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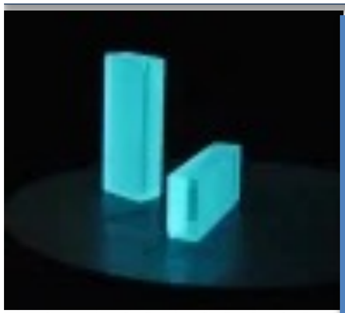
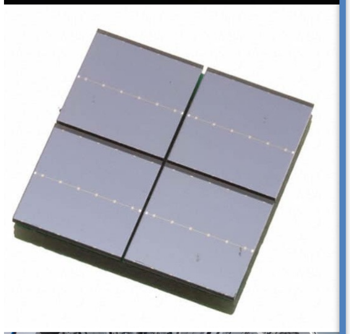
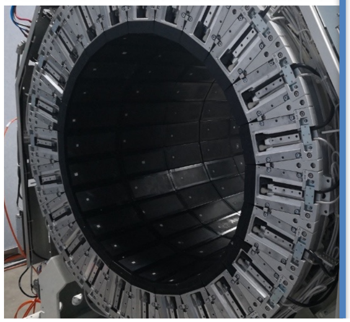
Advancing Medical Care through Discovery in the Physical Sciences
DOE/NIH Workshop, July 12-13, 2021





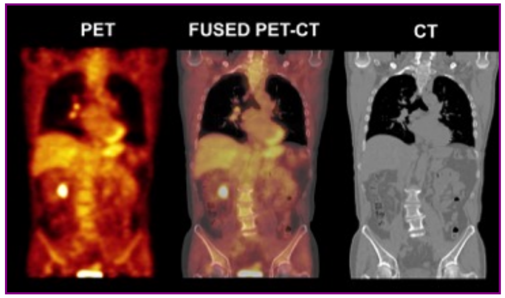


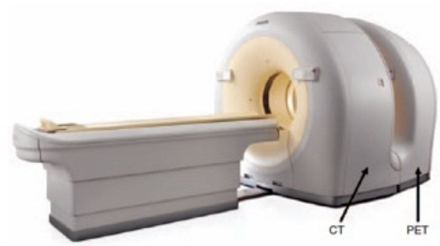
Crystals, Cameras and Detectors: State-of-the-Art Challenges and Emerging Technologies

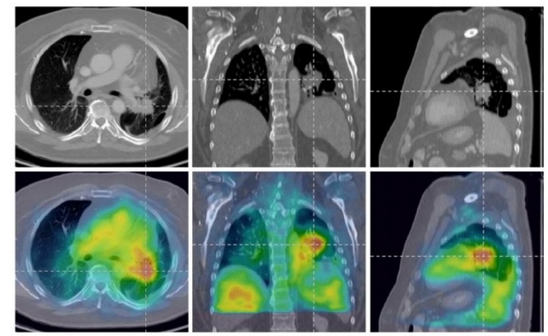
Simon R. Cherry

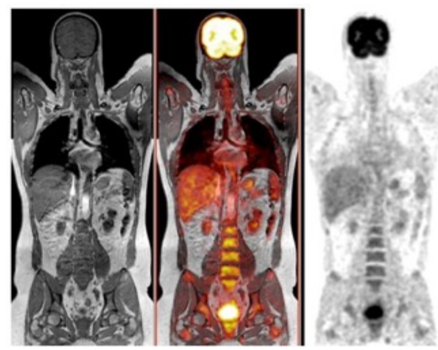
Departments of Biomedical Engineering and Radiology, UC Davis

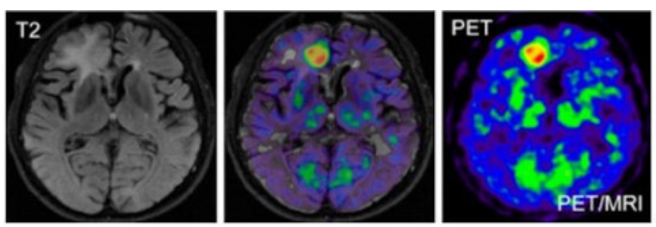
Clinical PET/CT, PET/MR, SPECT/CT





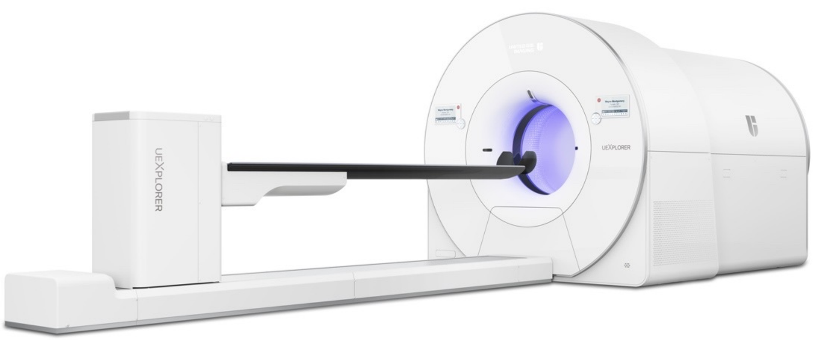



Total-Body and Long Axial FOV PET Scanners

Large increases in geometric collection efficiency lead to unprecedented image quality

Enables very fast imaging or low dose imaging

Need: Cost reduction

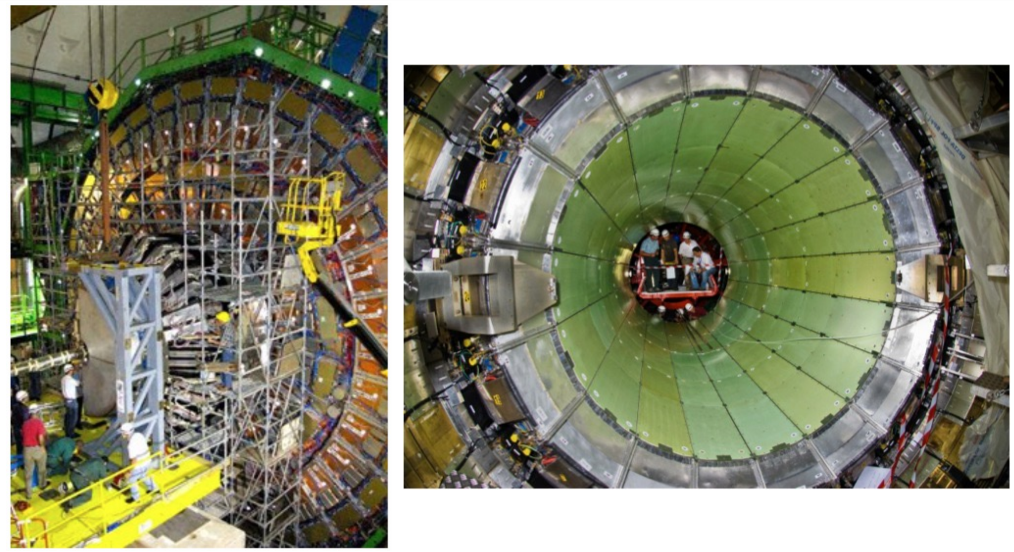


PennPET EXPLORER (140 cm)

