RICH 2016

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Cherenkov radiation in medical imaging

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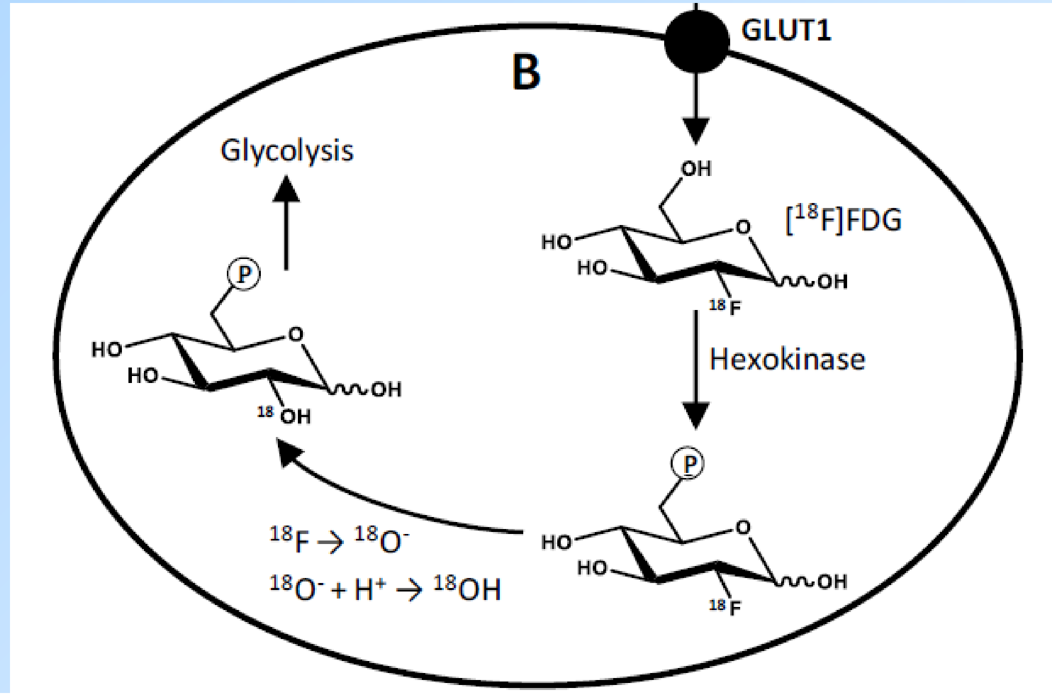
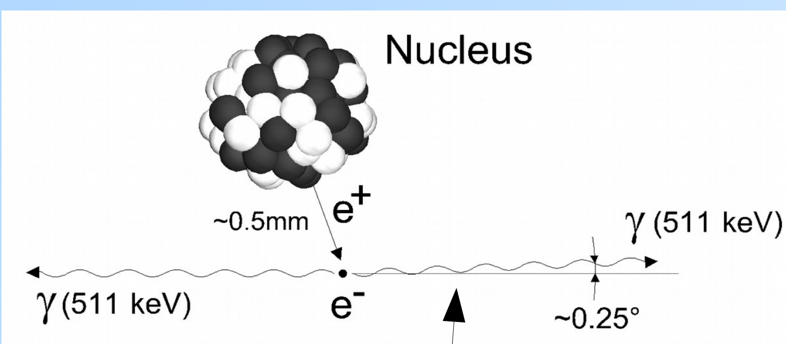
Outline:

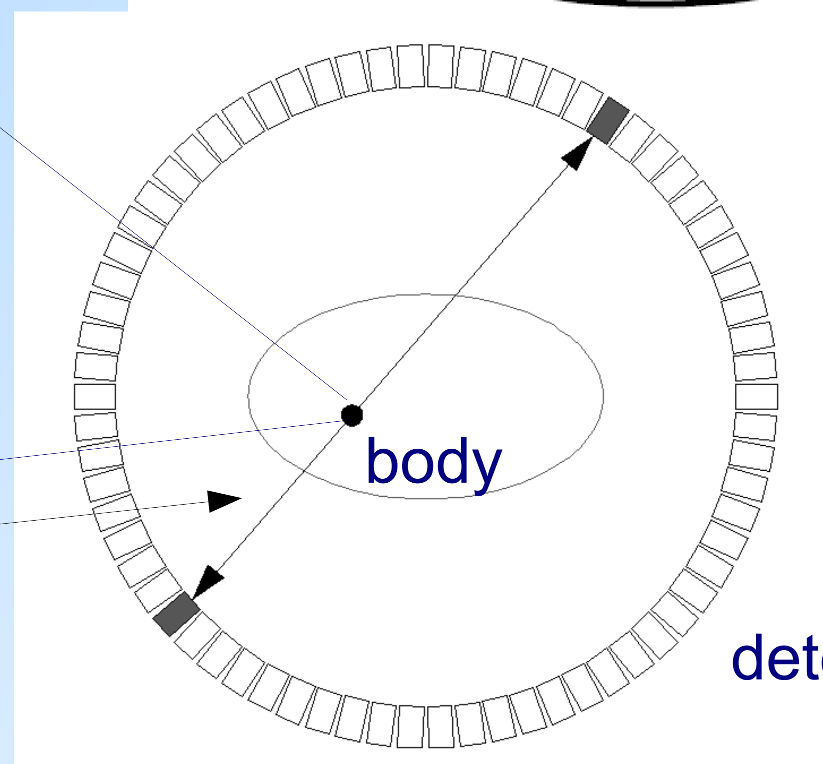
- Cherenkov radiation in PET applications
  - Cherenkov TOF-PET
  - Calypso project
- CLI – Cherenkov Luminescent Imaging
- Summary

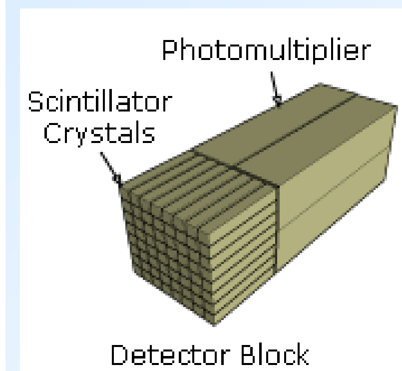
Imaging with PET

- functional imaging with biomarkers containing β^+ emitter
- fludeoxyglucose (FDG) is most commonly used – indicates the uptake of glucose









line of response (LOR)

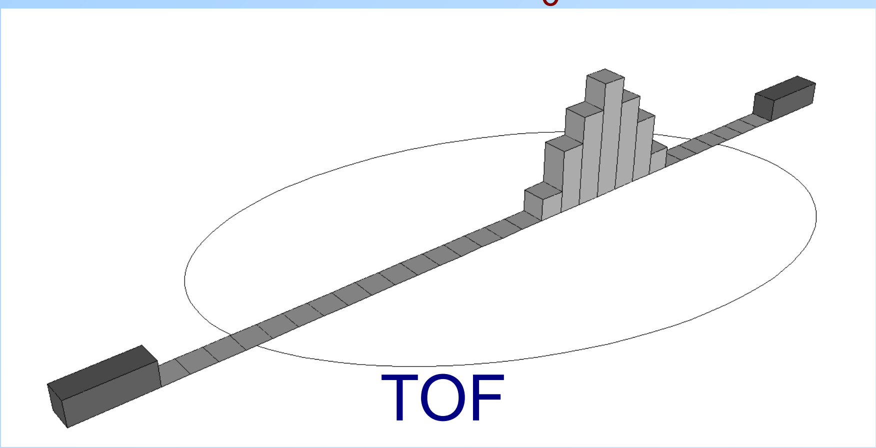
detector ring

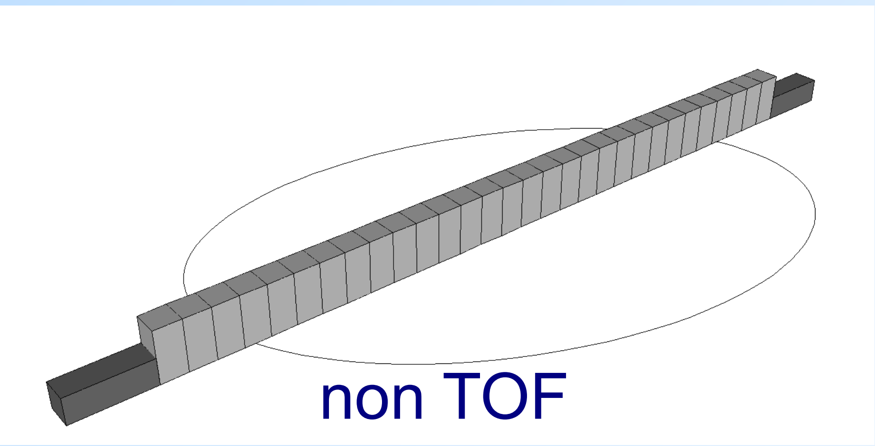
TOF-PET

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

- localization of source position on the line of response:

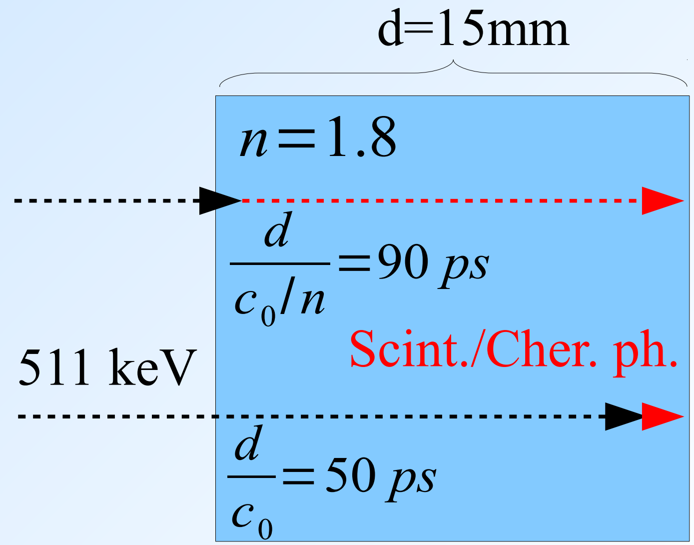
$\Delta t \sim 66\text{ps} \rightarrow \Delta x = 2c_0\Delta t \sim 1\text{cm}$





- PET systems based on SiPM readout are reaching CRT of 300 ps – small crystals $\sim 3 \times 3 \times 3\ \text{mm}^3 < 100$ ps

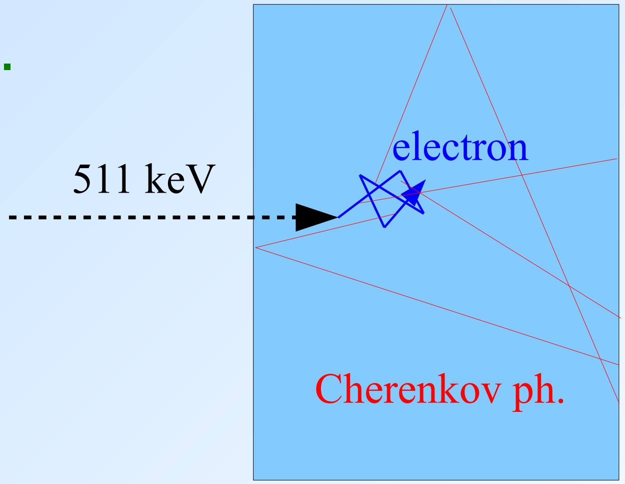
Depth of interaction contributes to the timing uncertainty in addition to detector TTS, scintillation process, optical path length ...



TOF-PET with Cherenkov light

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

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



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

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

→ detection at a single photon level!

Cherenkov radiator

Cherenkov radiator PbF_2:

- 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%

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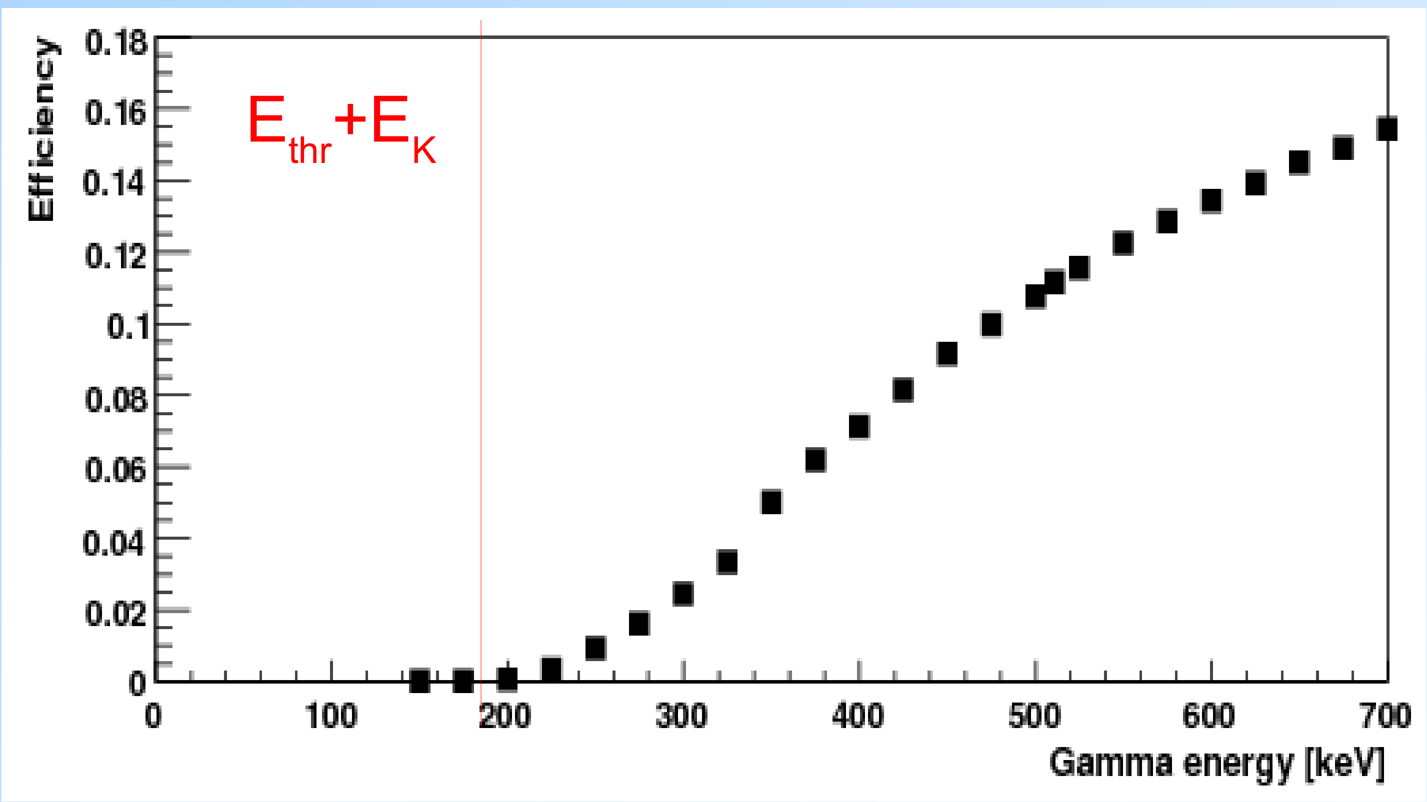
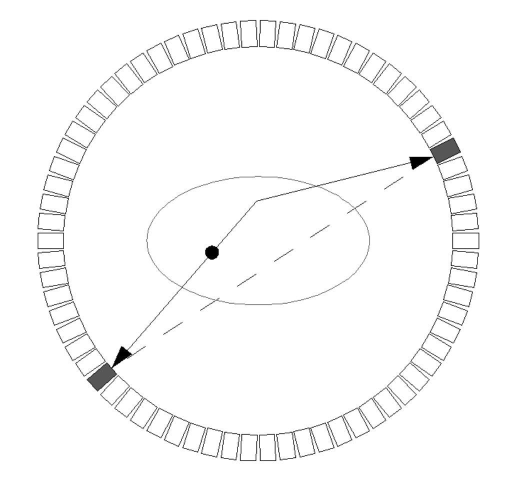
Suppression of scattered gammas

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; efficiency drops with gamma energy → intrinsic suppression





'scattered events'

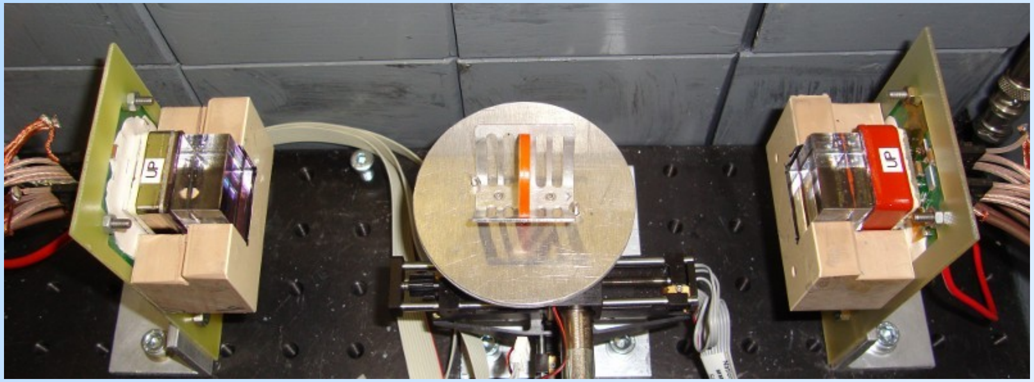
Excellent timing with MCP-PMT

Two detectors in a back-to-back configuration:

- Cherenkov radiators:

25x25x(5, 15) mm^3 PbF_2

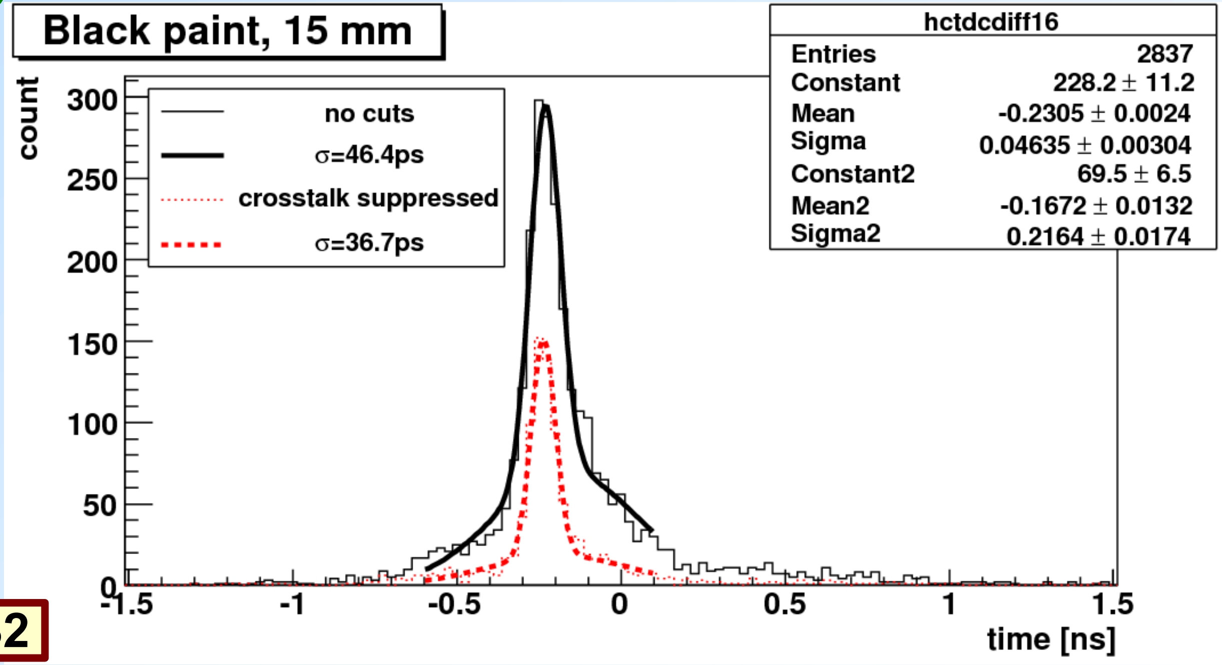
- MCP-PMT photodetectors:
  - single photon timing ~ 50 ps FWHM
  - active surface 22.5x22.5 mm^2



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)



