Development of Innovative PET Detectors at IRFU

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for the CaLIPSO group

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Biomedical Imaging

- Clinical Issues
  - Early diagnostics
  - Personalized (appropriate and optimal) therapy
  - Speed-up of the development of the new diagnostic and/or therapeutic bio-molecules.

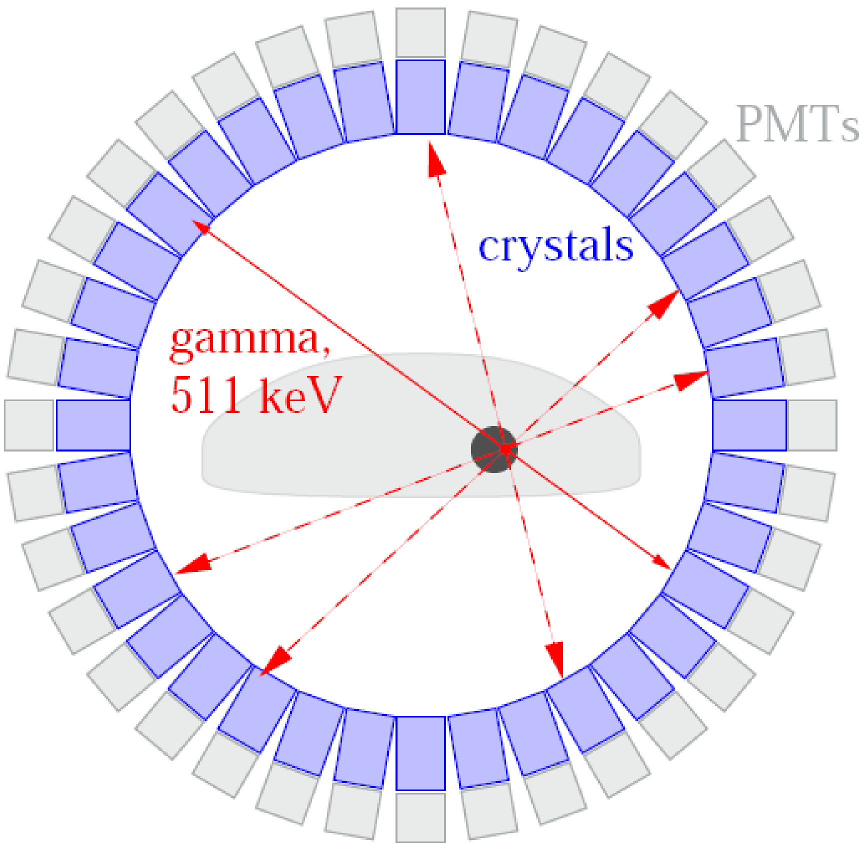
⇩

- Need to generalize the use of the quantitative and multi-modal molecular imaging technique.
  - Need to have multi-modal imaging with high resolution and high sensitivity
  - Increase the number of protocols guided by the imaging
  - Increase the applications filed (e.g. pediatric)
  - Facilitate access for the patient (cheaper, smaller, portable)
  - Dose reduction for the medical protocols

Positron Emission Tomography

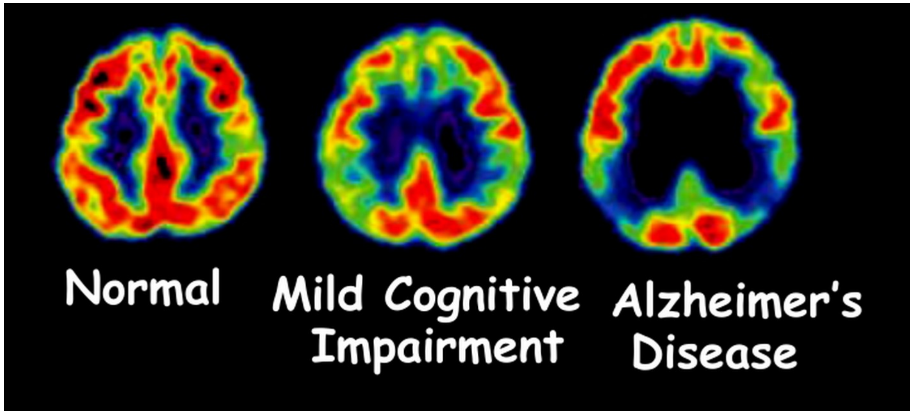
- PET is a nuclear imaging technique used widely in oncology, cardiology and neuropsychiatry.
- Allows to detect at picomol level the the biochemical activity.
- PET scan in a nootshell:
  - Inject one of the radioactive tracer

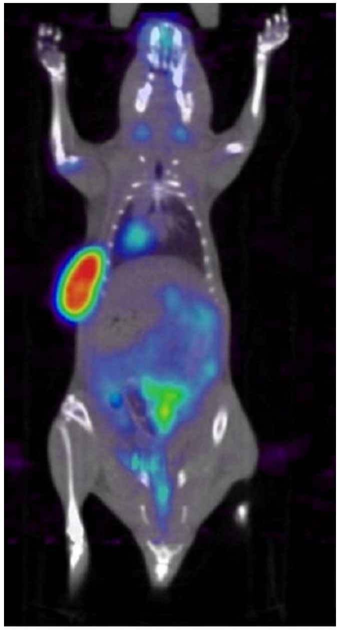
    e.g. ^{18}F-FDG, τ~110 min, ~one hour rest time
  - emits positrons ⇨ annihilation with an electrons ⇨ two 511 back-to-back gamma.
  - Gamma detection in coincidence ⇨ register ~100M lines-of-responce ⇨
  - 3D image reconstruction

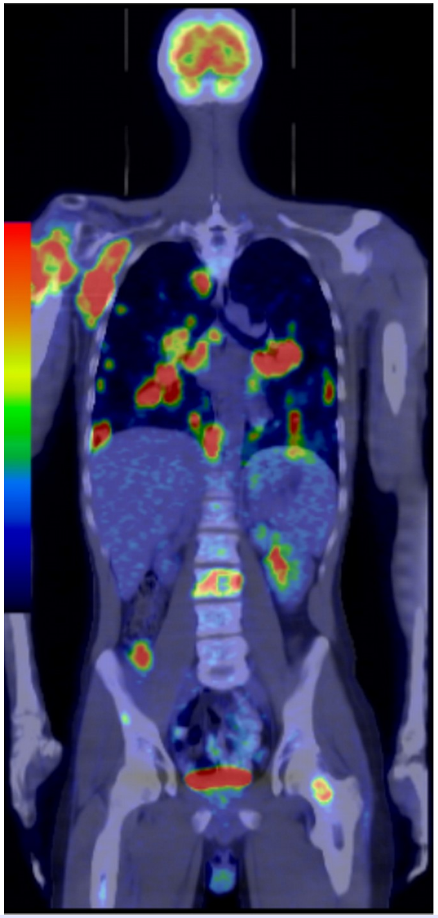


Scanner Types

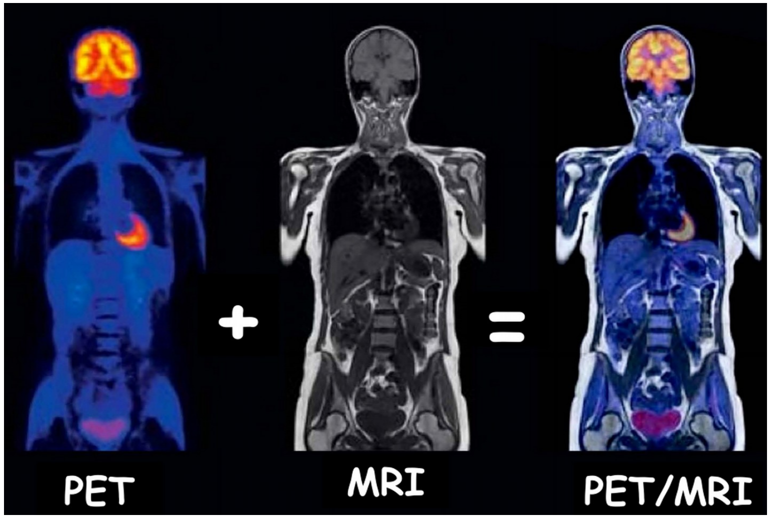
- Preclinical (small animals)
  - Small aperture
  - High spatial resolution
  - Small sensitivity
- Brain scanner
  - Limited aperture
  - High sensitivity
  - Good spatial resolution
- Whole-body
  - Large aperture
  - High sensitivity
  - Low spatial resolution
  - Full body dose ~ **5 – 15 mSv**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