Siemens Vision Quadra (106 cm)

UIH uEXPLORER (194 cm)

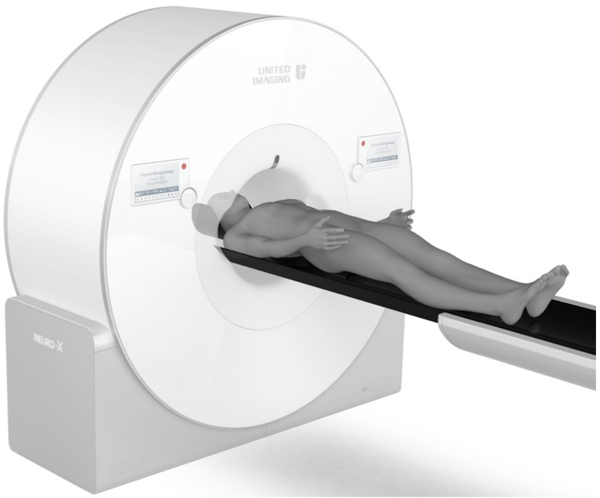
Latest generation PET scanners are complex instruments!



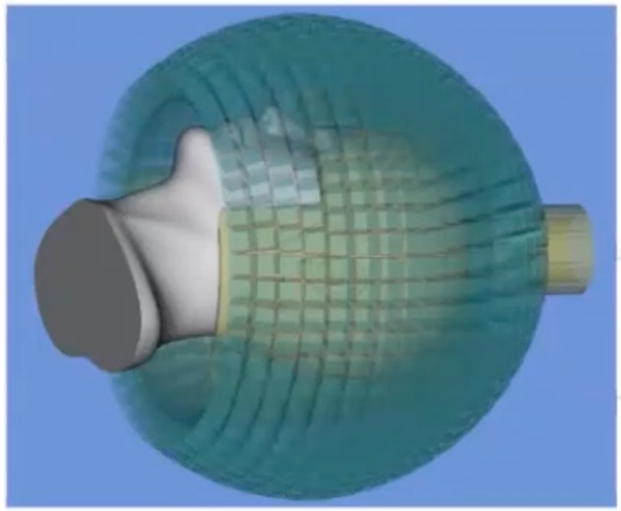
uEXPLORER
# of crystals: 564,480
# of photodetectors: 53,760
# of electronic channels: 53,760
Mass: ~11,000 kg

CMS EM Calorimeter at CERN
# of crystals: 75,848
# of photodetectors: 137,048
# of electronic channels: 75,848
Mass: ~100,000 kg

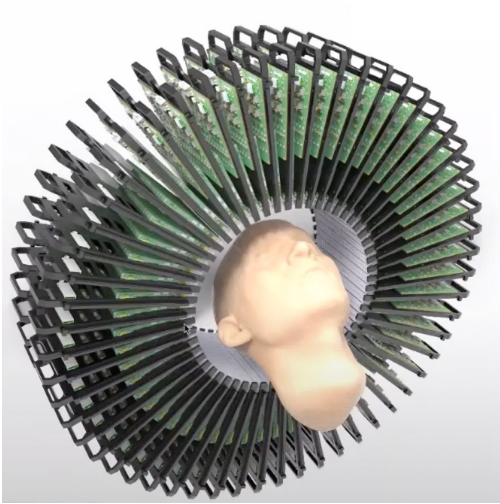
Next Generation Brain PET



neuroEXPLORER
PI: Richard Carson, Yale



HSTR
PI: Ciprian Catana, MGH

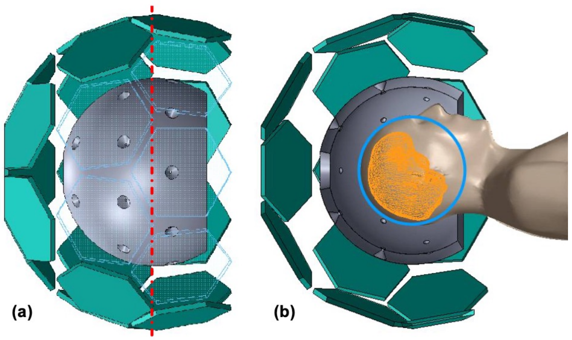


SAVANT
PI: Georges El Fakhri, MGH

Efforts are focusing on some combination of improved:
spatial resolution (with depth encoding), sensitivity, time of flight performance
Needs: Detectors that can deliver on all four at a reasonable cost

SPECT Imaging

Brain SPECT

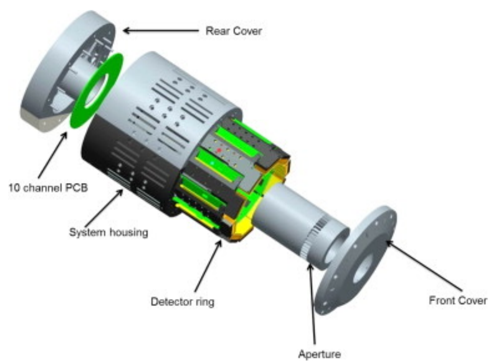


Zeratkaar et al, *IEEE Trans Med Imag 39*: 4209 (2020)

CZT-based SPECT systems
(e.g. VERITON, Spectrum Dynamics)

Desmonts et al, *EJNMMI Physics* 7: 18 (2020)

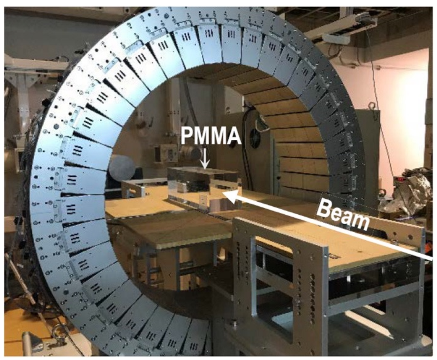
Preclinical SPECT/MRI

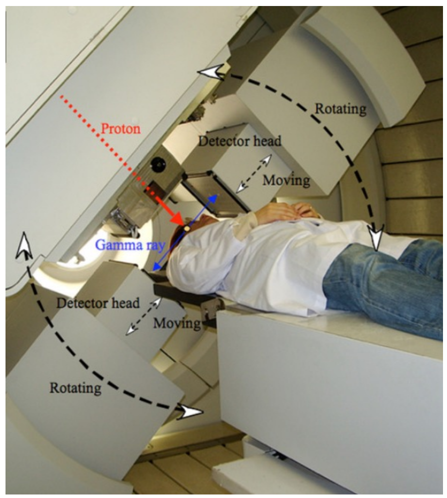


Lai et al, *Phys Med Biol 63*: 045008 (2018)

