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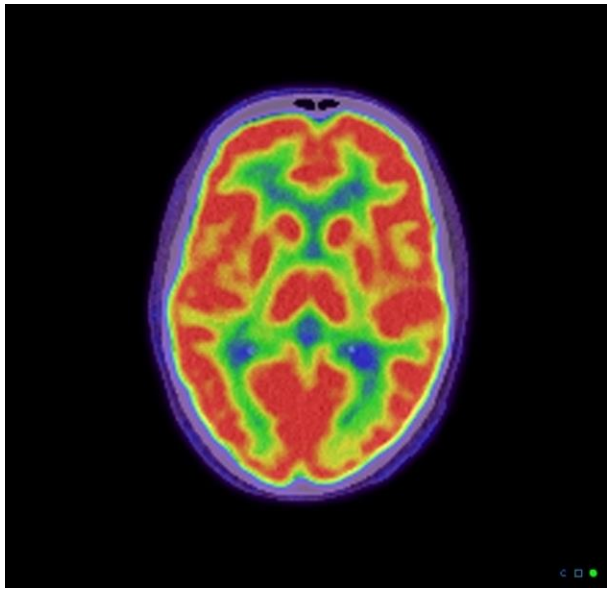
Univerza v Ljubljani
Fakulteta za matematiko in fiziko

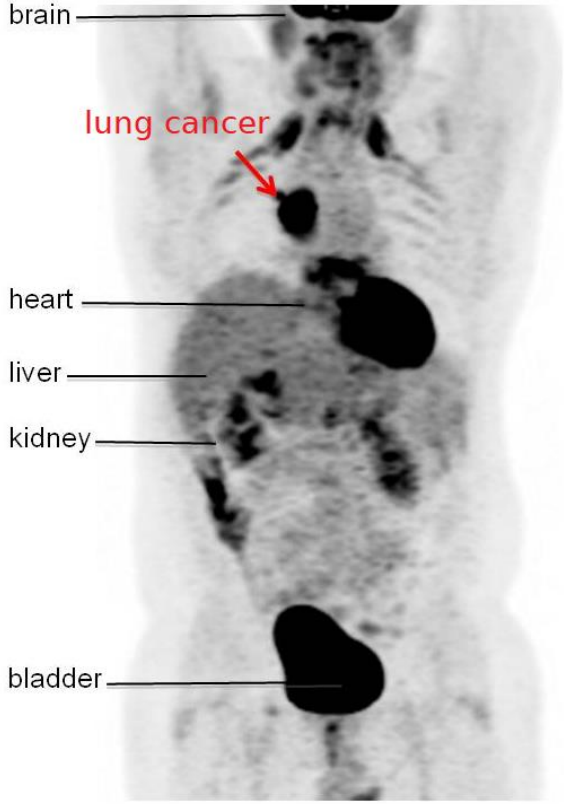
Thesis topic defense: Positron emission tomography with ultra-fast flat panel detectors

Author: Matic Orehar
Mentor: assist. prof. dr. Rok Dolenec

Positron emission tomography (PET)

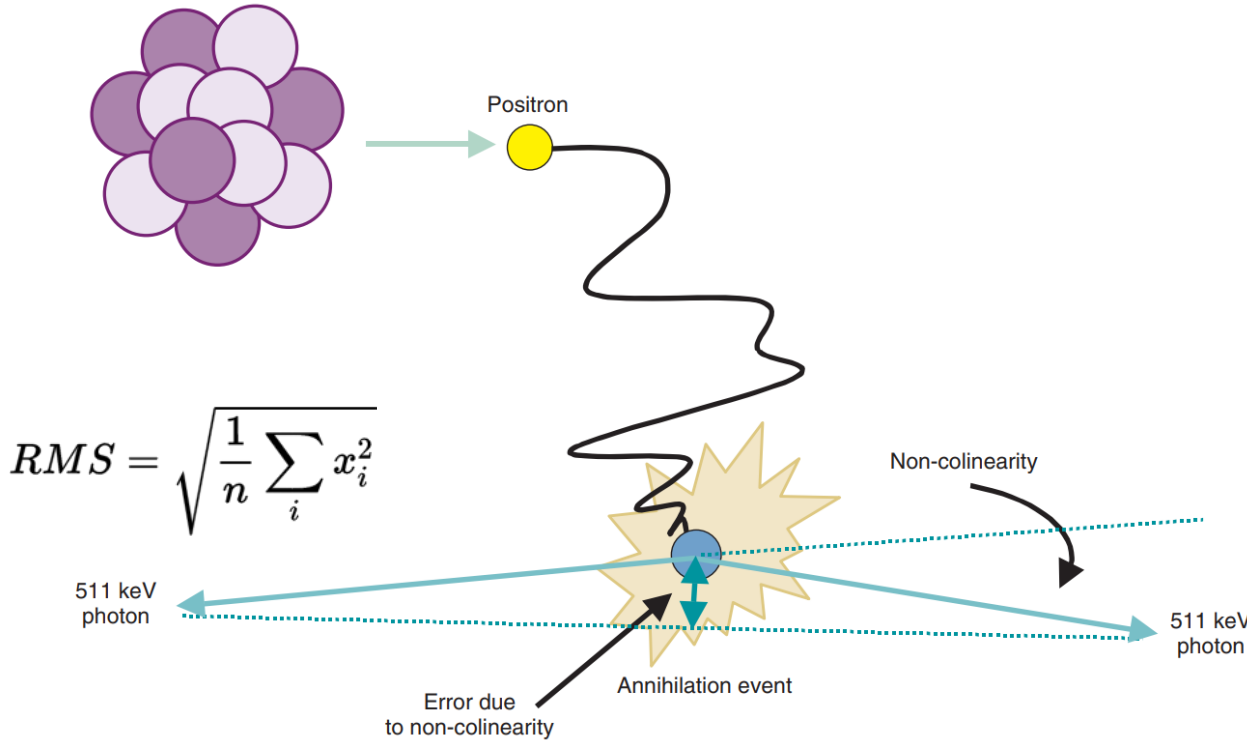
- Tomographic imaging technique used in Nuclear medicine
- Functional and molecular imaging (imaging metabolic and other physiological processes)
- Radiopharmaceuticals injected into the body



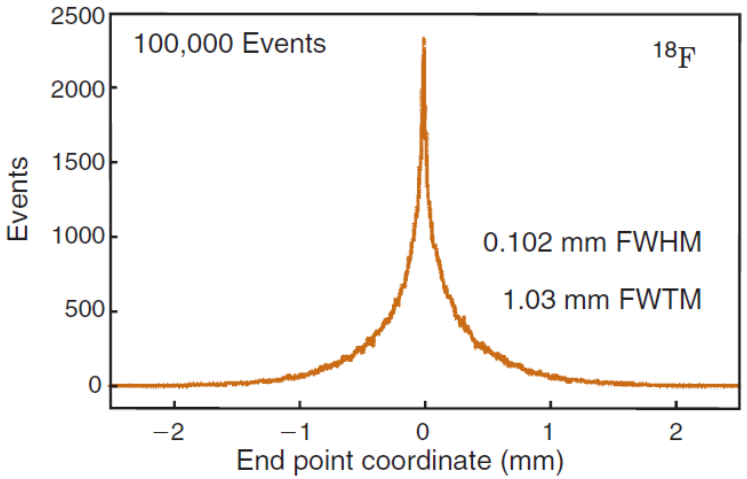


Positrons

- Positron emitted via β^+ decay, loses kinetic energy and annihilates with an electron
- Extrapolated range in water up to 2 cm
- Range characterized as root mean square of effective ranges
- Two back-to-back 511 keV photons are emitted
- Angular distribution is gaussian, centered around 180° with 0.5° FWHM