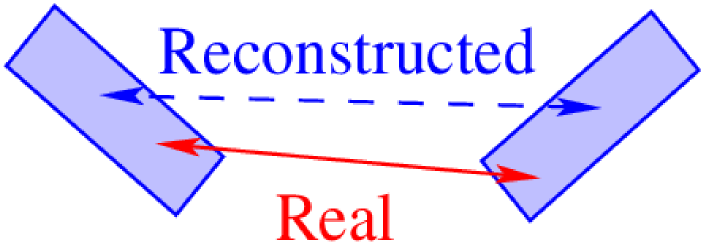


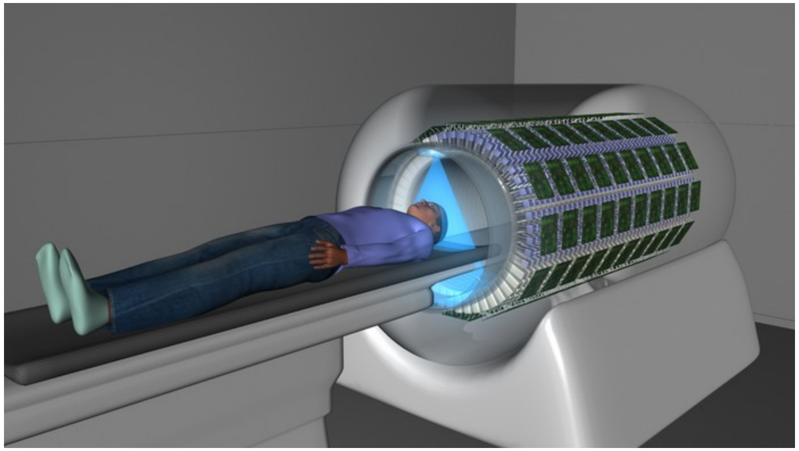


PET Evolution

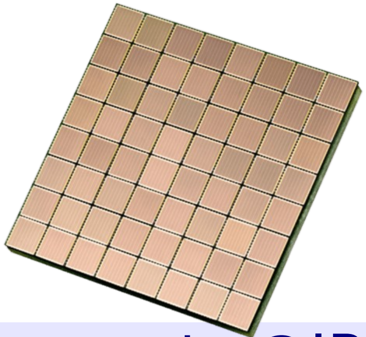


- Combined modalities: CT/PET, MRI/PET
- Improvement sensitivity: total-body PET → 40 fold improvement in sensitivity
- Reduce bias: depth-of-interaction reconstruction



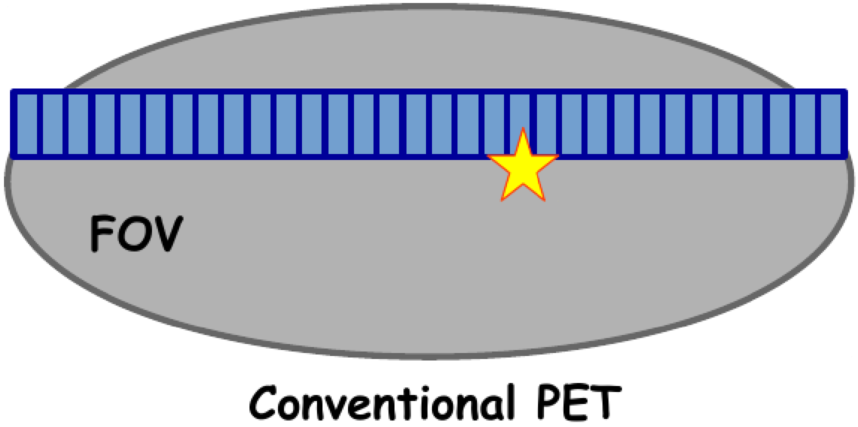


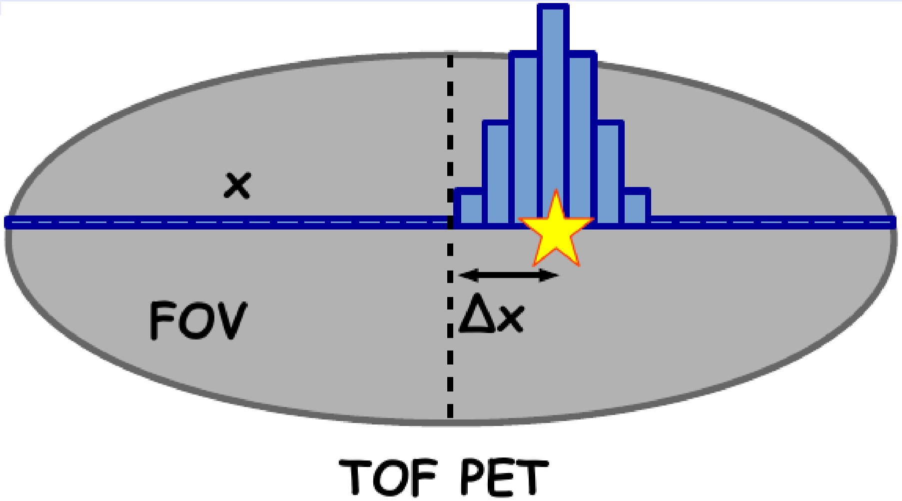
- New developments in electronics, detection



- Time-of-flight technique (TOF) ⇨ see next slides

TOF Technique





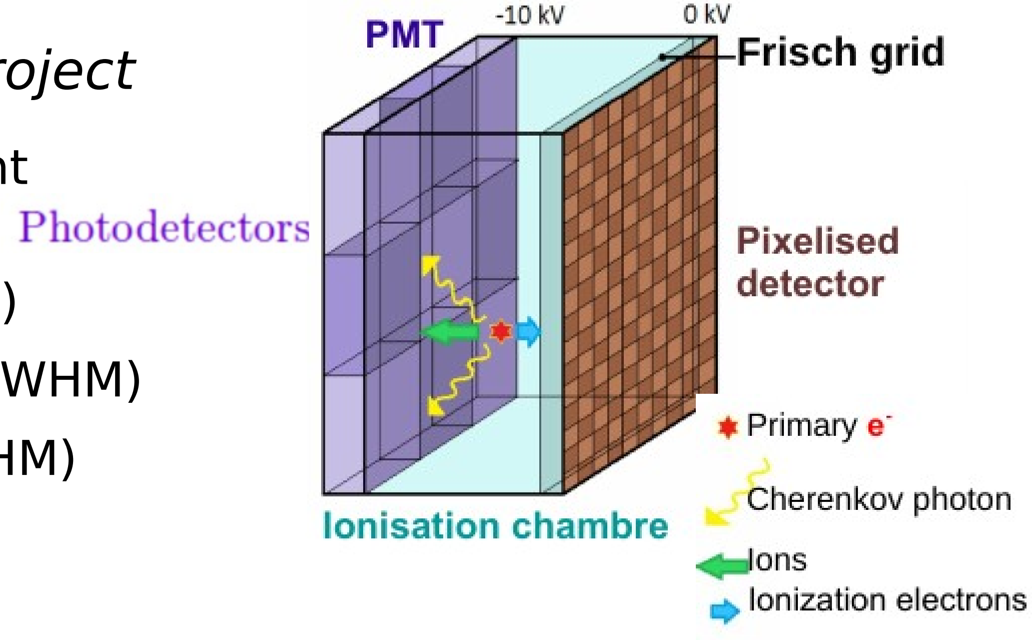
- TOF techniques: measure the difference in time between two photons ⇨ improve S/B
- Contrast of the image directly correlated to the S/B and available statistics.
- TOF gain estimation:

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

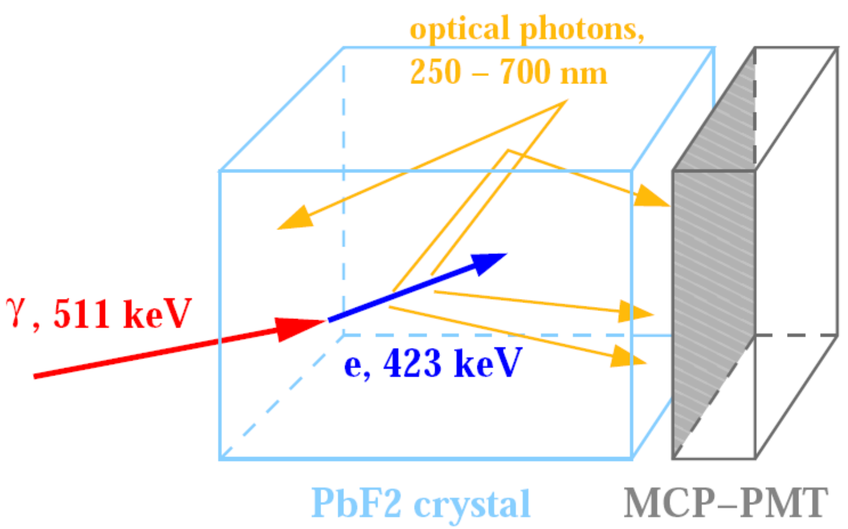
D=30 cm ⇨ CRT=**150 ps** (FWHM) ⇨ G~2.9 ⇨ **8x lower dose**

