Paris-Saclay Multimodal Biomedical Imaging Lab

CaLIPSO group: development of the ultra-fast gamma detectors for particle physics and Positron Emission Tomography

Viatcheslav Sharyy
Dominique Yvon

DPhP's CSTD
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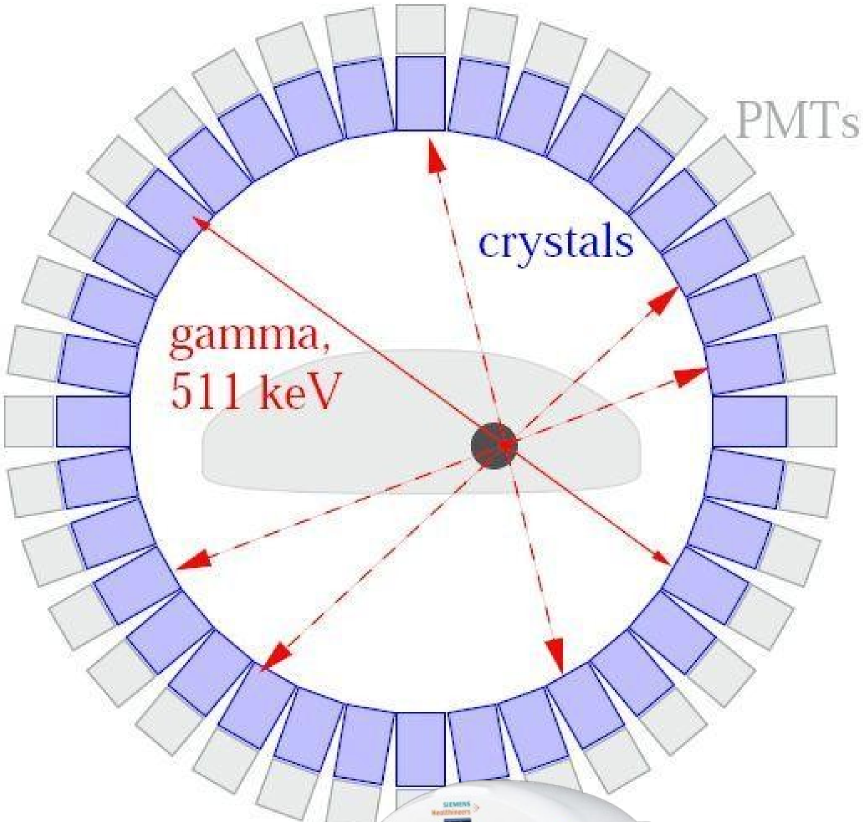
Introduction

- Fast photodetectors :
  - Timing layers at LHC
  - Cherenkov detectors for particle identification
  - Timing measurements at test beams
- Time-of-Flight Positron Emission Tomography
- Main components:
  - Cherenkov Radiators or Fast Scintilation Crystals
  - Fast photodetectors: MCP-PMT / SiPM
  - Dedicated electronics
  - Adequate time reconstruction for signals and events

Positron Emission Tomography

- PET is a nuclear imaging technique used widely in oncology, cardiology and neuropsychiatry.
- Allows to detect at pico-mol level the the biochemical activity.
- PET scan in a nutshell:
  - Inject one of the radioactive tracer

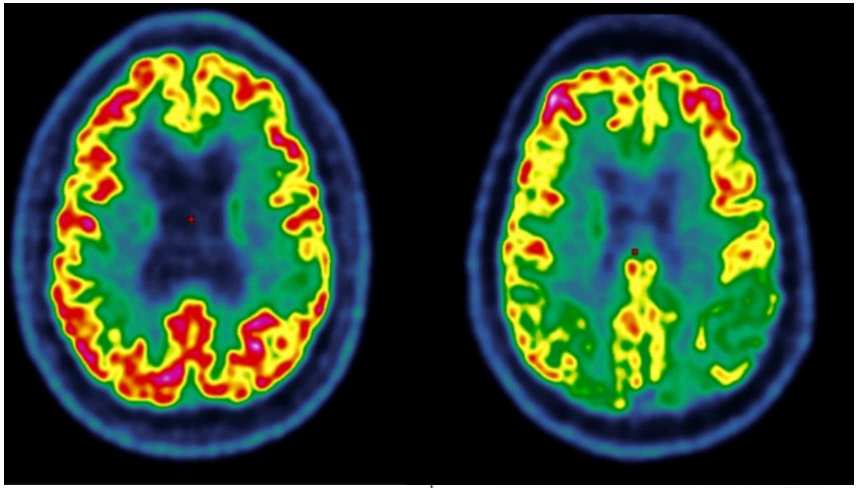
    e.g. ^{18}F-FDG, τ∼110 min, ~1/2 hour rest time
  - emits positrons ⇨ annihilation with an electrons ⇨ two 511 back-to-back gamma.
  - Gamma detection in coincidence ⇨ register ~100M lines-of-responce ⇨
  - 3D image reconstruction

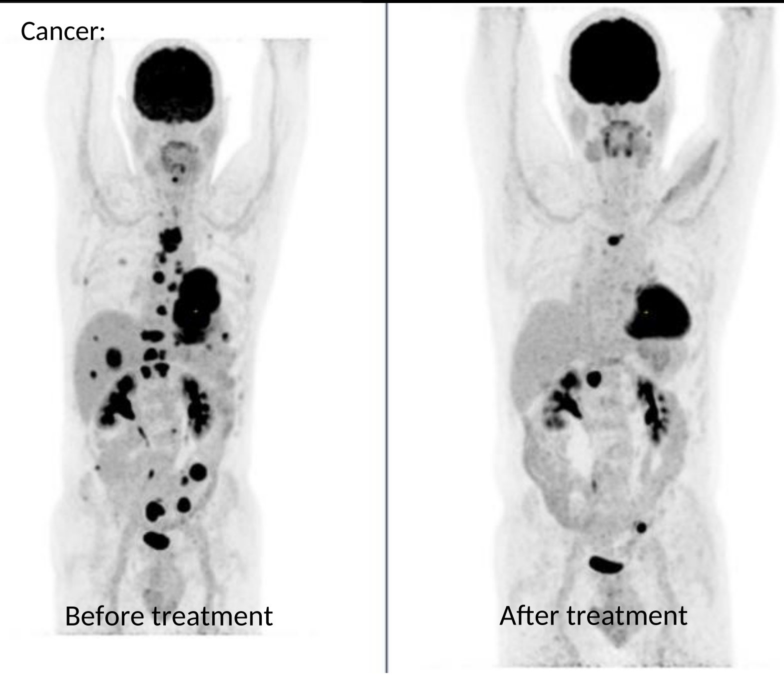


SIEMENS Biopgraph Vision PET/CT scanner
Credit: https://www.siemens-healthineers.com

Scanner Types

- Preclinical (small animals)
  - Small aperture
  - High spatial resolution (~1 mm)
  - Small sensitivity
- Brain scanner
  - Limited aperture
  - High sensitivity
  - Good spatial resolution (1.6 - 3 mm)
- Whole-body
  - Large aperture (~ 0.9 m)
  - High sensitivity
  - Low spatial resolution (4 - 6 mm)
  - Full body dose ~ **5 – 15 mSv** (natural radioactivity per year France : 2 mSv)

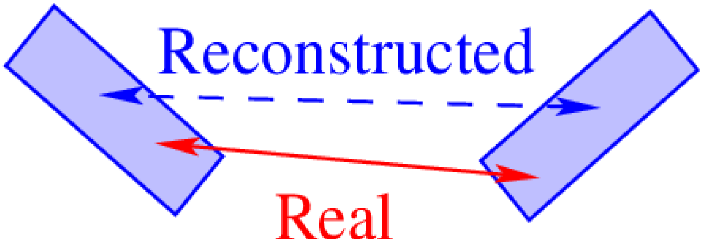




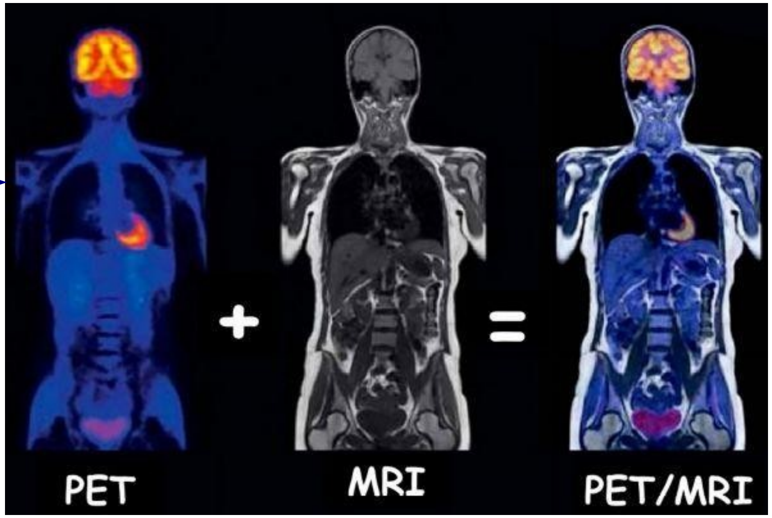
Credit: SHFJ

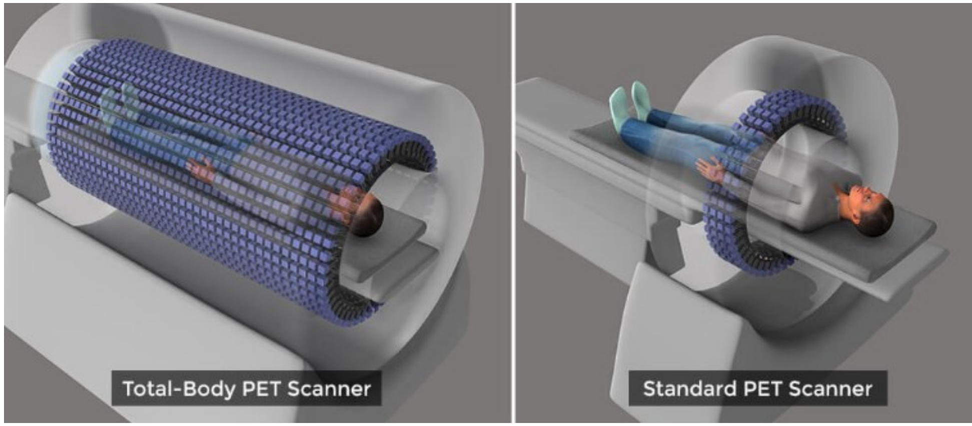
PET Evolution

- Combined modalities: CT/PET, MRI/PET
- Improvement sensitivity: total-body PET
  → 40 fold improvement in sensitivity
- *Reduce bias: depth-of-interaction reconstruction*



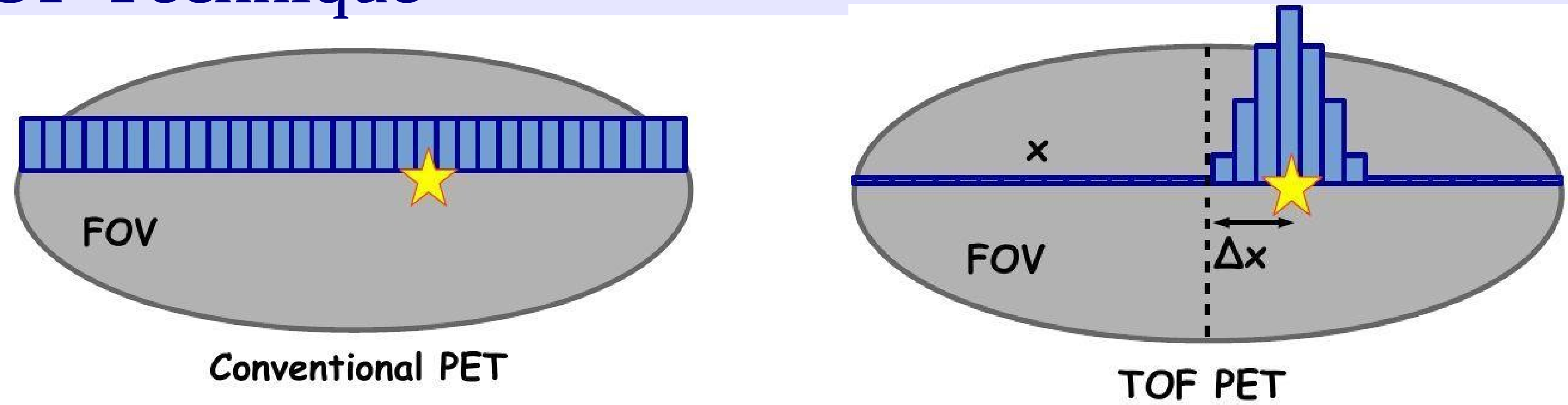
- Time-of-flight technique (TOF) ⇨ see next slides
- New developments in electronics, and gamma-detection





Credit: Simon R. Cherry, University of California, Davis
https://www.cancer.gov

TOF Technique



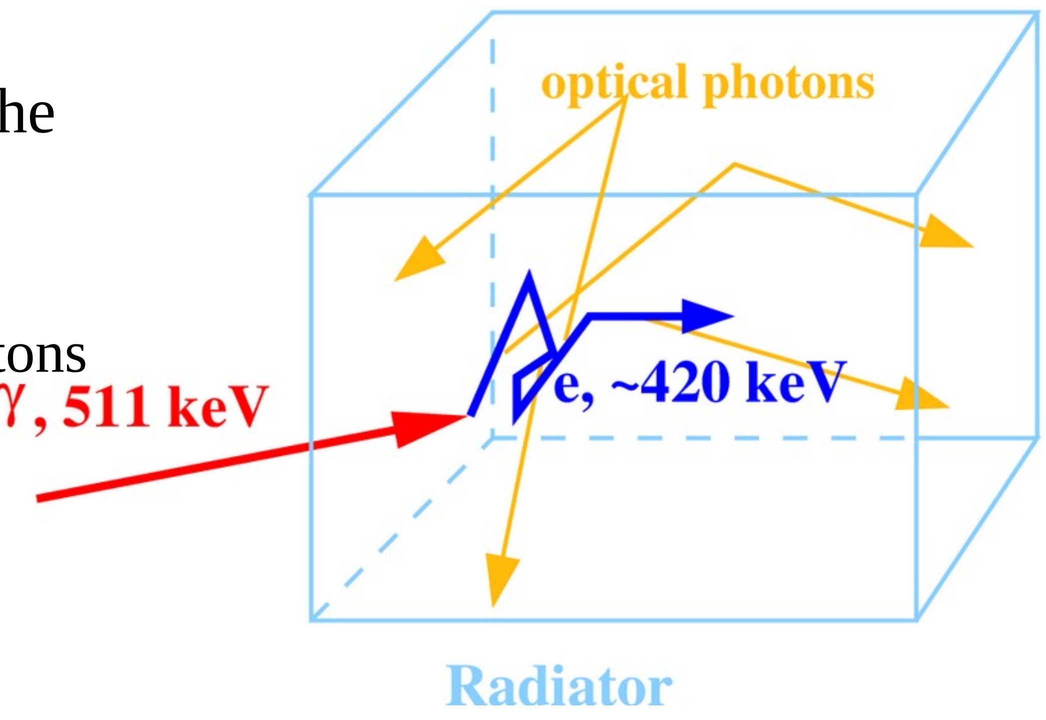
- TOF techniques: measure the difference in time between two photons ⇨ improve S/B
- Contrast of the image directly correlated to the S/B and available statistics.
- TOF gain estimation:

$$G = \frac{S/N_{TOF}}{S/N_{noTOF}} \sim \sqrt{\frac{D}{\delta x}} \sim \sqrt{\frac{D}{c/2\ \delta t}}$$