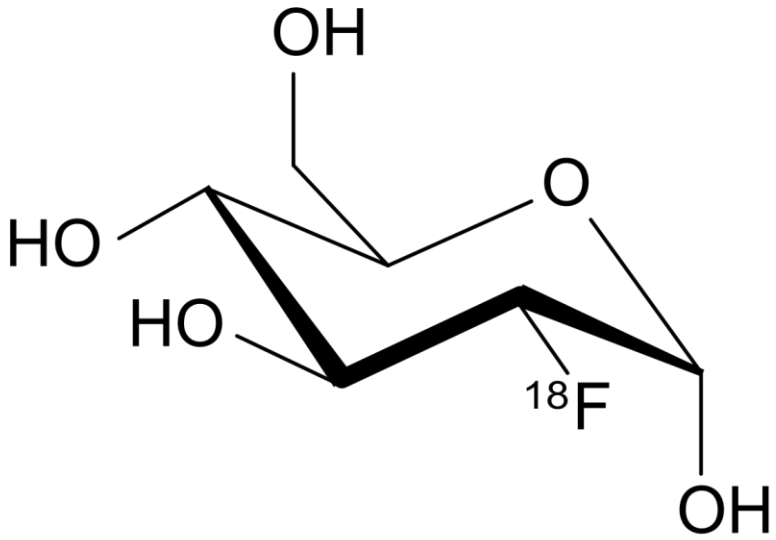
Effective positron range in water



Radionuclide	Half-Life	β^+ fraction	Maximum β^+ Energy	How Produced
^{11}C	20.4 min	0.99	960 keV	Cyclotron
^{13}N	9.96 min	1.00	1.19 MeV	Cyclotron
^{15}O	123 sec	1.00	1.72 MeV	Cyclotron
^{18}F	110 min	0.97	635 keV	Cyclotron
^{62}Cu	9.74 min	0.98	2.94 MeV	Generator (from ^{62}Zn)

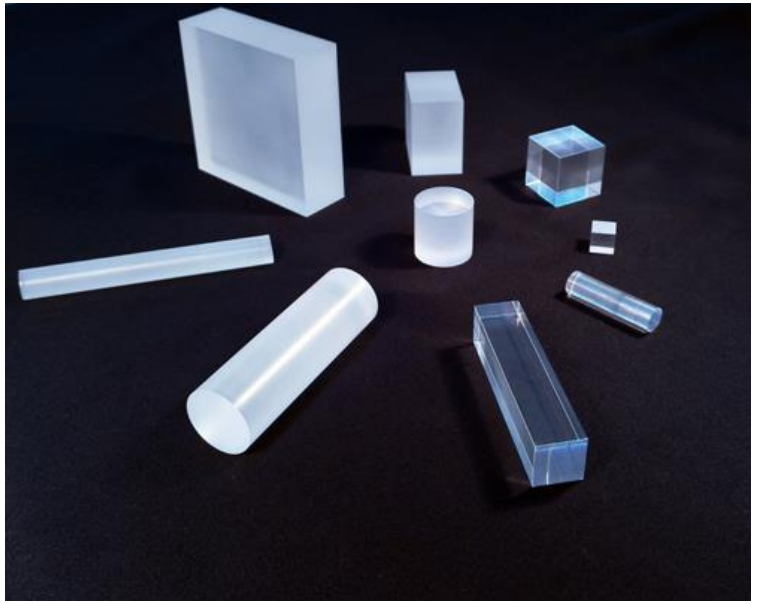
FDG (Fluorodeoxyglucose)

- Common radiopharmaceutical for PET
- Uptake of FDG reflects glucose metabolism in tissues
- After ^{18}F decays into ^{18}O and binds H^+ from the environment the molecule becomes regular glucose
- Detection and staging of cancer
- Diagnostics of neurodegenerative diseases (Alzheimer's, Parkinson's disease)

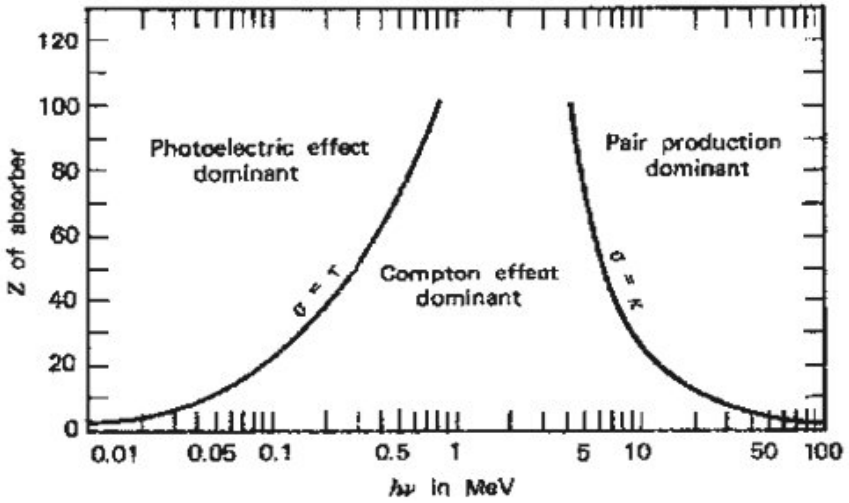


Scintillators

- Scintillators convert gamma rays to visible photons
- Number of visible photons proportional to deposited energy
  - Photoelectric effect and Compton scattering

