Detector Development for Nuclear Medical Imaging of Breast Cancer

William W. Moses
Lawrence Berkeley National Laboratory
January 12, 2000

Outline:

- Breast Cancer / Mammography
- Positron Emission Tomography
- Detector Development at LBNL

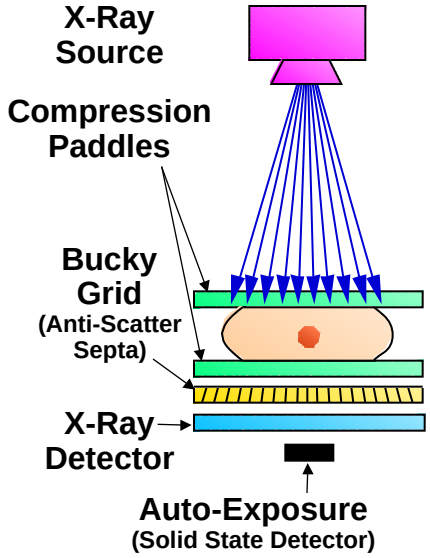
Breast Cancer Statistics

- 1 Woman in 8 Develops Breast Cancer
- 186,000 New Cases per Year in U.S.
- 46,000 Deaths per Year in U.S.
- Second Leading Cause of Cancer Death in Women
  - (slightly lower than lung cancer)

BUT

- Early Detection ⇒ Very High Cure Rate
  - Cancer hasn't spread into the axillary nodes ⇒ less likely to die of breast cancer than people who have never had breast cancer

Early Detection via X-ray Mammograms



- Breast compressed to ~5 cm thickness.
- X-rays pass through breast, then "Bucky Grid" for scatter rejection.
- X-rays that pass through breast and Bucky Grid are detected in 2-D detector.
- Exposure controlled by integrated current in solid state (Si) detector.

Low Energy X-Ray Image

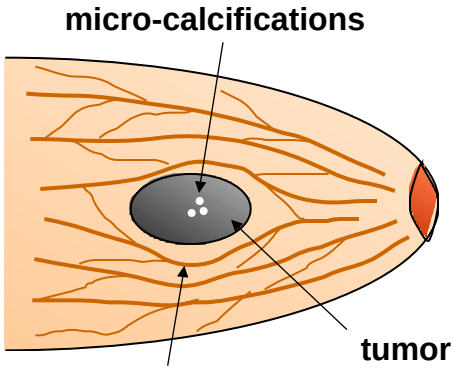
Mammography Images

Abnormal Mass

Microcalcifications

- Typical Contrast ~2%
- 25% – 80% False Positive Readings

Advantage of Nuclear Medical Imaging



- X-Ray Mammography images structure (*i.e.* electron density)
- Nuclear Medicine images function (*i.e.* metabolic rate)

Images the Tumor, Not Secondary Effects

Positron Emitting Drug for Mammography:

FDG (^{18}F-fluoro-deoxy-glucose):

>4x greater uptake in tumors than normal tissue

>95*% Sensitivity (i.e. probability that it has high uptake in breast cancer tumors)

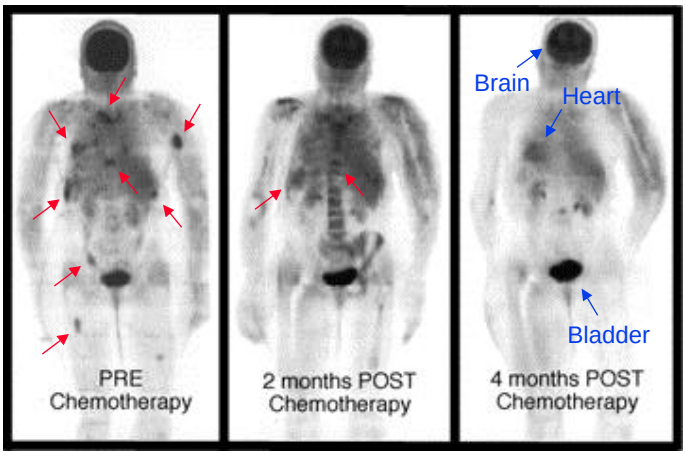
>80*% Selectivity (i.e. probability that objects with high uptake are actually breast cancers).

