Evolution of PET technology – from early days, to the PennPET Explorer

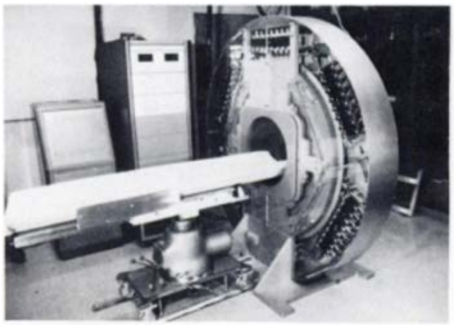
Joel Karp, David Mankoff
Department of Radiology

P30 Didactics Lecture, April 6, 2020

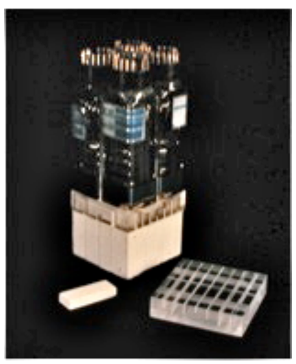
PET with multi-rings geometry (and septa)

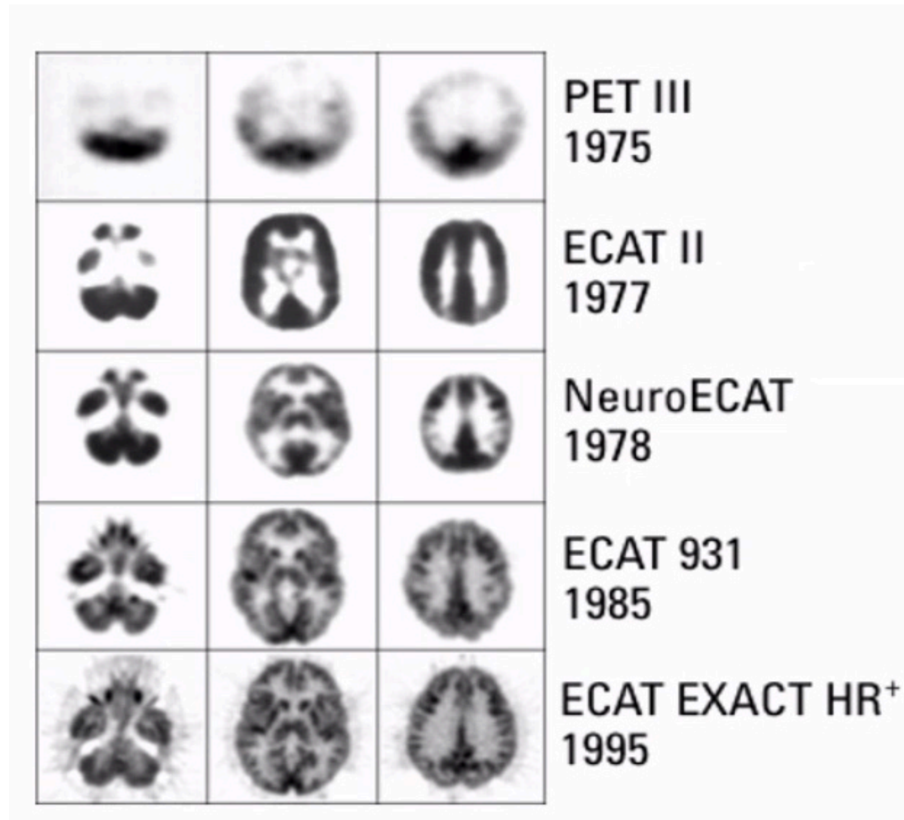
mid 1970's

Washington University
UCLA



mid 1908's
Casey, Nutt Block detector





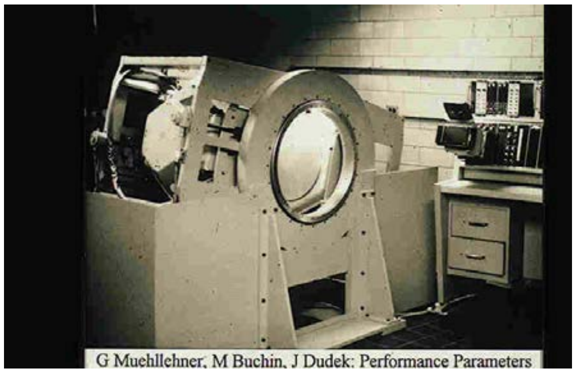
Higher spatial resolution with Anger-logic and multi-crystal BGO block

PET with Anger Cameras

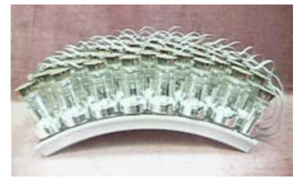
University of Chicago 1975

2 Anger cameras in coincidence:

- Thick crystals
- No collimation
- Rotating



University of Pennsylvania 1998

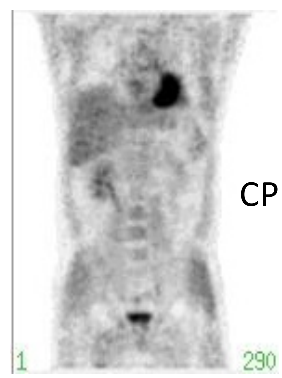


- 6 Curve-Plate detectors
- No Collimation – 3D
- Stationary

UGM Medical Systems
ADAC Laboratories C-PET

Iterative reconstruction – improved image quality
AC with ^{137}Cs singles Transmission scan – more accurate quantitation
Count-rate capability limited with NaI(Tl) – sufficient for FDG
Improved with pixelated detector with GSO – Allegro scanner

Higher sensitivity with 3D imaging acquisition and reconstruction



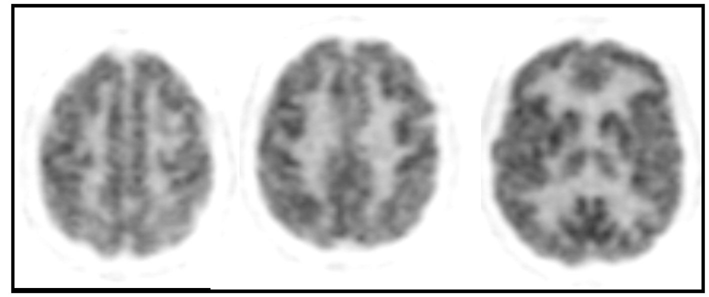
CPET

Allegro

Brain PET with Anger-logic Detectors

2001 G-PET Brain Scanner

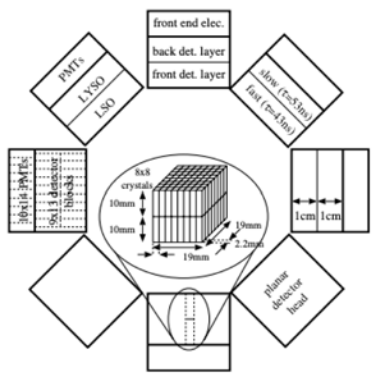
Pixelated GSO detector



Spatial resolution ~ 3.7 mm

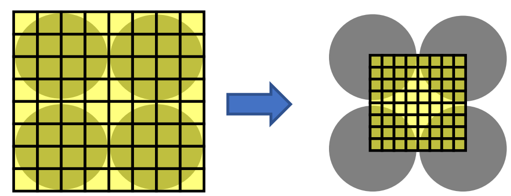
25.6 cm axial FOV

Siemens HRRT PET scanner



Spatial resolution ~ 2.7 mm

Dual-layer block detectors with smaller crystals and quadrant sharing arrangement of PMTs



Higher spatial resolution and sensitivity with dedicated brain PET

Also, improved quantification primarily due to a reduction in partial-volume effects (Van Helden *et al* (VUMC), JNM 2009).

TOF Positron Emission Tomography scanners

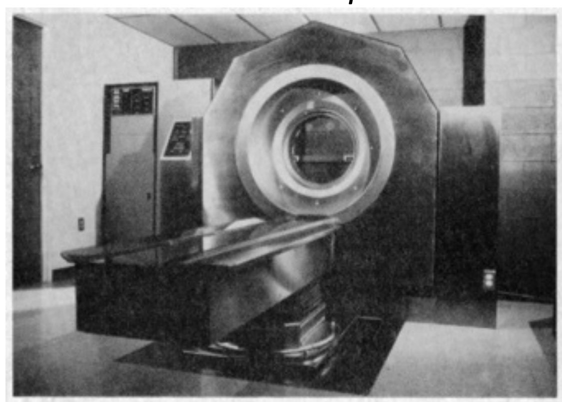
Washington University

CEA-LETI, Grenoble, France

University of Texas

1979-1983

Super PETT 1



Ter-Pogossian et al, TMI 1982

1-to-1 coupling

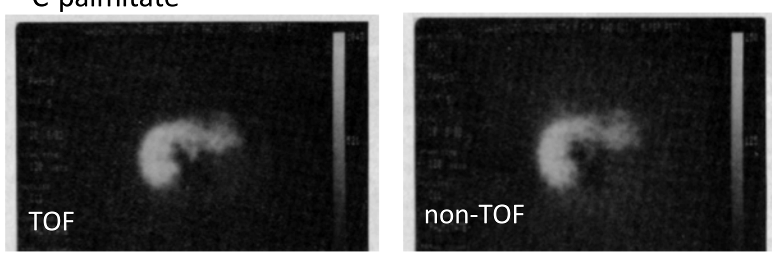
(25 mm ϕ x 45 mm : 28 mm ϕ PMT)

