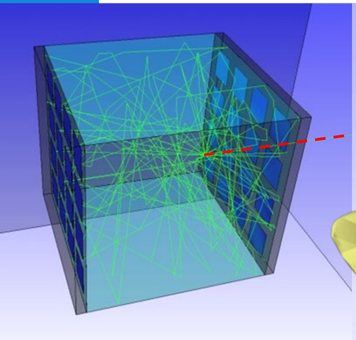

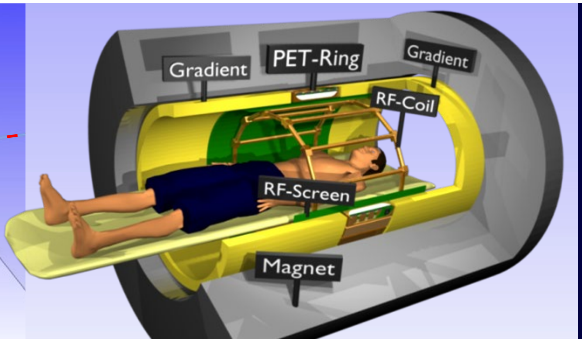

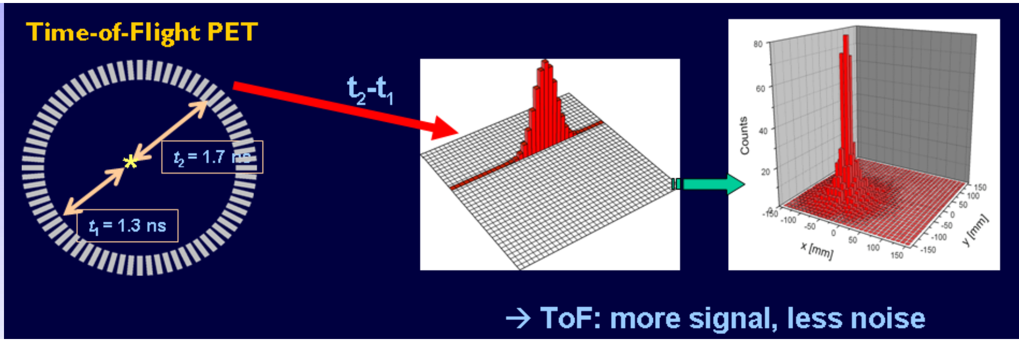

Silicon photomultipliers in medical imaging

16th Vienna Conference on Instrumentation, Feb 21-25, 2022

TU Delft
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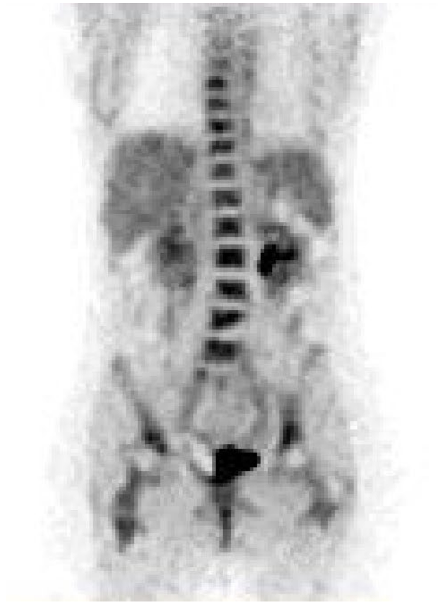
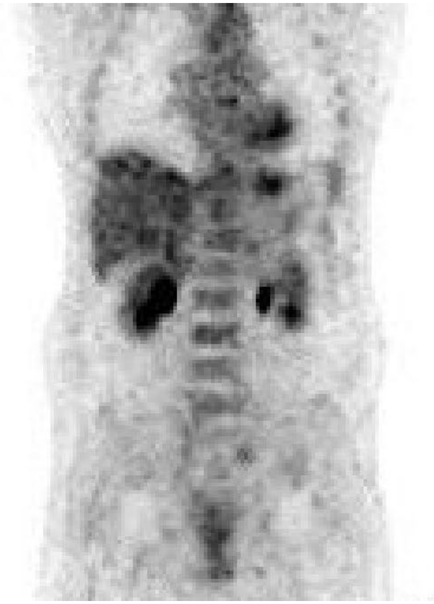
d.r.schaart@tudelft.nl

Mid-2000's: PET in the pre-SiPM era

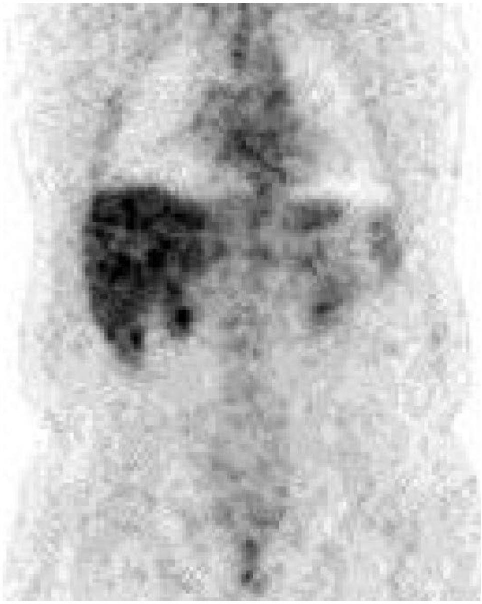
Typical image quality of positron emission tomography (PET) in the mid-2000's



58 kg



89 kg



127 kg

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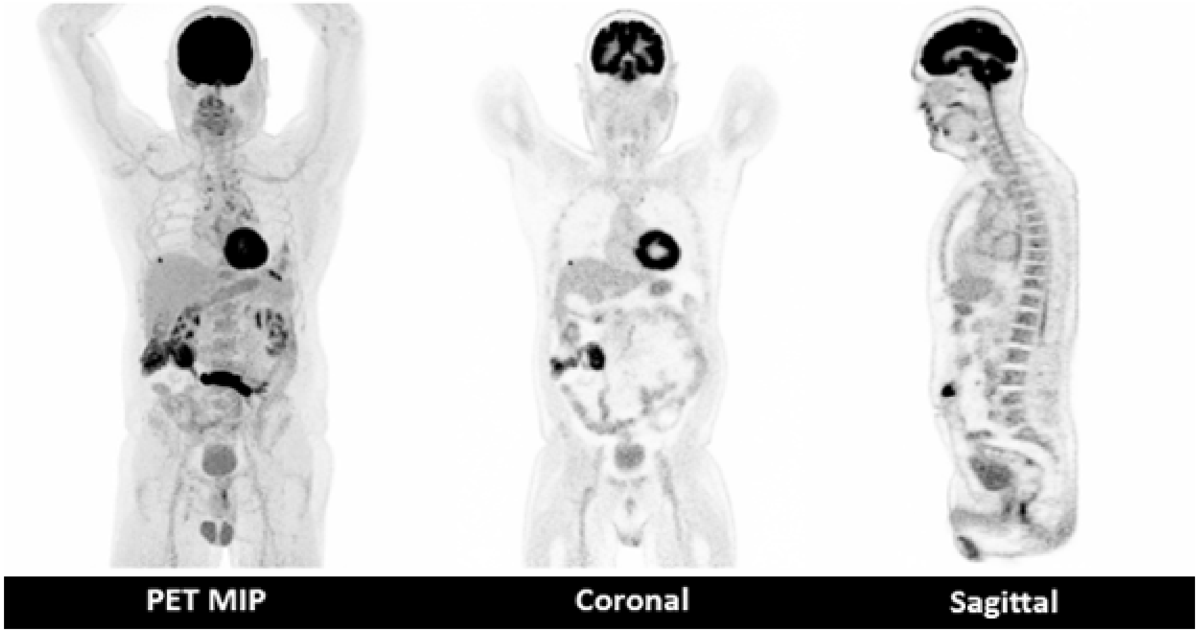
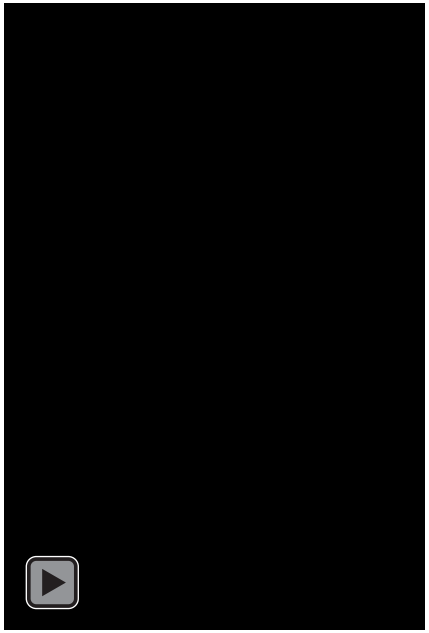
Delft University of Technology

Courtesy: Philips

Today: SiPM-based PET is the state-of-the-art

Typical image quality of PET scanners using silicon photomultipliers (SiPM)





Left: UMC Groningen, The Netherlands

Right: JS Reddin et al, U Penn, Philadelphia, USA

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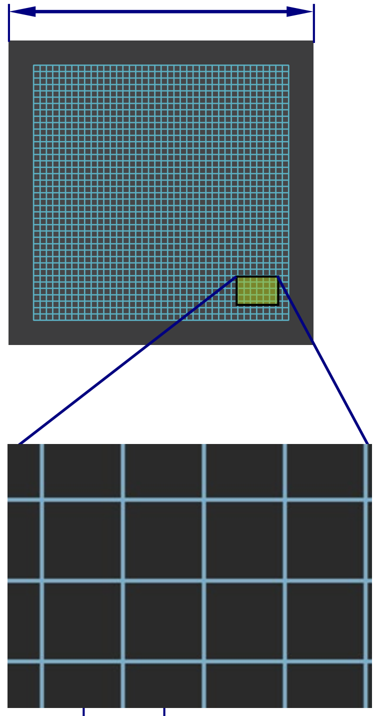
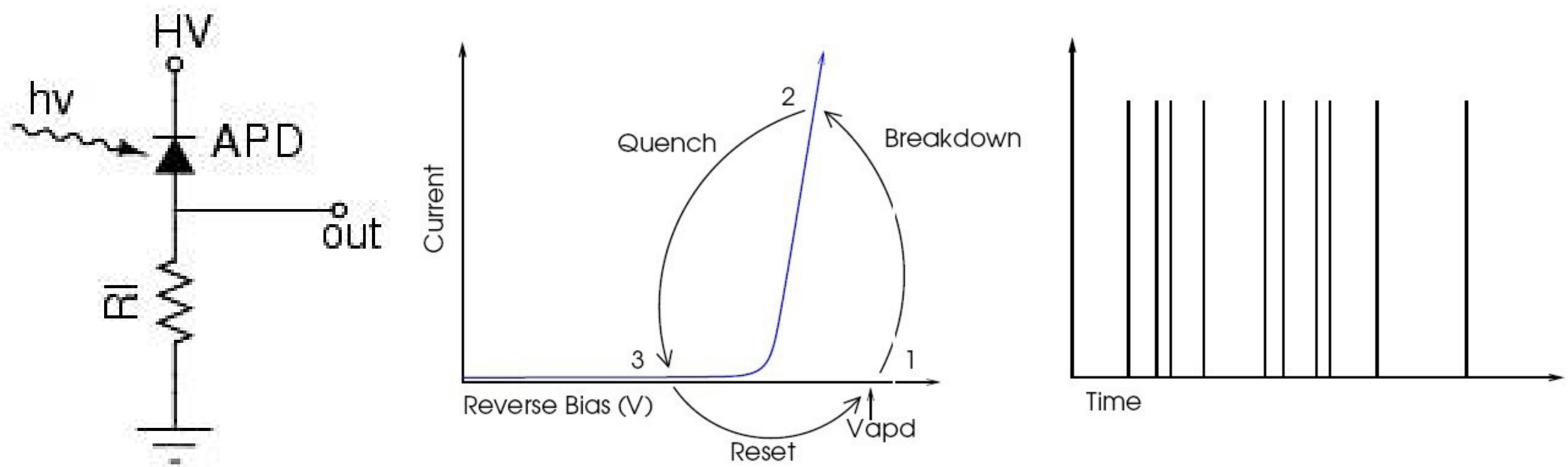
The silicon photomultiplier (SiPM)

- a disruptive photosensor technology



- Array of many self-quenched single-photon avalanche diodes (SPADs) connected in parallel
- Increasingly interesting as replacement for PMTs:
  - high gain (> 10^6)
  - high PDE (up to ~60%)
  - excellent SPTR (down to ~50 ps FWHM)
  - compact and rugged
  - transparent to γ-photons
  - insensitive to magnetic fields

Single-photon avalanche diode (SPAD)



Above the breakdown voltage, electrons generate a Geiger discharge

- Quenched by a series resistor
- A binary device: “on” or “off”
- Very large gain (~10^6) => sensitive to single photons
- High temporal resolution (< 100 ps for single photons)

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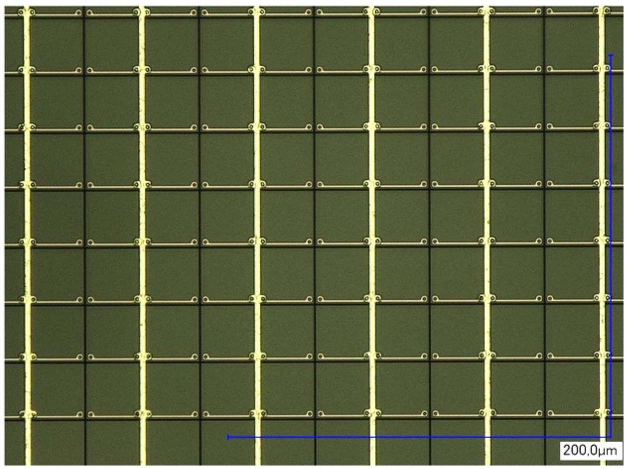
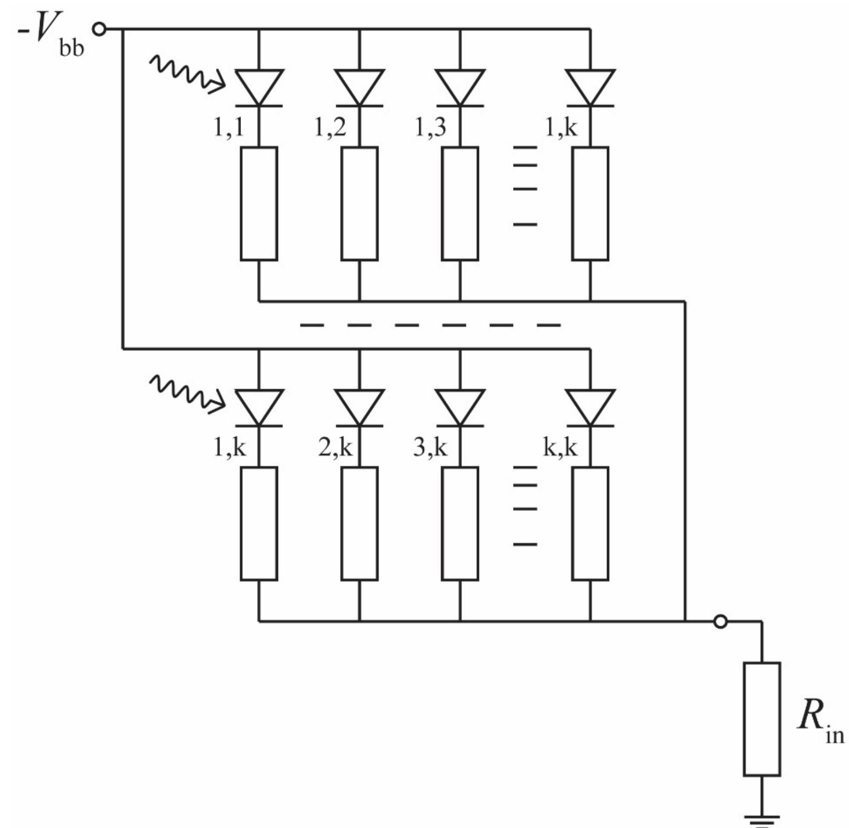
Figure: J. O’Keeffe, Sensl

SiPM: parallel array of many SPADs



Courtesy S. Brunner (Broadcom)

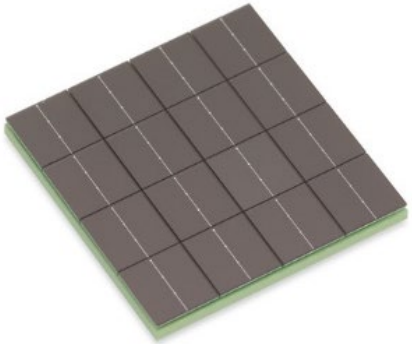


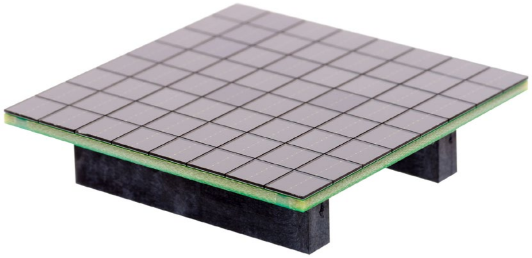
- Array of many (order 10^2 - 10^4) SPADs connected in parallel
- The combined output current is proportional to the incident photon flux under sparse illumination conditions

Schaart 2021, Physics and Technology of Time-of-Flight PET Detectors, Phys Med Biol 66 09TR01

Imaging applications: SiPM arrays

Four-side buttable arrays of SiPMs with high fill factor are nowavailable from various manufacturers. The best devices have photodetection efficiencies > 50%, single-photon time resolutions < 100 ps FWHM, and low dark count rate.





