Positron Emission Mammography (PEM)

A dedicated breast PET scanner developed at IHEP

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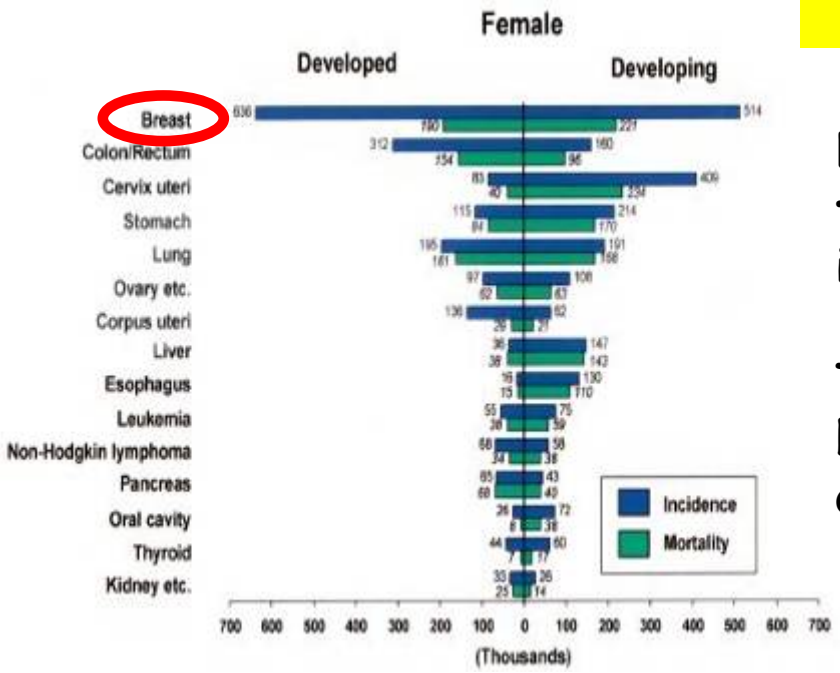
Institute of High Energy Physics

Outline

- **Introduction of PEM**
- **PEM equipment (PEMi)**
- **PEMi performance**
- **Industrialization**
- **Conclusion**

Introduction of PEM



About breast cancer

Breast cancer is one of the most common female malignant tumors, and the incidence is trending to rapidly ascend.

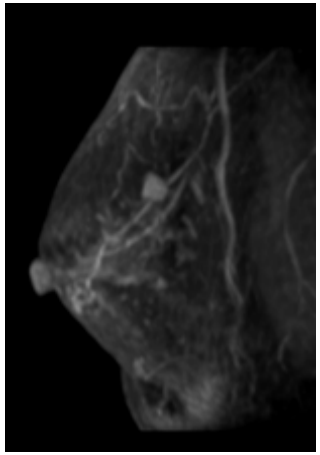
The earlier detection of breast cancer, the higher survival rates and the lower expense of therapy.

Imaging technology plays an important role in the basic and clinic research of breast cancer. It's a powerful tool to detect the cancer at early stage.

D. M. Parkin, F. Bray, J. Ferlay, and P. Pisani, "Global cancer statistics, 2002," CA: A Cancer Journal for Clinicians, vol. 55, pp. 74-108, 2005.

Introduction of PEM

Imaging technologies used in breast cancer



X-ray mammography

general survey of breast cancer, morphological information

ultrasonic echography

non-radiate, better imaging result for dense breast, morphological information

MRI

high sensitivity, unique advantages of discovery of small lesions

PET

PET is a functional imaging technique that has demonstrated large potential for breast cancer detection.

Introduction of PEM

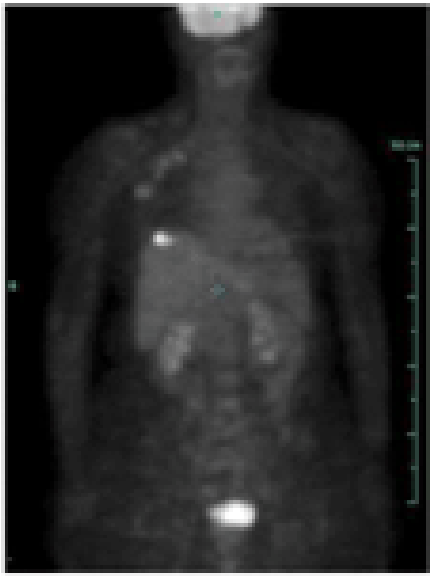
Limitations of whole-body PET for detecting breast cancer:

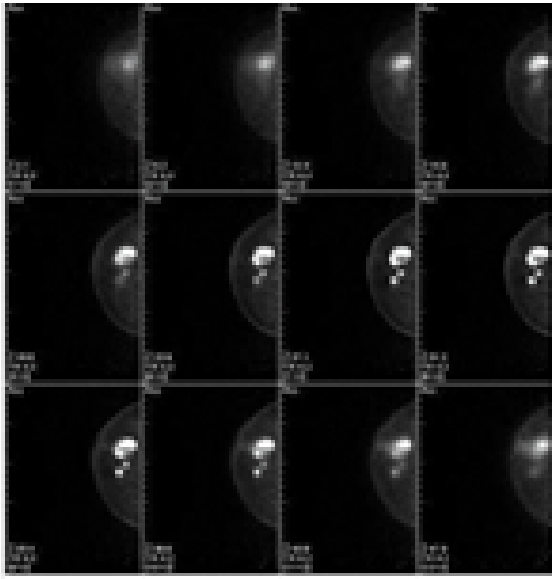
- **breast immobilization**
- **biopsy capability**
- **sufficient contrast-to-noise ratio for millimeter-sized lesions**

Significant progress has been achieved in the design of commercial PET in the last decade allowing significant progress made in the design of dedicated positron emission mammography (PEM) units.

Introduction of PEM

PEM system is a PET device dedicated to breast cancer detection,
with higher spatial resolution, efficiency and sensitivity.



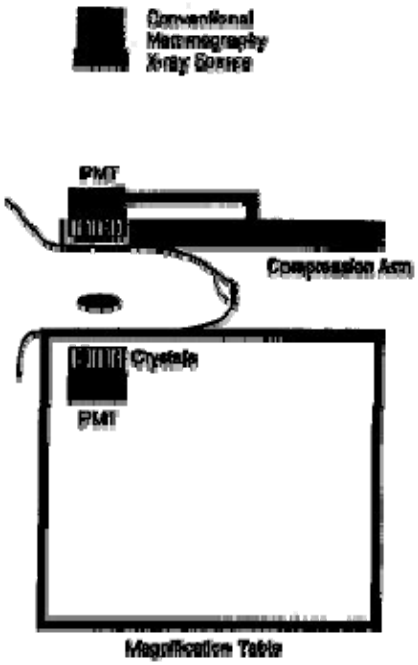


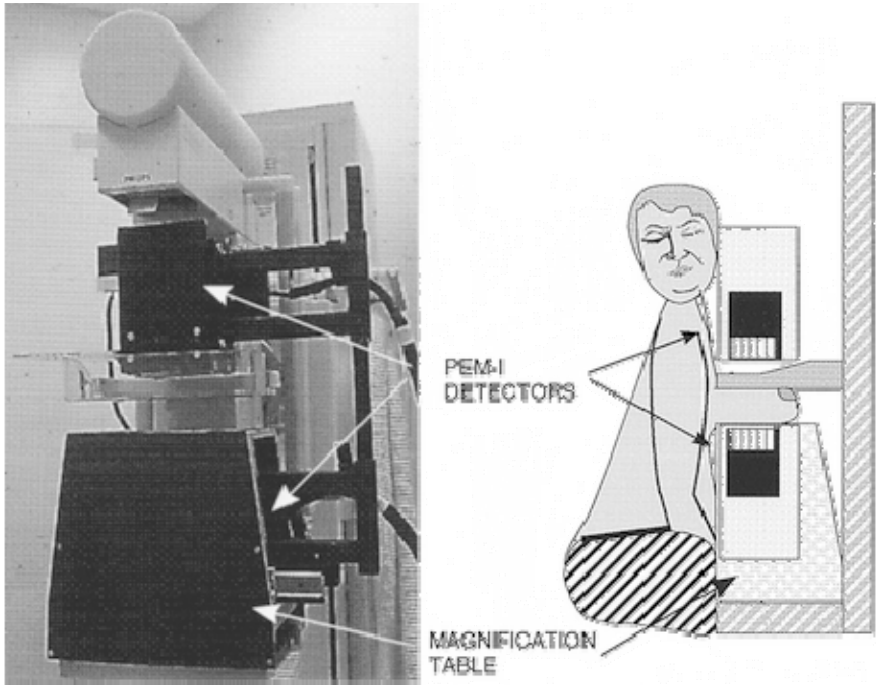
By placing the detectors close to the breast, the PEM geometry subtends more solid angle around the breast than a whole body PET scanner. The PEM can detect smaller breast cancers than whole body PET.

Combining the quantitative capabilities of PET with millimeter resolution, PEM can image the earliest *in situ* forms of breast cancer.

Introduction of PEM

First Feasibility Study for PEM





In 1994, Thompson *et al.* studied the feasibility of PEM for the first time. Their results suggested that the spatial resolution of about 2 mm should be possible when using narrow crystals and the efficiency could reach about ten times that of a conventional brain scanner.

Introduction of PEM

Application of PEM

Clinic

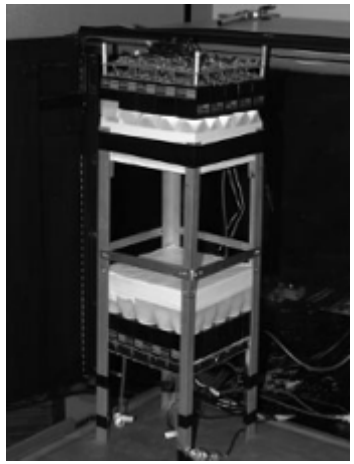
- Biopsy guidance
- Surgical planning
- Surveillance for recurrence
- Statistical analysis of patients imaging data

Research (Pre-clinical)

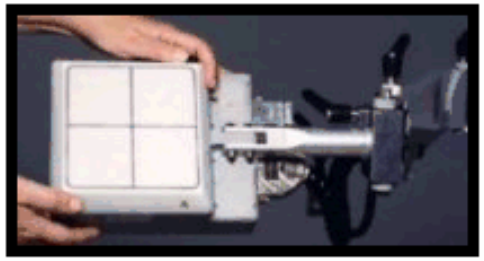
- Discovery of drugs
- Development of radiotracers
- Gene imaging

Introduction of PEM

Developments of PEM

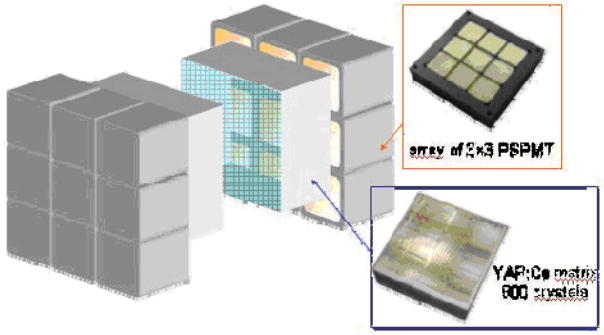


UCLA，MaxPET（2001）

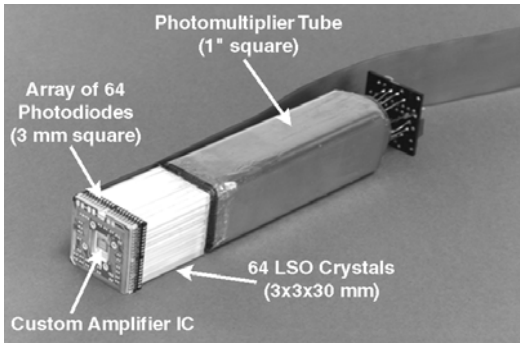


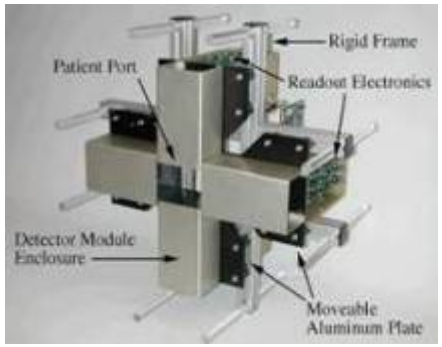
Compact scintimammography gamma camera for early detection of breast cancer

Jefferson Lab， PEM（2005）



FIIG，YAP PEM （2006）

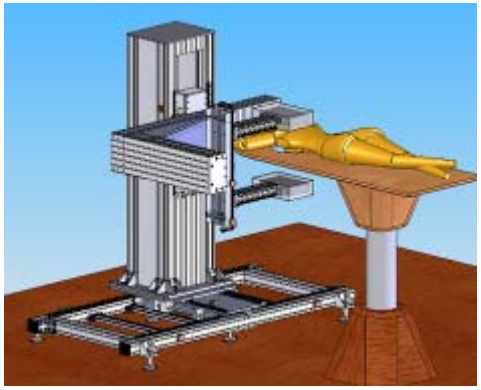


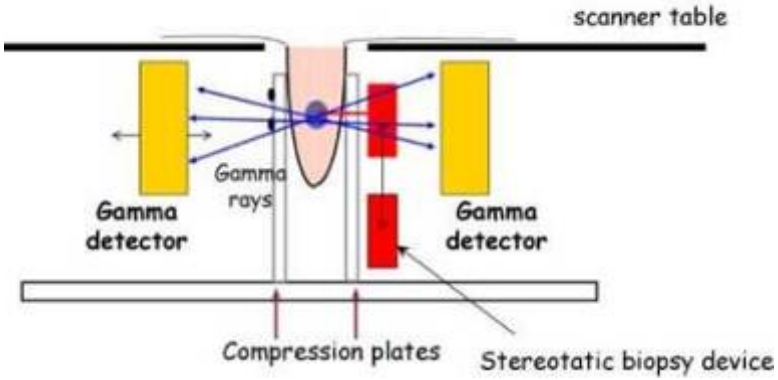


LBNL，LBNL PEM（2006）

Introduction of PEM

Developments of PEM



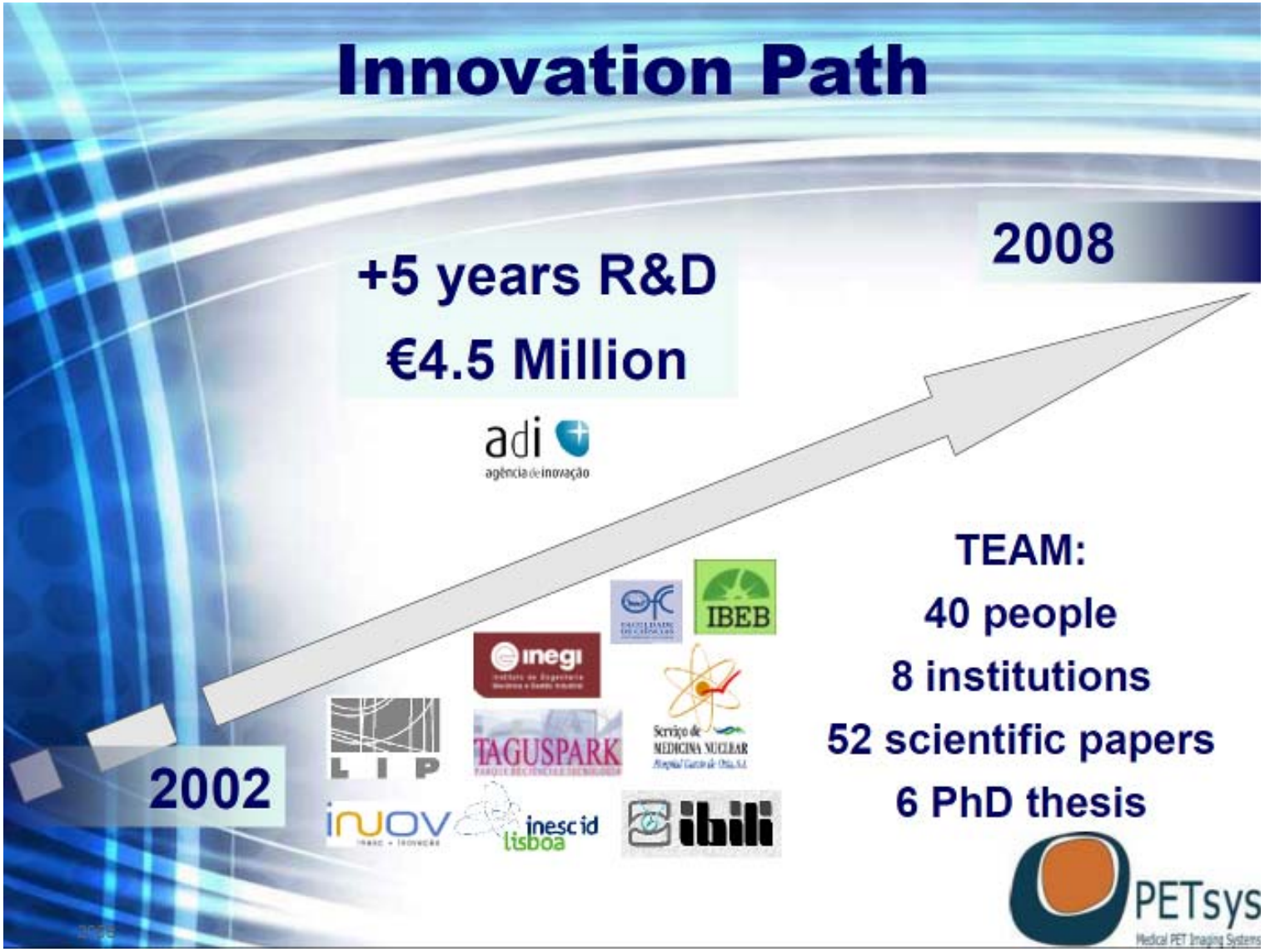


CERN，ClearPEM

PEM Detector Module Assembly

University of Texas，PEM（2008）

Introduction of PEM

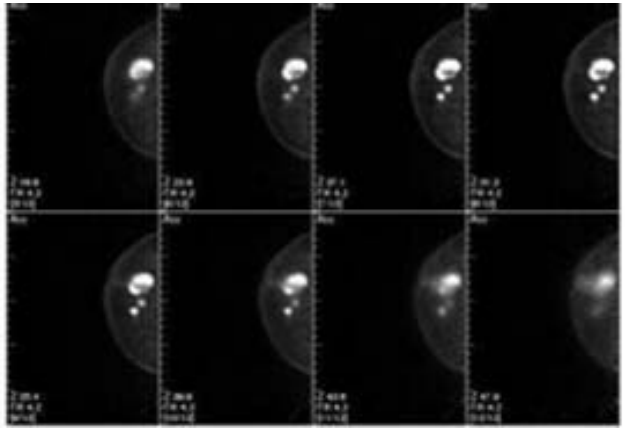


Introduction of PEM

Commercialization of PEM

PEM Flex™ Solo

NAVISCAN PET Systems Corp.
（2006, the first Commercial PEM）



- **Spatial Resolution ： 2 mm**
- **Filed of View (FOV): 16.3cm×24cm**
- **Scan Time ： 4~10 min**
- **Data Acquisition Mode：3D**

Outline

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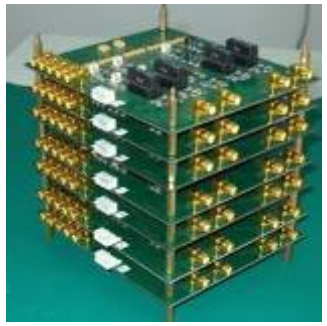
PEM technologies @IHEP

An animal PET scanner and a PET/CT scanner were developed by IHEP for metabolic and anatomic imaging of rodents and small primates.