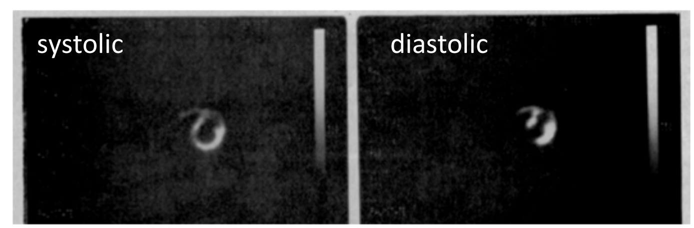
4 rings x 96 detectors CsF

Δt = 500 ps

Imaging with short-lived isotopes – ^{11}C, ^{15}O, ^{13}N

^{11}C-palmitate





Retrospective gating from list data

Higher count-rate imaging and TOF-assisted reconstruction with fast timing detectors

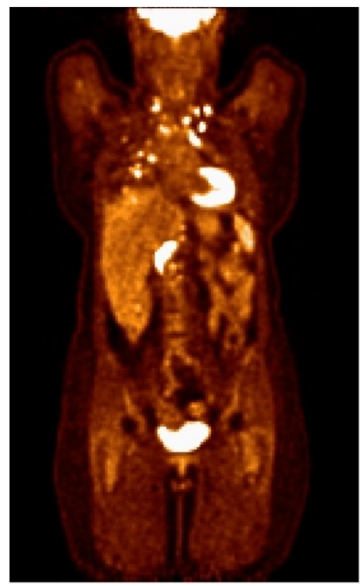
Modern PET-CT with 3D TOF

LSO/LYSO - high light output enabled extension of block design *and* pixelated Anger-logic detector
- stopping power enabled high sensitivity, along with 3D imaging
- fast rise/decay of scintillation enabled precise timing for TOF

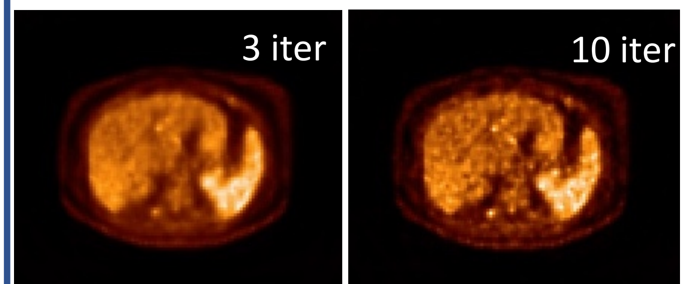
Philips Gemini TF

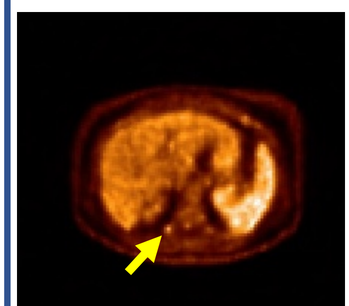
Anger-logic pixelated detector
– high spatial resolution and TOF

Fully 3D TOF PET-CT



noTOF





TOF

Higher contrast
Lower Noise

Improved lesion detectability and quantitative accuracy for clinical FDG imaging with TOF

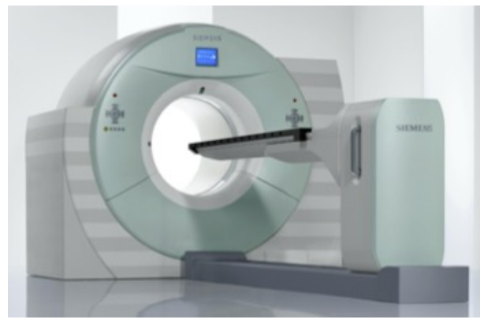
Commercial TOF PET/CT – all vendors

TOF 500-600 ps

2006 → 2010

Philips Gemini/Ingenuity TF

Siemens mCT

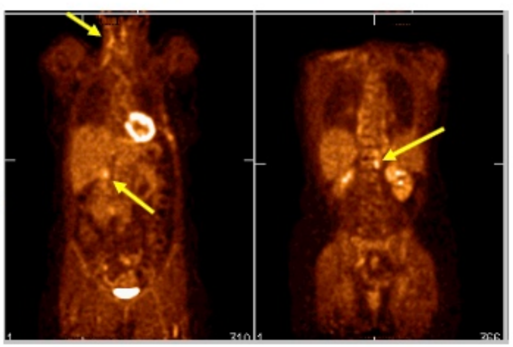


GE Discovery 690

8 min tot (1 min/bed)

Light patient:
61 kg BMI = 22.2

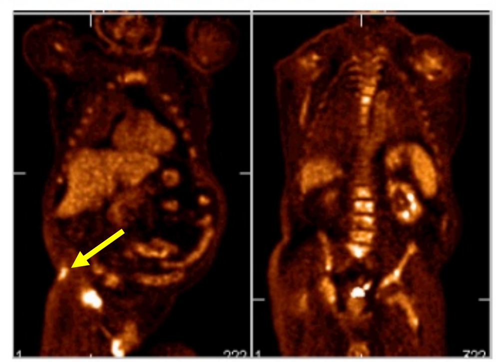
Head & neck cancer
- liver, spine lesions



27 min tot (3 min/bed)

Heavy patient:
115 kg BMI = 38

Abdominal
Cancer



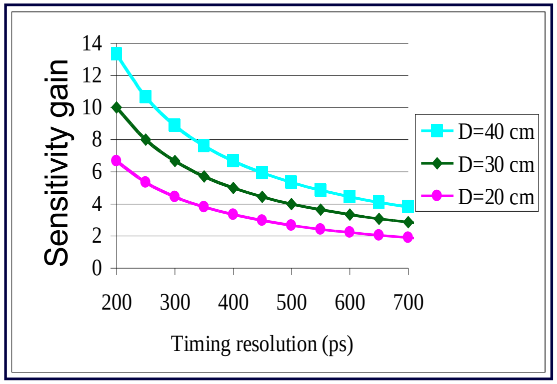
Benefits of TOF lead to shorter scans (light patient) or improved image quality (heavy patients)

Images courtesy of Univ. Pennsylvania PET Center

Improving Timing resolution

Benefits of TOF increase with better timing resolution

- Improved Signal-to-Noise
- Improved Quantitative Accuracy



Gain in SNR = $(D/\Delta x)^{1/2}$

Reduce statistical uncertainty or jitter in determining time stamp

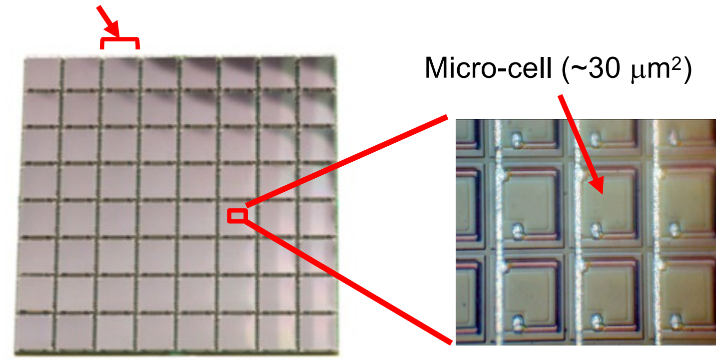
- New scintillators
  - Lanthanum Bromide
  - Ceramics (e.g., GluGAG)
  - LSO with optimized (e.g., Ca or Mg) dopants
- Improved detector designs
  - Dual-sided read-out
  - Thin layers of stacked detectors
  - Monolithic detectors – with depth-of-interaction
- New photo-sensor technology
  - Multi-channel PMTs
  - **Silicon photo-multiplier**

New Photo-sensor: Si-PMs

- Small APDs operating in Geiger mode with hundreds of micro cells per mm^2:
  - Small, compact design
  - Can operate in MR
  - High gain, no need for amplification
  - Very high QE
    - Photo Detection Efficiency (PDE) = QE x Fill ~ 25-50%
  - Fast timing characteristics
  - Potential for low encoding (e.g. 1-to-1)
  - Multiple vendors
    - Hamamatsu, SensL, FBK/Broadcom, PDPC

SiPM (~ 4 mm^2)

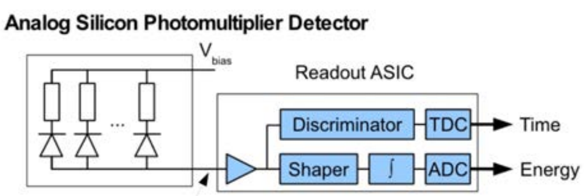
Micro-cell (~30 μm^2)

