Advances in Novel Prototype Imaging Systems:

# *Total-Body Positron Emission Tomography*

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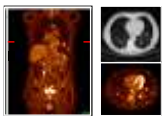
## Positron Emission Tomography

Tracer activity: FDG
10-15 mCi = 370-550 MBq




20 minutes whole-body (multi-bed scan)
200 M events total

Low Dose CT (for AC): ½ rem
PET : 1 rem (FDG)

## Advances in PET Instrumentation

mid 1970's
Washington University

University of Chicago

4 decades...

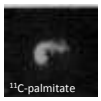
PET/CT

- Fully-3D (no inter-plane septa)
- Iterative reconstruction
- CT for anatomic correlation and attenuation correction
- Improved scintillators – fast, dense, bright (LSO, LYSO)
- Time-of-flight

## TOF PET Detectors

*Wash. U.* 1981-2
CsF 25 mm ϕ x 45 mm
28 mm ϕ PMT
Δt = 500 ps
1-to-1 coupling

Super PETT 1



Wash U. $^{11}$C-palmitate

*Philips* 2006-
LYSO 4 mm x 4 mm
39 mm ϕ PMTs
Δt = 500 ps
Anger-logic

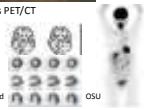
Gemini TF
PET/CT

U. Penn

*Philips* 2017-
LYSO 4 mm x 4 mm
4 mm² SiPMs
Δt = 300 ps
1-to-1 coupling

64-channel device

Vereos PET/CT



UH, Cleveland OSU

## TOF PET/CT scanners from all major vendors

PMT-based PET/CT: 2006 -> present *Timing resolution 500-600 ps*

Philips Ingenuity TF

Siemens mCT

GE Discovery 690

SiPM-based PET/CT: 2017 -> *Timing resolution 250-400 ps*

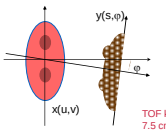
Philips Vereos

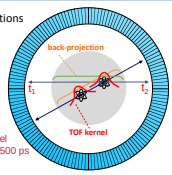
GE Discovery MI

Siemens Biograph Vision

## Time-of-flight (TOF) assisted Reconstruction

Image reconstruction from projections



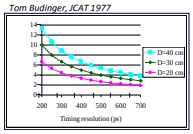




TOF kernel
7.5 cm ~ 500 ps

Signals from different voxels are coupled due to back-projection in reconstruction, thus SNR > $(N)^{1/2}$

TOF information reduces coupling of signals, thus improves SNR

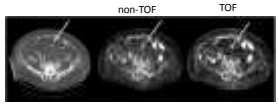
*Tom Budinger, JCAT 1977*




Gain in sensitivity = D/Δx

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

non-TOF TOF

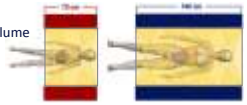


## Why large Axial FOV?

- Commercial PET/CT (~15-25 cm AFOV)
  - Total body PET - sequential beds
  - Best cost-benefit for clinical FDG

Assume tracer is static
Multi-bed acquisition

- High Sensitivity per volume
  - Lower dose
  - Reduce scan time



Sensitivity Gain

| | single organ | whole-body |
|---|---|---|
| 70 cm | 2.3 | 9.0 |
| 140 cm | 2.5 | 25.0 |
| 200 cm | 2.5 | 40.0 |

Point source sensitivity falls off due to geometry AND attenuation

- Simultaneous imaging of large volume
  - Dynamic imaging of multi-organ systems, multiple lesions
  - Kinetic modeling for biologic parameter calculation, e.g., flow, flux of tracer

Beyond Detection:

## How Can Molecular Imaging Guide Cancer Therapy?

- Measure therapeutic target expression:
  - *Choose targeted drugs most likely to be effective*
- Assess drug delivery:
  - *Does the drug reach the target?*
- Guide drug dosing:
  - *Choose a dose that balances efficacy and toxicity*
- Identify factors mediating therapeutic resistance
  - *Measure the In vivo biology of cancer response*
- Specific applications for Total-Body PET
  - Therapeutic target expression
  - Drug delivery
  - Radionuclide theranostic agent dosimetry – new tracers, e.g., $^{89}$Zr-labeled
  - Unique window on in vivo cancer biology

## Design Considerations

- Cost
  - Dominated by scintillator (LSO/LYSO) and photosensor (SiPM)
- Performance requirements
  - Retain, or improve upon state-of-the-art commercial PET/CT
- Scalable platform
  - Allow for different axial field-of-view

## Technology platform

- Philips digital SiPM detector tile: 1-to-1 coupling
- Design detector module
  - Thermal management of tiles for lower temperatures
- Detector ring: 23-cm axial length
  - 18 modules/ring