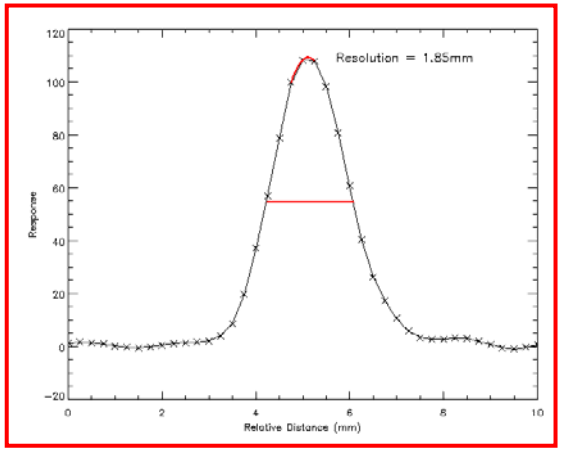
- **new type of position sensitive detectors**
- **high-speed data acquisition system with multi-channel**
- **data coincidence circuit without buckets**

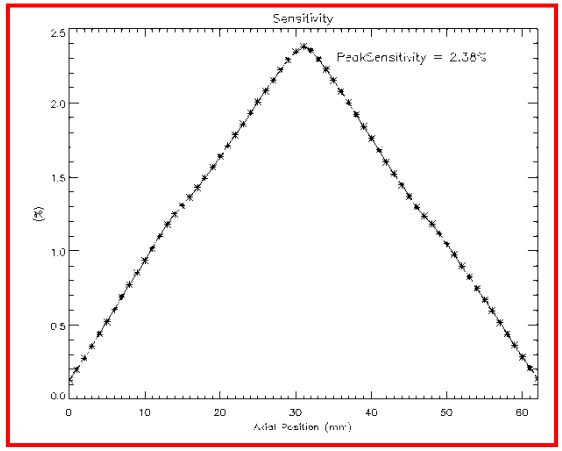


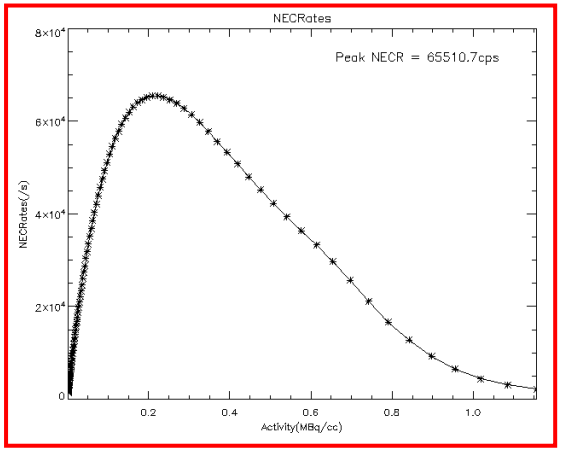
Animal PET@IHEP

● 技术指标 Technical index

Diameter of detector:	166mm	Spatial Resolution:	<2.0mm
Diameter of Entrance:	~160mm	X-ray Source Max Output:	90KV, 8W
Transverse FOV:	110mm	Focal Spot Size:	5um(min)
Axial FOV:	64mmor96mm	CT Active Area:	Ø 60mm
Spatial Resolution:	优于2.0mm	CT Resolution:	~80um

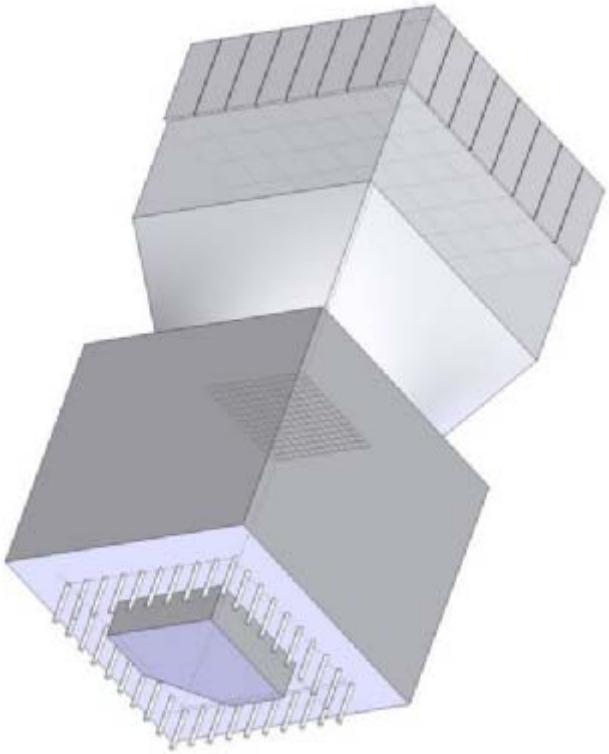


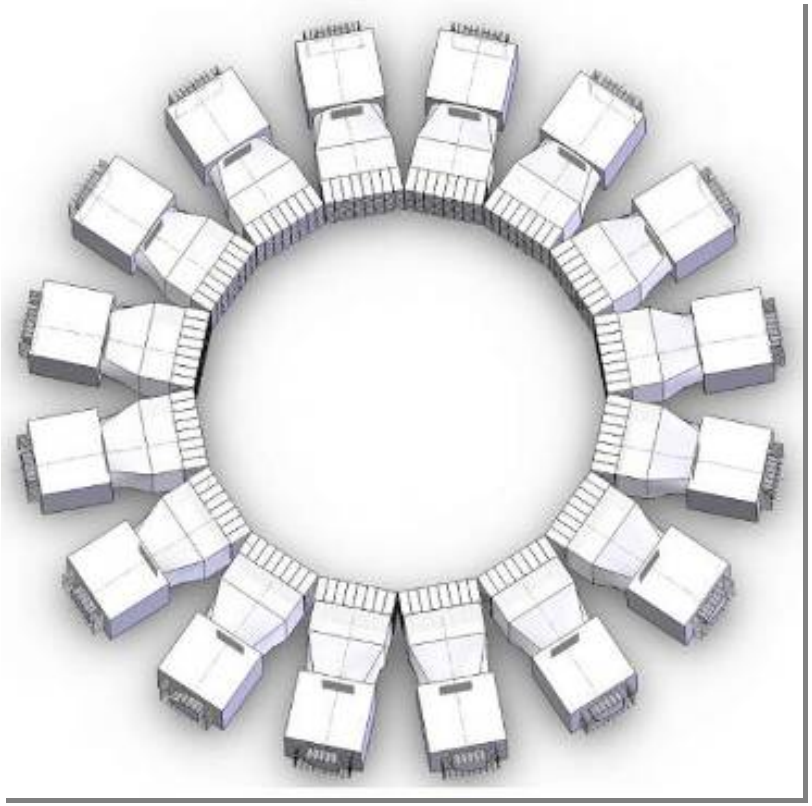


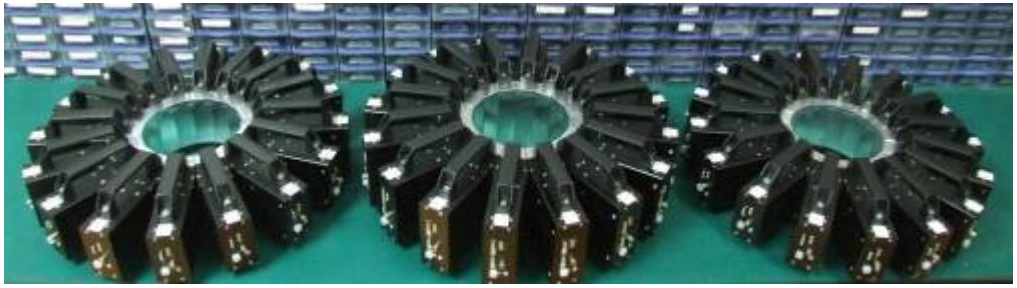


The bench mark has reached advanced level compared with commercial available ones.

Animal PET@IHEP







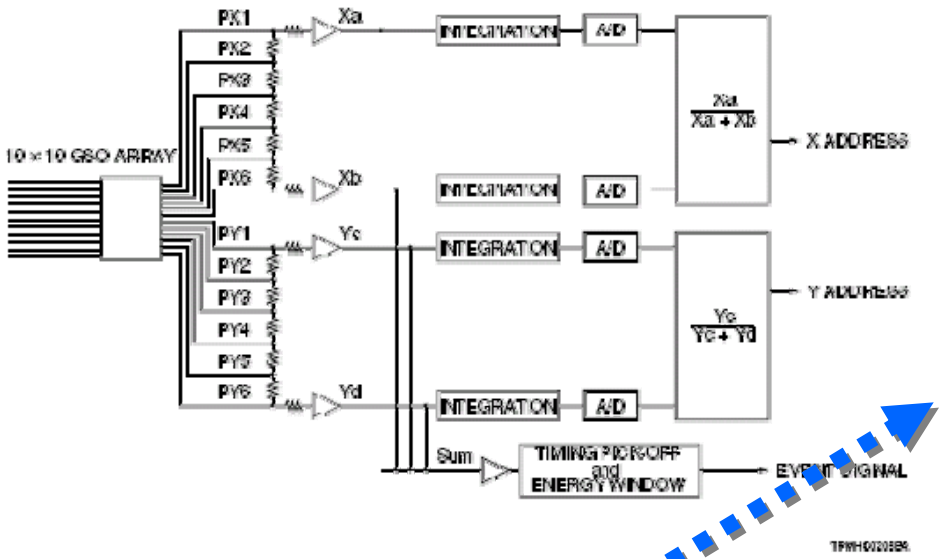
Patent：ZL200510105211.2

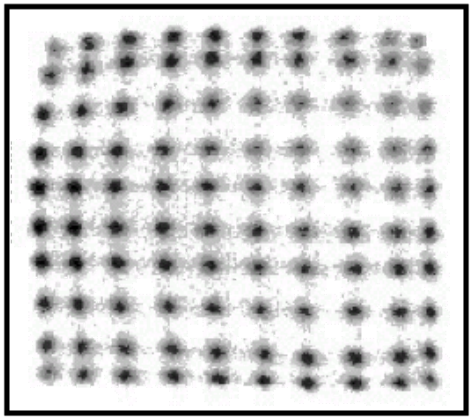
Animal PET@IHEP

HAMAMATSU

Circuit Diagram Example and Positioning Histogram

PRELIMINARY DATA

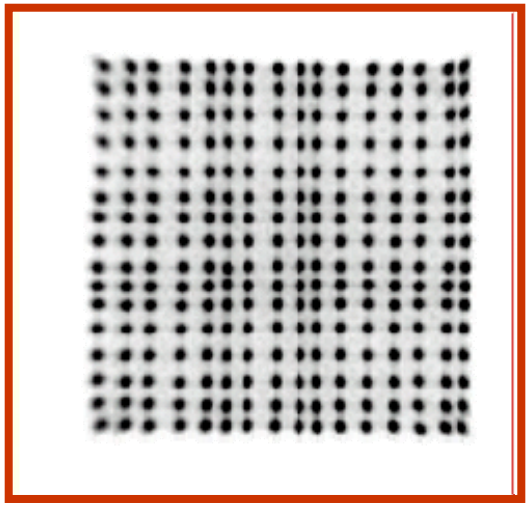




Positioning histogram of a 10 × 10 array of 2.0 mm × 2.0 mm × 20 mm GSO elements for 511 keV γ-rays.
(crystal pitch is 2.2 mm)

10×10 Array
Area: 20×20 mm

16×16 Array
Area: 32×32 mm



Animal PET@IHEP

MicroPET II (UCLA, CTI-Concorde)

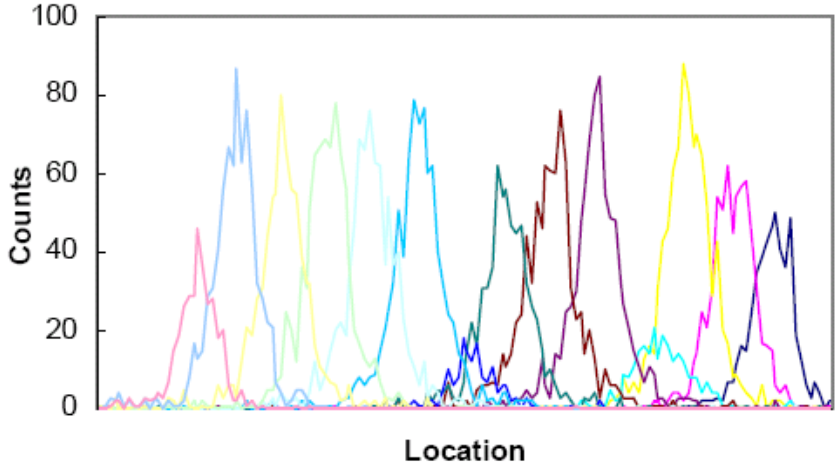
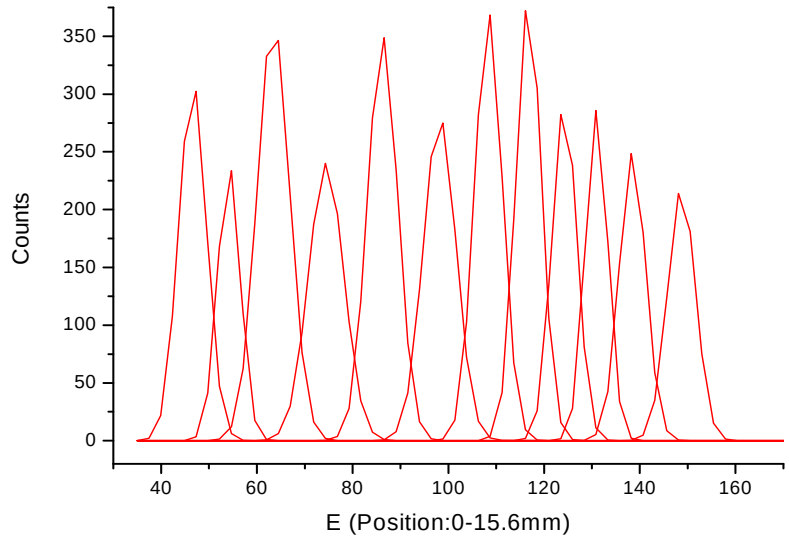


Figure 6. Intrinsic spatial resolution of the system measured with a ^{22}Na point source with 0.5 mm diameter nominal size. FWHM fit with Gaussian curves ranged from 1.04 to 1.66 mm with a mean of 1.26 mm without compensation for source size.

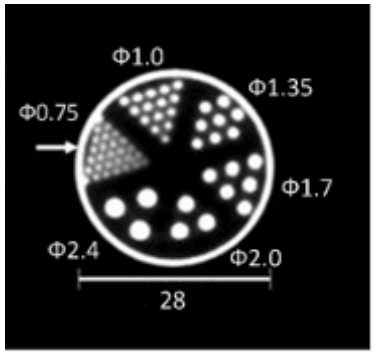
Animal-PET (IHEP)

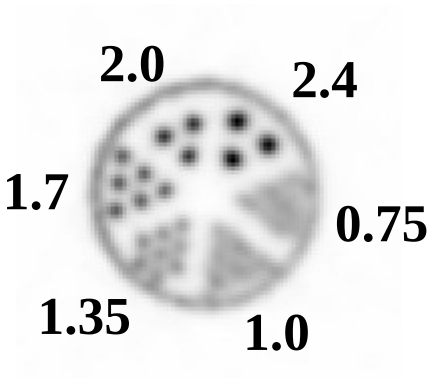


MicroPET II	Animal-PET
0.975x0.975x12.5 mm^3	1.2x1.2x10 mm^3
0.175 mm gap	0.10 mm gap
FWHM ~ 1.26 mm	FWHM < 1.2 mm

3 times detection area with same PMT!

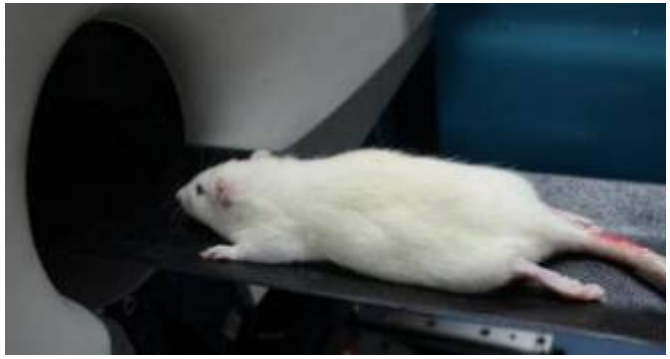
Performance of animal PET





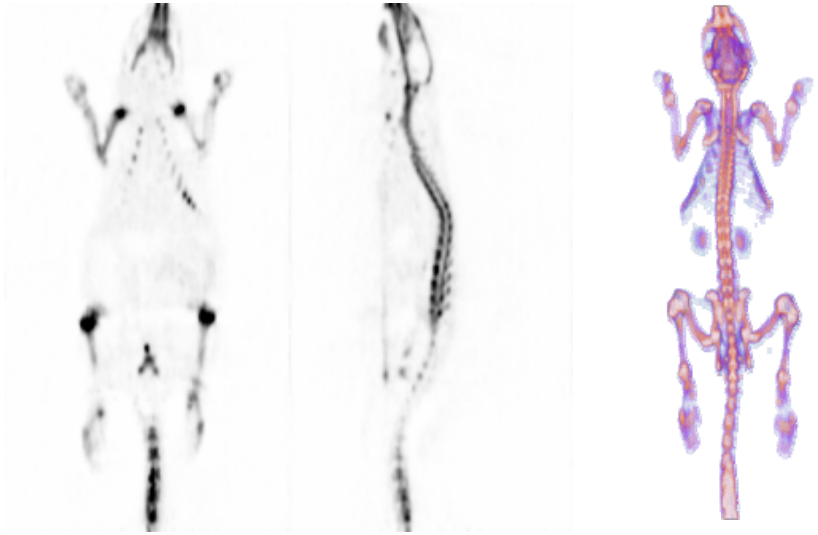
Derenzo Phantom Imaging

- Sealed phantom with FDG
- 0.5 mCi activity



Rat, 200g , 2.1 mCi of $^{18}F^{-}$

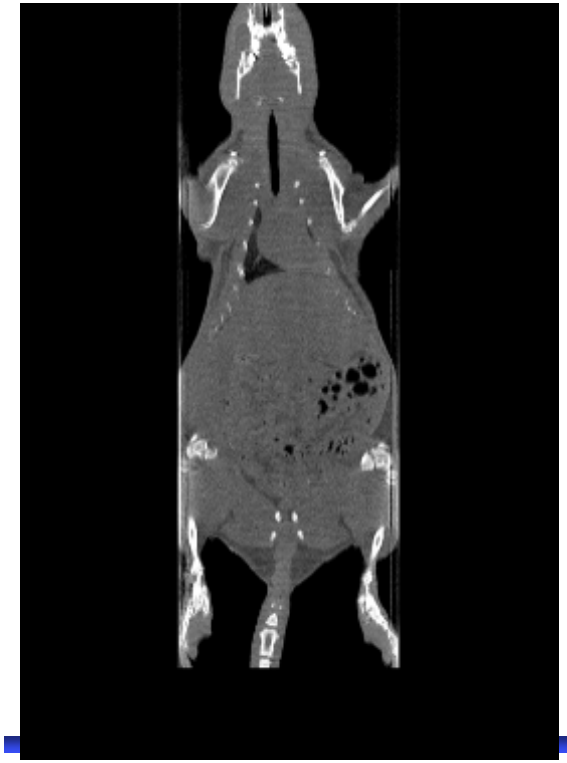
scanned for 20 min per bed in four bed positions