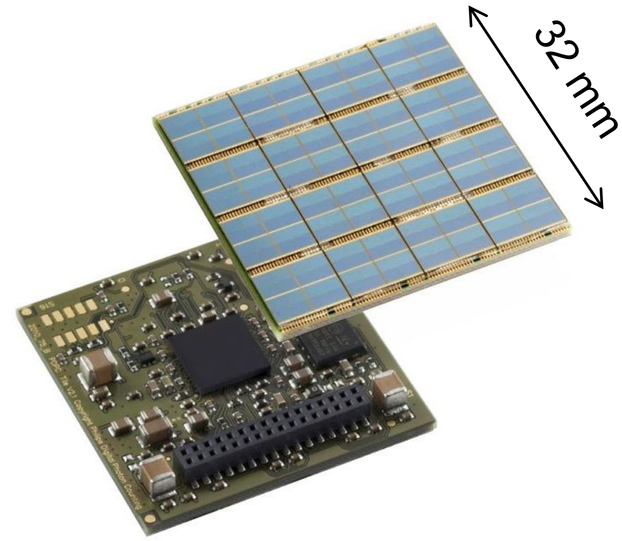
BROADCOM connecting everything

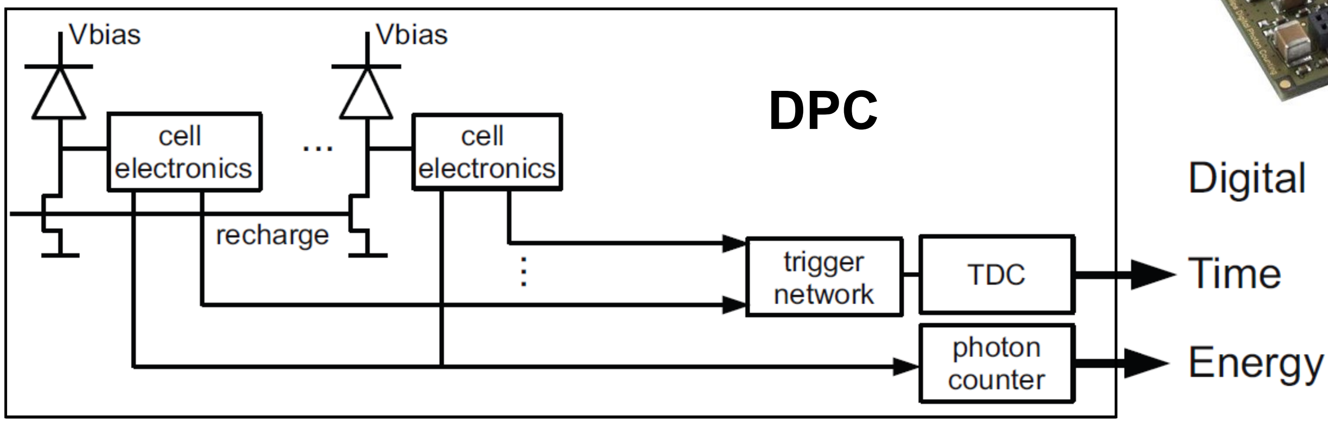
HAMAMATSU PHOTON IS OUR BUSINESS

onsemi

Digital Photon Counter

Frach et al, 2009 IEEE Nucl. Sci. Symp.
Conf. Record 1959-1965





++ small single-photon time jitter
++ negligible noise at the single photon level
++ high photon detection efficiency
+ MR-compatible

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

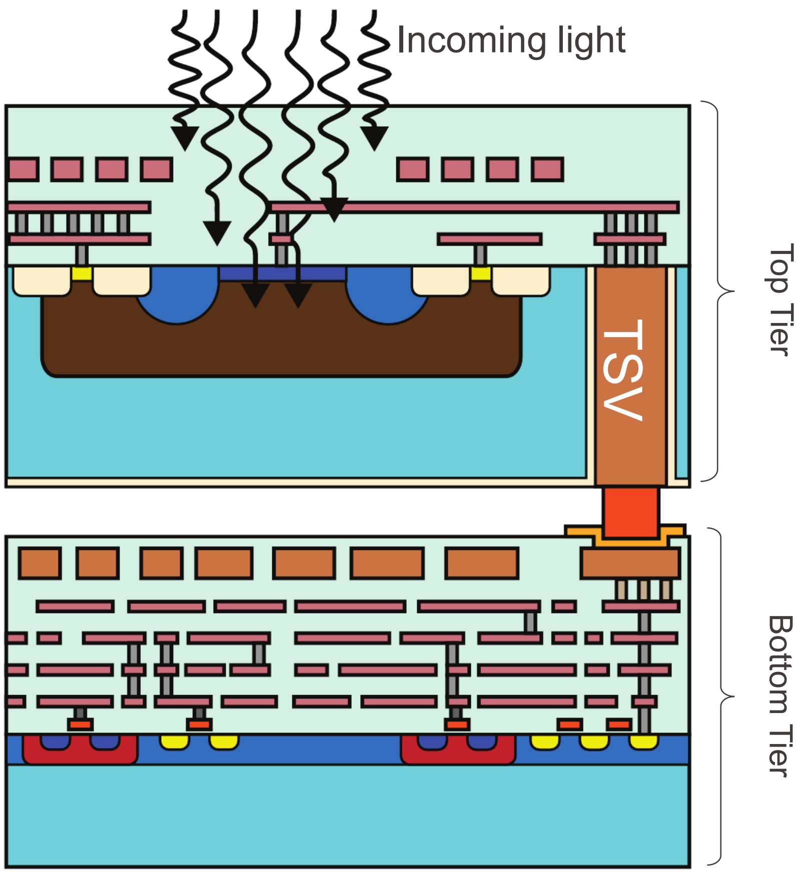
See also: D. R. Schaart et al "Advances in Digital SiPMs …," NIM A 809, 31-52, 2016

Example of a 3D integrated digital SiPM

3D Multichannel Digital SiPM (3D MD-SiPM)

3D FSI Architecture:

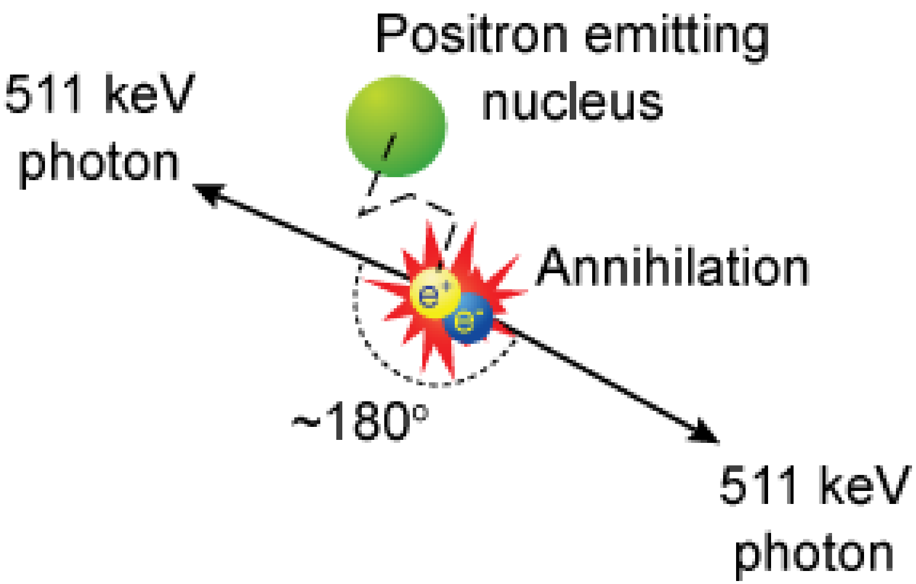
- Fill factor maximization
- Good blue/NUV sensitivity
- Enhanced compactness
- Multi-timestamp capability
- High spatial resolution
- Integration heterogeneity
- Higher complexity
- Higher cost

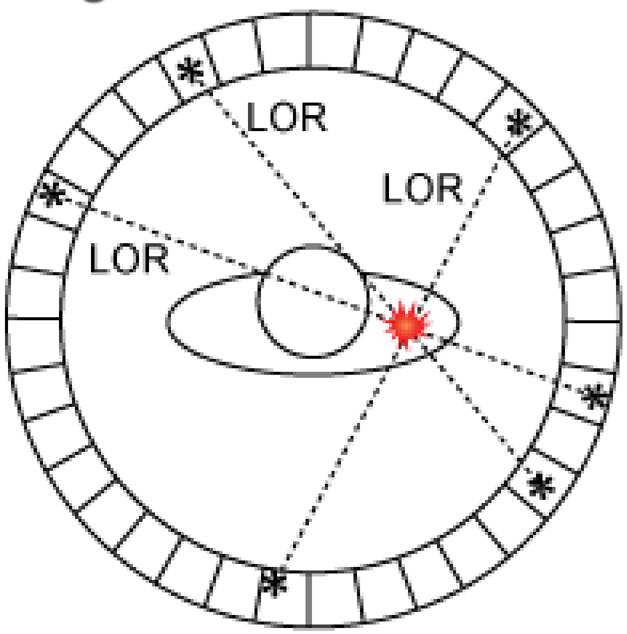


See also: F. Gramuglia et al. 2020
IEEE NSS/MIC Conf Record pp. 1-3

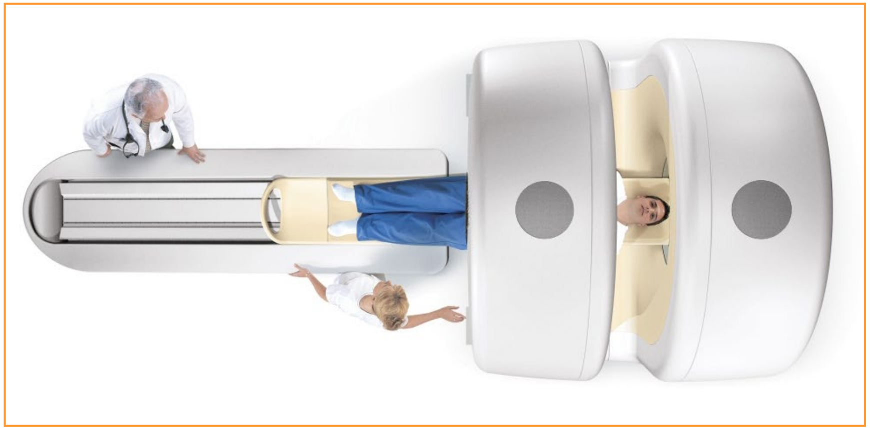
Why use SiPMs in PET?

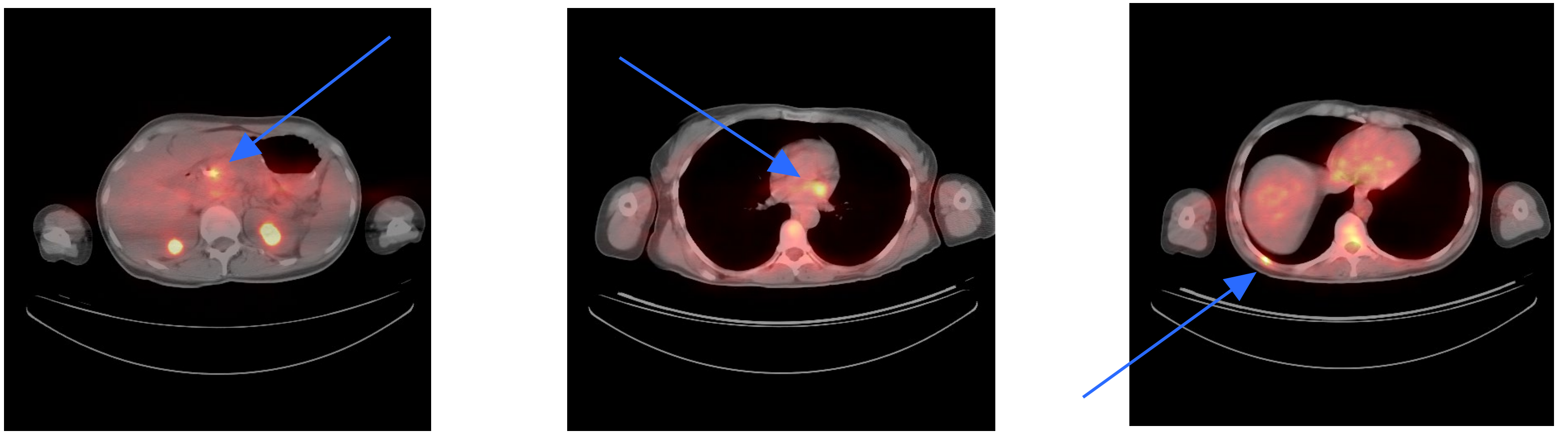
Positron Emission Tomography





PET/CT

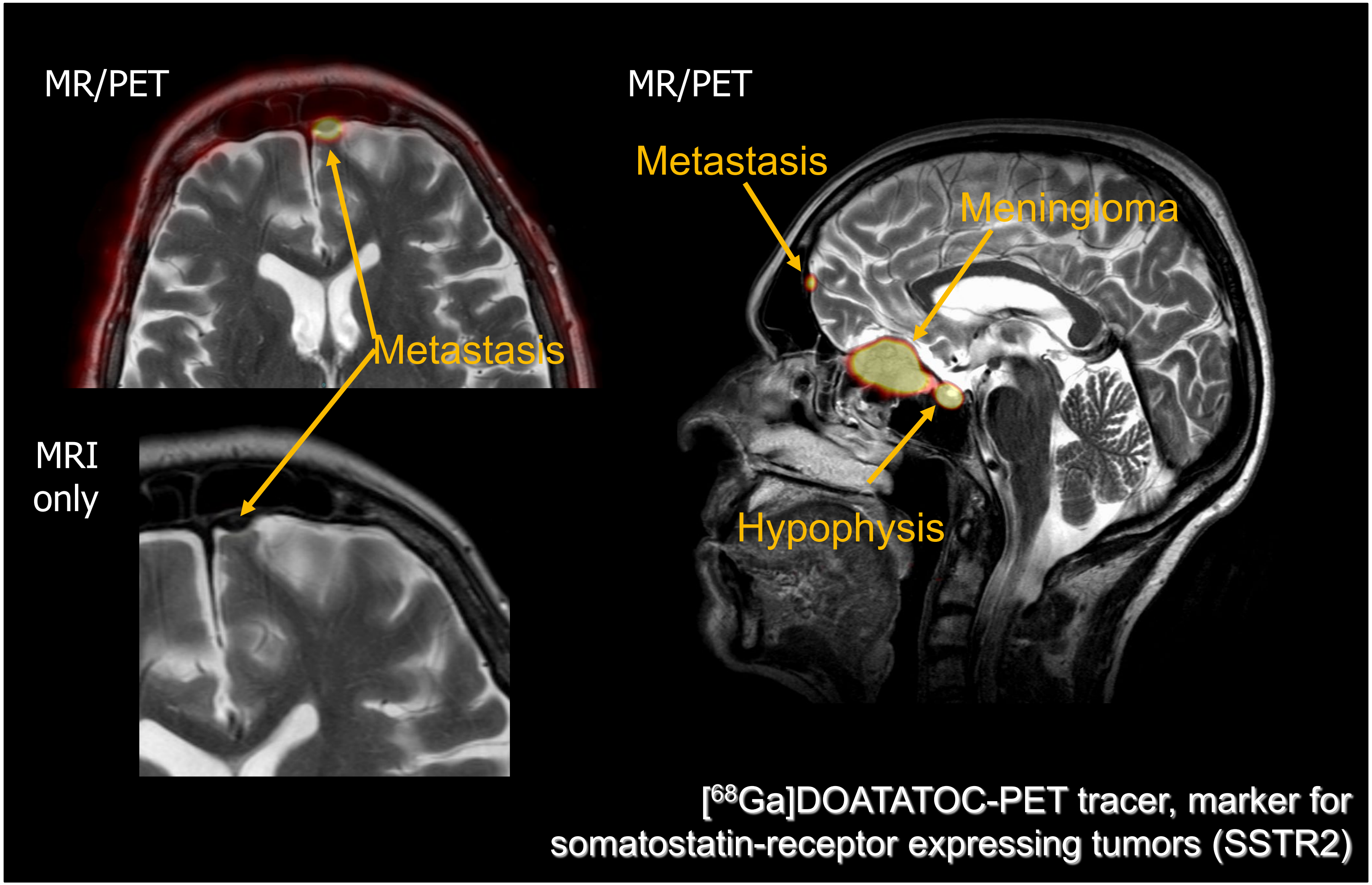




PET/CT (fused images): primary pancreatic cancer with suspicious chest wall and mediastinum lesions

Courtesy of A.A. Lammertsma, VUmc PET Centre, and Philips

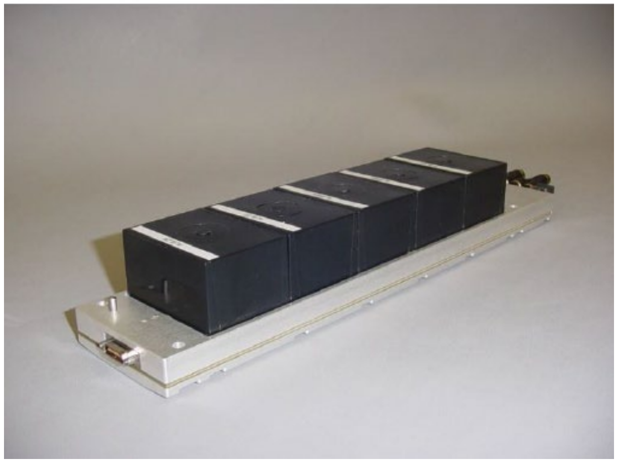
Multimodality: PET + MRI



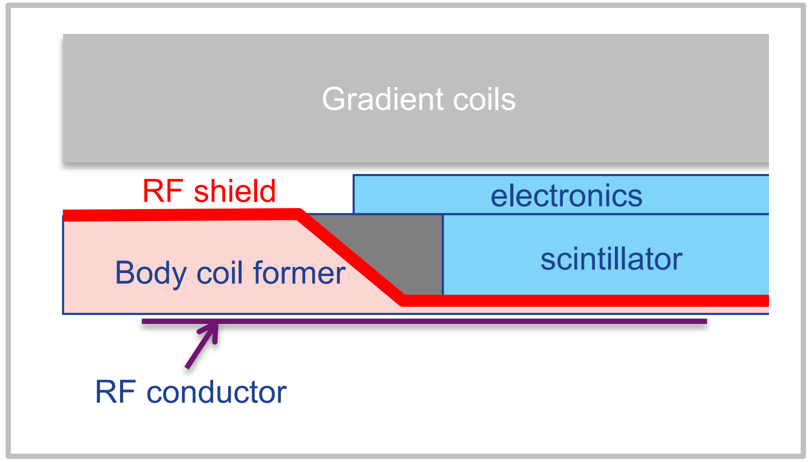
PET/MR System Research

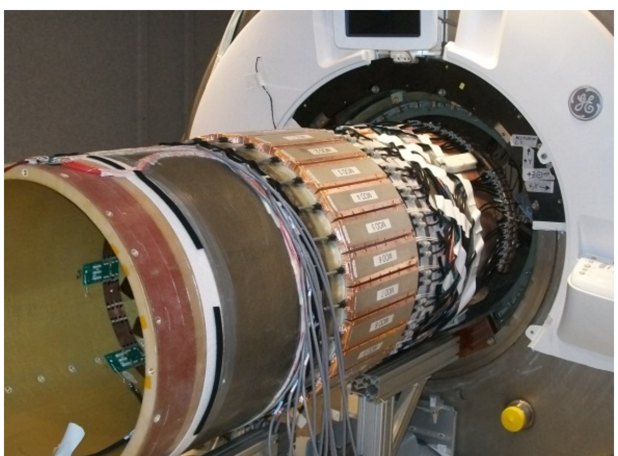
GE Healthcare

Compact PET ring in isocenter of magnet



PET detector module (unshielded)



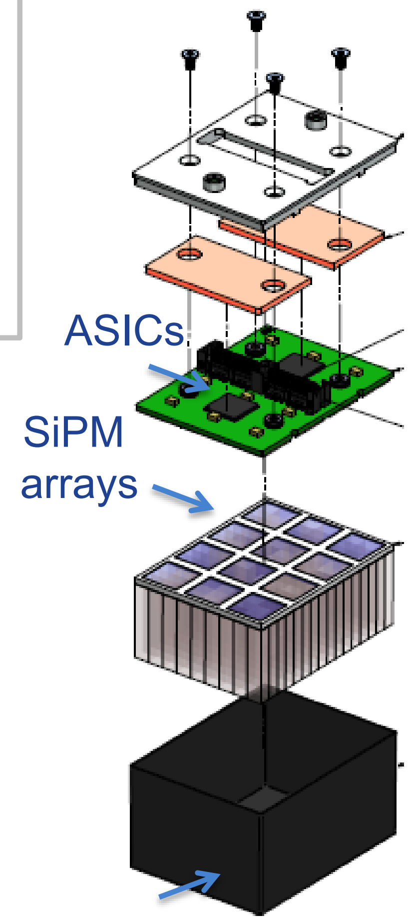


PET ring & MR body coil insertion

PET detector design goals

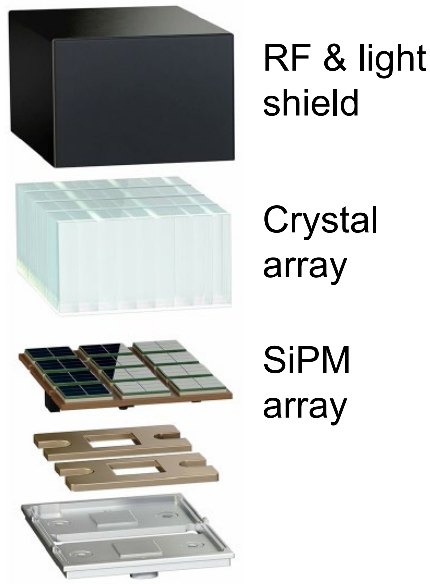
Measured performance	
Timing res	< 400 ps
Sensitivity	> 22 kcps/MBq
FOV	60 x 25 cm
Spatial res	4.1 mm (axial)
Energy res	< 12%

