APS Meeting, Denver, April 13-16, 2019

Session H02: New Detectors for Medical Imaging: Translating Discoveries from Nuclear and Particle Physics to Medicine

Ultrafast detection in positron emission tomography using Cherenkov light

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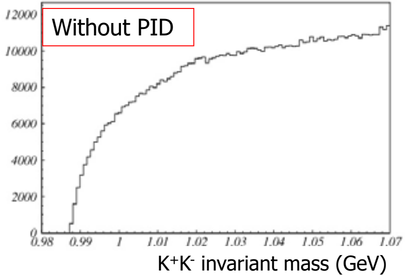
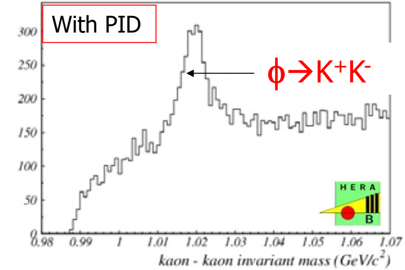
Beyond the simple Cherenkov based TOF-PET

Conclusions and summary

Particle identification – type of particles that were produced in a reaction - one of the essential features of experiments





Very often the interesting reaction is burried in a large number other reactions (background).

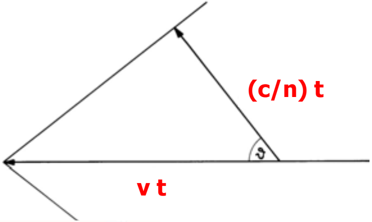
One important tool: select only reactions (events) with the right type of particles = identify each of them →particle identification (PID)

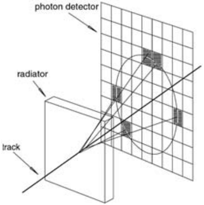
Example: the decay $\phi \rightarrow K^+K^-$ only becomes visible after particle identification is taken into account.

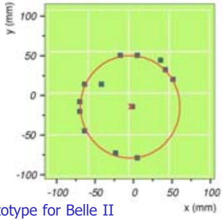
One of the important PID methods: use of Cherenkov radiation

A charged track with velocity v=βc exceeding the speed of light c/n in a medium with refractive index n emits polarized light at a characteristic (Cherenkov) angle, **$\cos\theta = c/nv = 1/\beta n$**

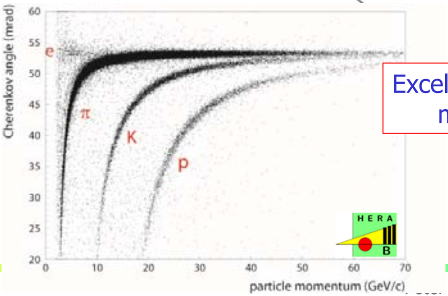
Cherenkov photons detected on a plane → ring
(Ring Imaging Cherenkov counter, RICH)
ring radius → Cherenkov angle → velocity







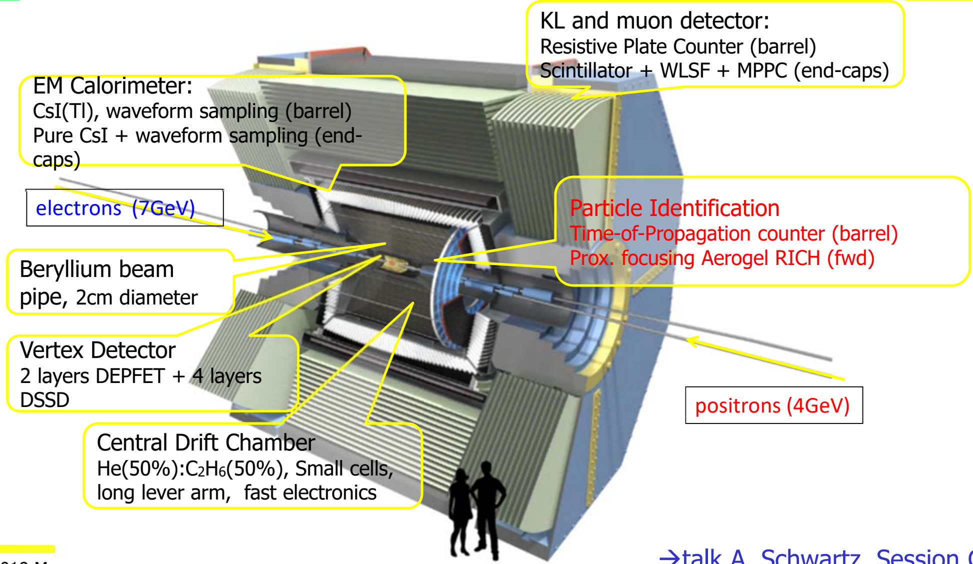
ARICH prototype for Belle II



Excellent identification method

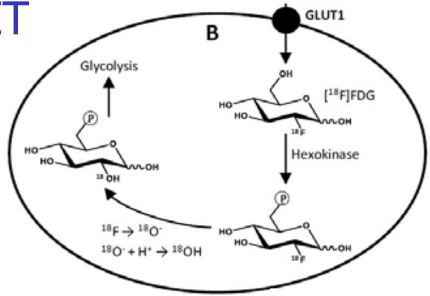
Very low light level = few detected photons → Needs a fine granularity sensor for single photons with low noise

Cherenkov detectors in Belle II



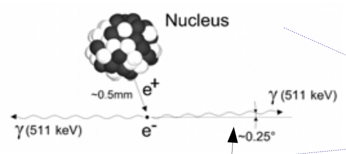
→talk A. Schwartz, Session G03

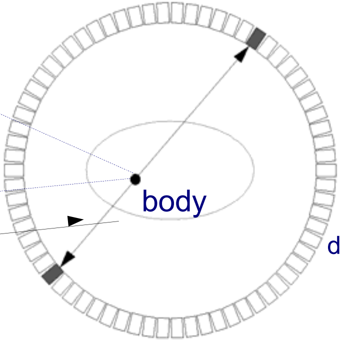
Medical Imaging with PET

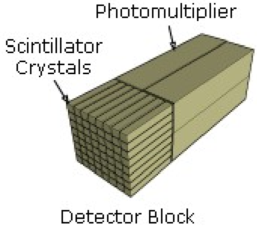


Positron emission tomography:
Functional imaging with
biomarkers containing a beta+ emitter

Fluorodeoxyglucose (FDG) is the
most commonly used marker – indicates
the uptake of glucose







detector ring

line of response (LOR)

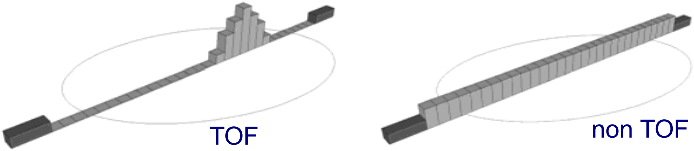
TOF-PET

Time-of-Flight difference of annihilation gammas is used to improve the contrast of images obtained with PET

Localization of source position along the line of response:

$\Delta t \sim 66\text{ps} \rightarrow \Delta x = c_0 \Delta t/2 \sim 1\text{cm}$

Δt = coincidence resolving time, CRT

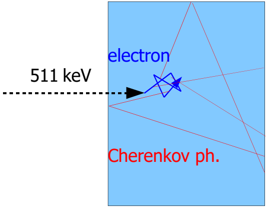


However, PET systems based on SiPM readout are reaching CRT of ~300 ps, and only with small crystals ~3x3x3 mm^3 CRT<100 ps

Annihilation gamma detection with Cherenkov light

Novel photon detectors – MCP-PMT and SiPM – have excellent timing resolution →
TOF resolution limited by the spread in photon emission and arrival time

Cherenkov light is promptly produced by a charge particle traveling through the medium with velocity higher than the speed of light c_0/n. Photoelectron emits Cherenkov light in ~1ps.