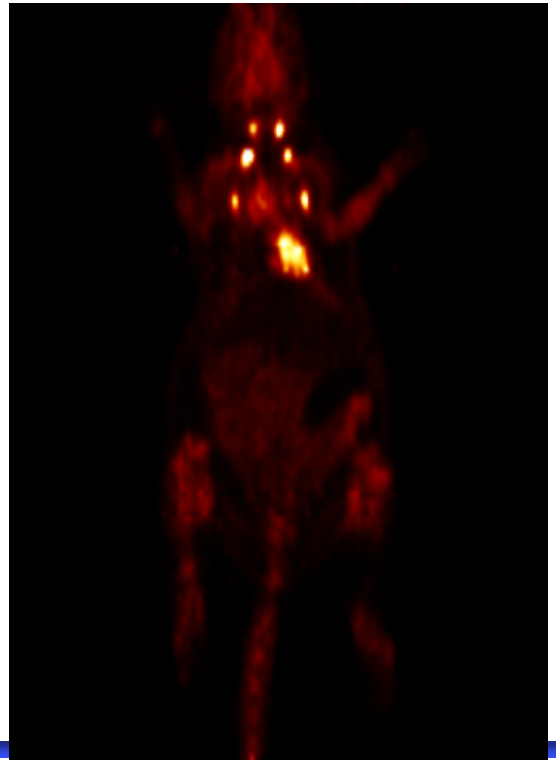
Bone imaging of a rat

Performance of animal PET

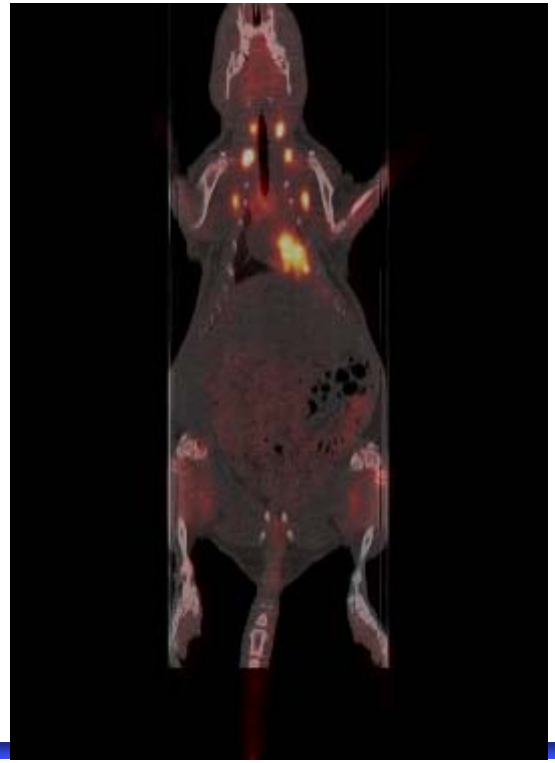
- Rat, 100g , 1.5 mCi of ^{18}F-FDG solution
- scanned for 10 min per bed in three bed positions



CT

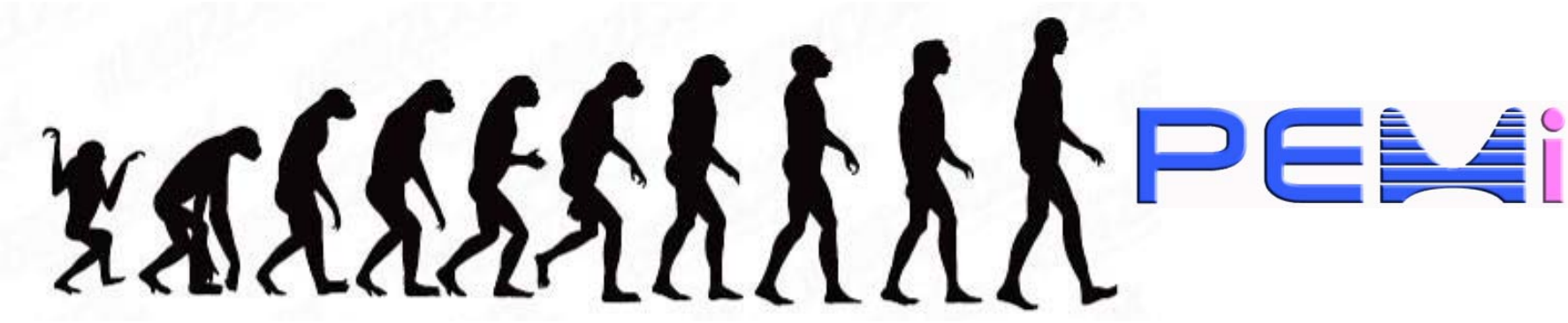


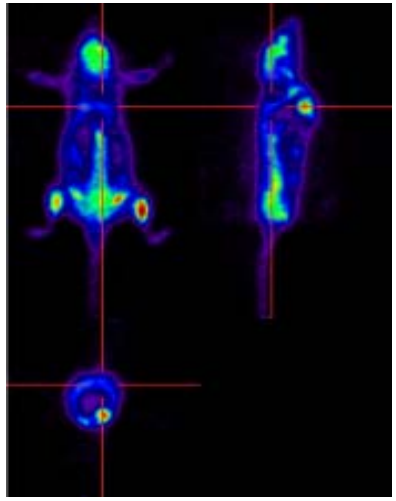
PET（ ^{18}F-FDG ）



PET-CT

Evolution is "from animal to human"





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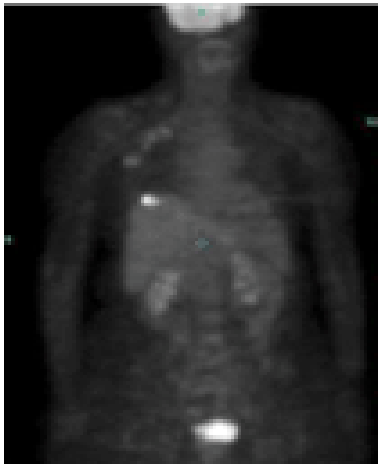

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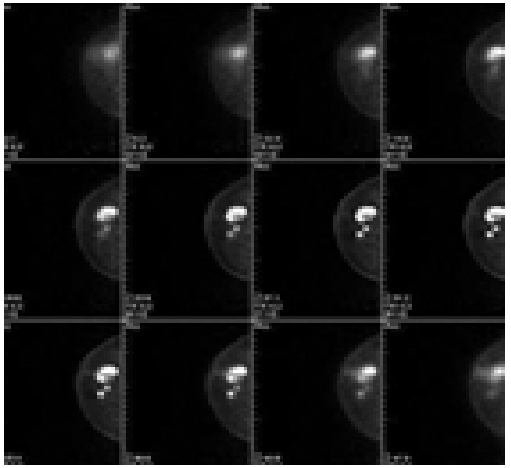
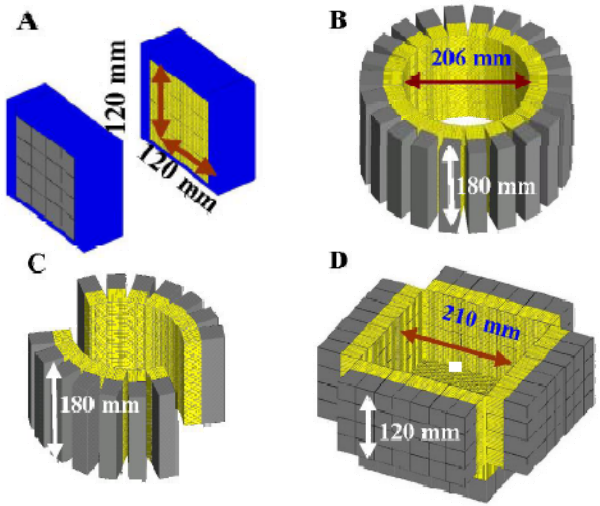
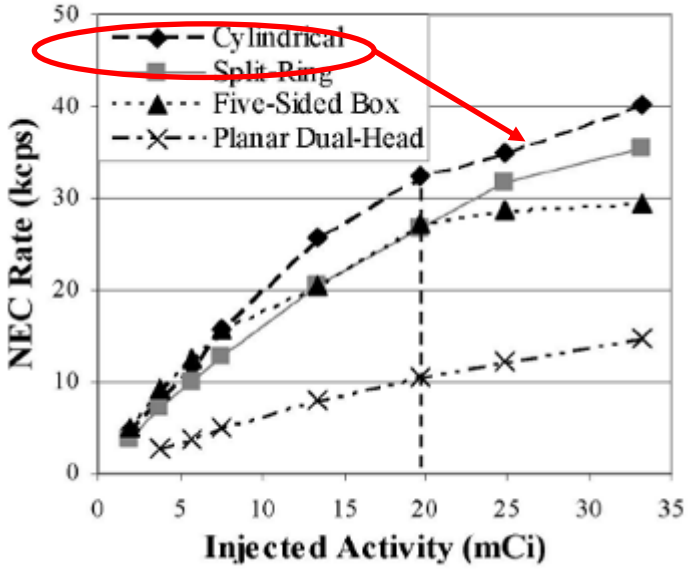


PEM scanner offered a chance for people to detect human body with the resolution of animal imaging!!

PEMi equipment





This study showed the NECR of new scanner (CYBPET), is much better than WB-PET, at low activity concentration. As an instance, the NECR of CYBPET is about 2 times greater than WB-PET in the activity concentration less than 3.2 (μCi/cc) for a 8mm lesion. This matter is noticeable, because of low activity concentration in the breast and its lesion, a relative high NECR in the low activity concentration is very important for visibility of small tumors.

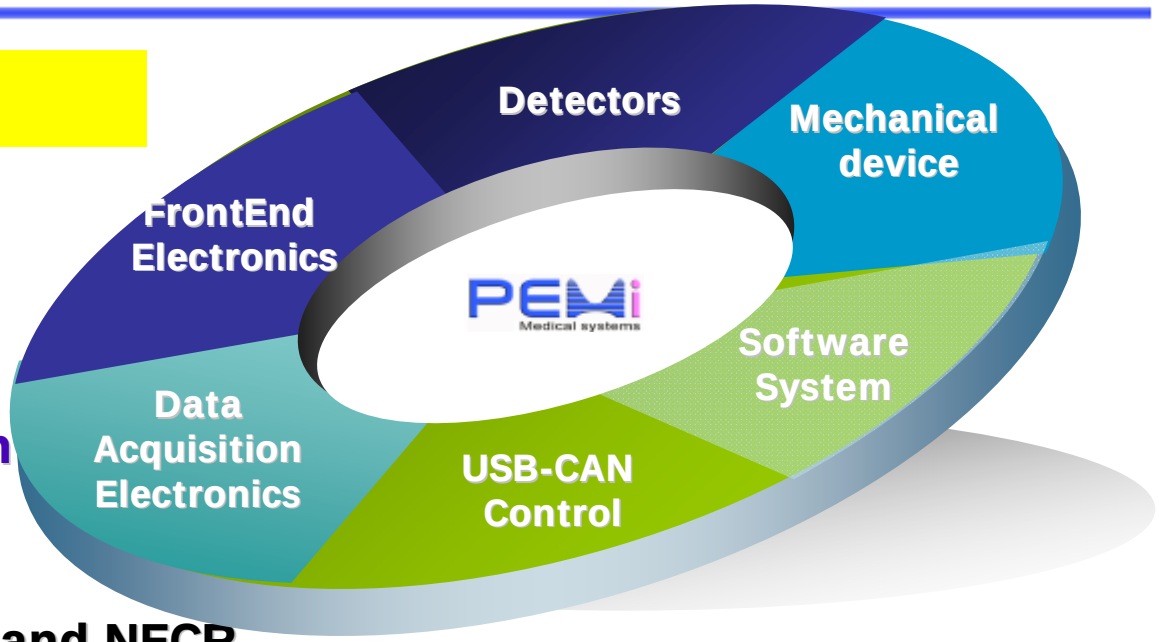
PEMi Medical systems

PEMi equipment

Scanner developed and assembled @ IHEP

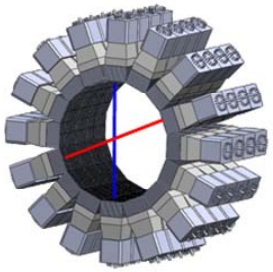
PEMi equipment

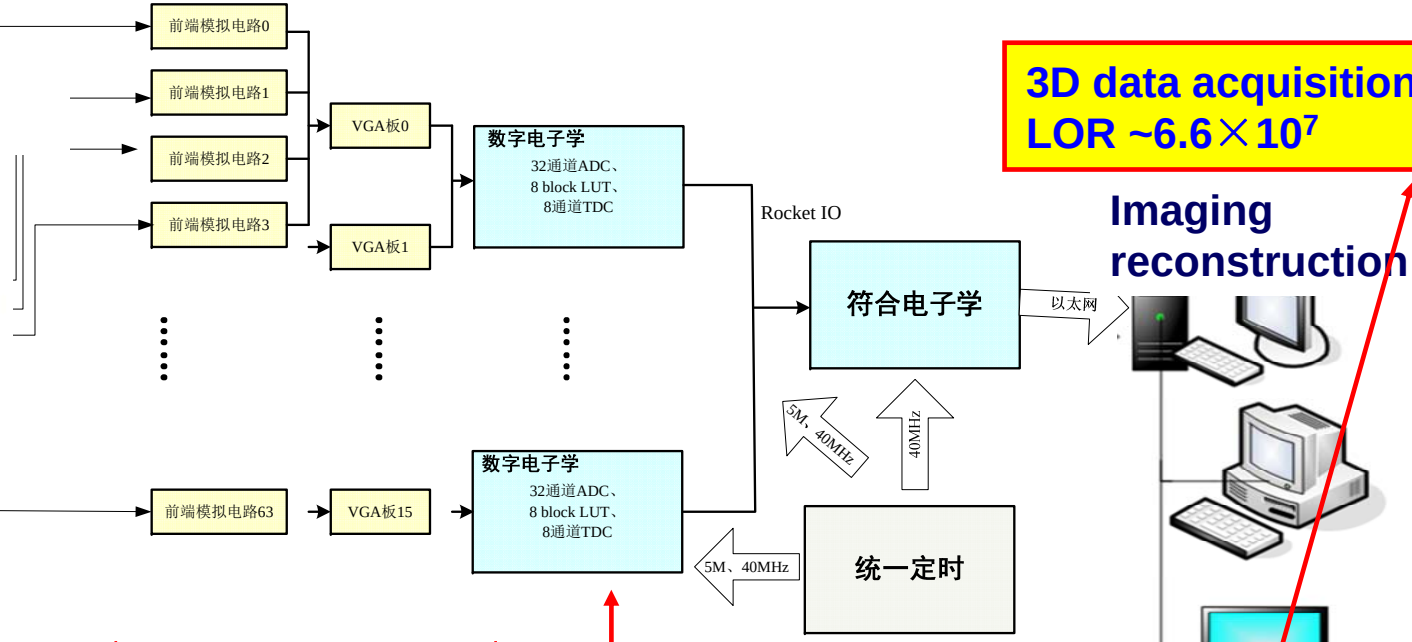
Characteristics of PEMi



- Prone position scan mode
- Cylindrical detector design
- High Detection Sensitivity and NECR
- High Spatial Resolution
- High detection efficiency and high-quality imaging
- Real-time data correction and 3D image reconstruction
- Medical image based on DICOM standard

Detector ring



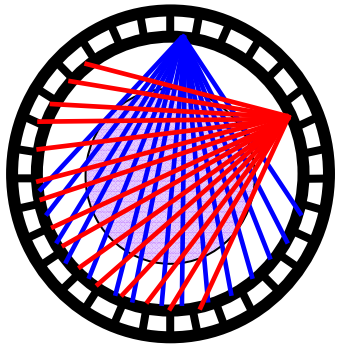


3D data acquisition，LOR ~6.6×10^7

Imaging reconstruction

FrontEnd Electronics

Data Acquisition Electronics

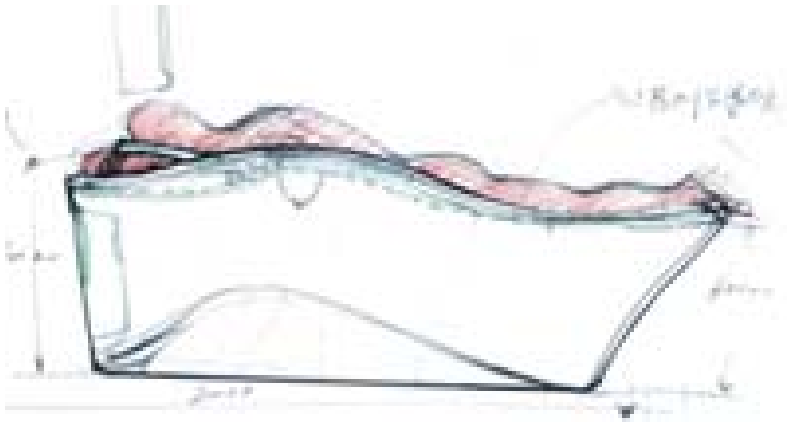


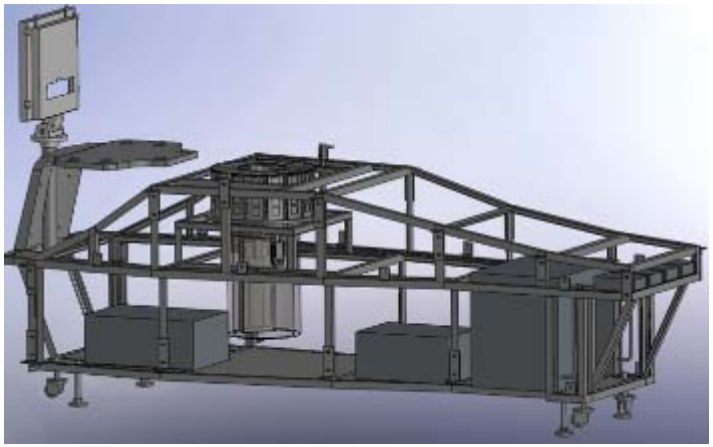
10 *mCi* tracer：~10^6 events per detector

64 detector blocks, ability of data acquisition 14.4 Gb/s

PEMi equipment

Mechanical and industrial design



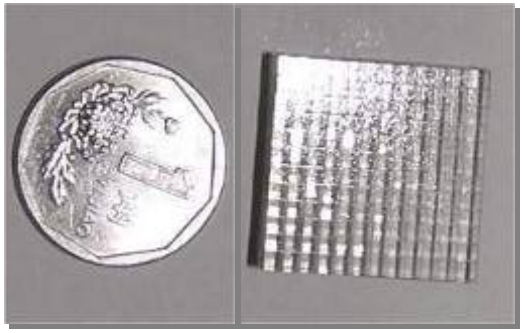


Ring-shaped detector and Prone position

- **Focus on the balance between structure and function**
- **Based on the human engineering**
- **Patient friendly**