Developments @ IRFU, CEA-Saclay

- **High spatial resolution** for the brain /preclinical PET: *CaLIPSO project*
  - Dual read-out: ionization and light
  - Innovative liquid as a detection medium: TMBi (trimethylbismuth)
  - Spatial resolution: 1x1x1 mm3 (FWHM)
  - Resolution in time < 150 ps (FWHM)

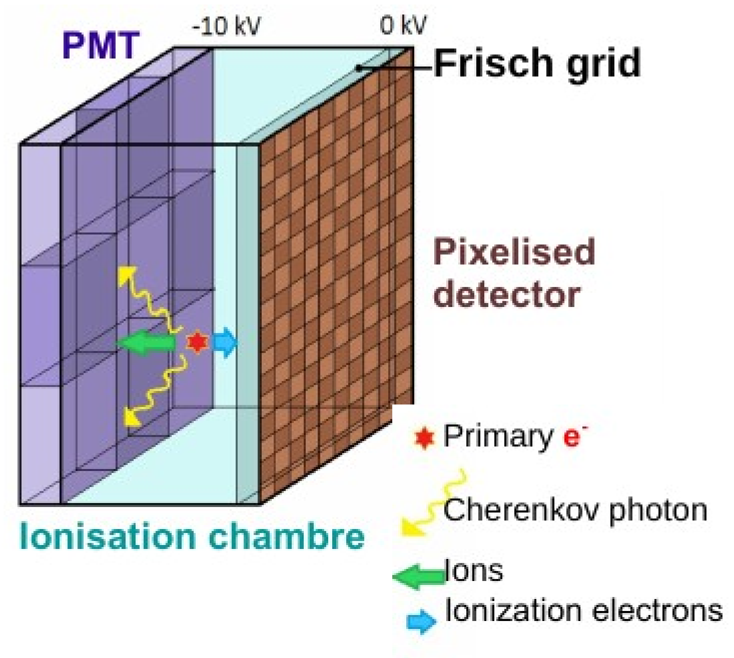


- **High TOF resolution** for whole-body/brain PET : *PECHE → ClearMind projects*
  - Use Cherenkov light for the detection
  - Crystals as a detection medium
  - Resolution in time < 100 ps (FWHM)



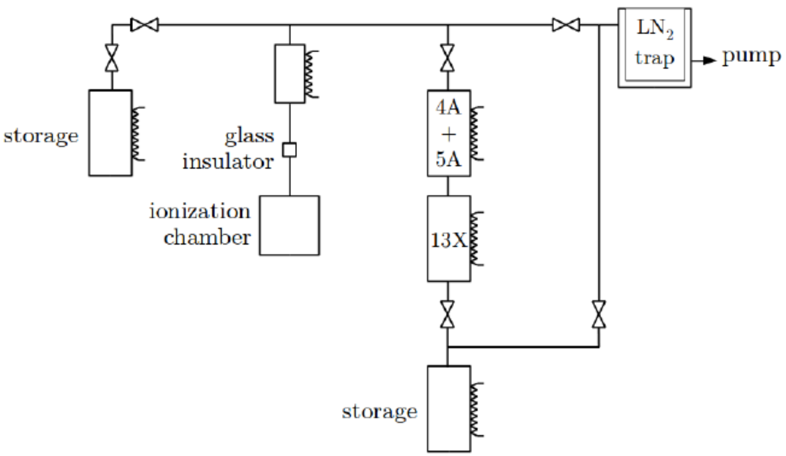
CaLIPSO project

- **Tri**M**ethyl **Bi**smuth (**TMBi**), Bi(CH_3)$_3$
  - **Bi, Z = 83, highest Z** non radioactive element.
  - Photoelectric / (Photoelectric + Compton) ~ 47%
  - Limpid (λ> 400 nm), dielectric, chemically stable
  - Density 2.3 g/cm^3, refraction index ~ 1.6



- Two axes of development
  - Cherenkov light signal detection: efficiency, time resolution
  - Ionization light detection: ionization yield, electron drift speed, purification

Purification Set-up



M. Farradèche

- Use a 1cm thick test cell
- TMBi very reactive → limited choice of materials (ceramic, stainless steel)
- Require use of ultra-high vacuum technologies

Ionization yield Measurement

$$G_{fi} = \frac{I}{e\,\Delta\epsilon}$$

I → measured

$e\,\Delta\epsilon$ → simulated

$$G_{fi} = G_{fi}^{0}\,(1 + \alpha E)$$

- Use a 1 cm thick test cell with parallel plate geometry.
- Measure a small (~100 fA current) induced by a radioactive source between two electrodes.
- Reduce the external noise: clean outer surfaces, decoupled from the common electrical network.

M. Farradèche et al. , “Free ion yield of Trimethyl Bismuth used as sensitive medium for γ detection”, Submitted to JINST, arXiv: 1809.08115

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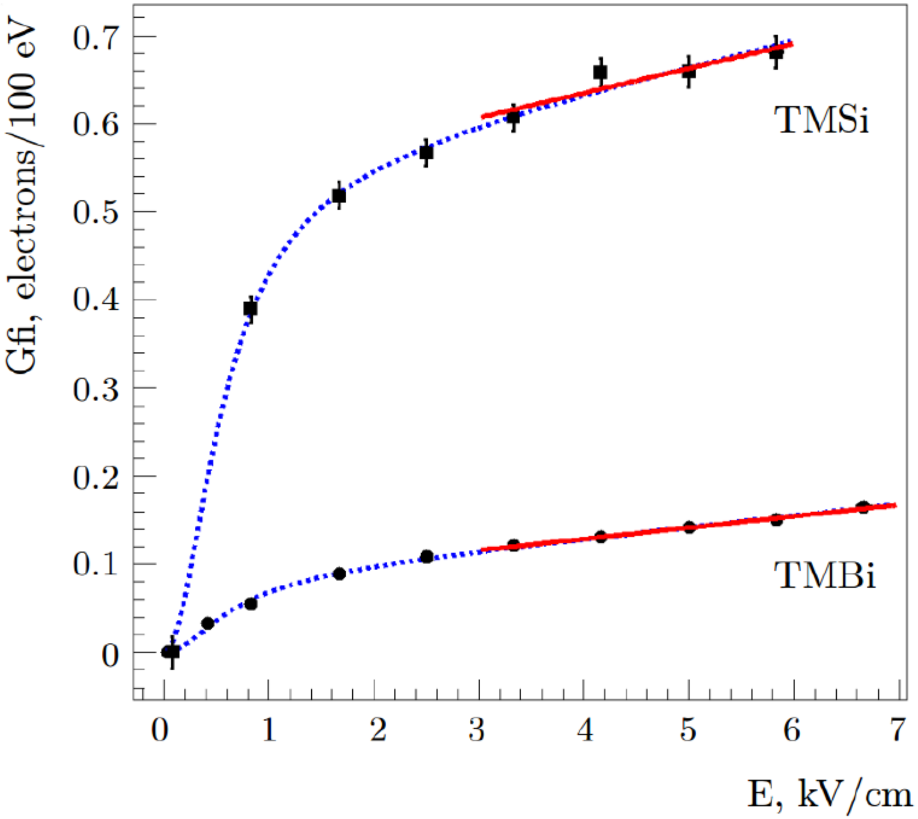

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Cherenkov Light Detection

C. Canot

PECHE	CALIPSO OPTICAL PROTOTYPE

Cherenkov Radiator

PbF_2 crystal	TMBi liquid + Sappfire window

Optical gel OCF452

Micro-Channel-Plate Photo-Multiplier
(Planacon by Photonis)