Disadvantage of Cherenkov light is the small number of Cherenkov photons produced per interaction

$$N \approx \frac{370}{eV\,cm}\, l\, \Delta E\, \sin^2 \vartheta_C \approx 370 \times 0.01 \times 2 \times 0.75 \approx 8$$

→ detection at a single photon level!

Cherenkov radiator PbF_2

An excellent candidate Cherenkov radiator for detection of annihilation gammas:

- high gamma stopping power
- high fraction of gamma interactions via photoeffect → electrons with maximal kinetic energy → more Cherenkov photons
- high transmission for visible and near UV Cherenkov photons

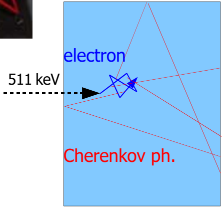
	ρ (g/cm³)	n	e^- Cherenkov threshold (keV)	Cutoff wavelength (nm)	Attenuation length (cm)	Photofraction
PbF_2	**7.77**	**1.82**	**101**	**250**	**0.91**	**46%**
LYSO	7.4				1.14	32%
$LaBr_3$	5.1				2.23	15%

Excellent TOF PET timing with MCP PMTs

Pioneering experiment, two detectors in a back-to-back configuration:

- Cherenkov radiators: 25x25x(5, 15) mm^3 PbF_2
- MCP-PMT photodetectors:
  - single photon timing ~ 50 ps FWHM
  - active surface 22.5x22.5 mm^2

black painted, Teflon wraped, bare



Timing resolution (black painted):

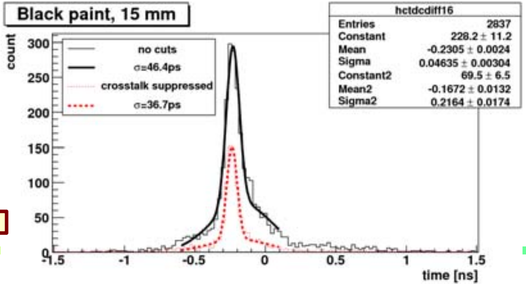
- ~ 70 ps FWHM, 5mm crystal
- ~100 ps FWHM 15mm crystal

Efficiency (Teflon wrapped):

- ~ 6%, single side

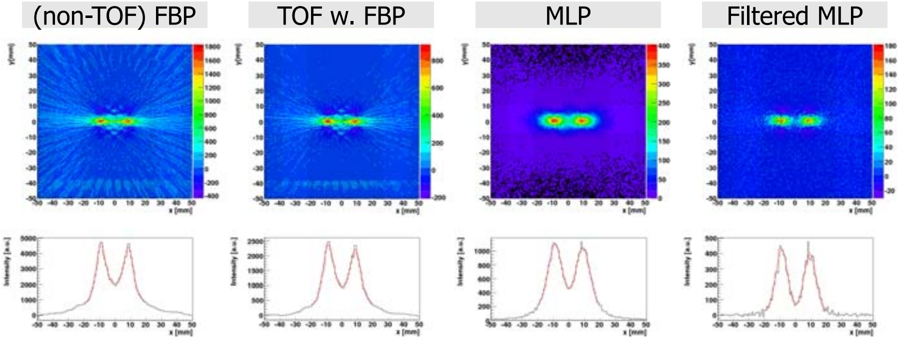
(typically ~ 30% for LSO)

NIM A654(2011)532



Reconstruction - experiment

Two ^{22}Na point sources at +10 mm and -10 mm 4x4 segmented, black painted PbF_2 radiators

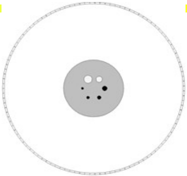


→ A simple, very fast Most-likely-point (MLP) method (~histograming of points) already gives a reasonable image

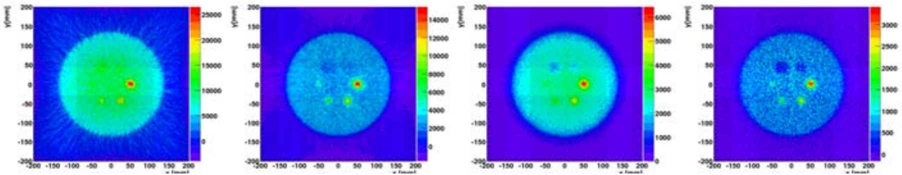
→ NIM A732 (2013) 595

Reconstruction - simulation

- Hot spheres activity concentration: 3x phantom background
- Statistics equivalent to 163 s of PET examination
- 4x4 segmented, Teflon wrapped PbF_2 radiators
- 20 mm thick axial slices



(non-TOF) FBP | TOF w. FBP | MLP | Filtered MLP



First tries, have to understand how the possible improvements in the detection efficiency will influence the performance:

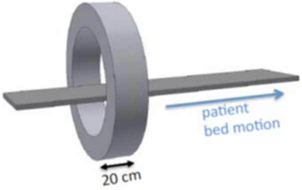
- Black painted (better TOF resolution) → better contrast
- Teflon wrapped (higher statistics) → better contrast-to-noise ratio (despite the tails in the timing distribution)

→ NIM A732 (2013) 595

Cherenkov based PET scanner?

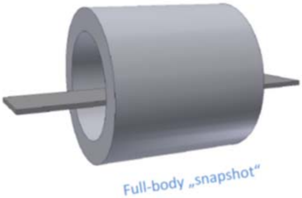
PbF_2 not a scintillator → considerably cheaper!

Smaller attenuation length than LYSO – small parallax error



→ Cheaper normal scanner or

→ Total/half body device



Extending axial FOV 20 cm → 200 cm:
estimated 6-fold increase in SNR →

- Better image quality
- OR Shorter scanning time
- OR Less injected activity: 8 mSv → 0.2 mSv

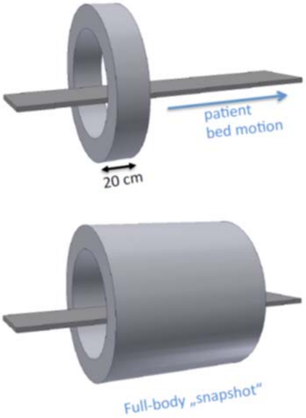
EXPLORER, first total-body scanner, is currently under test at UC Davis

Cherenkov based PET scanner

PbF_2 not a scintillator → very fast and considerably cheaper!
PET scanner feasible?

→ Carry out a feasibility study, groups led by

- Sibylle Ziegler, TU Munich
- Alberto Del Guerra, University of Pisa
- Peter Križan & Samo Korpar, JSI, Ljubljana
- Irene Buvat, IMIV, Orsay, CEA
- Edoardo Charbon, TU Delft
- Paul Lecoq, CERN
- Gabor Nemeth, Mediso Ltd
- Florian Wiest, KETEK GmbH
- Stefan Ritt, Paul Scherrer Institute



One of the outcomes → a preliminary MC simulation study →

Cherenkov based PET scanner, MC study

The main building block of the simulated scanner was a gamma detector composed of a PbF_2 crystal and a SiPM as light sensor.

