Medical Physics at LIP: PET with RPCs

Alberto Blanco

On behalf the RPC R&D group from LIP-Coimbra

Overview

- Positron Emission Tomography (PET).

- Resistive Plate Chambers (RPC) technology and RPC-PET concept.

- Small animal RPC-PET concept.

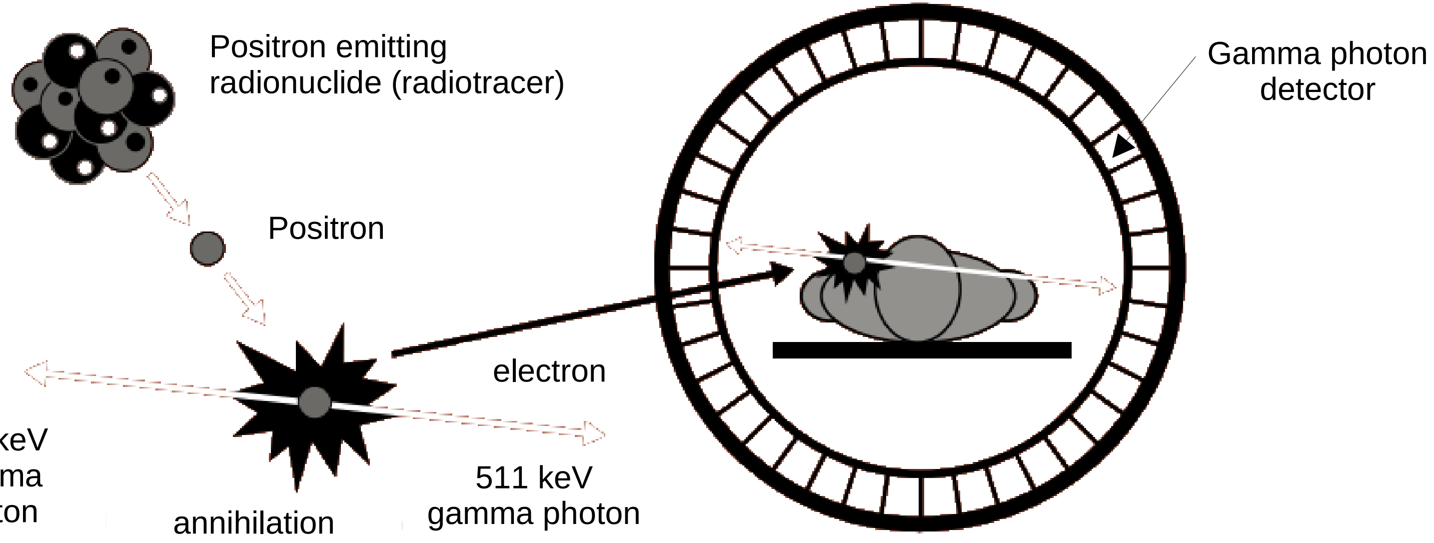
- Human brain RPC-PET concept.

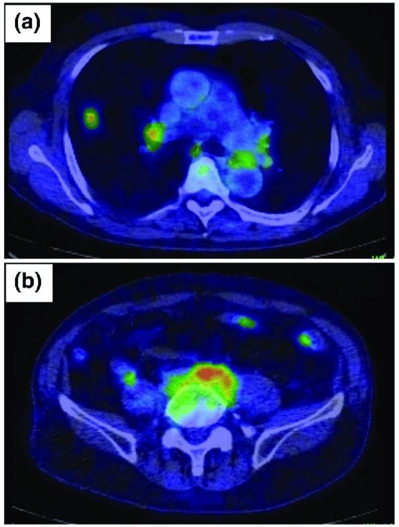
Positron Emission Tomography. PET

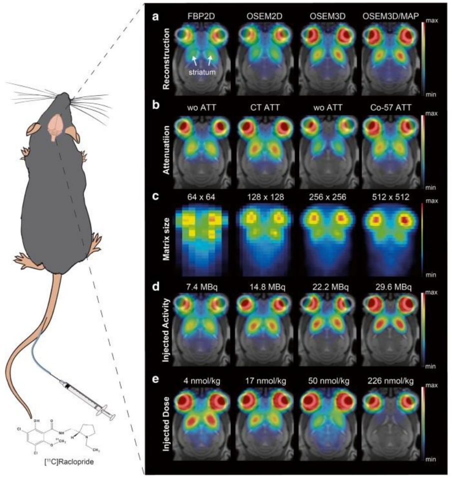
Positron emission tomography (PET) is a **functional imaging technique** that uses radioactive substances known as radiotracers to visualize and measure changes in metabolic process, and in other physiological activities.

Positron emission
and positron-electron annihilation

PET scanner



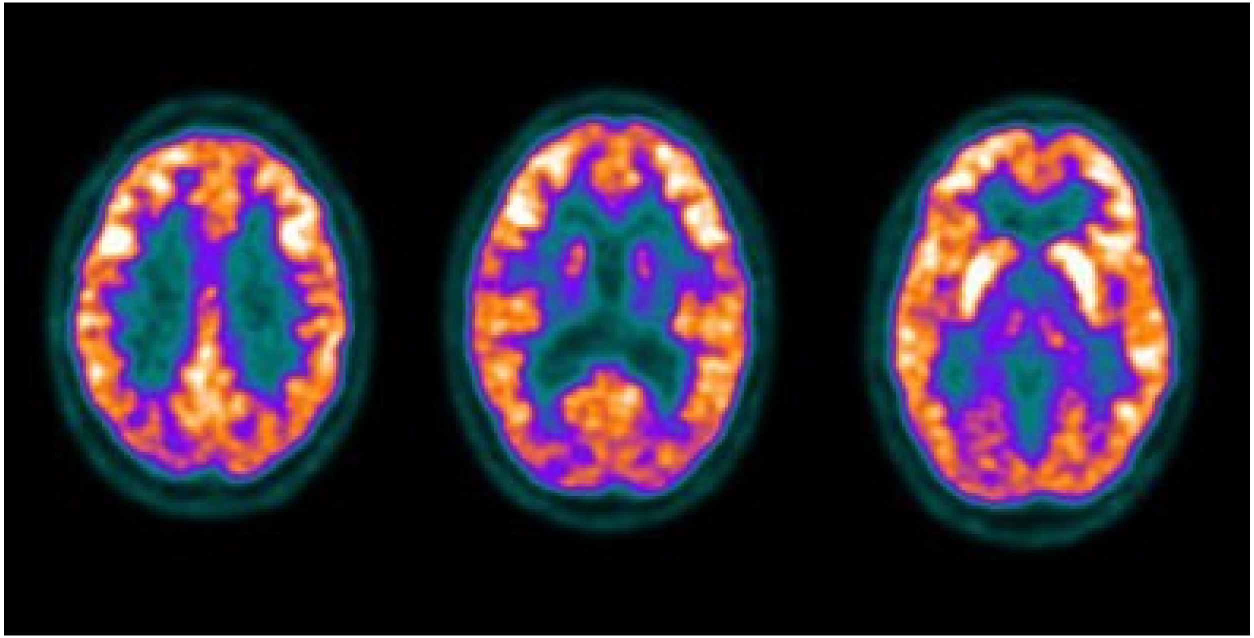




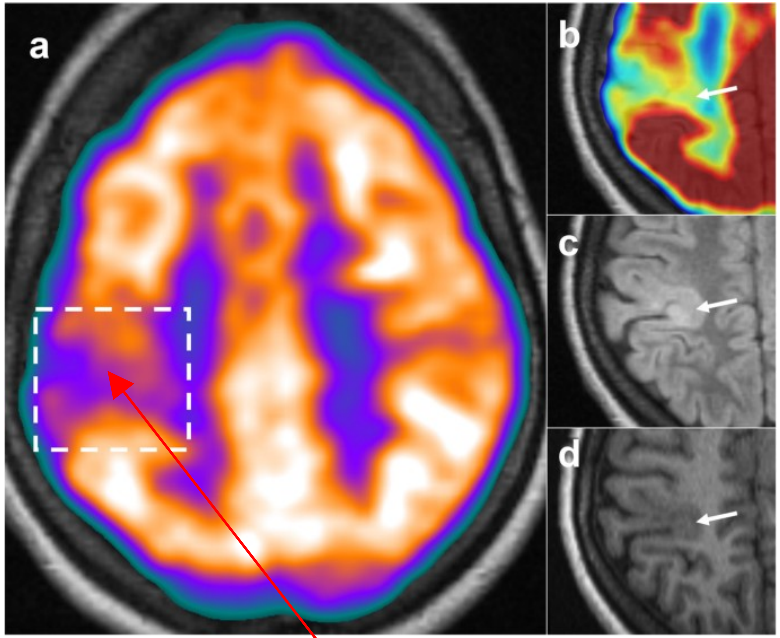
High spatial resolution needed.

Epilepsy. PET-FDG.

- 30% of patients do not respond to pharmacological treatments.
- In cases of focal epilepsy, the therapeutic option is surgery.
- Surgery consists of a resection of the area of the brain responsible for the seizures



Normal brain metabolism



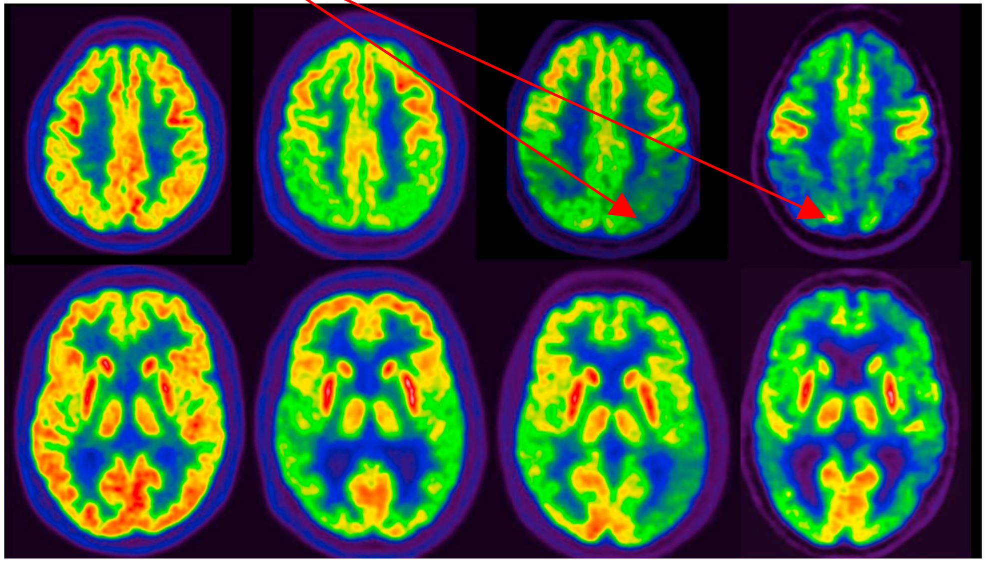
Patient with inconclusive lesion in MRI shows cortical dysplasia.

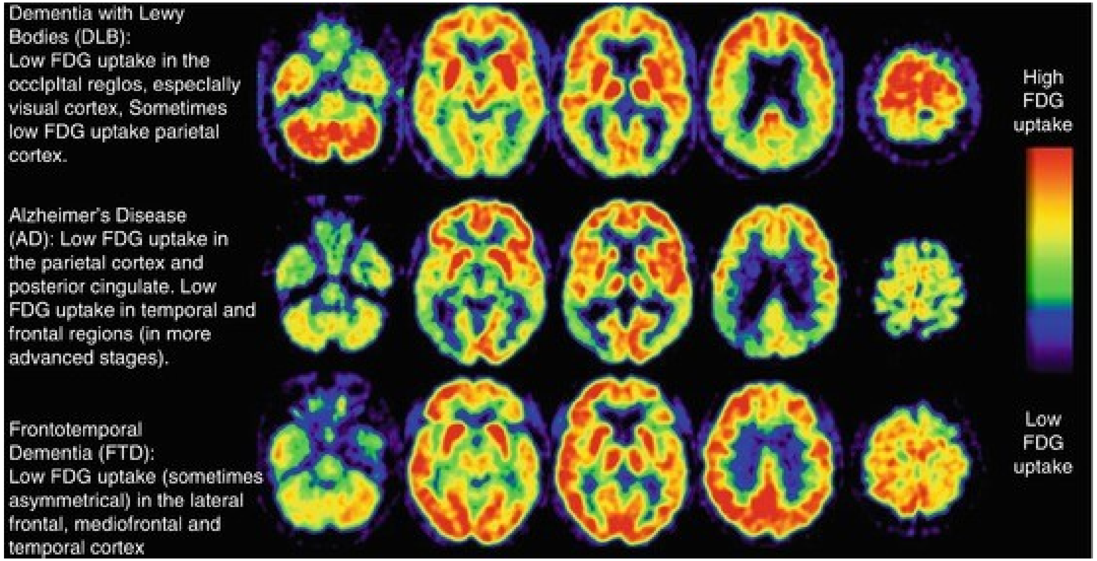
High spatial resolution needed.

Alzeimer. PET-FDG.

Alzheimer's patients show **loss of metabolism in posterior regions** resulting in cortical atrophy.

Differential diagnosis. Different diseases present FDG hypo-metabolisms in different regions of the brain.



