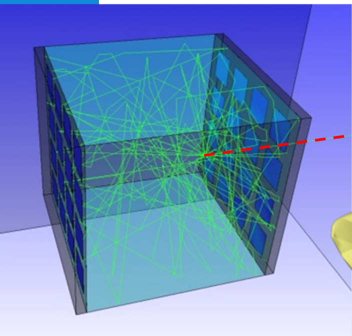
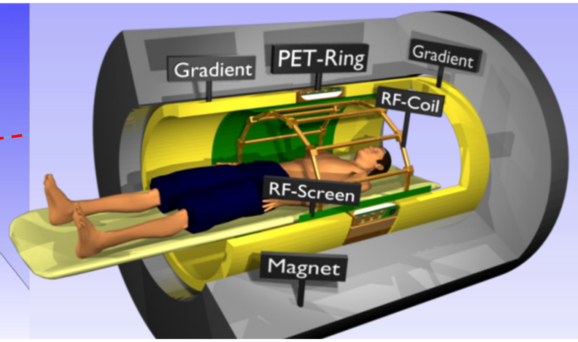
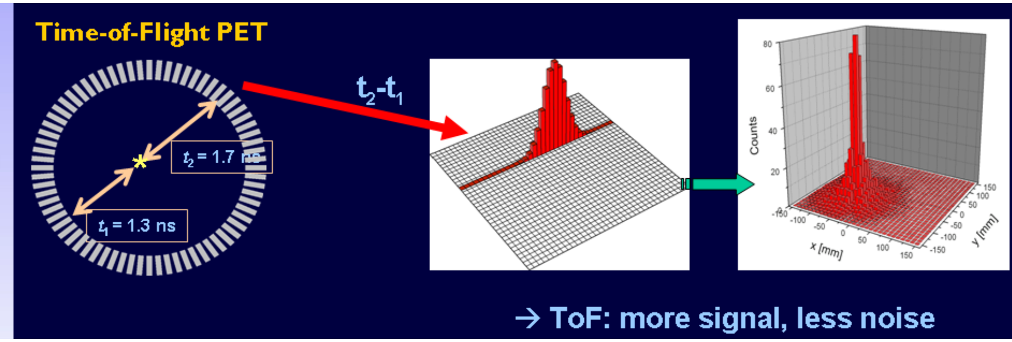






Is sub-100 picosecond time resolution feasible in realistic TOF-PET systems?

MEDAMI 2014, Alghero, Italy, September 6, 2014

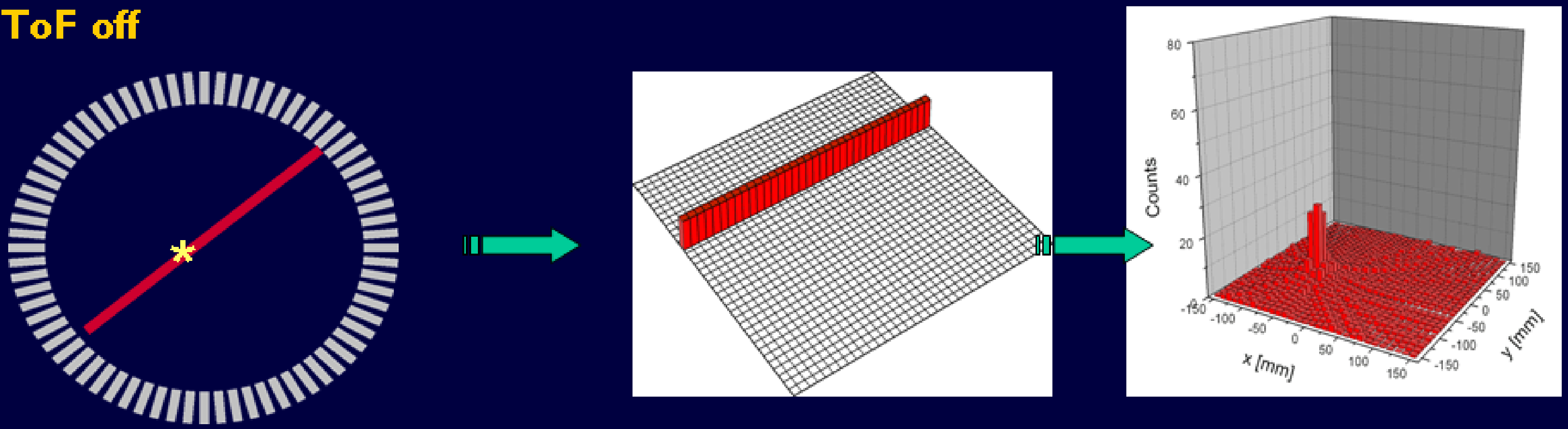
TU Delft

Dennis R. Schaart
Delft University of Technology

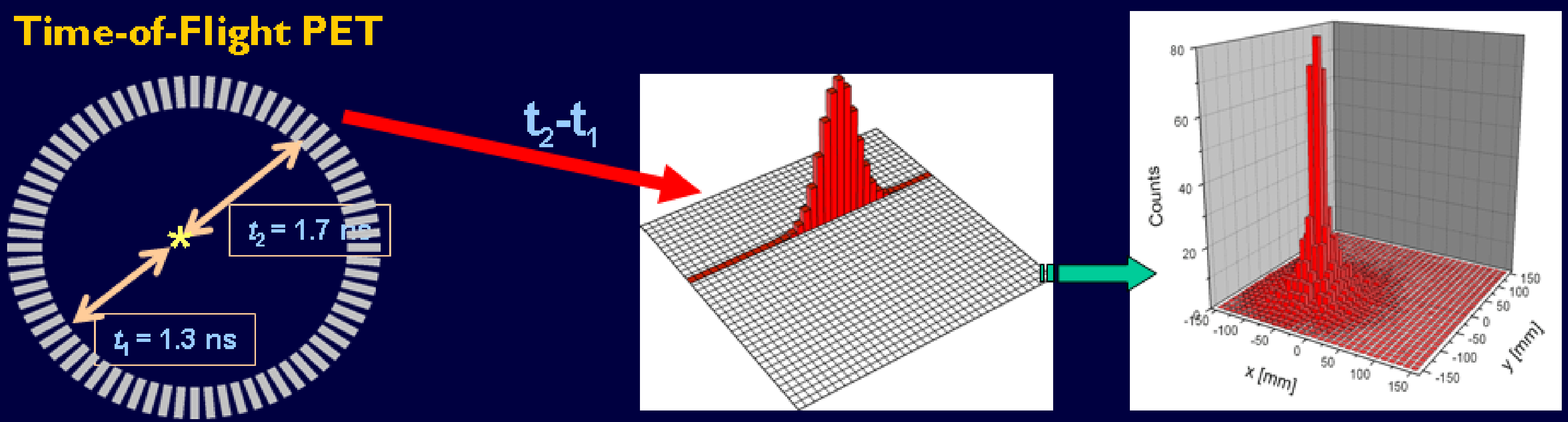
d.r.schaart@tudelft.nl

Time of Flight PET Systems

Conventional PET/ ToF off

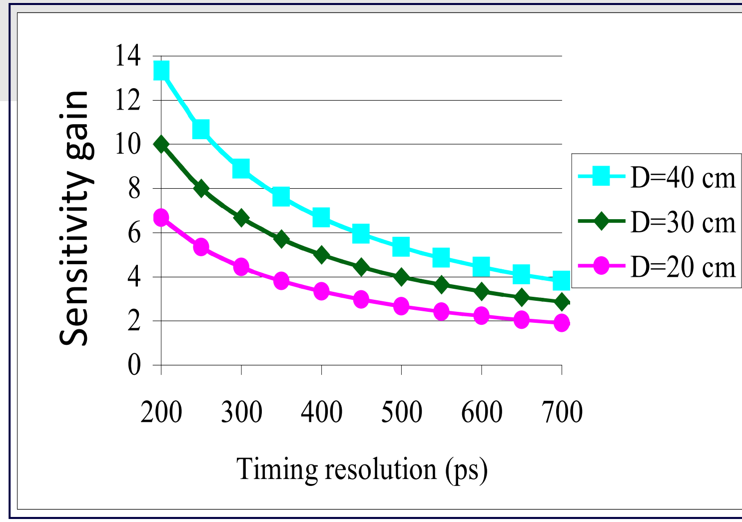


Time-of-Flight PET



→ ToF: more signal, less noise

Motivation towards improved TOF

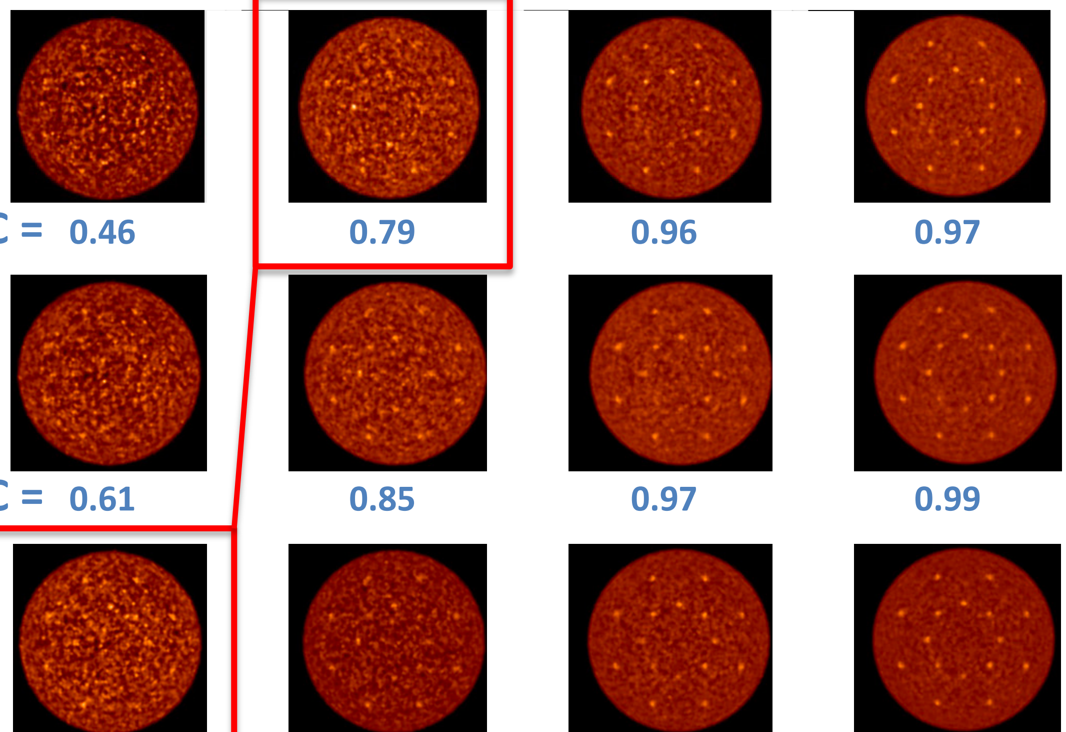


Tom Budinger, JCAT 1977

Gain in SNR = $(D/\Delta x)^{1/2}$

Gain in sensitivity = SNR^2 = $D/\Delta x$

Activity (µCi/cc): 1, x2, x4, x8



	1	x2	x4	x8
600ps ALROC =	0.46	0.79	0.96	0.97
450ps ALROC =	0.61	0.85	0.97	0.99
300ps ALROC =	0.73	0.92	0.99	0.99