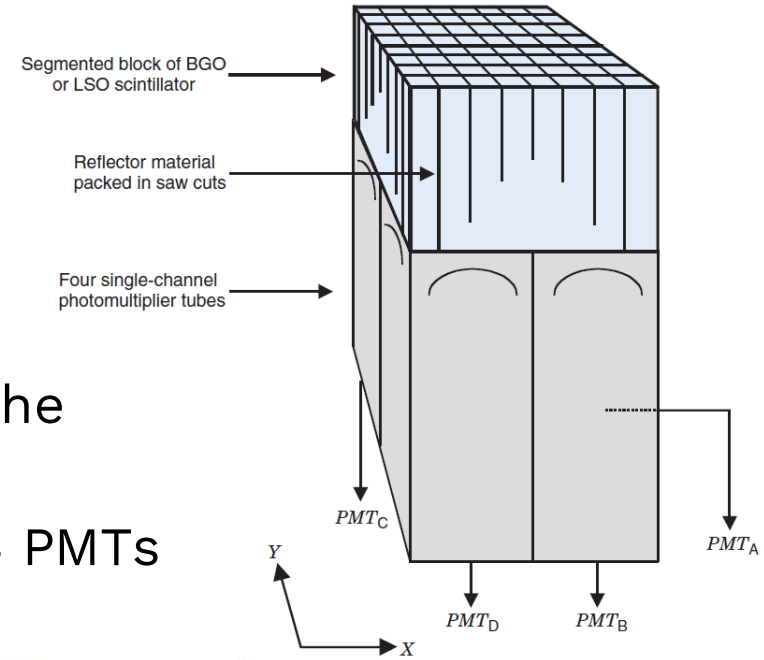


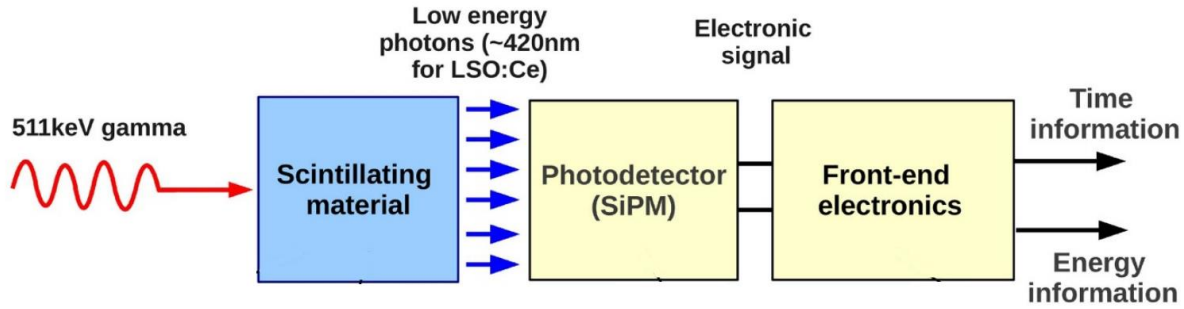
Property	NaI(Tl)	BGO	LSO(Ce)
Density (g/cm^3)	3.67	7.13	7.40
Effective atomic number	50	73	66
Decay time (nsec)	230	300	40
Photon yield (per keV)	38	8	20-30

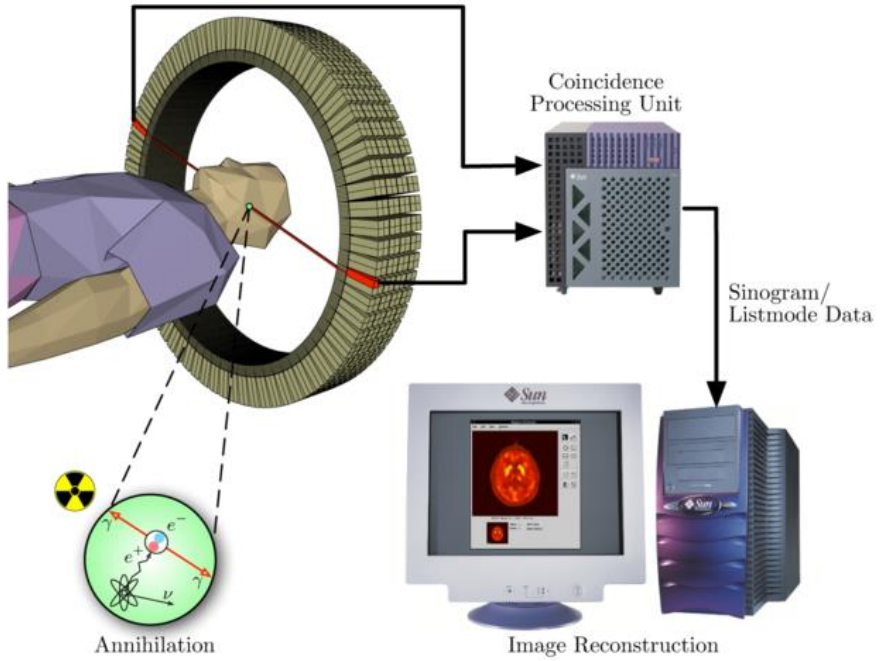


PET Detectors

- Photodetector converts photons to an electrical signal
- Block detectors used to increase spatial resolution but keep the cost relatively low
- Block detector example: Scintillators partially cut and share 4 PMTs
- Sensitivity depends on:
  - Efficiency of gamma ray detection
    - 511 keV gamma attenuation coefficient
    - Scintillator thickness
    - Photon detection efficiency
  - Geometrical acceptance of the scanner (5 %)

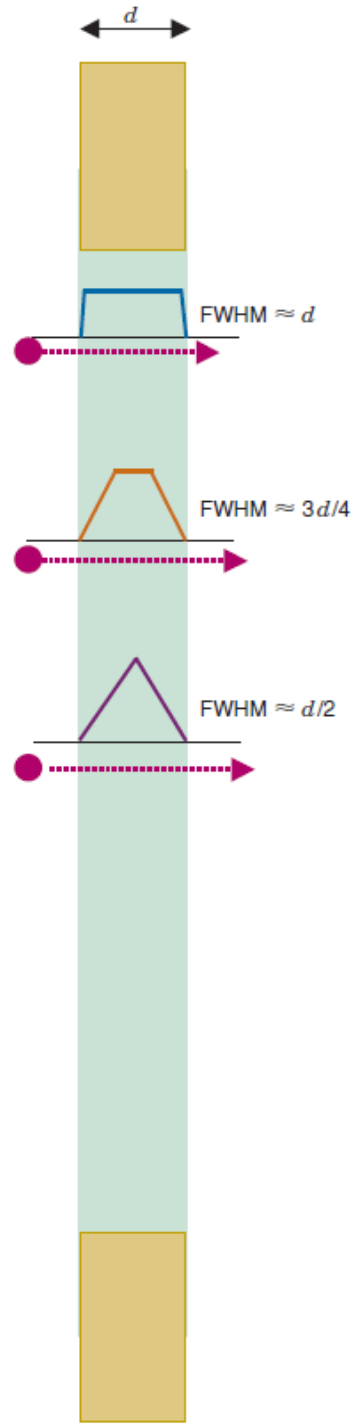






Spatial resolution

R_{det}:



- Detector resolution determined by the size of detector elements
  - Point response profile depends on the distance from detector elements
- Contribution of noncollinearity of annihilation photons depends on distance between detector elements

$$R_{180^\circ} = 0.0022 \times D$$

- Contribution of positron range (R_{range}) is RMS of effective range
- System resolution is the combination of all 3

$$R_{sys} \approx \sqrt{R_{det}^2 + R_{range}^2 + R_{180^\circ}^2}$$

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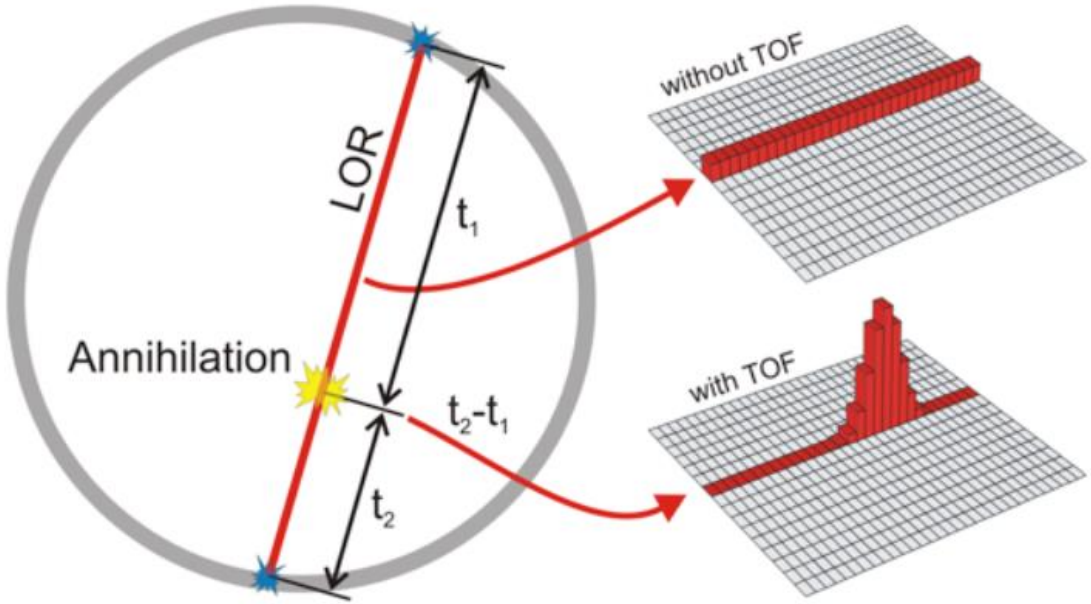
Time-of-flight

