3Dπ - Three Dimensional Positron Identification with Liquid Argon Total-Body TOF-PET

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LAr TOF-PET Workshop
GSSI: June 18th 2018

Simulation work carried out by Xinran Li (Princeton) and Alejandro Ramirez (University of Houston)

Principle of Traditional PET: The Signal

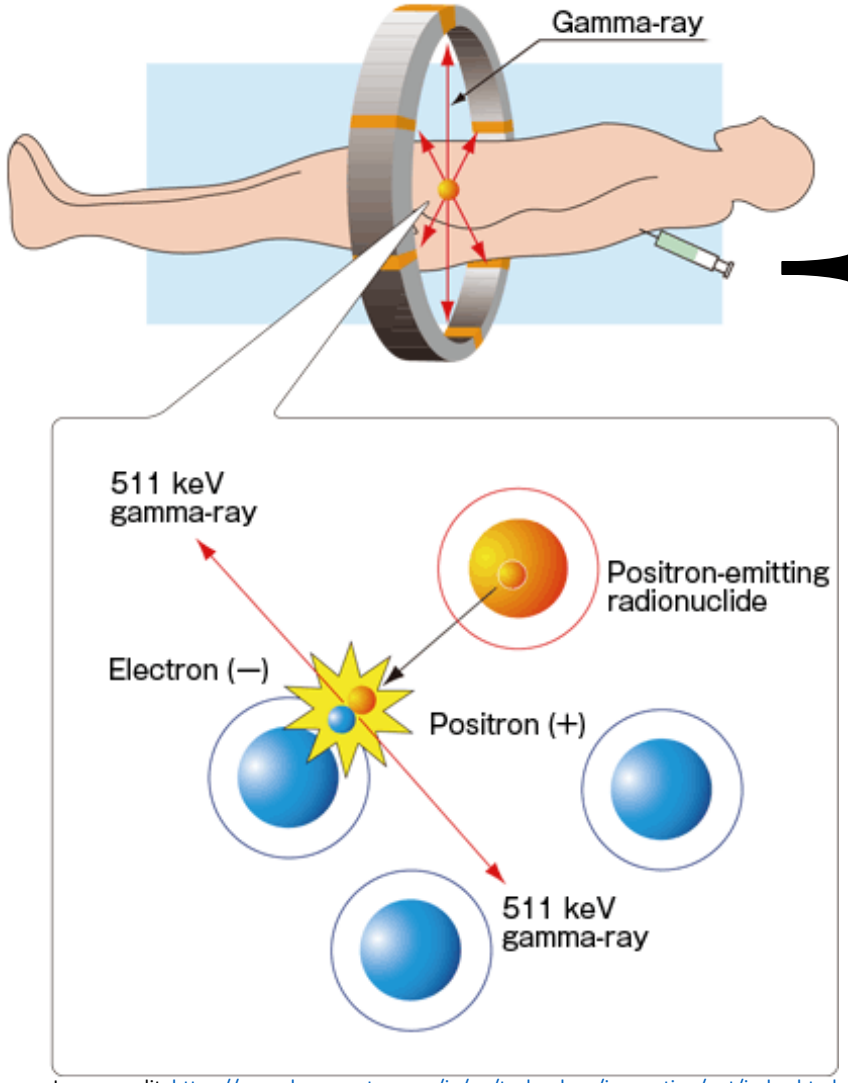


Image credit: https://www.hamamatsu.com/jp/en/technology/innovation/pet/index.html

Radionuclide	Half-life
^{11}C	20 min
^{13}N	10 min
^{15}O	2 min
^{18}F	110 min

Most widely used radiotracer in the form of F-18 FDG

PET is a functional scan:

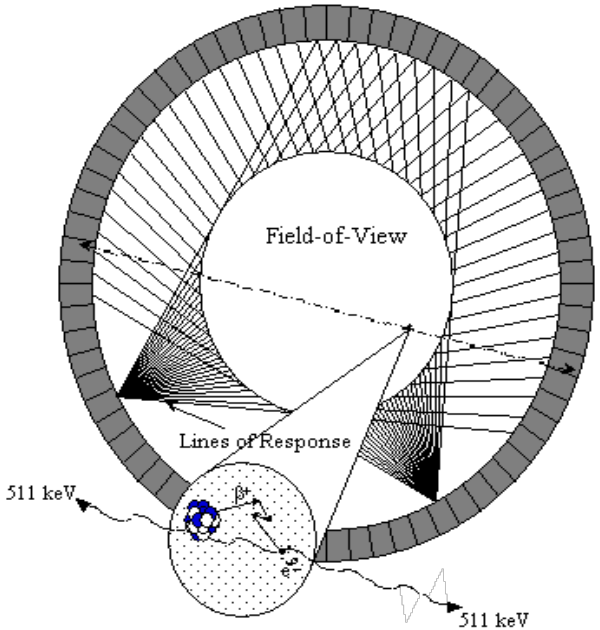
- Measurement of metabolic activity of the cells of body tissues
- Does not show anatomic features
- Used mostly for patients with brain and heart conditions or cancer
- Can detect the onset of a disease before anatomical changes occur

FDG most commonly used to look for cancer metastasis

- Other radiotracers used to image other types of molecules of interest

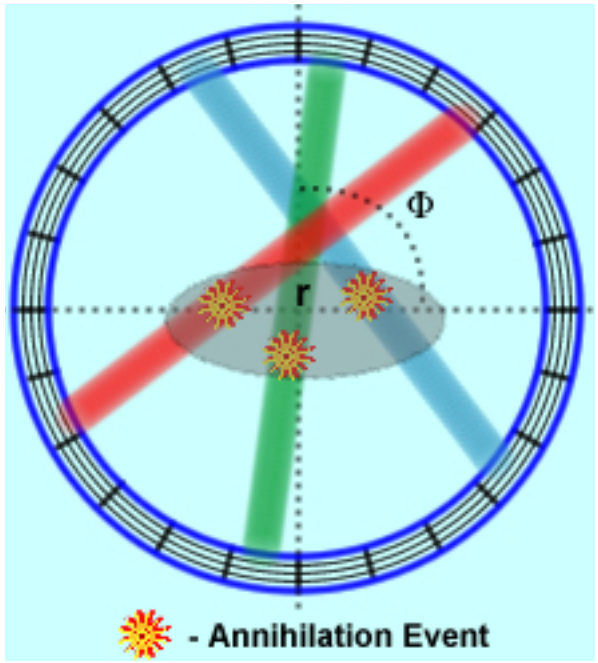
Principle of Traditional PET: Image Recon.

Produce LORs for coincident gammas
Coincidence defined by various cuts



http://www.europeanmedical.info/nuclear-medicine/positron-emission-tomography-41-the-physical-principles-of-pet.html

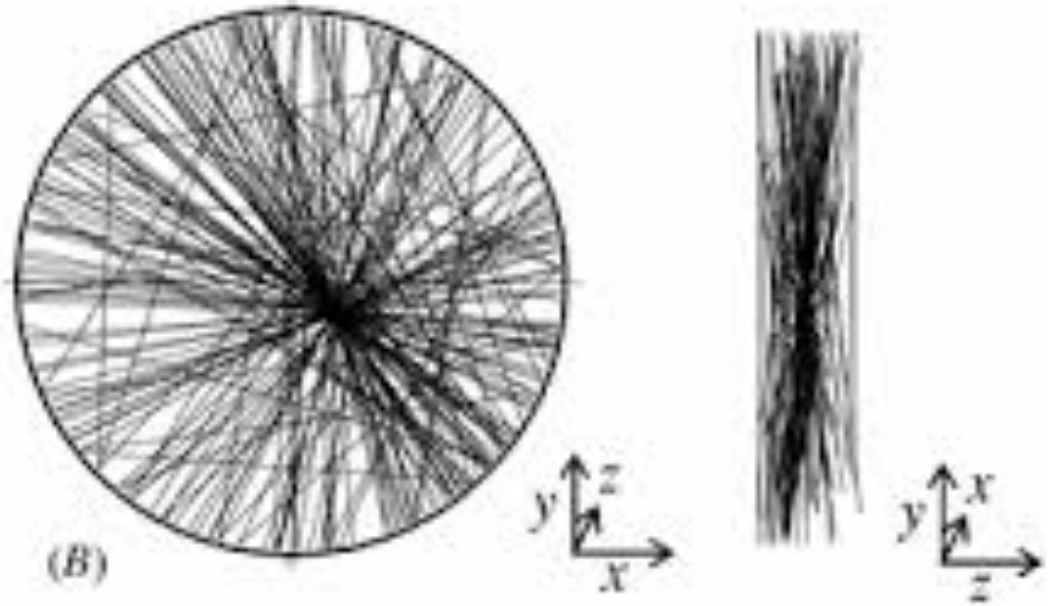
http://www.people.vcu.edu/~mhcrosthwait/PETW/Petandsingormasathome.html



Width of LOR determined by resolutions for Gamma scattering position detection

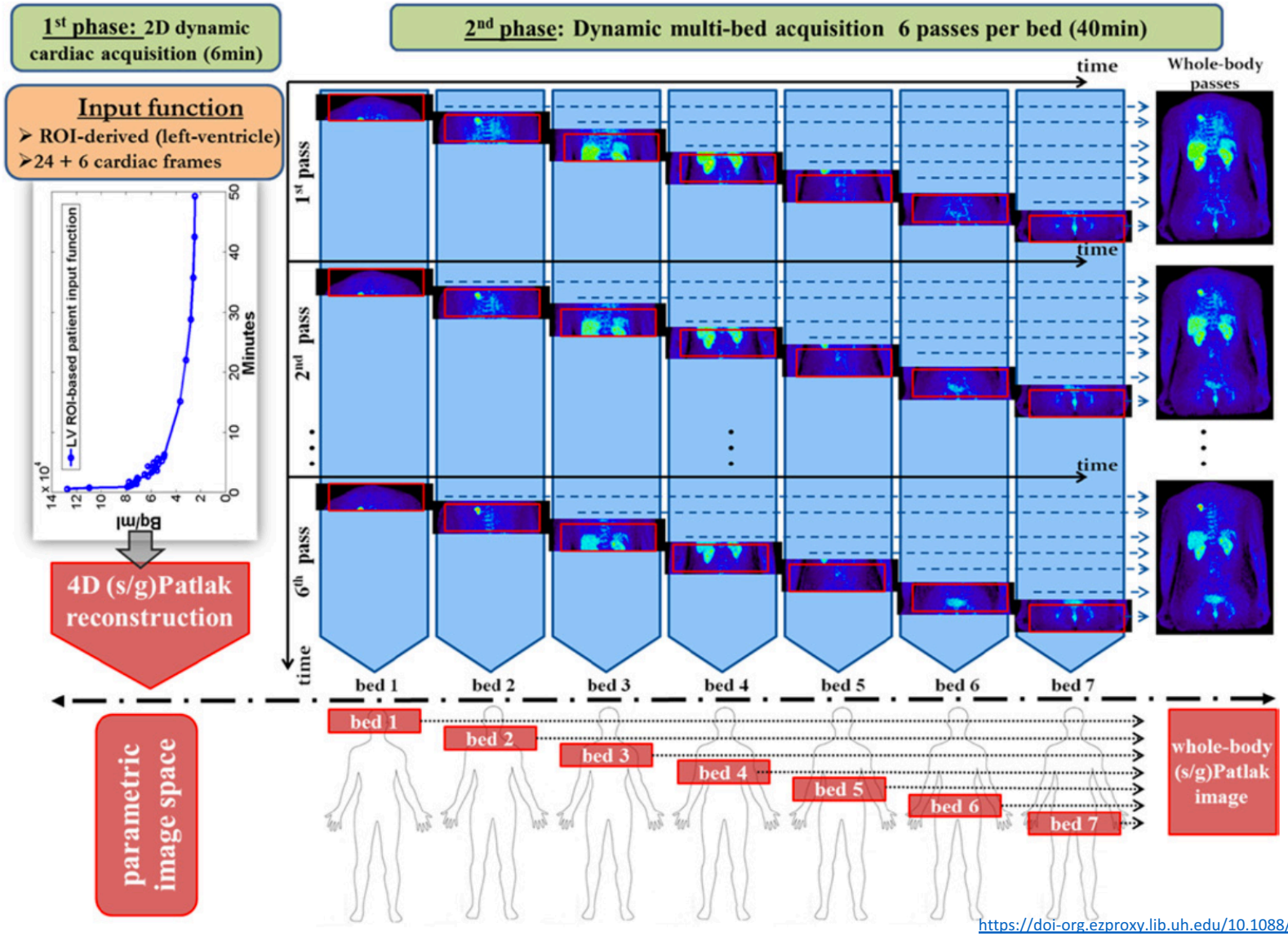
This is the resolution in the tangential and axial directions