35-cm diameter phantom
1 cm lesions with 3:1 uptake

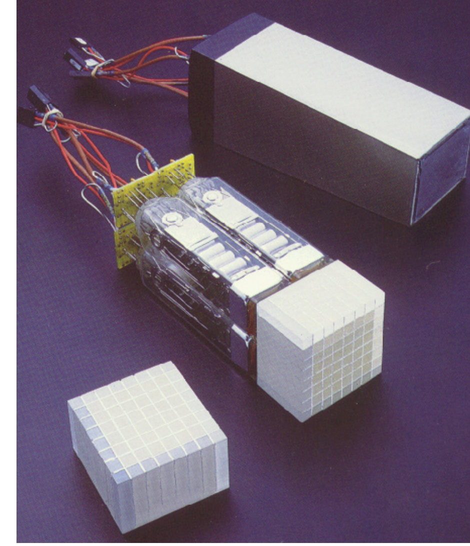
Improved detectability with TOF – depends on count density (activity)

Approximately equal: 2x timing resolution and ½ counts

Surti, SNM2014

PMT-based TOF-PET systems

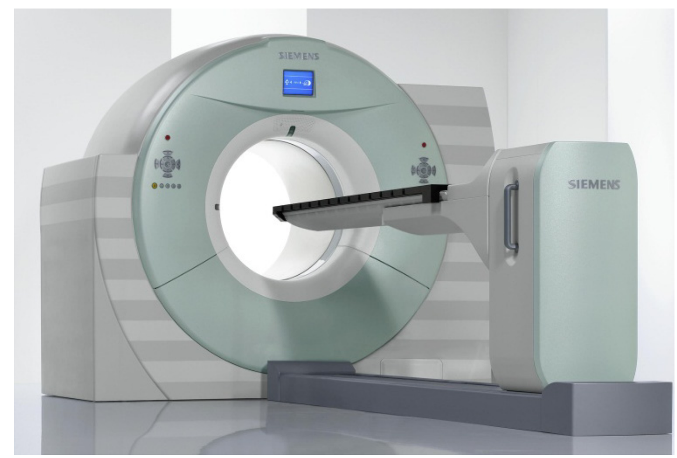
- Commercial TOF PET/CT scanners available from several manufacturers
- All based on PMTs
- Coincidence resolving time (CRT): 500-700 ps FWHM



PMT-based PET detector

Philips Gemini TF

GE Discovery 690

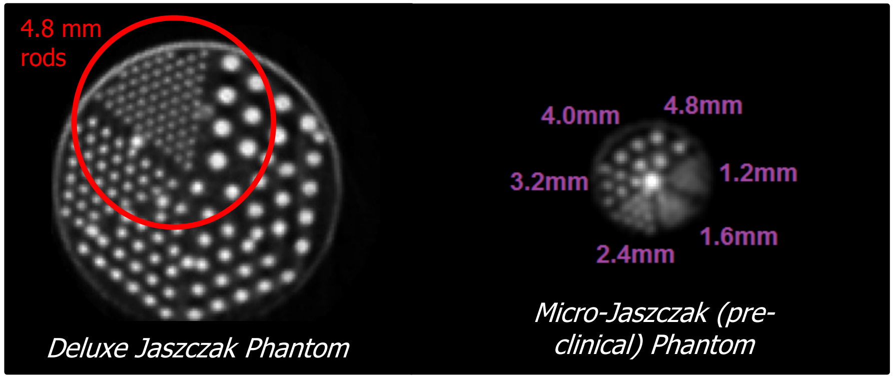


Siemens mCT

TU Delft
Dennis R. Schaart
Delft University of Technology

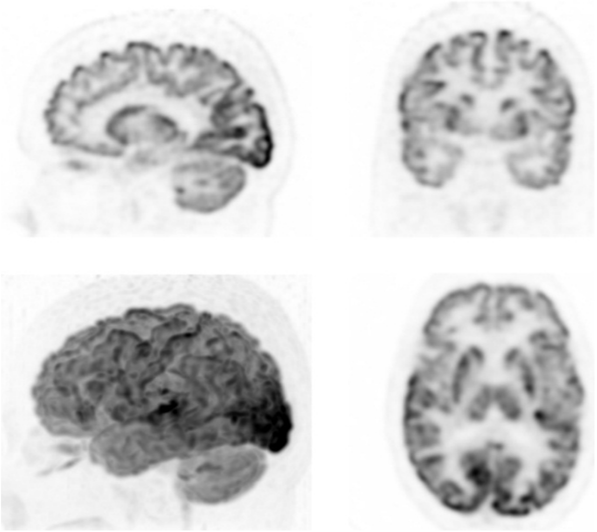
Vereos fully digital PET/CT system

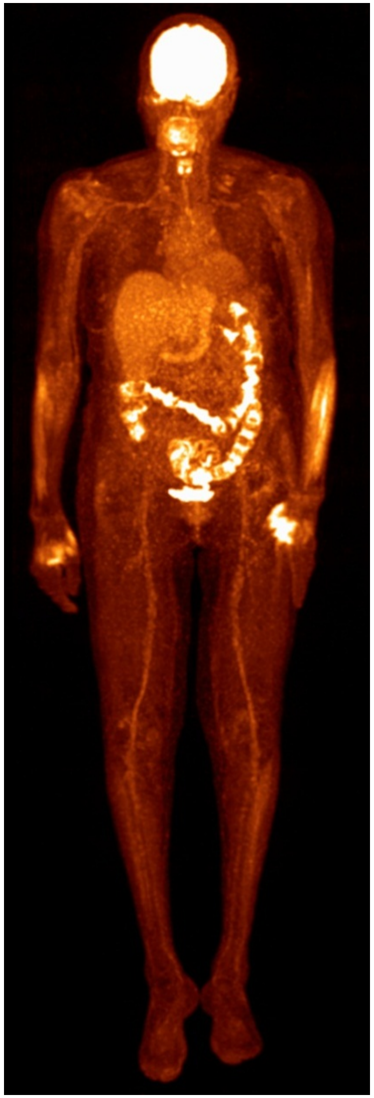
Coincidence resolving time (CRT) **350-400 ps FWHM** due to digital photon counting



Deluxe Jaszczak Phantom

Micro-Jaszczak (pre-clinical) Phantom





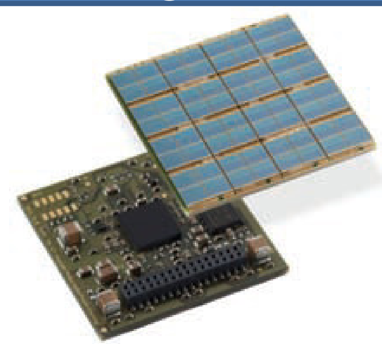
Images: Philips

Initial characterization of a prototype digital photon counting PET system

M. Miller et al, Philips Healthcare, Highland Heights, OH and Case Western Univ., Cleveland, OH

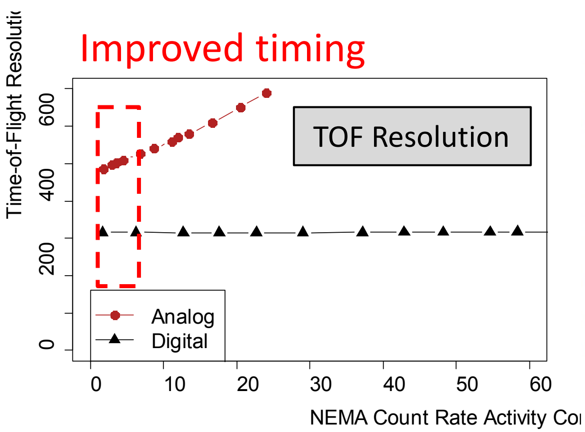
Research Prototype: Combined Gemini TF and Digital

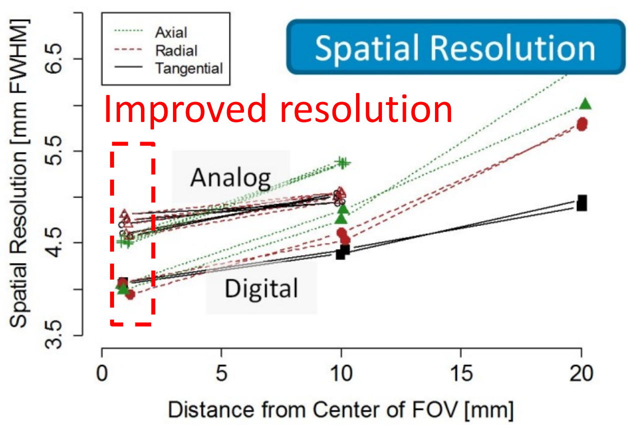
Digital Photon Counting Detectors

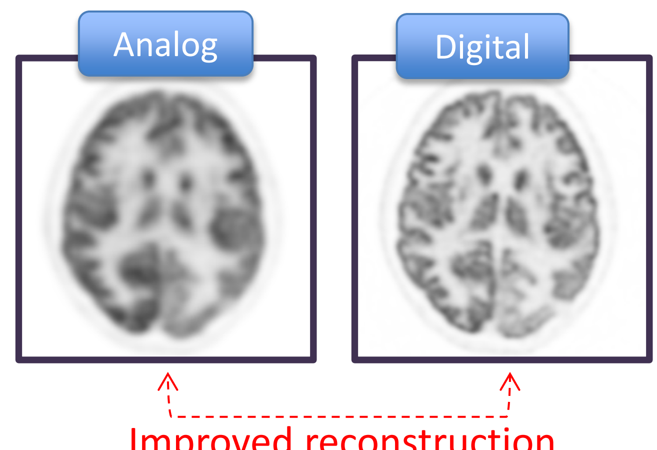


Commercial Design

Detector design	Digital Photon Counting
Number of detectors	23,040
Number of crystals	23,040
Crystal size	4 x 4 x 19 mm
Crystal material	LYSO
Ring diameter	76.4 cm
Transaxial FOV	Up to 676 mm
Axial FOV	164 mm
Coincidence window size[1]	4.0 ns
Lower level discriminator	450 keV







