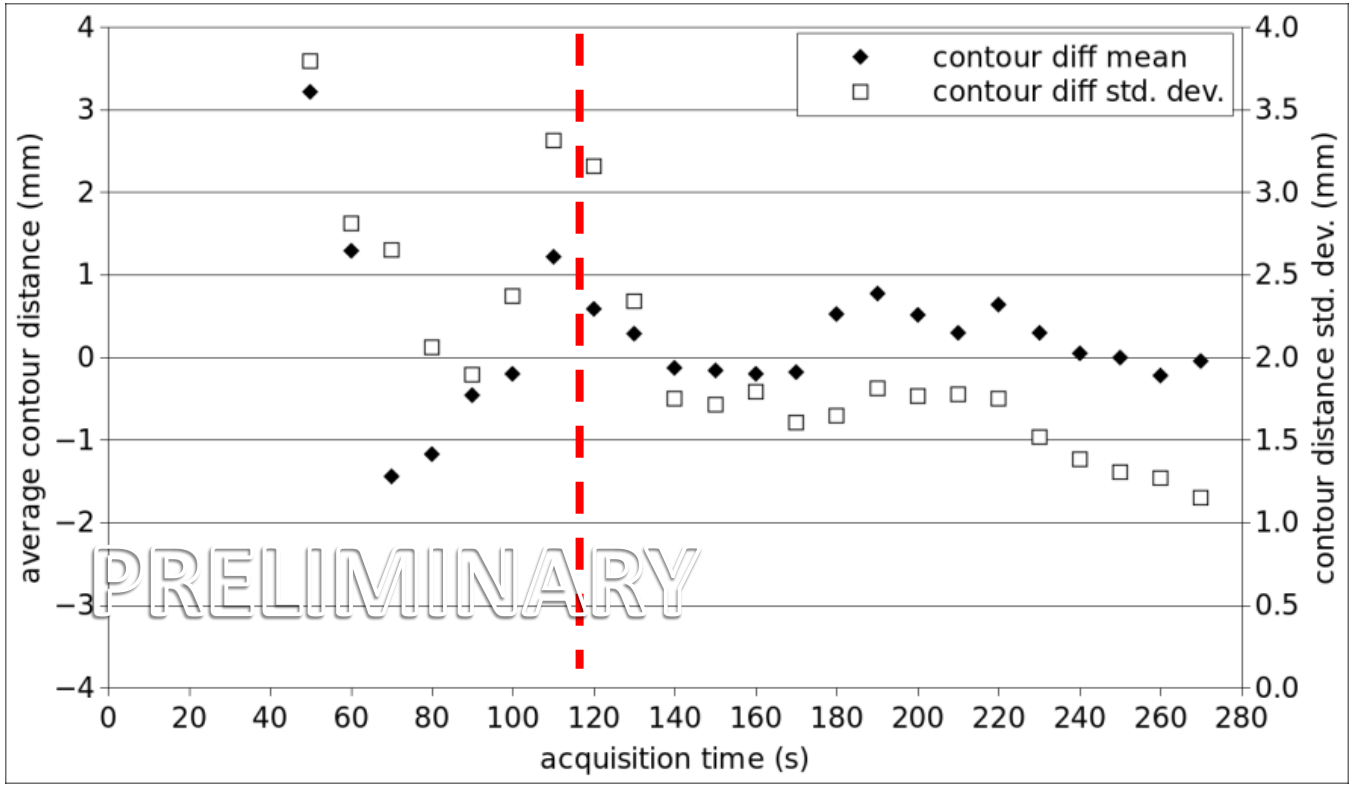


After 120 s average range difference in the interval (-2.2 ,+3.5) mm

…. very sensitive to mobile support positioning (manual alignment with treatment room laser)