- D=20 cm ⇨ Coincidence Time Resolution (CTR)=**150 ps** (FWHM) ⇨ G~2.9 ⇨ **8x lower dose**
- Best commercial detectors: ~210 ps (FWHM, CTR)
- In the Lab: below 100 ps, but on small crystals → low efficiency

Use of the Cherenkov photons

- The 10ps time-of-flight capabilities is a contemporary "holy grail" for PET.
- Current performance are limited by the several factors:
  - Time scale of the scintillation: rise time and quantity of the “fast” photons
  - Fluctuation in time during photon collection within a crystal
  - Performance of the photodetectors (TTS, Efficiency)
  - Limitations of the read-out electronics



- To overcome these limitations our strategy is to use the ***Cherenkov photons.***

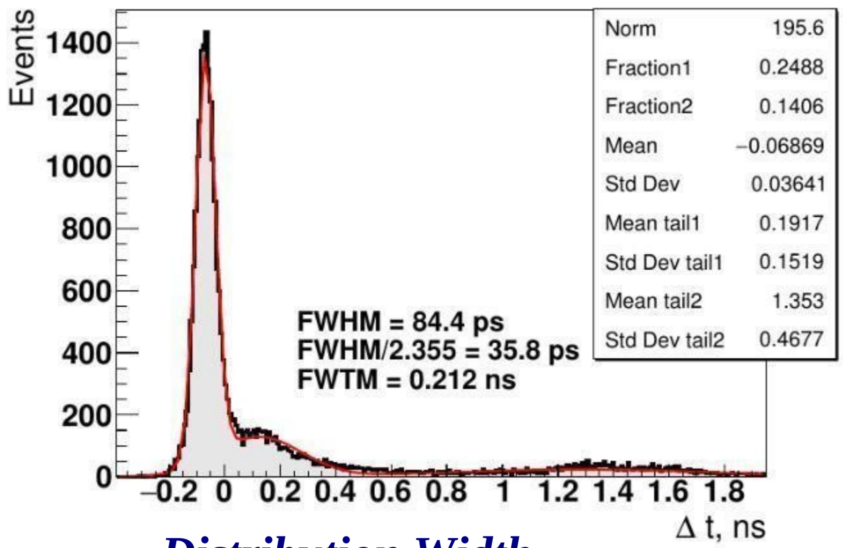
Cherenkov photons: Two Approaches

- Use pure Cherenkov radiators: PbF2, Pb glass
  - very good timing performance, but difficult to use with SIPM, *low detector efficiency*, limited suppression of the Compton background
  - see, e.g. Kopar et. al., 2011, Canot et al. 2019, Ota et al., 2021
  - Results: CTR FWHM; 30 ps – 300 ps
- Use scintillation + Cherenkov: BGO, LYSO
  - limited improvement, because of the low number detected Cherenkov photons per event
  - See e.g. Kwon et al. 2016, Brunner at al. 2017, Kates et al. 2019, Kratochwil et al. 2020, Gundacker et al. 2023
  - Results: CRT, FWHM : 100 – 300 ps (BGO), bellow 100 ps (LSO).
- In most of those studies → small crystals (3x3x3 mm^3), two channels, use scope or conventional electronics
- ***Our Goal*** → study with a “scanner size” module, MCP-PMT, multiple channels, custom made electronics.

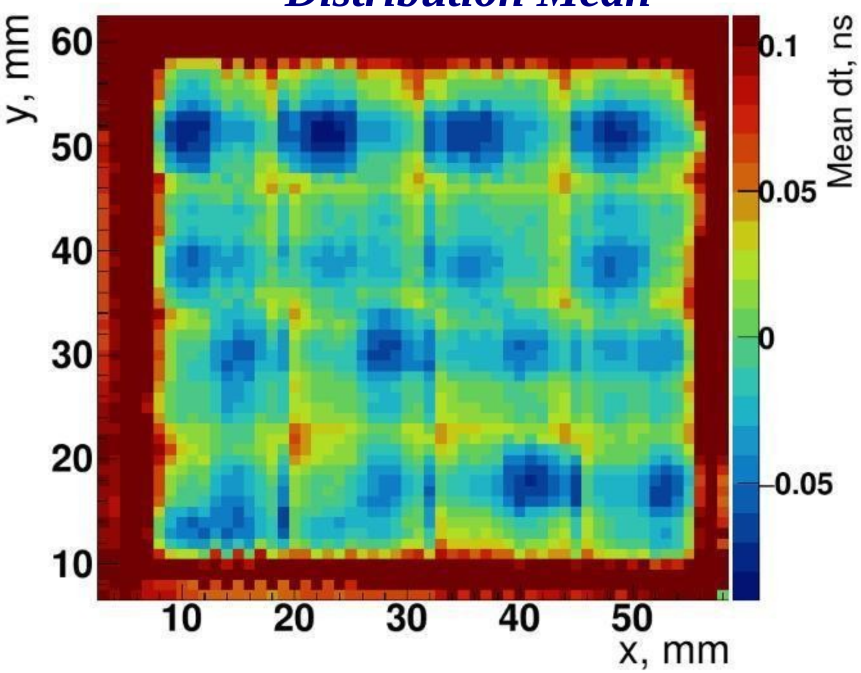
MCP-PMT readout scheme

Previous Studies: MCP-PMT Pixel Readout

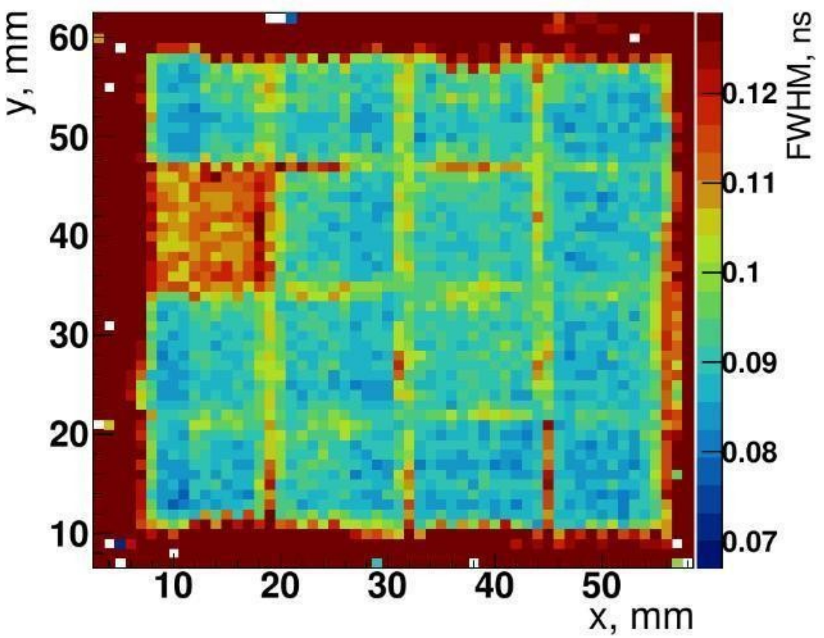
- Measure time difference between MCP-PMT *Planacon* from Photonis (25µm pores) and pulse laser (20 ps beam duration)
- Drawbacks: signal sharing between channels, signals time propagation fluctuation inside channel, limited spatial resolution



Distribution Mean



Distribution Width

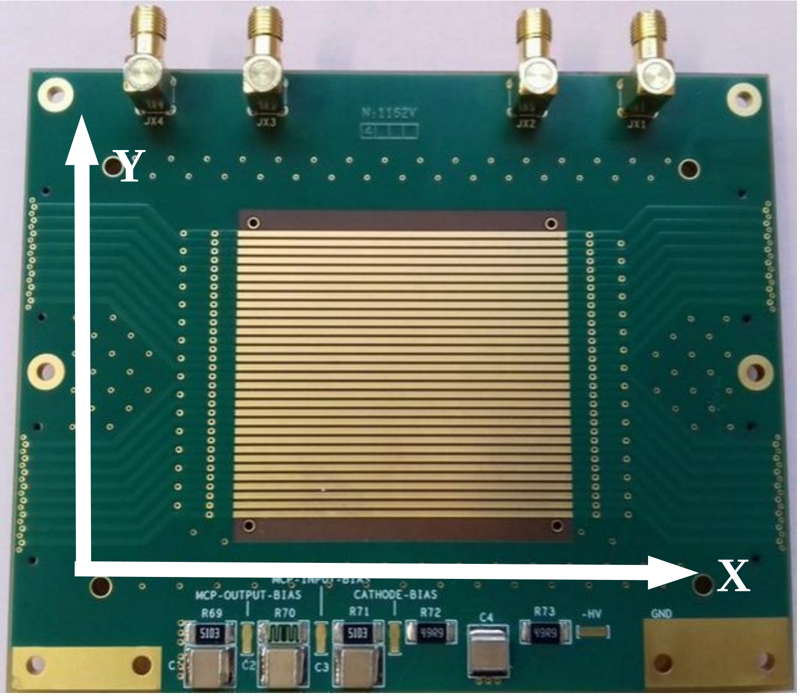


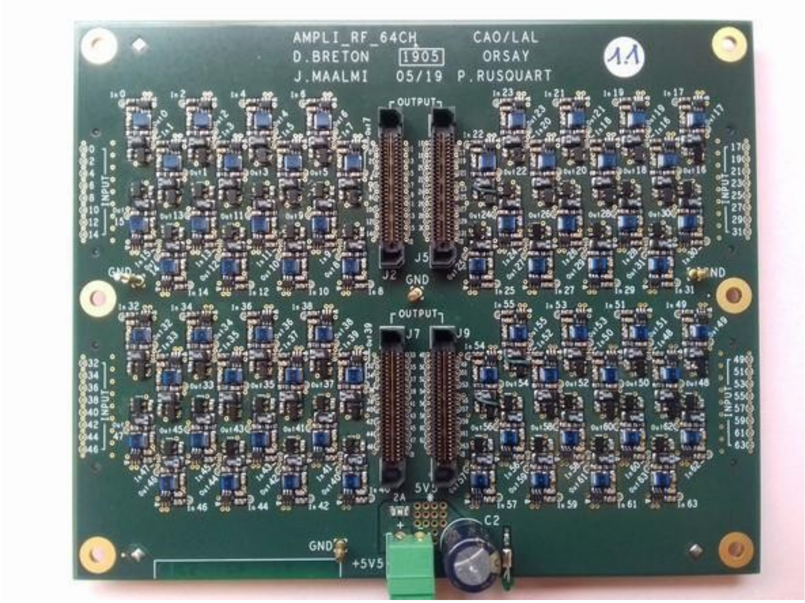
⇒ Propose to use a "continuous" readout

C. Canot et al, *2019, J. Inst. 14 P12001*

Transmission Line Read-out

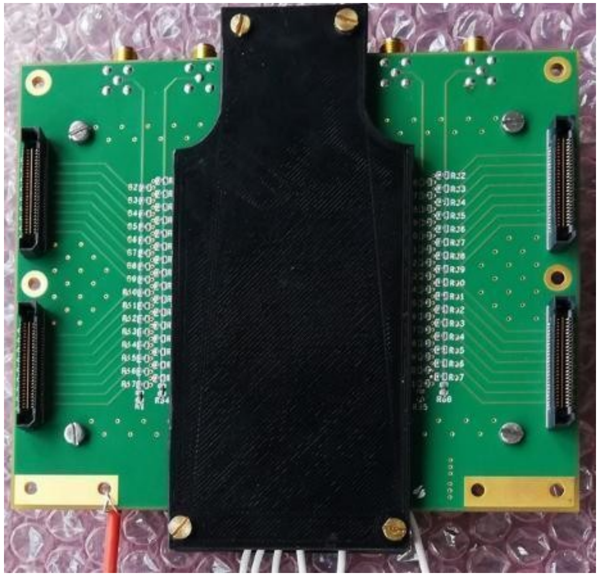
- Use 32 lines (50 Ohm impedance) to readout 32x32=1024 pixels
- Signals are readout from both ends.
- Amplifiers (IJCLab): 2x20dB, 700 MHz
- *SAMPIC digitizer:* 6.4 GSample/s, 64-channels
- Use *charge on lines* for **y-coordinate**
- Use *time difference* between right-left signals for the **x-coordinate**

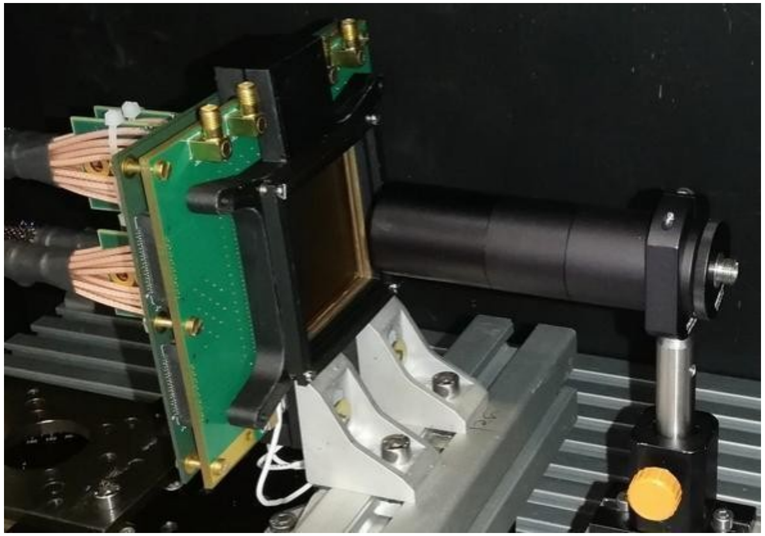


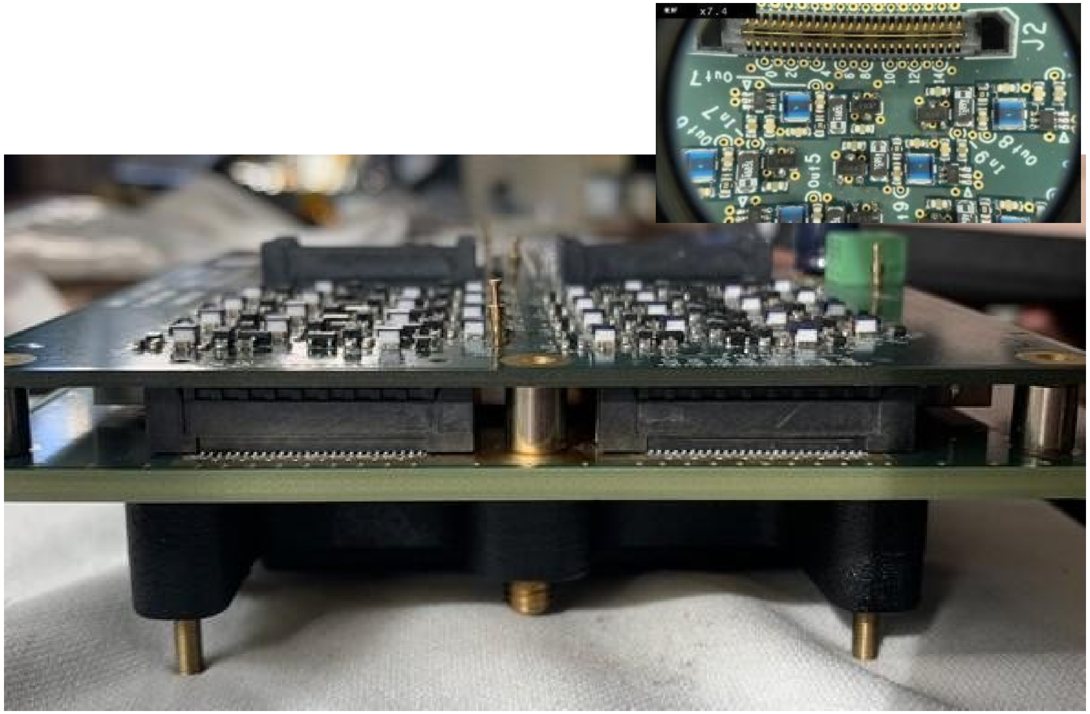


Readout Tests

- Use *Planacon MCP-PMT XP85122* from *Photonis (10µm pores)*
- Use the pressure-sensitive anisotropic conductive interface: *3M adhesive tape* or *Shin-Etsu MT-type of Inter-Connector*
    - reworkable, but require careful pressure adjustment
- Use 20 ps pulsed laser for tests in the single-photon regime

