THE PICOSEC MC-NET PROJECT

ENDO TOFPET US
Endoscopic TOFPET & Ultrasound

MARIE CURIE ACTIONS

EndoTOFPET-US: an endoscopic Positron Emission Tomography detector for a novel multimodal medical imaging tool

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on behalf of the EndoTOFPET-US collaboration

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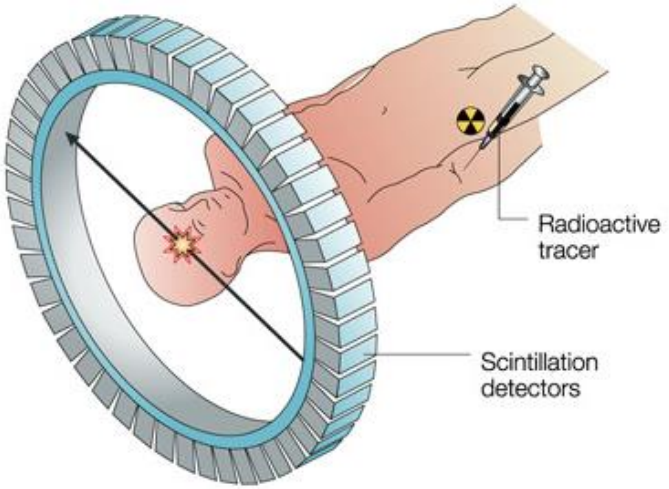
Outline

- Introduction and motivation
- EndoTOFPET-US detector
- External plate
  - Photodetector and crystals
  - Readout ASICs
  - Integration
- Internal probe
- Simulations and image reconstruction
- Conclusions and outlook

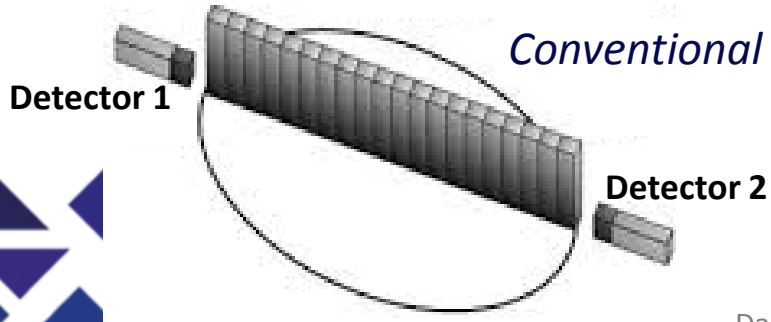
PET principles

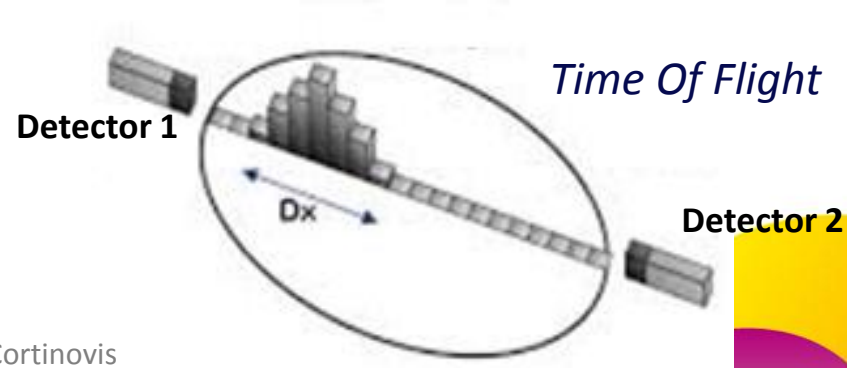
- **PET is a non-invasive, diagnostic imaging technique for measuring the metabolic activity of cells in the human body**



- β^+ radio-labeled compound (e.g. ^{18}FDG) is injected in the patient
- The positron annihilates with e^- from tissue, forming back-to-back 511 keV photon pair
- 511 keV photons detected in time coincidence
- Image reconstruction

Time Of Flight (TOF) PET uses TOF information to reduce background from neighboring organs



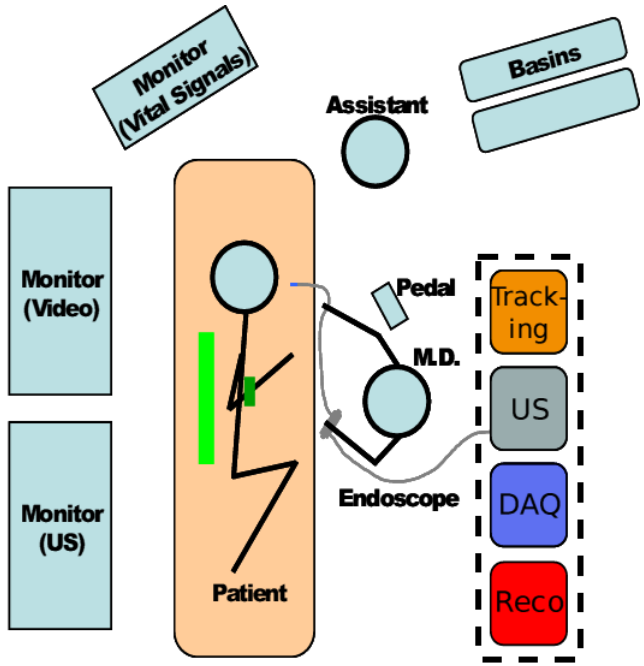


Medical requirements

Pancreatic cancer
- No early symptoms
- Low survival rate
- Imaging with US and CT

Prostate cancer
- Most frequent cancer in men
- Early detection improves prognosis
- Imaging with US and MRI

Limitations of standard full body PET, small organs and proximity to sources of background noise



EndoTOFPET-US

GOAL: ***Test of newly specific developed biomarkers***

- **Endoscopic approach → High spatial resolution**
- **Time Of Flight → High Signal to noise ratio**

