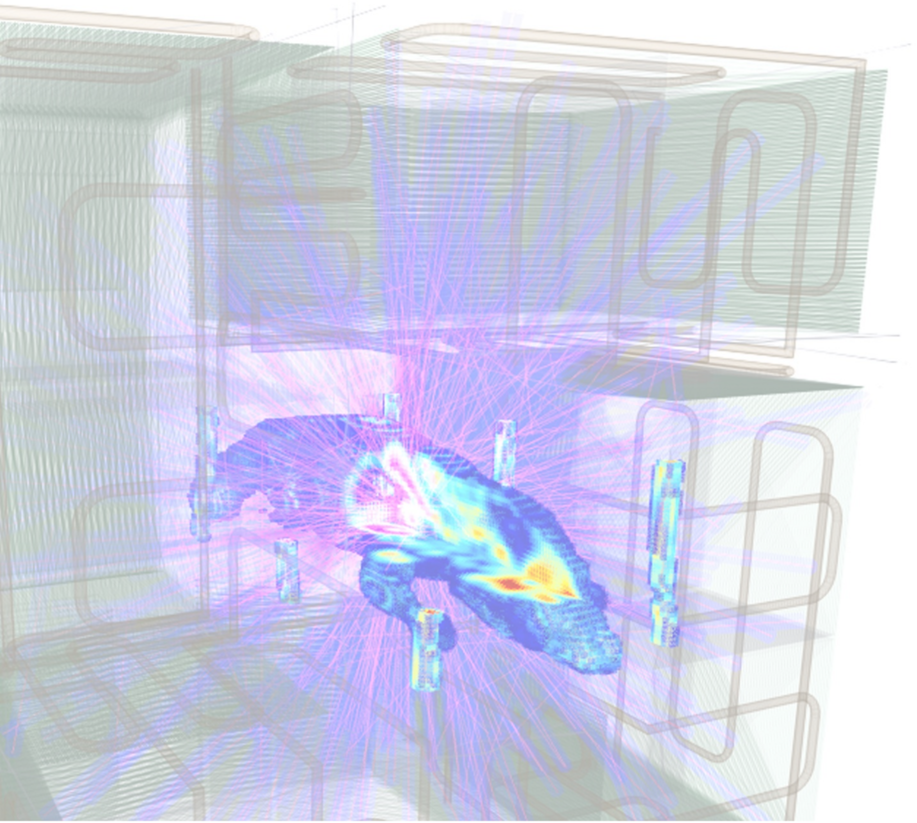
100µPET

An ultra-high-resolution silicon-pixel-based PET scanner



Swiss National Science Foundation

EPFL

UNIVERSITÉ DE GENÈVE

UNI LU

25th iWoRiD

3rd July 2024

Mateus Vicente (UNIGE)
on behalf of the 100µPET collaborators

Introduction

Positron Emission Tomography (PET)

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- PET is a nuclear medicine method to study metabolic processes in the body
  - A radiotracer is injected in the body; Regions with abnormal metabolism will present an excess of radiotracer;
    The radiotracer emits positrons, which "walks around" until annihilating with electrons of the nearby tissue;
    The two back-to-back 511 KeV photons from the annihilation are detected in coincidence;
    Lines-of-Response **(LoR)** are defined by the volume between the sensitive elements detecting the two photons;
    LoRs are processed to generate density maps of the detected annihilations;
  - Due to the lack of spatial resolution, PET imaging must be done in hybrid mode (combining MRI or CT measurements)

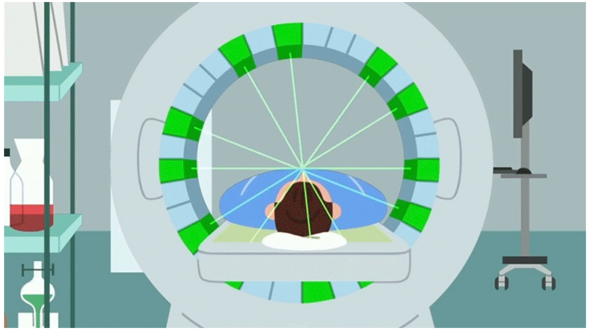
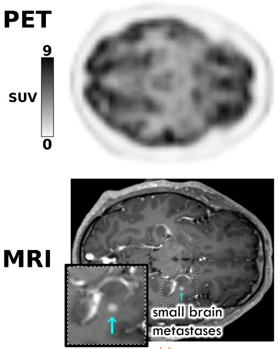


Image from here



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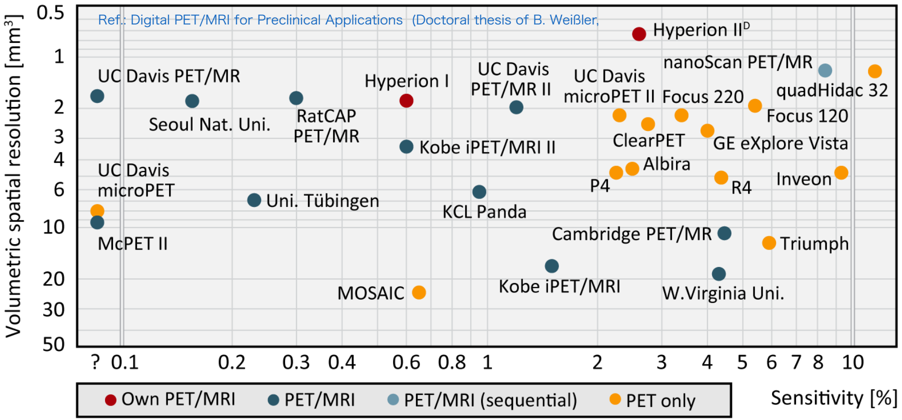
Overview of current small animal PET scanners



