TOTAL-BODY
METABOLIC IMAGING

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Acknowledgements

Funding:
UC Davis Research Investments in
Science and Engineering Program
R01 CA170874
R01 CA197608
with support from
NIH

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Whole-Body PET/CT

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Whole-Body PET/CT
**Sensitivity: Every Count Counts**

Current scanners do not maximize the sensitivity for whole-body imaging (<1% of the available signal collected)

- PET provides the most sensitive non-invasive molecular assay of the human body
- All PET studies are limited by statistics, radiation dose, or both

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**Total-Body PET: Maximizing Sensitivity**

- 40x gain in effective sensitivity for total-body imaging!
- 4-5x gain in sensitivity for single organ imaging
- Total-body kinetics
  - All tissues/organisms simultaneously
  - Better temporal resolution

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**EXPLORER**

**CONVENTIONAL PET**

**EXPLORER**

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**CONVENTIONAL PET**

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Total-Body PET: Maximizing Sensitivity

CONVENTIONAL PET

EXPLORER

Not a New Idea!


Terry Jones, circa 1990

Challenges

• Scale of system
  - >250,000 detectors
  - >5,000 channels of electronics
  - >400 kg of scintillator
  - Power consumption, temperature control

• High-performance detectors
  - Time-of-flight (TOF)
  - Depth-of-interaction (DOI) encoding
  - High resolution

• Big data (10 mCi in FOV)
  - 150 million singles/sec
  - 20 million coincidences/sec
  - 1.5 GB/sec data rates
  - 10-40TB storage per day

• Cost
  - ~$15M for first prototype
Count-Rate Simulations

- SimSET + pulse-processing code based on Siemens mCT
- No multiplexing: equivalent to parallelized acquisition
- Axial length: 215 cm
- Timing resolution: 530 ps

Count-Rate Simulations

\[ \text{NECR} = \frac{T^2}{T + S + \left( \frac{D_{\text{sim}}}{D_{\text{exp}}} \right) R} \]

T = true events
R = randoms
S = scatter events
D = diameter

Predicted Sensitivity Gains versus Siemens Biograph mCT

Pediatric Total Body Phantom: 20.0 (0.3 mCi)
Adult Total Body Phantom: 43.9 (10 mCi)
Brain: (Voxtiss 8, 6:1 brain to body) 4.2 (10 mCi)
**Image Better**

- > 6-fold improvement in SNR
  - Reconstruct at higher spatial resolution
  - Detect smaller lesions
  - Detect low-grade disease
  - Better statistics for kinetic modeling

**Image More**

Regional tissue kinetics & arterial blood input functions with high statistical quality

**Image Longer**

- 40-fold greater dynamic range
  - can image for five more half lives
  - $^{11}C$  
    - > 3 hours
  - $^{18}F$  
    - > 18 hours
  - $^{89}Zr$  
    - > 30 days
Image Faster

- Total-body PET in 15-30 seconds
  - Image in a single breathhold
  - Reduce respiratory motion
  - Higher resolution
  - Total-body kinetic imaging with high temporal resolution

Image Gently (Low Dose)

- 40-fold reduction in dose
  - Whole-body PET at ~0.15 mSv
  - Annual natural background is ~2.4 mSv
  - Return flight (SFO-LHR) is ~0.11 mSv
  - PET can be used with minimal risk – new populations

Image More Often
From Idea to Reality

$ = 2,000,000

Approaches

• Short Term
  – Use design based on existing commercial detectors and electronics – extend axial FOV
• Longer Term
  – Develop new detectors and electronics
  – Depth-of-interaction and time-of-flight
  – Higher spatial resolution
  – Collect singles events
    • Allows parallel and scalable data collection
    • more flexibility to optimize data

mini-EXPLORER

In collaboration with Mike Casey, Matthias Schmand, Maciej Kapusta, Siemens
Figure 9. LM-OSEM reconstructed images using the 45-cm long mini-EXPLORER scanner. Comparison results of with and without normalization among commercial companies. Specifically, United Imaging is clearly highly motivated to bring a product to market.
Computing Resources

