

# TIPP for Medical Applications

*Chin-Tu Chen, Ph.D.*  
*The University of Chicago*  
&

*Peter Weilhammer, Ph.D.*  
*CERN*



*Wilhelm Röntgen*  
*First Nobel Laureate in Physics (1901)*  
*Discovery of X-Ray: 11/8/1895*  
*First "Medical" Image: 12/23/1895*

June 10, 2011, TIPP 2011, Chicago

## This Overview

- **Only a limited selection of medical applications**
- **TIPP 2011 papers largely not included**
- **Emphasis on**
  - **PP/HEP connections**
  - **Emerging, forward-looking, next-generation**
  - **Potentials for routine and wide-spread use  
(commercialization)**
  - **Impacts to medicine & health-care**

*More on Medical Applications:*

- *TIPP 2011 Tuesday 6/14/2011, 10:30am  
Patrick Le Du: “Application Outside HEP”*
- *TIPP 2009, Peter Weilhammer: “Particle Physics  
Instrumentation and Its Impact on Medical Imaging”*



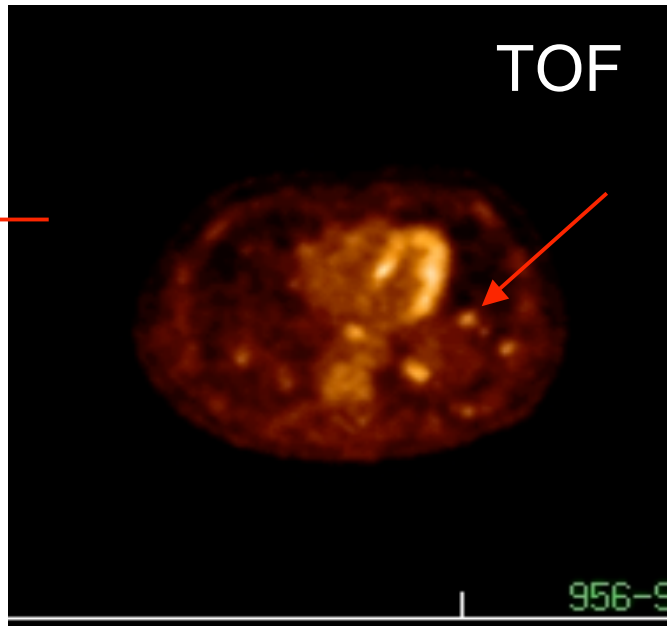
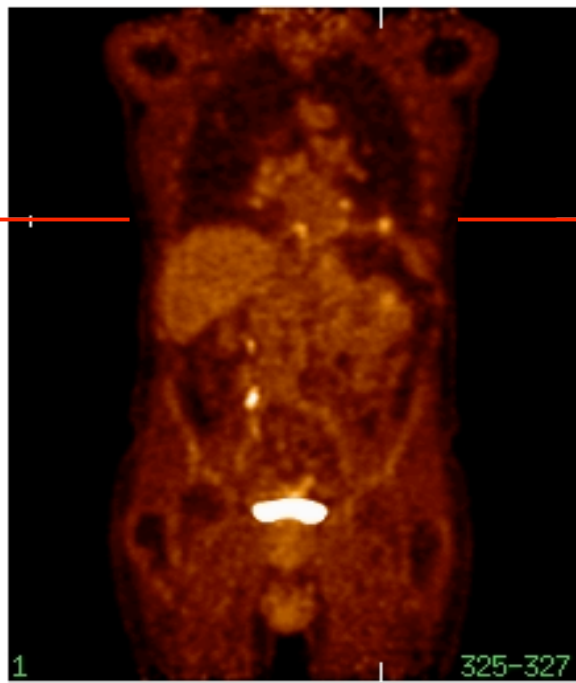
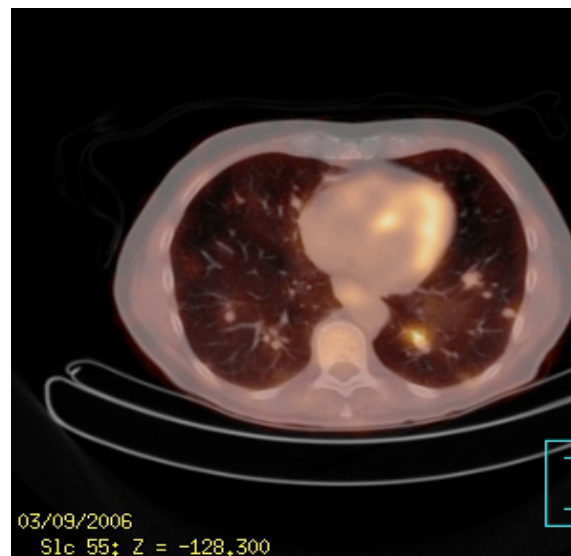
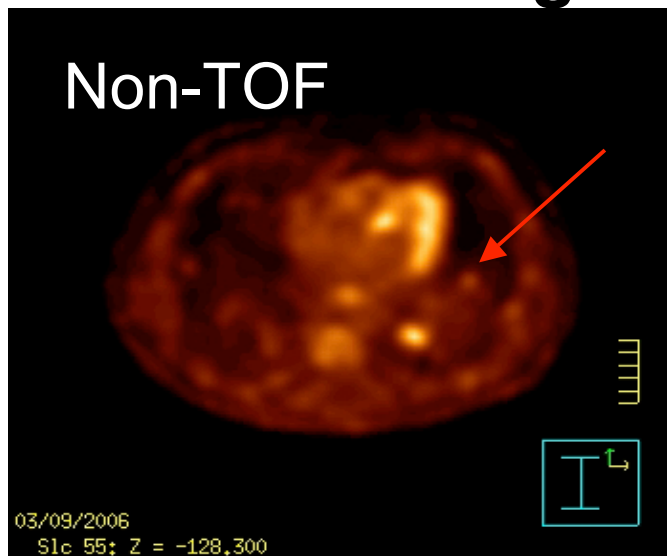
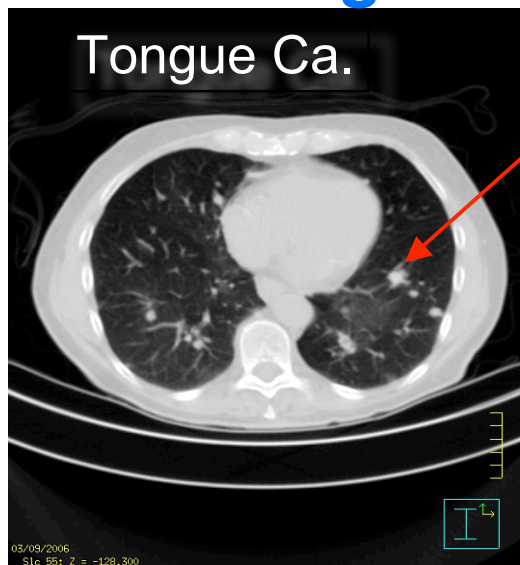
# Common Ground of PP/HEP & Medicine

- **Diagnostic Imaging**
- **“Radiation” & “Particle” Therapy**
- ***“Thera[g]nostics”* (Diagnostics + Therapeutics)**

*“.....Medical Applications serve as ideal ‘prototyping’ test and validation platforms of realistically feasible small-scale for PP/HEP Technology and Instrumentation.....”*

*- In Discussion with Marcel Demarteau*

# TruFlight™: Enhanced Diagnostic Confidence

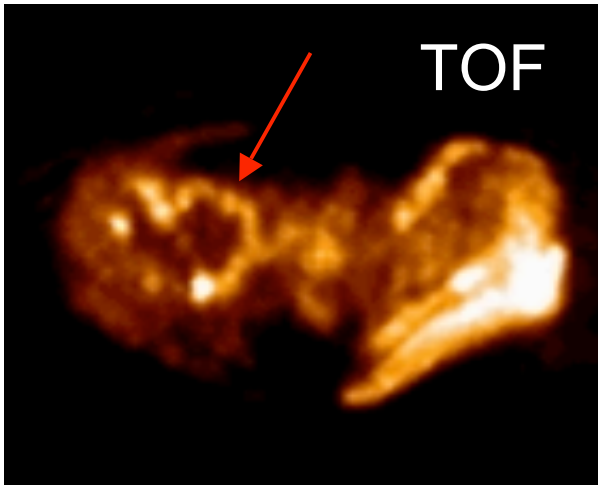
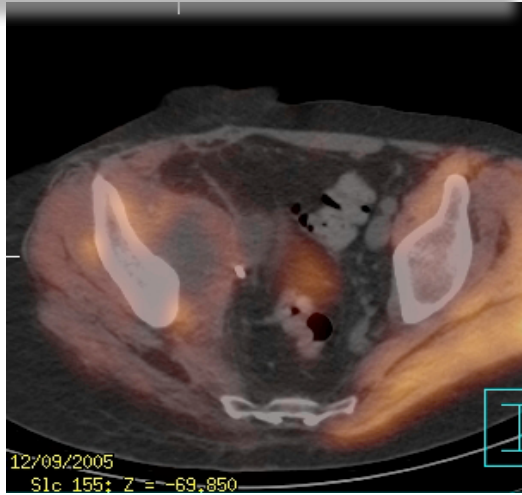
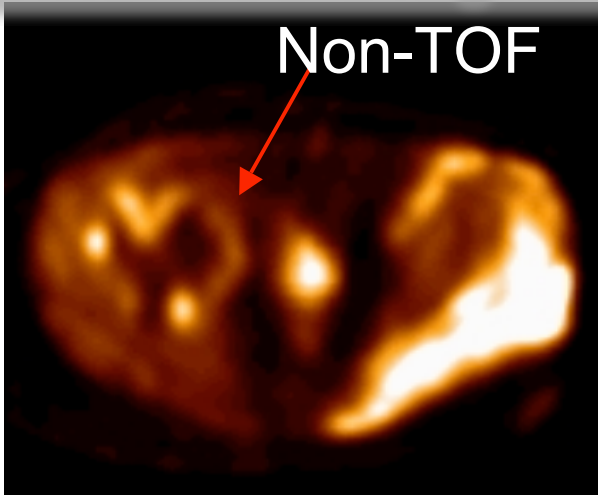
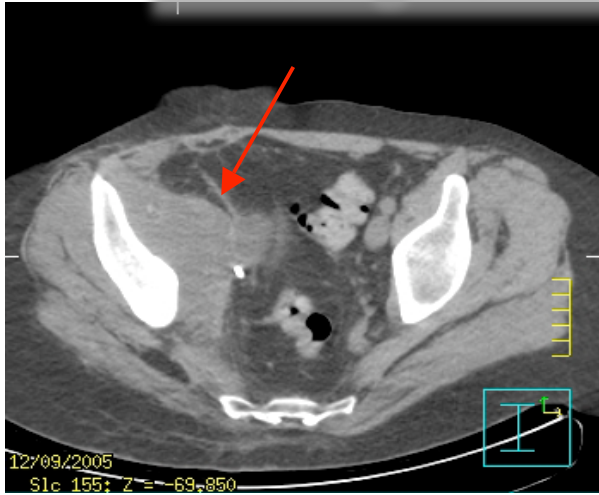


*improved detectability of small mets in lung*

*67 kg; BMI = 29.0  
9.8 mCi; 1 hr post-  
(2min/bed)*

Data courtesy of J. Karp, University of Pennsylvania

# TruFlight™: Enhanced Diagnostic Confidence



Lymphoma within iliopsoas muscle w central area of nec

*improved delineation of lymphoma activity*

116 kg; BMI = 31.2  
14 mCi; 2 hr post-inj

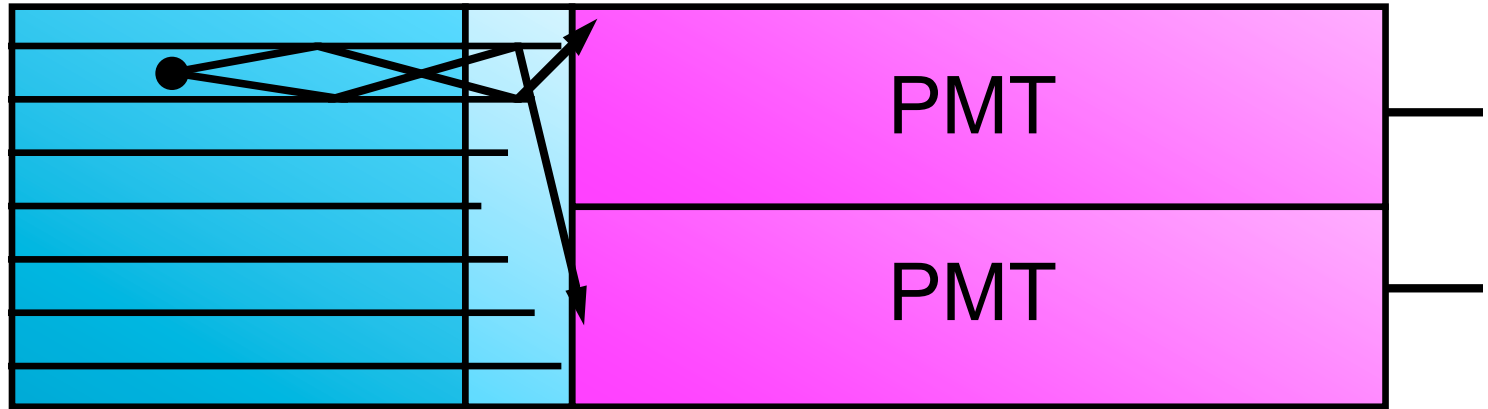
Data courtesy of J. Karp, University of Pennsylvania