The performance of a single gamma detector was first investigated in depth using GEANT4. The simulation was then transferred to GATE and a scanner was simulated.

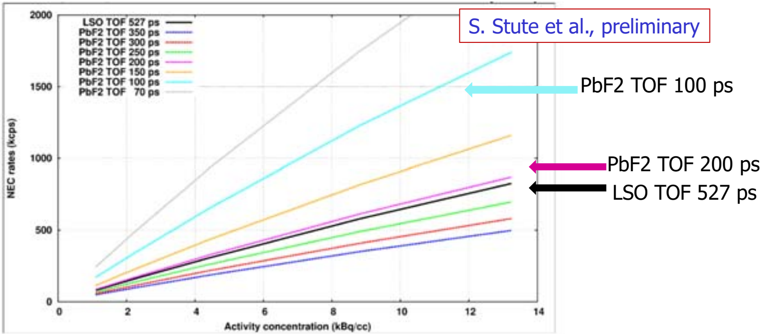
The performance of the scanner based on the Cherenkov method was compared to that of a state-of-the-art LSO scanner.

We studied:

- The standard axial length size scanner (axial extent 218 mm (4 blocks, sampled into 109 slices of 2 mm), diameter 854.8 mm (crystal-to-crystal, front face). diameter of.
- An axially extended 1m long scanner

Cherenkov based PET scanner, MC study

Comparison of LSO and PbF_2 standard axial length scanners: NEC rate, noise-equivalent count rates*



NEC rates vs. activity for the two scanners, following the Conti formula (with-TOF). Several assumptions on TOF resolution are presented for the PbF_2-based scanner.

*NEC rate, noise-equivalent count rate: corrected for random and scatter coincidences.

Cherenkov based PET scanner, MC study

First preliminary Monte Carlo simulation studies have shown that a Cherenkov-PET scanner using Lead fluoride with the same size of detector elements and the same ring geometry as a state-of-the-art LSO based PET scanner will have

- 20% improved spatial resolution, as is now achieved using one-to-one coupling.
- Sensitivity will be about one half, but noise equivalent count rate can be expected to be as good as or better than the standard PET scanner, if TOF resolution is 200 ps or better.

Remained to be proven: are SiPMs as light sensors really feasible for the detection of the few Cherenkov photons?

SiPM for Cherenkov TOF PET?

Advantages:

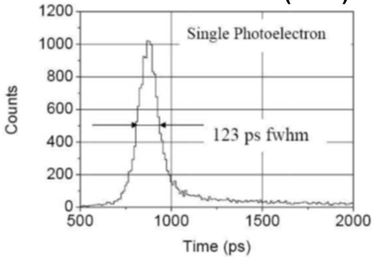
- high PDE – more than 50%
- flexible granularity
- low operation voltage
- operation in magnetic field
- affordable price (potentially)

Disadvantages:

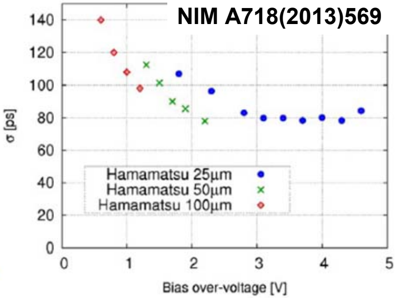
- high dark count rate ~ 100kHz/mm^2 (→cooling)
- single photon timing - resolution not yet below 100 ps FWHM (specially for large area devices)

→ Explore new devices and test them

NIM A504 (2003) 48



S.Gundacker et.al.
NIM A718(2013)569



SiPMs in a back-to-back configuration

Back-to-back with [22]Na source.

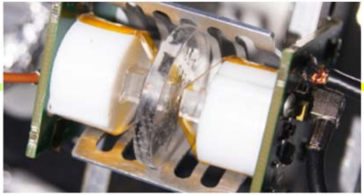
Cherenkov radiator (PbF_2): 5 x 5 x 15 mm black painted, Teflon wrapped, bare

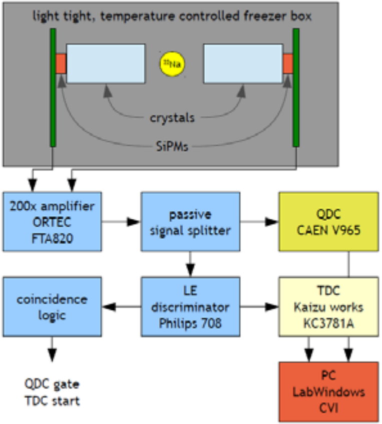
Readout: (timing ~25 ps FWHM)

- custom board with NEC μPC2710TB amp.
- amplifier: ORTEC FTA820
- discriminator: Philips sc. 708 LE
- TDC: Kaizu works KC3781A (25ps)
- QDC: CAEN V965

SiPMs 3x3 mm^2 :

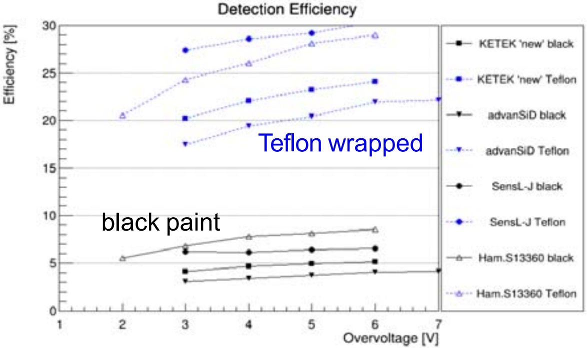
Producer	Model	Pixel pitch [μm]	Vbr [V]
Hamamatsu	S10931-050P, 'old'	50	69
Hamamatsu	S12641-PA050	50	65
AdvanSiD	ASD-NUV3S-P-40	40	26
KETEK	PM3350TP	50	25
SensL-J	MicroFC-30050-SMT-GP	50	25





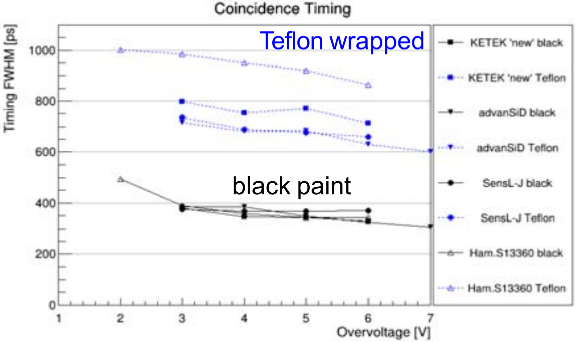
NIMA 804 (2015) 127

Single side efficiency



- best efficiency: ~30% with SensL SiPM and Teflon wrapped crystals
- T = -25°C

Coincidence time resolution



- best timing: ~300 ps with AdvanSiD
- T = -25°C

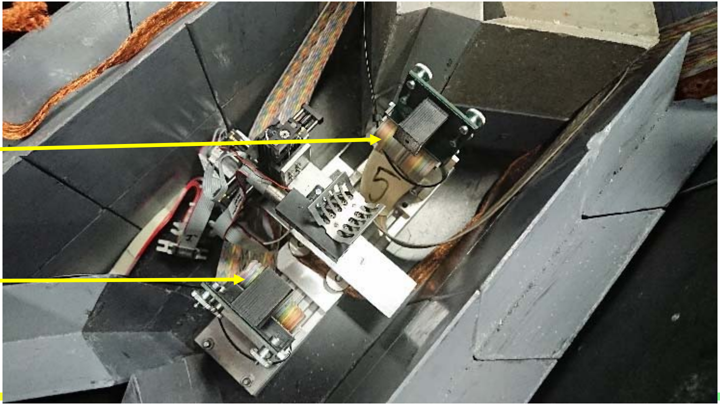
(note: 5x5mm^2 crystal on 3x3mm^2 SiPM!)

