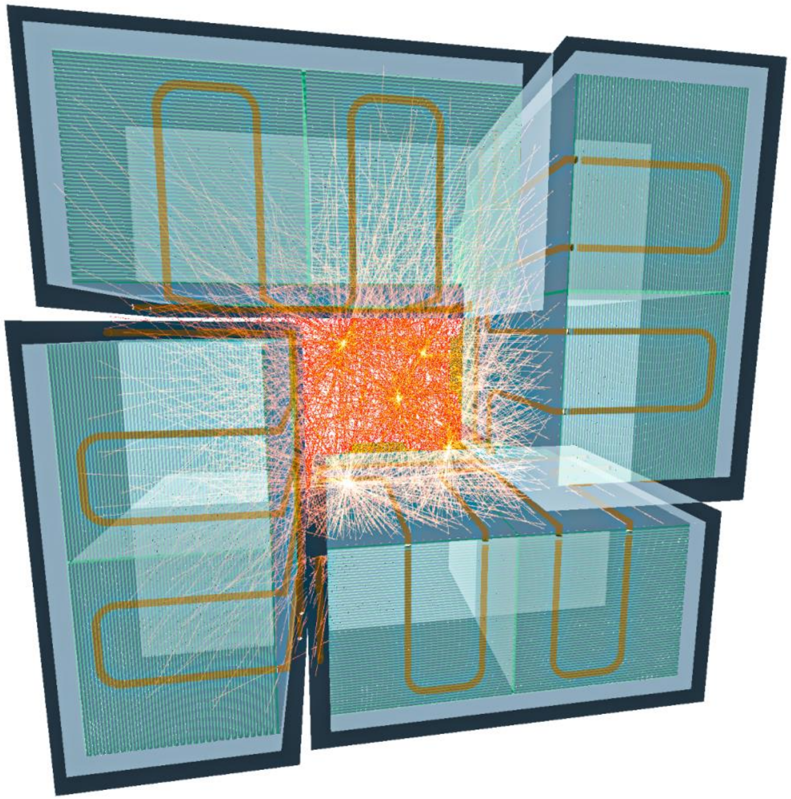

100μPET: Ultra-high-resolution PET imaging with MAPS

D. Ferrere, University of Geneva
On behalf of 100μPET collaborators

UNIVERSITÉ
DE GENÈVE
FACULTÉ DES SCIENCES

The Project & Collaborators

The **100µPET** project: molecular imaging with ultra-high resolution

- **SNSF SINERGIA** grant among **UNIGE** (scanner construction) **EPFL** (imaging) and **UNILU** (medical application studying atherosclerosis in ApoE+/- mice)
- **Deliverable:** Small-animal PET scanner with monolithic silicon pixel detectors

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Giuseppe Iacobucci
- project P.I.
- System design

Lorenzo Paolozzi
- Sensor design
- Analog electronics

Didier Ferrere
- System integration
- Laboratory test

Sergio Gonzalez-Sevilla
- System integration
- Laboratory test

Yannick Favre
- Board design
- RO system

Stéphane Débieux
- Board design
- RO system

Franck Cadoux
- Mechanical design

Thanushan Kugathasan
- Lead chip design
- Digital electronics

Roberto Cardella
- Sensor design
- Laboratory test

Mateus Vicente
- System integration
- Laboratory test

Jihad Saidi
- Detector simulation
- Data analysis

Luca Iodice
- Chip design
- Firmware

UNI LU

Martin Walter
- P. I.

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- PET imaging
- Translational imaging

Vincent Taelman
- Molecular biology
- Radiopharmacy

EPFL

Michäel Unser
- P. I.

Pol del Aguila Pla
- Statistical signal processing

Aleix Boquet-Pujadas
- Signal/image processing
- Physical modeling

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Swiss National Science Foundation
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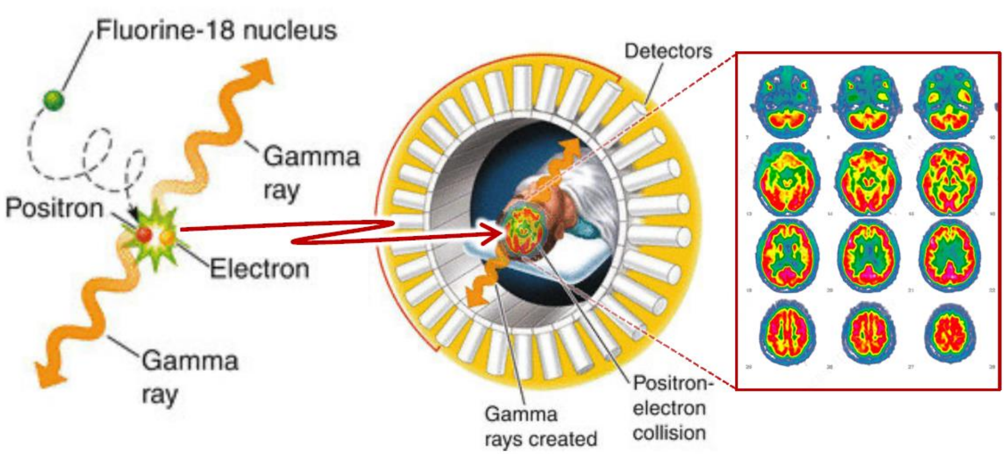
Sinergia
ATTRACT
UNIVERSITÉ DE GENÈVE UNITEC

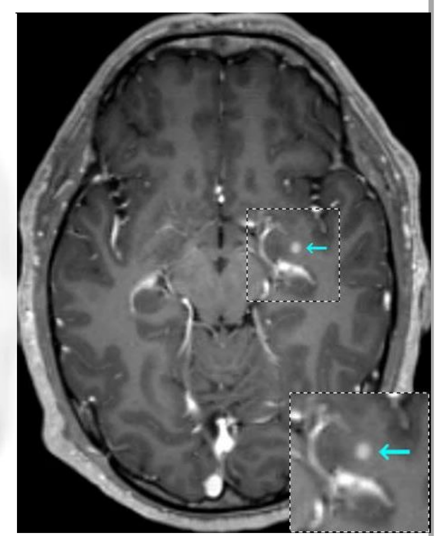
Positron Emission Tomography (PET)

- PET is a nuclear medicine method to study metabolic processes in the body
- Radiotracer is injected in a body → Positrons from the radionuclide annihilates with electrons of the nearby tissue → Two **back-to-back** 511 KeV photons are emitted and detected in **coincidence**
- **Lines-of-Response (LoR)** are defined by the volume between the **sensitive elements** detecting the two photons
  - Lines-of-response are processed to generate density maps of the detected annihilations
  - Today, due to the lack of spatial resolution, PET imaging must be done in hybrid mode (combining MRI or CT measurements)



PET

PET + MRI



Ref

Positron Emission Tomography (PET)

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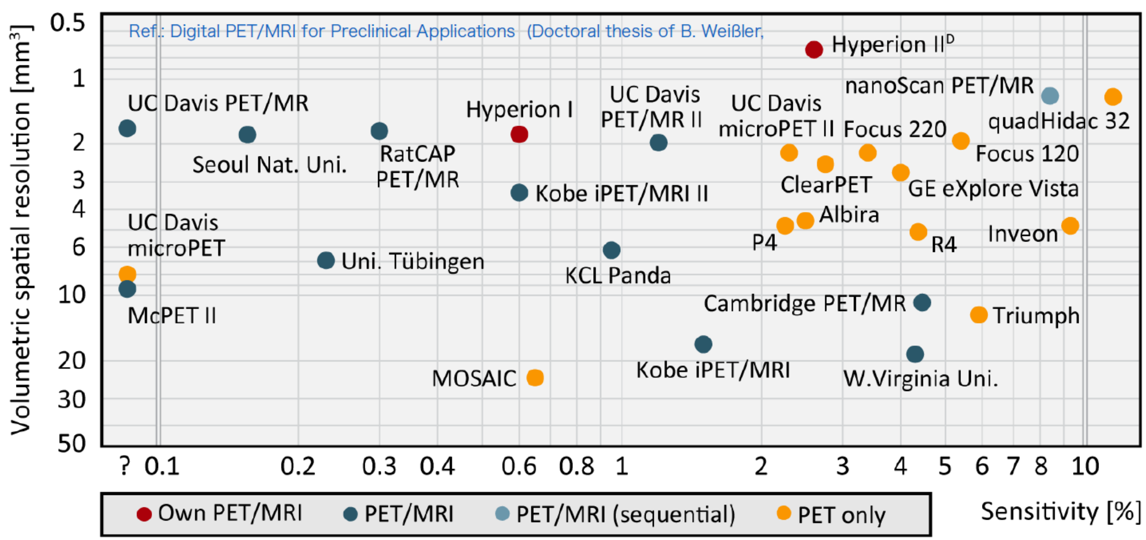
  - Today, due to the lack of spatial resolution, PET imaging must be done in hybrid mode (combining MRI or CT measurements)

  → <u>**Goal:**</u> improve the spatial resolution of PET scanner

Typical resolution today: 1 – 2 mm

Volumetric spatial resolution and **sensitivity** are the two key ingredients for performance

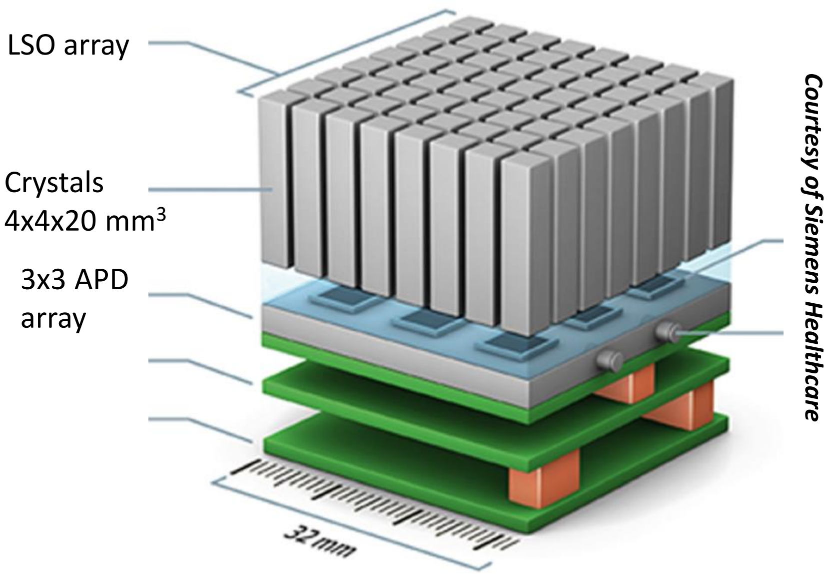
Overview of current small animal PET scanners



Detector Granularity - DOI and LOR

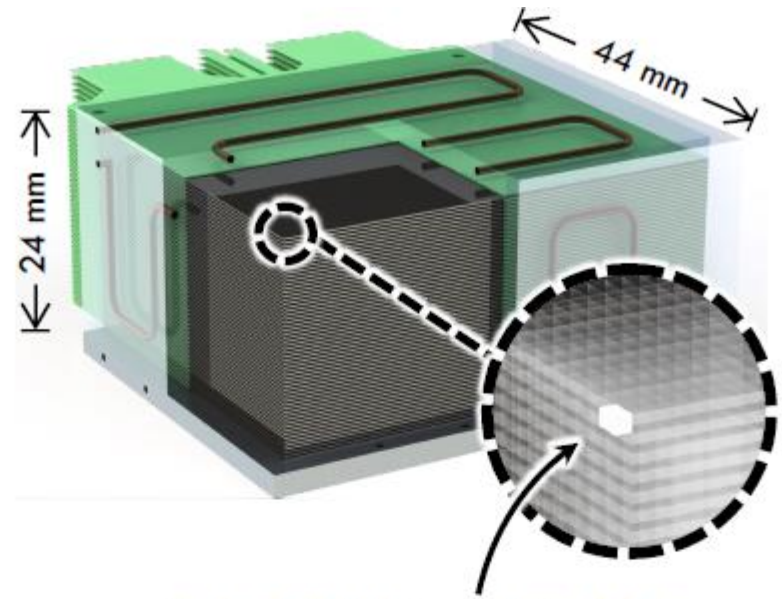
→ Ultra-high resolution is obtained by increasing the granularity inside a detection volume thanks to small silicon pixel size (~100 microns)