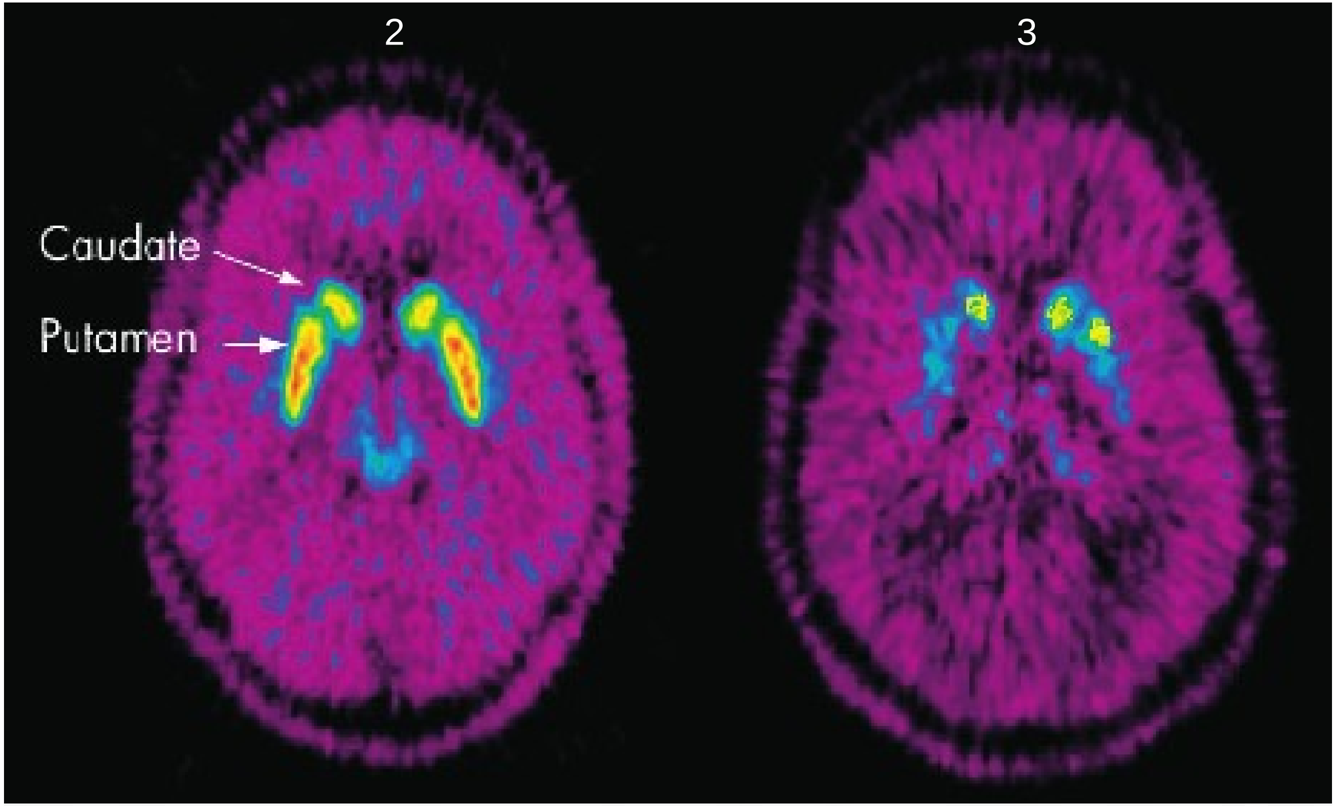


Process of neurodegeneration in brain metabolism in an Alzheimer's patient.

Evolution with time

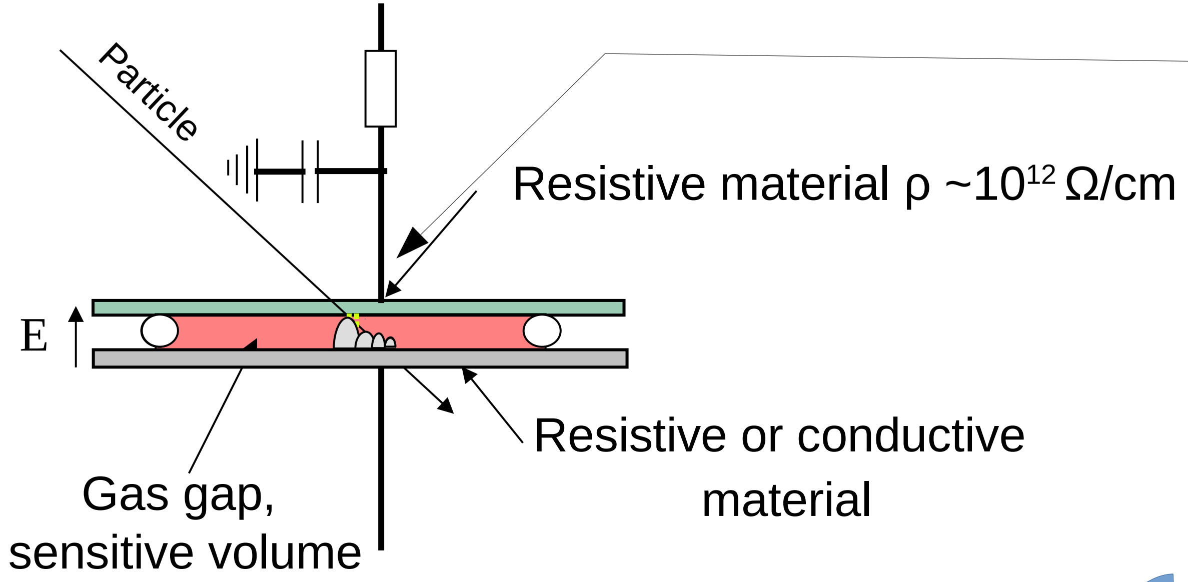
High spatial resolution needed.

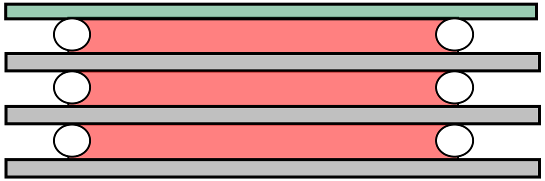
Parkinson. PET-FDOPA.



1 Healthy volunteer
2 Parkinson's patient showing asymmetric loss of the right putamen and caudate preservation (striatum)

Resistive Plate Chambers.



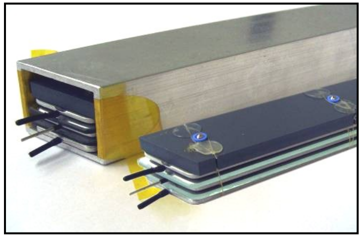


Multi-gap configuration

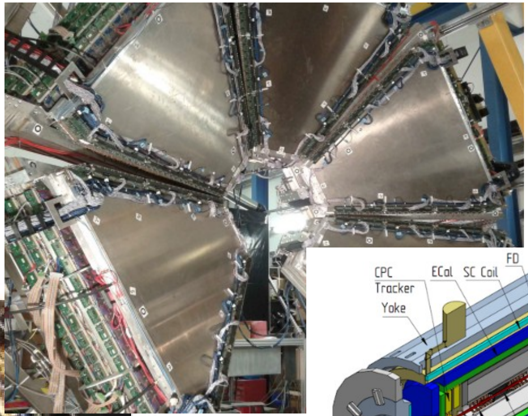
Avalanche multiplication

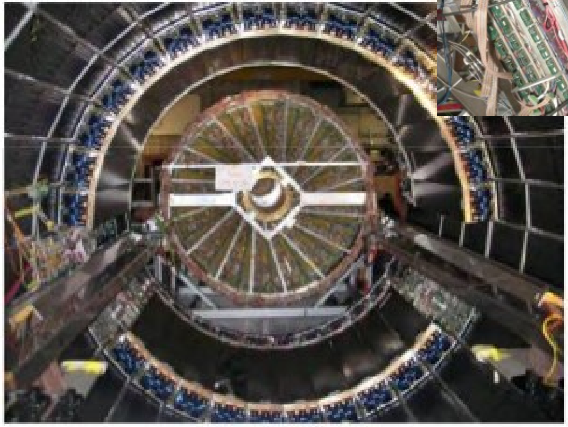
$$n_e(x,y,z,t)=n_o e^{\alpha v_e t}\frac{1}{(4\pi D_e t)^{3/2}}\exp\left(\frac{x^2+y^2+(z-v_e t)^2}{4 D_e t}\right)$$

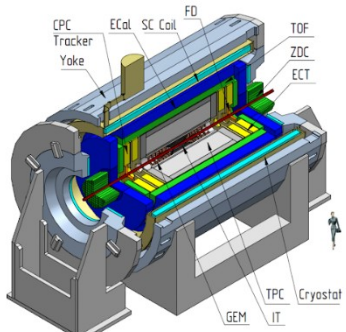
Capability to detect the crossing position (100 um) and time (100 ps) with high precision



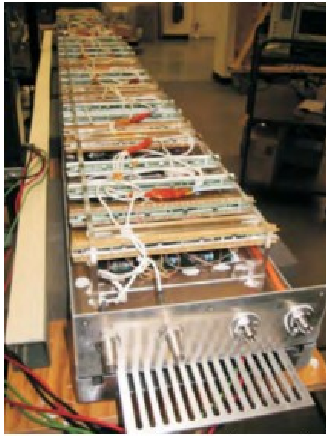
HADES@GSI
10.1016/j.nima.2008.12.090



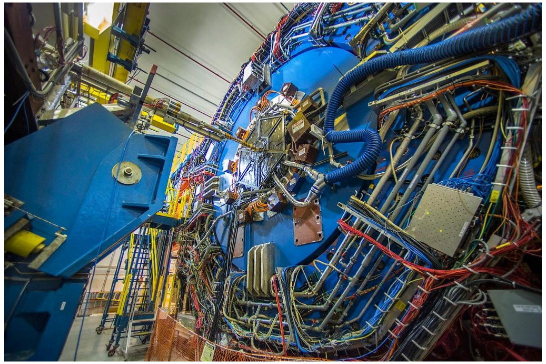


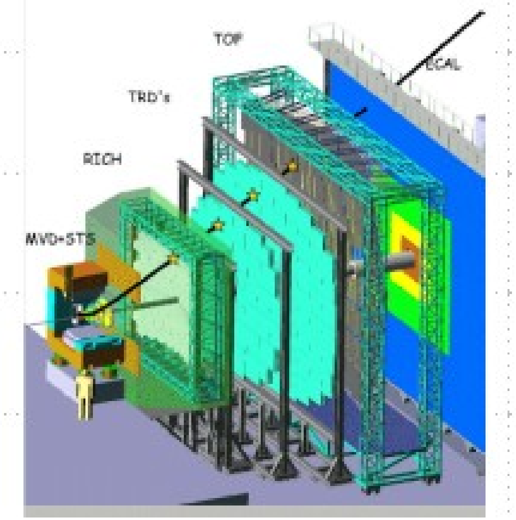


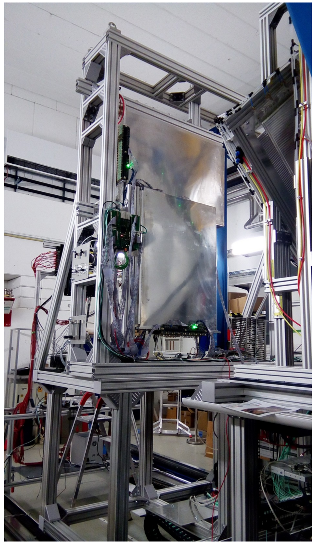
MPD, BM@N at NICA facility
10.1051/epjconf/201817112001



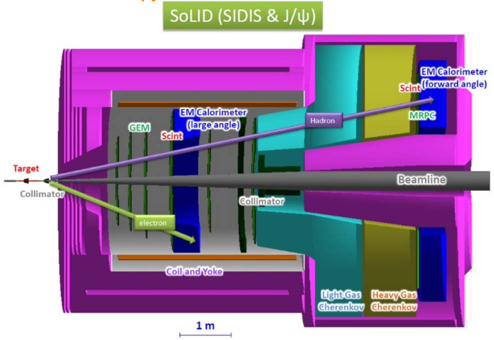
START@RHIC
10.1016/j.nima.2010.07.086







FD-HADES@GSI

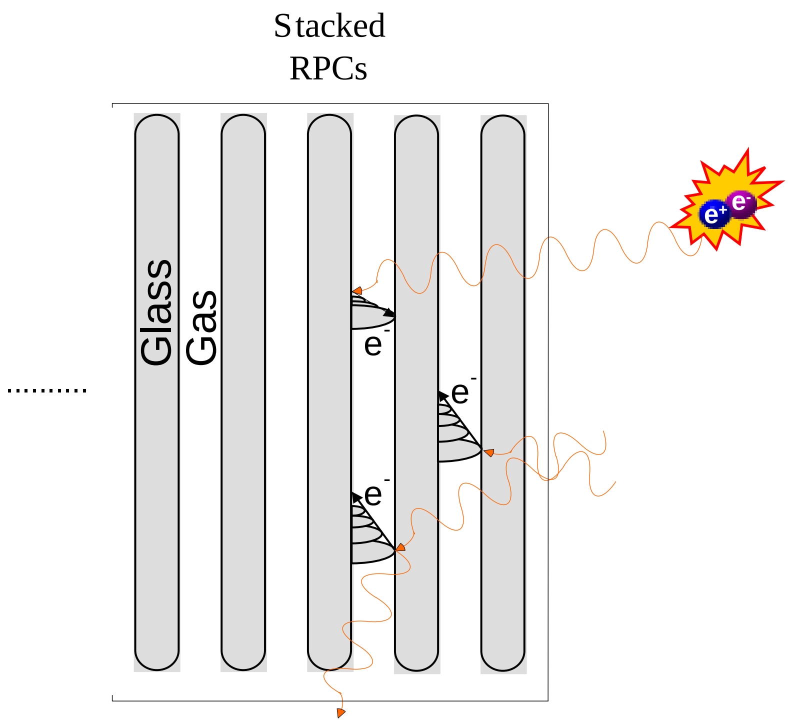


FOPI@GSI
10.1016/j.nima.2004.07.002

SoLID (Jefferson Labs)
arXiv:1409.7741v1 [nucl-ex] 26 Sep 2014

CBM@FAIR
10.1088/1748-0221/14/09/C09020

The converter-plate principle



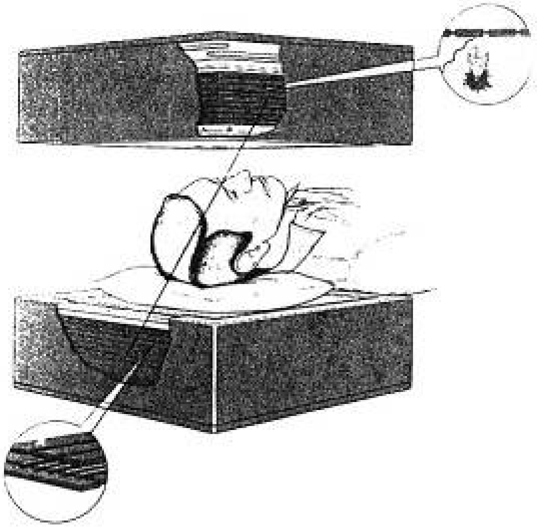
Use the electrode plates as a gamma converter, taking advantage of the natural layered construction of the RPCs.