Introduction

PET with the 100µPET scanner

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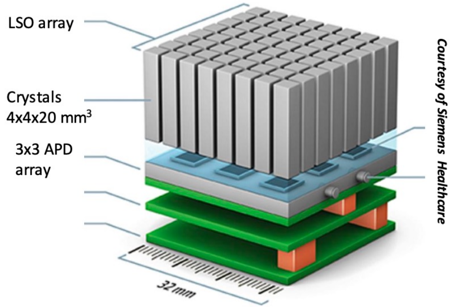
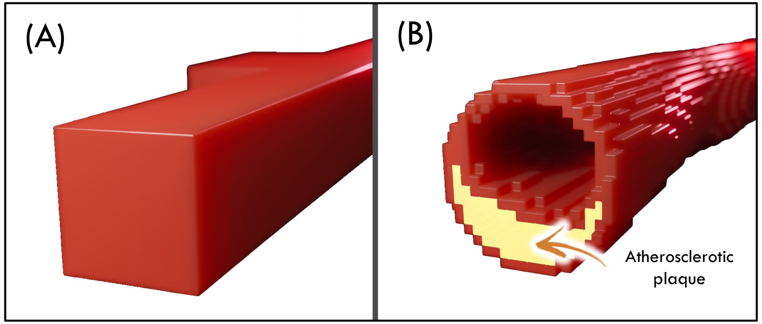
- Current PET scanner technology employs arrays of scintillating crystals with typical size $\gtrsim 1\,mm^3$
  - Small blood vessels can only be visualized in their entirety (A).
- To access ultra-high resolution molecular imaging, one must **reduce the LoR volumes** by exploiting:
  - Better timing resolution for coincidence measurement (TOF-PET), or increased detection volume granularity
- The **100µPET** SNSF Synergia project: **UNIGE** (scanner production) **EPFL** (imaging reconstruction) and **UNILU** (medical study)
  - Ultra-high resolution imaging by employing **multi-layer stacks of monolithic pixel detectors**, allowing the study of changes in small blood vessels, as atherosclerotic plaques (B)

PET tower with LSO crystals

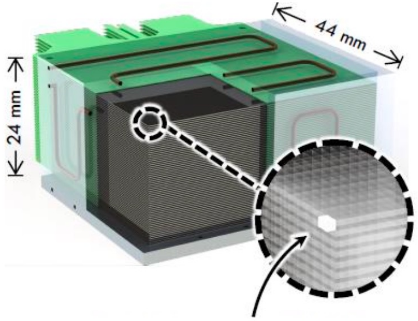


DOI: 20 mm
Sensor granularity: **320 mm³**



Images: © Xavier Ravinet - UNIGE

100µPET stack



Pixel pitch: 150 µm | DOI: 550 µm
Sensor granularity: **0.012 mm³**

The 100µPET team
and other collaborators

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The 100µPET project

Giuseppe Iacobucci
- project P.I.
- System design

Yannick Favre
- Board design
- RO system

Roberto Cardella
- Sensor design
- Laboratory test

Sergio Gonzalez-Sevilla
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- Laboratory test

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- Firmware

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- Translational imaging

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- Molecular biology
- Radiopharmacy

Michäel Unser
- P. I.

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- Signal/image processing
- Physical modeling

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- Laboratory test
- Data analysis

Jordi Sabater
- Detector simulation
- Laboratory test

Andrea Pizarro
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- Data analysis

Théo Moretti
- Laboratory test
- Data analysis

Chiara Magliocca
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- Sensor simulation

Ivan Semendyaev
- Laboratory Tests
- Data Analysis

Stefano Zambito
- Laboratory test
- Data analysis

Leonardo Cecconi
- Chip Design
- Firmware

also have a look at:

Matteo's talk on MONOLITH

Rafaella's talk on FASER

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Swiss National Science Foundation

European Research Council

Sinergia

ATTRACT

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The 100μPET scanner

ASIC, module/layer, tower

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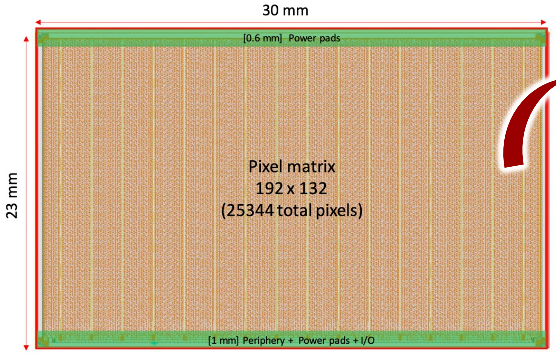
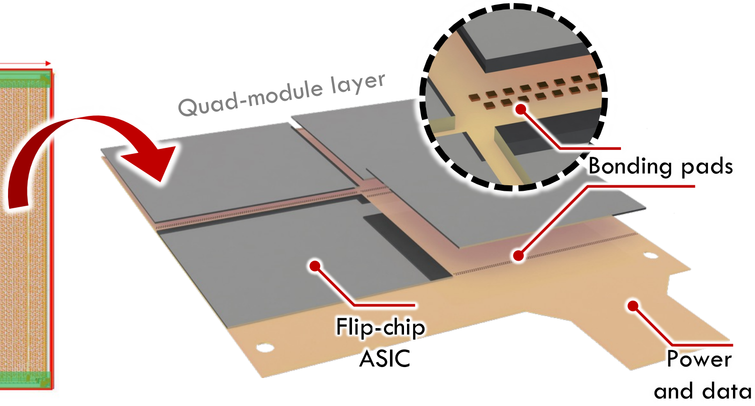
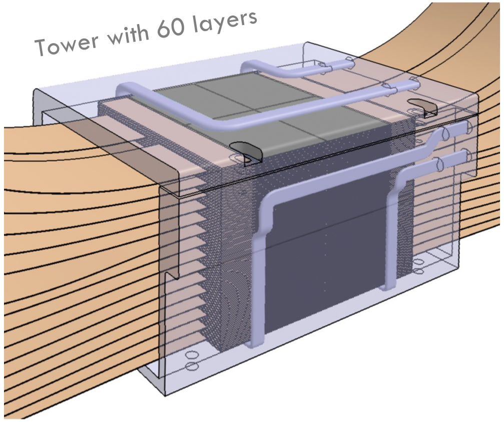
- Multi-layer stack of CMOS imaging sensors
  - **100μPET** MAPS: **130 nm** SiGe BiCMOS; **2.3 x 3 cm^2**; **150 μm** pixel pitch; **270 μm** thick; **4 kOhm*cm** p-substrate; **~0.5W** power
    - Designed foreseeing flip-chip bonding, the size and pitch of the bonding pads allows integration with standard PCB/FPC production
  - Single silicon detection layer composed by **2x2 ASICs** flip-chip to a flex printed circuit, covering **24 cm^2**
    - In addition to the thin MAPS, a **50 μm thick layer of Bismuth** is added above the MAPS to increase the photon convertion rate
  - **60** detection layers + cooling block compose each scanner **tower**, with 4 towers per scanner (for a grand total of **960 chips!)**