S. Korpar, IEEE/NSS 2015

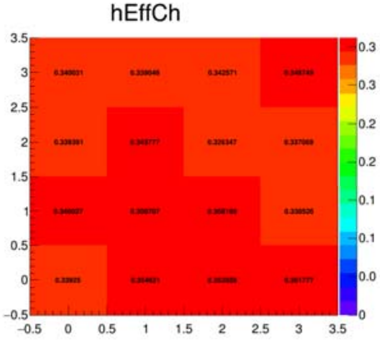
The first pair of PET 4x4 modules PbF_2+SiPMs in test

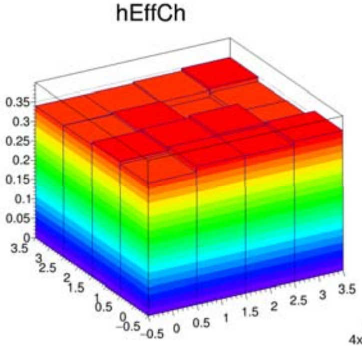
The module:

- a 4×4 array of 3×3×15 mm^3 PbF_2 crystals coupled to
- a 4x4 array of Hamamatsu S13361-3075 SiPM photosensors.



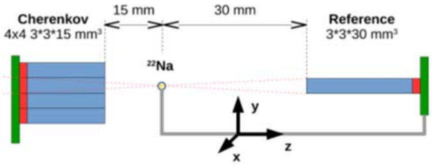
Efficiency of the 4x4 module





Set up and the method:

- Use LSO as a reference detector (triggers an annihilation gamma)
- Check if the associated gamma was detected in the PbF_2+SiPM array



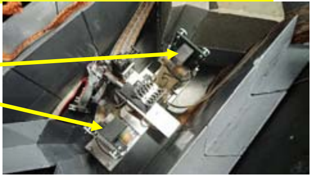
Efficiency: ~35%

Uniform over the 4x4 module

R. Dolenec et al., @RICH2018, to be published in NIMA

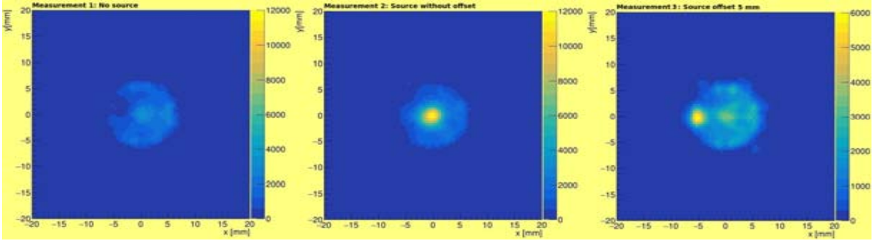
Pair of 4x4 PbF_2+SiPMs modules, reconstruction of a point source

Pair of back-to-back modules: 4×4 arrays of 3×3×15 mm^3 PbF_2 crystals coupled to 4x4 arrays of Hamamatsu S13361-3075 SiPMs



Two modules and a rotating source to form a virtual PET ring with R=51mm

Reconstructed images for a ^{22}Na point source:



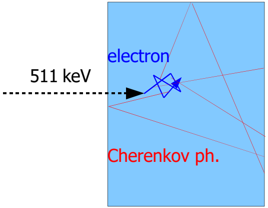
no source | source on the axis | source 5 mm off axis

no source = random coincidences due to SiPM dark counts & electronic pick-up noise, limited by the geometric acceptance of the virtual PET ring (only two modules).

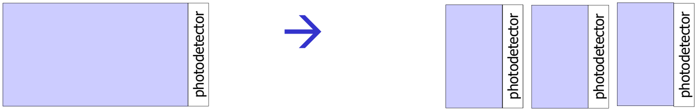
SiPMs as sensors for Cherenkov PET, summary

Summary of studies with 15mm crystals and SiPMs as sensors

- Efficiency: as high as 35% (for a teflon wrapped PbF2 crystal)
- TOF resolution: 300 ps FWHM (for a black painted crystal) limited by SiPM response (slides in backup)



Combine the best of the two options? 15mm →3x 5mm



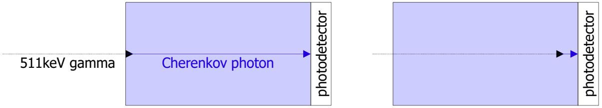
…currently under simulation study

Limitations of fast timing

Cherenkov photons are produced promptly, but still need time to reach the photodetector.

Gamma rays travel faster than Cherenkov light!

Radiator dimensions, refractive index → intrinsic travel time spread due to different gamma interaction depths.



d = 15 mm, n = 1.8: $t = d \cdot n / c_0 = 90$ ps $t = d / c_0 = 50$ ps   → $\Delta t = 40$ ps

For a 15 mm crystal the resulting FWHM contribution is ~90-50=**40 ps**

It gets even worse if the sensor is on the upstream side of the crystal

d = 15 mm, n = 1.8: $t = 0$ ps $t = d / c_0 + d \cdot n / c_0 = (50+90)$ ps   → $\Delta t = 140$ ps

For a 15 mm long crystal the resulting FWHM contribution is **~140 ps**

Limitations of any very fast photon timing 2

Gamma rays travel faster than light!

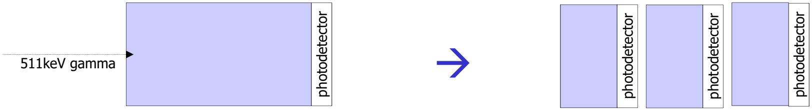
Radiator dimensions, refractive index → intrinsic travel time spread due to different gamma interaction depths

→ 40ps FWHM contribution in a 15mm long crystal if sensor downstream

This limitation is common to all very fast light emission mechanisms.

Can in principle be mitigated by

- a multi layer configuration with shorter crystals, or by
- measuring the depth of interaction (DOI)



DOI in Cherenkov based γ detectors

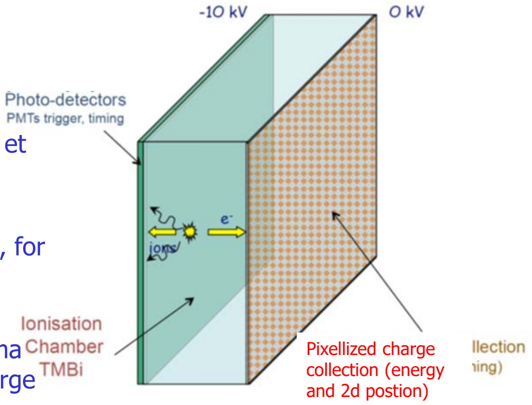
By measuring DOI we would

- Improve the timing
- Further mitigate the paralax error

A very interesting novel concept: CaLIPSO (D. Yvon et al., CEA Saclay)

Use a heavy high Z liquid, TriMethyl Bismuth (TMBi), for gamma conversion and dual mode detection

- Cherenkov light for timing
- Ionisation for energy measurement and 3d gamma interaction point determination (2d pixels for charge collection and drift time)

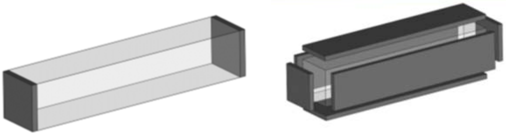


D. Yvon et al., IEEE TNS, 61 (2014) 60.

N.B. Again a nice example of HEP → medical imaging

More ideas: Cherenkov++ …

2 sided or 6 sided readout



→

S. Ziegler et al., Cherencube

Combine Cherenkov photons (time) and scintillator photons (efficiency): pioneered by P. Lecoq et al., S. Brunner et al.