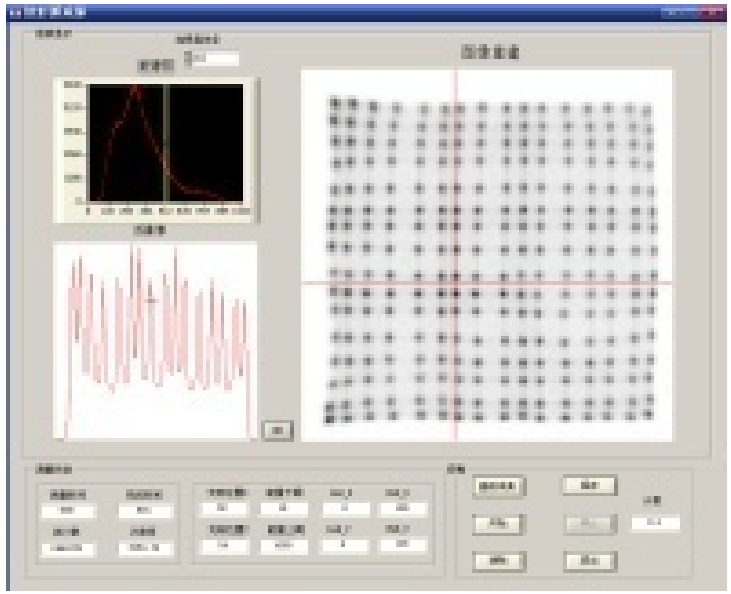
PEMi equipment

Detector Modules



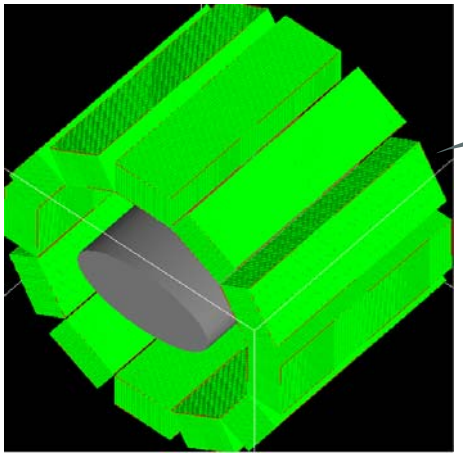
16 Detector modules

- 64 blocks
- 16384 LYSO scintillation crystals (1.9 mm×1.9 mm×15 mm)
- 64 Photo-multipliers (PS-PMT)

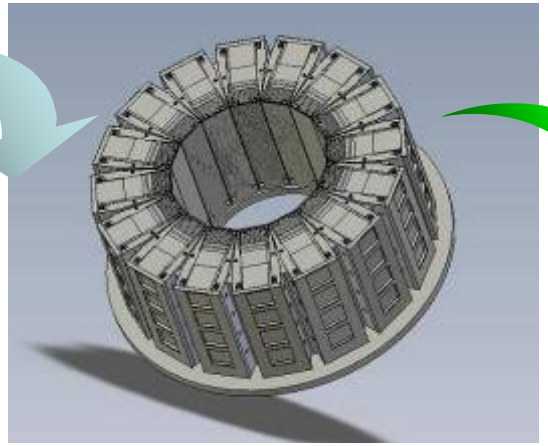


PEMi equipment

Detector Modules



GEANT4 simulation



Solid work cartography

Detector ring

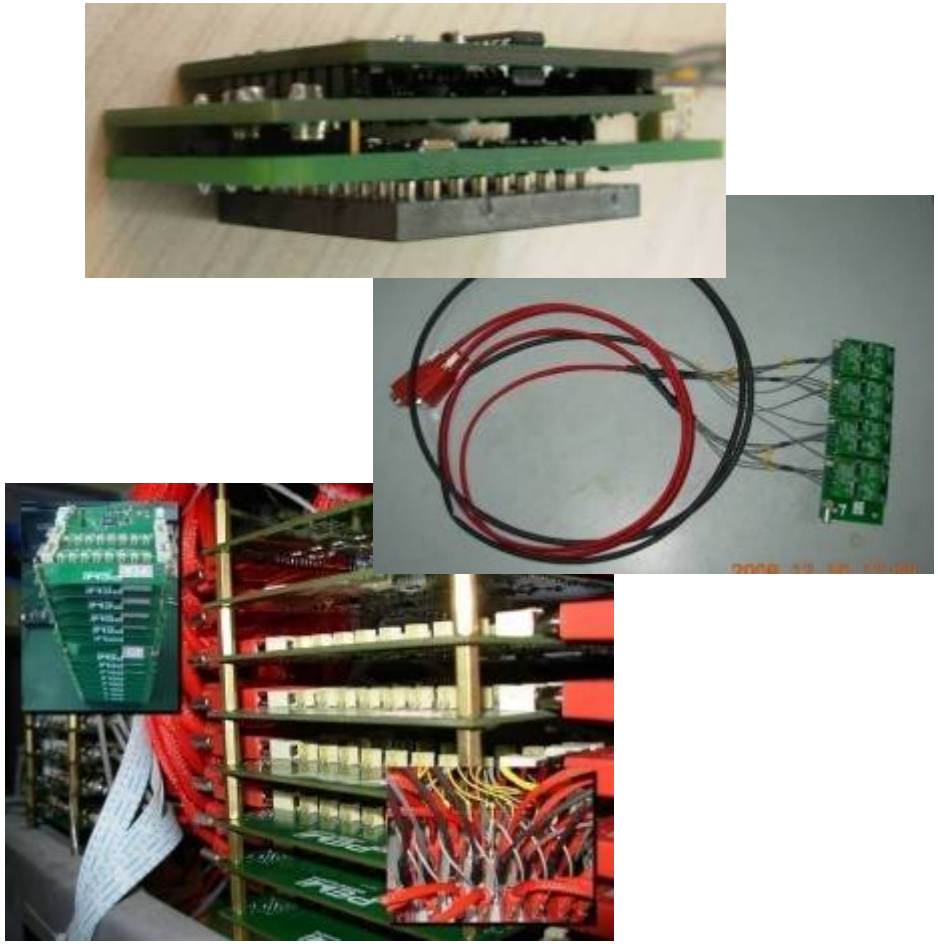
- 1 module = 4 detector blocks
- 1 detector ring = 16 modules
- Diameter of breast entrance: 160 mm
- Axial FOV: 128 mm, Radial FOV: 110 mm

PEMi equipment

Front-End Electronics

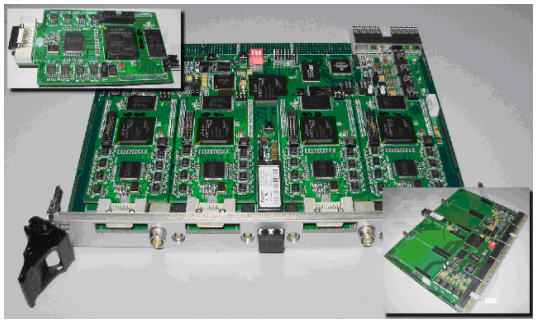
Main features of frontend electronics:

- **Built-in PMT voltage divider**
- **Timing signal output**
- **Signal amplifying and shaping**
- **Signal gain adjusting**



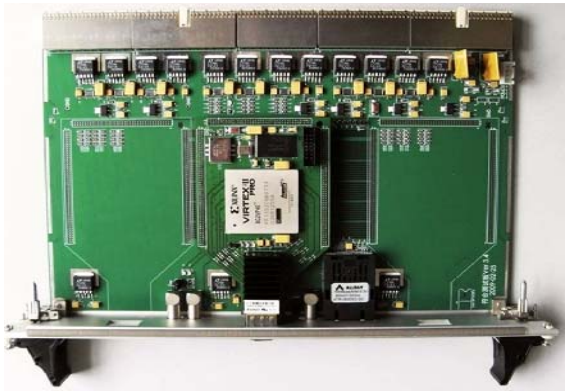
PEMi equipment

Data Acquisition Electronics



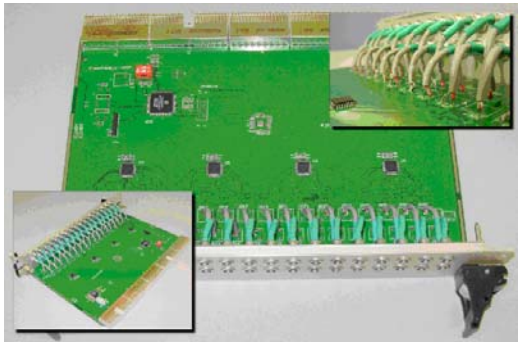
8 CSM （Continuous Sampling Module）

- Real-time parallel A/D sampling of signals
- Data synchronization processing



1 CPM（Coincidence Processing Module）

- A standalone coincidence circuit
- Analysis onboard
- Data Transmission



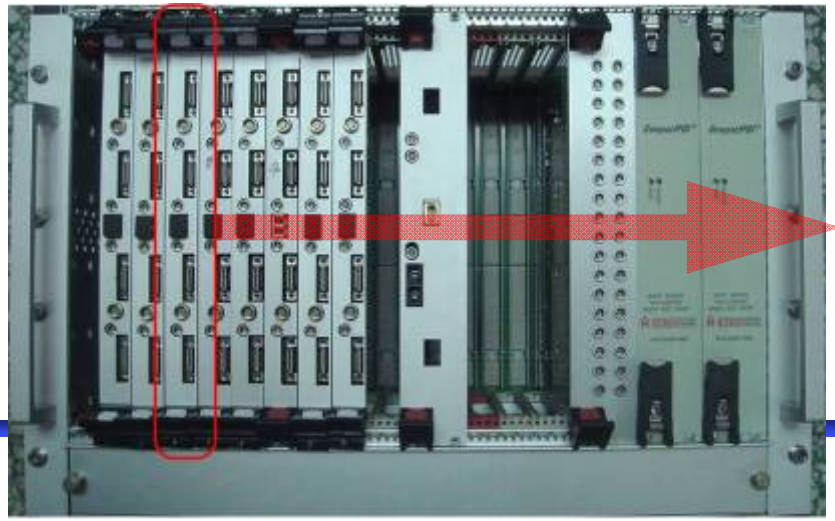
1 CGM（Clock Generation Module）

- Global clock fan-out

PEMi equipment

Continuous Sampling Module:

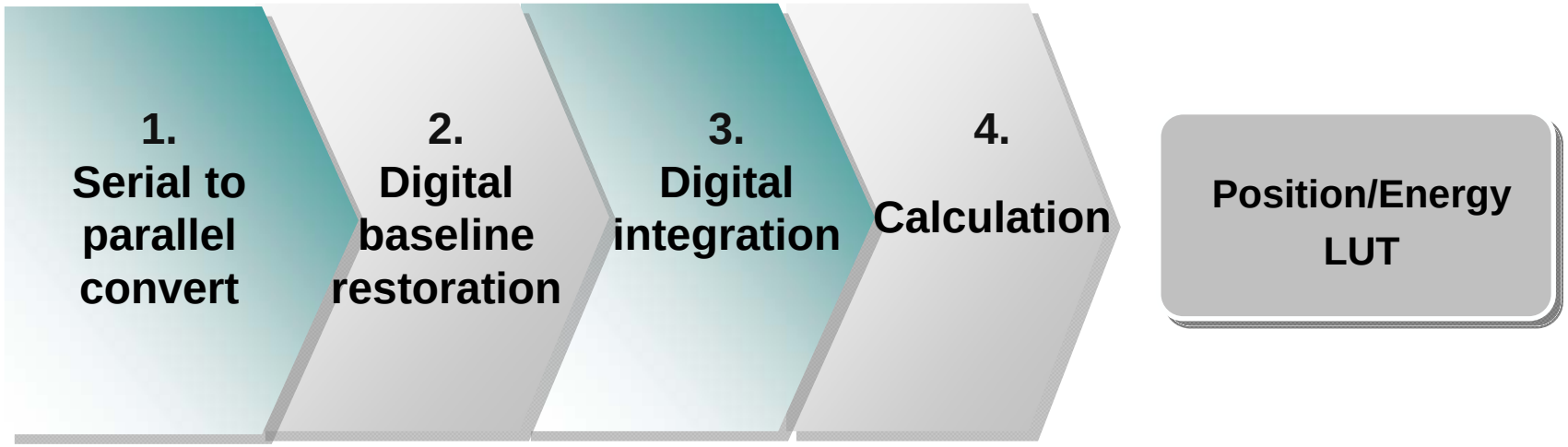
- **Motherboard-daughterboard Structure**
  - 1~4 daughter-boards are optional
- **Digitized Signal Sampling and Process**
  - 32 channels analog signals processing/unit
- **FPGA as MCU**
  - Flexible logic design



PEMi equipment

About Daughter-board:

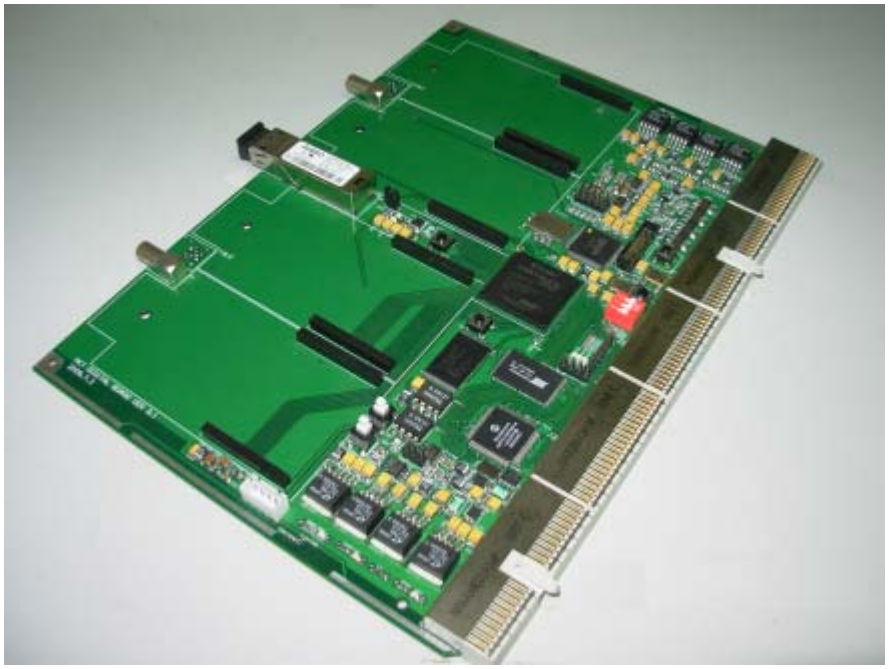
- **Analog to Digital Convert (ADC)**
  - **8 channels**
  - **40MHz/12bit**
- **Logic design in FPGA**



PEMi equipment

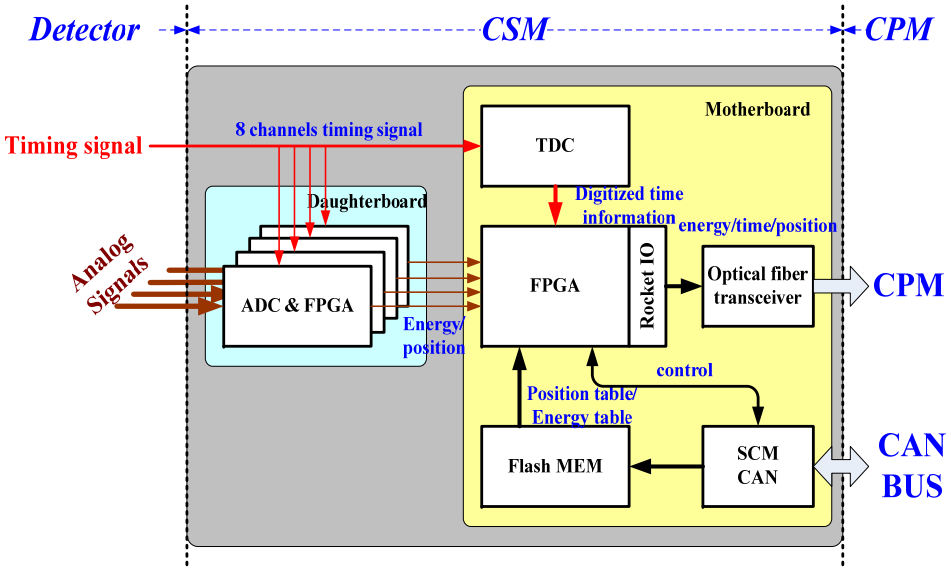
About Motherboard:

- **FPGA**
  - Receive daughterboard data
  - Flexible logic design for different system
- **Time to Digital Convert (TDC)**
  - 8 channel digitized time information
  - Time resolution: 320ps
- **Flash MEM**
  - Position table storage
  - Energy table storage



PEMi equipment

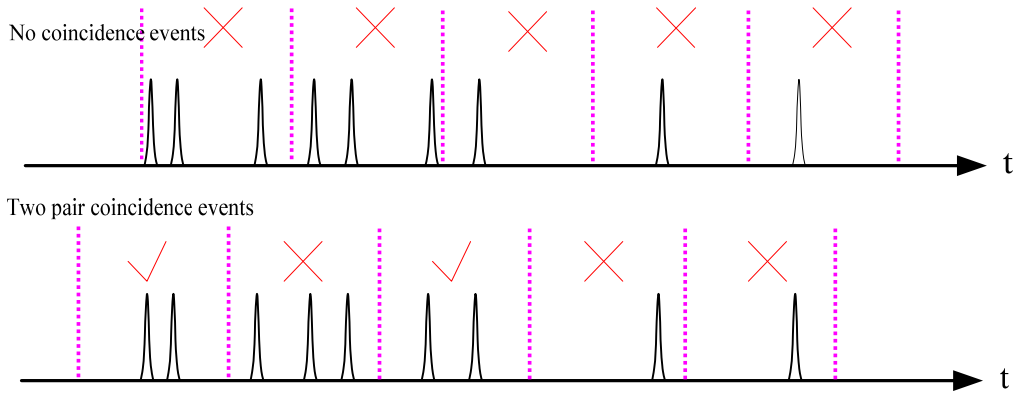
About Motherboard (cont.):



- **CAN BUS**
  - Controlling the boards
  - Rewrite position/Energy table in the Flash MEM if needed
  - Sent system reset signal
- **Optical Fiber Transmitting**
  - Gigabit data transmitting
  - Number of CSM works for the system is flexible
- **Power supply**
  - Get +3.3V/+5V from compact PCI crate

PEMi equipment

Coincidence Processing Module:



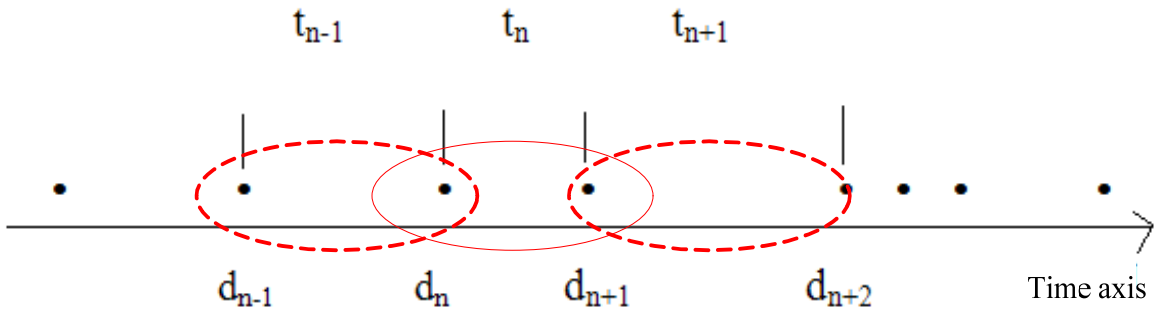
Fixed Time Window:

The same data,

but the different results

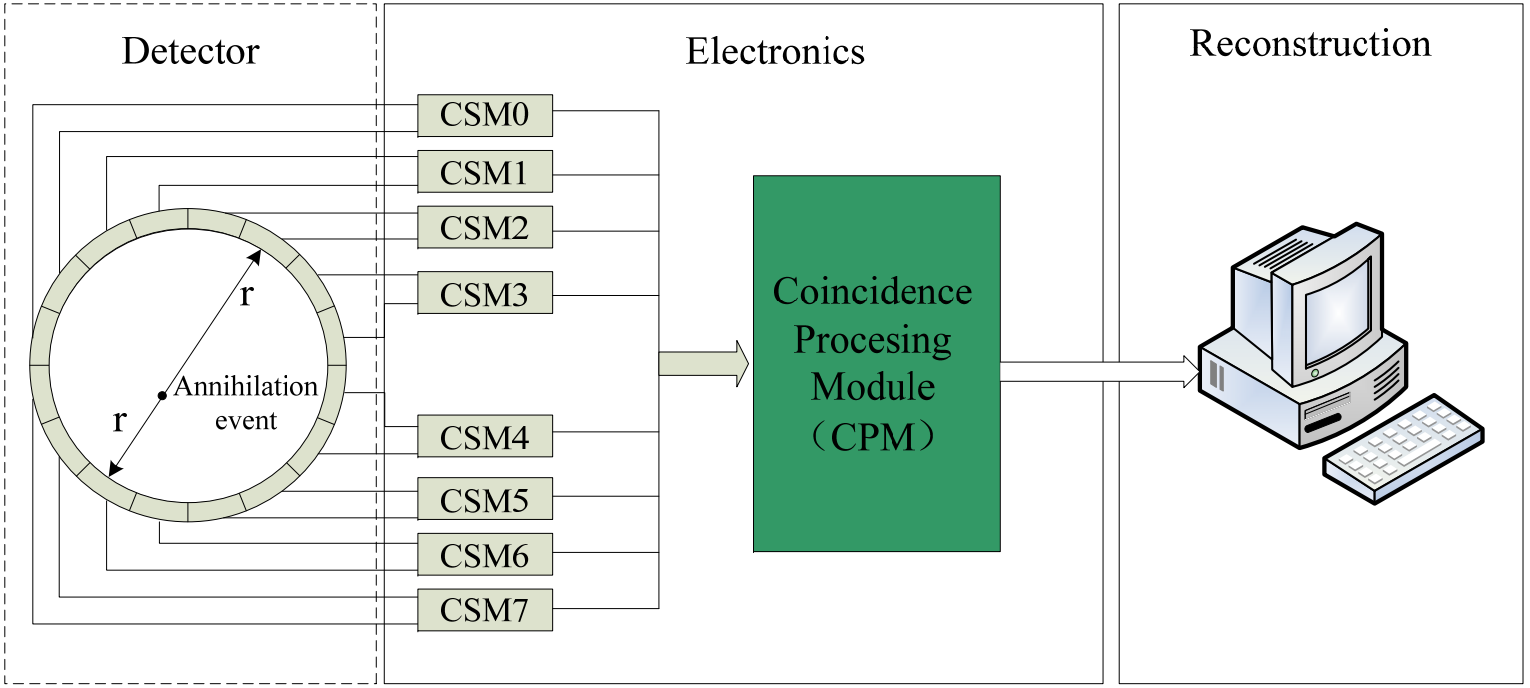
Sliding Time Window:

$$t_{n-1} > T_w \&\& t_n \leqslant T_w \&\& t_{n+1} > T_w$$



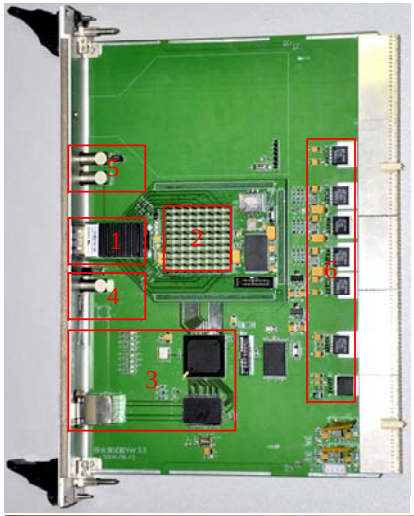
PEMi equipment

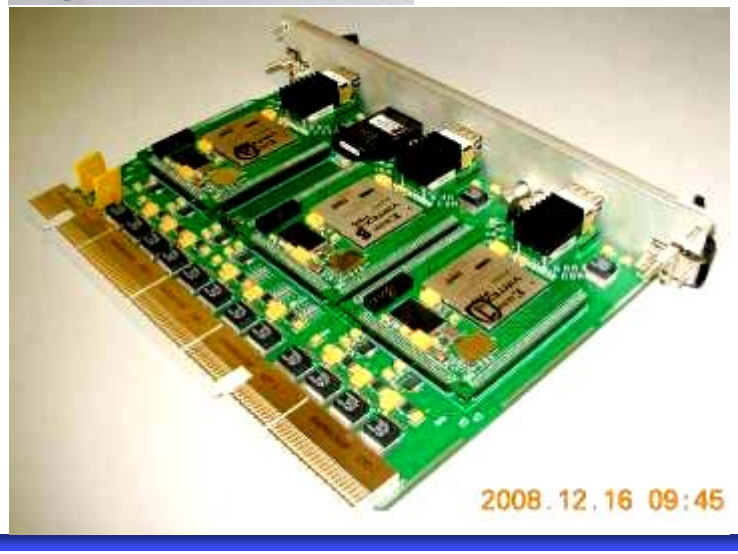
Coincidence Processing Module:



PEMi equipment

Hardware Architecture



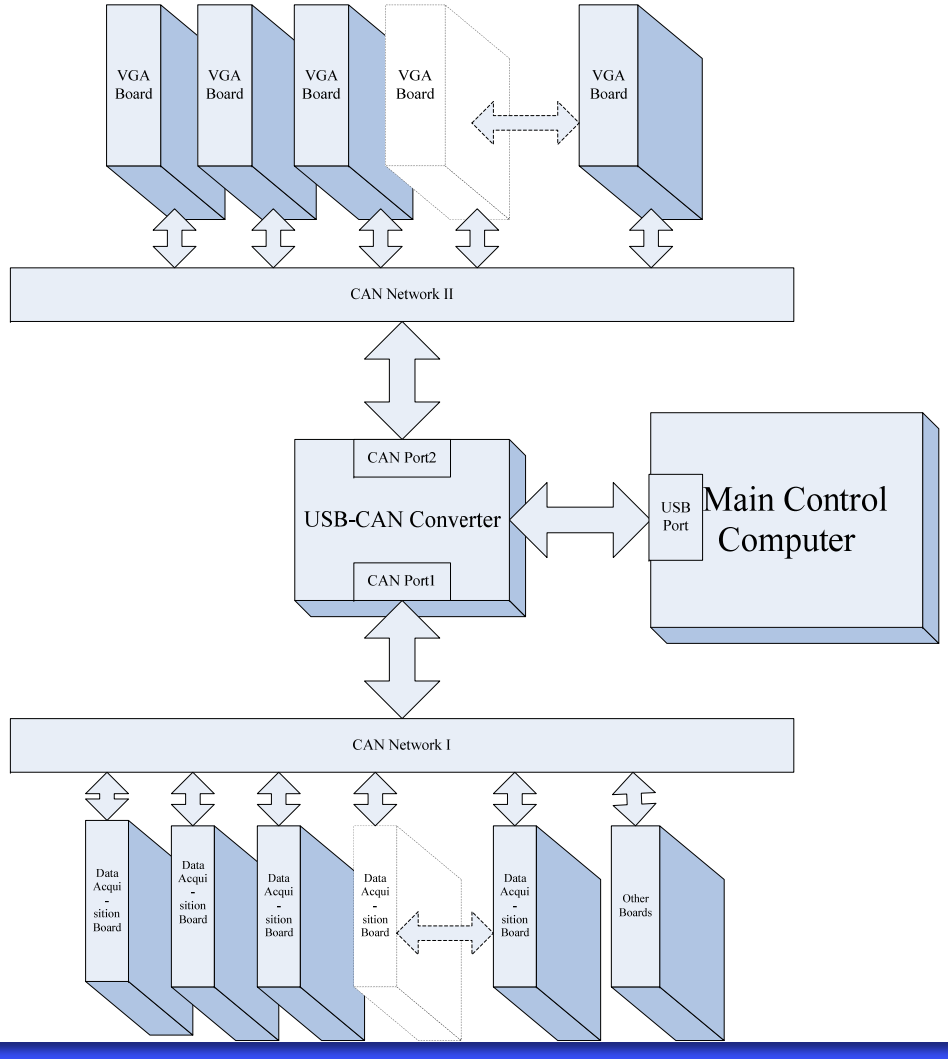


1. **Data Receiving:**
   - Optical fiber
2. **Coincidence Processing:**
   - FPGA
3. **Data Transmitting:**
   - Gigabit Ethernet
4. **Totally 288 detectors:**
   - 1 FPGA supports 96 detector
5. **System Controlling:**
   - CAN Bus

cPCI standard with 6U dimension

Control Network Based On CAN-BUS

1 Digital resistors Parameters
2 Sensor Information

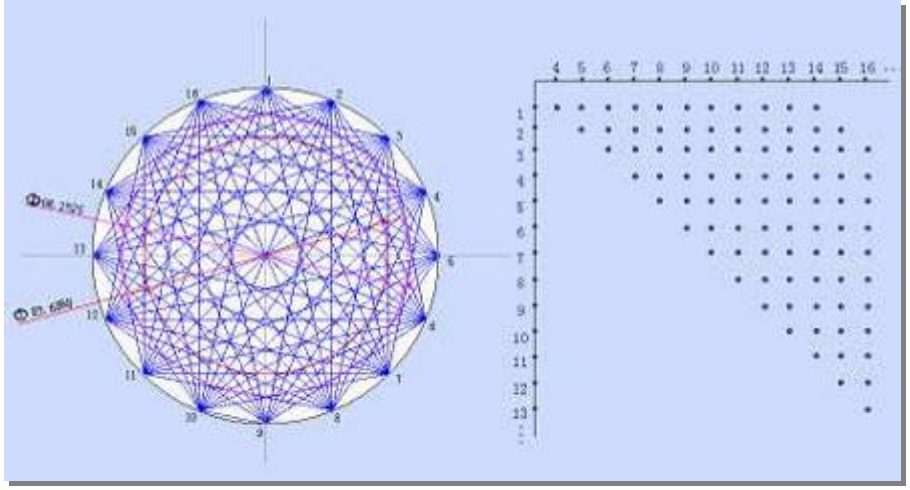


1 Operation Mode
2 Position tables, Energy tables
3 Sensor Information

PEMi equipment

Summary of Data Acquisition Electronics

- ✓ Multi-channel data acquire based on cPCI architecture
- ✓ Integrated data processing electronics based on FPGA
- ✓ High-speed data transmission based on Giga-bit network

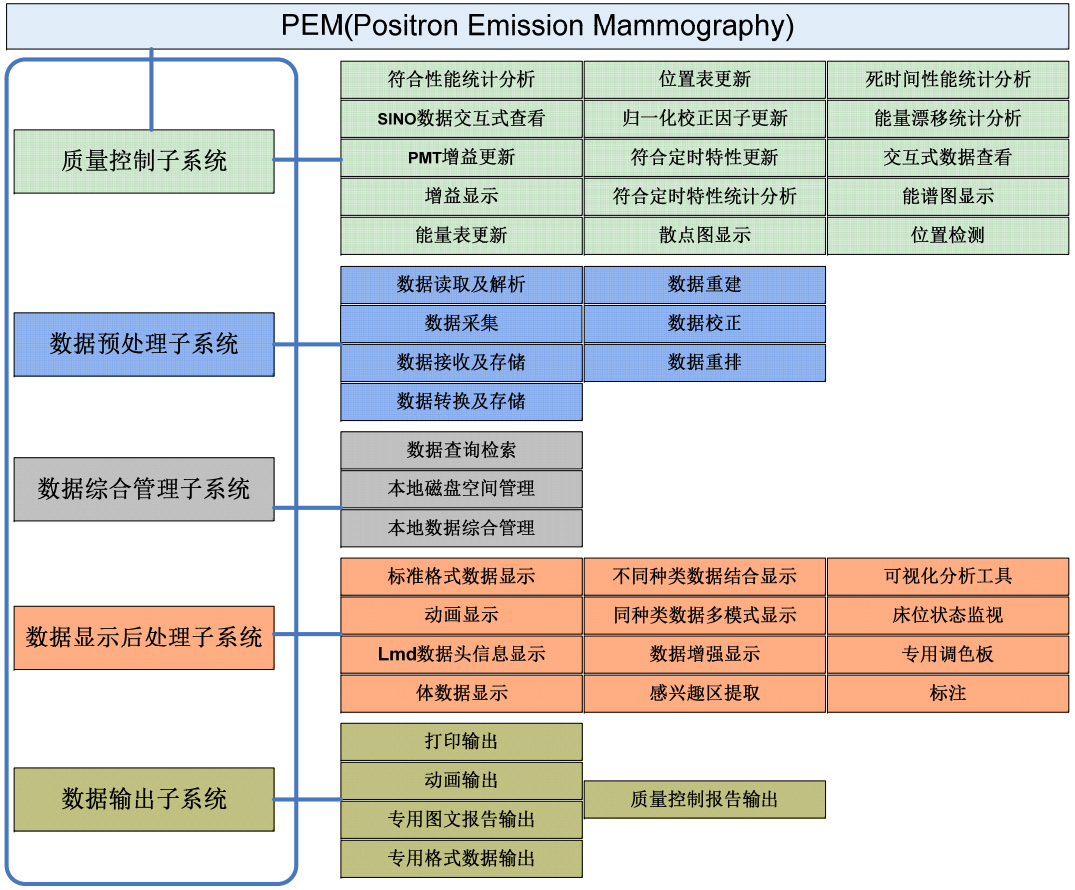


PEMi equipment

Software System

Software system includes:

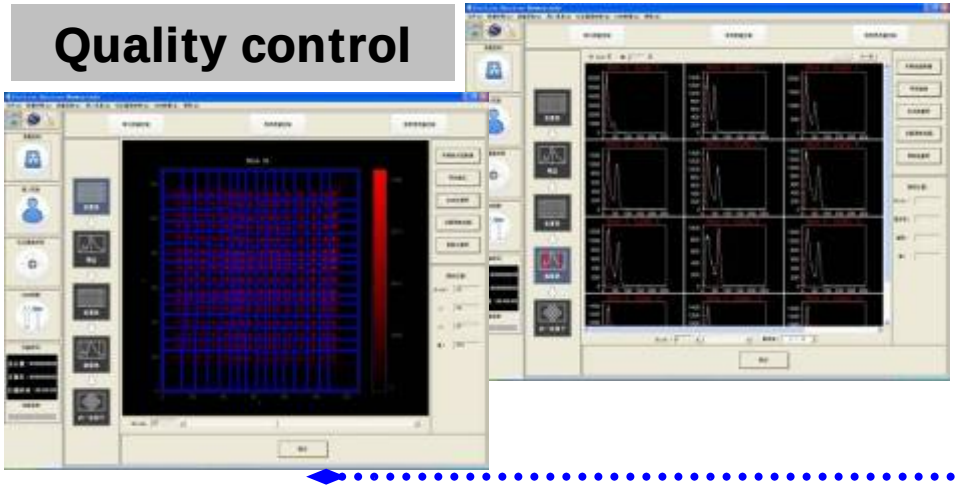
- **Quality Control**
- **Data pre-processing**
- **Data integration processing**
- **Data display**
- **Data output**

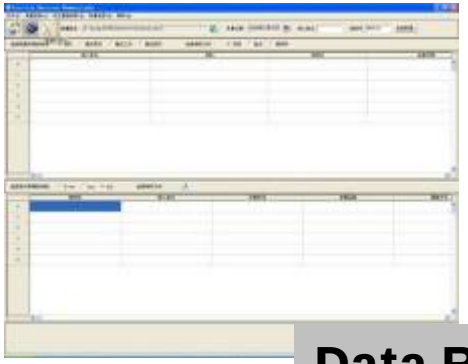


PEMi equipment

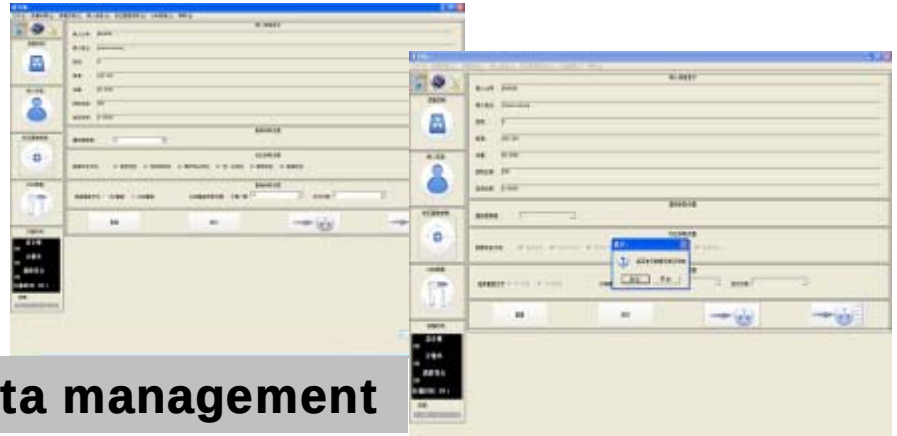
Software System

Quality control



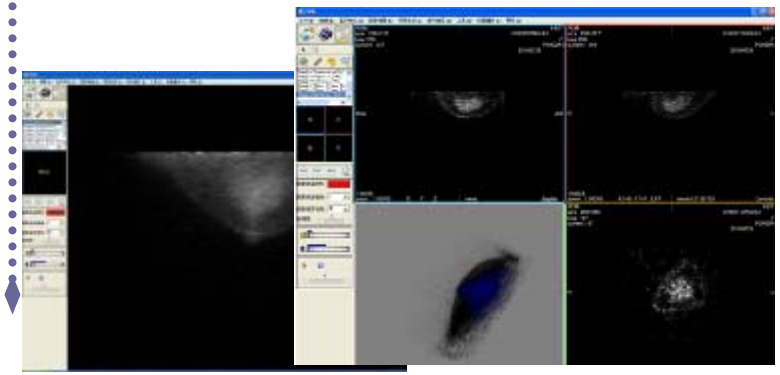


Data Retrieval



Data management

Data integration display

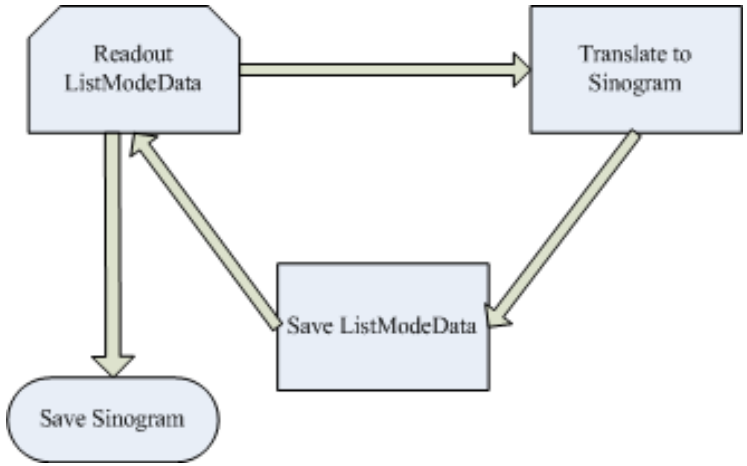


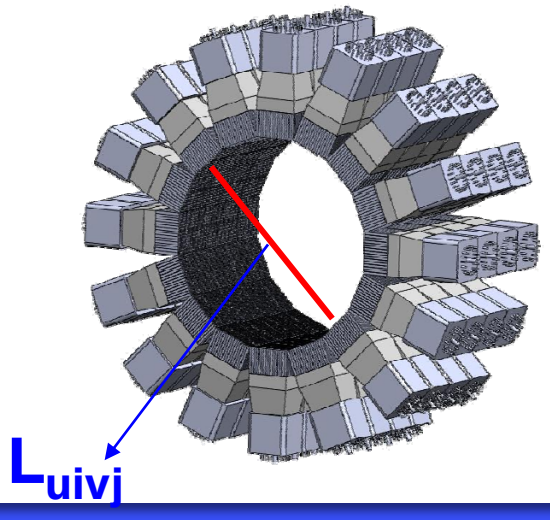
PEMi equipment

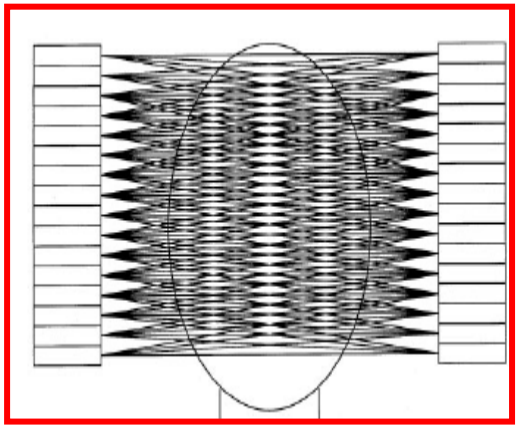
Data Correction

Correction Methods:

- Decay correction
- Dead time correction
- Random correction
- Normalization
- Scatter correction
- Attenuation correction

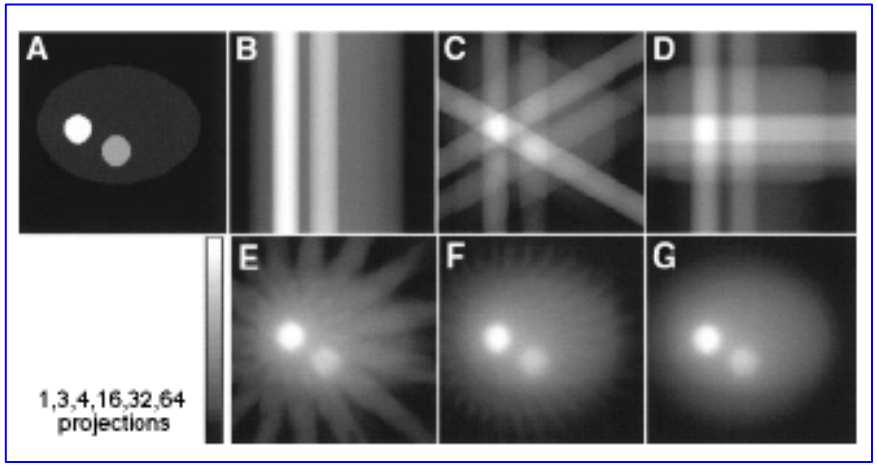




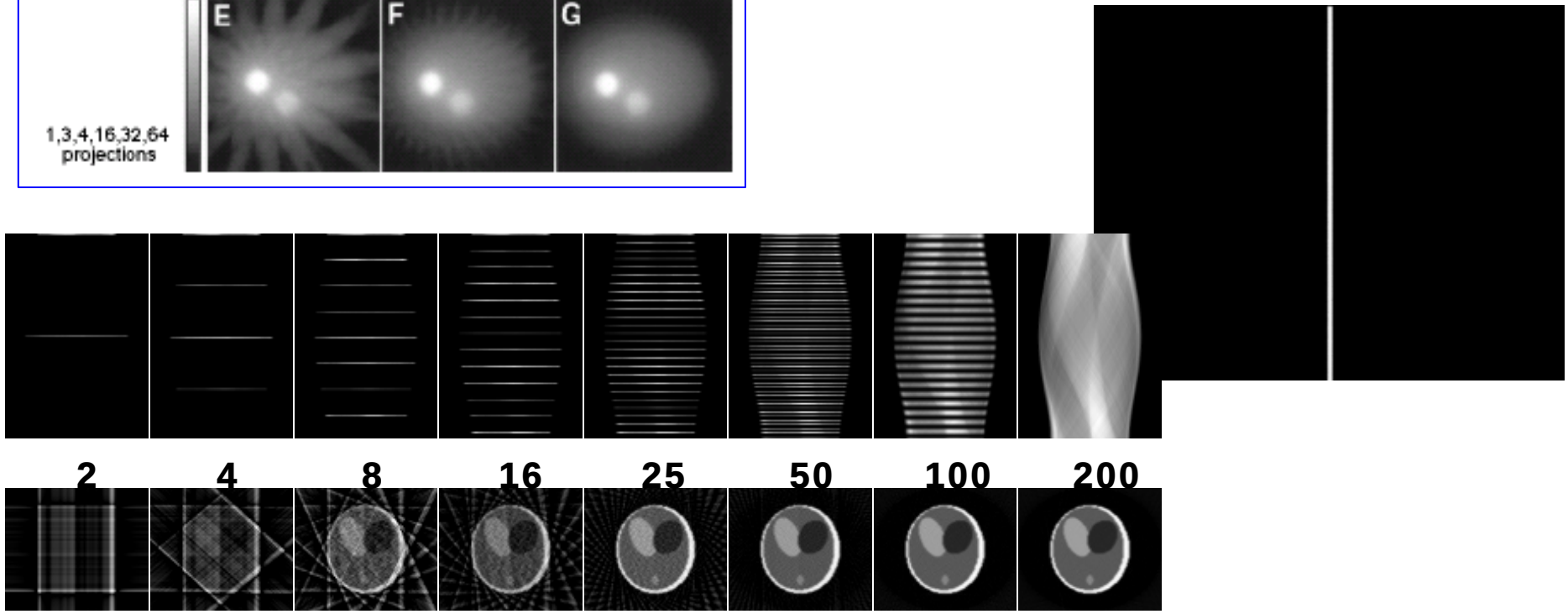


PEMi equipment

Reconstruction Algorithms

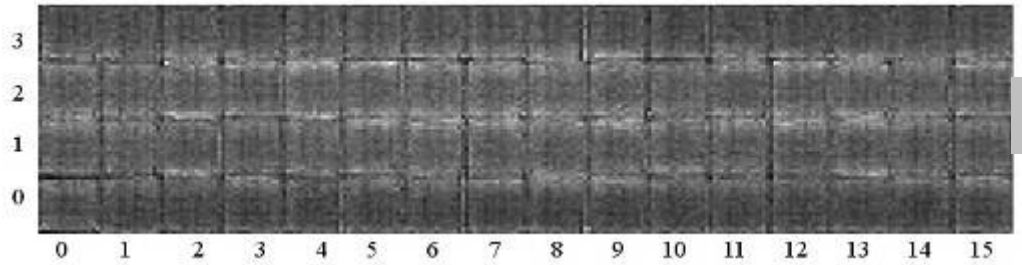


- FORE+FBP
- FORE+OSEM、3D OSEM

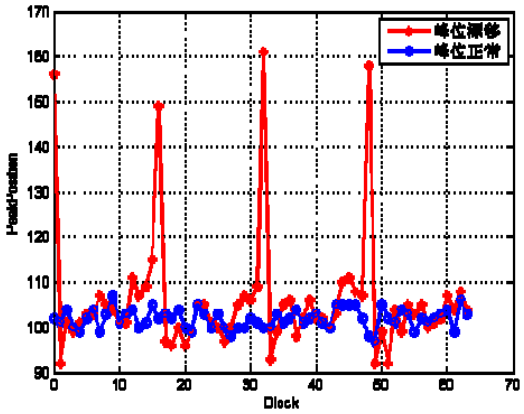


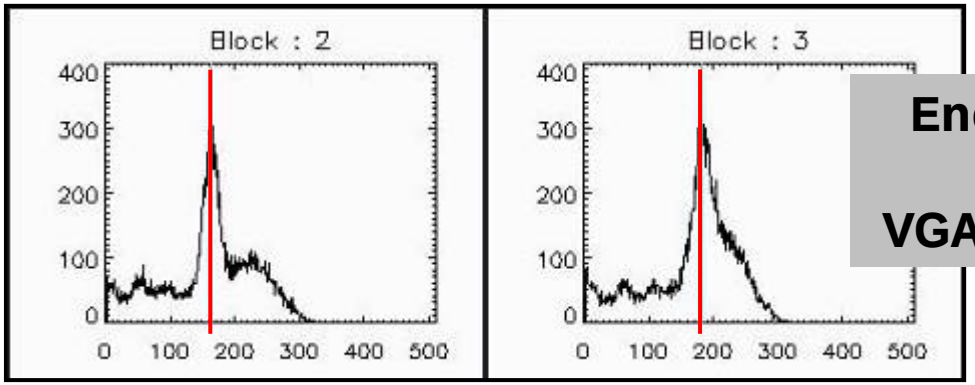
PEMi equipment

Quality Assurance & Control



Singles



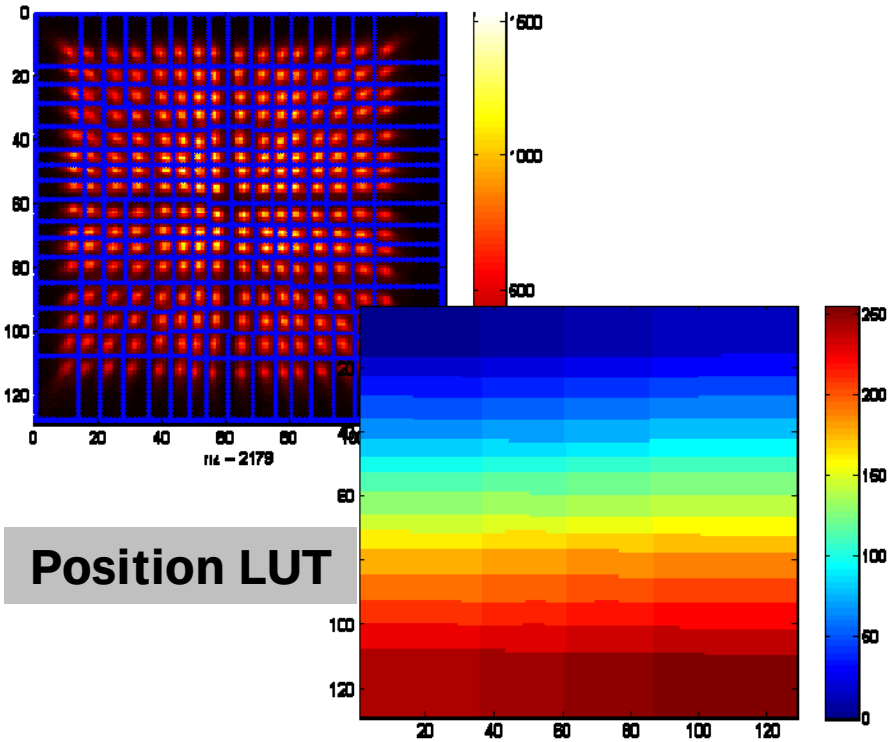


Energy & VGA Gain

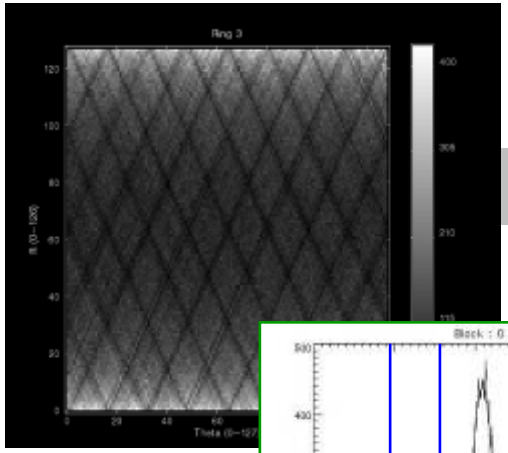
The daily quality control procedure quantitatively monitors the working quality of the scanner overtime.

PEMi equipment

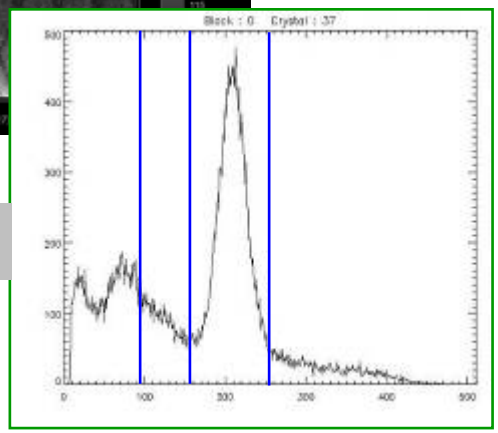
Quality Assurance & Control (cont.)



Position LUT



Sinogram



Energy LUT

Regular calibrations not only optimize image quality, but also provide the means to discover the potential for image artifacts before the patient scanning. Meanwhile, the calibrations also provide the system with a benchmark for counting variations.

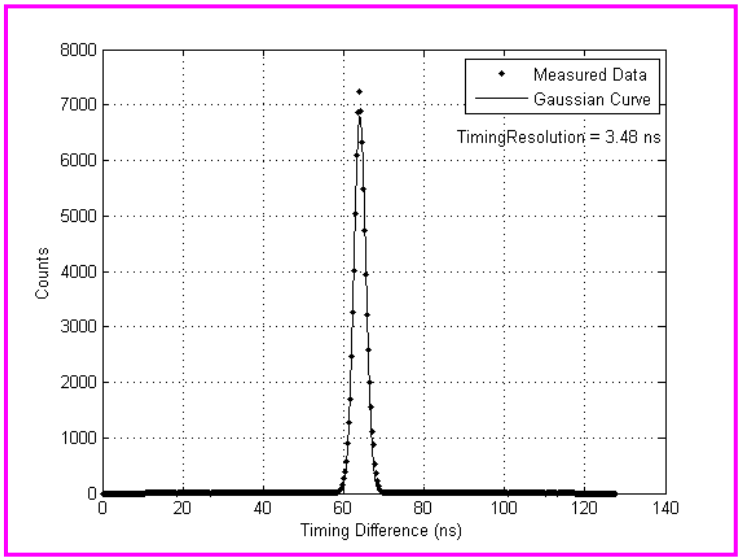
Outline

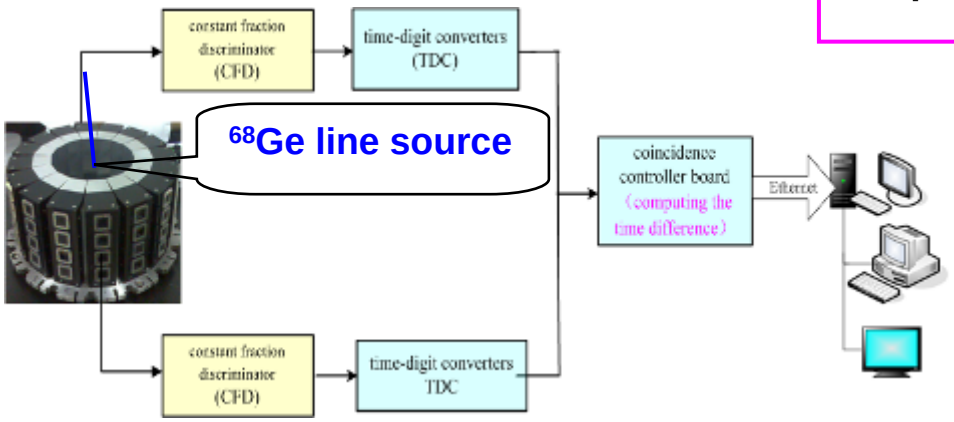
- Introduction of PEM
- PEMi equipment
- PEMi Performance
- Industrialization
- Conclusion

PEMi performance

Timing Resolution

^{68}Ge line source





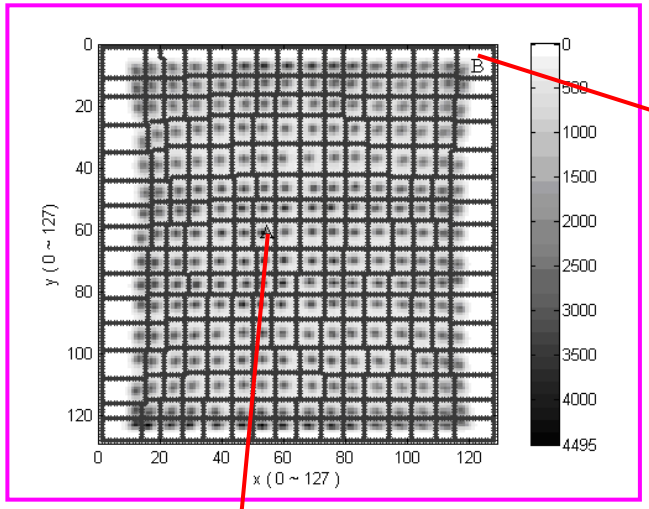
Timing Resolution：

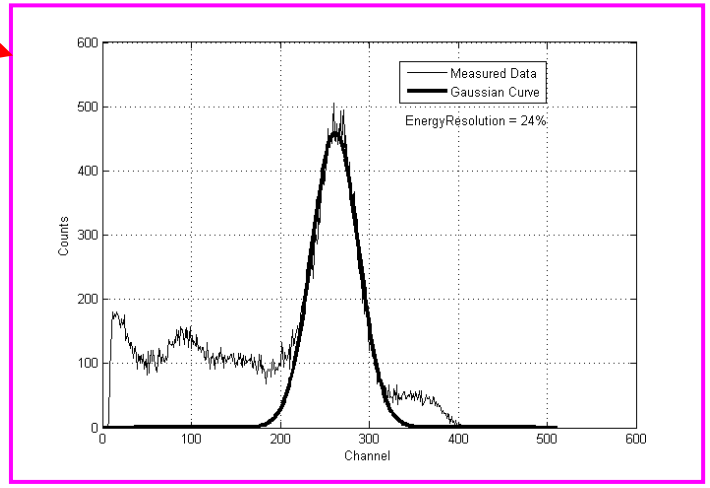
3.48 ns~4.13 ns;