[Blanco 2002]

Time resolution for 511 keV photons:
(our routine lab-test tool)

90 ps for 1 photon

300 ps FWHM for the photon pair



A previous work on PET with gaseous detectors (21 lead plates + 20 MWPCs = 7% efficiency)

“The Rutherford Appleton Laboratory´s Mark I Multiwire Proportional Counter Positron Camera” J.E. Bateman et al. NIM 225 (1984) 209-231

Disadvantages

- Certainly a much smaller efficiency… it is still to be seen if this is a fatal flaw.
- No energy resolution, but there is an equivalent energy sensitivity (more later).

Detector scatter (vs. “misidentified fraction” in crystal blocks)

Advantages

Increasing system sensitivity

Inexpensive => large areas possible => large solid angle coverage

Excellent timing => TOF-PET possible

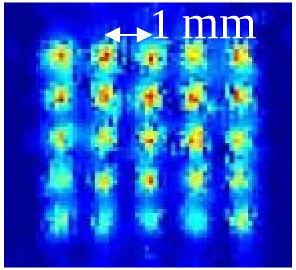
Total body Human PET

Increasing position accuracy

Gaseous detectors routinely deliver 0.1 mm resolution

Full 3D localization possible => no gross parallax error

The very small gap minimizes intrinsic errors



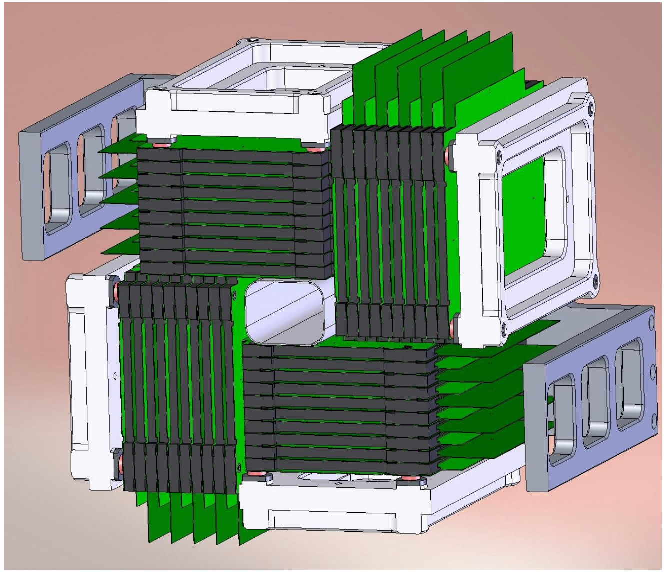
Simulation: 0.51mm FWHM

Small Animal / brain PET

Lowering costs

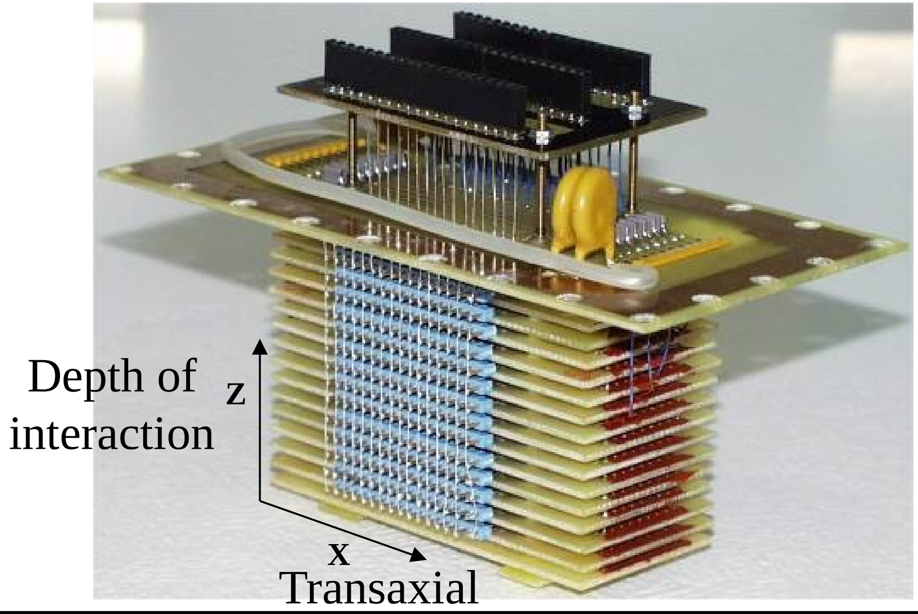
Applications can be also optimized for low cost at the expense of other characteristics

Small animal PET

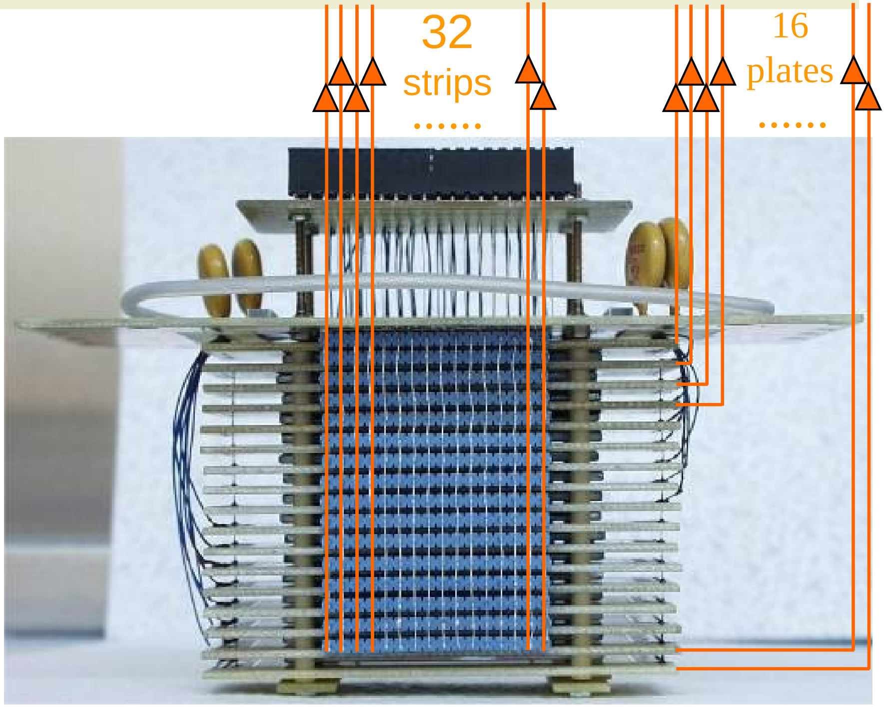


Aimed at **verifying** the concept and show the **viability** of a **sub-millimetric spatial resolution**.

16 stacked RPCs



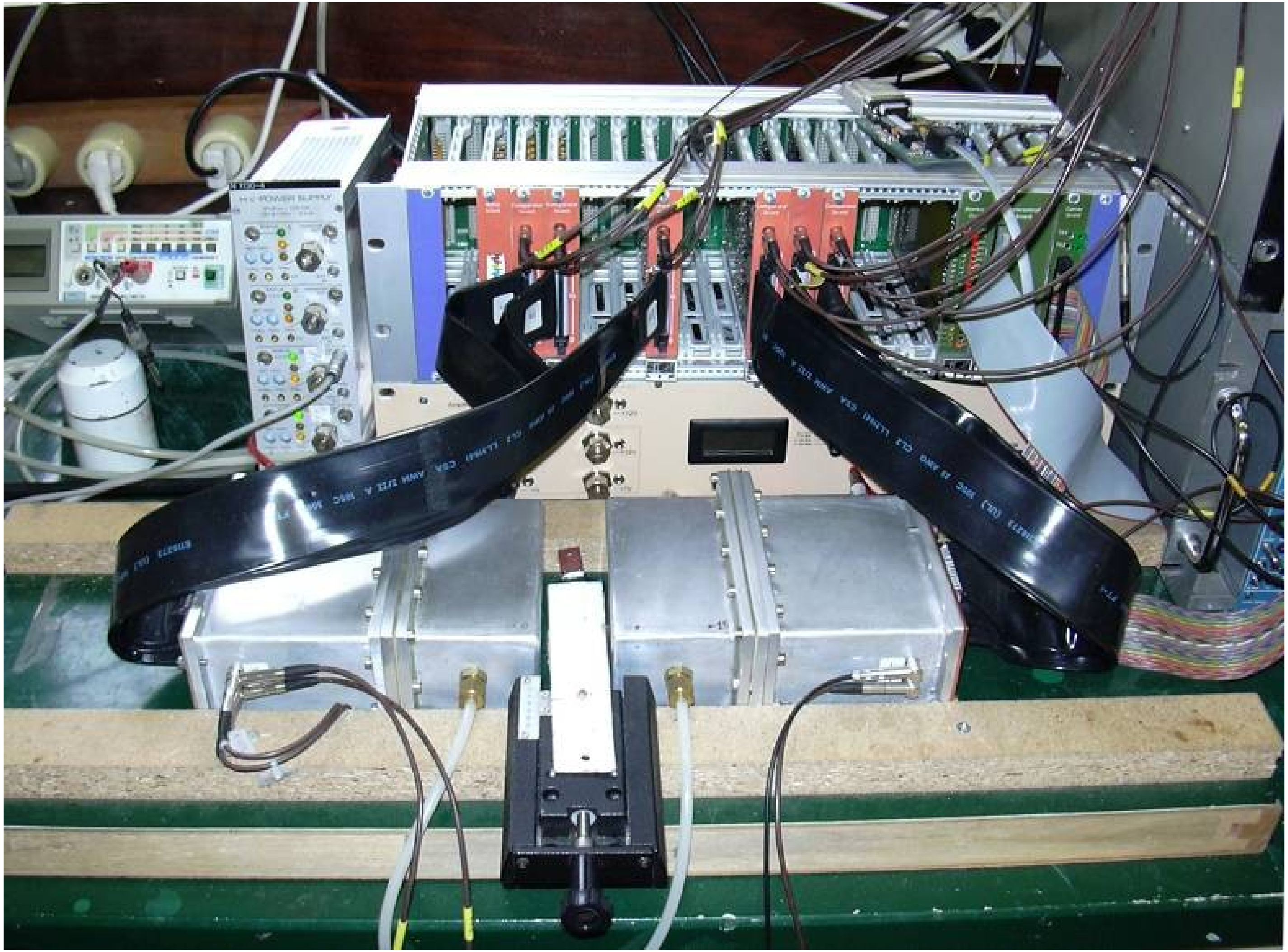
Charge-sensitive electronics allowing interstrip position interpolation



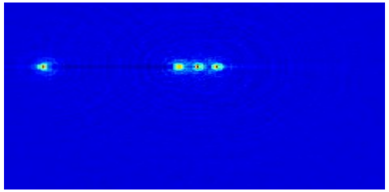
(now enjoying a second life as an exhibition item)

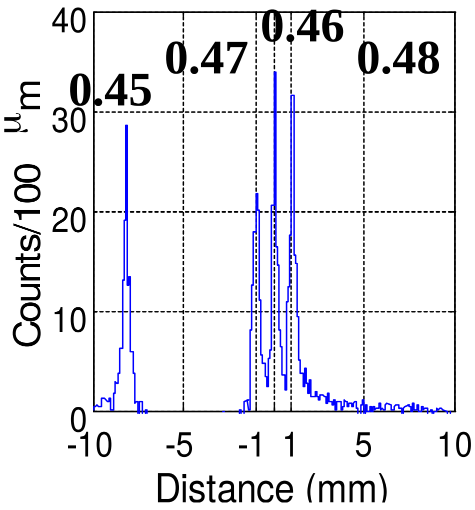
2D measurement of the photon interaction point

System in action



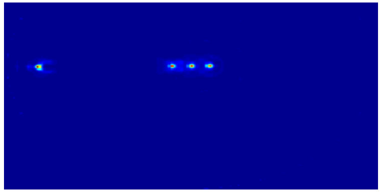
Filtered Back Projection FBP
~ 465 um FWHM

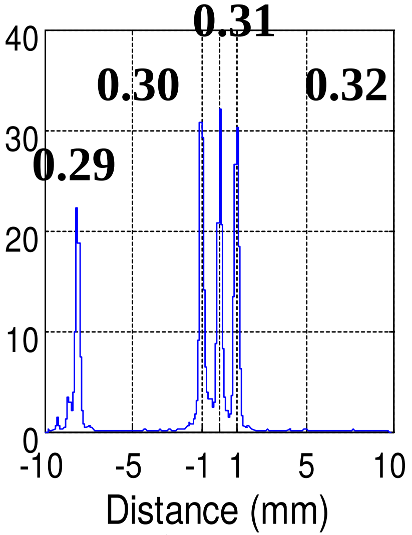




[A.Blanco, IEEE MIC 2004, PhD thesys]

