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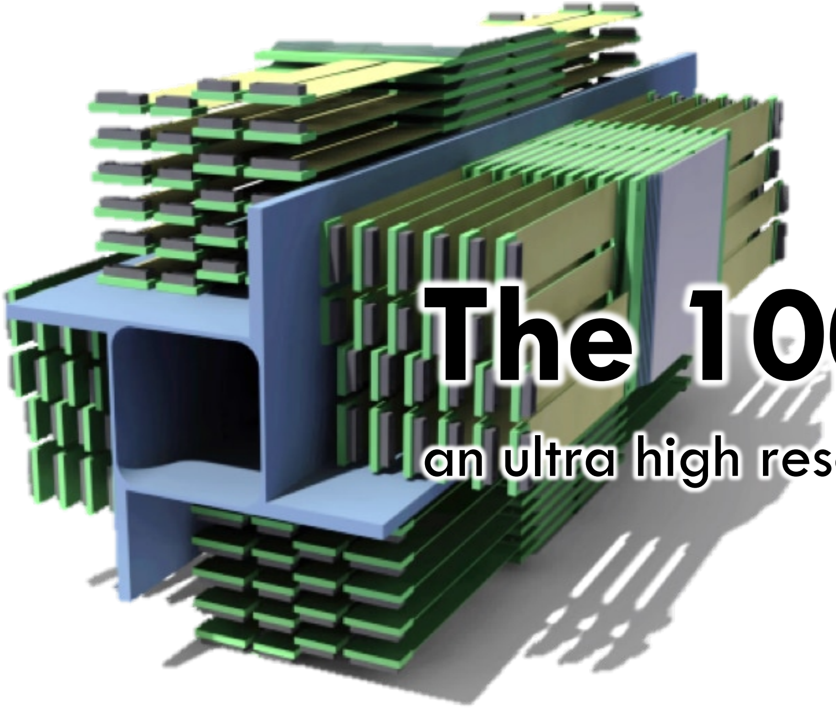

The 100µPET project:

an ultra high resolution small-animal PET scanner

17th "Trento" workshop 2–4 Mar 2022

Mateus Vicente
on behalf of the 100µPET collaborators

Introduction

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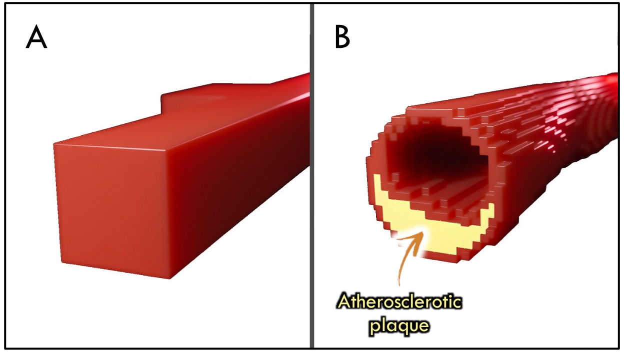
- The **100µmPET** project: molecular imaging with ultra-high resolution
  - First silicon small-animal scanner prototype
    - **SNSF SINERGIA** four years project (from 2021 Q2)
    - Three partners:
      - **UNIGE**: Construction of the 100µPET small-animal scanner
      - **EPFL**: Sophisticated imaging reconstruction with ML and NN to cope with the 10^{15} possible line-of-repsonse
      - **HUG**: Study the onset and progression of atherosclerotic plaques in arteries to better understand, monitor and treat atherosclerosis in ApoE$^{+/-}$ mice



With today's PET technology, small blood vessels can only be visualized in their entirety (A). The proposed new PET technology will allow the study of changes in the lining of small blood vessels, such as atherosclerotic plaques (B).
Images: © Xavier Ravinet - UNIGE

Positron Emission Tomography (PET) imaging

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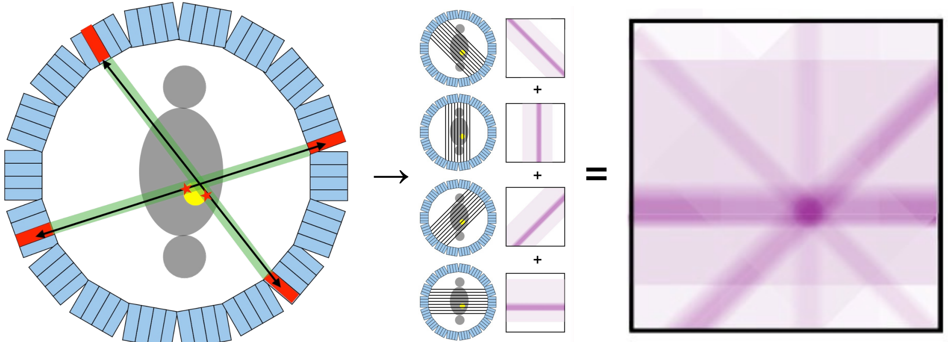
- PET is a nuclear medicine method to study <u>metabolic processes</u> in the body
  - Radiotracer is injected in a body; Positrons from the radionuclide annihilates with electrons of the nearby tissue
    ←→ <u>Two **back-to-back** 511 KeV photons are emitted and detected in **coincidence**</u> ⏱