PET tower with LSO crystals



DOI: 20 mm
Sensor granularity: **320 mm³**

100µPET stack

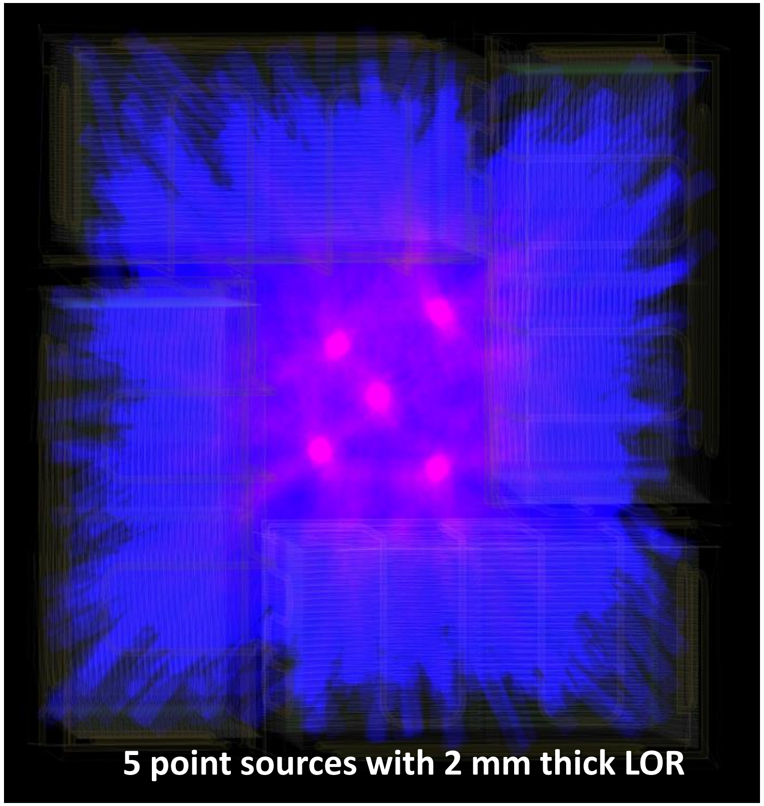


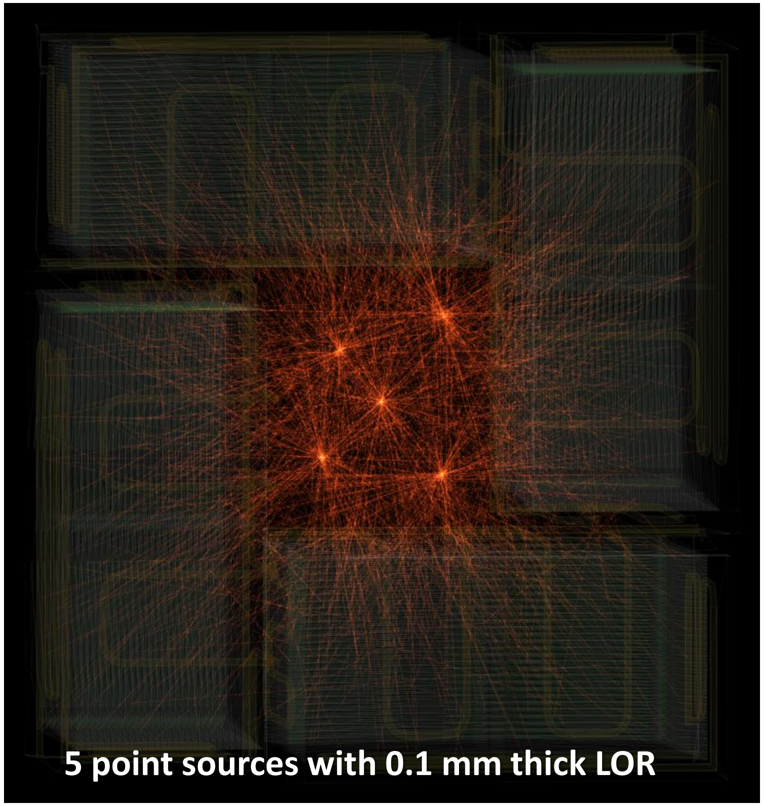
Pixel pitch: 100 µm | DOI: 400 µm
Sensor granularity: **0.004 mm³**

Scanner granularity: ~80'000 times finer with silicon pixel sensors
LOR volume: ~1'600 times smaller **& DOI: 50 times** smaller

Detector Granularity - DOI and LOR

→ Ultra-high resolution is obtained by increasing the granularity inside a detection volume thanks to small silicon pixel size (~100 microns)

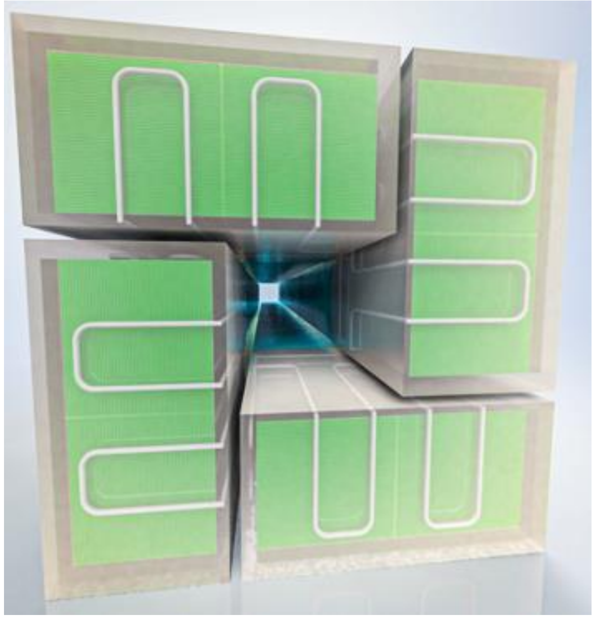


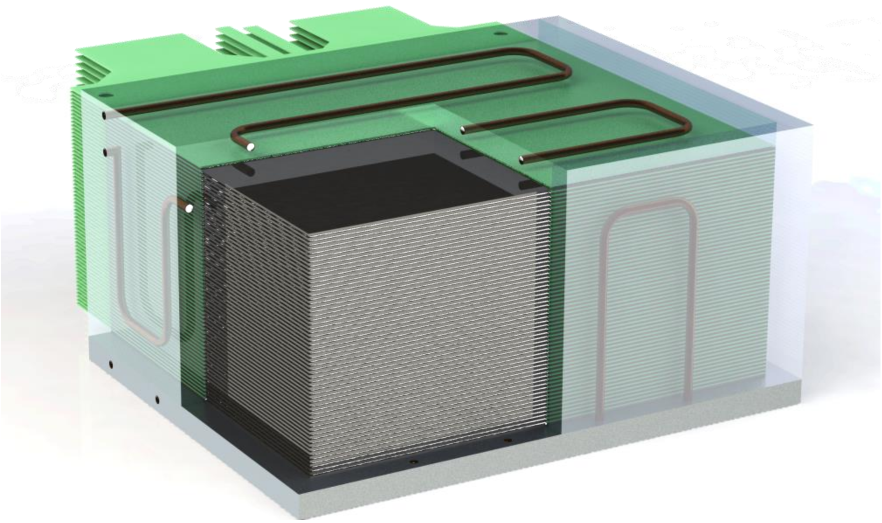


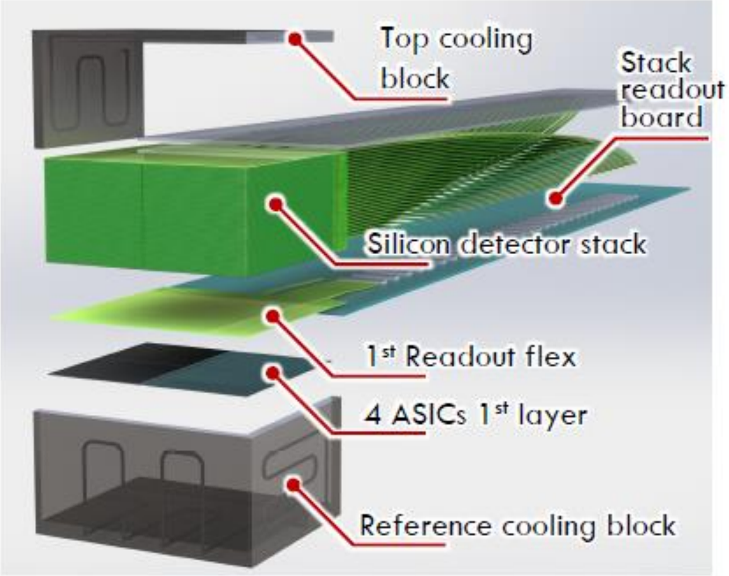
Only a factor of 20

100µPET Layout using MAPS

- The 100µPET Scanner consists of 4 towers with a total of 960 chips!
- A tower is composed of 60 Si-detection layers
- Multi-layer stack of CMOS imaging sensors based on silicon pixel detectors used in HEP
  - Monolithic 100µPET ASIC: 130 nm SiGe BiCMOS* using high resitivity wafer (4 kΩ.cm)
  - Large size reticle sensor-asic: 30 x 22 mm^2
  - Optional 50 µm thick Bismuth layer to increase the photon conversion efficiency (w.r.t. only silicon)





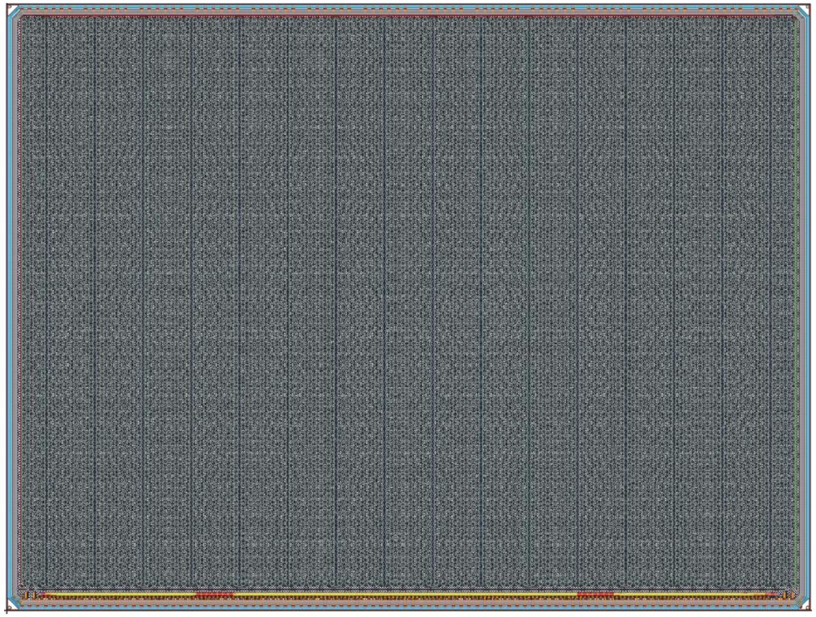


The Sensor-Asic Design - MAPS

- **SiGe technology** developed in the framework of monolithic timing pixel development profited from ~8 years of R&D development now used for FASER preshower upgrade and for 100µPET *(Monolith talk this afternoon)*
- **Asic design** largely inspired from the FASER chip *(tomorrow's talk)* – In-house design and submission booked for October 24th

Main features	
Depletion depth	250 [µm]
Pixel (hexagonal) pitch	**~ 160 [µm]**
Nb of pixels	**25344**
Max cluster size	< 25 pixels (5x5)
Front end noise (ENC)	**200 [electrons]**
Operation Threshold	3000 [electrons]
Power consumption	**70 [mW/cm^2]**
Time resolution RMS (Qin > 5 ke-)	**200 [ps]**
TOA and TOT	Per each super-pixel line
Readout speed	**50 [Mb/s]**
Event size	143 [bits]
Max expected data rate	40 kHit/s @ 20 MBq
Chip readout daisy chained	1 readout line / 4 chips

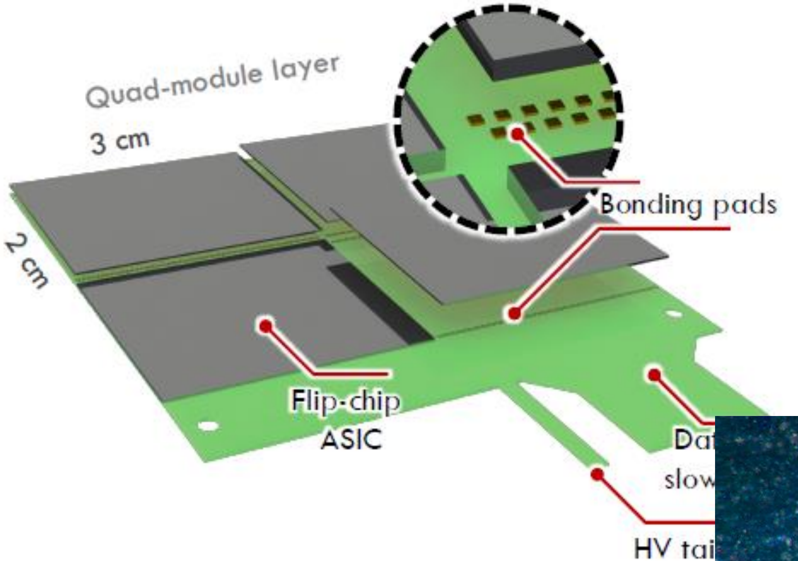
Chip size: ~ 30.2 x 22.8 mm^2



16 Super columns of 11 Super pixels of 144 pixels

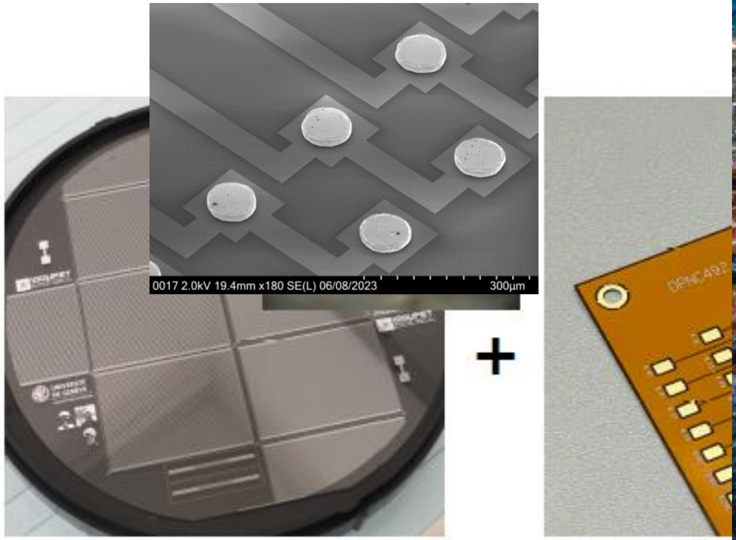
100µPET Module Construction

Baseline concept: Single module layer → Si to FCP interconnection

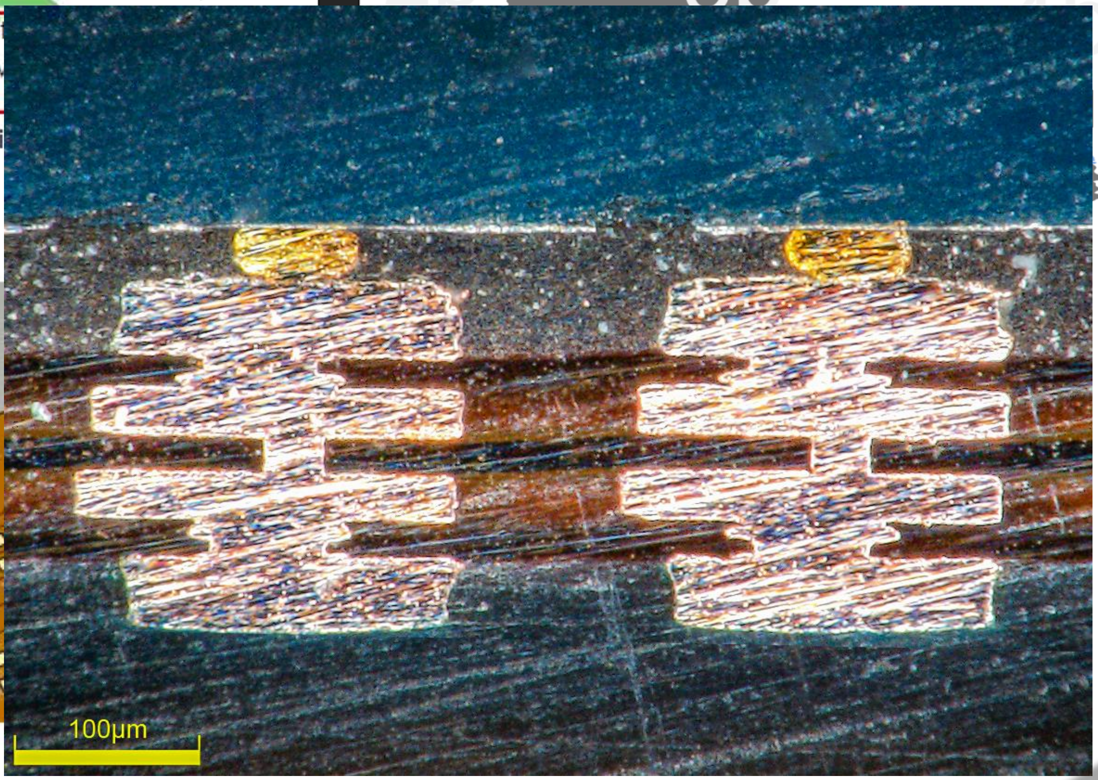


Flip-chip bonding thanks to:

- SET ACCURA100 machine
- Fused silica detector pattern matching flex PCB structure
- Flex PCB design on purpose to match the qualification bonding test



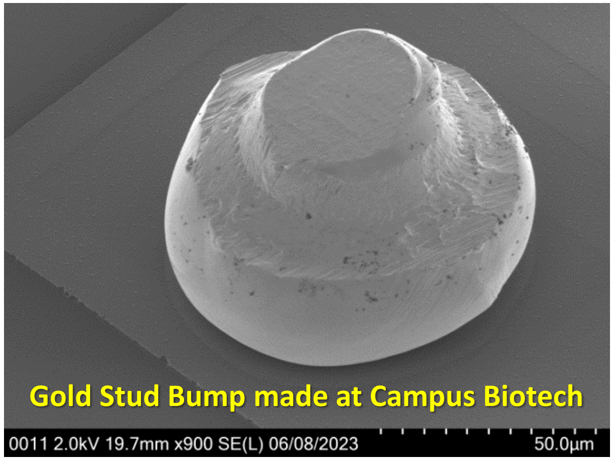
Pad wafer with 6 full chain dies

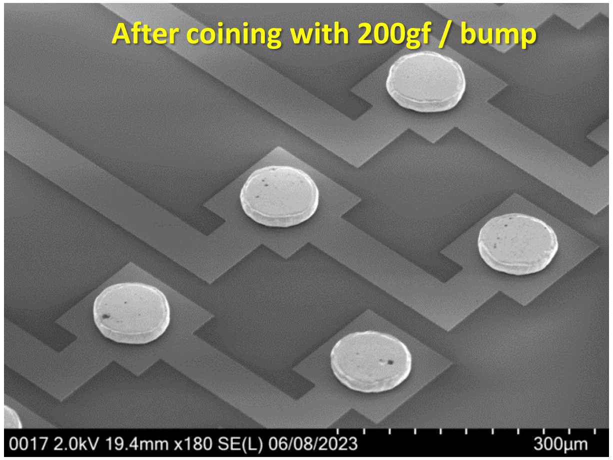


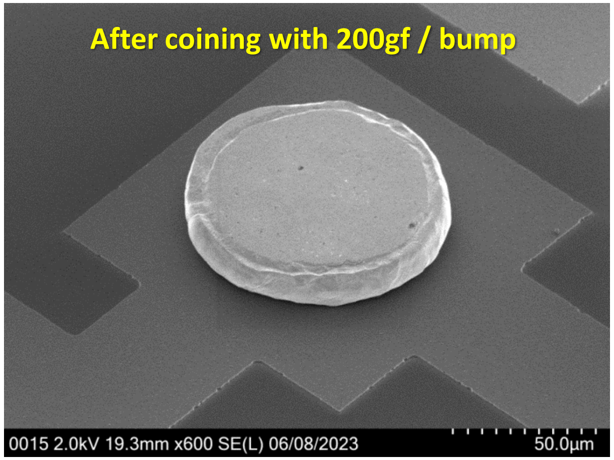
Interconnection Qualification

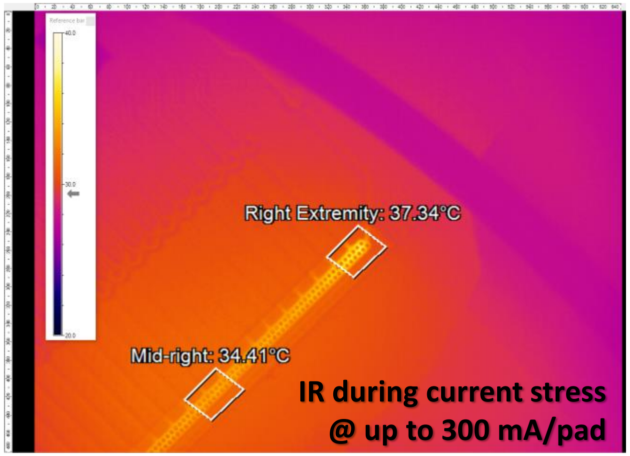
- **Several interconnections techniques were tested with the optimal method → Gold stud bumps with NCP**

Most reliable electrical contact and passed all the qualification tests including current stress test up to 300 mA









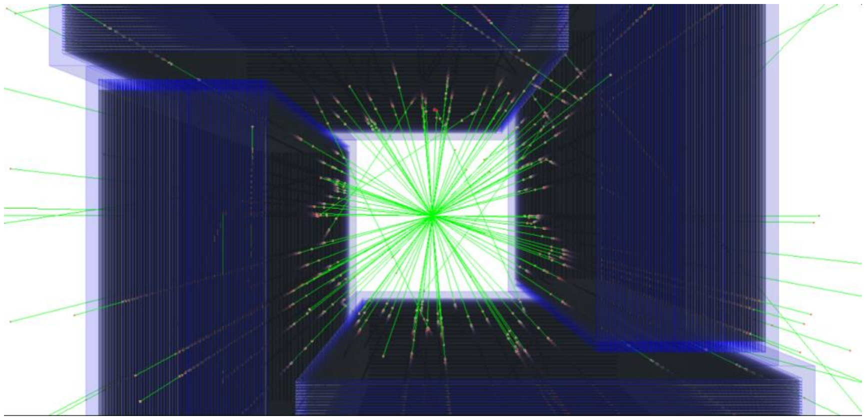
During current stress tests → IR image checked

IR Inspection area (Interconnection pads underneath)

100µPET – Performance Simulation (1/2)

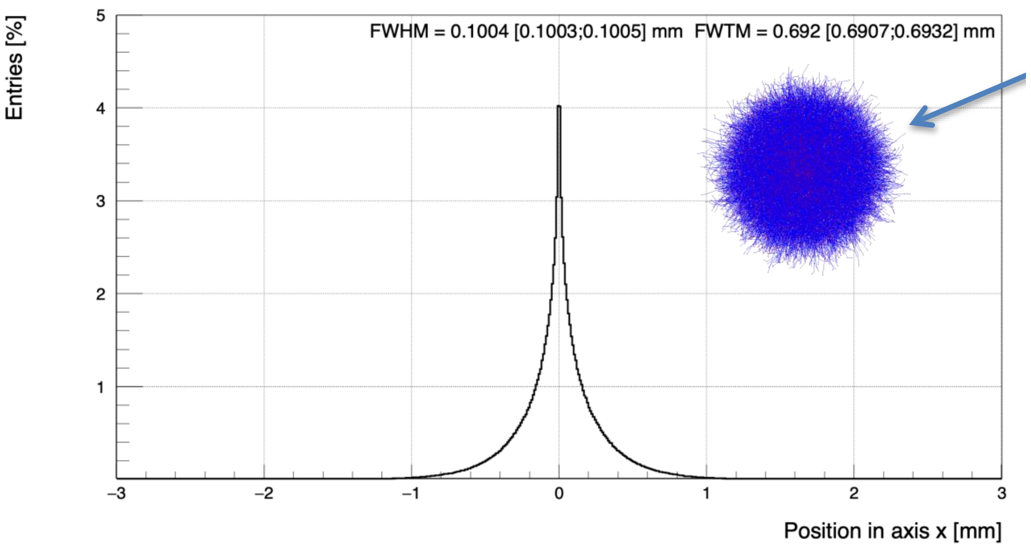
Monte Carlo simulation with Geant4 and Allpix2 allows:

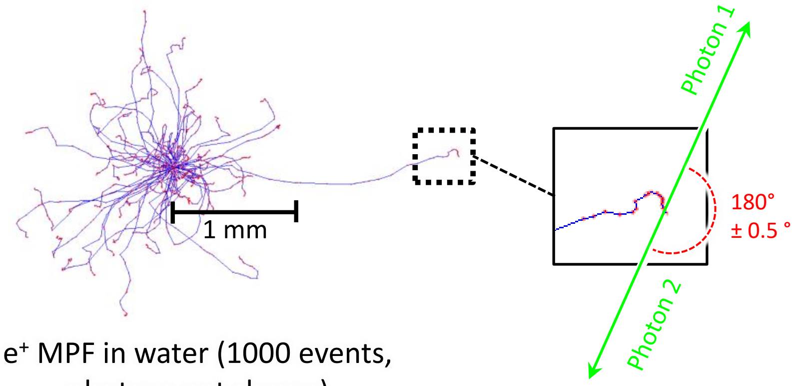
- Positron emission & photon conversion
- Detector performance with pixel asic
- Detector effects on sensitivity and resolution



Full scanner geometry (w/ or w/o Bi layers) + **water volume**

- Positron mean free path and annihilation from [^{18}F]FDG with acolineaity effect
- Photon interactions (scattering and photoelectric effect)
- Sensor/ASIC response + pixel clustering



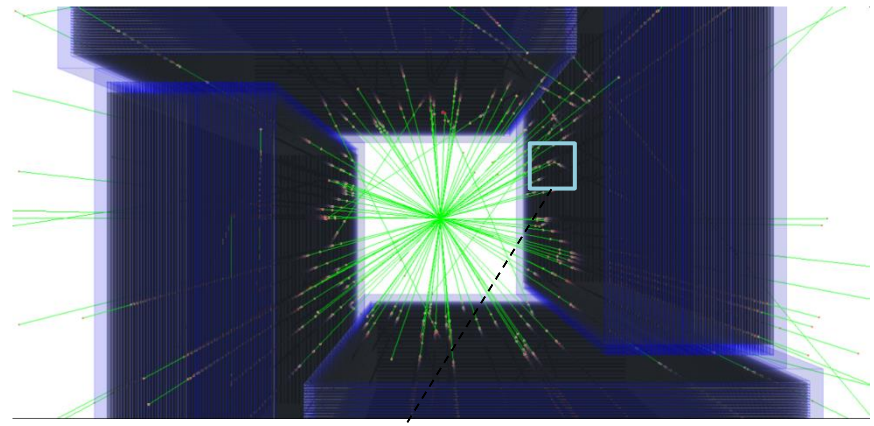


e⁺ MPF in water (1000 events, photons not shown)

100µPET – Performance Simulation (2/2)

Monte Carlo simulation with Geant4 and Allpix2 allows:

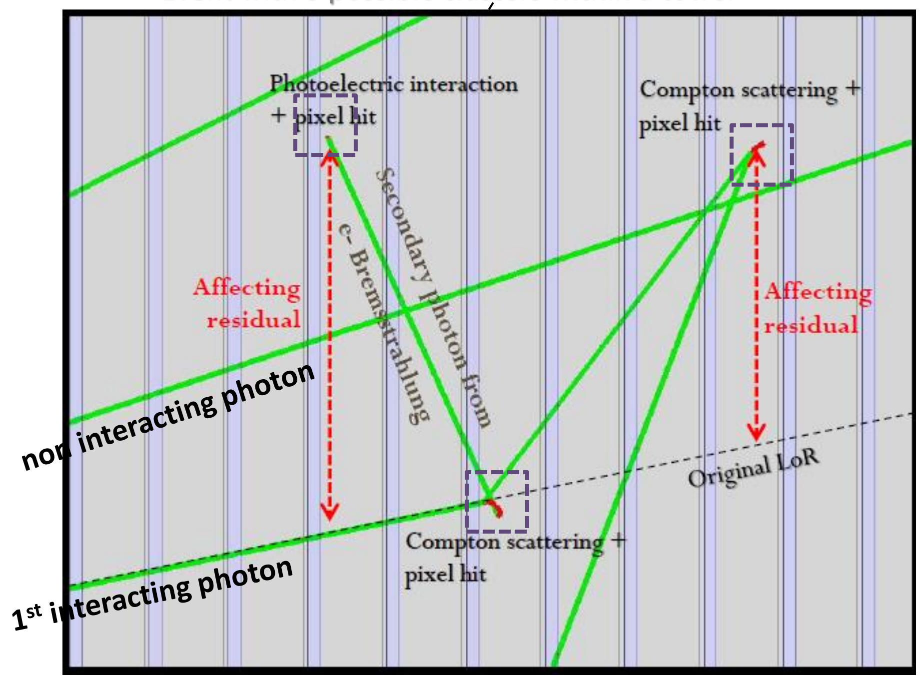
- Positron emission & photon conversion
- Detector performance with pixel asic
- Detector effects on sensitivity and resolution