- TOF information can be used in image reconstruction to increase Signal to noise ratio (SNR)
- Current state of the art timing resolution **FWHM 214 ps**
- Material properties of scintillators
  - Rise time, Light yield
- Decrease crystal length
  - Minimize travel time spread
  - Reduce parallax error
  - Loss of gamma detection efficiency

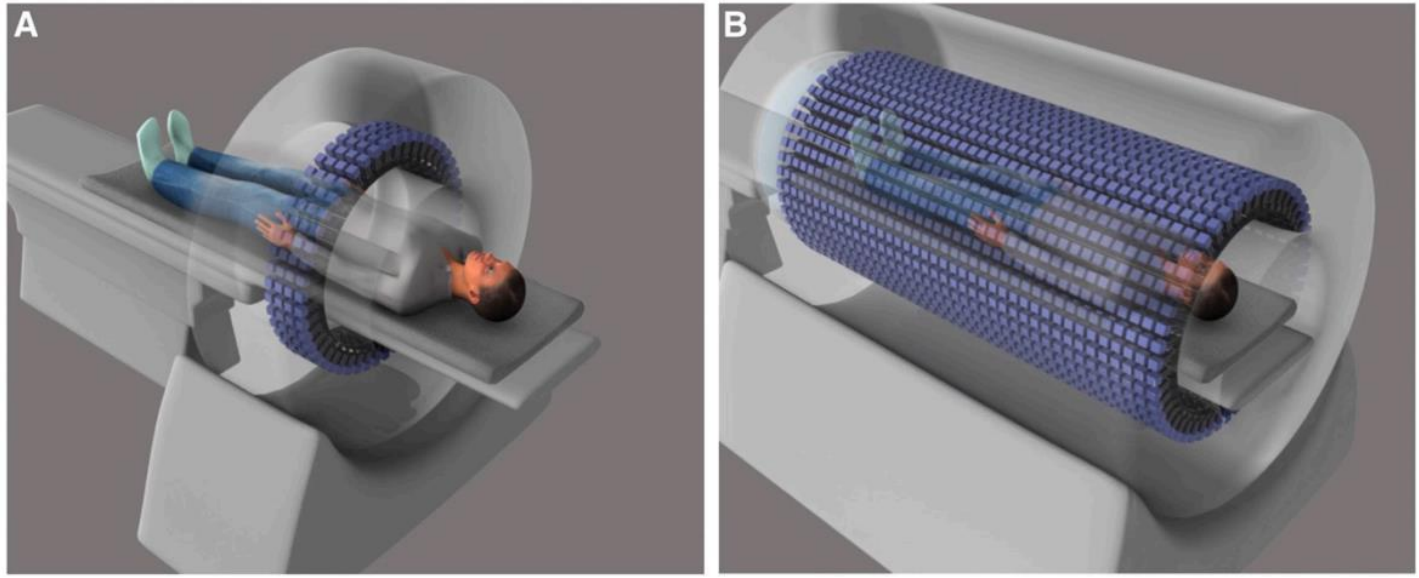


$$\Delta x = \frac{\Delta t \times c}{2}$$

$$SNR_{TOF} = \sqrt{\frac{D}{\Delta x}} SNR_{non\text{-}TOF}$$

Current research: Total-body scanners

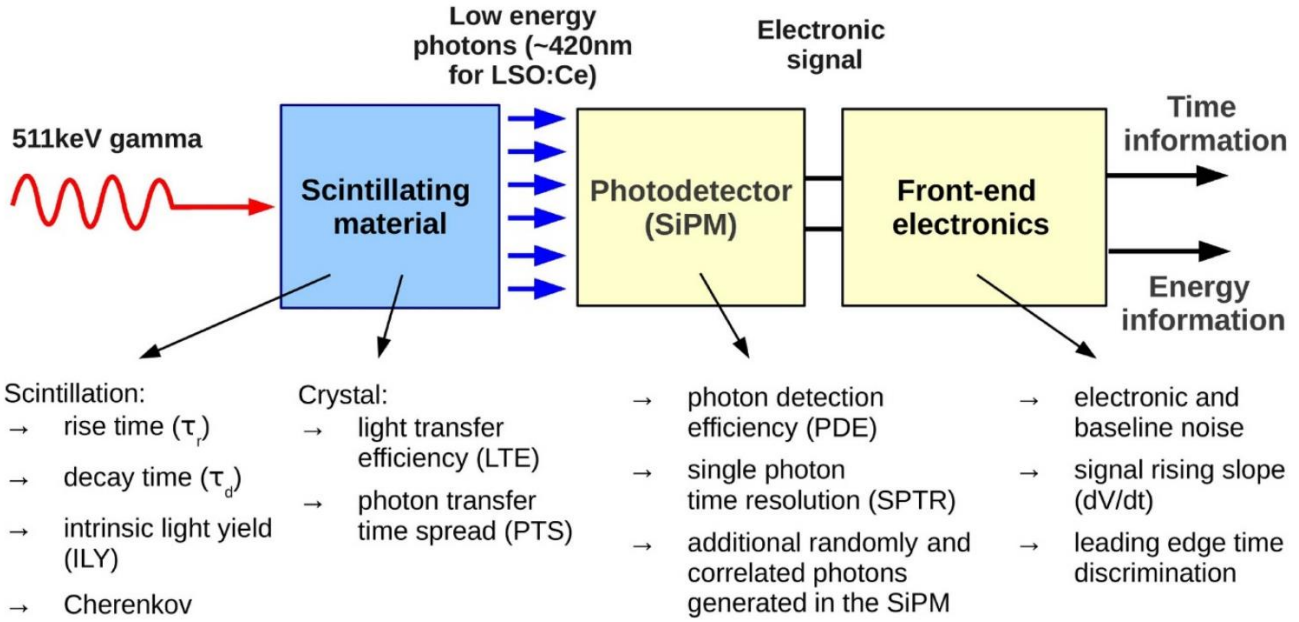
- Improving detector efficiency
- Increasing geometrical acceptance
  - Total-body scanner EXPLORER [1]
  - Extend axial field of view (FOV) from 20 cm to 200 cm
  - Axial FOV of 20 cm means only 5% of events have a chance to be detected
  - Up to 5-fold increase in effective sensitivity for single organ scans and up to 40-fold for total body scans
  - Very high cost (10 M$)



[1] Cherry, S. R., et al. (2017)

Current research: Time-of-flight

- Improving timing performance
- The 10 ps TOF-PET challenge *(Lecoq, P., et al. (2020))*
  - 10 ps CTR would allow reconstruction-less imaging, with mm resolution
  - Improvements required at every step of detection
  - Scalability of hardware is essential (power consumption)
  - 10 ps may not be realistically achievable
- *Gundacker et al.* Achieved 58 ps CTR with high-frequency electronics and small (2x2x3 mm^3) LSO crystals