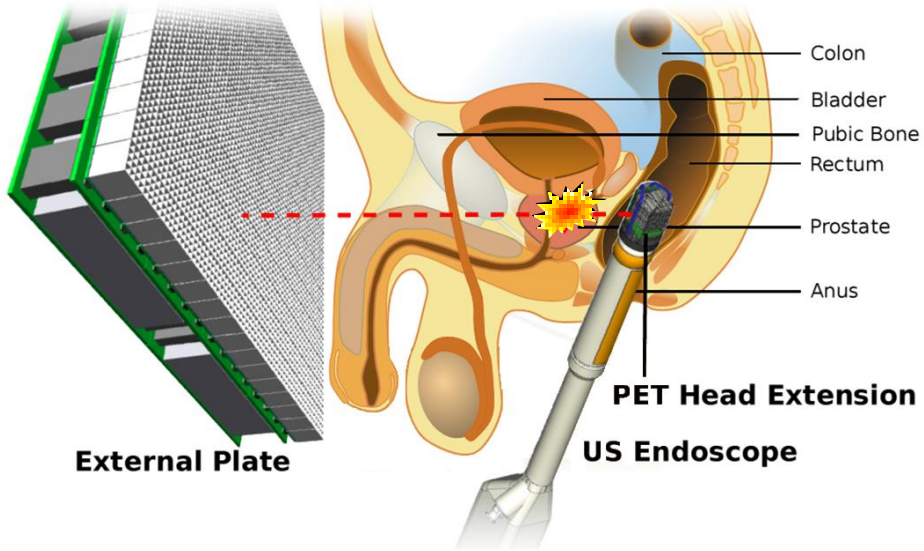
✓ ***Image guided surgery***

EndoTOFPET-US

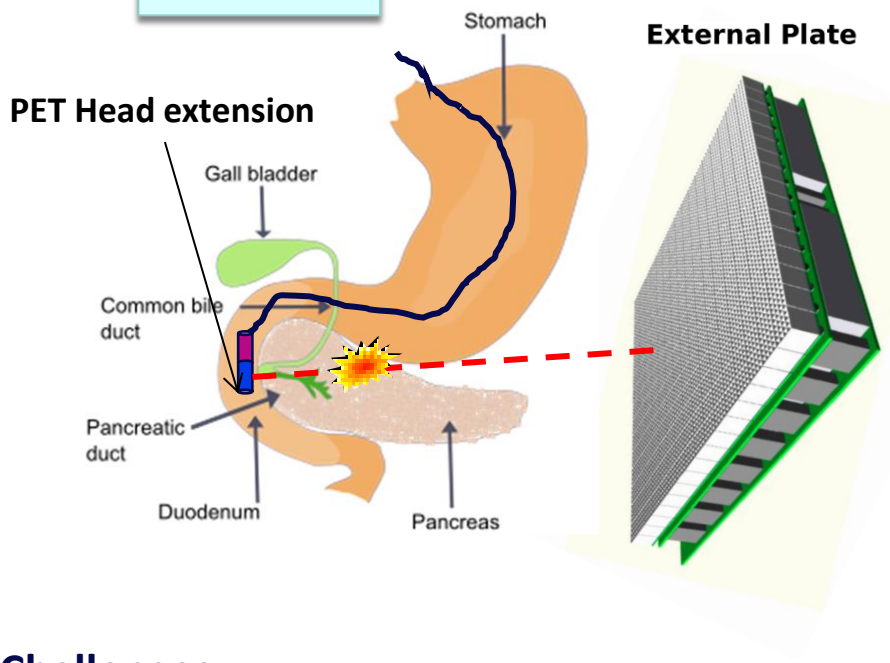
Endoscopic Time-Of-Flight PET & UltraSound

ENDO TOFPET US
Endoscopic TOFPET & Ultrasound

Prostate



Pancreas



➢ The system:

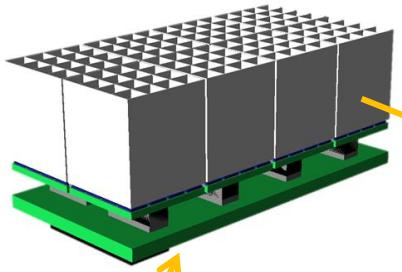
- PET detector mounted on an endoscopic ultrasound probe (two versions)
- External PET detector

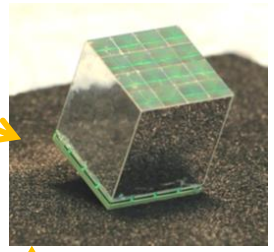
➢ The Challenges:

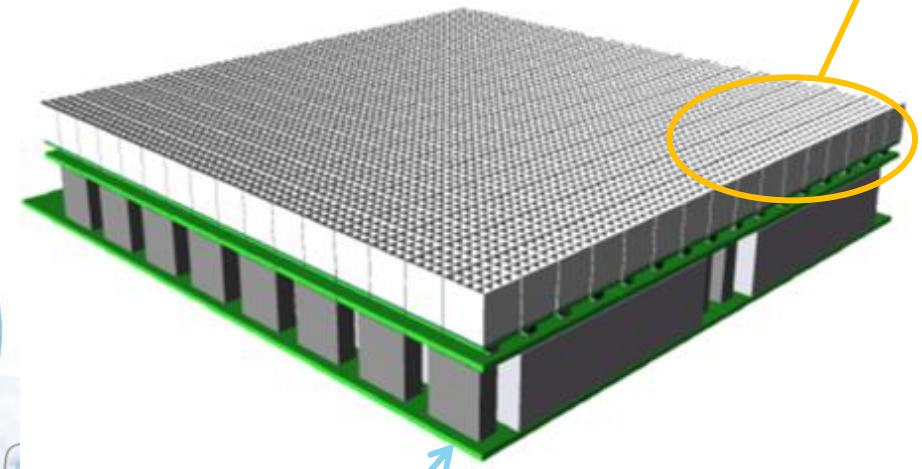
- Asymmetric design
- Fusion between US and PET images
- Excellent time resolution: **200 ps FWHM** (3 cm)
- 1 mm spatial resolution (PET image)

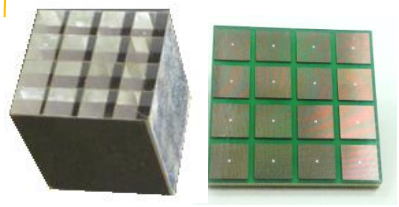
External plate design

- Plate area: **23 x 23 cm²**
- 4096 channels
- Dedicated ASICs
- Cooling embedded in detector housing
- Mounted on a movable arm









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4x4 LYSO:Ce crystals

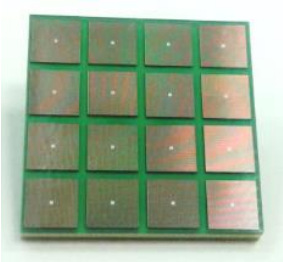
+

Hamamatsu MPPC (SiPM)

4x4 discrete array

Components characterization

- **Characterization of all 4096 SiPMs (256 arrays) for the external plate**



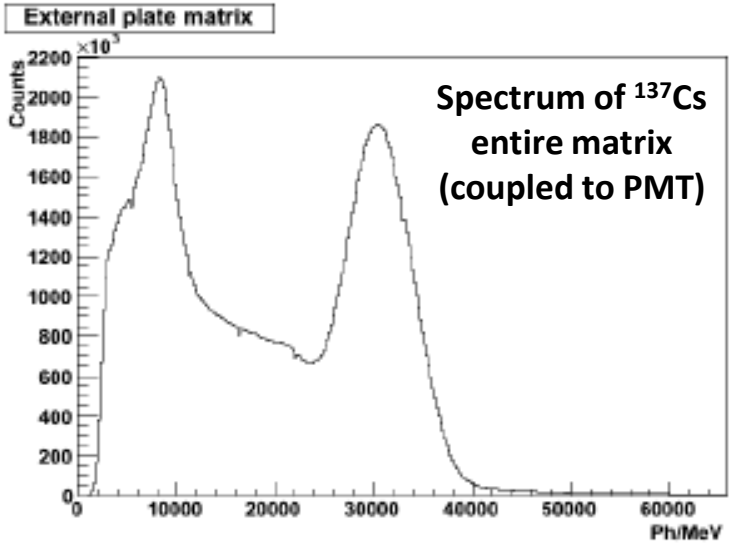
Through-Silicon-Via (TSV)
4x4 **MPPCs**
3 x 3 mm^2 active area

Quantity	Average value
Gain	(**0.48** ± 0.02)x**10^6** V^{-1}
Breakdown voltage (U_{bd})	**64.29** ± 0.2 V (@25 °C)
Dark Count Rate	**1.4** ± 0.4 **MHz** (@25 °C)
Correlated noise	~ **30%**
U_{bd} temp. dependence	**70.1** mV/°C

- **4x4 LYSO:Ce scintillators**
  - Crystal size 3.5 x 3.5 x 15 mm^3
  - Crystal pitch 3.6 mm
  - Coating: ESR reflector by 3M