    <u>**lines-of-response (LoR)**</u> are defined by the volume between the **sensitive elements** detecting the two photons (also called volume-of-response)

    - PET images are reconstructed from the **projections of the LoRs**

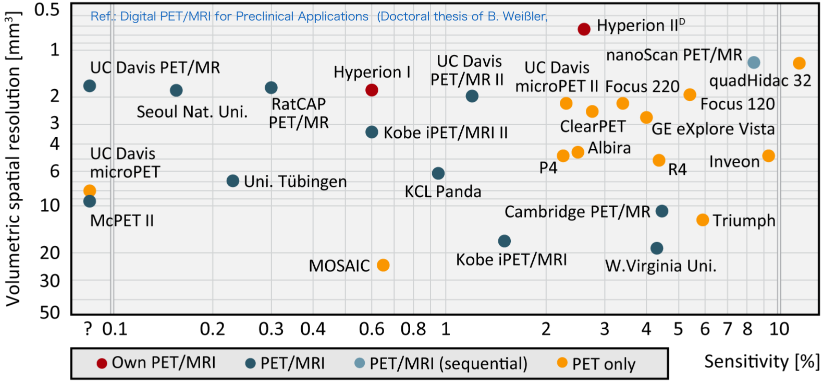


2D position histogram with source position reconstructed

★ Positron annihilation
⟷ Photons trajectory
Radiotracer
Line-of-response
Human body
Detection's sensor volume

(Above) PET example with 2 positron annihilations

Overview of current small-animal PET scanners



Positron Emission Tomography (PET) imaging

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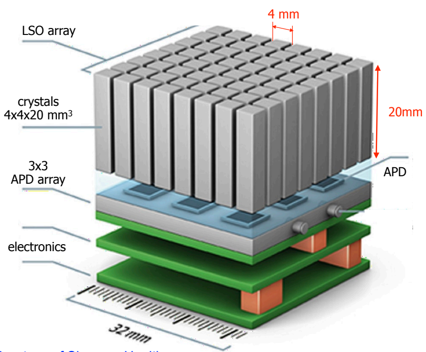
- To access ultra-high resolution molecular imaging ➔ **Reduce the LoR volumes** by exploiting:
  - Better timing resolution for coincidence measurement; Improved depth-of-interaction measurement;
  - Improved spatial resolution with higher detection volume granularity ➔ **HEP based silicon pixel detectors**
    - The higher 100μPET granularity will reduce the noise-like combinatorics artifacts during projection of LoRs

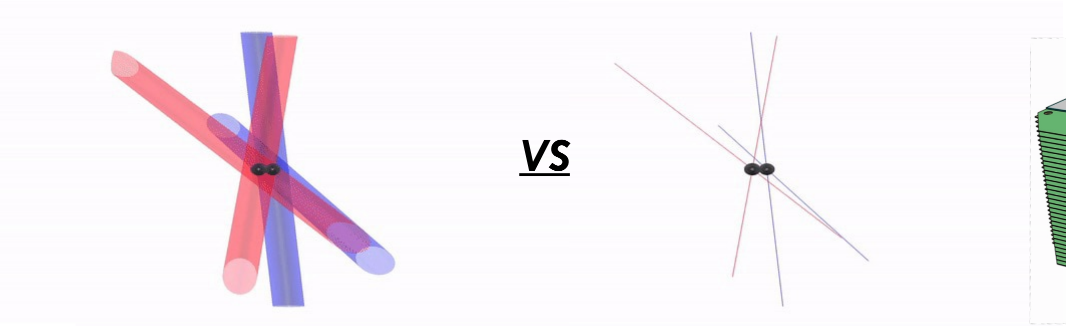


Courtesy of Siemens Healthcare

DOI: 20 mm
Pixel pitch: 4 mm
LOR volume: 20x4x4 = **320 mm³**

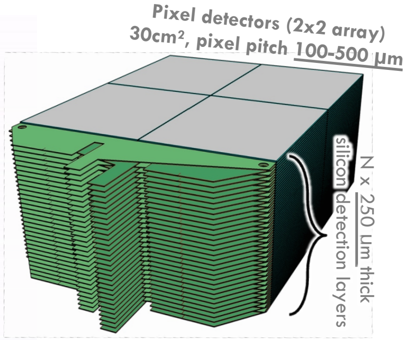
Two spherical sources
Two annihilations from each

Same two sources
Same four annihilations



Large LoR volumes produce "ghost" crossings of the LoR's

Higher spatial resolution (thinner LoR) avoids ghost crossings of LoR's



DOI: 0.2 mm
Pixel pitch: 0.1 mm
LOR volume: 0.2x0.5x0.5 = **0.05 mm³**

LoR volume 160'000 times smaller!

