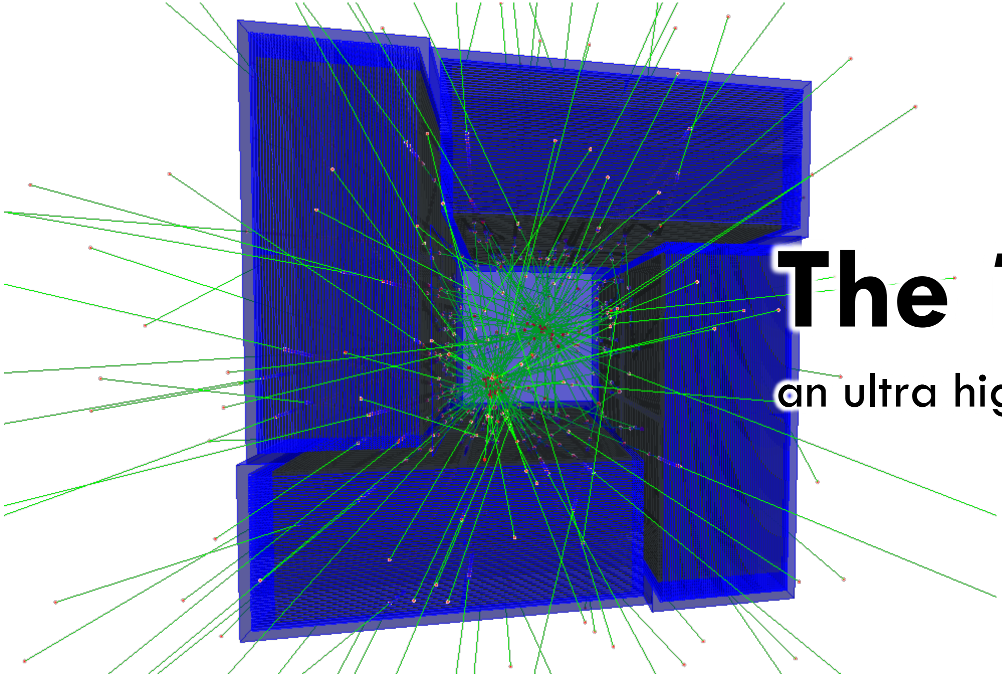

The 100μPET project:

an ultra high resolution small-animal PET scanner

UNIVERSITÉ DE GENÈVE

VERTEX 2021 – YSF talks
28/09/2021

Mateus Vicente
on behalf of the 100μPET collaborators

Introduction

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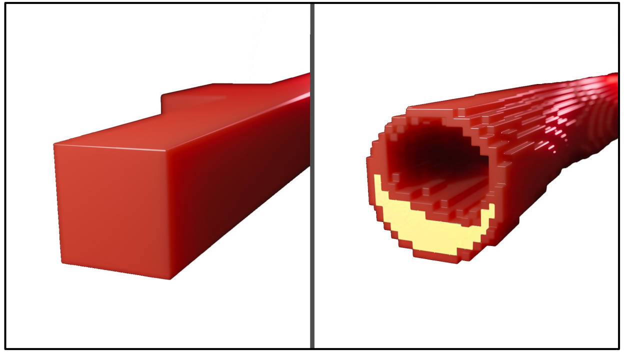
- The 100µmPET project: molecular imaging with ultra-high resolution
  - First silicon small-animal scanner prototype
    - SNSF SINERGIA four years project (from 2021 Q2)

    FNSNF Swiss National Science Foundation — Sinergia

    Université de Genève, Faculté des Sciences — HUG Hôpitaux Universitaires Genève — EPFL

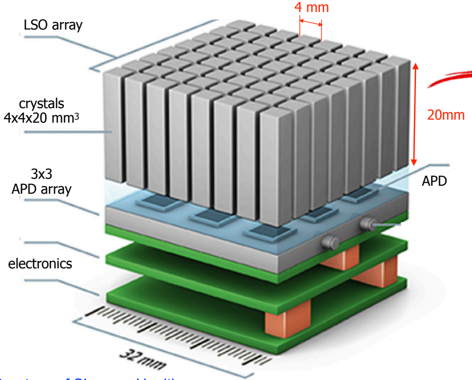
    - Three partners:
      - **UNIGE**: Construction of the 100µPET small-animal scanner
      - **EPFL**: Sophisticated imaging reconstruction with ML and NN to cope with the 10^{15} possible line-of-repsonse
      - **HUG**: Study the onset and progression of atherosclerotic plaques in arteries to better 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