SCHOOL OF MEDICINE CASE WESTERN RESERVE UNIVERSITY

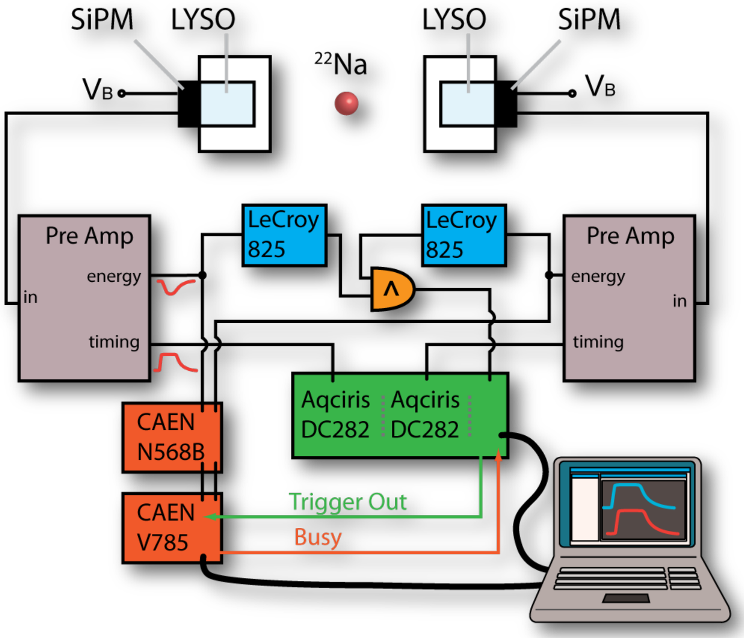
University Hospitals Case Medical Center

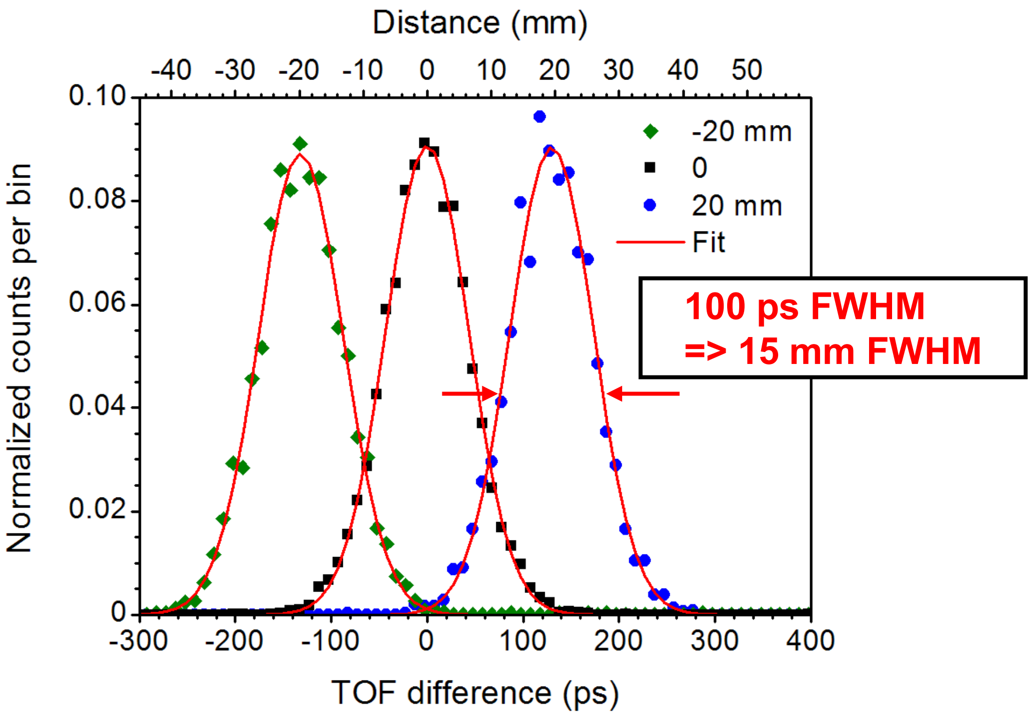
PHILIPS

2009: 100 ps barrier broken with SiPMs

Made possible by the combination of:

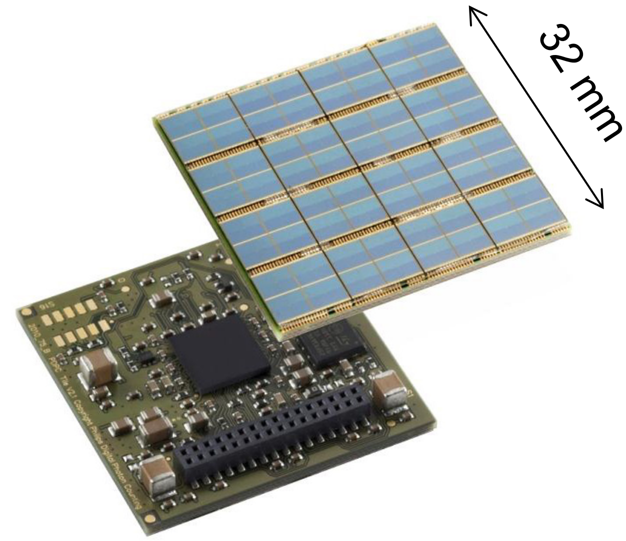
- Small $LaBr_3$:Ce(5%) crystals (3 mm x 3 mm x 5 mm)
- Silicon Photomultipliers (Hamamatsu MPPC-S10362-33-050C)
- Digital Signal Processing (DSP)

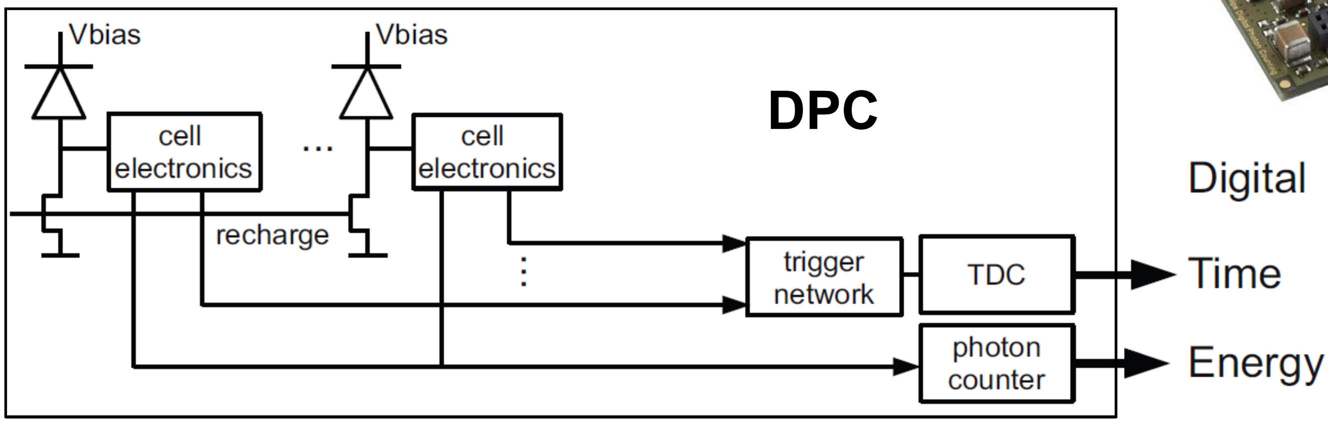




D.R. Schaart et al, Phys Med Biol 55, N179-N189, 2010

Digital SiPMs





- ++ small single-photon time jitter
- ++ negligible noise at the single photon level
- ++ ~ 30% photon detection efficiency
- \+ MR-compatible

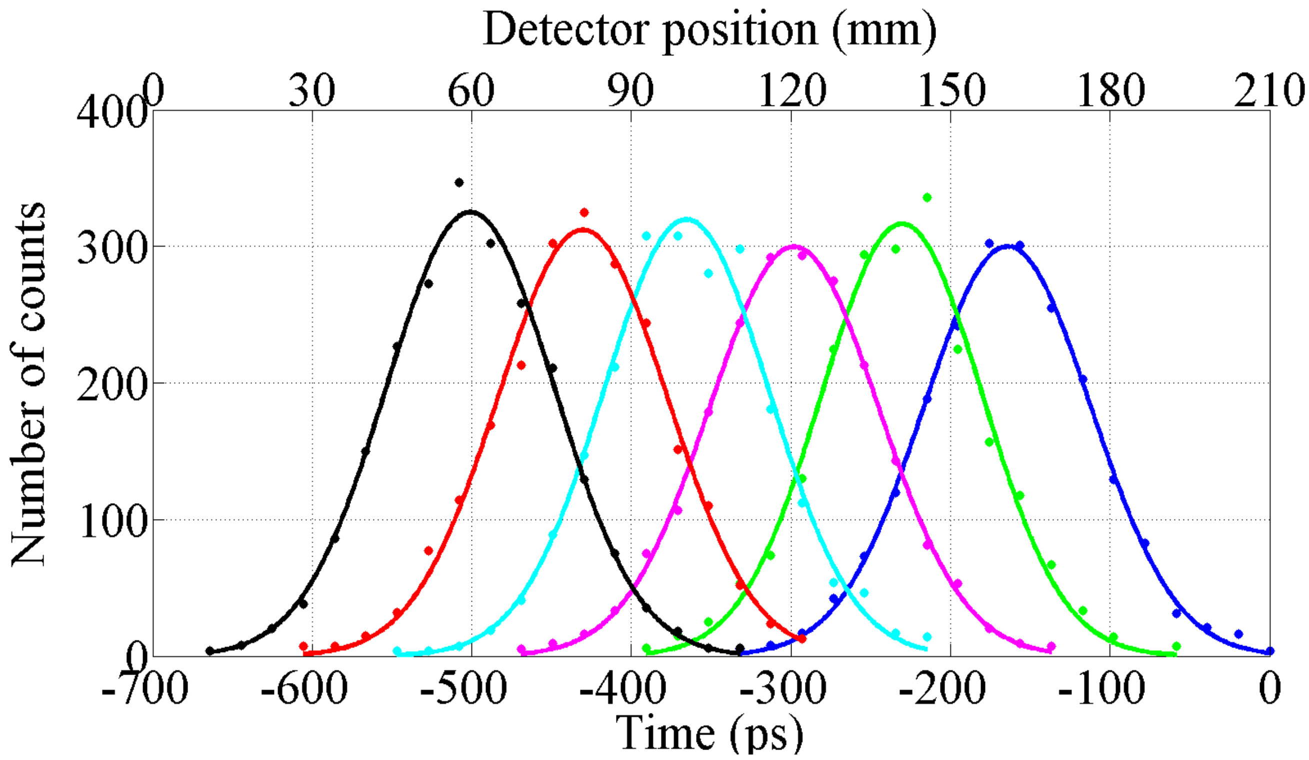
16 Si dies (4 x 4)
Each Si die:
→ 1 timestamp
→ 4 pixels values (no. of counts)