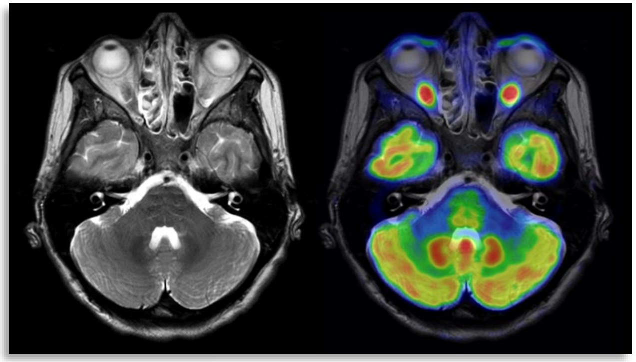
Construction of PET detector block



GE Signa SiPM-based PET/MRI system

Based on analog silicon photomultipliers (SiPMs)





System Performance	
CRT	< 400 ps FWHM
Sensitivity	21 cps/kBq
FOV	60 x 25 cm
Spatial res.	4.1 mm
Energy res.	< 12%

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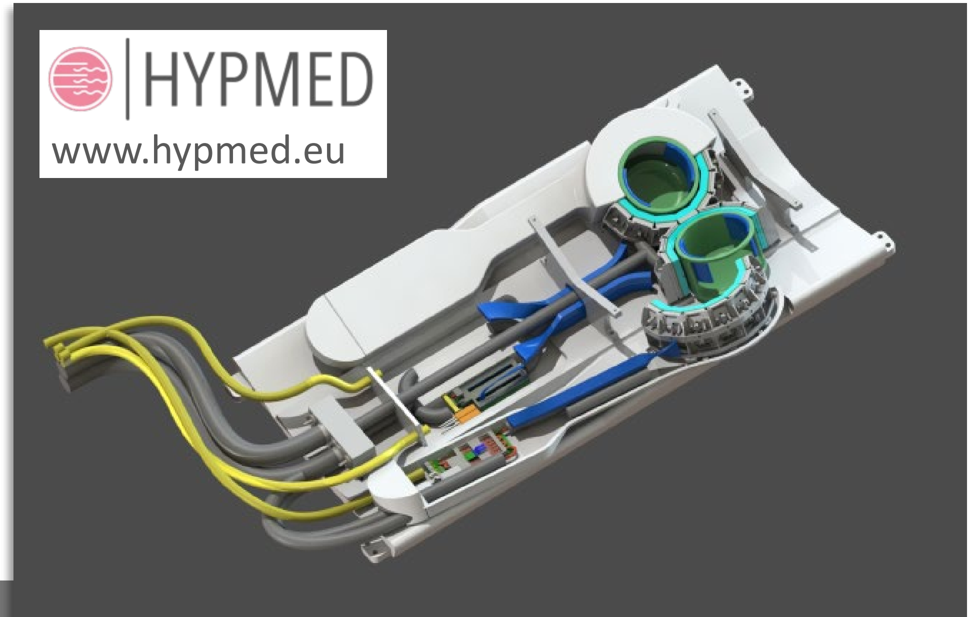
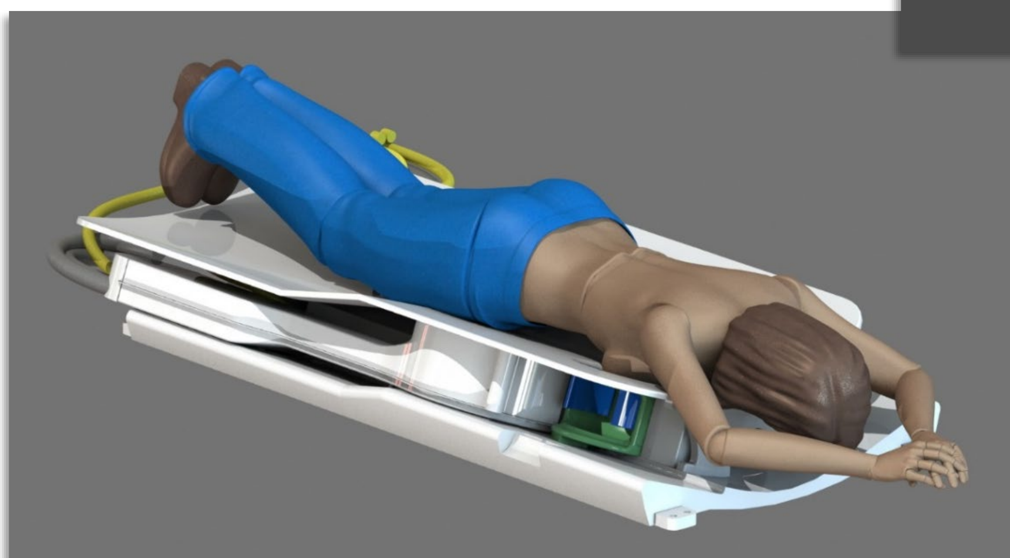
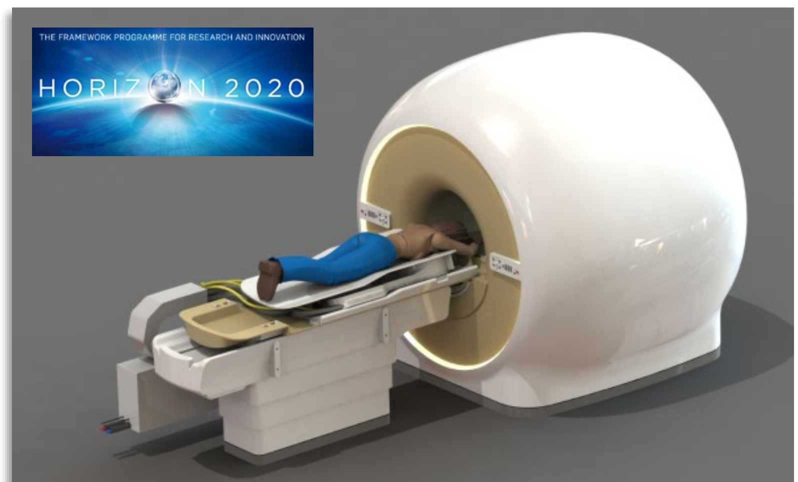
Images: PMB 60 R115, gehealthcare.com

HYPMED: a new device for breast PET/MRI imaging

- MRI-transparent PET detectors integrated with breast MRI coil
- Equipped with integrated biopsy unit
- PET rings can be opened for breast positioning and biopsy
- For use in standard MRI system







PET performance requirements

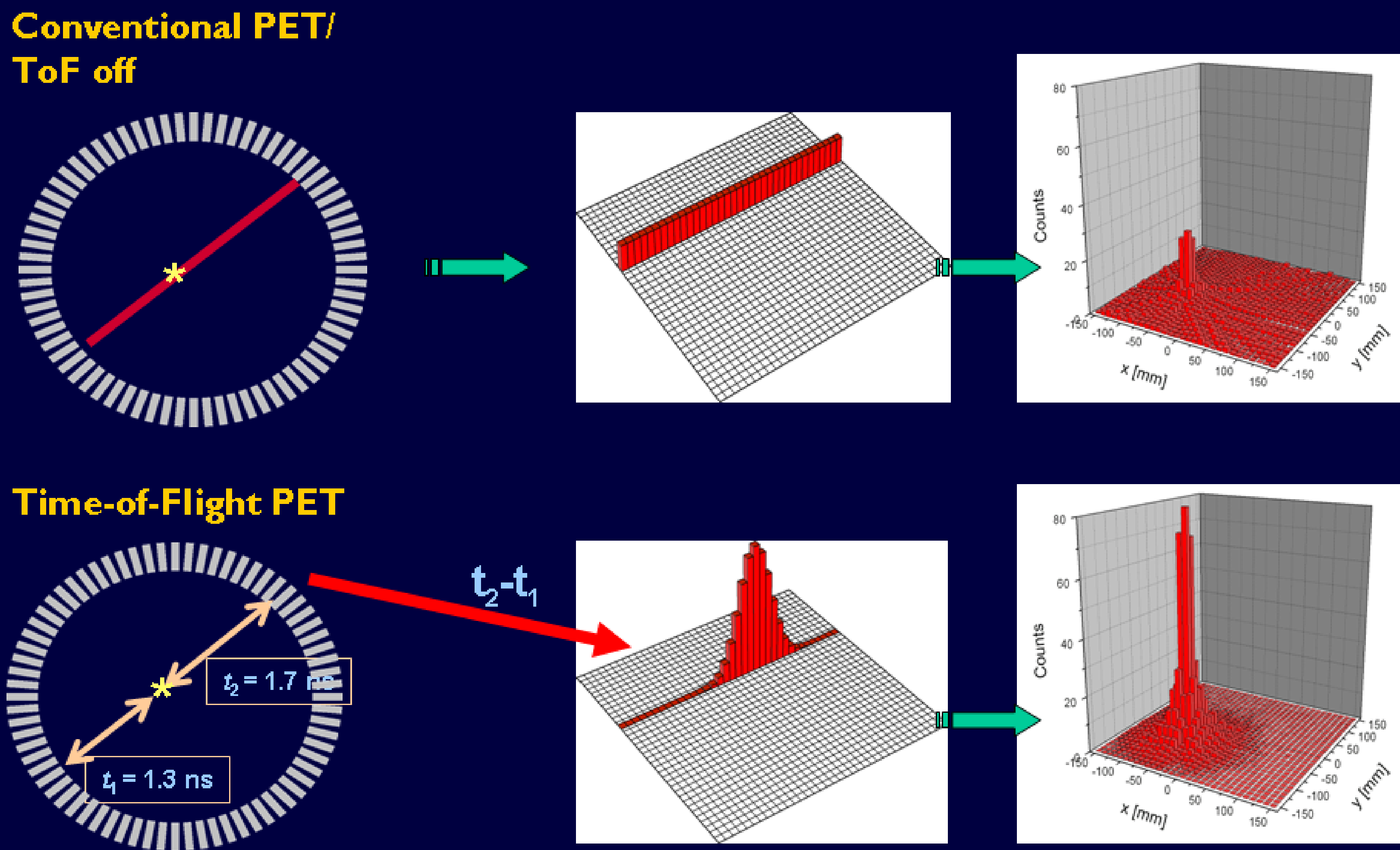
Important requirements in clinical PET:

- Tracers, with high specificity, readily available, and affordable
- Low radiation burden
- Short scan times
- Flexibility (e.g. combinations of imaging and therapeutic modalities)
- Cost-effectiveness

Technologically, this necessitates:

- High system sensitivity (cps/Bq)
- High spatial resolution and DOI recovery => high sensitivity!
- Quantitative accuracy and reproducibility (< 5%) => high sensitivity!
- Compact, flexible, scalable, and cost-effective detector technologies

Time of Flight PET Systems



→ ToF: more signal, less noise

A FOM for rational detector design

system geometrical efficiency

patient diameter

$$\mathrm{FOM}_{\mathrm{det}} = \eta_{\mathrm{det}}^{2} \frac{\eta_{\mathrm{geom}}}{\$} \frac{D}{\Delta t}$$

detection efficiency

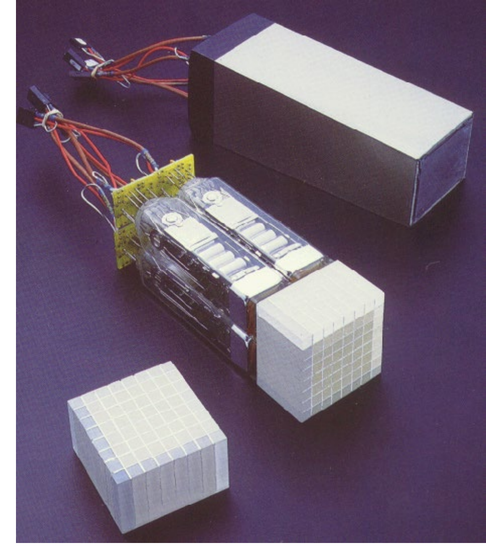
total cost of detectors

time resolution (specified in terms of the system coincidence resolving time: CRT)

Schaart 2021, Physics and Technology of Time-of-Flight PET Detectors, Phys Med Biol 66 09TR01

The first TOF-PET systems

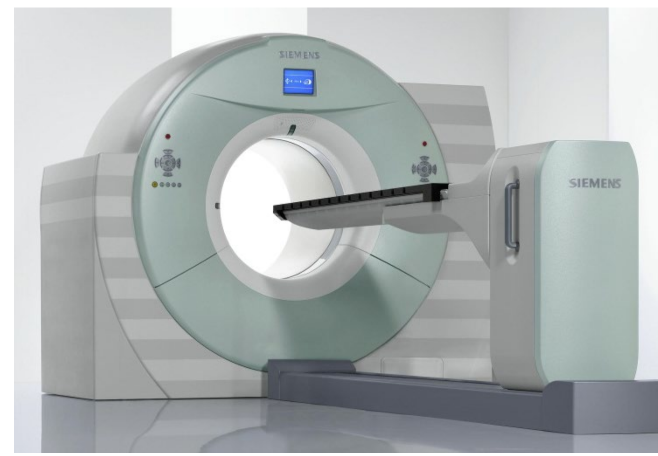
- Commercial TOF PET/CT scanners based on PMTs available from several manufacturers since 2006
- Coincidence resolving time (CRT): 500-700 ps FWHM



PMT-based PET detector

Philips Gemini TF

GE Discovery 690



Siemens mCT

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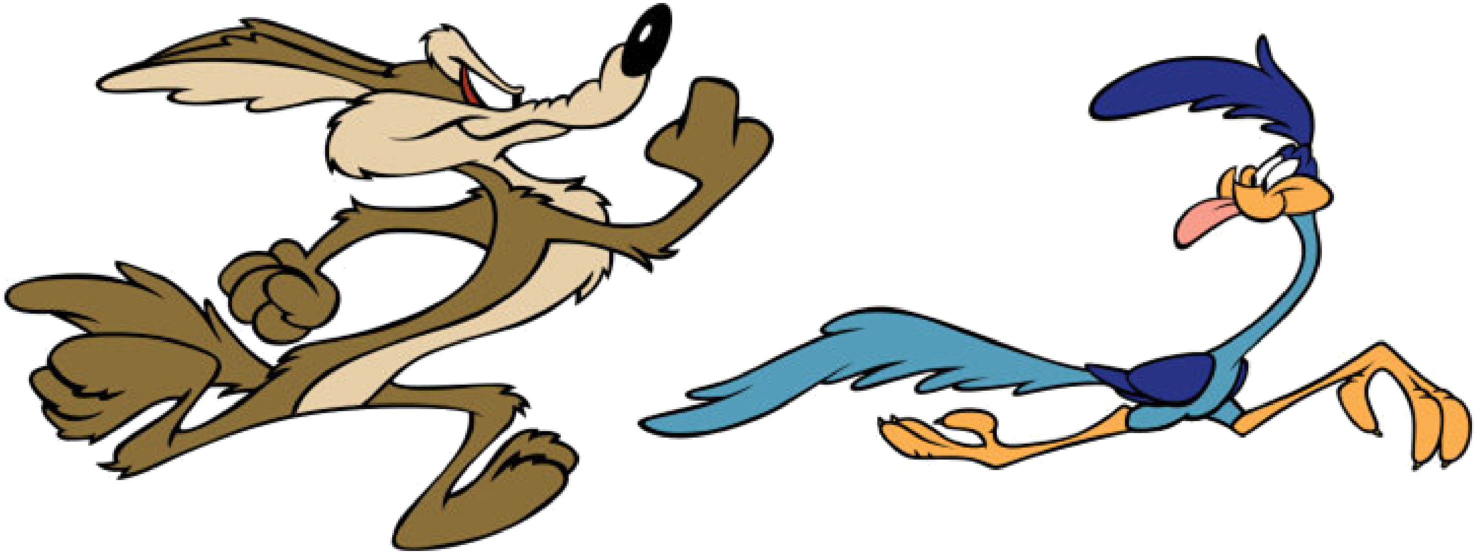
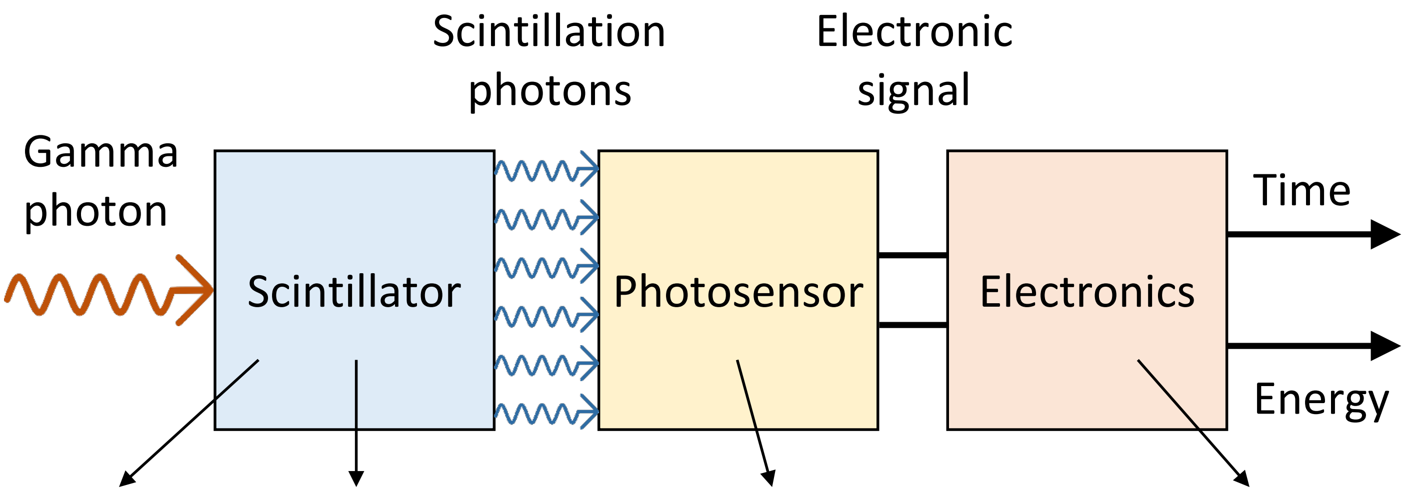
Faster is better