Maximum likelihood-expectation maximization with resolution modeling (ML-EM) ~ 305 um FWHM

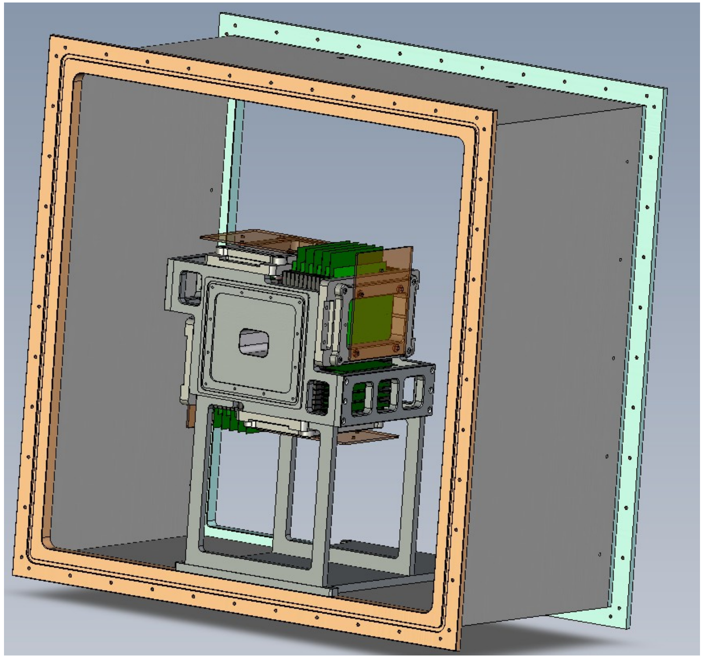


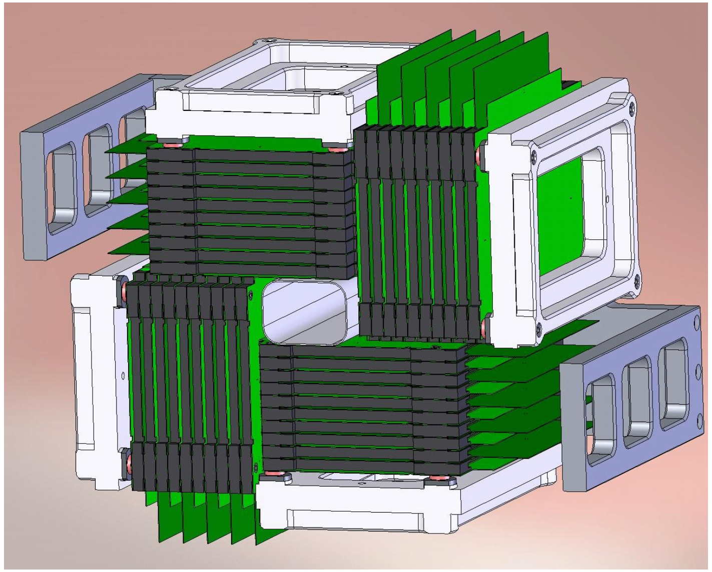


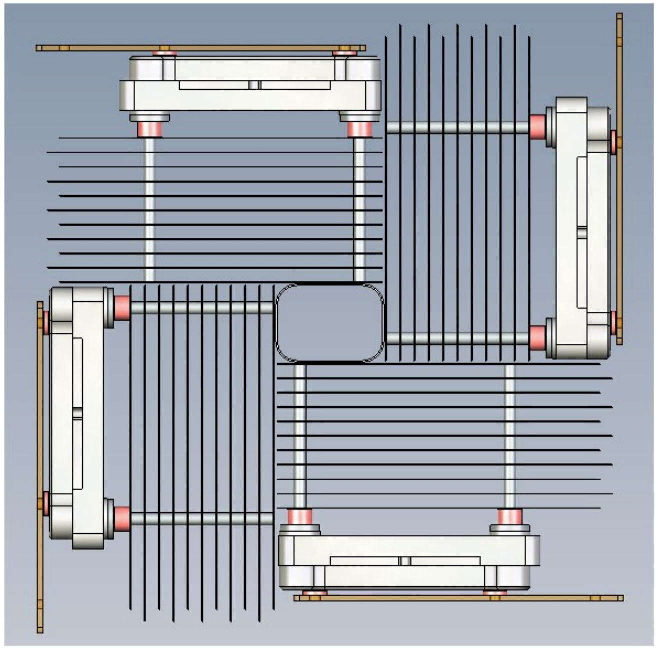
Proceeding IEEE MIC (2004) M2-177

Homogeneous spatial resolution over the entire field of view

Full scanner for mice – project

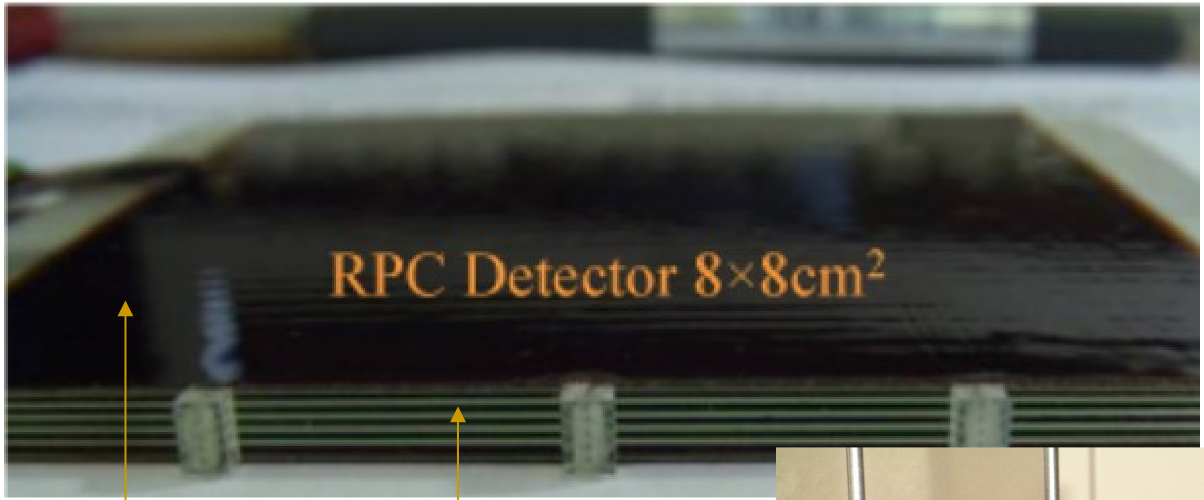






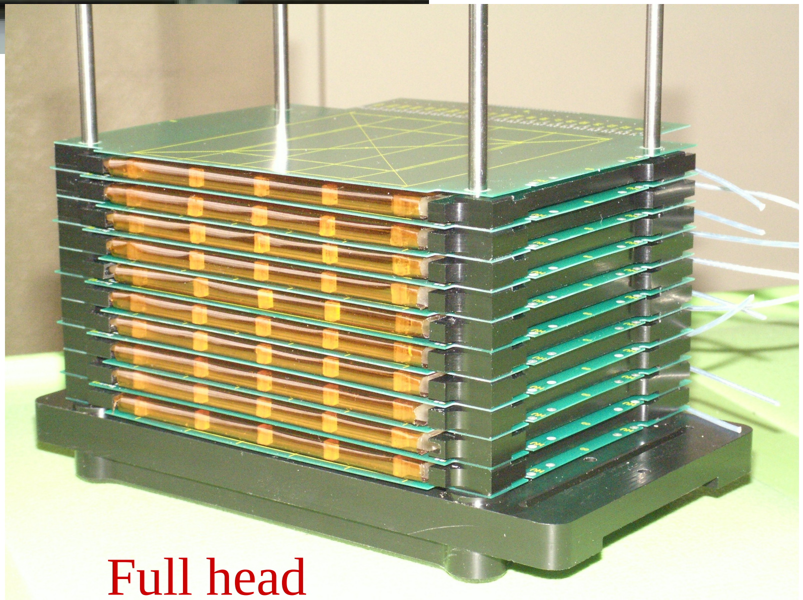
Almost 4PI
coverage

Detector & readout



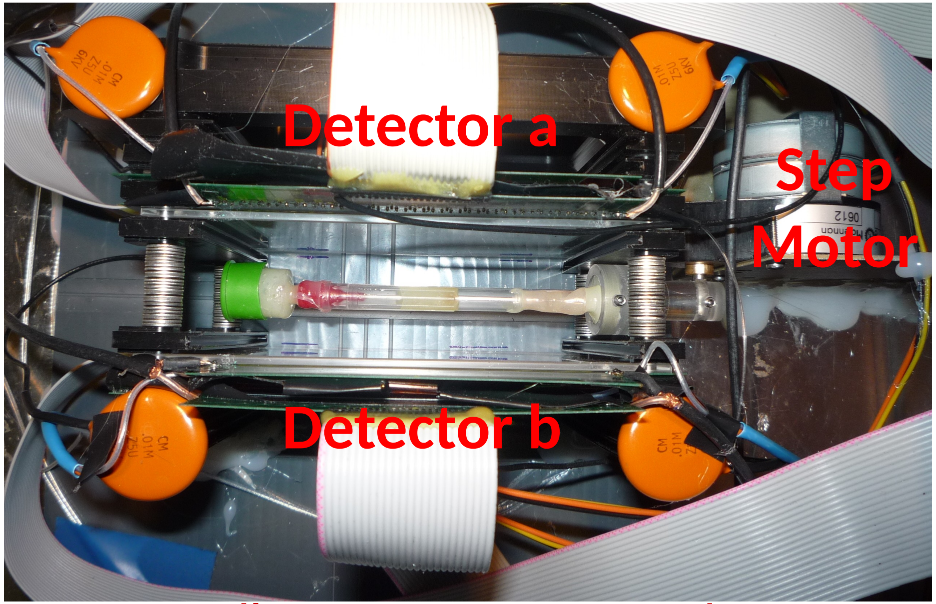
HV distribution layer
(signal-transparent)
kapton insulation

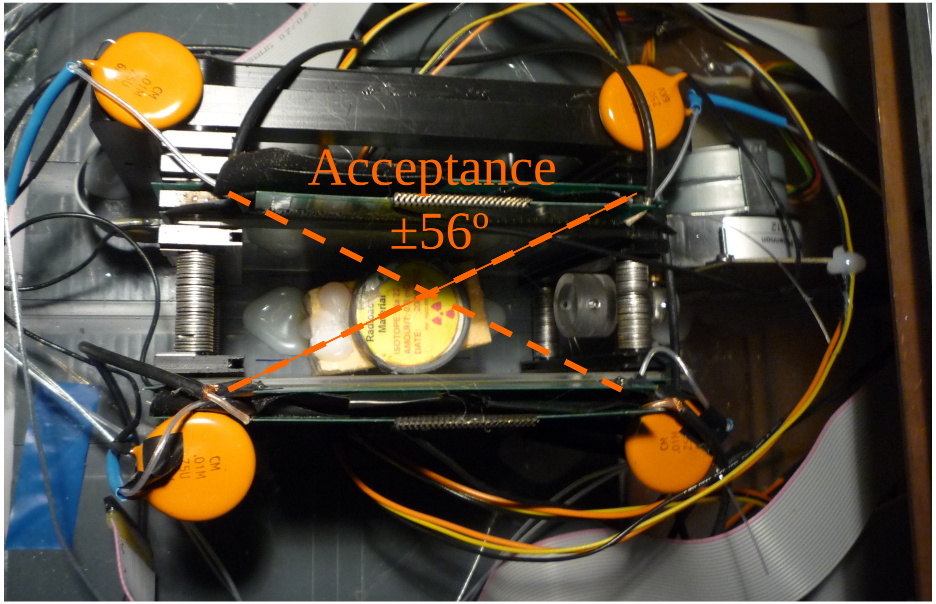
5 gaps 0.35 mm
6 x 0.38mm glass
~5 mm thick



Preliminary resolution tests in simplified geometry but realistic readout

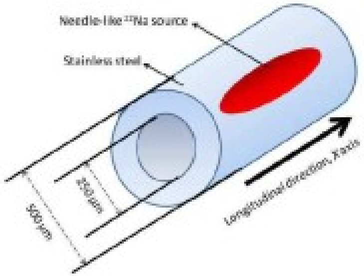
Two detectors with XY localization





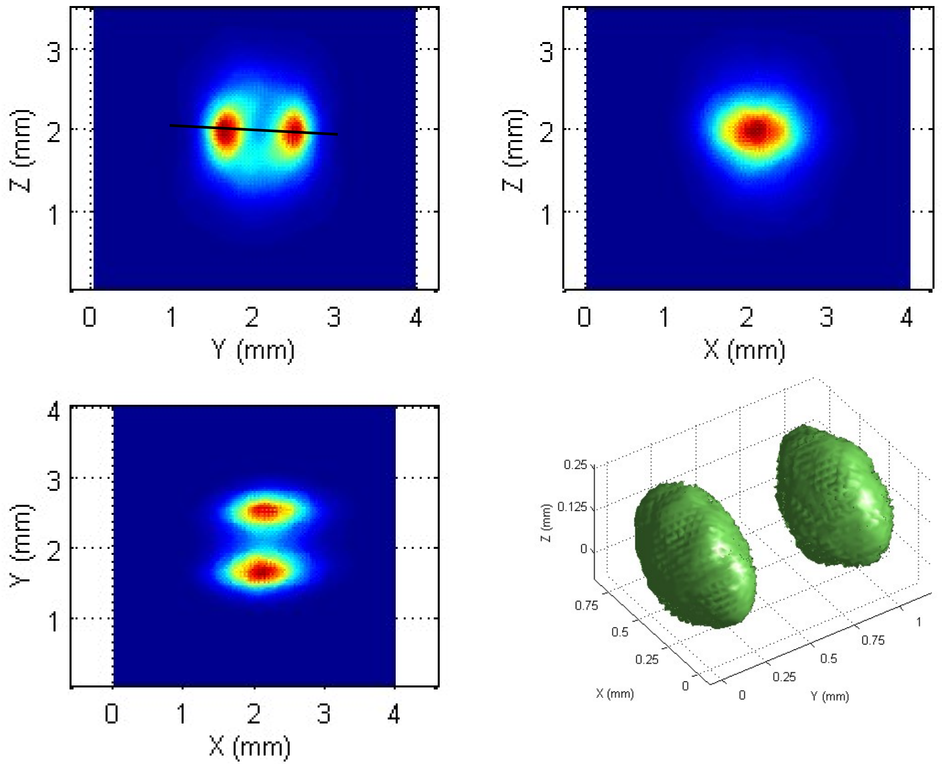
Needle source, 0.2 mm int.