See: Thomas Frach, IEEE NSS/MIC, Orlando, FL October 28, 2009

DPC timing resolution

Two coincident detectors:

- DPC-3200-44-22 dSiPM arrays
- 3 x 3 x 5 mm^3 LSO:Ce,Ca crystals



Timing spectra at different positions of one of the two detectors. The step size is 20 mm. The average coincidence resolving time (CRT) is **123 ps FWHM**.

Understanding SiPMs and Timing

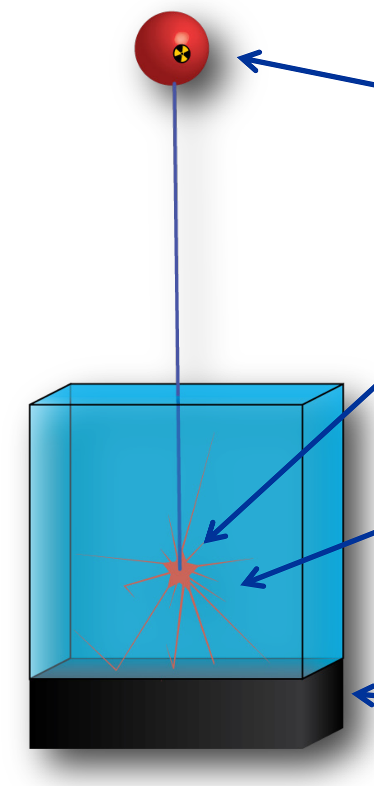
Understanding timing:

- S. Seifert et al, "The Lower Bound on the Timing Resolution of Photon Counting Scintillation Detectors," Phys Med Biol 57, 1797-1814, 2012
- S. Seifert et al, "A Comprehensive Model to Predict the Timing Resolution of SiPM-Based Scintillation Detectors: Theory and Experimental Validation," IEEE Trans Nucl Sci 59, 190-204, 2012
- S. Seifert et al, "Accurate measurement of the rise and decay times of fast scintillators with solid state photon counters," J Instr 7, P09004, 2012
- J. Huizenga et al, "A fast preamplifier concept for SiPM-based time-of-flight PET detectors," NIM A 695, 379-384, 2012
- H.T. van Dam et al, "Sub-200 ps CRT in monolithic scintillator PET detectors using digital SiPM arrays and maximum likelihood interaction time estimation," Phys Med Biol 58, 3243-3257, 2013

Understanding analog and digital SiPMs:

- S. Seifert et al, "Simulation of Silicon Photomultiplier Signals," IEEE Trans Nucl Sci 56, 3726-3733, 2009
- H. T. van Dam et al, "A comprehensive model of the response of silicon photomultipliers," IEEE Trans Nucl Sci 57, 2254-2266, 2010
- H.T. van Dam et al, "The statistical distribution of the number of counted scintillation photons in digital silicon photomultipliers: model and validation," Phys Med Biol 57, 4885-4903, 2012
- V. Tabacchini et al, "A Model for the Trigger and Validation Probabilities in a Digital Silicon Photomultiplier," J. Instrumentation 9, P06016, 2014

Scintillation photon counting statistics



γ emission

γ absorption → at $t = \Theta$

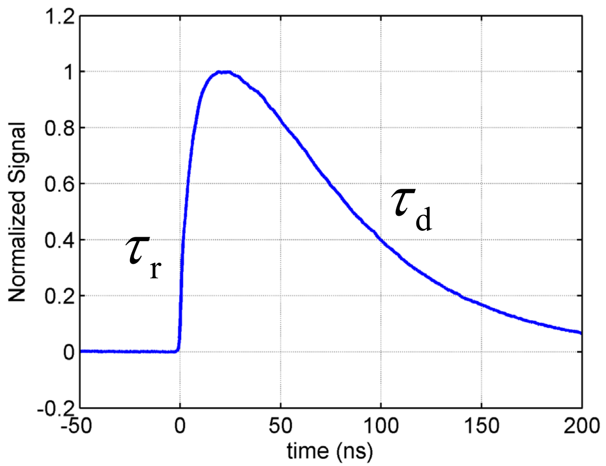
Emission of N_{sc} optical photons → $T_e = \{t_{e,1}, t_{e,2}, \ldots, t_{e,Nsc}\}$

Detection of N optical photons → $T_d = \{t_{d,1}, t_{d,2}, \ldots, t_{d,N}\}$

$N = \eta N_{sc}$, where η is the photodetection efficiency (PDE)

Ξ (= estimate of Θ)

Calculation of CRT_{LB}



Parameters included in the calculation:

- Scintillation light yield Y
- Photodetection efficiency η
- Scintillation pulse shape,
  - → For example, bi-exponential pulse with rise time constant τ_r and decay time constant τ_d
- Probability density function describing the single-photon timing uncertainty
  - → comprises optical path length variations in crystal, transit time spread (TTS) of sensor, trigger jitter, etc.
  - → for a very small crystal and near-perfect detector readout, this contribution is dominated by the photosensor TTS
  - → here represented by a Gaussian with standard deviation σ

The math involves order statistics, it can be found in:

S. Seifert, H.T. van Dam, and D.R. Schaart, "The lower bound on the timing resolution of scintillation detectors," Phys Med Biol 57, 1797-1814, 2012