# What Timing Can An LSO Module Achieve



**Crystal  
Geometry**



**Light Sharing**

**PMT  
Quality**

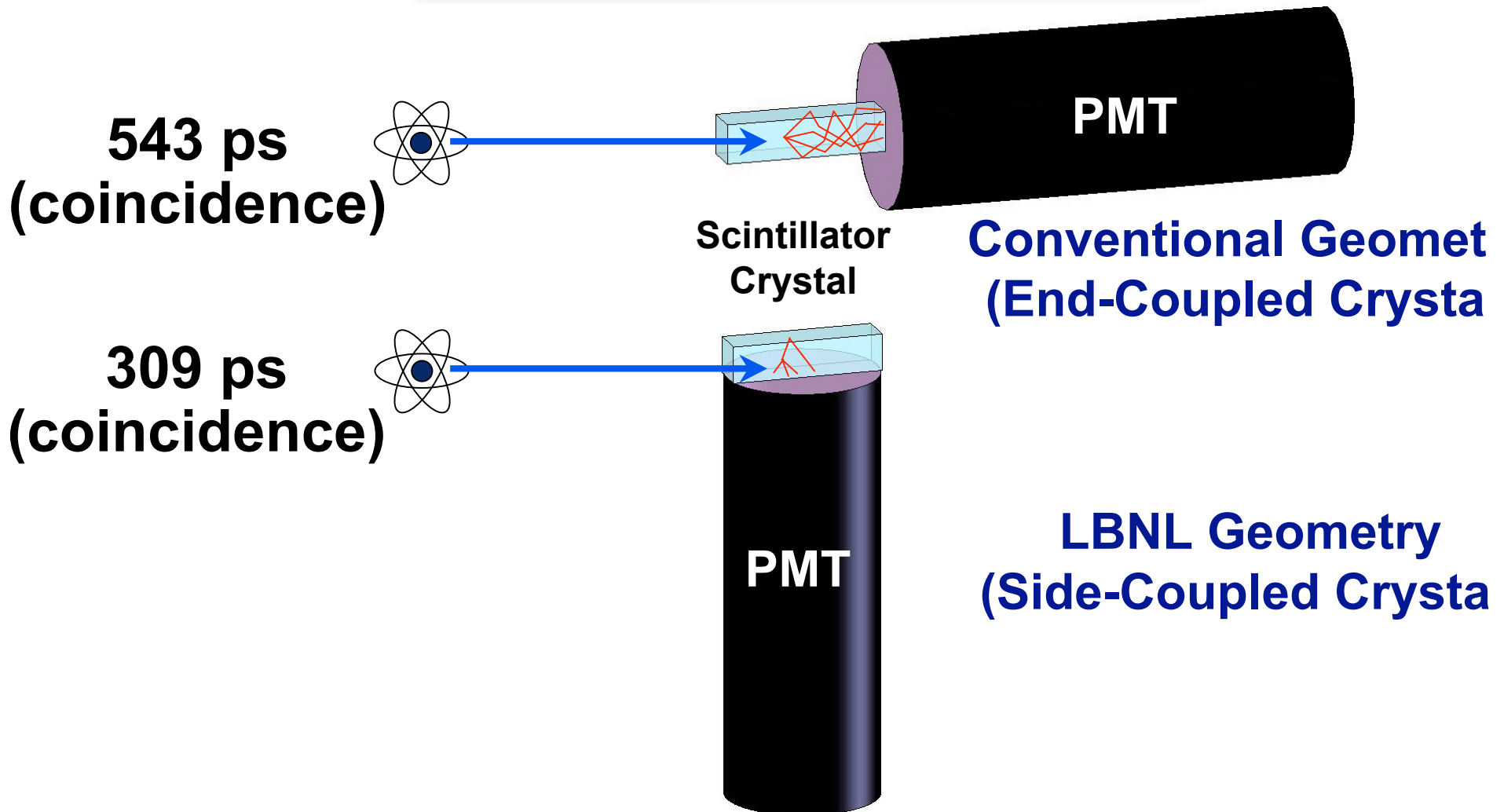
**Multiple  
PMTs**

**Predicted Limit  
Measured Value**

**550 ps  
575 ps**

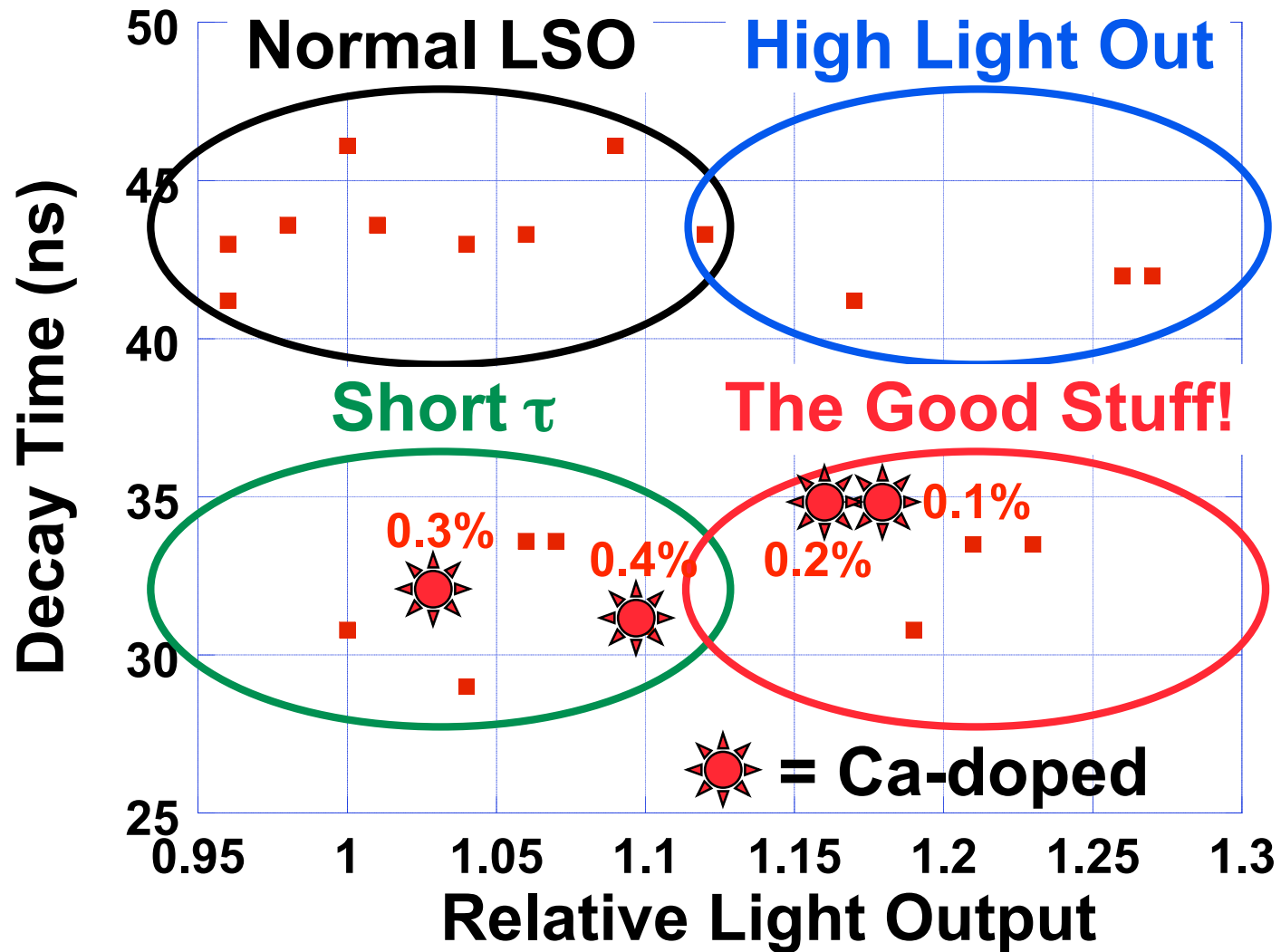
**Already Near LSO Block Detector Theoretical L**

# Side-Coupled Design



**Shorter Optical Path Length & Fewer Reflections**

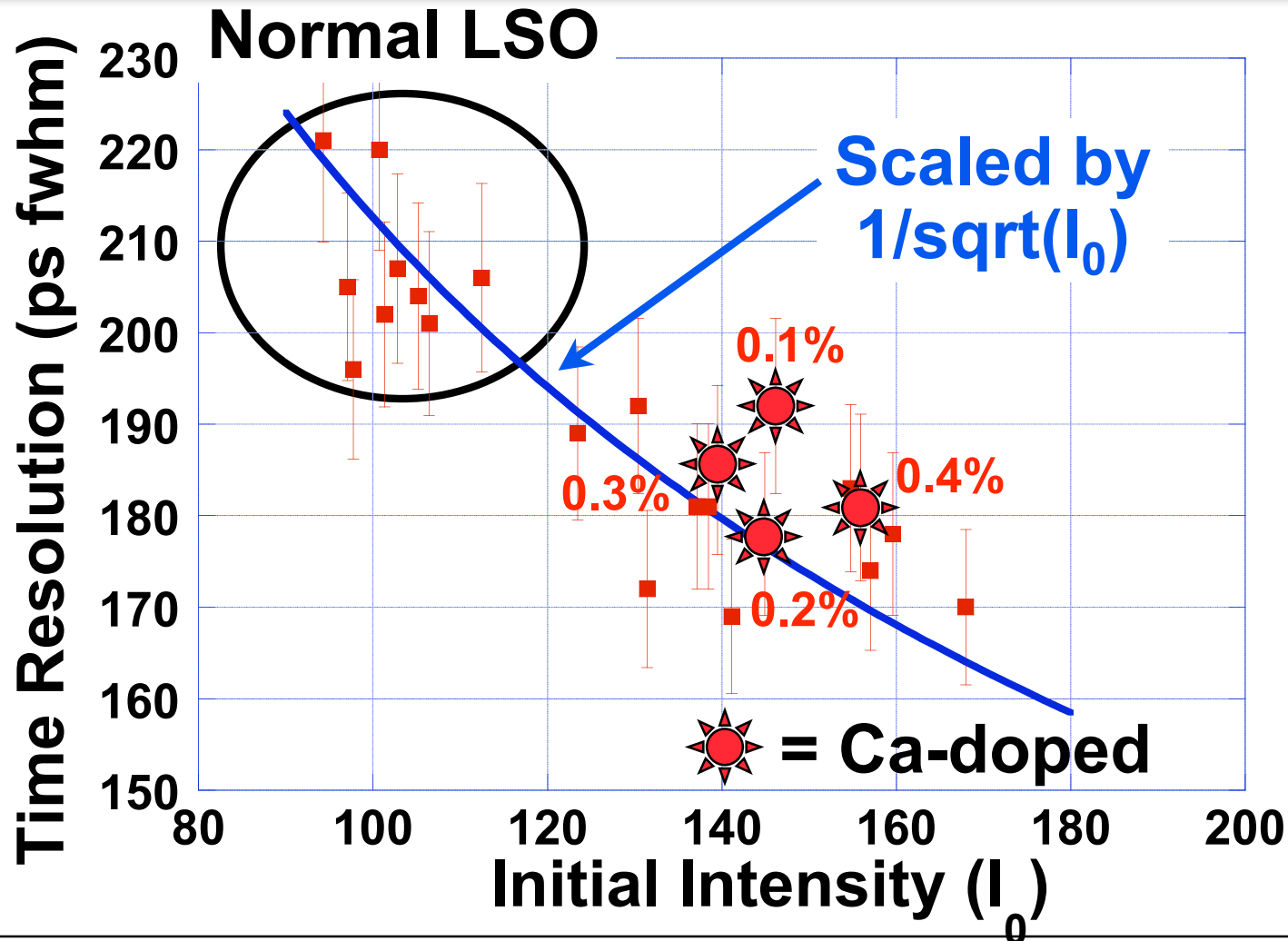
# Optimization: LSO Composition



**Ca-Doping Gives High Light Output & Short**

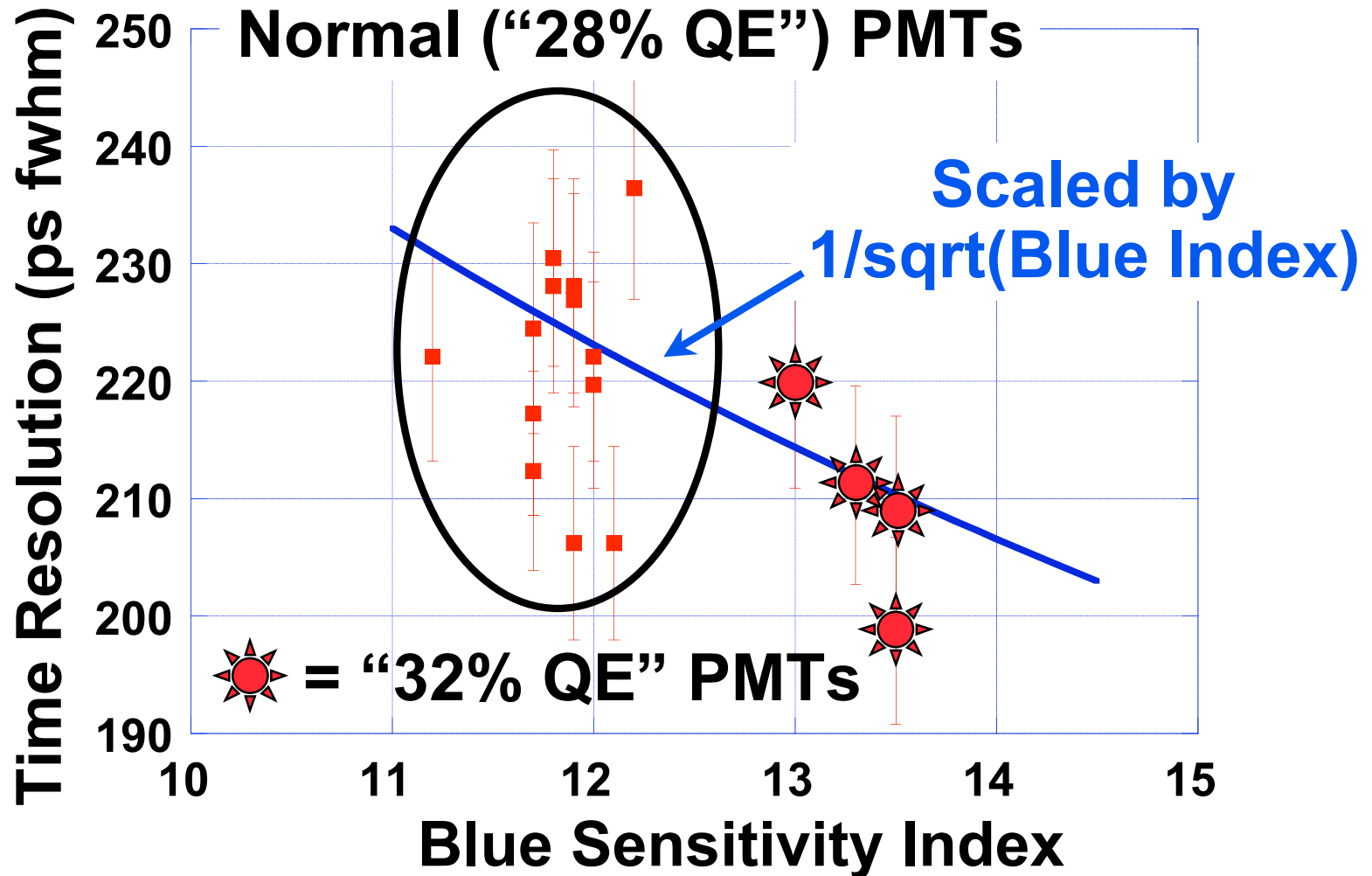


# Measured Results: LSO Composition



- **Ca-Doping Gives Good Timing Resolution**
  - **~15% Improvement Over Normal LSO**

# Measured Results: High QE PMTs



- Increased QE Improves Timing Resolution by
  - Expect 10% Improvement with 35% SBA PM

# Additional Improvements

Hardware	Coinc. (ps fwhm)	TOF Gain
End-Coupled Crystal	543	4.3
Side-Coupled Crystal	309	7.6
Co-Doped LSO	258	9.1
32% QE PMT	219	10.6

- TOF PET with *Significantly* Better Timing is Possible
- To Achieve, We Must “Think Outside the Block Detector”



# Detector Module Design

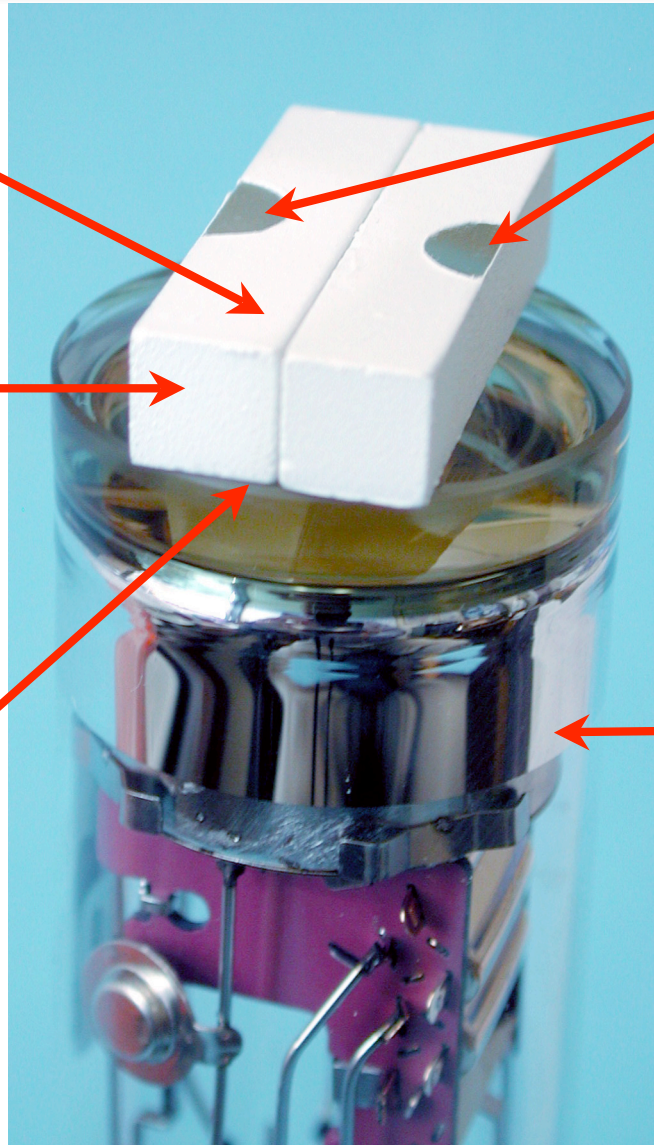
**Two LSO Crystals**  
(each 6.15 x 6.15 x 25 mm<sup>3</sup>)