Silicon pixel detectors at UNIGE

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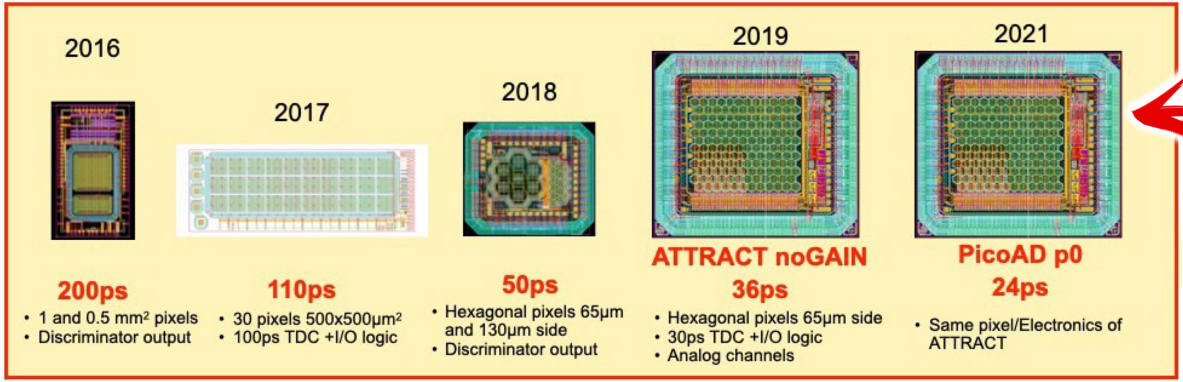
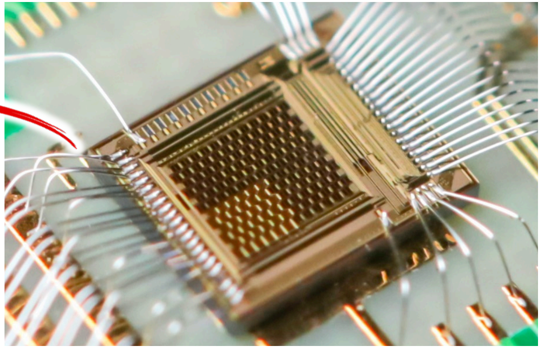
- Long tradition at UNIGE with hybrid silicon detectors:
  - pixel detectors for **ATLAS IBL** and **ITk** upgrade; strips (ATLAS **SCT, AMS, DAMPE**)
- In 2015: kick-off R&D on monolithic pixel sensors in **SiGe BiCMOS** technology
  - Aiming MAPS with timing resolution below 100ps
    - **MONOLITH** project, see talk by Magdalena Munker
    - **FASER pre-shower** detector, see talk by Lorenzo Paolozzi

innovations for high performance microelectronics
Leibniz-Institut für innovative Mikroelektronik

Monolithic prototype ASICs for timing purposes





The Thin Time-of-Flight (TT-PET) project

The 100µPET predecessor

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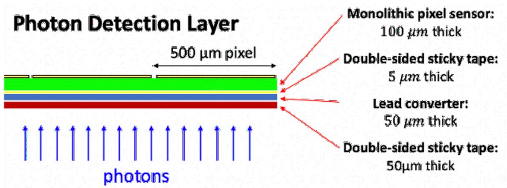
- A **SNSF SINERGIA** project from 2016 to 2019

(1)



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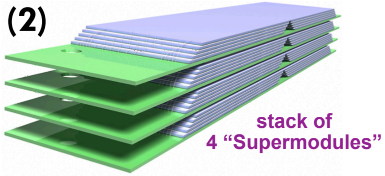

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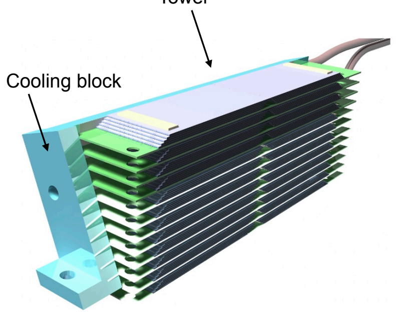
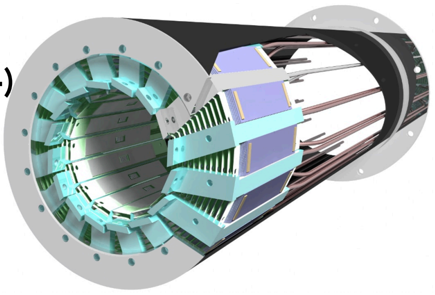
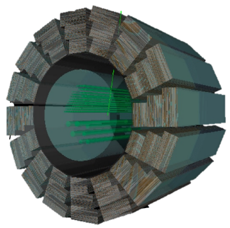


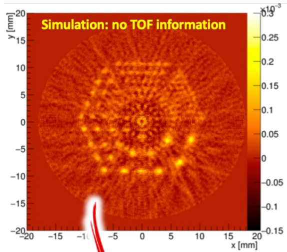
"Tower" of 12x5 = 60 detection layers
+ cooling block