Commercial Amplifiers
2.5 GHz, 20 dB, ZKL2R7+
1.5 GHz, 40 dB, ZKL1R5+

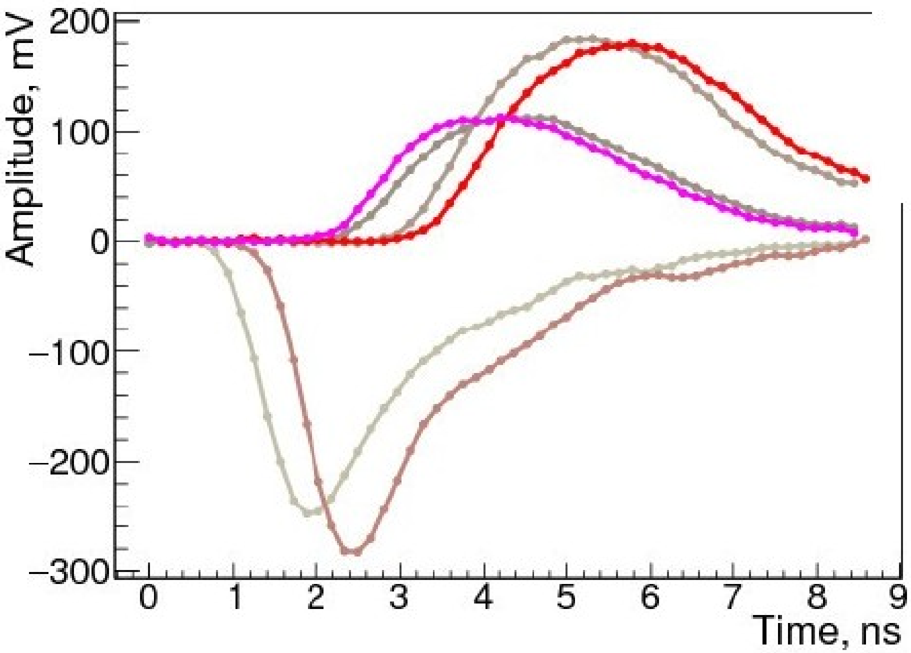
Digitization: **SAMPIC**
Time Waveform Digital Converter

C. Canot, “Détecteur optique Cherenkov de photons 511 keV …”, PhD thesis (in French), 2018

Read-out Electronics

Signals numerisation with the **SAMPIC** module:

> **A 32-channel, 10-GSPS Time and Waveform Digital Converter module**, developped by **IRFU** and **LAL.**



Typical signal with 6.4 GS/s

* provides digitized waveform with 64 samples, 1.6 GS/s to 10 GS/s

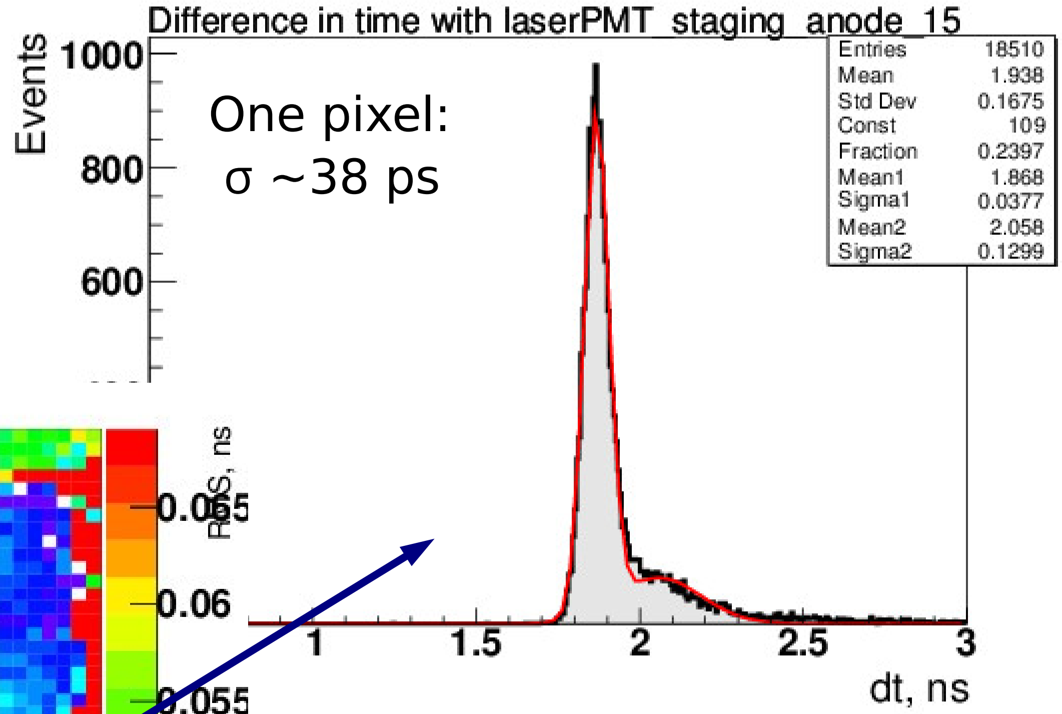
* extremely good resolution in time :
< 5 ps (σ)

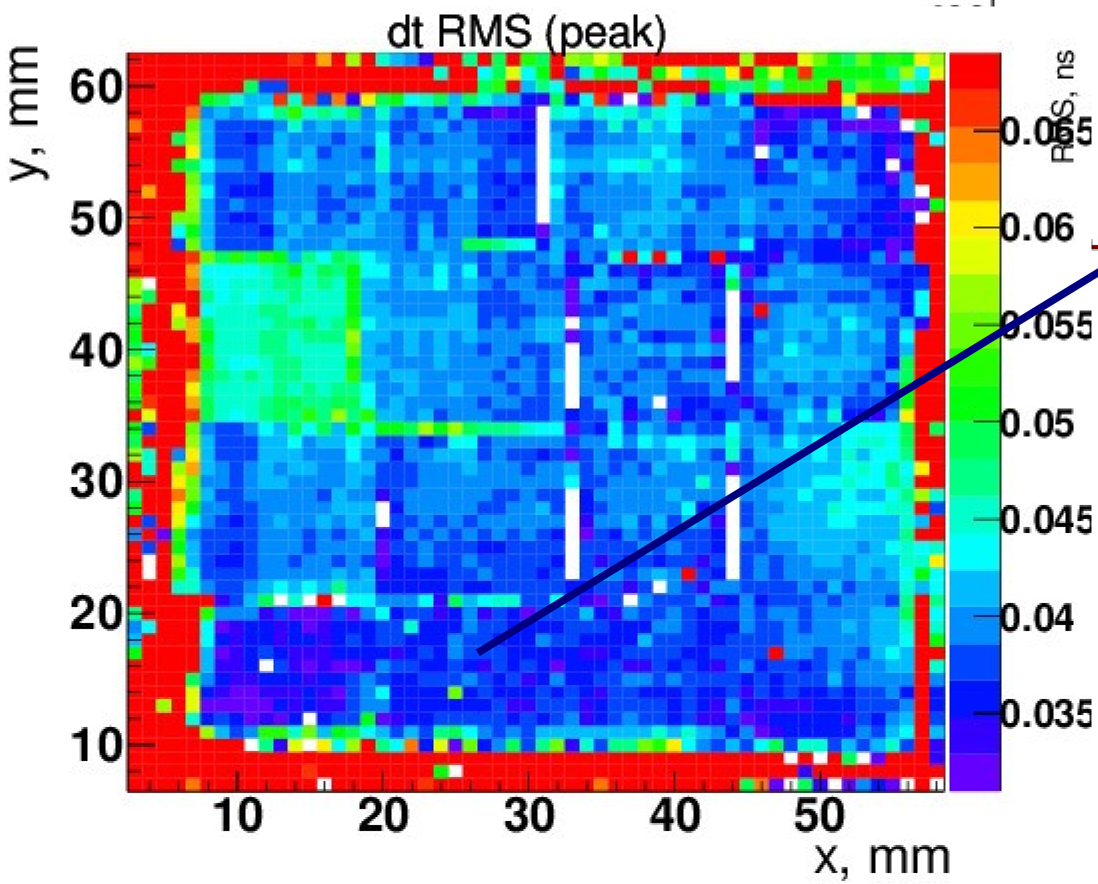
* allows to use on-line the configurable Constant Fraction Discriminator (CFD) algorithms