Scintillation detectors and time resolution



Emission
- Light yield
- Decay time
- Rise time

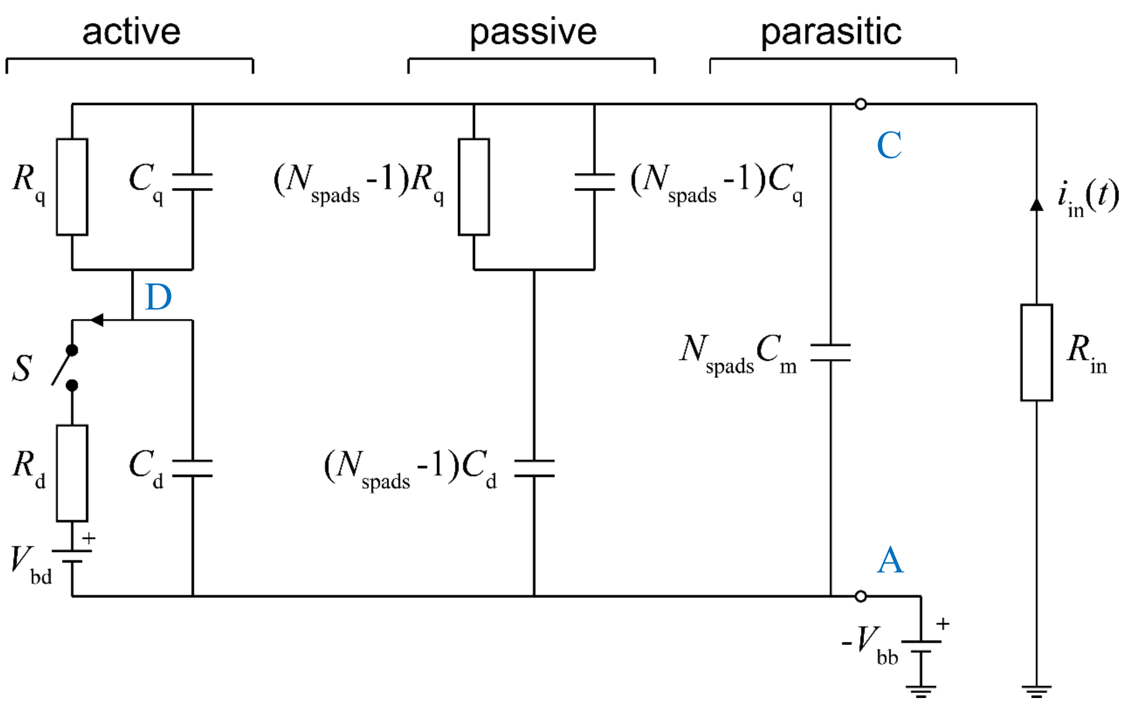
Crystal
- Optical transfer efficiency (OTE)
- Optical transfer time spread (OTTS)

Photosensor
- Photodetection efficiency (PDE)
- Single-photon time resolution (SPTR)
- Crosstalk
- Dark counts

Electronics
- Noise
- Bandwidth
- Transient response

D.R. Schaart et al, Time-of-Flight in Perspective, IEEE TRPMS 5, 598-618, 2021

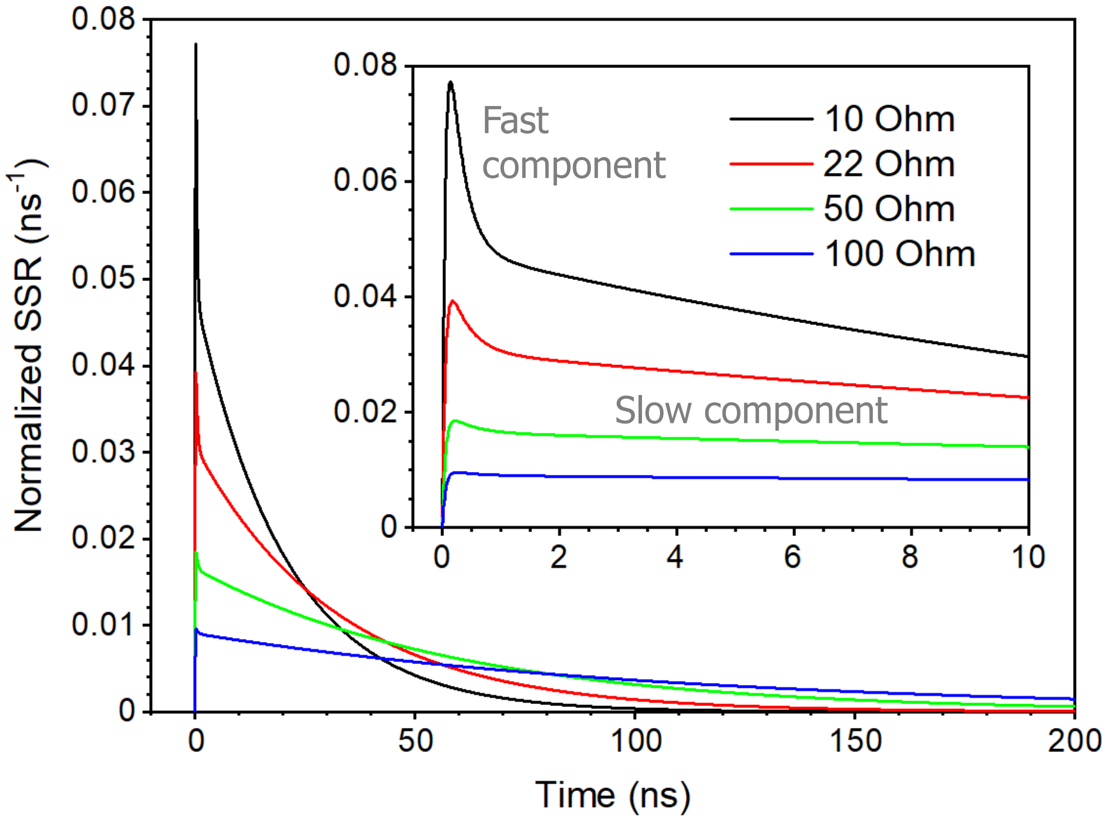
SiPM equivalent electrical circuit



C_d	Diode capacitance
C_m	Parasitic capacitance per SPAD
C_q	Parallel capacitance of R_q
$i_{in}(t)$	Current through R_{in}
N_{spads}	Number of SPADs in SiPM
R_d	Internal resistance of diode
R_{in}	Input resistance of readout circuit
R_q	Resistance of quench resistor
V_{bb}	Reverse bias voltage
V_{bd}	Breakdown voltage
$V_{ob} = V_{bb} - V_{bd}$	Voltage-over-breakdown

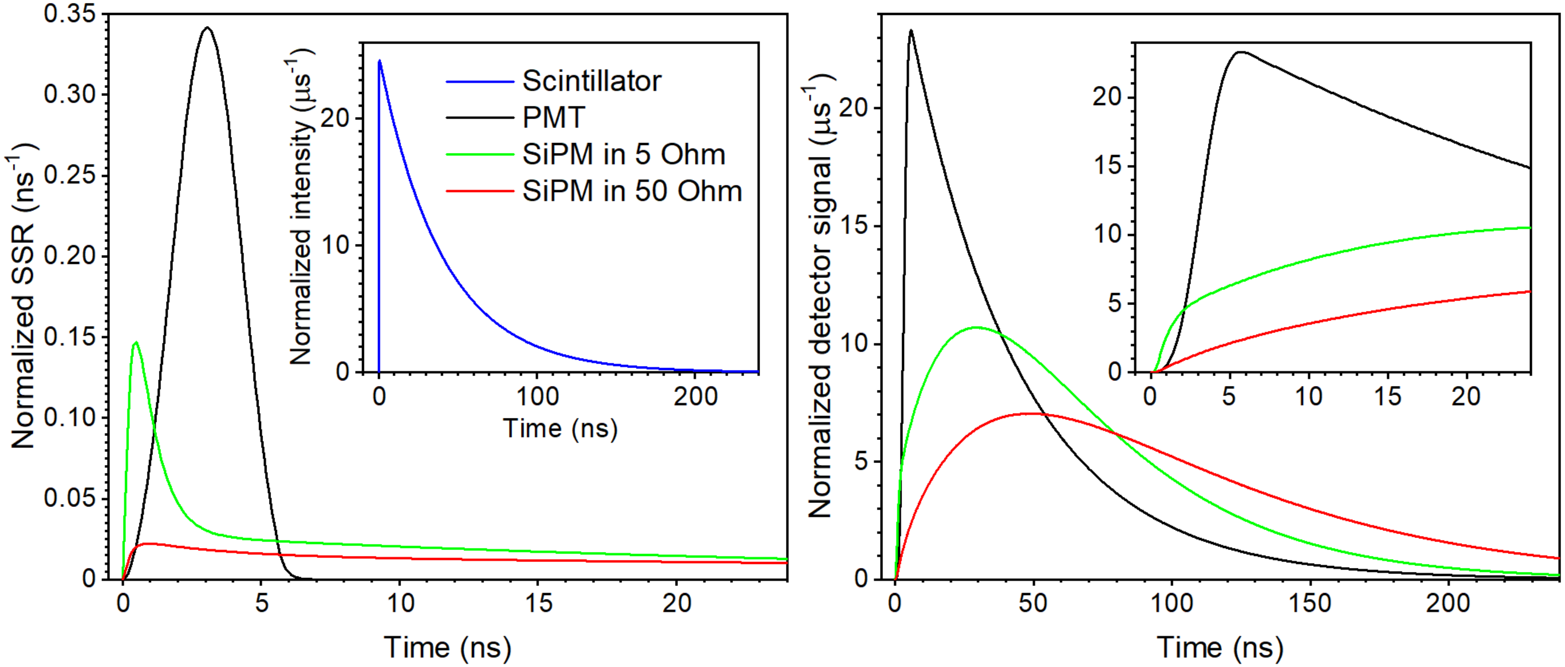
Seifert et al 2009, Simulation of silicon photomultiplier signals, IEEE Trans Nucl Sc. 56 3726-33

SiPM single-SPAD response



SiPM single-SPAD response (SSR) of a typical SiPM for R_{in} = 10Ω (black), 22Ω (red), 50Ω (green), and 100Ω (blue), calculated using the model of Marano et al, IEEE Sensors J. 14, 2749-2754, 2014.

Signal shape of scintillation detectors



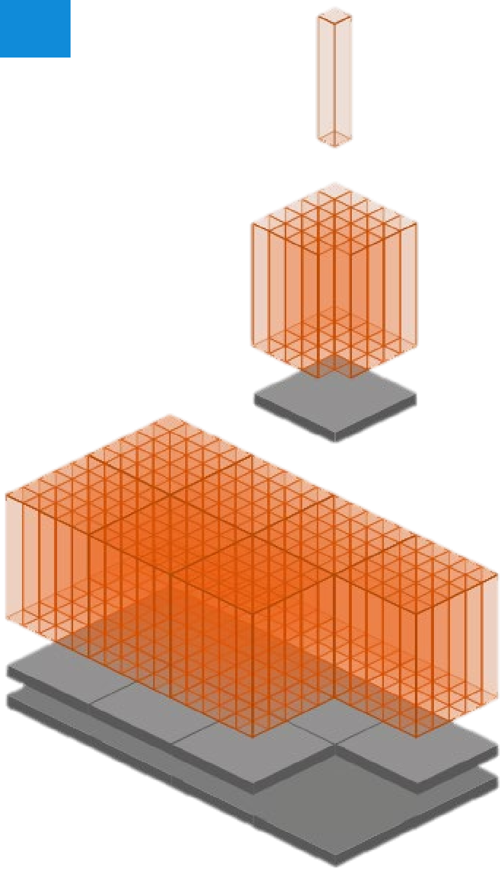
Left: the SER of a typical fast PMT, calculated according to Hyman 1965 (black) and the SSR of a typical SiPM, calculated according to Marano 2014 for R_{in} = 5Ω (green) and R_{in} = 50Ω (red)

Inset left: the emission function of scintillator with 100 ps rise time and 40 ns decay time

Right: the output current, i.e. the convolution of the scintillation pulse and the SER of a PMT-based scintillation detector (black) or the SSR of a SiPM-based detector (green: R_{in} = 5Ω; red: R_{in} = 50Ω)

Siemens Biograph Vision PET/CT system

Based on analog silicon photomultipliers (SiPMs)



PMT-based detector

SiPM-based detector

System Performance	
CRT	215 ps FWHM
Eff. sensitivity	100 cps/kBq
FOV	26.3 cm
Spatial res	3.7 mm
Energy res	~10%

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Delft University of Technology

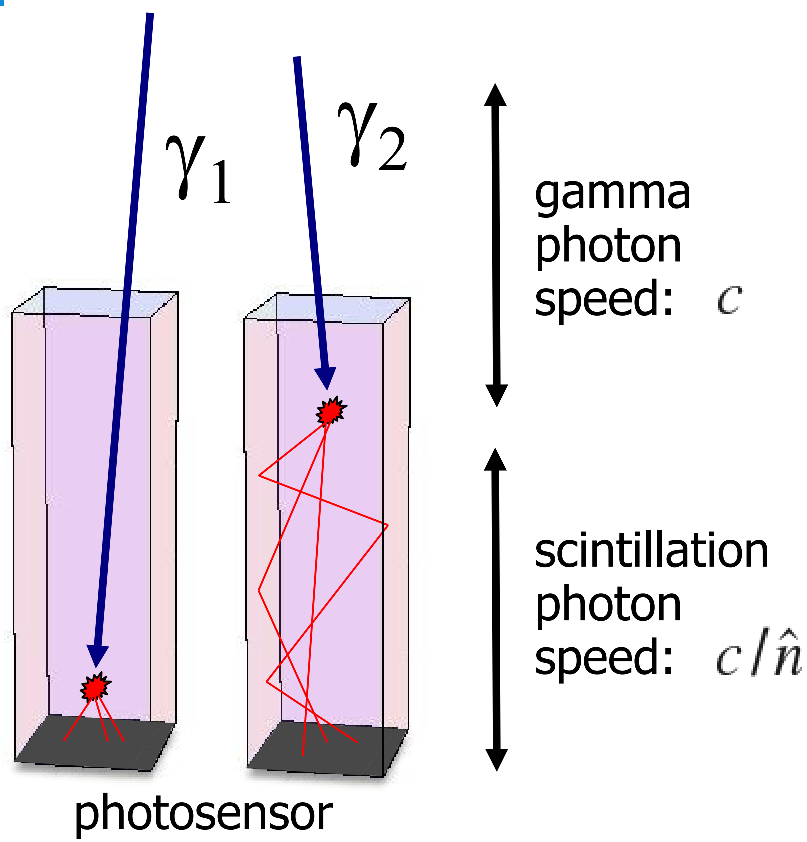
Images: siemens.com

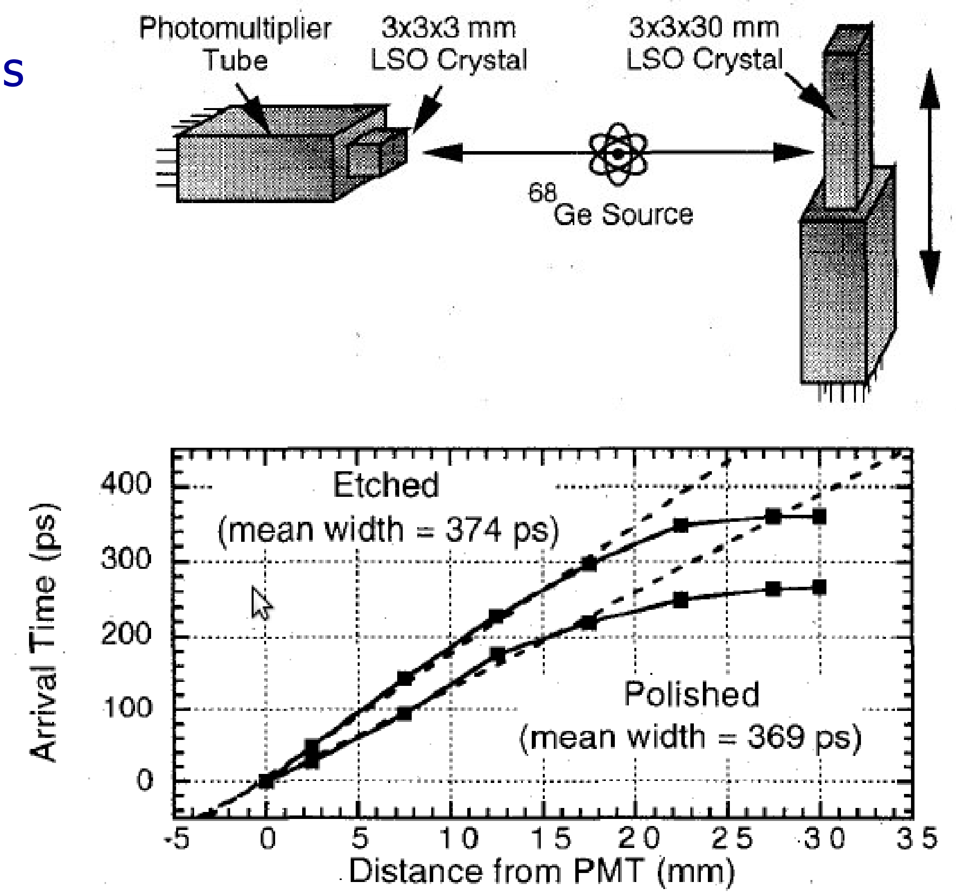
The End

… or just the beginning?

DOI-dependent signal delay in crystal

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

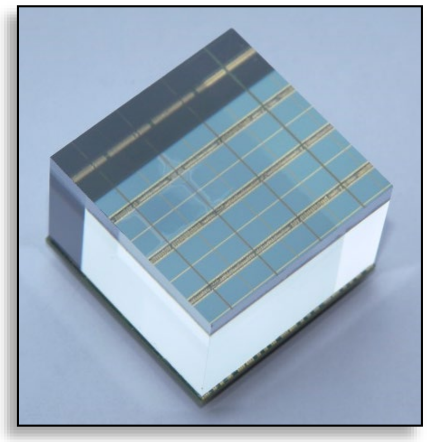




WW Moses and SE Derenzo

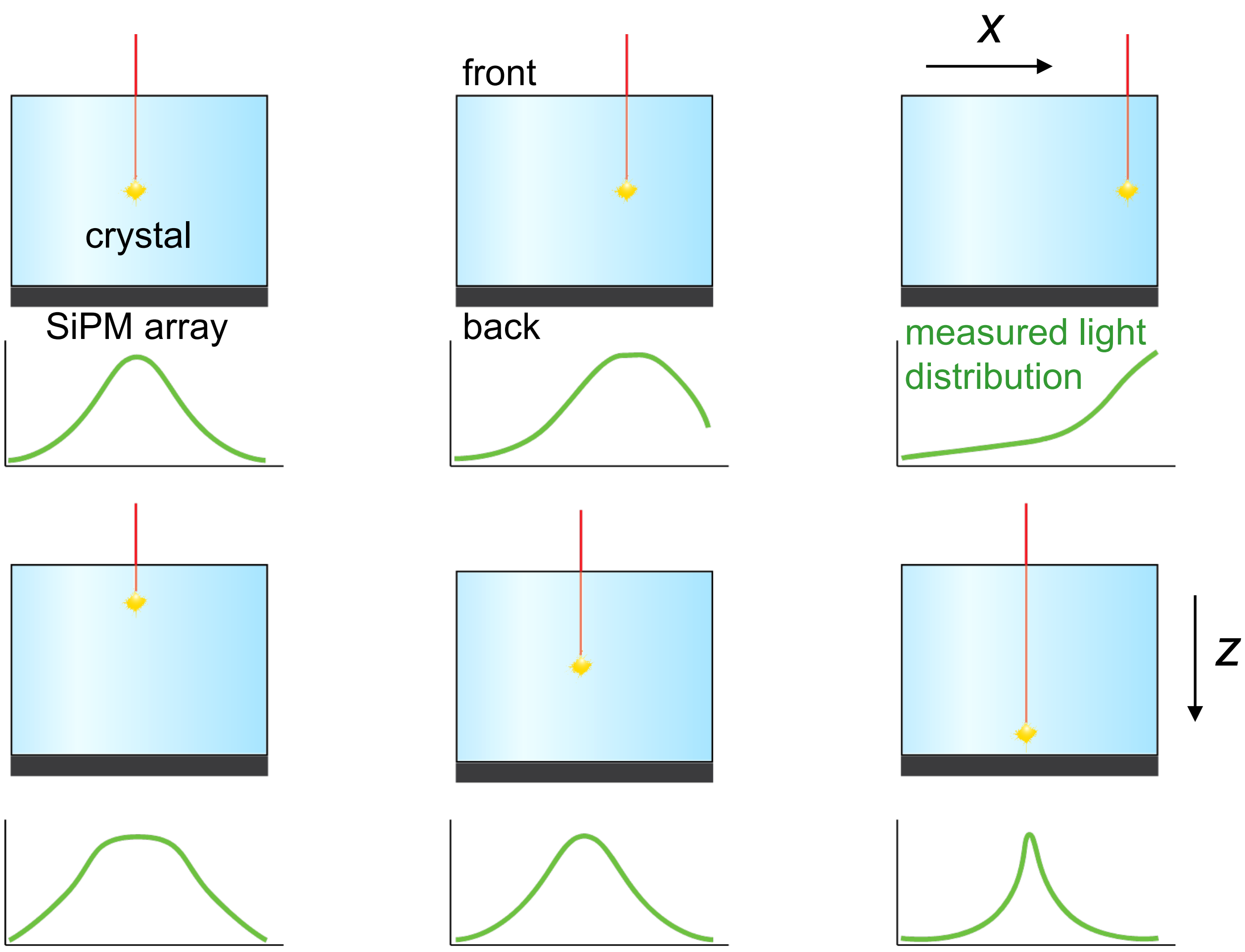
IEEE Trans. Nucl. Sci. 46, 474-478 (1999)