Project all LORs in axial and transverse planes
Density of LORs will form the projected image



https://doi.org/10.1088/0957-0233/16/3/029

Whole-Body PET



Axial FOV is typically 20-30 cm

→ 85% of body outside FOV

This is fine for imaging certain parts of body, Such as brain and heart

Whole-body scan must be “sliced-up”

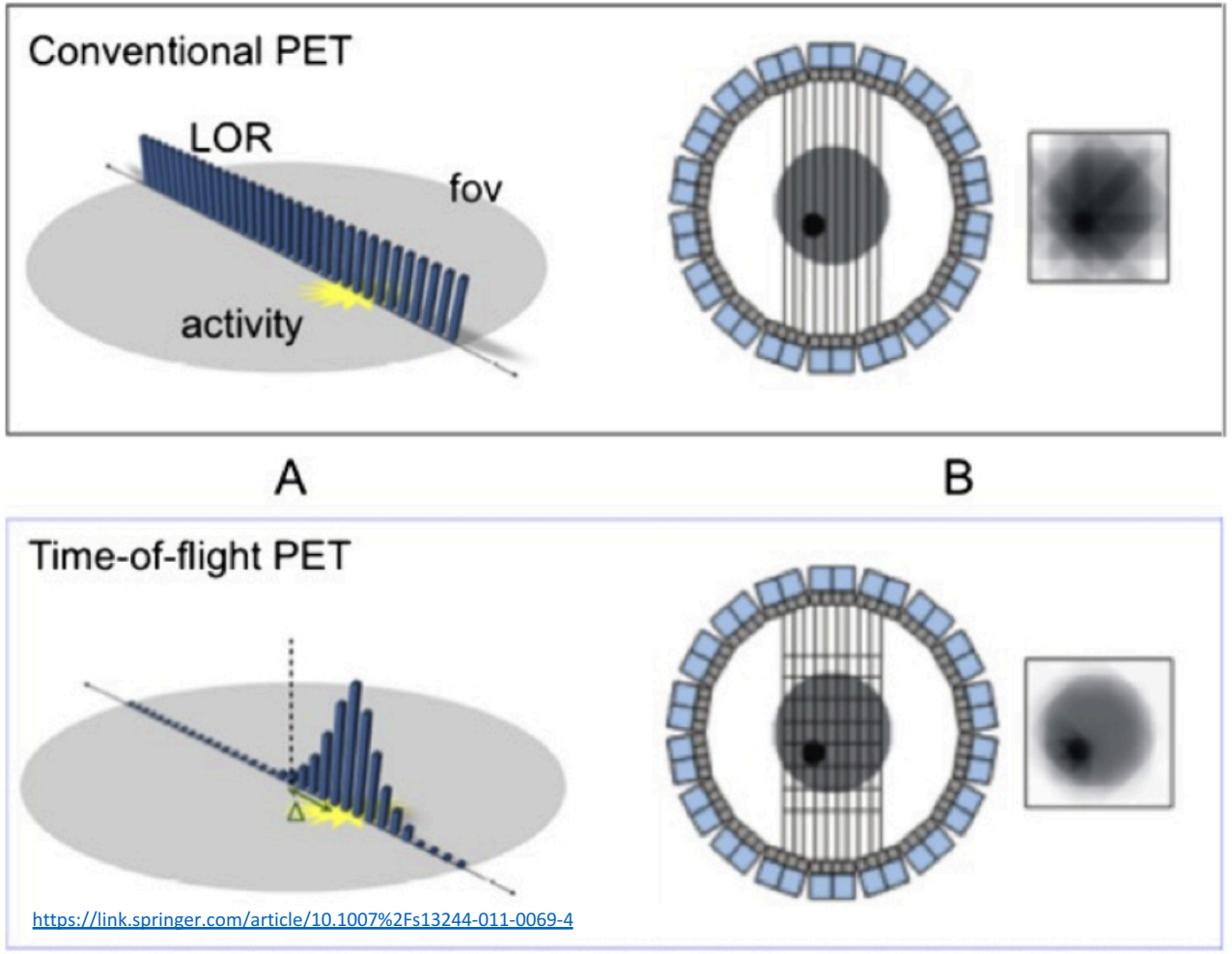
Final whole-body image formed by overlapping the images from each slice

Obvious disadvantages to this!!

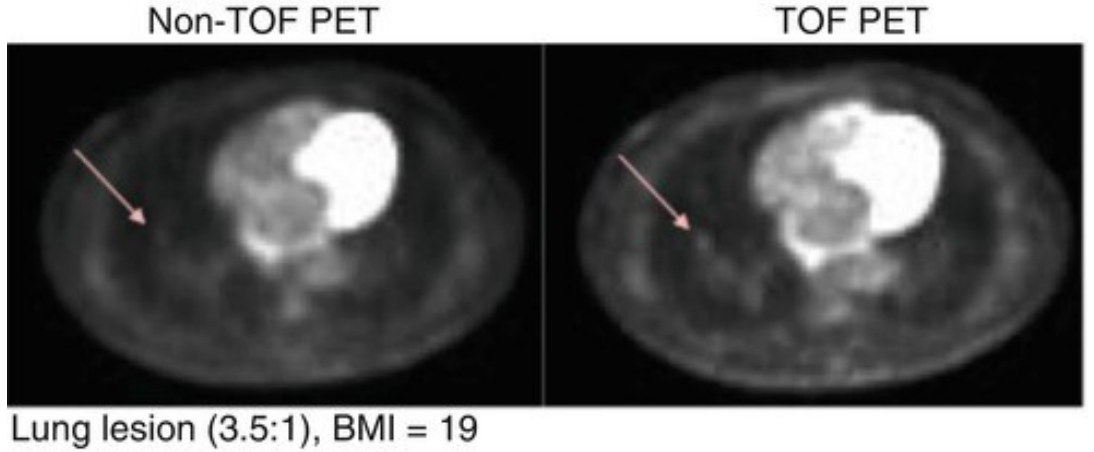
https://doi-org.ezproxy.lib.uh.edu/10.1088/0031-9155/61/15/5456

TOF-PET

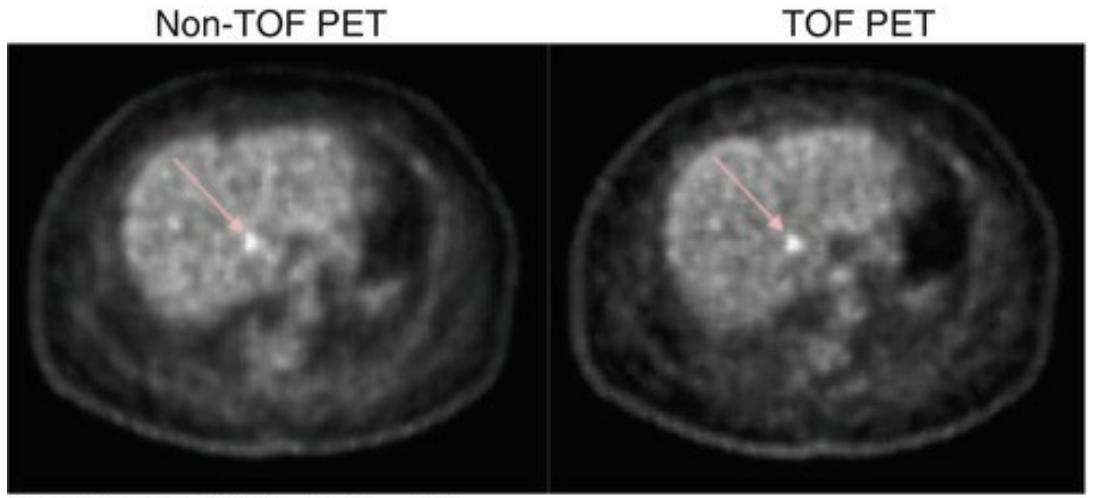
Typical TOF timing resolution is O(few hundred ps) → few cm spatial resolution



https://link.springer.com/article/10.1007%2Fs13244-011-0069-4



Lung lesion (3.5:1), BMI = 19



Lung lesion (2:1), BMI = 42

https://radiologykey.com/pet-physics-and-instrumentation/

Limitations of Current Commercial Technology

- Best for imaging individual parts of the body
  - Small sensitivity for gamma detection means higher activities required
    →Introduces more false coincident events and deteriorates image quality

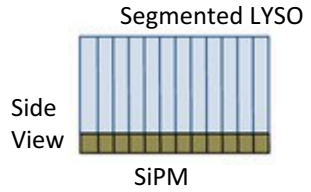
- Whole-body scans introduce further limitations:
  - Most of body outside the FOV, plus small sensitivity for detecting gammas in the FOV
    →Patient dosage must be able to account for this
    →Cannot image multiple body parts at same time, thus no dynamical data from all tissues of interest

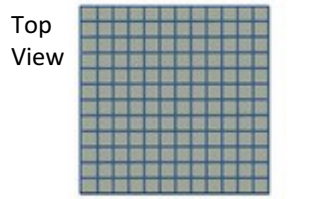
  - Long scans times due to slicing and stitching
    →Patients must be entirely still for 10s of minutes to more than an hour
    →Small movements can introduce image artifacts
    This can lead to uncertainty in diagnosis and even false positives
    →A single device is limited in the number of patients it can scan per day (higher administrative costs)

Limitations of Current Commercial Technology

- Timing resolution in TOF-PET limit the ultimate SNR
  - →Inherent timing resolution of the photosensors and electronics
  - →Rise and decay times of the detector scintillation
  - →Individual cell geometry is important, affects light propagation time
- Hard to do follow-up scans due to patient dosage limitations
  - →Also must be careful of exposure limits for medical staff
- Certain populations cannot be scanned
  - →Pregnant woman, infants, children, adolecents, and elderly
  - →People who live far from radiotracer productions, short half-lives limit the ability to distribute them across large distances

TOF-PET with Depth of Interaction (DOI)





Traditional scanners readout scintillator cells from one side only

→Based on intelligent recon. of light propagation

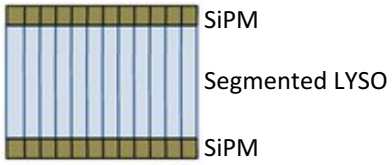
→Gives information on radial depth of gamma scattering

→Reduces the width of the kernal in the TOF reconstruction

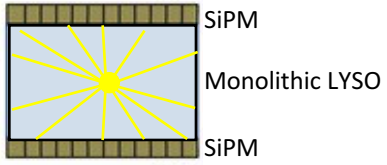
→Limited by charge and timing resolution, plus crystal segmentation