Quantitative comparison 3: Overall view

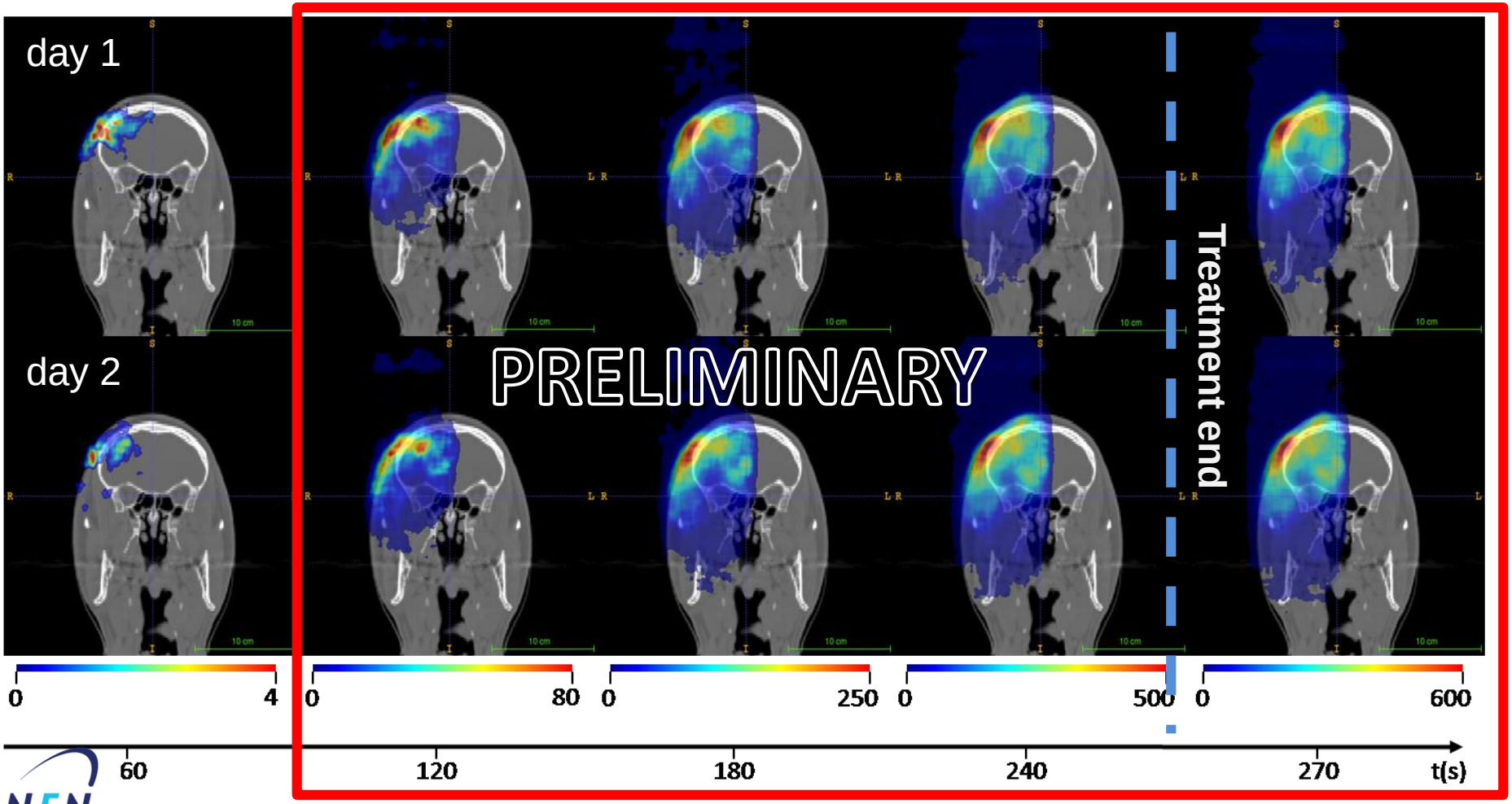




Comparison without preferable direction → after 120 s avg. contour distance < 1 mm