**Reflector**  
(on all five faces of  
each crystal, including  
the face between the  
two crystals)

**Optical Glue**  
(between lower crystal  
faces and PMT)

**Hole in Reflector**  
**On Top Face**  
**Crystals**

**PMT**  
(Hamamatsu  
R-9800)



**Two Side-Coupled Scintillator Crystals per PMT**

## How Far Can TOF PET Go?

- **100 ps Timing Resolution**
- **23x Effective Efficiency Increase**
- ***Very Fast Reconstruction***

**Acquire & Reconstruct Image in <1 Minute**

# Conclusions

## **Benefits of TOF are *HUGE*:**

- 5x effective efficiency gain w/ 500 ps timing
- Greatest improvement in large patients
- Faster reconstruction algorithm convergence

## **Rebirth of TOF PET Due To New Scintillators:**

- 575 ps for LSO, 350 ps for LaBr<sub>3</sub>

## **Still *LOTS* To Do:**

- Electronics
- Module Design
- Reconstruction
- Photodetectors
- Scintillators
- Evaluation

***Much More Improvement To Come!***



# UChicago, Argonne, Fermi, +.....

## Large-Area Picosecond Photo-Detector (LAPPD) Project

### *Next-Generation MCP-PMT*



Project with 4 primary goals:

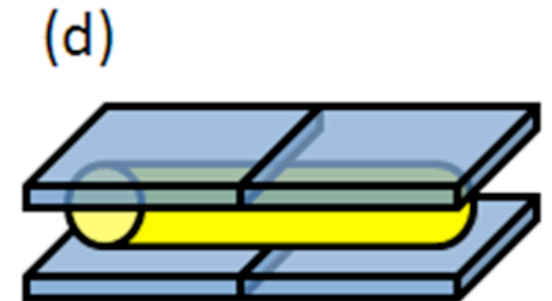
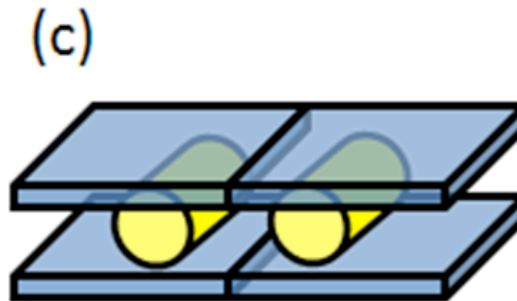
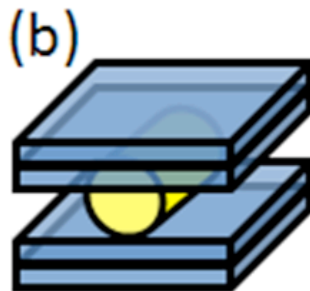
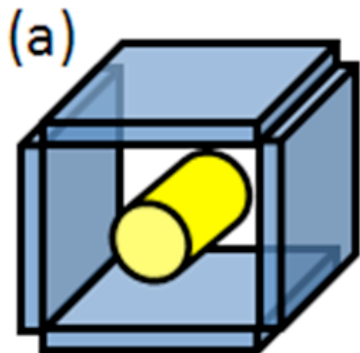
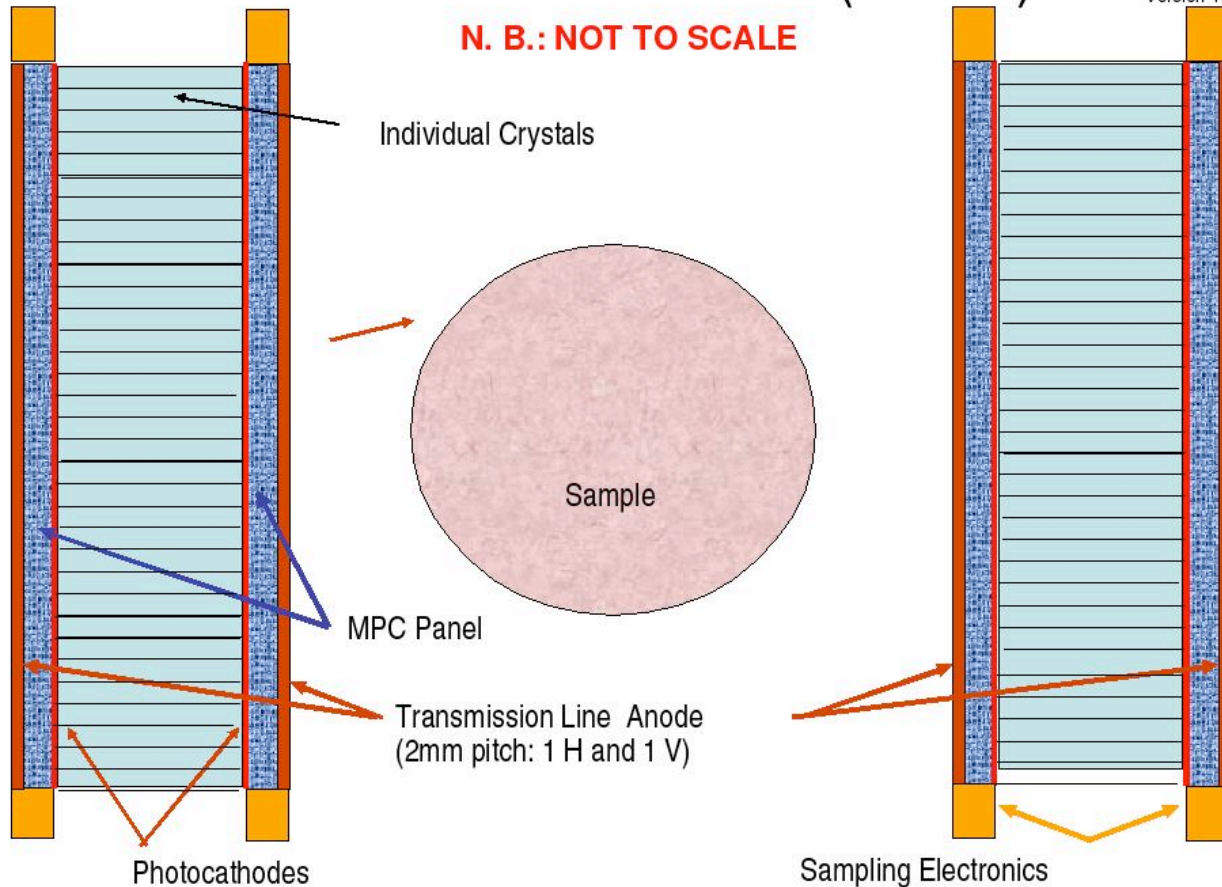
1. Low-Cost LAPPD with good timing and spatial resolution (~\$10/sq-in area cost)
2. Large-Area TOF particle/photon detectors with picosecond time resolution
3. Understanding photo-cathodes so that high QE cathodes can be reliably made with tailored spectral response, and new materials & geometries can be developed
4. Produce commercializable modules within 3 years & transfer technology to industry

# Panel-Based DOI-Coded TOF PET

## Micro-Channel Micro-PET (MCMP)

7/21/08  
Version 1.0

N. B.: NOT TO SCALE



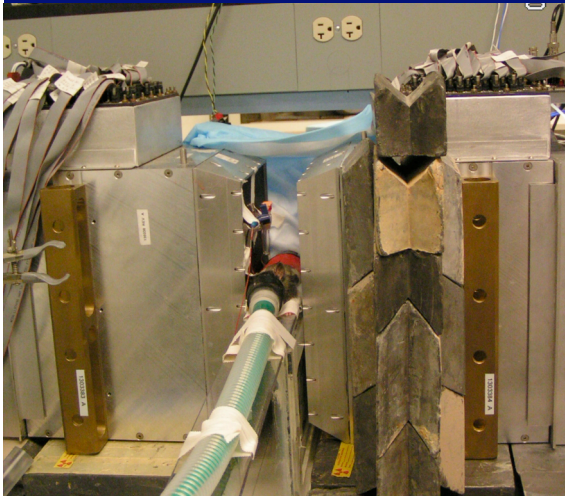
### Potential Applications:

- (DOI+TOF)-PET/CT
- Reconfigurable, Integrative, Modular "Super-Modules"
- [a] High-Resolution "Cube"
- [b] High-Sensitivity "Multi-Layer"
- [c] High-Throughput "Multi-Object"
- [d] Whole-Body

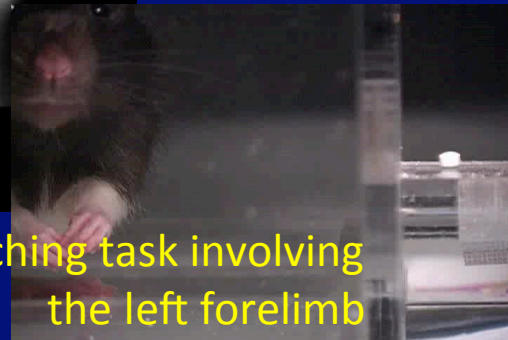
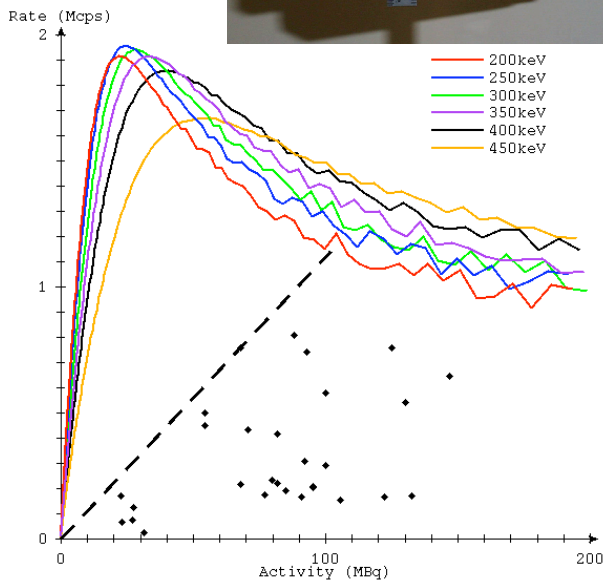
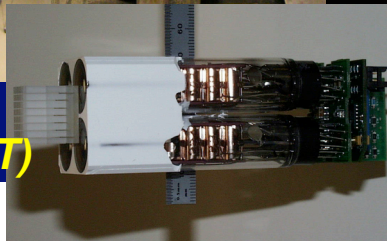
UC, ANL, FNAL, etc.

# High-Sensitivity Dual-Panel DOI-PET

- Sensitivity 25-30% (3-10 folds increase)
- High-throughput, multi-object
- Novel reconstruction/no rotation
- Super-resolution recovery
- Uniform resolution within large FOV
- Pre-clinical drug development
- Clinical or research brain imaging



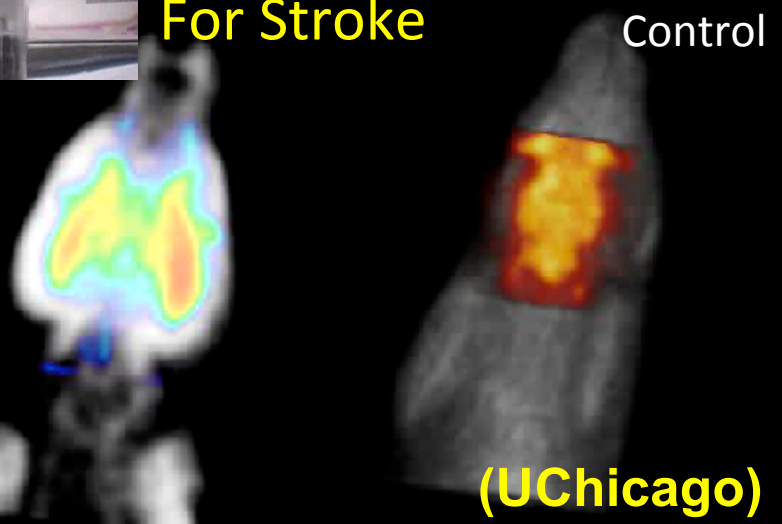
**Q-Sharing  
PMT (HRRT)**



Reaching task involving the left forelimb

FDG imaging of a rat's brain shows increased FDG uptake in the right brain due to the motor task performed by the left forelimb of the subject.