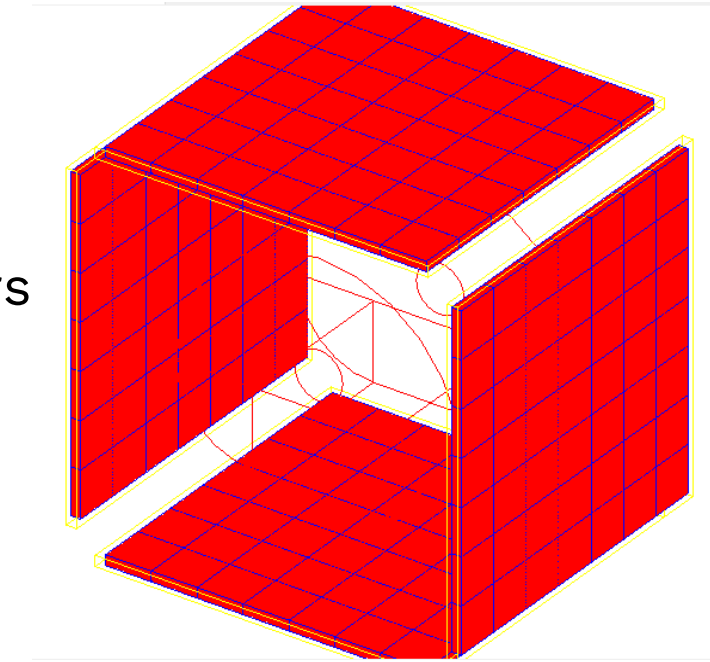
$$SNR_{TOF} = \sqrt{\frac{D}{\Delta x}} SNR_{non\text{-}TOF}$$

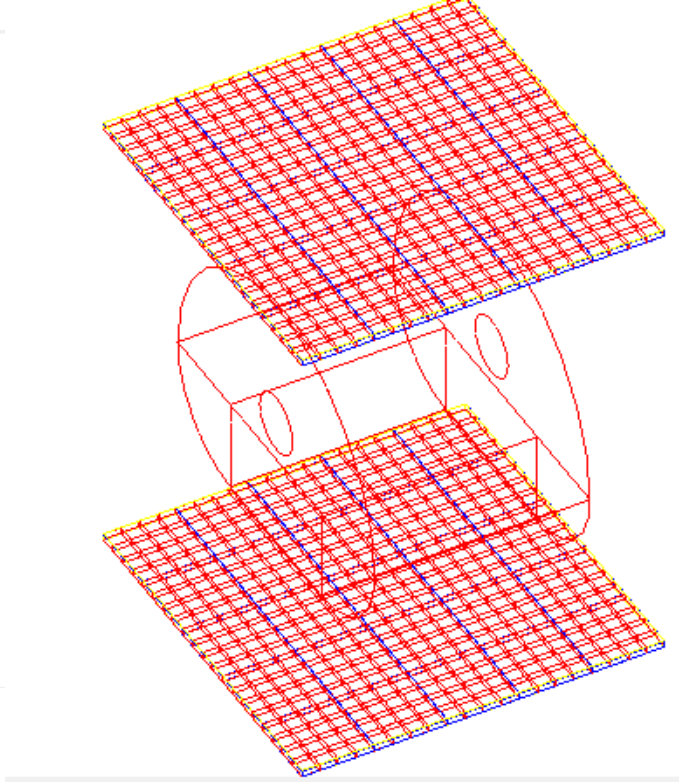
Research questions

- Excellent coincidence timing resolution (CTR) facilitates new detector geometries such as flat panel detectors and open geometry
- Researchers from FMF and IJS are developing a PET detector, planned to reach 70 ps CTR by closely integrating the photodetector and electronics.
- Development of a flat panel TOF PET scanner, based on this fast detectors, will require extensive studies to:
  - Search for optimal design parameters
  - Experimentally verify the integrated detector performance

Flat panel detectors

- Why are they better than ring detectors
  - Modular
    - Two or four panels
    - Total-body
  - Cost-accessible (lower material cost)
  - Possible increase of axial field of view
  - Smaller, lighter, more compact
  - Mobile
  - Open geometry
  - Personalized configuration for each patient
    - Distance between panels and incline
- Excellent TOF compensates sensitivity loss, enables limited angular coverage reconstruction
- Not compromising performance compared to conventional scanners





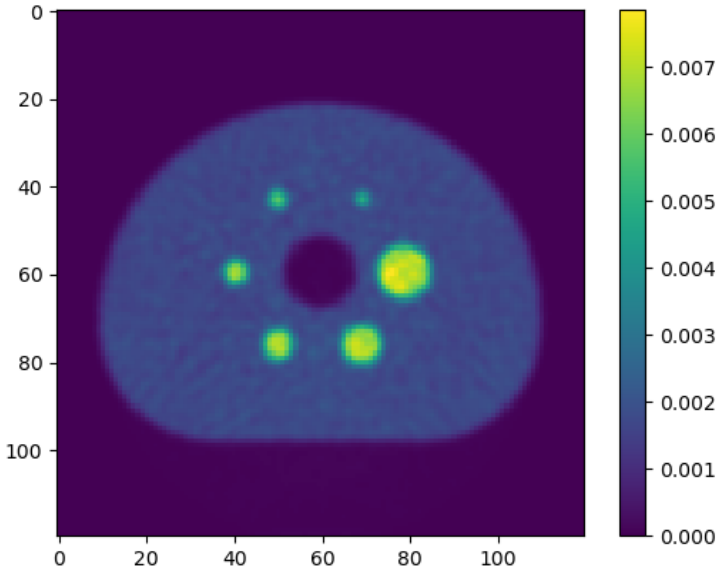
Tools

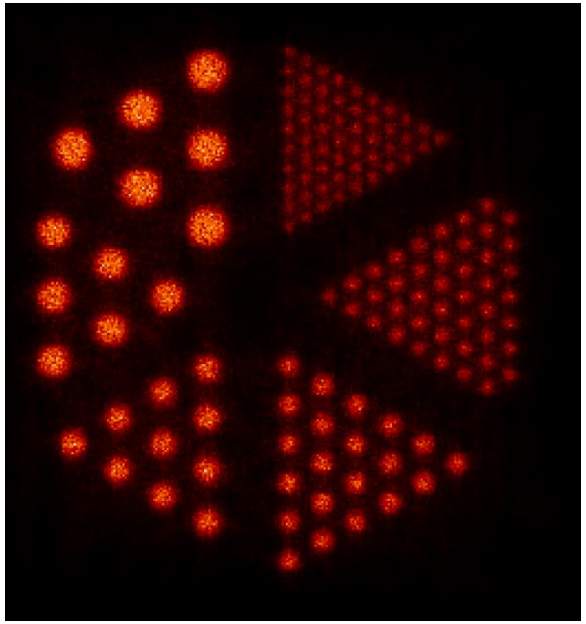
- GATE: Monte-Carlo simulation toolkit for medical physics applications (OpenGATE collaboration)
- CASToR: Customizable and Advanced Software for Tomographic Reconstruction
- SLING: Slovenian national supercomputing network

Slovensko nacionalno superračunalniško omrežje

Phantoms

- NEMA phantom
  - 6 spheres with high activity inside a body-shaped low activity container
  - Quantitative assessment of contrast and variability
- Derenzo Phantom
  - Multiple rods with different radii
  - Qualitative assessment of spatial resolution