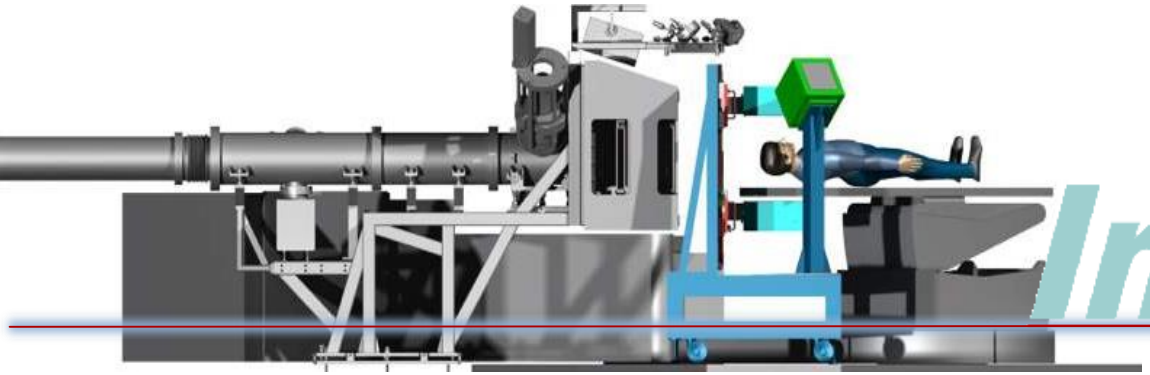
Time resolved & on-the-fly reconstruction

Agreement after 120 s



Conclusions

- INSIDE in-beam PET performances tested and assessed with PMMA phantoms
- Monte Carlo generated *a priori* images
- **First measurement during patient treatment**
- **Time-resolved and on the fly reconstruction**
- Future steps:
  - Test with carbon beams
  - Integration with INSIDE charged tracker
  - Integration with CNAO clinical workflow