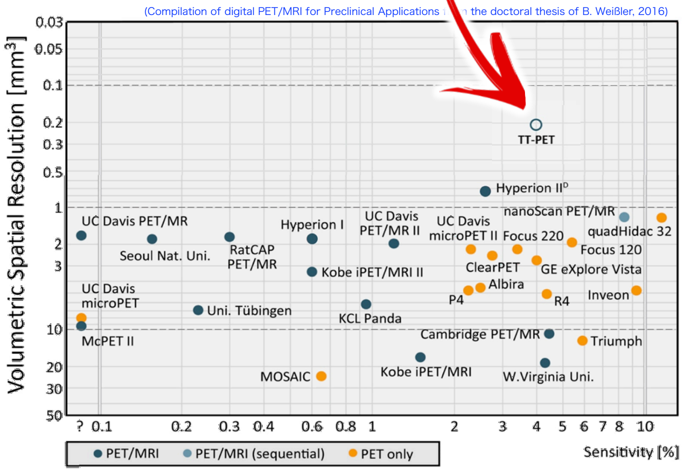
(4)



16 Towers all around to form the scanner



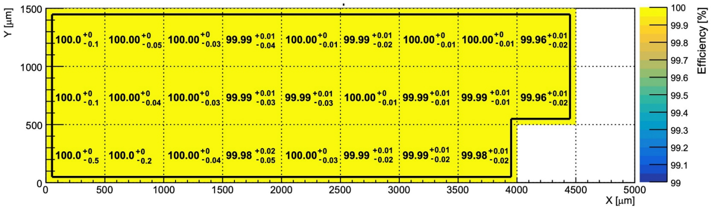


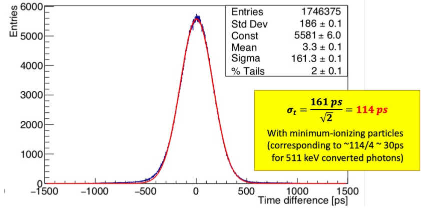


The Thin Time-of-Flight (TT-PET) project

- TT-PET project: from 2016 to 2019
  - Demostrator chip achieved target **performance,**

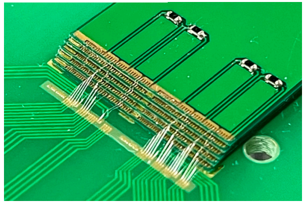
P. Valerio et al., JINST 14 (P07013) (2018),
L. Paolozzi et al., JINST 13 (P04015) (2018),
L. Paolozzi et al., JINST 14 (P02009) (2018)

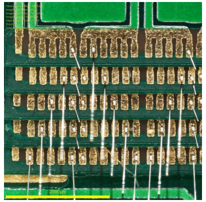




  - Scanner completely **engineered,**

D. Ferrere et al., arXiv:1812.00788



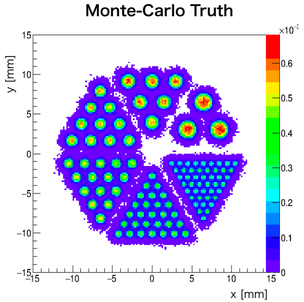


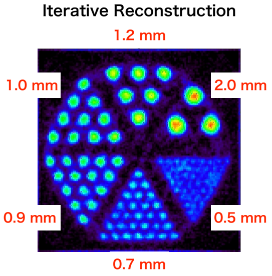
  - Performance **simulated**

E. Ripiccini et al., arXiv:1811.12381

  - Iterative imaging reconstruction **produced**

D. Hayakawa PhD thesis, http://dpnc.unige.ch/THESES/THESE_HAYAKAWA.pdf





Change of paradigm in PET imaging is possible with monolithic pixel detectors

- Can we do even better? Must reduce even further the “LoR volume”
  - by having better **spatial resolution,** pushing the position measurement down to the **intrinsic limits** given by the **positron mean free path** in body