Monte Carlo simulations

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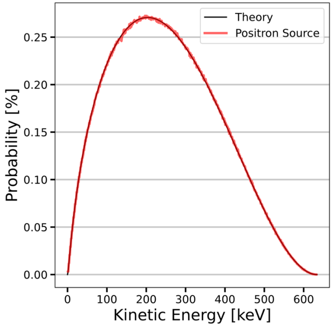
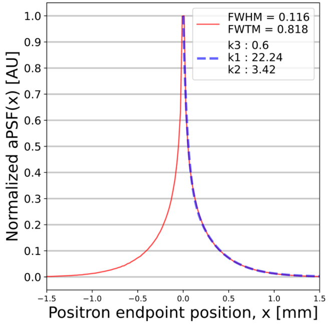
- **Performance** simulations with (Geant4 + AllPix^2)
  - Scanner geometry (silicon chips, flex, cooling block) + scatter water volume
  - positron spectrum (positron range and photons acollinearity)
  - Photon interactions + sensor/ASIC response + pixel clustering
    - No time information (event based) and **no energy window** used
      - LoR are crated on events with only 2 detections on 2 different towers

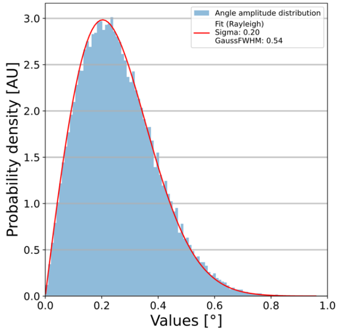
[^{18}F]FDG positron spectrum

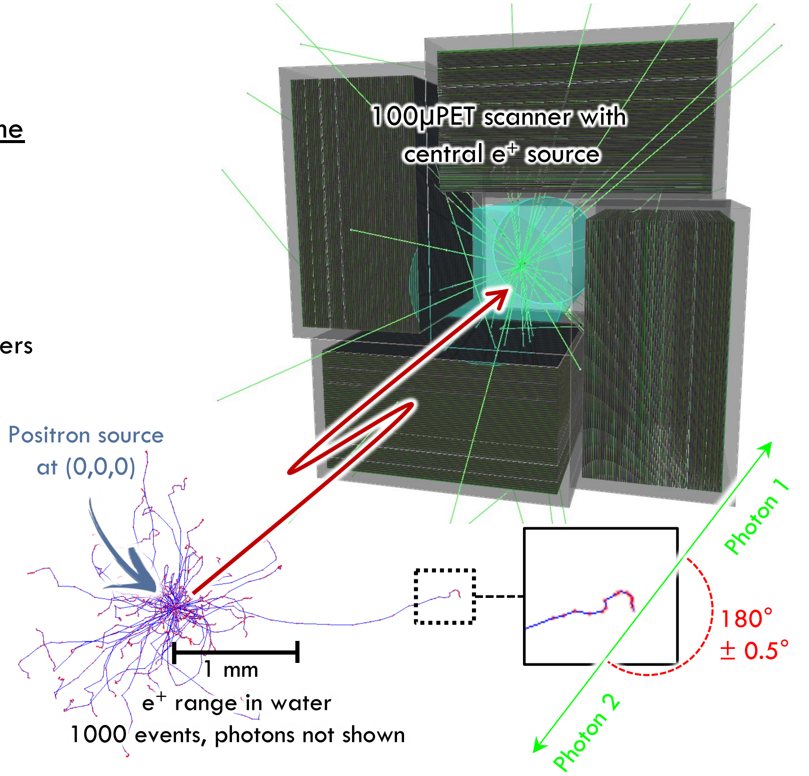


Positron range



Photons acollinearity





Monte Carlo simulations

Sensitivity and Point Spread Function

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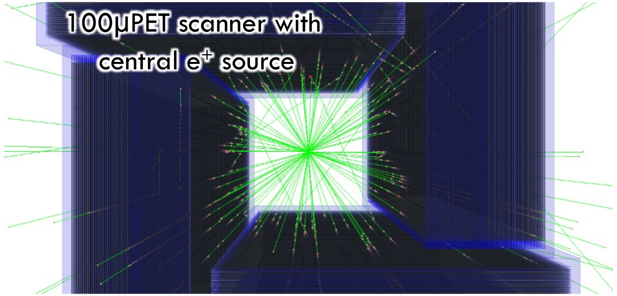
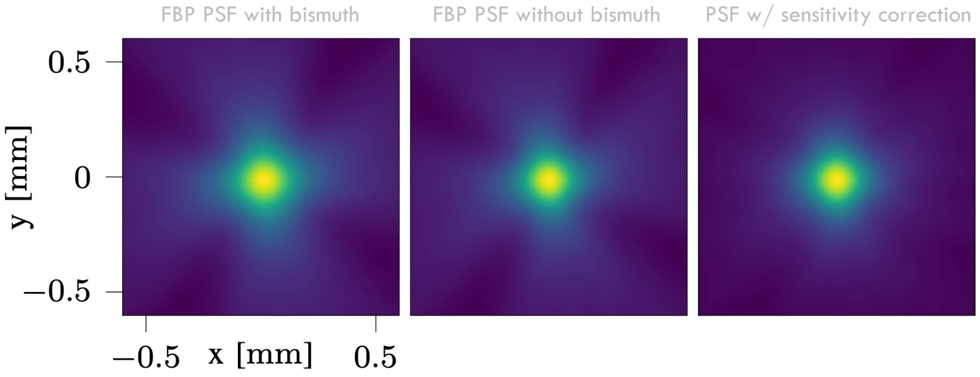
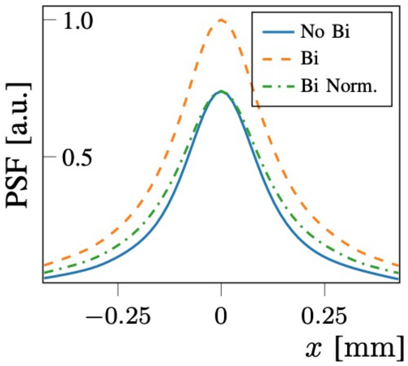
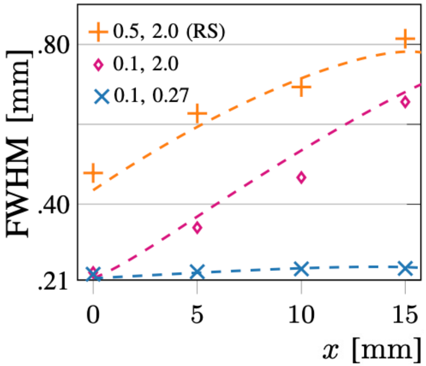
- Point source simulations
  - Sensitivity: LoR created / annihilations
    - **<u>5 / 3.1%</u>** (with / without 50 µm Bismuth layer)
  - Point spread function (PSF): Filtered back projection (FBP)
    - **<u>0.28-0.30 mm / 0.21-0.24 mm</u>** (w / wo Bi)









