Avanzamenti e prospettive future delle tecniche e dei metodi di rivelazione per l'imaging in medicina nucleare

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What is emission tomography?

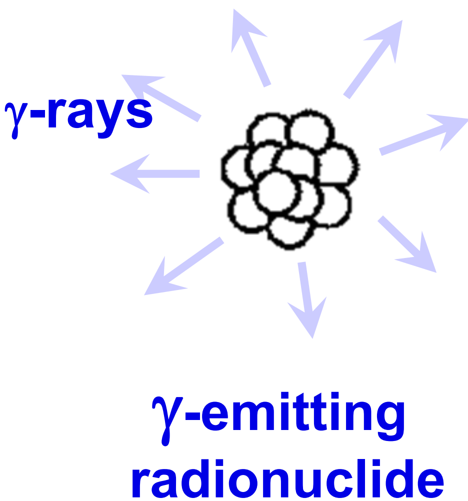
- Nuclear imaging techniques,based on the detection of photons in vivo, emitted by a radio-tracer injected into the patient.
- Diagnostic radiopharmaceuticals or tracers reflect physiological function with limited anatomical information

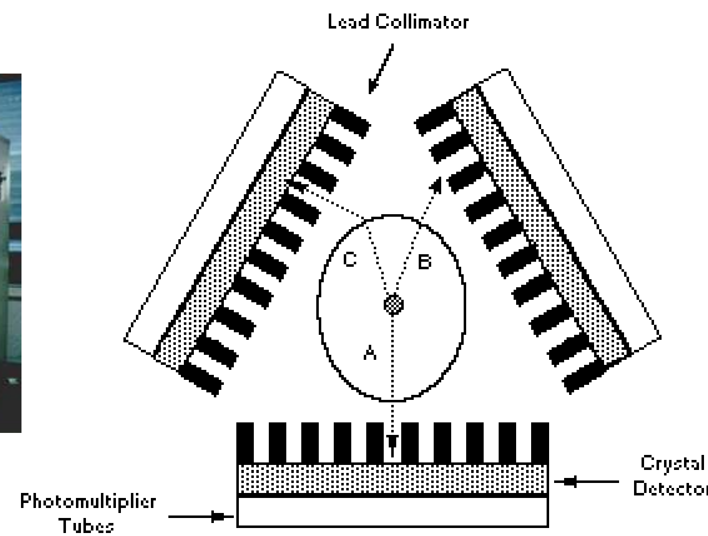
- Two different techniques:
    - **Single Photon Emission Tomography (SPECT):** a tracer molecule is labelled with single γ-emitting radionuclides. (Tc99m)
    - **Positron Emission Tomography (PET):** a tracer molecule is labelled with positron-emitting radionuclides (18F, 11C).

SPET basic physics: single detection

Most common nuclear imaging device (~ 22K units worldwide)

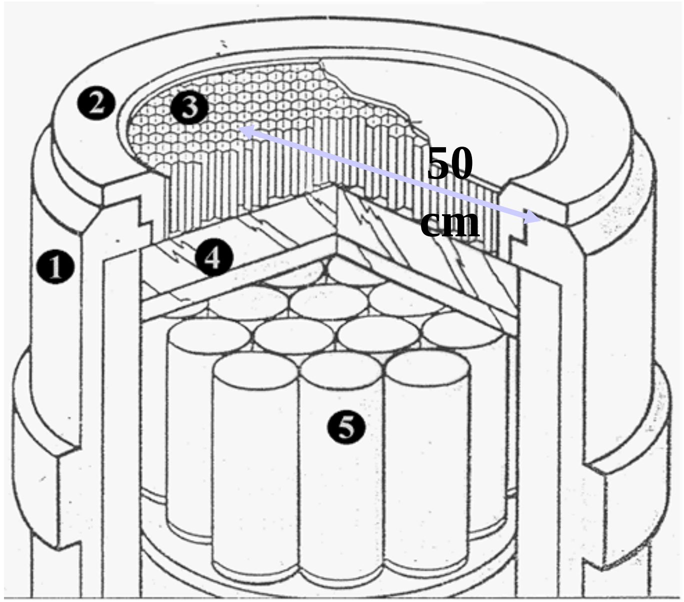
Single photon counting system Based upon NaI(Tl) scintillation detectors