- Excellent light yield: **32000 Ph/MeV**

  High light yield → High time resolution



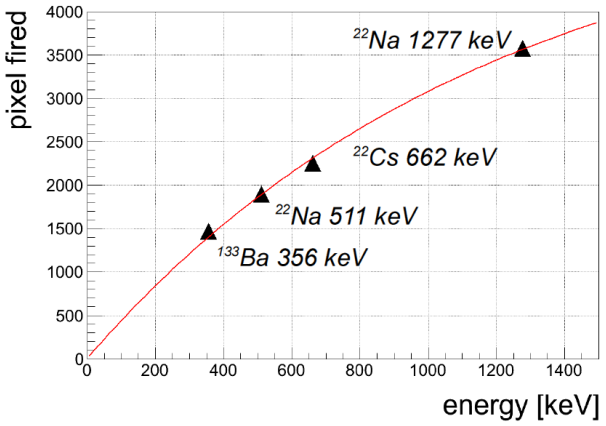
Detector modules characterization

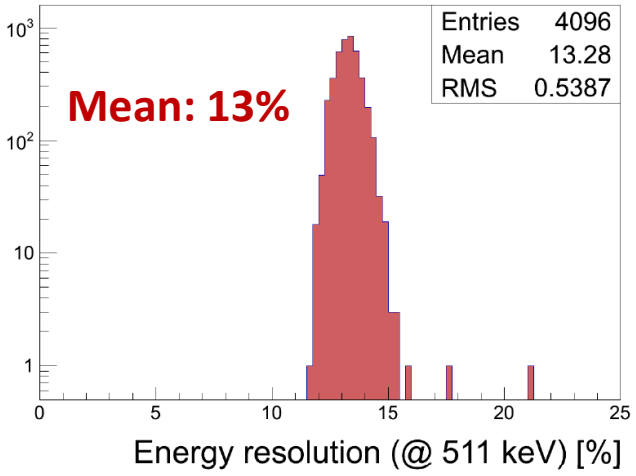
Energy resolution

SiPM has non-linear response due to the limited number of pixels

Linear correction and energy calibration is necessary

SiPM saturation curve for different gamma energies



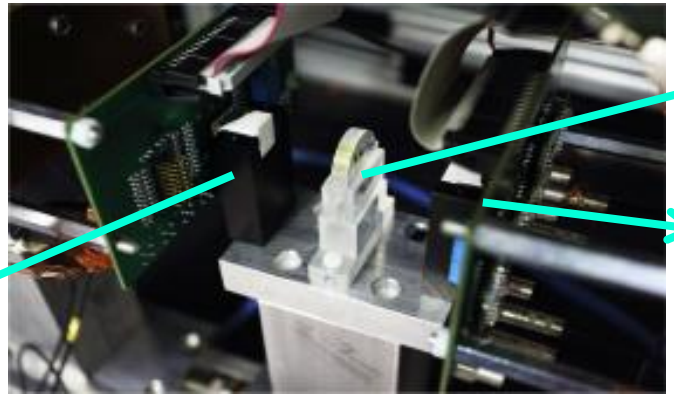


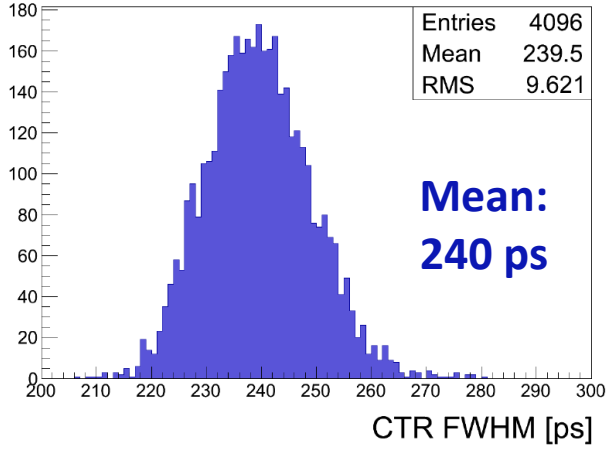
✓ 20% minimum required

Coincidence Time Resolution

Coincidence between two modules (1 is fixed as reference)

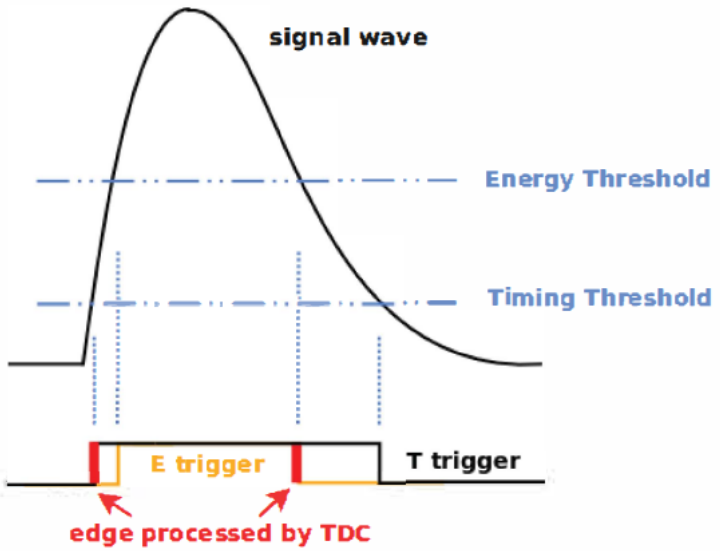
Read out provided by ASIC NINO





✓ Close to the goal of 200 ps

External plate ASICs



- **Timing** measurement: leading edge technique
- **Energy** measurement: Time-over-Threshold method

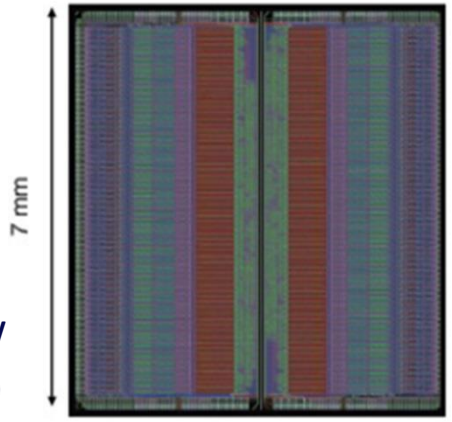
Requirements:

- Large channel density (4096 channels in 23 x 23 cm^2)
- Low noise, low timing jitter (< 30 ps)
- Low power consumption (<20 mW/ch)
- SiPM bias tuning (500mV adjustment range)

Two options:

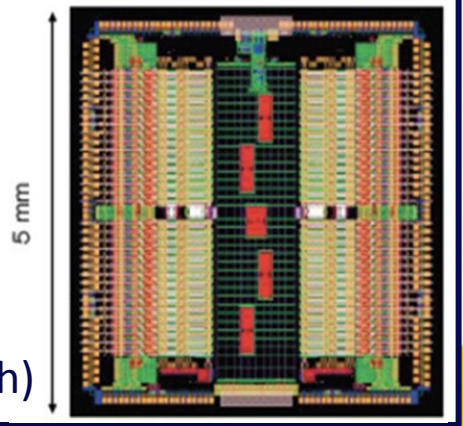
TOFPET

- Developed by LIP
- 128 channels
- Analog-based integrated TDC
- Optimized for low power (8 mW/ch)



STiC 3.0

- Developed by KIP
- 64 channels
- Digital-based integrated TDC
- Optimized for noise immunity (19 mW/ch)