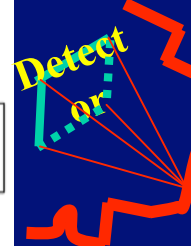
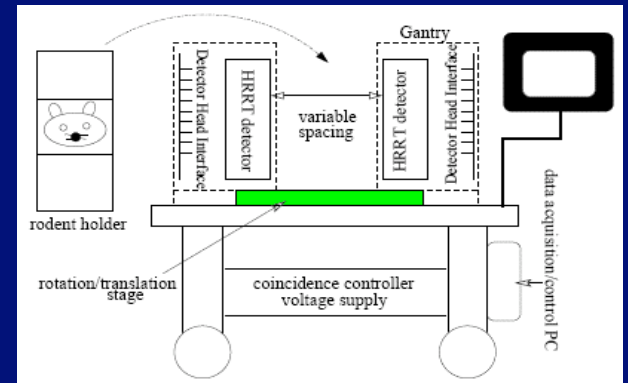
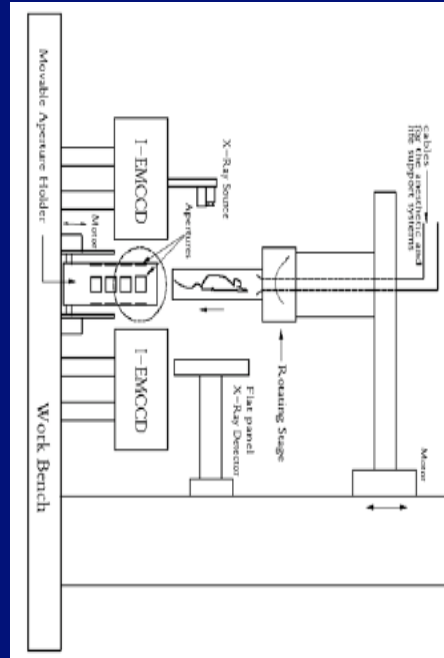
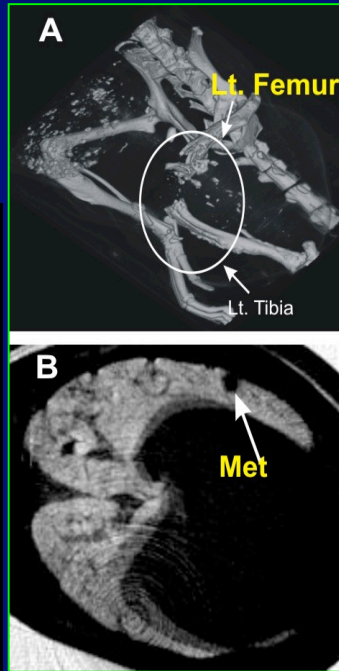
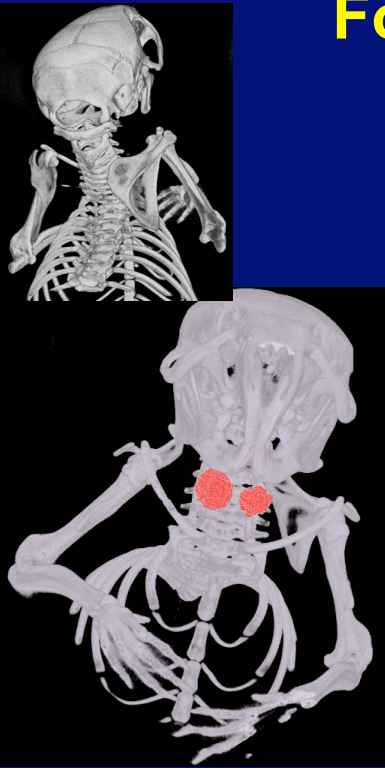
New CNS Drug Development For Stroke



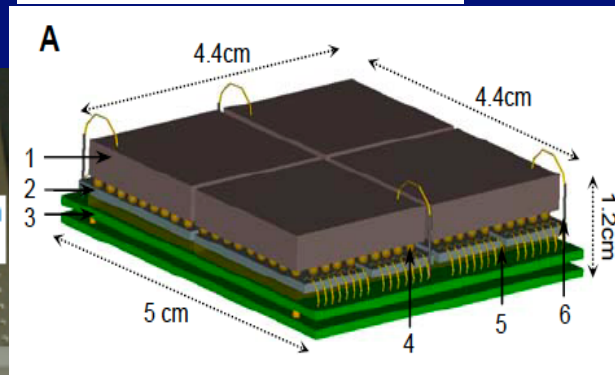
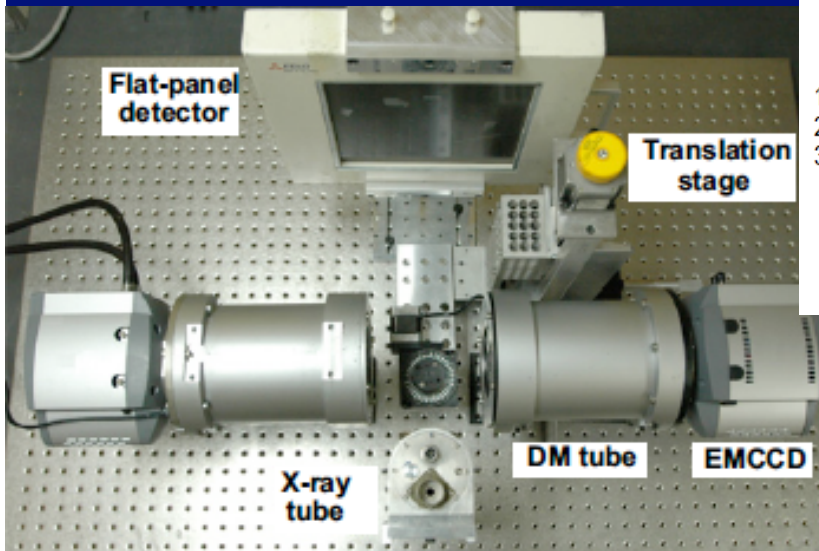
(UChicago)



# Modular, Re-Configurable, Integrative PET/SPECT/CT For Flexible Application-Specific Imaging



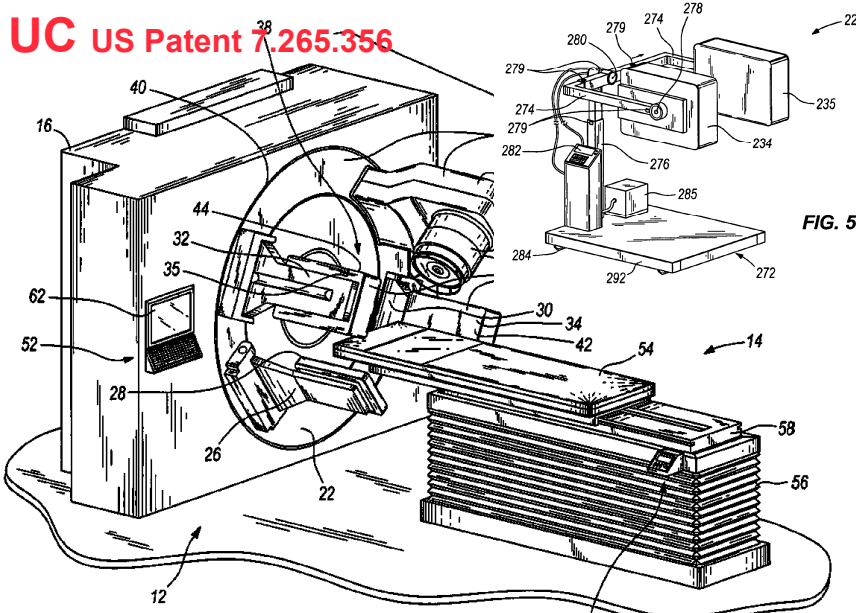
**Integrative:**  
Assemble & dis-assemble based on application-specific needs.  
**Flex-Configure:**  
Novel Recon for flexible scanning trajectories  
**Multi-Modality:**  
PET/SPECT/CT  
UIUC, WashU, UC



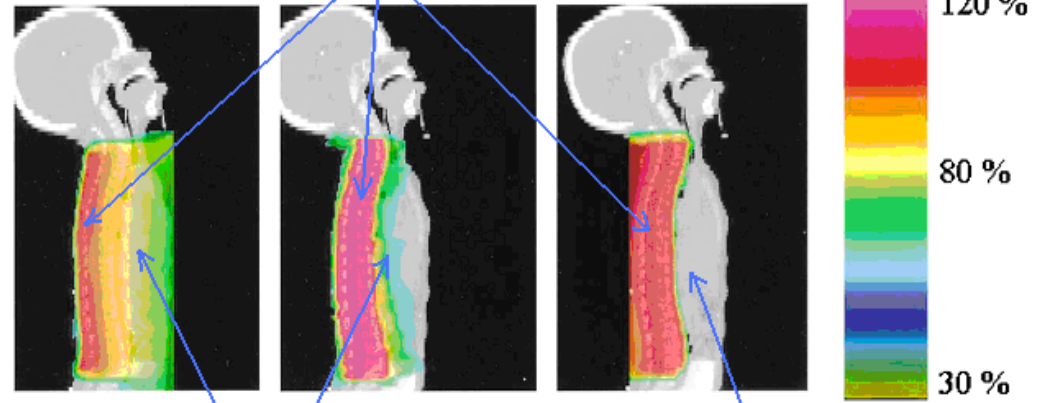
Semiconductor Detectors (CdTe/CZT)  
Energy Resolved Photon Counting (ERPC)