The 100μPET scanner

New SINERGIA project evolving from the TT-PET

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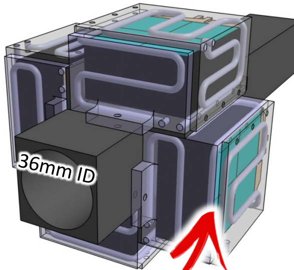
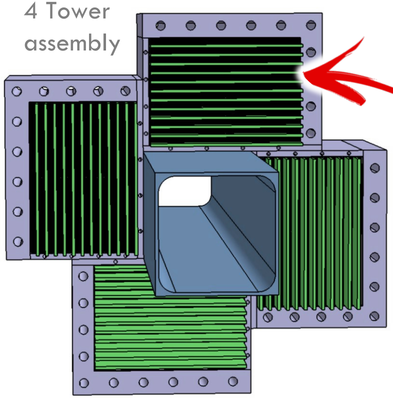
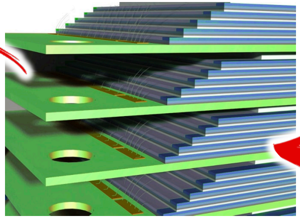
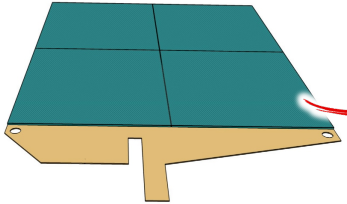
- Scanner **simplified** and **improved** design, avoiding acceptance inefficiency from cooling blocks
  - Monolithic **100μPET** detector ASIC: **2.5 x 3 cm^2** active pixel matrix; **100 μm** pixel pitch; **250 μm** thick silicon sensor
  - Single silicon detection layer composed by **2x2 chips** assembled, covering about **30 cm^2**!
  - **4 "towers"** compose the scanner. **60** detection layers on each tower = **960 chips!**
    - Large number of services and interconnections, requiring **innovative** design. Two possible designs under study
      - **5 silicon detector layers** (20 chips) stacked on a **PCB**, staggered for **wire-bonding. 12 modules** are stacked in a tower
      - **1 detection layer** (2x2 chips) are interfaced to a **FPC** via ACF bonding. **60 FPCs** are stacked in a tower

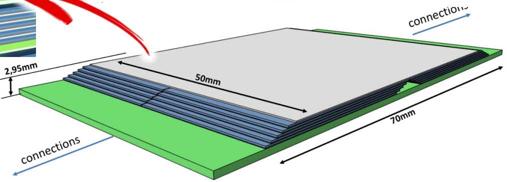


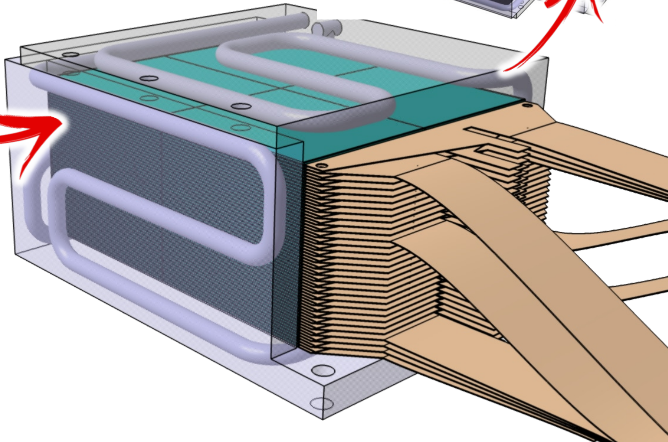
4 Tower assembly











The 100µPET scanner

Sensitivity and Resolution

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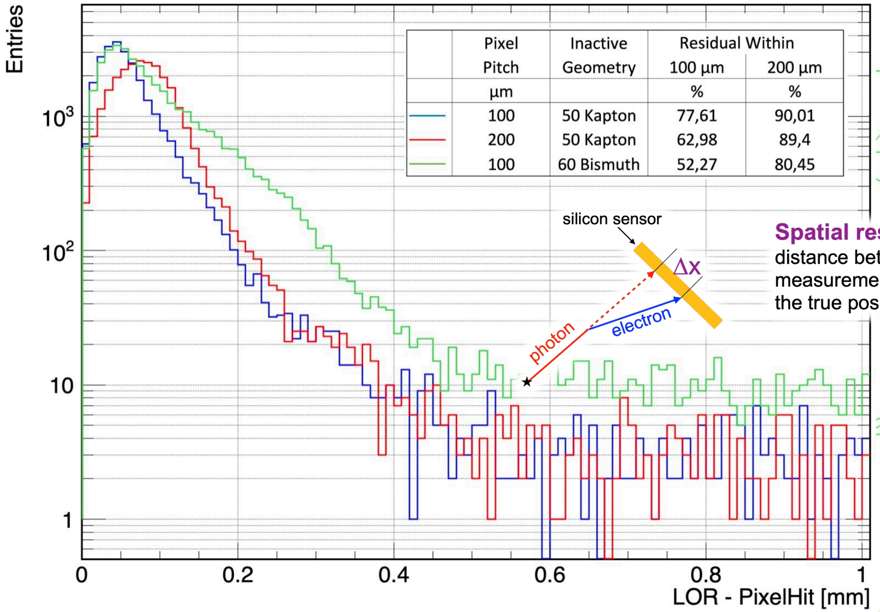
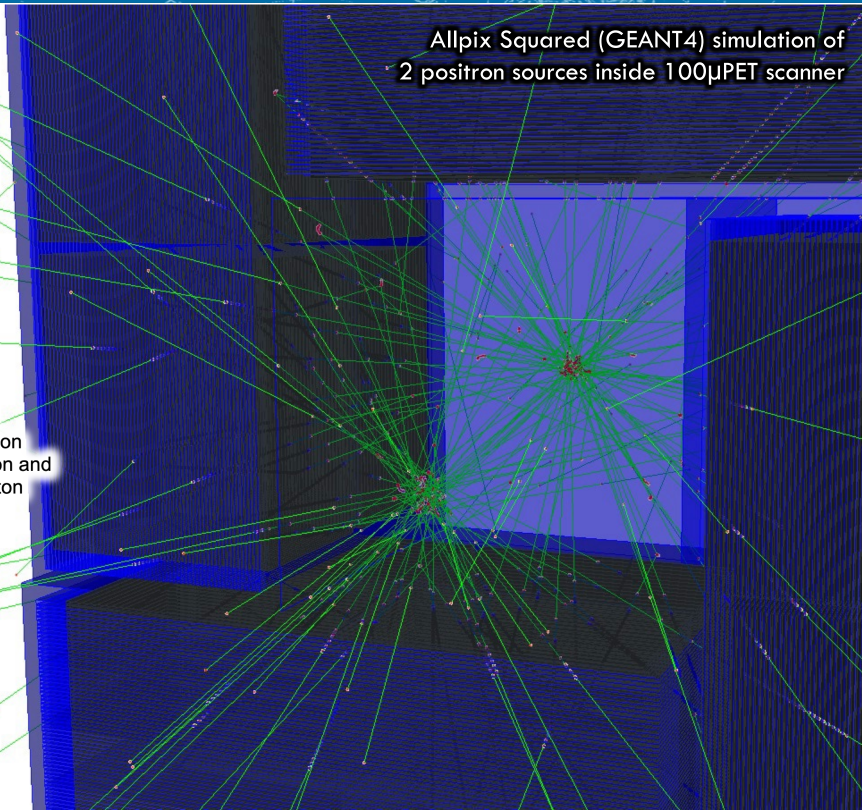
Monte Carlo simulations has shown a disruptive jump in the scanner's <u>resolution</u> and <u>sensitivity</u>