Planar (disk) source

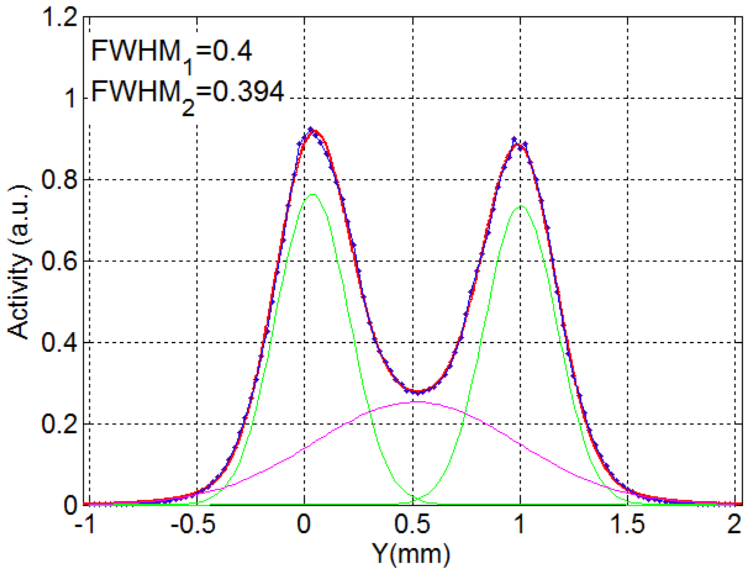


[P.Martins et al., JINST 2014 + PhD thesys]

Preliminary resolution tests in simplified geometry but realistic readout



[P.Martins et al., JINST 2014 + PhD thesys]

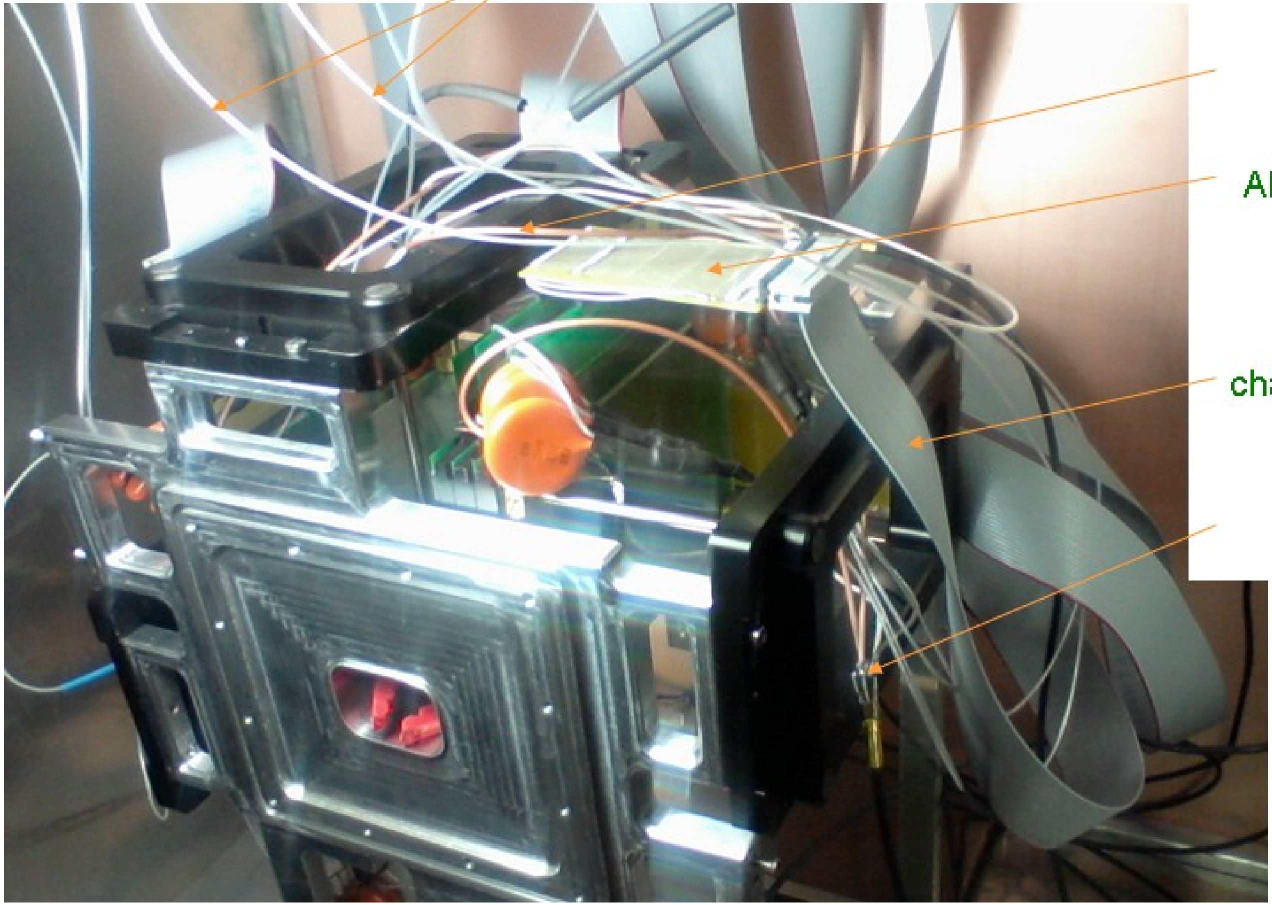


- Joint reconstruction of the source in 2 positions separated by 1mm.
- ~130k LORs in 3.5M 25um voxels.
- Color maps: planar profiles including peak density point. - Isosufaces: 50% rel. activity

- Reconstructed activity profile across the black line shown in the upper left panel.
- Resolution **~0.4mm FWHM +background** (Note: source is 0.2mm diam.)

Construction at LIP

±HV



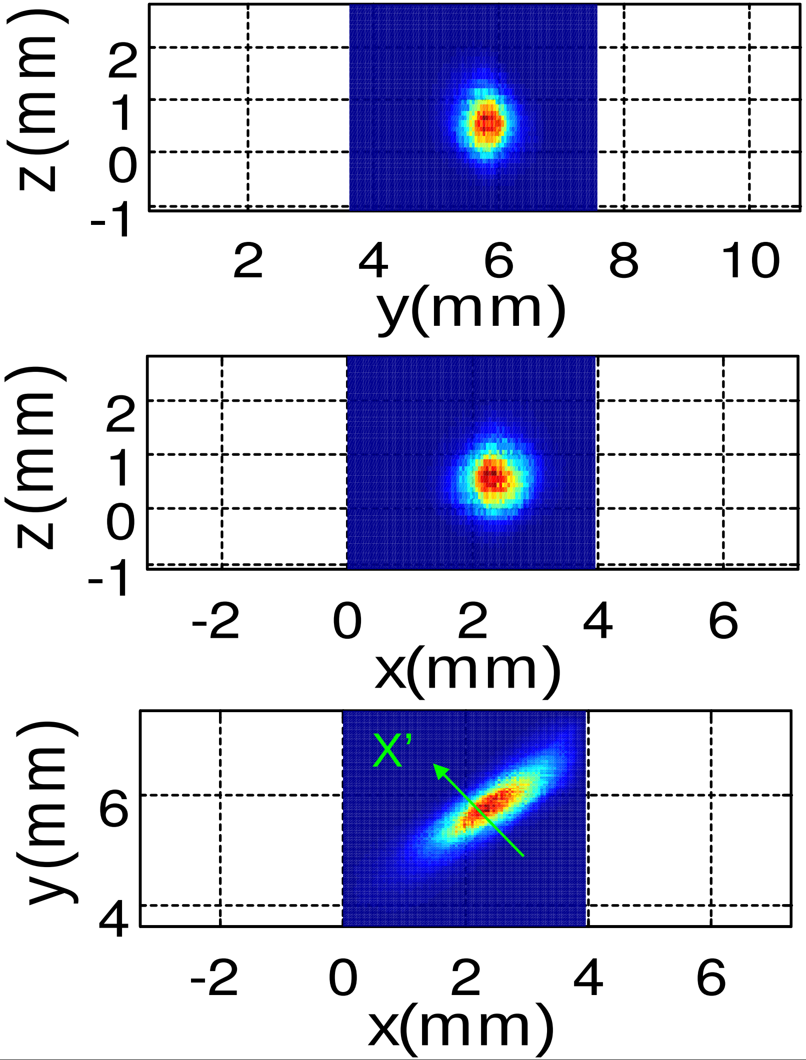
Auxiliary coarse Z determination

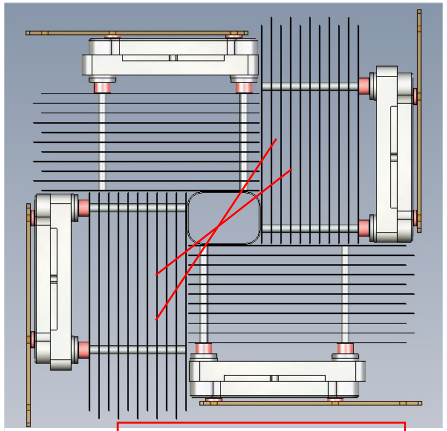
All electrodes readout in parallel

24 charge channels/coordinate/head

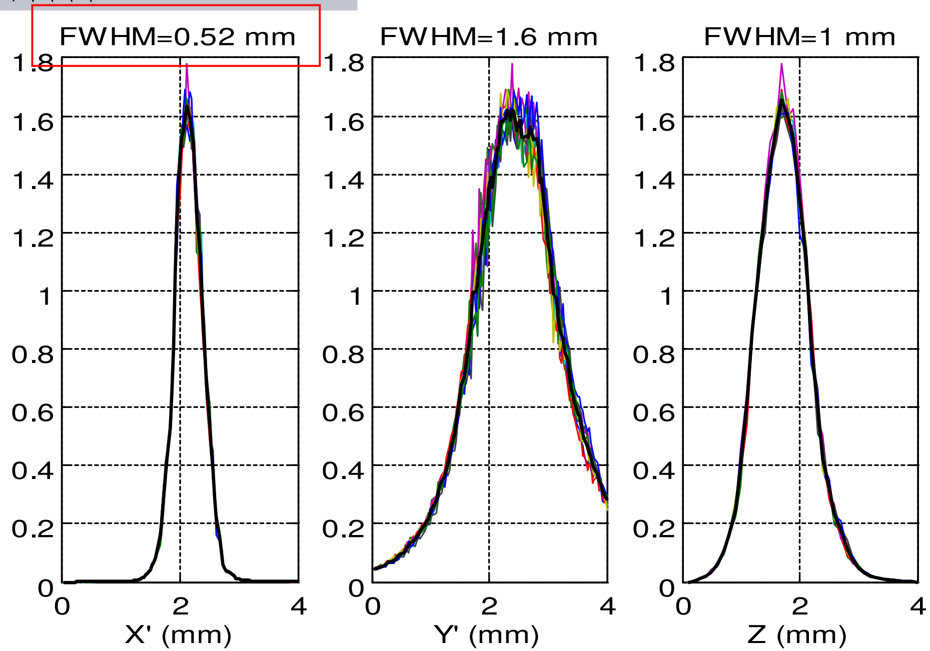
Time readout (for trigger)

Resolution in final geometry (2 heads only, needle source)



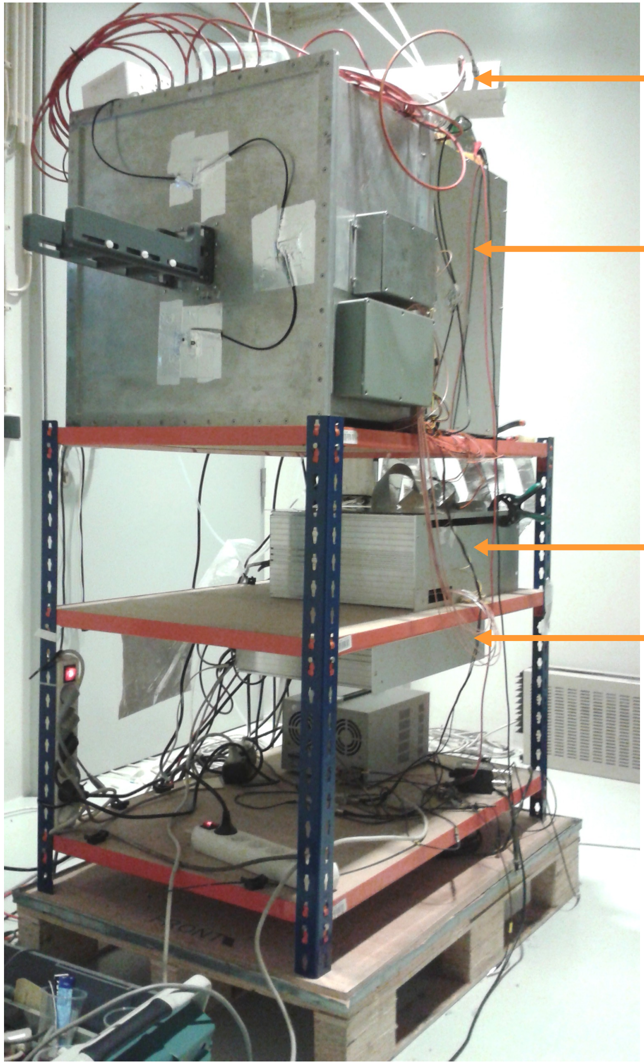


PRELIMINARY
Calibration not done in full.