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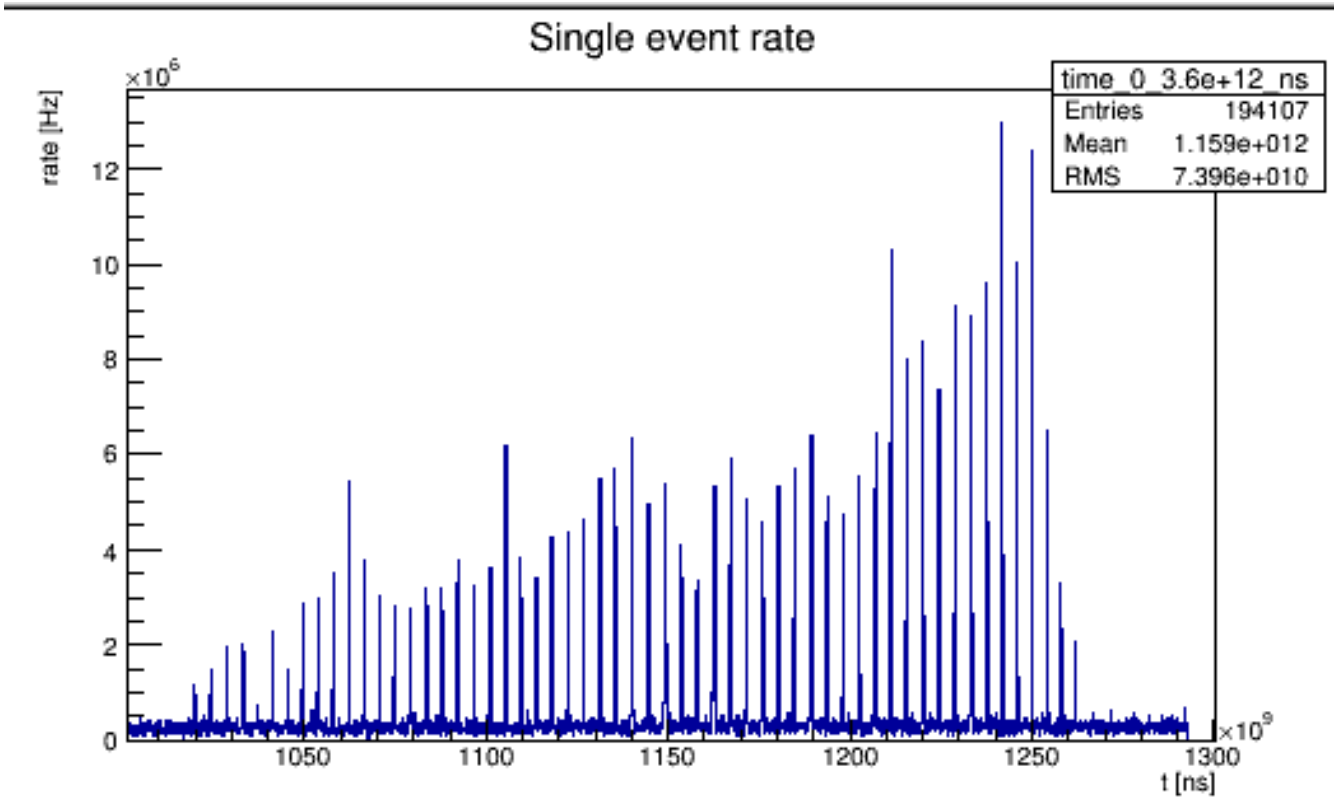
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RMS 7.396e+010
rate [Hz]
×10^6
0
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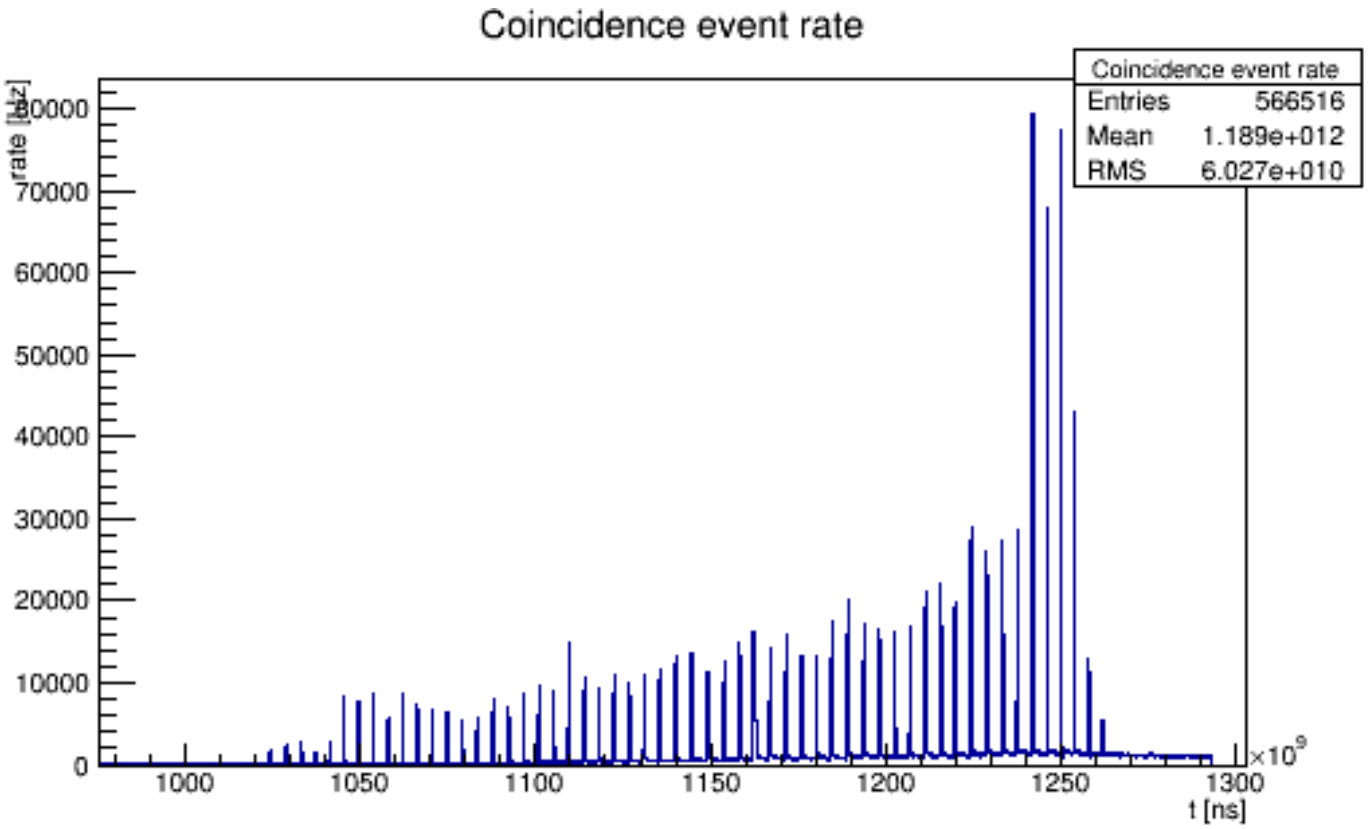
4
6
8
10
12
1050
1100
1150
1200
1250
1300
×10^9
t [ns]