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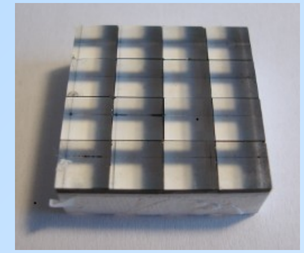
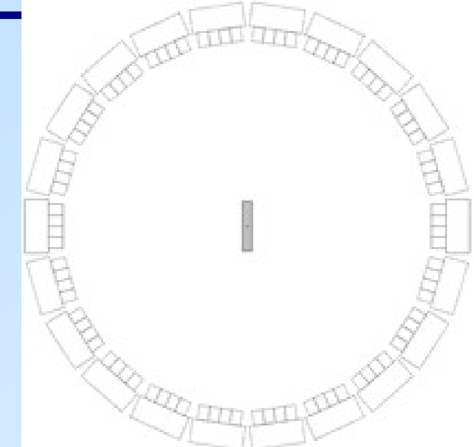
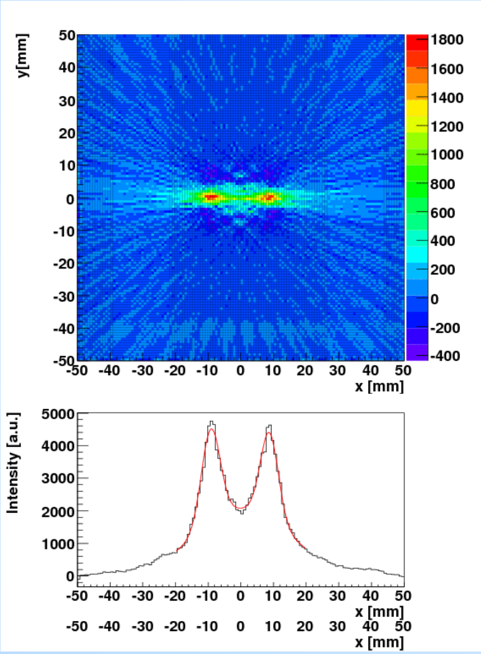
MCP-PMT: TOF PET reconstruction



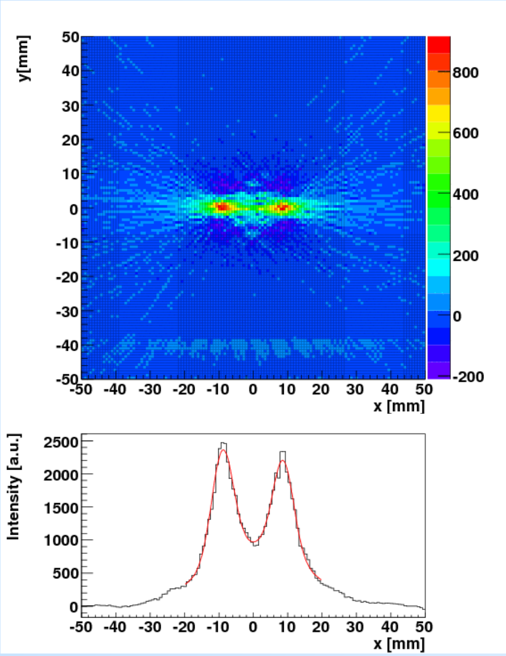


- ^{22}Na point sources at +10 mm and -10 mm
- 4x4 segmented, black painted PbF_2 radiators

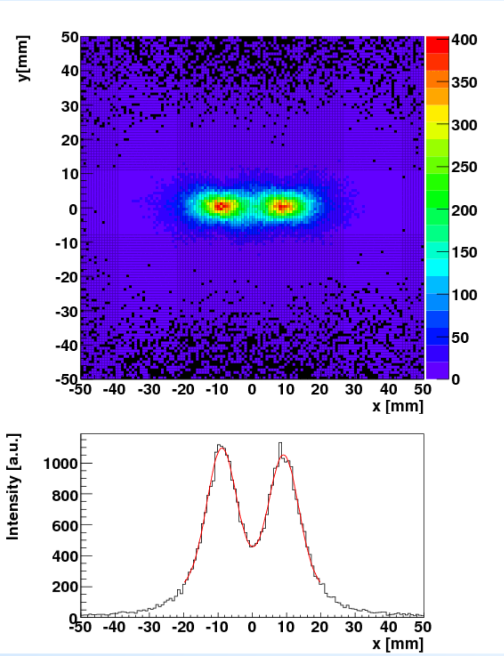
(non-TOF) FBP



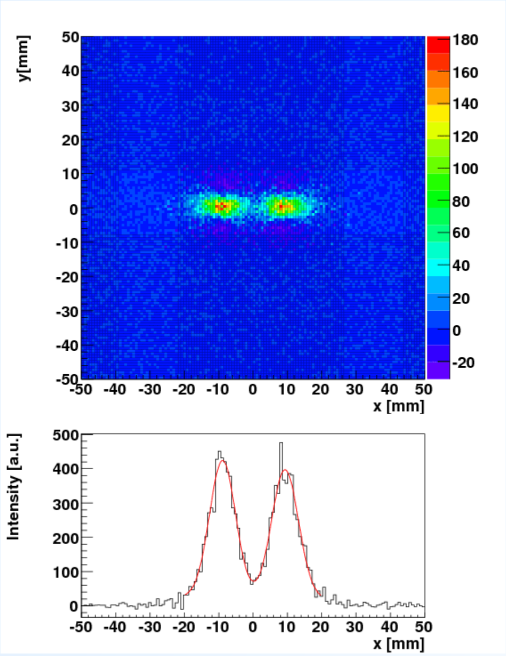
TOF w/ FBP



MLP



Filtered MLP



- Simple and very fast MLP (Most Likely Position)

→ already a reasonable picture

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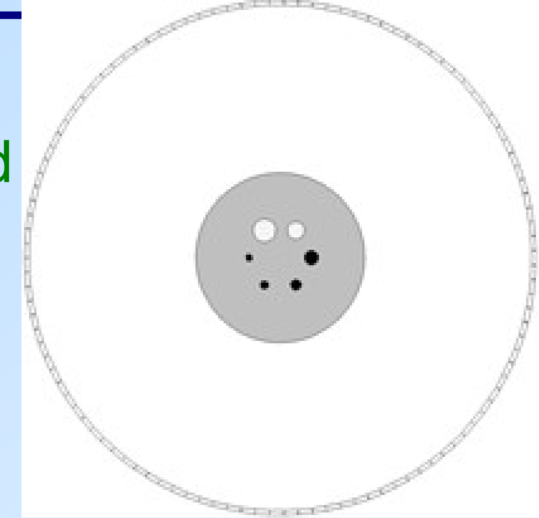
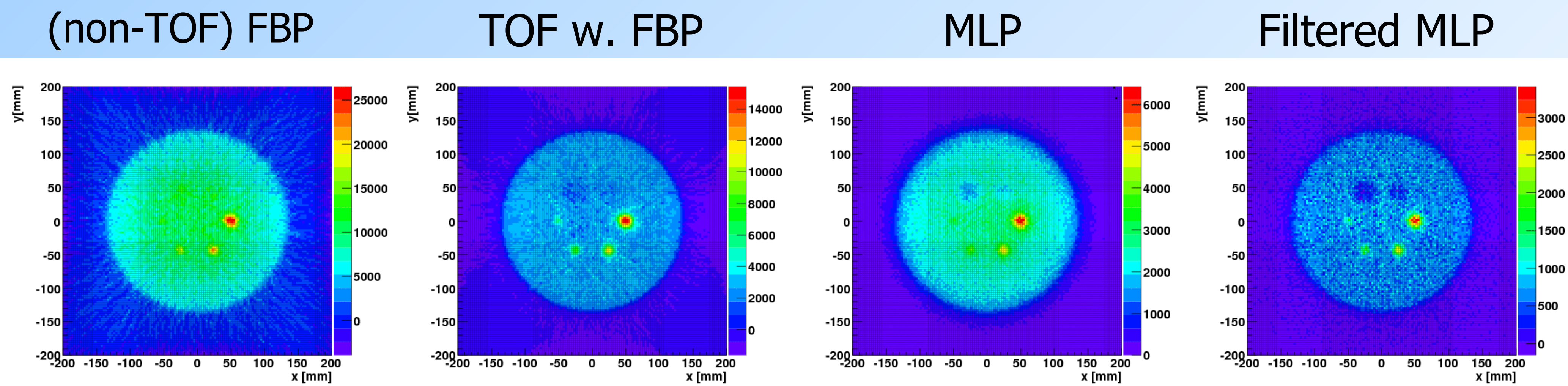
TOF PET reconstruction- simulation



- Hot spheres activity concentration: 3x phantom background (D(hot) = 10, 13, 17, 22 mm; D(cold) = 28, 37 mm)
- Statistics equivalent to 163 s of PET examination
- 4x4 segmented, Teflon wrapped PbF_2 radiator
- 20 mm thick axial slices

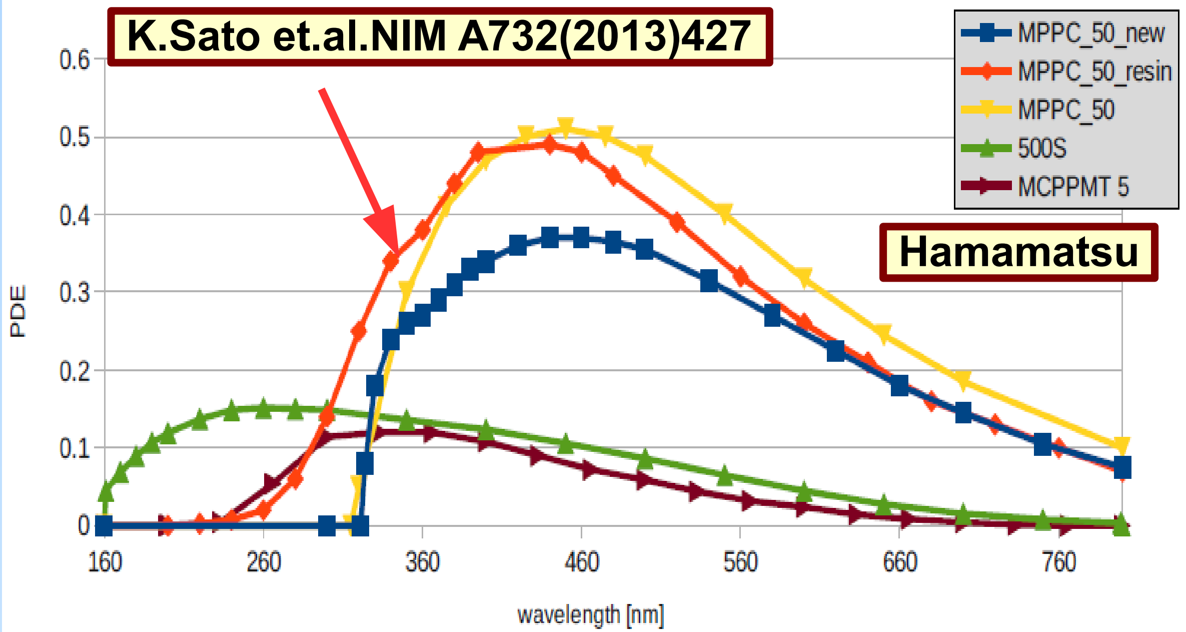


First tries, have to understand how the possible improvements in the detection efficiency will influence the performance:

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

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**
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**
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

Teflon wrapped

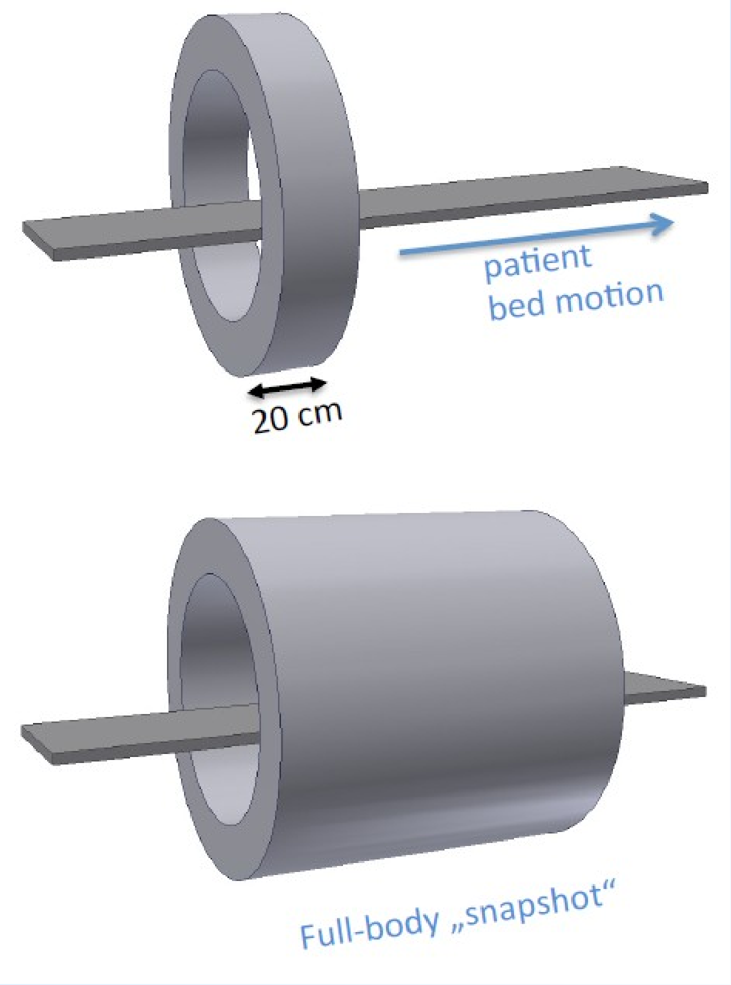
Black paint

Would Cherenkov based PET scanner be possible?

PbF_2 not a scintillator → considerably cheaper

Shorter attenuation length than LSO → smaller parallax error

→ Full body scanner



→ Join forces, groups led by:

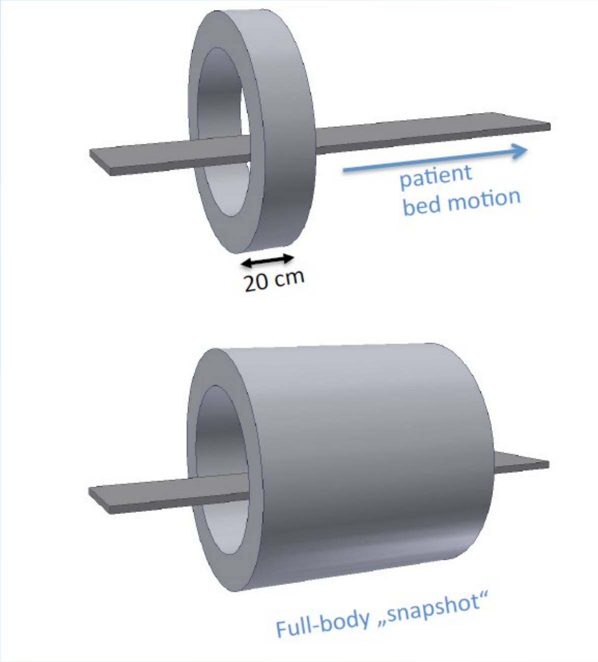
- Sibylle Ziegler, Technische Universität München
- Alberto Del Guerra, University of Pisa
- Peter Križan, J. Stefan Institute, Ljubljana
- Irene Buvat, IMIV, Orsay, CEA
- Edoardo Charbon, TU Delft
- Paul Lecoq, CERN
- Gabor Nemeth, Mediso
- Florian Wiest, KETEK
- Stefan Ritt, Paul Scherrer Institute

→ Carry out a feasibility study.

One of the outcomes → a preliminary MC simulation study →

Cherenkov based PET scanner – MC study

- Simulations were performed in order to estimate the performance of TOF PET scanner based on the Cherenkov method of gamma detection.
- The main building block of the simulated scanner was a gamma detector composed of a PbF_2 crystal (4x4x15 mm^3) 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 (4x4x20 mm^3) scanner.

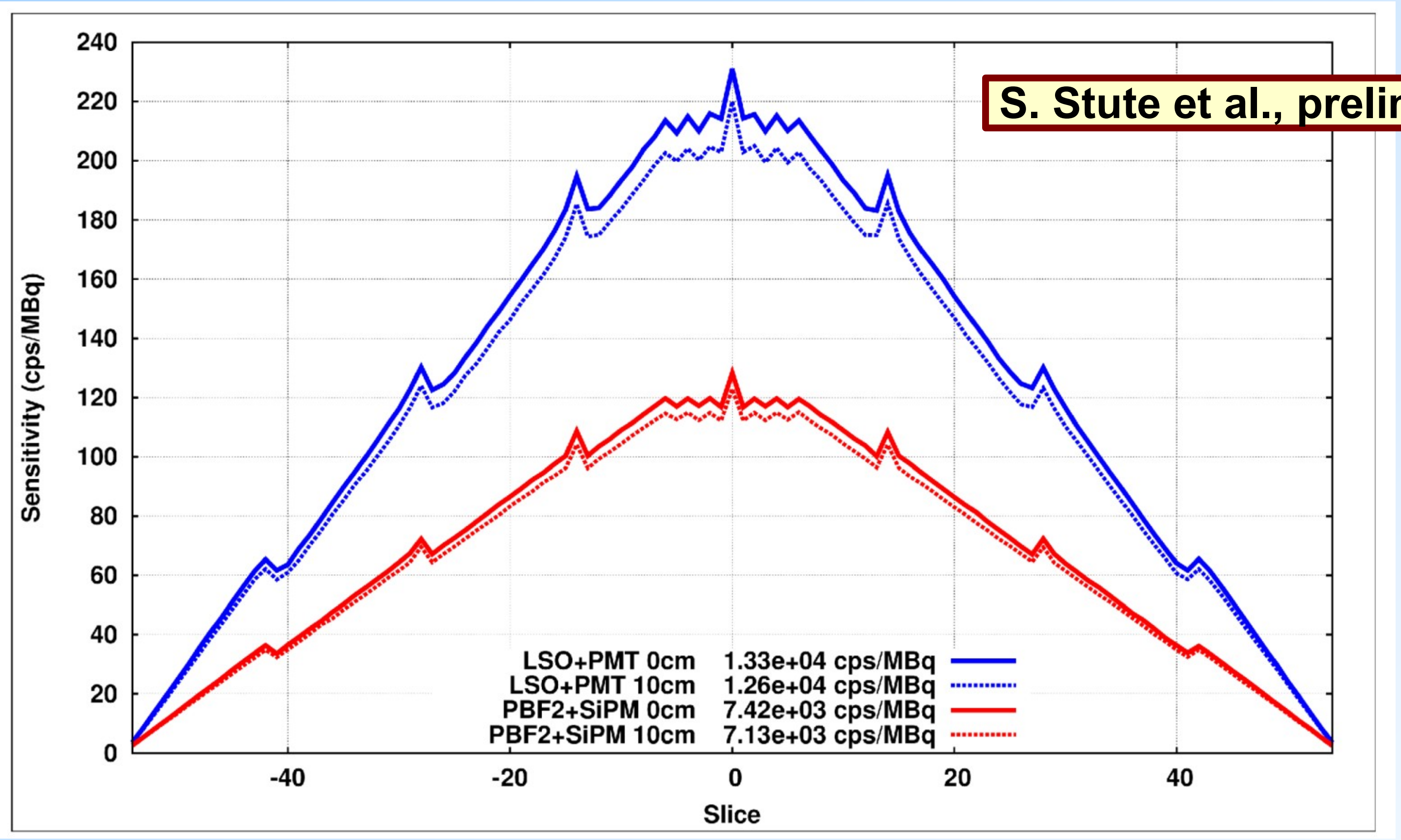


We studied:

- The standard axial length size scanner (axial extent 218 mm (4 blocks, sampled into 109 slices of 2 mm), diameter ~85 cm (crystal-to-crystal, front face).
- An axially extended 1m long scanner