S. Brunner: revival of BGO scintillator? (good TOF with Cherenkov, low price, high density and photo-fraction but still worse than PbF_2)

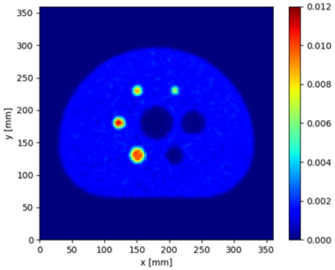
Harry van der Graaf: Tipsy as photodetector

More ideas around with multiple layer devices etc - stay tuned for more!

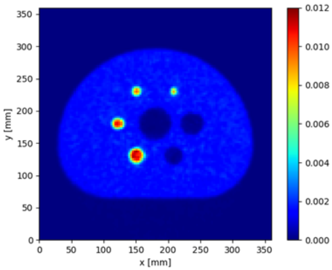
Image reconstruction, 6 sided readout

Reconstruction with CASToR (MLEM reconstruction method) on simulated data.

Assumed: 1 minute of data acquisition.



LSO scanner (Siemens Biograph TP)



PbF_2 Cherenkov scanner

(assumed: 6 sided readout, 100 ps TOF resolution, 100% QE)

Summary

Interplay of detector R&D for particle physics and medical imaging has a long history, and this will remain one of the sources of innovation in medical imaging.

Cherenkov radiation based annihilation gamma detectors offer a promising method for very fast detection and potentially cheaper devices or total body scanners.

Total body scanner: PbF_2 has another benefit, a shorter attenuation length → shorter crystals → smaller parallax error.

SiPMs have been proven to work as sensors for Cherenkov light from annihilation gamma absorption. The single side efficiency is comparable to LSO scintillator base detectors.

First tests of 4x4 modules with PbF_2 crystals and SiPMs as light sensors, efficiency measurement and source reconstruction.

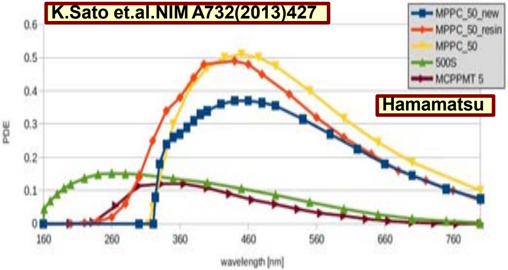
Improvements in SiPM timing would further boost this detection method.

More ideas around - stay tuned for interesting developments!

Back-up slides

Efficiency simulation

- Cherenkov fotons in range 200nm – 800nm
- PbF_2 radiator – 15 mm
- perfect coupling

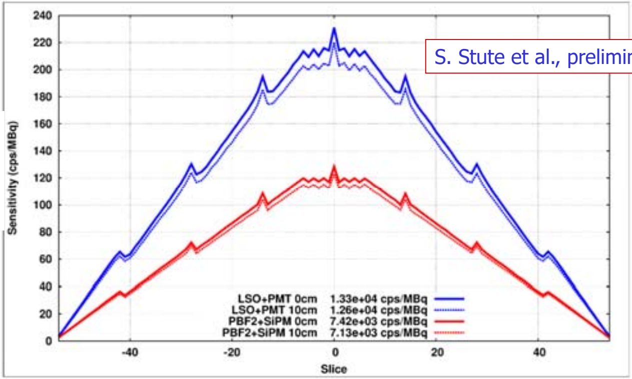


	C.Eff. [%]	C.T. [ps]	P(Nph>1) [%]	P(Nph>1)^2 [%]	
QE100	43.7	77	57.5	33	Teflon wrapped
MCPPMT_5	3.6	135	3.5	0.12	
MCPPMT_500S	6.4	132	6.4	0.41	
MPPC_50mum	18.7	93	21.6	4.7	
MPPC_50mum_Resin ⇨	21.0	96	24.4	6.0	
MPPC_50mum_NEW	14.0	99	15.6	2.4	
QE100	32.4	72	42.9	18	Black paint
MCPPMT_5	1.3	88	1.4	0.02	
MCPPMT_500S	2.5	91	2.8	0.08	
MPPC_50mum	8.6	69	10.1	1.0	
MPPC_50mum_Resin ⇨	10.1	73	11.9	1.4	
MPPC_50mum_NEW	6.0	70	6.8	0.5	

Cherenkov based PET scanner, MC study

The sensitivity for a standard scanner geometry with the two technologies: the state-of-the art LSO+PMT combination has a higher sensitivity than Cherenkov-PbF_2 because of a higher gamma detection efficiency. However, →

Axial sensitivity profiles following the NEMA standards, for the two scanners and at radial offsets of 0 and 10 cm; global sensitivity (all slices combined).



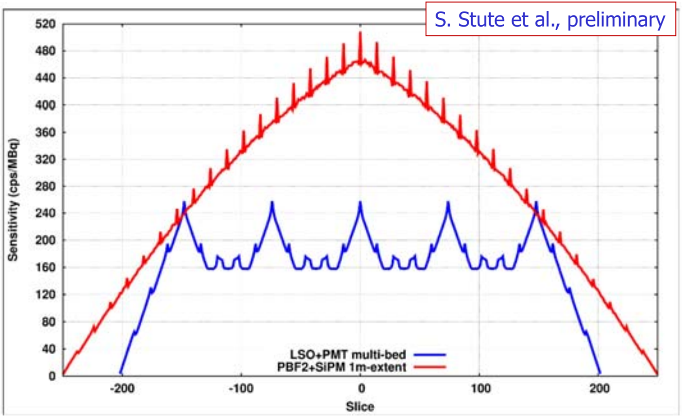
S. Stute et al., preliminary

Cherenkov based PET scanner, MC study

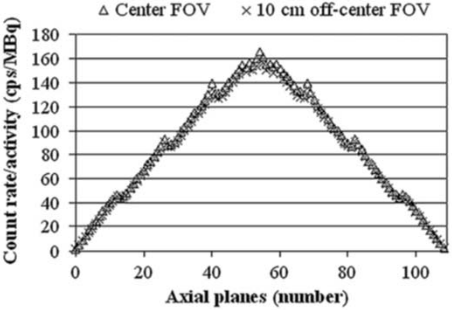
Comparison of the 1-meter axial sensitivities for the two technologies – note that this is only the theoretical sensitivity without taking TOF into account.

Axial sensitivity profiles following the NEMA standards at the center of the FOV, for the 1meter axial extent PbF_2-based scanner and for a multi-bed LSO-based scanner.