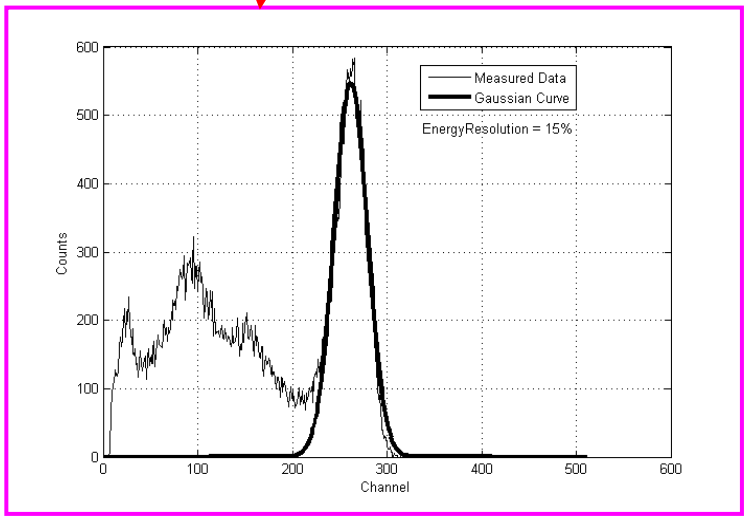
Average： 3.89 ns

PEMi performance

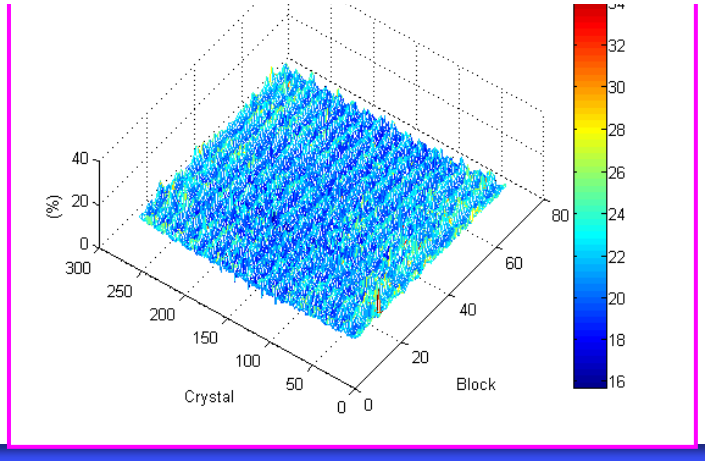
Energy Resolution







15%~35%, Average: 21%



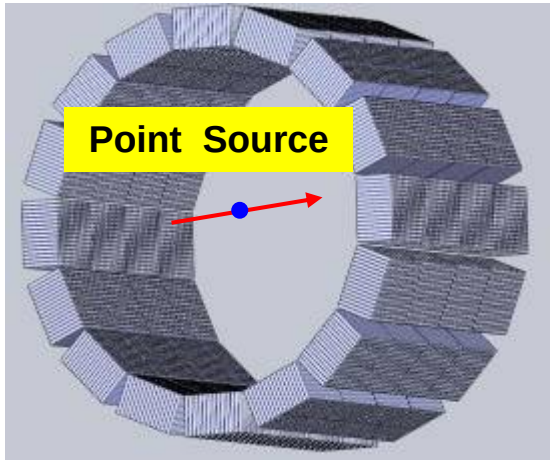
PEMi performance

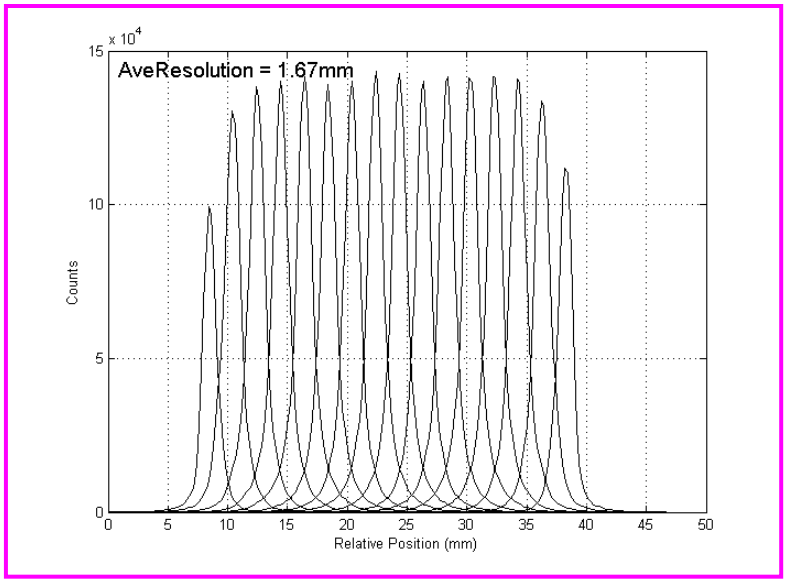
Intrinsic Spatial Resolution

Radionuclide：
^{22}Na Point Source；

Movement： along the central axis of the imaging aperture;

Step Size： 0.2mm





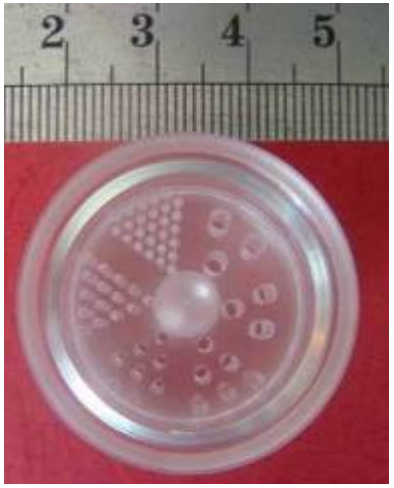
Intrinsic spatial resolution：

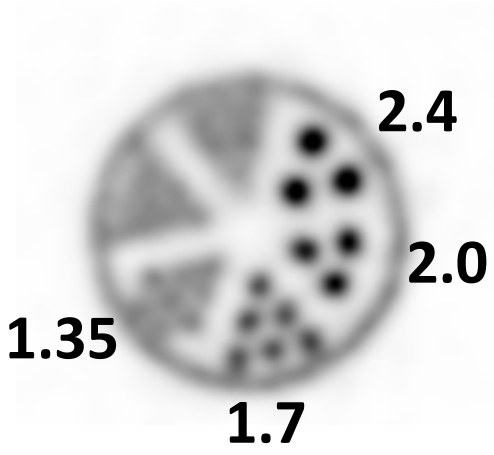
1.34~1.78 mm；

Average： **1.67 mm**

PEMi performance

Derenzo Phantom Imaging





ultra-micro hot spot phantom，
(Data Spectrum Corp., Chapel Hill, NC)

Rods Diameters： 2.4, 2.0, 1.7, 1.35, 1.00 and 0.75 mm

Reconstruction： FORE + 3D OSEM

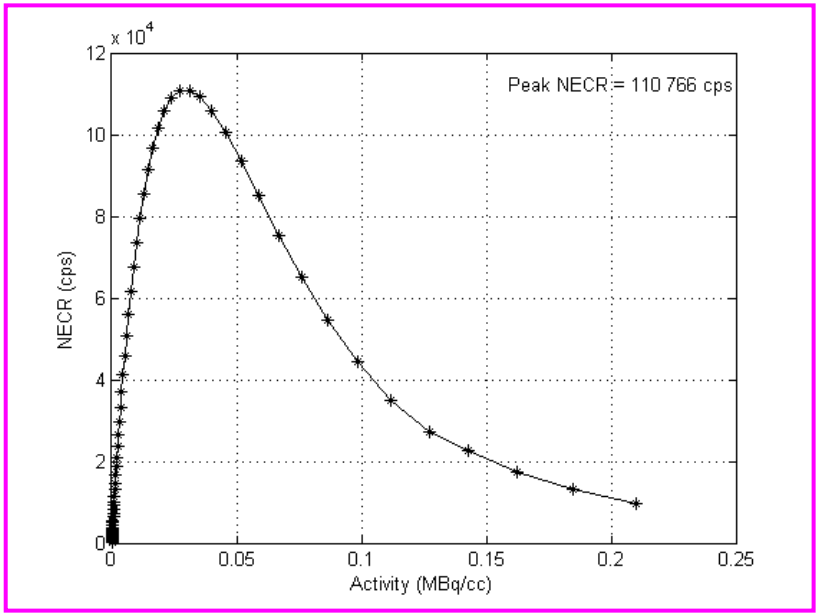
Resolving power：

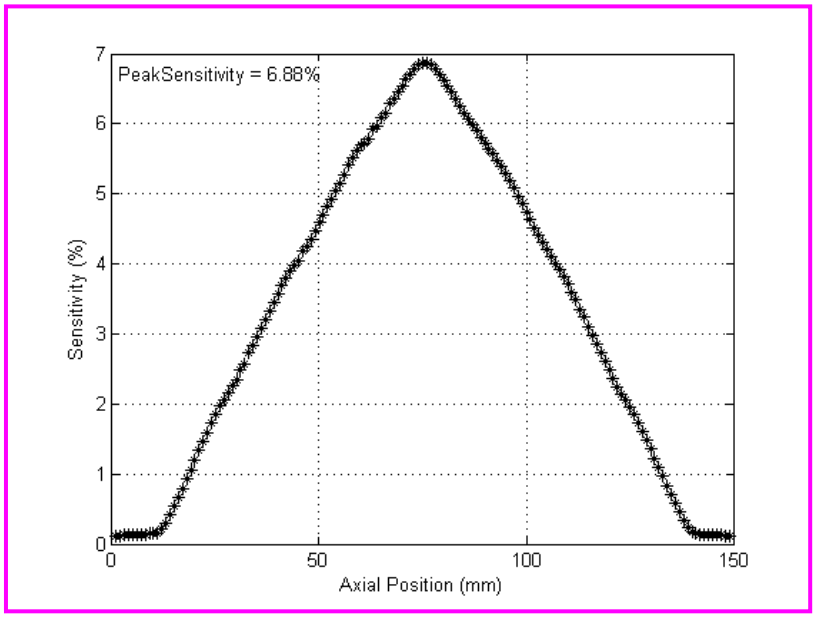
Identified "rods"： > 1.7mm；

Observed "rods"： 1.35mm

PEMi performance

NECR and Sensitivity





Energy Window：360~660 keV

Timing Window：6 ns

NECR（Peak）：110 kcps

Activity Concentration(Peak)：0.03MBq/cc；

Total Activity(Peak)：37.2MBq（1.005mCi）

Energy Window：360~660 keV

Timing Window：6 ns

Sensitivity（Peak）：6.88%

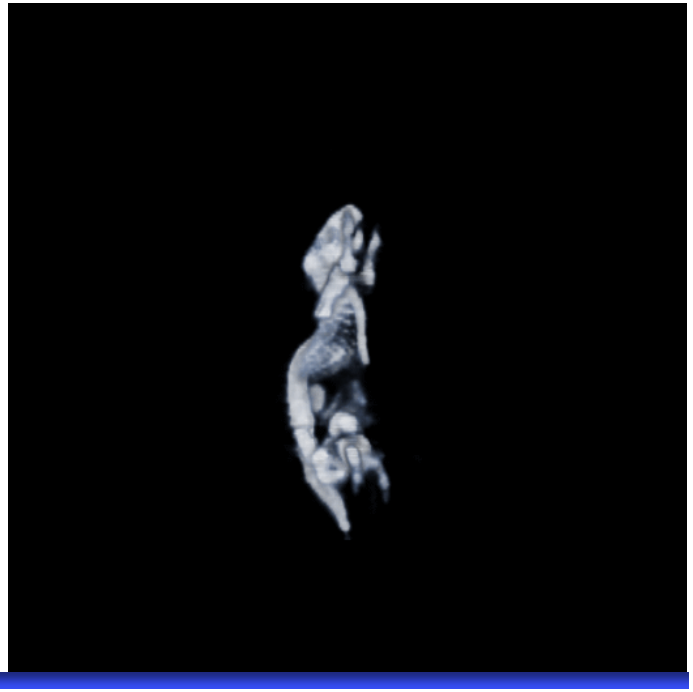
PEMi performance

Imaging Experiments

Self-made phantom imaging

Reconstruction

- FORE+ 2D, 3D OSEM
- normalization, random, attenuation and scatter correction applied



Bone scan of mouse

Outline

- Introduction of PEM
- PEMi equipment
- PEMi Performance
- **Industrialization**
- Conclusion

Industrialization

- For the regular of SFDA (State Food & Drug Administration)
- Defined as radioactive nuclear diagnosis device, and supervised as SFDA category Ⅲ medical instrument
- PEM must be passed through the compulsory inspection of BIMT before using it to clinical trials

Industrialization

Before upgraded

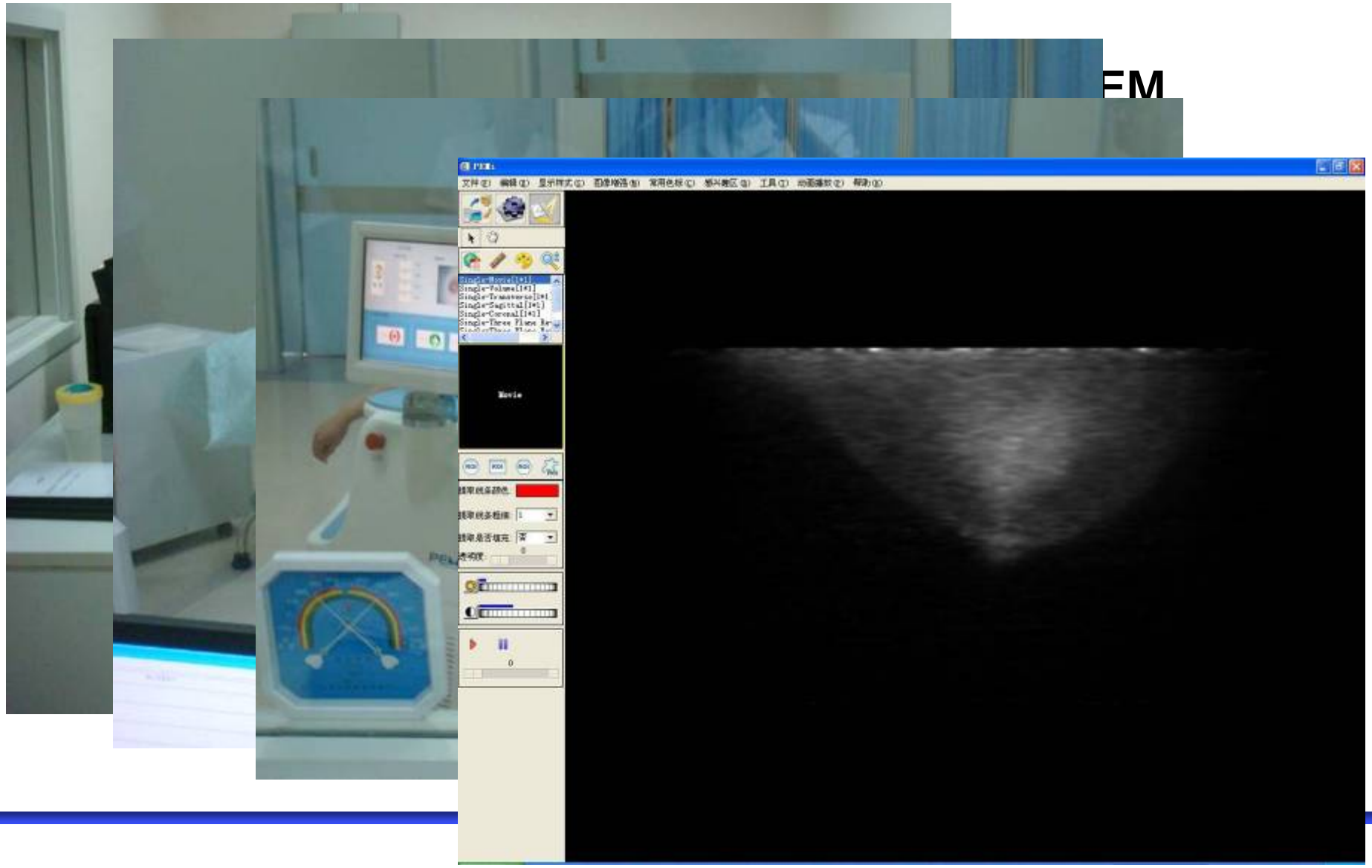
After upgraded

Industrialization- installation

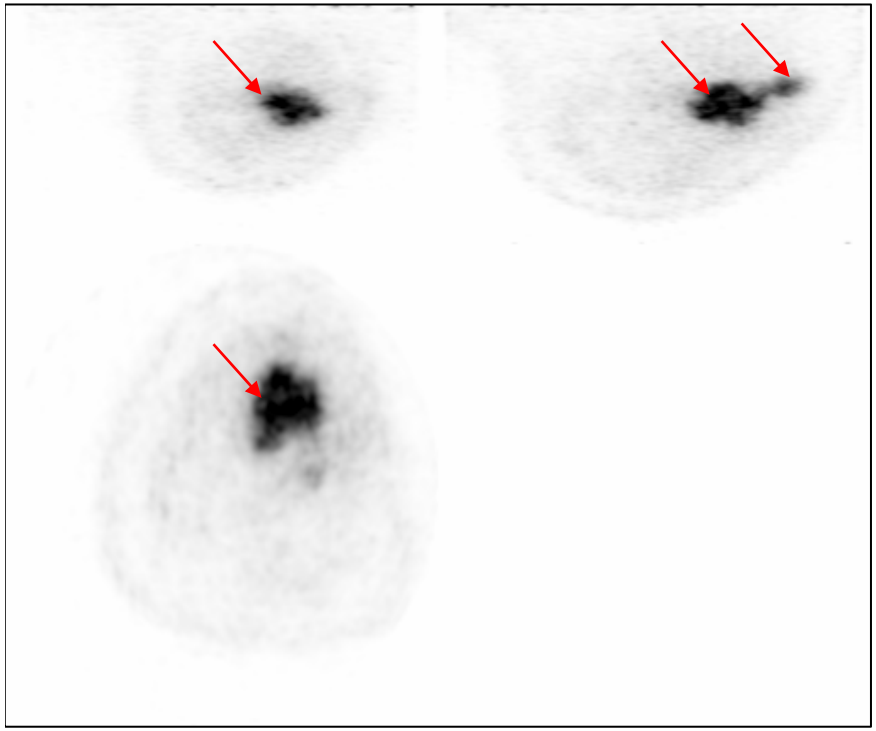
Institute of High Energy Physics, Chinese Academy of Sciences

Cancer Institute and

Industrialization-clinical trials



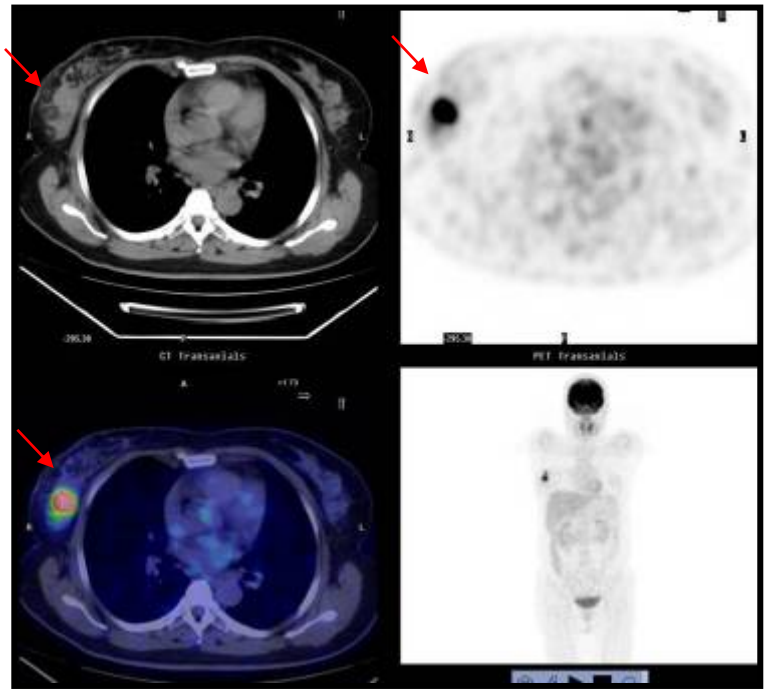
Industrialization-typical case



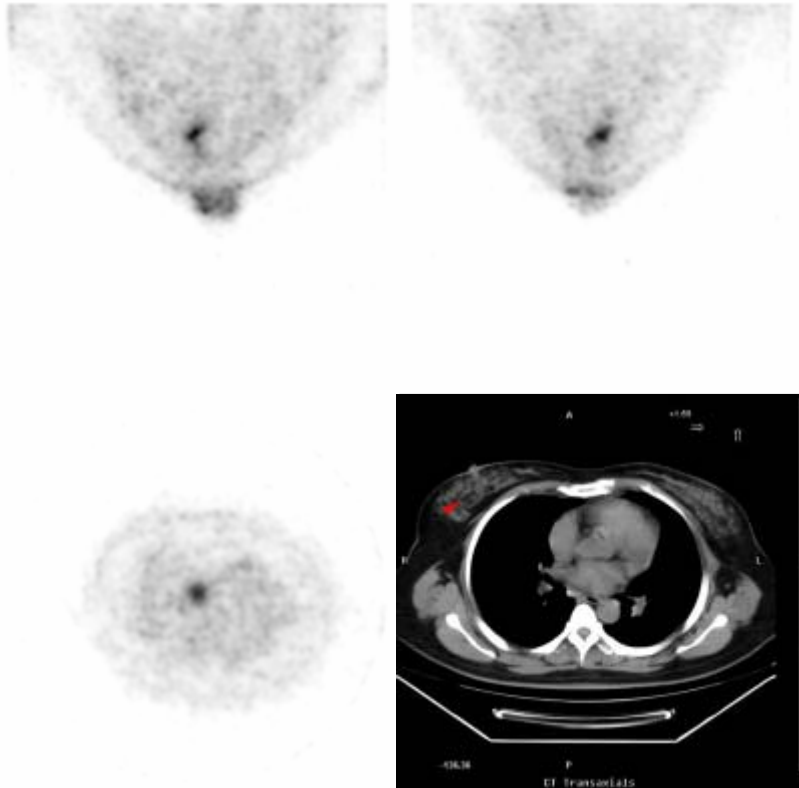
female，56 years old
solid intraductal papillary carcinoma in right breast