Proton and Ion Beam Range Verification

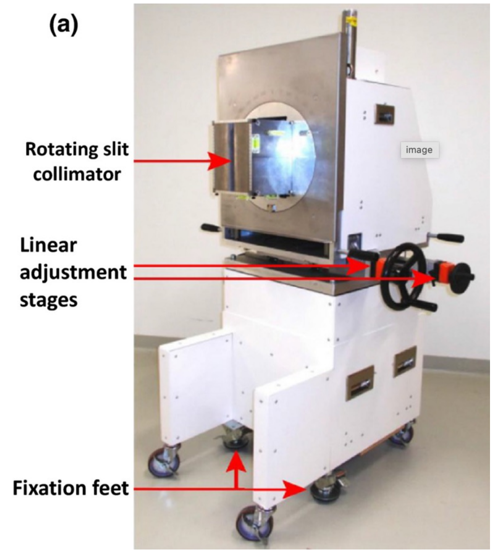
Coincidence (PET) Imaging

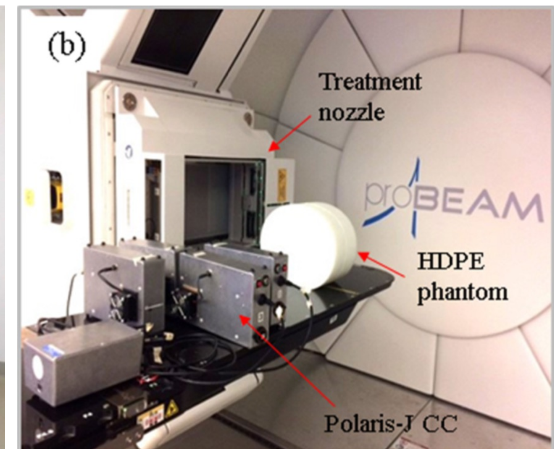




Mohammadi et al, *Phys Med Biol* 64; 145014 (2019)
Shao et al, *Phys Med Biol* 59; 3373 (2014)
Nishio et al, *Int J Radiat Oncol Biol Phys* 76; 277 (2010)

Prompt Gamma Imaging
(Collimated gamma camera or Compton camera)

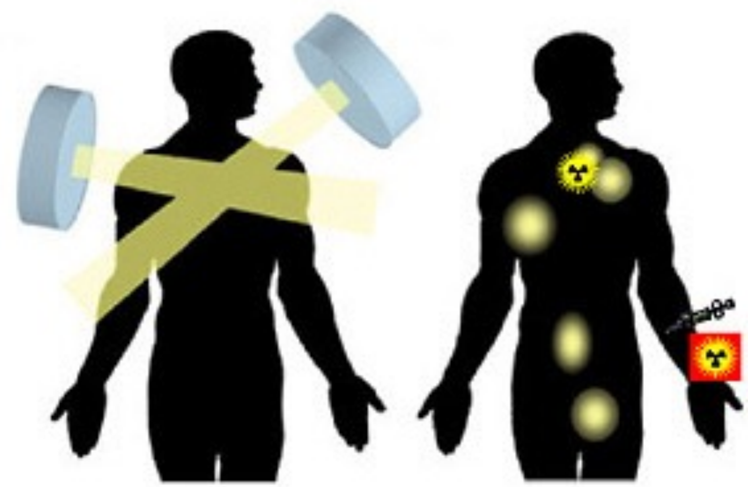




Richter et al, *Radiother Oncol* 118; 232 (2016)
Draeger et al, *Phys Med Biol* 63; 035019 (2018)

Radiation Therapy tomorrow?

- Deliver radiation internally!
  - Emergence of effective theranostic agents
  - Treat what you can't see
  - Eliminates motion and misregistration issue
- Challenges and opportunities:
  - Dosimetry and treatment planning
    - Imaging before treatment
  - Real-time imaging during treatment
    - Modulate dose given based on imaging?
  - Dose verification
    - Imaging after treatment

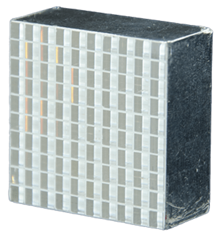


Courtesy Michael Zalutsky, Duke University

Opportunity: Optimal systems for whole-body Lu-177 imaging:
Gamma emissions at 208 keV (11%) and 113 keV (6.6%)