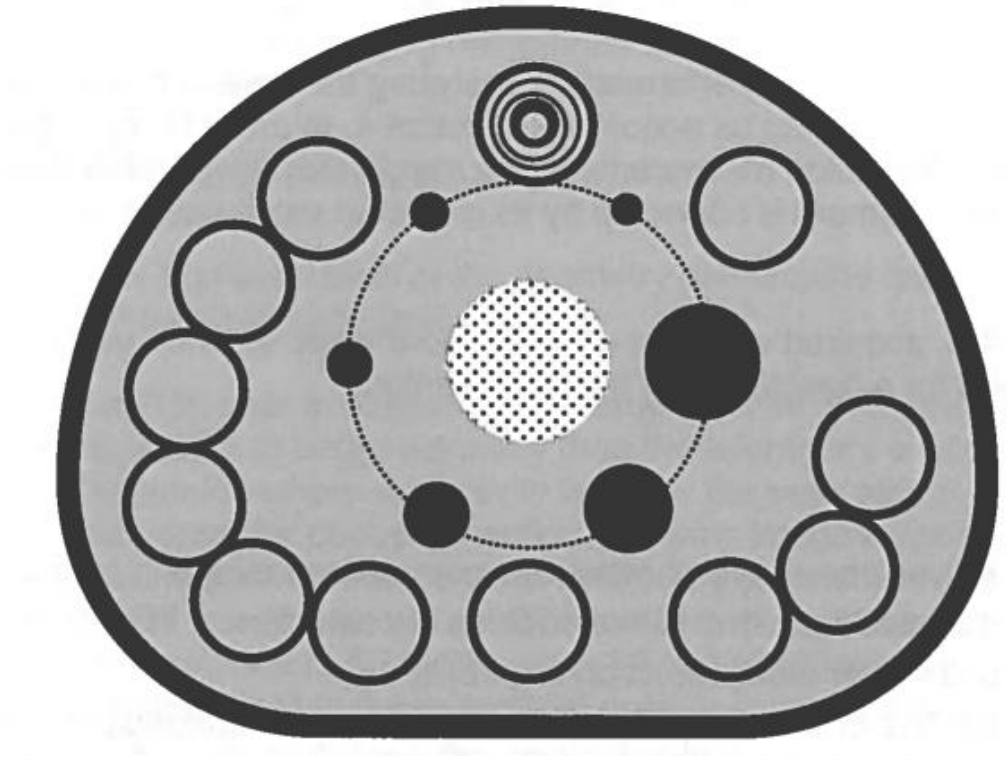


NEMA standard metrics for image quality

- Percent contrast recovery (CR)
  - Average counts inside Region of interest (ROI)
  - Average counts in 60 background spheres
- Background variability (BV)
  - Standard deviation of counts in background spheres

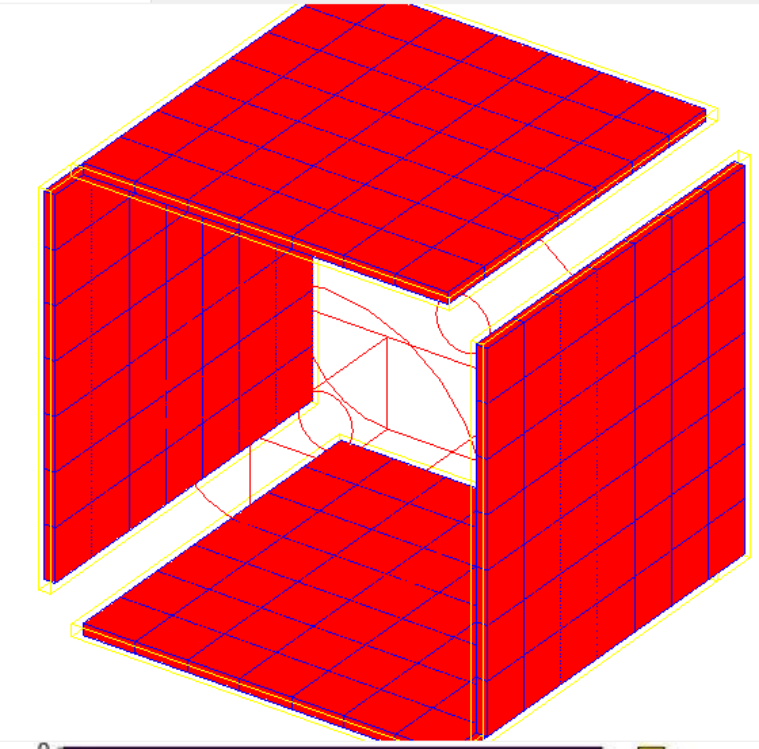
$$CR_i = \frac{S_i / \overline{Bk}_{i,60} - 1}{S_{i,Act} / Bk_{i,Act} - 1} \times 100$$

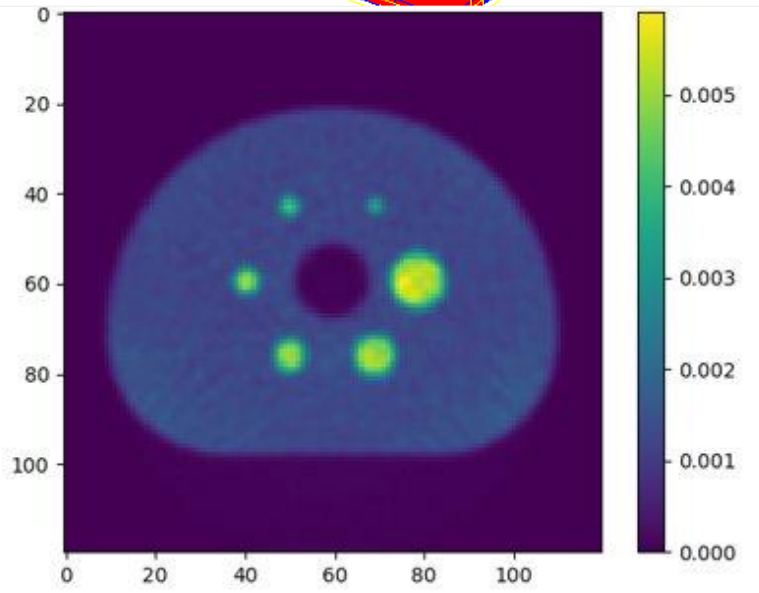
$$BV_i = \frac{\sigma_{i,Bk}}{\overline{Bk}_{i,60}} \times 100$$