Single positron annihilation per event:

- Event filtering for **unambiguous** line-of-response acceptance
- Only events with two scanner towers having each a single cluster charge
- No energy window for discriminating signals form Compton or Photoelectric interactions

Event with 3 possible clusters within a tower



Resolution of the positron source:

- Single point → Point Spread Function
- Derenzo phantom → assess image reconstruction

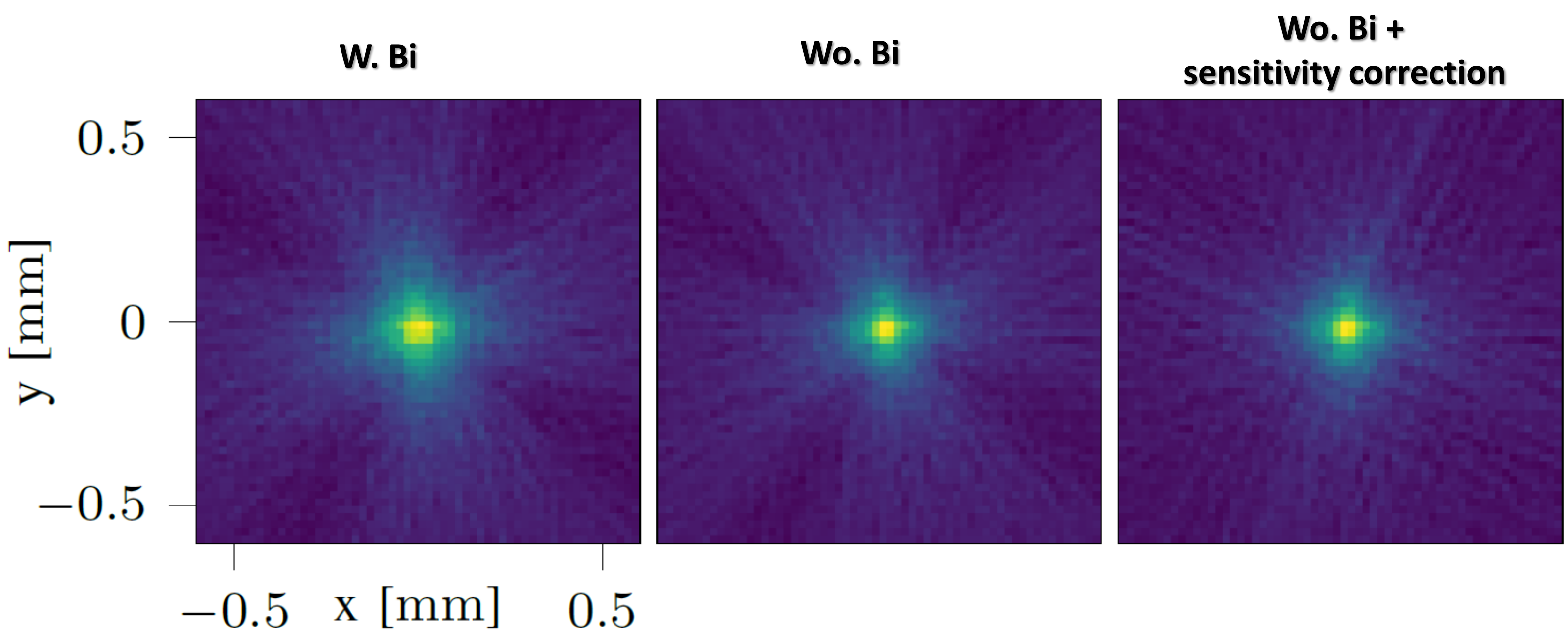
Performance with Single Point Source

- **Sensitivity:** amount of unambiguous LoR measured as a function of the total number of positrons
  - **3.3%** and **4.8%** detection efficiency, without and with Bi respectively
- **Spatial resolution:** Point Spread Function with FBP (Filtered Back Projection)
  - **0.22 mm** at minimum and **0.25 mm with Bi**
  - Due to acolinearity of the 2 photons → not a big change between 100 vs 150 µm pitch
  - **Negligible parallax distortion**

Point Spread Function from FBP
(values in mm)

off-axis (mm)		0	5	10	15
FWHM (100 µm)	No Bi	0.22	0.23	0.24	0.24
	Bi	0.25	0.26	0.27	0.28
FWHM (150 µm)	No Bi	0.24	0.25	0.26	0.25
	Bi	0.27	0.28	0.28	0.28

NB: *The mean-free path of the positron (100 µm FWHM and 1000 µm FWTM) is included in the simulation as well as the acolinerity*
→ Only unambiguous event were used



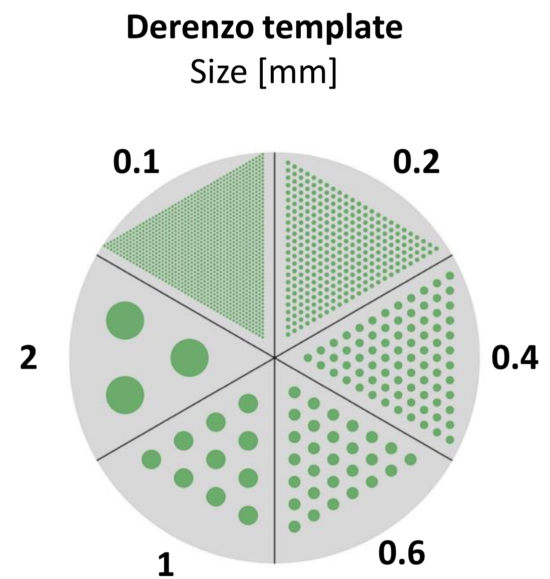
Derenzo Phantom for Imaging Reconstruction

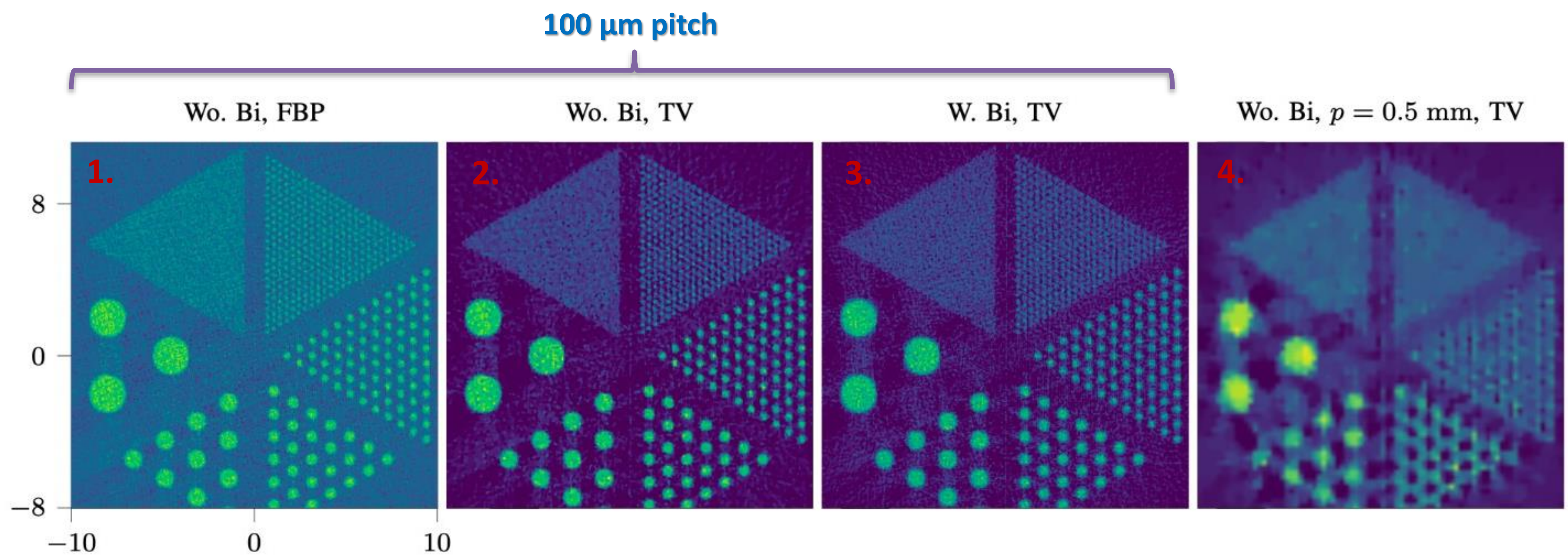
Derenzo phantom to test reconstruction to a given feature size:

- 2.0, 1.0, 0.6, 0.4, 0.2, 0.1 mm rods (no positron mean free path)

Reconstruction using the 100muPET scanner

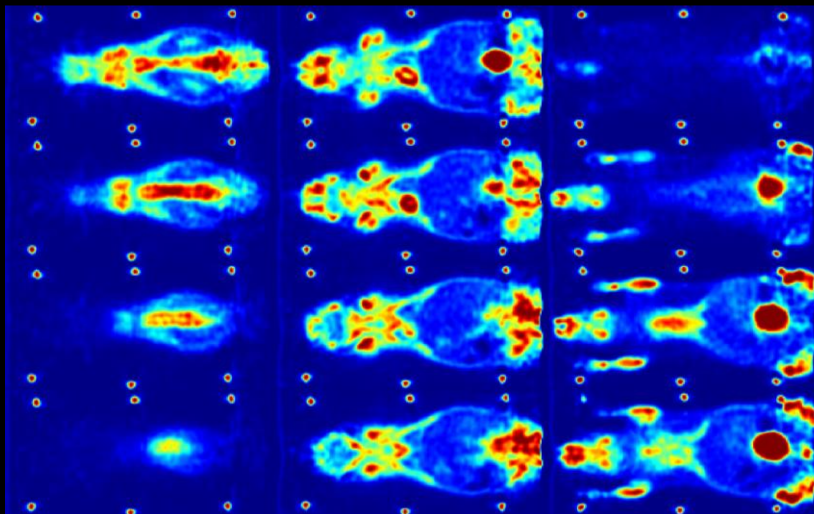
FBP: Filtered back projection
TV: Total Value



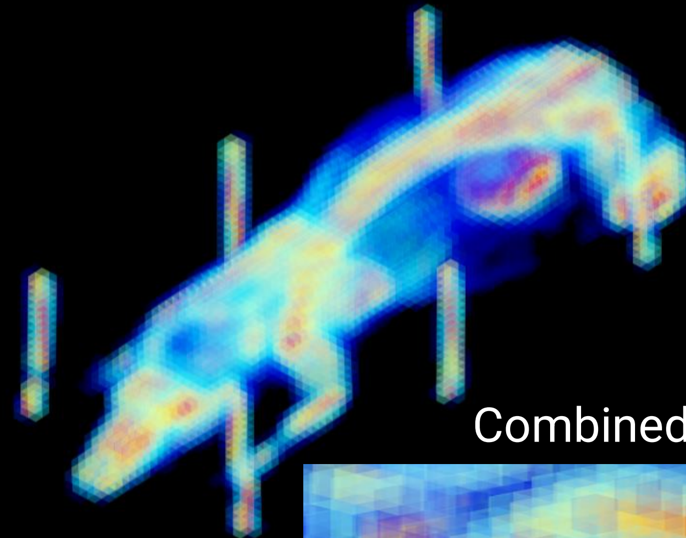


100μPET Artery Plaque

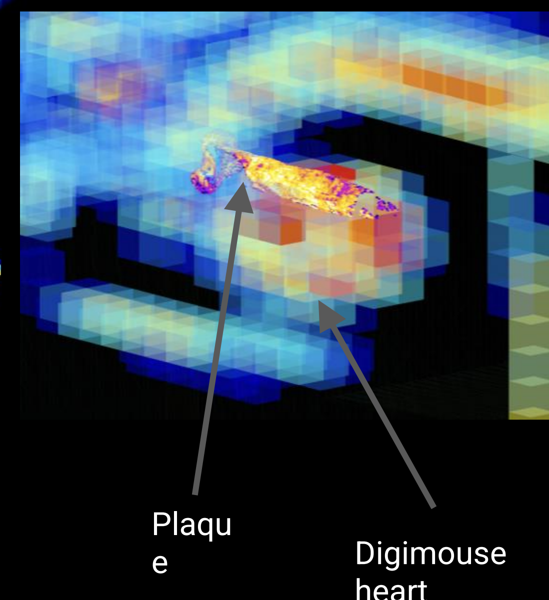
Digimouse: a 3D whole body mouse atlas from CT and cryosection data. doi: 10.1088/0031-9155/52/3/003



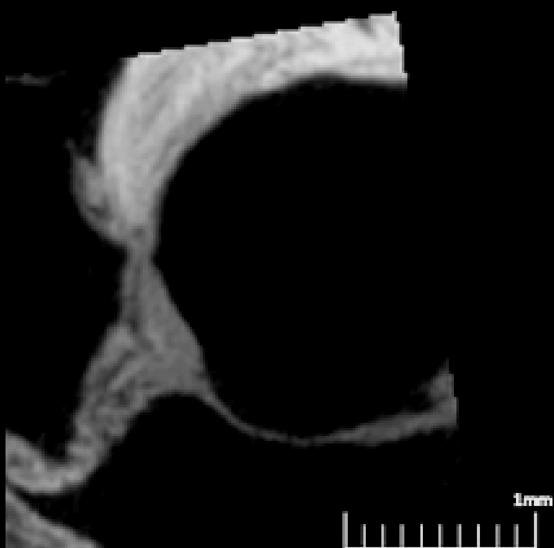
3D voxels from Digimouse PET scan (1 mm wide voxels)