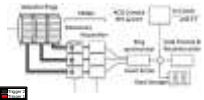
3.86 x 3.86 x 19 mm³ LYSO
PDPC digital SiPM (64 channels)

1st ring completed July 2017:
1½ year from initial design

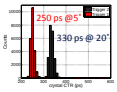
3 rings completed May 2018

## Technology challenges

- Data acquisition for multiple rings
  - Time alignment of rings – singles events



- Calibrations Timing and Energy
  - Lower temp for improved timing at equal sensitivity




- Data correction
  - Efficiency normalization
- Image reconstruction
  - Large data
  - Billions line-of-response

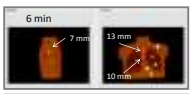


Uniformity test: meter-long cylinder


## Measurements : *CTN Torso Phantom*

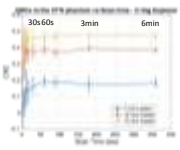
CTN Oncology phantom
- 30-cm axial length
- Lesions 7 -> 37 mm

Measure quantitative accuracy vs. scan time
- Lesion CRC – (T/B-1)/(Ratio-1)
- Lesion precision - %SD of replicate measures








Quantitative Accuracy for short scans

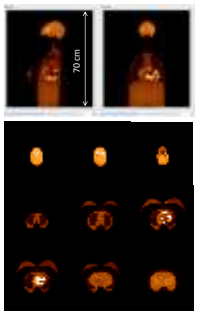
## PennPET Explorer : *Towards human imaging*

Aproved IRB approval of research protocol with new investigational device

Adult female: 162 cm (5'4")

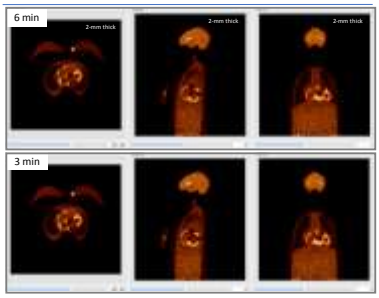
70 cm covers brain to lower abdomen

RSD Heart/Thorax + Striatal Phantoms – 60 cm axial length



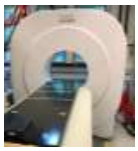

Dose = 0.1 µCi/ml

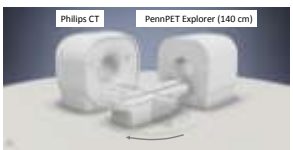
## *RSD Heart/Thorax + Striatal Phantoms*




## PennPET Explorer Status

- 3-ring, 70-cm AFOV system completed
  - Expansion ongoing to 6 rings, 140-cm AFOV
- Intrinsic performance measured
  - 4-mm spatial resolution
  - 250 ps timing resolution
  - 10% energy resolution
- Integration with commercial CT (in 2019)
  - rotating couch
  - minimize 'tunnel' effect





## Total Body PET - NIH Programmatic Overview

### The EXPLORER Project

Penn — UC DAVIS

**MiniEXPLORER-I**
- Applications prototype
- Non-human primate imager
- Siemens technology platform

**MiniEXPLORER-II**
- Technology prototype
- Companion animal/human brain imager
- UIH technology platform

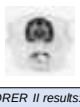
**PennPET EXPLORER**
- High TOF resolution
- Torso imager
- Philips technology platform

**uEXPLORER**
- High spatial resolution
- Total-body imager
- UIH technology platform

## UIH EXPLORER Detector Design

**Detector Module:**

Crystals: 2.76 x 2.76 x 18.1 mm LYSO
Block: 7 crystals (transaxial) x 6 (axial)
SiPMs: 4 per block - Sensl 6 mm J-series
Module: 5 blocks (transaxial) x 14 (axial)



- Primate imaging
- Demonstration of technology

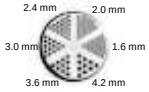
*MiniEXPLORER II results:*
Energy resolution: ~11.7%
Timing resolution: ~ 409 +/- 39 ps

## Human UIH EXPLORER

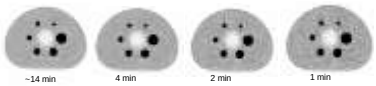
- Axial FOV: 194 cm
- Transaxial FOV: 68.6 cm
- Bore diameter: 76 cm
- 564,480 crystals
- 53,760 SiPMs
- 80 row CT

First Images

Mini-Derenzo
(not to scale with NEMA)




NEMA IQ - Spheres: 10 – 37 mm



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


## Summary

- Total body PET systems under development at several institutions
  - 70 cm – 200 cm axial FOV
- Human studies anticipated by 2019 at U. Penn and UC Davis
- Research applications will probe whole body kinetics
  - Guide cancer therapy
  - Clinical benefits - lower dose and reduced scan time
- Commercial interest from several vendors
  - Cost is a major consideration