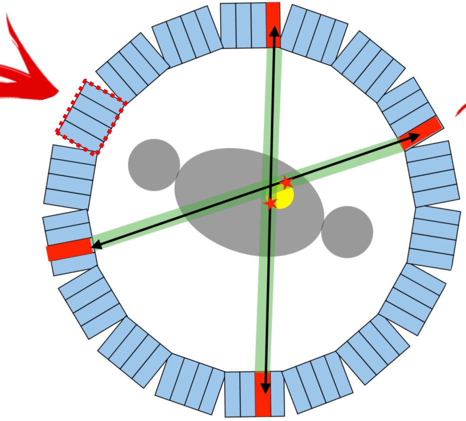
Positron Emission Tomography (PET) imaging

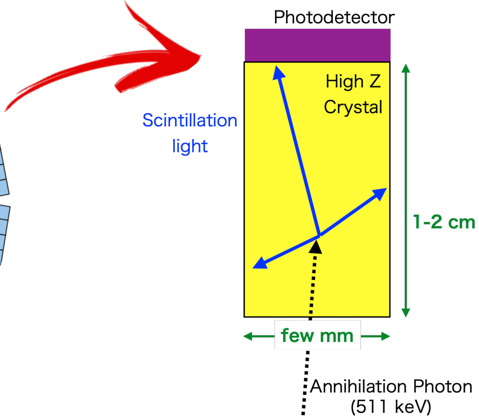
- PET is a nuclear medicine method to study metabolic processes in the body
  - A radiotracer is injected in a body and positrons from the radionuclide annihilates with electrons of the nearby tissue, emitting two **back-to-back** 511 KeV photons
    - The two photons are detected in **coincidence**, defining a **line-of-response (LoR) volume**



Courtesy of Siemens Healthcare

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





Positron Emission Tomography (PET) imaging

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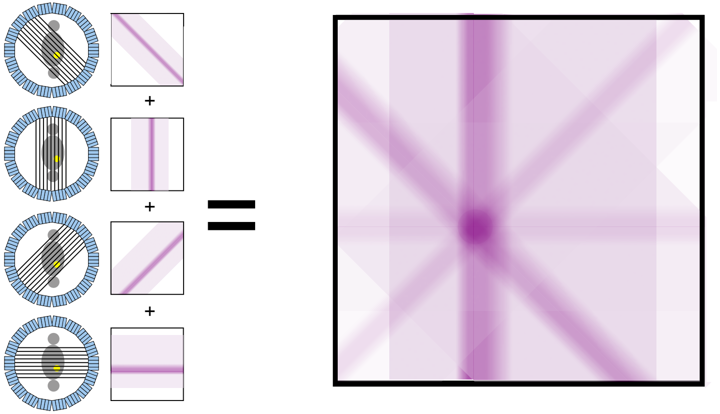
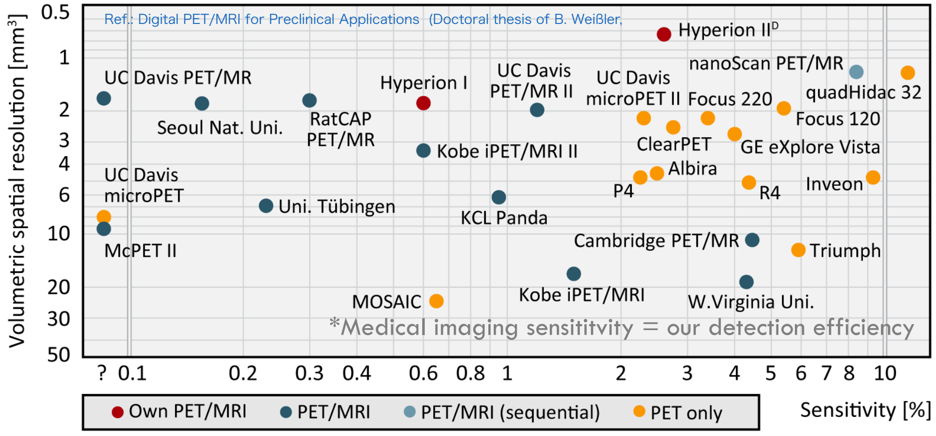
- PET images are reconstructed from the **projections of the LoRs**
  - To access ultra-high resolution molecular imaging ➔ **Reduce the LoR volumes** by exploiting:
    - Improved depth-of-interaction measurement
    - Better timing resolution for coincidence measurement
    - Improved spatial resolution with higher volume granularity ➔ **HEP based silicon pixel detectors**