* for tumors ≥1 cm diameter

•Excellent Tracer for Imaging Breast Cancer
•Emits Back-to-Back 511 keV Photons

PET Images of Breast Cancer Patient

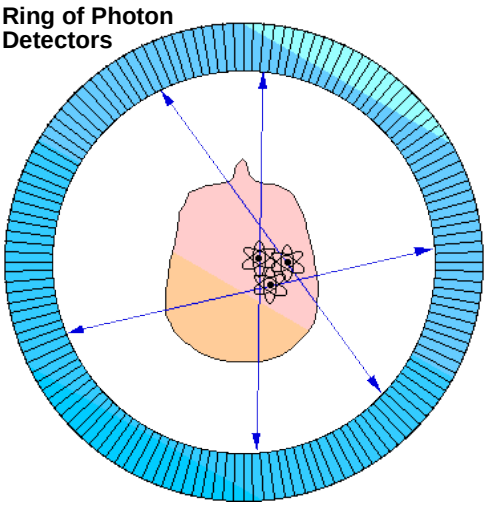
Metastases Shown with Red Arrows



Normal Uptake in Other Organs Shown in Blue

- Tumors Easily Seen (~5 mm spatial resolution)
- Typical Contrast ~400%

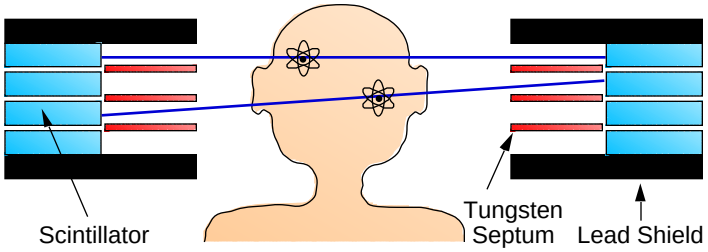
Positron Emission Tomography (PET)



- Patient injected with drug having β^+ emitting isotope.
- Drug localizes in patient.
- Isotope decays, emitting β^+.
- β^+ annihilates with e^- from tissue, forming back-to-back 511 keV photon pair.
- 511 keV photon pairs detected via time coincidence.
- Positron lies on line defined by detector pair.

Forms Planar Image of a "Slice" Through Patient

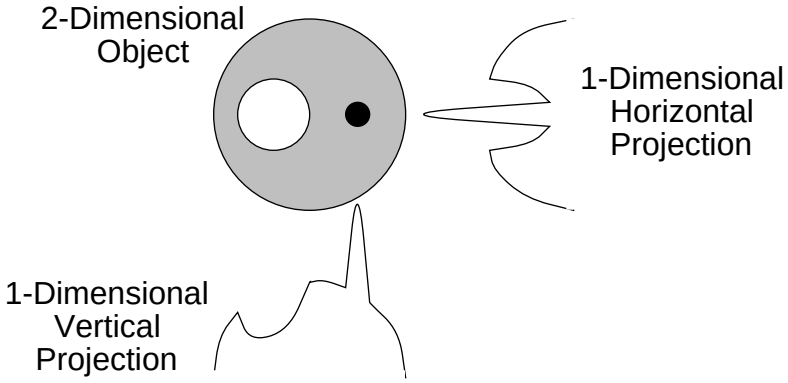
Multi-Layer PET Cameras



- **Can image several slices simultaneously**
- **Can image cross-plane slices**
- **Can remove septa to increase efficiency (“3-D PET”)**

Planar Images “Stacked” to Form 3-D Image

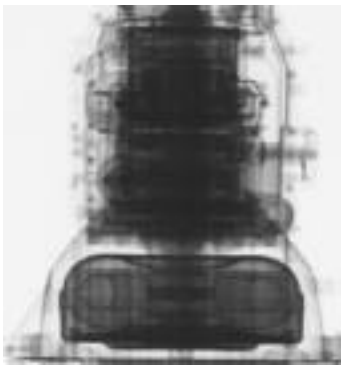
Form Images Using Computed Tomography

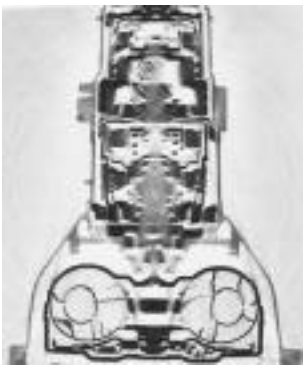


By measuring all 1-dimensional projections of a 2-dimensional object, you can reconstruct the object