# On-Board, In-Beam, In-Room CT, PET or SPECT for Radiation & Particle Therapy (Theranostics)

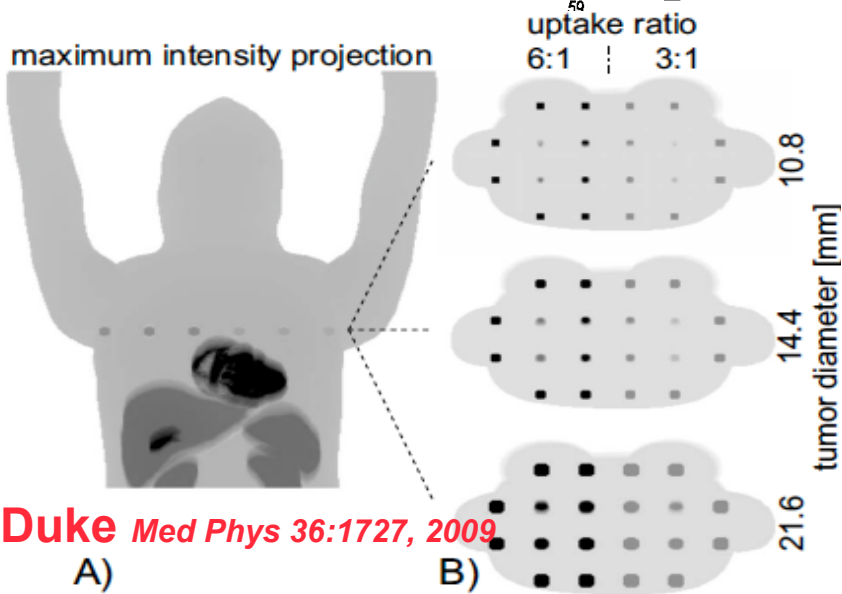
UC US Patent 7,265,356



Target organ: spinal cord **MGH IJROBP, 58:727, 2004**

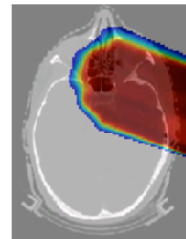


X-ray: dose bath of normal organs      Proton: sparing of normal organs



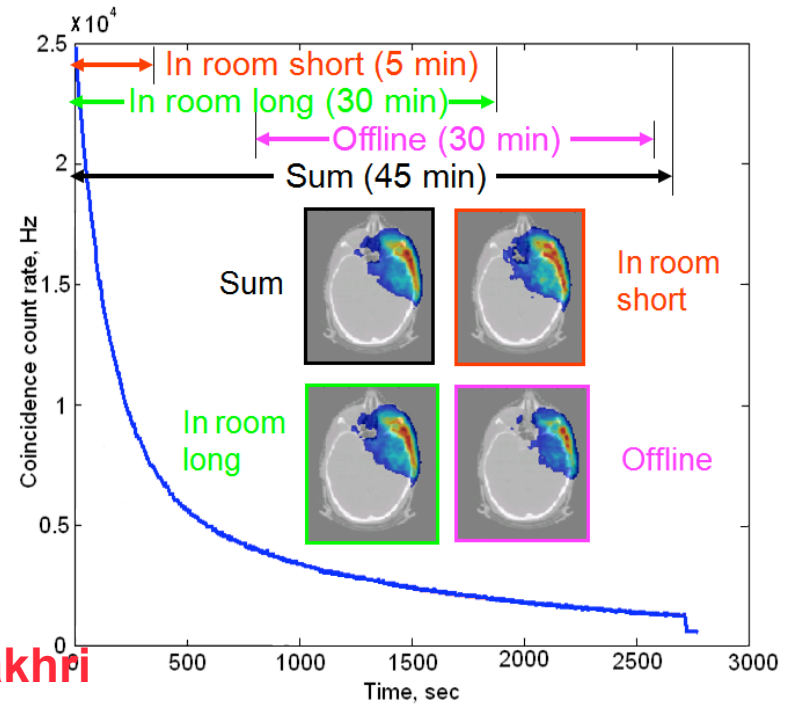
Duke Med Phys 36:1727, 2009

Dose distribution from treatment plan



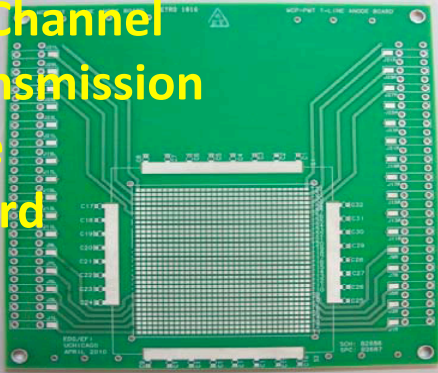
Beam Direction

MGH, El Fakhri

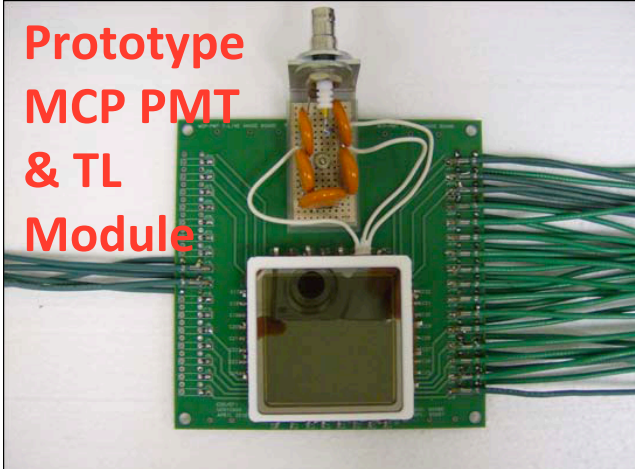


# Fast Electronics and All Digital PET

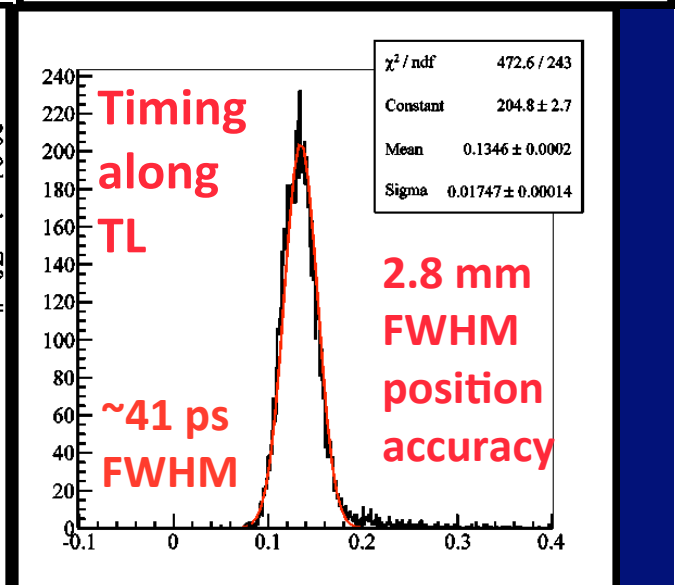
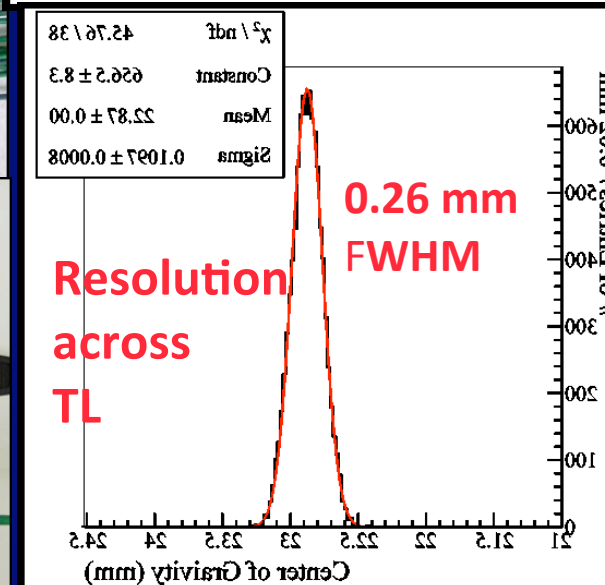
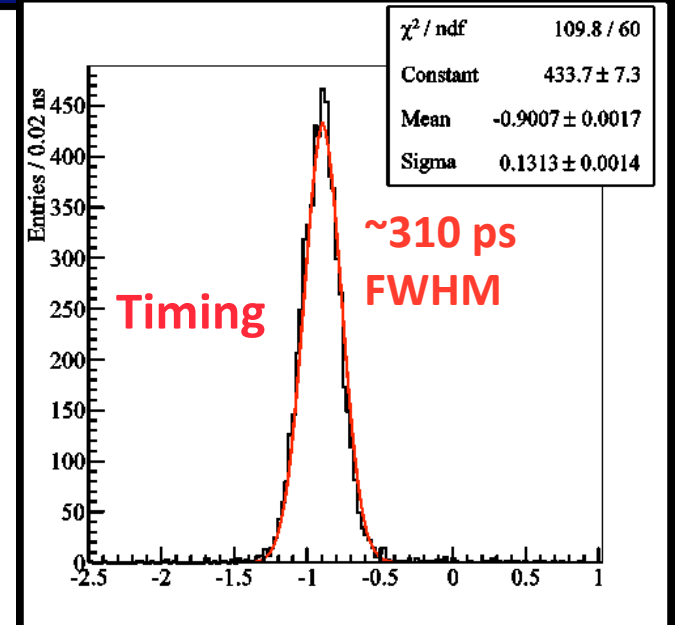
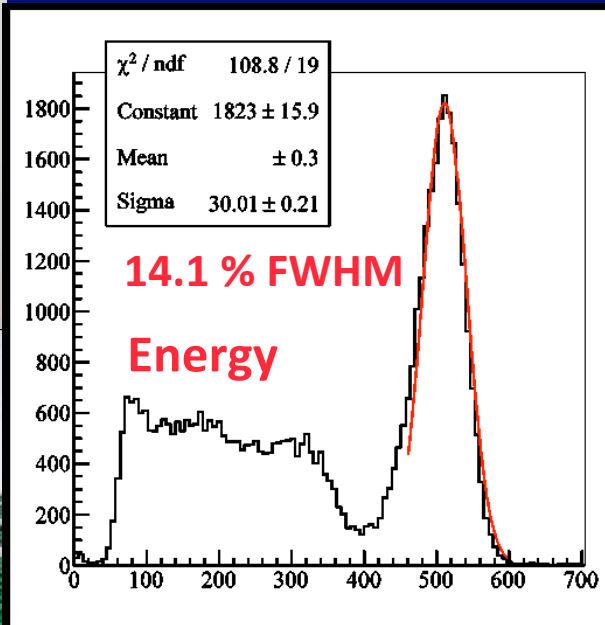
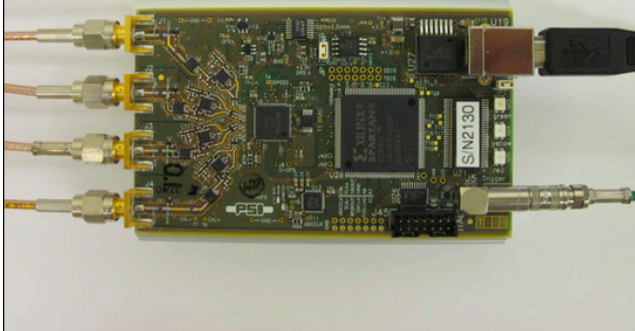
32-Channel  
Transmission  
Line  
Board



Prototype  
MCP PMT  
& TL  
Module

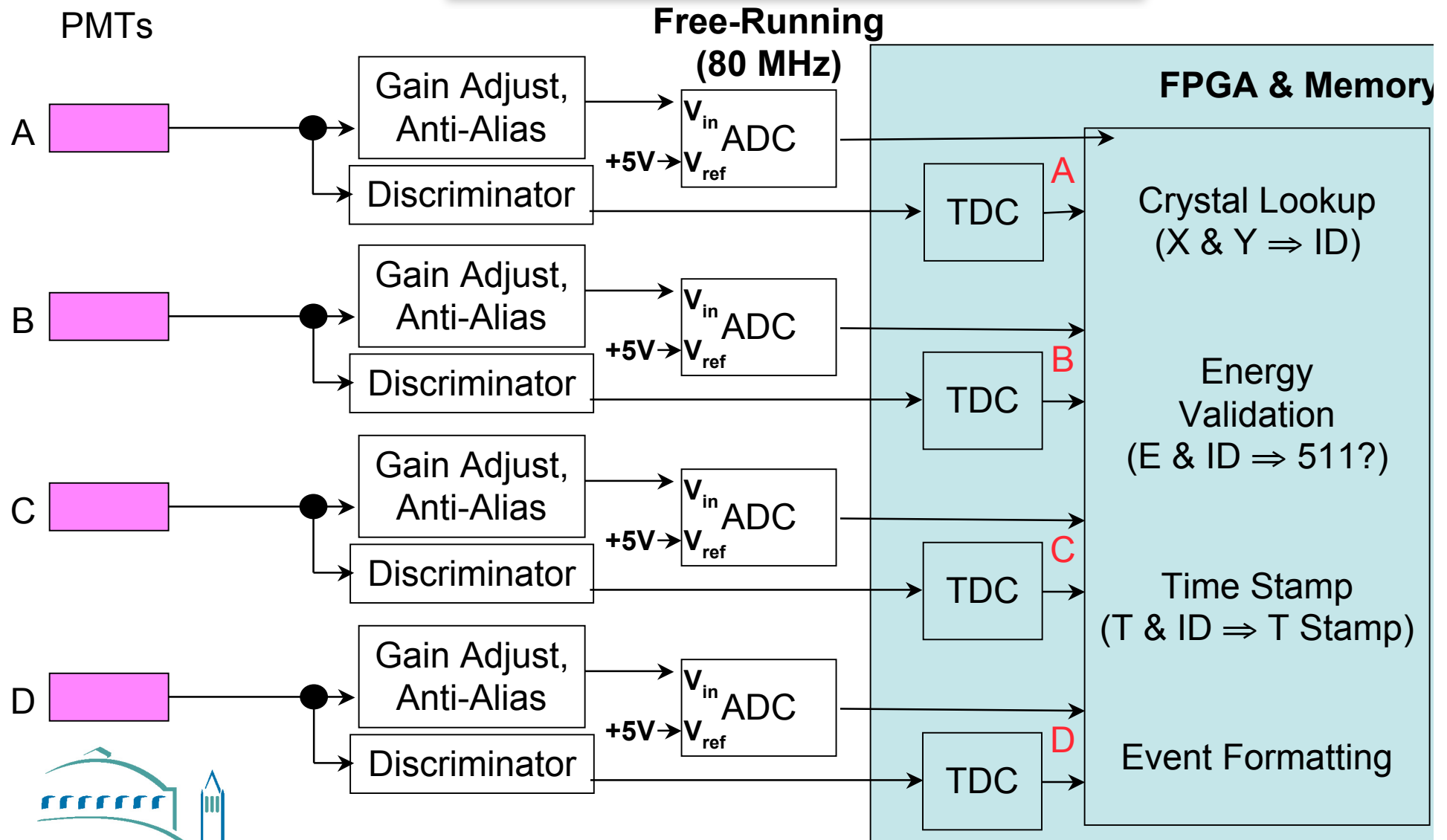


DRS4  
Evaluation Board



UC, ANL, etc.

# OpenPET Front End

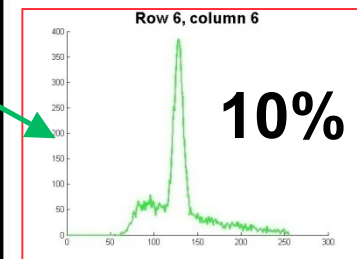
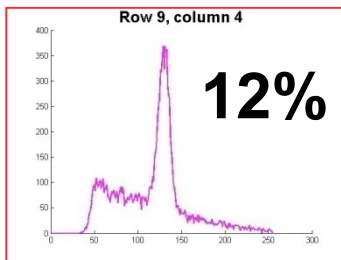
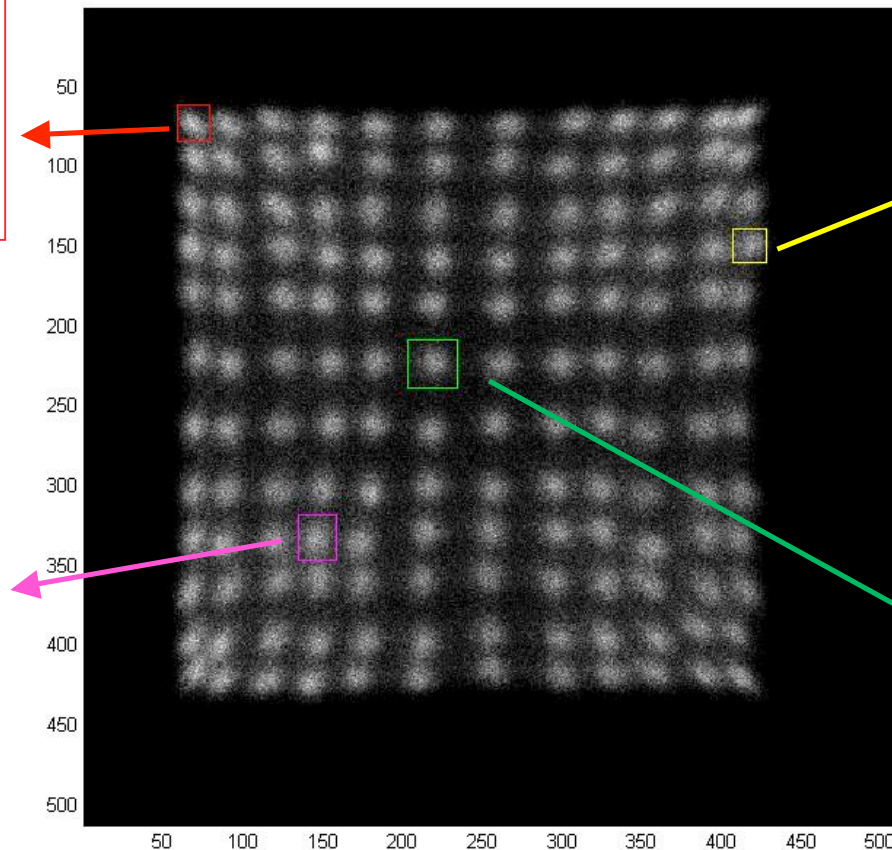
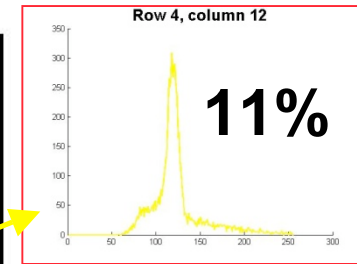
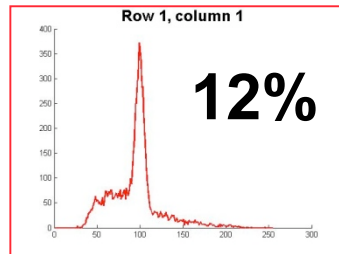


**Analog Done w/ Discrete, Digital Done w/ FPGA**



# Detector 1: Conventional Block Detector

12x12 array of 4x4x22 mm<sup>3</sup> LSO crystals  
4 Hamamatsu R-9800 PMTs



- Pre-Prototype Circuit Boards
- Excellent Flood Map and Energy Resolution

# Detector 2: SiPM Array

16x16 array  
3x3 mm<sup>2</sup> SiPMs



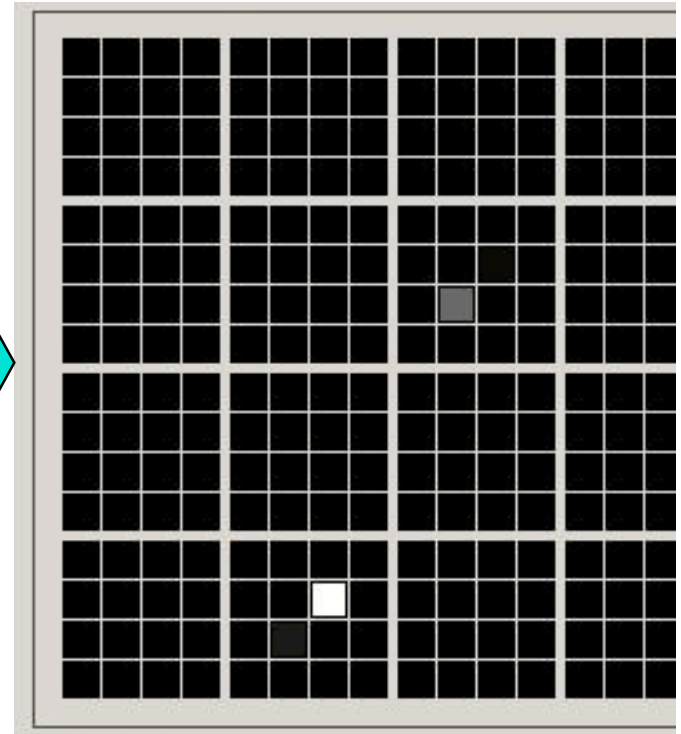
3x3x20 mm<sup>3</sup> &  
3x3x30 mm<sup>3</sup> LSO



Adapter Board

16x16 array  
to  
16 Row &  
16 Column  
Analog Sums

Natural LSO Activity

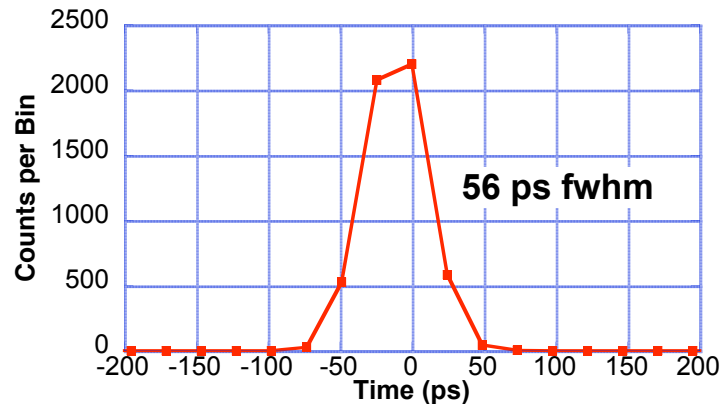


Pixel Intensity  $\propto$   
Energy x Count Rate

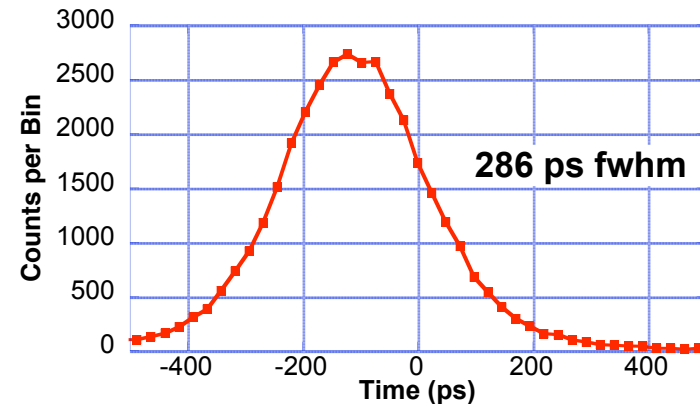
Same Electronics with *Very Different Type of Detecto*

# Timing Resolution

## Test Pulse

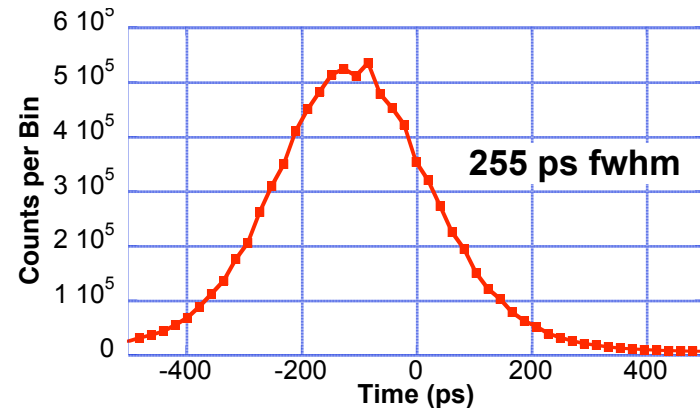
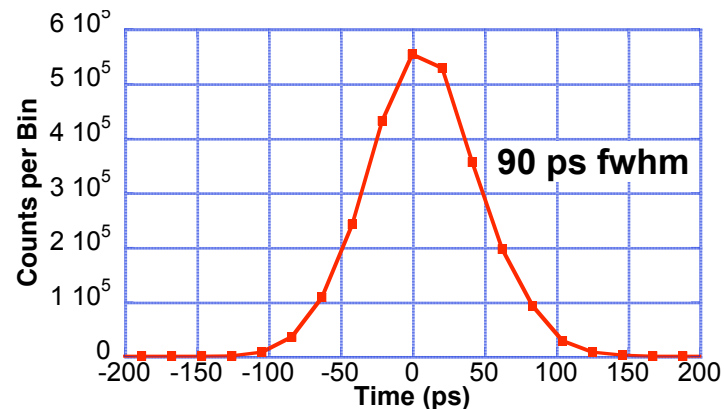


## TOF Module Pair



**HPTDC  
(CERN)**

**FPGA**



- 16 Channel TDC in Cyclone II FPGA
- Performance Good Enough for Time-of-Flight PET

# openPET Vision

## **Open Source**

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- Hardware, Firmware, and Software
- Schematics, Gerbers, BOM,...