- Efficiency can be increased with absorber layers



	Pixel Pitch µm	Inactive Geometry	Residual Within 100 µm %	Residual Within 200 µm %
blue	100	50 Kapton	77,61	90,01
red	200	50 Kapton	62,98	89,4
green	100	60 Bismuth	52,27	80,45

Spatial resolution Δx: distance between the position measurement of the electron and the true position of the photon



The 100μPET scanner

Sensitivity and Resolution

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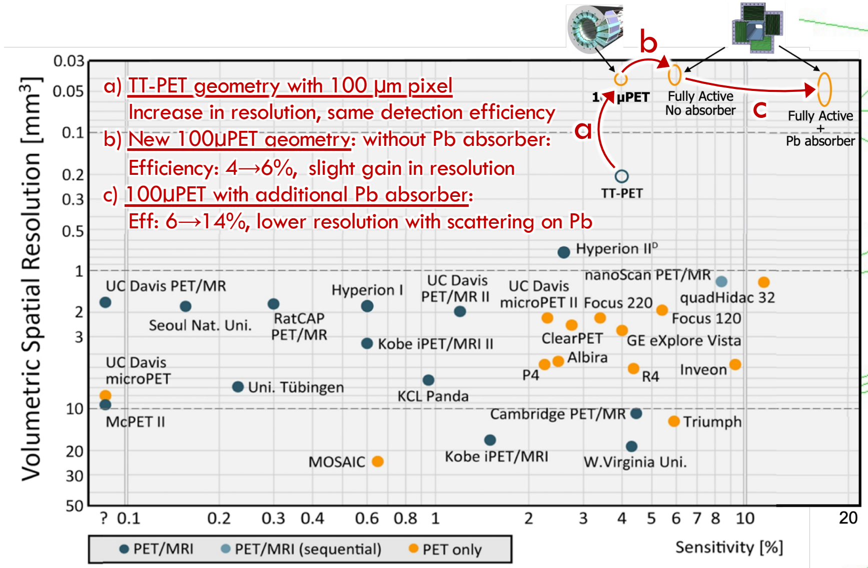
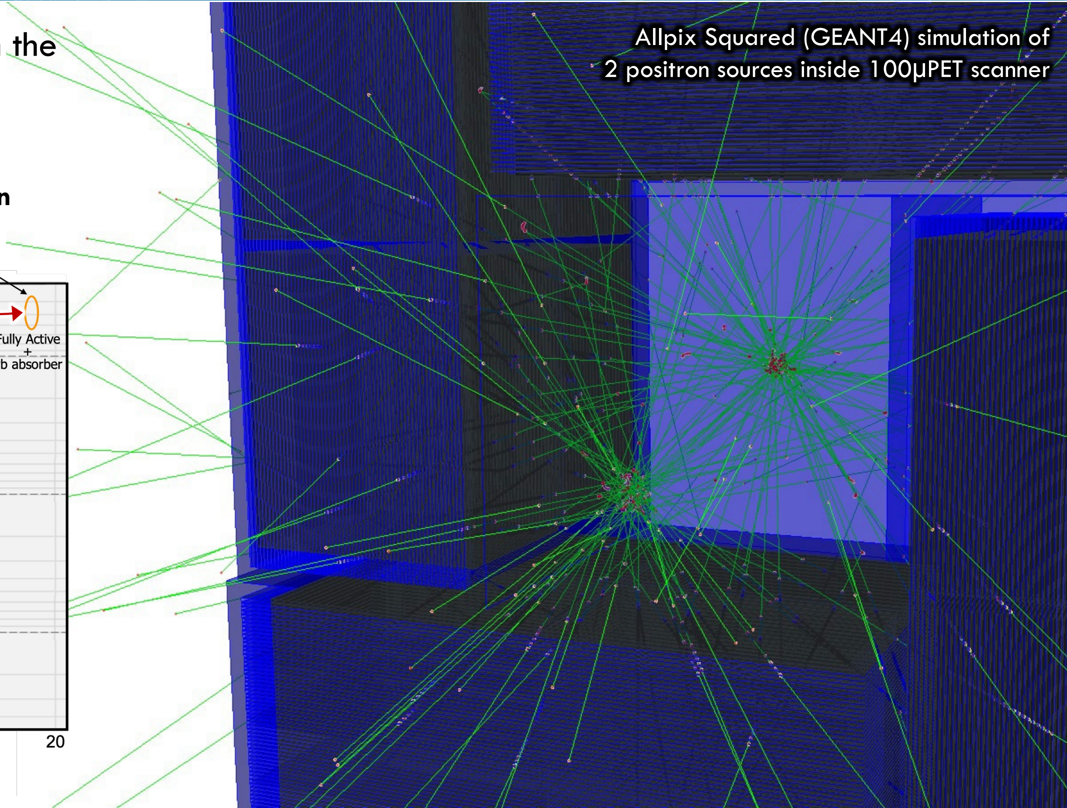
Monte Carlo simulations has shown a disruptive jump in the scanner's <u>resolution</u> and <u>sensitivity</u>