Installed at ICNAS (UC)

Upgrades



HV (mess)

Higher gain
trigger

DAQ
+
trigger

Comms
+
Power
management

Expected performance vs. other systems

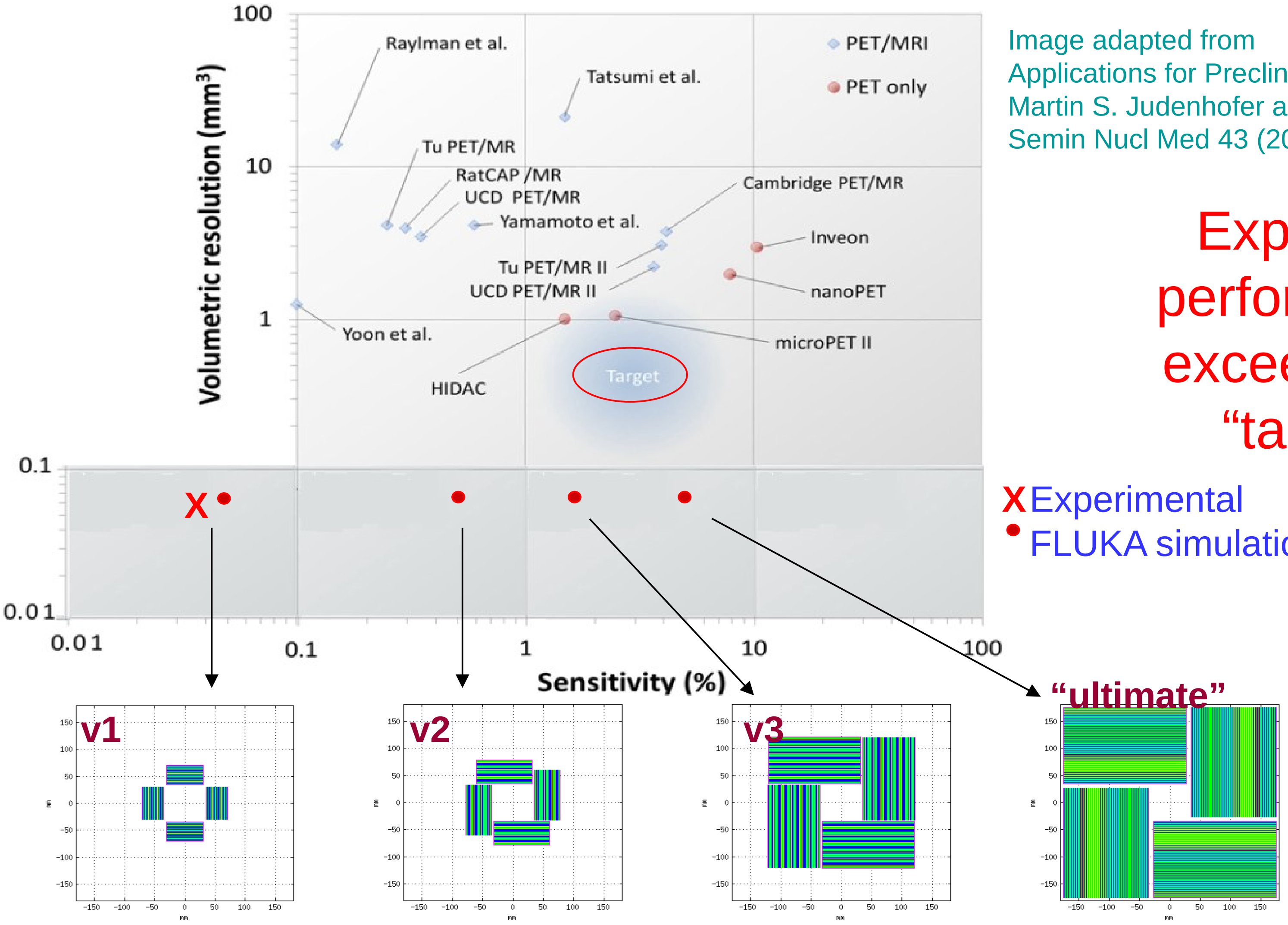
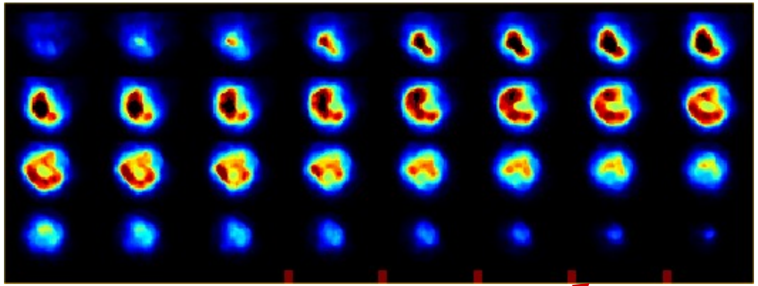


Image adapted from
Applications for Preclinical PET/MRI,
Martin S. Judenhofer and Simon R. Cherry
Semin Nucl Med 43 (2013)19-29

Expected performance exceeds the "target"

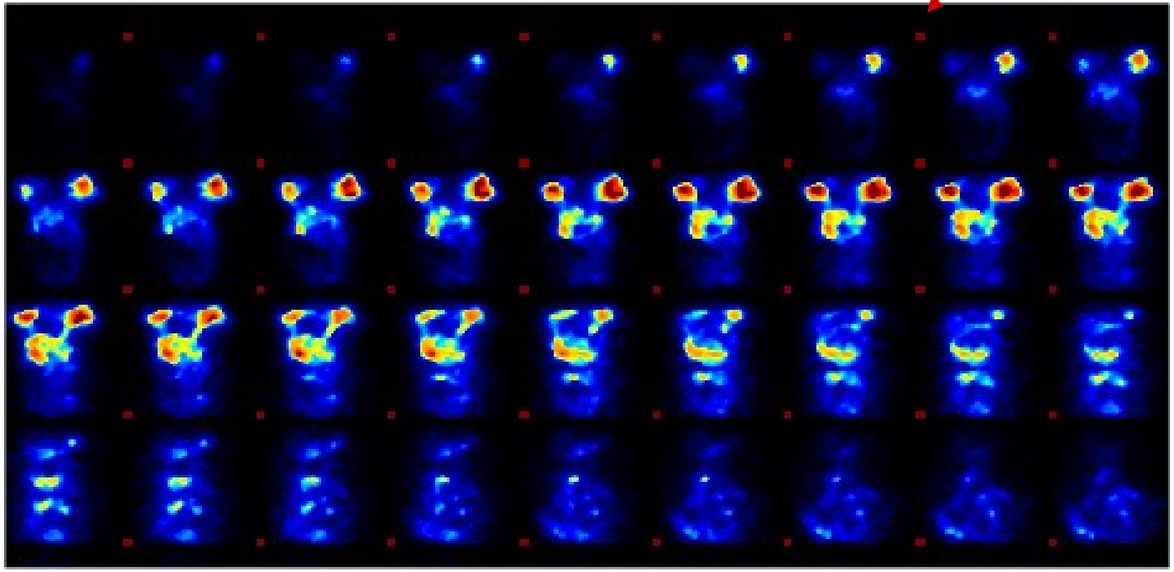
X Experimental
• FLUKA simulation

Some interesting images of mice

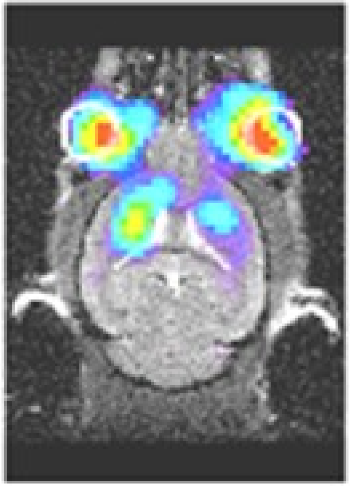


Live heart transaxial sections with ^{18}FDG

1 mm^2



Harderian glands and left striatum with ^{11}C-raclopride



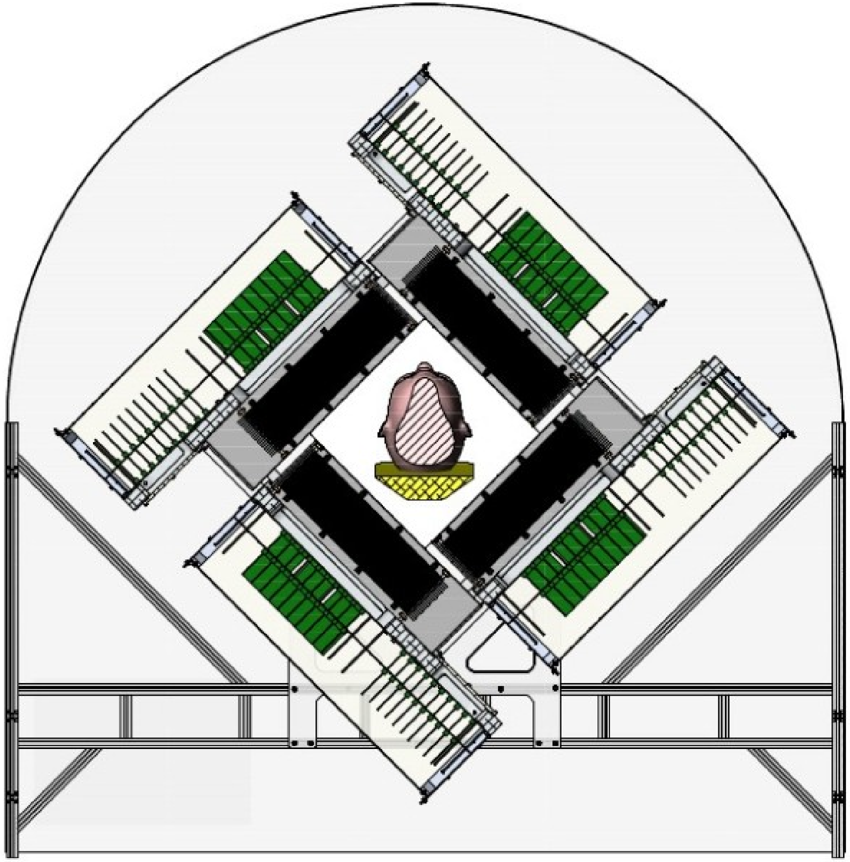
Co-registration with MRI

More than 500 scans performed so far (2015 - 2022).

S. Chiquita, M. Ribeiro, J. Castelhano, F. Oliveira, J. Sereno, M. Batista, A. Abrunhosa, A.C. Rodrigues-Neves, R. Carecho, F. Baptista, C. Gomes, P.I. Moreira, A.F. Ambrosio, M. Castelo-Branco, **A longitudinal multimodal in vivo molecular imaging study of the 3xTg-AD mouse model shows progressive early hippocampal and taurine loss**, Human Molecular Genetics, 28 (2019) 2174-2188.

C. Lopes, I.L. Ferreira, C. Maranga, M. Beatriz, S.I. Mota, J. Sereno, J. Castelhano, A. Abrunhosa, F. Oliveira, M. De Rosa, M. Hayden, M.N. Laco, C. Januario, M.C. Branco, A.C. Rego, **Mitochondrial and redox modifications in early stages of Huntington's disease**, Redox Biology, 56 (2022).