Advantage of Computed Tomography

Planar X-Ray | **Computed Tomography**





Allows Separation of Objects on Different Planes

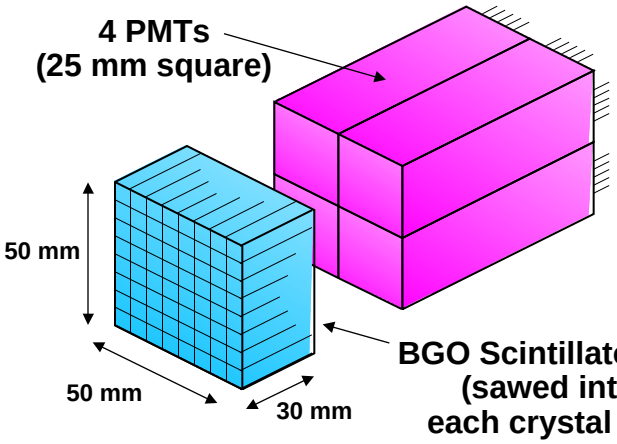
Images courtesy of Robert McGee, Ford Motor Company

PET Cameras

General Electric

Siemens / CTI

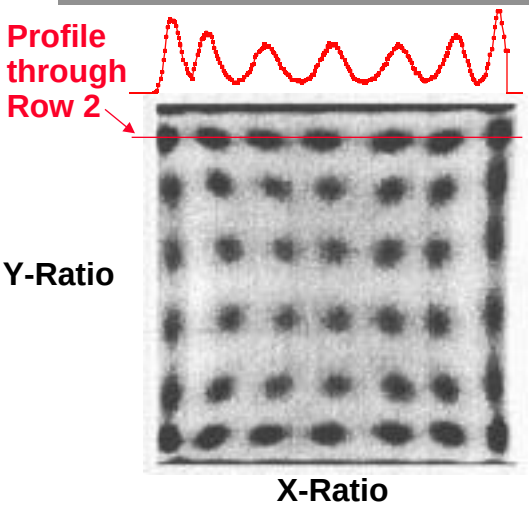
Conventional PET Detector Module



- Saw cuts direct light toward PMTs.
- Depth of cut determines light spread at PMTs.
- Crystal of interaction found with Anger logic (i.e. PMT light ratio).

Good Performance, Inexpensive, Easy to Pack

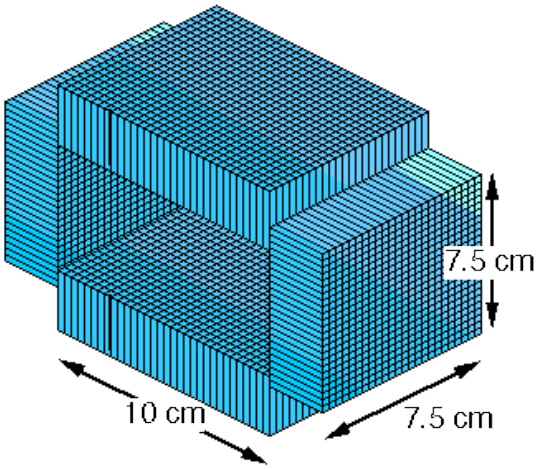
Crystal Identification with Anger Logic



- Uniformly illuminate block.
- For each event, compute X-Ratio and Y-Ratio, then plot 2-D position.
- Individual crystals show up as dark regions.
- Profile shows overlap (i.e. identification not perfect).