Overview of current small-animal PET scanners



Positron Emission Tomography (PET) imaging

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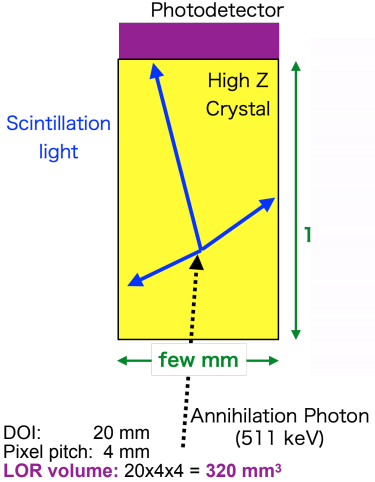
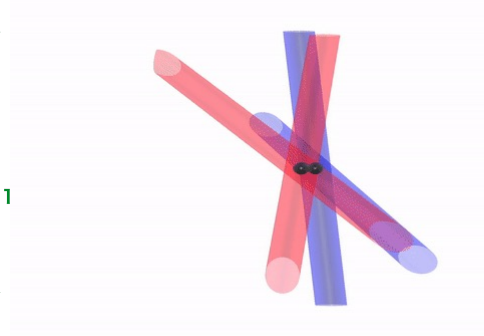
- The higher PET granularity will reduce the noise-like combinatorics artifacts during projection of LoRs

Conventional PET detectors



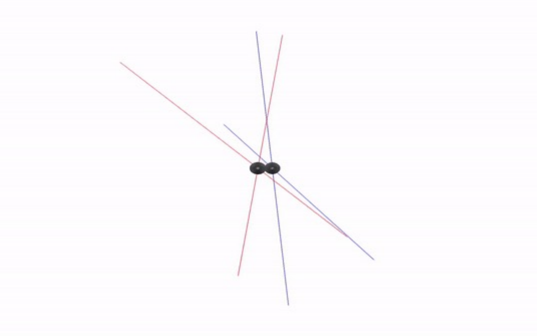
Two spherical sources
Two annihilations from each



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

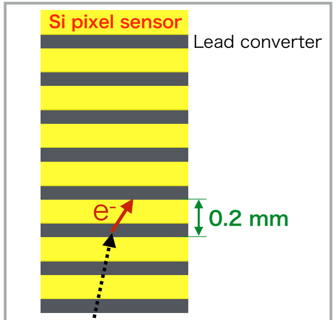
VS

Same two sources
Same four annihilations



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

Multi-layer silicon sensor Scanner



Multiple high Z conversion layers and fast timing pixel sensors with:
- 0.5 mm pixels
- 0.2 mm DOI uncertainty

LoR volume 160'000 times smaller!

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

The 100μPET predecessor

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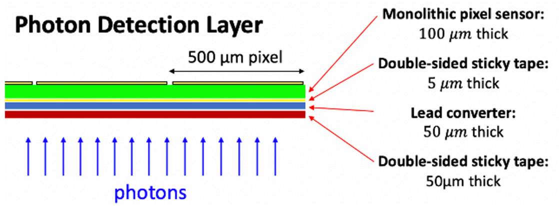
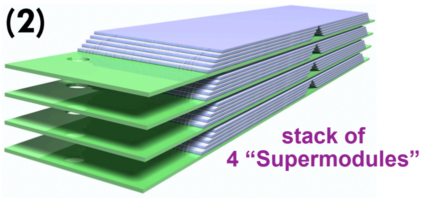
- A SNS SINERGIA project <u>from 2016 to 2019</u>