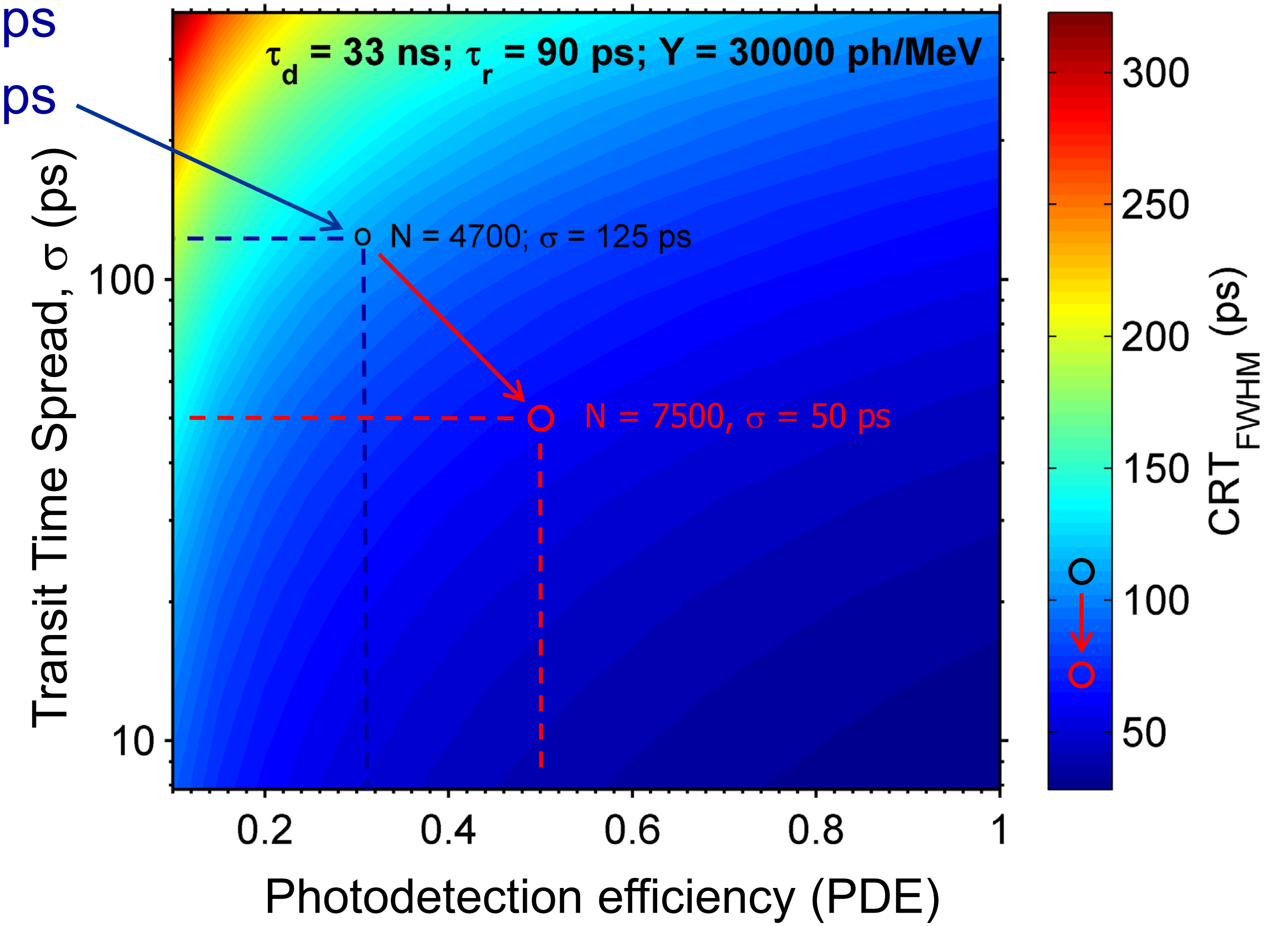
Lower bound on the CRT of LSO:Ce,Ca

Measured: ~125 ps

CRT_{LB}: ~110 ps

$$\mathrm{var}(\Xi) \geq \frac{1}{I_{T_d}(\Theta)}$$

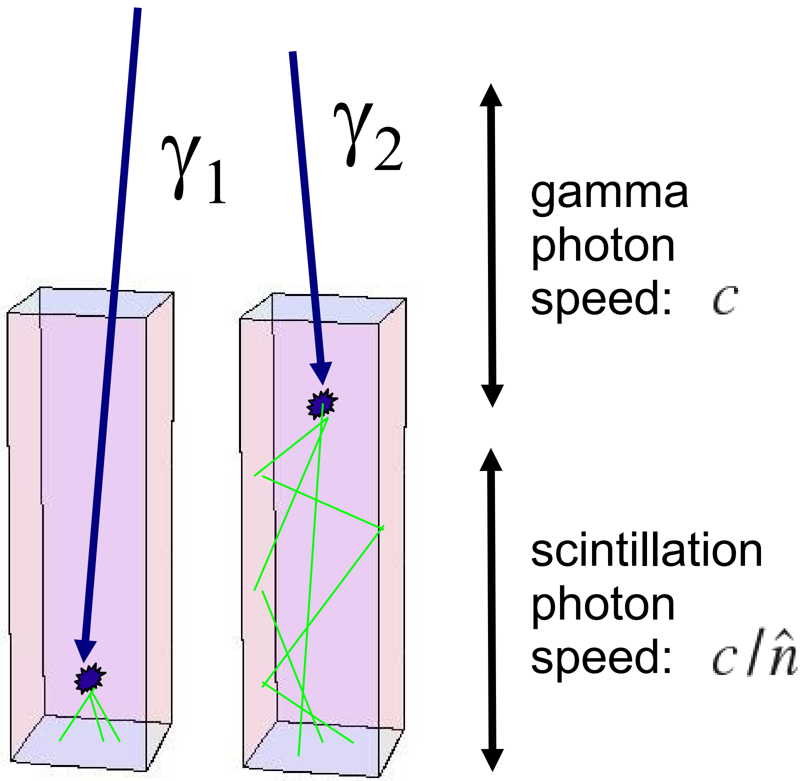
CRT < 100 ps seems feasible with further SiPM improvements (PDE and TTS)

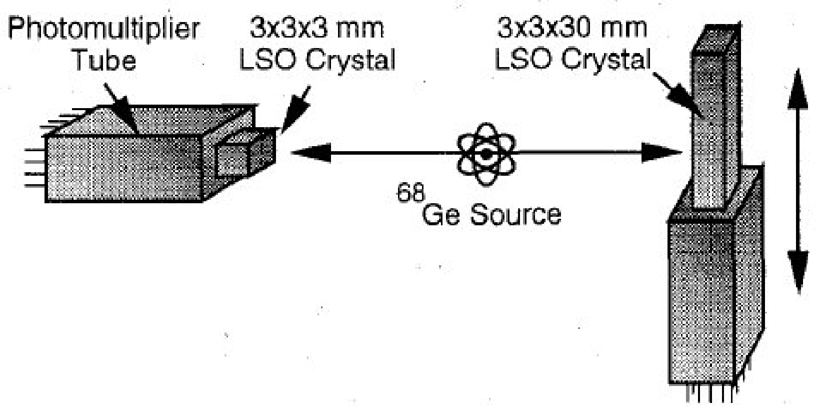


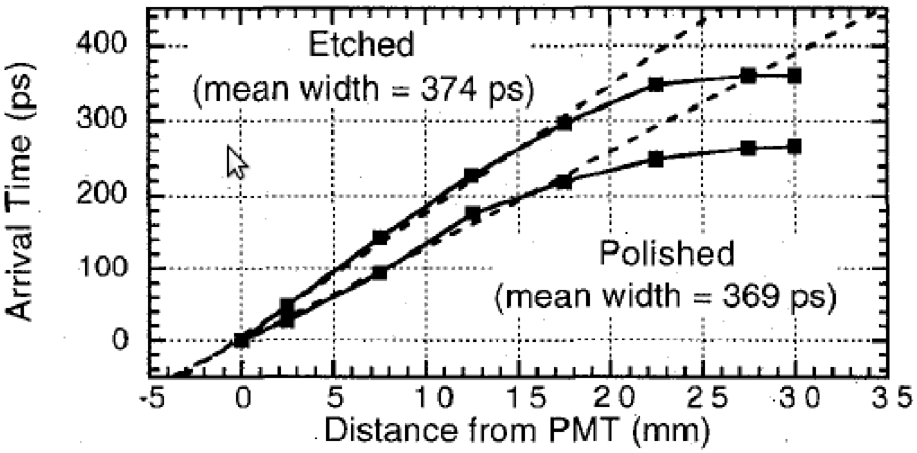
Lower bound on the CRT of LSO:Ce,Ca + MPPC as a function of PDE and TTS

DOI-dependent signal delay in crystal

Depth-of-interaction (DOI) variations deteriorate timing resolution



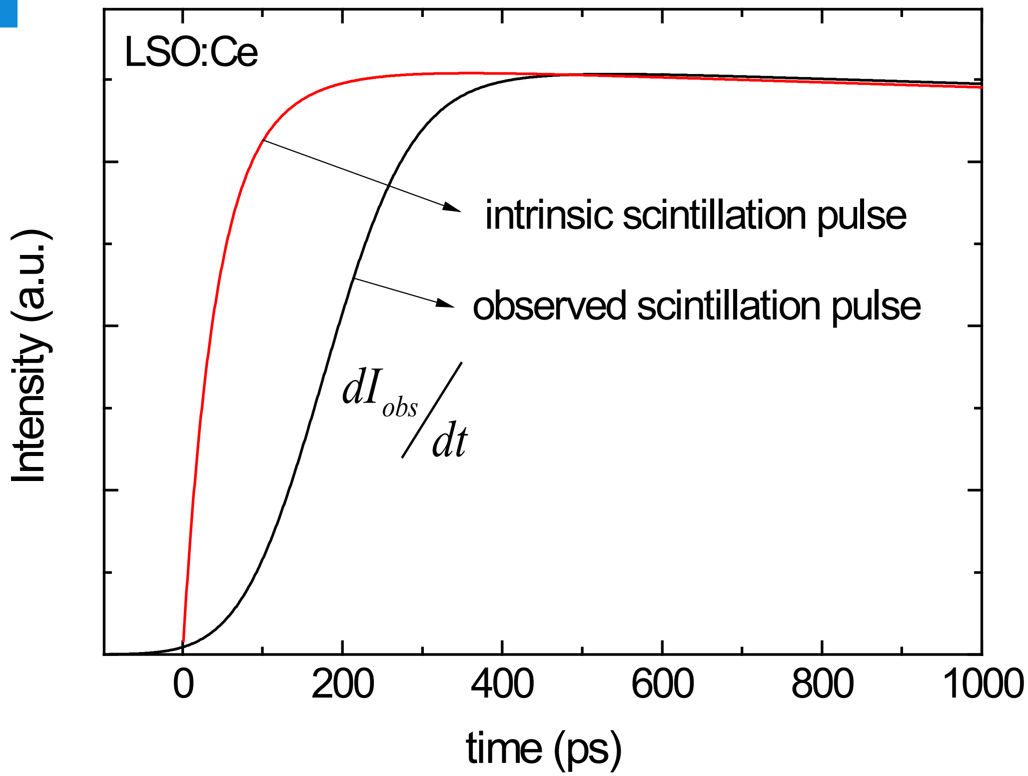




WW Moses and SE Derenzo

IEEE Trans. Nucl. Sci. 46, 474-478 (1999)

Factors influencing scintillation pulse shape

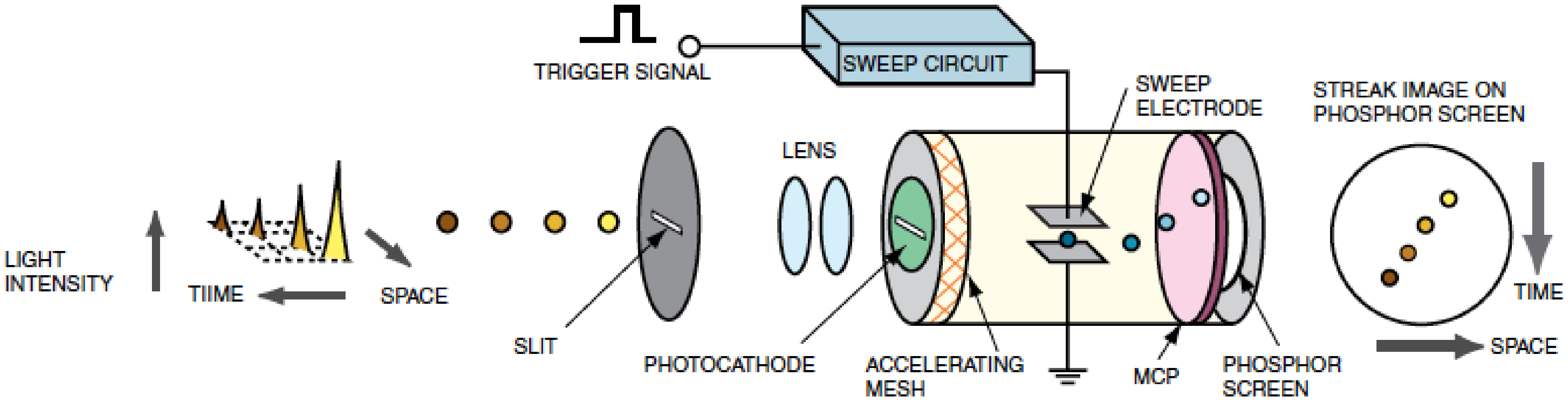


Intrinsic properties
- light yield
- decay time constant
- scintillation rise time

Optical transit time-spread
- dimensions of the crystal
- surface structure
- packaging

