Total Body PET: The Ultimate Molecular Imaging Tool:
Future Developments and Challenges in Scanner Design

Joel Karp
Department of Radiology
University of Pennsylvania

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 m² sensors (SiPM)
  - Long axial FOV scanner
    - 70 cm AFOV -> 32 liter scintillator, 1.7 m² sensors -> x 3 cost ~$2M (materials)
    - 140 cm AFOV -> 64 liter scintillator, 3.4 m² sensors -> x 6 cost ~$4M (materials)
    - 200 cm AFOV -> 90 liter scintillator, 4.8 m² 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

\[ \alpha \pm 15^\circ \]  
\[ \alpha \pm 44^\circ \]  
\[ \alpha \pm 63^\circ \]

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

<table>
<thead>
<tr>
<th>Scanner AFOV (cm)</th>
<th>20</th>
<th>70</th>
<th>100</th>
<th>140</th>
<th>200</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Point source in a 20 cm (\phi) cyl.</strong></td>
<td>1</td>
<td>2.4</td>
<td>2.7</td>
<td>2.8</td>
<td>2.8</td>
</tr>
<tr>
<td><strong>Uniform source in a 20 cm (\phi) cyl.</strong></td>
<td>1</td>
<td>10</td>
<td>18</td>
<td>29</td>
<td>46</td>
</tr>
<tr>
<td><strong>Uniform source in a 35 cm (\phi) cyl.</strong></td>
<td>1</td>
<td>14</td>
<td>24</td>
<td>38</td>
<td></td>
</tr>
</tbody>
</table>
How long is enough?

**Partial body coverage**

- Patient Height: 193 cm
- Average adult: 171 cm
- Image: 153 cm

**Full body coverage**

- Image: 140 cm
- Courtesy, Bernard Bendriem, Siemens

70 cm

193 cm
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

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

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

Courtesty, Drs. Knopp, Zhang, OSU

MIP images for BMI=24 patient

15min 5min 1.5min

MIP images for BMI=35 patient

Total scan 12 min 8 min 5.3 min

Sectional images for BMI = 43.6 patient

11 min scan

Courtesty, Dr. Mawlawi, MDACC

(5 ring scanner)

Courtesty, University of Pennsylvania
Long AFOV scanners: UIH uEXPLORER

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

- LYSO Detector Module
  - 2940 crystals
  - 5x14 blocks
  - 7x6 crystals/block

- Block flood map

- **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

Courtesy, Hongdi Li, UIH America
### Long AFOV scanners: PennPET Explorer

**PennPET Explorer**

- **PennPET Detectors:** 1:1 encoding, crystals: SiPMs
- **3.86 x 3.86 x 19 mm³ LYSO with PDPC digital SiPM**

- **TOF = 250 ps, 4-mm spatial resolution**

**Scalable platform for multi-ring PET**

- **3-ring**
- **6-ring**

- **CT - couch**

![PET Scanner Diagram]
TB-PET looking forward

Benefits of TOF increase with better timing resolution

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

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

Detectability task

2.6mm, 600ps
4.0mm, 300ps

Surti et al., TNS 2013

Measurements

<table>
<thead>
<tr>
<th>Siemens Biograph</th>
<th>mCT</th>
<th>Vision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>10</td>
<td>15.6 kcps/ml</td>
</tr>
<tr>
<td>TOF</td>
<td>525</td>
<td>215 ps</td>
</tr>
<tr>
<td>Spat. Resol</td>
<td>4.2</td>
<td>3.6 mm</td>
</tr>
</tbody>
</table>

CTN phantom

Vision
mCT

Measurements

10-mm lesions

ALROC

r=7cm
r=14cm

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

Molecules β-Cube

Existing Technology
Small animal imaging

Clinical Detector

8-by-8 SiPM array
L(Y)SO

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. Vandenbergh1, E. Mikhailova2, B. Brans3, M. Defrise4, T. Lahoutte5, K. Muyldermans, R. Van Horen6, D. Schaart7, J.S. Karp8

Courtesy, S. Vandenberghe, U. Ghent
"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

PennPET Explorer measurements (3 rings with gaps – prototype)

- 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

Inter-ring gaps: reduction of 1/3 detectors

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

TOF information for axial positioning and image reconstruction

Prototype with PMTs, updated with SiPMs

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

• 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
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