Can Decode Up To 64 Crystals with BGO

Positron Emission Mammography (PEM)

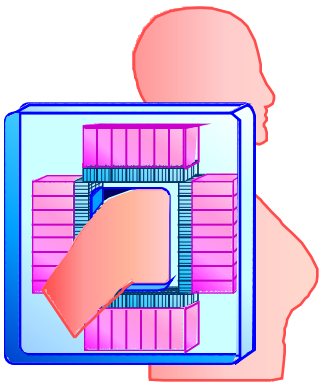


Compared to 2D PET

- 30x Higher Sensitivity
- 2x Finer Resolution
- 4x Lower Dead Time
- 10x Lower Cost

PET Camera Optimized for Breast Imaging

PET Camera for Axillary Nodes (ANPET)

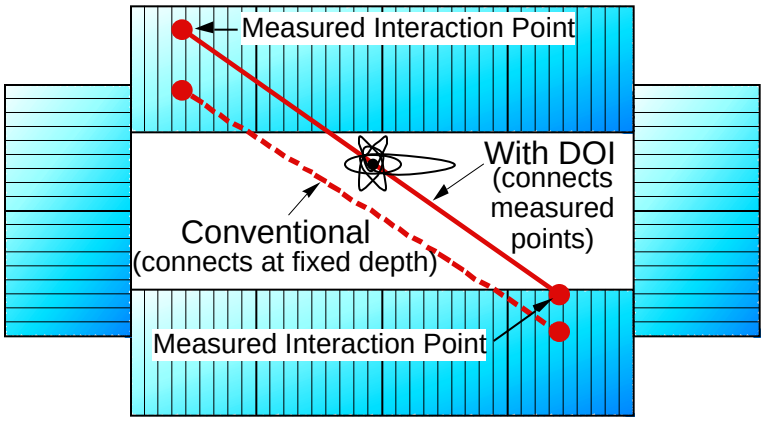


Compared to 2D PET

- 10x Higher Sensitivity
- 2x Finer Resolution
- 4x Lower Dead Time
- 10x Lower Cost

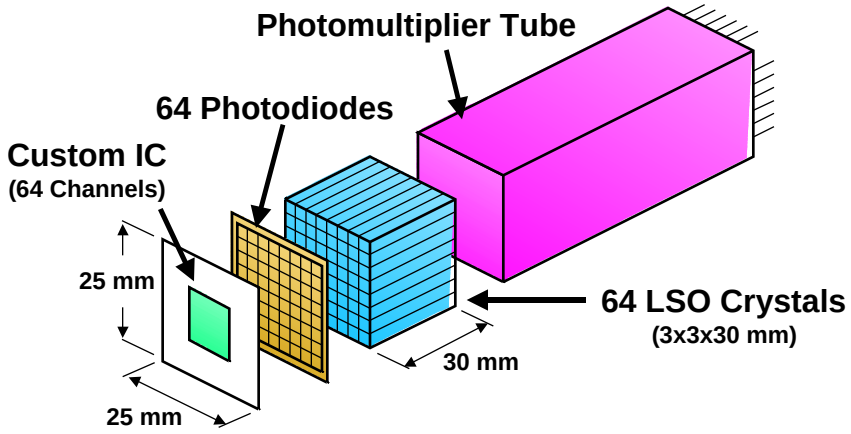
Determine Whether Disease has Spread

Need Depth of Interaction Measurement



Required DOI Resolution is ~5 mm

LBNL Detector Module Design



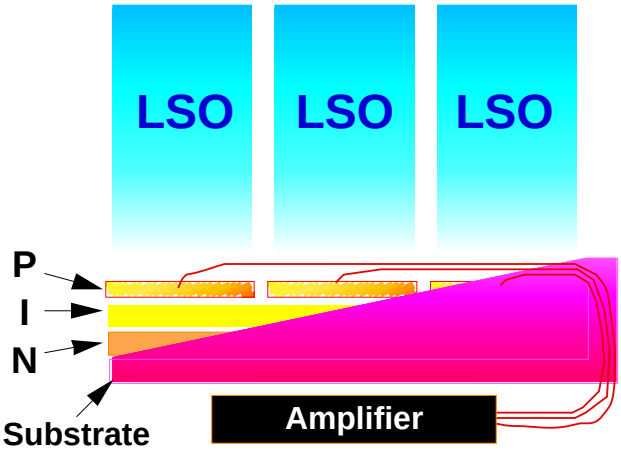
- PMT Provides Timing Pulse and Energy Discrimination
- PD Array Identifies Crystal of Interaction
- PD / (PD+PMT) Measures Depth of Interaction

Lutetium Orthosilicate (LSO) Scintillator

	BGO	LSO
Formula	$Bi_4Ge_4O_{12}$	Lu_2SiO_5:Ce
Atten. Len.	1.1 cm	1.2 cm
Photo Fract.	43%	34%
Photon/MeV	8,200	25,000
Decay Time	300 ns	40 ns
Emission λ	480 nm	415 nm
Radioactive?	No	Yes (300 dps/cc)