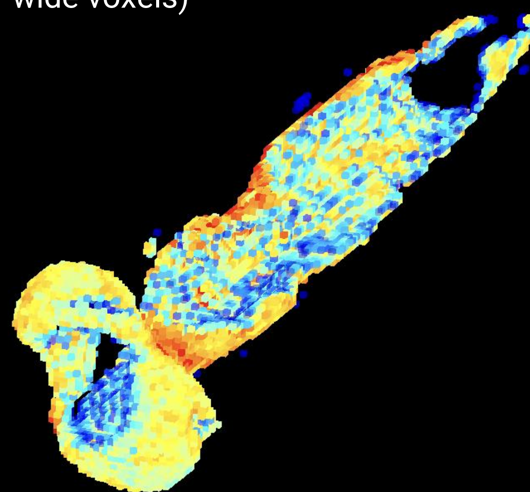
Combined parts



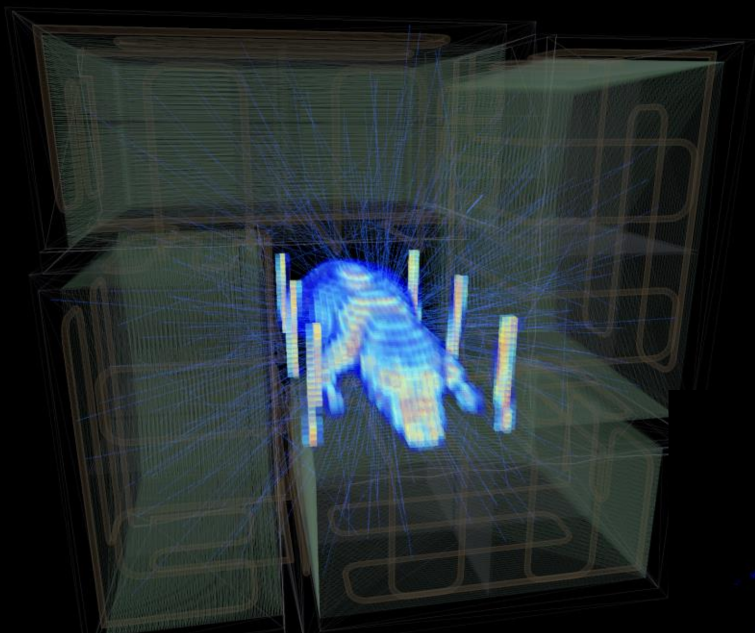
A volumetric method for quantifying atherosclerosis in mice by using microCT doi: 10.1371/journal.pone.0018800



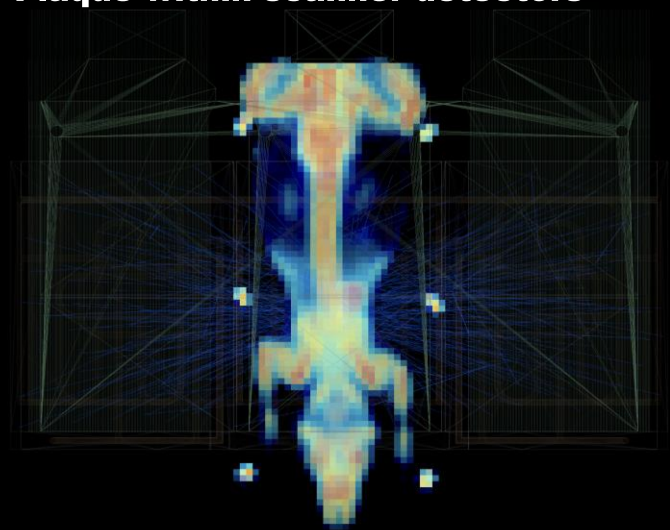
3D voxels from plaque (50 μm wide voxels)



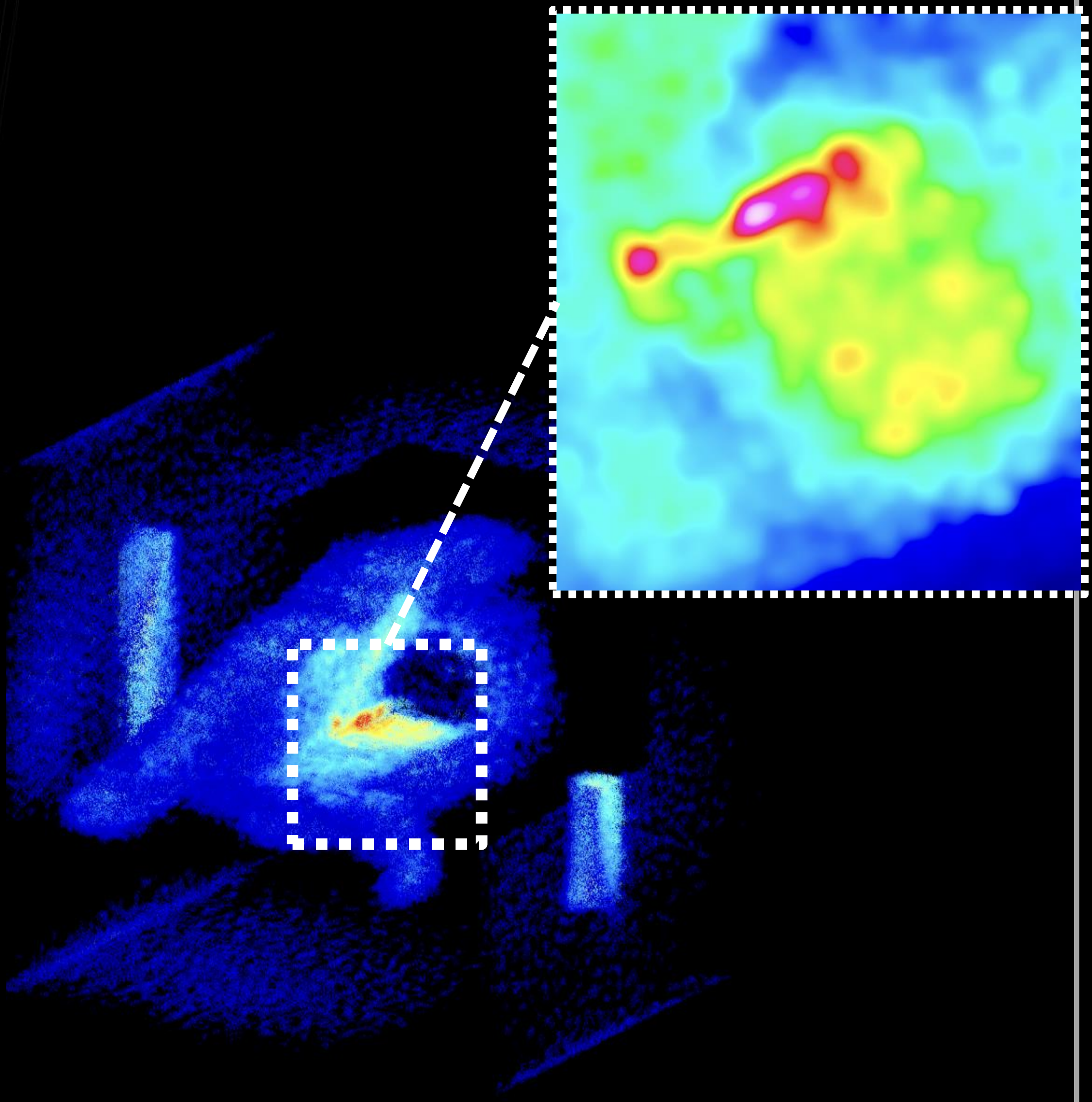
100μPET Artery Plaque



Monte Carlo simulation of Mouse + Plaque within scanner detectors

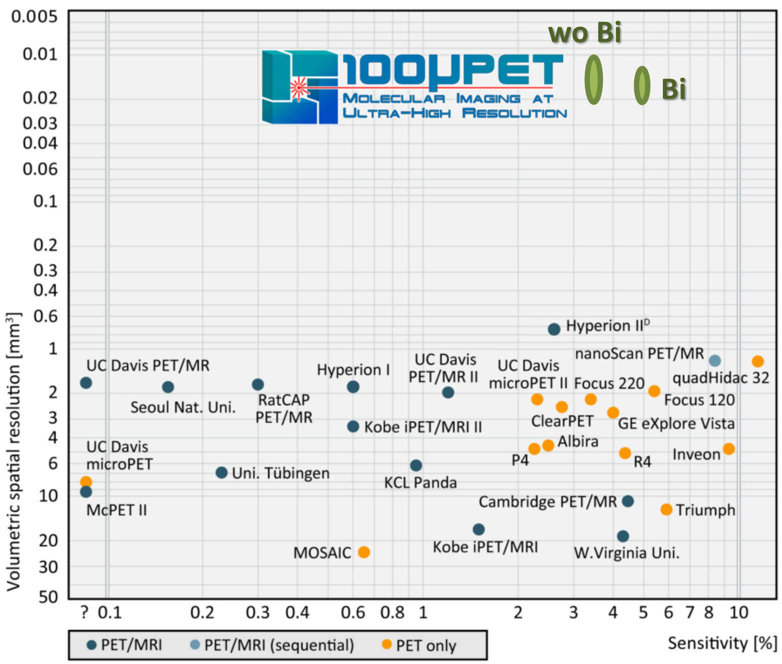


Reconstructed volume (110 μm voxels)



Summary & Conclusions

- **PET scanners** are important diagnostic tools for metabolic process imaging
- **Potential ultra-high-resolution** molecular imaging **using MAPS**
  - ASIC designed within the UniGE DPNC group (together with the FASER and MONOLITH projects)
  - Development of module construction technique based on flip-chip bonding for compactness
  - Monte Carlo simulation and imaging reconstruction are showing very promising performance
- **4.8%** and **3.3% scanner sensitivity** (w/ or w/o Bismuth layer)
  - ***0.22-0.28 mm PSF → 0.010 - 0.022 mm3* volumetric spatial resolution**
- **Delivery of a proof-of-concept** scanner for small animals **in 2025**
  - Silicon-sensor technology, specially with MAPS, advances and its cost will go down while larger scanners can be envisaged in the future
  - In the whish-list → additional feature: TOF ≲ 10ps, when delivered by the MONOLITH project

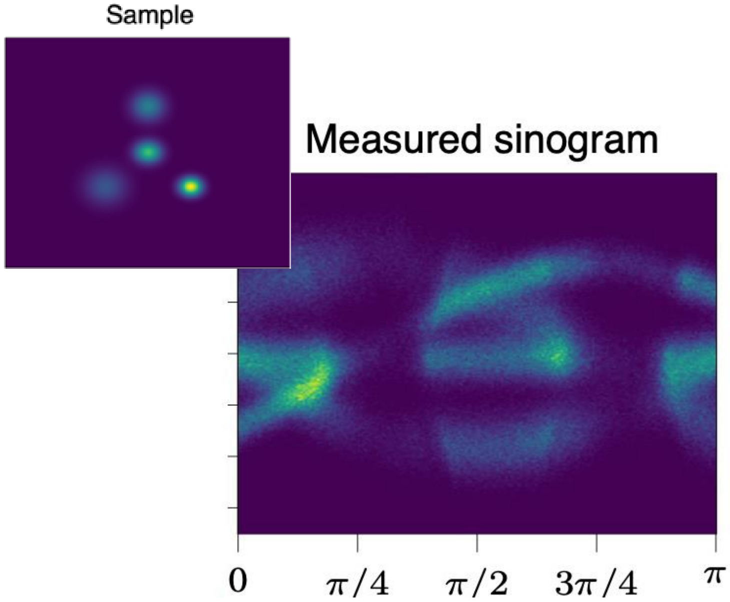


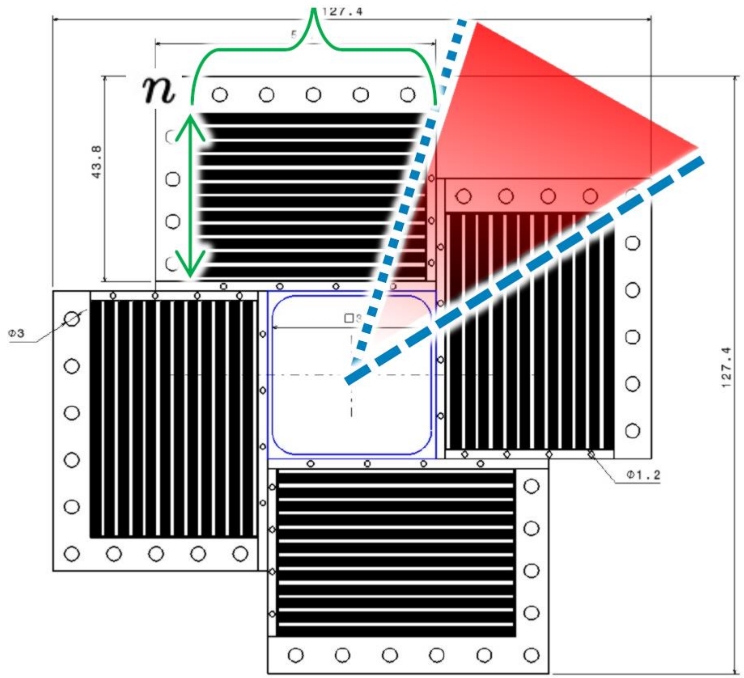
BACK-UP

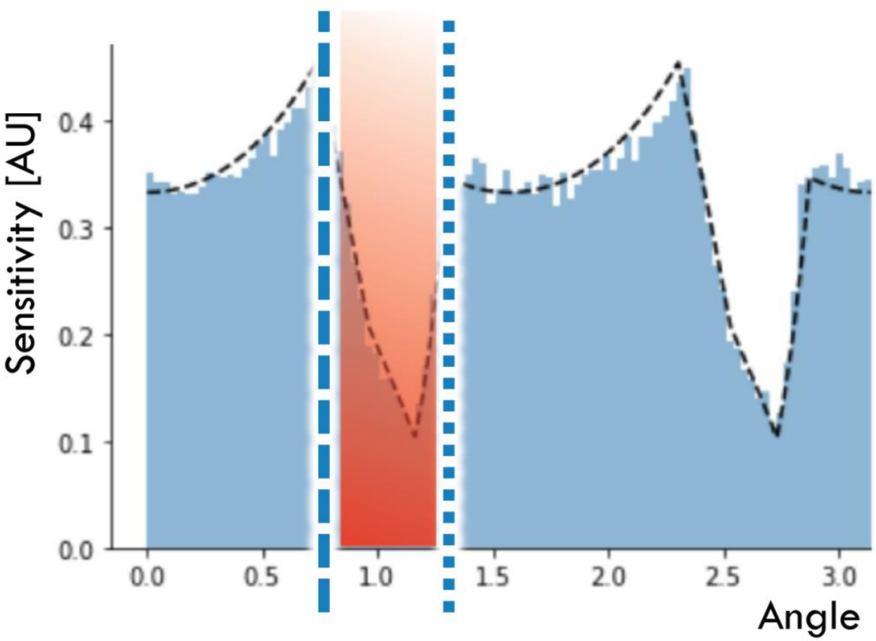
100µPET Detection Efficiency

The scanner sensitivity is driven by the photon stopping power of silicon detectors across all the stack

