EXPLORER

TOTAL-BODY METABOLIC IMAGING

UCDAVIS UNIVERSITY OF CALIFORNIA

Penn

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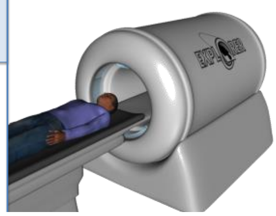

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Acknowledgements

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Suleman Surti

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Michael Casey (Siemens)
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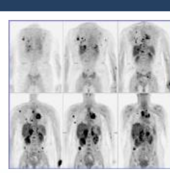
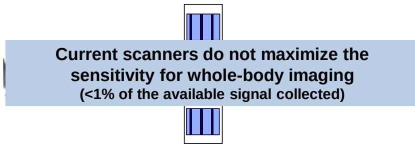
Whole-Body PET/CT



Sensitivity: Every Count Counts

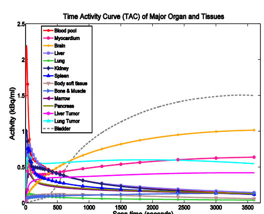


Current scanners do not maximize the sensitivity for whole-body imaging
(<1% of the available signal collected)

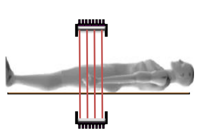
- PET provides the most sensitive non-invasive molecular assay of the human body
- All PET studies are limited by statistics, radiation dose, or both

Total-Body PET: Maximizing Sensitivity

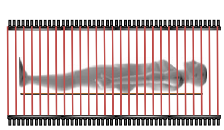
- 40x gain in effective sensitivity for total-body imaging!
- 4-5x gain in sensitivity for single organ imaging
- Total-body kinetics
  - All tissues/organs simultaneously
  - Better temporal resolution



Total-Body PET: Maximizing Sensitivity



CONVENTIONAL PET



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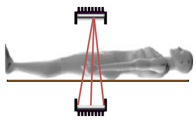
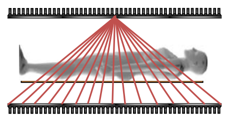
Total-Body PET: Maximizing Sensitivity



CONVENTIONAL PET



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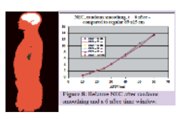
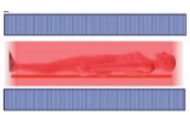
Not a New Idea!

Terry Jones, circa 1990



Badawi et al, *IEEE Trans Nucl Sci* 2000;47:1228–32

Watanabe et al, *IEEE Trans Nucl Sci* 2004;51:796–800.



Cherry, *J Nucl Med* 2006;47:1735–45.

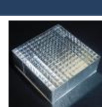
Eriksson et al.
IEEE Nucl Sci Symp Conf Rec 2008:1632–6.

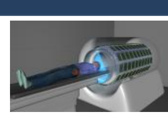
Borasi et al.
Eur J Nucl Med Mol Imaging 2010; 37:1629–32.

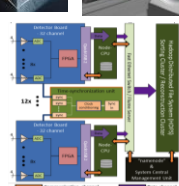
Crosetto
IEEE Nucl Sci Symp Conf Rec 2003; 2415–19.

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



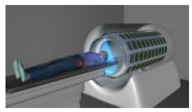




Count-Rate Simulations

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

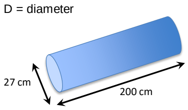
vs.

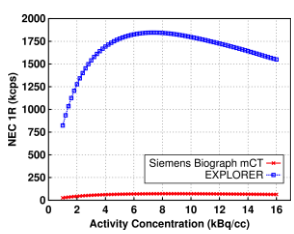


Count-Rate Simulations

$$NECR = \frac{T^2}{T + S + \left(\frac{D_{obj}}{D_{FOV}}\right) R}$$

T = trues
R = randoms
S = scatters
D = diameter



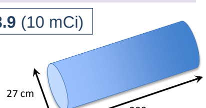


Predicted Sensitivity Gains versus Siemens Biograph mCT

$$NECR_{TOF} = \frac{D_{obj}}{\Delta x} \cdot \left(\frac{T^2}{T + S + \left(\frac{D_{obj}}{D_{FOV}}\right)^2 R} \right)$$