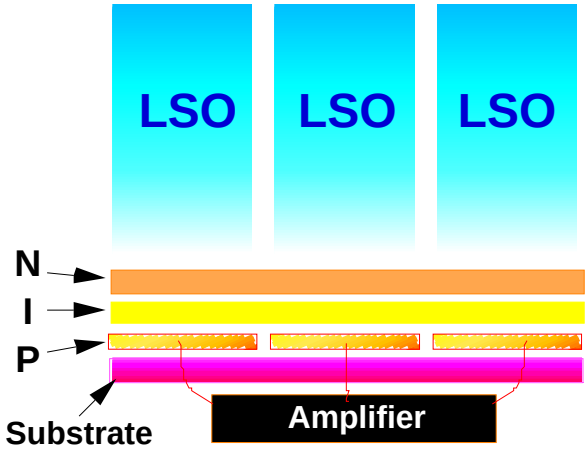
Recently Developed Scintillator

Conventional PIN Photodiode Array



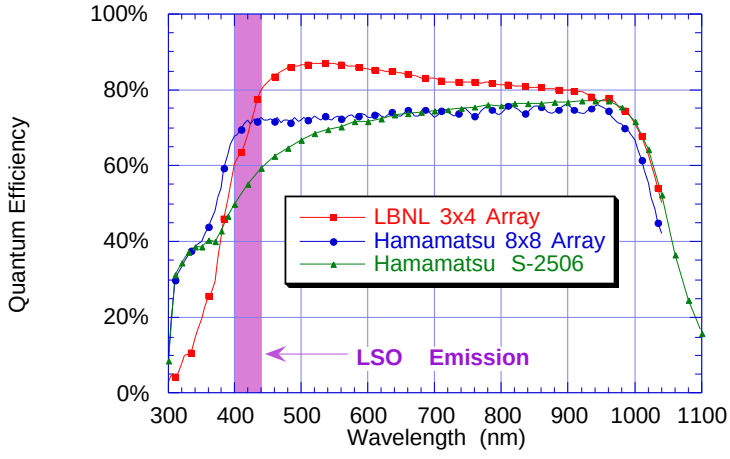
- Long Leads to Amplifier ⇒ Extra Capacitance ⇒ Extra Noise
- Vias at Edge ⇒ Dead Area

LBNL Back-Side Illuminated Photodiode



- Short Leads ⇒ Low Capacitance ⇒ Less Noise
- No Vias at Edge ⇒ Less Dead Area
- Very Low Dark Current ⇒ Less Shot Noise

Photodiode Array Performance

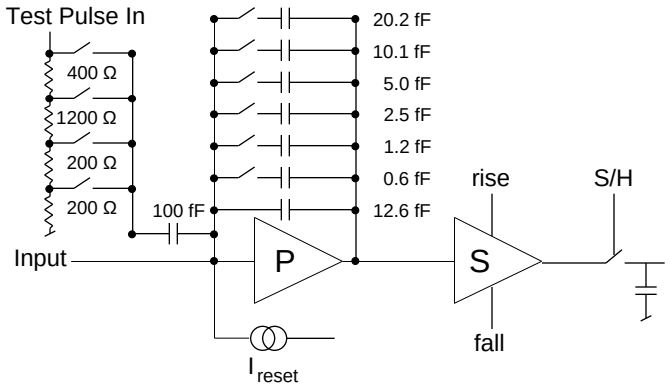


Dark Current (pA)

LBNL 3x4	20
Ham. 8x8	300
Ham. S-2506	100

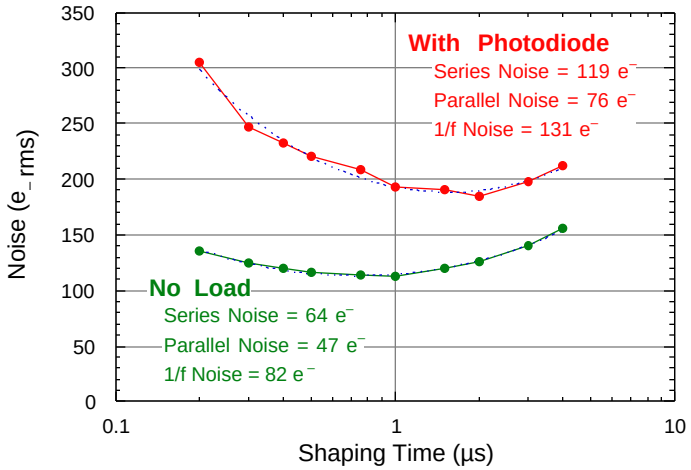
LBNL Photodiode has Superior Signal & Noise