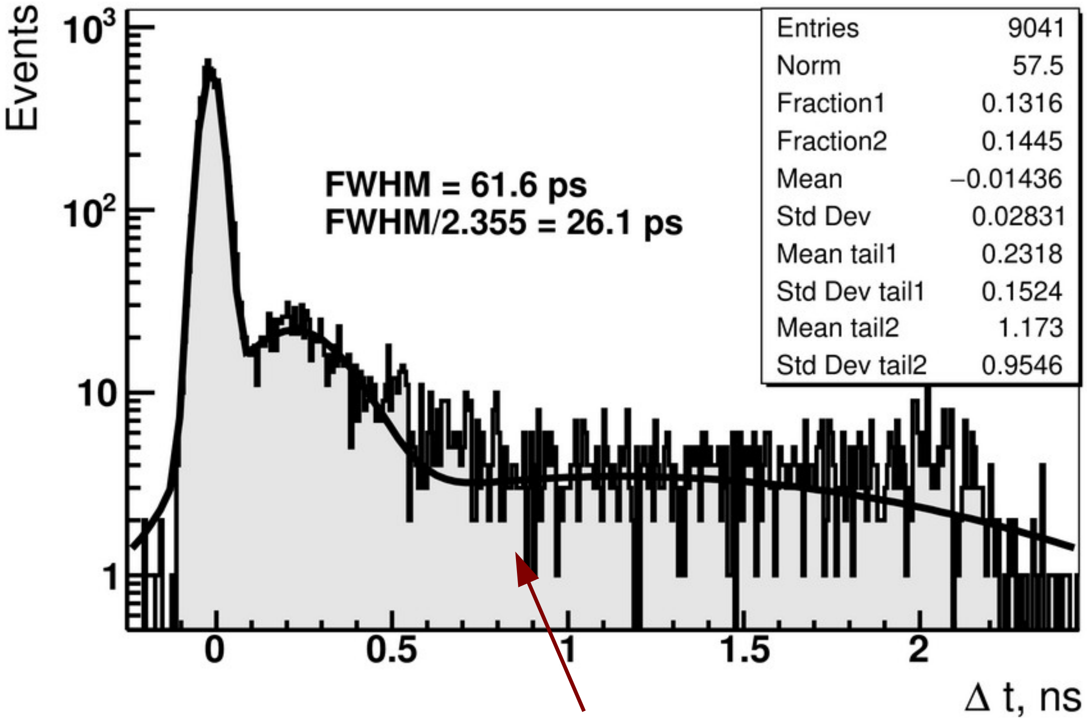




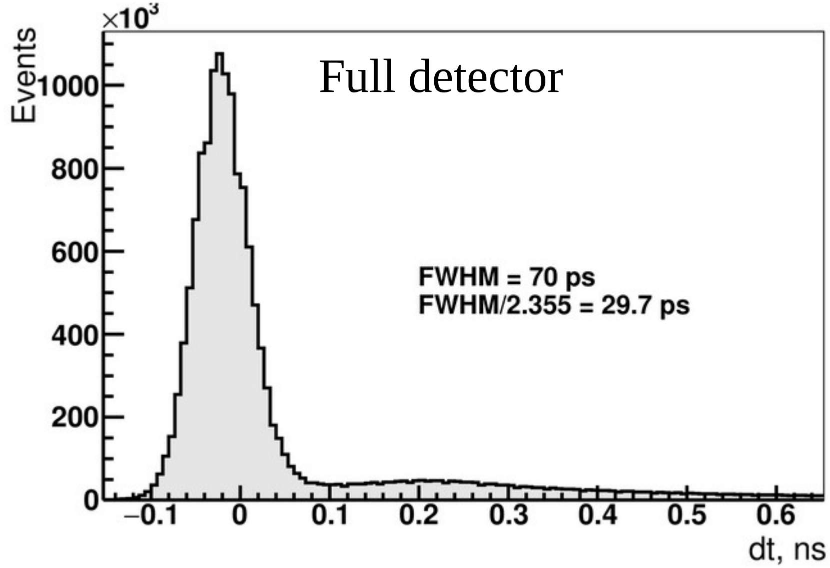


Time Resolution

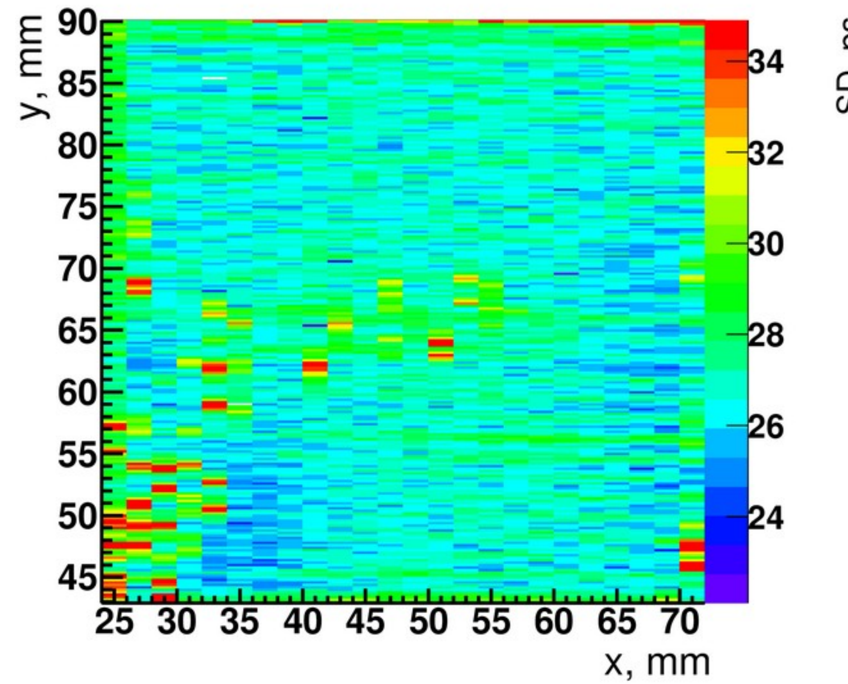
Single position (x, mm; y, mm) = (53,66)



Back-scattered electrons from the MCP surface ~27%



Time Resolution (SD)



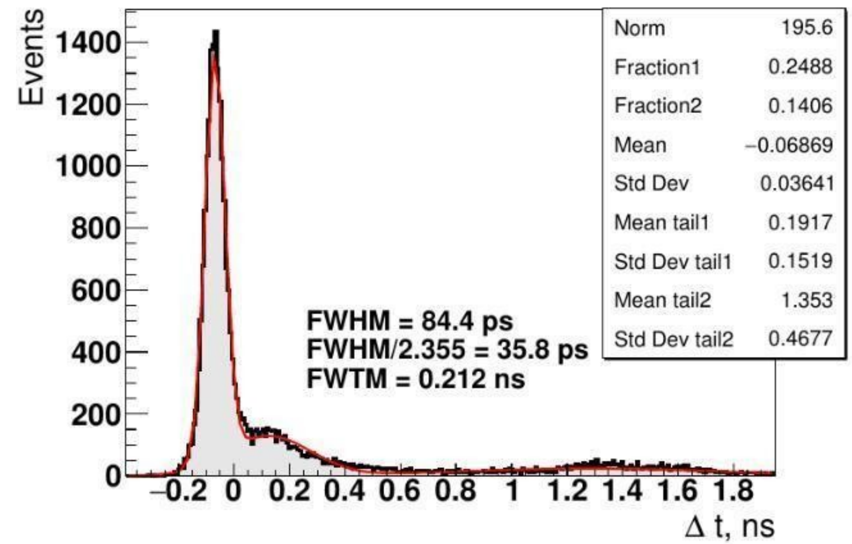
- For each event measure:
  - $dt = t_R + t_L - t_{LASER}$
- Scan all surface to measure PMT response in each position

M. Follin et al, 2022, NIM A, vol. 1027, p. 166092

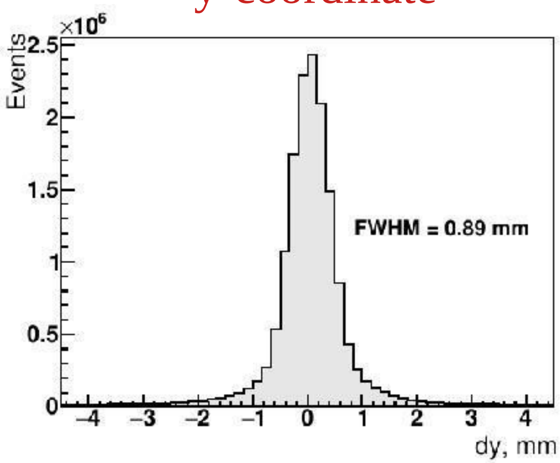
Single Photoelectrons Detection: Conclusion

- Obtain uniform quasi-continuous read-out with the limited number of channels
- Time resolution marginally improved vs the pixel readout
  70 ps (FWHM)
- Achievable spatial resolution is much improved (see following slides)

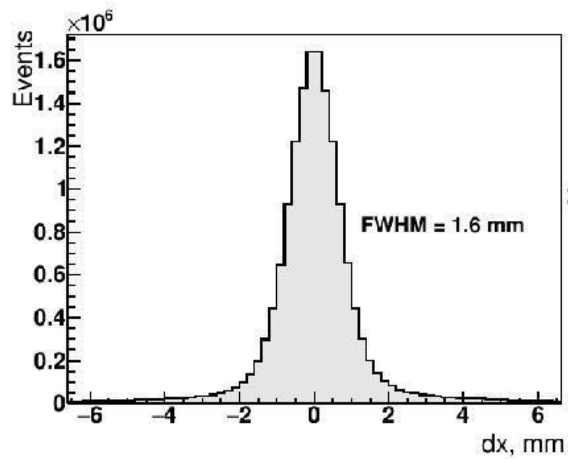
Pixelized read-out



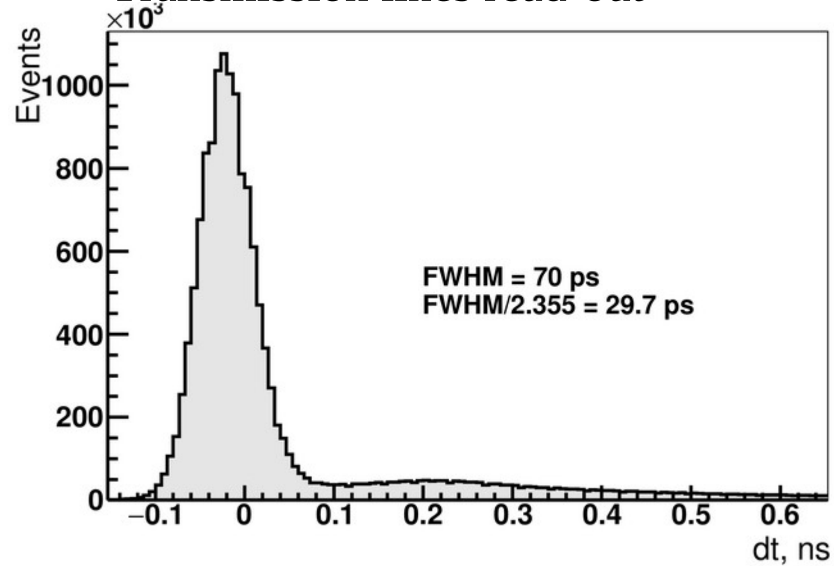
y-coordinate



x-coordinate



Transmission lines read-out

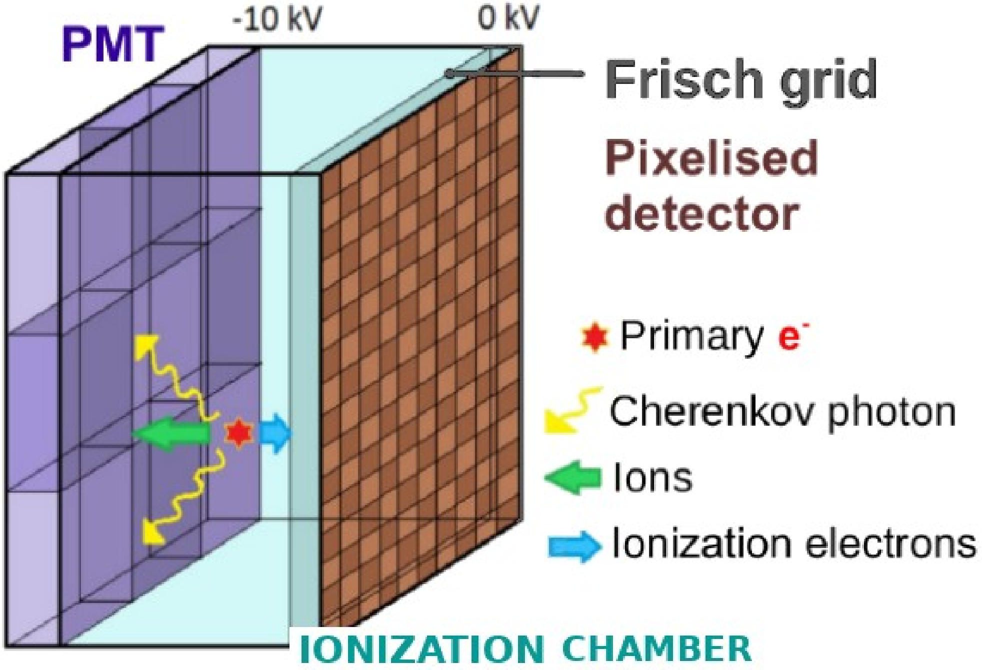


CaLIPSO/BoldPET project:
High spatial resolution for the brain
preclinical PET

for the BOLPET collaboration

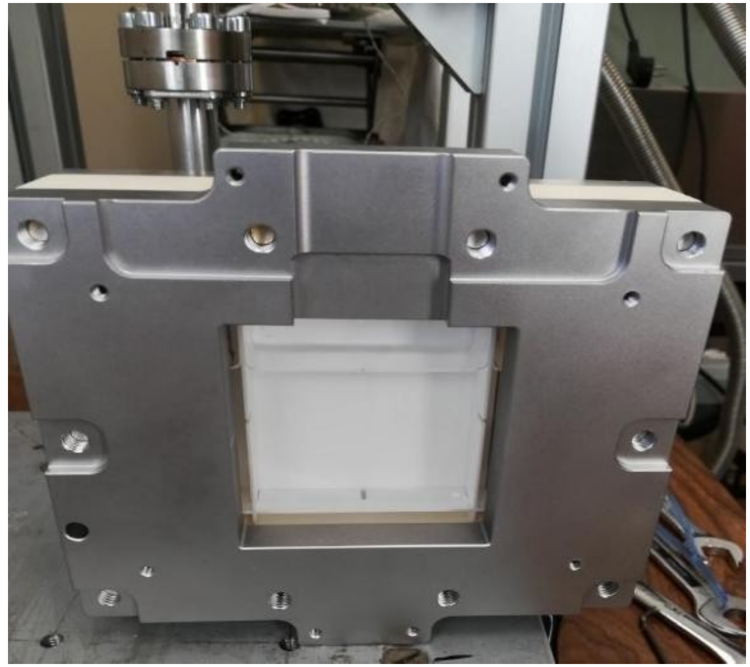
BOLD-PET project

- **High spatial resolution** for the brain *preclinical PET: CaLIPSO/ BOLDPET* project
- Dual read-out: ionization and light (Cherenkov signal)
- Innovative liquid as a detection medium: TMBi (trimethylbismuth)
- Spatial resolution: 1x1x1 mm^3 (FWHM)
- Resolution in time < 150 ps (FWHM)
- Use MCP-PMT for the optical signal read-out
  - Expected number of photons: 1-2
- Collaboration: IRFU, IJClab, Münster University