Monte Carlo simulations

Derenzo and Image Quality phantoms

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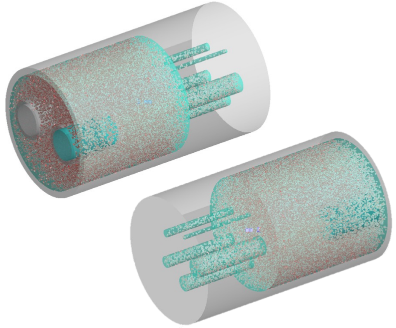
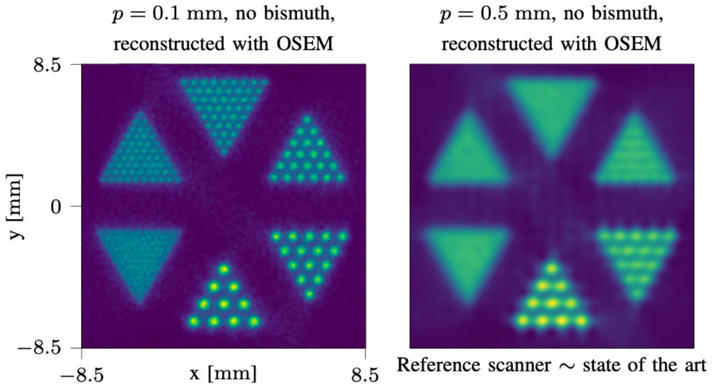
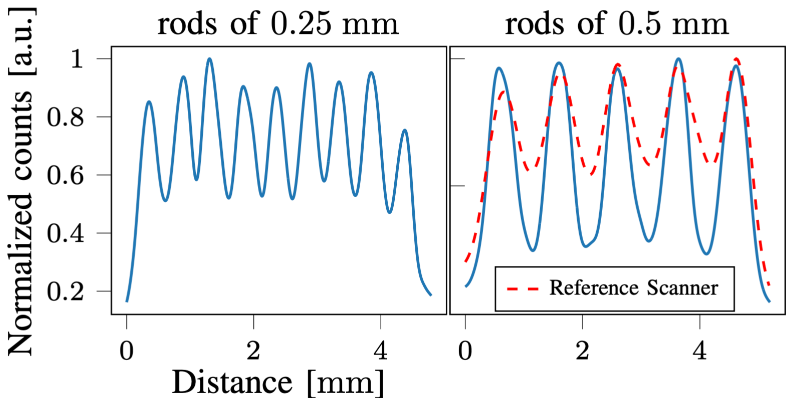
- Derenzo phantom: Rods diameters {0.2, 0.25, 0.3, 0.4, 0.5, 0.6} mm
  - Valey-to-peak ratio: **0.57** (0.25 mm rods), **0.25** (0.5 mm rods) (ref. scanner = 0.6)
- NEMA NU4 Image Quality phantom: Active rods and uniform volume + air/water volume
  - Spatial resolution + attenuation and SNR + scatter correction performance
    - Recovery coefficient: **0.6** (for 1 mm rod)
    - Standard dev. for the uniform volume: **4%**







Monte Carlo simulations

Atherosclerosis case study

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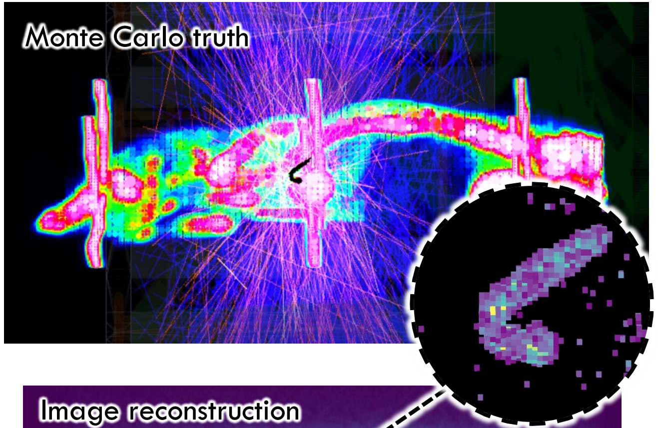
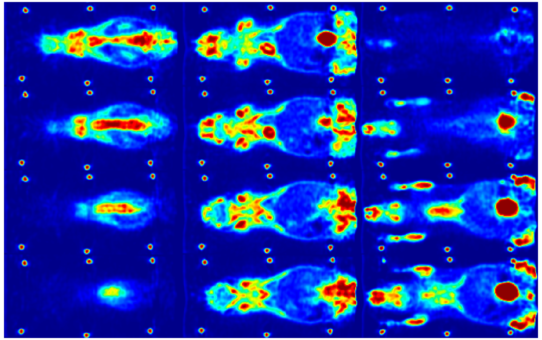
- Mouse phantom from Digimouse PET (background) + atherosclerotic plaque microCT (signal of interest)
  - Injected activity: 30 MBq
  - Measurement time: 20 min
    - Mouse volume = 45 mL ➟ **1.4 x 10^9** background annihilations
    - Plaque volume = 0.006 mL ➟ **8.4 x 10^6** plaque annihilation



Digimouse PET section



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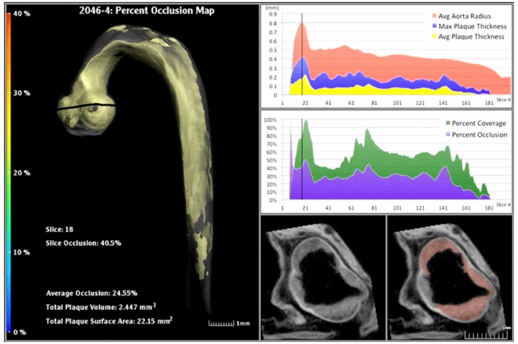
microCT of atherosclerotic plaque