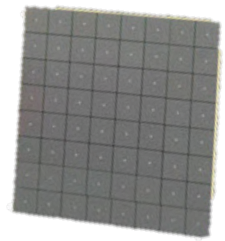
Radiation Detectors

annihilation photons or gamma ray



signal generation

scintillator



signal detection

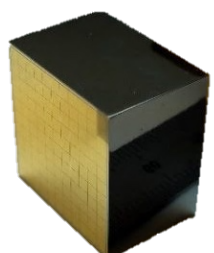
photodetector

signal processing/ analysis

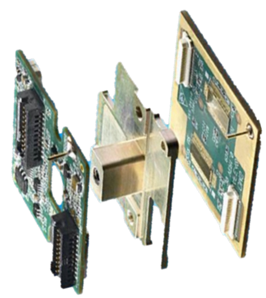
electronics

PET	LSO/LYSO	SiPM	ASIC
SPECT	NaI(Tl)	PMTs	ASIC/discrete

gamma ray



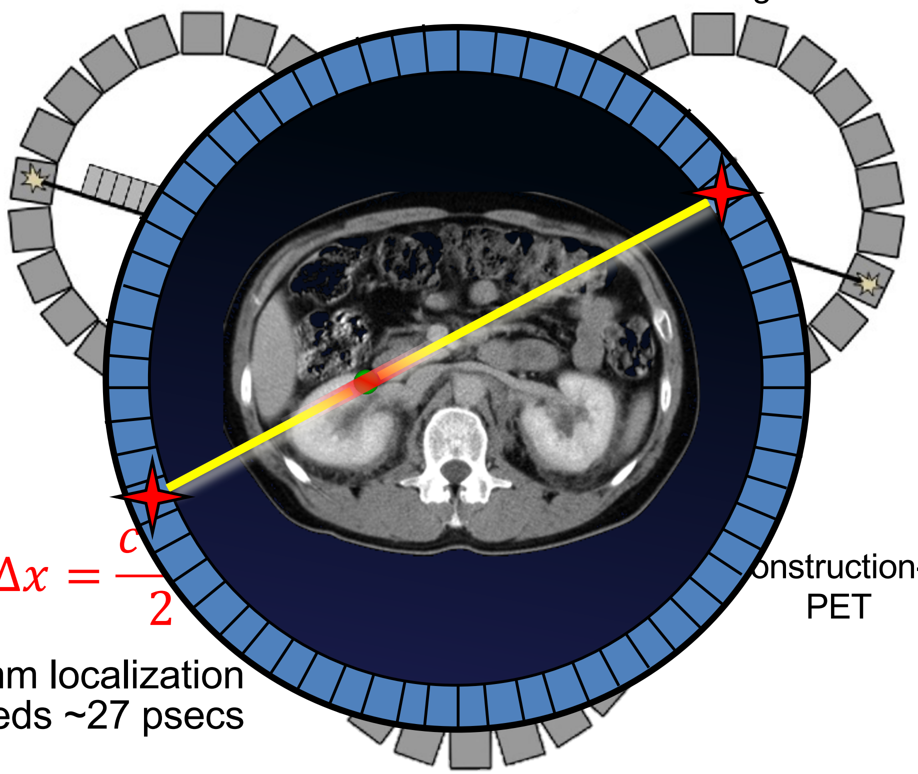
semiconductor



electronics

SPECT	CZT	ASIC

Time-of-Flight (TOF) PET



$\Delta x = \frac{c}{2}$

4 mm localization needs ~27 psecs

Sensitivity Gain ~ $\frac{2D}{c\,\Delta t}$

(for 30 cm object)

No TOF	1
500 ps	4
400 ps	5
300 ps	6.66
200 ps	10
100 ps	20
50 ps	40
25 ps	80

Adapted from Vandenberghe *et al*, EJNMMI Physics (2016) 3:3

Improving Timing Resolution

Material	Center emissions (nm)	Crystal size (mm^3)	SiPM used	Weighted PDE (%)[a]	CTR (ps)
LSO:Ce:0.2%Ca	420	$2 \times 2 \times 3$	NUV-HD 40 μm	59 ± 3	60 ± 3
LSO:Ce:0.2%Ca	420	$2 \times 2 \times 20$	NUV-HD 40 μm	59 ± 3	98 ± 3
LSO:Ce:0.4%Ca	420	$2 \times 2 \times 3$	NUV-HD 40 μm	59 ± 3	58 ± 3
LYSO:Ce	420	$2 \times 2 \times 3$	NUV-HD 40 μm	59 ± 3	69 ± 3
BGO	480	$2 \times 2 \times 3$	NUV-HD 40 μm	47 ± 3	158 ± 3
BGO	480	$2 \times 2 \times 20$	NUV-HD 40 μm	47 ± 3	277 ± 3
BaF_2	195/220 (fast)	$2 \times 2 \times 3$	VUV-HD 40 μm	$\sim 22 \pm 5$[b]	51 ± 3

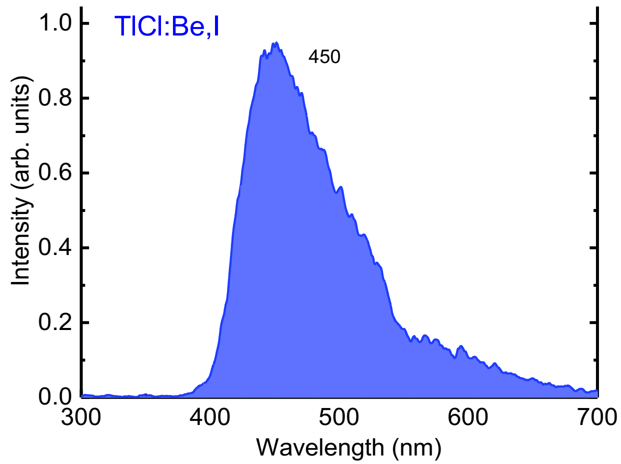
Gundacker et al, *Phys Med Biol* 65; 025001 (2020)

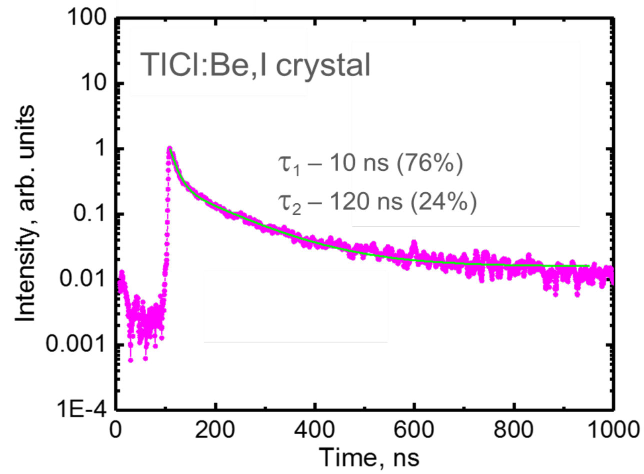
How to get to 20-30 ps?

- Incrementally through improvements in scintillators, light collection, photodetectors, electronics
- New approaches for signal generation, conversion and/or detection

New Scintillators: TlCl(Be,I)

Material	Density (g/cm³)	Effective Z (Z_{eff})	511 keV length (cm)	511 keV photo-fraction	Melting Point (°C)	Light Yield (ph/MeV)	Emission Wavelength (nm)	Decay time (ns)
BGO	7.1	73	1.09	42	1050	8,200	480	300
LSO:Ce	7.4	66	1.15	33	2050	30,000	420	40
TlCl:(Be,I)	7	77	0.97	46	430	~2,000	450	≤10