* acquisition of waveform and/or CFD time

MCP-PMT Calibration

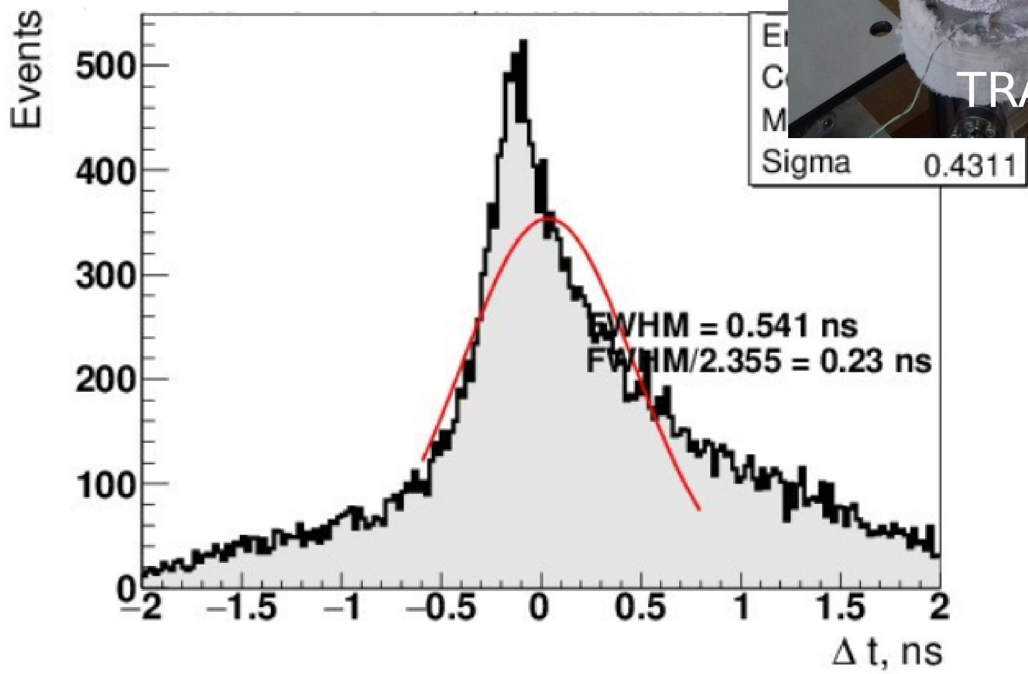
- 1 mm step size
- ~70kHz acquisition speed
- 3 hours per PMT





CaLIPSO optical Prototype

- Measure efficiency and time resolution at the test bench using ^{22}Na radioactive source → two 511 keV photons
- Measured eff.: ~25%



CRT = 540 ps (FWHM) →
DO3 Resolution = 500 ps

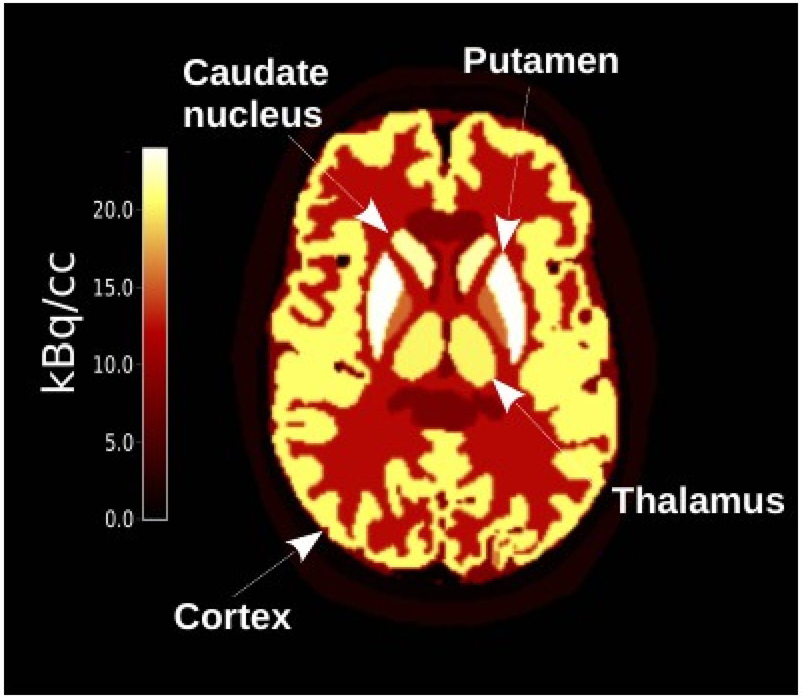
CRT : Coincidence Resolving Time

CALIPSO Potential in Simulation

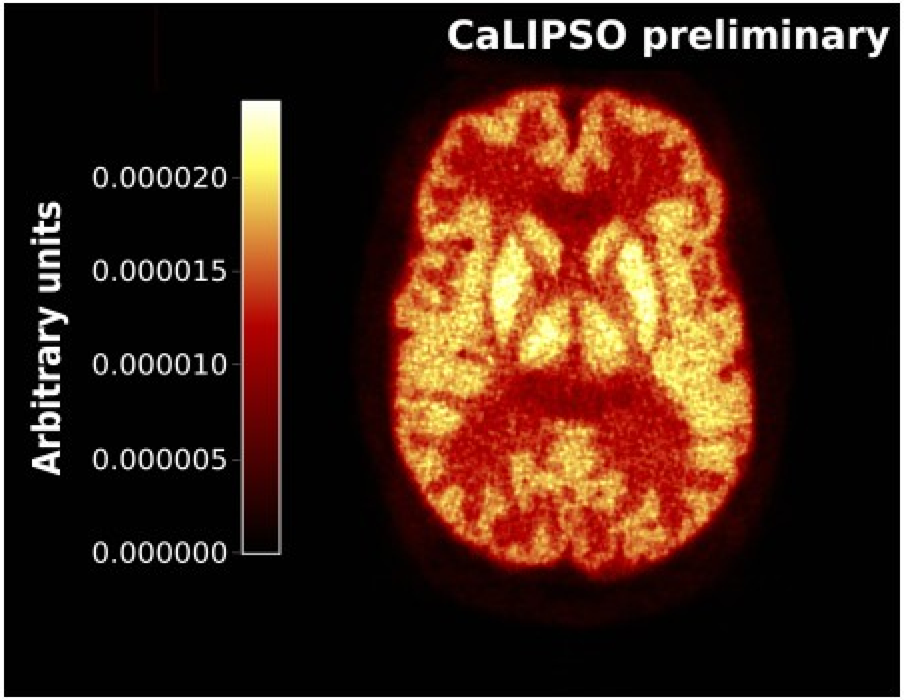
O. Kochebina

- Use GATE/Geant4 software for the simulation
- Simulate use 18F-FDG marker (glucose transporter could be used to study for Alzheimer disease)
- Demonstrate that CaLIPO indeed is able to hve a precision of about 1 mm^3

Simulated



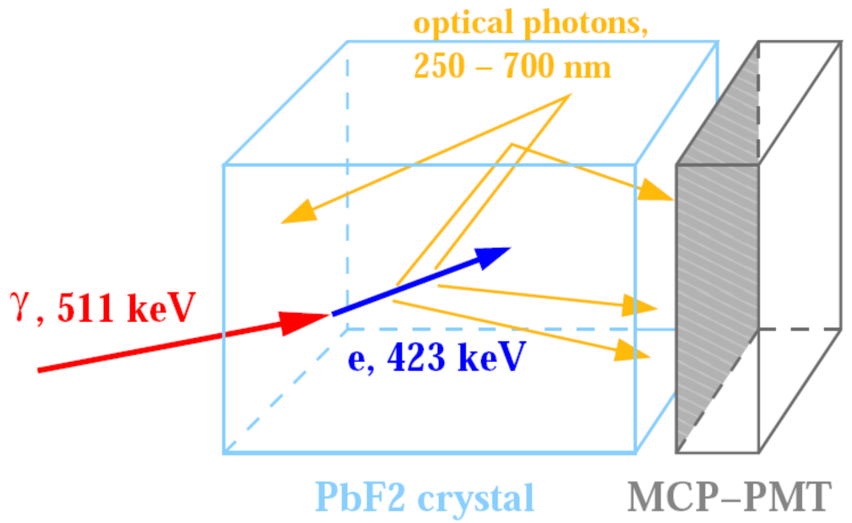
Reconstructed



O. Kochebina et al,
"Simulations and Image Reconstruction for the High Resolution CaLIPSO ...", 2018, e-Print: arXiv:1801.06411 [physics.med-ph], Submitted to IEEE TRPMS journal

Crystal Detector: Time Resolution

- PbF2 crystal (thickness 10 mm)
  - only Cherenkov radiation
  - Density 7.66 g/cm³, high photoelectric fraction : 46 %
  - refractive index : 1.82 @ 400 nm, transp. > 250 nm
- Test two equivalent detectors on the test bench with ^{22}Na source.