S. Stute et al., preliminary



NECR for a commercial PET scanner

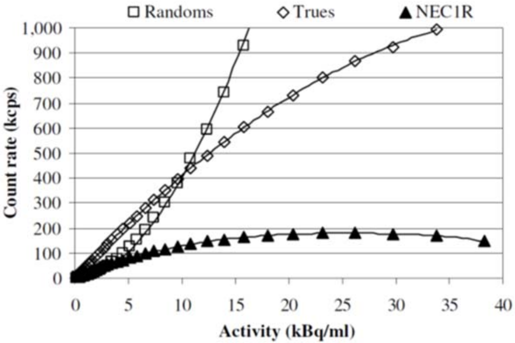


Results of an experimental study

B.W. Jacoby et al, Phys. Med. Biol. **56** (2011) 2375–2389

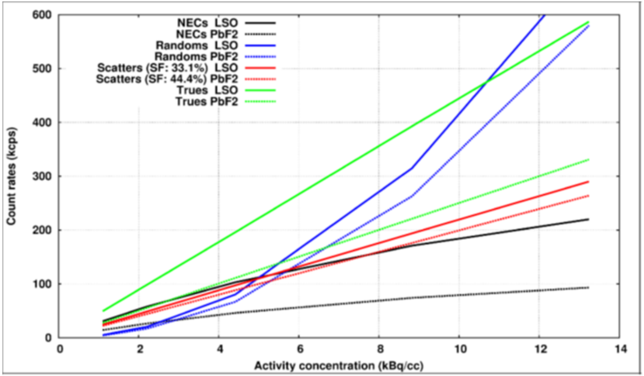
Axial sensitivity profile at 1 cm off-center FOV () and 10 cm off-center FOV (X) of the mCT scanner.

Comparison of the random, true and NECR rates as a function of the average activity concentrations within the 70 cm long NEMA scatter phantom



Count rates, LSO and PbF_2

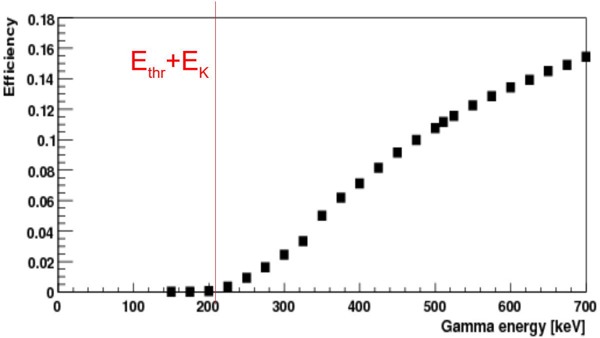
Count rates for different activities and for the two scanners, following the NEMA standards (no-TOF). Scatter fraction is 33.1% for LSO and 44.4% for PbF_2-based scanners.

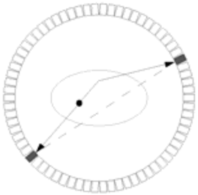


Intrinsic suppression of scattered events

Traditional PET: large number of photons → gamma energy → rejection of scattered events. Only events with detected energy in the photo-peak are used for reconstruction.

Cherenkov PET: a few photons detected → no energy information, but efficiency drops with gamma energy → intrinsic suppression



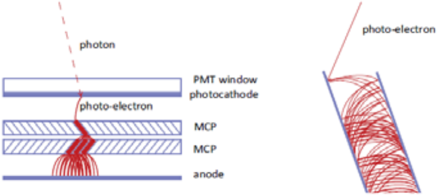


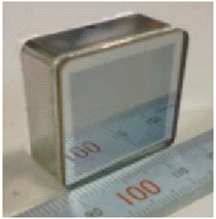
'scattered events'

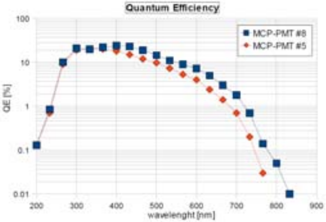
Very fast single photon sensor: MCP-PMT

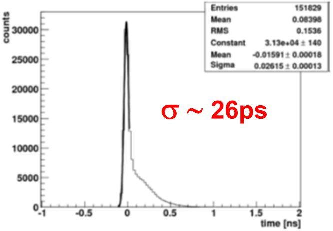
Example: Hamamatsu SL10 microchannel plate PMT

- multi-anode PMT with two MCP steps, 10 μm pores
- 16 (4x4) anode pads, pitch ~ 5.6 mm, gap ~ 0.3 mm
- box dimensions ~ 27.5 mm square
- excellent timing **~ 20ps r.m.s.** for single photons
- multi-alkali photocathode
- 1.5 mm borosilicate window
- gain > 10^6

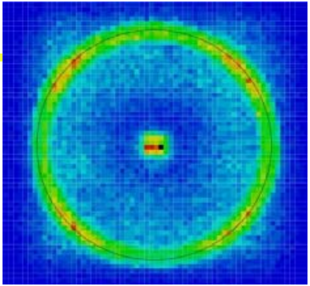








SiPMs as light sensirs for a RICH



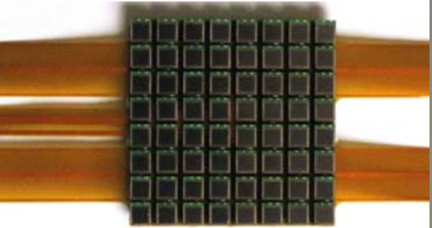
SiPMs in a RICH detector, first rings in 2007

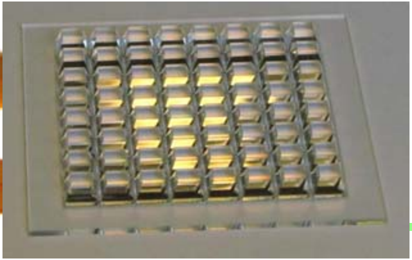
Korpar et al., NIM A594 (2008) 13; NIM A613 (2010) 195

A more recent study: a module of:

- a 8x8 SiPM array, Hamamatsu MPPC S11834-3388DF
- An array of pyramidal light guides

NIM A787 (2015) 203

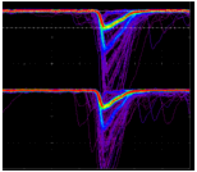


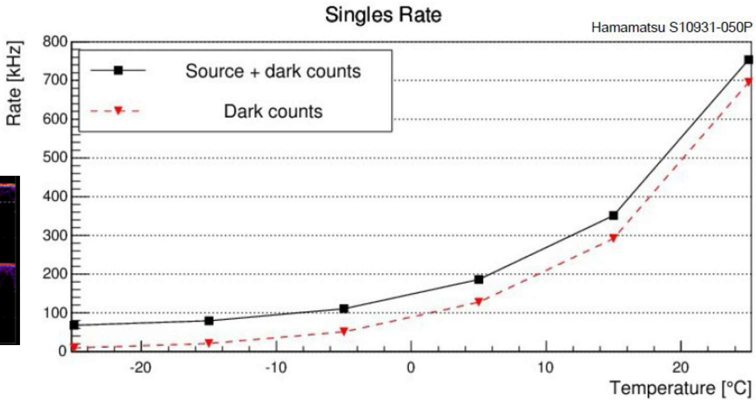


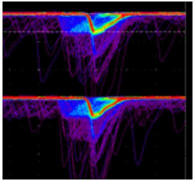
SiPMs, dark count rate vs temperature

Hamamatsu S10931-050P at constant gain (V_{ov} = 1.5V, recommended)