Cherenkov based PET scanner – MC study

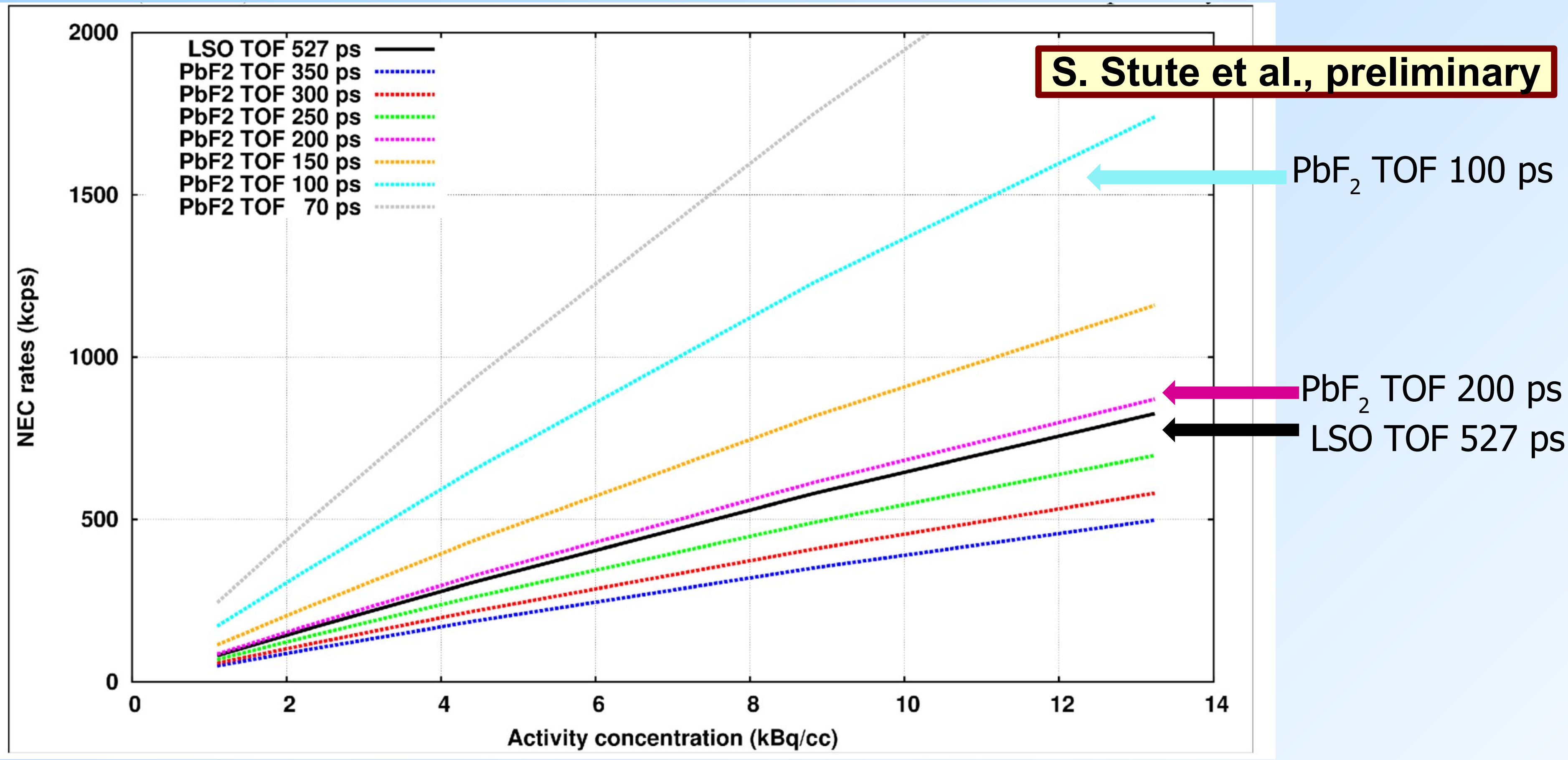
The sensitivity for a standard scanner geometry with the two technologies: the state-of-the art LSO+PMT combination has a higher sensitivity than Cherenkov-PbF2 because of a higher gamma detection efficiency.



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).

Cherenkov based PET scanner – MC study

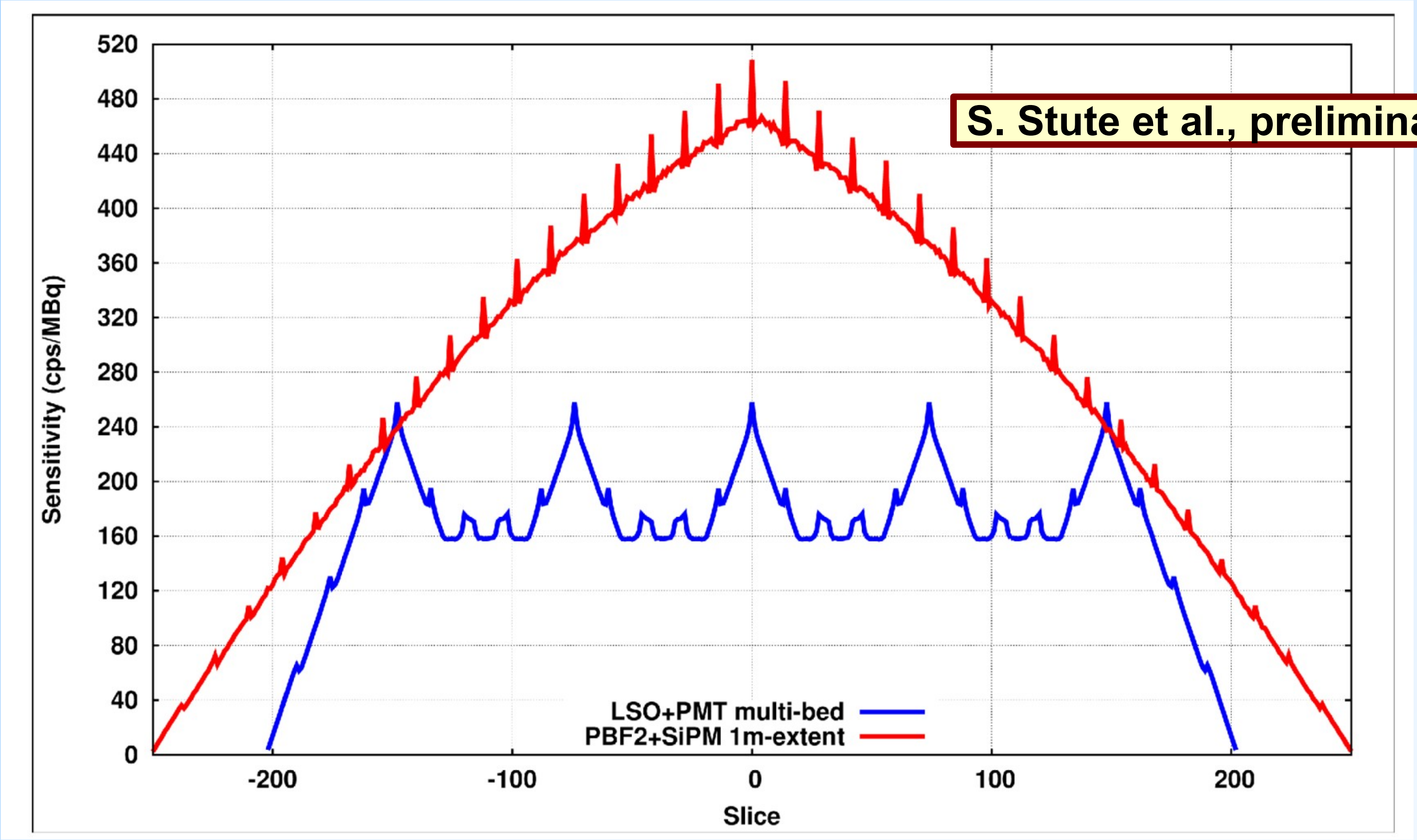
NEC rates: impact of improved TOF using the Cherenkov in PbF_2 for a standard axial length scanner.



NEC rates for different activities and for the two scanners, following the Conti formula (with-TOF). Multiple TOF resolution are presented for the PbF_2-based scanner.

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.

Cherenkov based PET scanner – MC study summary

• 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.

Back-to-back setup with SiPMs

Back-to-back with ^{22}Na source.

Cherenkov radiator (PbF_2):

- 5 x 5 x 15 mm^3 (SiPM),

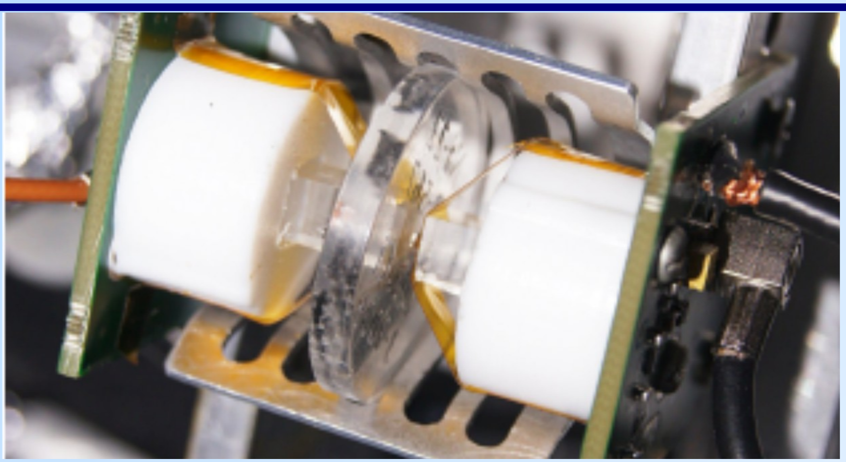
black painted, Teflon wrapped, bare

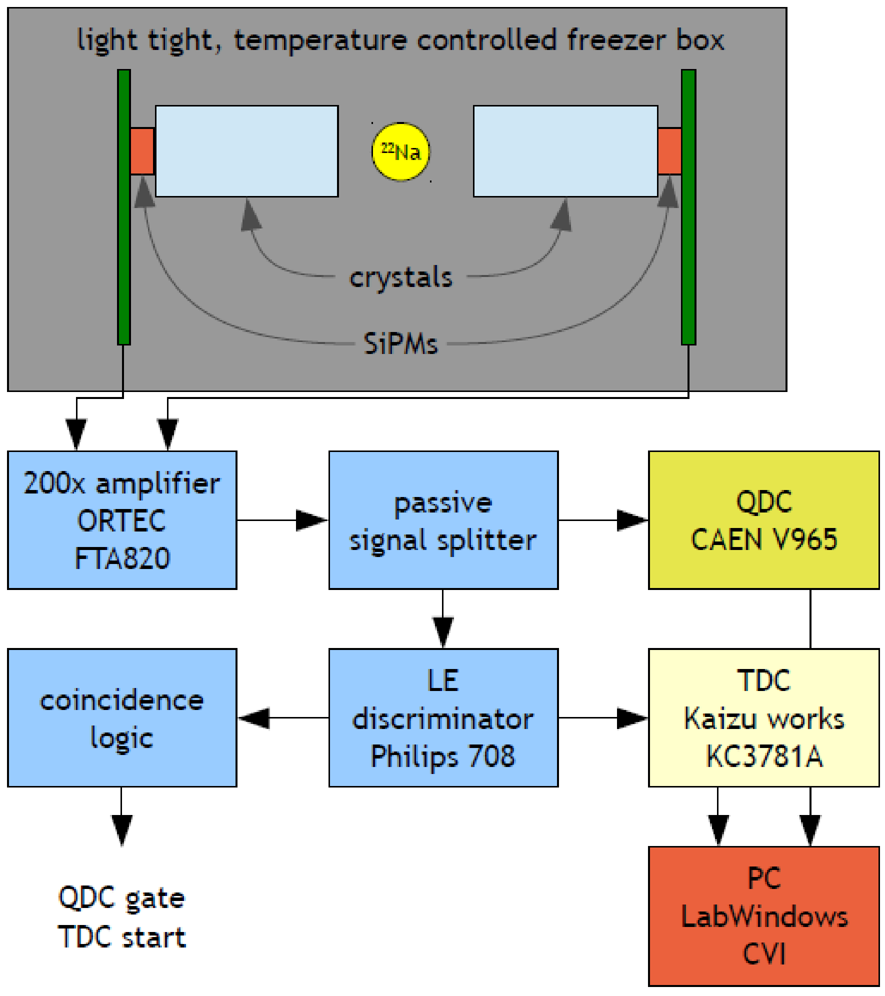
Readout: (timing ~25 ps FWHM)

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

3x3 mm^2 SiPMs:

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

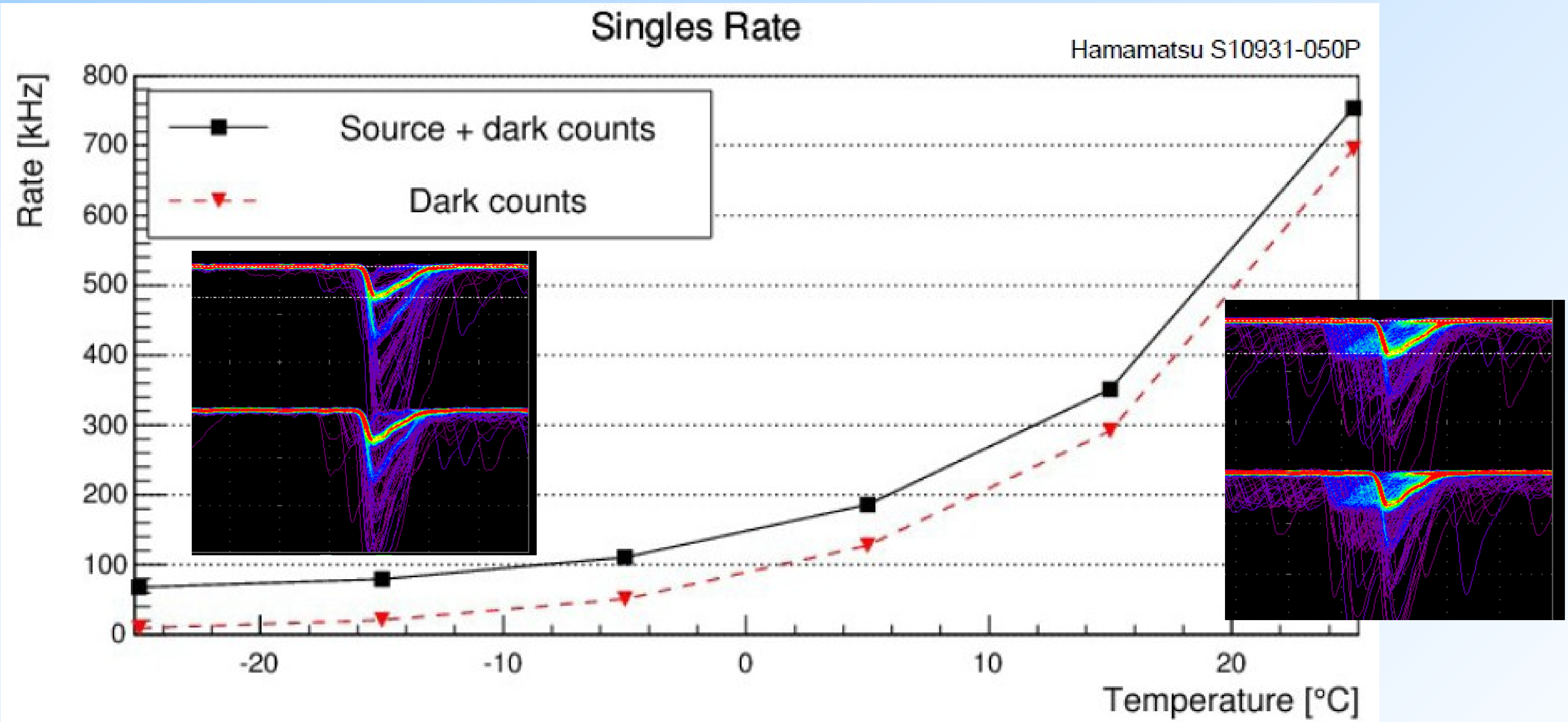




Dark count rate vs. temparature

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

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



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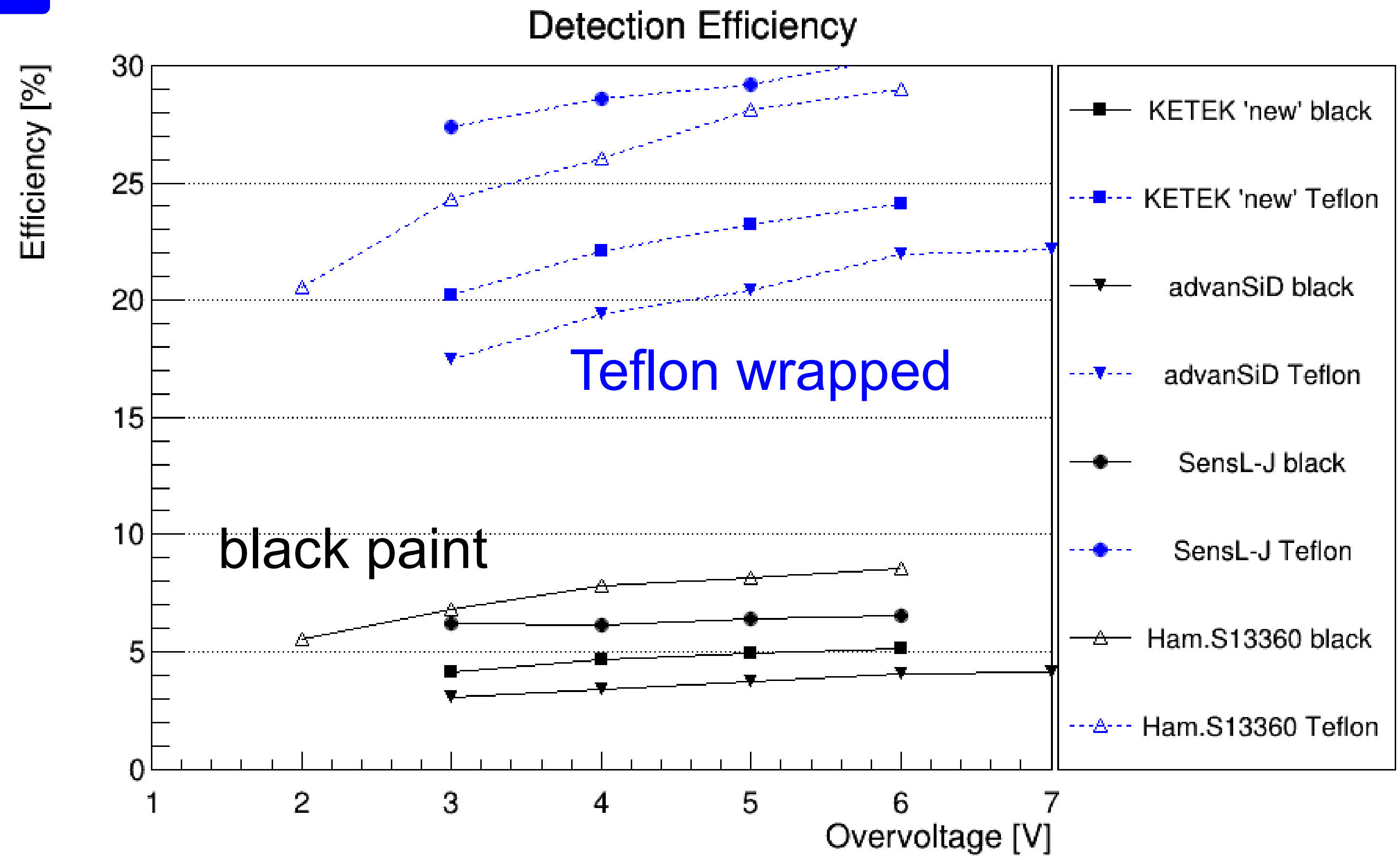
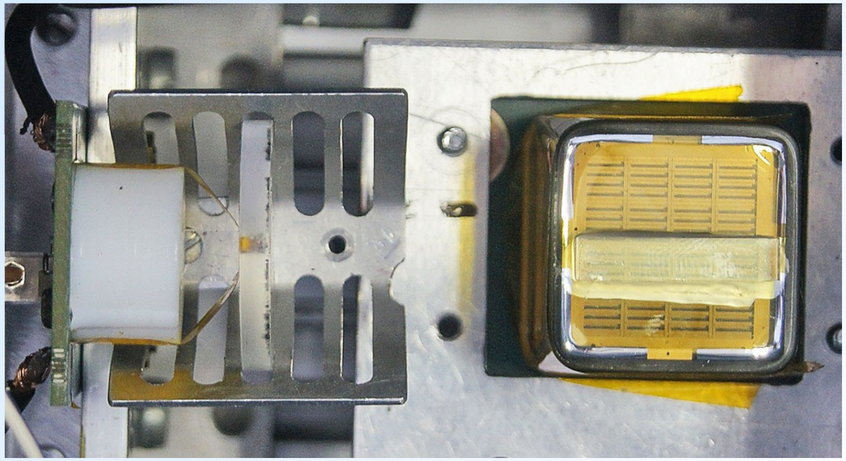
Single side efficiency