Amplifier Block Diagram



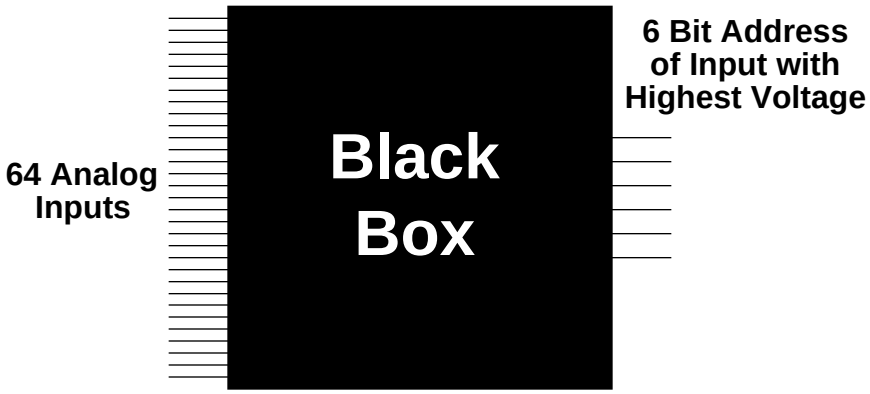
- **Amplifier Characteristics**
  - **Rise Time (0.2 – 100 µs)**
  - **Fall Time (0.2 – 100 µs)**
  - **Dark Current Sink (0 – 1000 pA)**
  - **Power / Channel (1 – 20 mW)**
  - **Gain (individual channel control, 50 – 200 mV / 1000 e⁻ input)**

Amplifier Performance



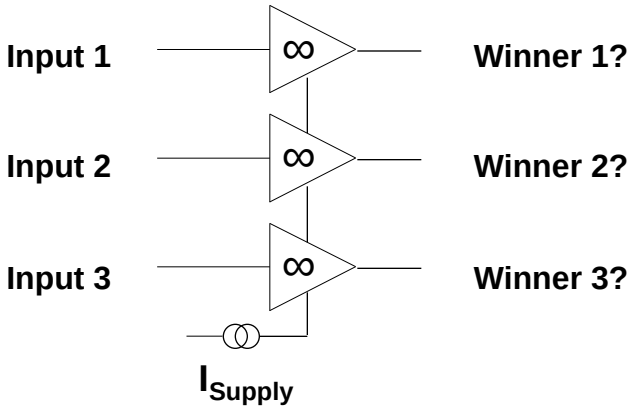
Plan to Operate at 0.5 – 1.0 µs Shaping Time

The Crystal Identification Problem



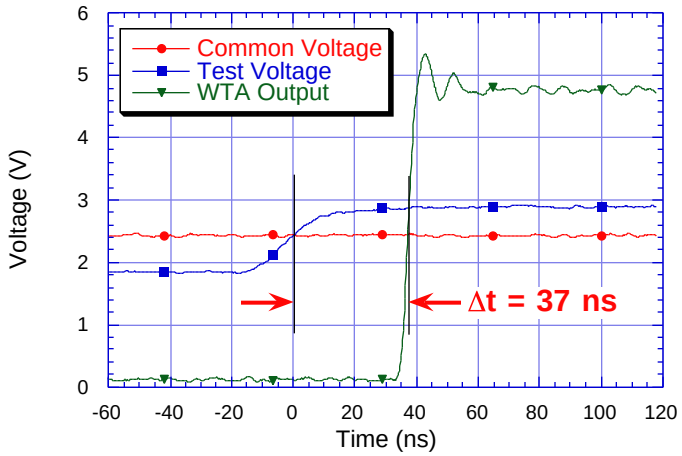
Provide Digital Address of Input with Highest Voltage in <100 ns