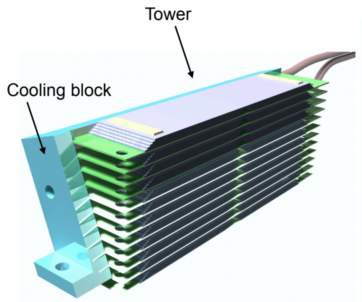
(1)



(2)

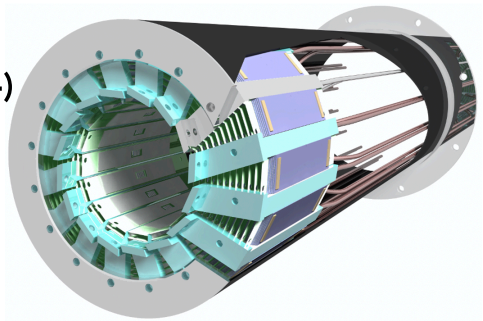


(3)



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

(4)

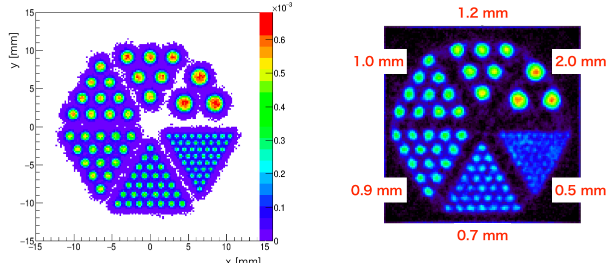


16 Towers all around to form the scanner

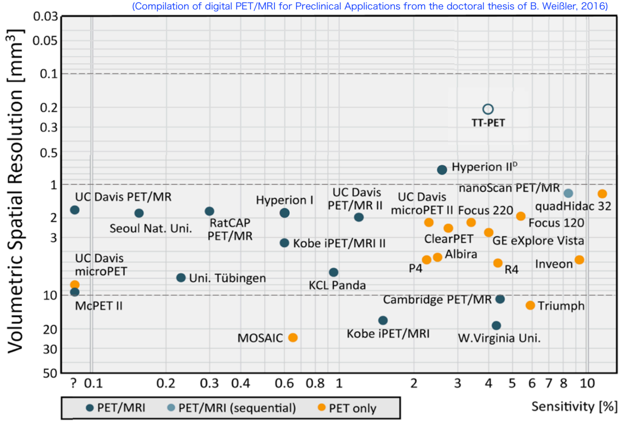
Scanner performance simulation with derenzo phantom

Unprecedeted high spatial resolution

Monte-Carlo Truth   Iterative Reconstruction



(Compilation of digital PET/MRI for Preclinical Applications from the doctoral thesis of B. Weißler, 2016)



The Thin Time-of-Flight (TT-PET) project
Timing and efficiency

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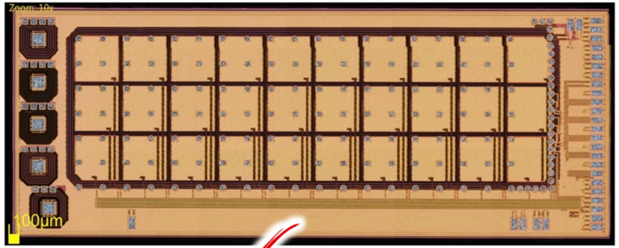
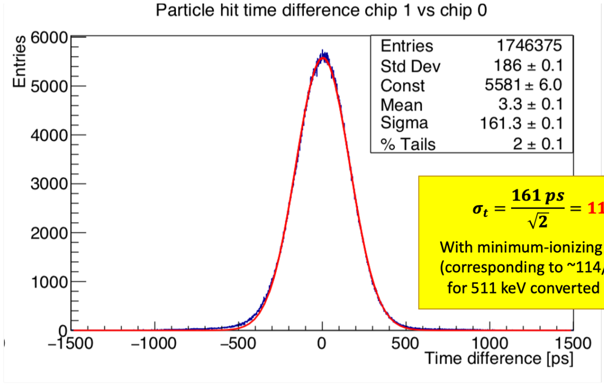
- TT-PET demonstrator <u>monolithic</u> chip produced, containing:
  - Matrix of 3x10 pixels of area 500x500 µm^2
  - Pre-amplifier + discriminators
  - 20 ps binning TDC
  - Read-out logic and serializer
- Test beam results from CERN SPS
  - **114 ps** timing achieved with **>99.9 detection efficiency**!