Move to readout both sides of scintillator, two photosensors see the same cell

→Charge and time difference between sensors reduces DOI uncertainty



Monolithic crystals can help further reduce the DOI uncertainty

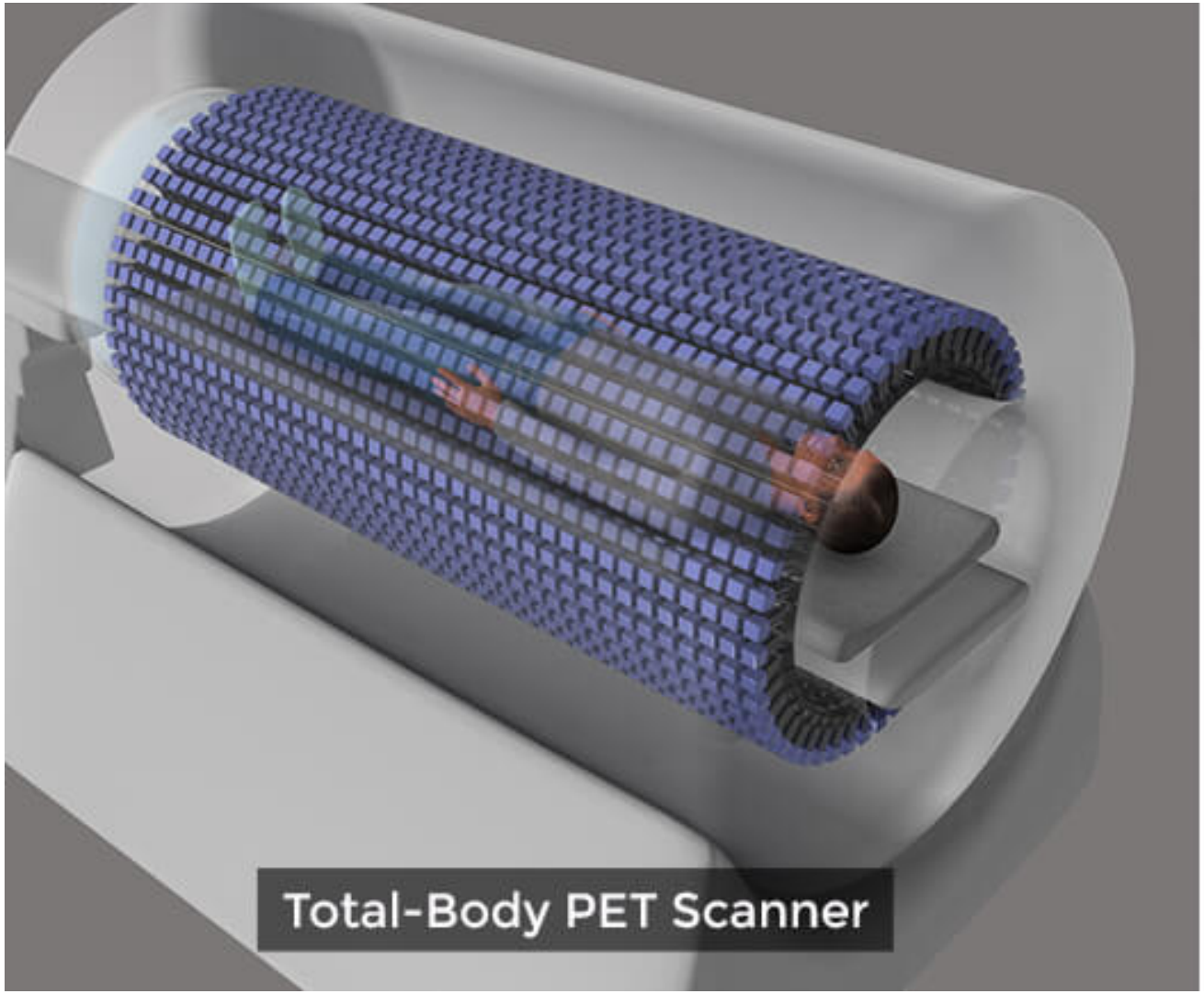


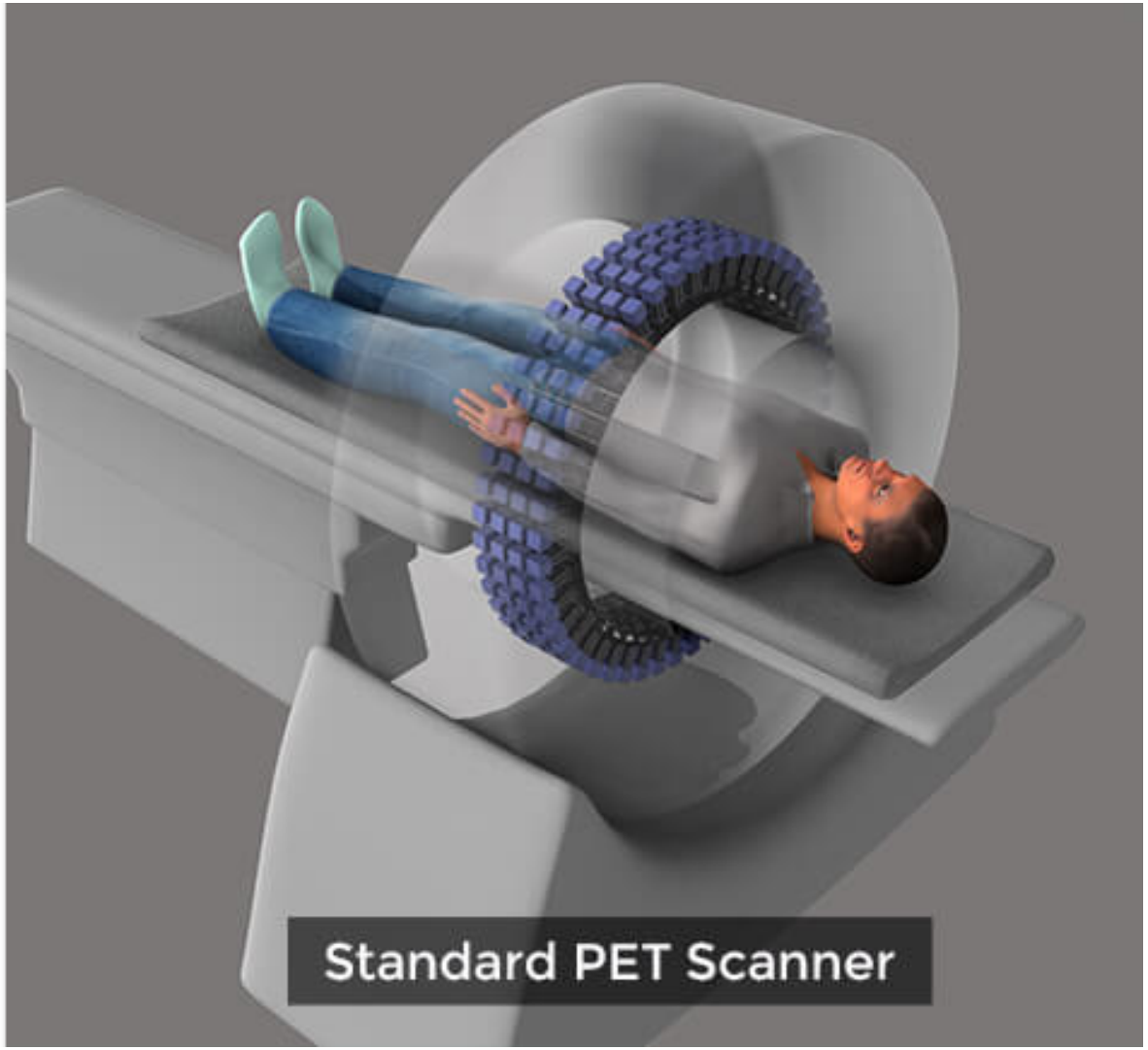
Sensitivity to 511 keV Gammas

$$S \propto \frac{a \cdot \epsilon^2 \cdot e^{-\mu t}}{r^2}$$

- Ability to detect gammas depends on the detector area (a), as seen from a point source at a given position
- Detector efficiency ($\boldsymbol{\varepsilon}$) comes in as the square due to need to detect two gammas to form a coincidence
- $\boldsymbol{\mu}$t gives the probability for interaction given a detector thickness t
  - Better to use materials with higher $\boldsymbol{\mu}$ (high Z and high density), or compensate with larger detector thickness
- Denominator brings in the typical flux spreading of $1/r^2$

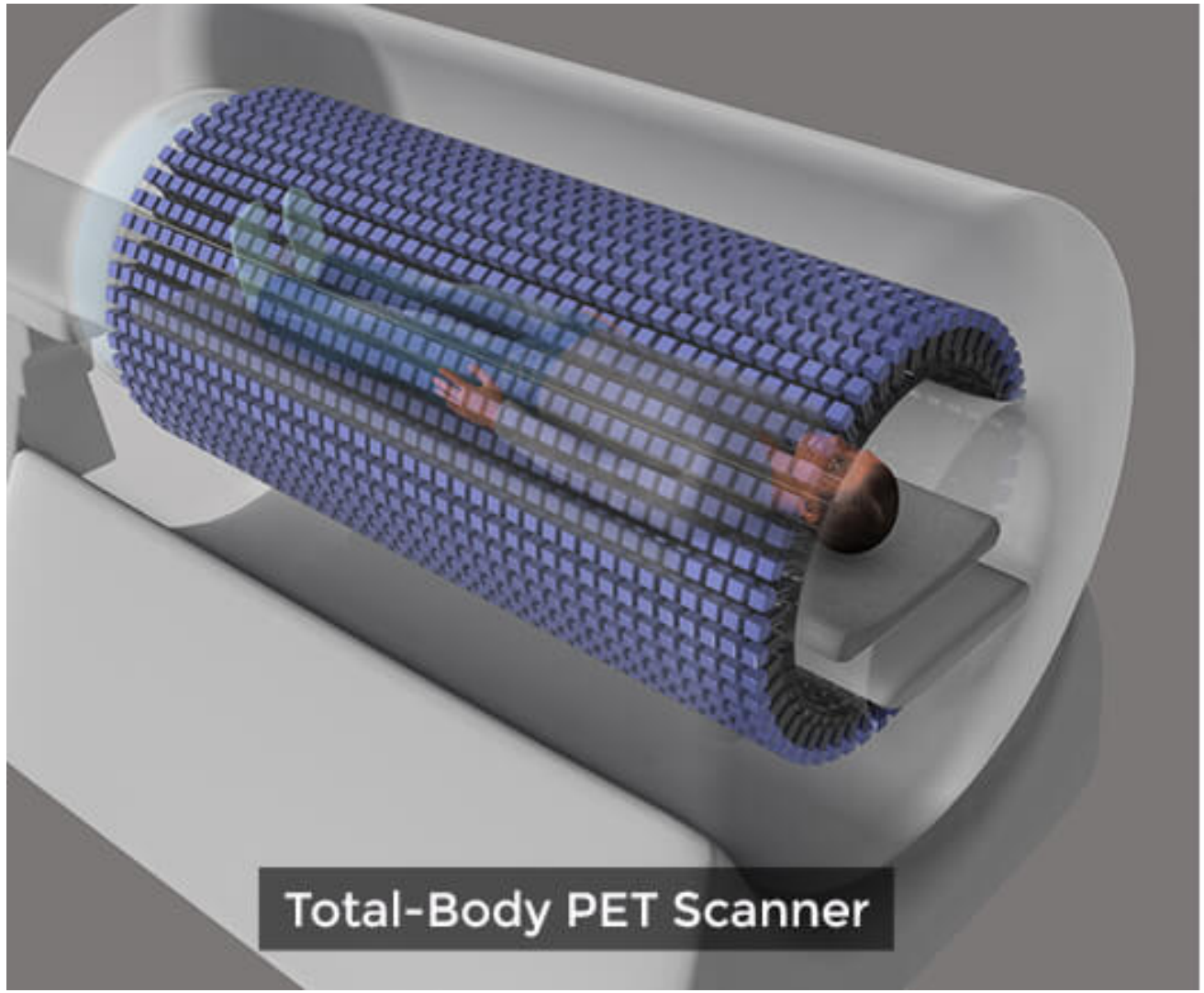
Total-Body TOF-PET





https://www.cancer.gov/news-events/cancer-currents-blog/2017/total-body-pet

Total-Body TOF-PET

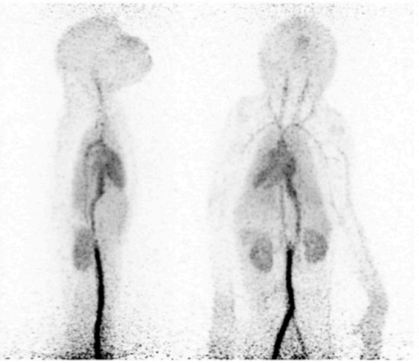


https://www.cancer.gov/news-events/cancer-currents-blog/2017/total-body-pet

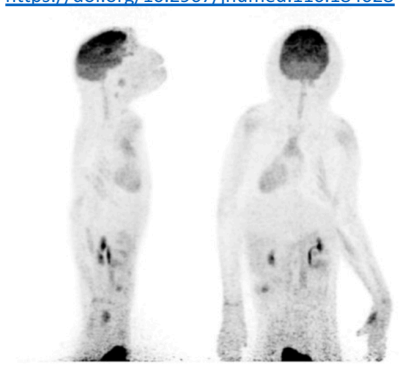
EXPLORER Consortium

- First implementation of total-body concept
- Based on traditional scanner technology
  →Just add more rings next to each other!
- More than 560,000 LYSO crystals and 53,500 SiPMs
- Estimated cost is O($10M) for CT/PET version
  →compared to O($2M) for current commercial device
- Prototype results are very promising
  (sensitivity gain expected is 30-50)