- Efficiency can be increased with absorber layers
  - It is a compromise **between efficiency** and **resolution**





ASIC prototypes

The MonPicoAD ATTRACT and MONOLITH ERC projects

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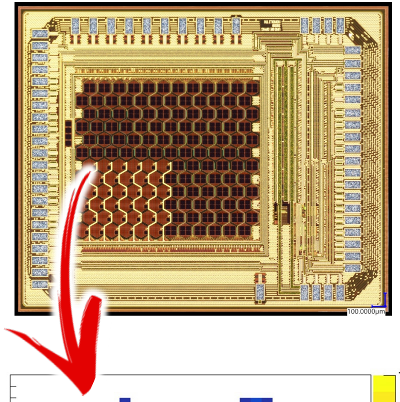
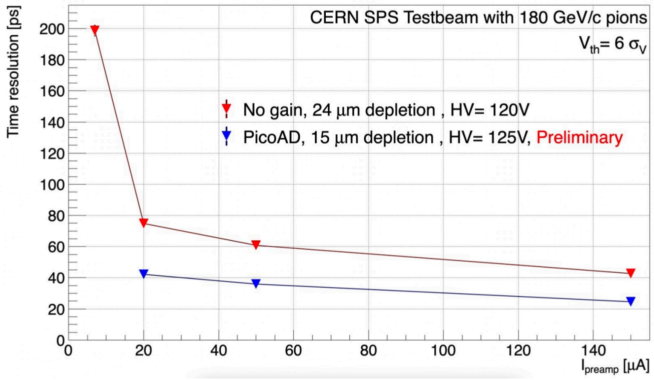
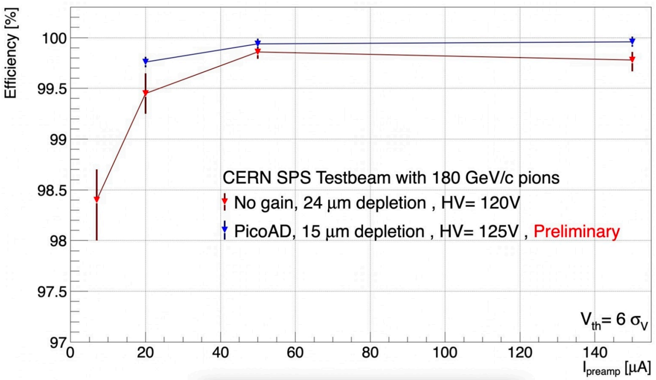
- 100μPET ASIC will spin-off from noGAIN and PicoAD prototypes
  - Hexagonal **65 μm** wide pixel (equivalent 100μm XY pitch) for R&D investigation
- Tested at CERN SPS H8 beam-line in Q2 2021
  - >99.5% detection efficiency (on both prototypes)
  - Timing resolution of **36.4 ± 0.8 ps** (without gain) and **24 ± 0.7 ps*** (with gain layer)