Monolithic scintillator detectors



32 mm x 32 mm x 22 mm monolithic LYSO:Ce crystal on digital silicon photomultiplier (dSiPM) array

Monolithic scintillator operating principle

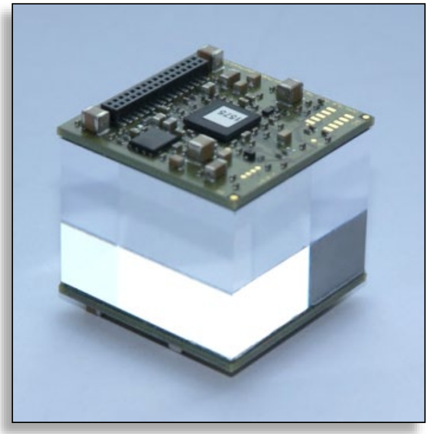


See e.g.: A. Gonzalez-Montoro et al., IEEE Transactions on Radiation and Plasma Medical Sciences 5, 282-305, 2021

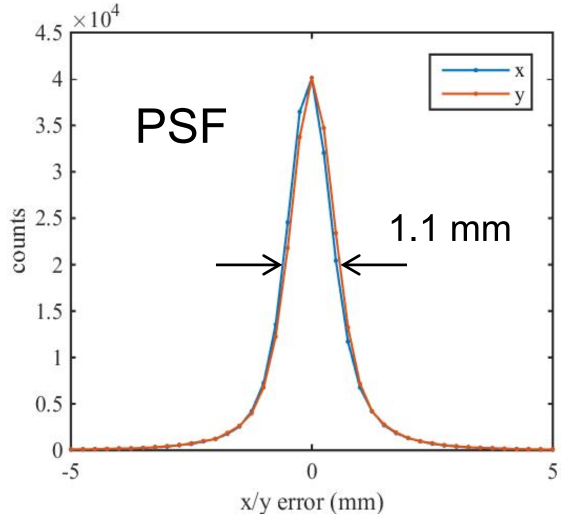
Performance summary

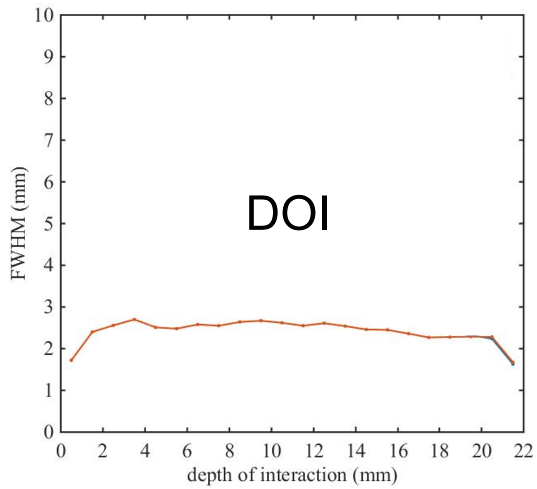
A practical detector for PET/CT and PET/MRI with high spatial resolution, excellent CRT, and high detection efficiency

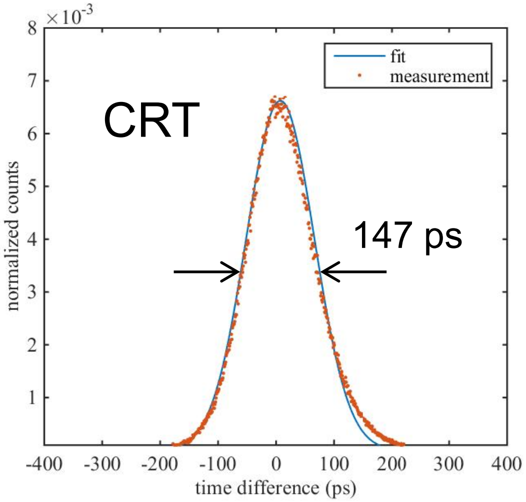
Performance parameter	BSR* monolithic	DSR** monolithic	3x3x5 mm³ crystal***
Energy resolution	**~10%**	**~10%**	~10%
Spatial resolution	**1.7 mm**	**1.1 mm**	N/A
DOI resolution	**3.7 mm**	**2.4 mm**	N/A
Coincidence resolving time	**214 ps**	**147 ps**	~135 ps



32 mm x 32 mm x 22 mm commercial-grade LYSO:Ce with double-sided (DSR) dSiPM readout







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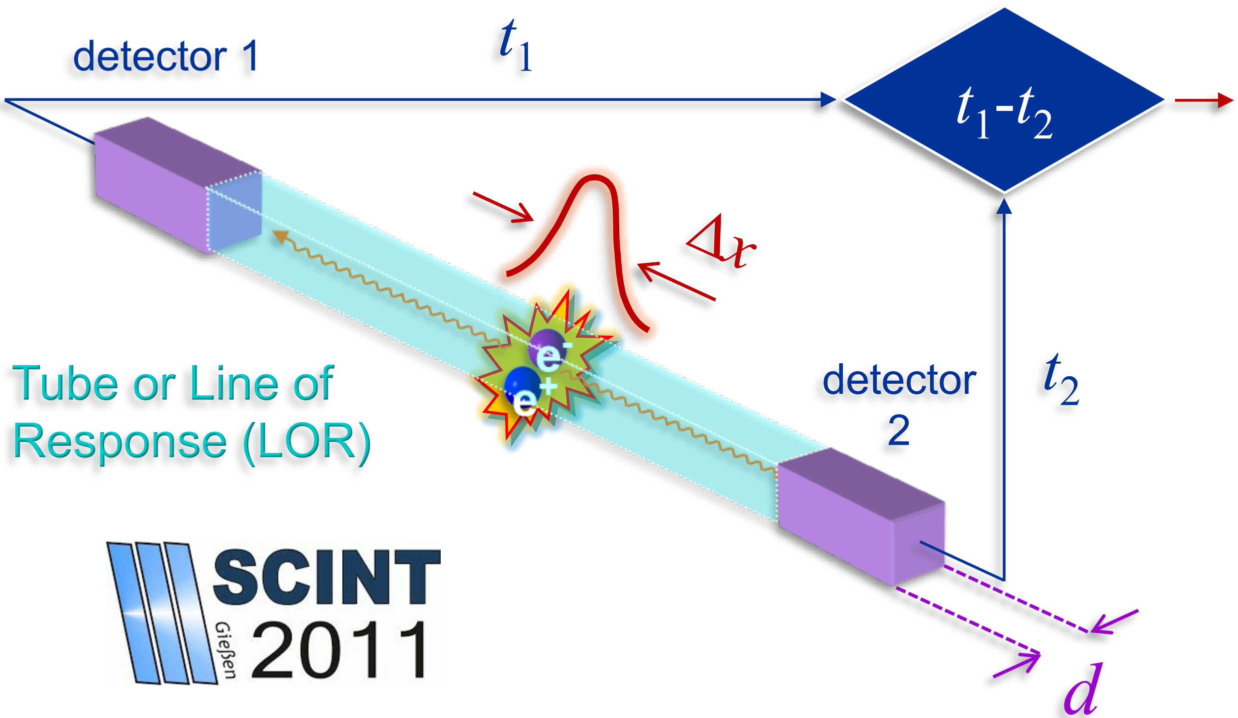
* G. Borghi et al, Phys Med Biol 61, 4904–4928, 2016
** G. Borghi et al, Phys Med Biol 61, 4929–4949, 2016
*** J.Y. Yeom et al, Med Phys 41, 122501, 2014

The holy grail: “10-picosecond PET”

With a CRT of ~10 ps events an be localized directly:

- image reconstruction no longer necessary!
- real-time image formation feasible
- makes TOF imaging applicable to small subjects (e.g. mice, rats)



$\Delta x = c \cdot CRT / 2$

Aim: $\Delta x \leq d$

$\Rightarrow CRT \leq 2d / c$

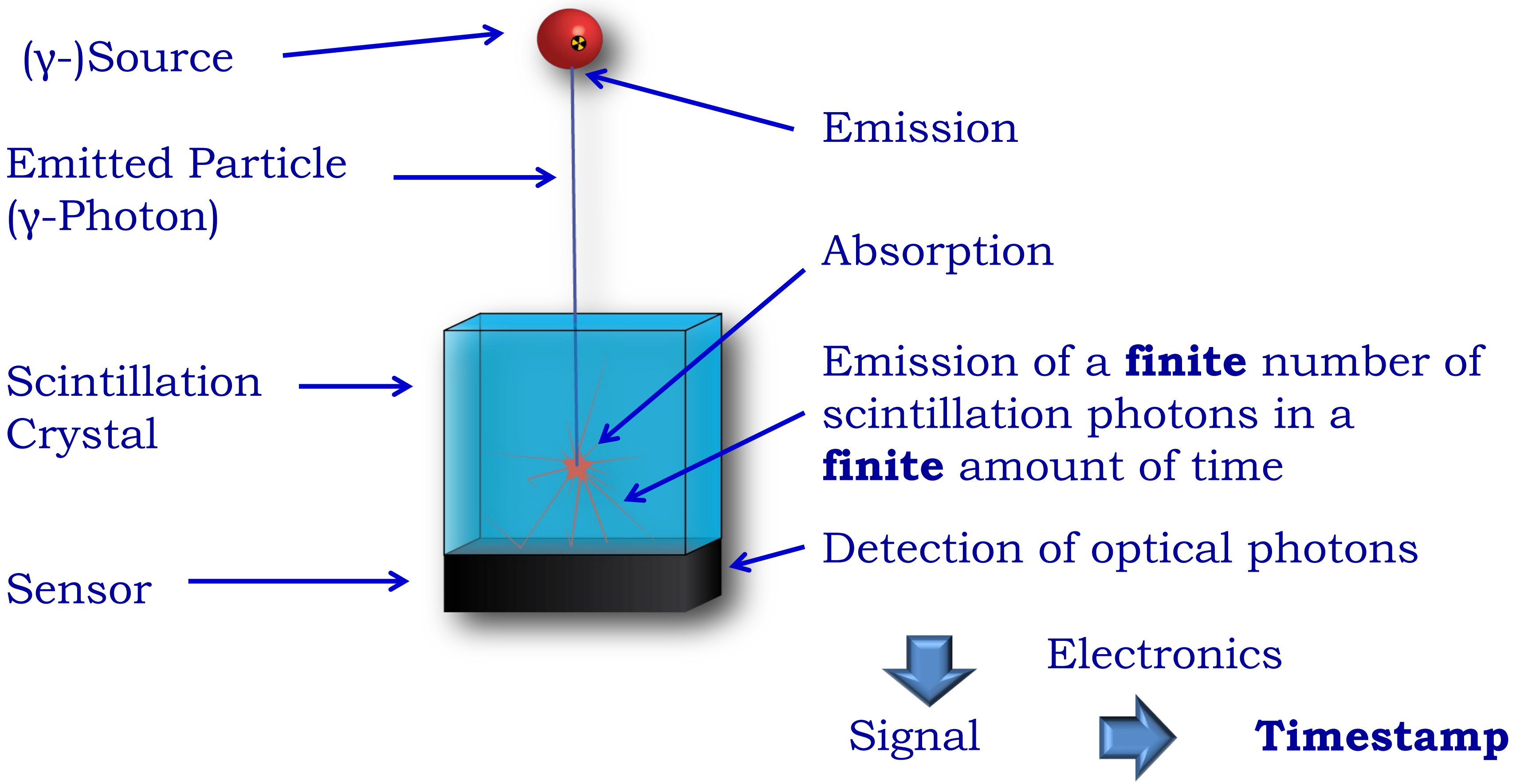
Clinical PET:

$2\ \text{mm} \leq d \leq 4\ \text{mm}$

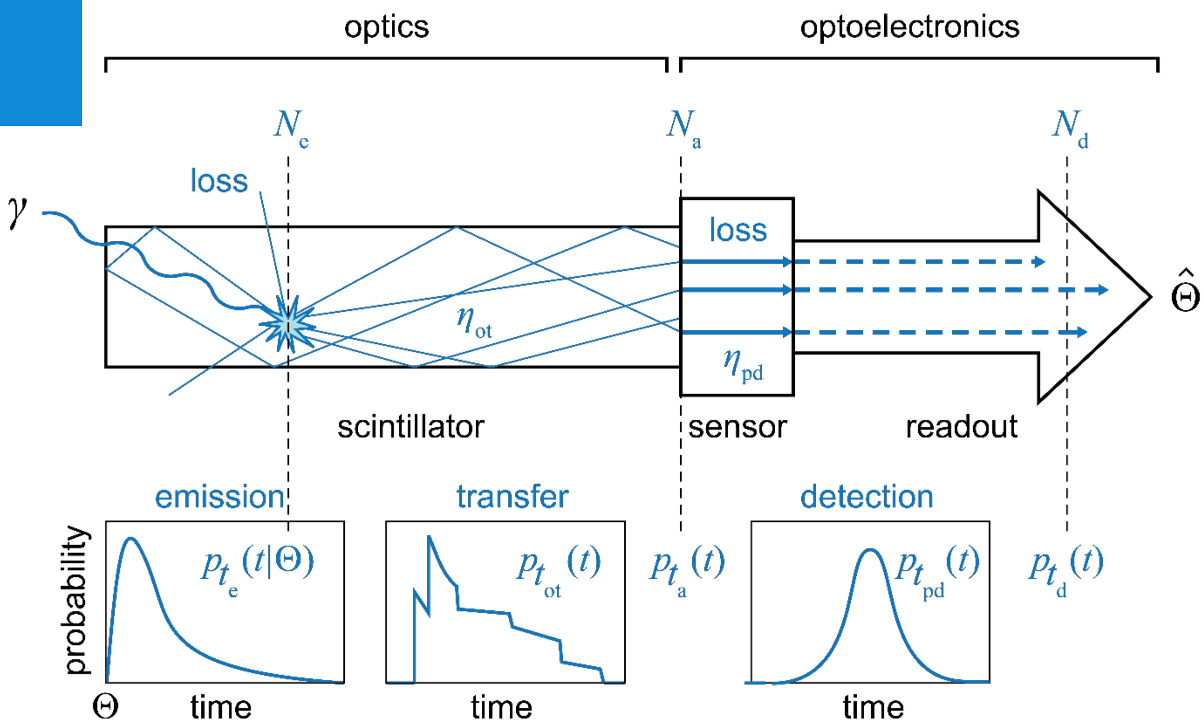
$\Rightarrow CRT \leq 20\ \text{ps}$

Dennis R. Schaart
Delft University of Technology

Scintillation detector timing is governed by photon counting statistics



Overview of relevant processes and parameters



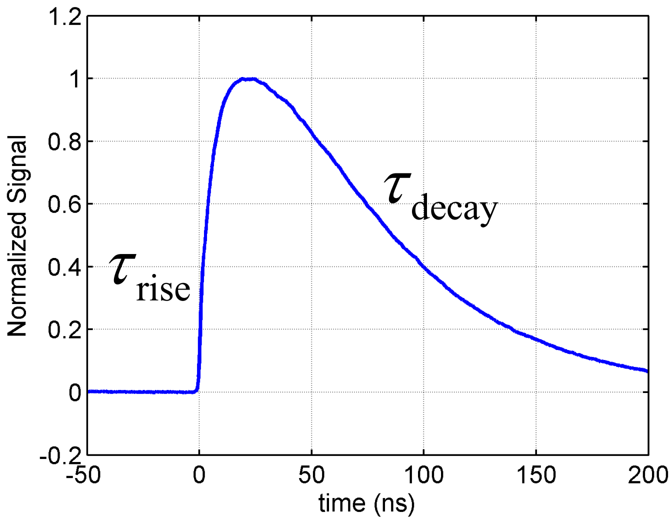
N_a	Number of photons arriving at photosensor
N_d	Number of detected photons
N_e	Number of emitted photons
$p_{t_a}(t)$	Photosensor illumination function
$p_{t_d}(t)$	Detected photon distribution
$p_{t_e}(t)$	Photon emission function
$p_{t_{ot}}(t)$	Optical transfer time distribution
$p_{t_{pd}}(t)$	Single-photon timing spectrum (SPTS)
η_{ot}	Optical transfer efficiency (OTE)
η_{pd}	Photon detection efficiency (PDE)
Θ	True time of interaction
$\hat{\Theta}$	Estimated time of interaction

$$p_{t_d}(t) = p_{t_e}(t\,|\,\Theta) * p_{t_{ot}}(t) * p_{t_{pd}}(t) = p_{t_e}(t\,|\,\Theta) * p_{t_{trans}}(t)$$

$$p_{t_{trans}}(t) = \int_{-\infty}^{\infty} p_{t_{ot}}(t - t'\,|\,\Theta)\, p_{t_{pd}}(t')\, dt'$$

Transfer time distribution of information carriers

Cramér–Rao lower bound on CRT (CRT_{LB})



Parameters determining CRT_{LB}:

- Scintillation light yield Y
- Photodetection efficiency (PDE)
- Scintillation pulse shape (emission function):
  - → For example, bi-exponential pulse with rise time constant τ_{rise} and decay time constant τ_{decay}
- Probability density function describing single-photon timing uncertainty:
  - → includes optical transit time spread (OTTS), single-photon time resolution (SPTR) of sensor, trigger jitter, etc.