Brain PET



$30\times30\times30$ cm^3 field of view

Acceptance solid angle = 66%

Installed at ICNAS Pharma

Motivation:

- Resolving the smaller brain structures, often involved in severe neurological disorders (e.g. Parkinson, Huntington, addictions)
- Better characterization of the lesions from strokes
- Improve the oncological therapeutic planning by better detection and characterization of tumors

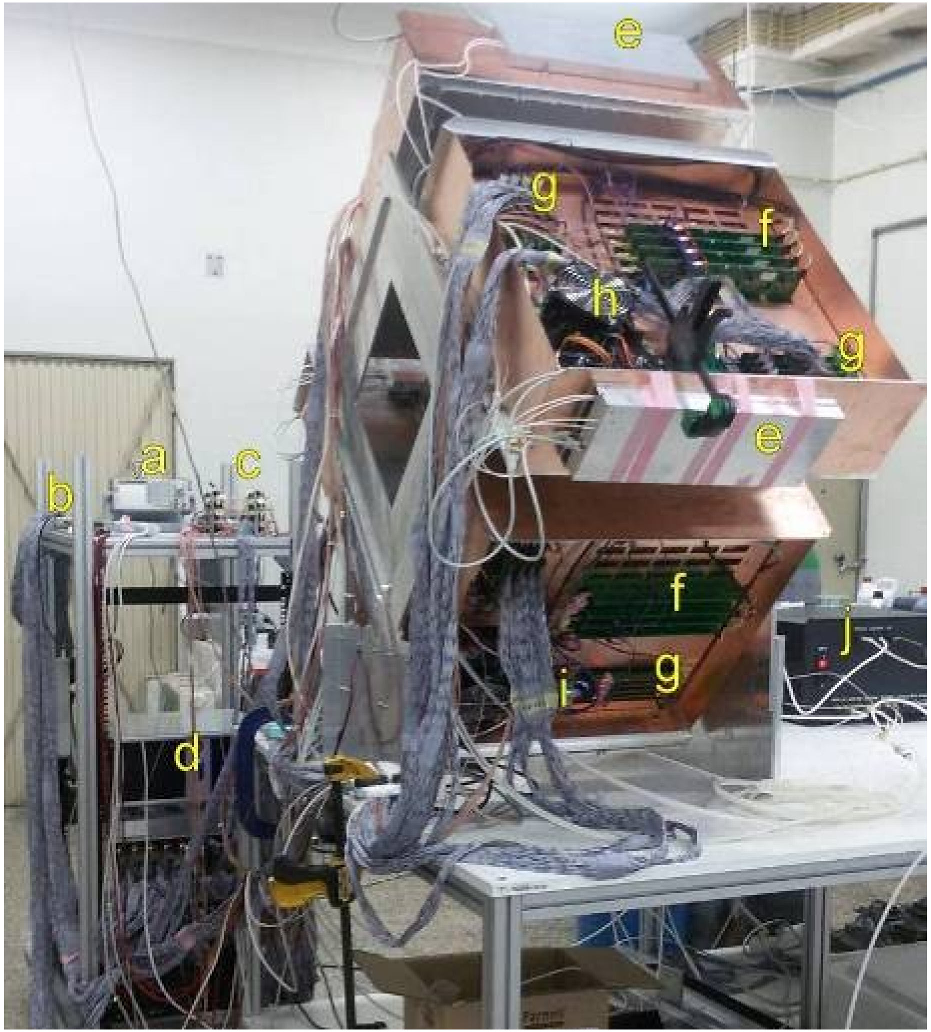
Specific project goals:

1 – best image resolution possible

2 – modest sensitivity of 0.1 %
(this is a demonstrator)

3 – fit the budget and the schedule (2.5y)

Instrumentation overview

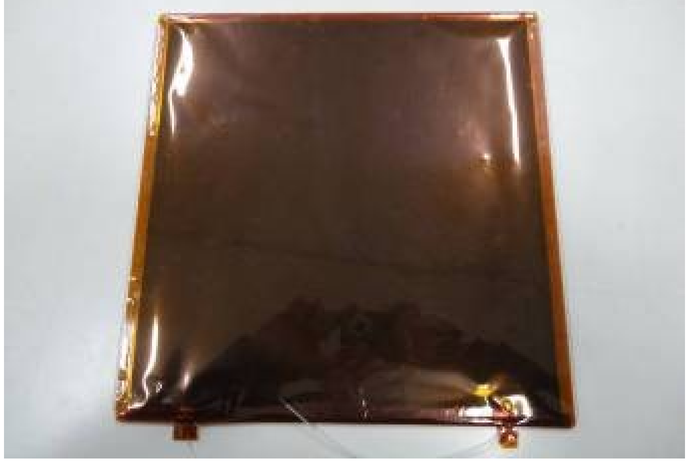


a) Pulse generator
b) Slow control main unit
c) Auxiliary comparators for trigger
d) DAQ system
e) HV power supplies
f) Timing amplifiers/comparators
g) Charge amplifiers
h) LV power supply
i) Local slow control
j) Gas system

DAQ system was developed by the TRB collaboration (trb.gsi.de)

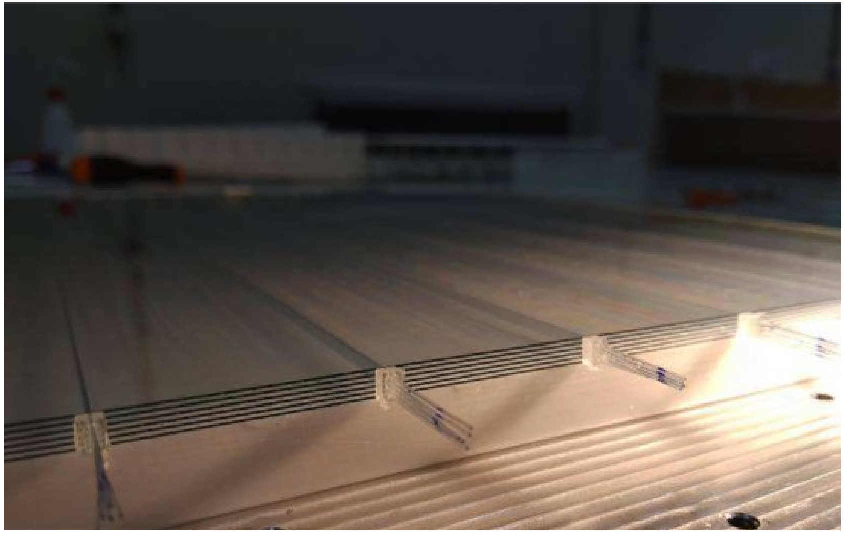
All other hardware developed at LIP

a) Readout electrodes
b) Cabling towards fast amplifers
c) Cabling towards charge amplifiers
d) RPCs (8 = 40 gaps total)
e) Empty space for twice more RPCs
f) Pulser cable

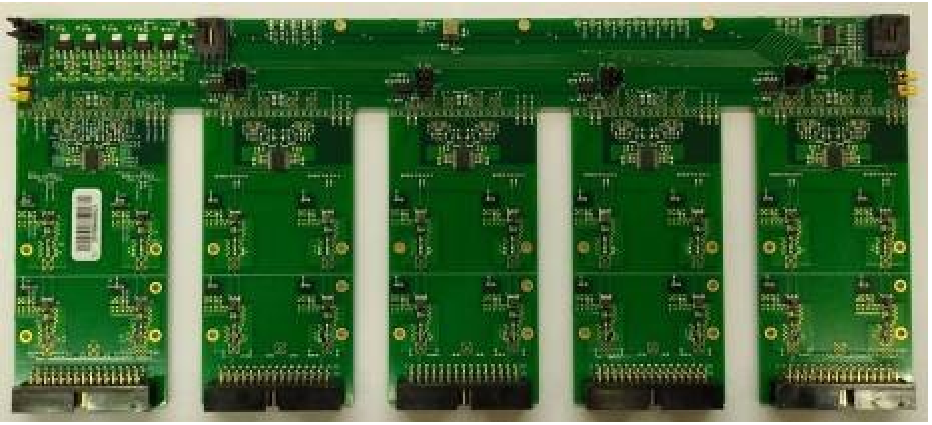


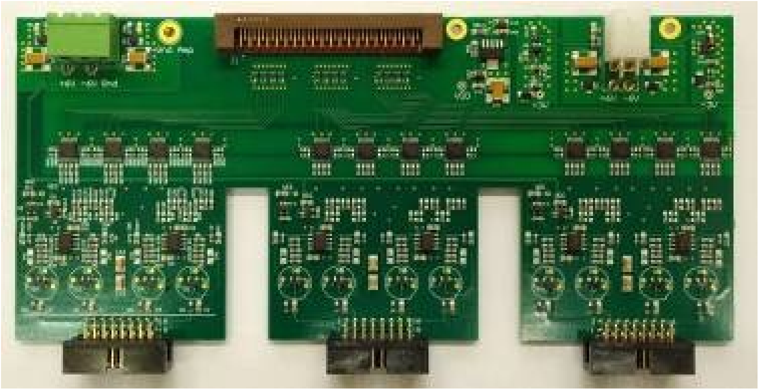
5-gaps MRPC: 30 x 30 cm^2 active area

Glass 0.33 mm, 0.35 mm gaps, ~4.5 mm thick



Front-end electronics (custom, discrete)





Timing amplifiers:

- 10 independent channels
- selectable polarity
- two-stage wideband amplification (2 x SPF5043Z => gain 60 @ 1GHz)
- comparator MAX9601 as 200 ns one-shot
- individual LVDS outputs
- wired OR output for trigger
-noise floor ~20 uA at input (50 ohm) <=> 50 mV on the comparator

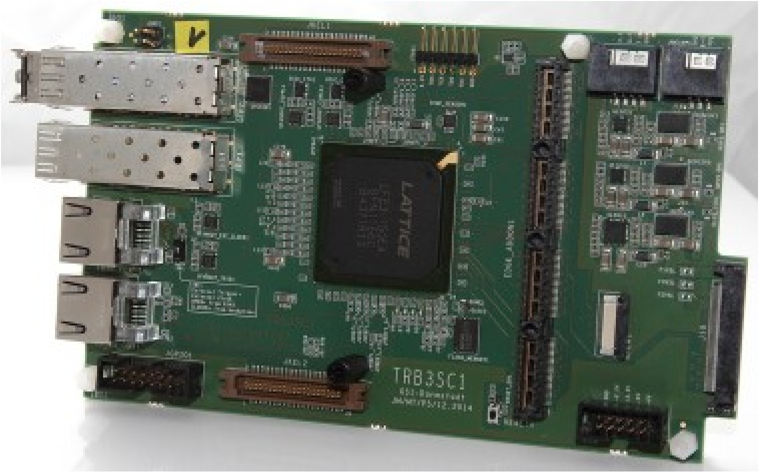
Charge amplifiers:

- 24 channels
- bipolar
- 50 mV/pC
- 20 us integration time
- readout by streaming ADCs
- digital pulse proccessing

- two independent systems (1/crate = 1 head pair)
    - 8 x 48ch streaming ADCs
    - 8 x 1GbE links
    - central trigger processor
- switch for data aggregation into 2 x 10GbE links
- server for event building and storage (~2 h)
- acquisition rate limited only by the 1GbE links

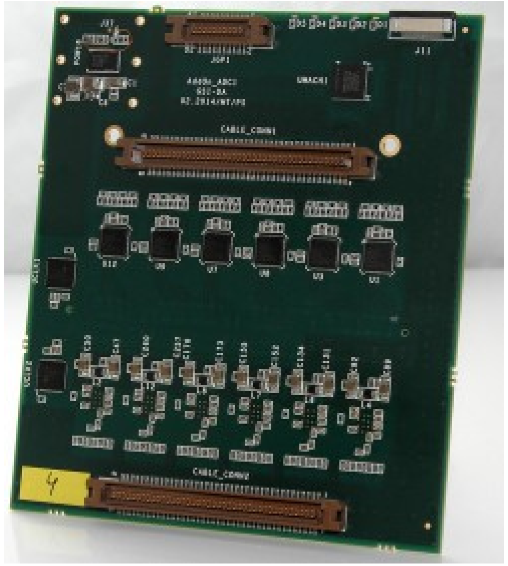
Developed by the TRB collaboration

(trb.gsi.de)



TRB3sc

- base module for numerous addon boards
- 1GbE link
- many firmware options
  - 48 ch 10 ps TDC
  - central trigger processor
  - digital pulse processing for ADCaddon
  - etc.



ADCaddon

- 48 ch 40 MHz streaming ADC

Gas system

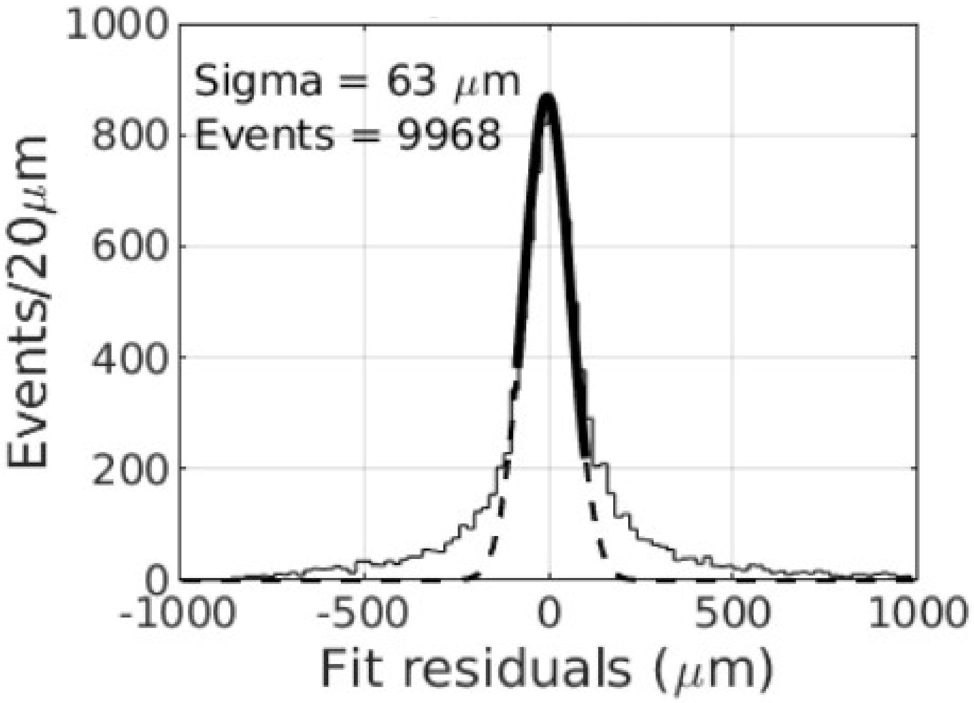
Very nice gas system:

- flow splitted equally between the 4 heads
- separate exit bubblers
- flow and humidity measurement in each bubbler
- temperature, etc.
- local RPI for control & measurement