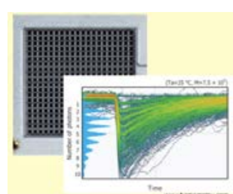


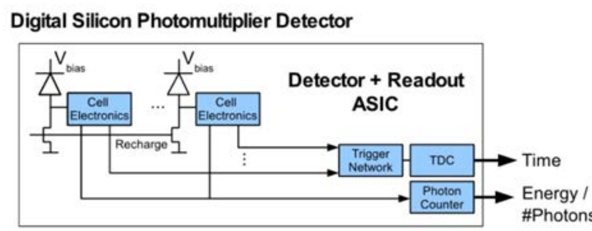
SiPM multi-channel array

- Analog devices requires ASIC for signal processing

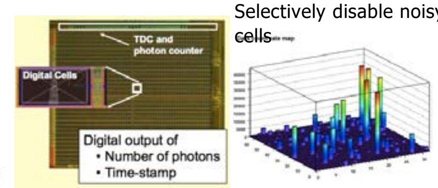
Digital devices have electronics embedded on chip







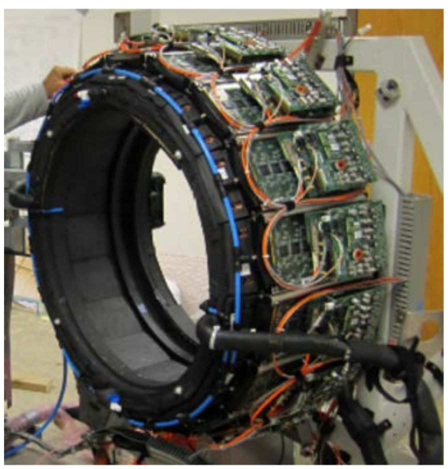
Selectively disable noisy cells

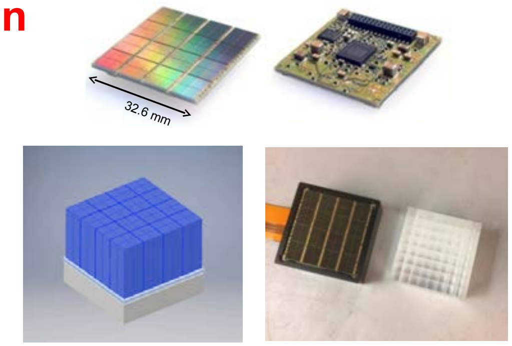


Philips Digital Photon Counting (PDPC)

Philips Vereos

2012 pre-production, 2017 production





- 3.86 x 3.86 x 19 mm^3 thick LYSO
- Axial FOV: 16.4 cm
- TOF: 320ps

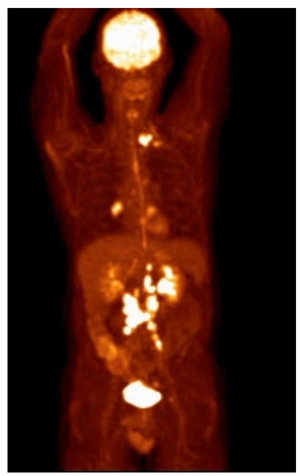
Digital SiPM chip is a 8x8 channel device

- 1 crystal per SiPM channel

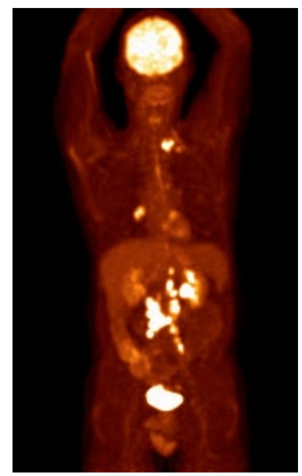
MIP images for BMI=24 patient 13.4 mCi, 60 min p.i.

Courtesy, Drs. Michael Knopp, Jun Zhang, Ohio State Univ.

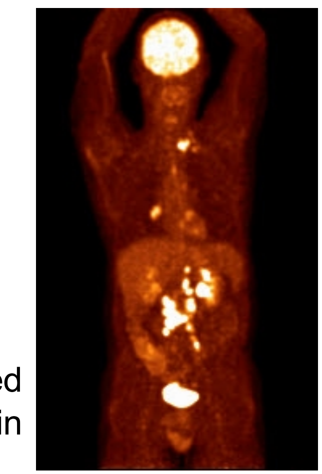
90s/bed
15min



30s/bed
5min



9s/bed
1.5min



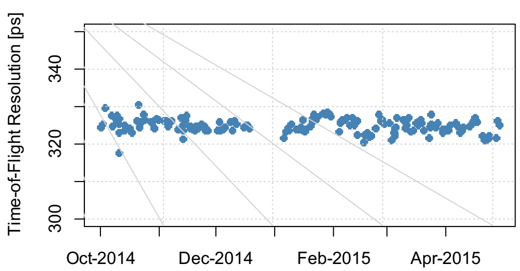
High quality images in short scan time

Philips Vereos

Characterization of the Vereos Digital Photon Counting PET System
Miller et al, SNM 2015

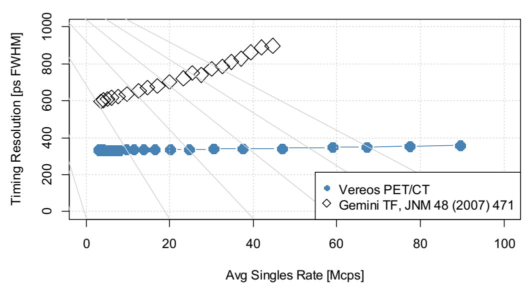
THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER
Wright Center of Innovation in Biomedical Imaging
PHILIPS

TOF and count stability better than 1 % over 7 months



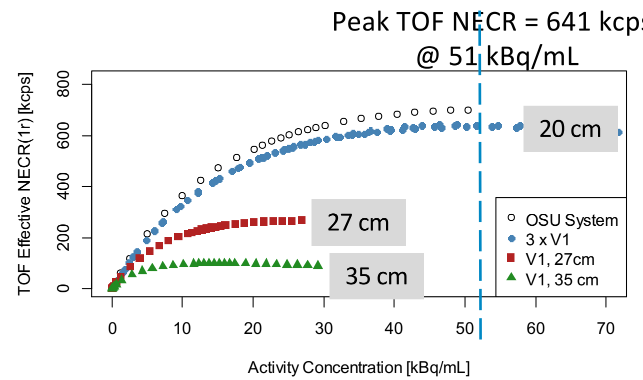
TOF Resolution Stability Over Time

TOF resolution stable within 5% up to peak NECR



TOF Resolution Stability Over Count Rate

First-class count rate performance



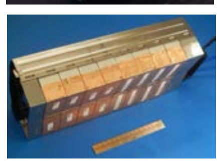
Spatial Res = 4.1 mm at center
5.1 mm at 20 cm

Siemens Biograph Vision

2018

- 3.2 x 3.2 x 20 mm³ thick LSO
- Axial FOV: 26.3 cm
- TOF: 215 ps

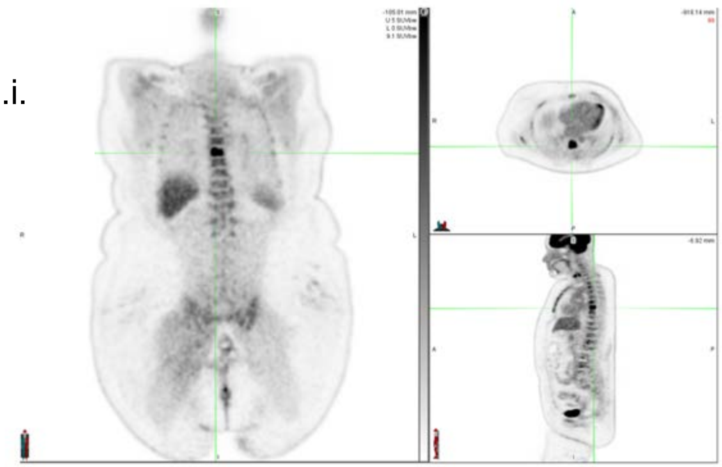
Mini-block, 5x5 array of crystals coupled to a SiPM chip with 4x4 array of channels
- ~ 1.5 crystals per SiPM channel