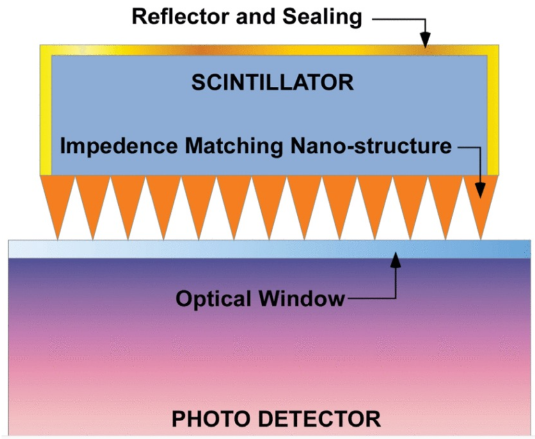


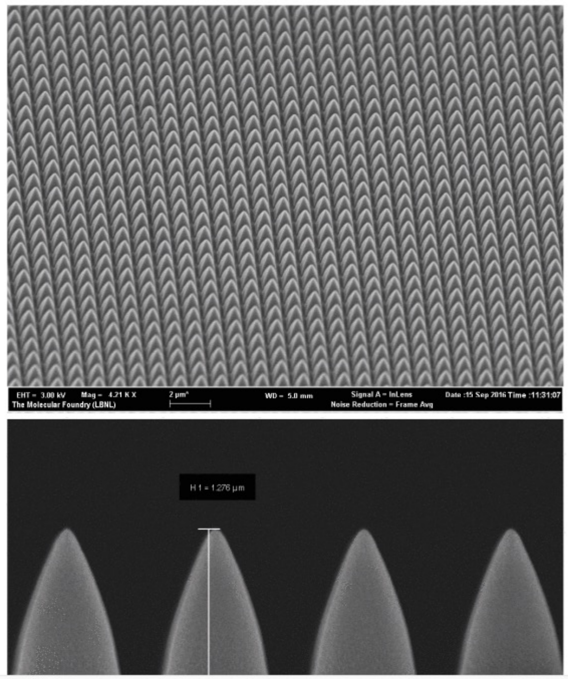


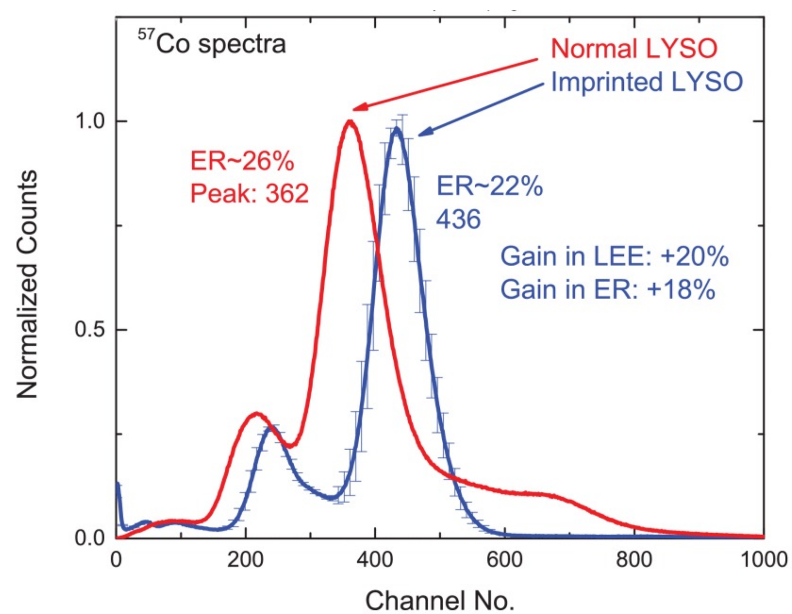
RMD
A Dynasil Company

Significance: Not lutetium-based (cost, background)
Exceptional stopping power and decay time

Photonic Structures to Improve Light Collection





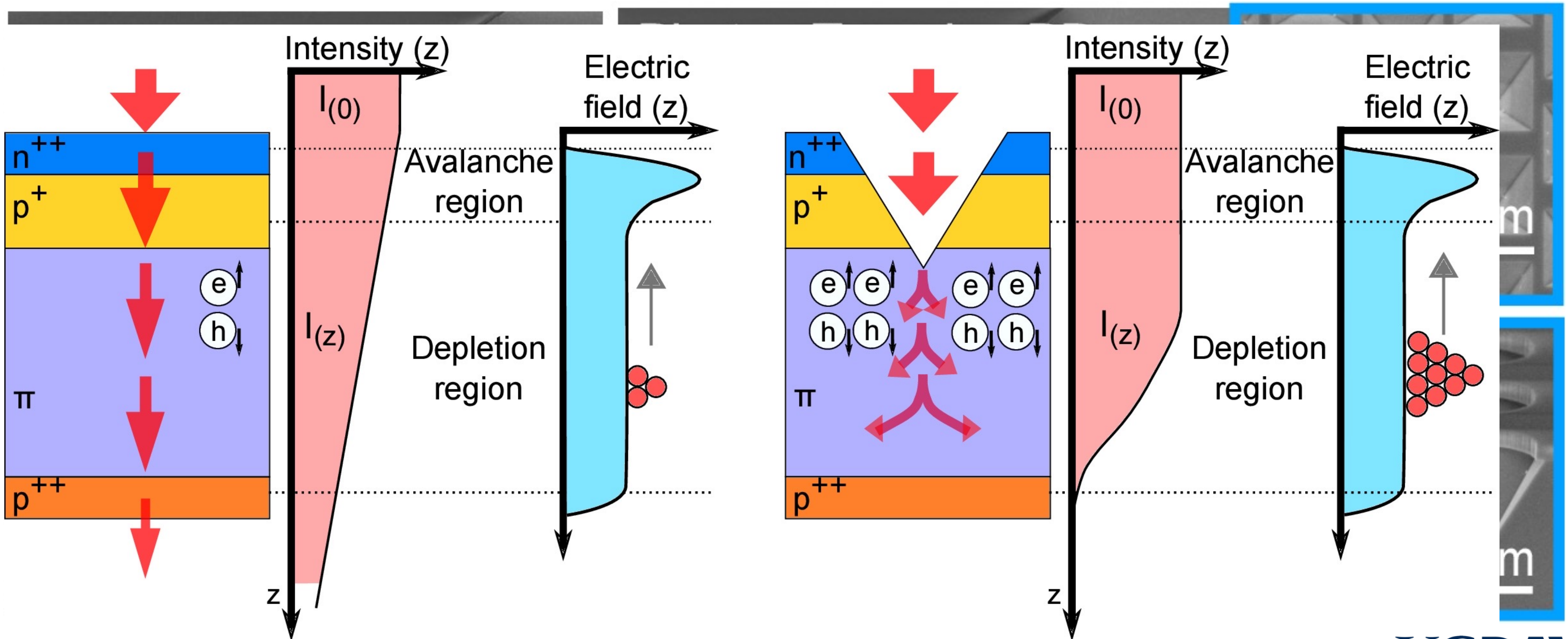


Singh et al, *IEEE Trans Nucl Sc*i 65; 1059 (2018)

Photon Trapping SiPM Architectures

Control photodiode

Photon trapping photodiode



Bartolo-Perez et al, *Optics Express* 29: 19024 (2021)