The "Winner Take All" Solution



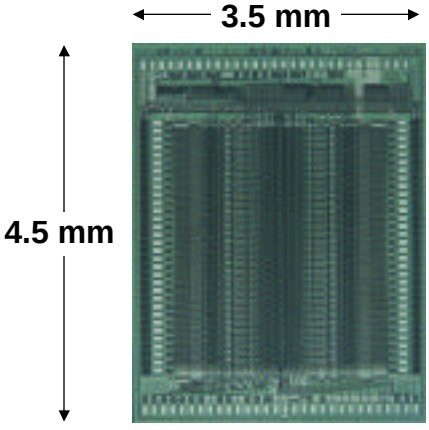
- Amplifiers Fight for Limited Supply Current
- Output is Digital Bit Identifying Winner

WTA Propagation Time



Well Under 100 ns

64 Channel IC Prototype Completed



Inputs

- 64 PD Signals
- Sample & Hold
- Rise, Fall, & Reset Control

Outputs

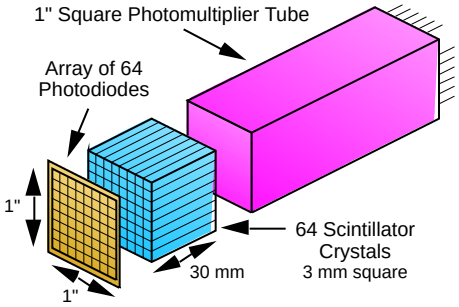
- Voltage of Winner
- Address of Winner

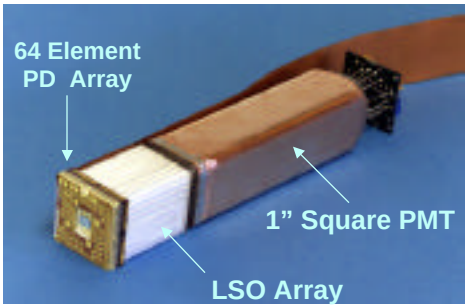
Input / Output

- Serial Control (Xicor Protocol)

Submitting New Version Soon...

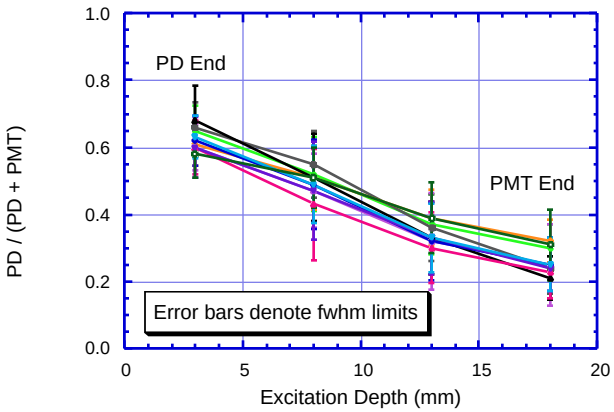
Prototype Detector Module





64 Channel Prototype Built & Tested

Depth Estimator PD / (PD+PMT) is Linear with Excitation Depth



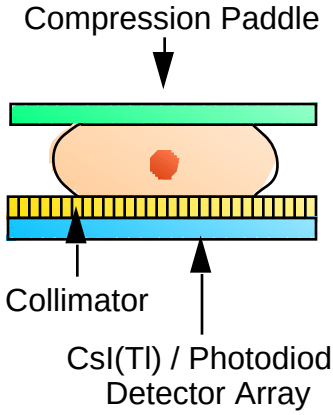
- **Depth Resolution is 7–13 mm fwhm**
- **Distribution Similar in All Channels**

Prototype Detector Performance

Quantity	Conventional Module	This Module	Effect
Timing Resolution	~4 ns fwhm	0.75 ns fwhm	Improved Random Rejection
Energy Resolution	20% fwhm	25% fwhm	Degraded Scatter Rejection
Crystal Size	4.0 x 4.4 mm	3.0 x 3.0 mm	Improved Position Resolution
Correct ID Fraction	53% (Center 1) 66% (Center 5)	65% (Center 1) 91% (Center 5)	Improved Position Resolution
D.O.I. Resolution	none	7–13 mm fwhm	Reduced Radial Elongation