https://doi.org/10.2967/jnumed.116.184028



0- to 30-s scan



55- to 60-min scan

Total-Body TOF-PET: Immediate Advantages

- Entire body within the FOV
  →True 3D annihilation vertex reconstruction

- Scan entire body at once
  →Capture dynamical information from multiple parts of the body, can begin to use systems kinetic modeling approaches that are currently hindered

- Increases sensitivity for gamma detection by greatly increasing the detector area, there is a trade off here in how this advantage can be used…

- $SNR \propto \sqrt{\frac{D}{\delta t}}$ (Diameter of object being imaged), decreased timing resolution → image quality improves

Ultimately 20 ps resolution would give ~3 mm spatial resolution, cannot do better than this due to e^+ momentum and non-colinearity of two gammas

Trading off the Gain in Sensitivity

$$SNR \propto \sqrt{S \cdot A \cdot T}$$

Sensitivity, Activity, Scan time

1. **Keep patient dose and scan time same, increases SNR**
   - Higher spatial resolution leads to smaller/lower-contrast structures/lesions to be detection and improved quantification in static and dynamic scans
   - Broadens the dynamic range, can follow radiotracers for longer times as they decay away, up to 5-6 additional half-lives, compared to traditional 3!
   - Increased rate of gammas in the device leads to more randoms, degrades SNR

2. **Keep the SNR and activity constant, decrease scan time**
   - Scans times reduced from O(10min) to O(10sec)
   - Improved image quality due to less patient movement

3. **Keep SNR and scan time constant, decrease patient dosage**
   - Injected activity reduced from O(10mCi) to O(100μCi), effective dose less than 0.2 mSv
   - Improved image quality with less randoms and dead time at lower activities
   - Could use longer lived isotope like ^{89}Zr, could allow for follow-up scans 30d after initial scan without further injection
   - Improves the ability to do multi-tracer studies with isotopes with much different half-lives
   - This opens the door to imaging the sensitive and distant populations

Liquid Argon as Scintillator for 511 keV Gammas

- Compton scatters in LAr vs photoelectric conversion in LYSO
  - Fast scintillation w/ decay time of ~6 ns (also long lifetime component O(1 μs), can be suppressed)
  - Need to shift 128 nm scintillation photons
- 40,000 scintillation photons per MeV, ~30% more than LYSO
- Energy resolution O(few %) for multiple Compton scatters
  - No non-linear quenching effects
- Scalable, monolithic and homogenous format
  - Uniform response
  - Cost much reduced (1/5,000 for argon from the atmosphere vs LYSO)
- Attenuation length O(100 mm) (12 mm for LYSO), compensate with thickness
- Cryogen will control photosensor and electronics temperature/gain

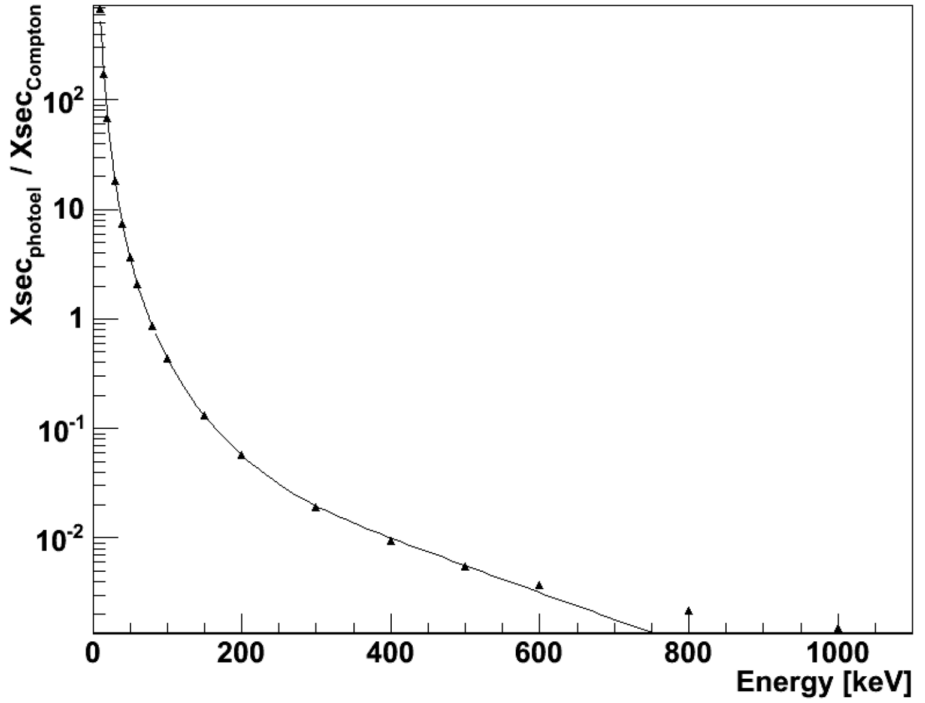
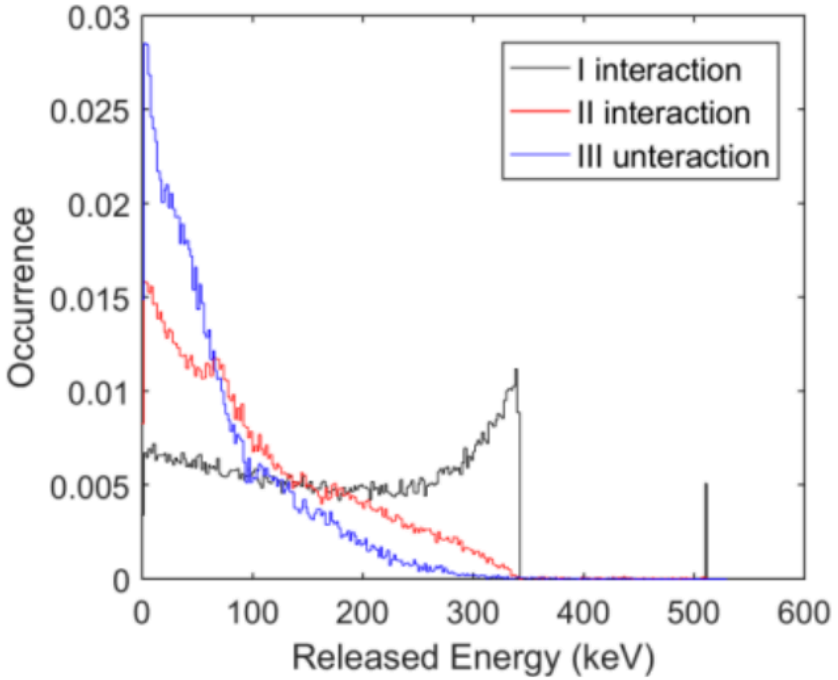


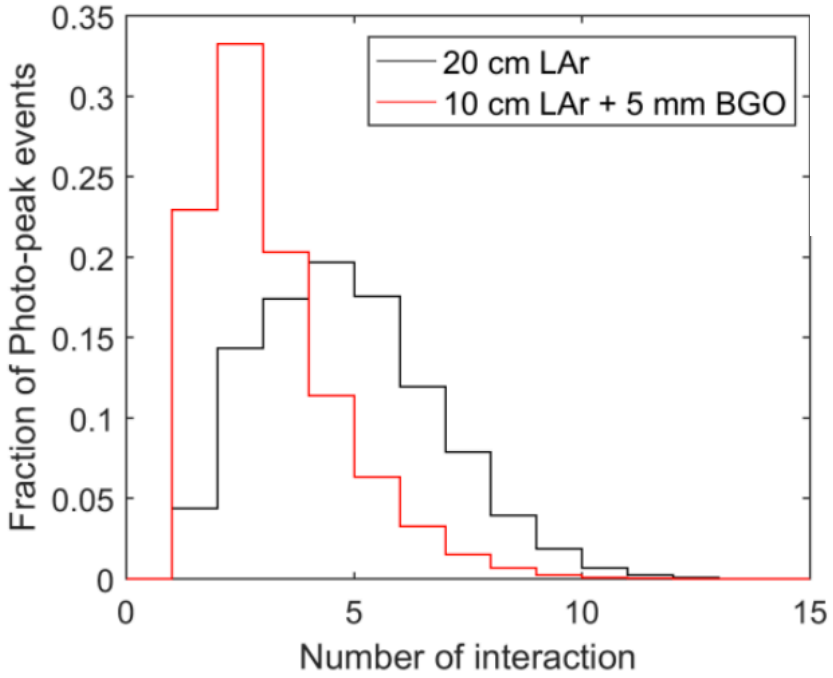
Image from ArDM

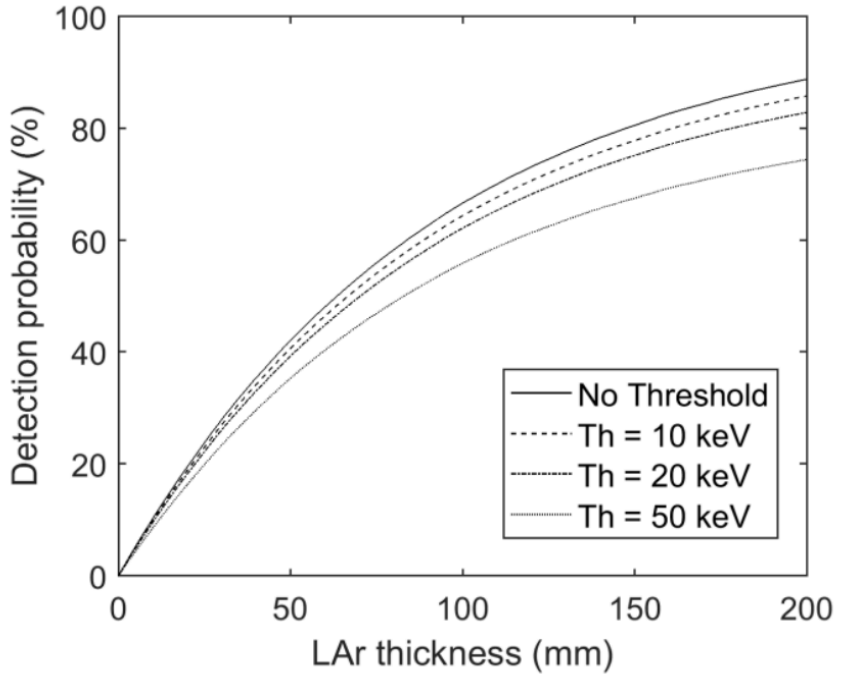
- Low-radioactivity argon can be used → limits rate of randoms (raises cost of LAr, still O(100) times cheaper less than LYSO)

