Total Body PET: The Ultimate Molecular Imaging Tool:

Future Developments and Challenges in Scanner Design

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Joint EFOMP/AAPM Symposium,
Annual AAPM, July 16, 2020

Funding and Disclosures

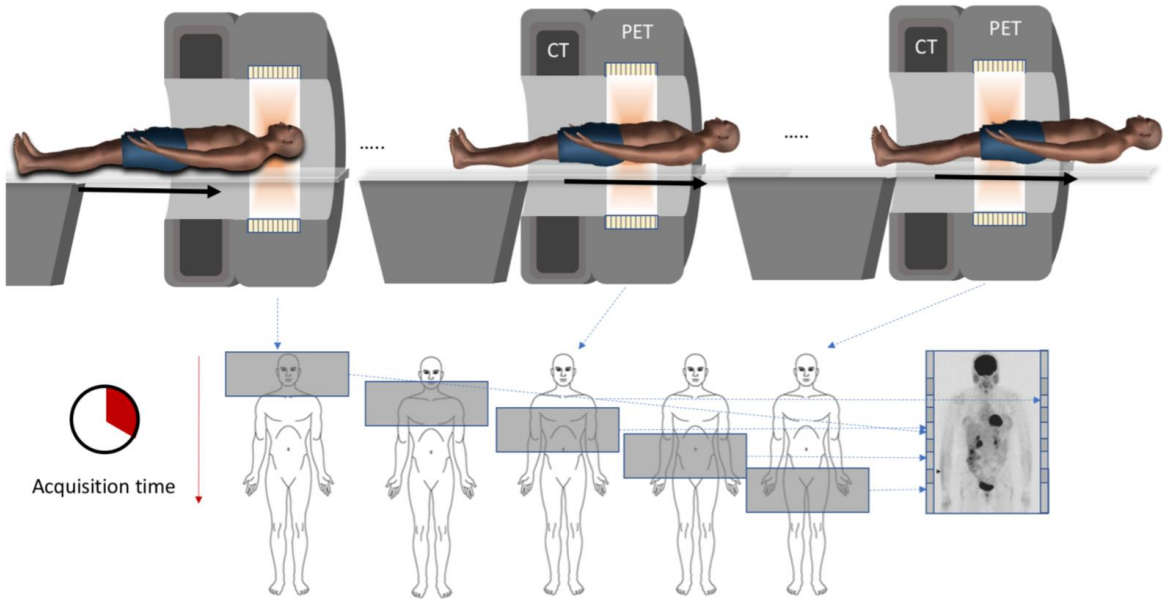
Funding support:

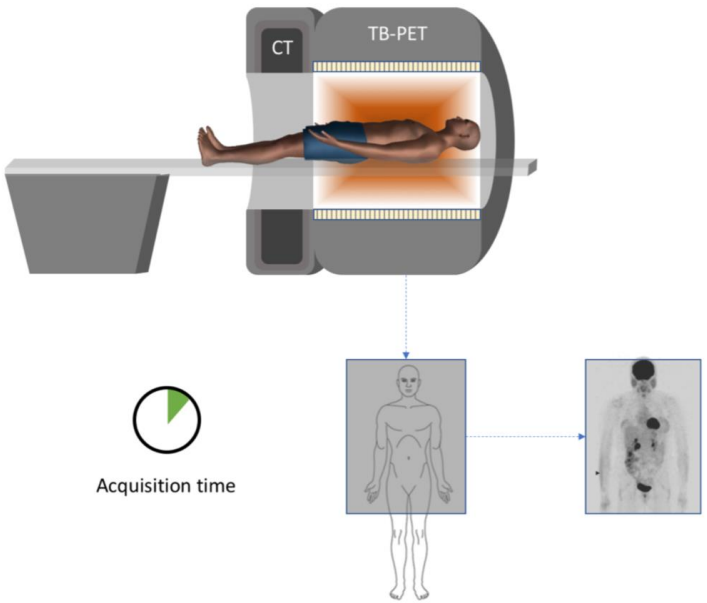
NIH R01-CA113941
NIH R01-CA206187
NIH R01-CA225874
NIH R33-CA225310

Disclosures:

Research contract with Philips Healthcare
Research contract with Siemens Healthcare

What is TB (Total-Body) PET?





- Standard PET: AFOV 15 -26 cm
  - Sensitivity limited by acceptance of oblique coincidence pairs
  - Multi (or continuous) bed positions for whole-body survey
  - Satisfactory for tracers with stable uptake, e.g., FDG at 1 hr p.i.

- TB-PET: Higher Sensitivity per volume
  - Sensitivity increases dramatically with axial length
  - Single bed position can capture all major organs
  - Capability of whole-body dynamic imaging

Illustrations courtesy S. Vandenberghe et al, EJNMMI Physics, 2020

What are the questions going forward?

- What are the important clinical and research applications for TB-PET?

- What are the key scanner requirements, beyond longer axial length?
  - TOF resolution (effective sensitivity) vs geometric sensitivity?
  - spatial resolution?

- What about cost?
  - purchase cost
  - operational cost - reliability

- What is the optimal axial length of a scanner for TB-PET?
  - ***Depends on all of the above***

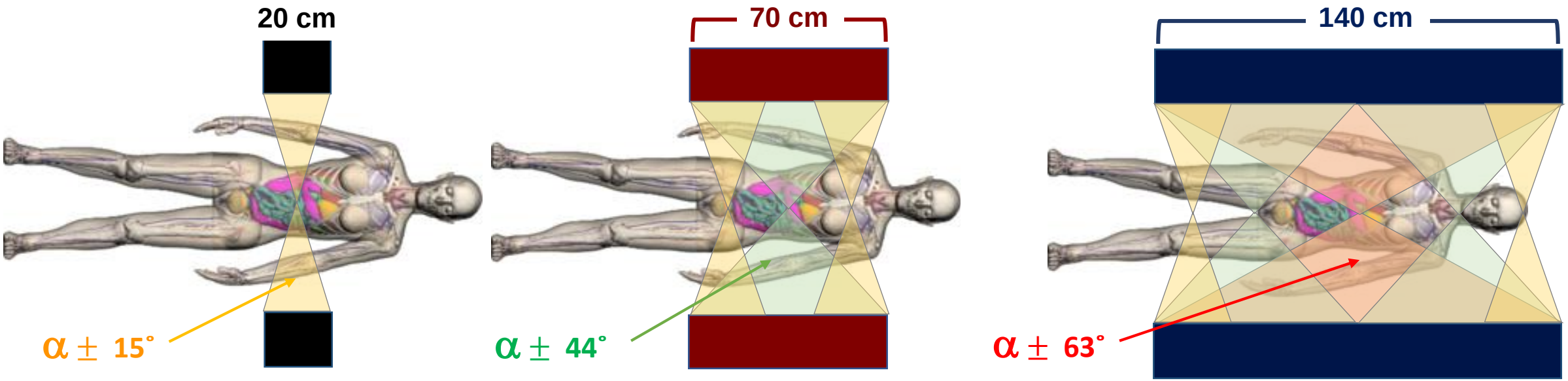
Total Body PET Design: Practical Considerations

- Cost
  - Dominated by scintillator and photosensor (SiPM) materials
  - Commercial (state-of-the-art) scanner: typical PET/CT purchase price $2M
    20-25 cm AFOV -> 10-12 liter scintillator, 0.5 m^2 sensors (SiPM)
  - Long axial FOV scanner

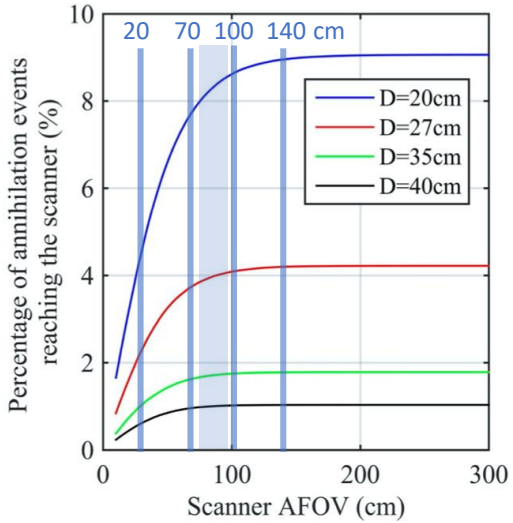
70 cm AFOV	-> 32 liter scintillator,	1.7 m^2 sensors	-> x 3 cost	~$2M (materials)
140 cm AFOV	-> 64 liter scintillator,	3.4 m^2 sensors	-> x 6 cost	~$4M (materials)
200 cm AFOV	-> 90 liter scintillator,	4.8 m^2 sensors	-> x 8.4 cost	~$5.6M (materials)

- Reliability and operational cost
  - Multiple scanners – electronics, computers, etc.
  - > 100,000 SiPM devices (channels) – with temperature control
  - *But….much redundancy as long as majority of scanner detectors are functional*

Axial acceptance angle increases with axial length



Point source



Uniform source (35-cm diam.)