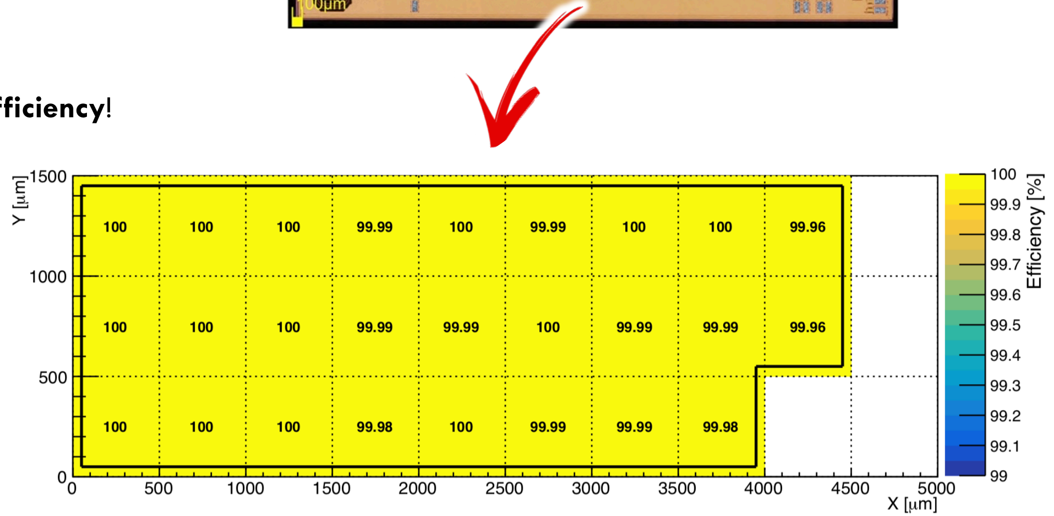
TT-PET prototype with 500 x 500 µm^2 pixels





$$\sigma_t = \frac{161\,ps}{\sqrt{2}} = 114\,ps$$

With minimum-ionizing particles (corresponding to ~114/4 ~ 30ps for 511 keV converted photons)



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

- By the end of the TT-Project in 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**

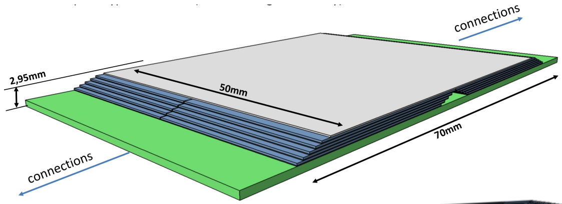
  E. Ripiccini et al., https://arxiv.org/abs/1811.12381
  - Iterative reconstruction **produced**

  D. Hayakawa PhD thesis, http://dpnc.unige.ch/THESES/THESE_HAYAKAWA.pdf
- Simulations and prototyping work showed that a change of paradigm in PET imaging is possible with monolithic pixel sensors
- Can we do even better? Must reduce even further the "LoR volume":
  - either by having better time resolution, or
  - By having better **spatial resolution**, pushing the position measurement down to the **intrinsic limits** given by the **positron mean free path in body**