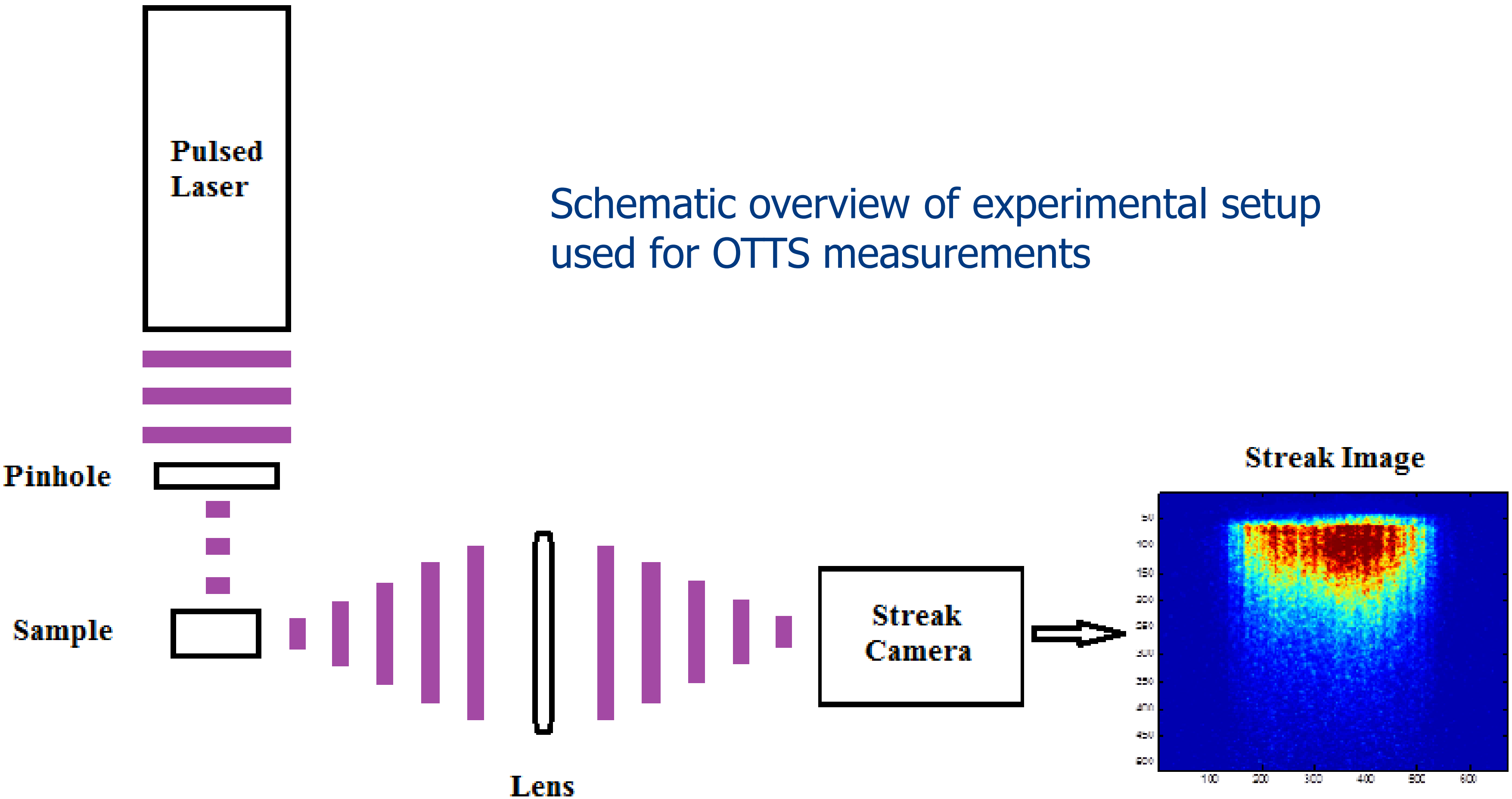
Self-absorption
- possibly with re-emission

Optical transit time spread (OTTS) measurement with a streak camera



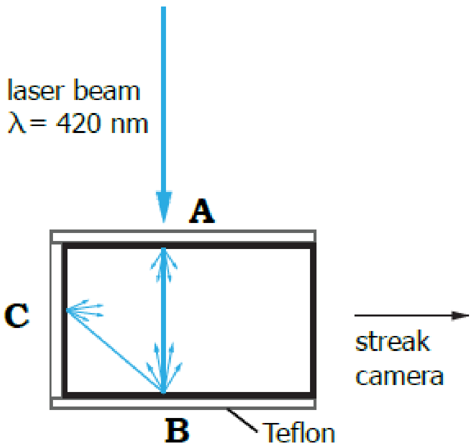
Schematic overview of streak camera principle

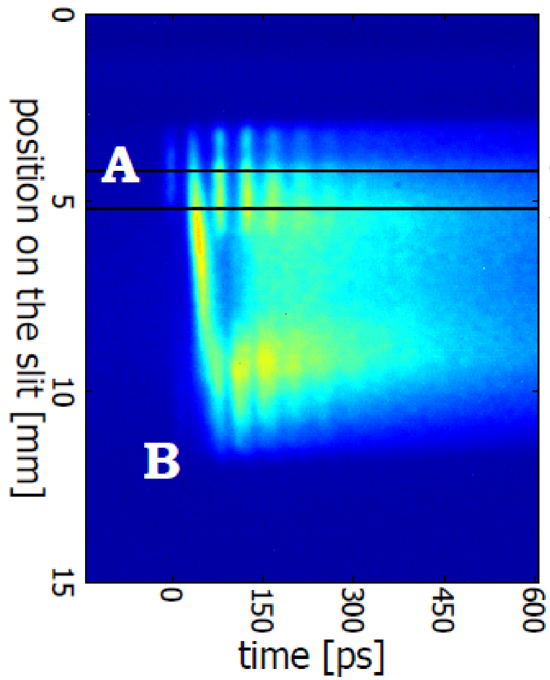
Optical transit time spread (OTTS) measurement with a streak camera

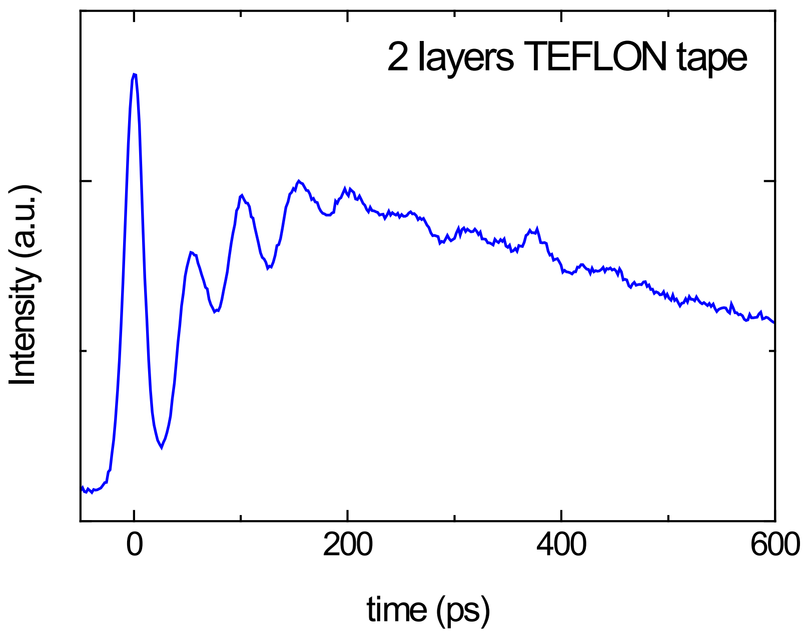


Schematic overview of experimental setup used for OTTS measurements

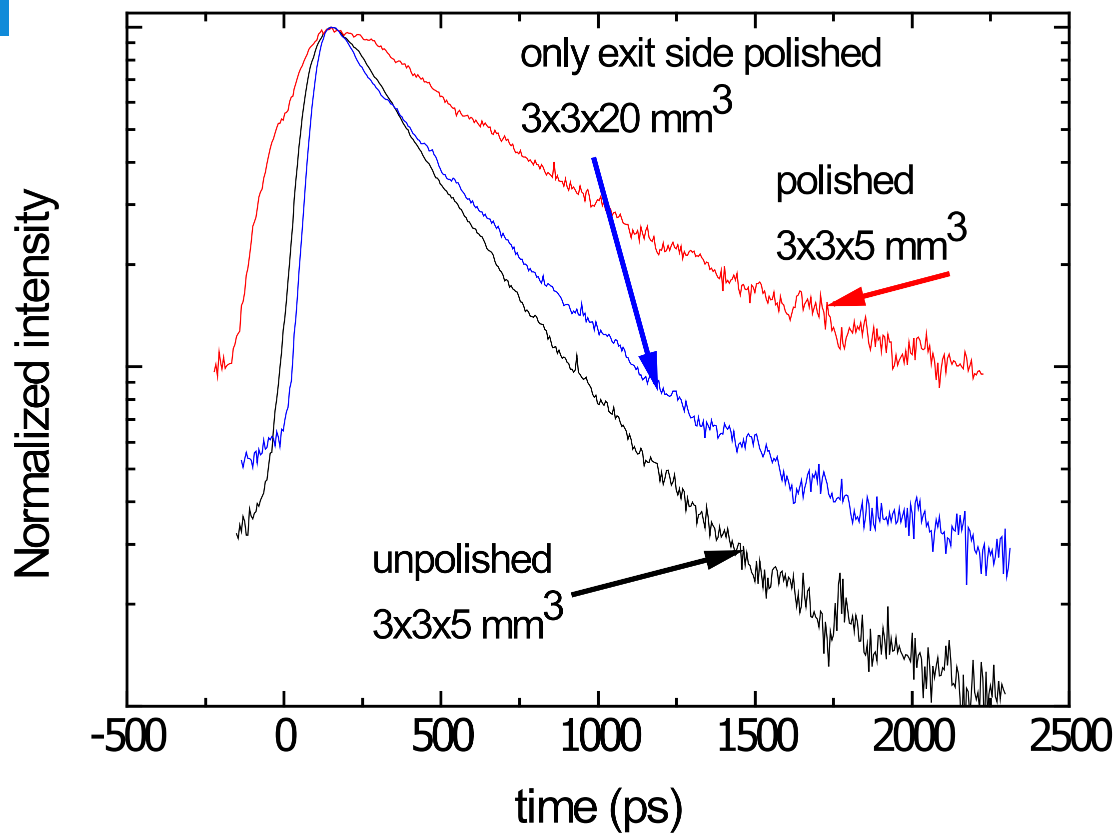
Polished LYSO 3x3x5 mm^3 crystal







Optical transit time-spread (OTTS)



- Optical transit time-spread increases with the length of the crystal
- Light trapping in polished crystals increases the photon collection time
- OTTS easily > 100 ps