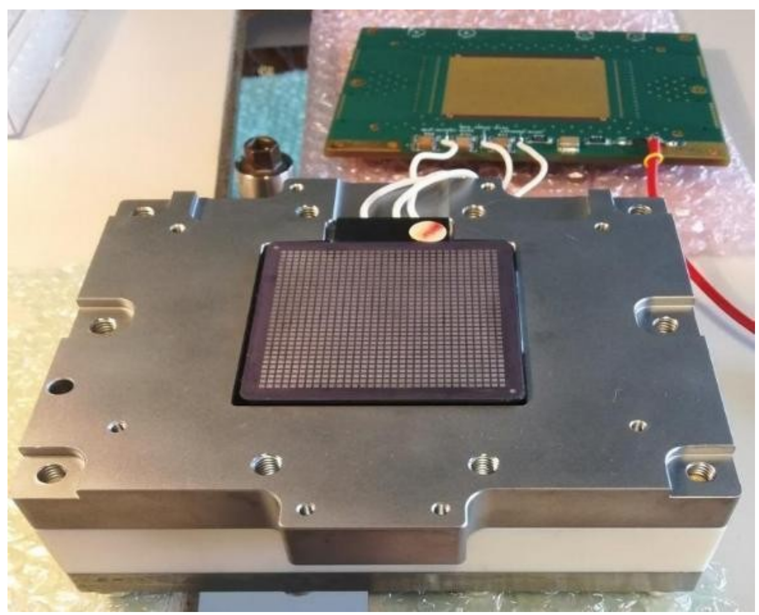


CEA Patent 2010: D. Yvon, J-Ph Renault, « Détecteur de photons à haute énergie », WO2011/117158 A1

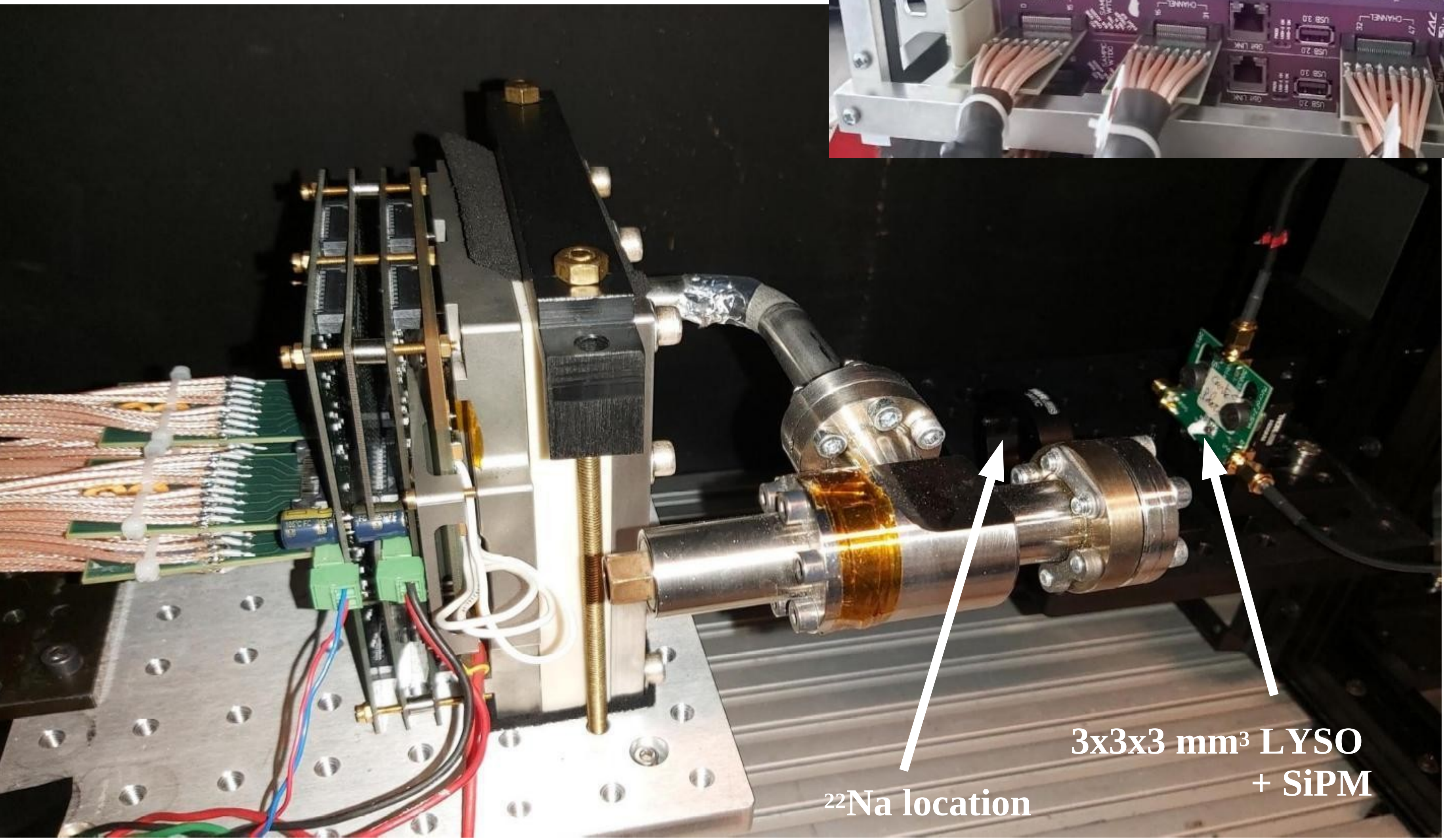
Test With Optical Prototype



- Cell size
  - 60 x 60 x 20 mm^3
- Filled with TMBi
  - ref. Index 1.6 (@425nm)
  - Density 2.3 g/cm^3
- *MCP-PMT XP85122* from *Photonis*
  - *10 µm pores*

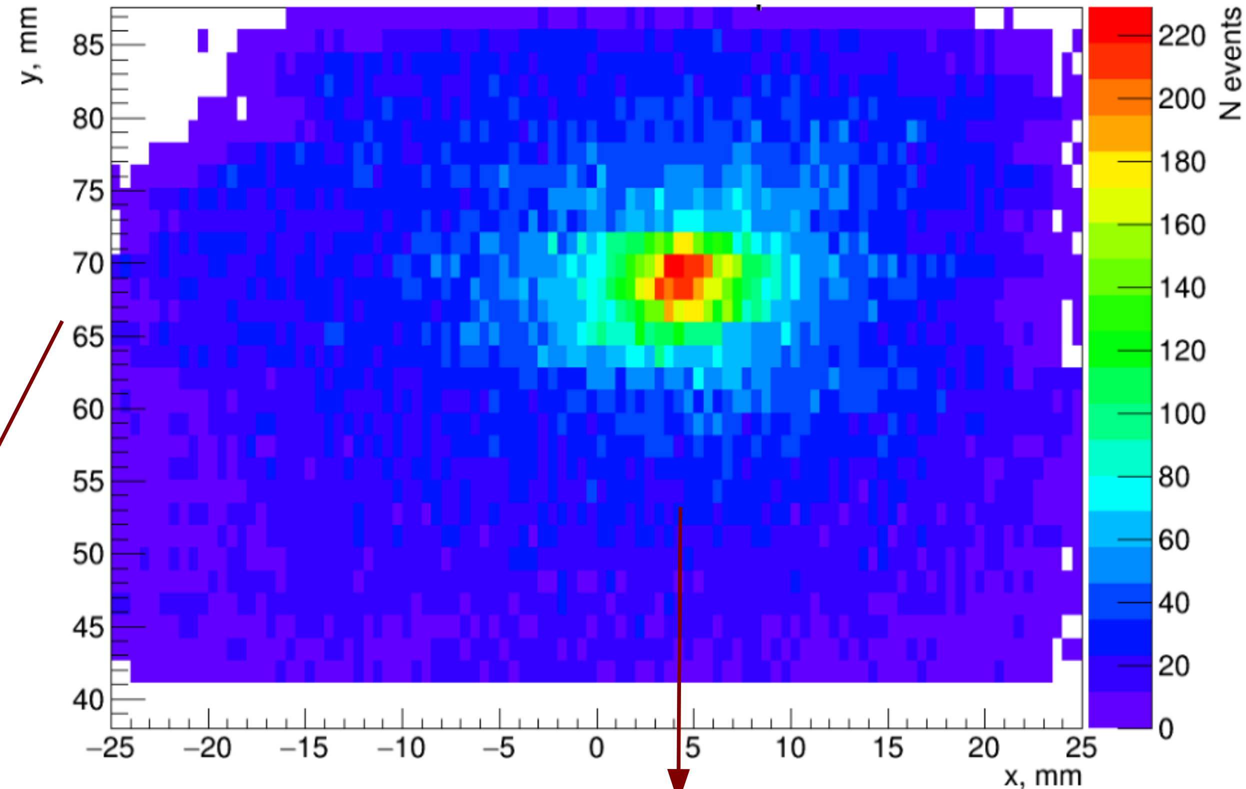


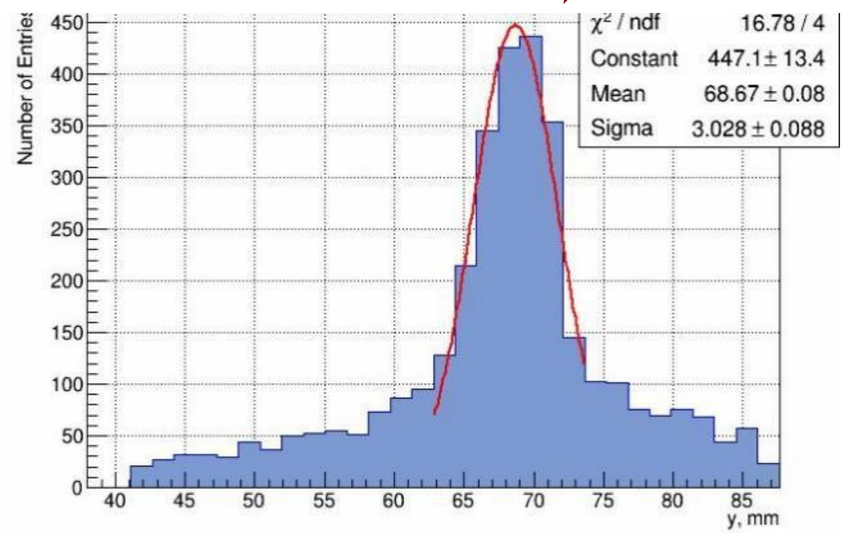
Test Bench: Measurement with ^{22}Na source

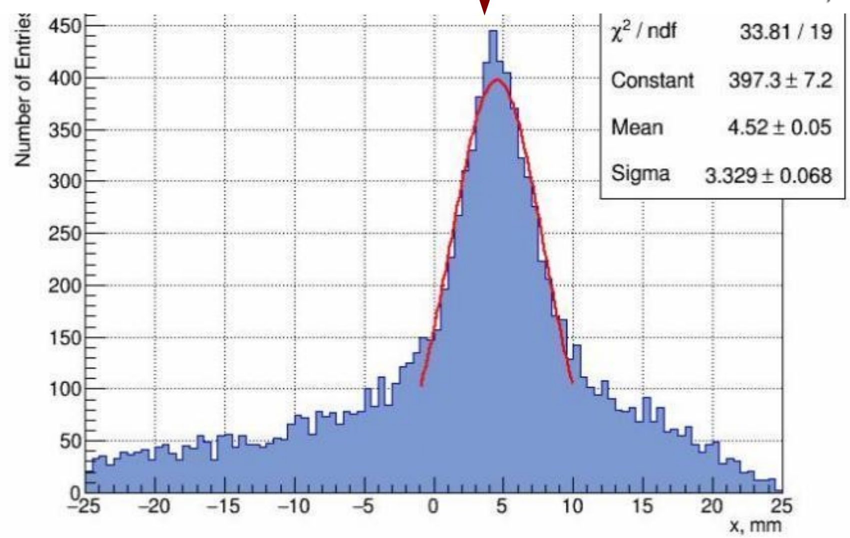


Spatial resolution

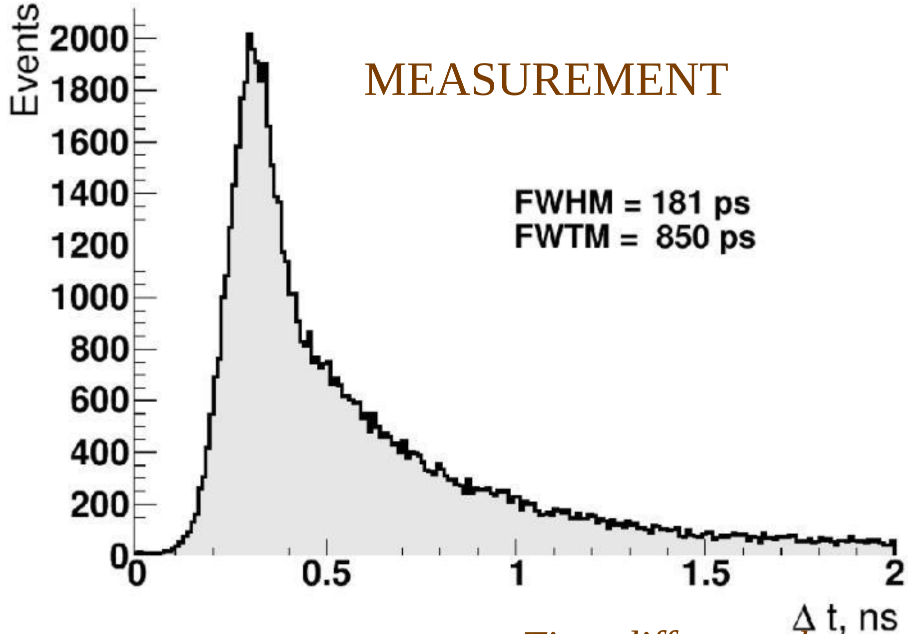
- Coincident Gamma beam of a size ~2x2 mm^2 (FWHM)
- The core of the distribution of about ~ 7x7 mm^2 (FWHM)

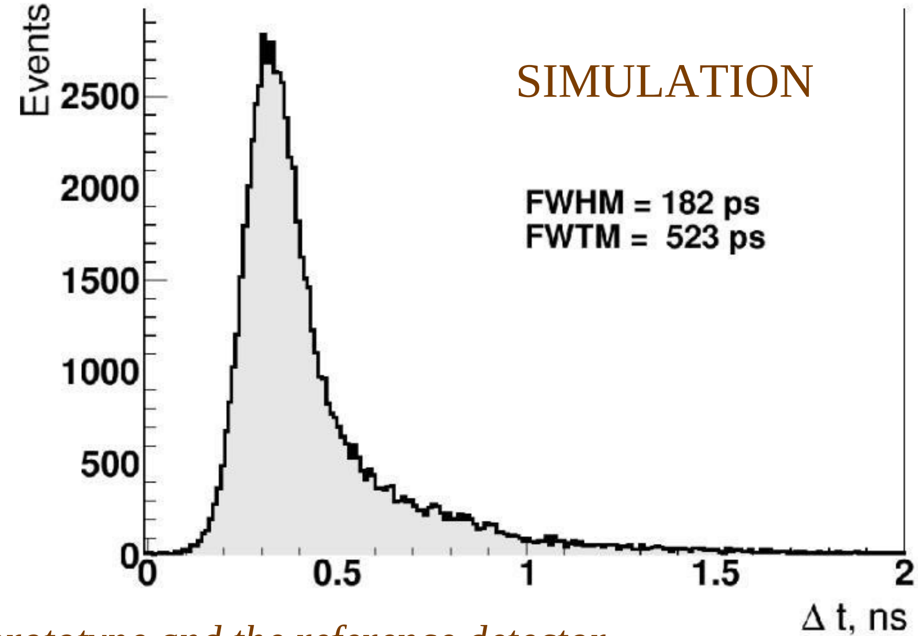






Time Resolution





Time difference between the prototype and the reference detector.