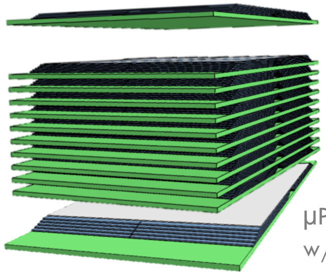
The 100µPET scanner

New SINERGIA project evolving from the TT-PET

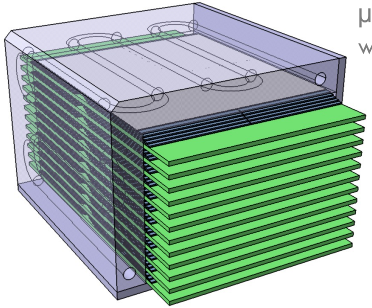
- Major scanner simplified and improved redesign, **avoiding acceptance inefficiency** from cooling blocks
  - **µPET quad-module** (current base-line): **6 cm x 5 cm, x5** chips staggered ➔ **150 cm^2** detector module!
  - **12 quad-modules** are stacked together in a **tower,** and **4 towers** compose the scanner ➔ **60** detection layers **x4** = **<u>960 chips!</u>**
    - The power density per unit of volume is very high: **250 W,** to be contained in a very small volume
    - The amount of services and interconnections are much denser, requiring **innovative** design



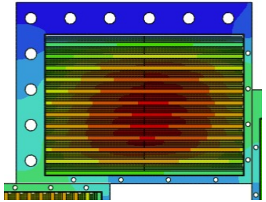
Quad-module



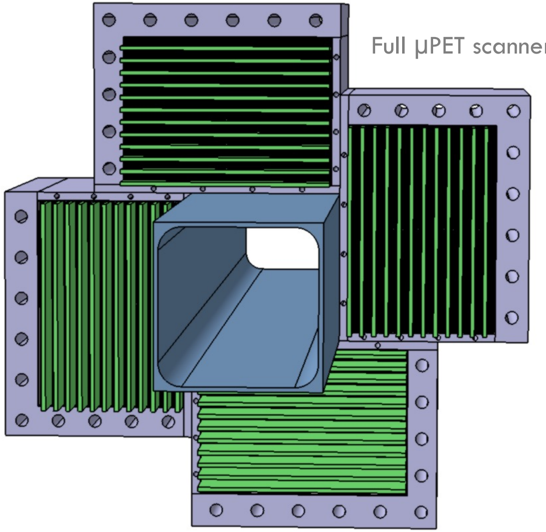
µPET tower w/ 12 modules



µPET tower w/ cooling block



Cooling FEA simulation



Full µPET scanner

The 100µPET scanner
Sensitivity and Resolution

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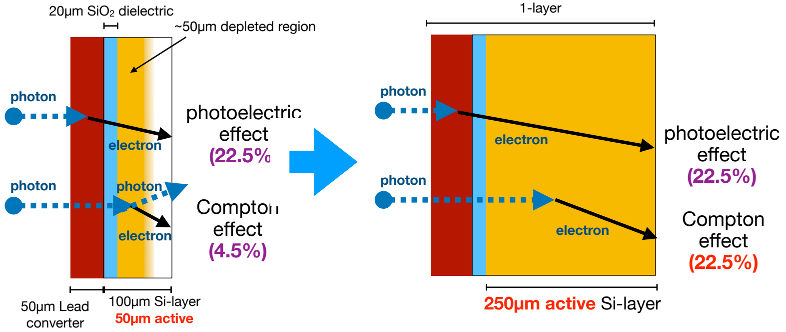
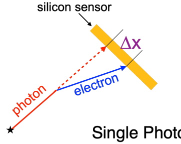
*single photon absorption efficiency

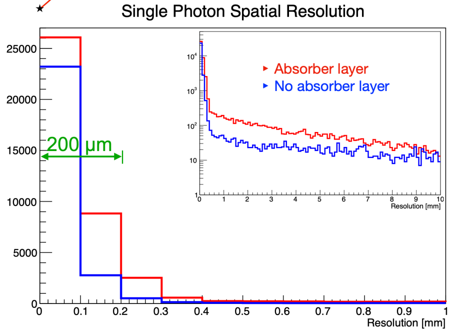
Monte Carlo simulations has shown a disruptive jump in the scanner’s resolution and sensitivity