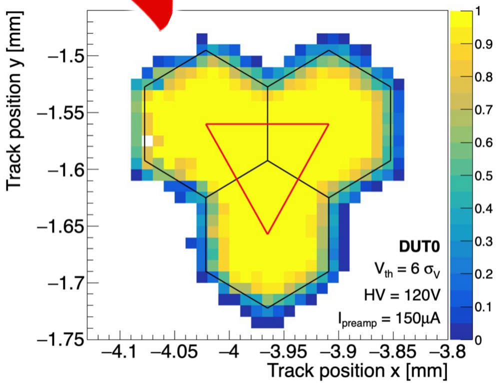
    *First PicoAD prototype. Sensor and front-end design still to be optimized + ps TDC

    - G. Iacobucci et al 2022 JINST 17 P02019 (no gain prototype)









Detector assembly prototyping

In collaboration with ALICE (CERN and INFN-Cagliari)

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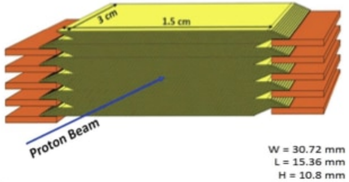
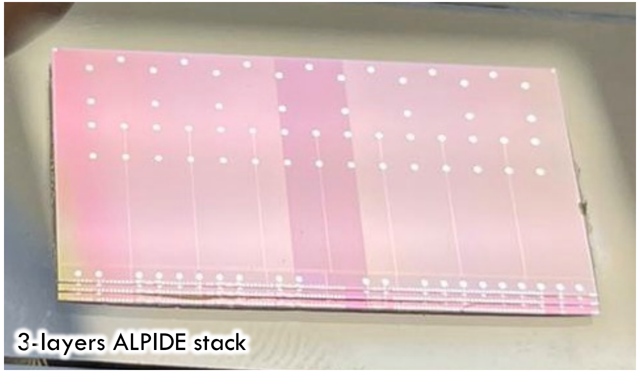
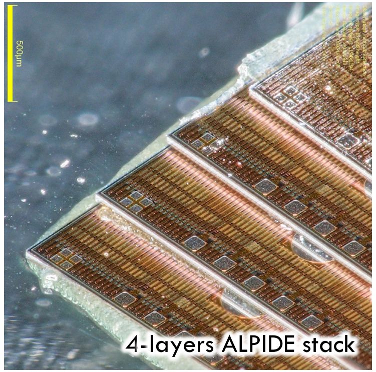
- Common interest in stacking MAPS for detection transition from 2D layers (pixels) to **3D volumes (voxels)**
  - Pixel chamber project: Solid state counterpart to the bubble chamber
    - Active target, hosting the primary IP in fixed target experiments
      - Stack of 216 ALPIDE chips (30x15x11 mm^3), resulting in a 3D volume with **10^8 voxels (29x27x50 μm^3)**

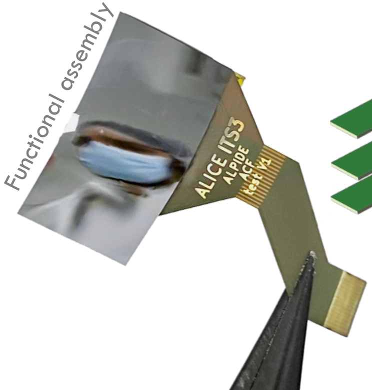


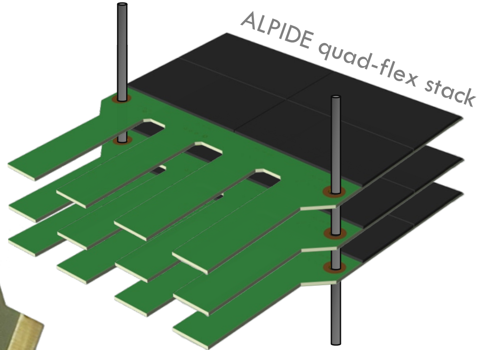
- R&D and prototyping work started stacking 50 µm thick ALPIDE chips
  - 2 stack versions: Staggered for wire-bonding and ACF bonded to flex
    - First mechanical assembly with 4 dummy chips stacked using 20 µm epoxy film. Stack to be wire-bonded soon
    - Successful single-module flex already produced. Stackable quad-module flex finalizing design


3-layers ALPIDE stack



4-layers ALPIDE stack




ALPIDE quad-flex stack

Conclusion and outlook

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- **PET scanners** are an important diagnostic tool that has been improving in an astounding way over the years and will continue to improve
- **Pixelated silicon sensors** have the **enormous potential** to enable ultra-high-resolution molecular imaging
- The **100µPET SNSF SINERGIA** project will deliver a small-animal scanner based on silicon technology with expected **0.3 mm spatial resolution,** **one order of magnitude resolution improvement**
  - **TOF below 10ps** could be added, when delivered by the **MONOLITH** project
- Innovative ASIC design and module construction techniques are being developed
  - Silicon-sensor technology will continue to improve and its **cost will go down**
    - In the future, scanners larger than those for small-animals could be realised