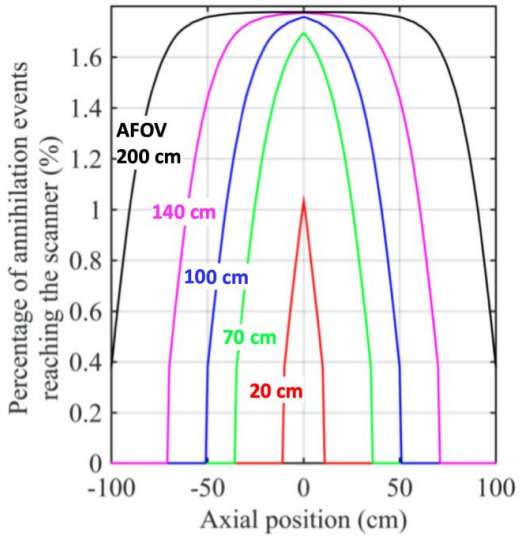


TABLE I

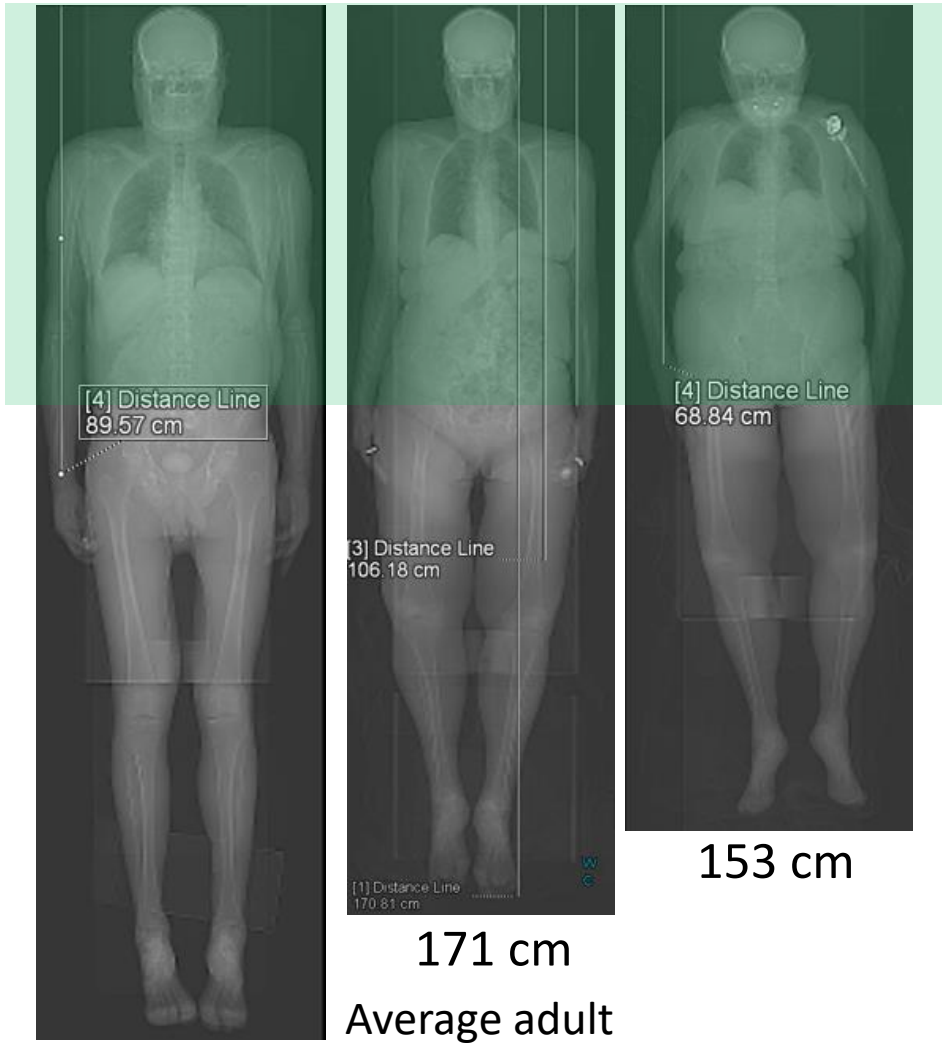
RELATIVE SENSITIVITY FOR SELECTED SCANNER AXIAL LENGTHS AS CALCULATED FOR THREE DIFFERENT IMAGING SETUPS. THE PHANTOMS ARE 200 CM LONG CYLINDERS.

Scanner AFOV (cm)	20	70	100	140	200
Point source in a 20 cm ϕ cyl.	1	2.4	2.7	2.8	2.8
Uniform source in a 20 cm ϕ cyl.	1	10	18	29	46
Uniform source in a 35 cm ϕ cyl.	1	14	24	38	56

How long is enough?