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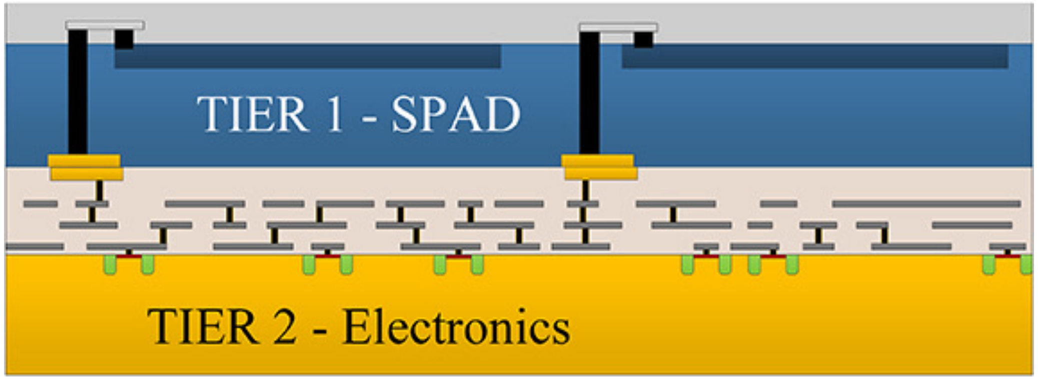
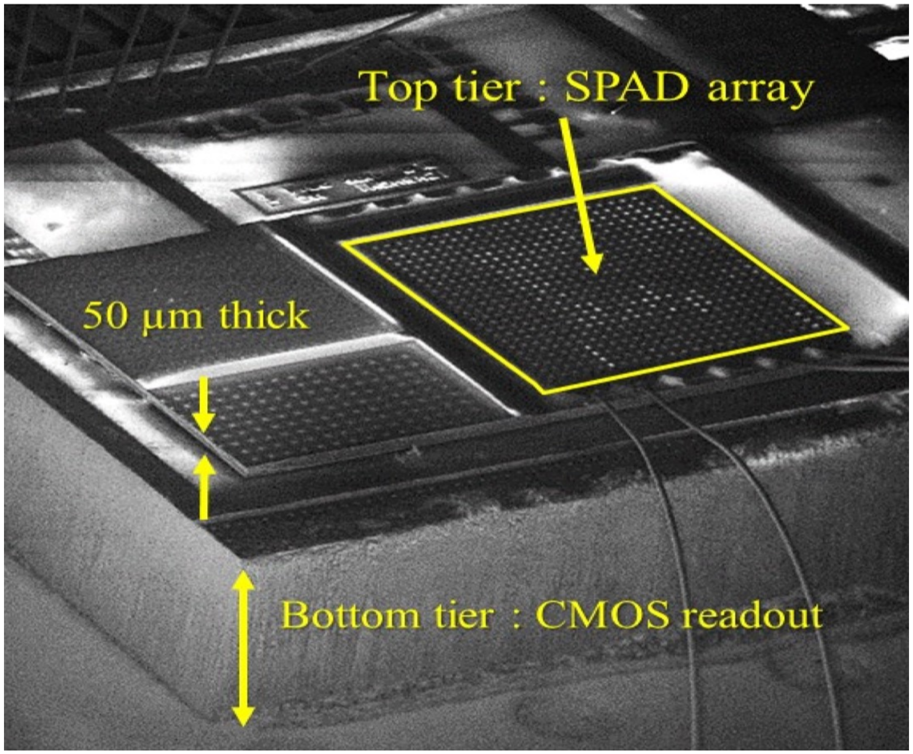
3-D Silicon Photomultipliers

Integrated CMOS electronics

Vertical integration retains high fill factor for photosensitive area

Realize timing performance of individual SPADs (<10 ps SPTR?)





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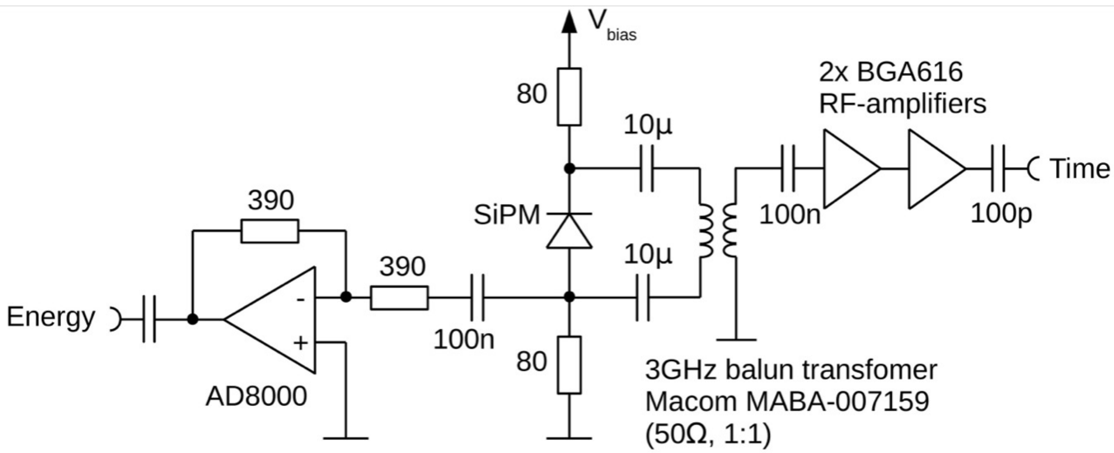
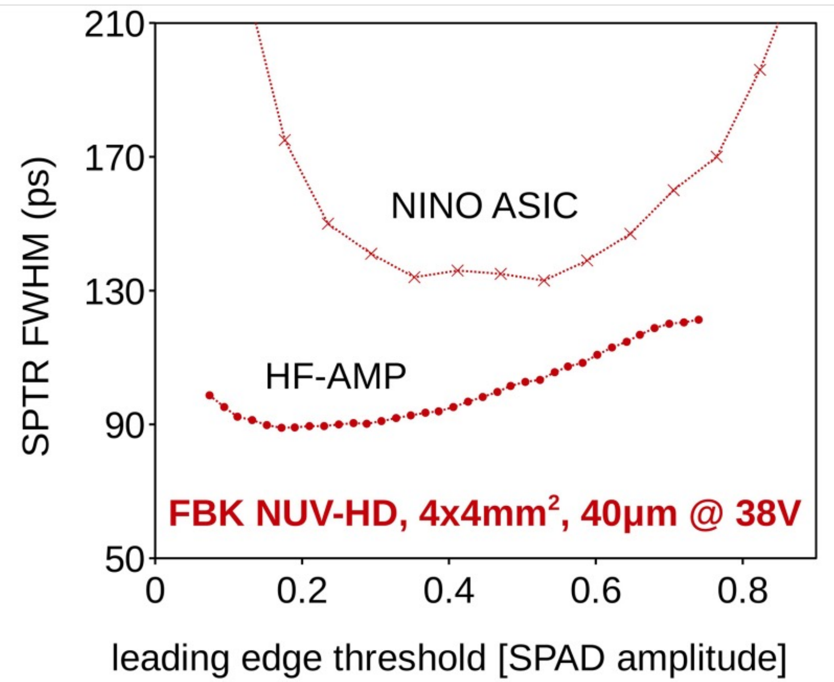
Pratte et al, *Sensors* 21; 598 (2021)