- dark noise reduces with temperature by ~ 2.4 x / 10°C

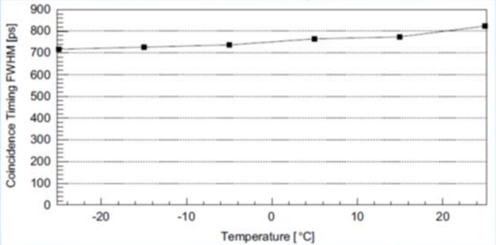


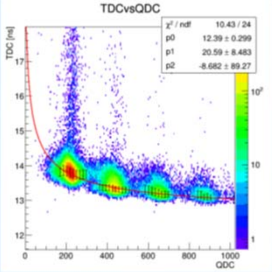


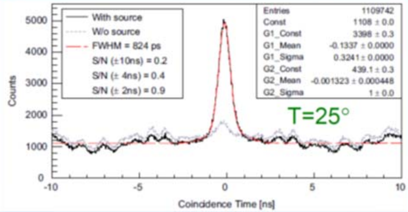


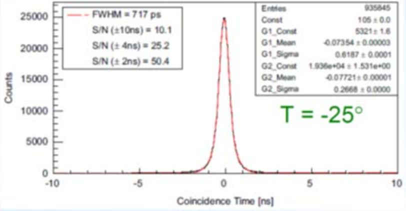
Coincidence time resolution vs temprature

- coincidence time resolution ~ 800 ps FWHM (Hamamatsu S10931-050P at V_{ov} = 1.5V)



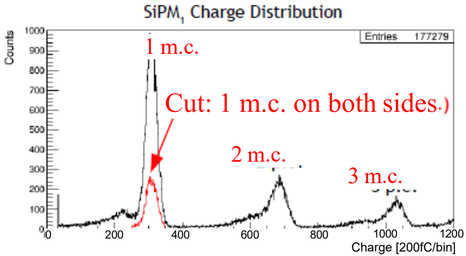




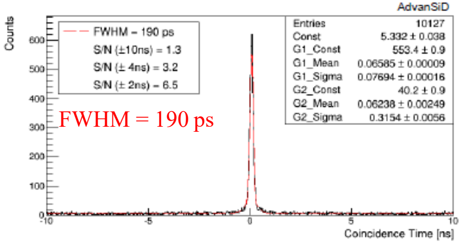


CRT with SiPM single cell hits on both sides

- Using only events with single micro cell signal on both sides:
  CRT= 190 ps FWHM
  (AdvanSiD, V_{OV}=7V, black-painted PbF_2, T=-25 °C)



- To get the resolution below 200 ps we need to improve the resolution for the events with more than 1m.c. signal; stronger suppression of optical crosstalk?

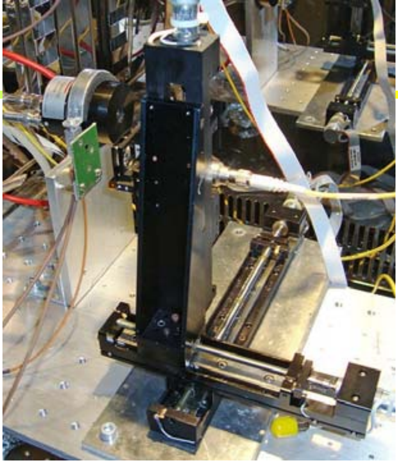


S. Korpar, IEEE/NSS 2015

Laser stage for SiPM timing studies

- PiLas diode laser system EIG1000D, 404nm and 635nm laser heads (ALS)
- ND filters (0.3%, 12.5%, 25%)
- optical fiber (single mode,~4μm core)
- focusing lens (min. spot size σ ~ 3μm)
- laser timing ~35 ps FWHM
- readout system the same as for CRT

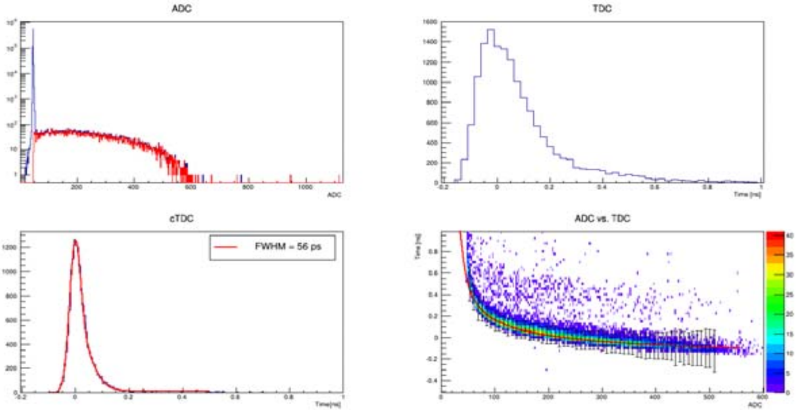
- Additional SiPM from KETEK with improved timing (@PhotoDet 2015)



Producer	Model	Pixel pitch [μm]	Vbr [V]
Hamamatsu	S12641-PA050	50	65
AdvanSiD	ASD-NUV3S-P-40	40	26
KETEK	PM3350TP	50	25
SensL-J	MicroFC-30050-SMT-GP	50	25

Reference sensor: MCP PMT

Hamamatsu MCP-PMT R3809U-52 (TTS ~ 25 ps FWHM)

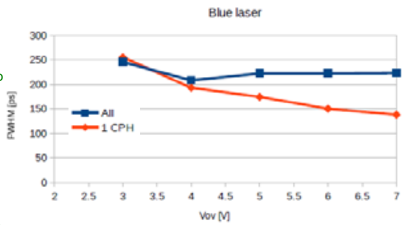


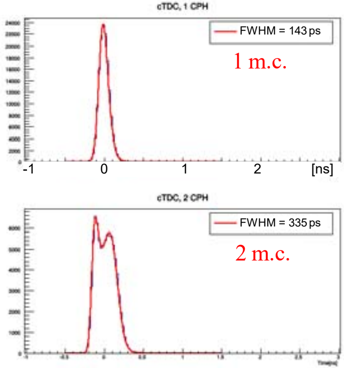
Red laser: 56 ps FWHM

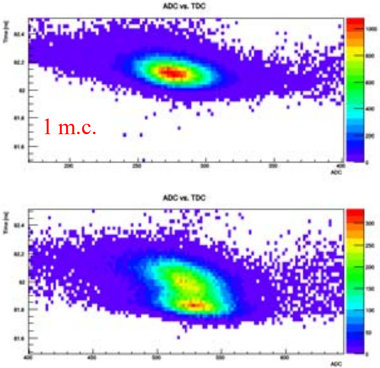
Estimate: 56 ps (measured) = 35 (laser) ⊕ 25 (MCP PMT) ⊕ 36 (electronics)

All vs. 1m.c. signal events

- AdvanSiD SiPM, V_{OV}=6V, T=-25 C
- blue laser λ=404nm
- events vith 2m.c. signal have two contributions: real double hit events with better resolution and optical crosstalk events