Partial body coverage

70 cm



153 cm

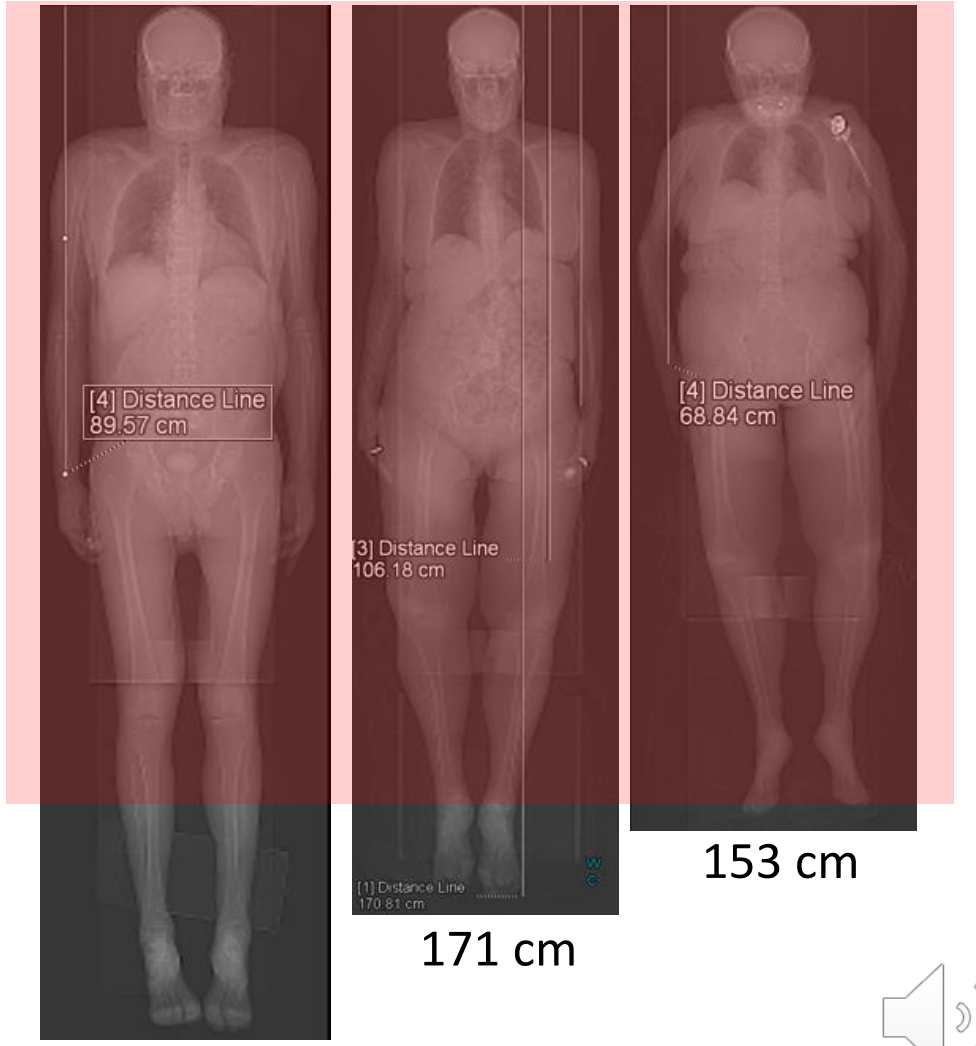
171 cm

Average adult

Patient Height 193 cm

Full body coverage

140 cm



153 cm

171 cm

193 cm

Courtesy, Bernard Bendriem, Siemens

Clinical scanners: State-of-the-art

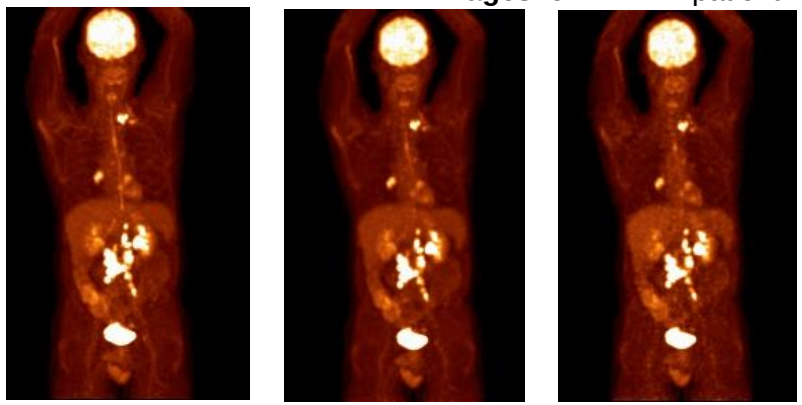
- PET axial field-of-view FOV: *15-26cm*
- CT scanner: *anatomic correlation & attenuation correction*
- Fully-3D: *higher sensitivity*
- Iterative reconstruction: *higher SNR*
- Lu-based scintillators: *LSO, LYSO*
- Time-of-flight: *improved with SiPMs*

Clinical scanners: State-of-the-art

Philips Vereos

- Axial FOV: 16.4 cm
- Spatial resolution 4 mm
- TOF: 320ps

MIP images for BMI=24 patient



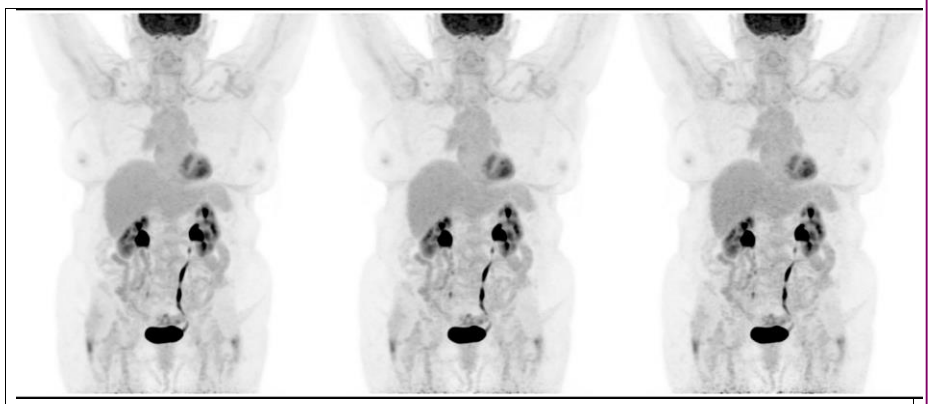
15min 5min 1.5min

Courtesy, Drs. Knopp, Zhang, OSU

GE MI Discovery

- Axial FOV: 15 cm, 20 cm, 25 cm
- Spatial resolution 4-5 mm
- TOF: 380 ps

MIP images for BMI=35 patient



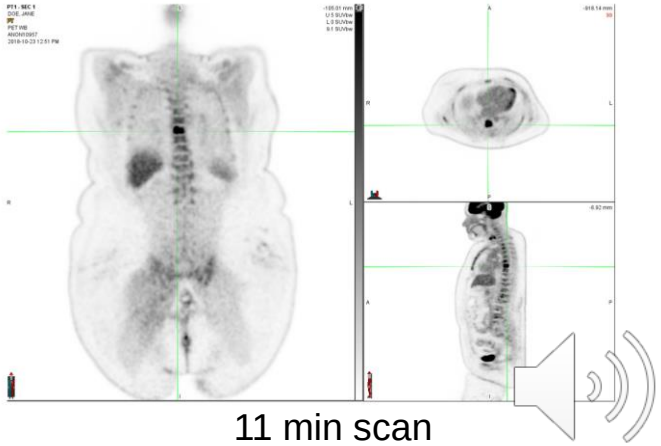
Total scan	12 min	8 min	5.3 min

Courtesy, Dr. Mawlawi, MDACC (5 ring scanner)