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



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

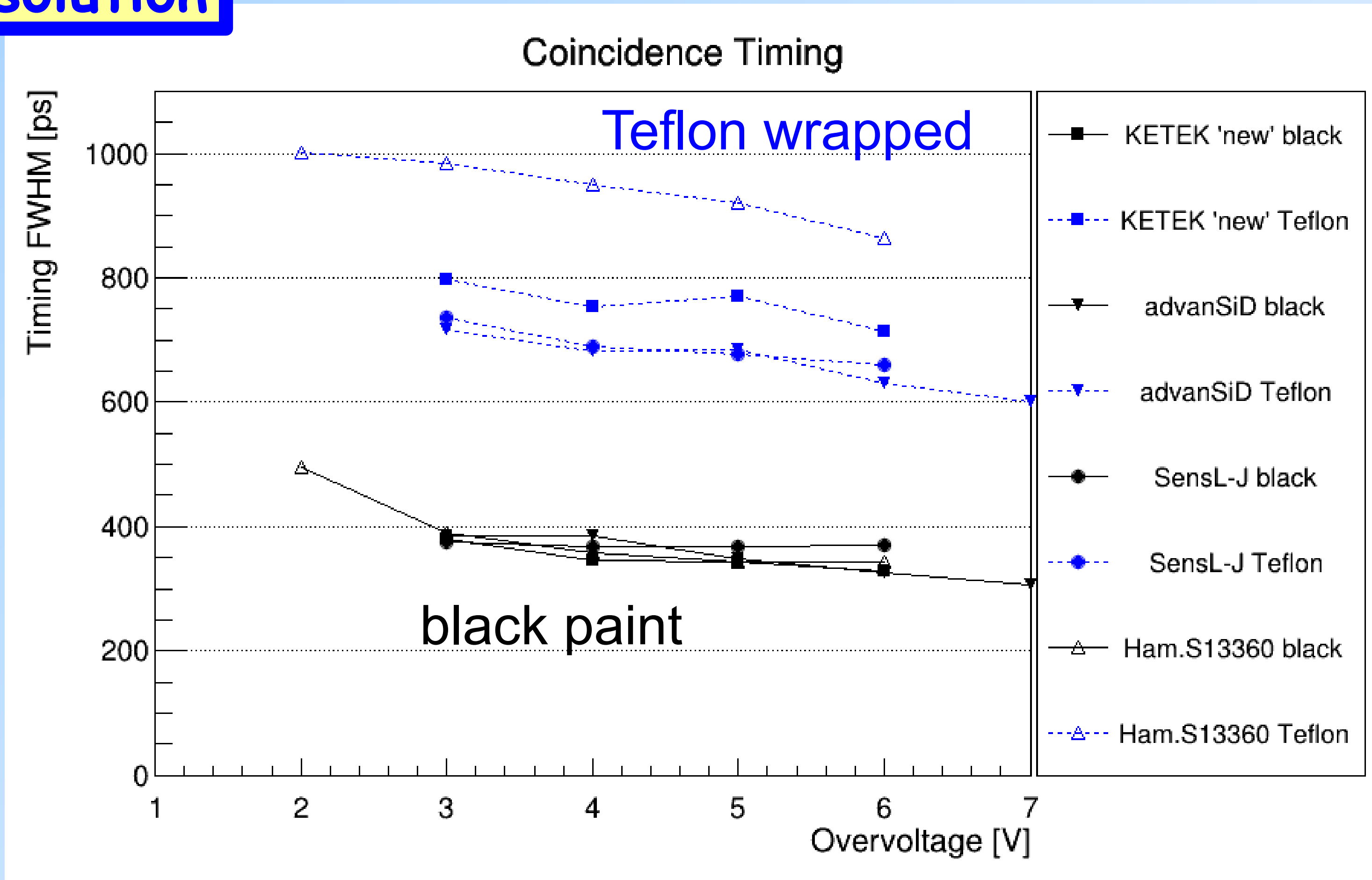
Producer	Model	Pixel pitch [μm]	Vbr [V]
Hamamatsu	S12641-PA050	50	65
AdvanSiD	ASD-NUV3S-P-40	40	26
KETEK	PM3350TP	50	25
SensL-J	MicroFC-30050-SMT-GP	50	25



Coincidence time resolution

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

(note: 5x5mm² crystal on 3x3mm² SiPM!)



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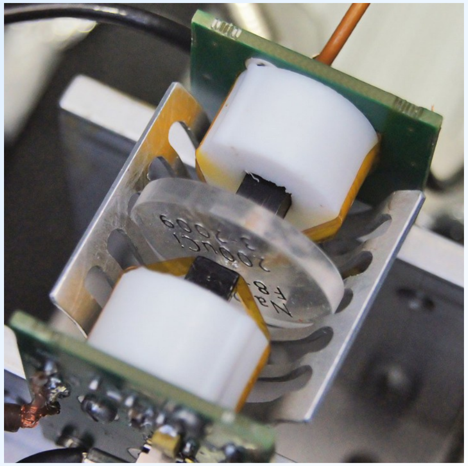
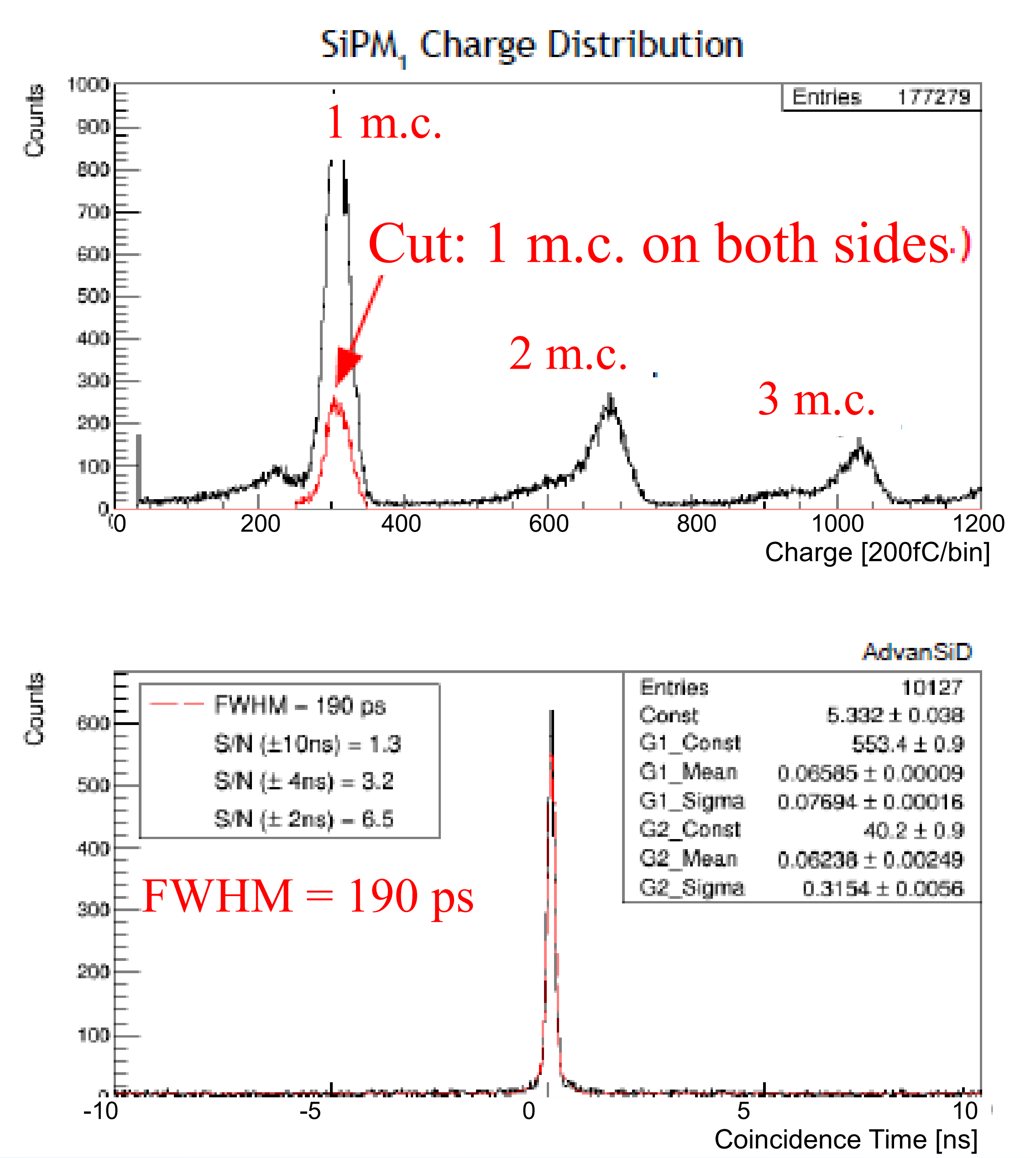
AdvanSiD	ASD-NUV3S-P-40	40	26
KETEK	PM3350TP	50	25
SensL-J	MicroFC-30050-SMT-GP	50	25



CRT using only single micro cell events

- 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)

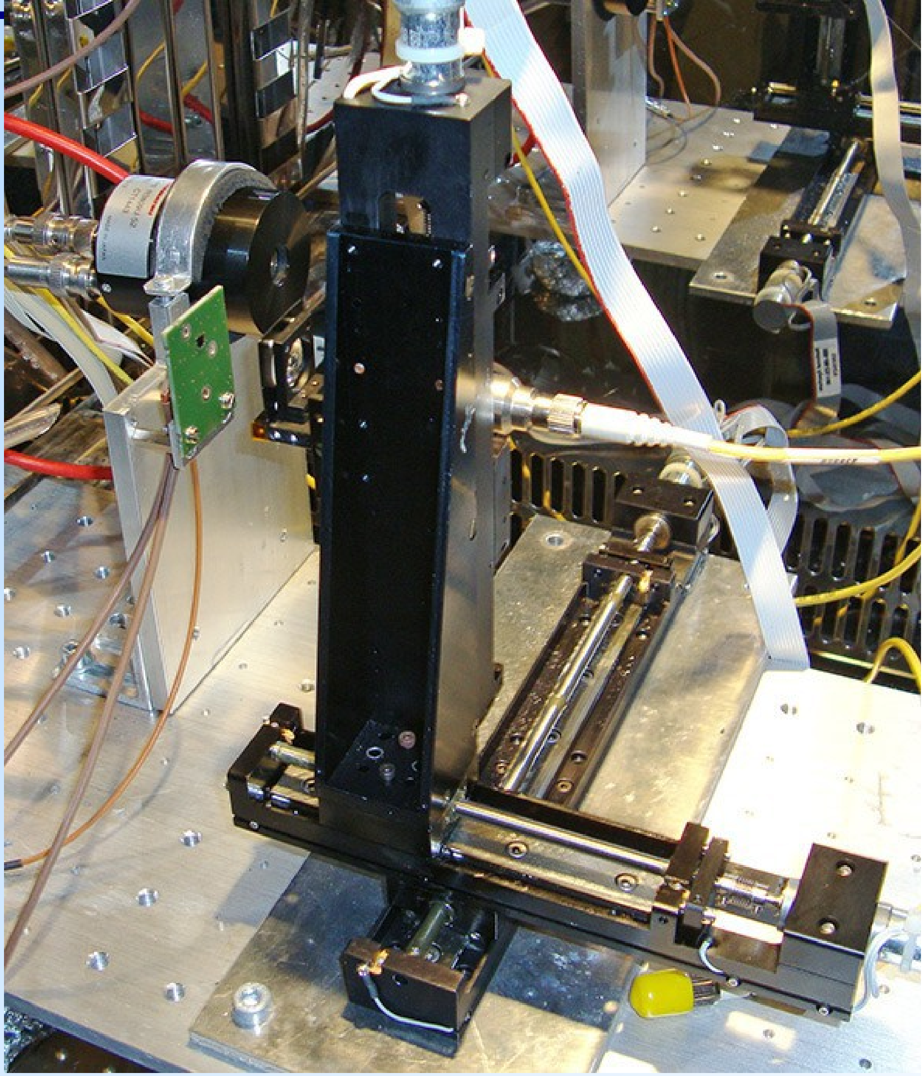
- To get the resolution below 200 ps we need to improve the resolution for the events with more than 1m.c. signal; stronger suppression of optical crosstalk?)



Laser setup with 3D stage

- 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]
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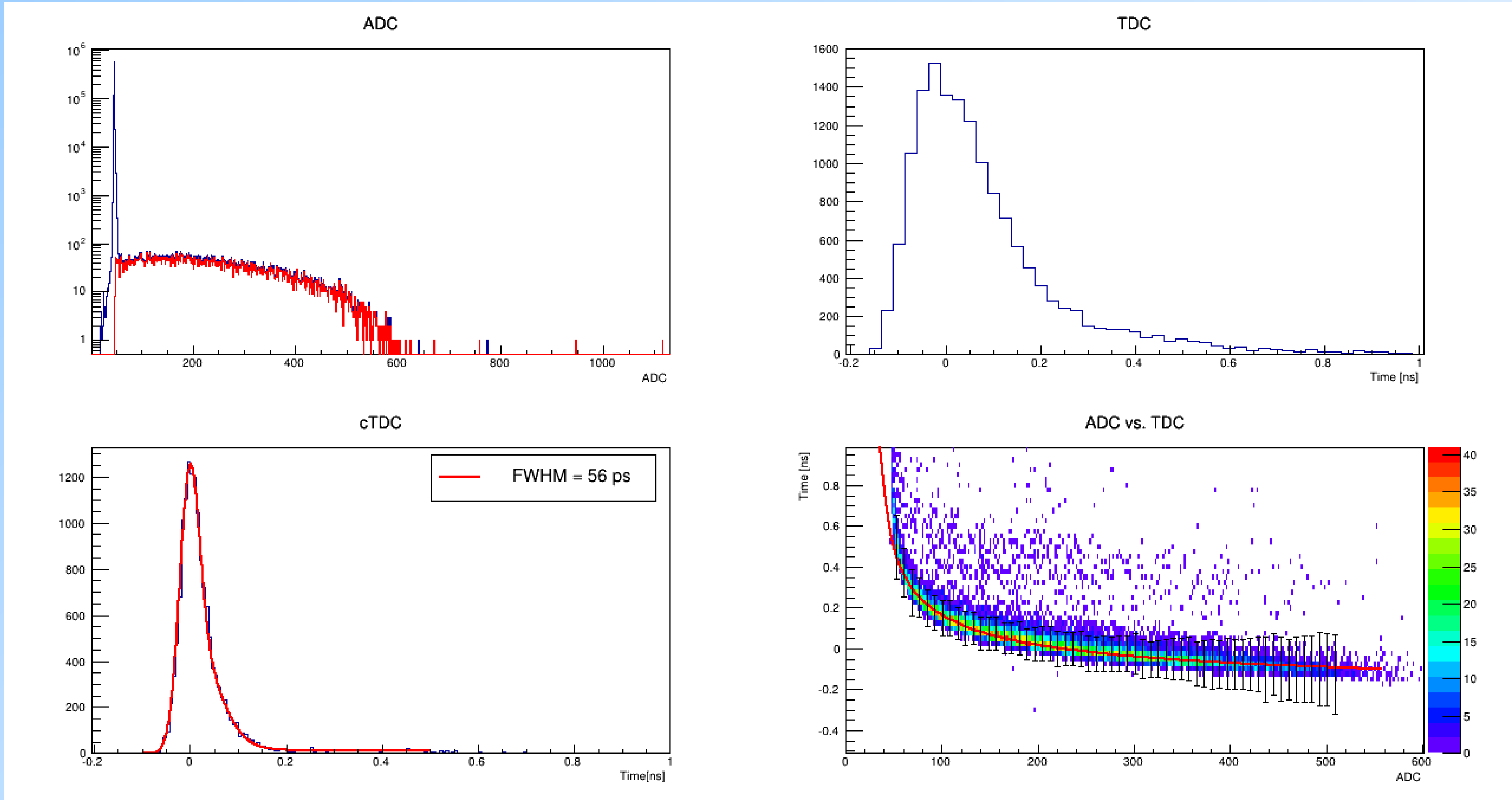
KETEK	PM3350TP	50	25
SensL-J	MicroFC-30050-SMT-GP	50	25

Reference sensor: MCP PMT

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

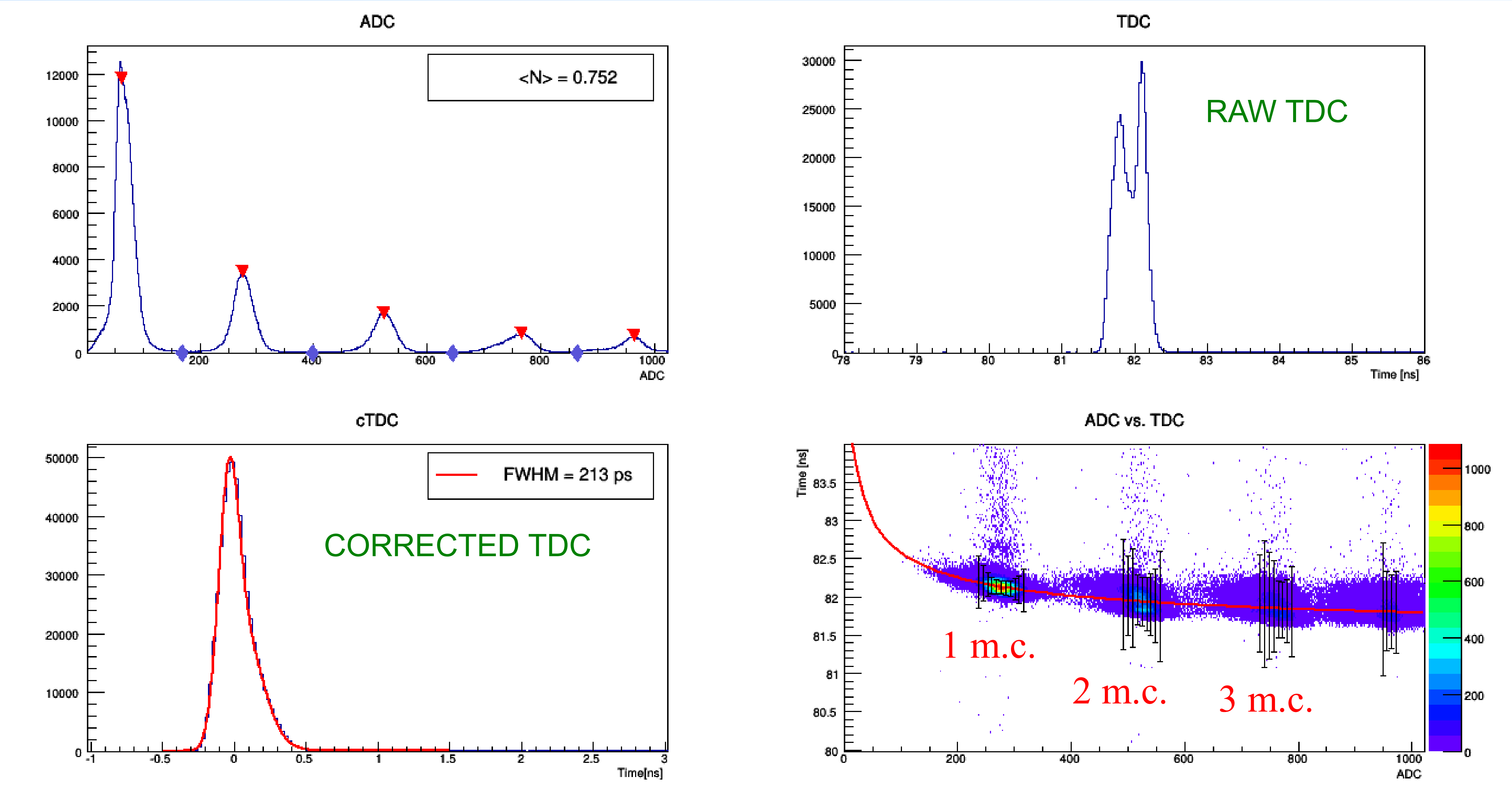


Red laser: 56 ps FWHM

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

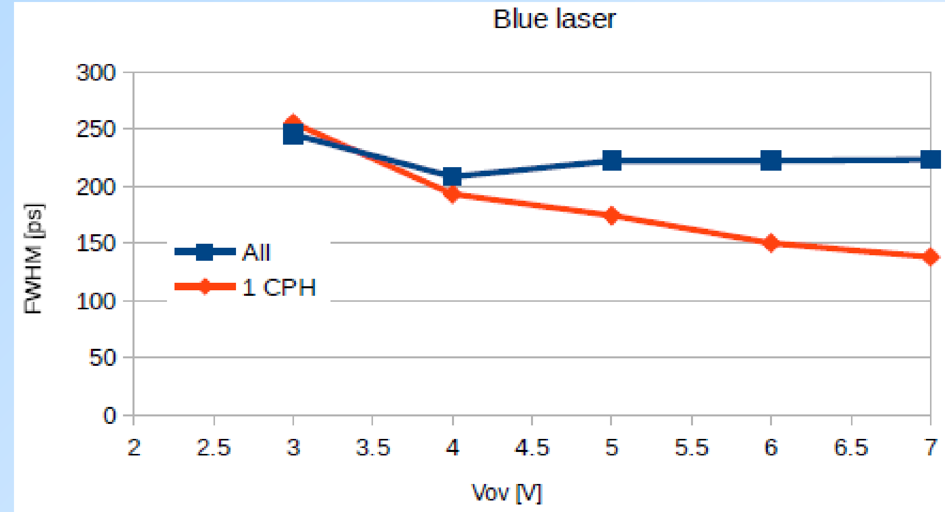
SiPM: Timing resolution with pico-second laser