High-Frequency Amplifiers





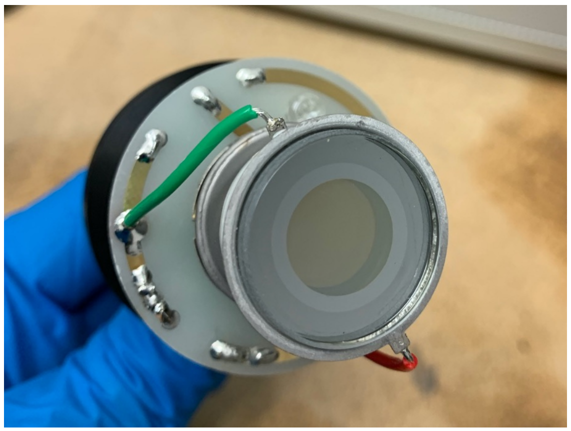
Cates et al, *Phys Med Biol* 63; 185022 (2018)
Gundacker et al, *Phys Med Biol* 64; 055012 (2019)

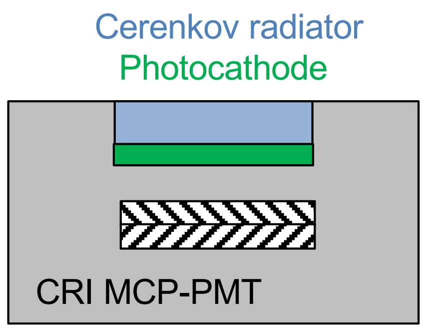
Different Luminescence Mechanisms?

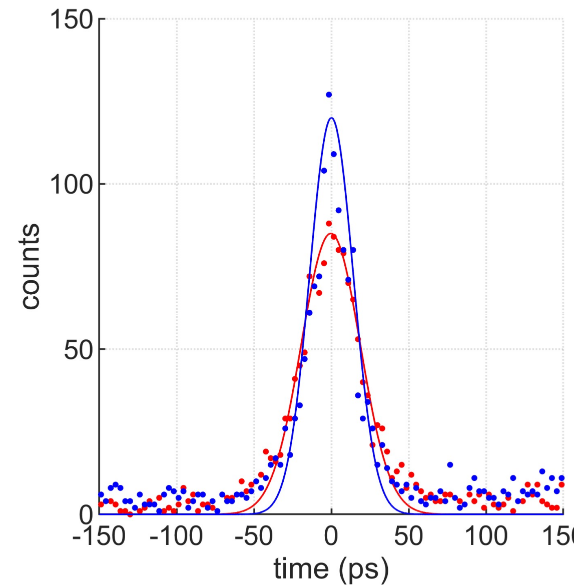
- Scintillation
  - Bright, but relatively slow in terms of initial photon flux (photons/ps)
- Cerenkov
  - Fast, prompt emission, but relatively few photons (~10-20)
- Other
  - Hot intraband luminescence
  - Quantum confinement in nanoscintillators

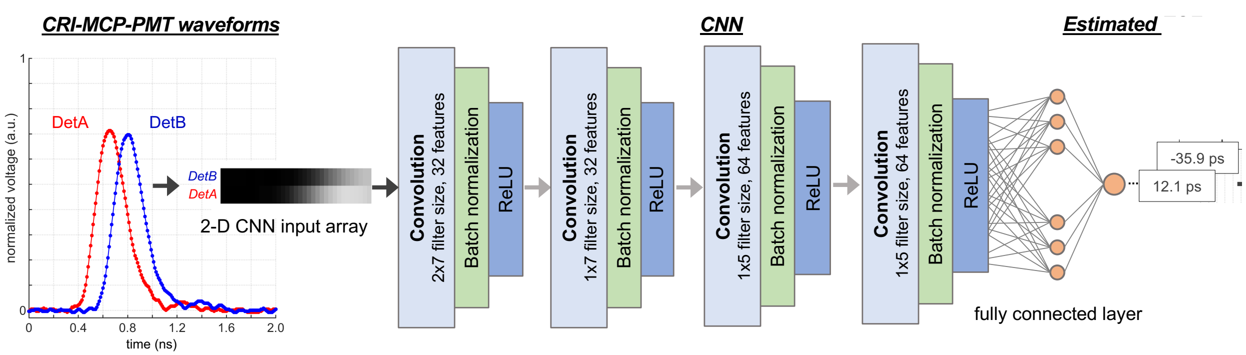
Lecoq, *IEEE Trans Rad Plasma Med Sci* 1; 473 (2017)

MCP-PMTs with Integrated Cerenkov Radiator and Deep Learning Timing Estimation









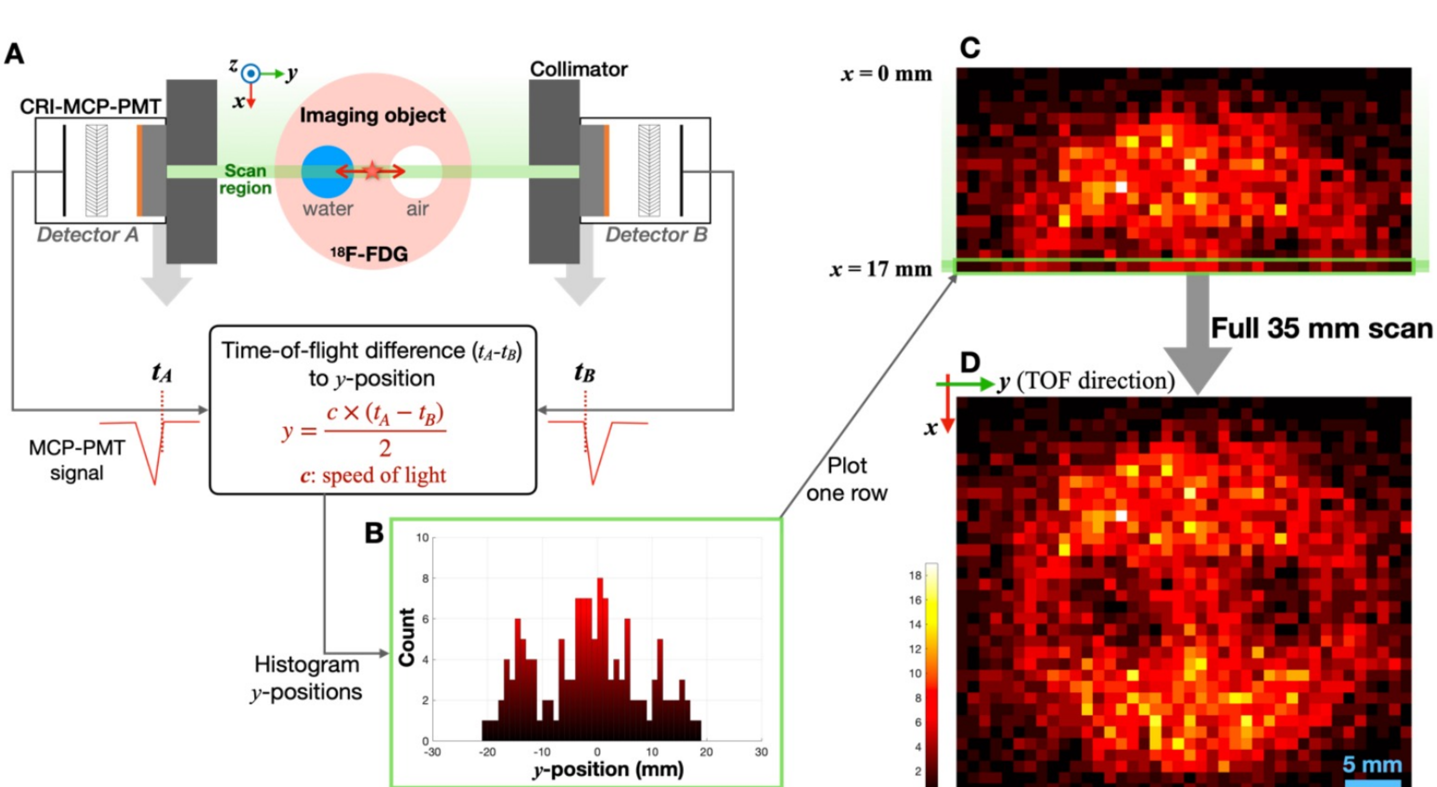
34.8 ps FWHM (leading edge)