Siemens Biograph Vision

- Axial FOV: 26.3 cm
- Spatial resolution 3.6 mm
- TOF: 215 ps

Sectional images for BMI = 43.6 patient



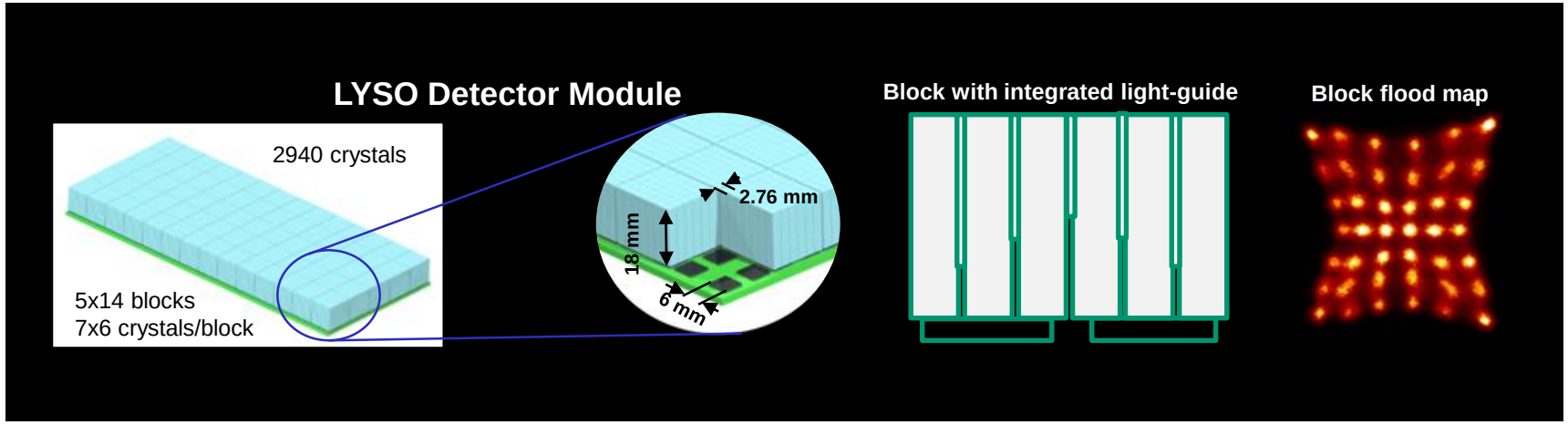
11 min scan

Courtesy, University of Pennsylvania

Long AFOV scanners: UIH uEXPLORER

uEXPLORER

uEXPLORER PET Detectors: **10:1 encoding, crystals:SiPMs**



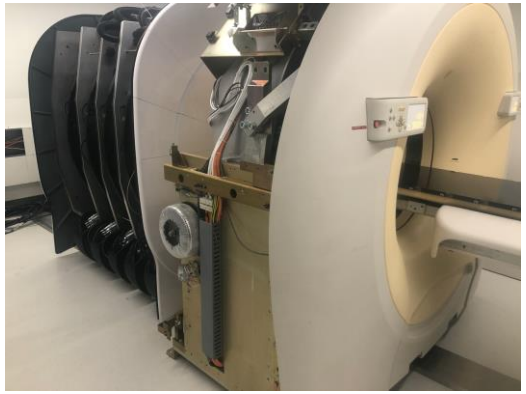
Courtesy, Hongdi Li, UIH America

- TOF = 505 ps, 3-mm spatial resolution

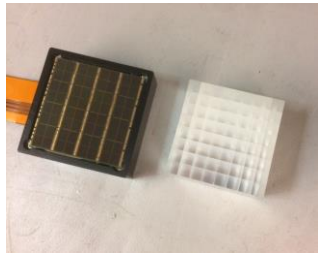
- Axial FOV: 194 cm
- Transaxial FOV: 68.6 cm
- Bore diameter: 76 cm
- 564,480 crystals
- 53,760 SiPMs
- 80 row CT

Long AFOV scanners: PennPET Explorer

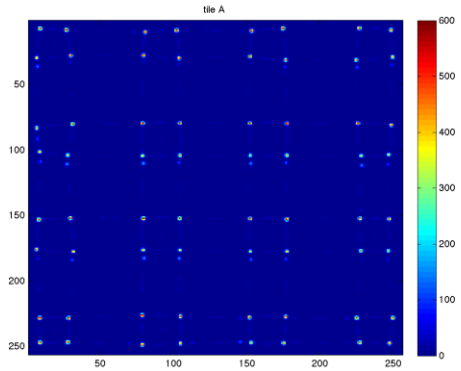
PennPET Explorer

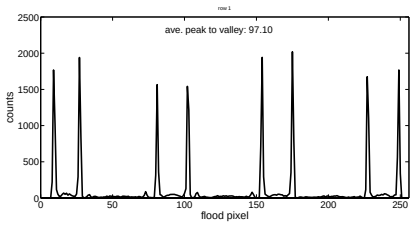


PennPET Detectors: **1:1 encoding, crystals:SiPMs**



2D flood





3.86 x 3.86 x 19 mm^3 LYSO with PDPC digital SiPM

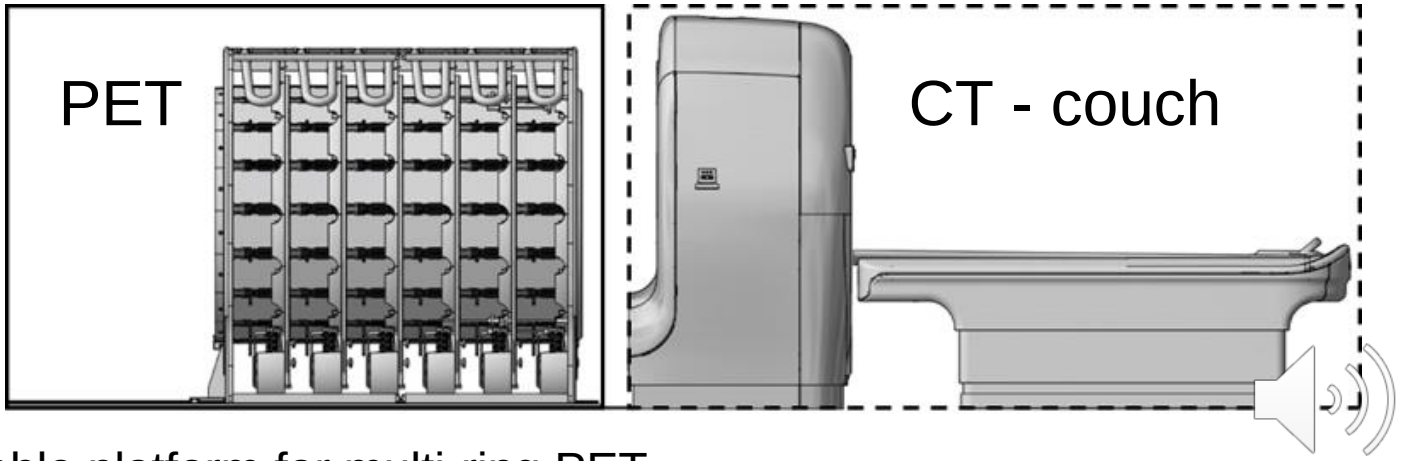
- TOF = 250 ps, 4-mm spatial resolution

3-ring

70 cm

6-ring

140 cm

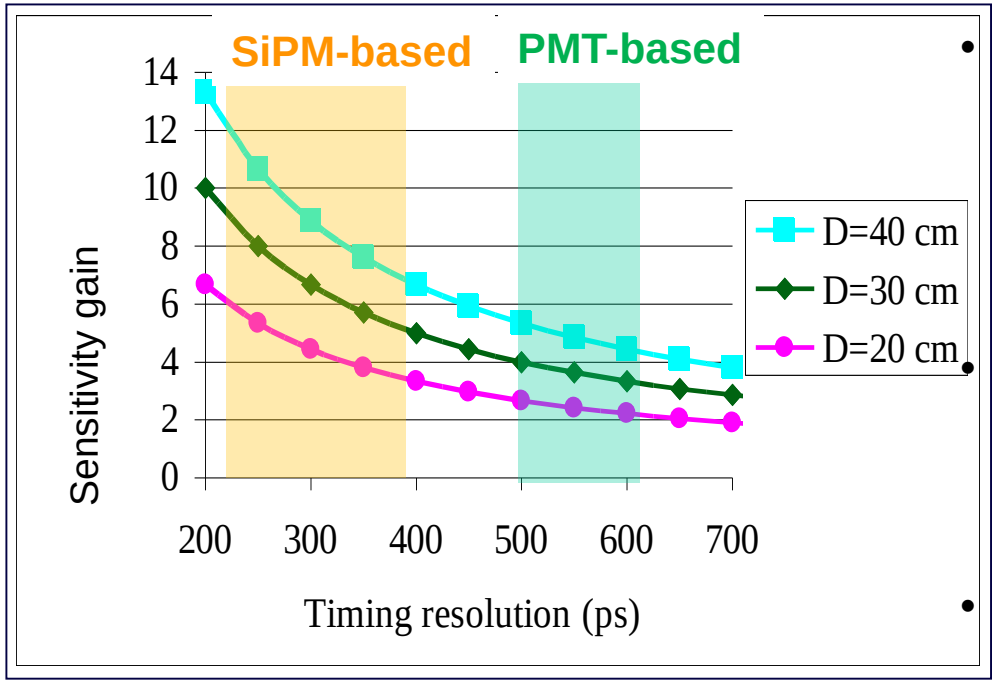


Scalable platform for multi-ring PET

TB-PET looking forward

Benefits of TOF increase with better timing resolution

- Improved Signal-to-Noise Gain = $(D/\Delta x)^{1/2}$
- Improved Quantitative Accuracy



The 10 ps challenge:
a step toward reconstruction-less TOF-PET

The10ps-challenge.org
P. Lecoq *et al*

New scintillators

- LSO with optimized dopants – *higher light, faster, better TOF*
- Ceramics (e.g., GluGAG) – *less costly*
- BGO with Cerenkov radiation – *less costly*