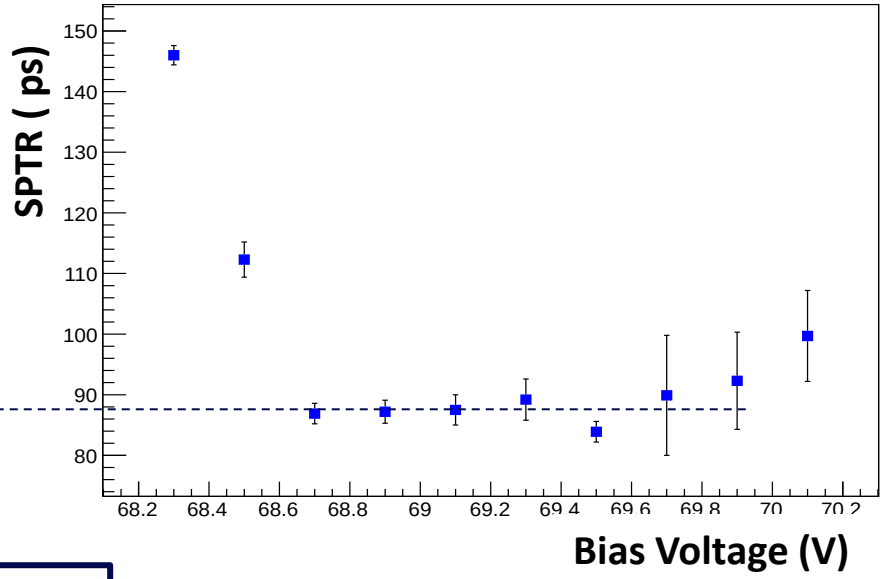


TOFPET

➢ **Single Photon Time resolution**

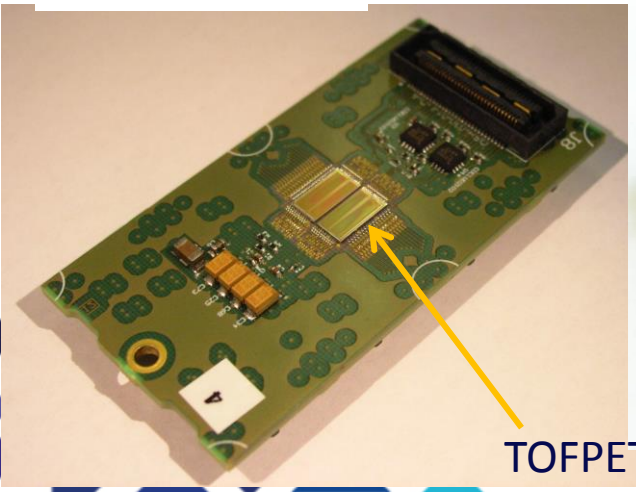
Measurement with single-photon laser pulse

~ 90 ps r.m.s

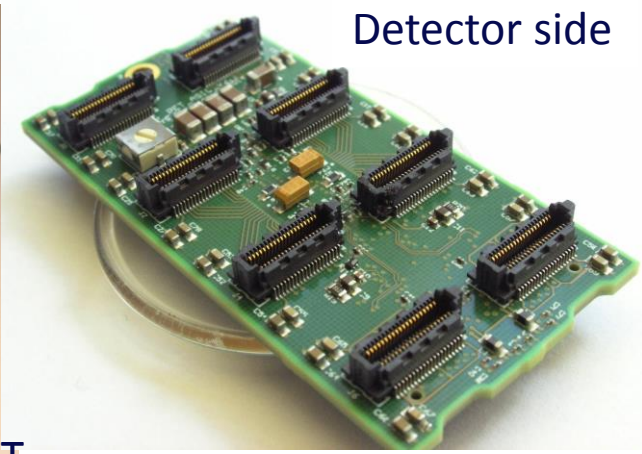


➢ **Final front end board:**

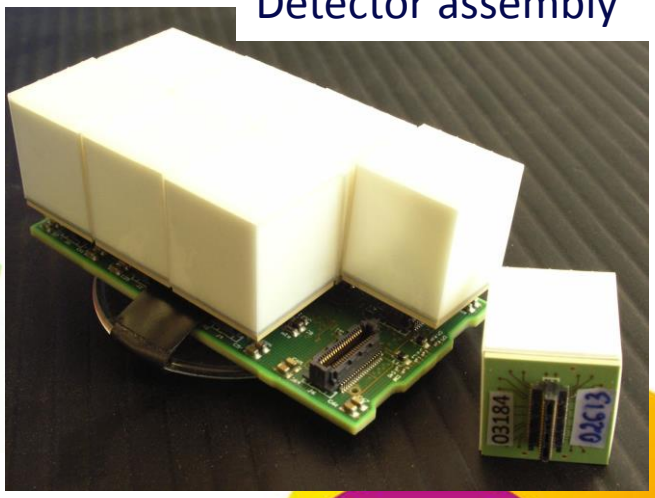
Cold plate side



Detector side

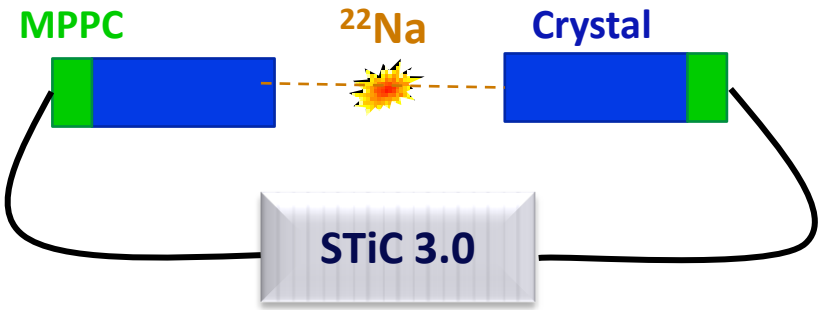


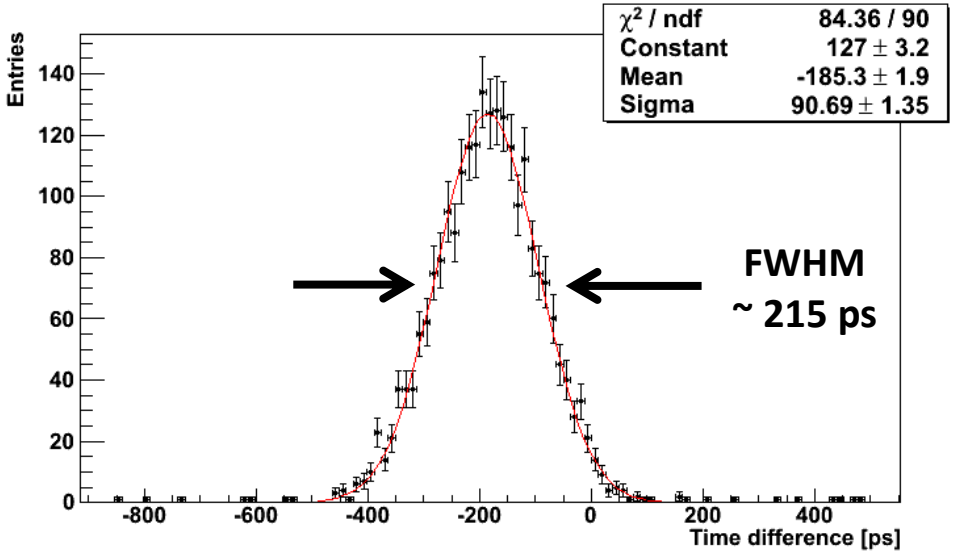
Detector assembly



STiCv3.0

➢ Coincidence Time Resolution:





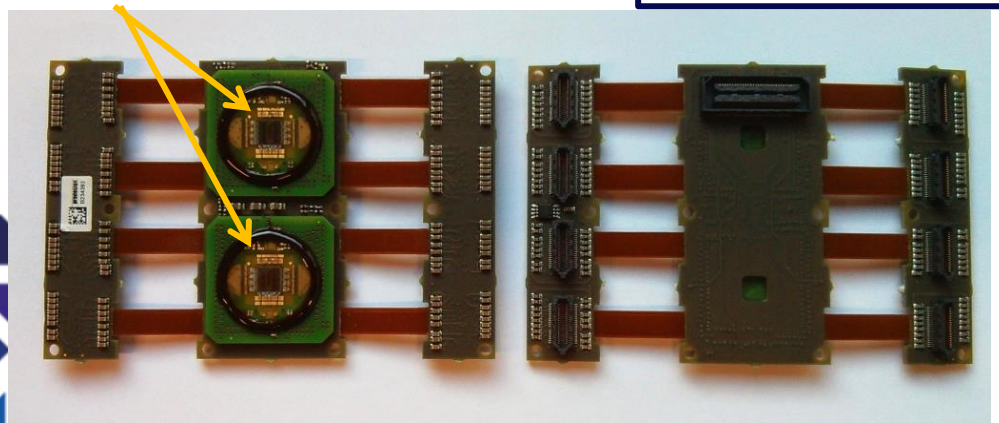
Crystals: LYSO 3.1x3.1x15 mm³

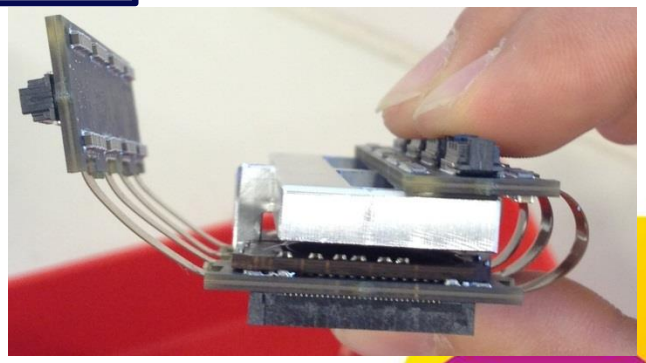
MPPC: Hamamatsu MPPC S12643-050CN(X)

Temperature: 18 °C

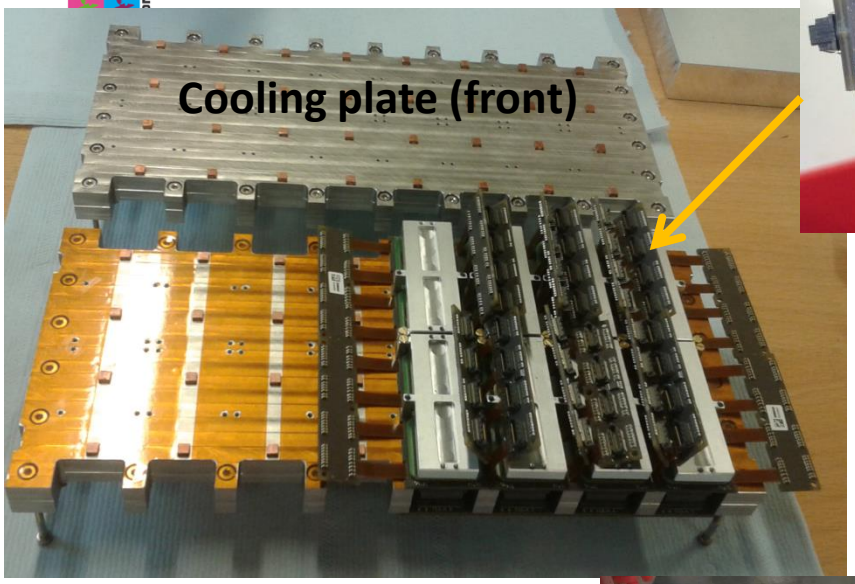
➢ Final front end board:

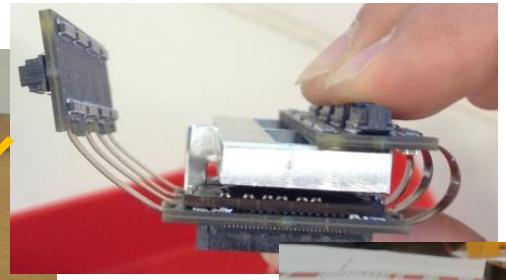
STiC 3.0



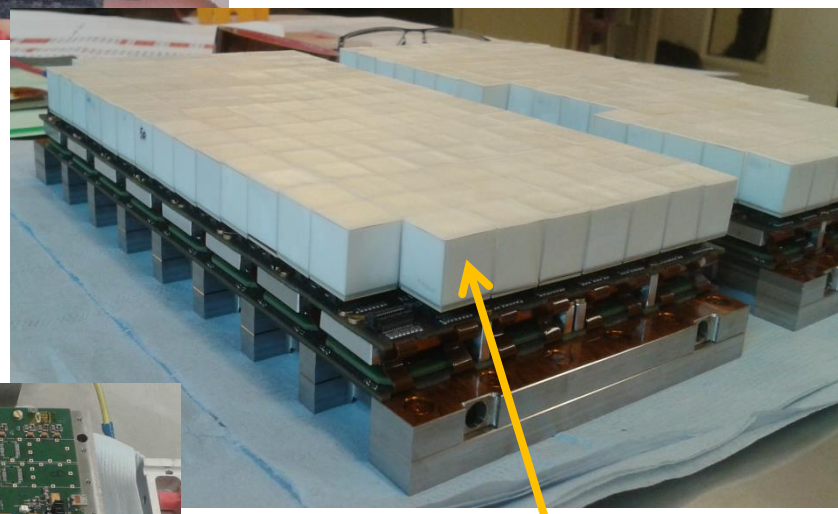


External plate integration

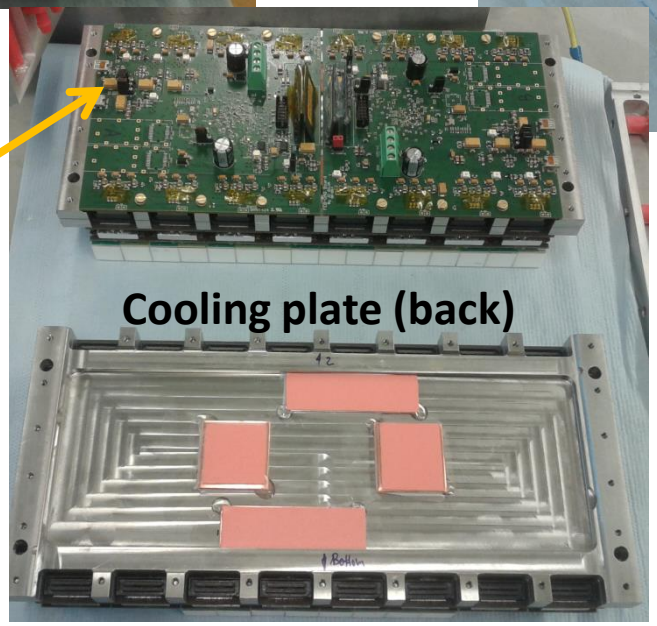




STiC 3.0 FEB/A

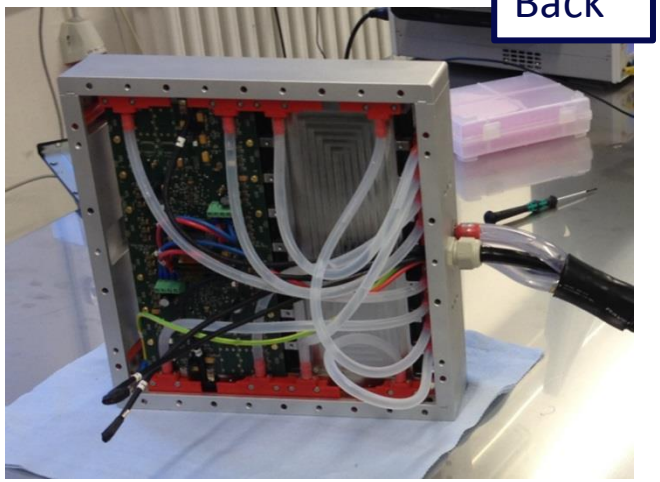


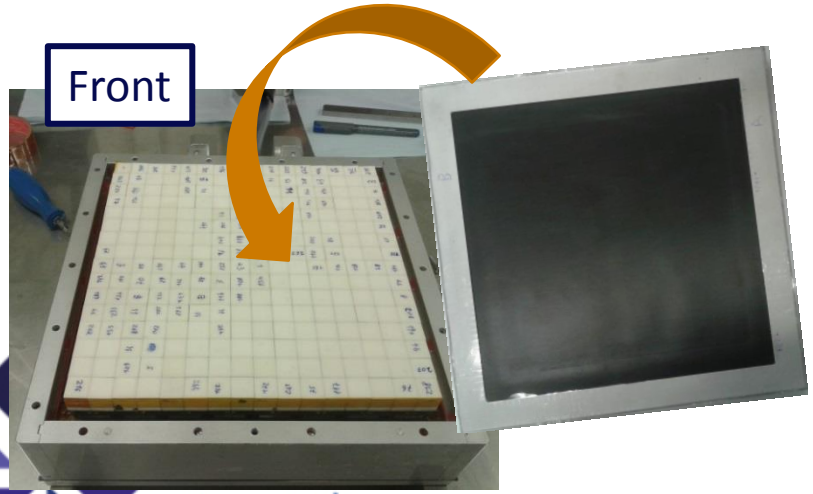
FEB/D

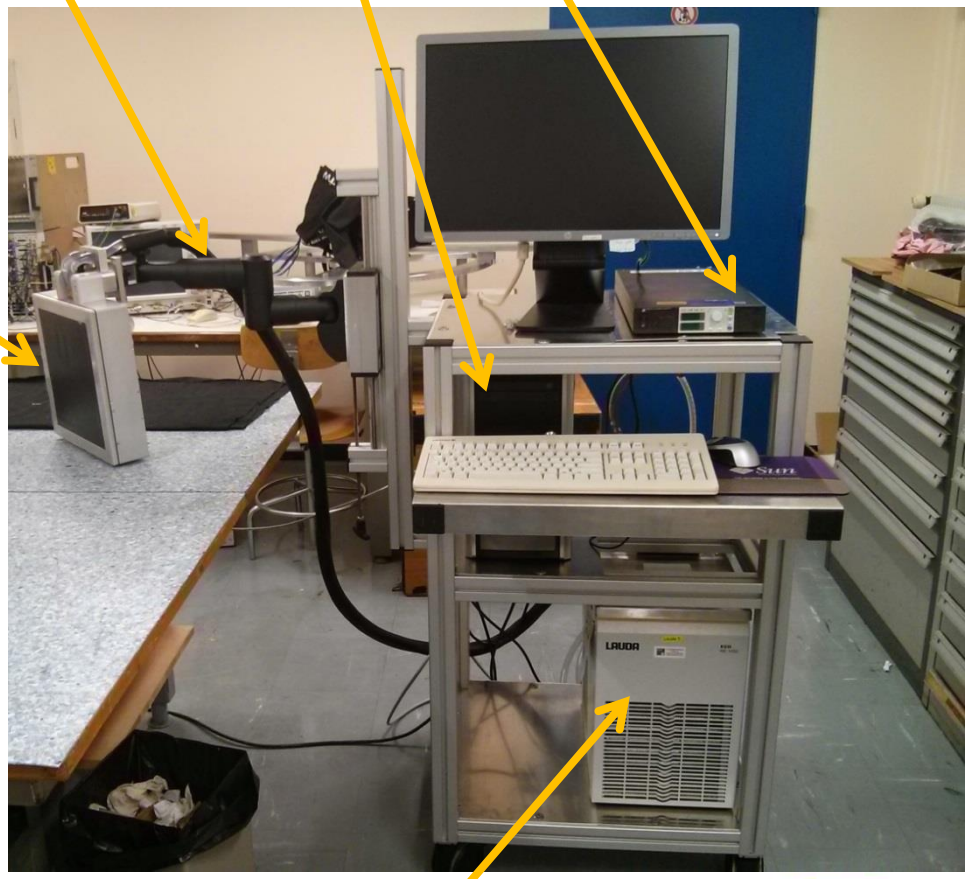


Crystals + MPPC module

External plate Integration



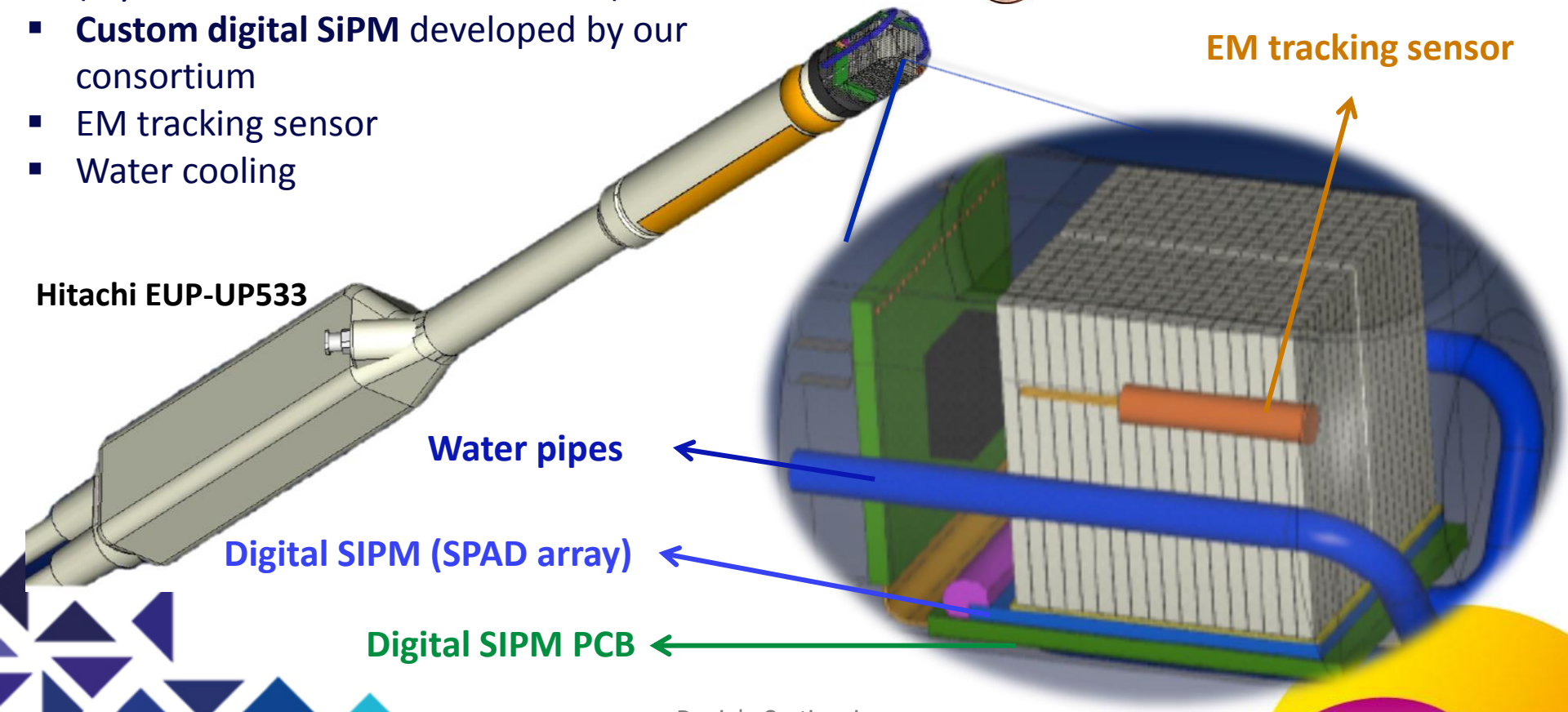




Endoscope extension (prostate)