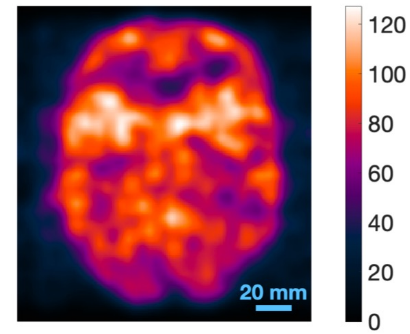
26.2 ps FWHM (CNN)

Sun Il Kwon and Eric Berg — UC DAVIS, UNIVERSITY OF CALIFORNIA

Ryosuke Ota and Tomohide Omura — HAMAMATSU

Reconstruction Free Imaging of Positron Emitters





Ota et al, *arXiv* 21.05.058052021 (2021)

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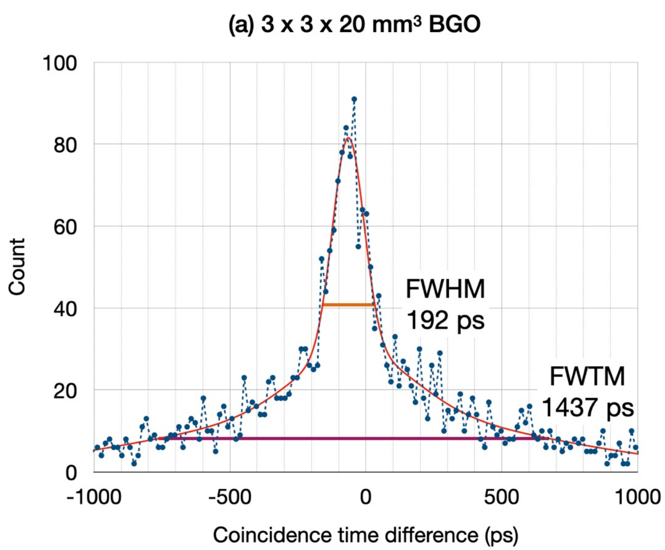
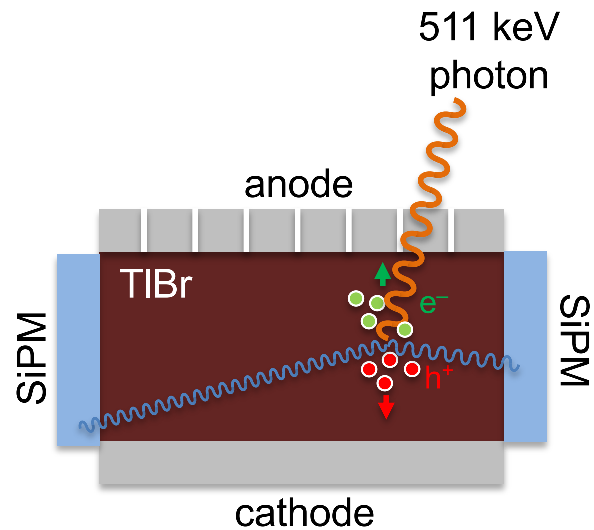
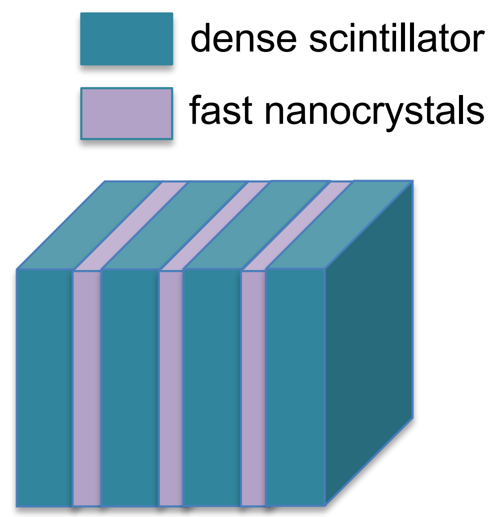
Hybrid Radiation Detectors



Cerenkov-scintillation
(BGO)



Cerenkov-semiconductor
(TlBr)



Metamaterials
Nanocrystals-scintillator

Kwon et al, *Phys Med Biol* 61; L38 (2016)
Kwon et al, IEEE MIC (2020)

Ariño-Estrada et al, *Phys Med Biol* 63; 04LT01 (2018)

Turtos et al, *Phys Med Biol* 64; 185018 (2019)

Summary

There is lots going on and many opportunities!

- New cameras are being developed:
  - Long axial FOV / total-body PET scanners
  - High performance brain PET/SPECT imagers
  - Preclinical systems, proton range verification etc….
  - Opportunity: Systems optimized for theranostics (Lu-177)
- Timing is a major emphasis in PET development
  - At ~30 psecs reconstructionless PET becomes possible
- Explore different luminescence mechanisms
- New SiPM architectures (3D digital, photon trapping structures)
- New detector materials (<cost?) and hybrid radiation detectors
- Integrating deep learning into detector signal processing