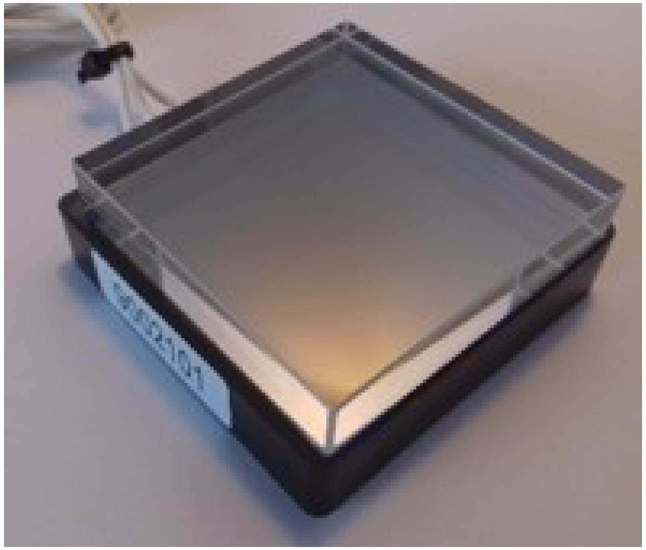
$$\sigma^2_{Détecteur} = \sigma^2_{Ch} + \sigma^2_{PM} + \sigma^2_{j} + \sigma^2_{a} / (dS/dt)^2$$

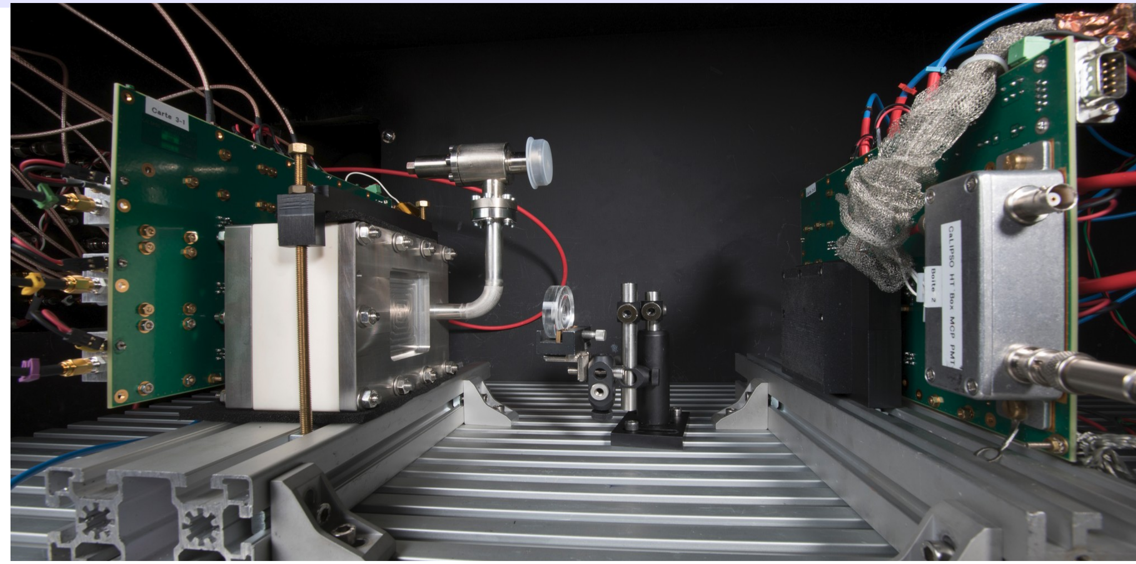
Simulation
PECHE ~ 50 ps (FWHM)
DO3 ~ 170 ps (FWHM)

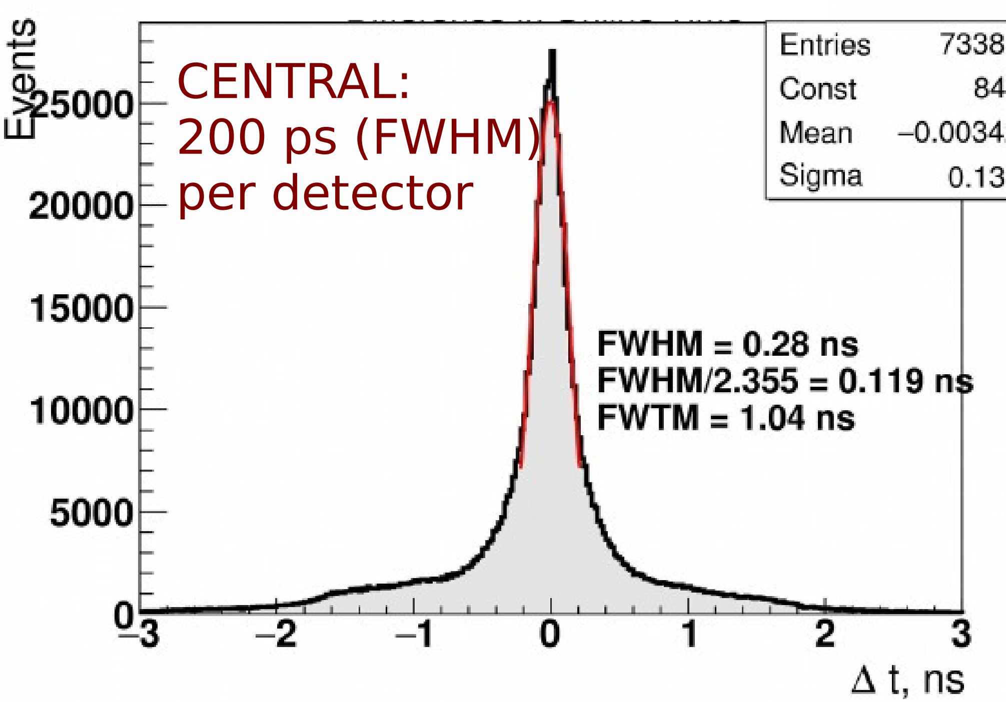
Measured PMT TTS:
130 ps (FWHM) + tails

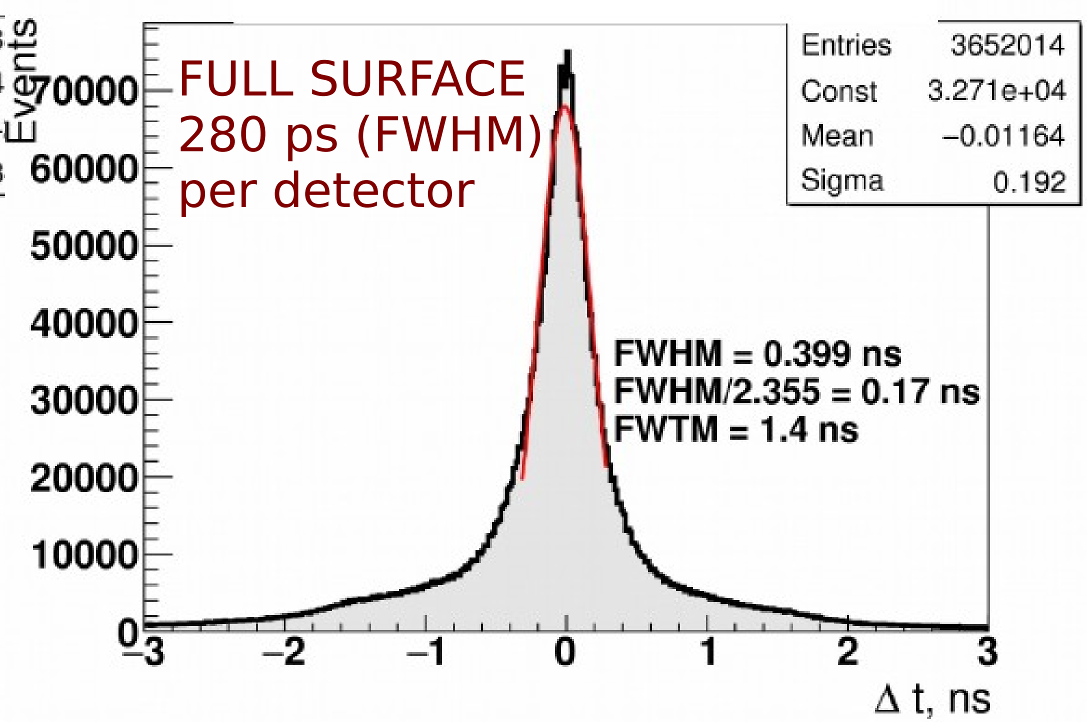
Mesured:
12 ps (FWHM)