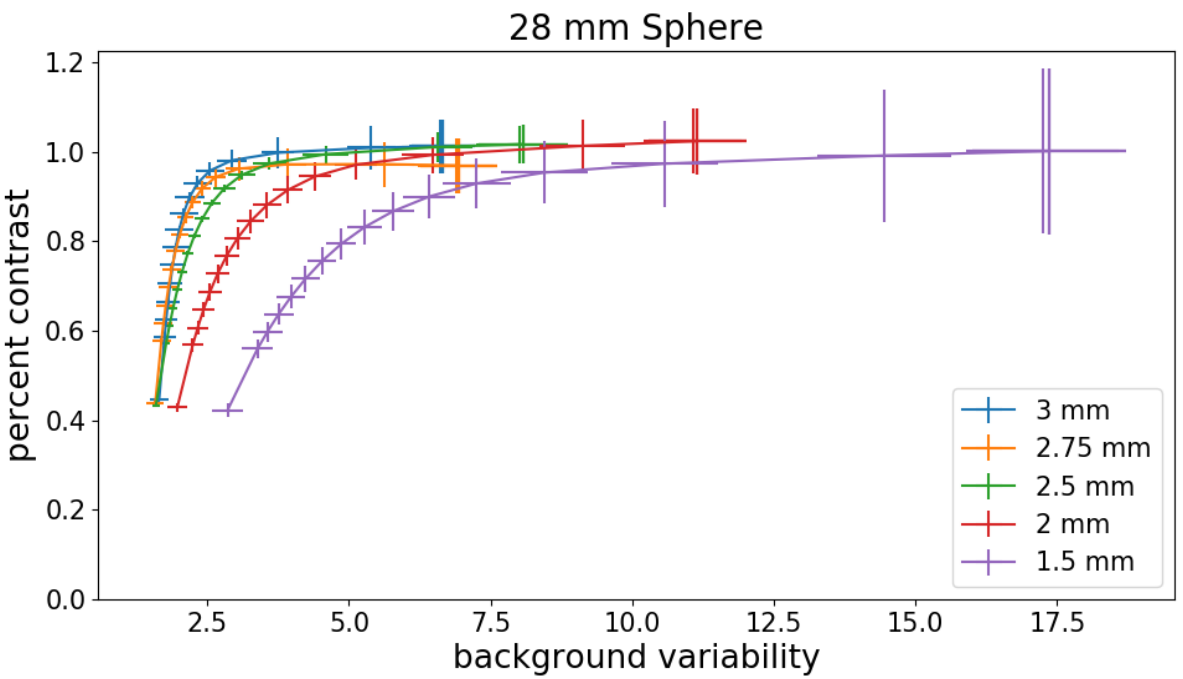
GATE (MC) simulations

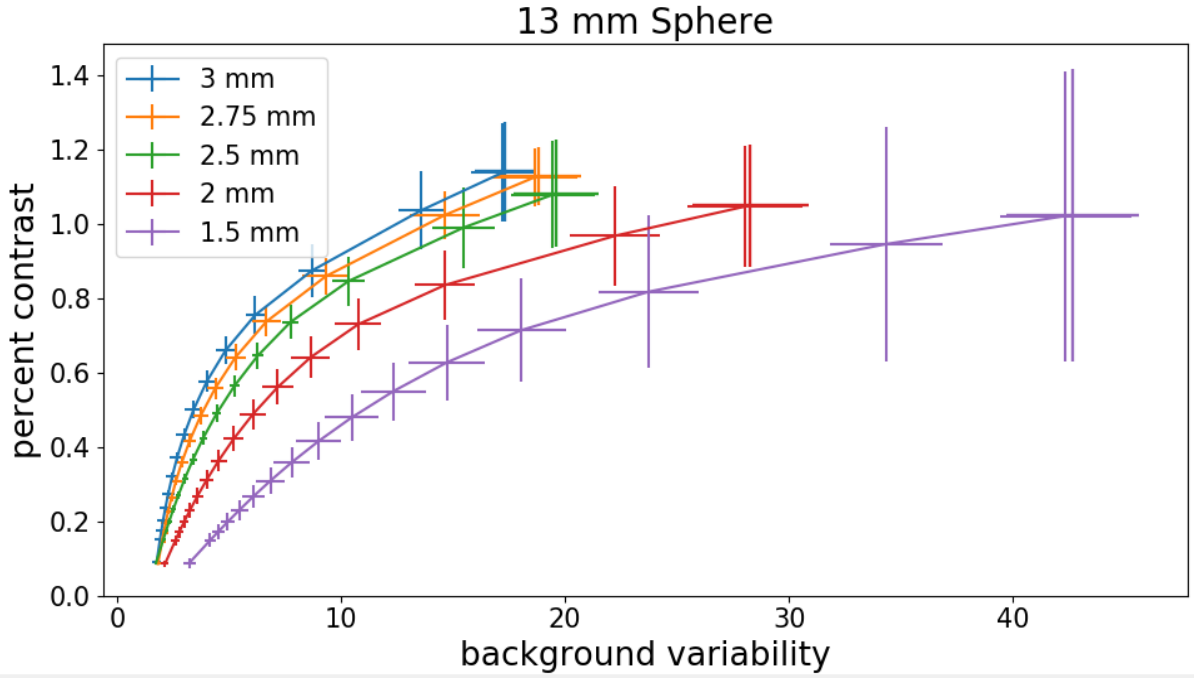
- 4 panels (30 x 30 cm)
- Distance between parallel panels 40 cm
- Each panel 100 x 100 crystals (LSO)
- Crystal dimension 3 x 3 x 10 mm
- Distance between centres of neighbouring crystals 3.01 mm
- Coincidence timing resolution (CTR) 100 ps
- Energy window 435 – 585 keV
- 1 minute scan
- NEMA phantom

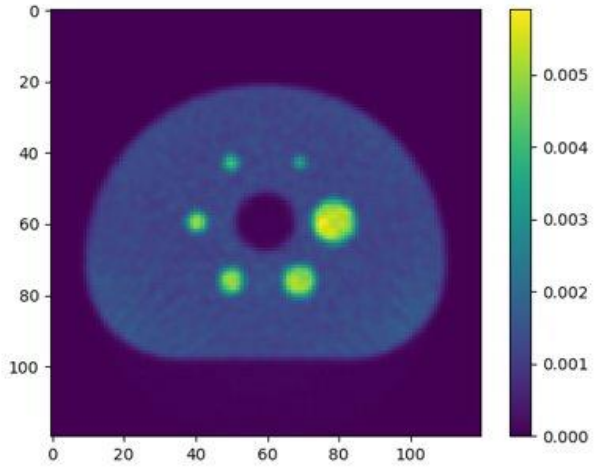




Crystal size optimization results







Conclusion

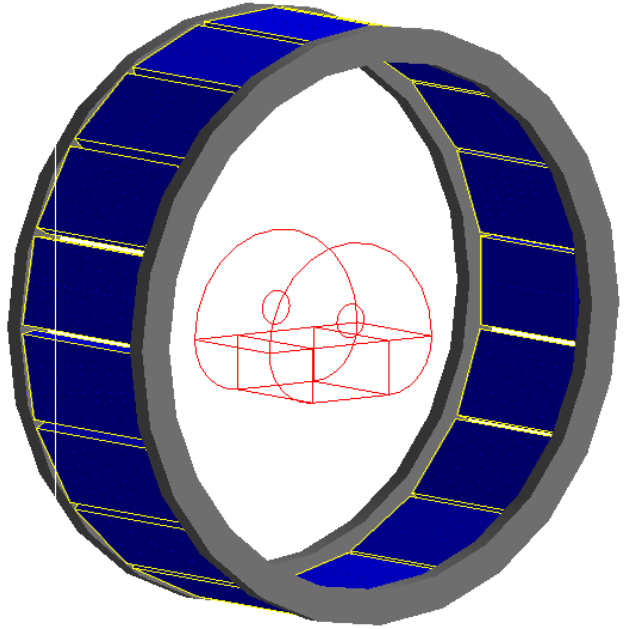
- PET is a widely established medical imaging modality
- Quality of obtained images can be improved with increase in geometric efficiency and improved timing resolution
- Current state-of-the-art CTR is 214 ps, laboratory experiments as low as 58 ps
- Improved timing resolution allows new detector geometries, e.g. flat panel detectors
- Research goals
  - Optimize flat panel TOF PET scanner design parameters
  - Study the integrated detector, enabling ultra-fast timing

Thank you
for your attention

Q & A

Siemens Biograph Vision

- Axial field of view 26.3 cm
- Crystal size 3.2 x 3.2 x 20 mm (LSO)
- Coincidence timing resolution (CTR) 214 ps FWHM



Radionuclide	Half-Life	β^+ fraction	Maximum β^+ Energy	How Produced
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^{13}N	9.96 min	1.00	1.19 MeV	Cyclotron
^{15}O	123 sec	1.00	1.72 MeV	Cyclotron
^{18}F	110 min	0.97	635 keV	Cyclotron
^{62}Cu	9.74 min	0.98	2.94 MeV	Generator (from ^{62}Zn)
^{64}Cu	12.7 hr	0.19	580 keV	Cyclotron
^{68}Ga	68.3 min	0.88	1.9 MeV	Generator (from ^{68}Ge)
^{76}Br	16.1 hr	0.54	3.7 MeV	Cyclotron
^{82}Rb	78 sec	0.95	3.35 MeV	Generator (from ^{82}Sr)
^{124}I	4.18 days	0.22	1.5 MeV	Cyclotron