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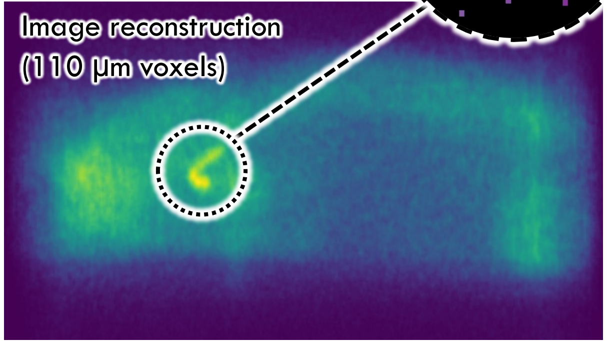

Monte Carlo simulations

Timing and count rate performance

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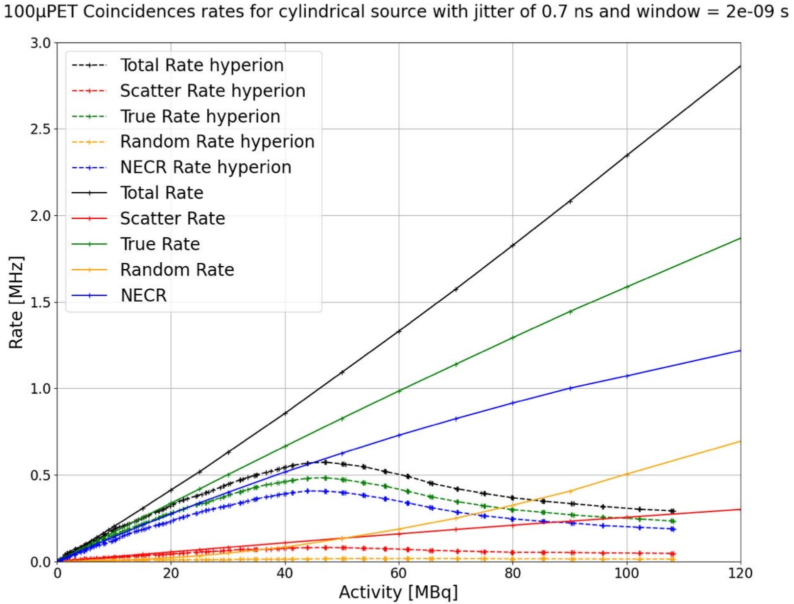
Offline time-stamping of annihilation events allow us to investigate multiple jitter and time-window scenarios using the same data-set

- Time between 2 decays follows an exponential distribution
  - Cumulative distribution function method is used to get the time between 2 consecutive decays
- The assigned time-stamp is smeared with a gaussian distribution representing the ASIC's jitter
- Data loss from ASIC's buffer saturation (MAX 350 kHz cycle rate) is also included



Monte Carlo simulations

Assembly and alignment study

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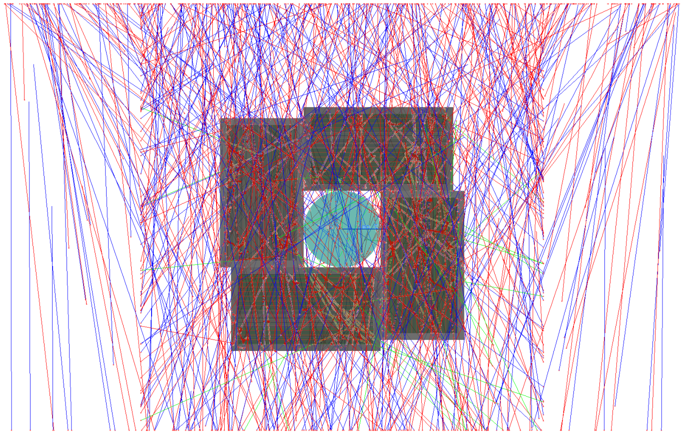
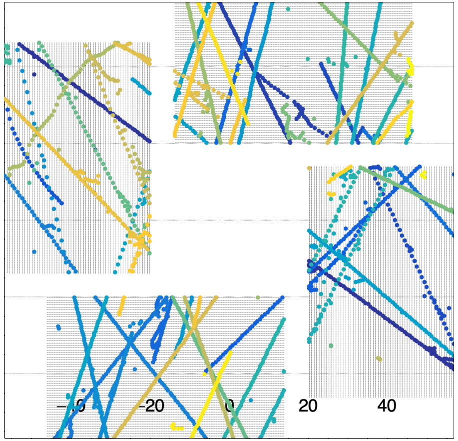
<u>Disclaimer</u>: the simulation results were obtained with all <u>voxels perfectly aligned</u> (impossible in real life)

- Spatial and temporal alignment à la HEP detectors using cosmic muons, or external particle beams (as from CERN SPS or a synchrotron light source)
  - Straight muon tracks with **Chi2/NDoF ~1** can be used for space/time alignment between different layers and towers
  - Many particle showers are seen. Maybe this voxel block can be used as an active target for a fixed target experiment? This is subject for another talk…

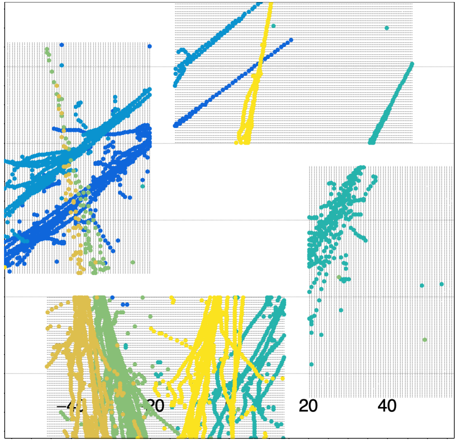
~1 day of cosmic run



Muons tracks with Chi2/NDoF ~1



Muons tracks with multiplicity > 500 pixel clusters



100µPET flip-chip module

Flip-chip verification

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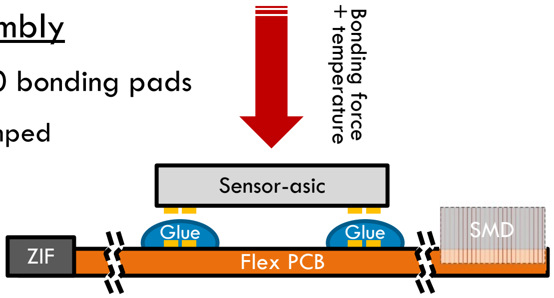
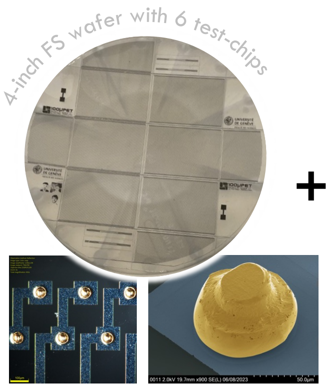
- A **modular** and **compact** scanner design is achieved with ASIC/flex flip-chip assembly
  - ACF/ACP and NCP flip-chip was investigated with dedicated test assemblies with 400-500 bonding pads
    - Pad-wafer produced at CMi-EPFL: 525 µm thick, Ti/Al metal patterning, Au stud or ENIG bumped
    - Flex to probe flip-chip bonding yield: 4 layers, ~180 µm total thickness, ENIG pad finishing
    - Flip-chip machine for the thermocompression using an epoxy adhesive (Araldite 2011), 20 kgf bonding force and 100 °C for 7 minutes