S. Seifert et al, "The lower bound on the timing resolution of scintillation detectors," Phys Med Biol 57, 1797-1814, 2012

Some essential findings from timing theory

Lower bound on the coincidence resolving time (CRT_{LB}):

$$\mathrm{CRT_{LB}} \propto \frac{1}{\sqrt{N_\mathrm{d}}}, \text{ with } N_\mathrm{d} \text{ the no. of detected photons}$$

$$\tau_\mathrm{rise} << \tau_\mathrm{decay} \;\wedge\; \mathrm{SPTR} << \tau_\mathrm{decay} \;\Rightarrow\; \mathrm{CRT_{LB}} \propto \sqrt{\tau_\mathrm{decay}}$$

$$\left.\begin{matrix} \\ \\ \end{matrix}\right\} \mathrm{CRT_{LB}} \propto \sqrt{\frac{\tau_\mathrm{decay}}{\mathrm{PDE} \cdot Y}}$$

Only if the previous condition does not apply:

$$\tau_\mathrm{rise} \downarrow \;\Rightarrow\; \mathrm{CRT_{LB}} \downarrow \quad \text{and/or:} \quad \mathrm{SPTR} \downarrow \;\Rightarrow\; \mathrm{CRT_{LB}} \downarrow$$

Schaart 2021, Physics and Technology of Time-of-Flight PET Detectors, Phys Med Biol 66 09TR01

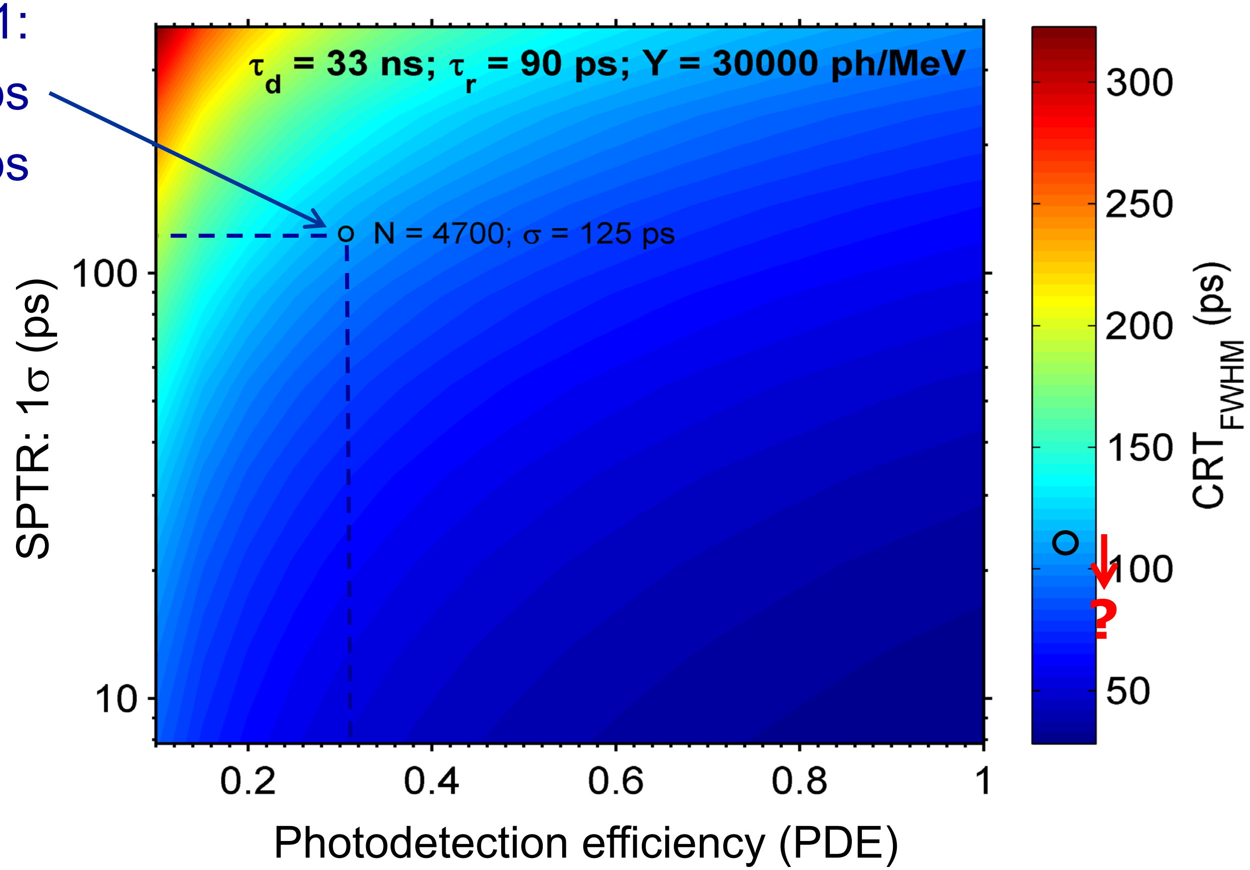
Lower bound on the CRT of LSO:Ce,Ca

Schaart et al ~2011:

CRT_{CRLB} ~110 ps

CRT_{EXP} ~125 ps

Prediction (2011): "CRT < 100 ps is feasible with further improvement of SiPM PDE and SPTR"



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

Lower bound on the CRT of LSO:Ce,Ca

Schaart et al ~2011:

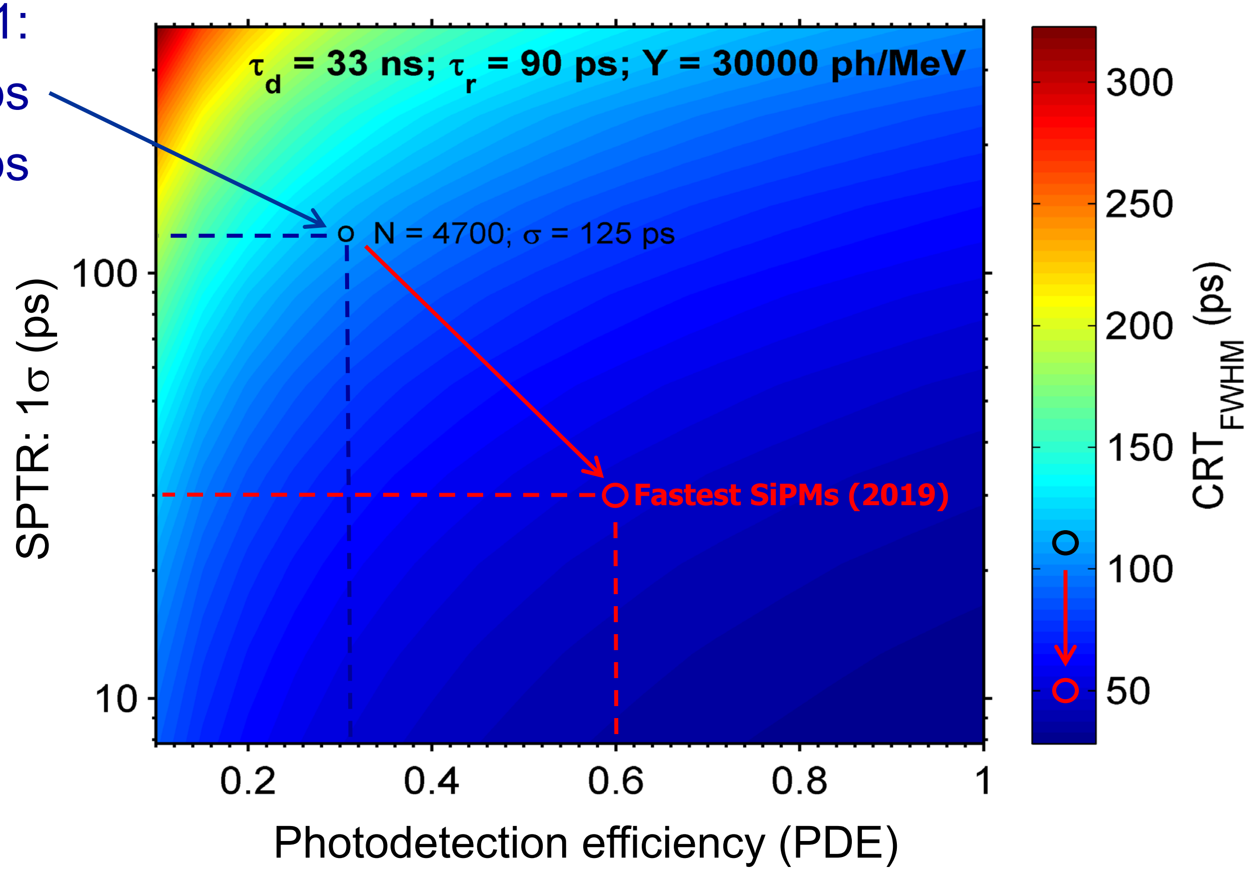
CRT_{CRLB} ~110 ps

CRT_{EXP} ~125 ps

Gundacker et al 2019:

CRT_{CRLB} ~50 ps

CRT_{EXP} ~60 ps



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

Best CRT with tiny LSO crystals to date

- Two 2 x 2 x 3 mm^3 LSO:Ce crystals codoped with 0.4%Ca in coincidence
- Read out with NUV-HD SiPMs from FBK (PDE ~60%, SPTR ~70 ps FWHM)
- 1.5 GHz bandwidth readout electronics (with corresponding high power dissipation)
- Lots of expensive digital readout and signal processing equipment

=> Results not very scalable, but showing that CRT a CRT of ~60 ps FWHM is physically possible!

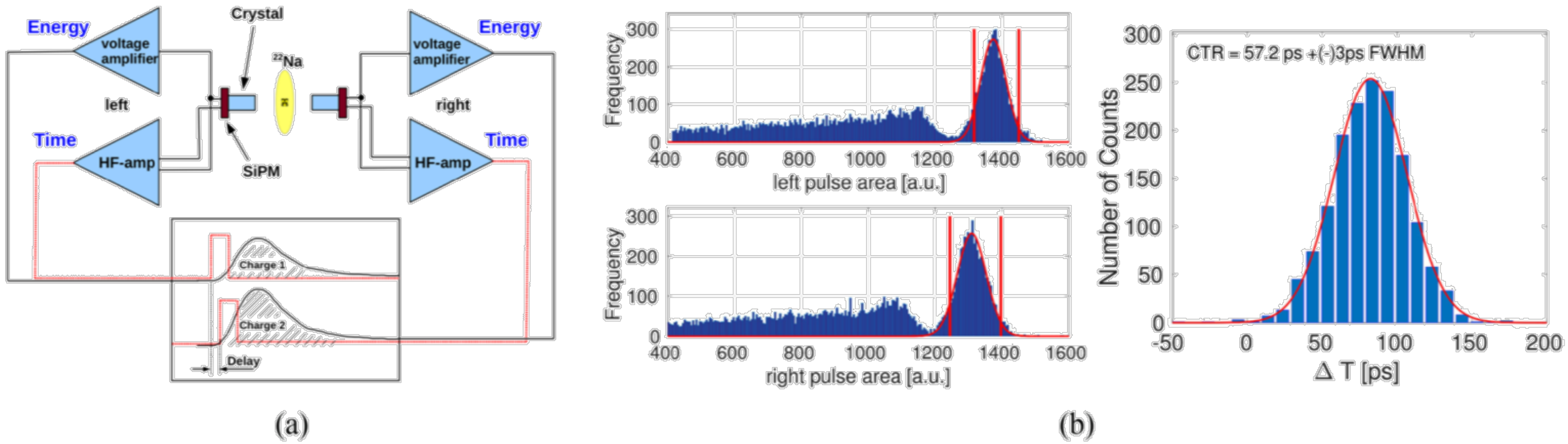


Figure 3. (a) In the CTR setup we readout the energy signal separately from the time signal to maintain highest time and energy resolution. (b) Example of measured energy spectra and photopeak selection with resulting delay time histogram and Gaussian fit giving the CTR in FWHM.

Gundacker et al 2019, High-frequency SiPM readout advances measured coincidence time resolution limits in TOF-PET, Phys Med Biol 64 055012

Conclusions (2011)*

CRT values obtained with current scintillators and SiPMs are close to the lower bound imposed by photon counting statistics

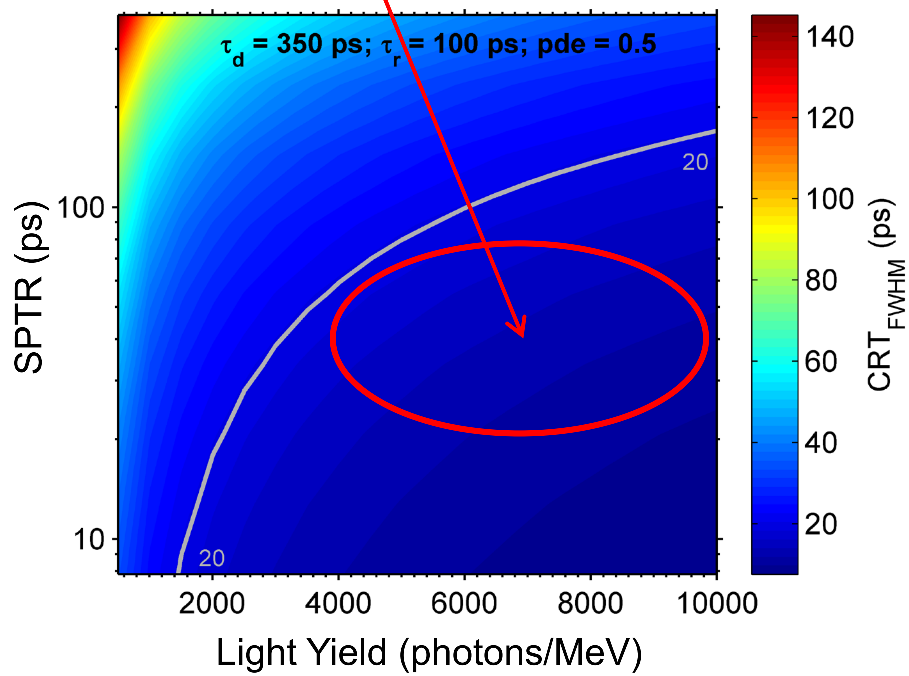
⇒ *further improvement only possible by decreasing the lower bound*

Key enablers required:

1. Bright (>> 10^3 ph/MeV), ultrafast (~ 1 ns) scintillation materials
2. Ultraprecise (SPTR << 100 ps), highly efficient (PDE → 1) photon counters
3. Detector design mitigating optical transit time spread (<< 100 ps) while maintaining high gamma detection efficiency (→ 1)

⇒ *None of these are available yet, but none are physically impossible*

CRT < 20 ps in principle feasible



Dennis R. Schaart
Delft University of Technology

* D.R. Schaart, "Scintillator needs for sub-100 ps PET," SCINT 2011

Conclusions (2022 update)

CRT values obtained with current scintillators and SiPMs are close to the lower bound imposed by photon counting statistics

⇒ *further improvement only possible by decreasing the lower bound*

Key enablers required:

1. Bright (>> 10^3 ph/MeV), ultrafast (~ 1 ns) scintillation materials
2. Ultraprecise (SPTR << 100 ps), highly efficient (PDE → 1) photon counters
3. Detector design mitigating optical transit time spread (<< 100 ps) while maintaining high gamma detection efficiency (→ 1)

⇒ *Items 2 and 3 are available; we are still looking for the scintillator (1)*

CRT < 20 ps in principle feasible

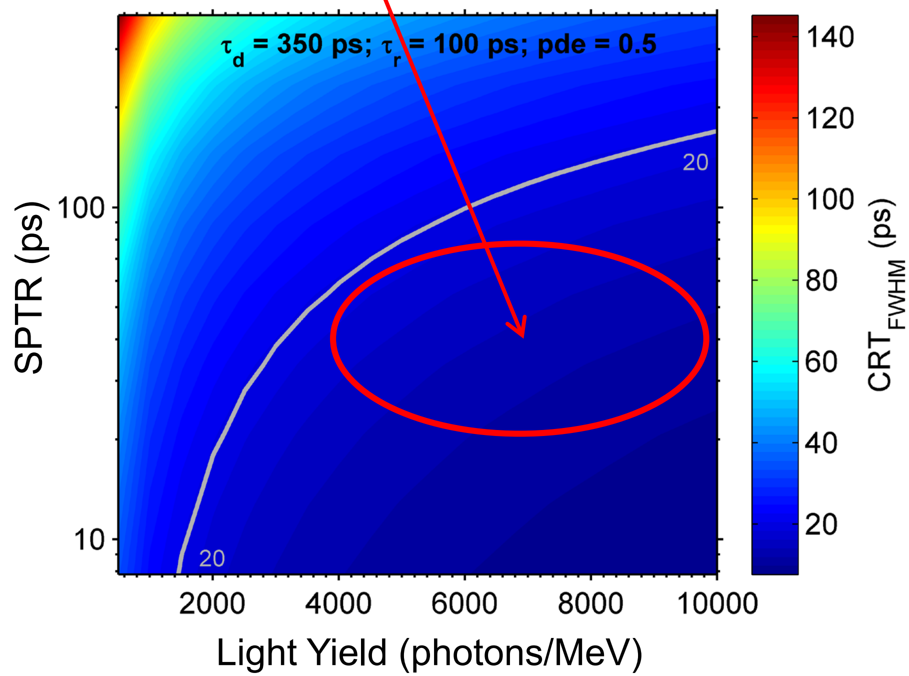
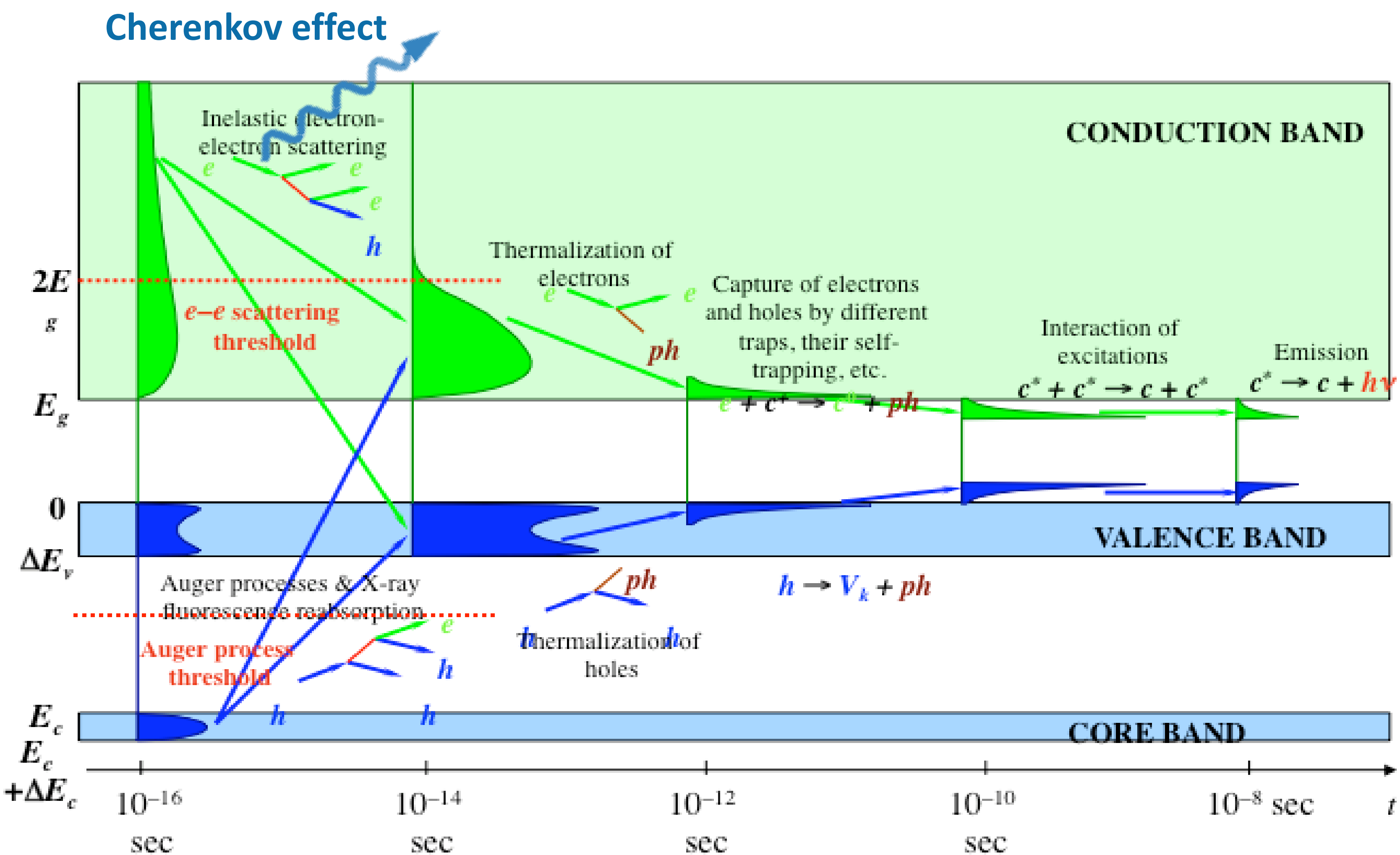