- Detector time resolution of about 150 ps (FWHM)
  - Limited mainly by the photon propagation in the demonstrator (see next slide)
- The detection of the ionization is more difficult than expected:
  - Low ionization yield
  - Reactivity of the TMBI
  - Require extremely high purity of the liquid

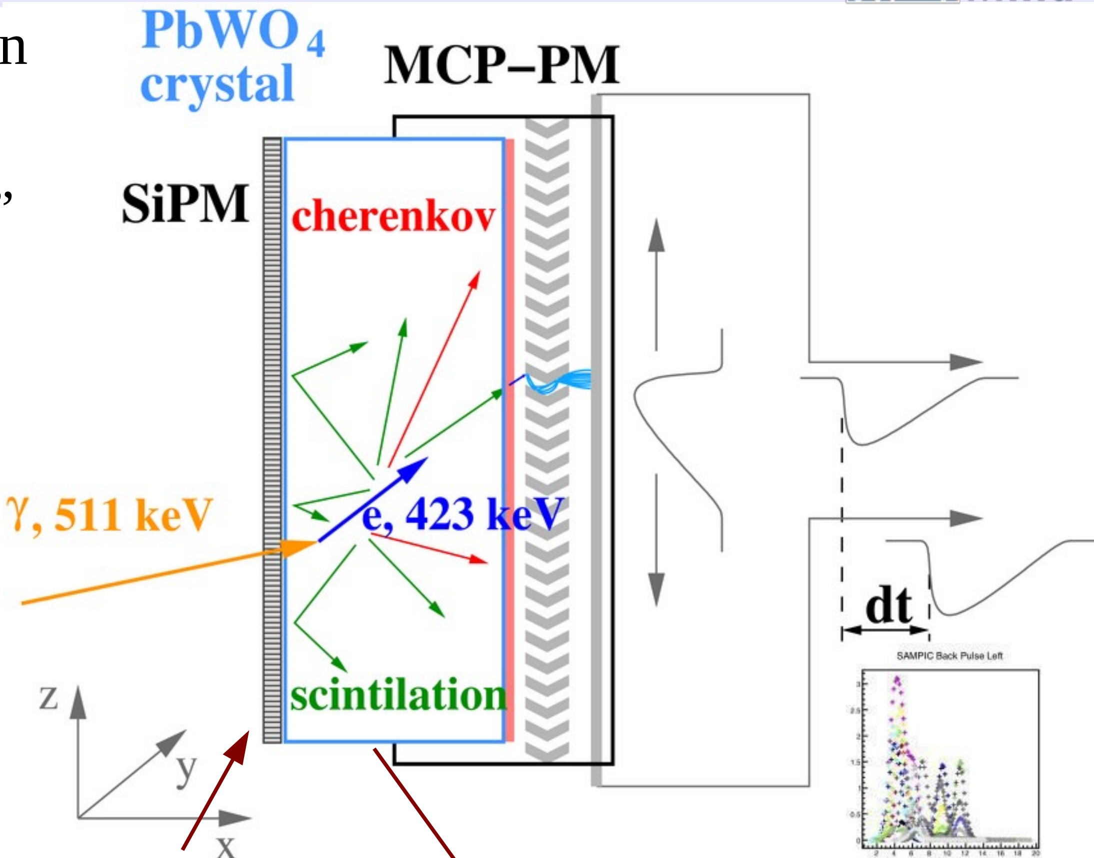
Roman Chyzh et al. 2024, JINST 19 P07018

ClearMind Project :
TOF, high spatial resolution,
efficient large PET detection module

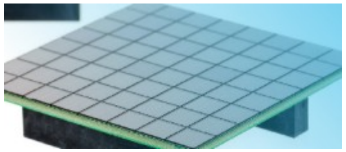
for the ClearMind Collaboration

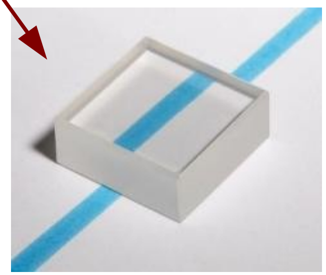
ClearMind Detector Project

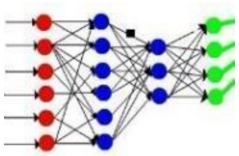
- Direct deposition of the photocathode on the $PbWO_4$ crystal
  - Single Photo-Electron: “Time -Maps”
  - increase the number of detected Cherenkov photons
  - additional fast scintillation photons
- Use of monolithic crystal
  - to reconstruct 3D interaction position
  - correct for DOI effect
- Use MCP for electron multiplication
- Use transmission line readout
  - Reduce number of channels and improve PMT calibration
- Record signal waveform (SAMPIC)
  - For optimal performances
  - Second crystal face instrumented MCP-PMT or SiPM Matrix



SiPM







Patent CEA, FR1759065, 2017

D. Yvon et al., 2020, JINST 15 P07029

Why photocathode deposit on crystal ?

- Cherenkov Photons in $PbWO_4$ @ 511 keV ~ 20
- **Regular assembly (optical gel)**
  - Refrac. index: $PbWO_4$ **~ 2.2**, Optical contact gel **~ 1.5**
  - $R_{Fresnel}$ ~ **3.6 %**, ….. But total reflection angle ~ 43°

    → **73% of solid angle reflected**....
  - ! Photons hardly escape the crystal !
- **PhotoElectric Layer deposited on Crystal**
  - Refraction index ~ 2.7 – 3
  - $R_{Fresnel}$ ~ 2.5 %, ….. no total reflection effect …..
  - ***Up to a factor 4*** in light collection efficiency + ***light collection time shortened*** !

…... But …..

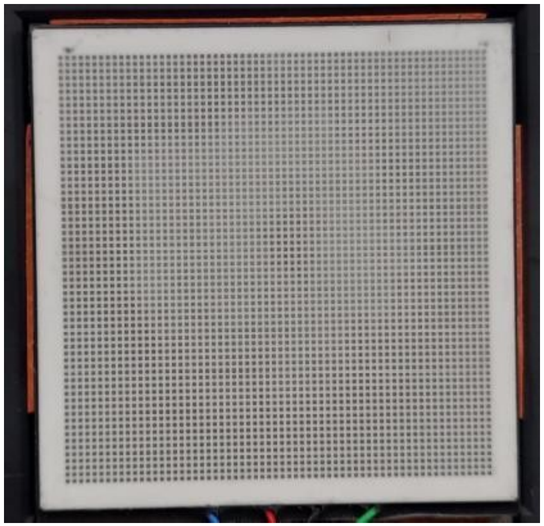
- **Difficult for crystals with High-Z components**.

ClearMind Collaboration

- CEA Saclay – DRF/IRFU
  - D. Yvon & V. Sharyy, Thomas Proslier, R. Belkacem, Z. Zobundzija, (+ D. Baudin, et al.)
- CNRS/IN2P3/IJC-Labs, Serv. d’Electronique : *Analog & Digital readout*
  - D. Breton, J. Maalmi et al.
- CNRS/IN2P3/CPPM – Marseille : *Optical simulation / PET imaging hardware simulator*
  - C. Morel, M. Dupont, Y. Boursier, et al.
- CEA-DES/ISAS: *Machine Learning / IA*
  - G. Daniel, (+ J-M. Martinez)
- CEA-DRF/ISVFJ/SHFJ : Medical Physicists. *Full scanner GATE simulation / Image reconstruction / IA*
  - O. Kochebina, C. Comtat, S. Jan

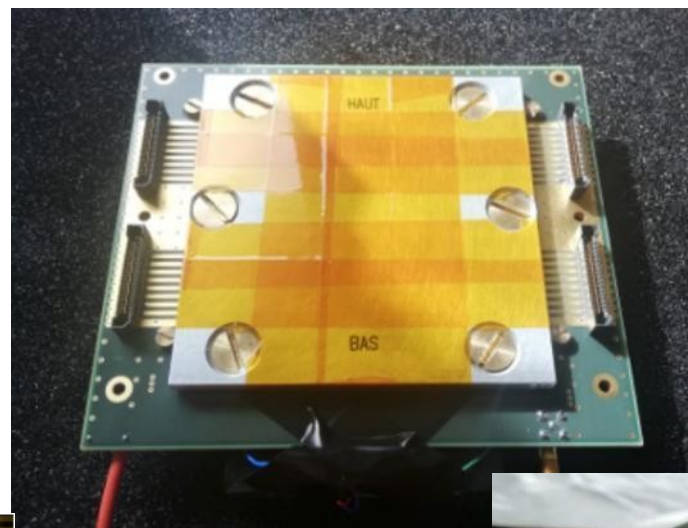
First Prototype (Photek): Lines read-out

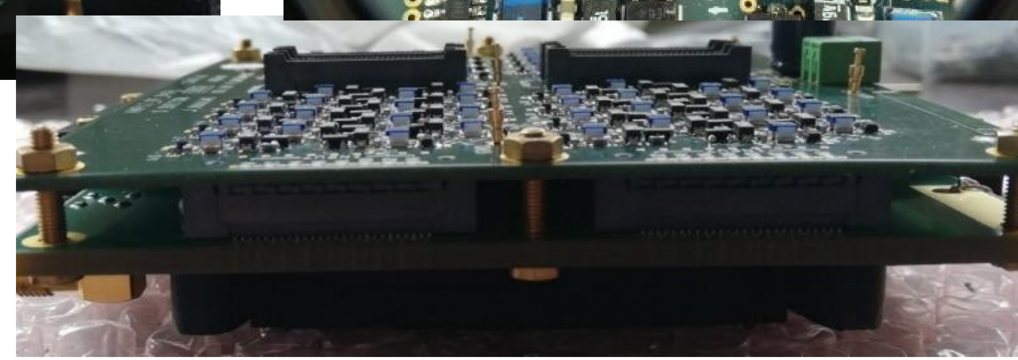
Anode



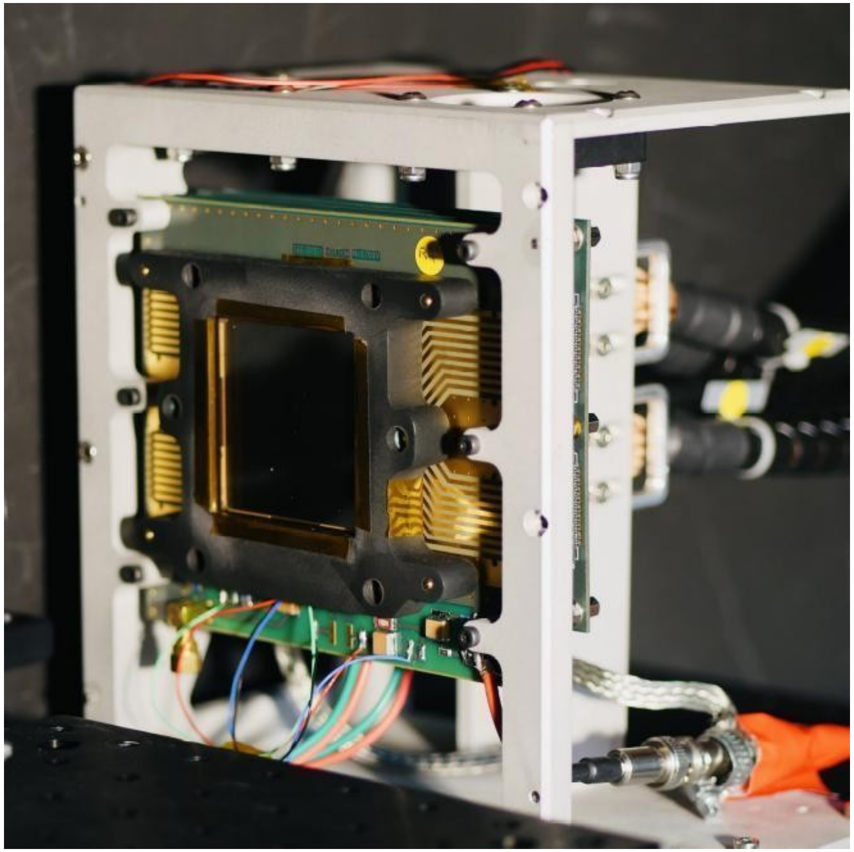
Readout Board

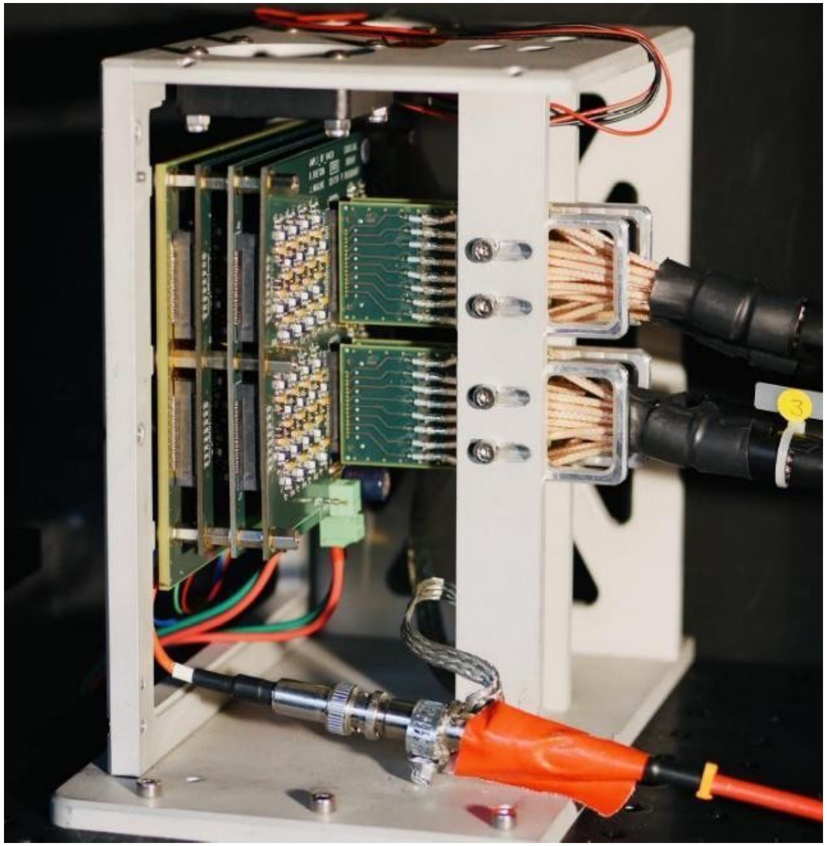
- Prototype produced by Photek on the base of MAPMT253 (*10 μm* pores)
- Transmission line readout :
  - 32 lines
  - Connected throw Shin-Etsu MT-Interconnect
  - Apply compression with metallic brace
  - Double stage amplification: 2 x 20 db, 700 MHz (IJC Labs)