- Gain of efficiency is optimal at ~60 silicon layers, with 60 mm width
- Efficiency can be further increased if heavy materials (high atomic number, as bismuth) are inserted between the silicon detection layers
- Holes in the scanner's acceptance have large impact in the sensitivity and Sinograms



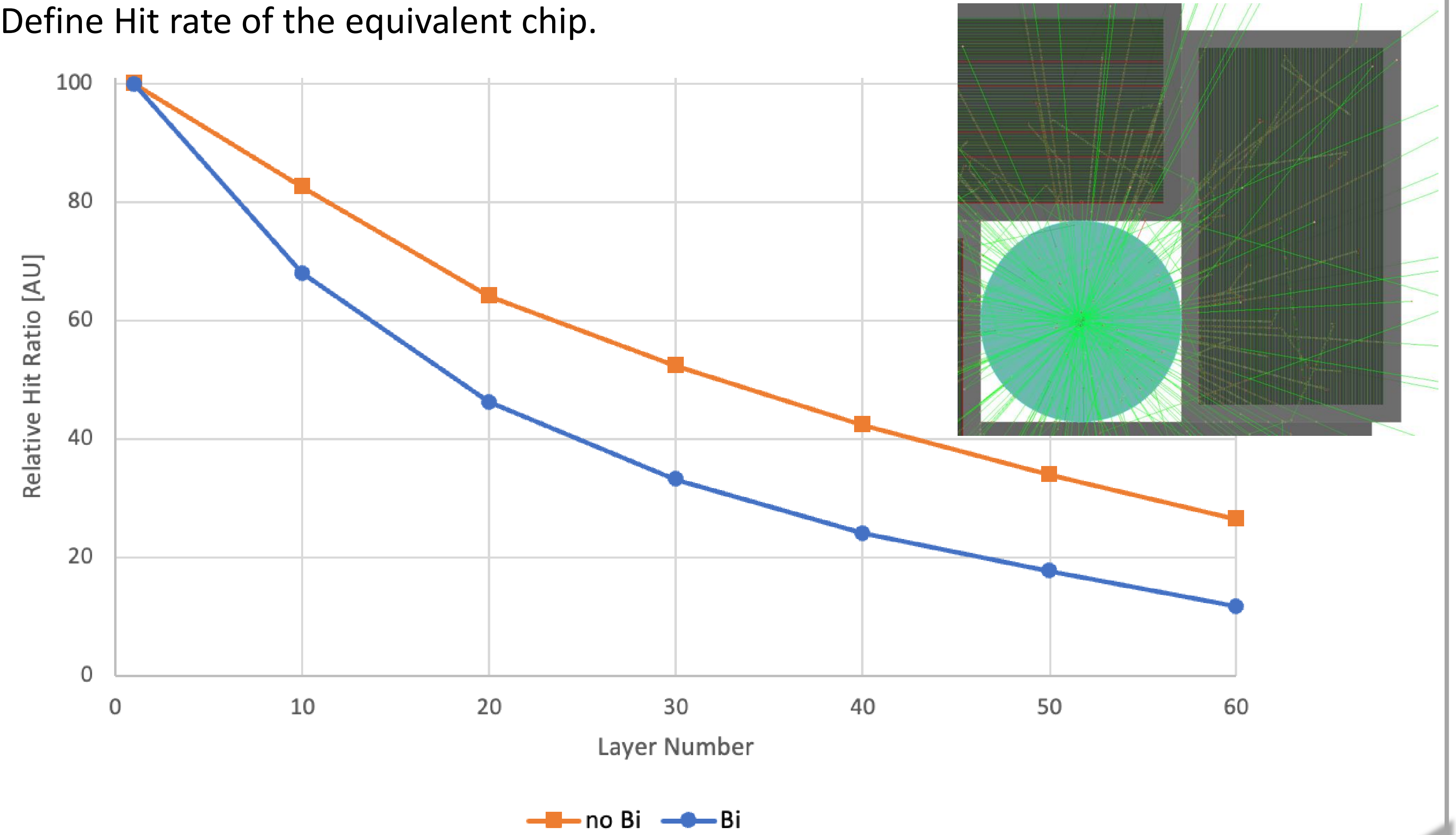




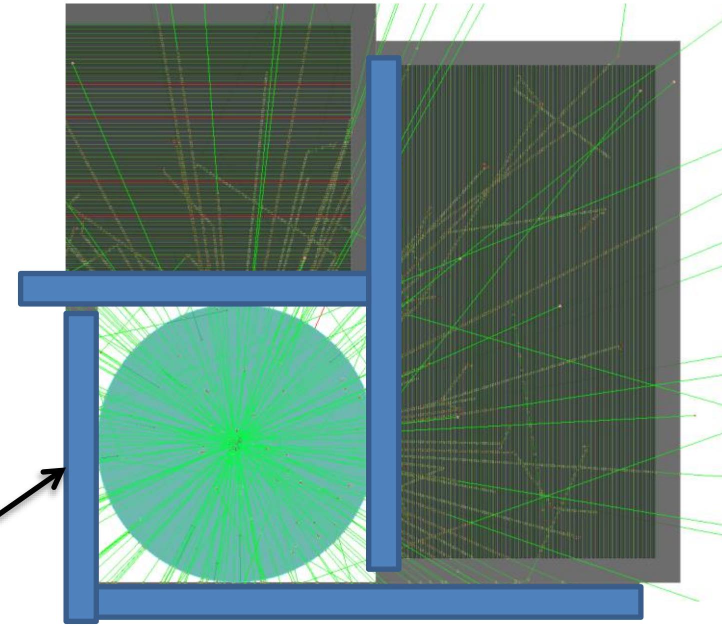
Hit Rate with Layer Number

Empirical strategy to estimate the maximum Hit Rate that a chip will reach during operation.

1. Simulate Some Events
2. Check Layer with highest number of Clusters.
3. Obtain the map of the position of each cluster on that plane
4. Define Hit rate of the equivalent chip.



Cooling Wall Thickness

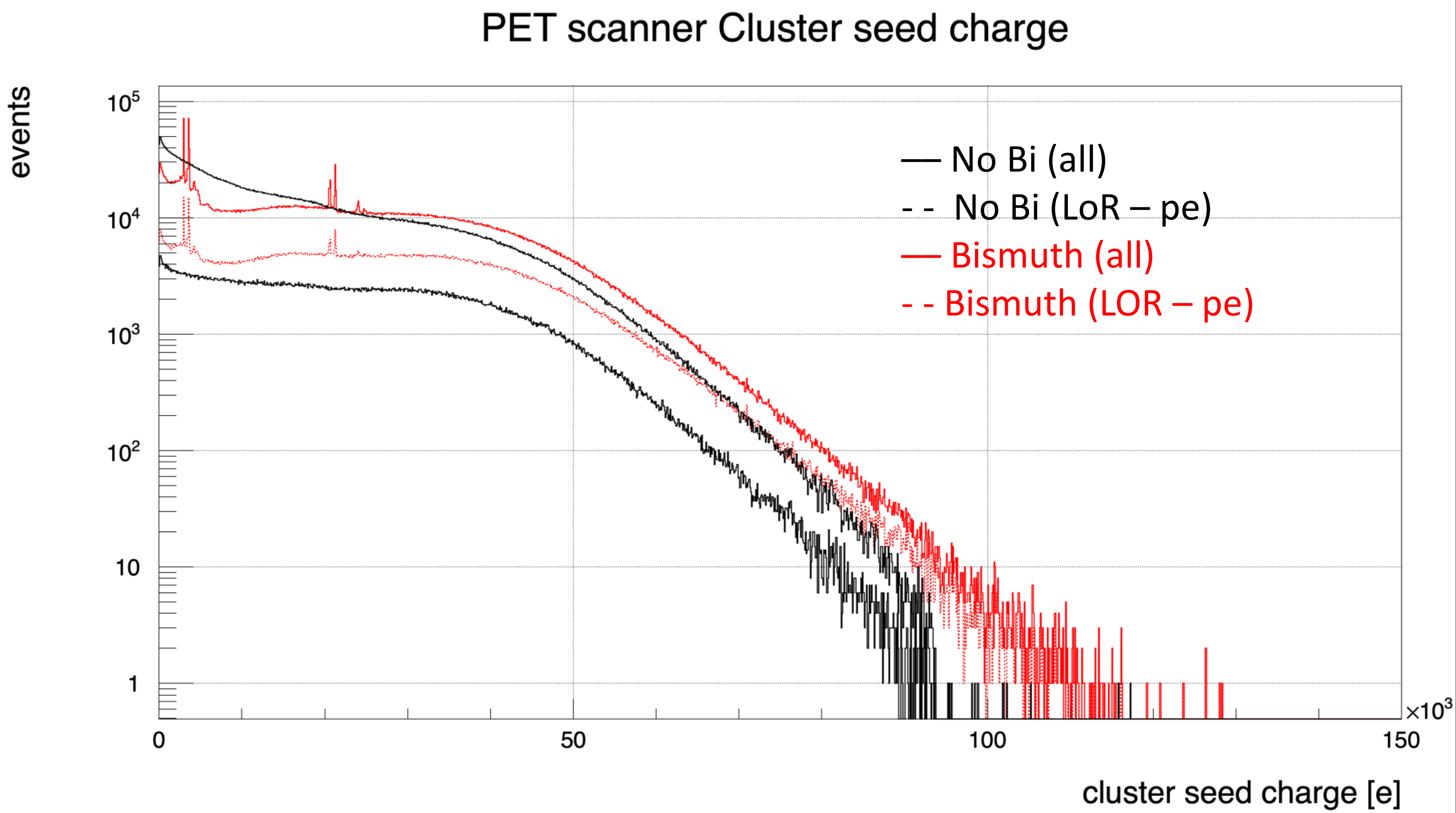


Kapton	50 µm	LOR EFFICIENCY		
Cooling wall thickness		1 mm	2 mm	3 mm
Different	10 keV	7.11%	6.51%	5.97%
	0 keV	7.19%	6.61%	6.08%
Opposite	10 keV	5.55%	5.21%	4.85%
	0 keV	5.53%	5.20%	4.86%

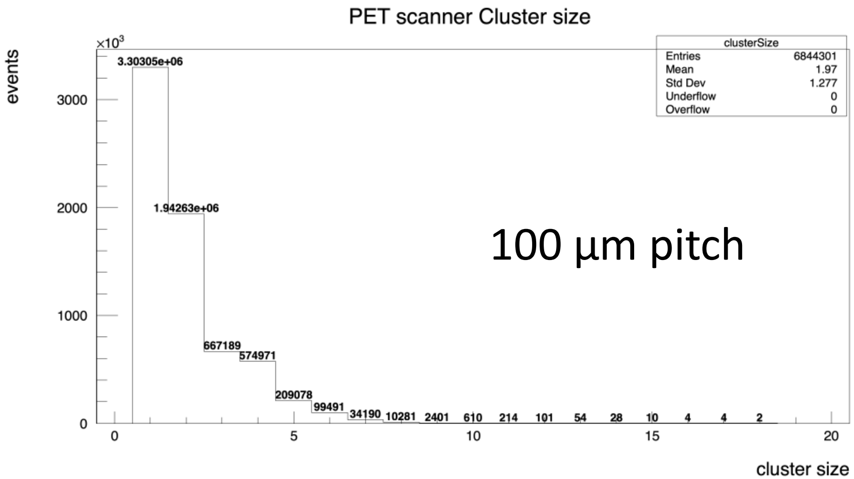
LOR Efficiency along the Scanner

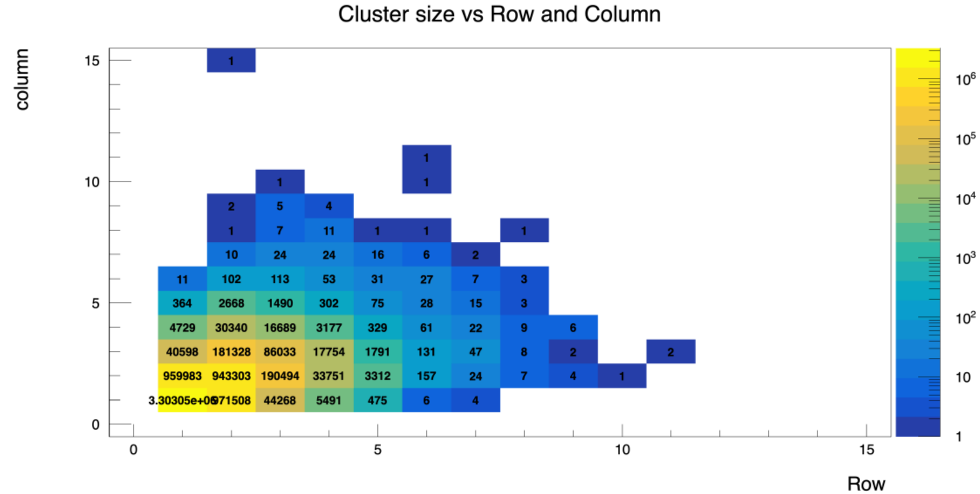
Distance from center [mm]	0	5	10	15
Bismuth	4.81%	4.77%	4.81%	5.08%
No Bismuth	3.29%	3.29%	3.38%	3.65%