Pads and gold stud

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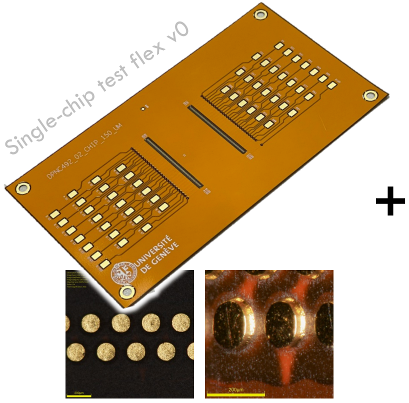

Bonding pads

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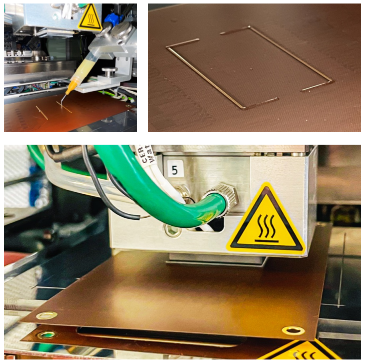
Glue dispensing and bonding



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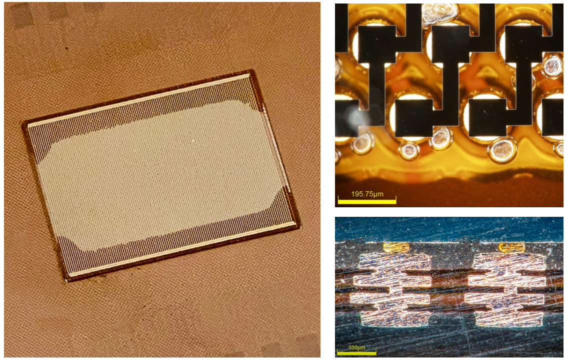
Bonded assembly and cross-section



Flip-chip qualification tests

Temperature cycles (TC) and current injection

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Molecular Imaging at Ultra-High Resolution
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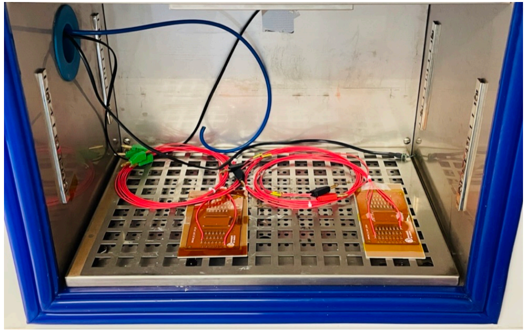
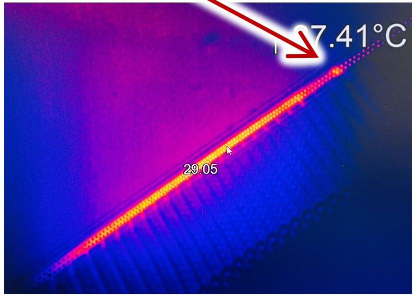
Au studs with NCP bonding was chosen for the assembly

- 100% yield connection among hundreds of pads
- (Direct) Current stress-tests to verify bonding failure
  - Limit DC to 200 mA, avoiding local heating exceeding Tg of the glue (60-80 °C)
    - Visible permanent defects (hot spots – higher bonding resistance) after reaching 300 mA
- 100 TCs from +5 to +60 °C
  - No effect on connections

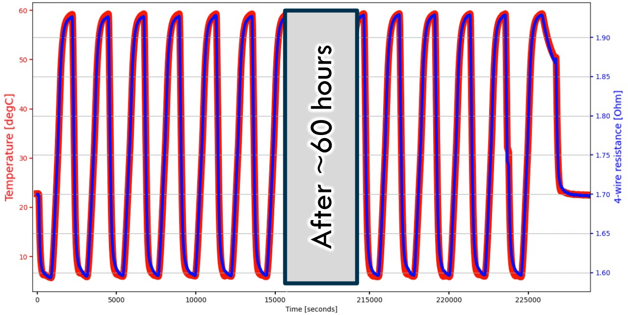
Bonded samples inside climate chamber



Bonded assembly and IR thermal image during DC injection



Temperature and resistance measurement during TC



100µPET pre-production

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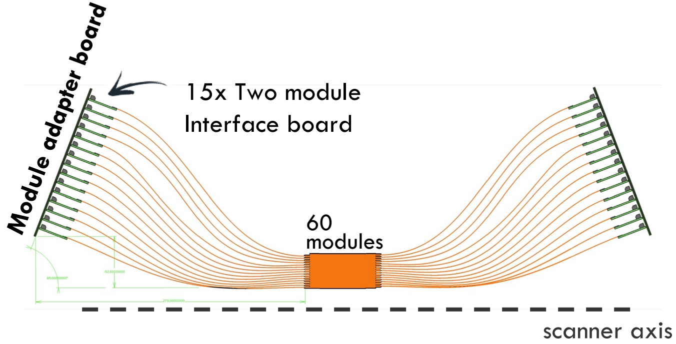
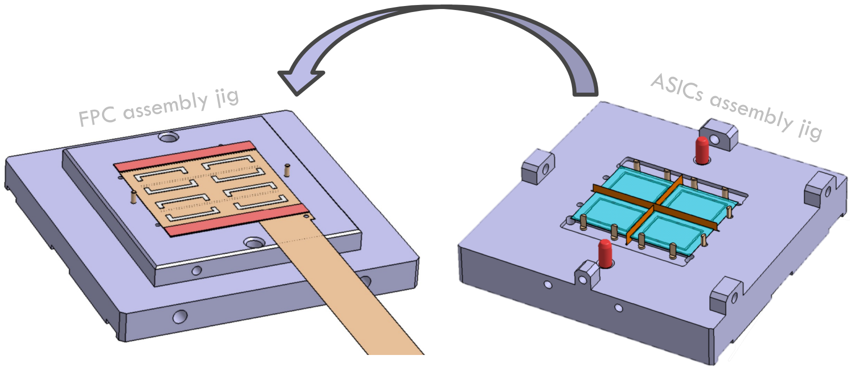
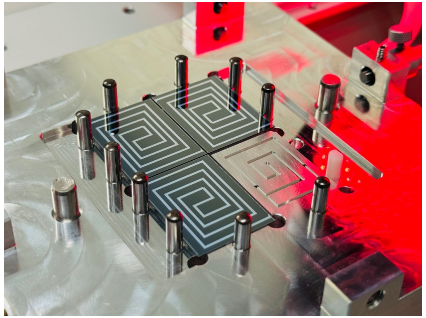
- Electro + thermal + mechanical prototype under design/production
  - Test-chip with the same dimensions, electronic interface and power consumption (resistance heater)
  - Test-flex with the same dimensions, circuit stack-up and ZIF connection to MAB
- Validation of module assembly, layer stacking, cooling performance and back-end connections