Timing deterioration in large crystals

Factors causing deterioration of photon counting statistics in large crystals:

- Different speeds of gamma and scintillation photons in crystal
- Increased light loss, especially in high-aspect-ratio crystals
- Increased optical path length straggling

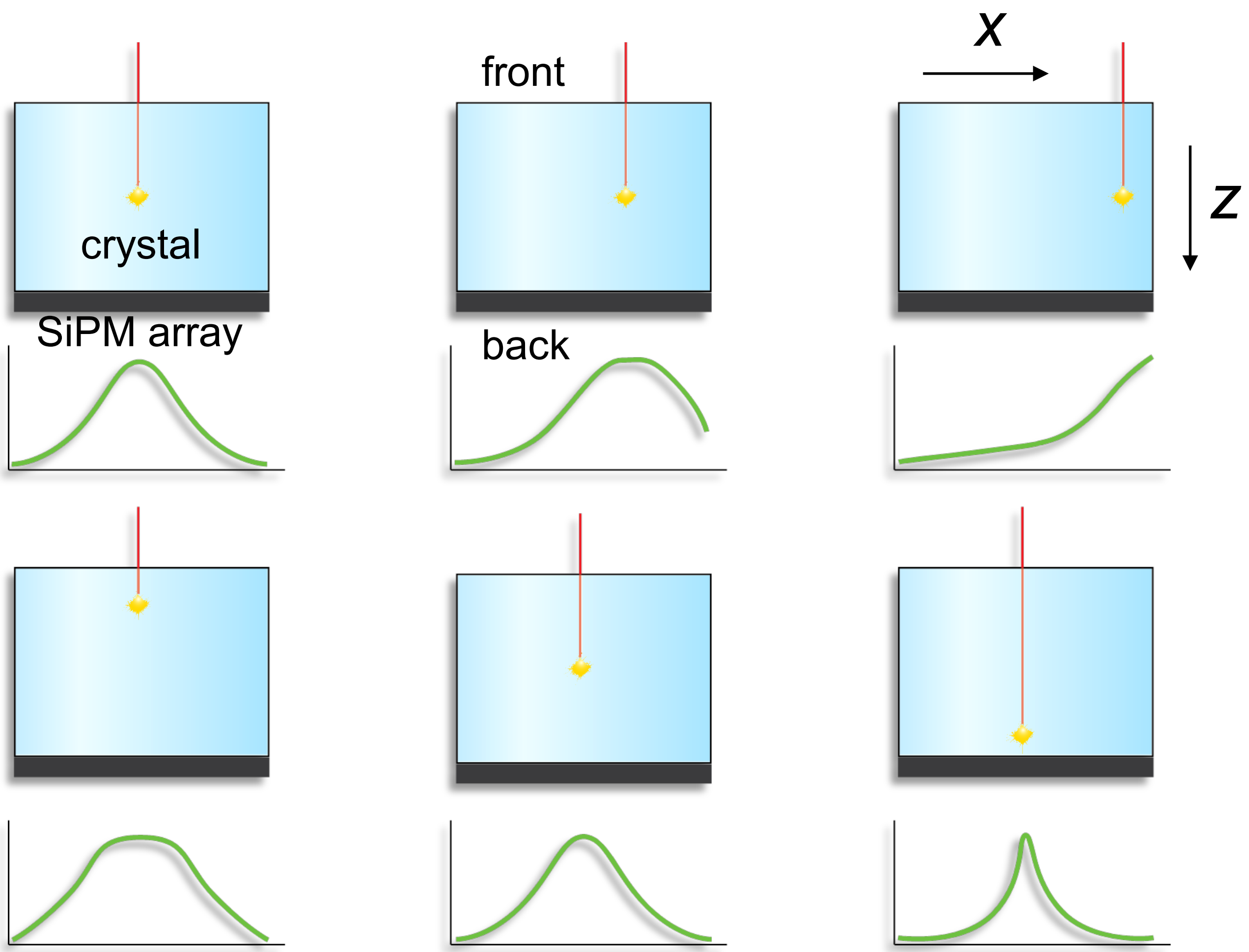
Possible solutions:

- Use many small crystals one-to-one coupled to SiPMs
  - → technically challenging, expensive
- DOI correction on time stamps
  - → limited by error on DOI
  - → does not mitigate light loss and optical path length straggling
  - → DOI schemes based on light sharing may cause timing deterioration

Let’s try something else…

(a practical approach towards 100 ps system resolution)

Monolithic scintillator detectors

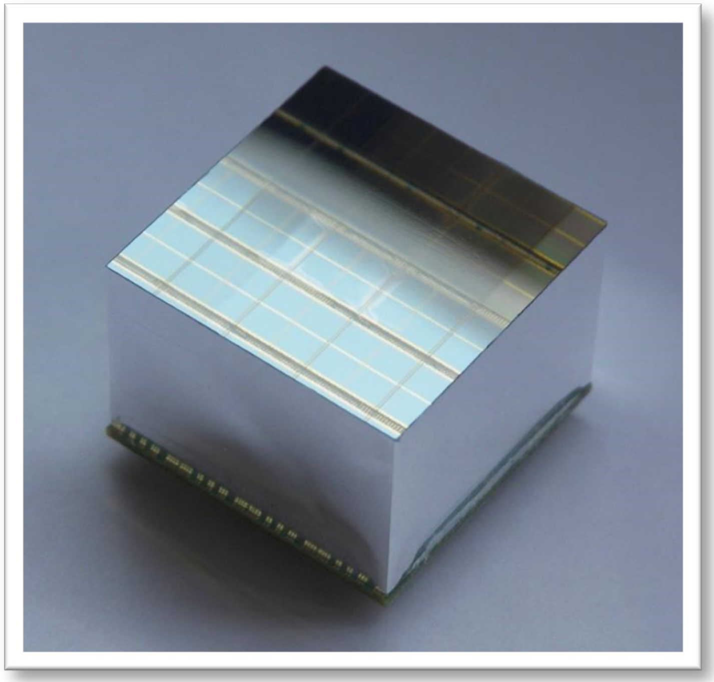


Light distribution depends on the entry point on the front surface…

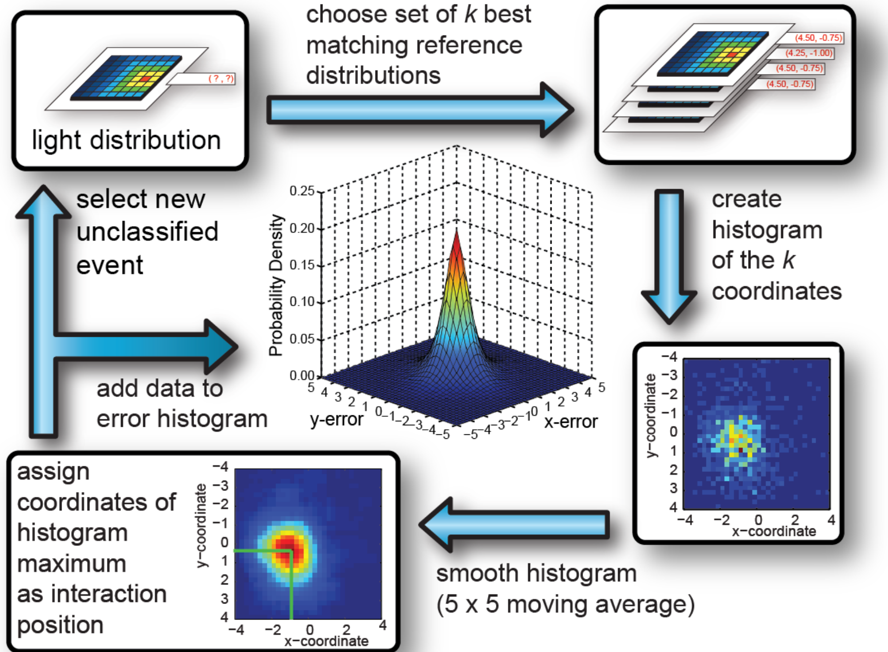
…and on the depth of interaction (DOI).

The monolithic scintillator detector

Monolithic TOF/DOI detector with improved performance due to Ca co-doped LSO scintillator, digital photon counters (DPCs), and optimized readout algorithms



32 mm x 32 mm x 22 mm LSO:Ce,Ca scintillator on PDPC digital SiPM array



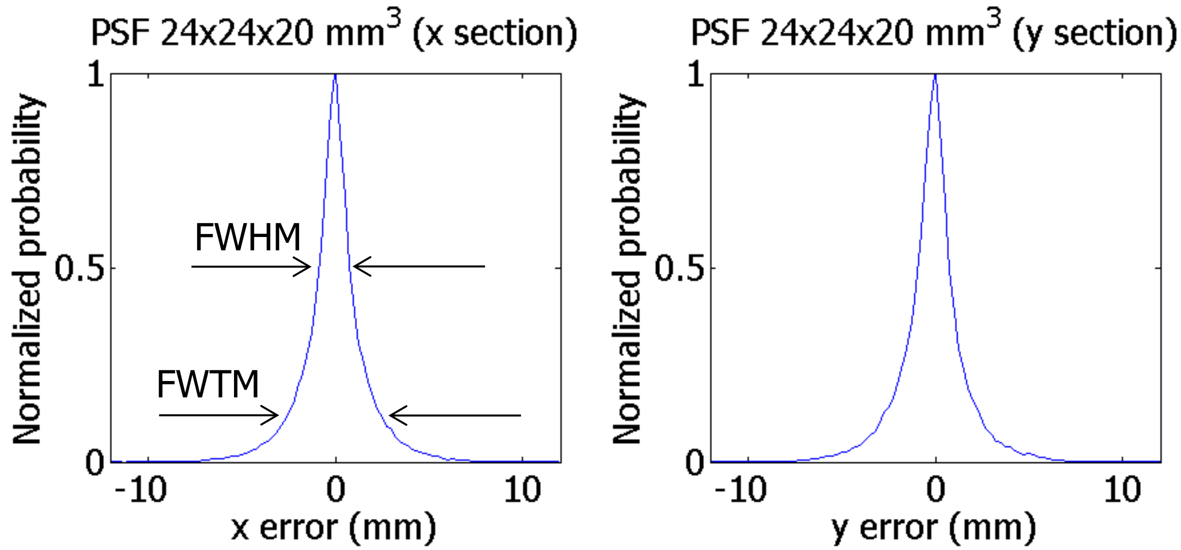
Fast & accurate nearest-neighbour algorithm, H.T. van Dam et al, IEEE Trans Nucl Sci 58, 2139-2147, 2011