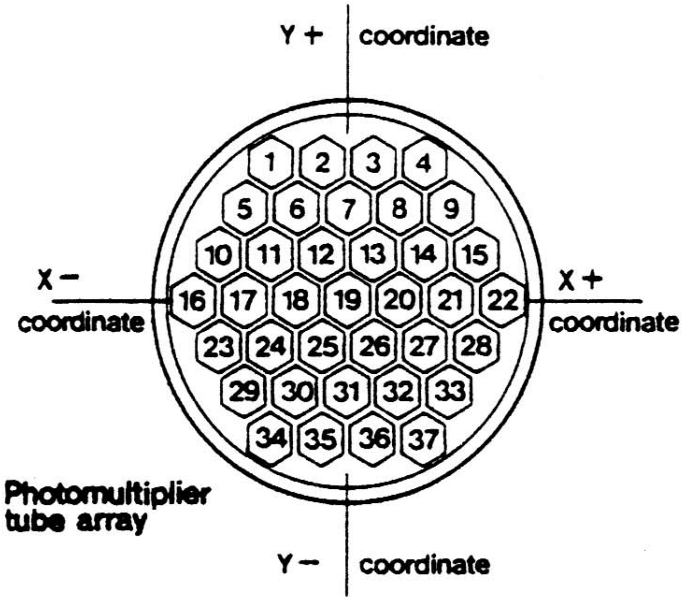


In contrast to PET scanners,
SPET radiation detectors typically rotate around the subject.