3D event localization – in plane electronic contribution

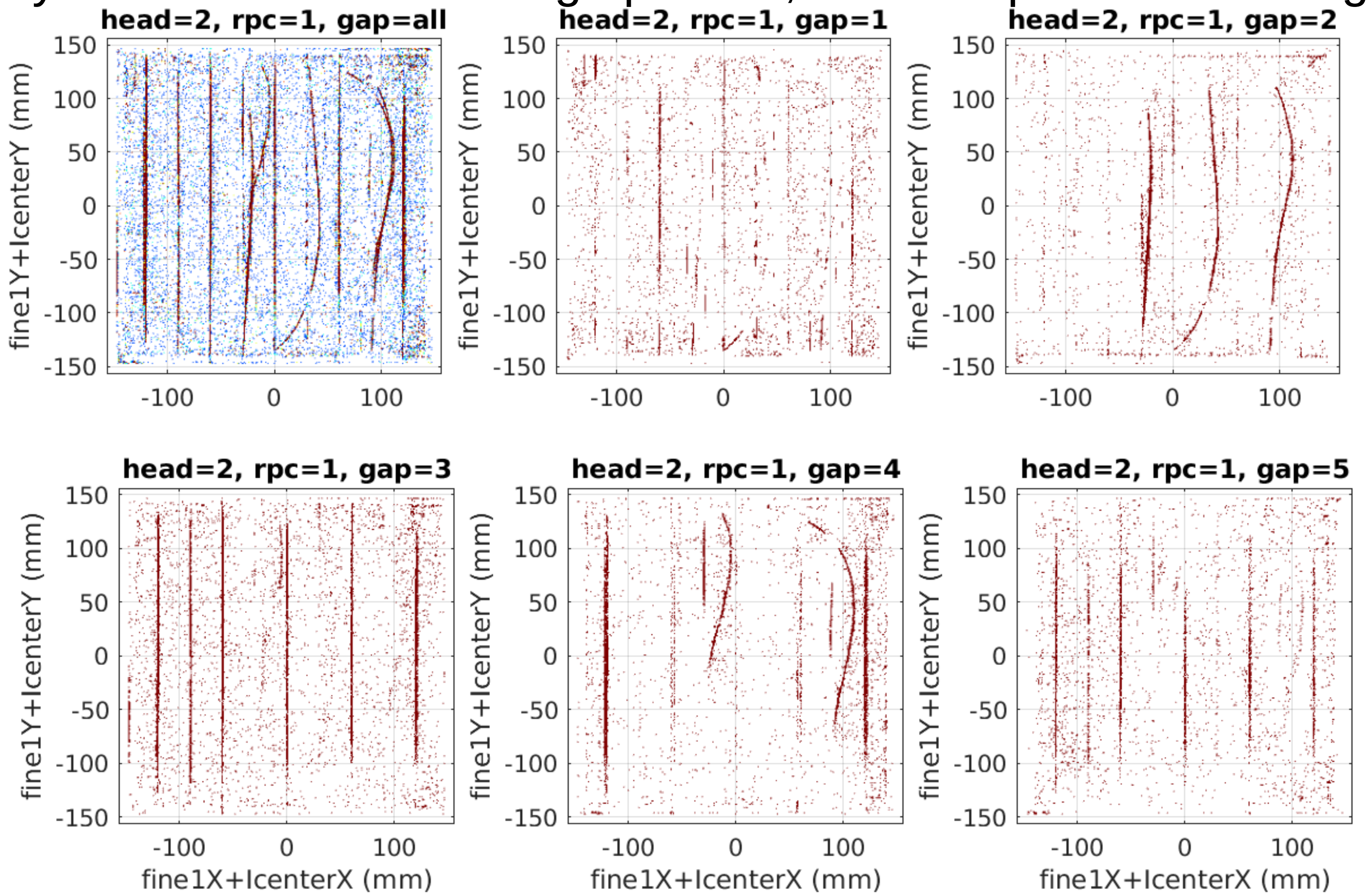
Difficult to determine with photons because there is always a parallax effect on the emitted electrons

Cosmic ray test with 3 full planes (all systematics in)



Fit of the residuals = 63 um sigma => 272 um FWHM/plane
(61 ps sigma time resolution)

Via analysis of the induced charge profiles, which depend on which gap has fired

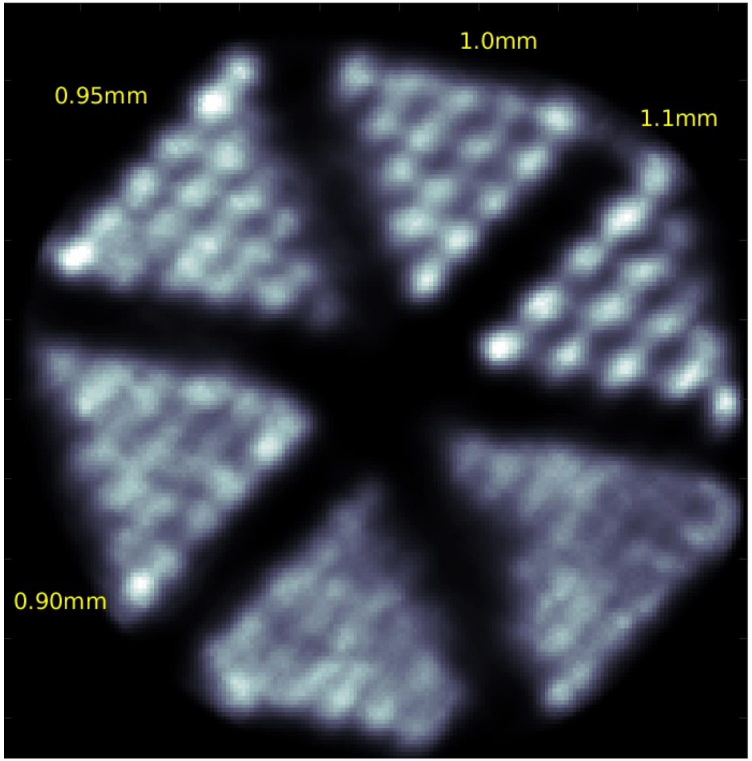


Self-trigger image of a chamber with loose spacing lines and deficient pressing

Image resolution

Data taken on the final scanner with a “Derenzo” or “hot-rod” phantom with ^{18}F.

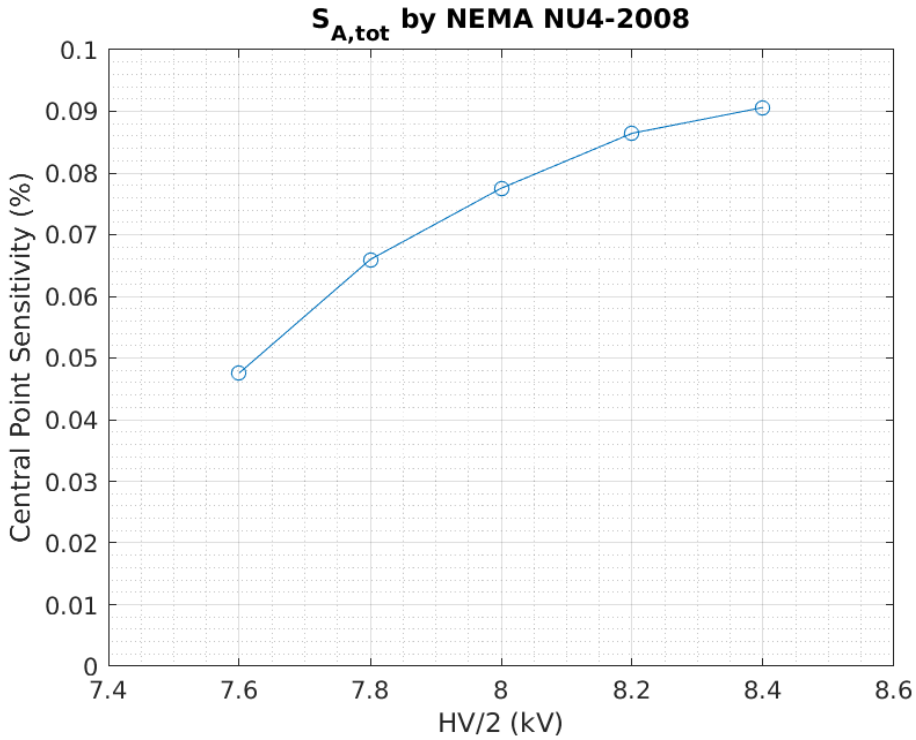
Radial resolution < 1mm (above the state-of-the-art)

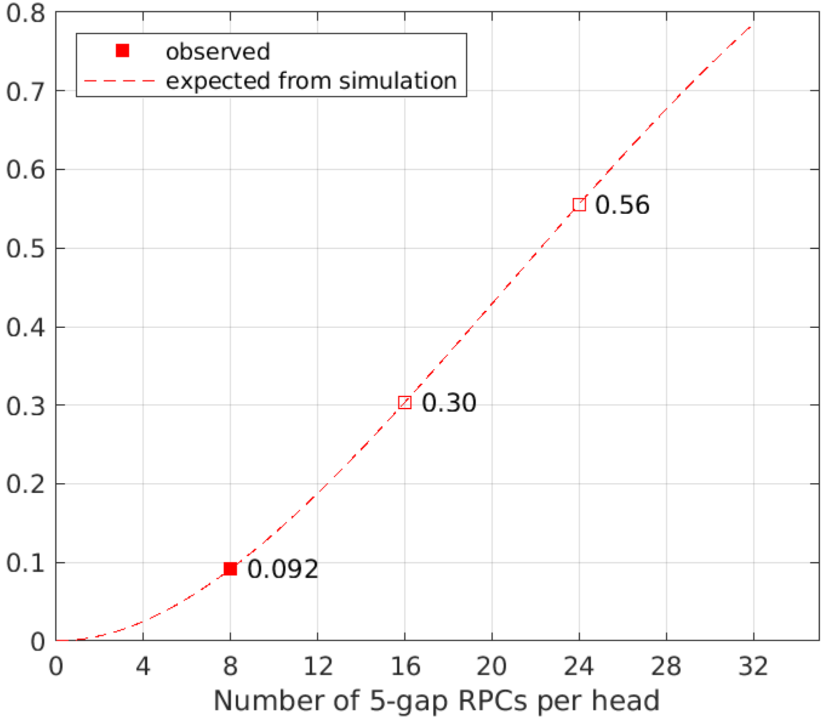


Moliner, L. et al., Sci Rep 9, 15484 (2019)
https://doi.org/10.1038/s41598-019-51898-z

PET Name	Algorithm	Isotope	10 mm FWHM radial	tang.	axial
Celestion	SSRB + FBP	^{18}F	4.5	4.7	4.4
Biograph mCT flow	FORE + FBP	^{18}F	4.33	4.33	4.25
Biograph mCT	FORE + FBP	^{18}F	5.0	5.0	6.4
Biograph mMR	FORE + FBP	^{18}F	4.0	4.0	4.1
Vereos	3DFRP	^{18}F	3.99	3.99	3.99
Ingenuity TF	3DFRP	^{18}F	4.84	4.84	4.73
Ingenuity PET/MR	3DFRP	^{18}F	4.7	4.7	4.6
Geminity		^{18}F	5.06	4.84	4.73
SIGNA PET/MR	FBP	^{18}F	4.4	4.10	5.34
Discovery MI	FBP	^{18}F	4.02	3.97	4.39
Discovery IQ	OSEM (VPHD)	^{18}F	4.2	4.7	4.8
Dedicated PETs					
CareMiBrain	SSRB + 2DFBP	^{22}Na	1.72	1.66	1.71
CareMiBrain	SSRB + 2DFBP	^{18}F	2.34	1.93	1.94
BrainPET-4layer MPPC	2DFBP	^{22}Na	1.8–2.1	1.8–2.1	1.8–2.1
NeuroPET	FBP	^{22}Na	3.2	3.2	3.5
Human Brain Insert	OP-3DOSEM	^{18}F	1.8	2.9	2.7
G-PET	3D-FRP		4.2	4.2	5.2
ECAT HRRT	2D FBP	^{18}F	2.6	2.7	3.0
jPET-D4	SSRB + 2DFBP	^{18}F	3.1	3.1	3.1
GAPD-PET		^{22}Na	3.0	3.0	—
PET-HAT	SSRB + 2DFBP	^{22}Na	4.0	4.0	—
MB-PET	MLEM	^{22}Na	1.02	1.21	1.27

Table 6. Spatial resolution (center axial





Sensitivity (probability of pair detection at low count rate) of 0.092%

But only half of the RPCs were installed. If all => triple the sensitivity.

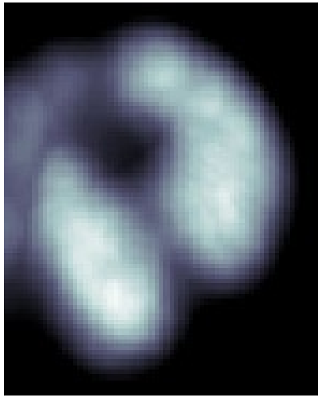
In the future could sextuple the sensitivity with 3x more RPCs.

Sensitivity is not so important. What matters is the noise-equivalent count rate (not yet)

Brain phantom imaging

Phantom of the cranium, brain and striatum nuclei

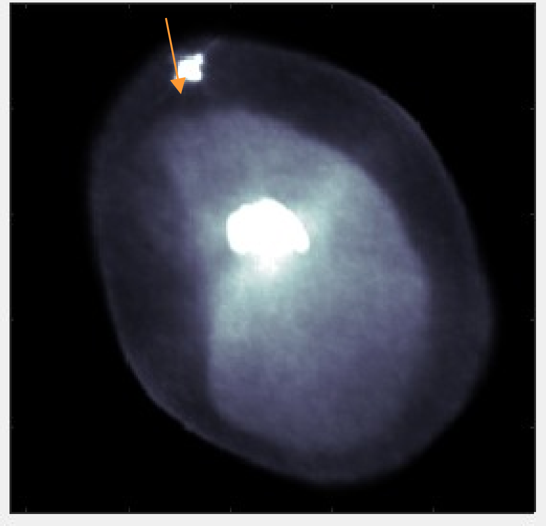
Striatum was filled with 8-fold more activity concentration than the brain



Detail showing the separation between chambers, which are externally touching

^{22}Na source

Global image of the brain (6 kBq/mL)



Striatum (50 kBq/mL)