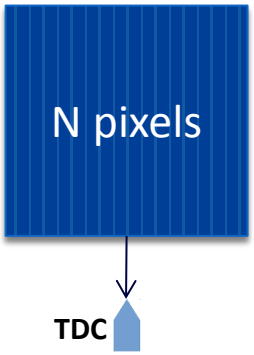
- Clamped on **US endoscope**
- 1 or 2 crystal matrices of **LYSO:Ce scintillators** (crystal size: 0.71 x 0.71 x 10 mm^3)
- **Custom digital SiPM** developed by our consortium
- EM tracking sensor
- Water cooling

➢ **23 mm** diameter



Multi-channel Digital SIPM

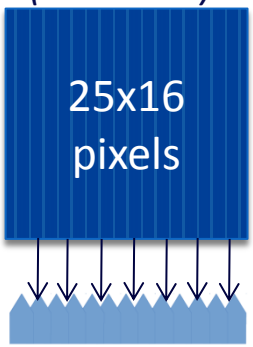
Standard analog SiPM



1 single timestamp

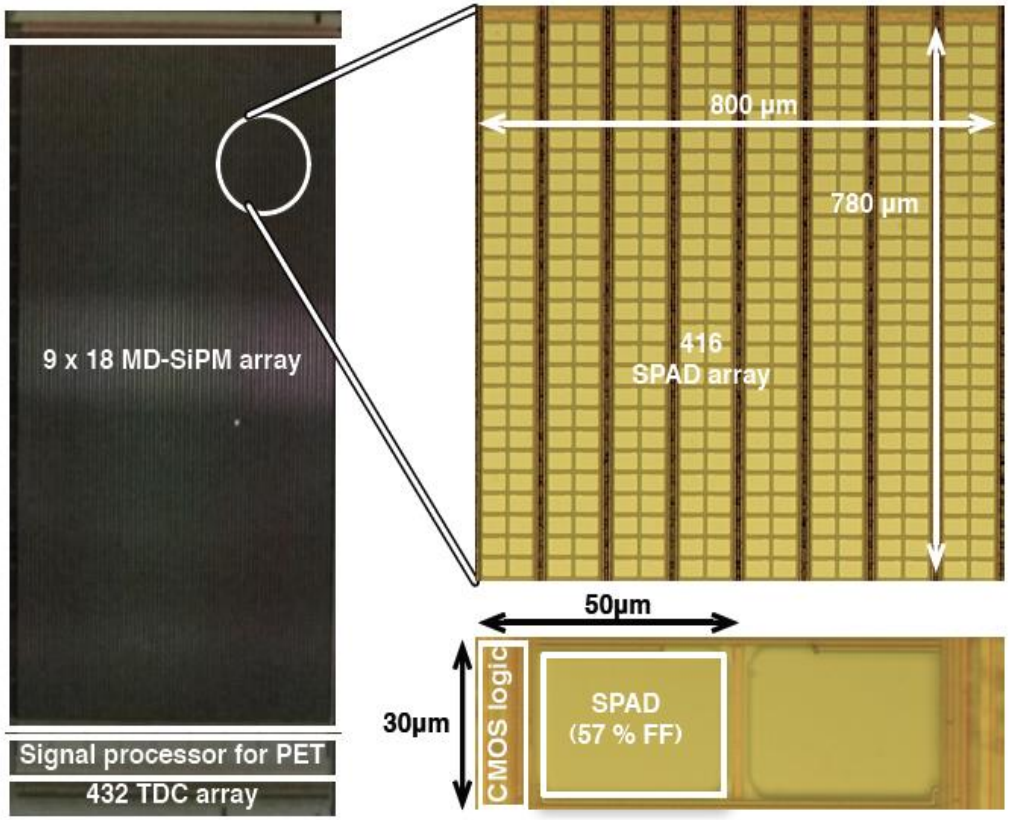
MD SiPM

(1 cluster:)



48 individual timestamp

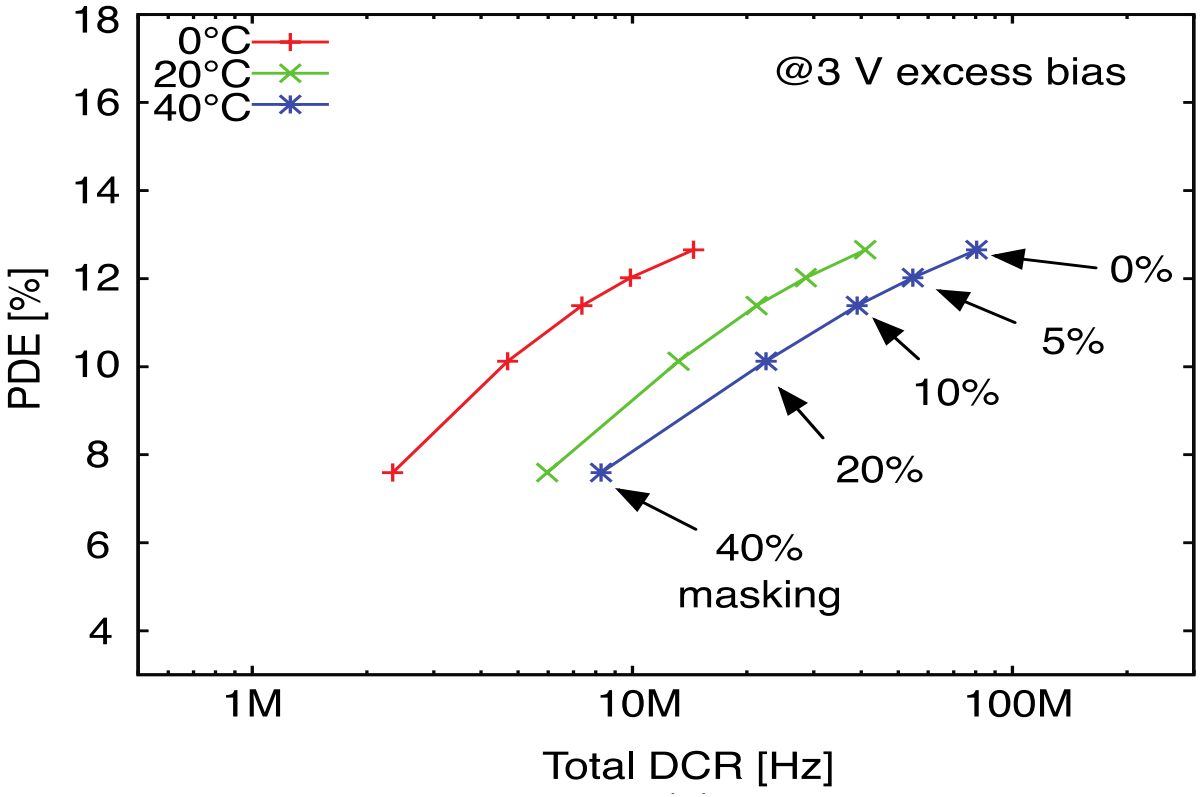
(1 cluster:)



- 9x18 clusters
- 50 x 30 µm^2 SPADs
- Active quenching
- Smart reset
- Masking high DCR channels

- **Timing:** 416 pixels / SiPM with single bit count
- **Energy:** 48 TDC / cluster < 50 ps time bin

Multi Digital SIPM
prototype characterization

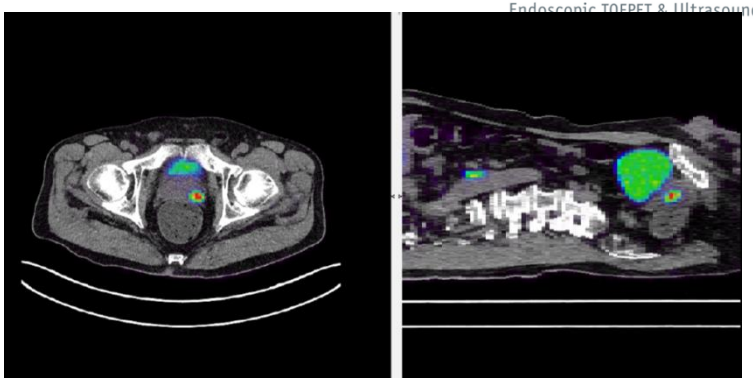


- High Dark Count Rate (DCR), but able to mask noisy pixels
- 41 MHz DCR without masking (20 °C, 3 V excess bias)
- **23 MHz** with **10 % masking**
- Photon Detection Efficiency **(PDE) ~ 12%**
- Additional cooling necessary