Capturing 511 keV Gammas in LAr

Figures taken from 3Dπ INFN proposal Morrocchi)

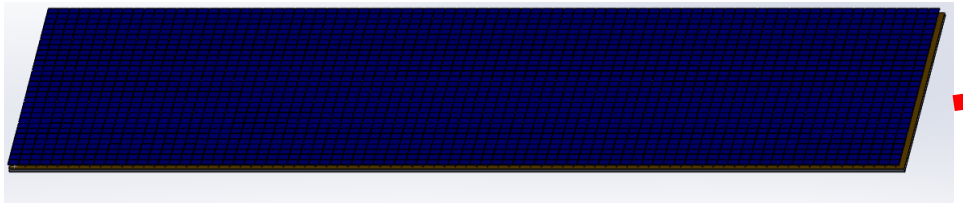


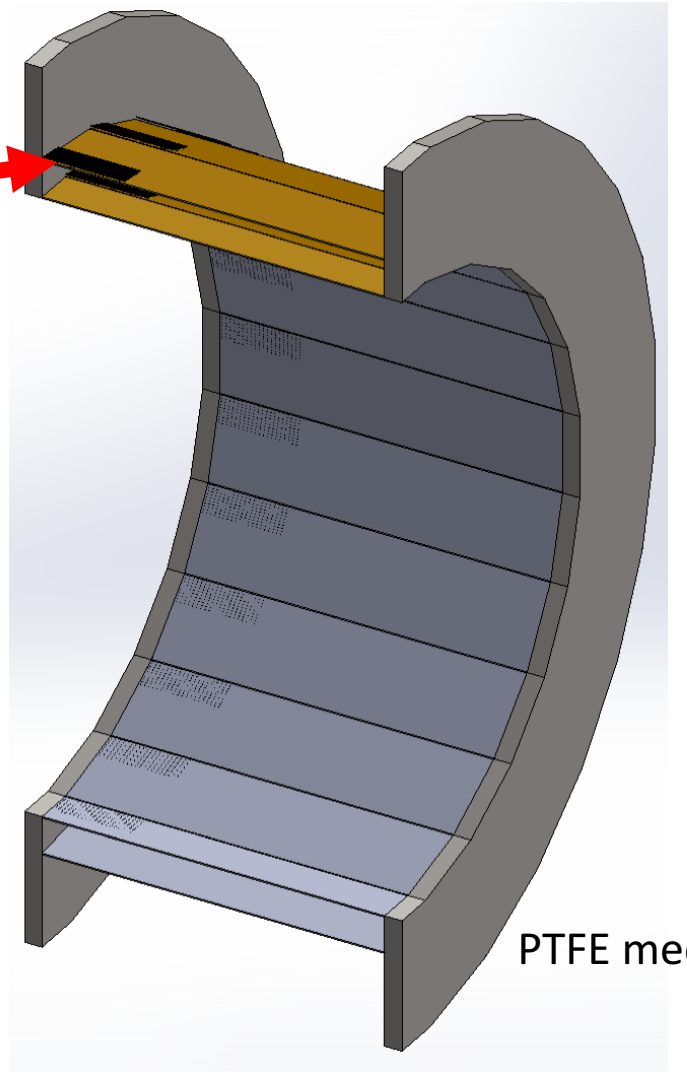




Conceptual Design of a LAr PET Detector

- Integrated cryogenic SiPM panels with readout
- SiPMs on boths sides of the panel



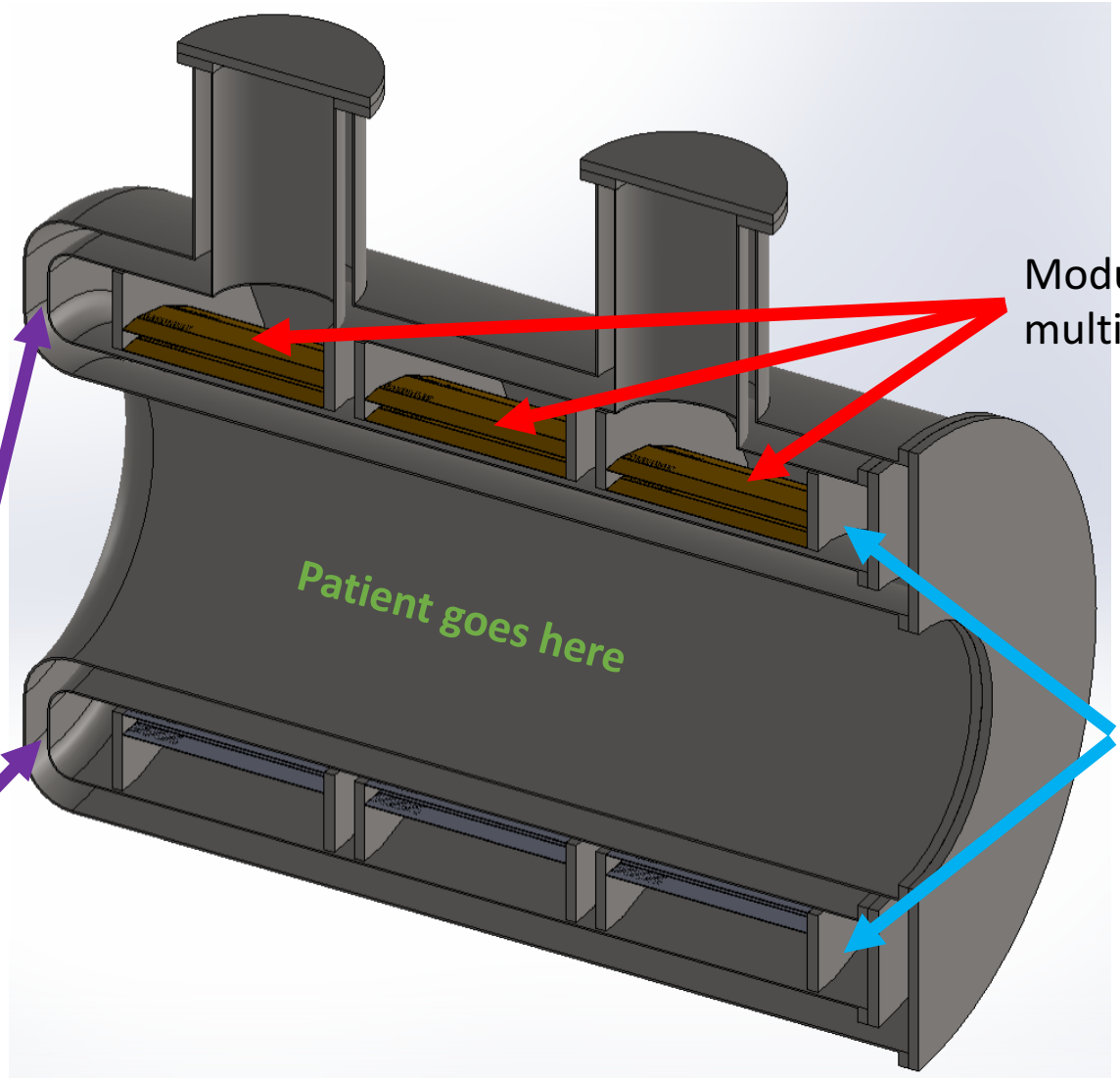


PTFE mechanical supports

- Modular concept, in which “rings” can be assembled and then placed into cryostat

- Each module would have 9 layers, providing the proper thickness to get >75% detection efficiency

Conceptual Design of a LAr PET Detector



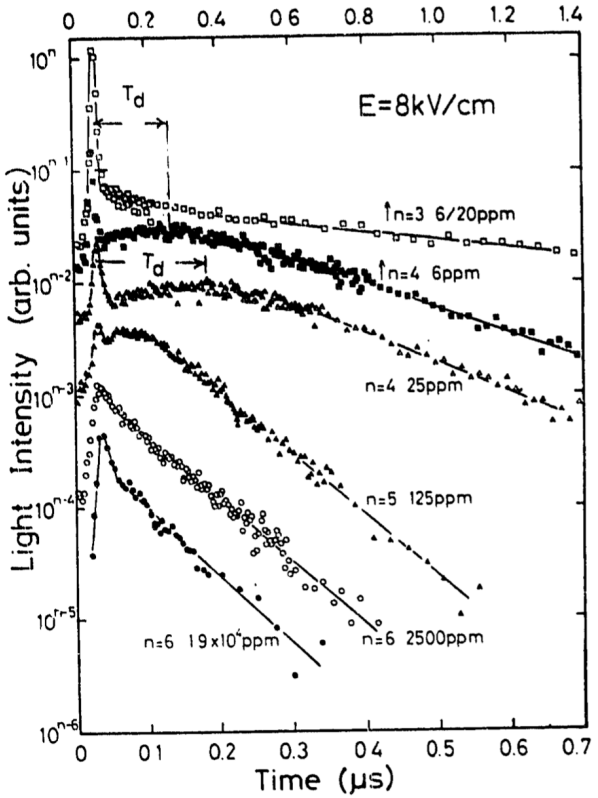
Modular SiPM detector assembly, multiple could be slid in from the side

Fill with LAr

Vacuum jacket around LAr

LAr+TPB vs. LAr+Xe

- LAr scintillates at 128 nm, low efficiency to detect this (<10%)
  - Caveat: long lifetime component gives light even after 1 μs
- TPB coated on all surfaces → shifts wavelength to ~420 nm
  - Caveat: TPB decay time is O(1ns), this hurts TOF resolution
- Possible solution, dope the LAr with some amount of Xe
  - Previous studies show it is possible at concentrations up to 10%
  - Greatly suppresses long lifetime component of LAr scintillation
    - At ~2% Xe concentration the long lifetime component is suppressed to a decay constant ~80 ns
    - LY may increase, fraction of scintillation light at 176 nm Xe wavelength
  - Increases density and effective Z, so shorter attenuation length



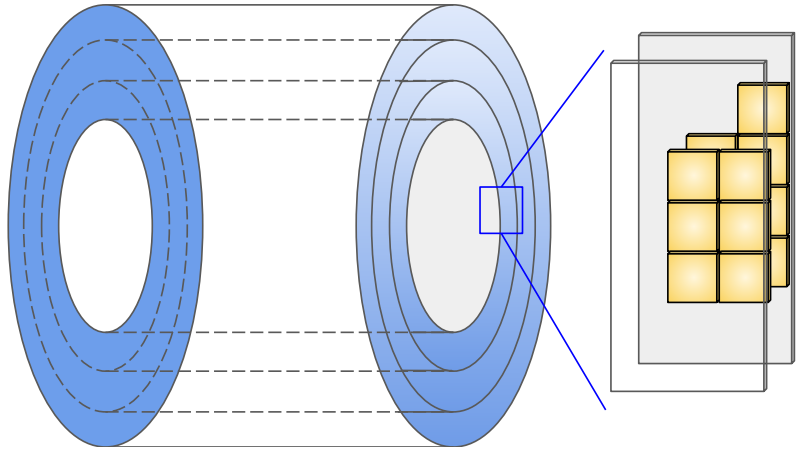
https://doi.org/10.1016/0168-9002(93)91413-H

Simulation Package Information

- Based on Geant4 package built for the DarkSide experiments
  - Optical properties of LAr scintillation and light propagation tuned with real data from DarkSide detectors
  - Response to electron recoils from gamma rays has been well studied and compared with real detector data