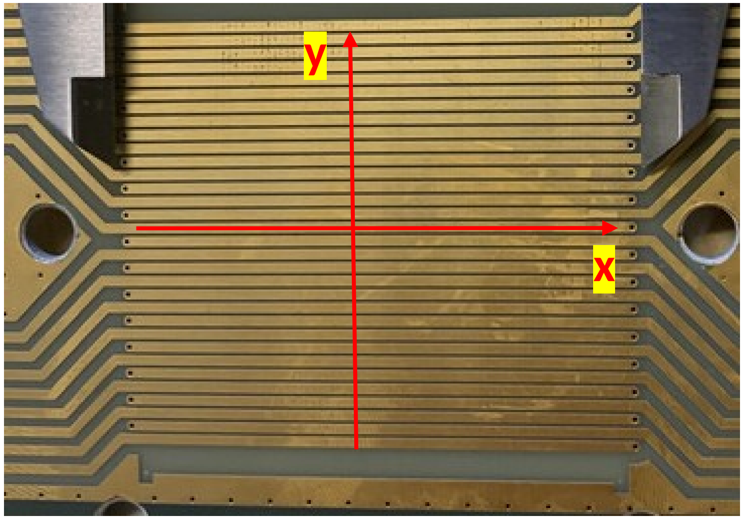
First Prototype Assembly

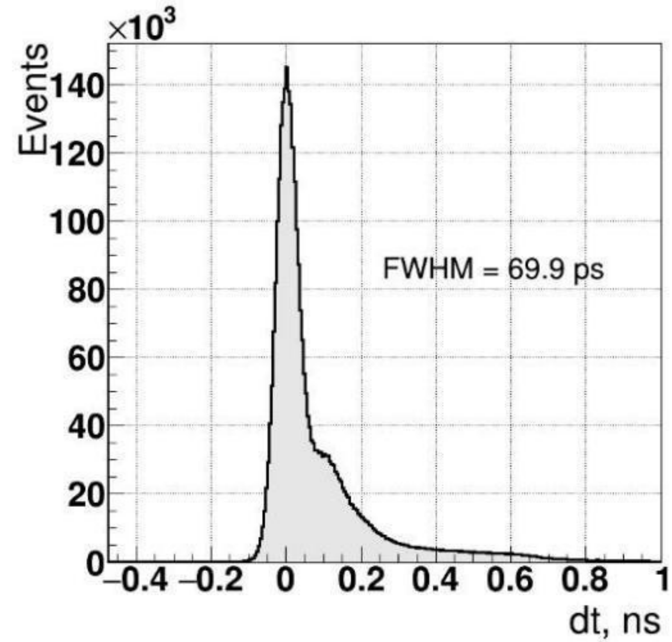




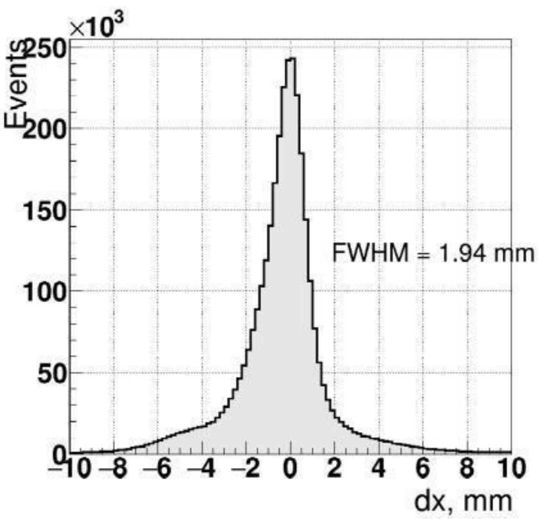
SAMPIC crate digitizes
the signals @ 6.4 GS/s
(IJC Labs/IRFU)

Single Photon detection

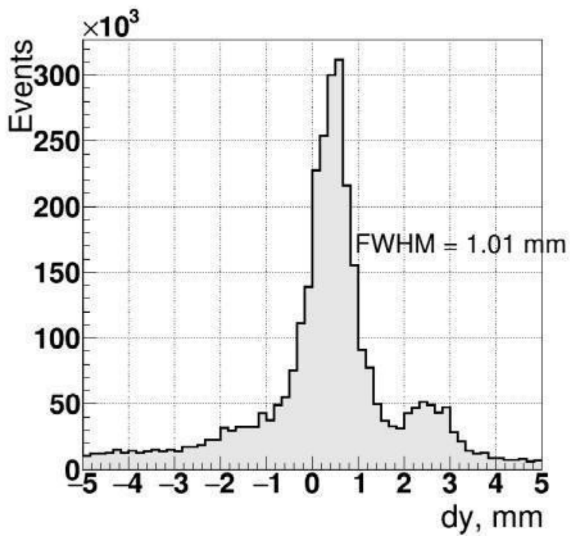




Time difference between the laser and the Clear Mind prototype signals over all the detector.

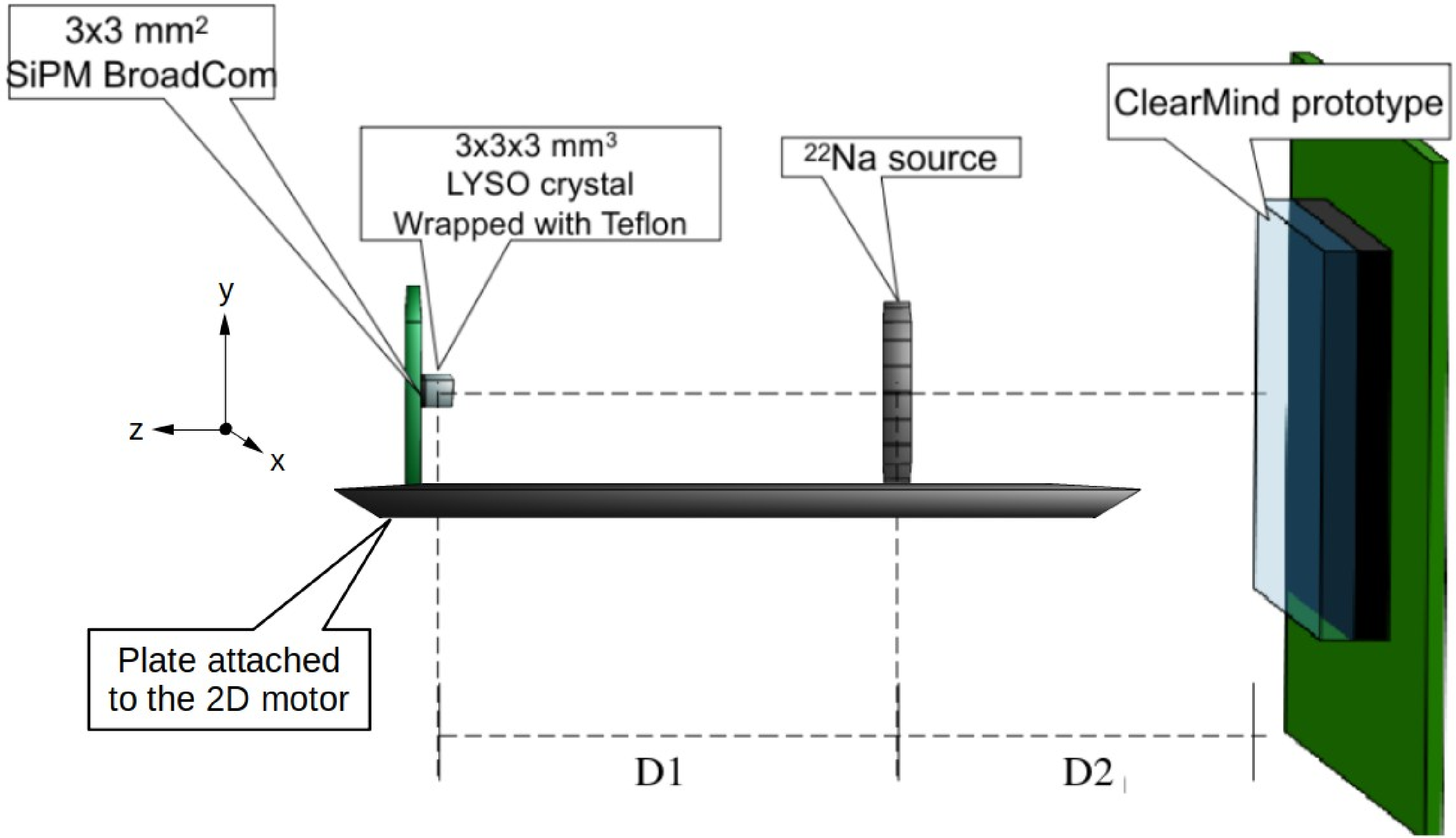


Reconstructed x-coordinate (along the transmission line)



Reconstructed y-coordinate (across the transmission lines)

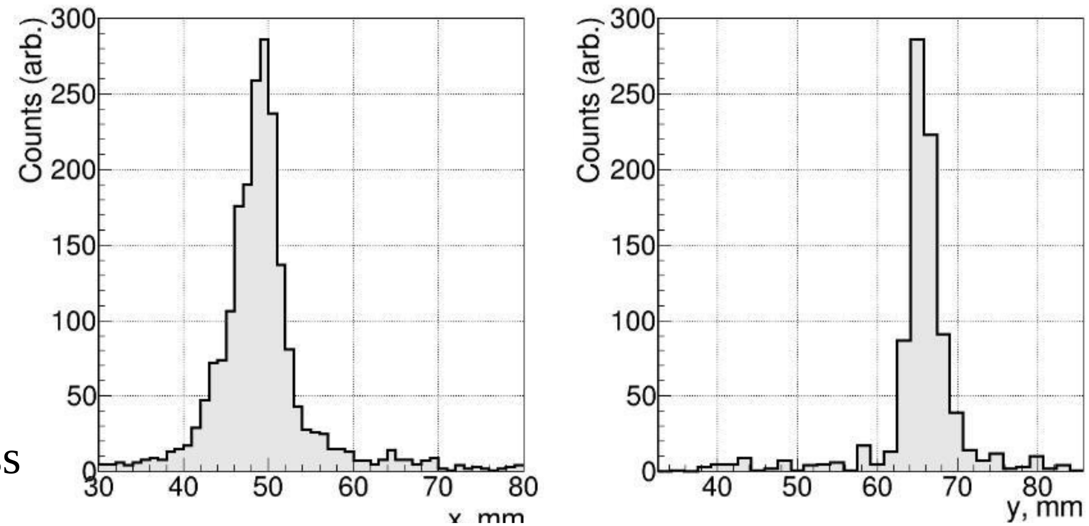
ClearMind-one Gamma detection test setup

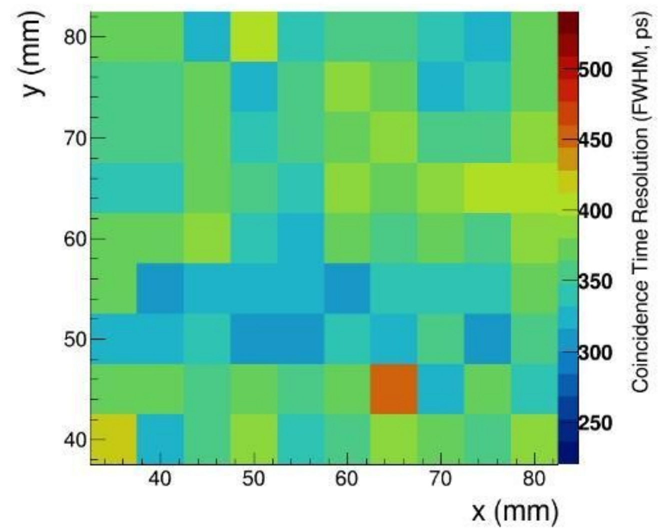


ClearMind-one Gamma detection

- Successful deposition of photocathode on $PbWO_4$ Optical window
  - But low Photocathode QE : 16%
  - Thick Passivation layer
- **Efficiency** on 5 mm thick crystal :
  - ***28 ± 3 %*** (28.6% Expected from MC)
- **Spatial resolution** (no IA) : ***3.5 mm*** across lines & ***5.4 mm*** along lines (FWHM)
- **Time resolution**
  - ***330 ps*** (FWHM) … far from our goals
  - ***48% of PE event*** include a detected Cherenkov photon.
  - Thick Passivation layer
    - → Lower Photon detection efficiency
    - → Reflections : Random delay of fast photon detection
  - MCP + Lead loaded glass detectors* achieve < 50 ps (FWHM)

Cherenkov Only → Severe loss in efficiency
→ No positioning





CRT versus positioning (FWHM)

A. Galindo-Tellez et al., JINST, 2024
**S.I. Kwon, Nature Photon, 2021,*
L. Chen, NIM A 2024

Ongoing developments with INCOM (USA)

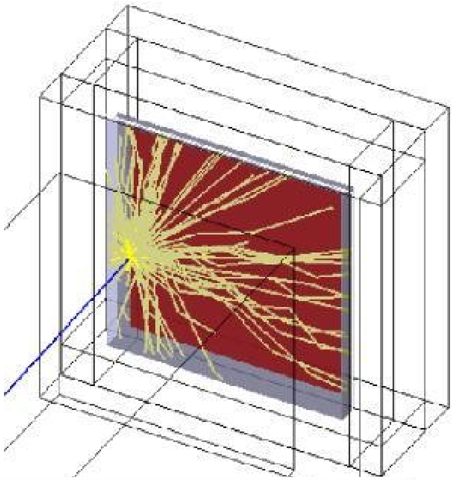
- Study and optimize timing and position resolution of MCP-PMT photo-detection
  - Using ***standard HRPPD MCP-PMT*** photo-detector
  - Tails minimization in MCP-PMT distribution in also important !
- ALD barrier coating compatibility with Photocathodes
  - High efficiency photocathodes (30%)
  - ***Recent progress with Thomas Proslier (IRFU) & M. Miserques (CEA-DES)***
- Lead Tungstate Window Sealing trials
- Fabricate 56 x 56 mm^2 thick scintillating crystal MCP-PMTs
- Maintain low contribution from Read-Out Electronics, e.g. :
  - Employ Pulse Shape Measurement Techniques
  - Implement ***Advanced Time Estimation Algorithms***
  - Keep Electronic Noise Levels at a Minimum Level
- Improve Depth of Interaction (DOI) Reconstruction Precision :
  - Correct for the time reconstruction biases
  - + Working on ***thicker crystal***

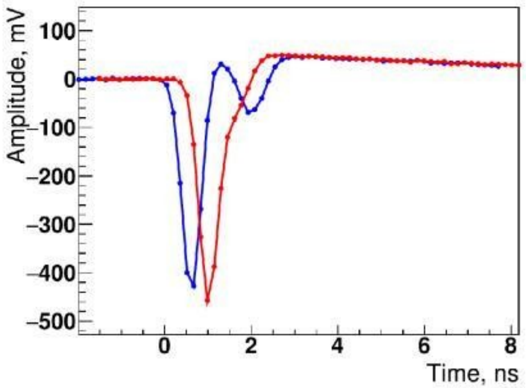
AAIMME Project :
Machine Learning for Molecular Imaging and the Medicine of the Future

for the AAIMME collaboration

Simulation

- Gate/Geant4 simulation is used to understand the detector.
- Detailed simulation of the optical photon propagation
  - Surface properties adjusted to the measurement with the optical microscope
- Innovative approach to the photocathode simulation
  - Specify the refractive index of the Bialkali photocathodes using the published measurement
  - Leave Geant4 to simulated the reflection and absorption at the photocathode
  - Parameterize the extraction probability and intrinsic quantum efficiency using the PMT photocathode calibration.
  - Use of the dedicated simulation for the thin layer frustrated transmission (CPPM Marseilles, added to Geant4 v11.2)
  - Will share this code inside DRD4 CERN collaboration
- Simulate in the detailed PMT response and signal shape using parameterized analytical functions.