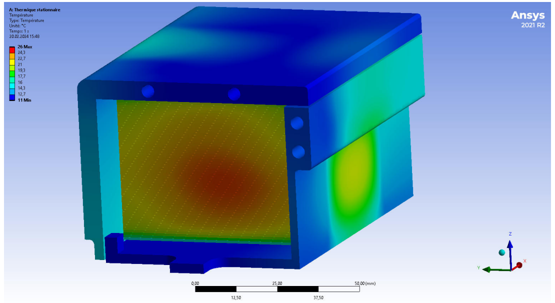




ASICs on jig



FEM simulation of cooling performance



100µPET module demonstrator

Design and production

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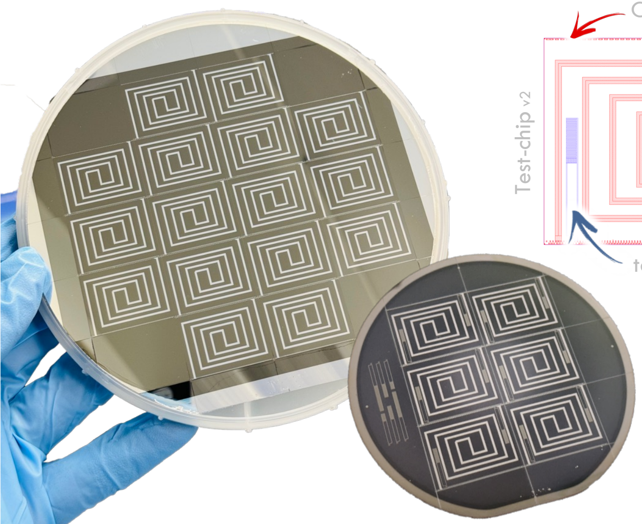
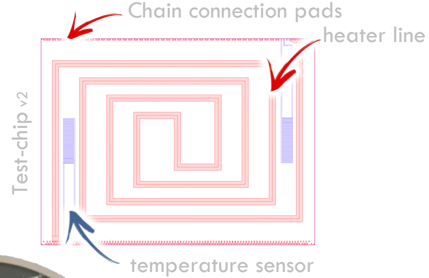
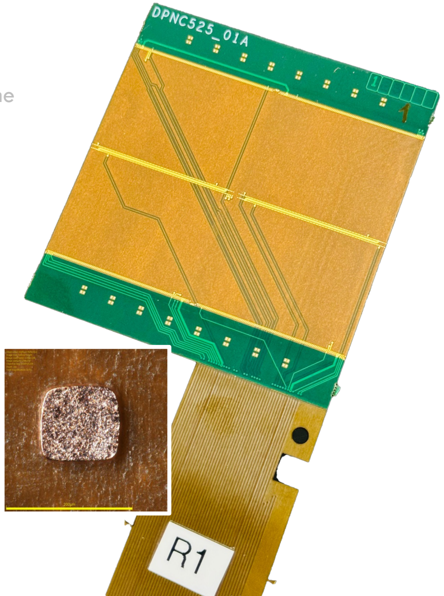
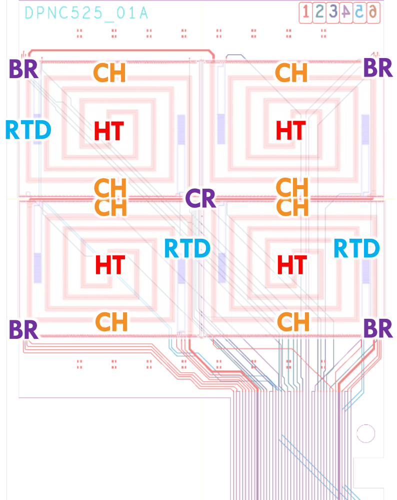
- **240x** 300 µm thick test chips:
  - 4x 4-wire single-bond resistance, 1x resistive heater (1 µm thick Al), 2 RTDs (PT1000-ish), 1x 162-pads chain and 1x 82-pads chain
    - 4x 4-inch wafers produced at NMP-FCBG and 15x 6-inch wafers from CMi (no RTDs)
- **60x** test flex (+ 2x beck-end prototype system)







3x Resistive Temperature Detectors
5x Bond Resistance (4-wires)
4x Heaters in series
8x Chains (4x w/ 162 pads, 4x w/ 82)