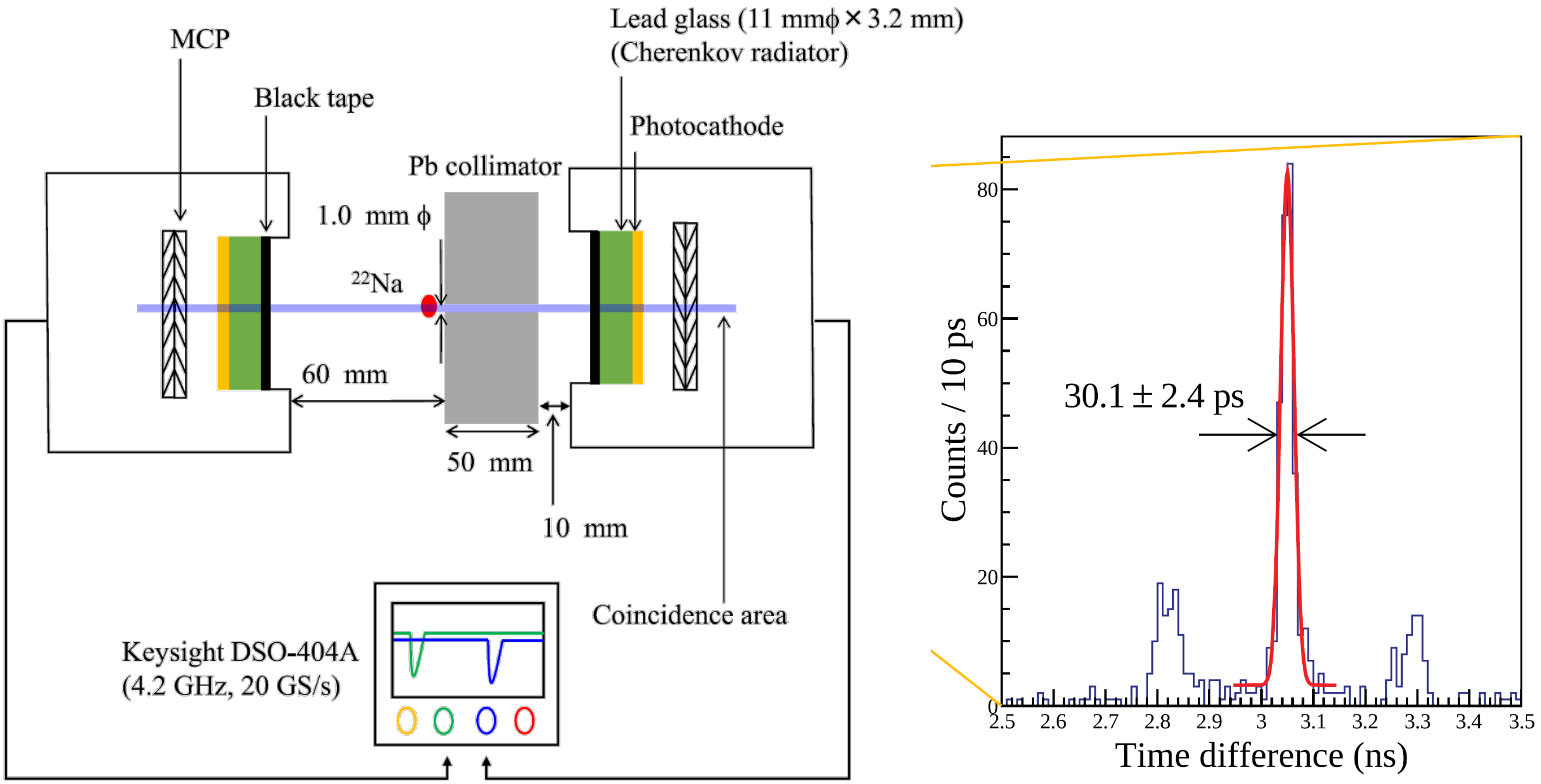
Figure: D.R. Schaart, "Scintillator needs for sub-100 ps PET," SCINT 2011

Other types of emission?



Based on: Vasil'ev, SCINT99

Best result with Cherenkov radiators so far

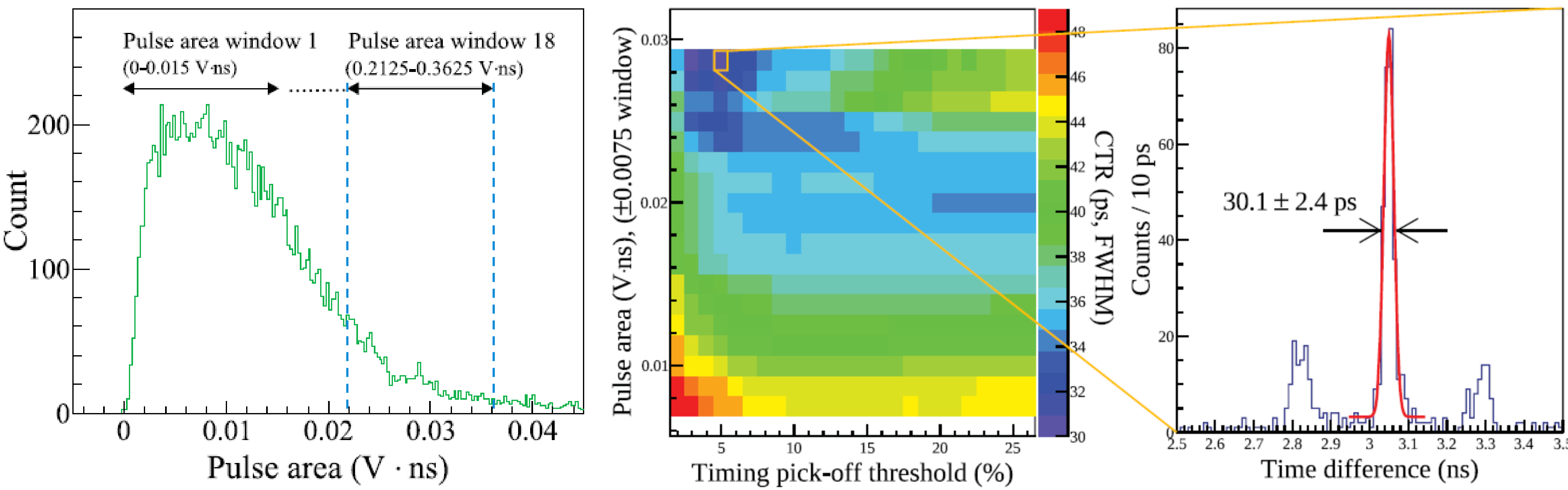


Ota 2019, Coincidence time resolution of 30 ps FWHM using a pair of Cherenkov-radiator-integrated MCP-PMTs, Phys Med Biol 64 07LT01

Best result with Cherenkov radiators so far

- MCP-PMT window replaced by 3.2 mm thick lead glass Cherenkov radiator
- Covered with black tape to suppress reflections
- 4.2 GHz bandwidth readout
- Event selection: events with max. no. of Cherenkov photons only

=> η_{det} very low, but results show that a CRT of ~30 ps FWHM is physically possible!



Dennis R. Schaart
Delft University of Technology

Ota 2019, Coincidence time resolution of 30 ps FWHM using a pair of Cherenkov-radiator-integrated MCP-PMTs, Phys Med Biol 64 07LT01

A FOM for rational detector design

$$\mathrm{FOM}_{\mathrm{det}} = \eta_{\mathrm{det}}^2 \frac{\eta_{\mathrm{geom}}}{\$} \frac{D}{\Delta t}$$

system geometrical efficiency

patient diameter

detection efficiency

total cost of detectors

CRT

Schaart 2021, Physics and Technology of Time-of-Flight PET Detectors, Phys Med Biol 66 09TR01

Faster is not always better…

A FOM for rational detector design

system geometrical efficiency

patient diameter

$$\mathrm{FOM}_{\mathrm{det}} = \eta_{\mathrm{det}}^{2} \frac{\eta_{\mathrm{geom}}}{\$} \frac{D}{\Delta t}$$

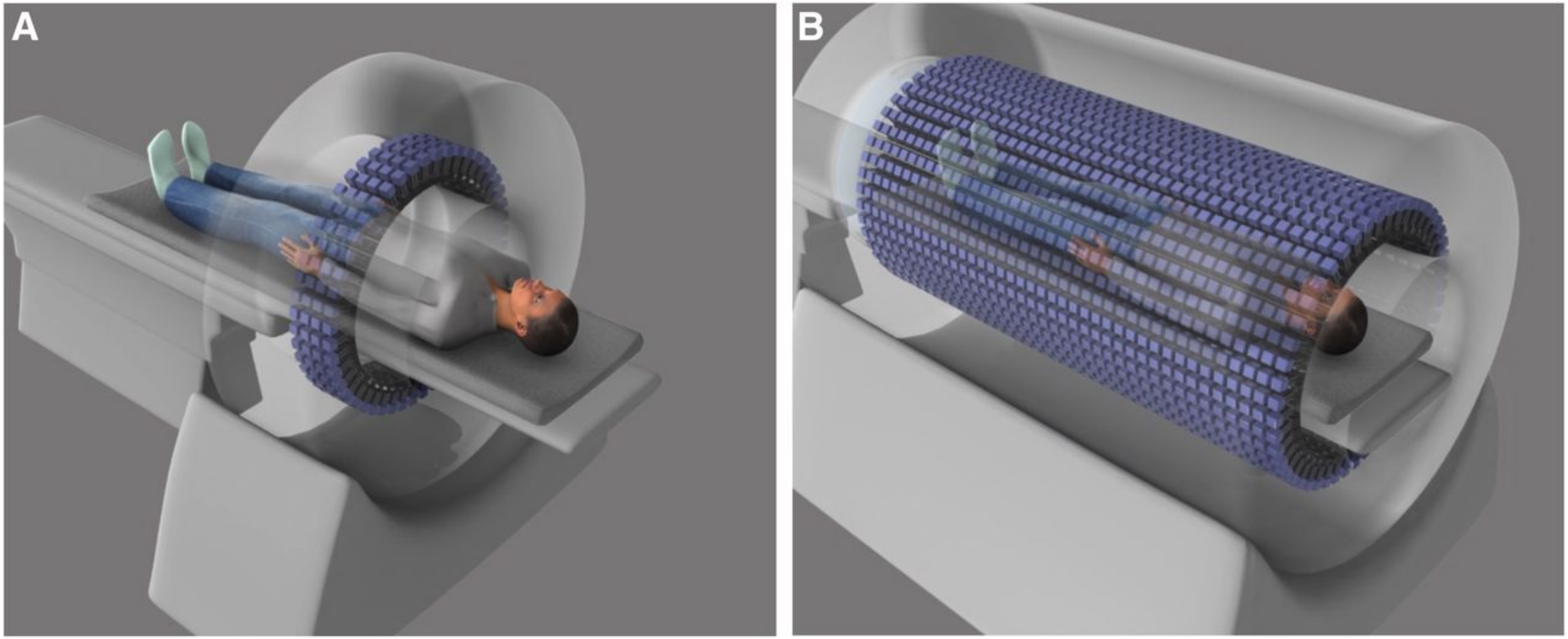
detection efficiency

CRT

total cost of detectors

Schaart 2021, Physics and Technology of Time-of-Flight PET Detectors, Phys Med Biol 66 09TR01

Total-body PET

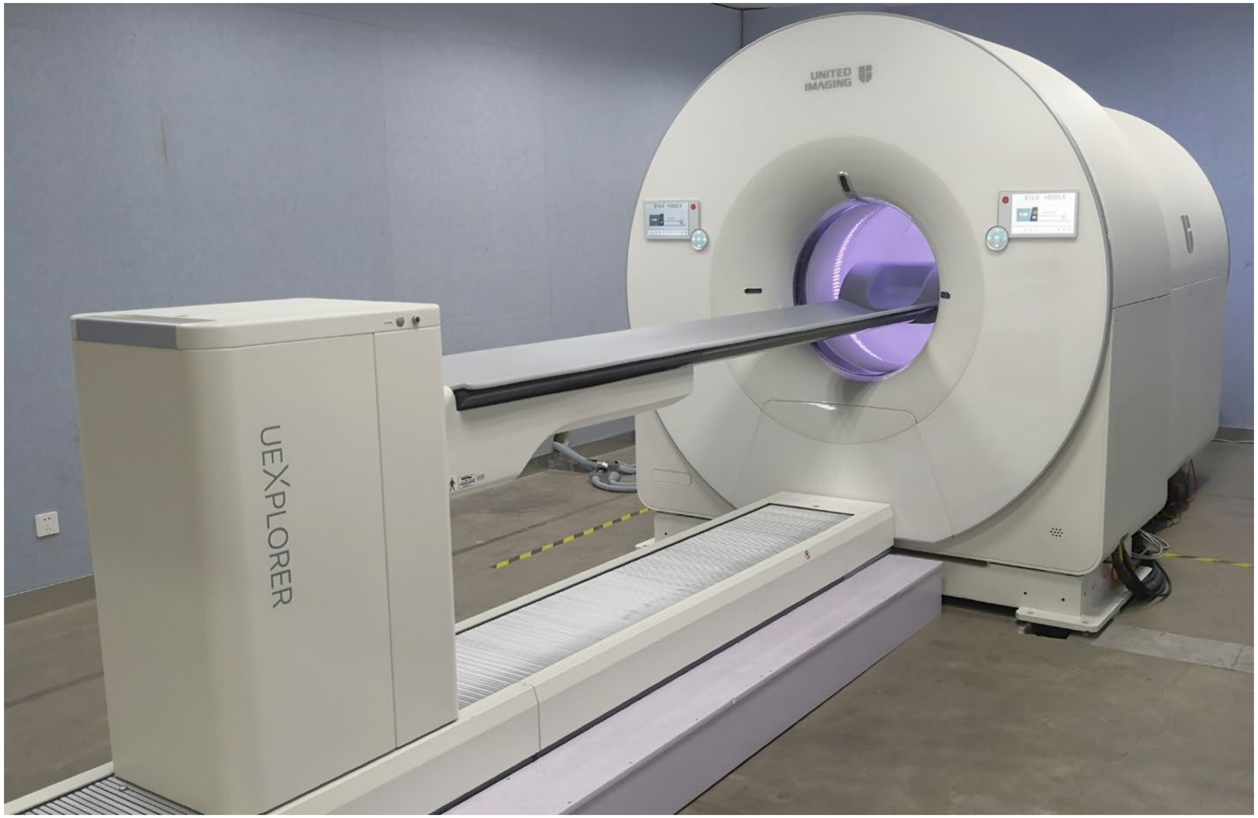


Conventional PET system

Total-body PET system

Total-body PET

Cost: ~$12M for first prototype, mainly determined by LYSO-based detectors



Berg *et al*, Total Body PET Workshop, Sydney 2018

A FOM for rational detector design

system geometrical efficiency

patient diameter

$$\mathrm{FOM}_{\mathrm{det}} = \eta_{\mathrm{det}}^{2} \frac{\eta_{\mathrm{geom}}}{\$} \frac{D}{\Delta t}$$

detection efficiency

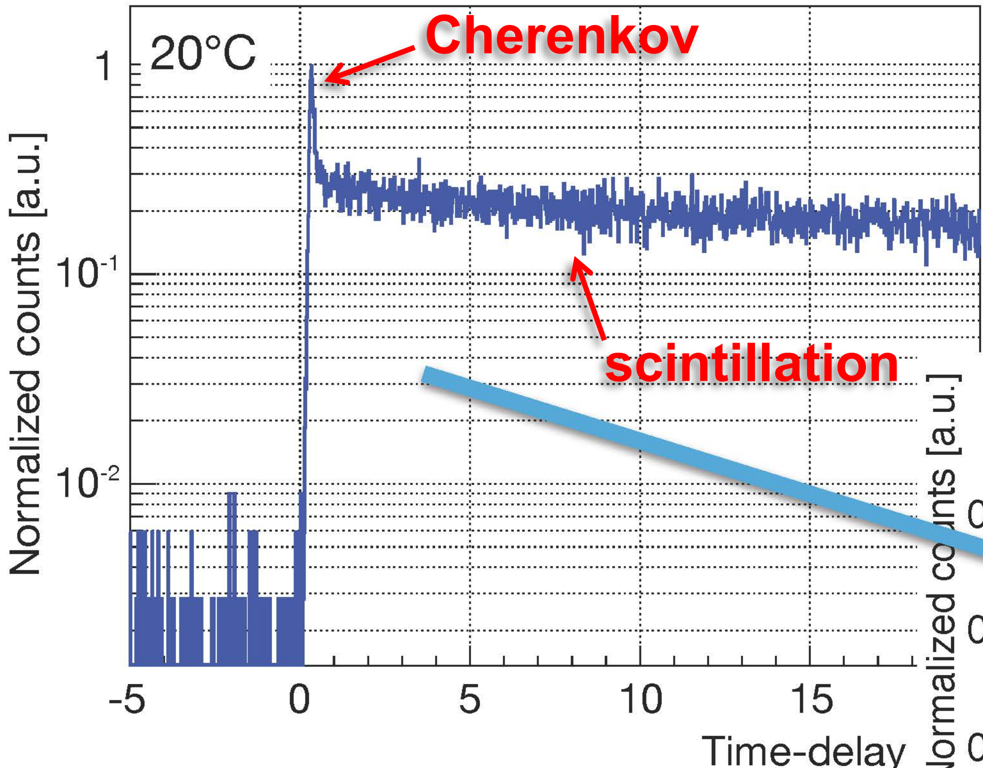
CRT

total cost of detectors

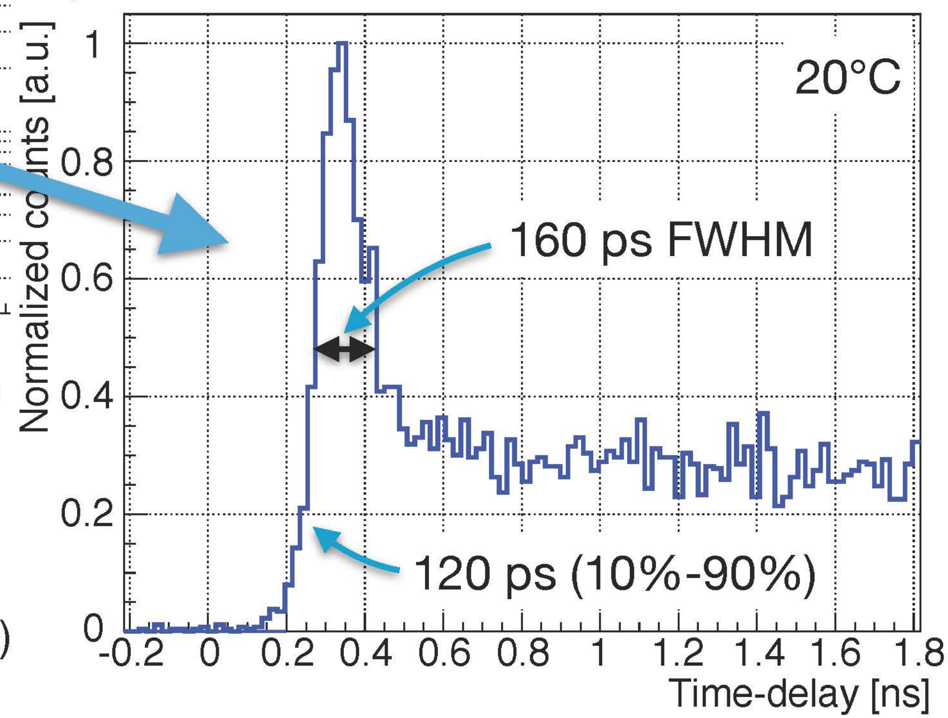
Schaart 2021, Physics and Technology of Time-of-Flight PET Detectors, Phys Med Biol 66 09TR01