Coincidence event rate
Coincidence event rate
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Mean 1.189e+012
RMS 6.027e+010
rate [Hz]
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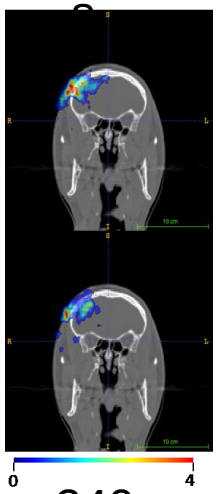
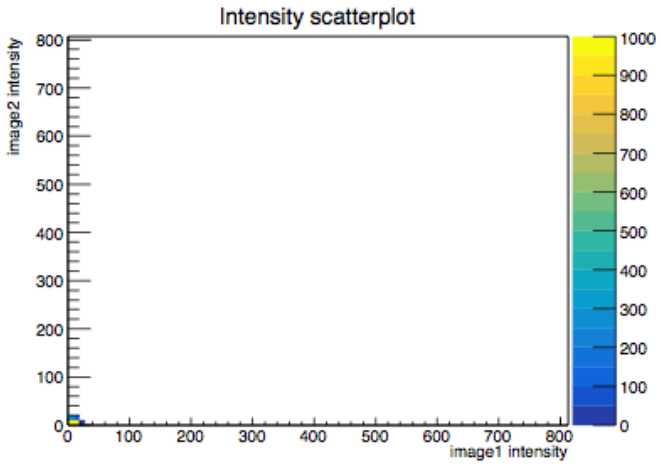
70000
60000
50000
40000
30000
20000
10000
0
1000
1050
1100
1150
1200
1250
1300
×10^9
t [ns]