Simulated signals read out at the left (blue) and right (red) ends of the line

Ch.-H. Sung et al.
NIM A Volume 1053, 2023, 168357

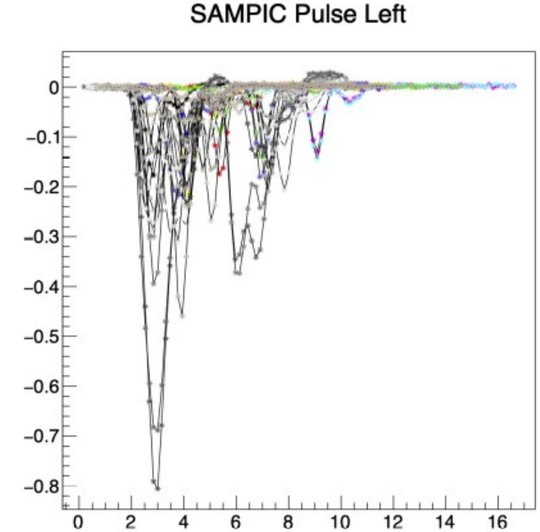
Ch.-H Sung, PhD thesis, Université Paris-Saclay, Orsay, 2022

L. Cappellugola et al.,
in 2021 IEEE NSS/MIC Conference

2D Spatial Reconstruction

- Develop an innovative method of NN gamma vertex 2D reconstruction → modify the Loss function:
  - Estimate the uncertainties σ_x, σ_y
  - take into account the physical boundaries of the detector with a truncated gaussian

Set of pulses as registered recorder for a 511 keV energy deposit (simulation). Only the pulses registered on one side of the transmission lines are shown.



$$-\log(L(\theta)) = \sum_i \sum_{z\in\{x,y\}} \log\left(\Phi\left(\frac{b-\mu_{\theta,z}(\mathbf{s_i})}{\sigma_{\theta,z}(\mathbf{s_i})}\right) - \Phi\left(\frac{a-\mu_{\theta,z}(\mathbf{s_i})}{\sigma_{\theta,z}(\mathbf{s_i})}\right)\right)$$

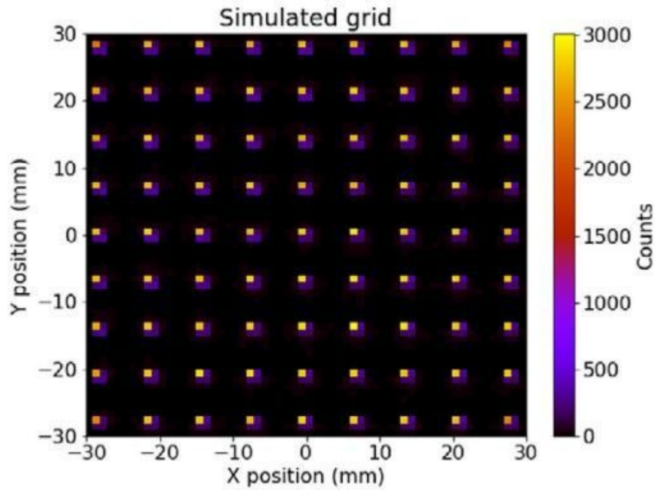
$$+\frac{1}{2}\log(2\pi\sigma_\theta^2(\mathbf{s_i})) + \frac{(z_i-\mu_{\theta,z}(\mathbf{s_i}))^2}{\sigma_{\theta,z}^2(\mathbf{s_i})}$$

G. Daniel et al.,
Engineering Applications of Artificial Intelligence, Volume 131, 2024, 107876

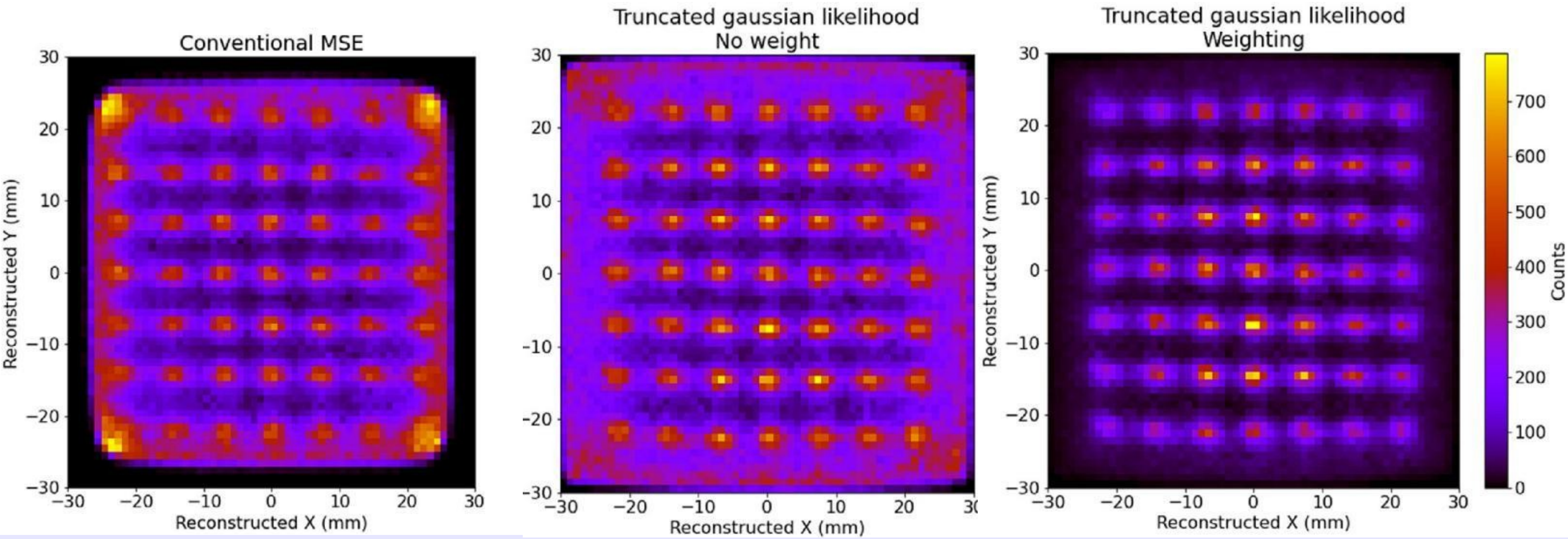
Φ: Erf function

$[a, b]$: detector boundaries

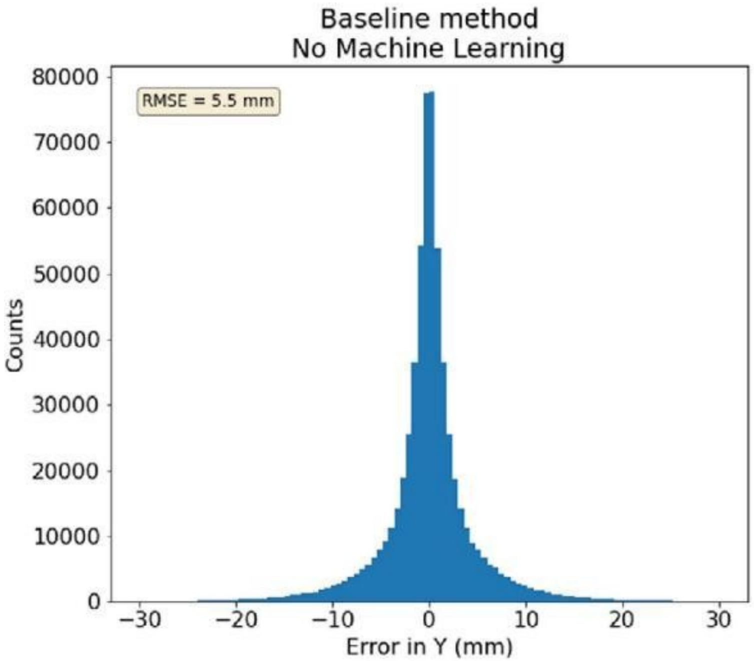
Grid of sources

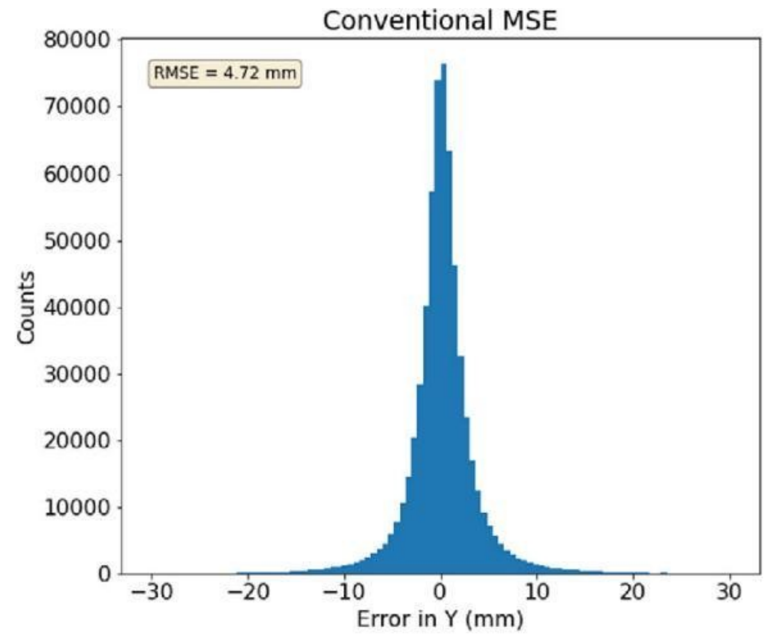


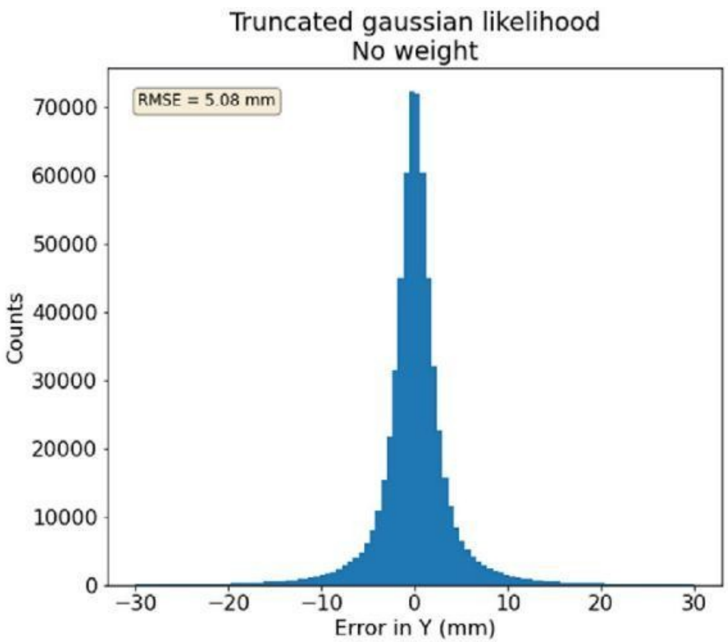
- Simulate a grid and reconstruct in three different approaches:
  - Preprocessing using robust statistics
  - Conventional
  - Account for the physical limits throw the truncated Gaussian
  - Account in addition for the uncertainties (weighting)

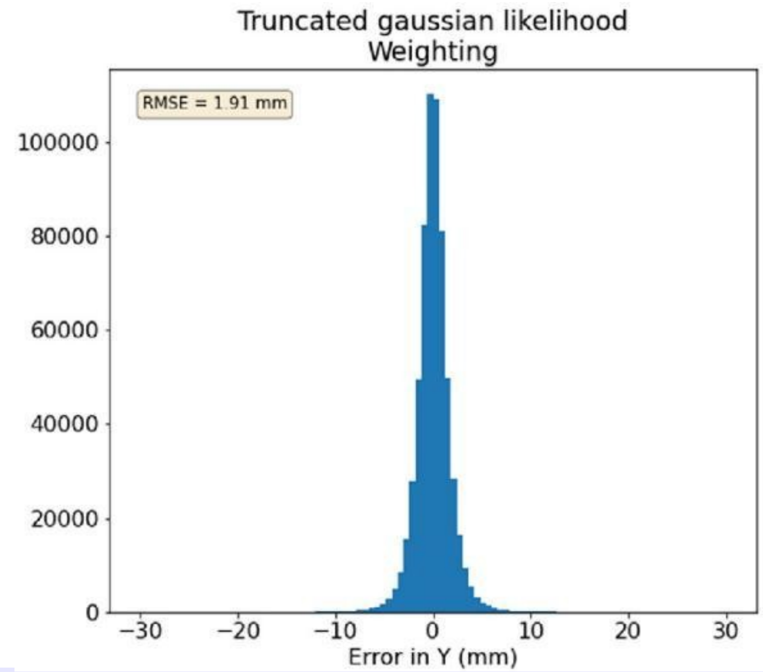


Reconstruction Precision in X (along lines)