Imaging of Radio-isotopes : Anger Camera Basic



1. Housing
2. Lead shield
3. Collimator
4. NaI(Tl) crystal
5. PMTs

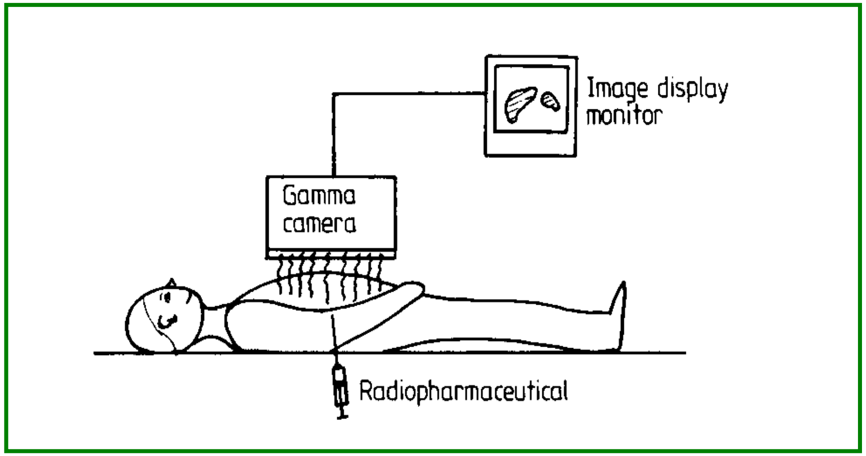


Four output signals

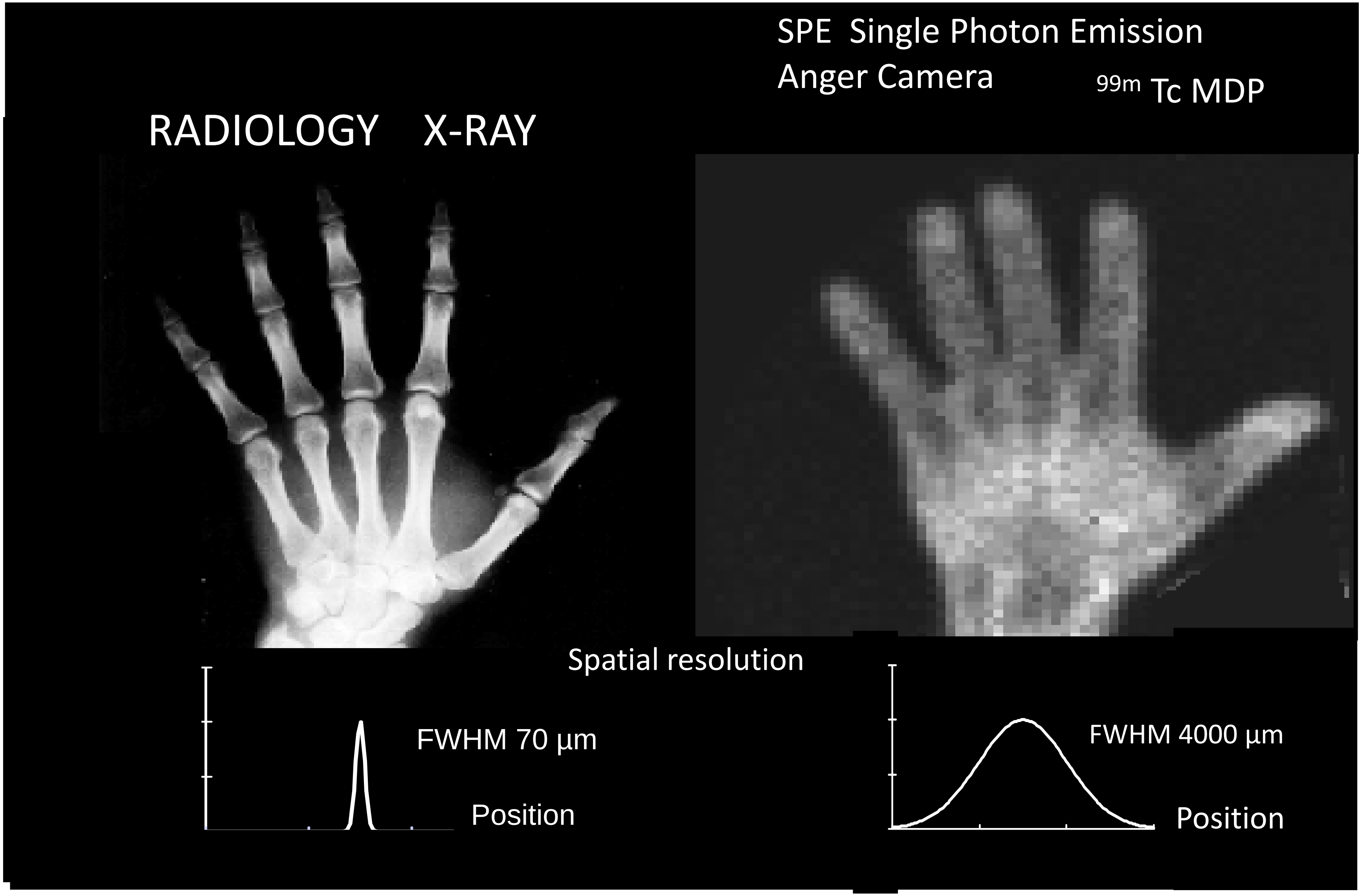
$$X=(x^+-x^-)/(x^++x^-)$$

$$Y=(y^+-y^-)/(y^++y^-)$$

Intrinsic Saptial Resolution ≈ 4 mm

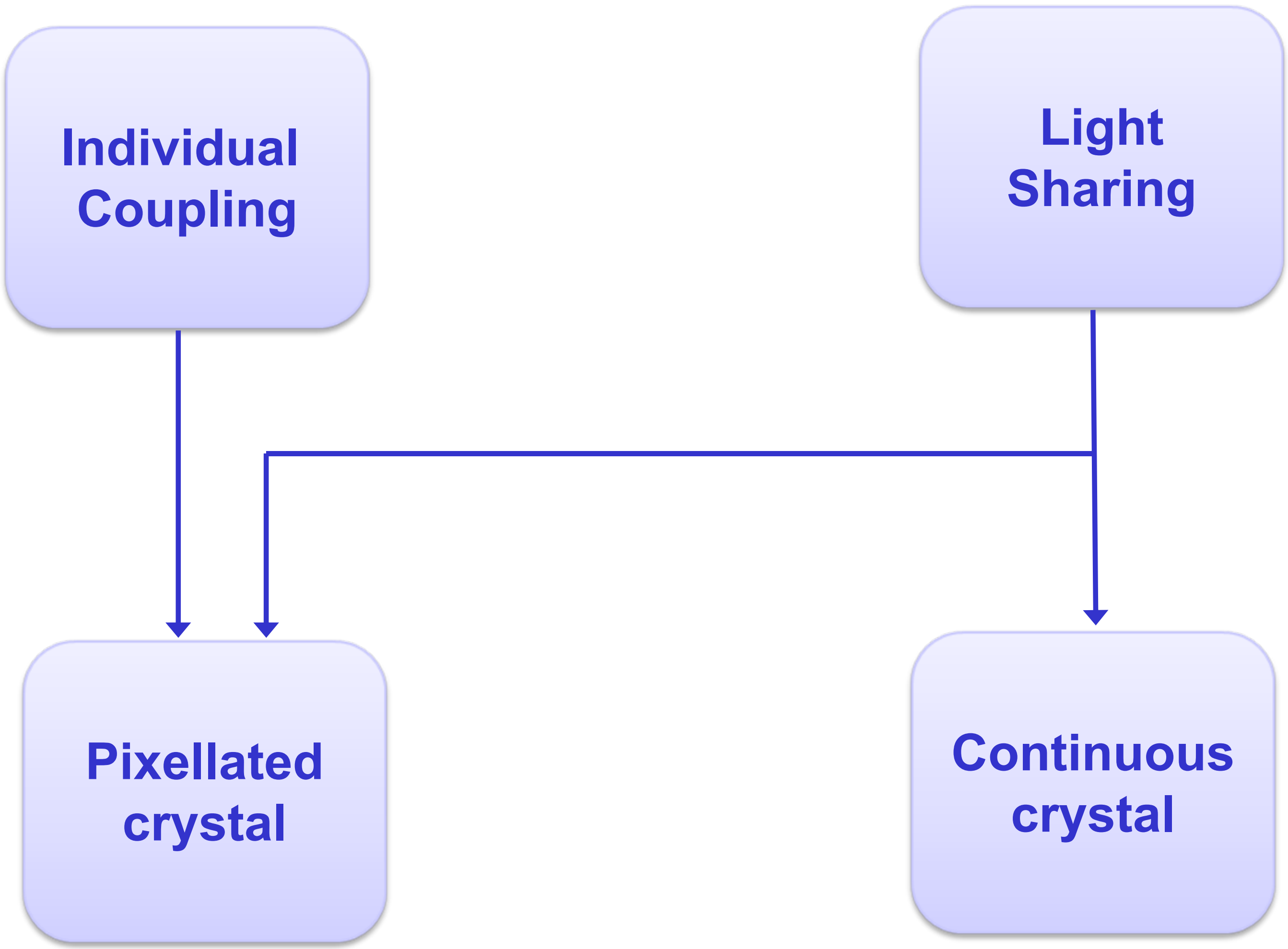