S. Seifert et al, First Characterization of a Digital SiPM based Time-of-Flight PET Detector with 1 mm Spatial Resolution," Phys Med Biol 58, 3061-3074, 2013

Sub-2 mm spatial resolution

Position estimation using "smooth" k-nearest neighbour method from Van Dam et al* with 100 reference events per position

** H.T. van Dam et al, IEEE Trans Nucl Sci 58, 2139-2147, 2011*



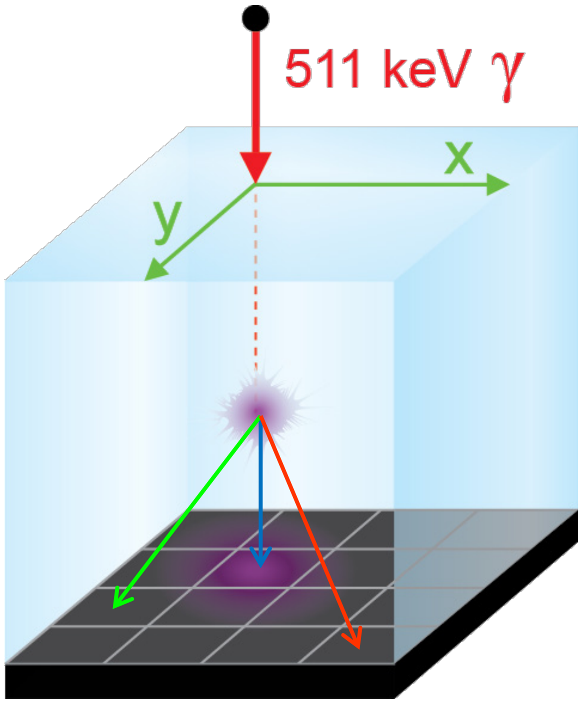
Crystal size (mm^3)	Average FWHM (mm)		Average FWTM (mm)	
	x	y	x	y
16 x 16 x 10	**1.24**	**1.25**	3.1	3.0
16 x 16 x 20	**1.60**	**1.67**	6.7	6.8
24 x 24 x 10	**1.08**	**1.06**	2.5	2.5
24 x 24 x 20	**1.61**	**1.64**	5.4	5.5

ML interaction time estimation (MLITE)

More than 1 timestamp available to estimate the interaction time → use of all this information

Calibration procedure:

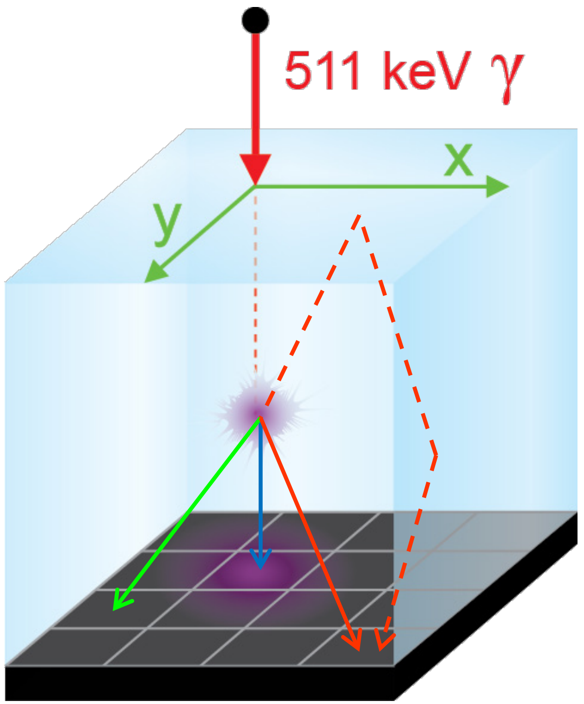
- Irradiate entire detector uniformly
- Determine position of each interaction
- Determine the 1st photon arrival time probability distribution on each dSiPM element for each interaction position

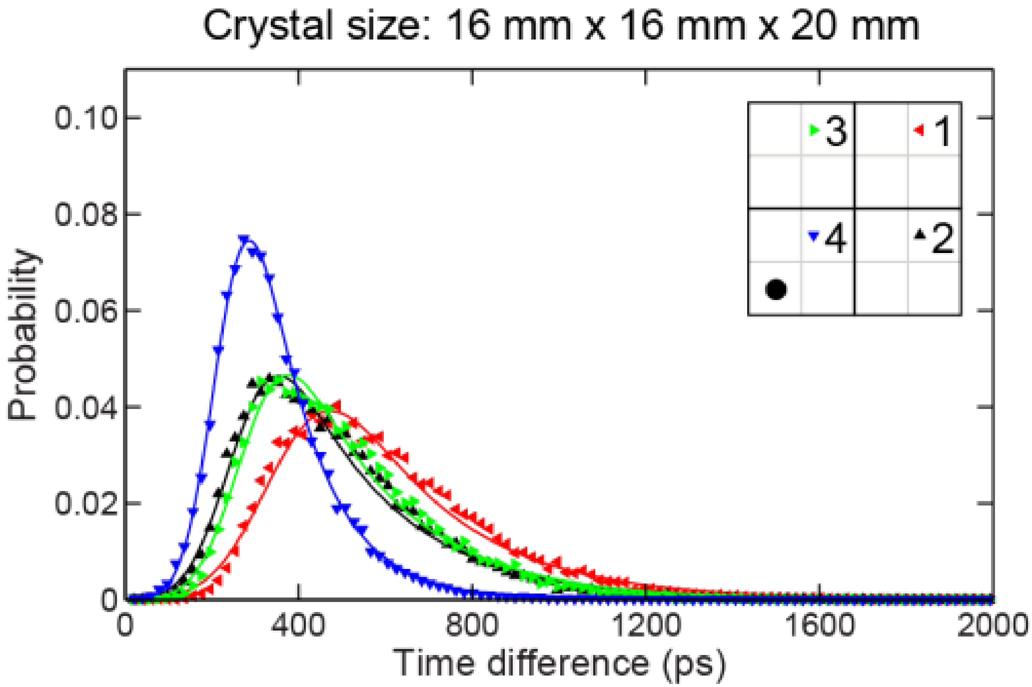


H.T. van Dam et al, Sub-200 ps CRT in monolithic scintillator PET detectors using digital SiPM arrays and maximum likelihood interaction time estimation, PMB 58, 3243-3257, 2013

ML interaction time estimation (MLITE)

Maximum likelihood interaction time estimation (MLITE), using measured 1st photon arrival time probability distribution for each (x,y,z) position





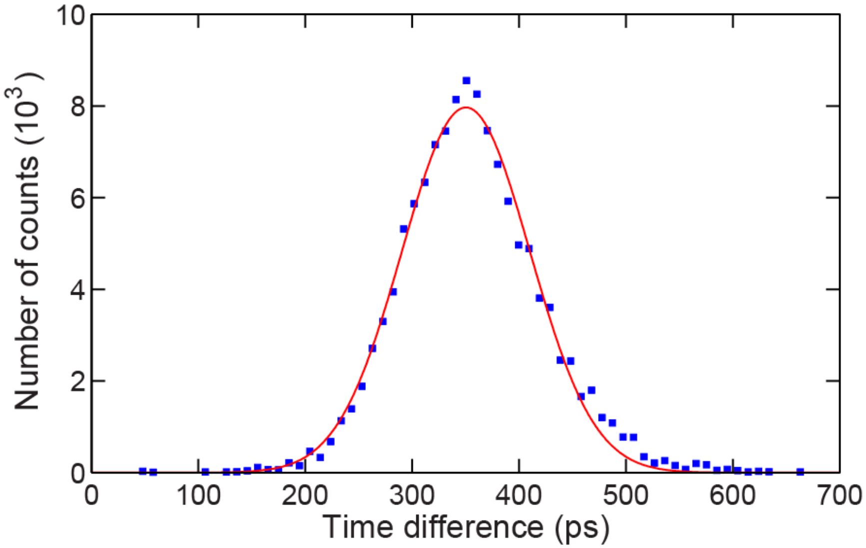
H.T. van Dam et al, Sub-200 ps CRT in monolithic scintillator PET detectors using digital SiPM arrays and maximum likelihood interaction time estimation, PMB 58, 3243-3257, 2013

Timing performance of monolithic scintillator detectors with MLITE

Use of MLITE method to determine γ interaction time

Crystal size (mm^3)	CRT FWHM (ps)
16 x 16 x 10	**157**
16 x 16 x 20	**185**
24 x 24 x 10	**161**
24 x 24 x 20	**184**

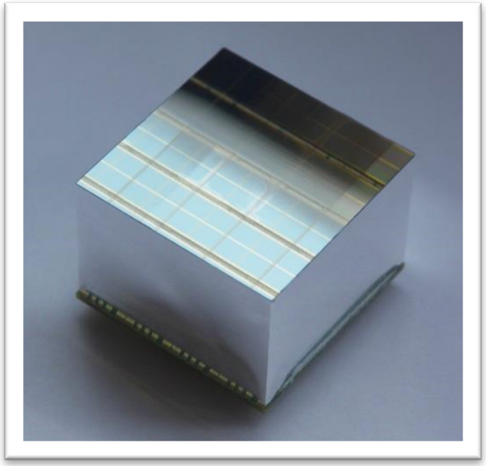
Timing spectrum of the 16x16x10 mm^3 monolithic LSO:Ce,Ca crystal in coincidence with a 3x3x5 mm^3 reference crystal



- Using only the earliest timestamp: CRT ~ 200 ps – 230 ps FWHM
- Without electronic skew correction: CRT ~ 350 ps FWHM

H.T. van Dam et al, Sub-200 ps CRT in monolithic scintillator PET detectors using digital SiPM arrays and maximum likelihood interaction time estimation, PMB 58, 3243-3257, 2013

Performance summary



Current results with L(Y)SO monolithic scintillators on dSiPM arrays:

Performance parameter		Monolithic	State of the art
Energy resolution	(% FWHM)	**11 - 12**	~12
Spatial resolution	(mm FWHM)	**1.0 - 1.6**	4 - 6
DOI resolution	(mm FWHM)	**3 - 5 mm**	None
CRT	(ps FWHM)	**160 - 185**	350 - 650

⇒ A highly promising detector for whole-body and organ-specific TOF-PET and PET/MRI