New photo-sensor technology

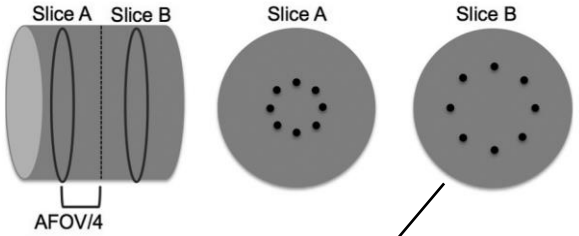
- SiPM with TVS technology – *improve fill factor, better TOF*
- SiPM with higher efficiency – *improve statistics, better TOF*

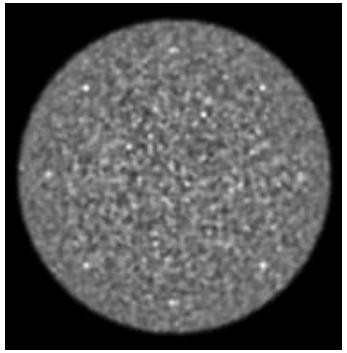
Improved detector designs

- Dual-side readout read-out – *reduce timing dispersion*
- Monolithic detectors – *with depth-of-interaction*
  - Fully digital, 3D Anger-logic detector with MLEM position processing
  - **< 150 ps TOF and < 2 mm spatial resolution**

Improving Timing resolution…or Spatial resolution…or both

Monte Carlo Simulations

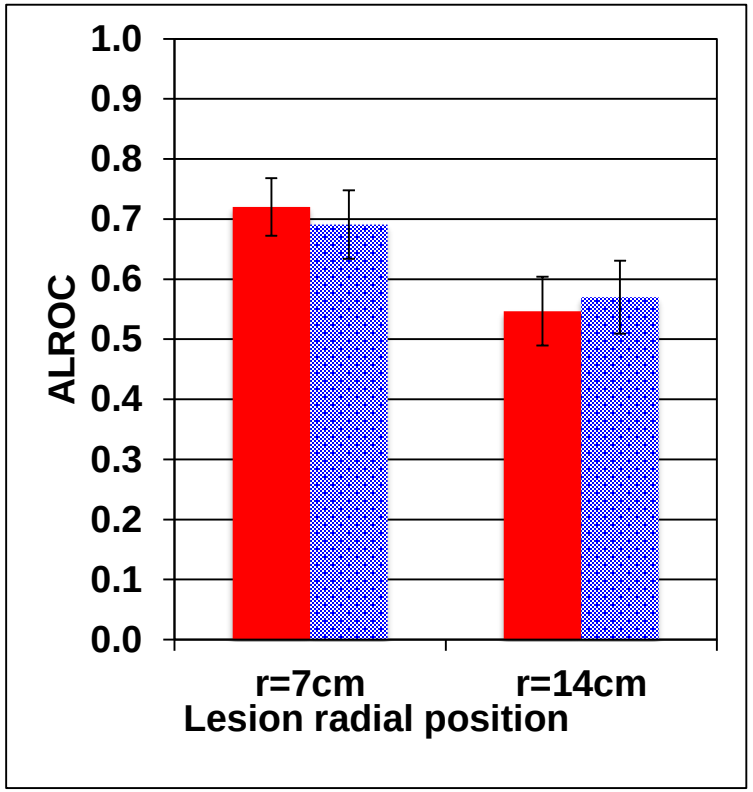




Surti *et al*., TNS 2013

Detectability task

2.6mm, 600ps 4.0mm, 300ps



0.10 μCi/cc, 3 min scan time/bed position, 5-mm diam. 6:1 uptake lesions

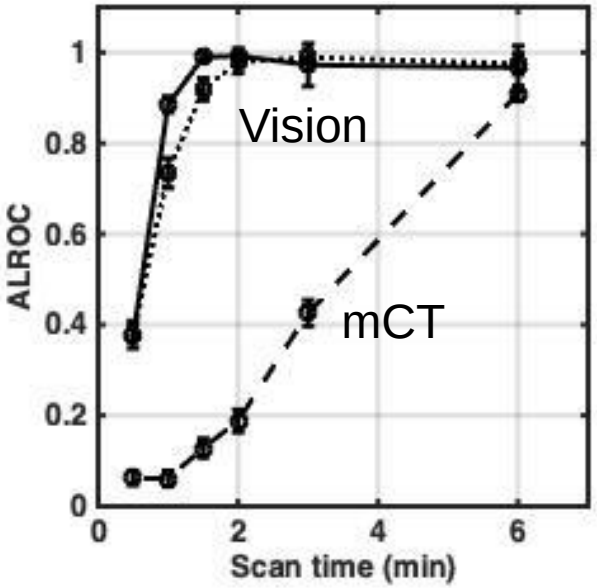
Measurements

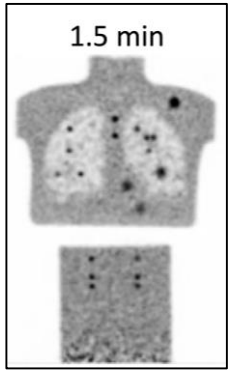
Siemens Biograph

	mCT	Vision
Sensitivity	10	15.6 kcps/ml
TOF	525	215 ps
Spat. Resol	4.2	3.6 mm

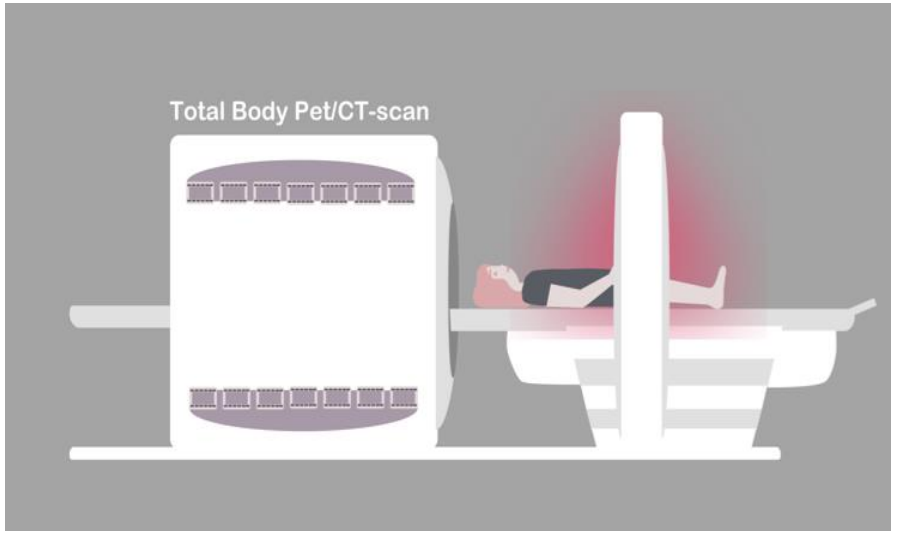
CTN phantom

10-mm lesions





PET20.0: EU version of Explorer: Combining high sensitivity of Total Body Time-of-Flight PET with high resolution monolithic detectors and depth-of interaction