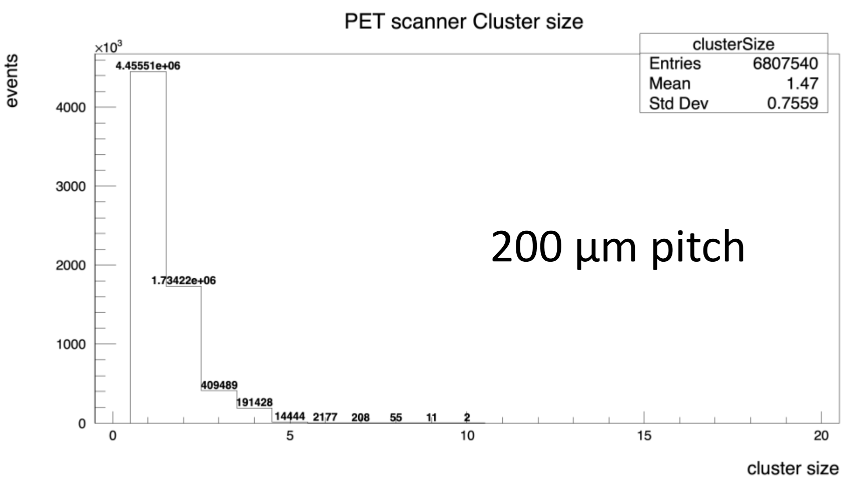
Cluster Seed Charge

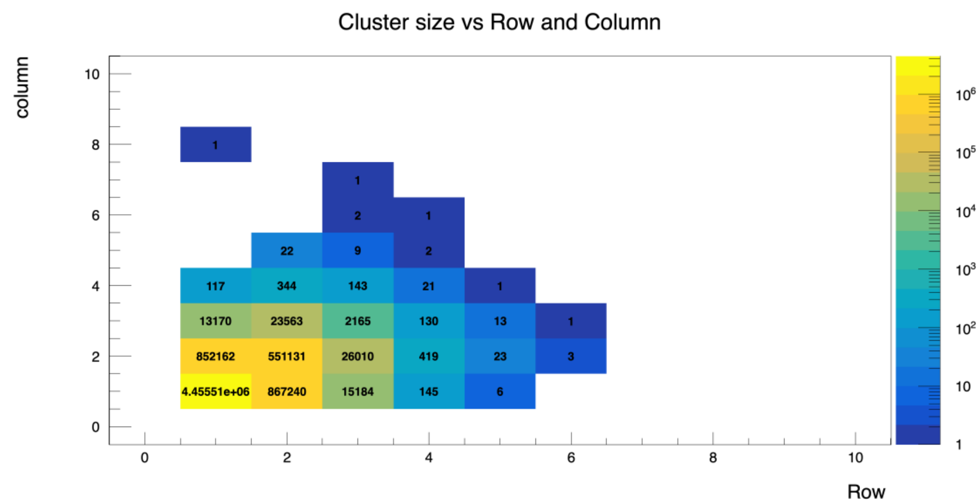


Cluster Size



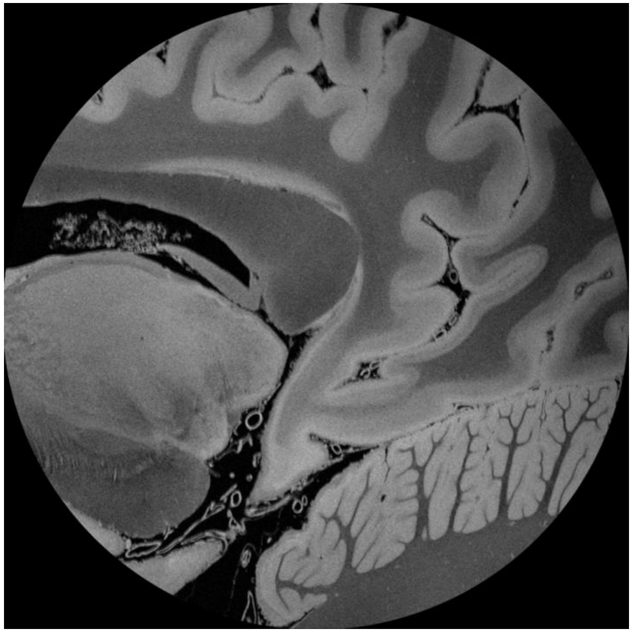






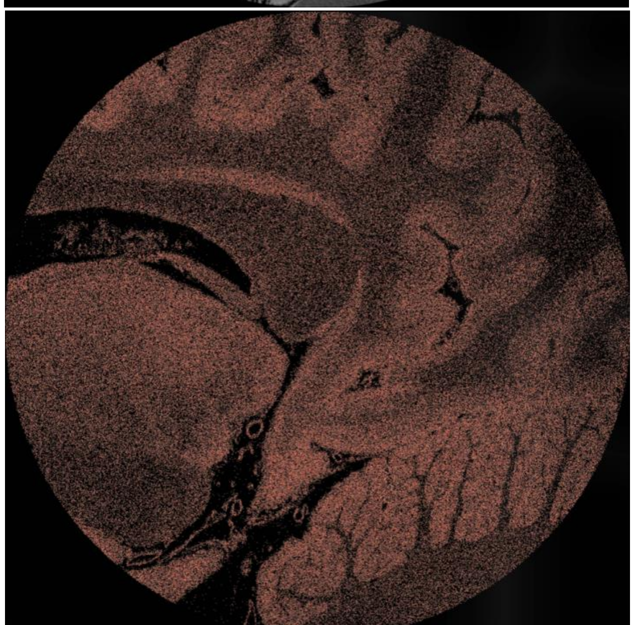
100µPET Human Brain Reconstruction

MRI image of a human brain



1. Original brain MRI image *Source: Openneuro dataset*
2. Random brain slide with 68 mm disk diameter was selected
3. Image reduced to 34 mm with artificial 50 µm resolution
4. Conversion of the MRI grey scale to annihilation events
5. Each pair and reconstructed within the 100µPET MC simulation reconstruction
6. Image reconstruction algorithm used finally

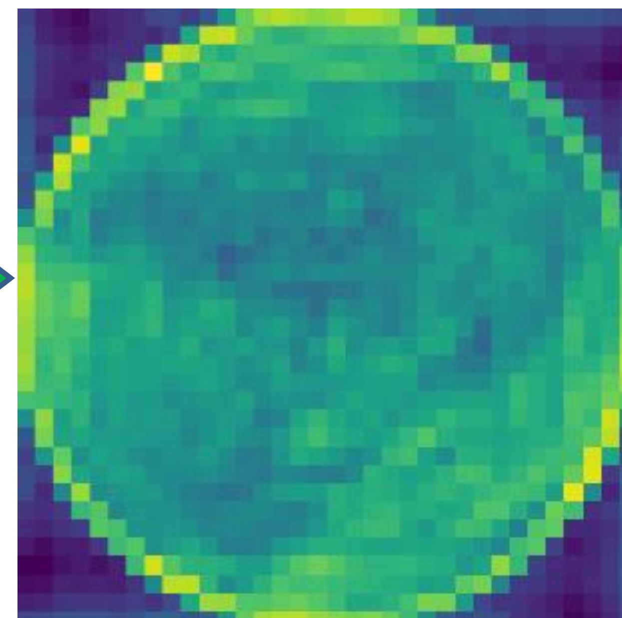
2 billion annihilation events generated



MC simulation with the

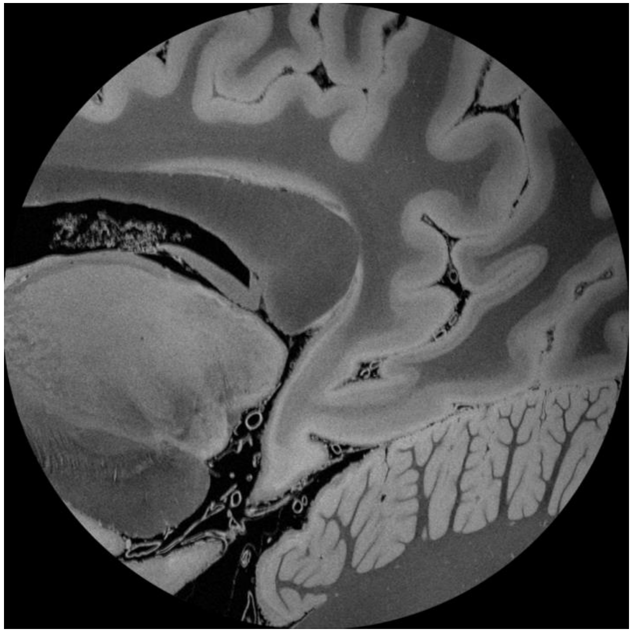
geometry of 100µPET

Reconstruction if 1 mm resolution



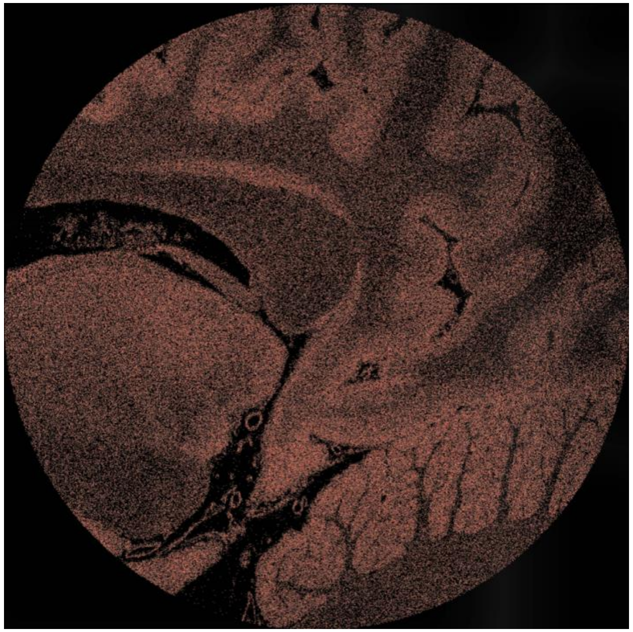
100μPET Human Brain Reconstruction

MRI image of a human brain



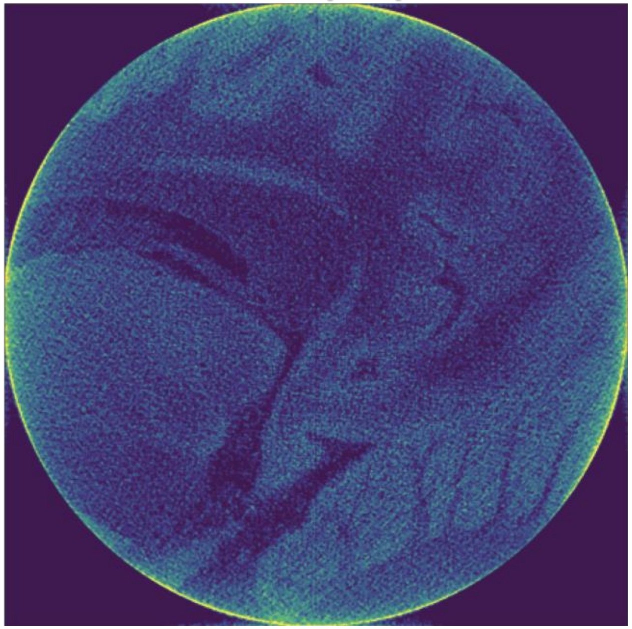
1. Original brain MRI image *Source: Openneuro dataset*
2. Random brain slide with 68 mm disk diameter was selected
3. Image reduced to 34 mm with artificial 50 μm resolution
4. Conversion of the MRI grey scale to annihilation events
5. Each pair and reconstructed within the 100μPET MC simulation reconstruction
6. Image reconstruction algorithm used finally

2 billion annihilation events generated



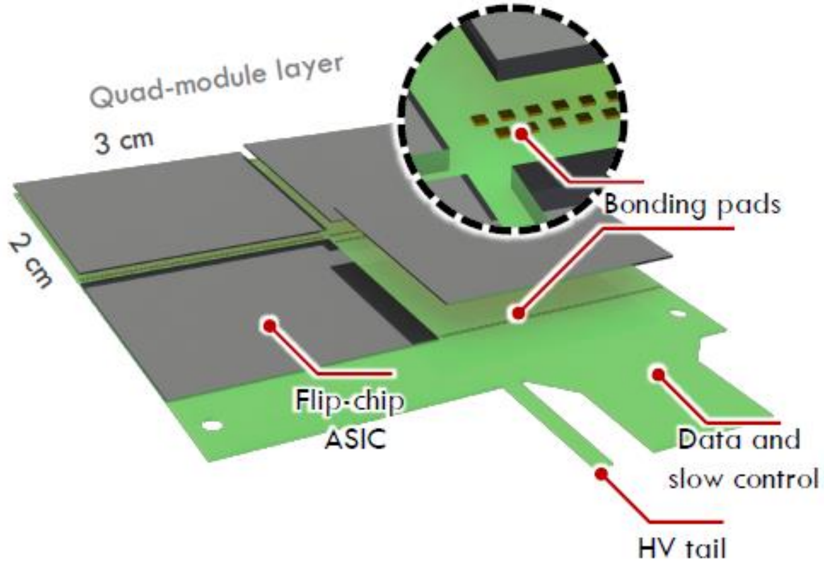
MC simulation with the geometry of 100μPET