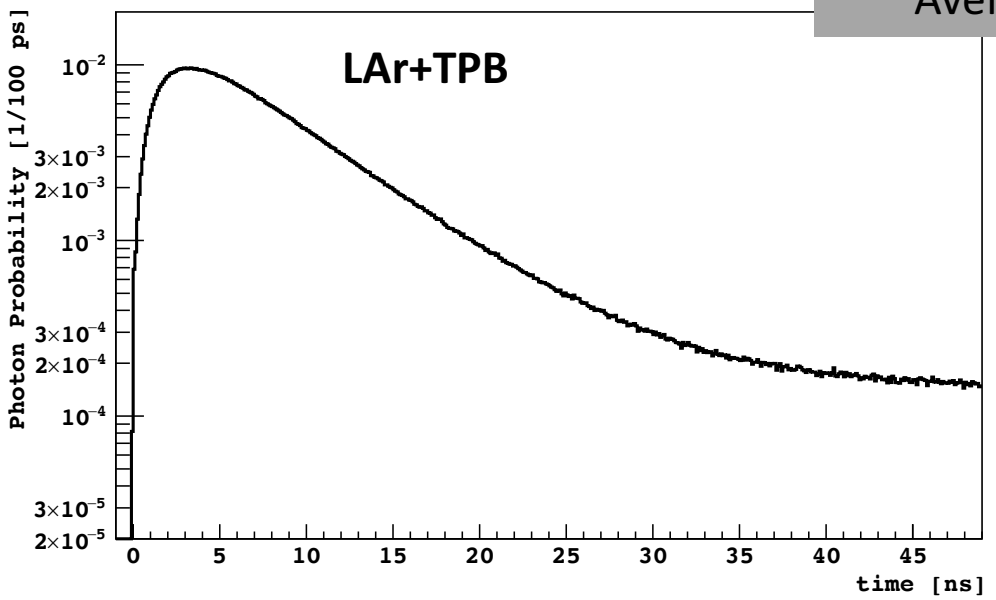
http://arxiv.org/abs/arXiv:1801.06653

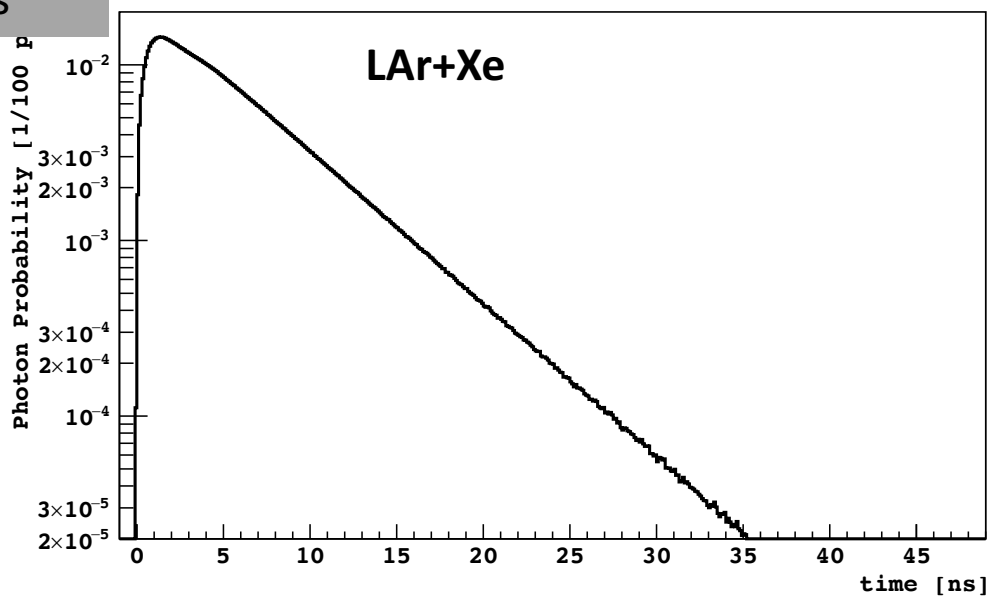
- Current simulations assume 9 layers of SiPM panels
  - Provide ~20 cm of LAr thickness → >70% of gammas scatter inside detector
  - Assumes minimal thickness of Ti cryostat (6 mm)
  - SiPMs assumed to have 40 ps intrinsic timing resolution
  - SiPM detection efficiency = 70% at 420 nm, 30% at 172 nm

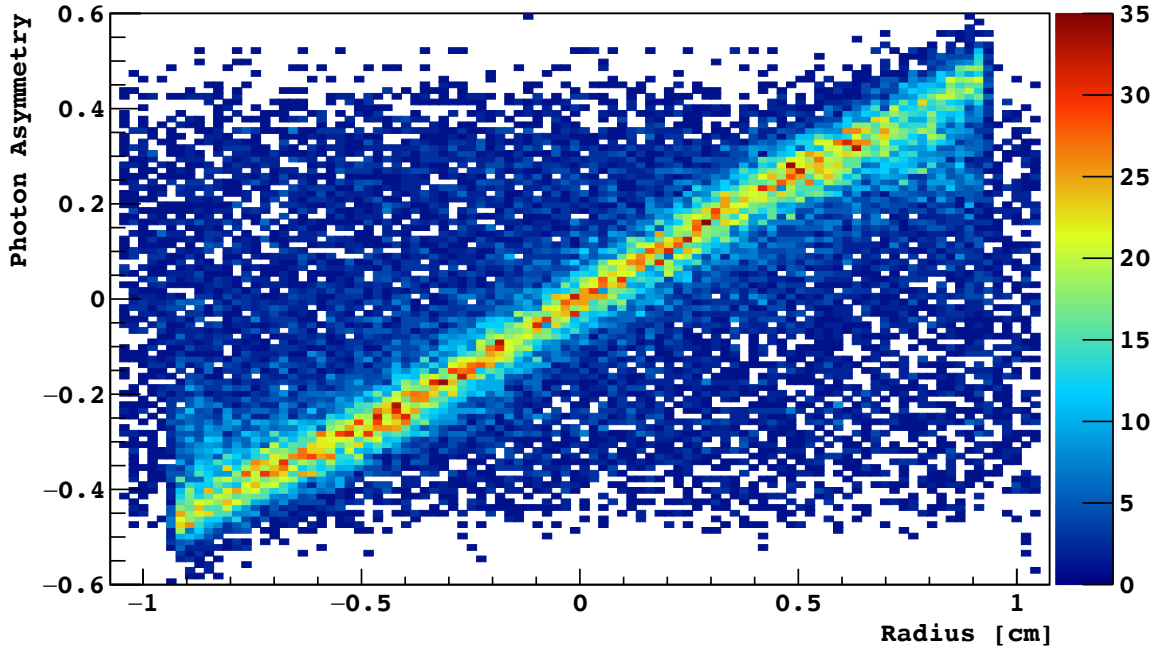


Simulations Outputs

Averaged waveforms



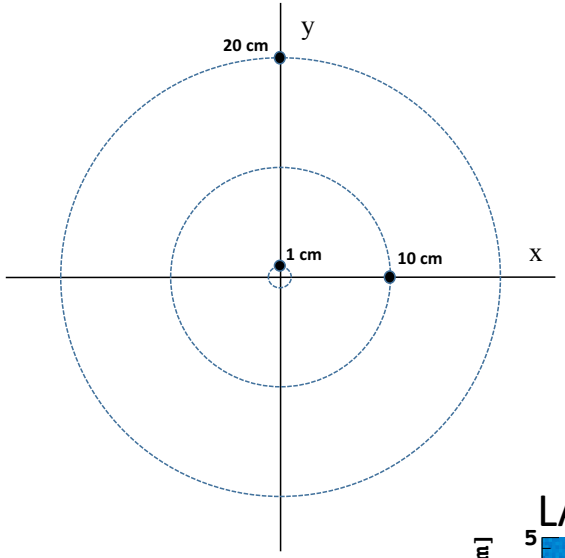




Light sharing asymmetry for between facing SiPMs, used for DOI

Similar results for LAr+TPB and LAr+Xe

NEMA NU 2-2012 Spatial Resolution Test



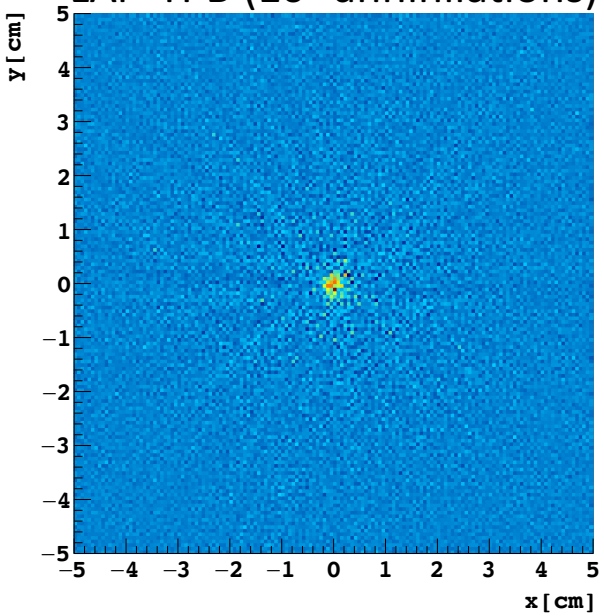
Source locations in the radial direction as shown

Two axial positions:

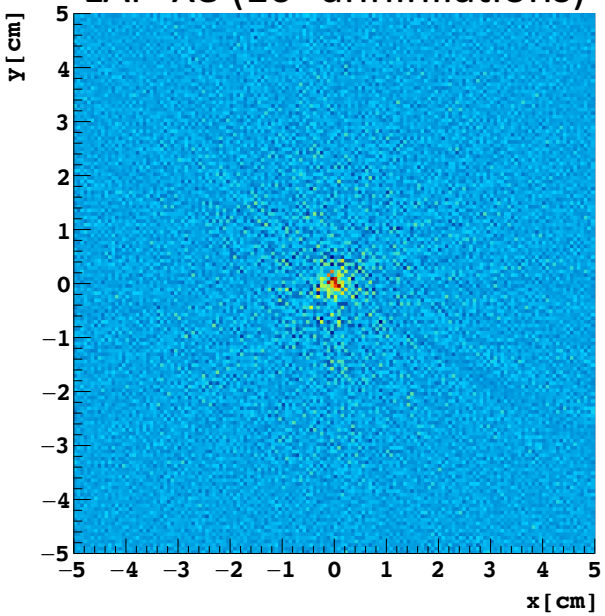
1) Center of FOV
2) 375 mm from center of FOV

Reconstruction done using simple filter back projection technique with no smoothing or apodization

LAr+TPB (10^4 annihilations)



LAr+Xe (10^4 annihilations)



NEMA NU 2-2012 Spatial Resolution Test

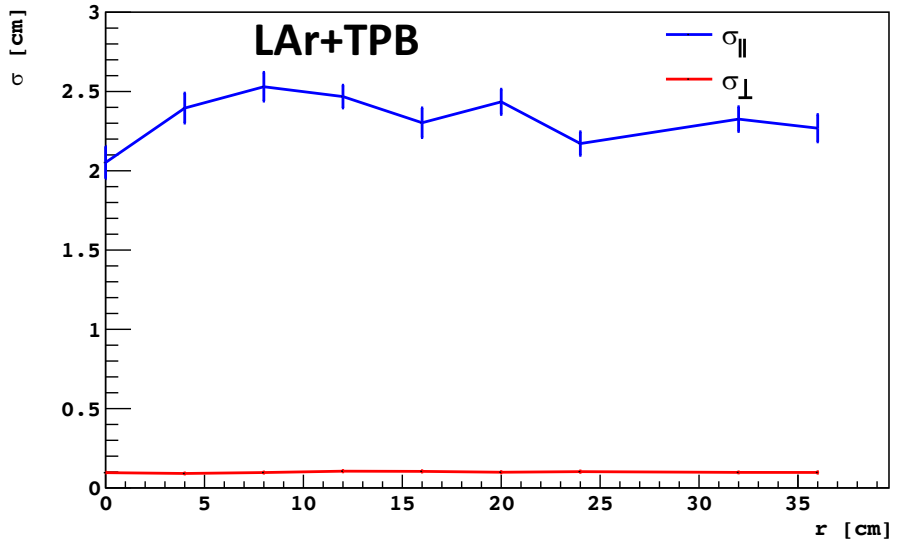
	LAr+TPB (center)	LAr+TPB (375 mm)	LAr+Xe (center)	LAr+Xe (375 mm)
y = 1 cm position				
σ_x[mm]	8.8	8.7	4.7	4.3
σ_y [mm]	11.3	11.4	4.1	5.5
σ_z [mm]	8.7	8.2	6	7.3
$\sigma_{transverse}$ [mm]	**10.0**		**4.7**	
σ_{radial} [mm]	**8.5**		**6.7**	
x = 10 cm position				
σ_x [mm]	8.7	8.0	4.5	5.4
σ_y [mm]	7.1	9.0	4.8	5.2
σ_z [mm]	11.2	7.6	6.7	6.8
y = 20 cm position				
σ_x [mm]	7.8	7.2	4.1	5.5
σ_y [mm]	8.4	7.2	4.2	5.7
σ_z [mm]	10.8	10.3	6.4	7.2
$\sigma_{transverse\ rad}$ [mm]	**8.1**		**5.0**	
$\sigma_{transverse\ tan}$ [mm]	**7.8**		**5.0**	
σ_{axial} [mm]	**10.0**		**6.8**	