- **Outperforms Conventional Detector Module**
- **Further Improvements Expected...**

Single Photon Variant



Good Single Gamma Emitting Drugs Exist

- Technetium-99m Sestamibi
- Emits 141 keV gamma

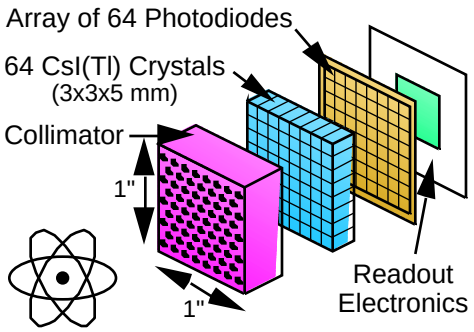
Collimate w/ Parallel Holes in Pb

Detect with CsI:Tl Scintillator / Photodiode Array

- ~4x more light than LSO
- CsI:Tl not dense or fast for PET

- **Uses Similar Components as PEM / ANPET Module**
- **Planar (not Tomographic) Images Formed**
- **Radiopharmaceutical Widely Available**

Components of the Detector Module



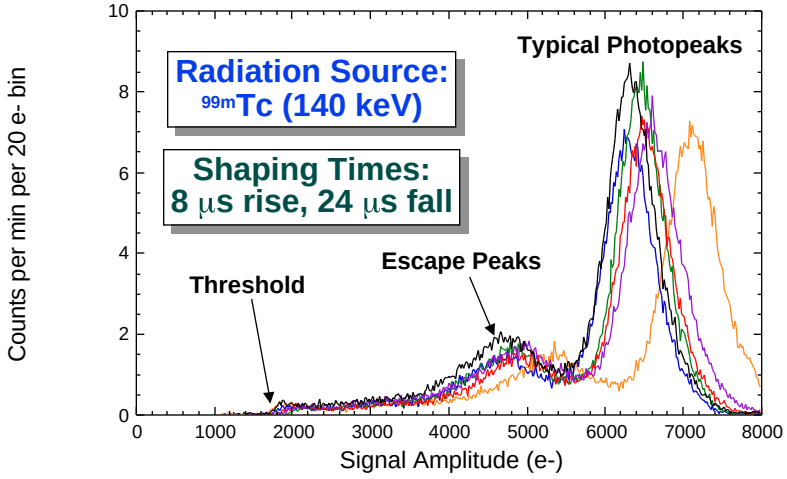
Same Custom IC as PET Module
- **Signal level is ~50% higher**

Same PD Array as PET Module
- **Optimized for 550 nm**

Collimators are "Off the Shelf"

- **Readout IC Mounted to Back of Photodiodes**
- **Easy to Scale Up to a Full Camera**

^{99m}Tc Spectrum in LBNL Detector



- **Average Energy Resolution = 10.7 ± 0.6% fwhm**
- **Conventional Camera (NaI:Tl / PMT) Typically 9% fwhm**

Conclusions

Nuclear Medicine Can Image Breast Cancer:

- Excellent Accuracy for ≥1 cm Tumors

Specialized Cameras Under Development:

- Higher Resolution & Efficiency, Lower Cost
- Image Breast and Axillary Nodes
- At LBNL and Other Institutions

Development at LBNL:

- Major Components Developed (Photodiode, Custom IC)
- Prototype Detector Module Shows Excellent Performance
- Lots of Work Yet To Do (Postdoc? – wwmoses@lbl.gov)

Acknowledgements

People:

Mark Andreaco*, Jean François Beche, Eric Beuville, Tom Budinger, Steve Derenzo, Greg Gruber, Matt Ho, Steve Holland, Michelle Huesman, Ron Huesman, Jenny Huber, Atul Joshi, Issy Kipnis, Brad Krieger, Tony Ko, Emmanuele Mandelli, Oren Milgrome, Chuck Melcher*, Marzio Pedrali-Noy, Ron Nutt*, Ola Pettersson, Amy Shustz, Patrick Virador, Nadine Wang, Matthew Weng

*CTI PET Systems, Inc.

Funding:

National Institutes of Health
Grants R01-CA67911, P01-HL25840, & R01-NS29655

State of California Breast Cancer Research Program
Grant 1RB-0068

U.S. Department of Energy
Office of Biological and Environmental Research