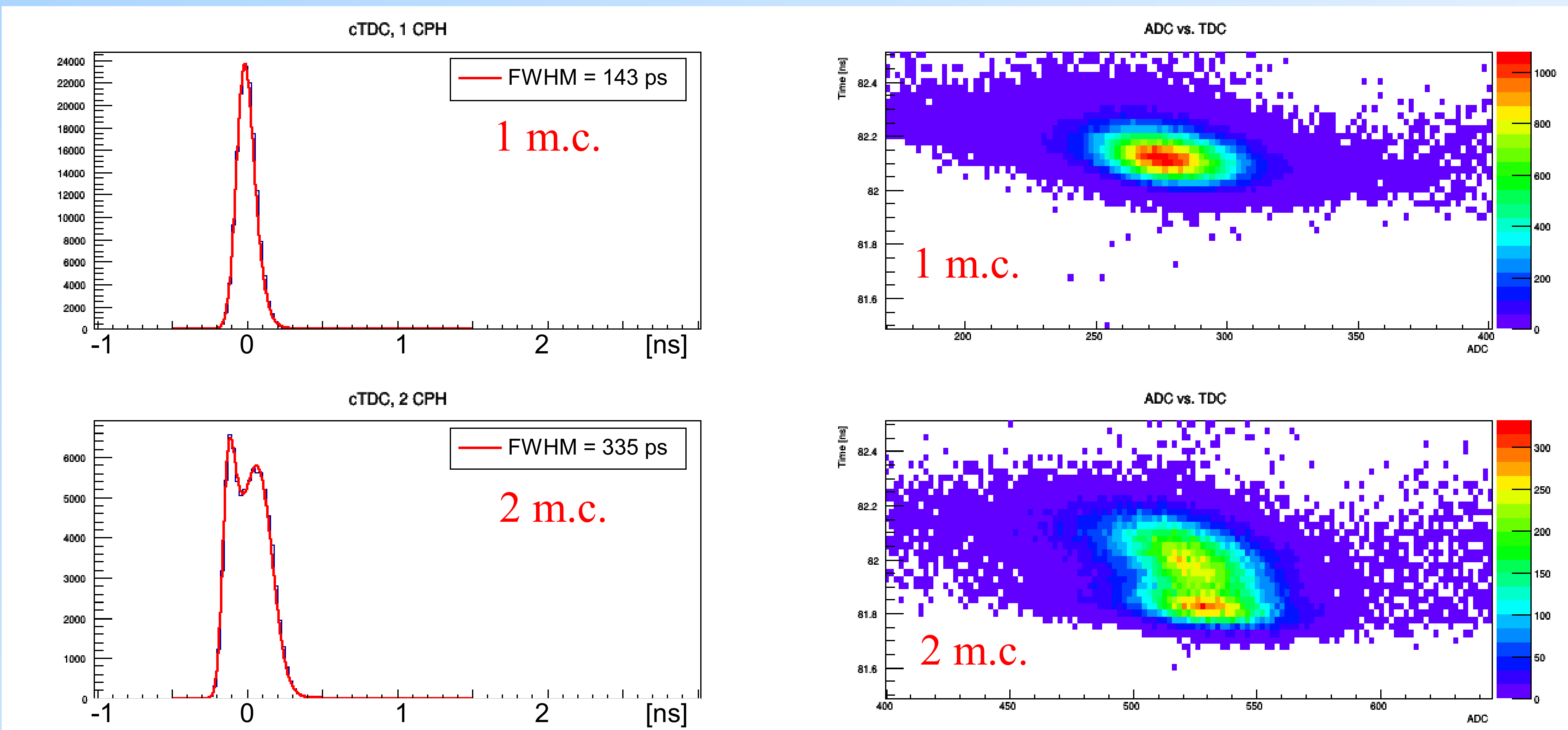
- AdvanSiD SiPM, V_{OV}=6V, T=-25°C
- blue laser λ=404nm



All vs. 1m.c. signal events

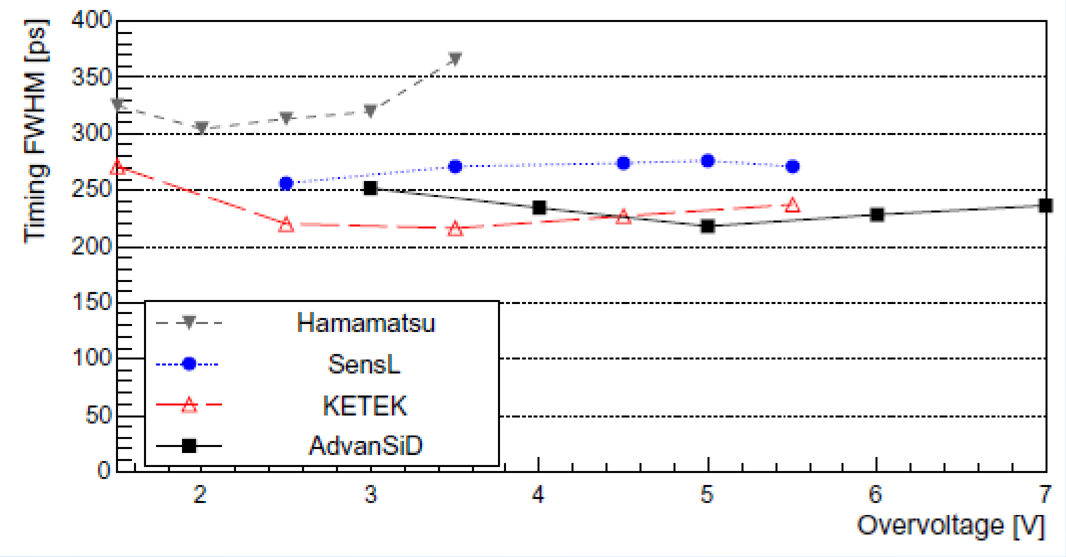
- AdvanSiD SiPM, V_{OV}=6V, T=-25°C
- blue laser λ=404nm
- events vith 2m.c. signal have two contributions: real double hit events with better resolution and optical crosstalk events

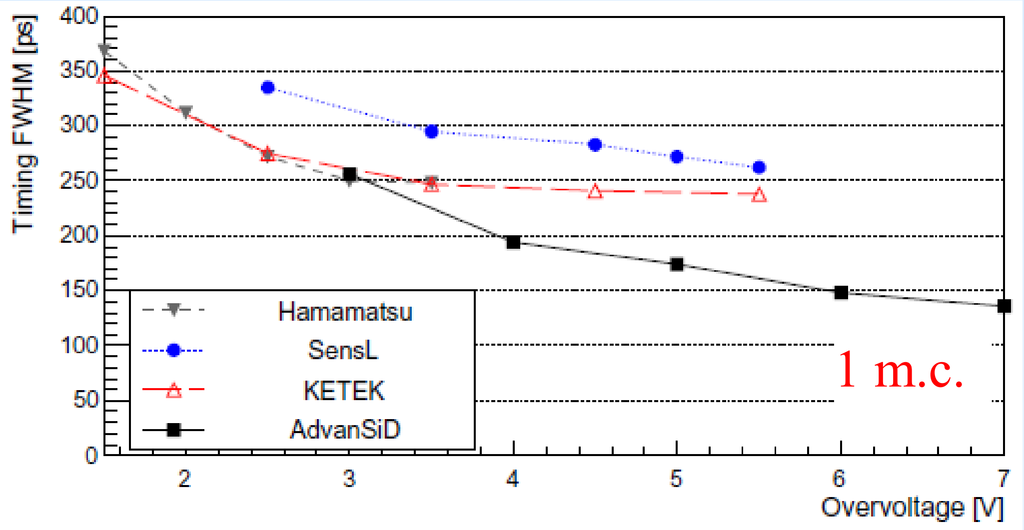


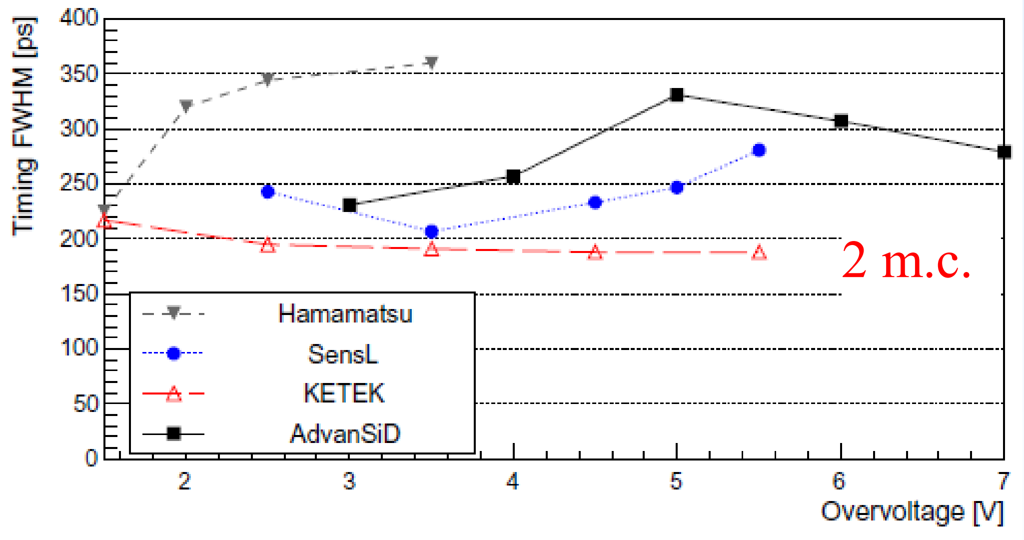


Timing resolution with laser pulses

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





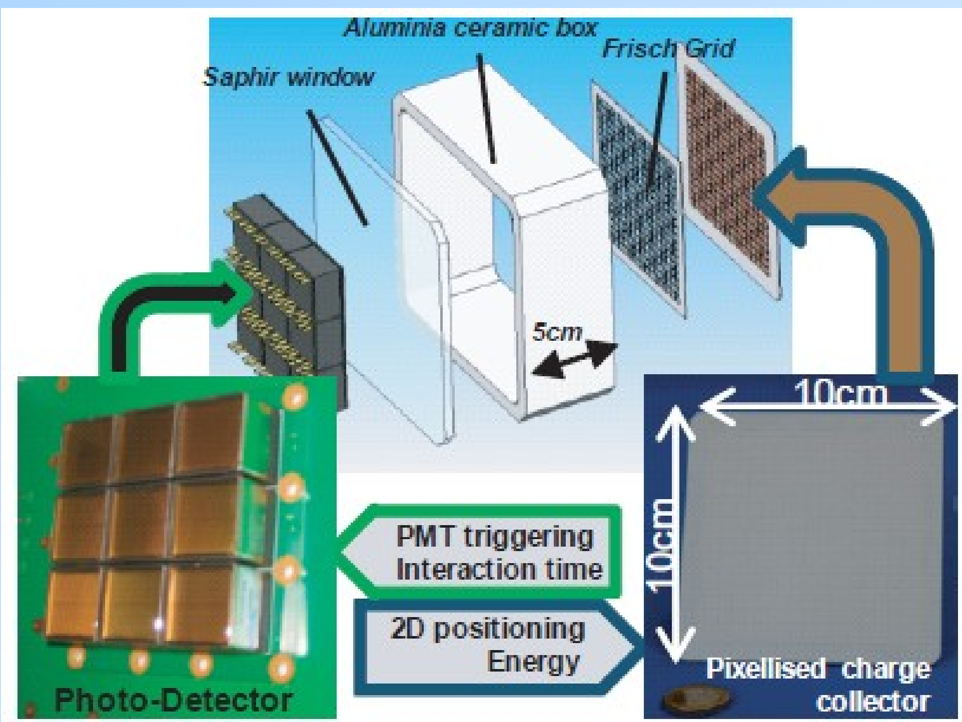


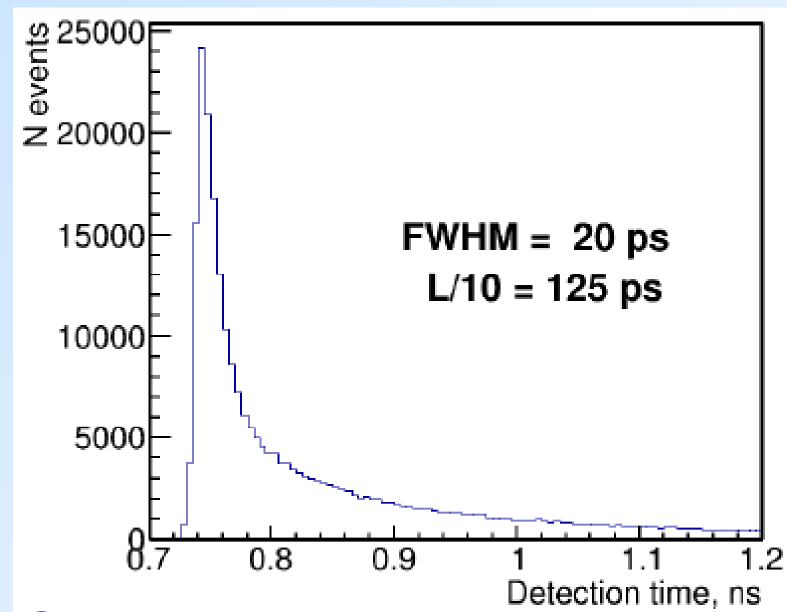
CaLYPSO detector

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

Development of high precision TOF-PET for brain imaging:

- use of liquid TMBi (TriMethyl Bismut $Bi(CH_3)_3$) for gamma detection
  - density 2.3 g/cm^3
  - att. length 2.5 cm
  - ph. fraction 47%
- position from ionization process – aiming at 1mm
- timing from Ch. photons detected by MCP-PMT – aiming at 100ps





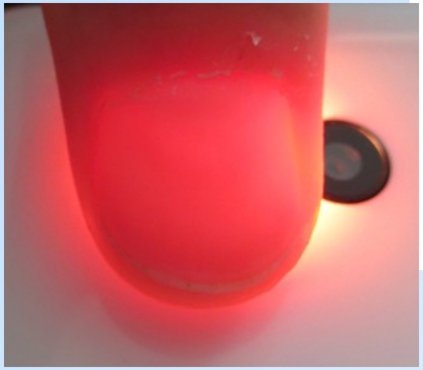
Simulated time response with DOI correction

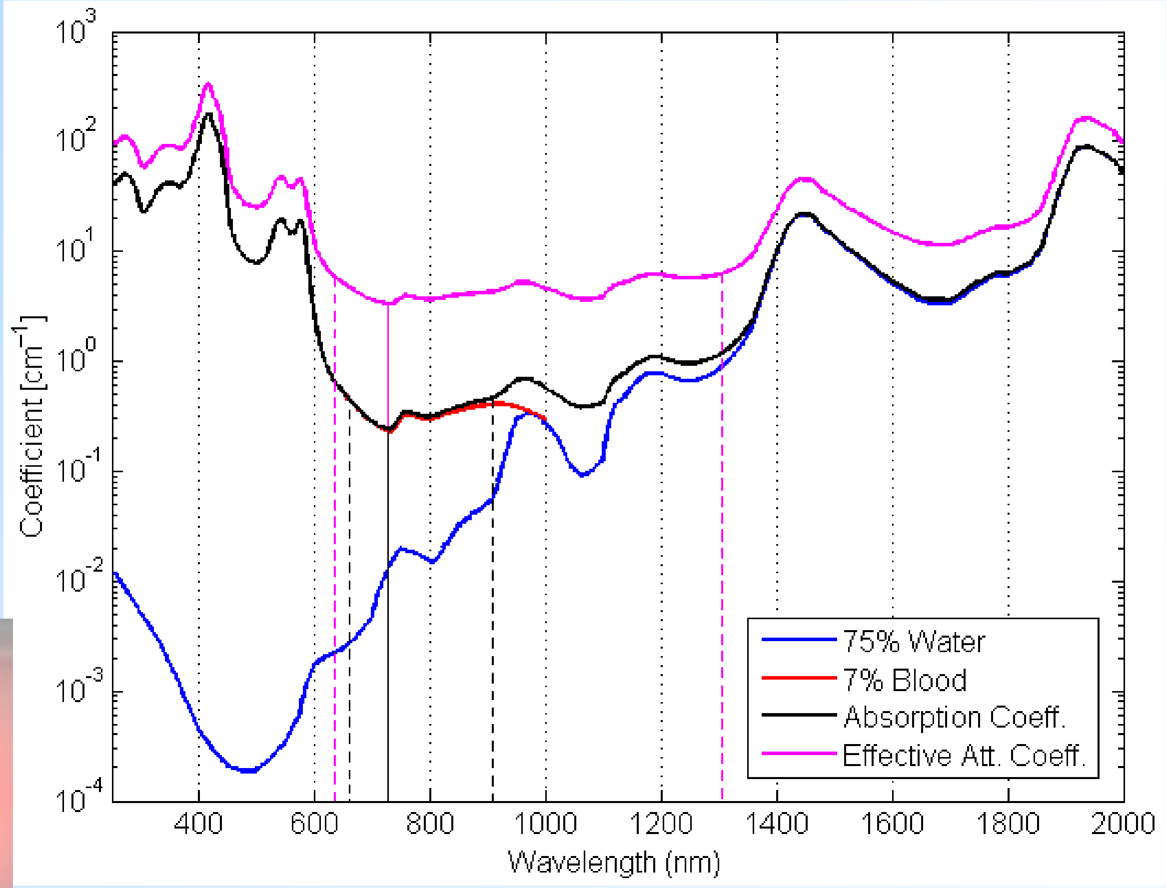
Cherenkov Luminescence Imaging - CLI

Imaging of the Cherenkov light produced in the tissue:

- standard PET markers and other beta emitters may be used: ^{18}F-FDG, Na^{18}F, Na^{131}I, ^{90}YCl$_3$
- main problems are:
  - low number of photons
  - absorption and scattering in the tissue