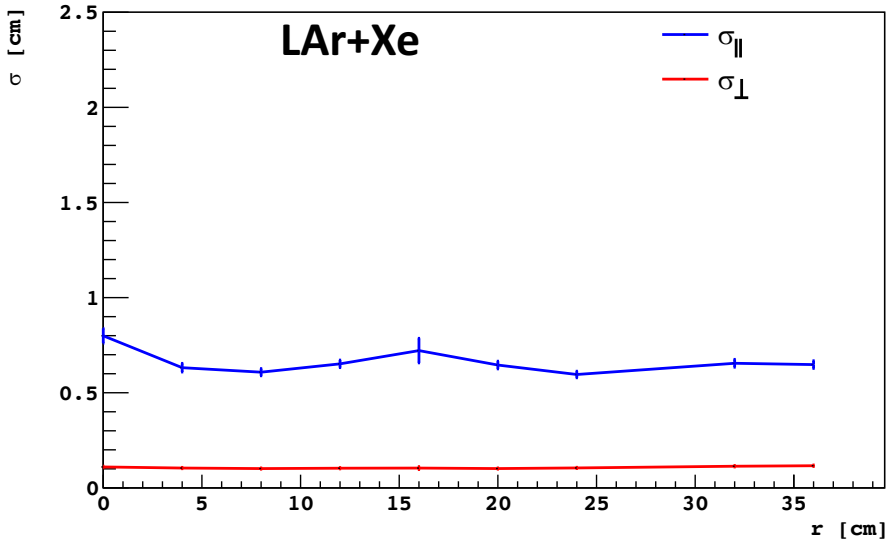
k projection
tion**

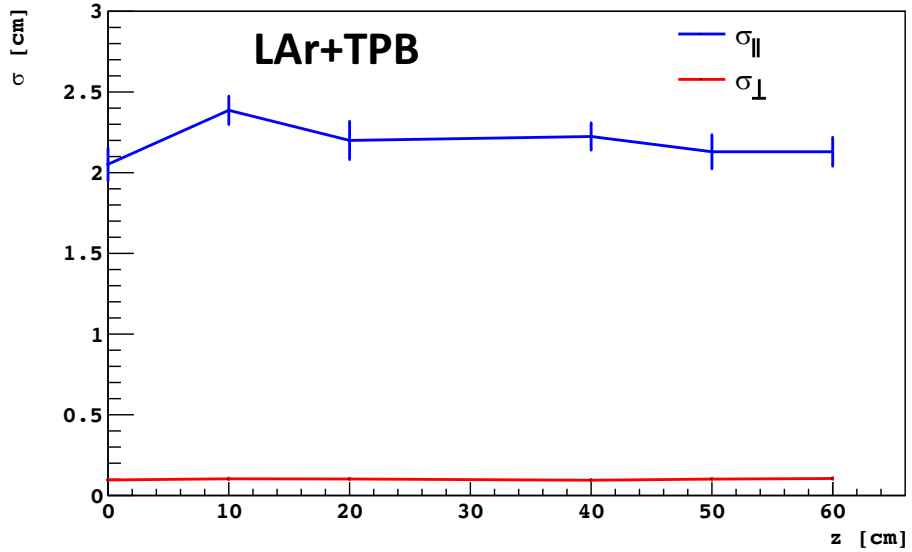
x [cm]

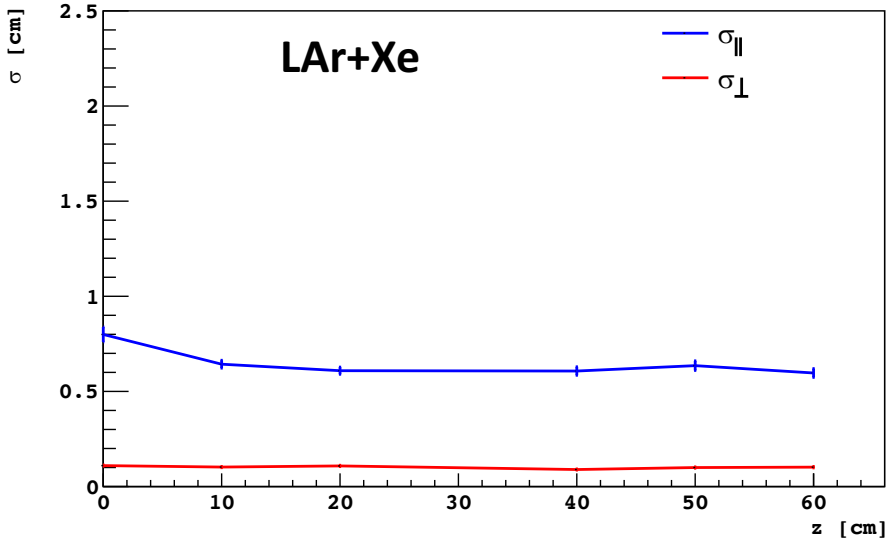
x [cm]