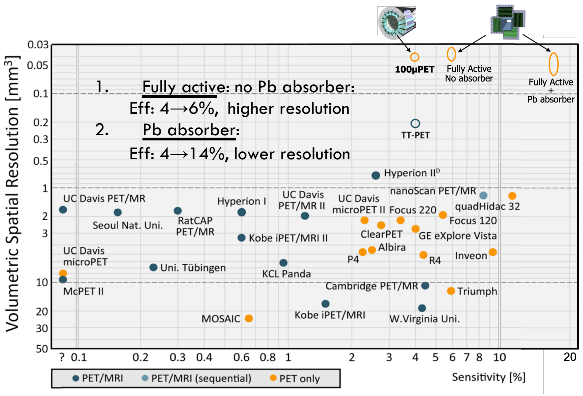
- Increase the active zone in the silicon sensor from **50 µm** to **250 µm** for higher sensitivity
  - also increasing the volumetric granularity with **100 µm pixel pitch**
- The thicker sensor changes the conversion efficiency* from 27% (22.5% photoelectric conversion in absorber and 4.5% from Compton effect in silicon) to **45%** (**additional 18%** from Compton in the thicker silicon sensor)
  - Efficiency can be increased with absorber layers
    - It is a **deal between efficiency** and **resolution**





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





The 100µPET scanner
Small pixel “ATTRACT” prototype

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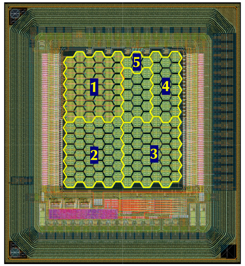
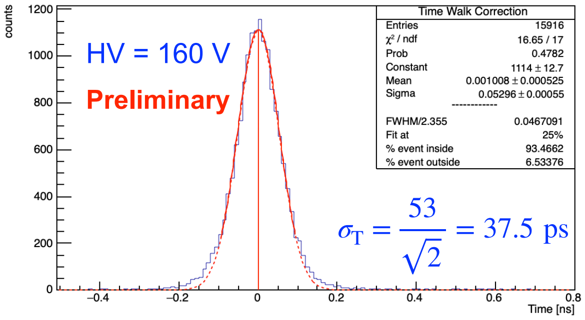
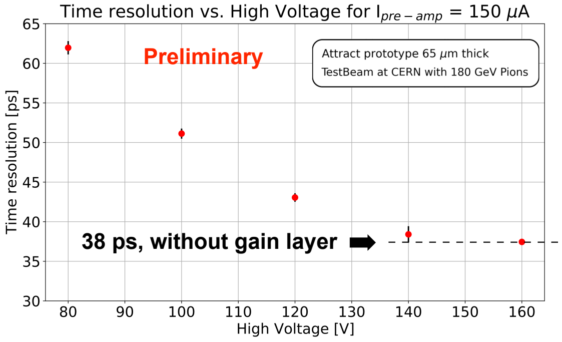
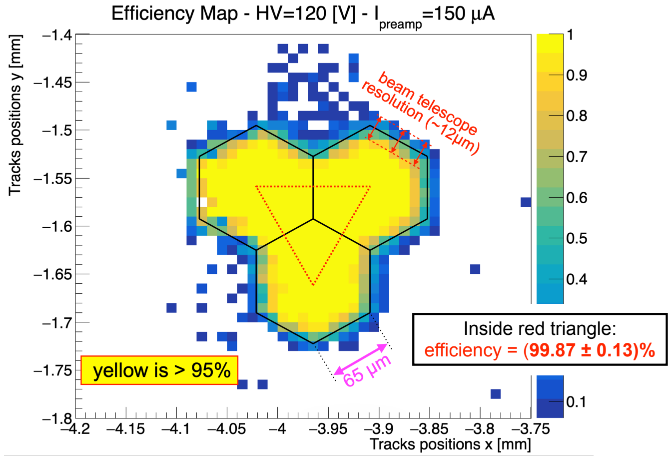
- MPW submission in 2019 funded by H2020 ATTRACT MonPicoAD project
  - Prototype chip with 5 different pixel matrices for R&D investigation
- Tested at CERN SPS testbeam in Q2 2021
  - Timing plateau at **~38 ps** and detection efficiency **>99%**



Time of flight between two sensors







Conclusions

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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** and **one order of magnitude better volumetric spatial resolution**
  - **TOF below 10ps** could be added, when delivered by the **MONOLITH** project
- Silicon-sensor technology will improve and its **cost will go down.** In the future, scanners larger than those for small-animals could be realised
  - (…maybe a human-head scanner with silicon is the following step…)