41 yo F with breast cancer
BMI 43.6

15 mCi FDG, 54 min p.i.
11 min scan
CBM @ 1.4 mm/s

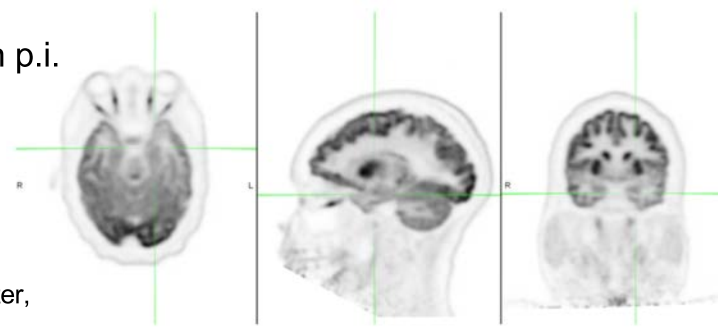
Bony metastasis in thoracic spine



27 yo F with drug resistant epilepsy

15 mCi FDG, 46 min p.i.
10 min scan

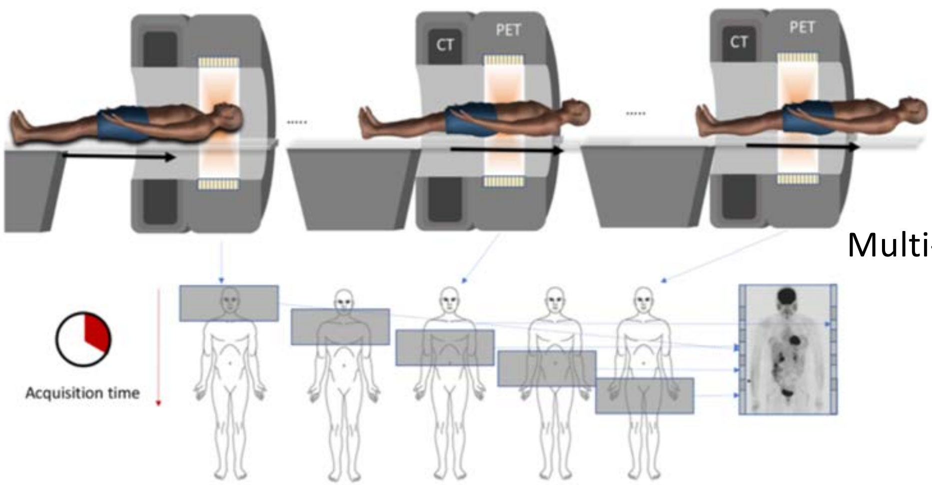
Decreased uptake consistent with left-sided seizure onset



Images courtesy PET Center, University of Pennsylvania

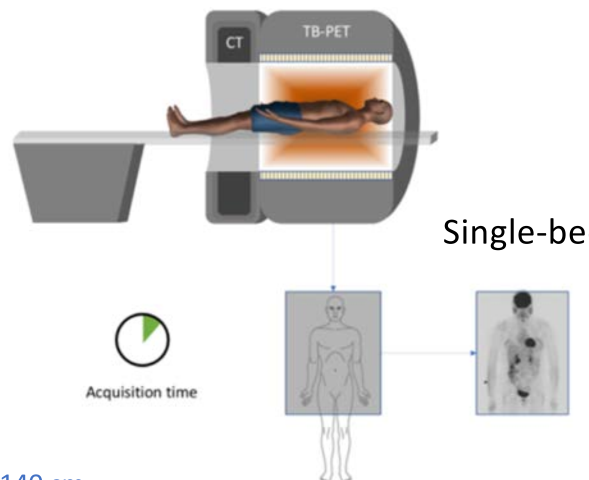
What is TB (Total-Body) PET?

Commercial PET-CT: Axial FOV 15-30 cm



Multi-bed acquisitions

Total-Body PET-CT: Axial FOV > 70 cm



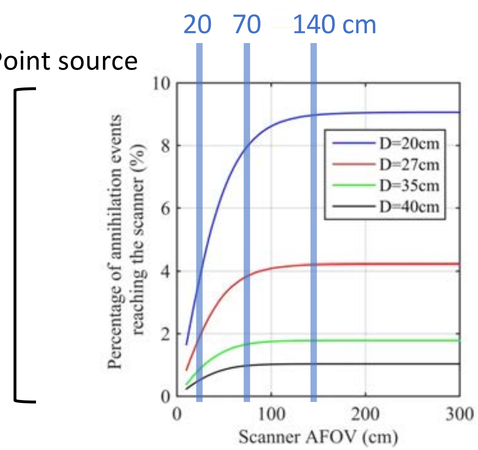
Single-bed acquisition

TABLE I

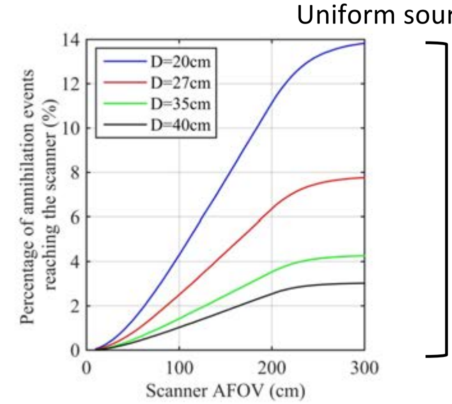
Relative sensitivity for selected scanner axial lengths as calculated for three different imaging setups. The phantoms are 200 cm long cylinders.

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	58

Point source



Uniform source



Research and Translational Applications

- High sensitivity
  - Reduce dose or scan time
  - Delayed imaging to capture slow biology
- Simultaneous imaging of large volume
  - Bio-distribution of new radio-tracers
  - Dynamic imaging of multi-organ systems
    - brain-body
- Improved quantitative accuracy of kinetic modeling for biologic parameter calculation

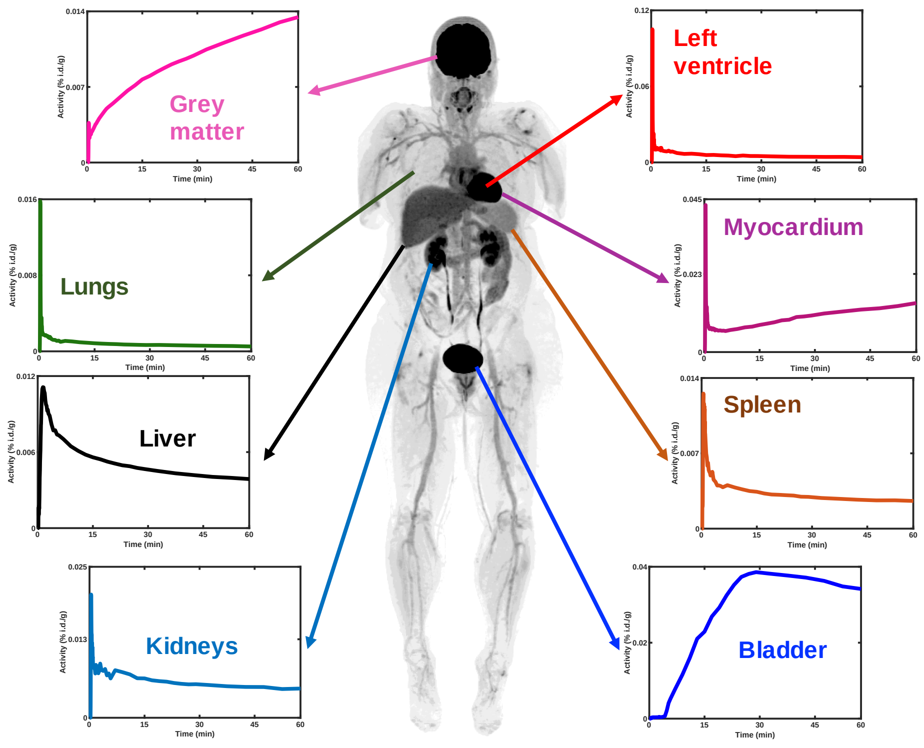


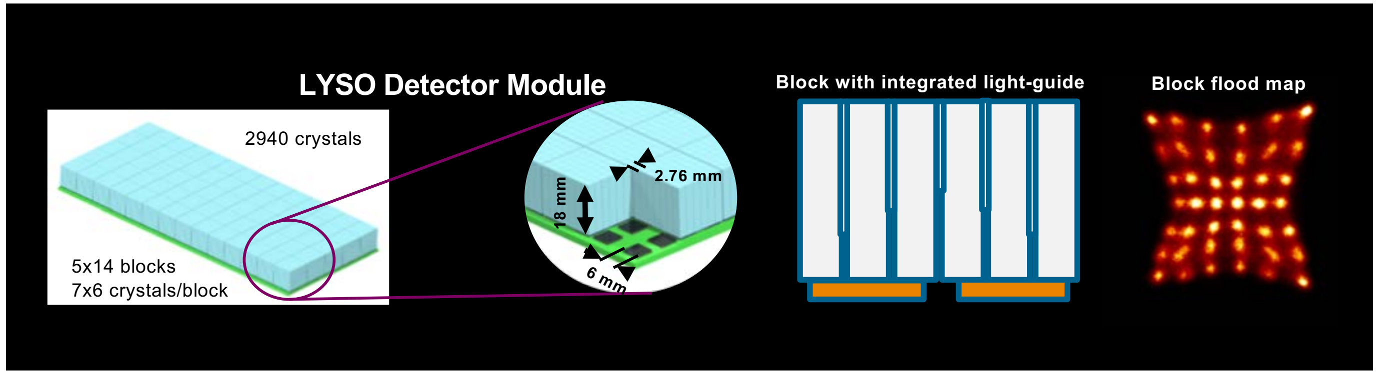
Image courtesy S. Cherry, UC Davis

Long AFOV scanners: Anger logic vs. 1-to-1 coupling with SiPMs

uEXPLORER

194 cm AFOV

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



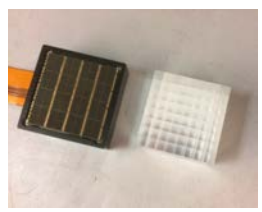
- TOF = 505 ps, 3-mm spatial resolution

Courtesy, Hongdi Li, UIH America

PennPET Explorer

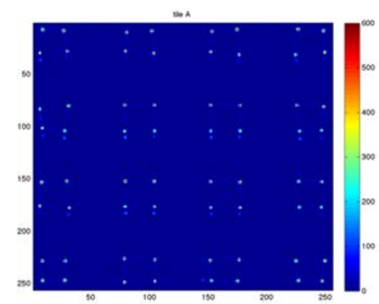
70-140 cm AFOV

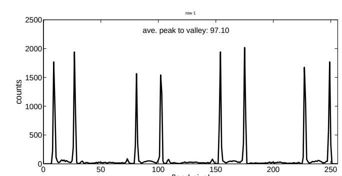
PennPET Detectors: **1:1 encoding, crystals:SiPMs**