Spatial Resolution: Dependence on Parameters

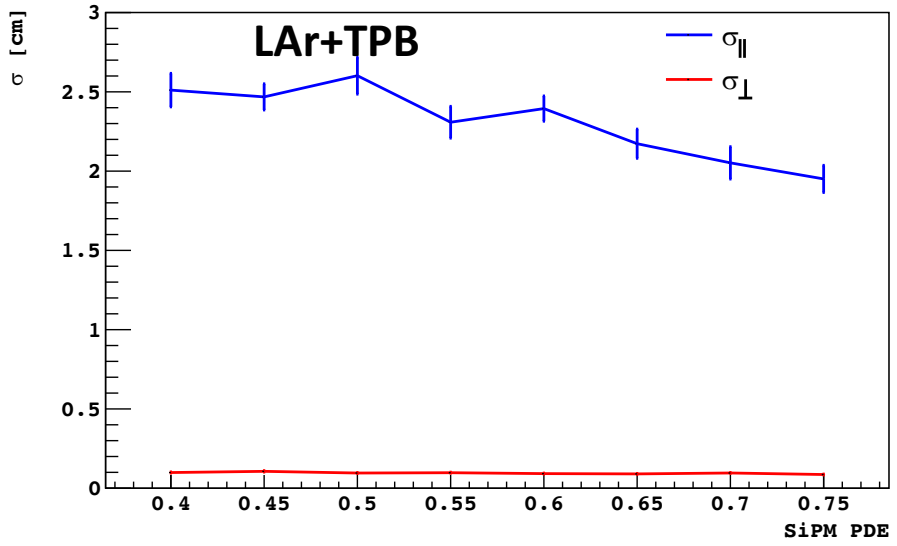


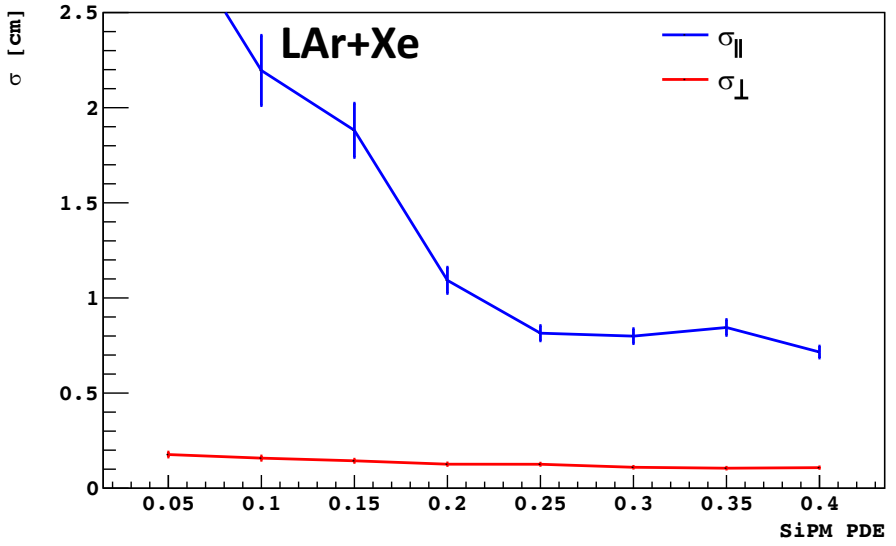


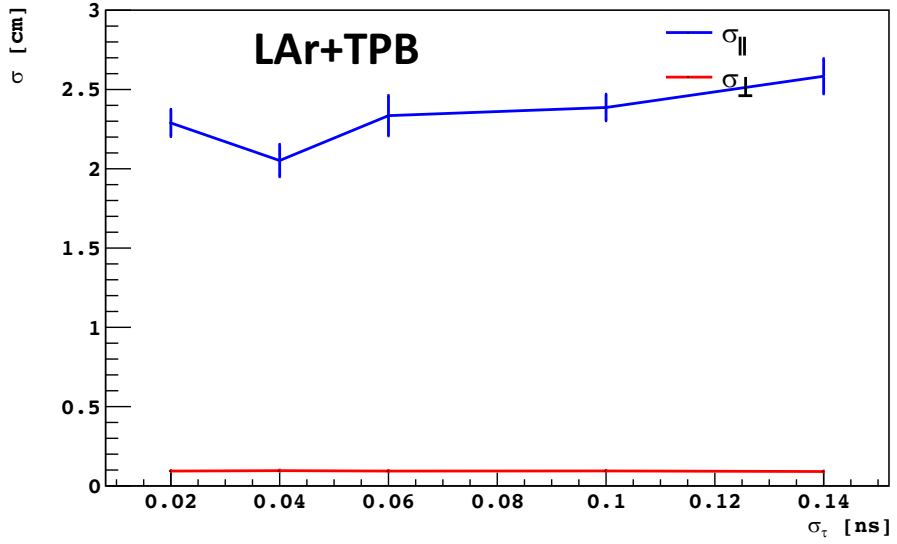


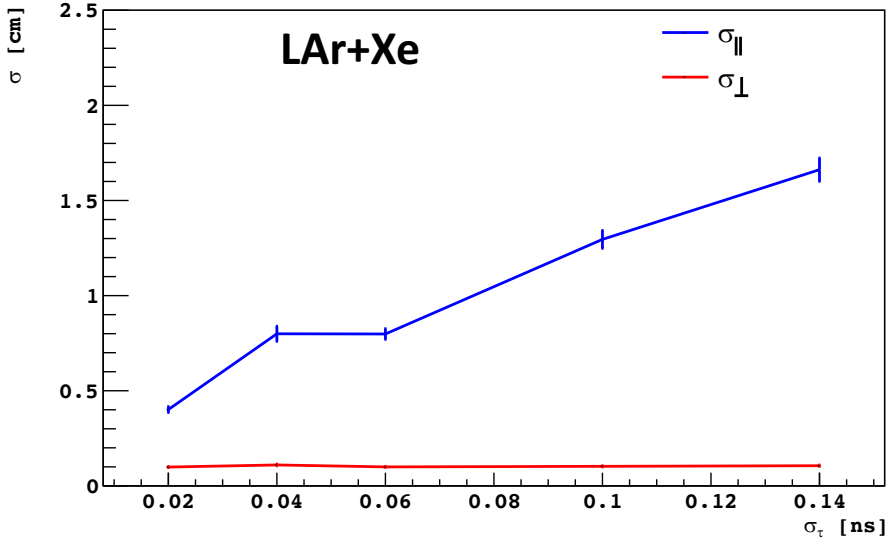


Spatial Resolution: Dependence on Parameters



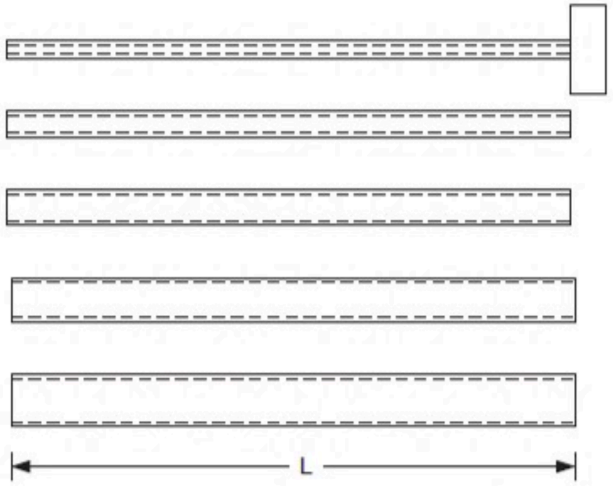






NEMA NU 2-2012 Sensitivity Test

Defined as number of counts per unit time detected by the device for each unit of activity present in the source [cps/kBq]



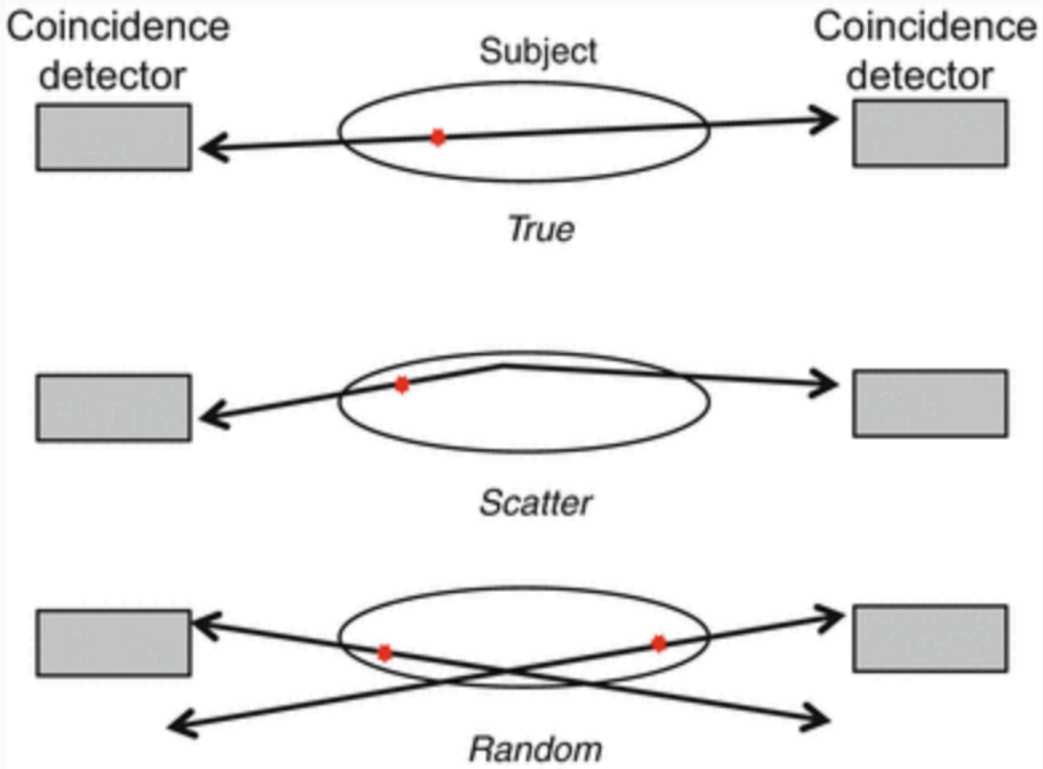
Tube Number	Inside Diameter (mm)	Outside Diameter (mm)	Length L (mm)
1	3.9	6.4	700
2	7.0	9.5	700
3	10.2	12.7	700
4	13.4	15.9	700
5	16.6	19.1	700

Figure 5-1
SENSITIVITY MEASUREMENT PHANTOM

- Simulate line source with varying thickness of attenuator (either Al or PTFE)
- Fit the count rate as a function of sleeve thickness
- Extrapolate back to 0-sleeve thickness, this is the sensitivity

	LAr+TPB	LAr+Xe
Sensitivity [cps/kBq]	505	513

NEMA NU 2-2012 Scatter Fraction, Randoms and Count Loss



https://radiologykey.com/pet-physics-and-instrumentation/

Scatter fraction is the ratio of scattered events to scattered+true events, measured at the noise equivalent count rate (NECR), affects SNR

$$SF = \frac{S}{T+S} \qquad NECR = \frac{T^2}{T+S+R}$$

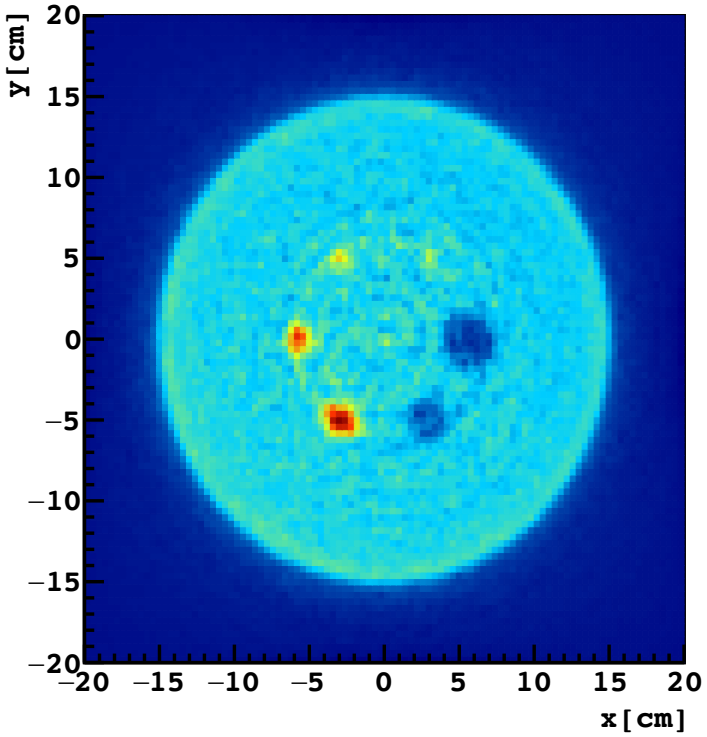
Randoms are detection of 2 gammas from two separate annihilations

Count loss gives the ability for the detector to work at higher and higher source activities

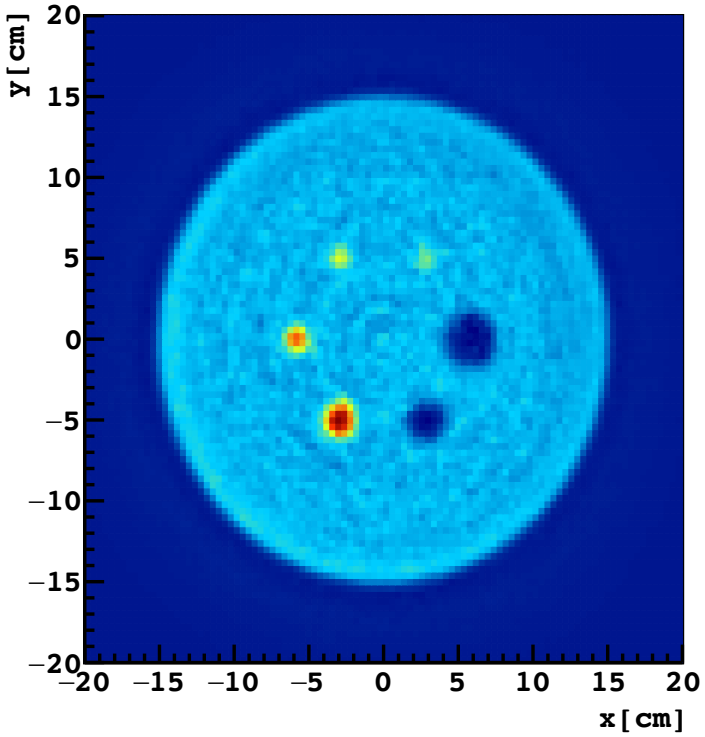
*****Simulations results too preliminary, still need to work on reconstruction*****

NEMA NU 2-2012 Image Quality Test

LAr+TPB

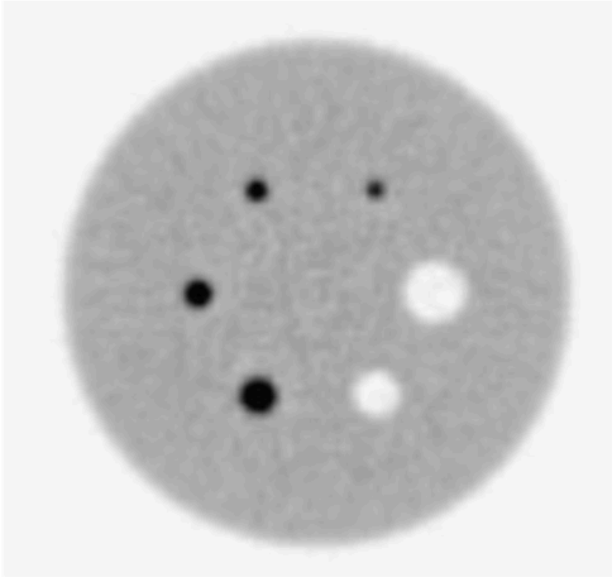


LAr+Xe



10^9 positron annihilations

LYSO



3.56×10^8 positron annihilations

Comparison to Commercial Technology

		LAr+TPB	LAr+Xe	GE Signa PET/MR	GE Discovery 710 PET/CT
Central position	$\sigma_{transverse}$ [mm]	10.0	4.7	4.30	4.73
	σ_{radial} [mm]	8.5	6.7	5.79	4.93
Off center position	$\sigma_{transverse\ rad}$ [mm]	8.1	5.0	5.79	5.35
	$\sigma_{transverse\ tan}$ [mm]	7.8	5.0	4.40	4.83
	σ_{axial} [mm]	10.0	6.8	7.26	5.62
	Sensitivity [cps/kBq]	**505**	**513**	22.2	5.458

First pass sensitivity gain is a factor of more than 23 larger than current commercial technology

Issues Still to be Addressed

- Finalize simulations and analysis for scatter fraction, count rate and loss, and randoms based on real backgrounds
- Move on to accuracy and uncertainty estimations, along with full image reconstruction analysis
- Design is very preliminary, only simple parts in the simulation
- Process of Xe doping in LAr needs to be further studied at concentrations up to 10% to fully understand scintillation light time profile and spectrum
- Engineering study to confirm mechanical stability of design and procedures for filling and emptying the LAr

Closing Remarks

- The biggest gain in sensitivity comes from detector area increase
- Total-body PET will open up new research and clinical applications
- LAr could be the cheapest way to make a total-body device
- New algorithms required to understand the true performance of LAr PET, but the potential looks very promising!
- We should build a prototype as soon as possible!!