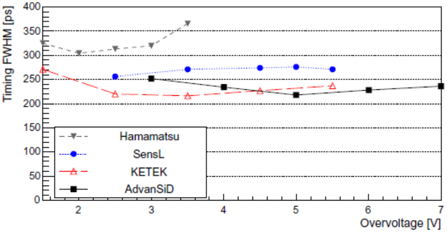


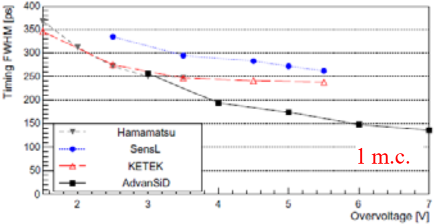


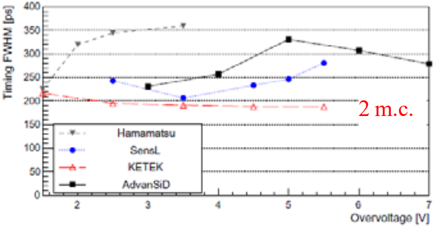


Timing resolution with laser pulses

- Uniform illumination of SiPMs, T=-25°C
- Timing for all events (left), and events with single and double micro cell signal (right)

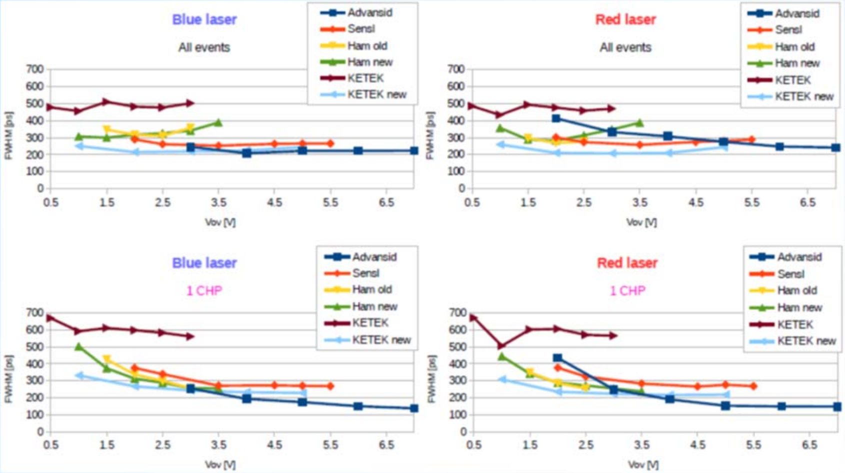






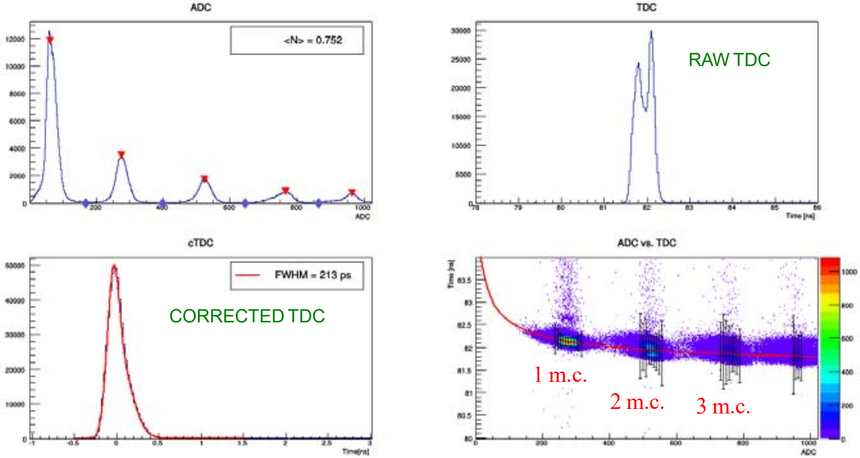
SiPM timing with uniform illumination

- Uniform illumination of SiPMs, T=-25°C
- Timing for all events (top) and events with single micro cell signal (bottom)



SiPM: Timing resolution with pico-second laser

- AdvanSiD SiPM, V_{OV}=6V, T=-25 C ^{o}
- blue laser λ=404nm



The first PET detector module with 4x4 PbF_2 + $3x3mm^2$ SiPMs in test

The module:

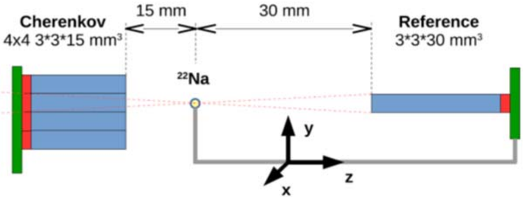
- a 4×4 array of 3×3×15 mm^3 PbF_2 crystals coupled to
- a 4x4 array of Hamamatsu S13361-3075 SiPM photosensors.

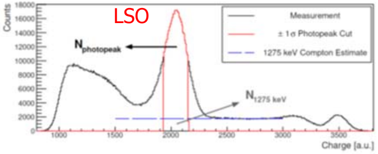
<u>Efficiency measurement</u>

Set up and the method:

- Use LSO as a reference detector (triggers an annihilation gamma)

- Check if the associated gamma was detected in the PbF_2+SiPM array

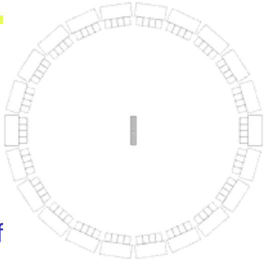




Reconstruction

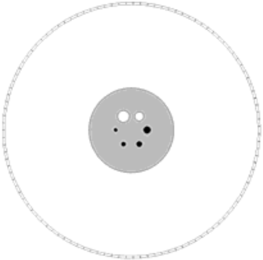
Cherenkov PET tested experimentally

- data equivalent to one PET ring obtained with only two detectors
- source rotated in discrete steps
- data collected at each step for the same amount of time
- D = 185 mm, H = 22.5 mm

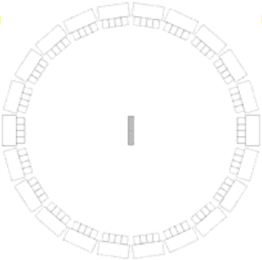


Full body PET scanner simulated

- D = 800 mm, 15 rings (H = 340 mm)
- phantom with d = 270 mm, 4 hot spheres (d: 10 - 22 mm) and 2 cold spheres (d = 28, 37mm)

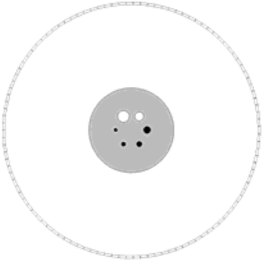


Reconstruction



Reconstruction algorithms:

- **Filtered backprojection (FBP):** basic non-TOF algorithm
- **TOF weighted FBP:** pixels along LOR incremented with TOF response defined weight
- **Most likely position (MLP):** point of decay on LOR calculated from TOF information
- **Filtered MLP:** MLP image deconvoluted for TOF response



Cherenkov based TOF PET - summary

- main advantage prompt emission
- main disadvantage low number of photons
- requires very fast single photon sensor with high PDE.

- We have studied several SiPMs from different producers to find the best candidate for the application → the best value for the efficiency reached 30% and the best CRT was ~300 ps (will improve with SiPM and crystal size matching).
- Performance of SiPMs is constantly improving and hopefully it will reach optimal performance → coincidence efficiency > 10% and timing < 200 ps FWHM