## **Active User Community**

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- Share Software and Expertise
- Module, Calibration, DAQ, Display,...

## **Fall, 2011**

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- Detector & Support Boards Available
- Work on Coincidence Board Begins

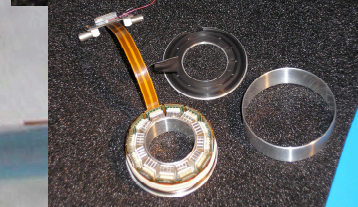
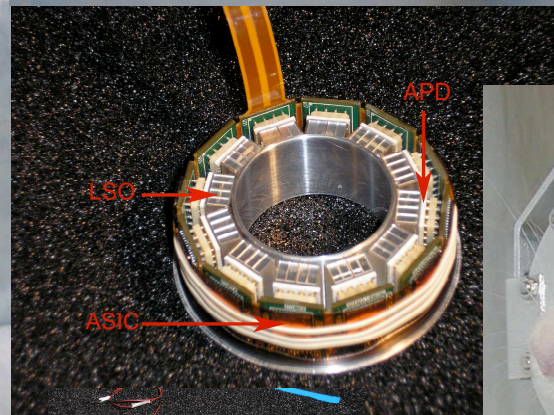
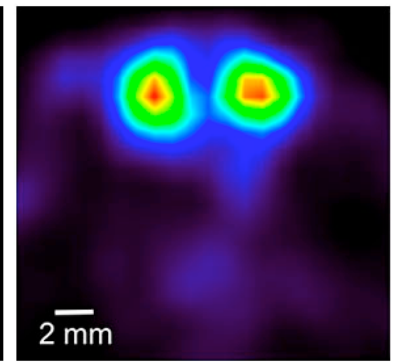
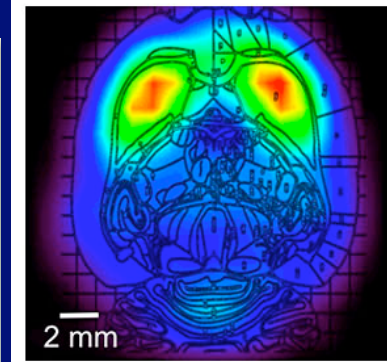
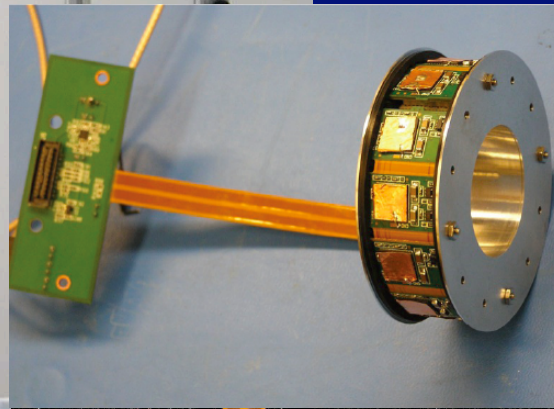
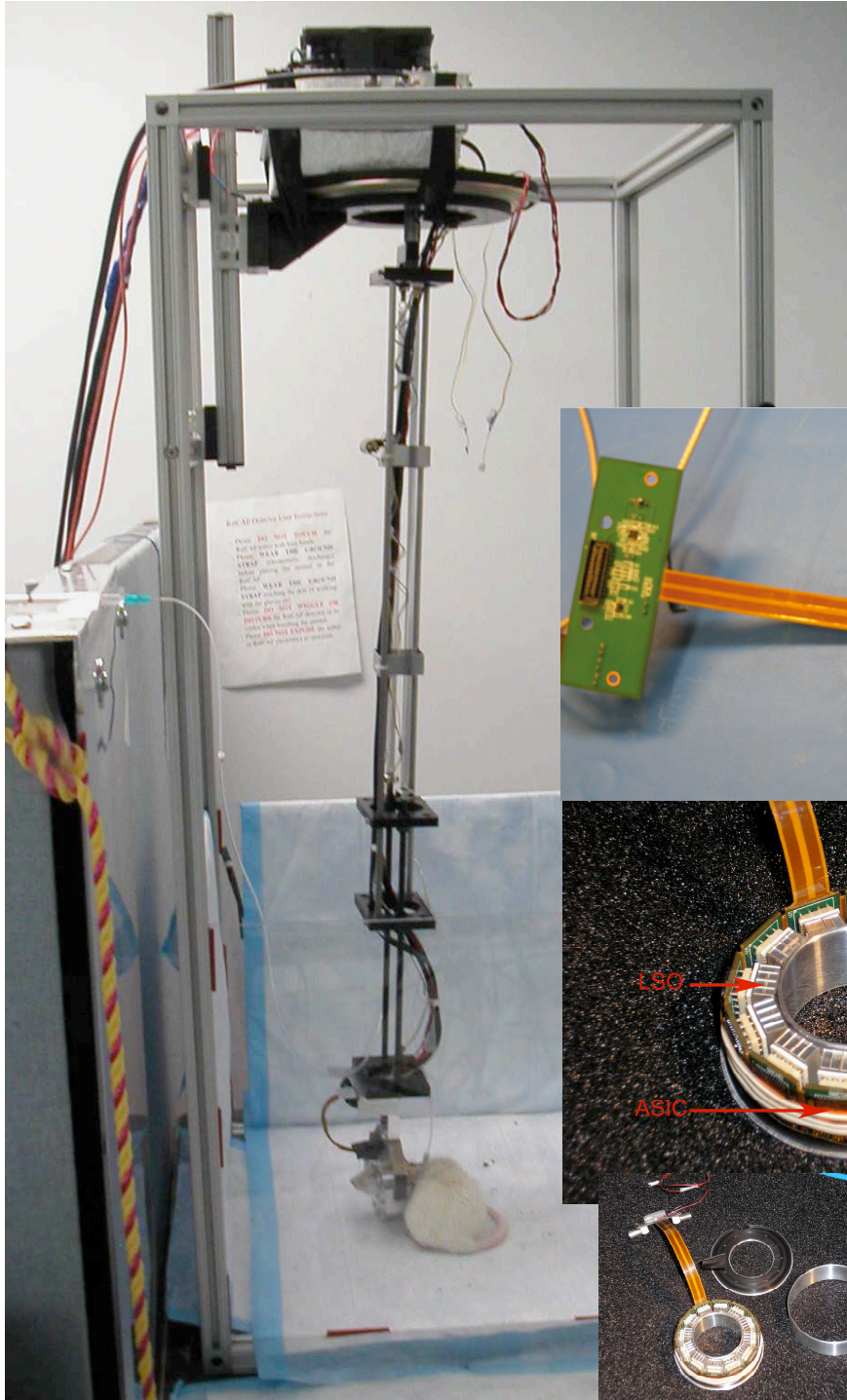


<http://OpenPET.LBL.gov>



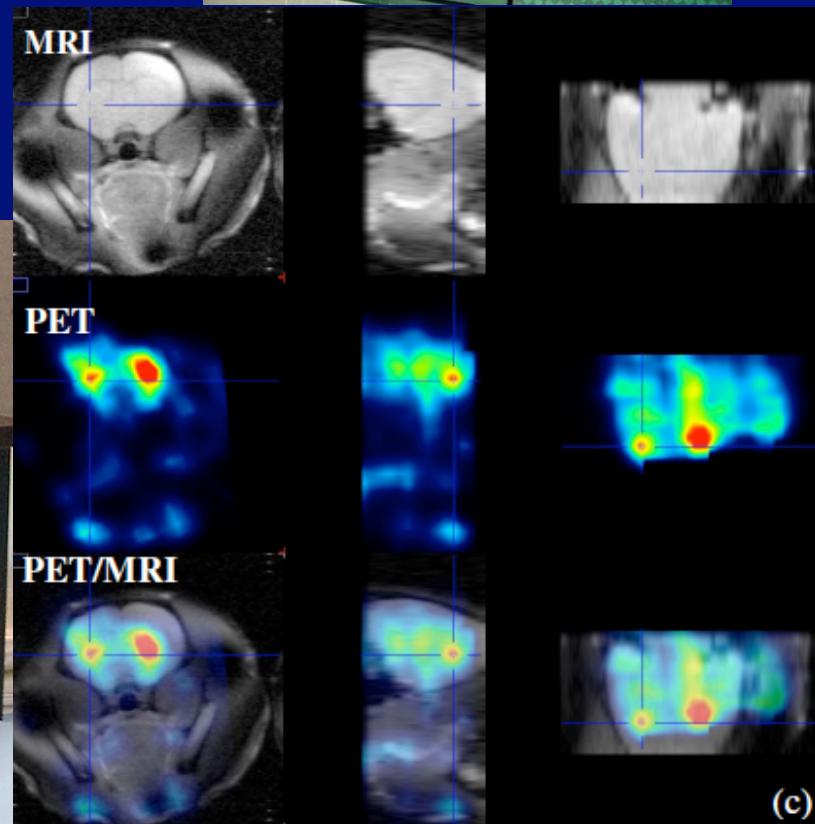
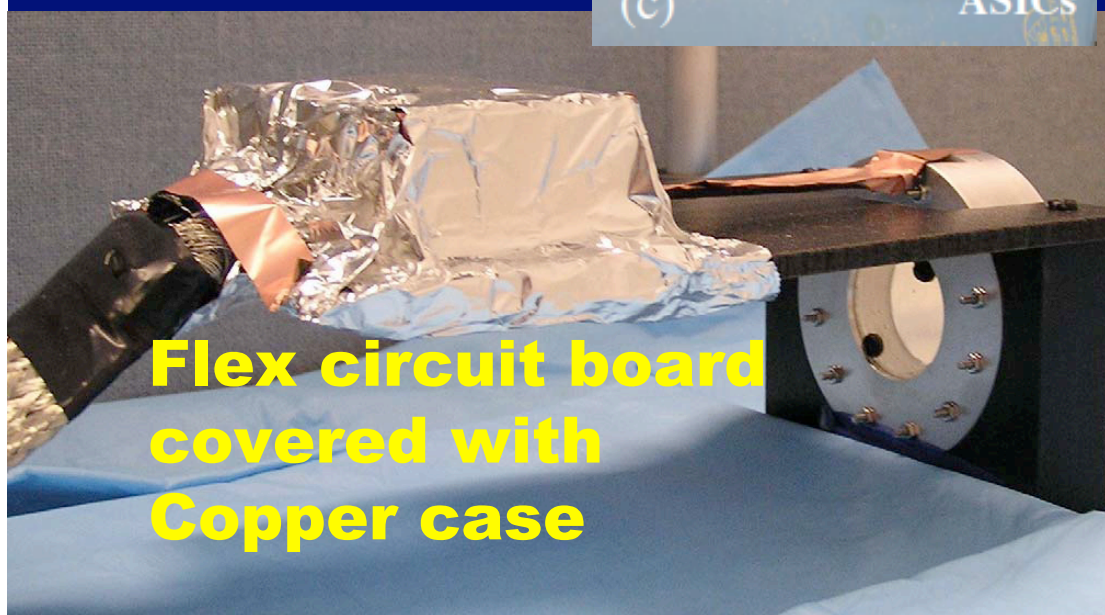
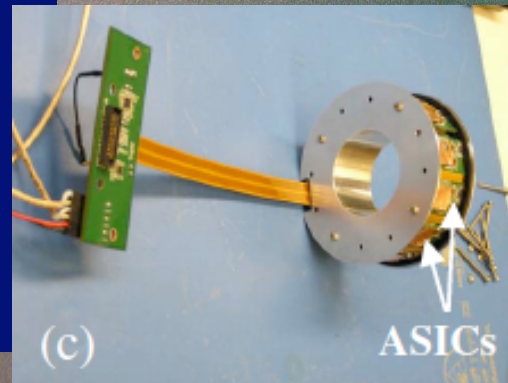
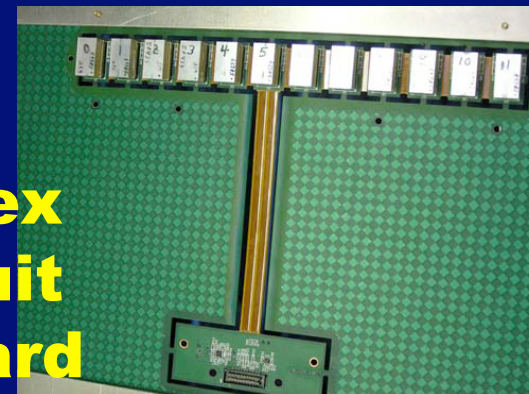
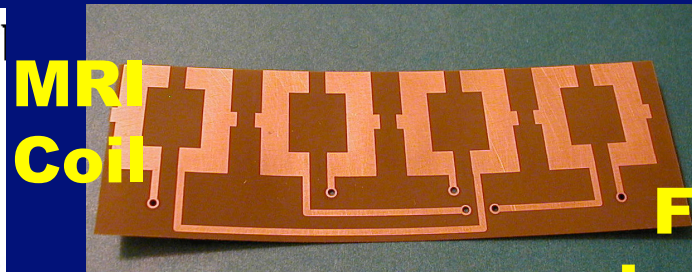
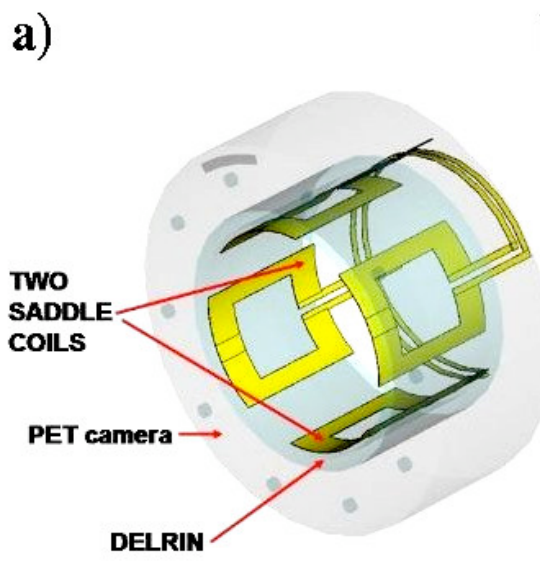
# RatCAP for PET Imaging of Awake Animals