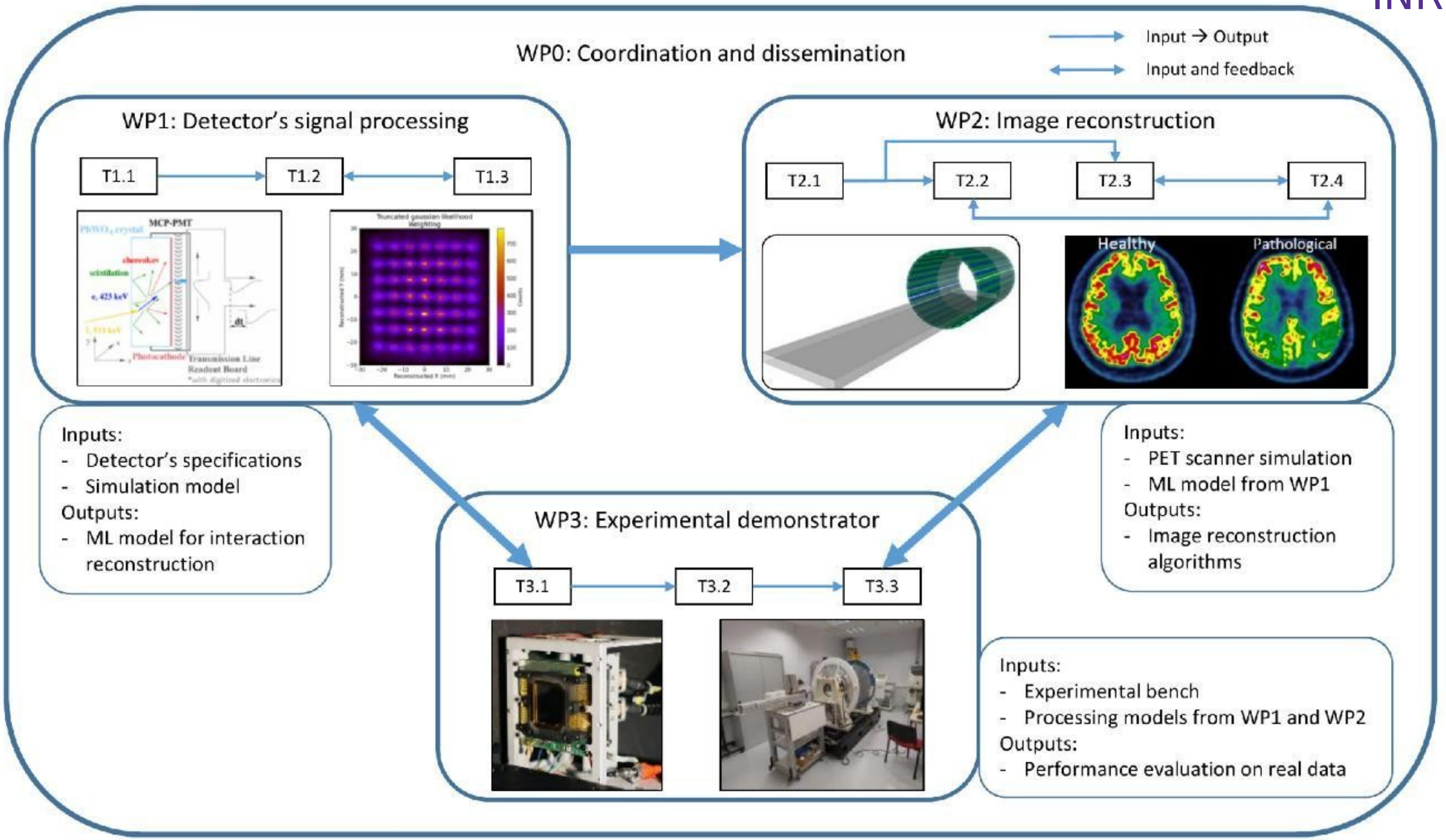




AAIMME Project: To be continued

- Encouraging results → ***uncertainties are needed*** at the image reconstruction level
- ANR AAIMME: time/DOI reconstruction, image reconstruction

CEA – DES / ISAS
CEA – DRF / IRFU
CEA – DRF / ISVFJ/SHFJ
CNRS – IN2P3 / CPPM
INRIA -IdF / OPIS



Chronography*

Cutting edge gamma detector instruments

for TOF-PET &

High-Speed Calorimeter

for the future collaboration

* **Ch**erenkov and c**r**oss-lumi**n**escence timing for highly time-res**o**lved ionizin**g** **ra**diation detectors for **ph**ysics and societ**y**

Chronography Collaboration

- CEA Saclay & BIOMAPs Orsay
  - D. Yvon, V. Sharyy, Thomas Proslier & Olga Kochebina, Claude Comtat, Sébastien Jan
- FZU, Univ. Prague
  - Robert Kral, Martin Nikl
- Univ. Tartu
  - Vitali Narginoi, Marco Kirm
- Institute for Crystal Growth (IKZ), Berlin
  - Iroki Tanaka
- CERN
  - Etiennette Auffray
- Univ. Marseilles, CPPM
  - Christian Morel, Univ. Marseilles, CPPM
- *No Industrial accepted to be involved yet*
  - St Gobain Cristaux (V. Ouspensky, Luxium Solutions), Hellma, Korth Kristalle, MEGA Materials

Chronography goals : Two breakthroughs

- **Ultra-fast, bright, dense scintillating crystal of heavy compounds**
  - ***Cherenkov yield*** : *high optical index* and *UV transparency*
  - **Cross-luminescence** scint., ***intrinsic*** *(ps), shortest* ***decay times (sub-ns)***, *yield* ~1000 ph/MeV
- Study ternary Rb, Cs and Ba *fluorides* containing a second, heavy, cation
  - From ***Lu*** (Z=71) ***to lead and bismuth***,
  - High Gap → Deep UV transparent → More Cherenkov light.

    → Cross-luminescent crystal, ***an ambitious challenge***.
- **Light extraction and detection of dense UV-scintillating crystals**
  - SiPMs : QE ~15% in the deep UV. Optical contact damps photons l < 200 nm.
  - ***MCP-PMT : Thin optical, deep UV coating*** to passivate the crystal surface
    → before photocathode deposition : optical window of a cutting edge MCP Gamma detector.
    → ***no total reflection at the crystal/grease interface***, thanks to frustrated transmission
    → improves fast photon collection time and light collection efficiency (up to a factor 4)
  - Good commercial ***deep UV photomultiplier photocathodes reach 30% efficiency***
- **Fully meet the specifications of a gamma detector for TOF- PET imager.**

Tasks Sharing

Chronography Technology Development

Chronography Pixelated & Monolithi Detector PoC

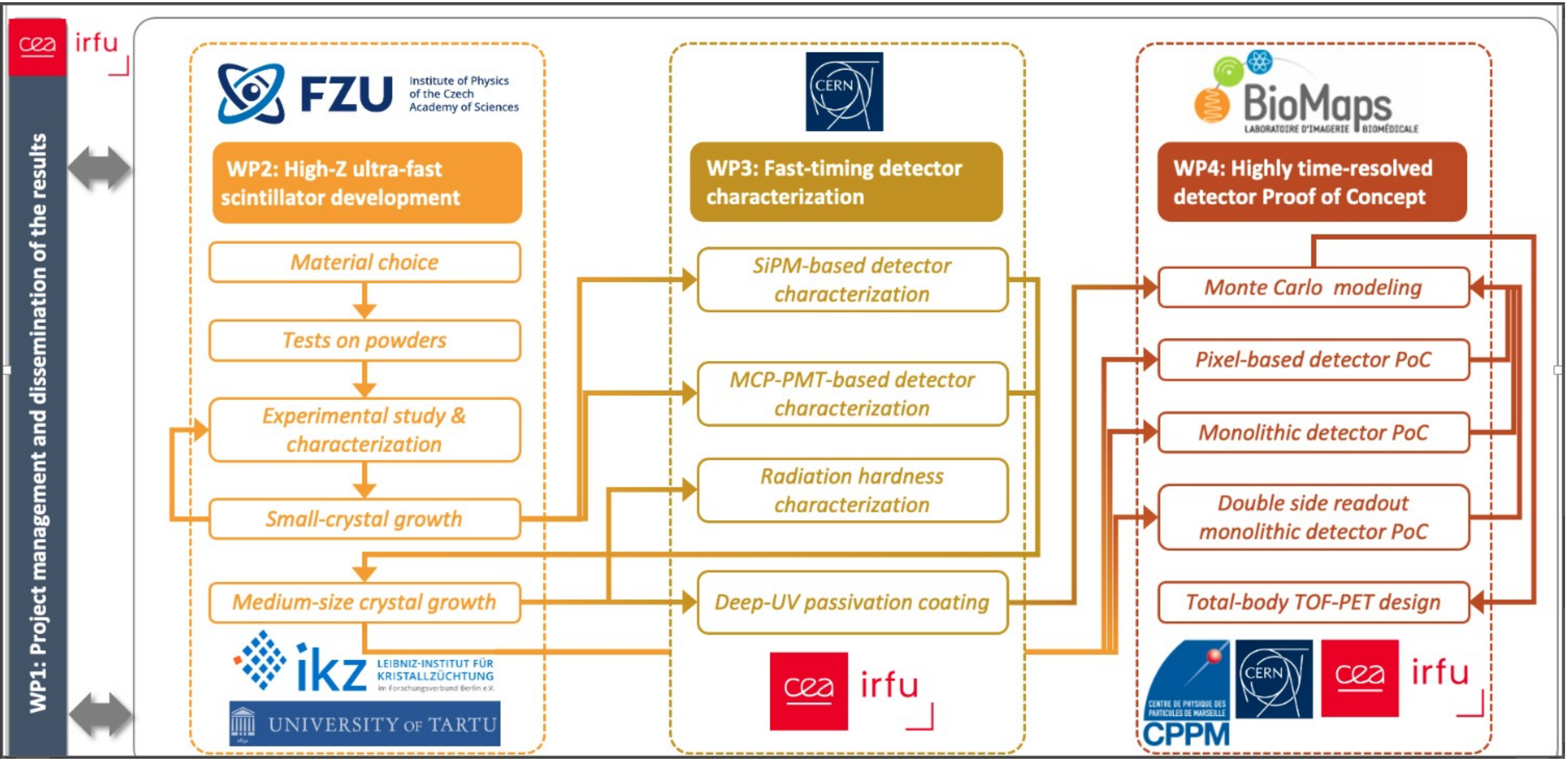
Powder material preselection & characterization	Crystal selection & characterization	Large crystal growth	Components and pixel-detector characterization	TOF-PET detectors' PoC	TOF-PET scan Monte Carlo des
ikz LEIBNIZ-INSTITUT FÜR KRISTALLZÜCHTUNG; FZU Institute of Physics of the Czech Academy of Sciences; UNIVERSITY OF TARTU	ikz LEIBNIZ-INSTITUT FÜR KRISTALLZÜCHTUNG; FZU Institute of Physics of the Czech Academy of Sciences; UNIVERSITY OF TARTU	ikz LEIBNIZ-INSTITUT FÜR KRISTALLZÜCHTUNG	CERN; cea irfu	CERN; cea irfu; CPPM	BioMaps; CPPM; cea irf

Advisory BOARD

1/ Crystal : 1/ LUXIUM France, Saint Gobain, 2/ CRYTUR
2/ Photodetector : Photonis (techno ambitieuse : MCP-PMP) + Broadcom
3/ Industrial Machines Manufacturer : InViScan, SIEMENS, Philips
4/ BIG pharma : Servier, Astrazeneca,Sanofi
5/ Other : ANDRA
6/ Expert-researcher ?

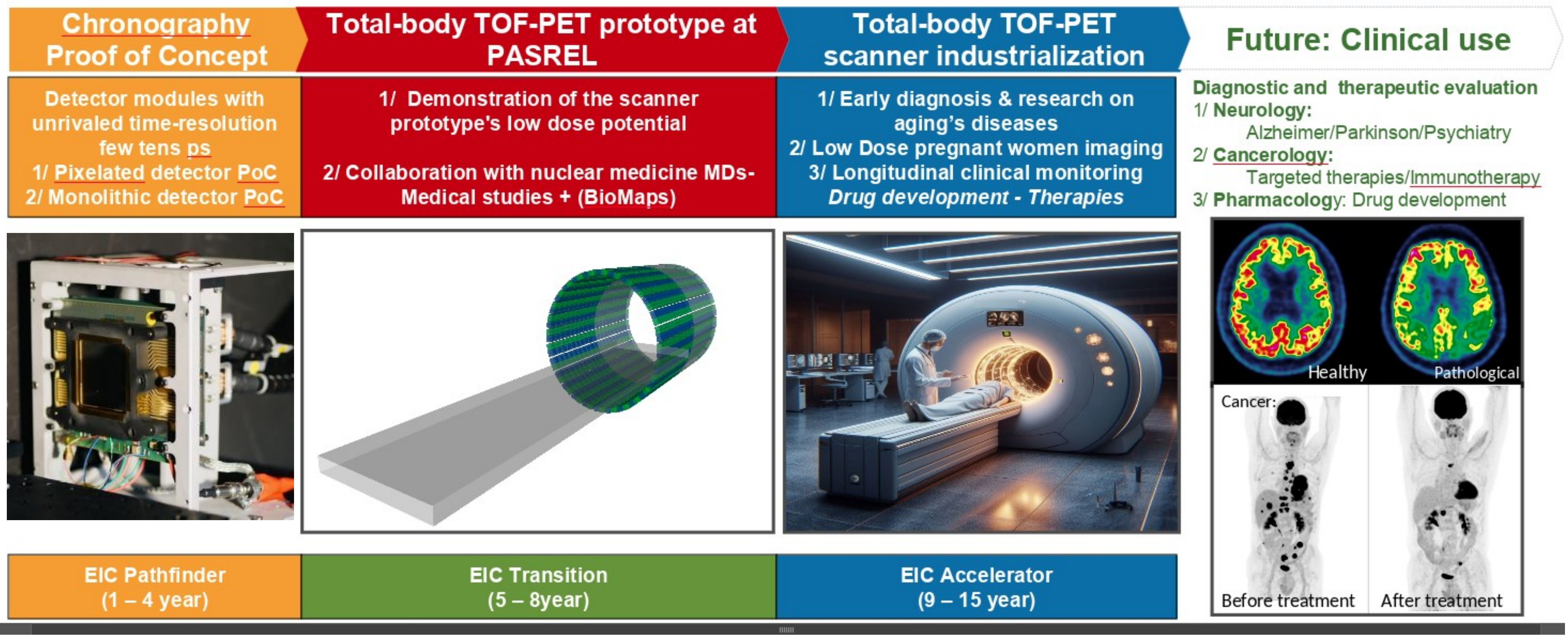
Crystal development / Gamma Detector Dev. & Models / PET Scan optimization

Work Package Organisation



Organisation / Crystal development / Single pixel detec. and related technologies / Proof of Concept detectors and PET Scan modeling

Long term vision



From a detector prototype

To a PET-Scan prototype (PASREL)

To PET-Scan industry

To medical applications

Conclusion : Instrumental skills in lab

- Expertise in fast photo-detection technologies and MeV gamma-ray detectors.
- At the forefront of fast single-photon detection, with MCP-PMTs and SiPMs.
- Tests benches on key photodetector characteristics
  - Quantum efficiency, time response, Positioning accuracy
  - high-performance, fast electronics (analog amplifiers and SAMPIC).
  - => original and high-performance photo-detection chain.
- Extensive experience in Monté-Carlo simulations for gamma ray detectors (Geant4 & GATE)
- Innovative AI approaches for event reconstruction.
- Closely following advances in scintillation crystal technologies (Crystal Clear collab.)

Conclusion : Positioning within IRFU and CEA

- Representing IRFU at the Crystal Clear collab. (Scintillators Crystal dev. & applications, Dominique).
- Representing IRFU at DRD-6 collab., (WP3, crystal calorimeters, Dominique).
- Representing IRFU at DRD-4 collab., (Photodetectors, MCP-PMTs, Instruments & simulations, photocathode models, Slava).
- Associated Researchers to the UMR BioMaps (CEA-SHFJ + Univ. Paris-Saclay + INSERM + CNRS) (Dominique, Slava),
  Headed by Prof. V. Lebon, leader of the *PASREL Research Hospital* being build in Saclay
- Membre du CoPil RTR Physique-Biologie de la DRF (Dominique).
- Membre de CSTD du DPhP (Slava)

- Coordinator of two collaborations, ***ClearMind*** (France) and ***Chronography*** (Europe).
- Major contributor to the AAIMME collaboration (CEA, CNRS, INRIA, Univ. Paris-Saclay).

Our request

- ManPower :
  - ***Ambitious, rich and motivating, scientific and technological program***.
    Major prospects for valorization.
  - Program in synergy with the major priorities of CEA and active prospects at CERN
  - Yet ***only two permanent scientists*** take care of it. Dominique will be 60 in 2025.

*For an ambitious future to these developments, **strengthening the group** is needed in the short term*

- Budget :
  - *ANR funding, P2I prototype and DPhP R&D budget* will cover the planned program with INCOM.
  - *Chronography project cannot be carried with French expertise alone*.
    The budget for the European collaboration : 3.1 M€, including 1.4 M€ for the CEA.
    EIC funding application : 4% success rate.
  - The competition is increasely powerful, particularly in the USA/Japan.

We are asking the CSTD and the heads of labs
support for
our scientific and technological program and
reliable source(s) of funding for this ambitious project