Crystal Detector: Time Resolution

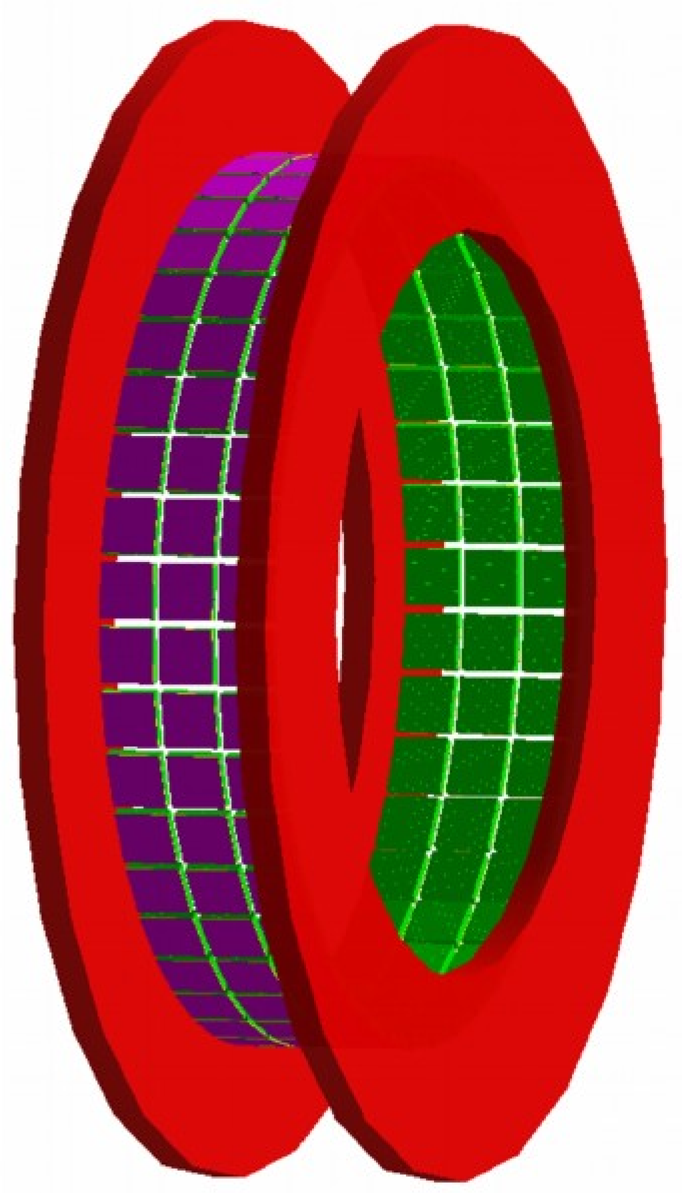








Cherenkov Scanner: Simulation



M. Alokhina
Cotutelle:
Psris-Sud / TSNUK, Kyiv

Material: PbF_2 (8 256 crystals)