## LSO + APD





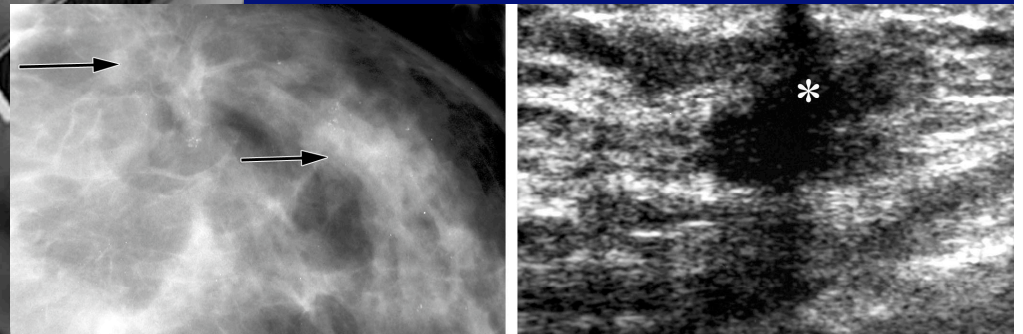
# Simultaneous PET/MRI Based on RatCAP in Small Animals & for Breast Imaging



# Large-FOV Positron Emission Mammography



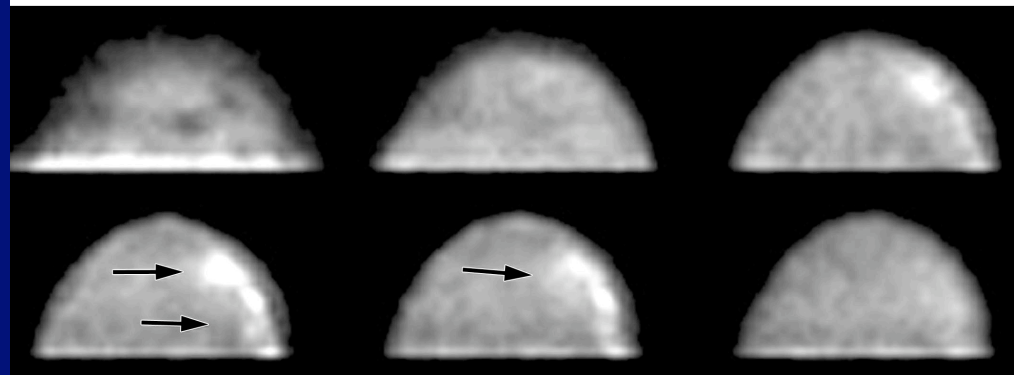
- A large field-of-view (15 cm x 20 cm) PEM
- Two-Panel pixelated LGSO/LYSO
- Coupled to an array of PSPMTs



b.

DOD & NIH Funded  
large-scale clinical trials  
Conducted at Duke Univ.

**Jefferson Lab**

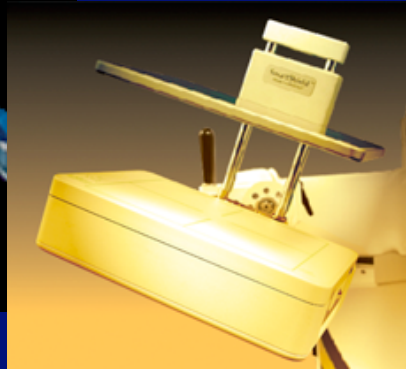




# Molecular Breast Imaging (BMI)



Dilon 6800 Acella  
Expanded FOV  
20 cm X 25 cm



Dilon 6800  
Gamma  
Camera  
15cmX20cm



Dilon 6800 Gamma Camera

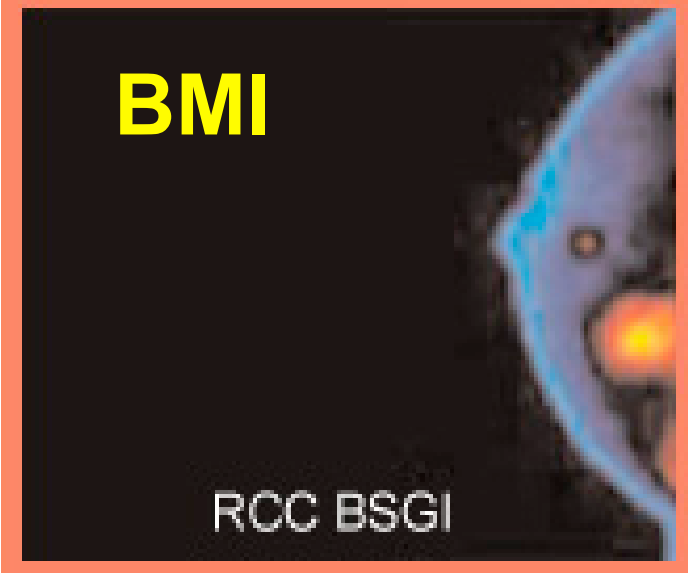
Successful Technology  
Transfer to and  
commercialization by  
Dilon Diagnostics

**Jefferson Lab**



RCC mammogram

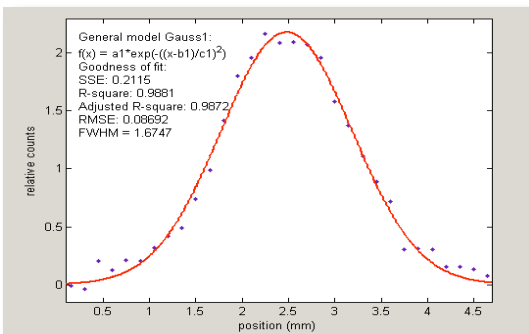
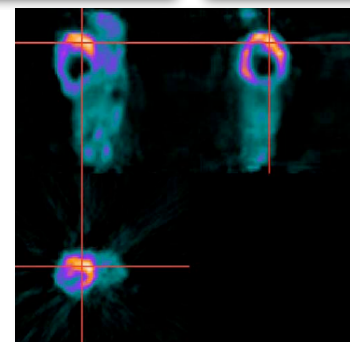
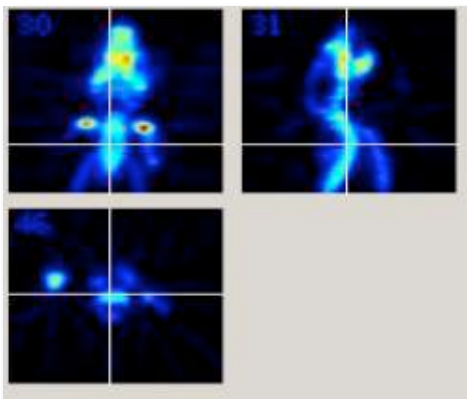
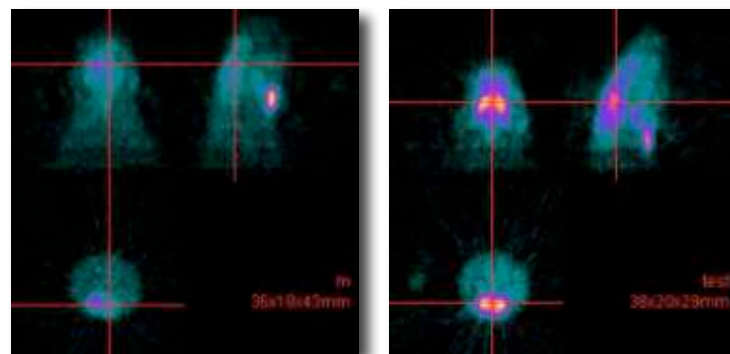
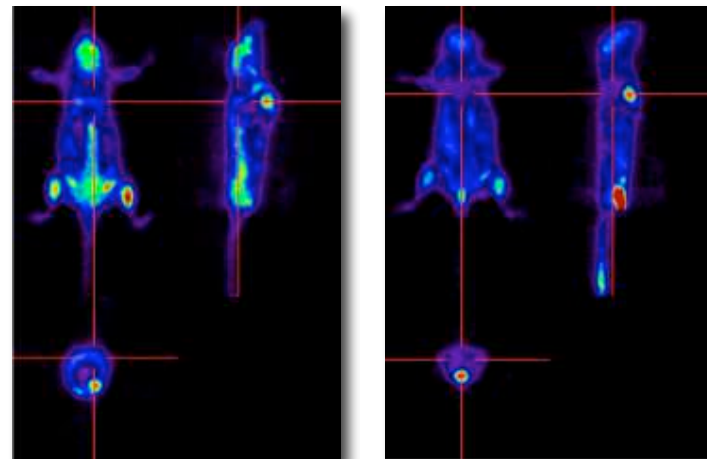
**BMI**



RCC BSGI



## High resolution & high counting-rate animal PET scanner

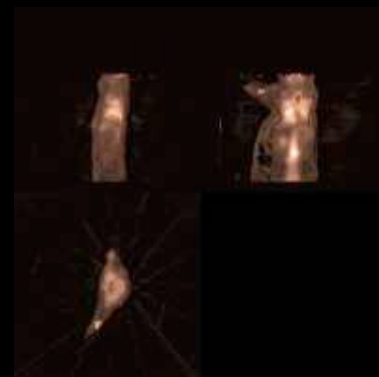
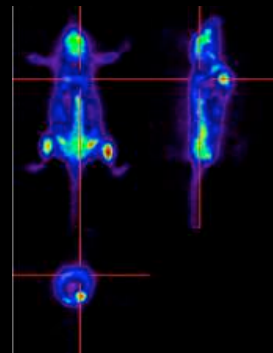


**CFOV resolution: 1.67 mm**

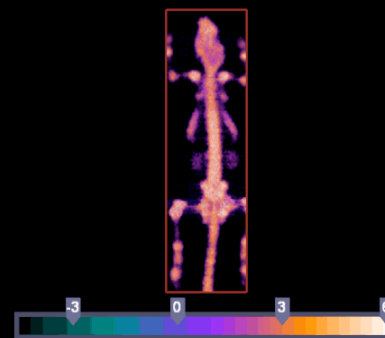


## Scanners for Molecular Imaging

$\mu$ PET、  
 $\mu$ PET/CT



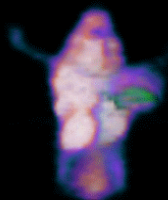
$\mu$ SPECT/CT





## Scanners for Molecular Imaging

**Optical  $\mu$ PET**



**$\mu$ CT**



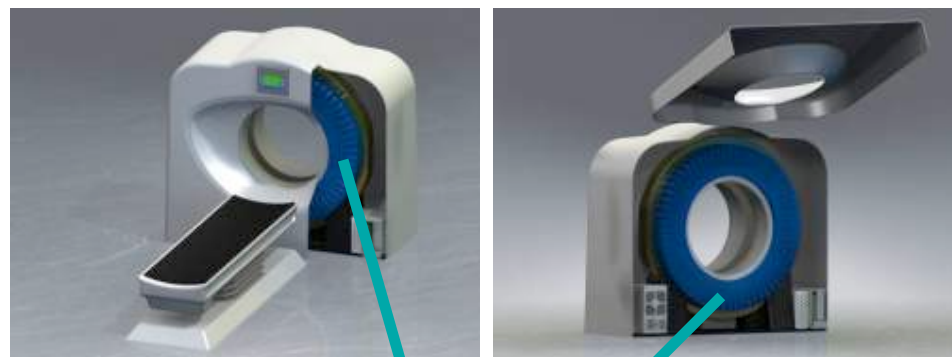


## High Resolution whole-body PET Scanner (currently detector research)

### Designed Feathers:

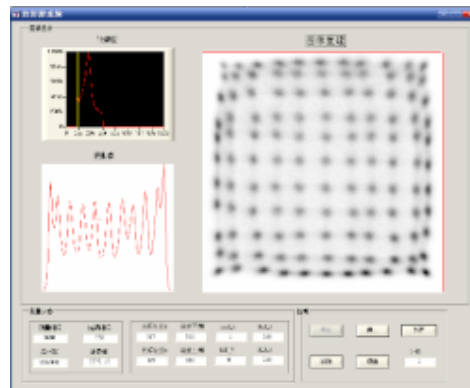
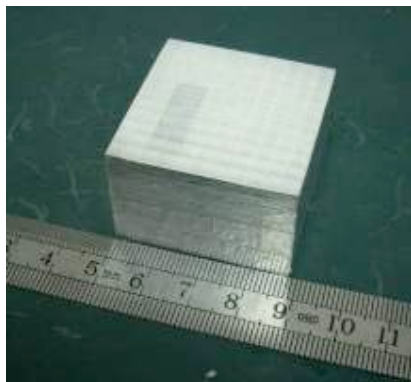
- Gantry aperture: >650 mm
- Axial FOV: >150mm
- Spacial Resolution: ~3.5mm
- Crystal material: LYSO
- Crystal number: 30976
- Detector number: 256
- Dia. of detector ring: 810mm

*LYSO: an patent-free Cerium-doped Lutetium  
Yttrium Oxyorthosilicate ( $\text{Lu}_{2(1-x)}\text{Y}_2\text{SiO}_5:\text{Ce}$ )*

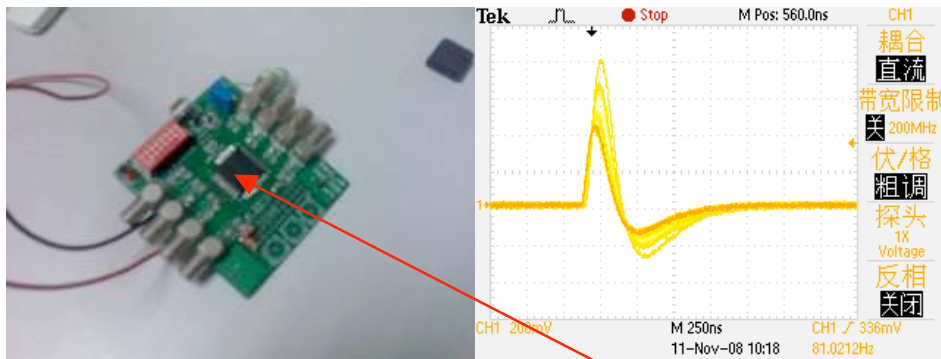




## Performance of detector and electronics



Detectors and flood-histogram for 11x11 crystal array



Front-end electronics (ASIC) and 32-Chanel digital board

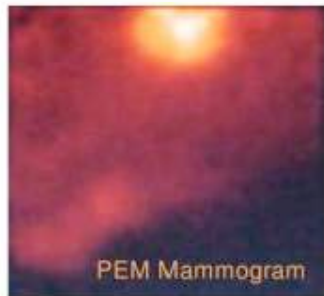


## PEM (Positron Emission Mammography)

**Mammography is a morphological technique**



Images courtesy of L.P. Adler, Cancer Center, Philadelphia



*A PEM system is a PET device dedicated to breast cancer detection, and has higher gain and lower noise.*

**Morphological**  
Sensitive to tissue density

**Functional**  
Sensitive to metabolism

**Sensitivity to small tumors (1-2 mm)**

**The PEM system we designed is prone-style, with annular detector structure.**

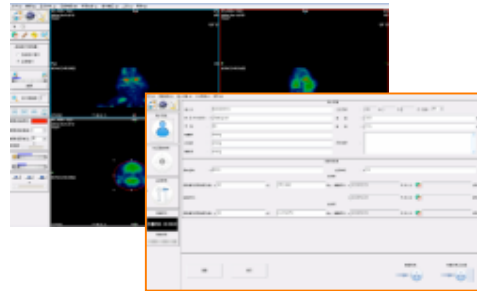
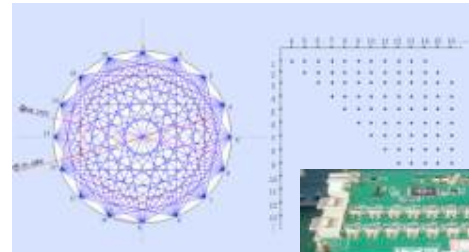




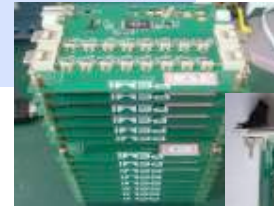
Design and production of PEM system have been completed.  
Performance testing is under way.