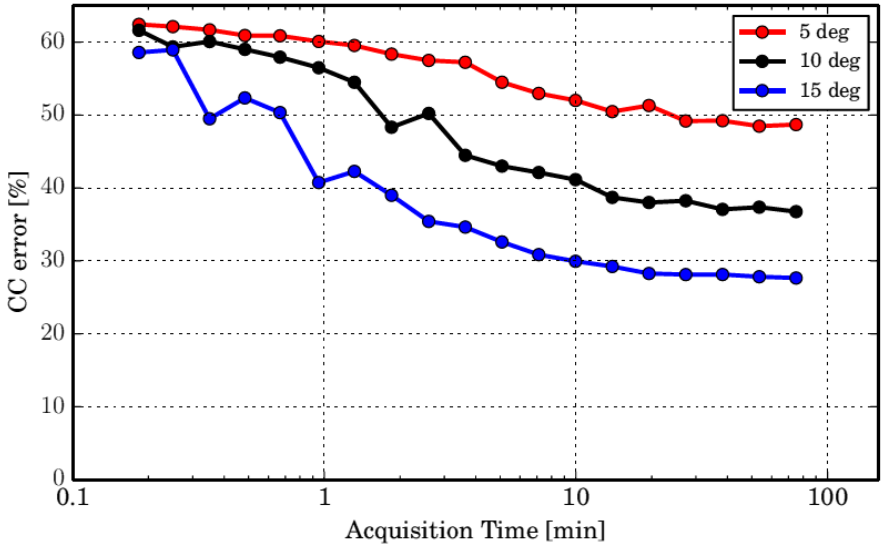
Full system simulation and image reconstruction

- Dedicated software framework for simulation of asymmetric, non-rigid, freely-moving detector system based on GAMOS
- Full-body PET/CT DICOM import
- Parallelization on computing cluster
- Custom iterative image reconstruction based on ML-EM

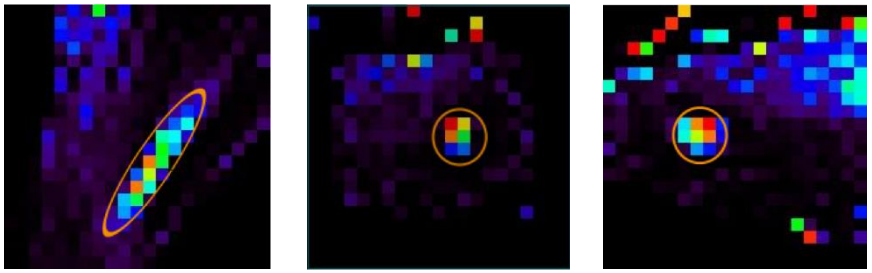
- Image resolution of about 1 mm possible
- Scan time of about 10 minute sufficient
- Some detector movement is beneficial



Full-Body PET/CT scan with prostate-specific membrane antigen (PSMA)



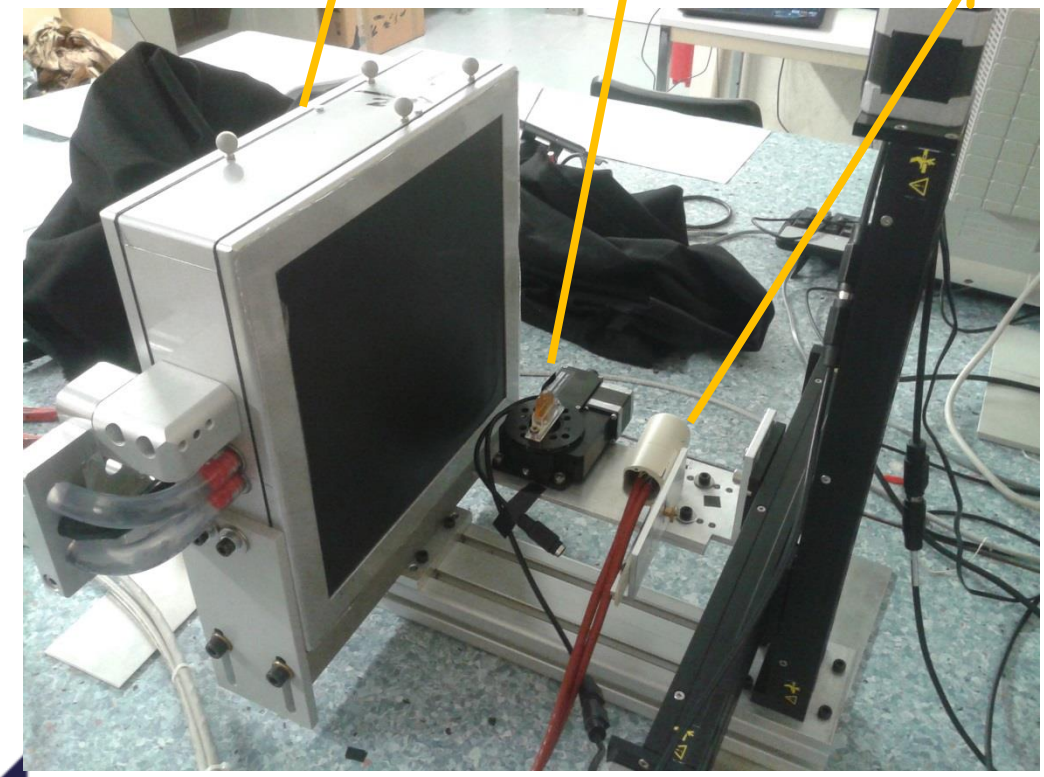
Cross correlation (CC) error (image quality) vs. scan time



(a) transverse (b) Coronal (c) Sagittal

Reconstructed image of the prostatic lesion of this patient after 3 min acquisition

First prototype commissioning



FIRST PROTOTYPE:

- EndoTOFPET-US external plate (3072 channels)
- Temporary internal probe
  - 32 crystals of 3.2x3.2x15 mm^3
  - 2 Hamamatsu 4x4 MPPCs
  - Readout with TOFPET ASIC

✓ System integration with the DAQ
✓ System validation
✓ Detector calibration

✓ Delivered to Marseille hospital for pre-clinical tests

Conclusions and outlook

- ✓ **EndoTOFPET-US is a novel multimodal imaging tool specifically developed to improve the diagnosis for pancreatic and prostate cancer**
- ✓ **Technology transfer from High Energy Physics to medical imaging**

- ✓ **Very challenging system:**
  - **Extreme miniaturization**
  - **Asymmetric design**
  - **Coincidence Time Resolution of 200 ps FWHM**
  - **Spatial resolution of 1 mm**
  - **Fusion with US**

✓ **Successful commissioning of the first EndoTOFPET-US prototype**

✓ **Prototype delivered to Marseille hospital for pre-clinical tests**

PICOSEC

MARIE CURIE ACTIONS

ENDO TOFPET US

Endoscopic TOFPET & Ultrasound

Thanks for your attention!

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PEOPLE

CERN TU Delft DESY fiberoptics UNIVERSITÄT HEIDELBERG KLOÉ LIP UNIVERSITÀ DEGLI STUDI DI MILANO BICOCCA TECHNISCHE UNIVERSITÄT MÜNCHEN life.augmented SURGICeye