A closer look at good old BGO

SiPMs enable taking timestamp from Cherenkov, energy from scintillation signal

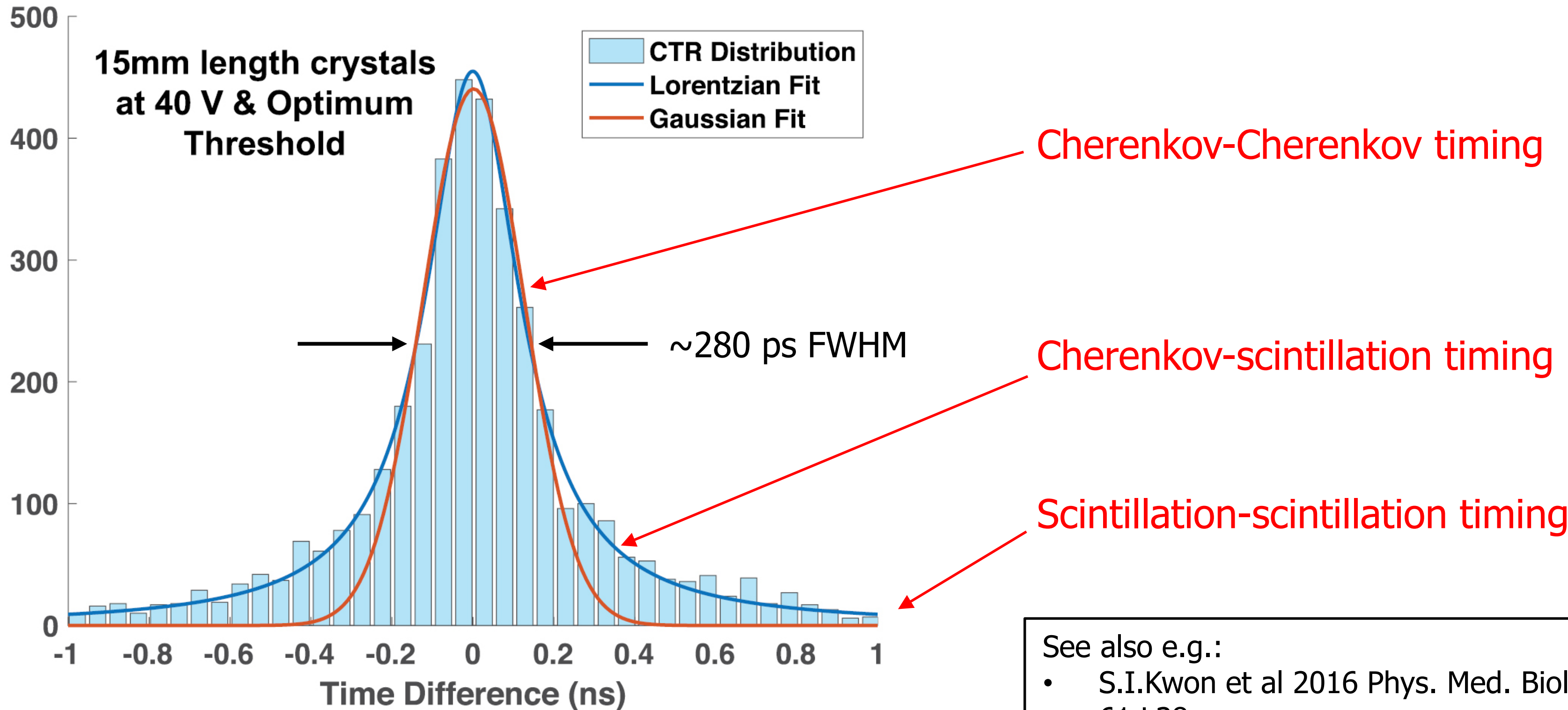


BGO luminescence response to 511 keV annihilation photons



- TCSPC using Philips DPC
- BGO (3 x 3 x 5 mm^3) in coincidence with LSO:Ce:Ca (3 x 3 x 5 mm^3)
- Event selection for 511 keV (start and stop)

Non-Gaussian timing spectra due to Cherenkov statistics



CTR distribution for 15 mm length BGO crystals with optimum SiPM bias and leading edge threshold with both Lorentzian (blue) and Gaussian (red) fits.

See also e.g.:

- S.I.Kwon et al 2016 Phys. Med. Biol. 61 L38
- S. Gundacker et al 2019 Phys. Med. Biol. 64 055012
- S.I. Kwon et al 2019 Phys. Med. Biol. 64 105007
- N. Kratochwil et al 2020 Phys. Med. Biol. 65 115004

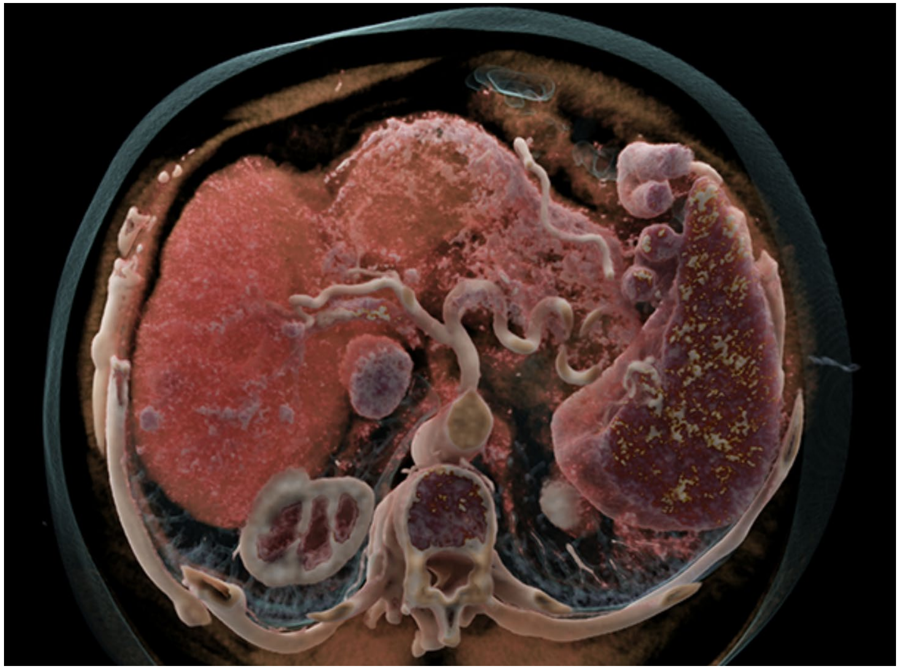
J.W. Cates and C.S. Levin 2019 Phys. Med. Biol. 64 175016


One more thing...

Photon-Counting CT (PCCT)

Energy-resolved X-ray detection enables tissue-resolved CT imaging

Siemens NAEOTOM Alpha
photon-counting CT scanner



Clinical PCCT image,
Erasmus Medical Centre,
Rotterdam, the Netherlands

Photon-Counting CT (PCCT)

Photon-counting detectors instead of energy-integrating detectors

- Count individual photons & assign them to an energy bin
- Many advantages: ‘The more information, the better’

Challenges?

- X-ray absorption efficiency (energies ≤ 150 keV)
- Pulse pile-up (fluence rate > 100 Mcps/mm^2)

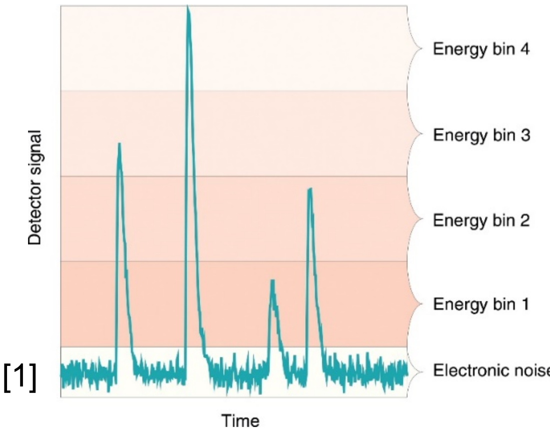
PCCT currently based on direct-conversion detectors

- CdTe/CZT: costly production; limited no. of manufacturers

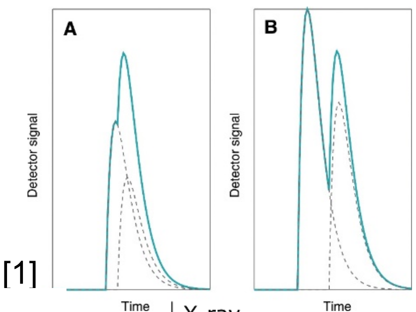
Silicon:

- Low density (2.3 g cm^{-3}) and atomic number (14)

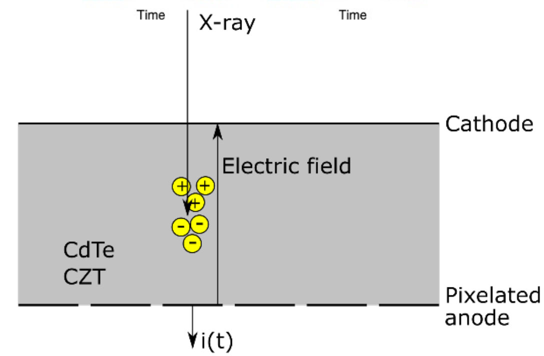
[1]



[1]



[2]



Fast pulses & pixel miniaturization

TUDelft
Dennis R. Schaart
Delft University of Technology

SiPM-based PCCT?

Silicon photomultiplier (SiPM)

- 1.0 x 1.0 mm^2 prototype from Broadcom Inc.
- Ultrafast single-SPAD response: $\tau_{recharge}$ = 7-10 ns

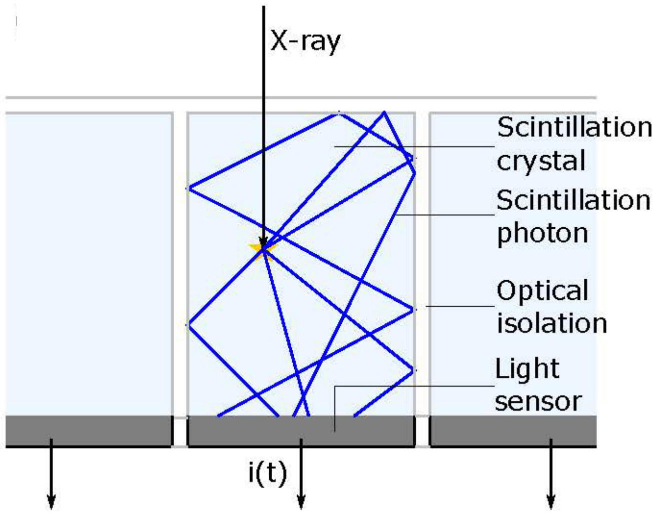
Crystals:

0.9 × 0.9 × 1.5 mm^3 $Lu_{1.8}Y_{0.2}SiO_5$:Ce (LYSO:Ce)

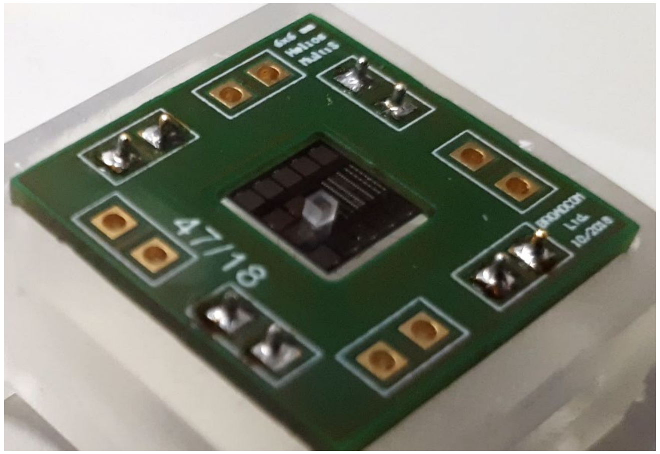
- 3.0 mm CdTe equivalent absorption efficiency
- τ_{decay} = 33 ns; positron emission tomography

0.9 × 0.9 × 4.5 mm^3 $YAlO_3$:Ce (YAP:Ce)

- 1.5 mm CdTe equivalent absorption efficiency
- τ_{decay} = 29 ns; commercially available material

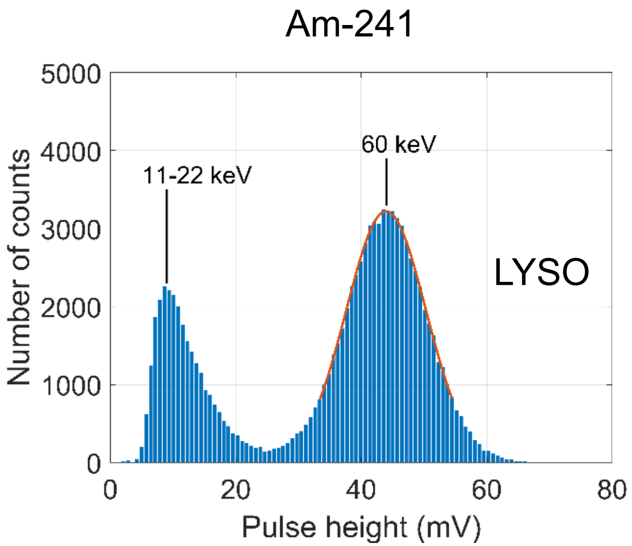


SiPM-based PCCT detector concept

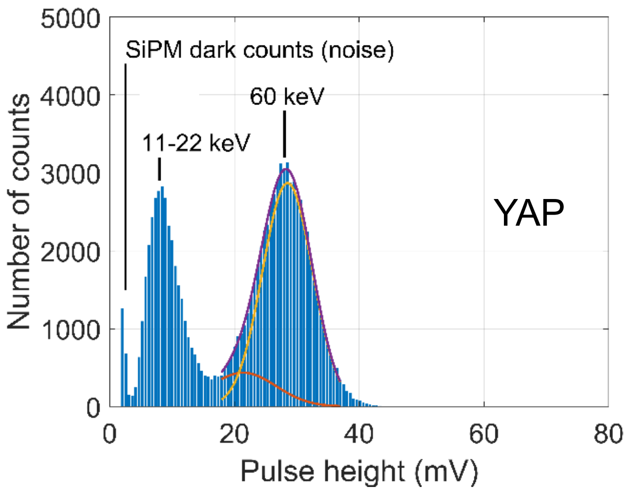


Single-pixel detector prototype

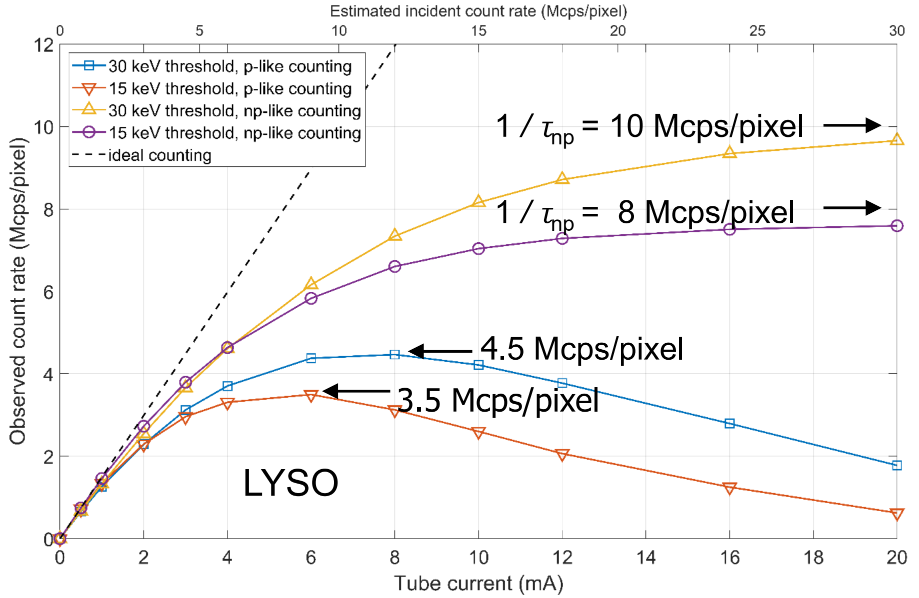
Results



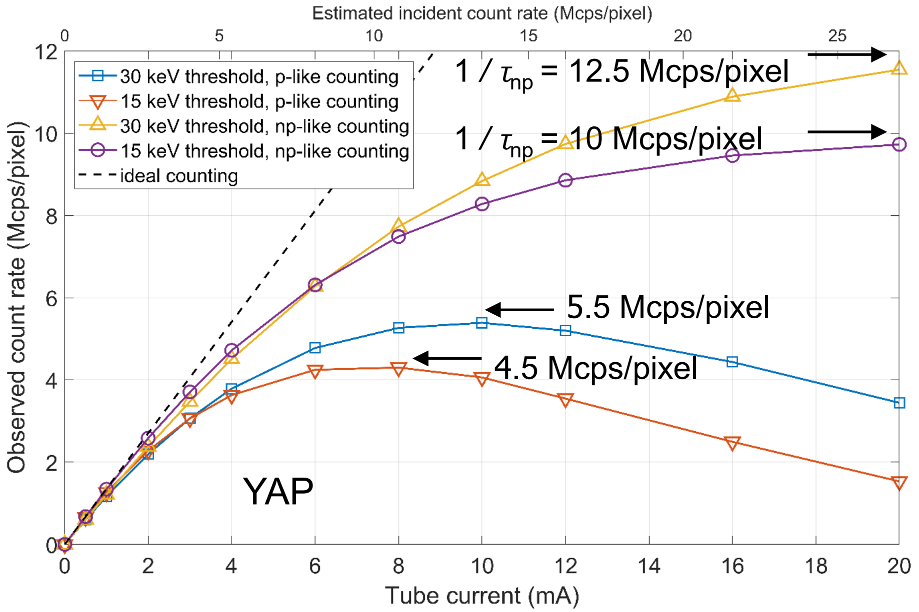
Am-241
11-22 keV
60 keV
LYSO
Number of counts
Pulse height (mV)



SiPM dark counts (noise)
11-22 keV
60 keV
YAP
Number of counts
Pulse height (mV)



Estimated incident count rate (Mcps/pixel)
30 keV threshold, p-like counting
15 keV threshold, p-like counting
30 keV threshold, np-like counting
15 keV threshold, np-like counting
ideal counting
$1 / \tau_{np}$ = 10 Mcps/pixel
$1 / \tau_{np}$ = 8 Mcps/pixel
4.5 Mcps/pixel
3.5 Mcps/pixel
LYSO
Observed count rate (Mcps/pixel)
Tube current (mA)



Estimated incident count rate (Mcps/pixel)
30 keV threshold, p-like counting
15 keV threshold, p-like counting
30 keV threshold, np-like counting
15 keV threshold, np-like counting
ideal counting
$1 / \tau_{np}$ = 12.5 Mcps/pixel
$1 / \tau_{np}$ = 10 Mcps/pixel
5.5 Mcps/pixel
4.5 Mcps/pixel
YAP
Observed count rate (Mcps/pixel)
Tube current (mA)

Thank you!