✓High-resolution imaging reflect more lesions in detail

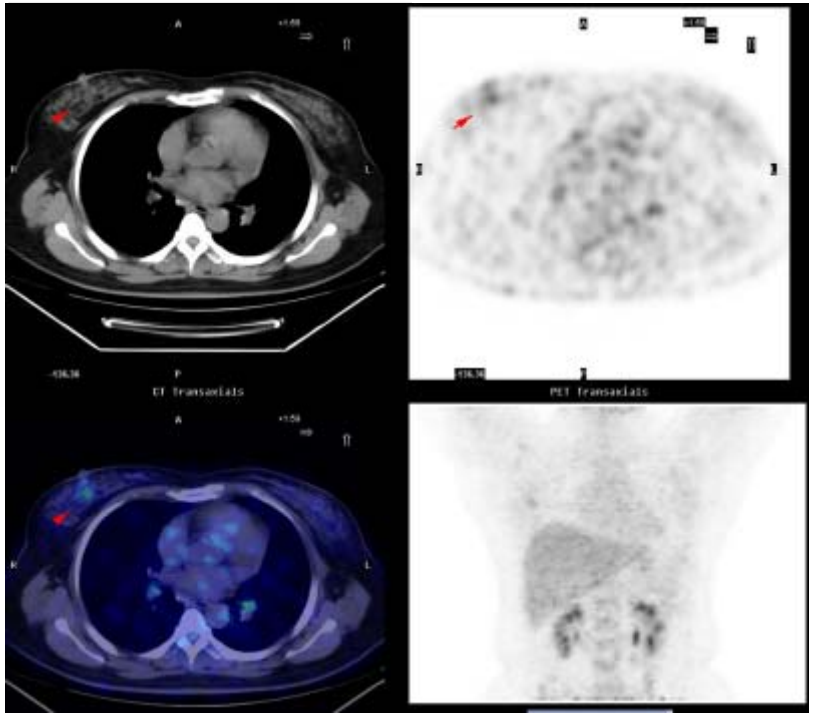
✓Benefit to adjuvant diagnosis



Industrialization-typical case



✓High-resolution and high-sensitivity facilitated the discovery of minimal change



female，49 years old

X-ray、CT、MRI

Suspected

Outline

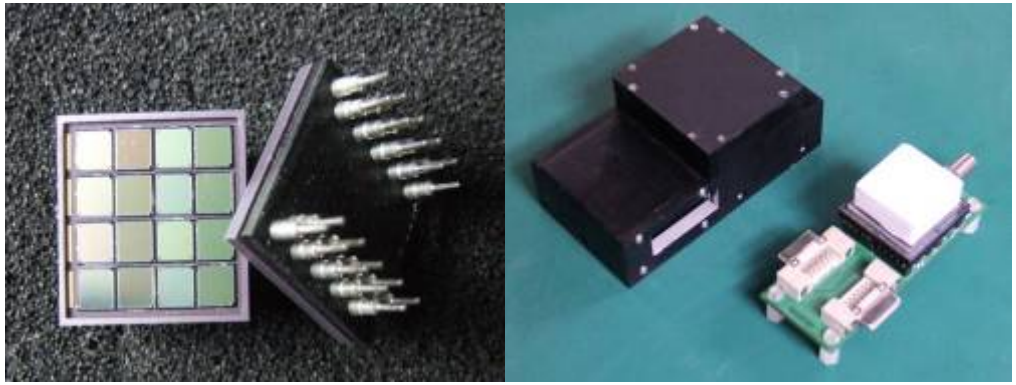
- Introduction of PEM
- PEMi equipment
- PEMi Performance
- Industrialization
- Conclusion

Before Conclusion

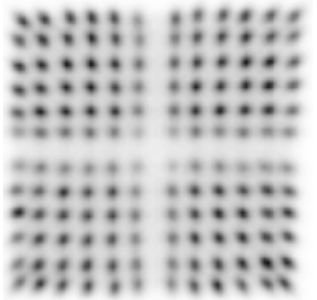
Possible upgrade of detector, electronics and others.

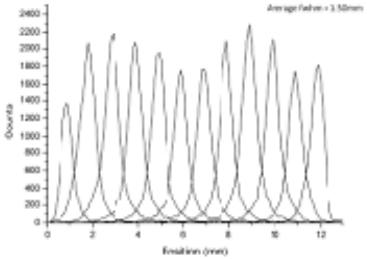
- **Detector: use of SiPM**
- **Electronics: more compact and integrated circuits**
- **Multi-modality ability: (eg. Integrated with a breast CT)**
- **puncture instrument add-on: in that case the planner detector may be needed**

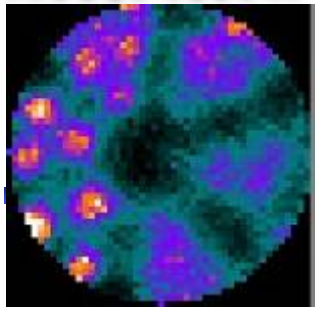
SiPM Detector

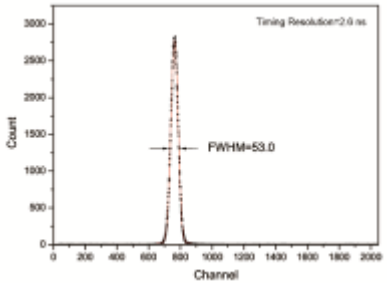


- 12×12 LYSO matrix
- 2×2 SPMArray4
- Quartz glass light guide





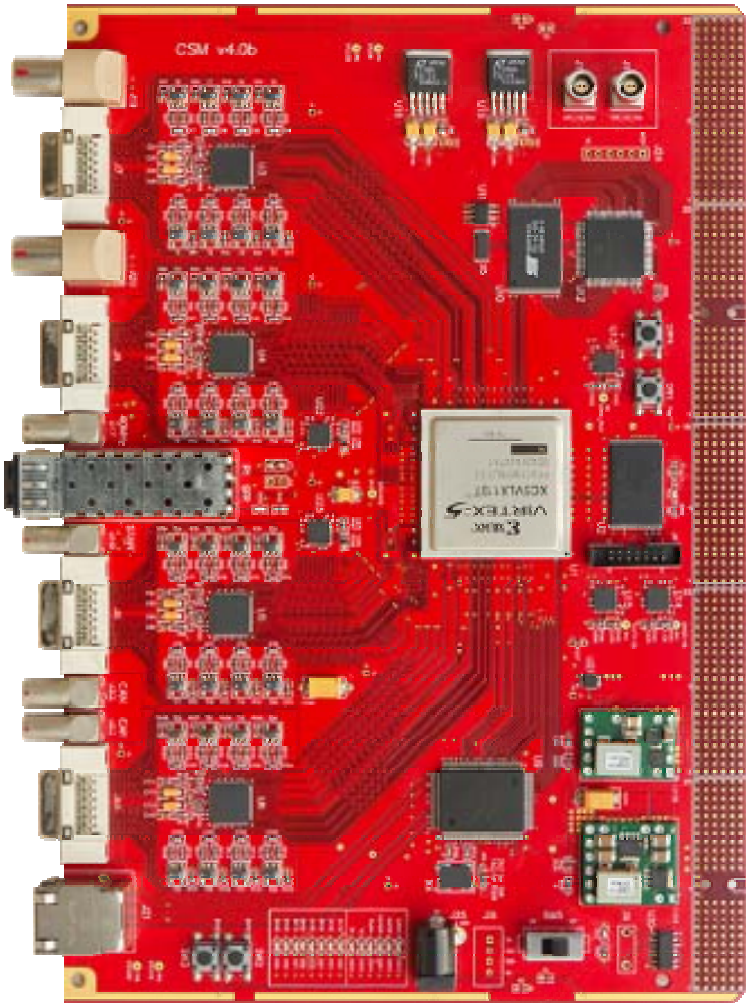




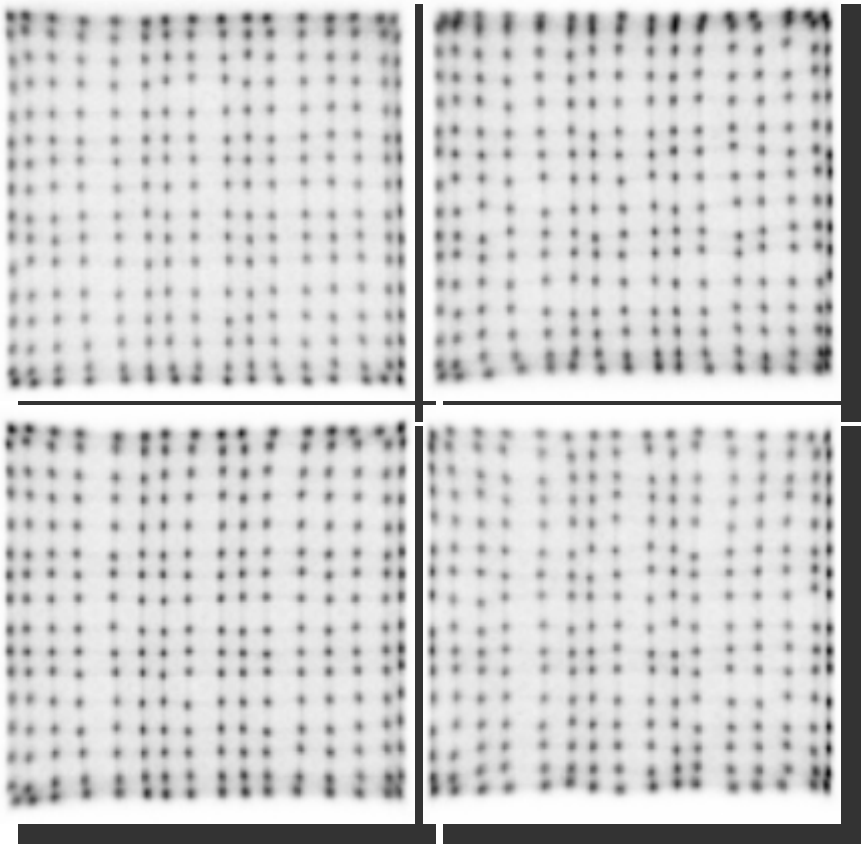
- ✓ All the crystals in the matrix can be identified
- ✓ Average energy resolution=17%
- ✓ Intrinsic spatial resolution ~ 1.5 mm
- ✓ Timing resolution = 2.6 ns
- ✓ 1.7 mm hot FDG phantom can be identified
- ✓ Insensitive to 1.5T magnetic fields

Upgrade of Sampling electronics

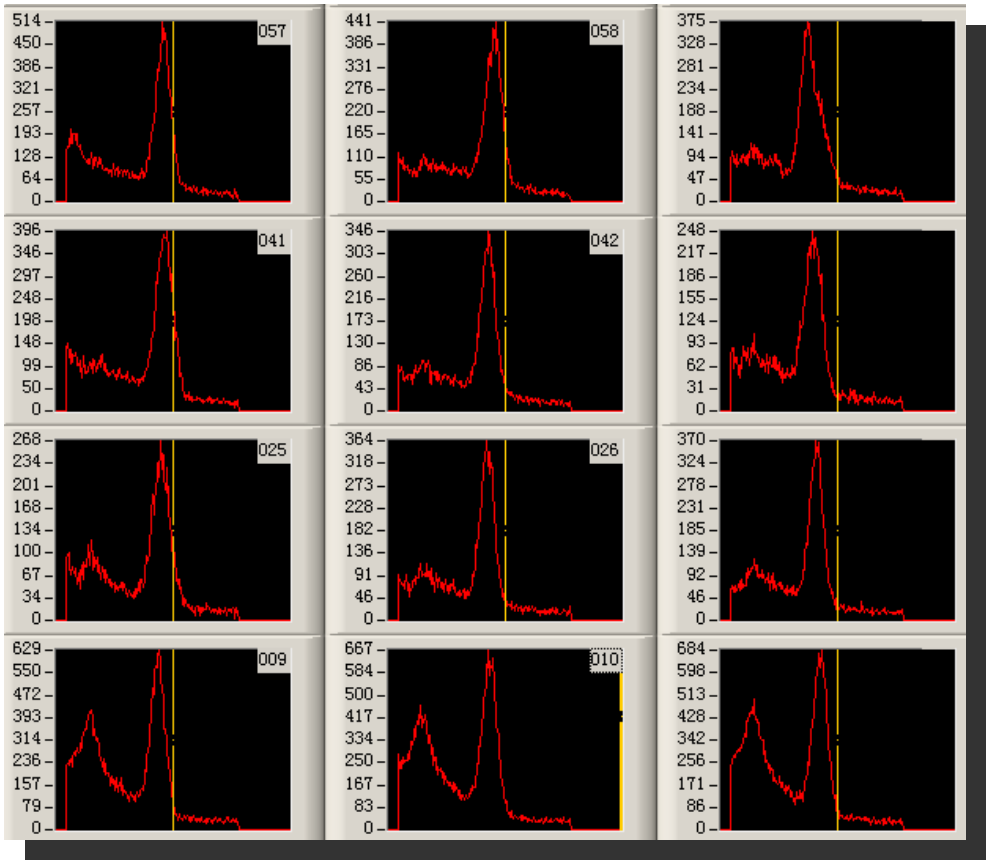
- high speed ADCs, which cope with 32 analog signals.
- Precision time measurement of up to 50.5ps time resolution inside FPGA.
- On board variable gain amplifier for the input analog signals.
- 3.75Gbps optical links to new CPM, 1Gbps Ethernet to computer.
- Same size as the old CSM board, 9U CPCI, 8-layer PCB.
- Instead of Multi-Board structure, new CSM use a single board.



Upgrade of Sampling electronics

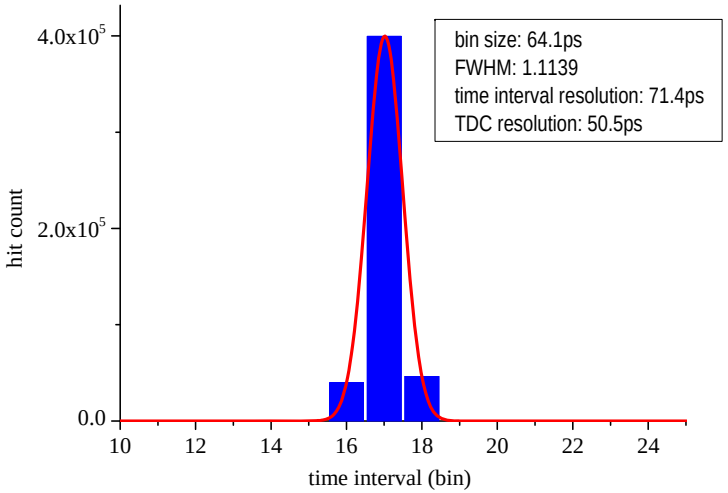


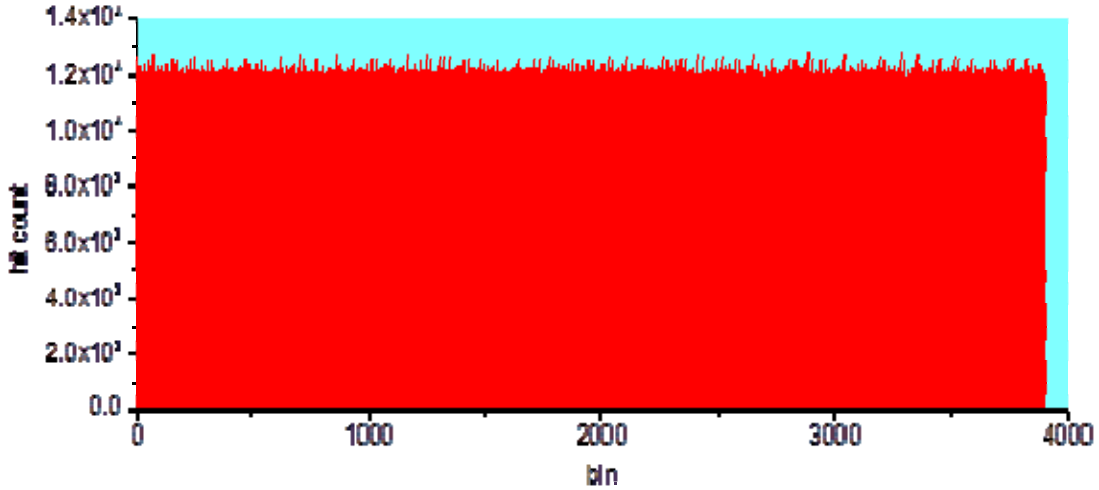
Example of flood images



Example of energy spectra

Upgrade of Sampling electronics





Time resolution of build-in TDC

Differential nonlinearity of TDC

Upgrade of Coincidence electronics

- **No bucket needed**
- **Stand-alone Mode:**

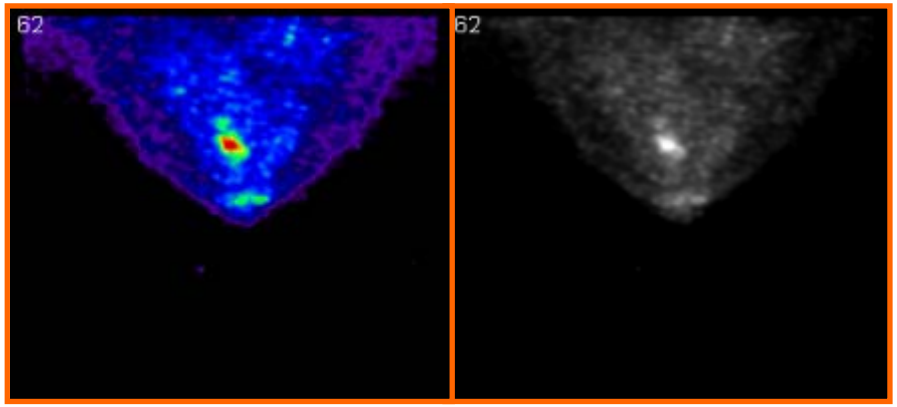
For small and medium scale detectors, it can run in a stand-alone mode!

- **Cascade Mode:**

Add single fiber channel which not only can be used for self testing but also can be used to cascade CPMs.

Conclusion

We have developed a dedicated PET for breast cancer detection with cylindrical geometry named PEMi. The initial performance results reflect a promising potential of this system for early breast cancer detection.



Detector rings	64		Radial image resolution	1.58 mm
Number of slices	127		Axial image resolution	1.30 mm
Radial FOV	110 mm		Sensitivity	6.88%
Axial FOV	128 mm		Energy resolution	21%
Intrinsic resolution	1.67 mm		Timing resolution	3.89 ns

Thanks for your attention!