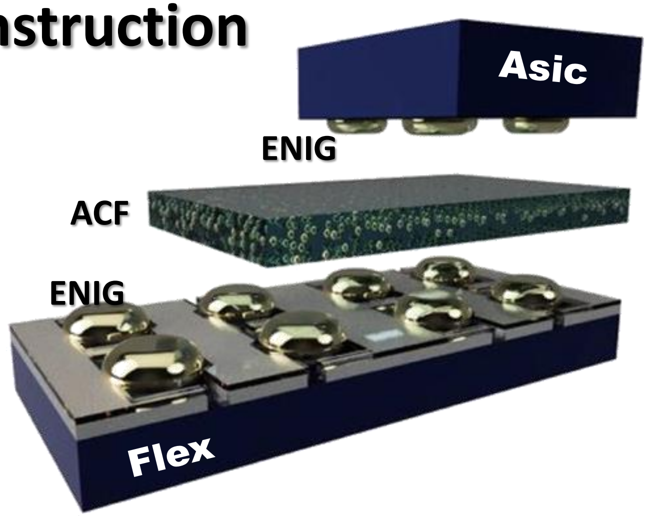
Image reconstruction algorithm with 100 μm pitch

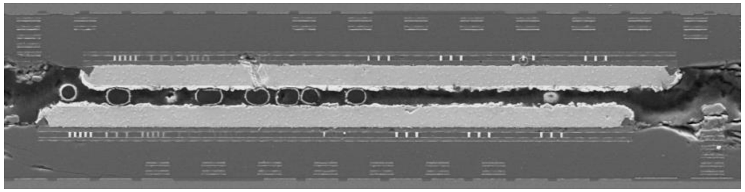


100µPET Module Construction

Baseline concept: Single module layer → Si to FCP interconnection

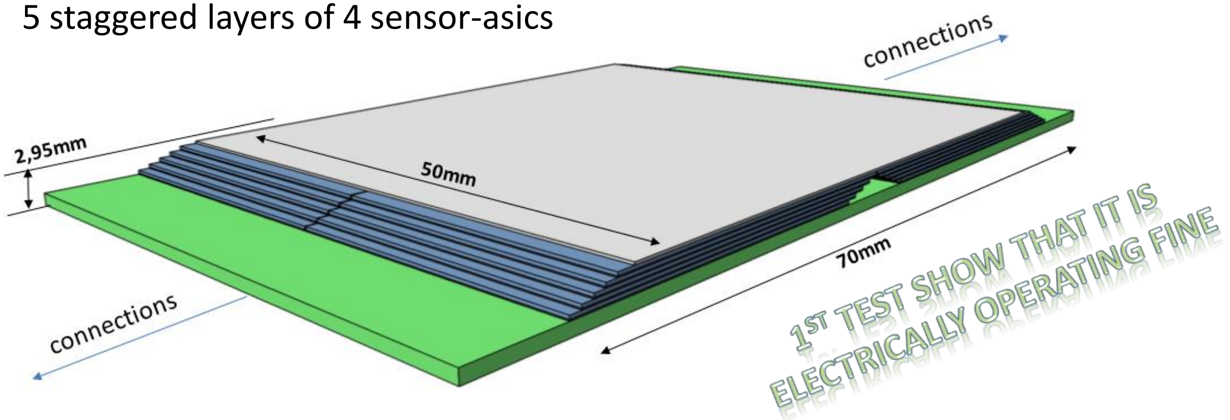


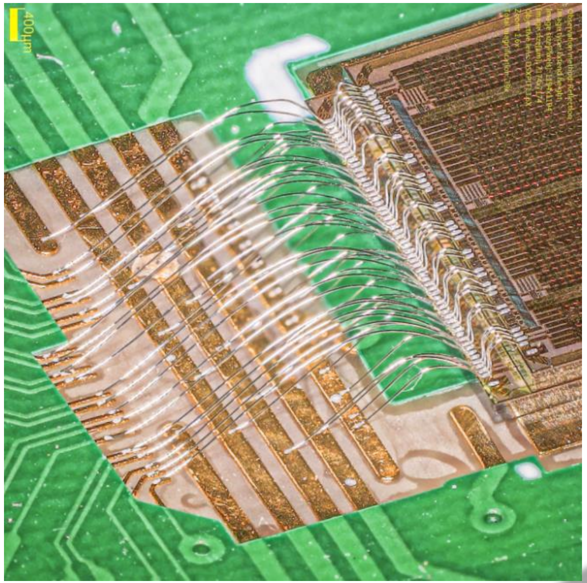




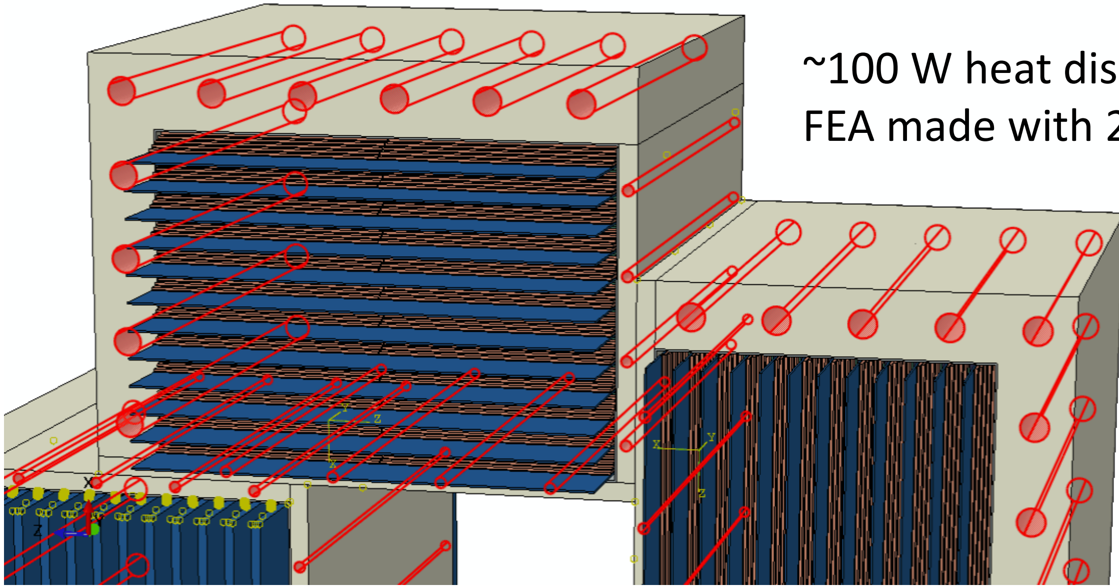
Alternative concept: Super-module with 5 layers of 2x2 sensor asics
→ wire bonding interconnection

5 staggered layers of 4 sensor-asics





Thermal Management



~100 W heat dissipation expected in a tower
FEA made with 250 W (below)

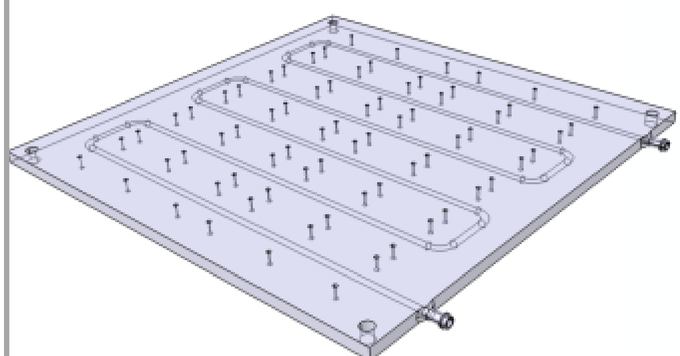
Assuming using water:

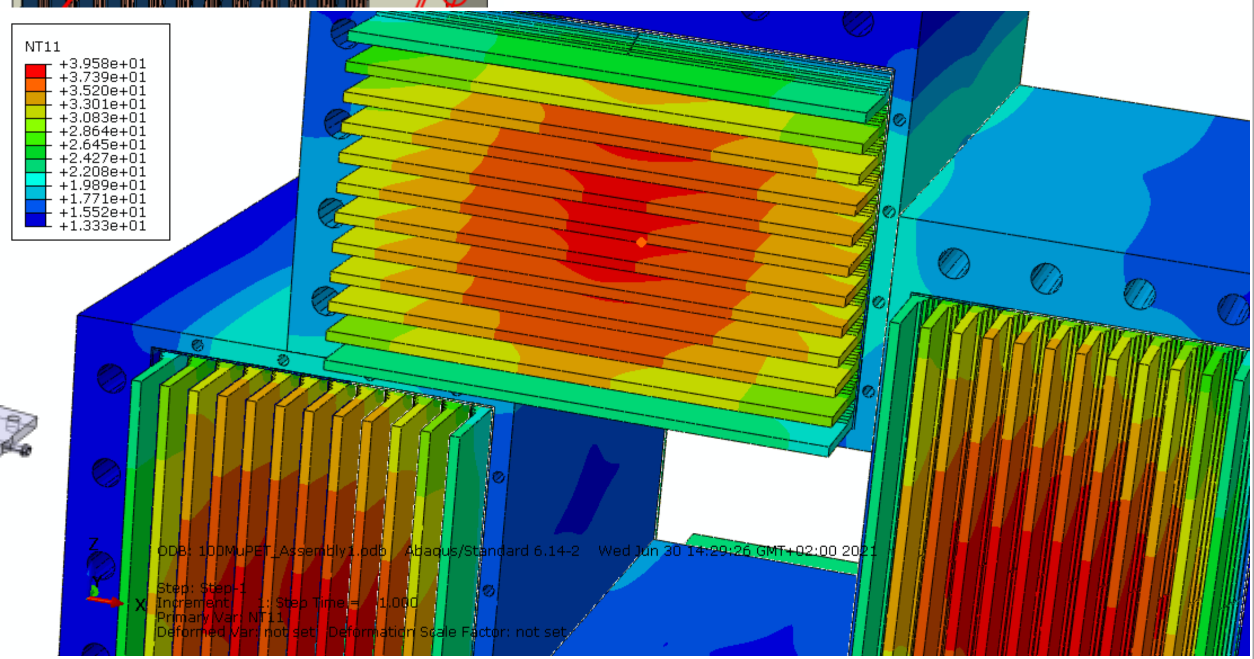
- Tcool: 12°C
- HTC: 8000 W/mK

→ A max temperature of ~39°C with 250 W/ tower

→ **Extrapolating max temp of ~ 25°C for 100 W**

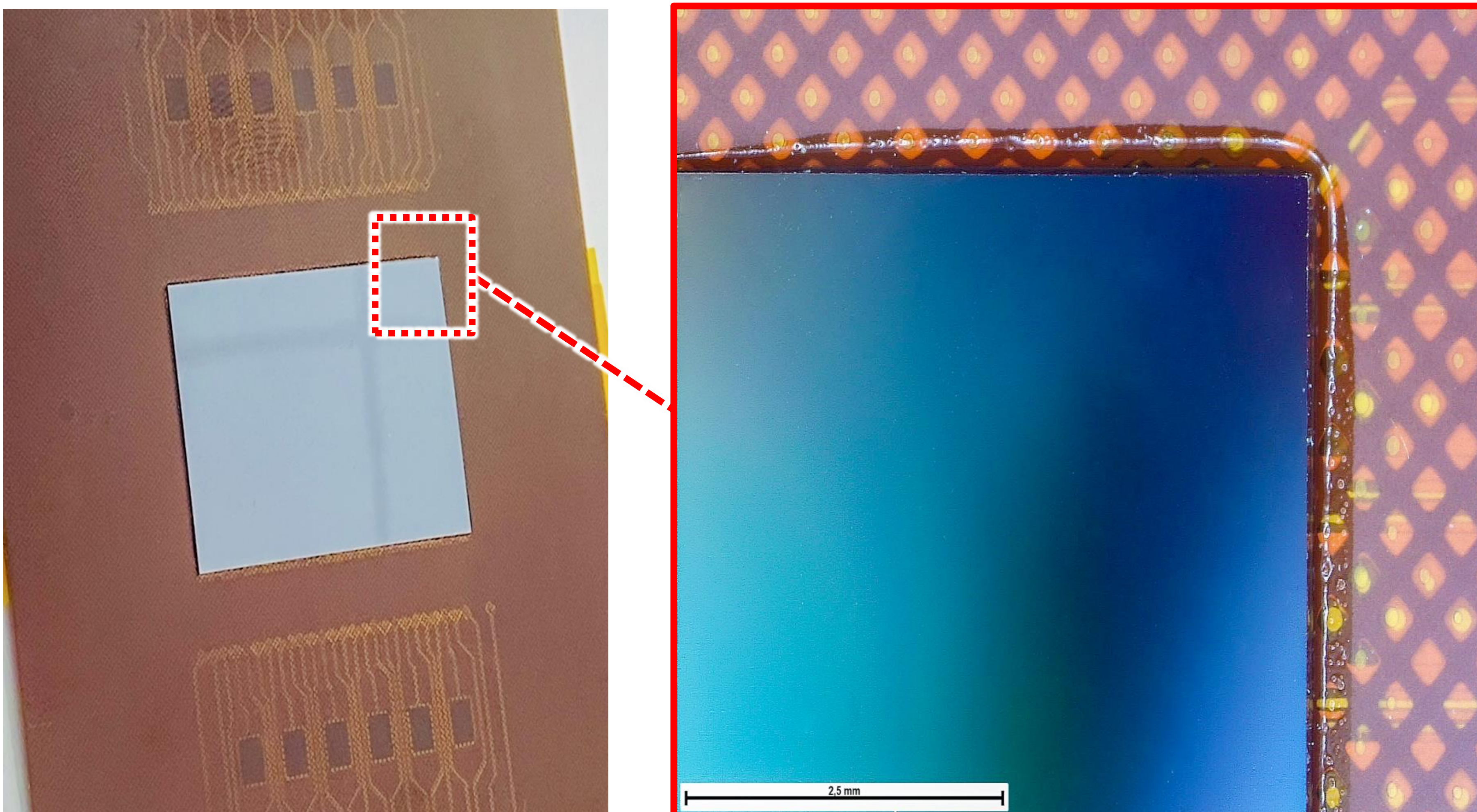
Like for FASER project the blocks can be manufactures **in 3D metal printing** in order to have an optimal heat exchange.





Abaqus Unified FEA

Silicon to Flex PCB Interconnection



Silicon to Flex PCB Interconnection – Cross Section