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

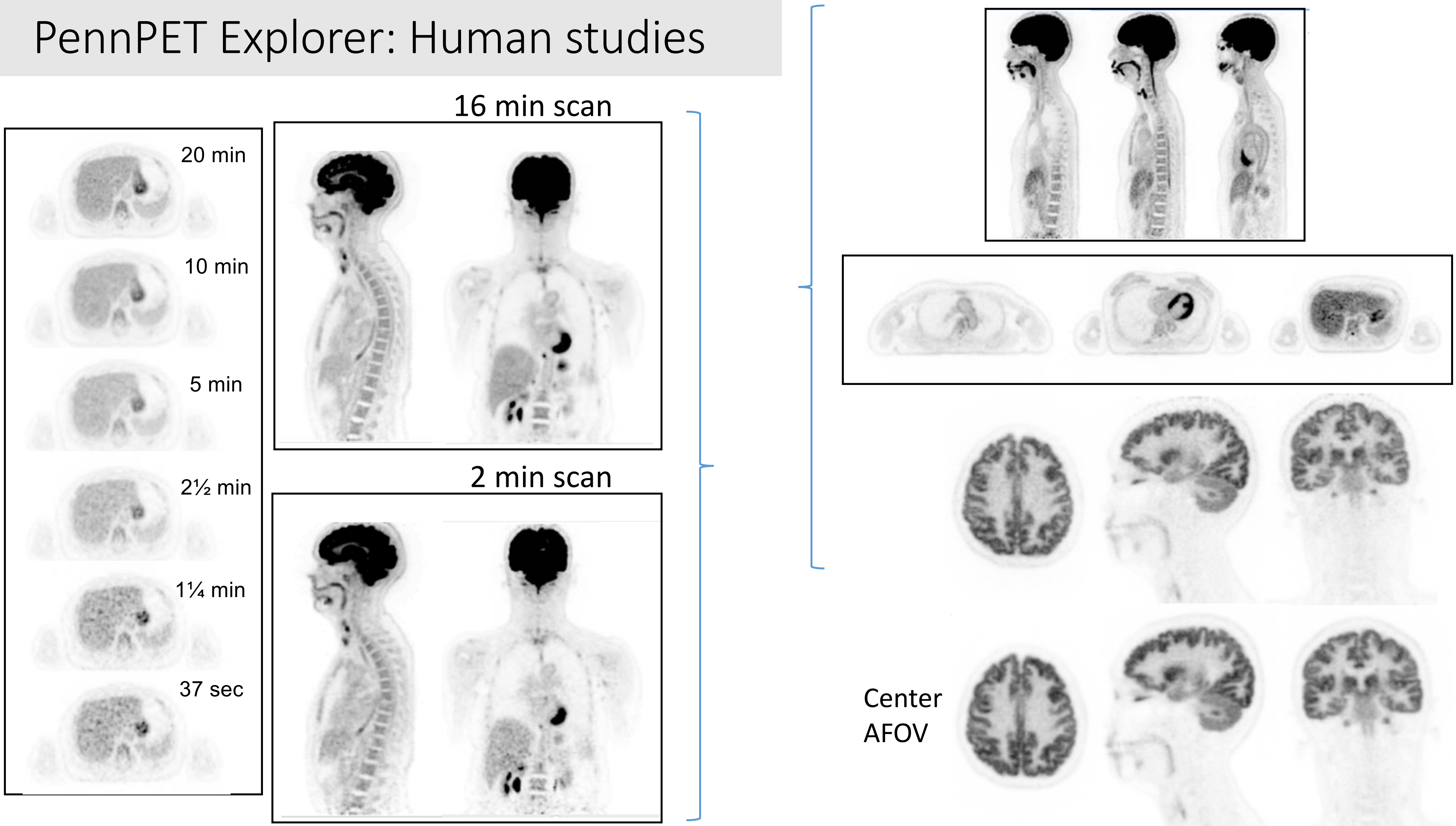
2D flood





- TOF = 250 ps, 4-mm spatial resolution

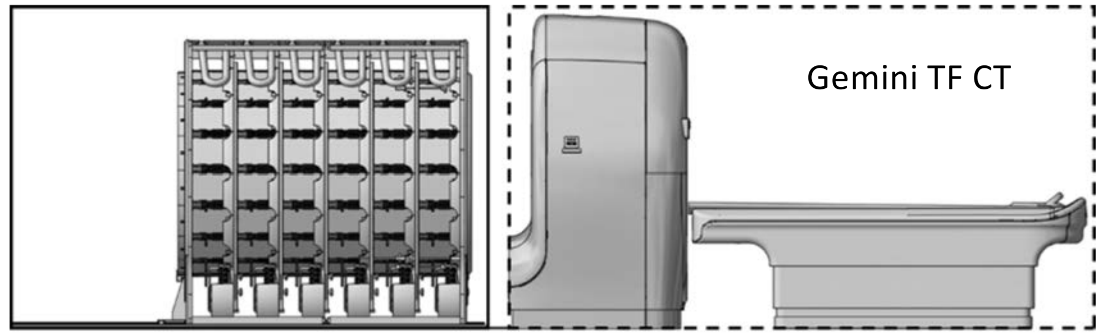
PennPET Explorer: Human studies

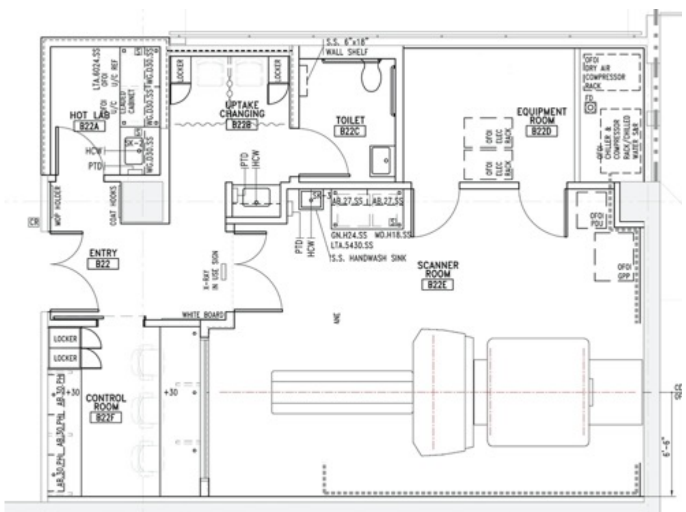


Scalable: 3 rings to 6 rings

3-ring PennPET Explorer

6-ring – 1.4 meter

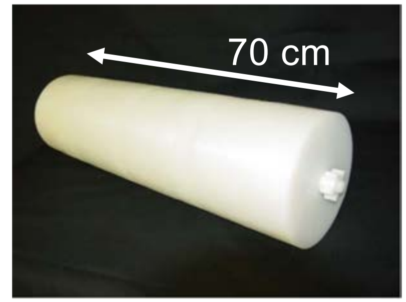




PennPET Explorer Imaging Facility -Stemmler B22

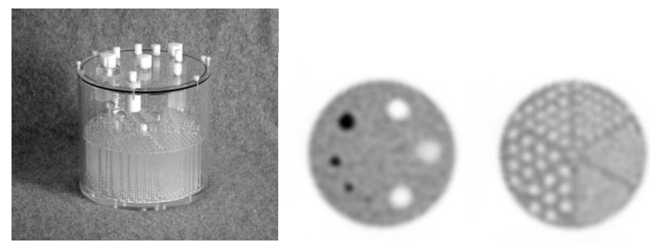
Summary

- Complete expansion to 6 rings



- Acceptance testing
  - Gemini TF CT completed
  - PET – will follow NEMA 2018
    - Designed for scanners with standard AFOV
    - Spatial resolution, sensitivity, count-rate capability, image quality

- Quantitative calibrations
  - ACR phantom – SUV cylinders, background
  - Routine QC – daily, monthly/quarterly, annual



- Resume human imaging – research IRB
  - Emphasize applications for whole-body PET

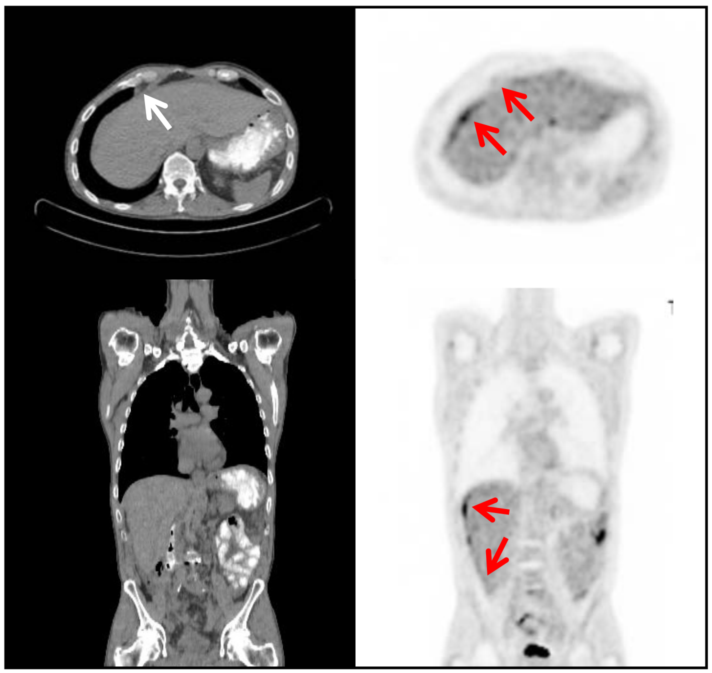
PennPET Explorer: Clinical studies

M 60 y.o, 173 cm, BMI 20.1

15 mCi FDG

Clinical PET/CT scan

1 hr p.i.