Red and near infrared light can penetrate/scatter through ~1cm of a tissue





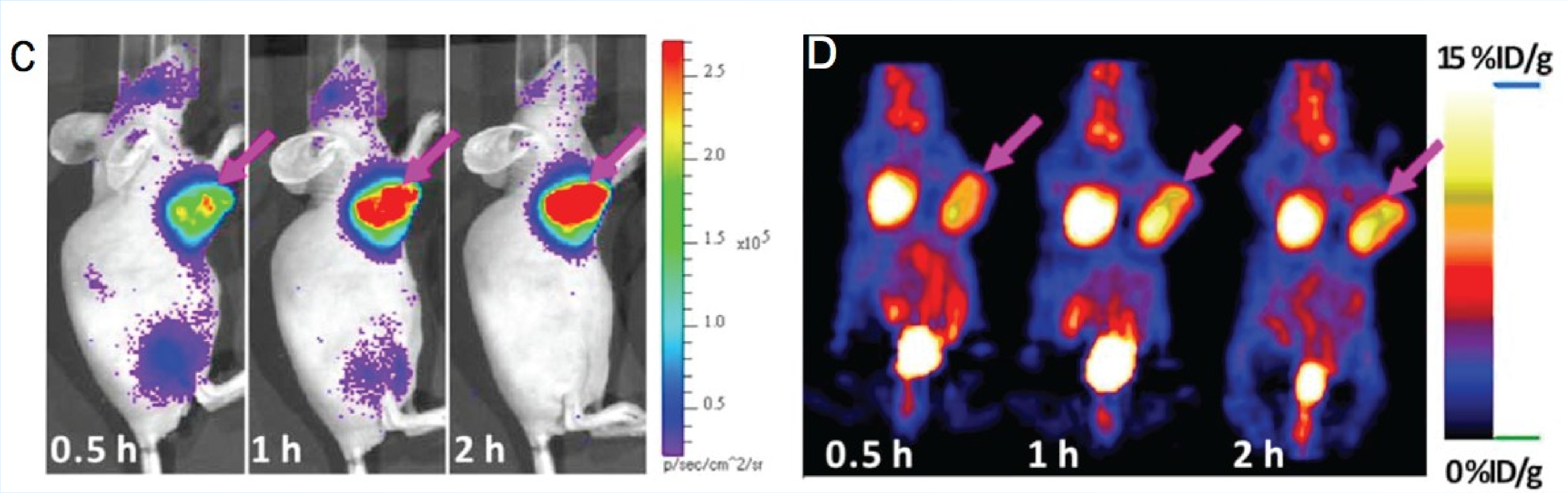
Absorption coefficients for main tissue components

Planar CLI – radio-tracer imaging

- use of sensitive CCD camera to visualize the Cherenkov light produced in the tissue – under the skin
- comparison of the planar CLI and PET image for mice with tumor

CLI image of nude mice with injected tumor

PET image of the ame mice



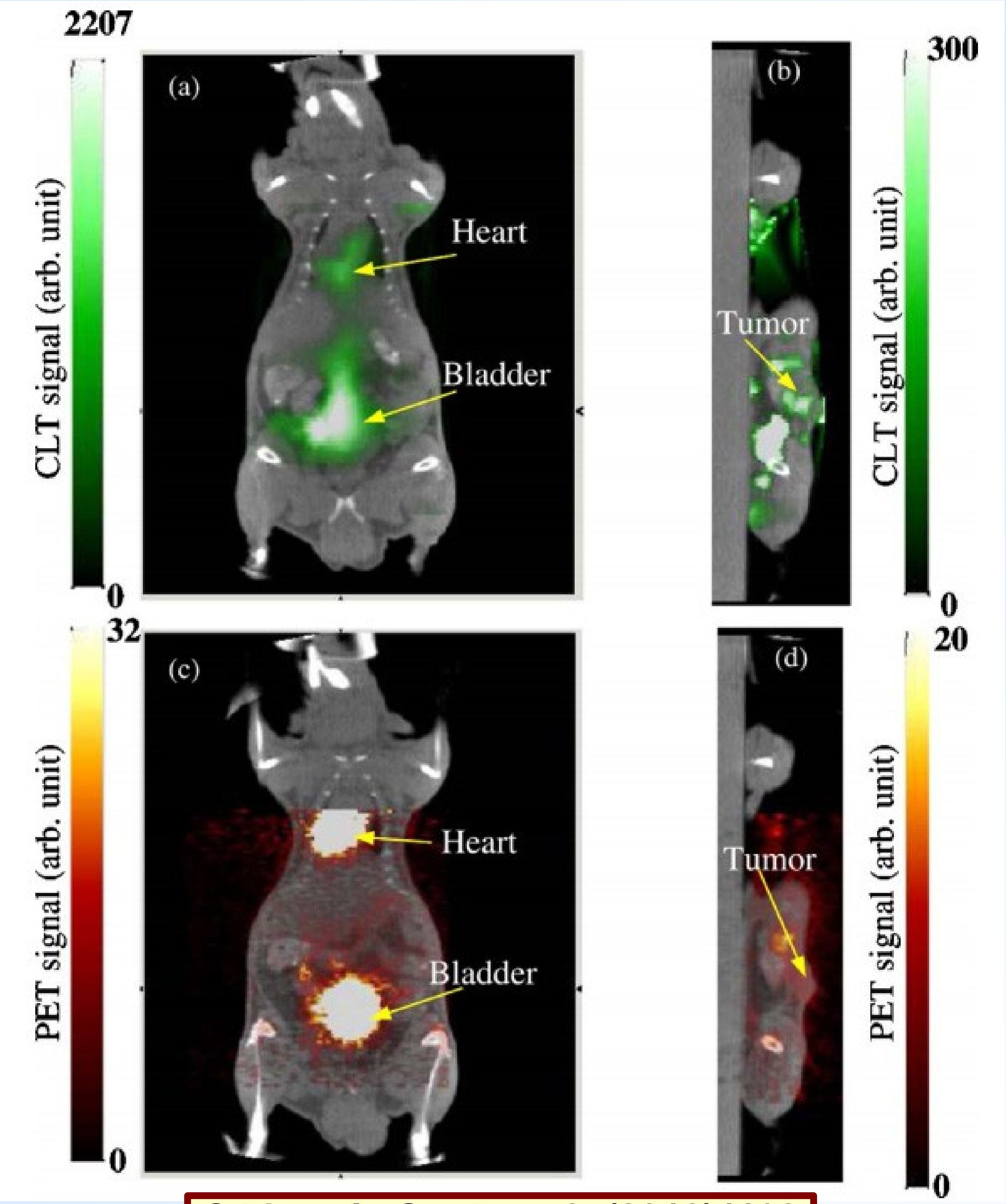
(images taken 0.5h, 1h, 2h after ^{18}F-FDG injection)

H.Liu et al., PLoS ONE 5(3): e9470

Cherenkov Luminescence Tomography - CLT

- small animal tomography by making the images from different view points around the object and using filtered back-projection

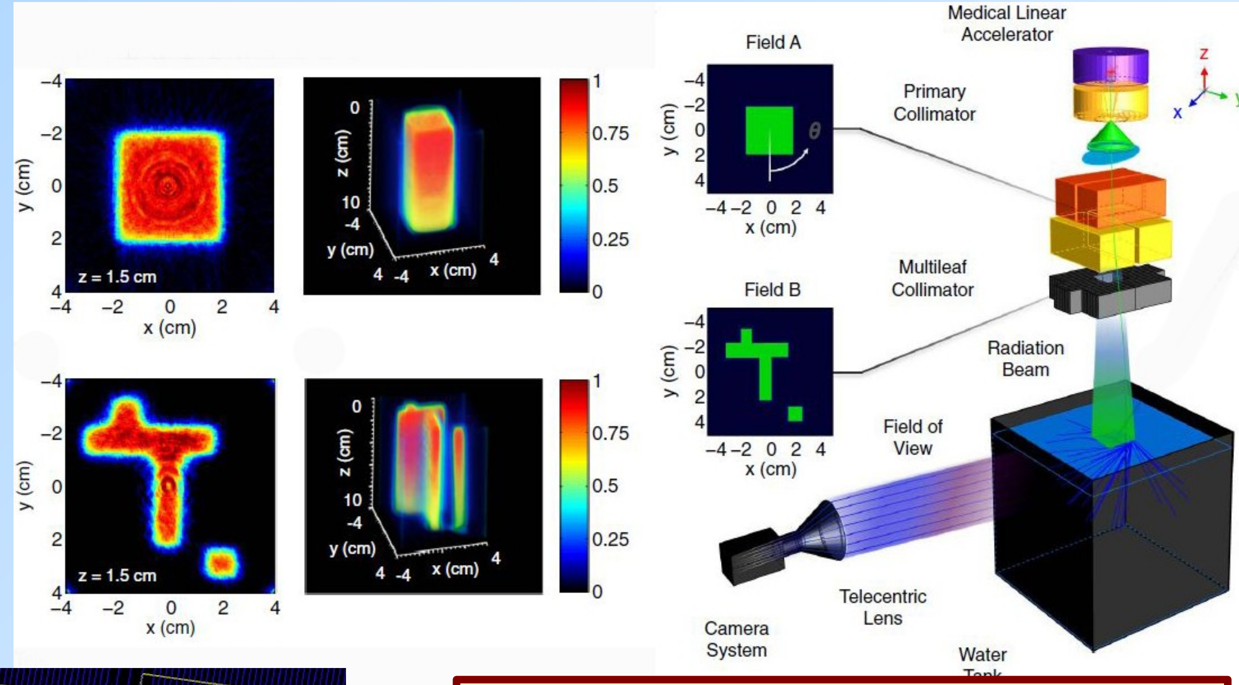
- comparison of CLT and PET images of mice with tumor



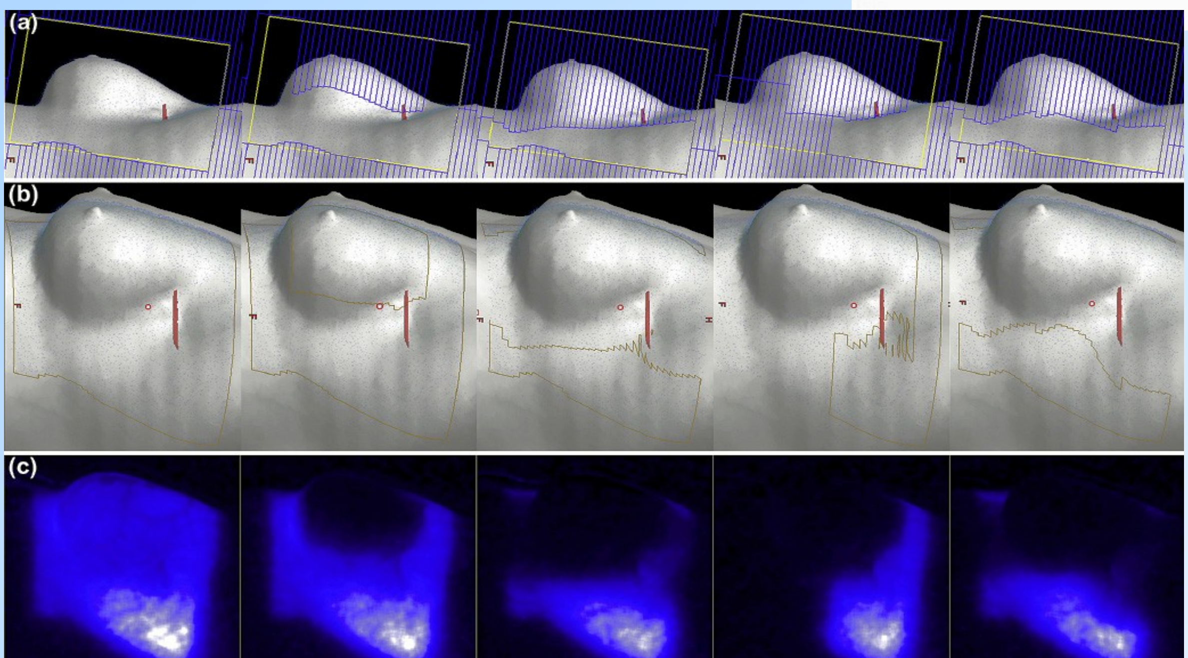
C.Li et al., Opt.Lett. 35(2010)1109

Cherenkov Luminescence Imaging Dosimetry - CLID

- measuring of the 1MeV photon beam profile in the water based phantom



A.K.Glaser et al.,Opt.Lett. 38(213)634



A.E.Spinelli et al.,J.Biomed.Opt.18(2013)020502

- monitoring of irradiated area by CLI during radiotherapy (Cherenkography)

Summary

- **Cherenkov TOF PET** uses Cherenkov light produced in the radiator by the electron produced in the 511 keV gamma interacting with radiator
  - main advantage prompt emission
  - main disadvantage low number of photons
- Initial tests with MCP-PMT prototypes showed that CRT < 100 ps FWHM can be achieved but efficiency was low
- Preliminary MC studies show that with SiPMs with higher PDE a competitive PET scanner with PbF_2 radiator may be possible
- Performance of SiPMs () is constantly improving and hopefully it will reach optimal performance → coincidence efficiency > 10% and timing < 200 ps FWHM
-
- **Cherenkov Luminescence Imaging** has recently emerged and uses Cherenkov light produced in the tissue imaged by CCD camera. The technique is investigated for many different applications: planar imaging, tomography, radiography, dosimetry, guided surgery, photoactivation therapy ...

BACKUP SLIDES

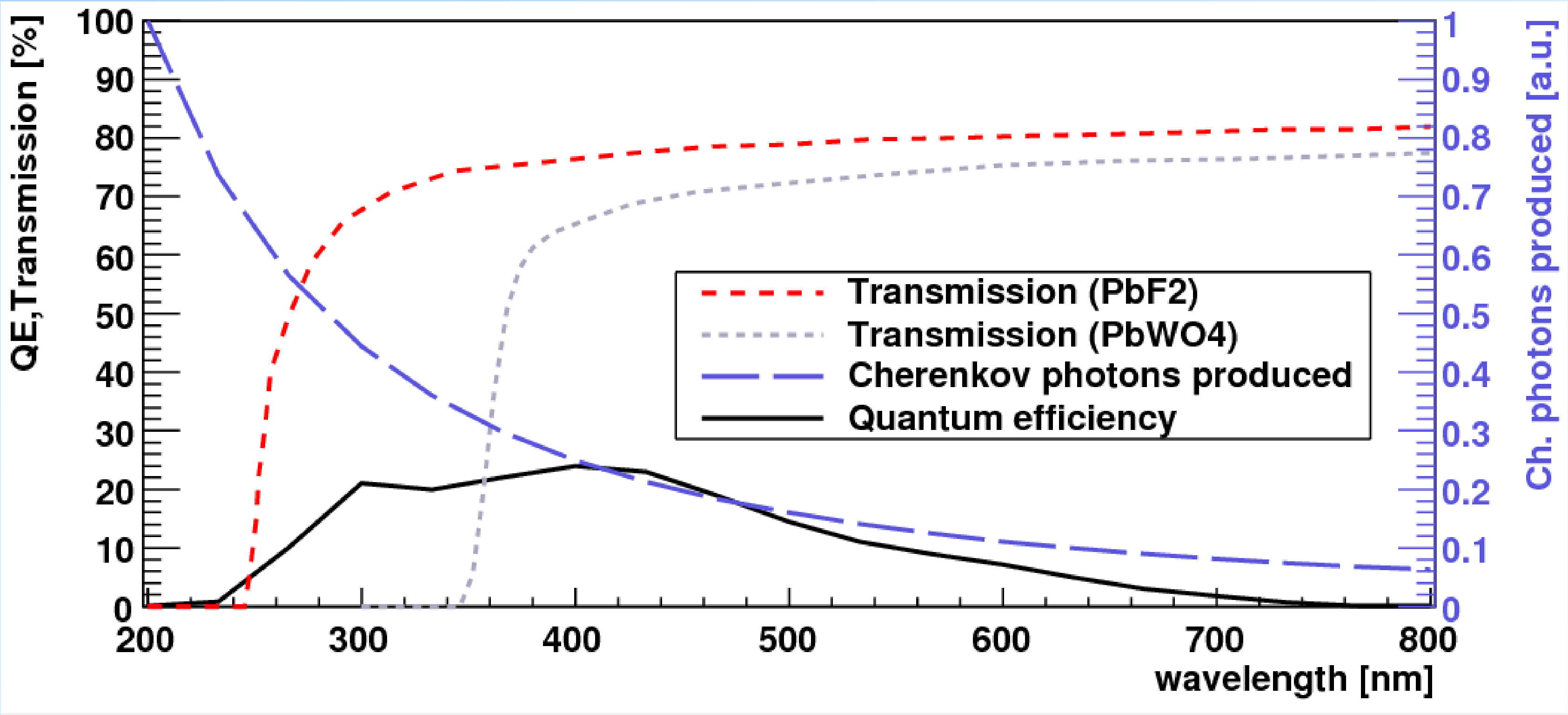
Scintillator propertis

- Properties of some commonly used scintilattors

	NaI(Tl)	BGO	BaF_2	LSO	$LaBr_3(Ce)$
ρ (g/cm^3)	3.7	7.1	4.9	7.4	5.1
μ_{511keV} (cm^{-1})	0.35	0.96	0.44	0.87	0.43
τ (ns)	230	300	0.6	40	17
LY (photons/MeV)	38000	6000	2000	29000	58000
Peak emission (nm)	415	480	220	420	356
Refractive index	1.85	2.15	1.52	1.82	1.88

Simulation: transmission and QE

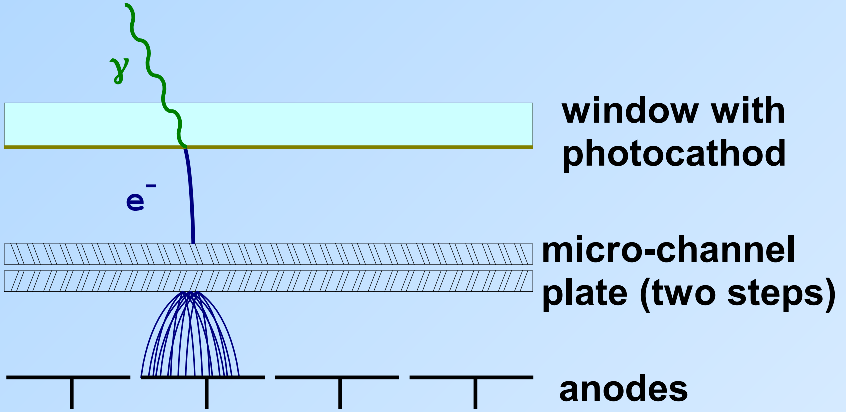
- Transmission of PbF_2 and $PbWO_4$ indicating the cut-off wavelength.
- QE used in simulation.