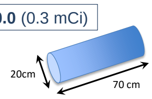
Adult Total Body Phantom:

43.9 (10 mCi)



Pediatric Total Body Phantom:

20.0 (0.3 mCi)



Brain: (Voxtiss 8, 6:1 brain to body)

4.2 (10 mCi)

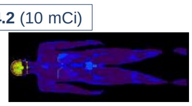
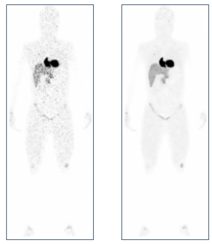


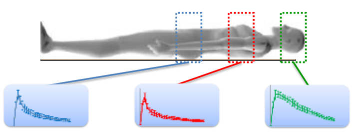
Image Better

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



Conventional PET EXPLORER

Image More



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

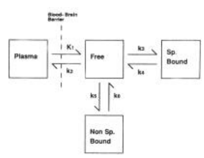


Image Longer

- **40-fold greater dynamic range**

  can image for five more half lives

- **^{11}C**

  > 3 hours

- **^{18}F**

  > 18 hours

- **^{89}Zr**

  > 30 days

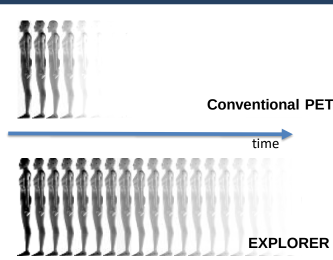


Image Faster

- **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

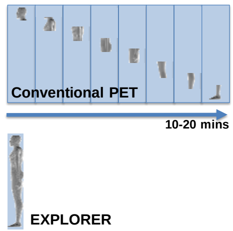
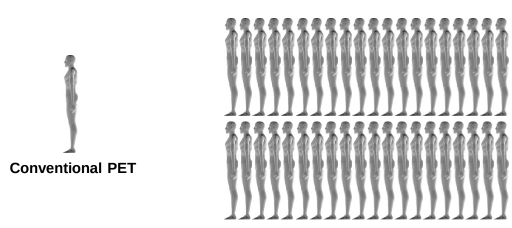


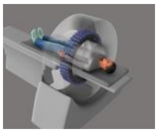
Image Gently (Low Dose)

- **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



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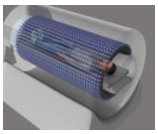

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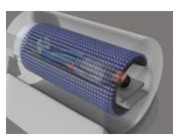
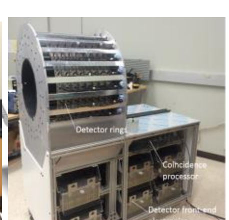
Approaches

- 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

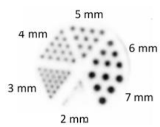


In collaboration with Mike Casey, Matthias Schmand, Maciej Kapusta, Siemens

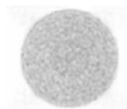
mini-EXPLORER

Detector efficiency maps

Reconstructed image
Derenzo Phantom



Reconstructed image
Uniform Cylinder

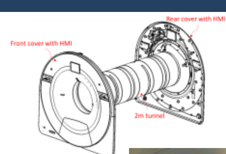


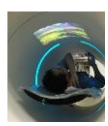
Scanner Mock-Up

Technologist/Scanner Interface
- Patient positioning
- On-bed injection
- Blood sampling
- Patient monitoring and communication (visual and audio)

Patient/Scanner Interface
- Ease of getting on and off bed
- Comfort for long dynamic studies
- Reducing chances of claustrophobia (light, sound etc…)

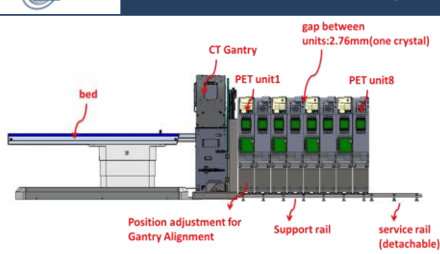
Engineering and Support
- Easy access for maintenance and part replacement
- Room size, physical plant requirements (power, temperature etc.…)
- Bed design, throw and support
- Integration with CT