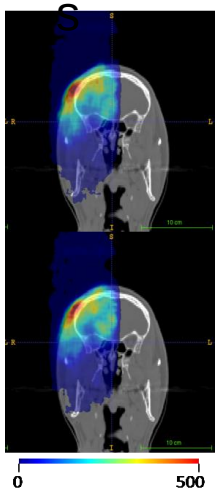
Correlation test

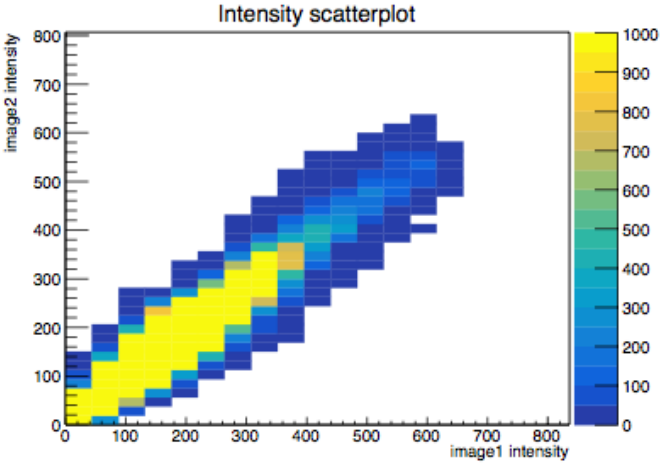
60 s





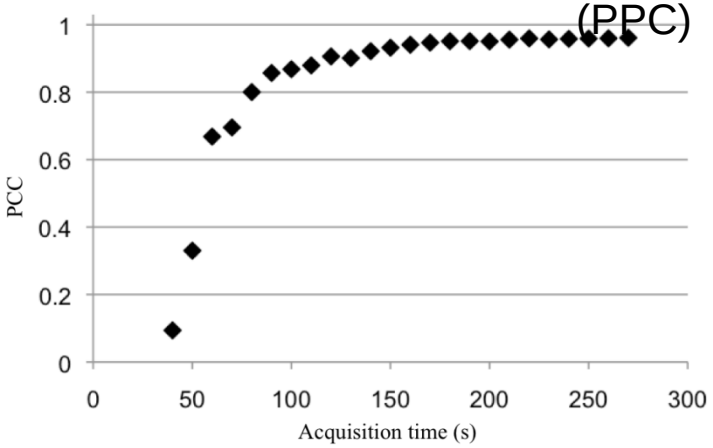
240 s





$$r = \frac{\sum_{i=1}^{n}\left(\left(x_i - \bar{x}\right)\left(y_i - \bar{y}\right)\right)}{\sqrt{\sum_{i=1}^{n}\left(x_i - \bar{x}\right)^2 \sum_{i=1}^{n}\left(y_i - \bar{y}\right)^2}}$$

Pearson Correlation Coefficient (PPC)



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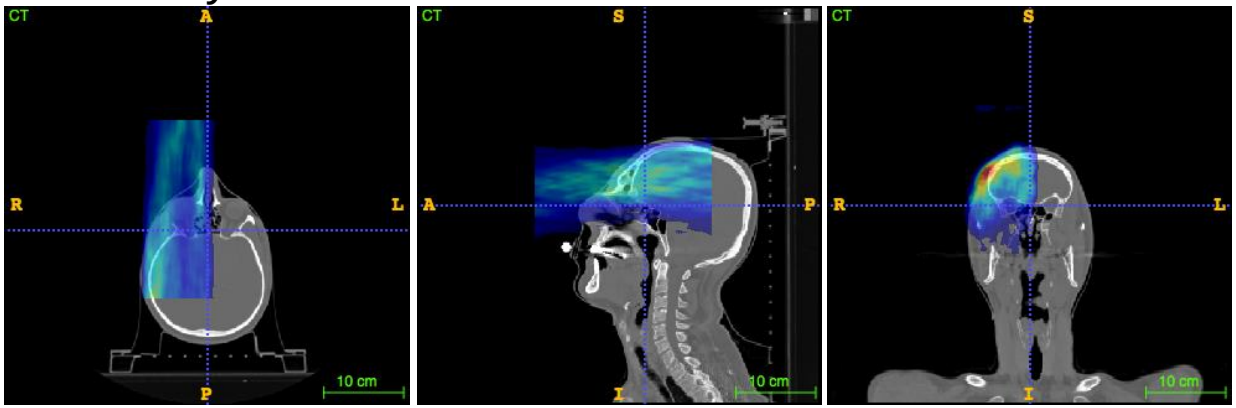
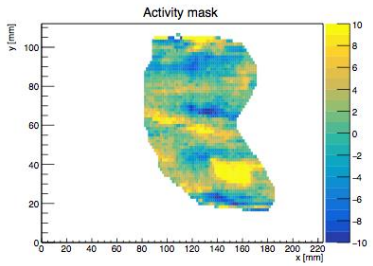
Activity distribution analysis

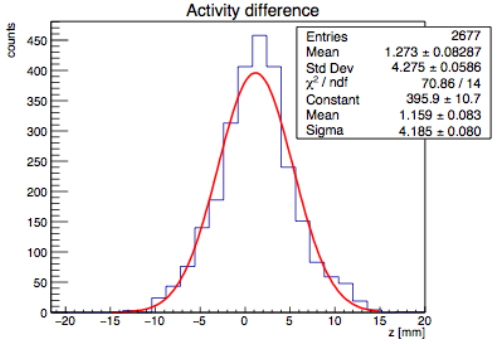
3D activity distribution at 240 s



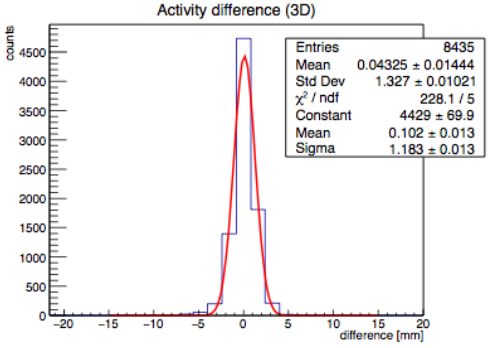
Activity selection (3D mask) to remove background and select the volume where the beam was actually



Beam's eye view



Overall view



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