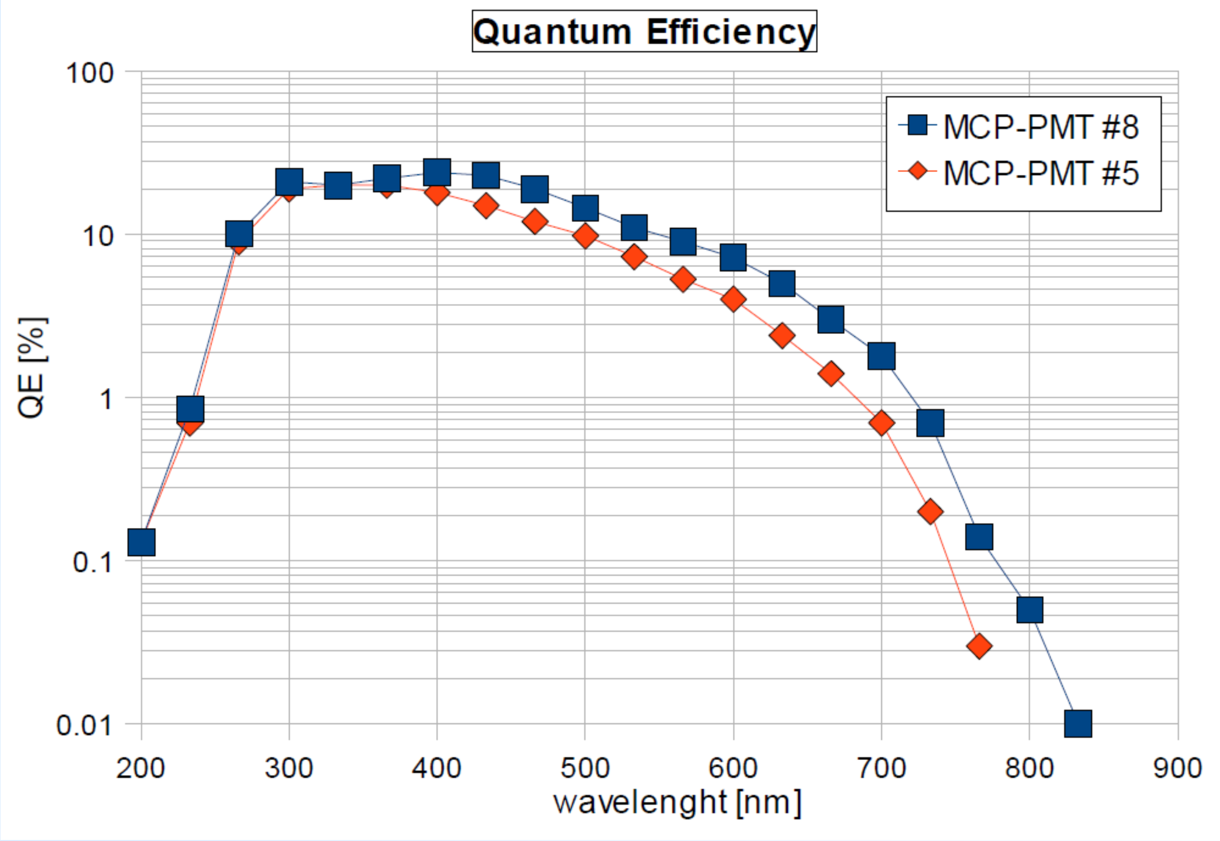


MCP-PMT properties

Hamamatsu MCP-PMT
(prototypes for Belle II TOP counter #5 and #8):

- multi-anode PMT with two MCP steps, 10 μm pores
- 16 (4x4) anode pads, pitch ~ 5.575mm, gap ~ 0.3mm
- box dimensions ~ 27.5 mm square
- excellent timing σ ~ 20ps for single ph.
- multi-alkali photocathode
- 1.5 mm borosilcate window
- gain > 10^6

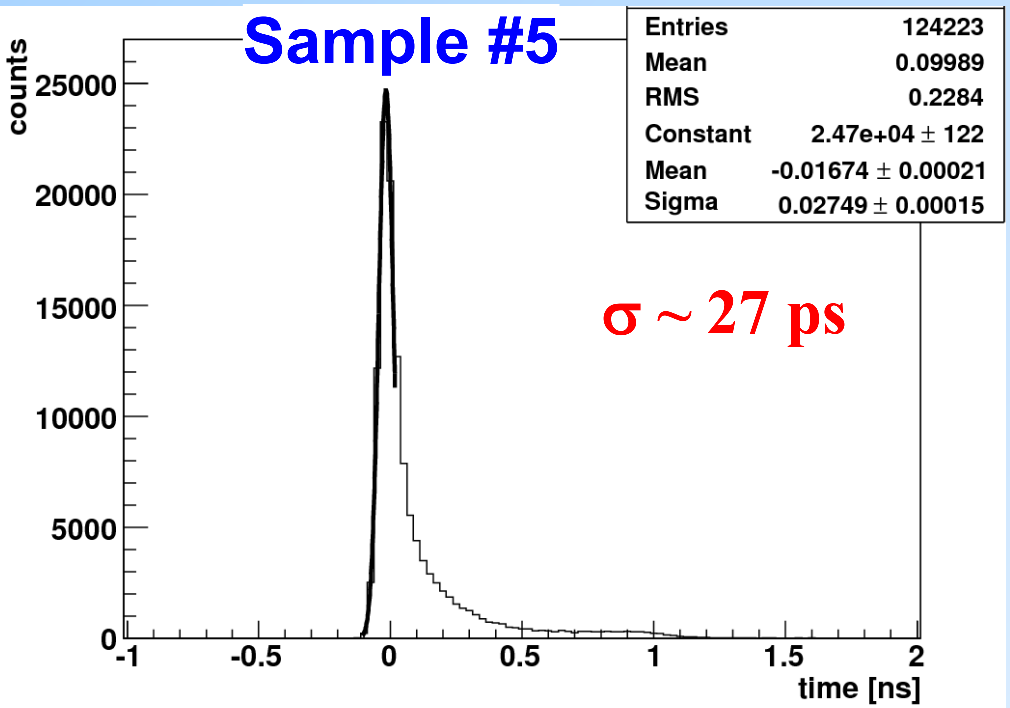


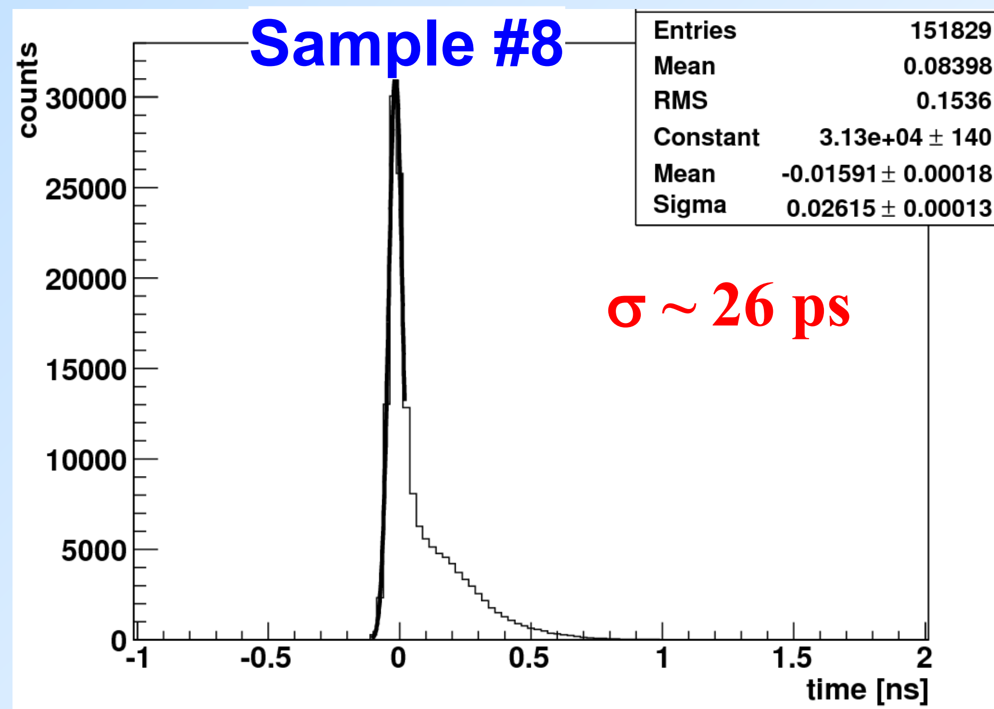


Tests with picosecond laser

Intrinsic resolution measured with pico-second PiLas laser, λ=406 nm, attenuated to single photon detection level:

- r.m.s. of prompt peak for both samples below 30 ps including contribution from laser ~15 ps and electronics ~11 ps
- intrinsic resolution ~ 20 ps

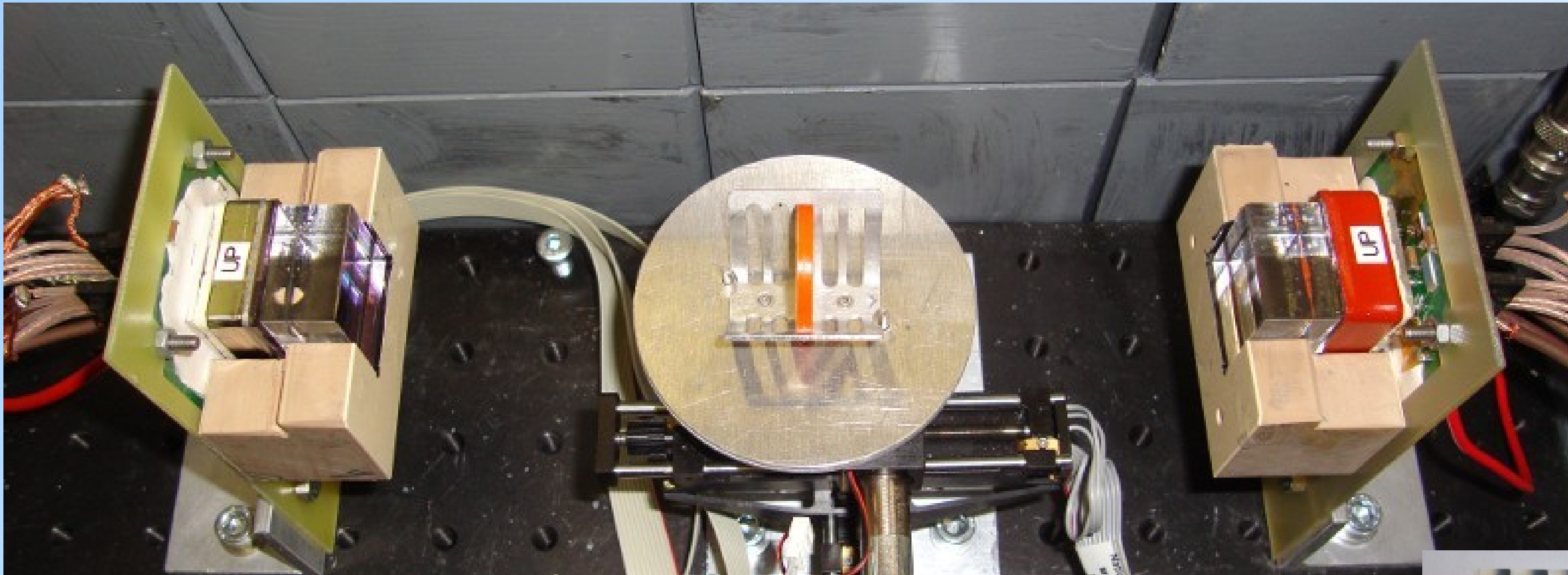




- tails are mainly produced by photoelectron back-scattering events

Setup

Two detectors in back-to-back configuration with 25x25x15 mm^3 crystals coupled to MCP-PMT with optical grease.

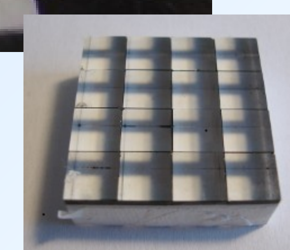


Cherenkov radiators:

-monolithic: 25 x 25 x 5,15 mm^3 (PbF_2, $PbWO_4$)

-4x4 segmented: 22.5x22.5x7.5 mm^3 (PbF_2)

-black painted, Teflon wrapped, bare



Samo Korpar
Univ. of Maribor and J. Stefan Institute

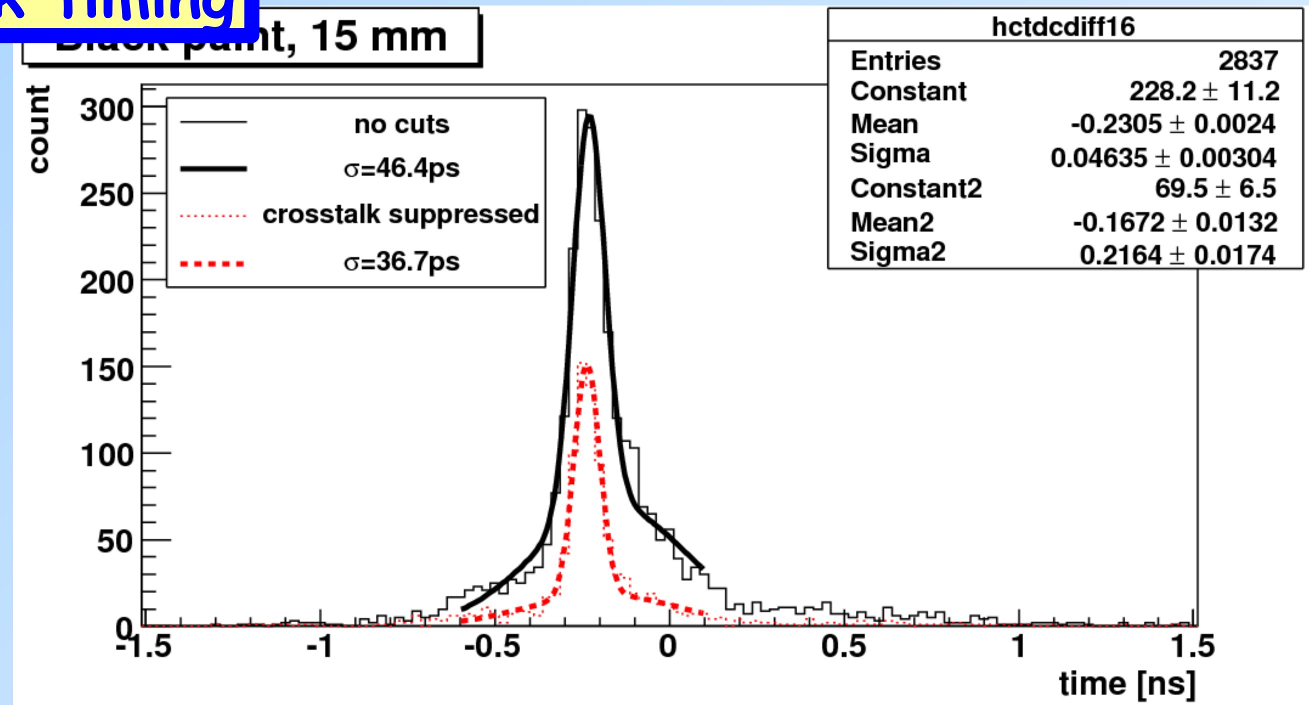
MCP-PMT: Back-to-back timing

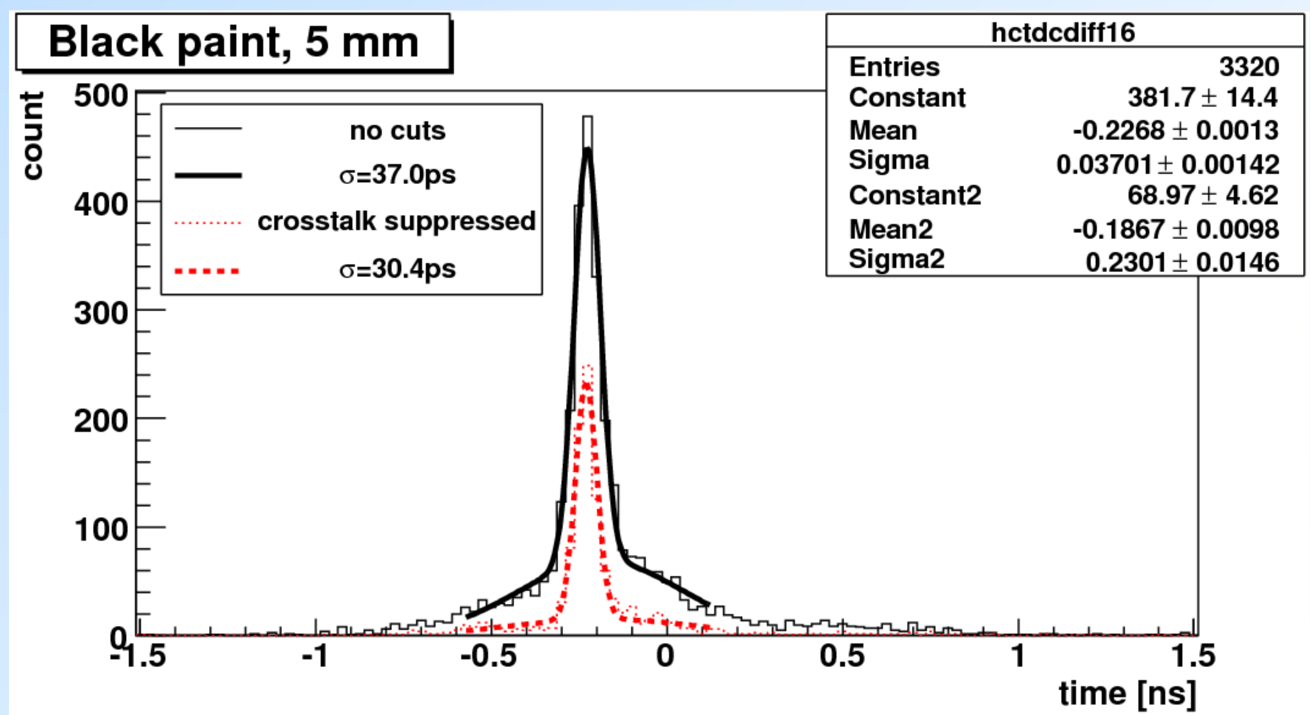
Data taken with black painted PbF_2 crystals:

- 15 mm: r.m.s. ~ 37 ps
  FWHM ~ 95 ps

- 5 mm: r.m.s. ~ 30 ps
  FWHM ~ 70 ps

NIM A654(2011)532



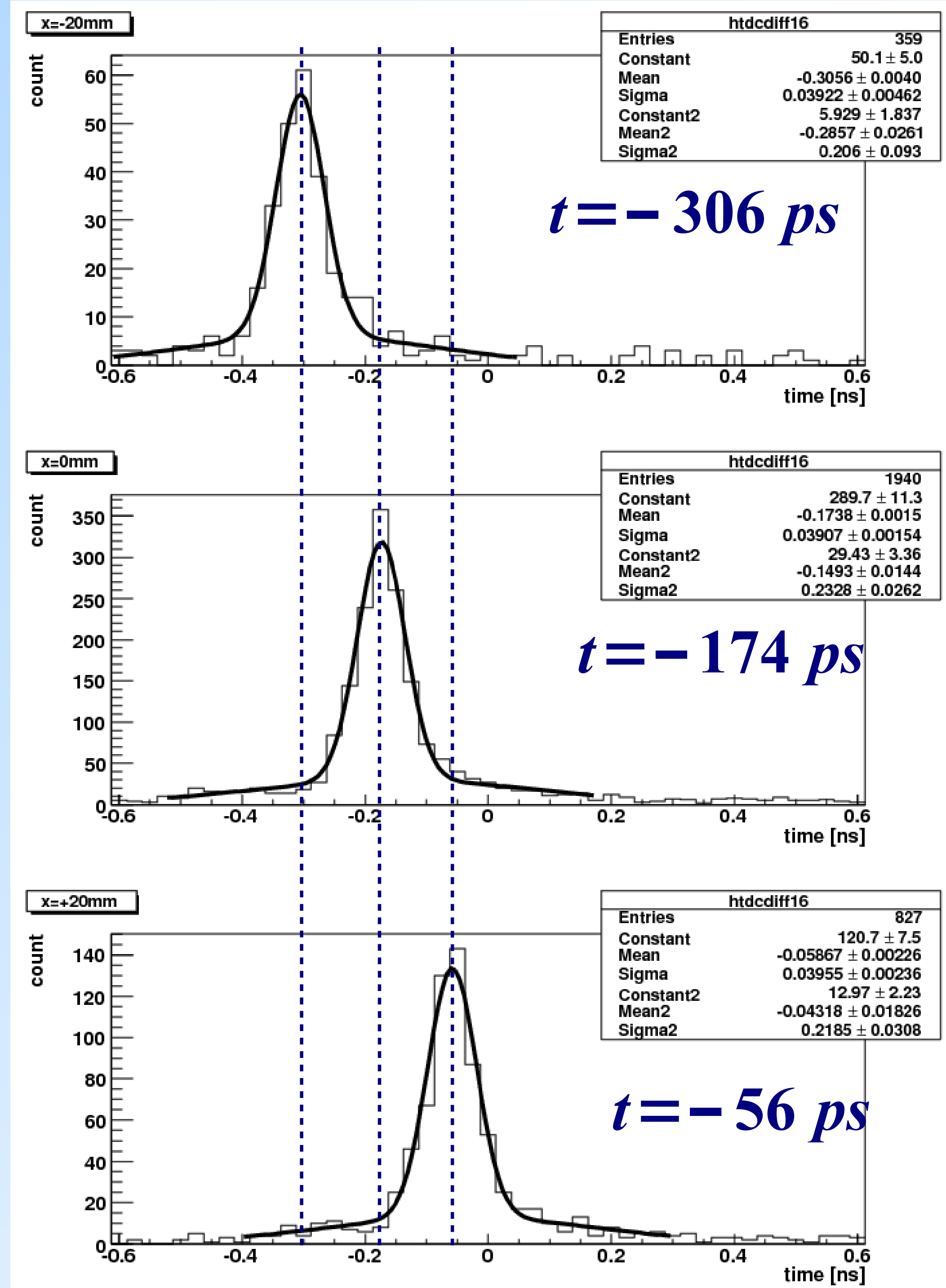


TOF PET position resolution

Data taken at three different point source positions spaced by 20 mm:

- average time shift 125 ps
- timing resolution ~ 40 ps, ~ 95 ps FWHM
- position resolution ~ 6 mm RMS, ~ 14 mm FWHM

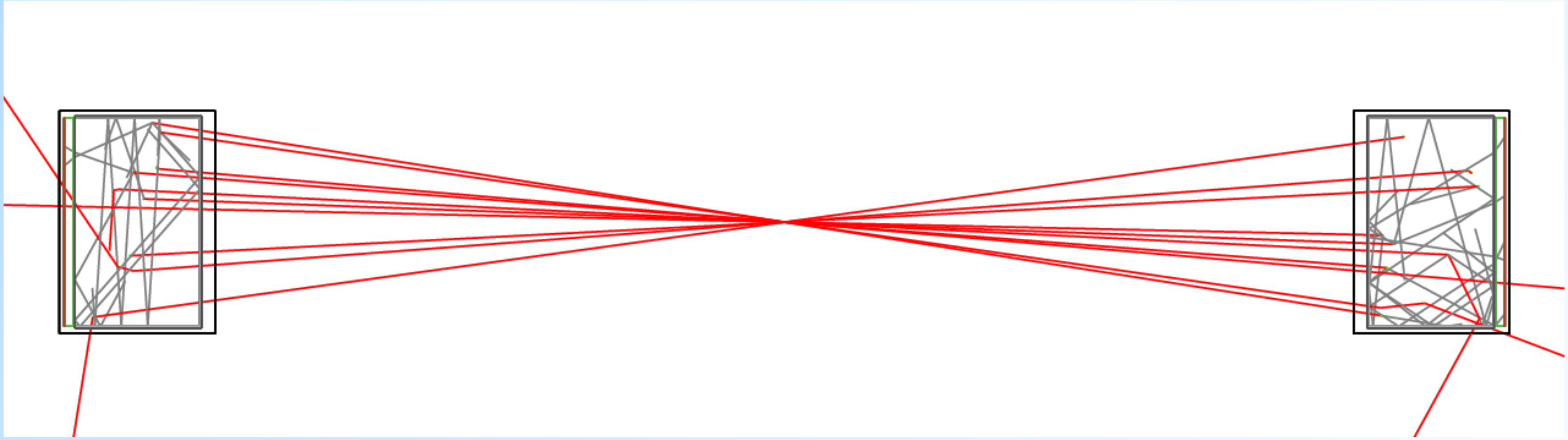
Black painted 15 mm PbF_2 crystals.