- Coincidence sorting
  - 10^6 singles/sec/core achieved
  - Requires ~64 cores to sort 8 hours of high-activity data in < 24 hours
- Data storage
  - 10-40 TB/day: distributed file system
- Reconstruction
  - 20 minute scan, 14FDG, 25 MBq:
  - ~1.6 billion coincidence events
  - Recon time: 3 min/iteration with GPU acceleration

Reconstruction Methodology

Reconstructed Image for 1st Frame (0-30 secs, 25 MBq)

OSEM
195x195x527 image array
3.42 mm voxels
10 subsets and 10 iterations
Gaussian post-smoothing

OSEM with kernel method
195x195x527 image array
3.42 mm voxels
10 subsets and 10 iterations

Contrast Recovery

EXPLORER
Siemens mCT

25 MBq injection, 20 minute scan, includes scatters and randoms
12 mm liver lesion, contrast 3.3:1
Attenuation Correction

- **Low-Dose CT**
- **Transmission Source**
  - Annulus or static transmission rods?
  - Use time-of-flight to separate transmission and emission
- **L(Y)SO background**
  - $^{176}$Lu equivalent to a ~25 MBq source
  - Use time-of-flight to separate transmission and emission

Current Status

- Project launched to build total-body PET scanner with unprecedented sensitivity
  - NIH funded development of first prototype
  - Simulations are being used to evaluate design trade-offs
  - Detector, electronics and image reconstruction development underway
  - Small-scale prototype just completed
  - Full-scale mock up in ~ 6 months
- Conceptual applications in clinical medicine and research have been formulated

Applications

- Systemic disease and therapies:
  - Cancer: Ultra-staging and micrometastasis
  - Infection
  - Cellular therapy and trafficking
  - Mind-body interactions
- Total body pharmacokinetics
  - Drug development
  - Toxicology
  - Biomarker discovery
- Low dose opens up new populations:
  - Expanded use in pediatrics
  - Use in chronic disease
  - Studies of normal biology
Metastatic Cancer
The Challenge

<table>
<thead>
<tr>
<th>No Mets</th>
<th>TCC</th>
<th>Micro Met</th>
<th>Subclinical</th>
<th>Clinical</th>
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<tbody>
<tr>
<td>PET Ultra-sighting</td>
<td>PET MRI CT US</td>
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</tbody>
</table>

Beyond SUV and Hotspot Imaging
Quantifying low levels of disease

- Image dynamically
  - Cancer cells have different kinetics than normal tissue
- Image late
  - Tumor contrast increases with time
- Employ advanced modeling
  - Image-derived input function
  - 4-D reconstruction
  - Spectral/factor/cluster analysis
- Detecting below the resolution threshold
  - Look for regional changes in FDG kinetics that indicate low levels of underlying disease

Extension to Other Systemic Applications

- Methods/paradigm can be also be applied to total-body imaging of
  - low level inflammation
  - low level infection
  - distribution of cellular therapeutics

Courtesy Abass Alavi

Total-Body Pharmacology

Quantification of “free” drug concentration in multiple organs using kinetic analysis
Modeling of drug absorption, distribution, metabolism and excretion (ADME)
Toxicology
Biomarker discovery
Move away from novel drug testing in animals

Multi-Organ Disease

Total-Body PET
A Renaissance for PET?

- Realising the full potential of PET
- Full implementation of the tracer kinetic principle
- Engaging “Systems Biology”
- Alleviating the radiation dose burden
- Impacting on clinical PET
Total-Body PET

**Image better**
- 2-fold increase in SNR
- Reconstruct at higher resolution
- Detect smaller lesions
- Detect low-grade disease
- Better statistics for kinetic modeling

**Image faster**
- Total-body PET in 15-30 mins
- Image in a single breath hold
- Reduce respiratory motion
- Higher resolution
- Total-body kinetic imaging with good temporal resolution

**Image longer**
- 40-fold increase in dynamic range
- Image for 5 more half lives
- T1 > 3 hours
- T90 > 10 hours
- T2 > 30 days

**Image gently**
- 40-fold reduction in dose
- Whole-body PET at 150 µSv
- PET in new populations (adolescents, pediatrics)
- Many repeat scans in an individual – follow disease trajectory

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