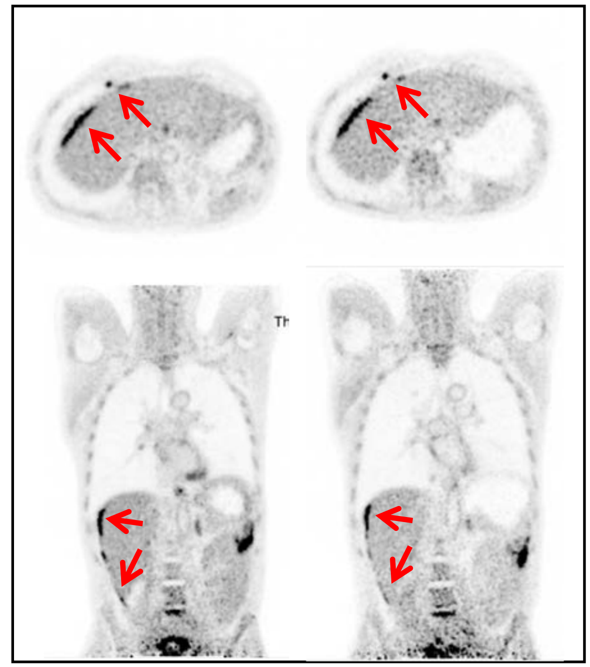
15 min scan

Disease of the peritoneum

Improved clarity of disease

PennPET scan

2.75 hr 4.25 hr (~ ¼ dose)

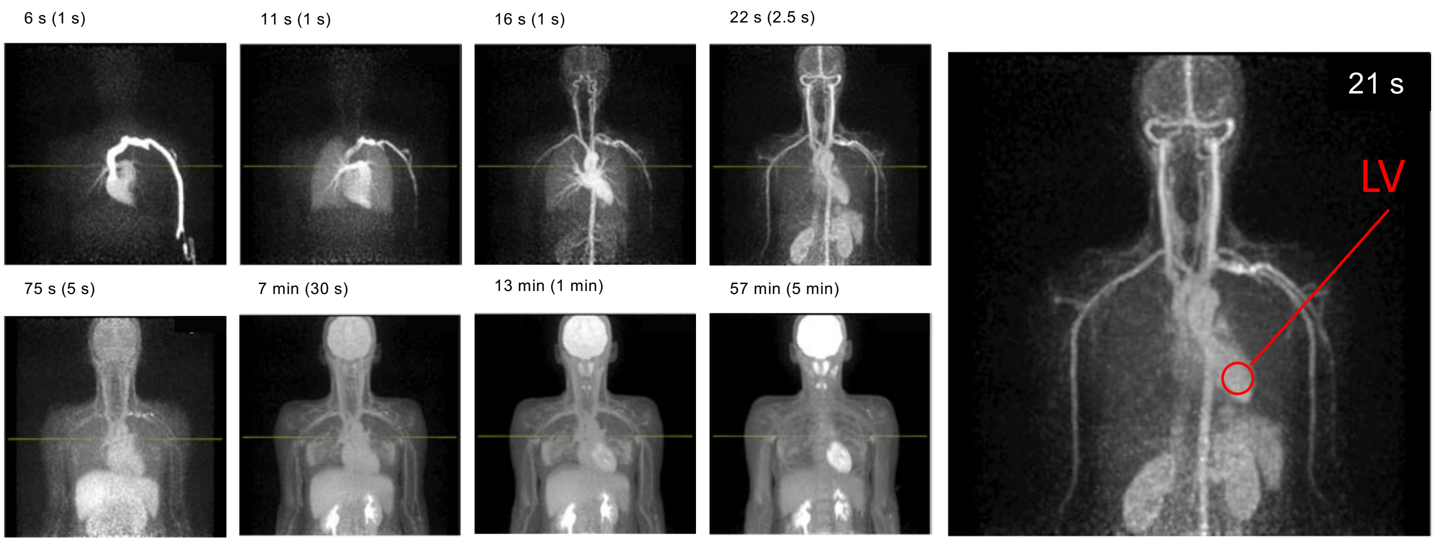


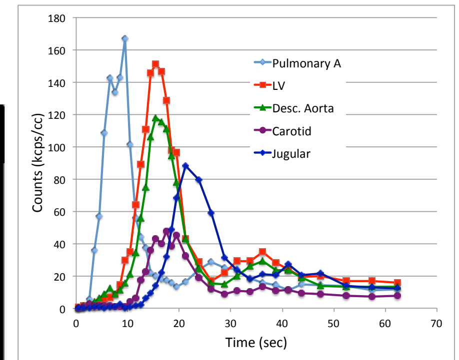
10 min scan 10 min scan

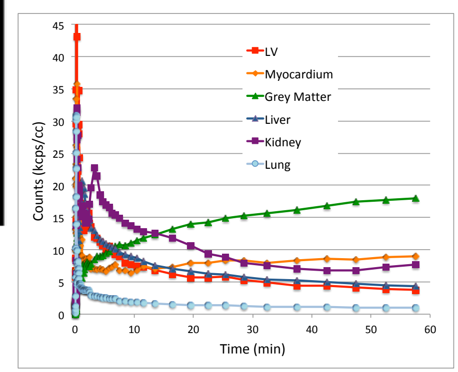
PennPET Explorer: Dynamic studies

F 29 y.o, 177 cm, BMI 19.3

15 mCi FDG

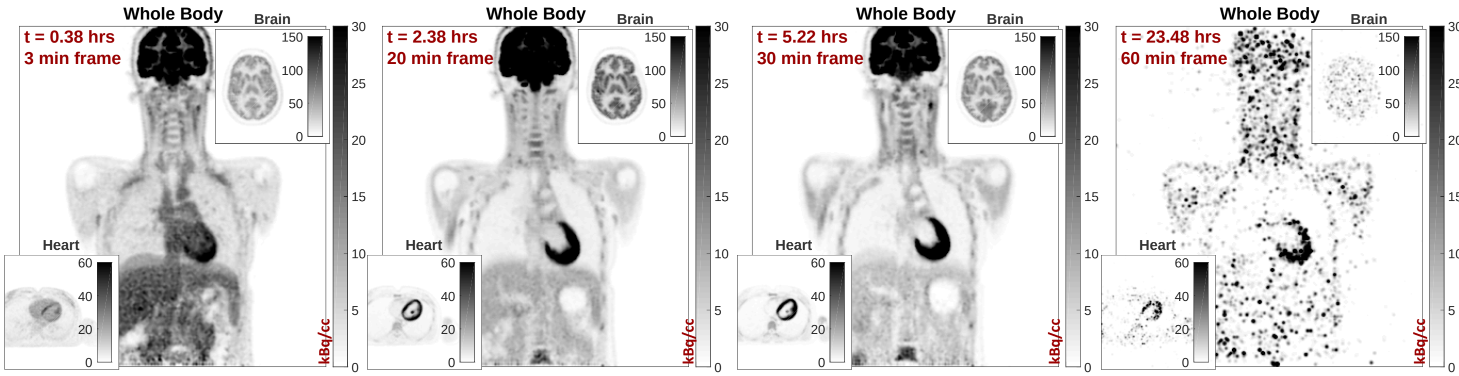


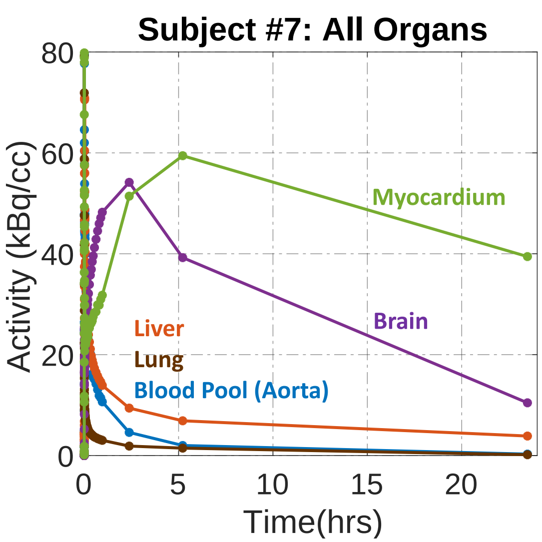




Bolus injection: TACs of blood input function measured at several vessels over first minute after injection, and TACs of major organs over first hour after injection