Detector ring  
of our PEM

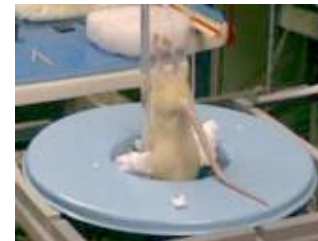
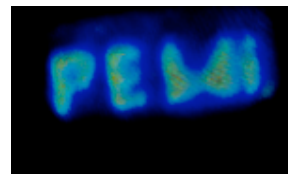


Reconstruction  
algorithm &  
user interface

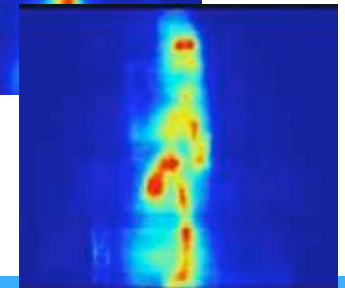
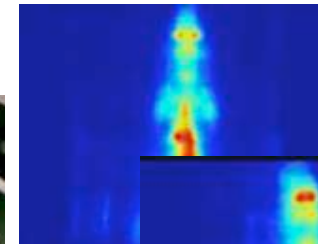


A/D &  
Coincidence  
system

Initial imaging  
results

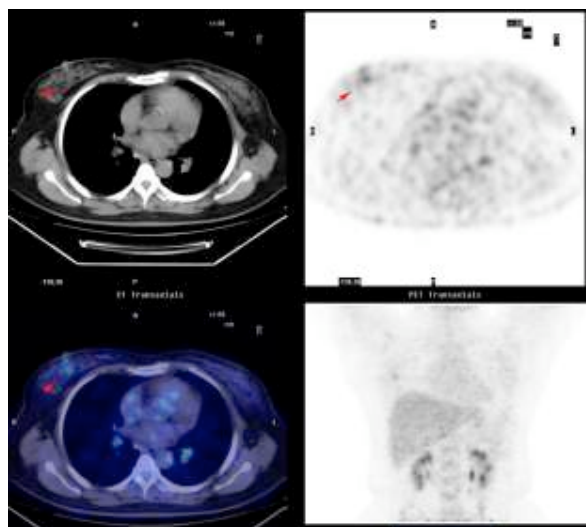
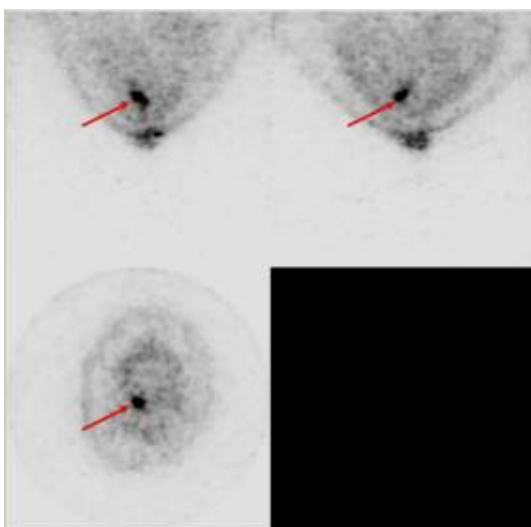
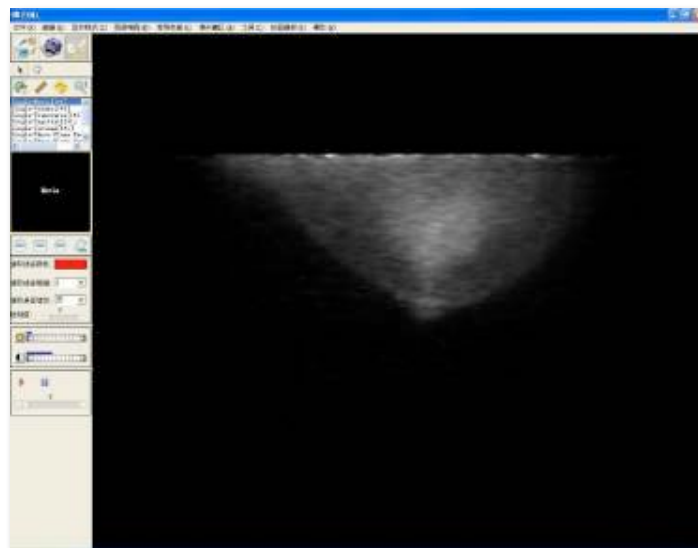


Rat imaging



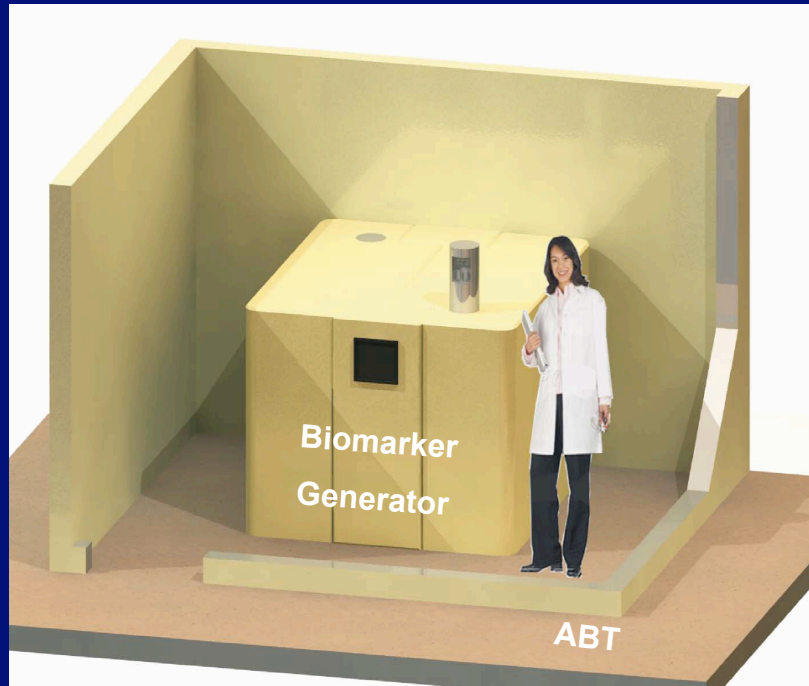
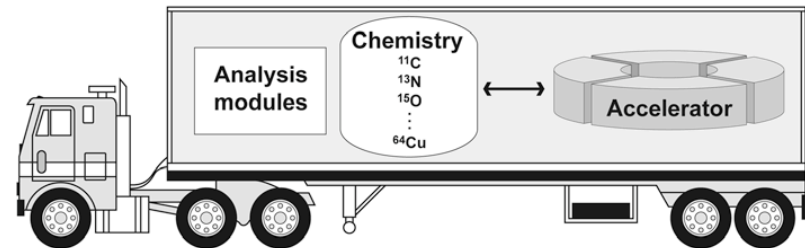
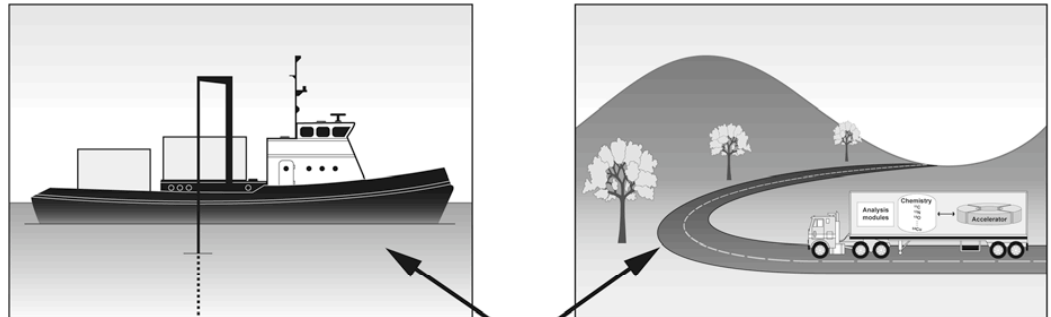


## PEM is in clinical trial stage for SFDA registration



# Radiotracer More Readily Available Mobile & Compact Biomarker Generator

## Expanding Radiotracer Applications

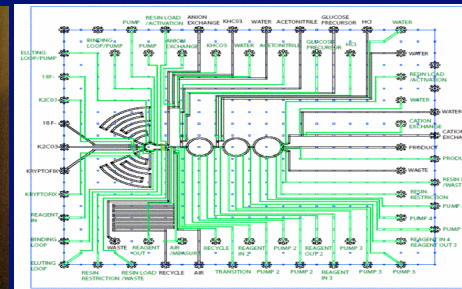


*Micro Accelerator*



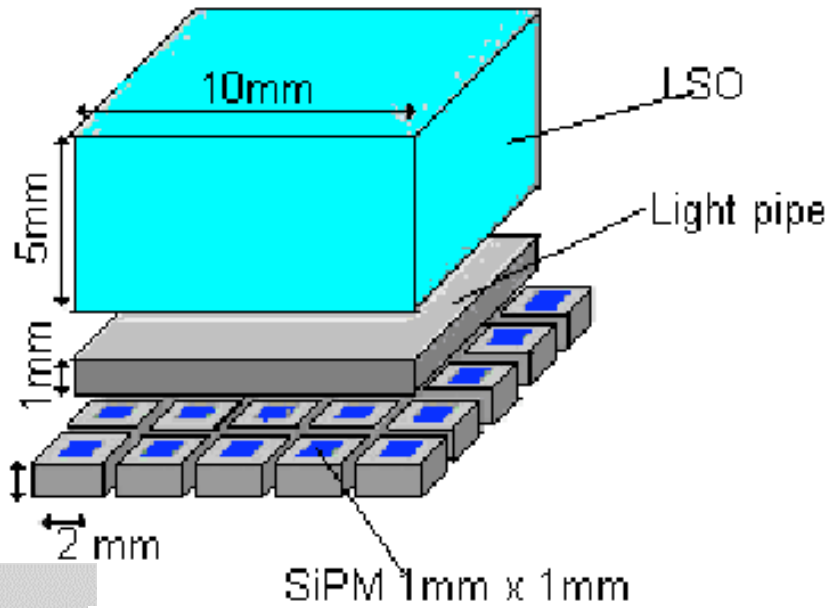
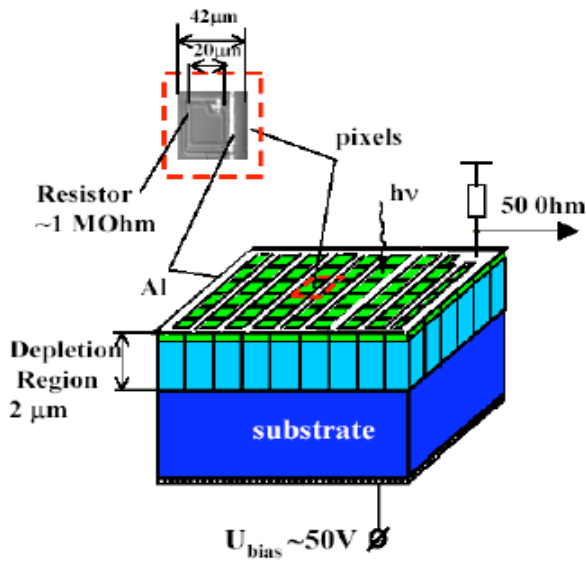
Courtesy of ABT

## Microchemistry & Microfluidics

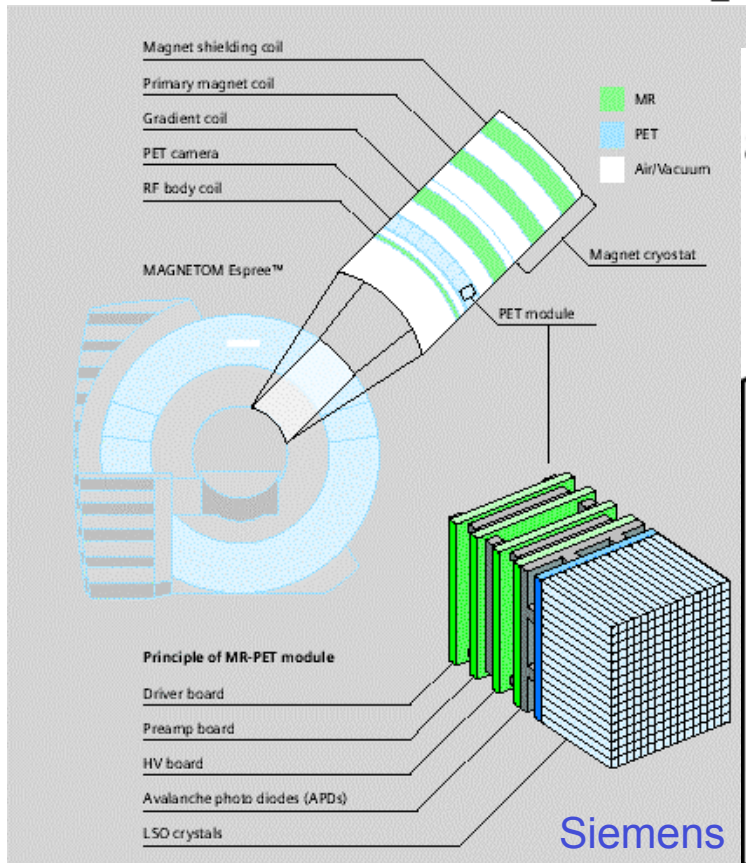
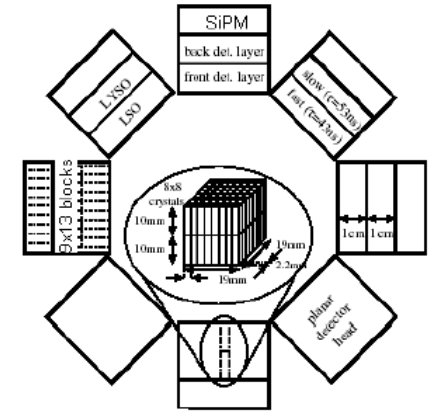


DOE/LBL

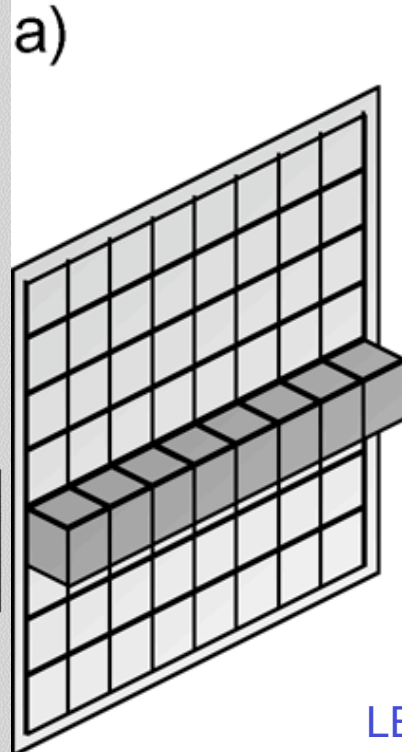




**Oh, YES !  
SiPM**



Siemens



LBL