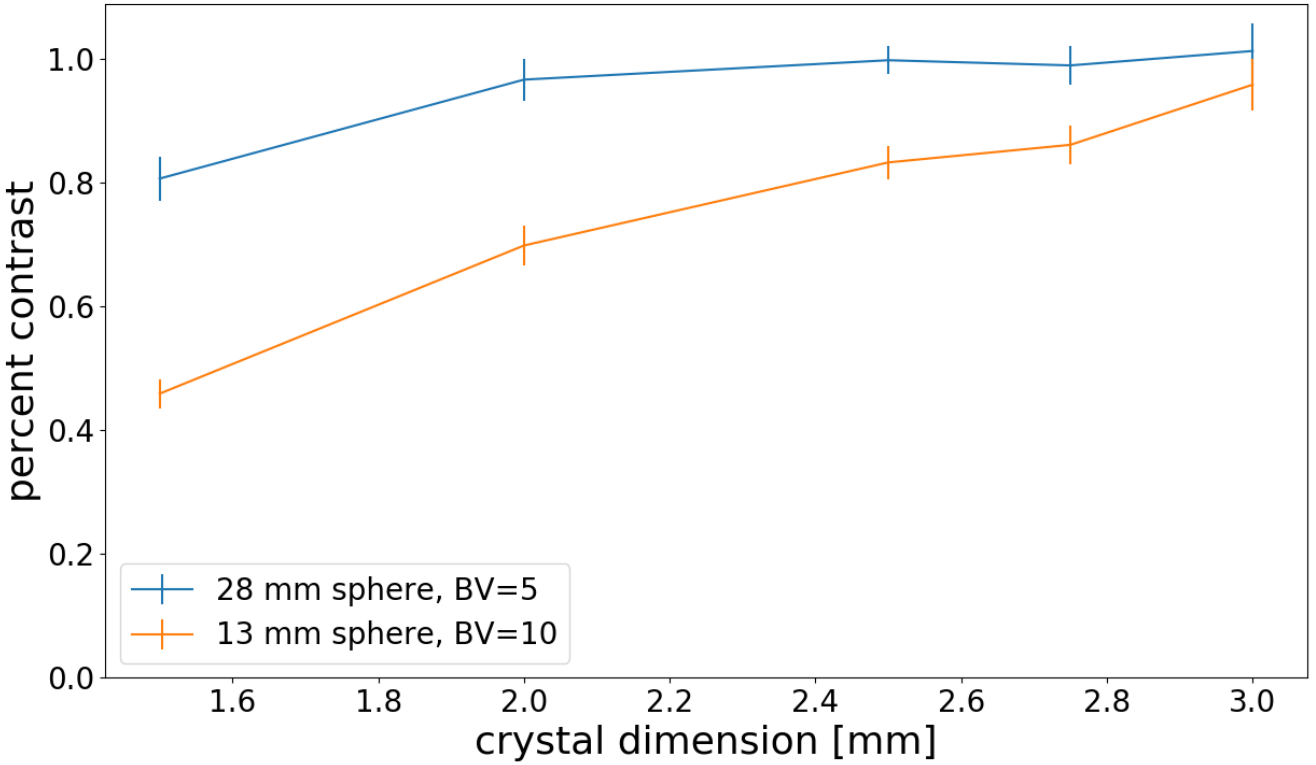
PROPERTIES OF SOME SCINTILLATOR MATERIALS USED IN NUCLEAR MEDICINE

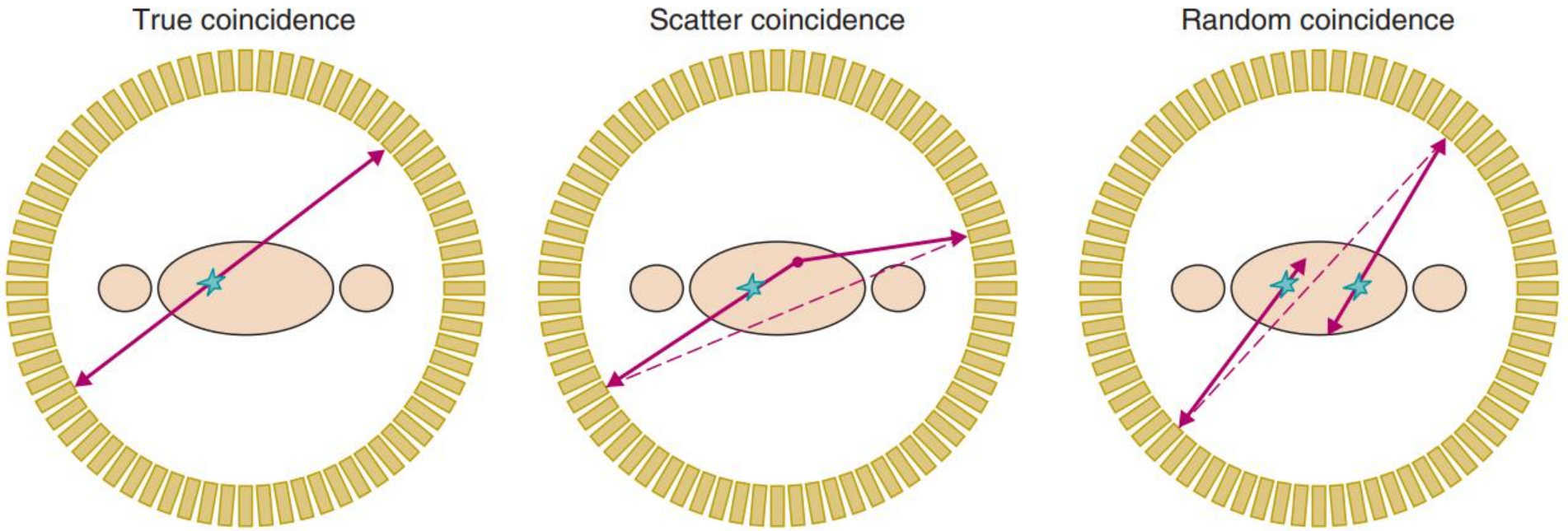
Property	NaI(Tl)	BGO	LSO(Ce)	GSO(Ce)	CsI(Tl)	LuAP(Ce)	$LaBr_3(Ce)$	Plastic*
Density (g/cm^3)	3.67	7.13	7.40	6.71	4.51	8.34	5.3	1.03
Effective atomic number	50	73	66	59	54	65	46	12
Decay time (nsec)	230	300	40	60	1000	18	35	2
Photon yield (per keV)	38	8	20-30	12-15	52	12	61	10
Index of refraction	1.85	2.15	1.82	1.85	1.80	1.97	1.9	1.58
Hygroscopic	Yes	No	No	No	Slightly	No	Yes	No
Peak emission (nm)	415	480	420	430	540	365	358	Various

*Typical values—there are many different plastic scintillators available.

BGO, $Bi_3Ge_4O_{12}$; GSO(Ce), $Gd_2SiO_5(Ce)$; LSO(Ce), $Lu_2SiO_5(Ce)$; LuAP(Ce), $LuAlO_5(Ce)$

Crystal size optimization results




True coincidence
Scatter coincidence
Random coincidence