Crystal size: 6.5x6.5x10 mm^3

Total number of PMTs: 129

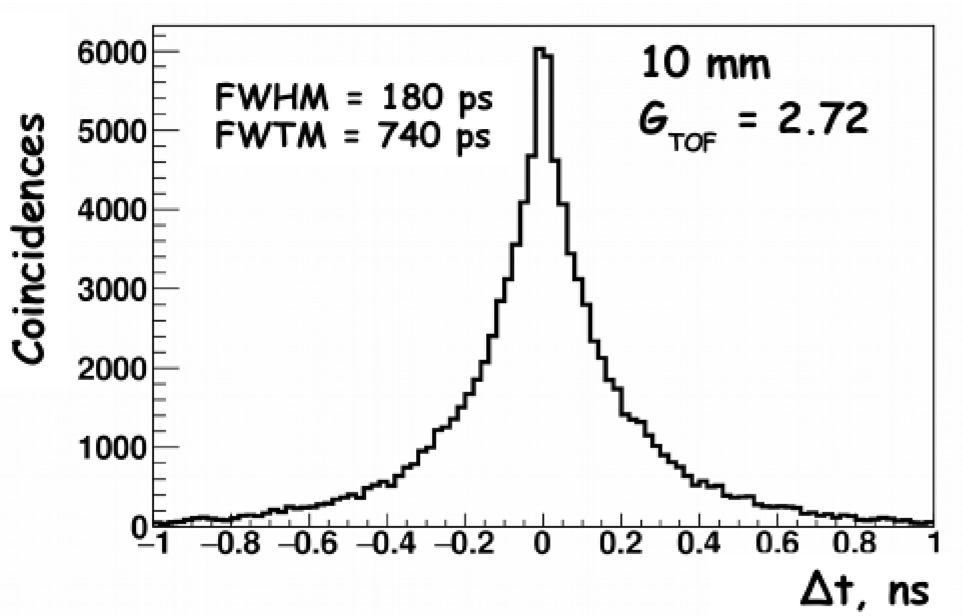
Coincidence window: 4.0 ns

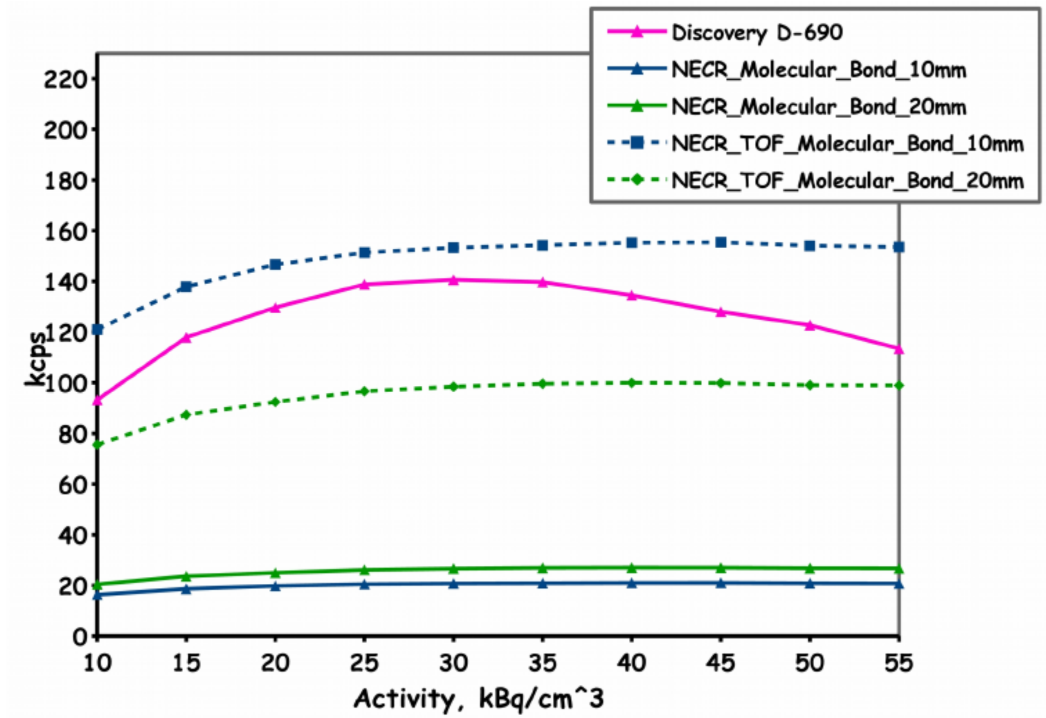
Axial FOV: 177 mm

Transaxial FOV: 81 cm

M. Alokhina, "Design of the Cherenkov TOF whole-body PET ...", PhD thesis, 2018

Performance: Noise Equivalent Count Rate





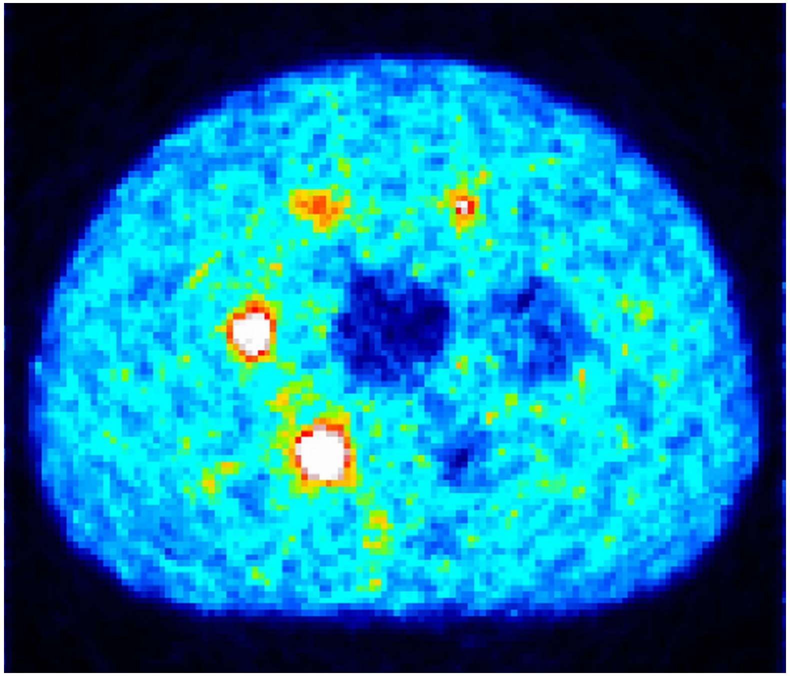
$$NECR = T^2/(T + S + 2R)$$

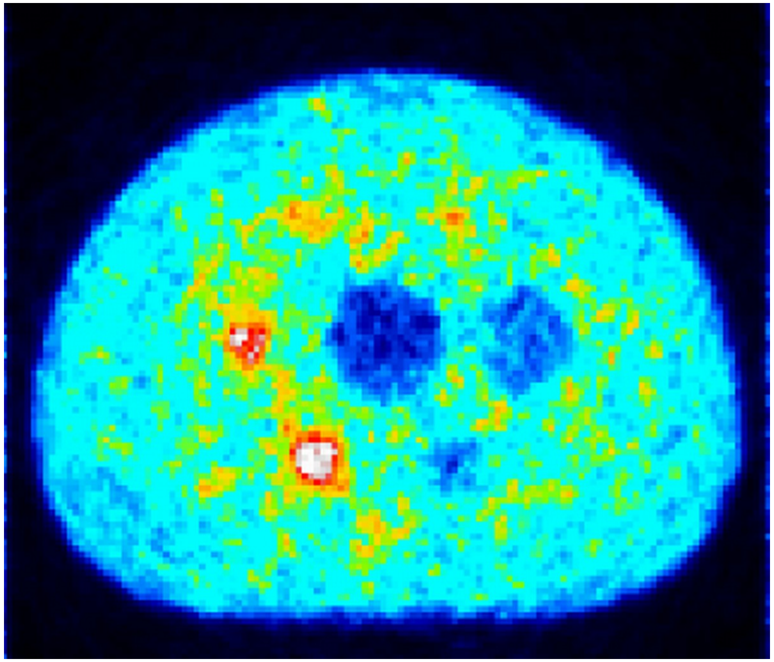
T – rate of true coincidences
S – rate of scatter coincidences
R – rate of random coincidences

$$NECR_{TOF} = D/\Delta x * NECR$$

Contrast Recovery

- Use iterative Maximum Likelihood Expectation Maximization (MLEM) imge reconstruction 3D algorithm with TOF.
- Open source code CASToR, French collaboration: ww.castor-project.org
- Use Image Quality Phantoms (NEMA 2-2012 standard) with two initial S/B contrast: x8 or x4
- Observe reasonable contrast recovery

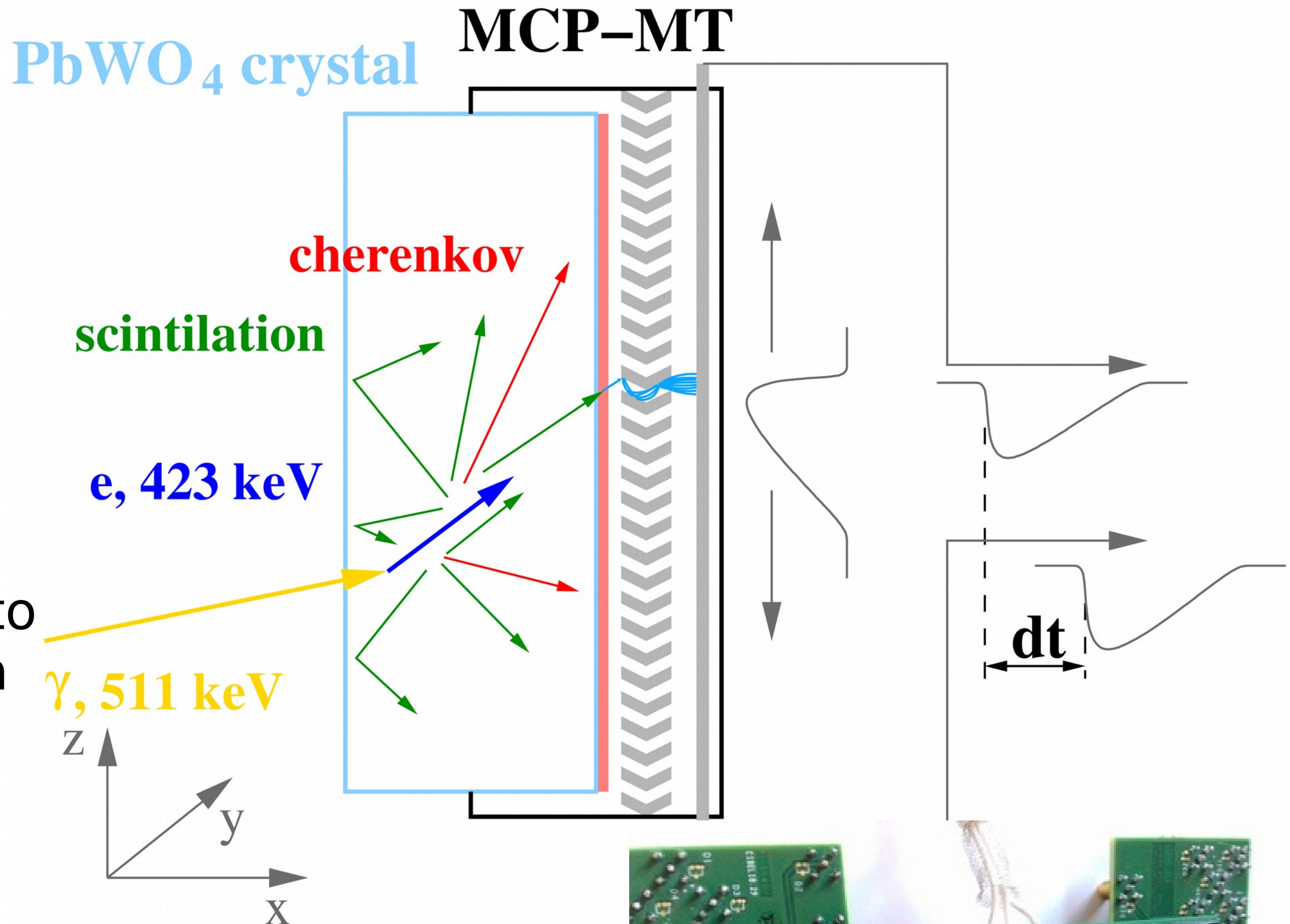


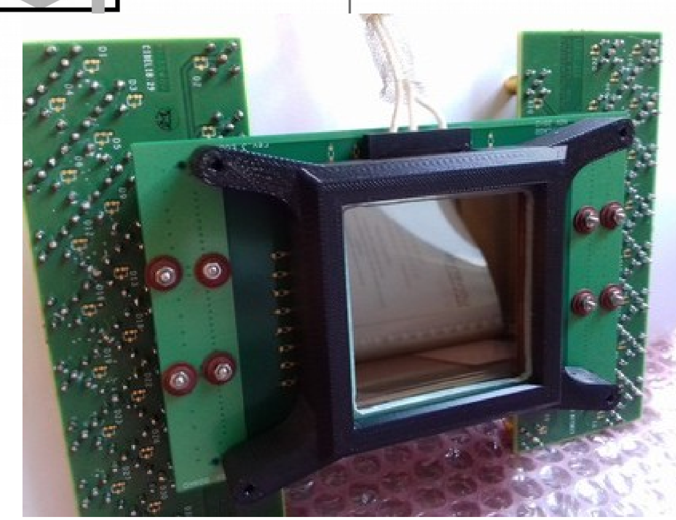


Reconstructed image of IQ NEMA Phantom.
Scan time 15 min, TOF 180 ps, initial contrast 8xBG

Further Developments: ClearMind

- Direct deposition of the photocathode on the PbWO4 crystal
  - increase the number of detected Cherenkov photons
  - additional fast scintillation photons
- Use of monolithic crystal to reconstruct 3D interaction position and
- correct for DOI effect
- Use MCP for electron multiplication
- Use delay line approach to reduce number of channels





Conclusion

- Development of the cutting-edge technology for use in PET, but not only.
- Main directions: high spatial precision and high TOF resolution
- Study a potential of the Cherenkov radiation for whole-body PET scanner by simulation and hardware test and identified main limitations for use of the Cherenkov technology.
- The ongoing developments at IRFU have an ambition to overtake the identified limitations.