System: 104 cm long axial FOV, 64 cm bore
Detector: 16 mm thick 5x5 cm LYSO

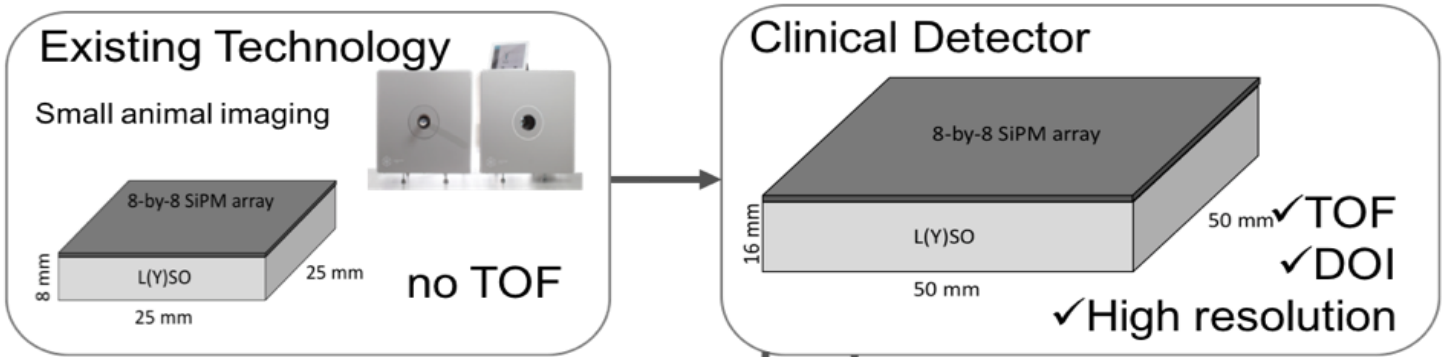
High resolution monolithic detectors of expected 1.3 mm intrinsic resolution

Point sensitivity of > 20 %

Scatter fraction < 33 %

System spatial resolution of 2.0 mm

Molecubes β-Cube



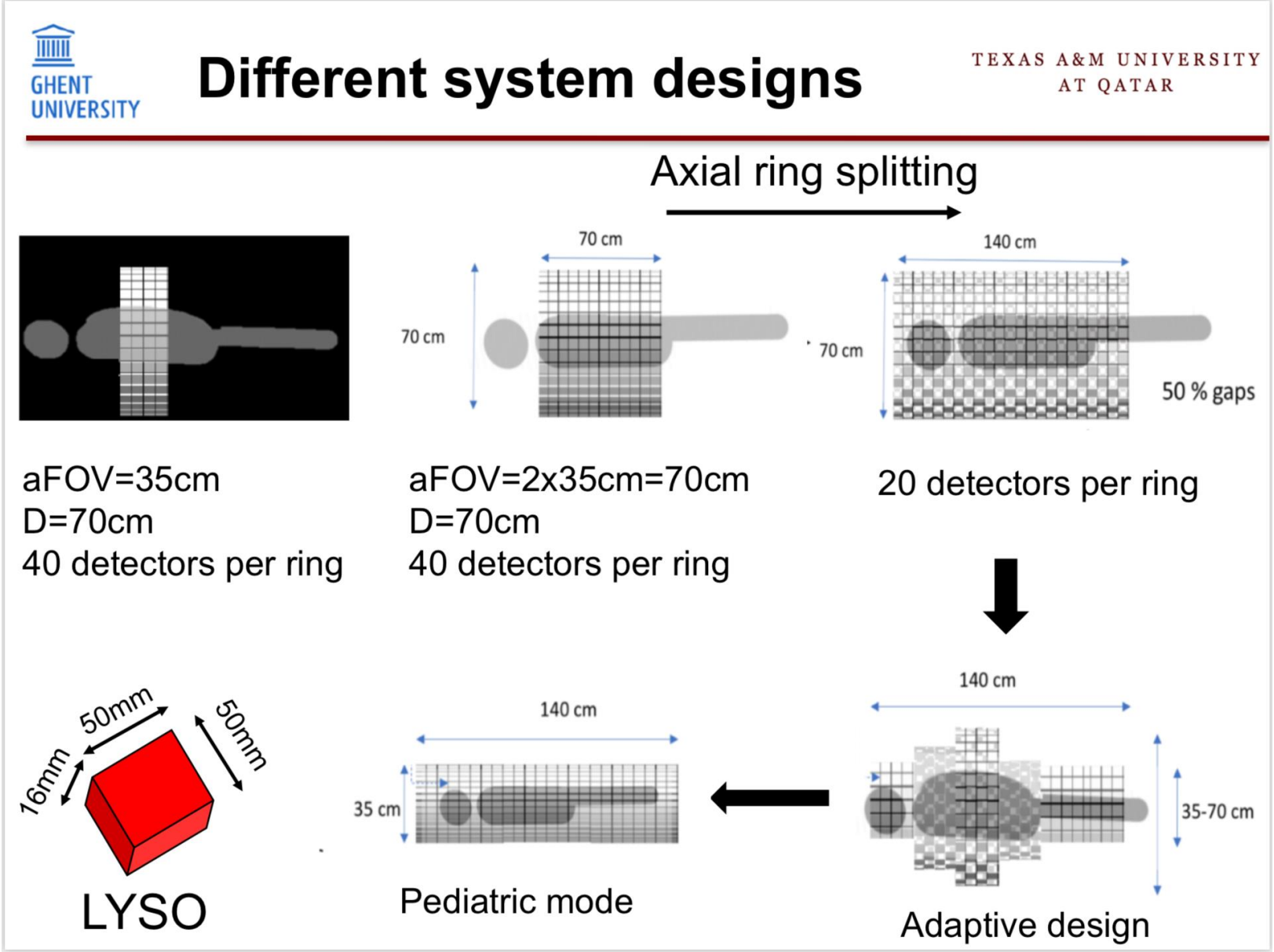
Univ. Ghent

PET 20.0: a cost efficient, 2.00 mm resolution Total body monolithic PET with very high sensitivity and an adaptive axial FOV up to 2.00 m

S. Vandenberghe[1], E.Mikhalyova[2], B. Brans[3], M.Defrise[4], T.Lahoutte[4], K.Muylle[4], R. Van Holen[1], D.Schaart[5], J.S. Karp[6]

Courtesy, S. Vandenberghe, U. Ghent

Adaptive scanner rings – Adult/Pediatric



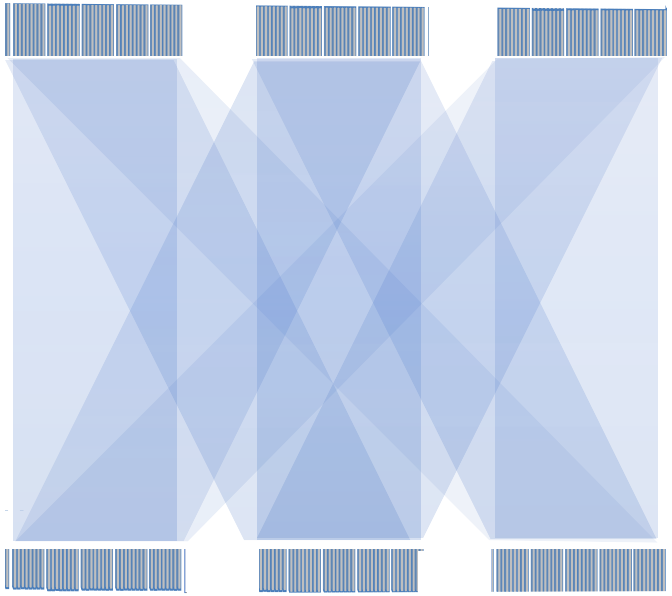
"Monte Carlo sensitivity and count rate study of a long axial FOV PET scanner with patient adaptive rings"

Abi Akl et al

MIC 2019, Manchester, UK

Reduce number detectors for more cost-effective solution

- Many lines-of-response for 3D image reconstruction, improved with very good TOF resolution



Inter-ring gaps: reduction of 1/3 detectors

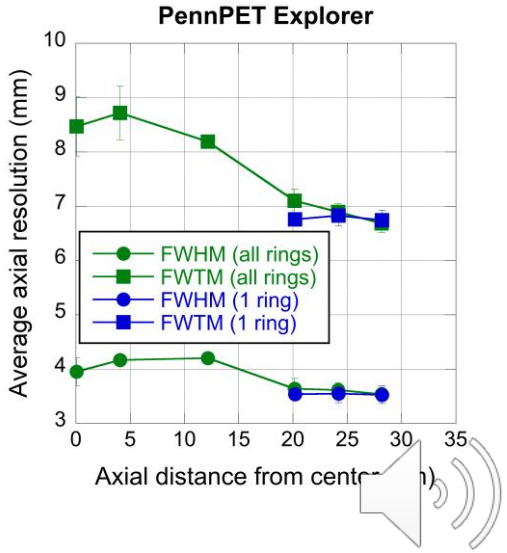
PennPET Explorer measurements (3 rings with gaps – prototype)

TOF-OSEM – 4 iter.