100µPET module demonstrator

Reference module

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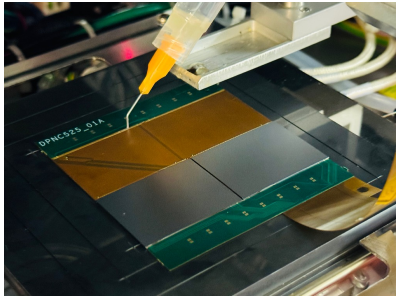
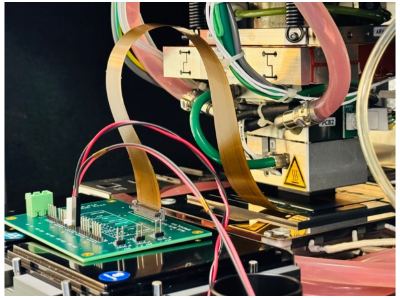
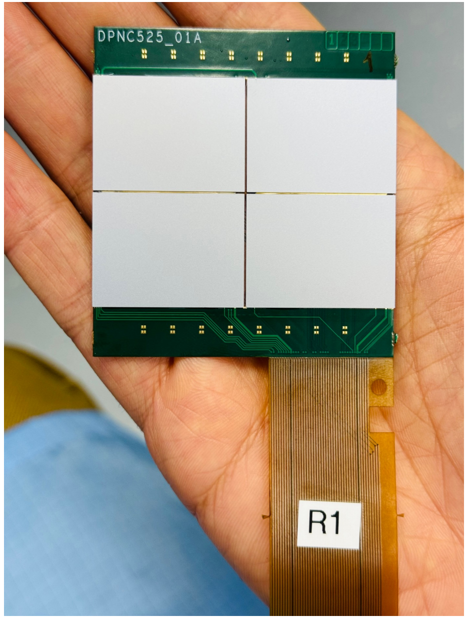
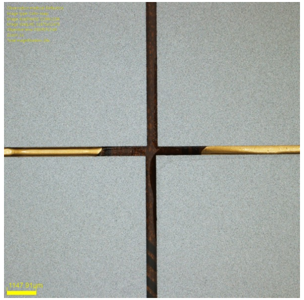
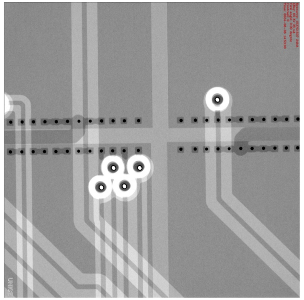
- Bonding reference module with flip-chip machine
  - We are putting in place the data-base tracking, handling the temporary storage, module quality control tests and etc











100µPET module demonstrator

Reference module characterization

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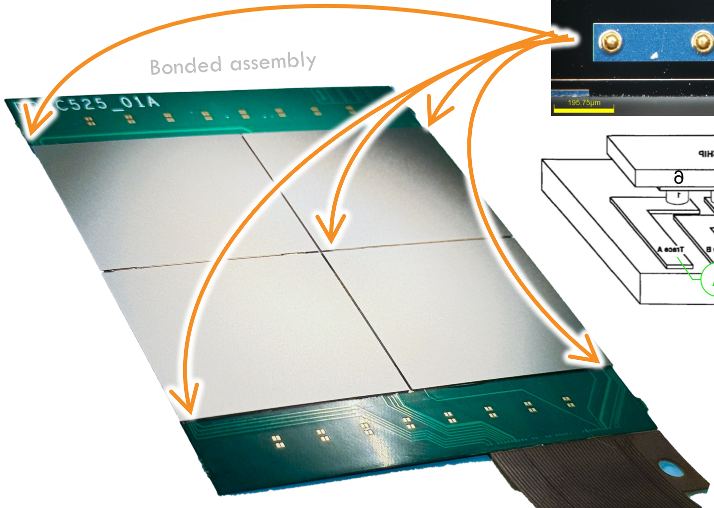
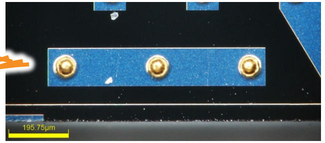
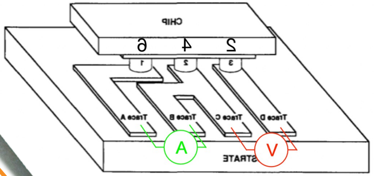
- Bond resistance of **<u>~10 mOhm</u>** and uniform over module's 4 corners and center
- Chains of pads indicating no open connection in ~1000 pads (**bonding yield >99.9%**)
- Heater system is working as expected, with <u>8°C</u> increase in temperature at <u>nominal module power (2W)</u>

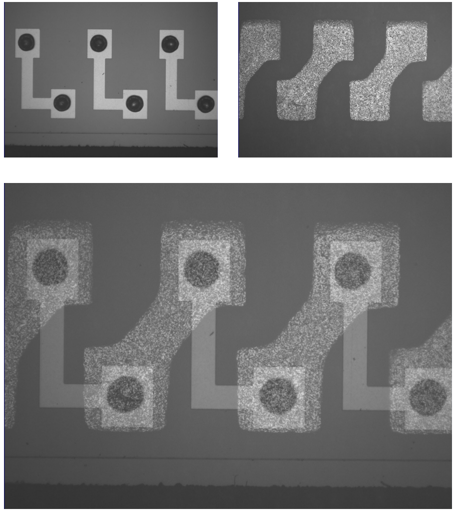


Pads for single-bump 4-wire measurement

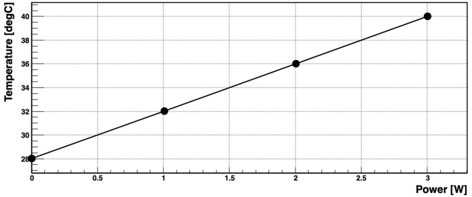


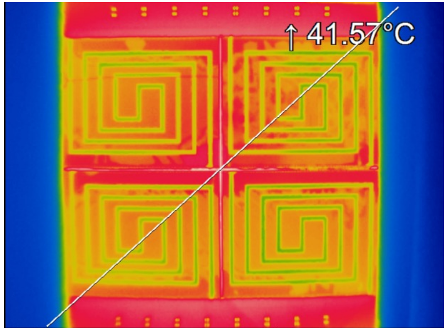


Pads for chain continuity test



Power injection on heater and thermal image





Summary and conclusions

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- Potential ultra-high-resolution molecular imaging using **MAPS**
  - 5% and **3.3% scanner sensitivity** (w/ or w/o Bismuth layer)
  - **0.21 mm** FWHM **PSF** → **0.017 mm^3** volumetric resolution
- ASIC designed within the UniGE DPNC group (ETA Sept 2024)
  - Monolithic SiGe; flip-chip bonding integration; **150 µm** pixels; **200 ps** time resolution (**~1ns** coincidence time-window)
- Flip-chip integration qualified with test-chips
  - Characterization tests indicates **good yield** and **reliability**
- Module and Tower demonstrators under construction
  - Module reference assembled and qualified.
- Side-task: simulations with High Z sensors
  - Lower the number of layer, scaling the assembly to larger areas
    - Interlaying Si with High Z, a single tower can be used as a Compton camera, allowing simultaneous PET and SPECT in the new scanner
    - Polarization measurement of photons allows scatter/random rejection (better SNR) using the entanglement information from the photons