PennPET Explorer: Delayed studies

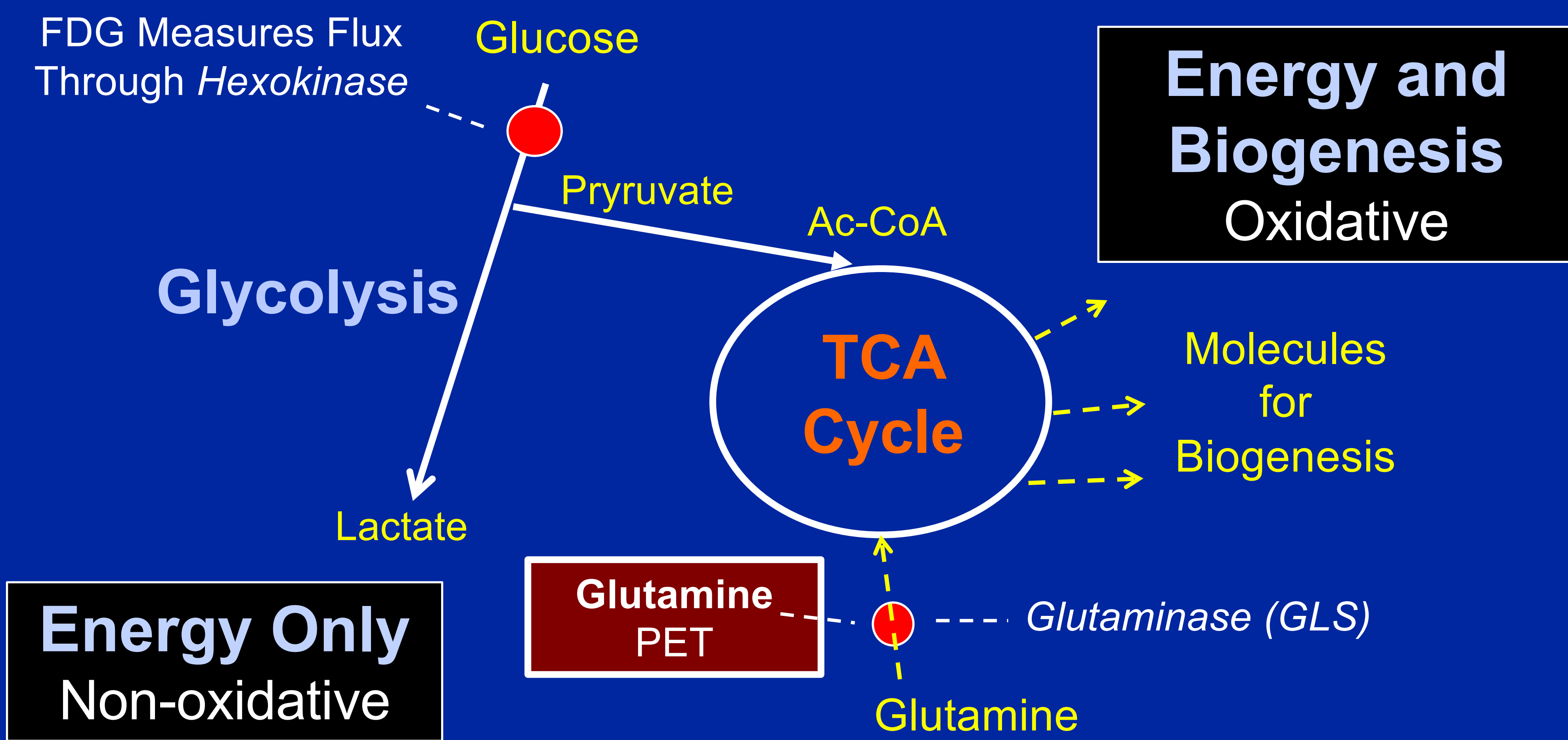




- Activity in the brain decreases over time more quickly than in myocardium implying that G6Pase is activated to break down [^{18}F]FDG-6P

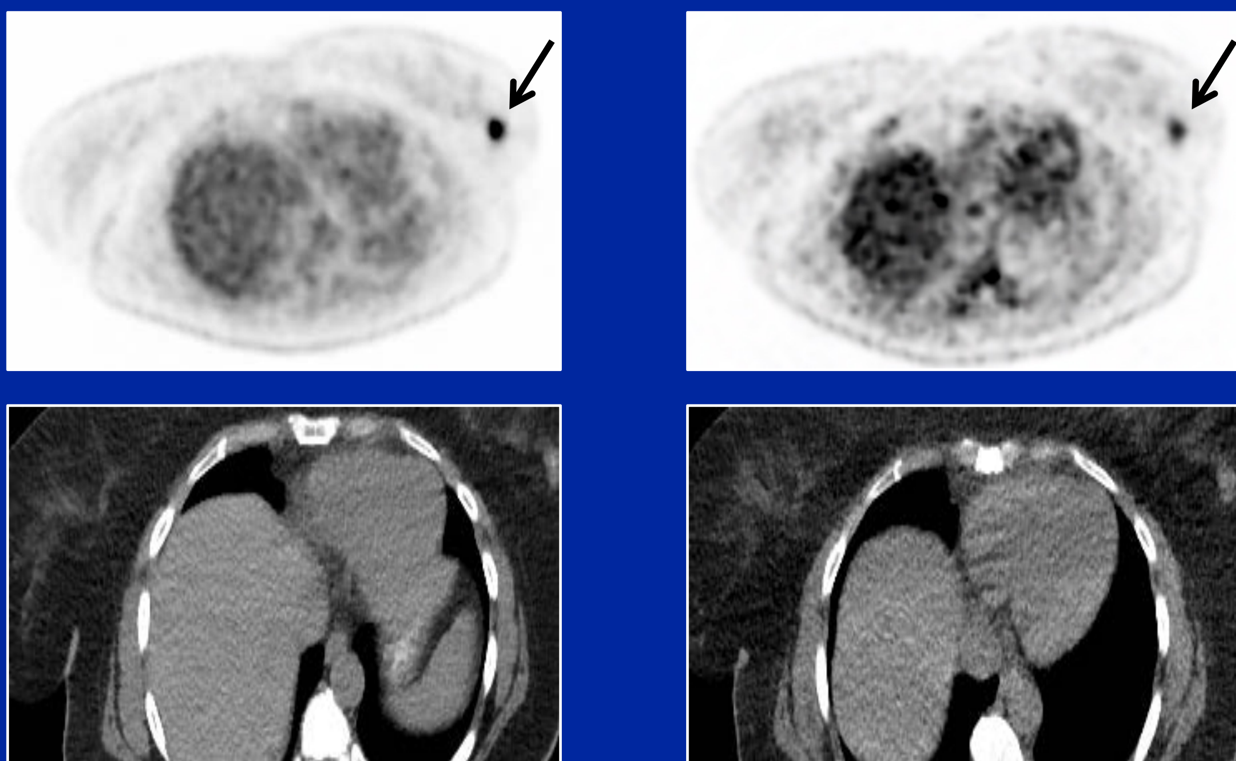
High Sensitivity enables the study of slow biological processes