Sensitivity-relaxed TOF-OSEM – 25 iter.

- Axial uniformity – no evidence of gaps
- Sensitivity-relaxed OSEM more uniform although more iterations required

- Axial resolution – no evidence of gaps
- Small degradation from center to edge due to large (unrestricted) axial acceptance angle



# rings	# rows (no gaps)	AFOV (cm)	Sensitivity (kcps/MBq)	# rows (2-row gaps)	AFOV (cm)	Sensitivity (kcps/MBq)	Application
3	21	71	101	15	64	52	EAFOV: *Head-neck, Torso, Pelvis-abdomen, Pediatric*
6	42	143	223	30	136	115	LAFOV: *Total Body*

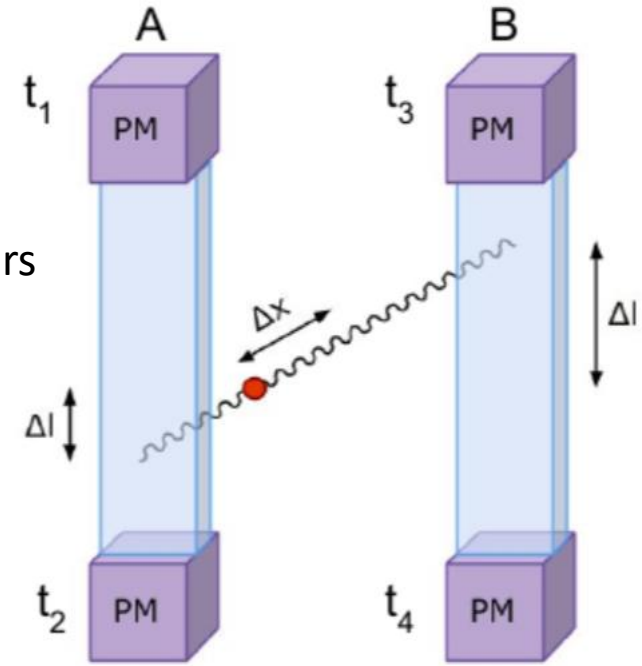
Alternative scintillators

J-PET: a new technology for the whole-body PET imaging*

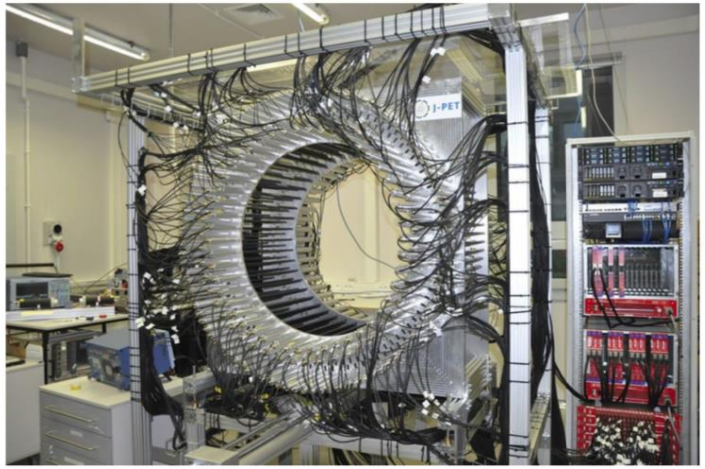
Moskal et al, Jagellonian Institute, Crakow, Poland