In collaboration with Hongdi Li, United Imaging

Gantry Design



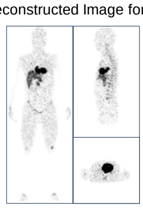
In collaboration with Hongdi Li, United Imaging

Computing Resources

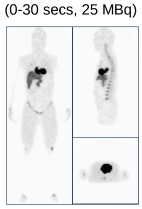
- **Coincidence sorting**
  - 10^6 singles/sec/core achieved
  - Requires ~64 cores to sort 8 hours of high-activity data in < 24 hours
- **Data storage**
  - 10-40 TB/day: distributed file system
- **Reconstruction**
  - 20 minute scan, ^{18}FDG, 25 MBq:
  - ~ 1.6 billion coincidence events
  - Recon time: 3 min/iteration with GPU acceleration

Reconstruction Methodology

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



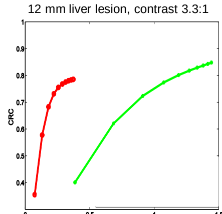
OSEM
195×195×527 image array
3.42 mm voxels
10 subsets and 10 iterations
Gaussian post-smoothing



OSEM with kernel method
195×195×527 image array
3.42 mm voxels
10 subsets and 10 iterations

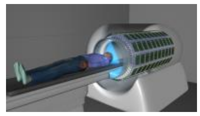
Contrast Recovery

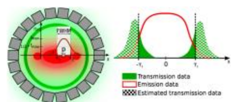
25 MBq injection, 20 minute scan, includes scatters and randoms
12 mm liver lesion, contrast 3.3:1



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

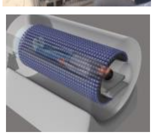




Mollet et al. *IEEE Trans Med Imaging* 31:1734-42 (2012)

Current Status

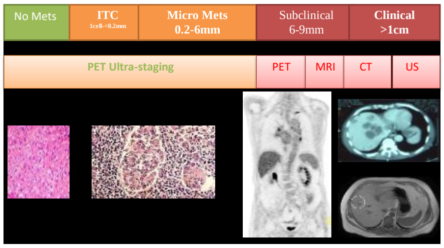
- Project launched to build total-body PET scanner with unprecedented sensitivity
  - NIH funded development of first prototype
  - Simulations are being used to evaluate design trade-offs
  - Detector, electronics and image reconstruction development underway
  - Small-scale prototype just completed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



Applications

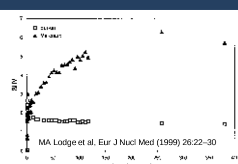
- **Systemic disease and therapies:**
  - Cancer: Ultra-staging and micrometastasis
  - Inflammation
  - Infection
  - Cellular therapy and trafficking
  - Mind-body interactions
- **Total body pharmacokinetics**
  - Drug development
  - Toxicology
  - Biomarker discovery
- **Low dose opens up new populations:**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

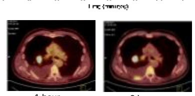
Metastatic Cancer
The Challenge



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





Courtesy Abass Alavi

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**

Total-Body Pharmacology

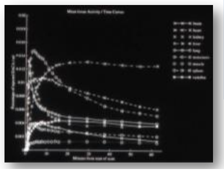
Quantification of "free" drug concentration in multiple organs using kinetic analysis

Modeling of drug **a**bsorption, **d**istribution, **m**etabolism and **e**xcretion (ADME)

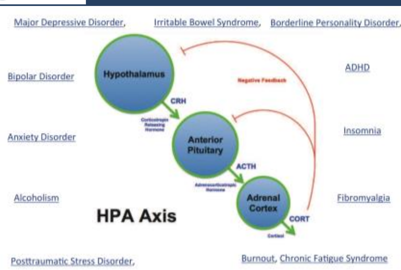
Toxicology

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

EXPLORER

Total-Body PET

Image better
- **> 6-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 secs**
- 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
- ^{11}C > 3 hours
- ^{18}F > 18 hours
- ^{89}Zr > 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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Acknowledgements

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