Energy Metabolism & Biogenesis



[^{18}F]FDG and [^{18}F]F-GLN PET/CT in Breast Cancer

[^{18}F]FDG | [^{18}F]F-GLN

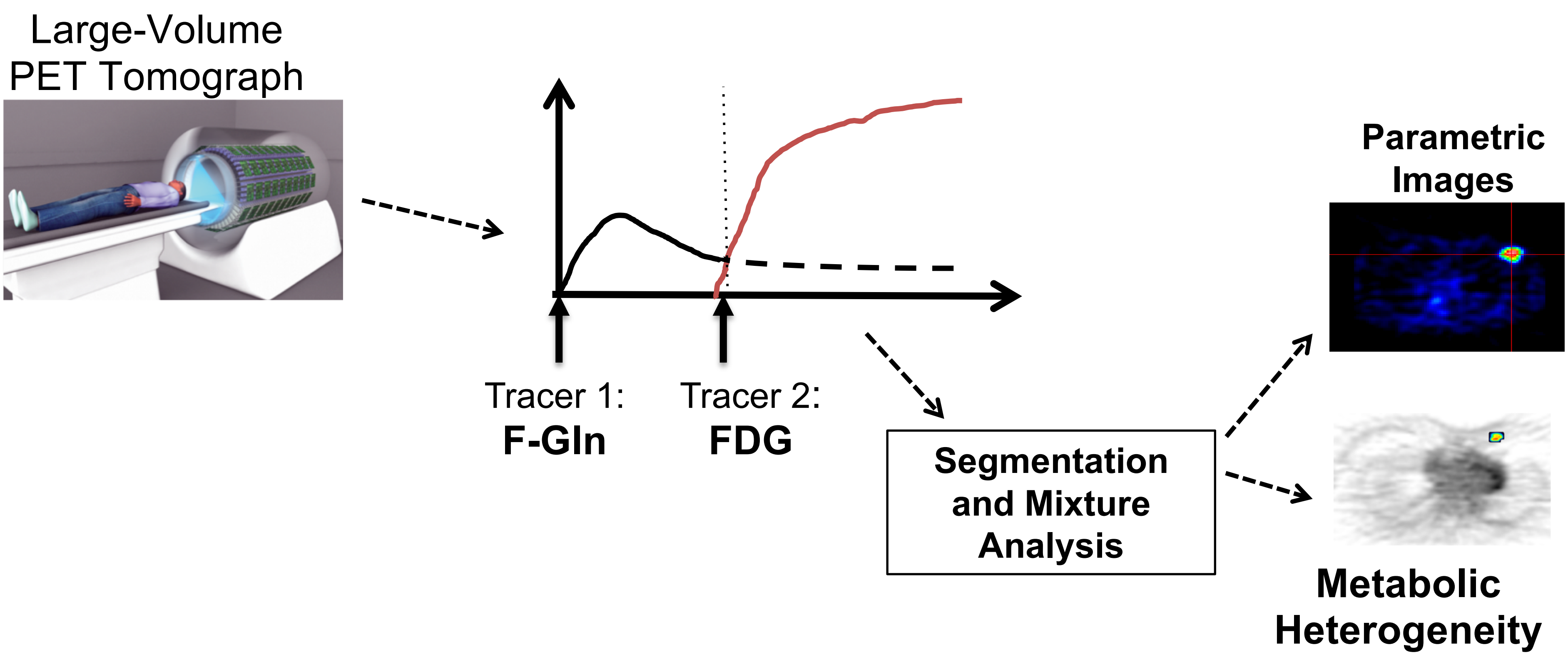


Perelman School of Medicine
University of Pennsylvania

(Austin Pantel)

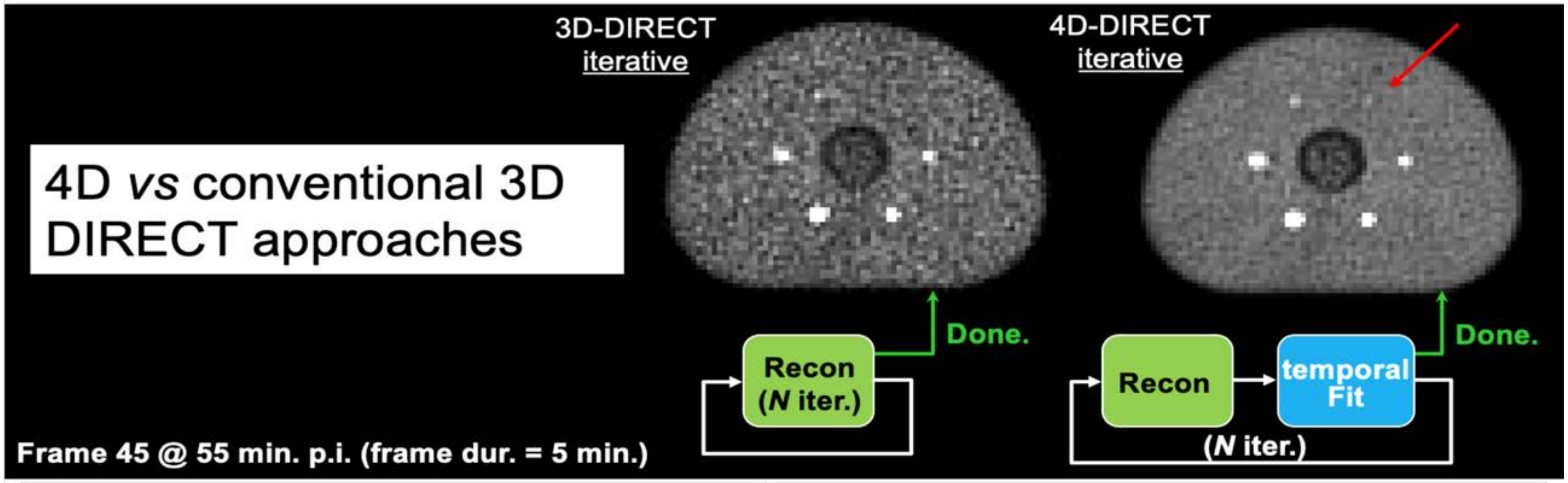
Total Body PET Enables Simultaneous Imaging of Glutamine and Glucose Metabolism

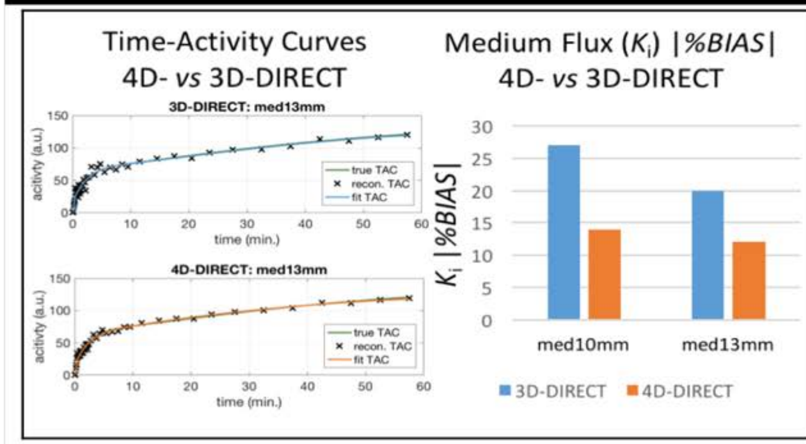
Mankoff, Karp, Kontos, O'Sullivan, Cancer Moonshot Grant R33-CA225310



Dynamic data analysis with 4D reconstruction tools

Matej & Gravel



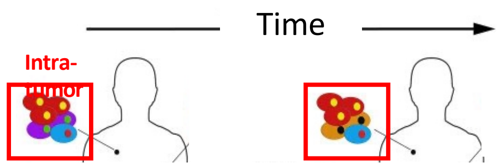


True, reconstructed and fit time-activity curves (left), with K_i absolute *%BIAS* (right) obtained from the iterative 4D-DIRECT reconstruction (orange) and from the iterative 3D-DIRECT reconstruction (blue) fitting methods at iteration 15, for the medium flux lesions of the dynamic IQ phantom.

Contributors: Paul Gravel, Margaret Daube-Witherspoon, Joel Karp, Yusheng Li, David Mankoff, Varsha Viswanath, and Samuel Matej.

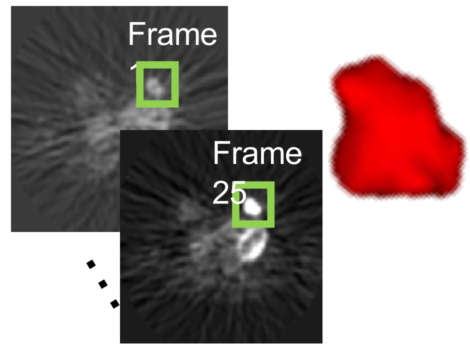
Funding: National Institutes of Health under Grants R33-CA225310 and R01-EB023274.

4D Imaging biomarkers of functional tumor heterogeneity (FTH)

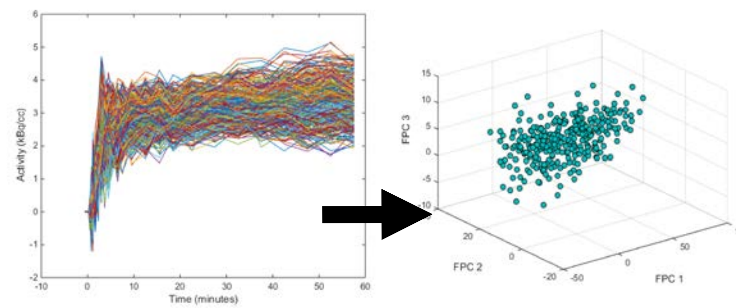


Spatial + Temporal = 4D functional tumor heterogeneity (FTH)

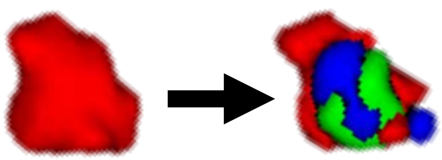
1. 3D tumor segmentation



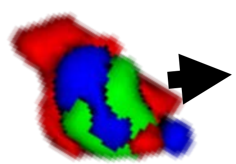
2. Summarize TACs using functional principal components



3. Segment tumors into 3 sub-regions using novel 4-D segmentation

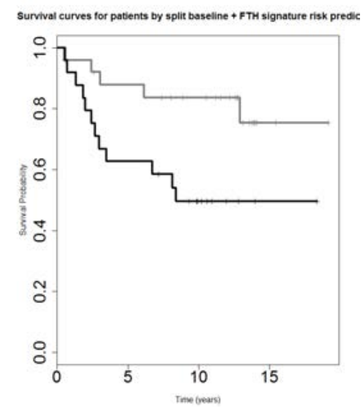


4. Radiomic biomarker: FTH imaging signature



FTH imaging signature

5. Recurrence free survival analysis



Chitalia and Kontos

Chitalia et al., *Radiomic Functional Intra-Tumor (Rad-FIT) clustering for characterizing functional tumor heterogeneity: Evaluation as a prognostic dynamic FDG-Pet biomarker for breast cancer*, in progress