GEANT4 simulation

Interactions in a single crystal and full Back-to-back setup were simulated in GEANT4, taking into account:

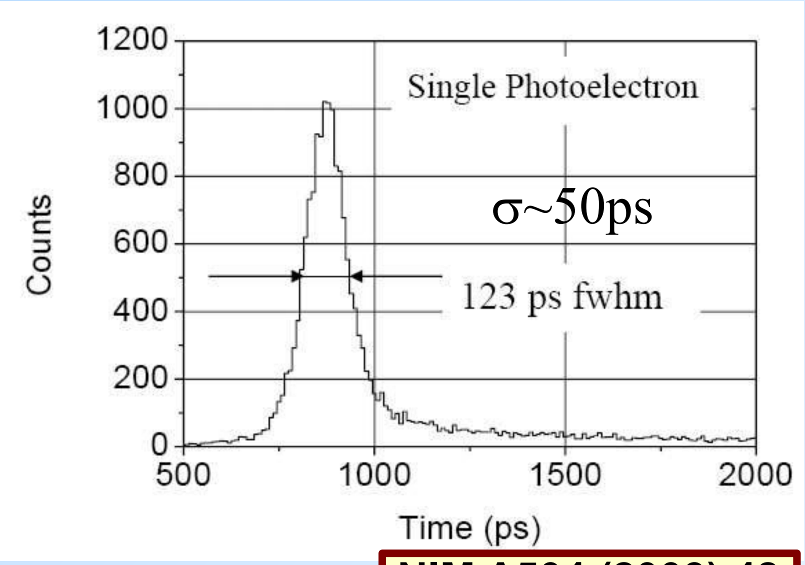
- gamma interactions with detector
- optical photons (Cherenkov and scintillation) produced between 200 nm – 800 nm (no scintillation assumed for PbF2)
- optical photon boundary processes (exit surface polished, other surfaces polished and wrapped in white reflector or black painted)
- photodetector window coupled with optical grease (n=1.5)
- photodetector QE (peak 24% @ 400nm)
- perfect photodetector timing – simulated timing resolution only includes photon travel time spread



SiPM for Cherenkov TOF PET?

Advantages:

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

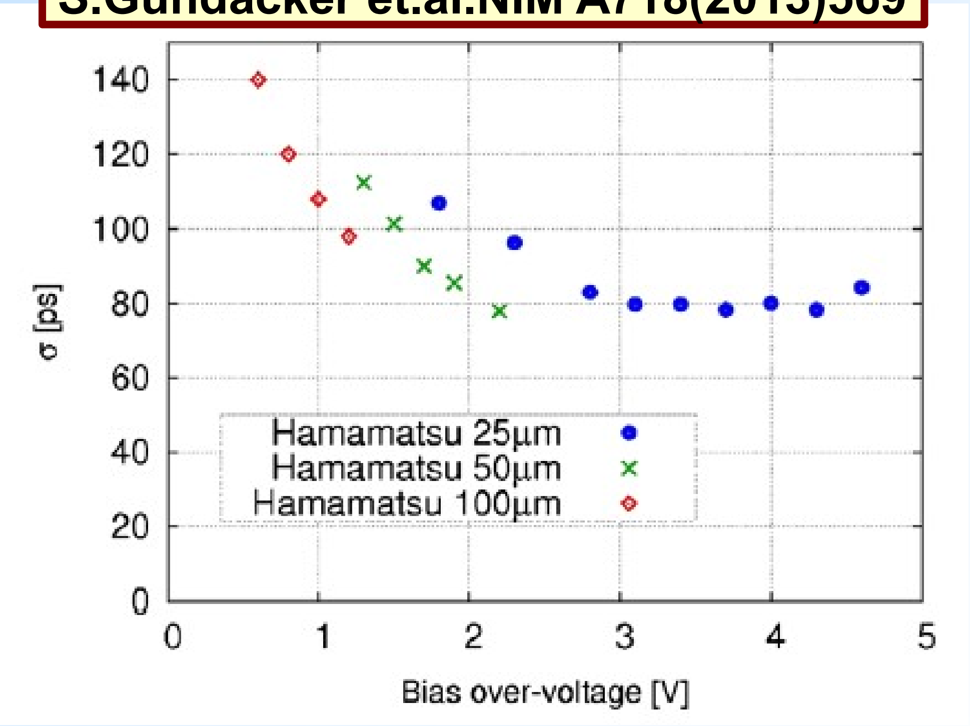


NIM A504 (2003) 48

Disadvantages:

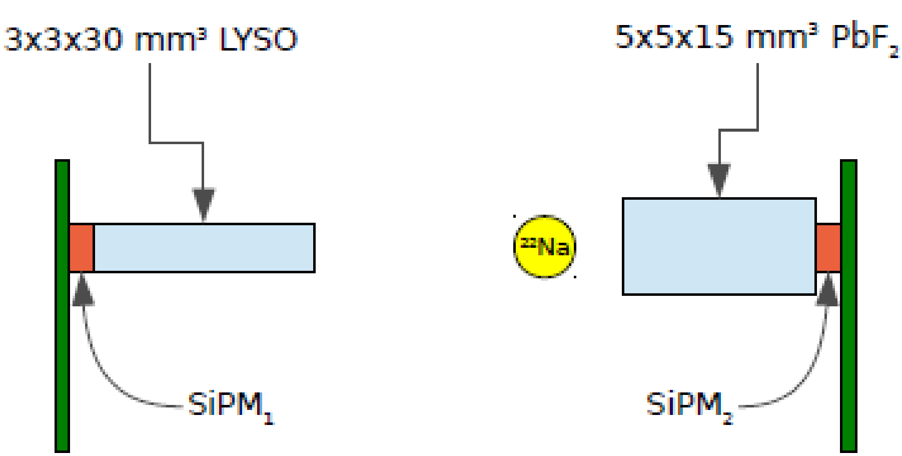
- high dark count rate (DCR) ~ 100kHz/mm^2 (cooling?)
- single photon timing resolution not yet below 100 ps FWHM (especially for large area devices)?

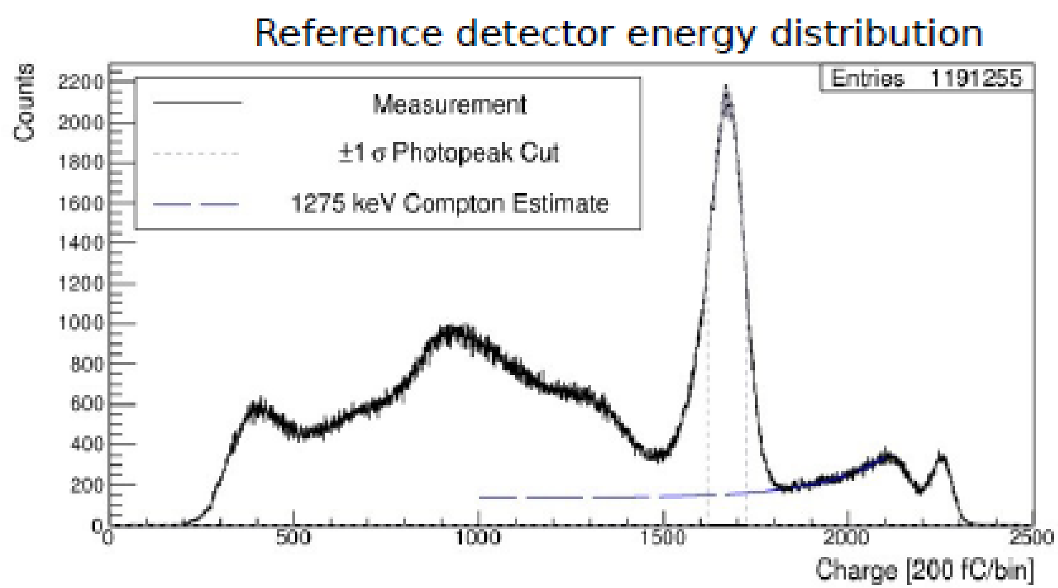
S.Gundacker et.al.NIM A718(2013)569



Efficiency measurements

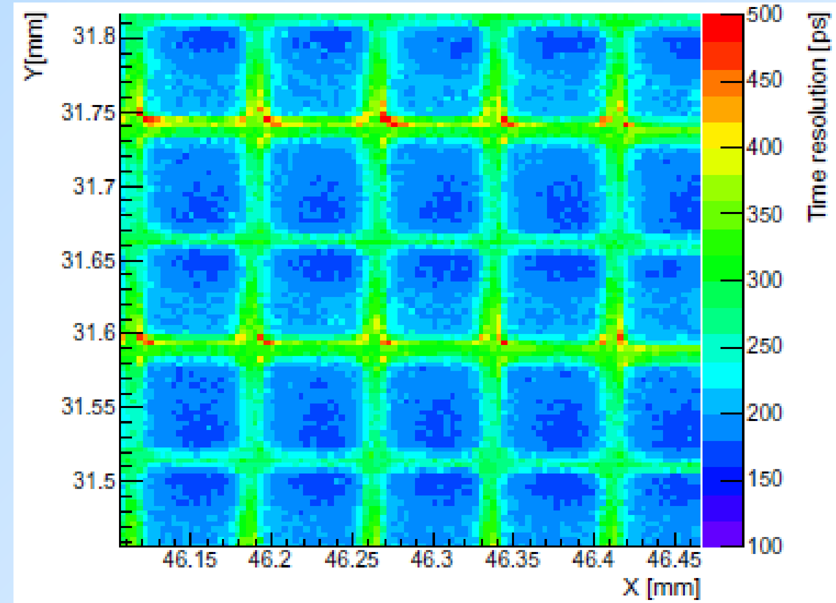
- one Cherenkov detector replaced with a reference scintillation detector
- tight collimation of coincidence gammas on Cherenkov detector
- photopeak cut on reference detector → single side detection efficiency on Cherenkov detector
- corrected for
  - SiPM dark count rate
  - Compton scatter of 1275 keV gammas from ^{22}Na

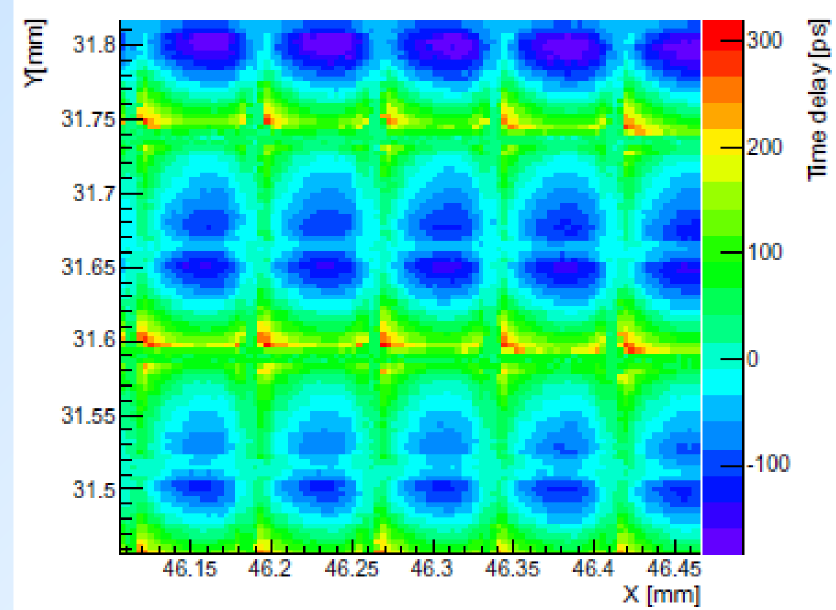


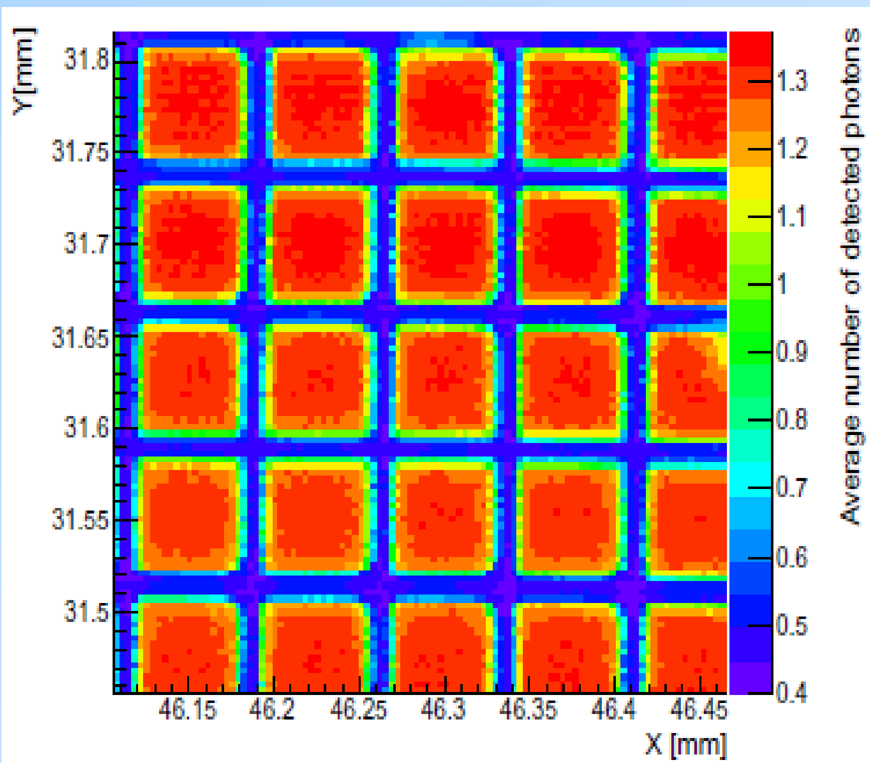


Timing resolution and delay vs. position - local

- Focused red laser ($\sigma \sim 3\mu m$), T=25°C, area ~250 x 250 μm^2
- Higher dark count rates and lover V_{OV}
- Timing resolution (right-top) and delay (right-bottom)[ps], vs. position
- Average number of detected photons (primary carriers) from P(0) (left)

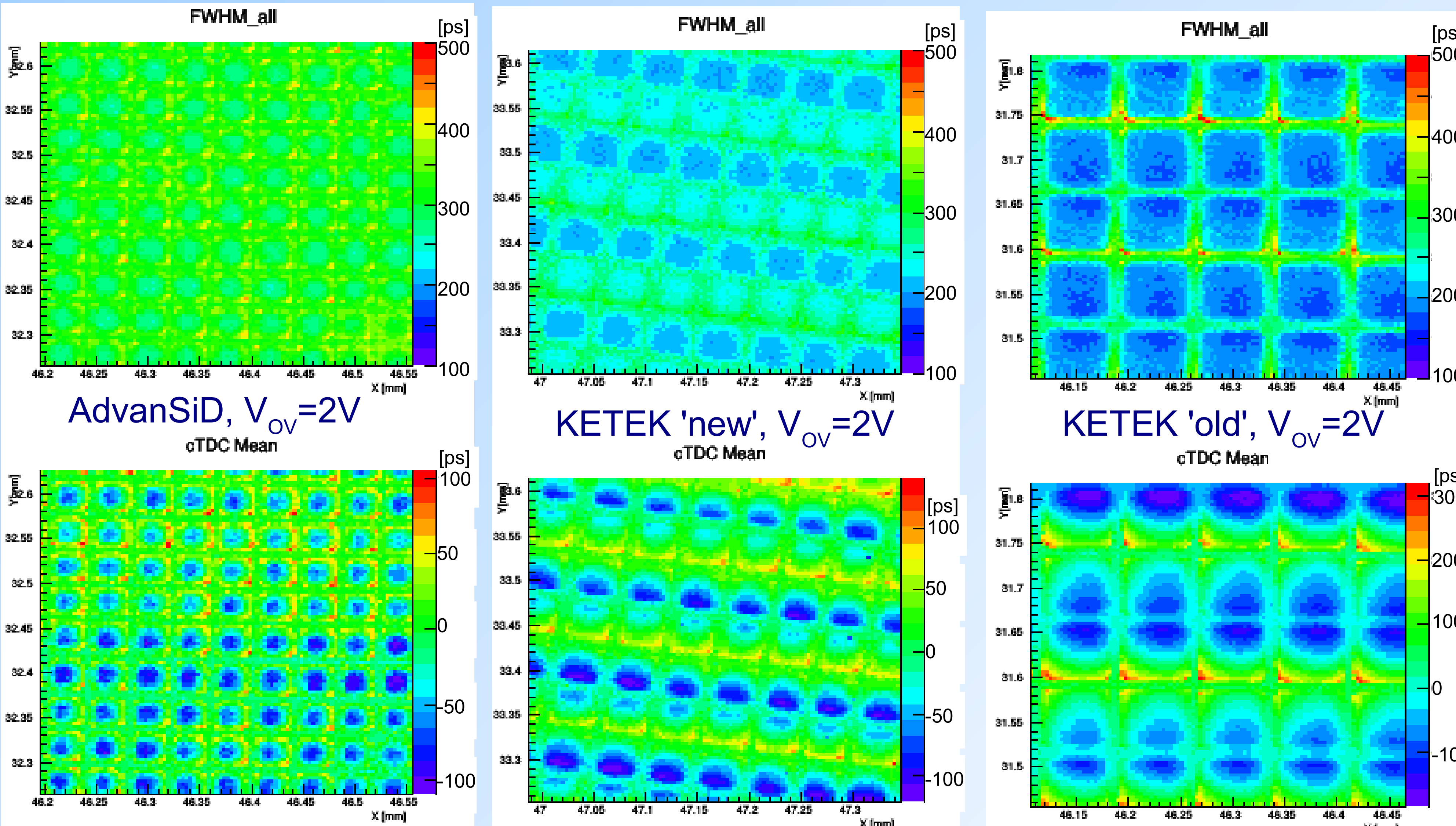






Timing resolution and delay vs. position - local

- Focused red laser ($\sigma \sim 3\mu m$), T=25°C, area ~250 x 250 μm^2
- Higher dark count rates and lover V_{OV}
- Timing resolution (top) and delay (bottom)[ps], vs. position



Timing resolution and delay vs. position

- Defocused red laser (σ ~ 300μm), T=25°C, ~ 3 x 3 mm^2
- Higher dark count rates and lover V_{OV}
- Timing resolution (top) and delay (bottom) vs. position