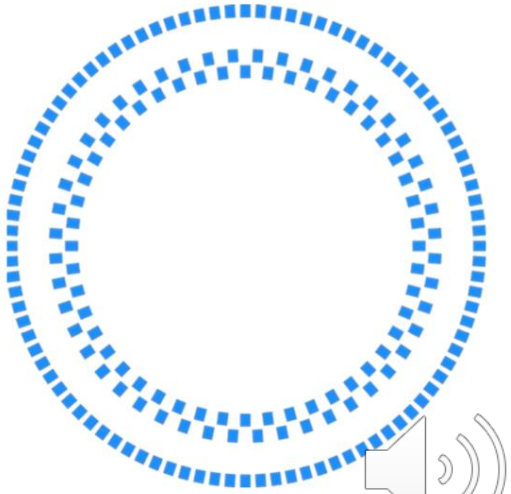
Plastic scintillators

50-100 cm long



Prototype with PMTs, updated with SiPMs



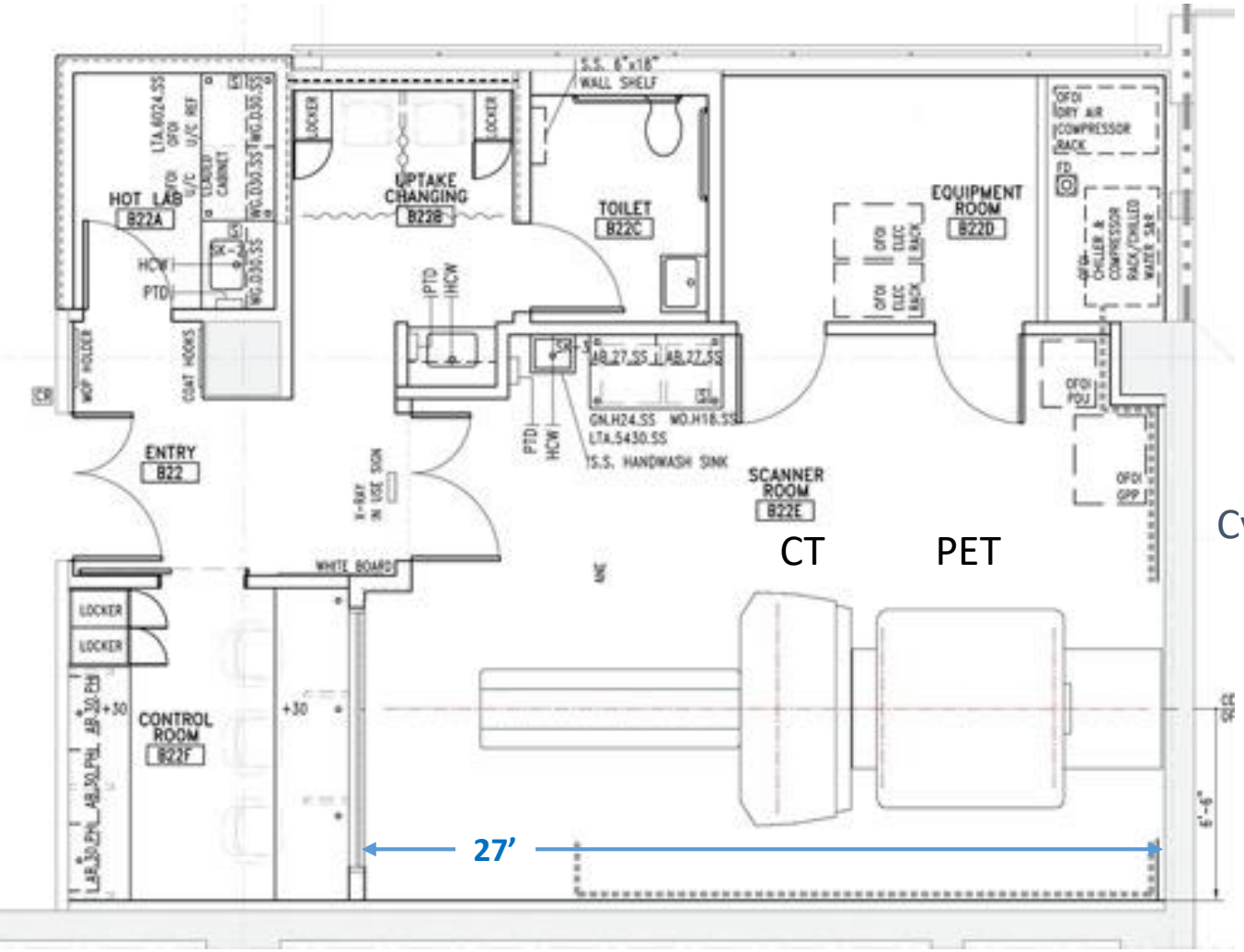


TOF information for axial positioning and image reconstruction

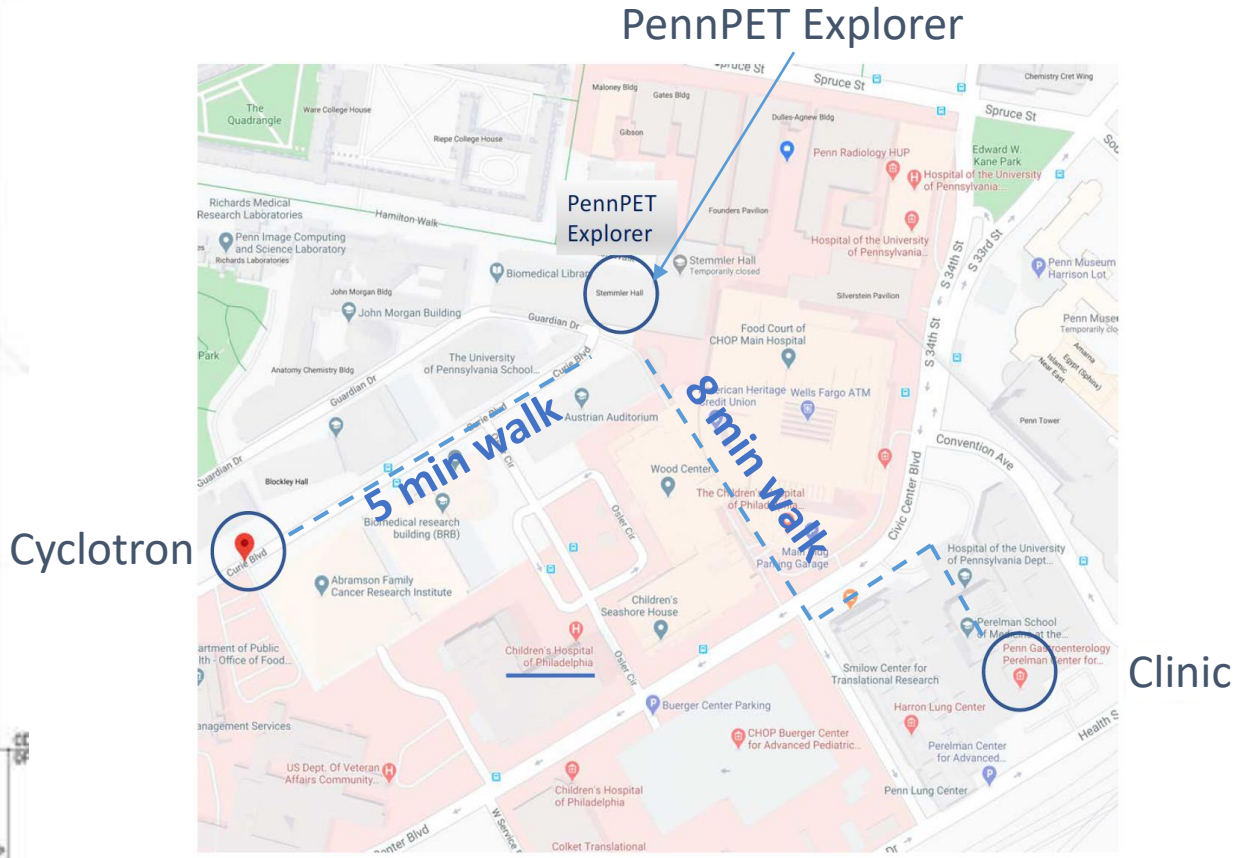
Multiple layers to improve sensitivity

Practical Considerations

Imaging Facility – room size and location



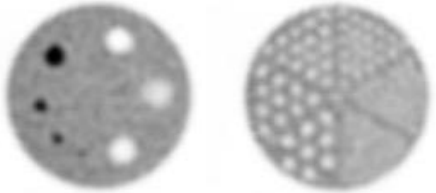
PennPET Explorer Imaging Facility in SoM

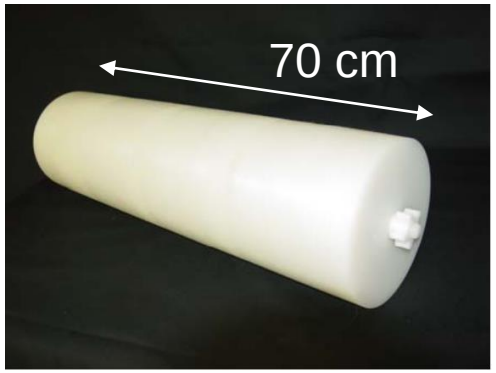


Penn School of Medicine (SoM) and
Perelman Center of Advanced Medicine (PCAM)

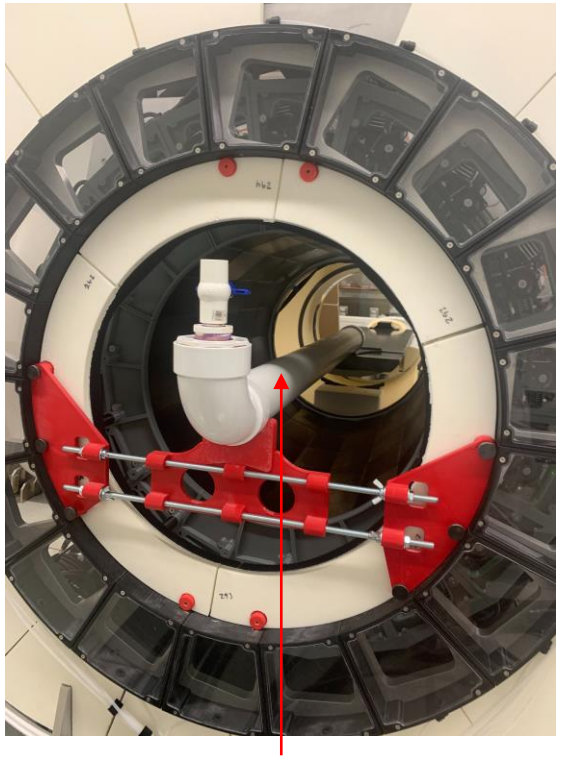
Practical Considerations

- Physical testing
  - Modify NEMA 2018
    - Designed for scanners with standard AFOV
  - Quantitative calibrations
    - ACR phantom – SUV calibration





NEMA Scatter/Count-rate phantom



10 cm x 150 cm 'long-pipe'

- Human imaging
  - Patient comfort in long bore - claustrophobia
  - Clinical imaging
    - Optimize workflow
    - Complementary scheduling with standard scanners in the clinic
  - Research imaging
    - Arterial/venous sampling (with long bore) vs image-derived input function

Potential Market

- There is enough excitement to predict sales in near term
- Extended AFOV (40-70 cm) can perform studies not currently possible
  - Low dose (pediatric) imaging
  - Head-Neck, Heart-Renal, Pelvis-Abdomen
- Long AFOV (70-200 cm) offers full, whole-body dynamic studies
  - Maximum sensitivity over larger axial coverage
- **Larger market will depend on support from vendors and clinician researchers**
  - Axial FOV and performance need to meet clinical needs
  - New applications take time to develop, publish, get reimbursement