Relation To Anatomic Imaging



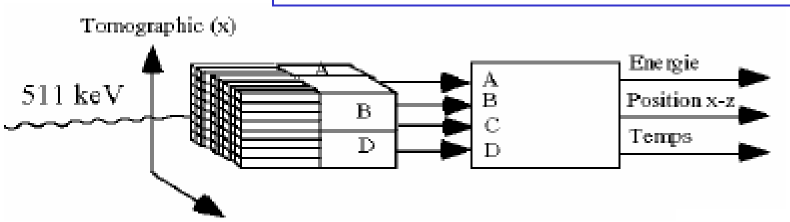
SPECT and PET detectors

Scintillation crystal read-out technique fall in the following categories



The most diffused PET Light Sharing: Block Detector

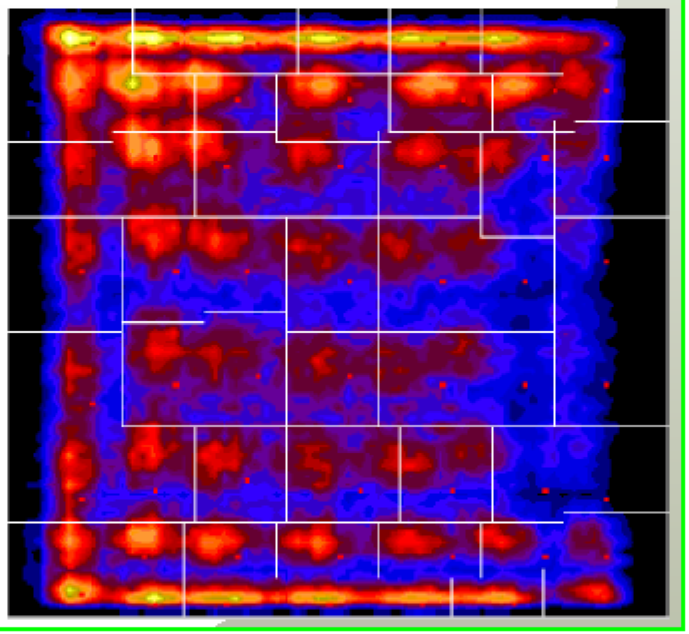
Casey & Nutt, *IEEE TNS* 33:460-3, 1986



x=(A+B)-(C+D)/(A+B+C+D)

z=(B+D)-(A+C)/(A+B+C+D)

EXACT HR Block

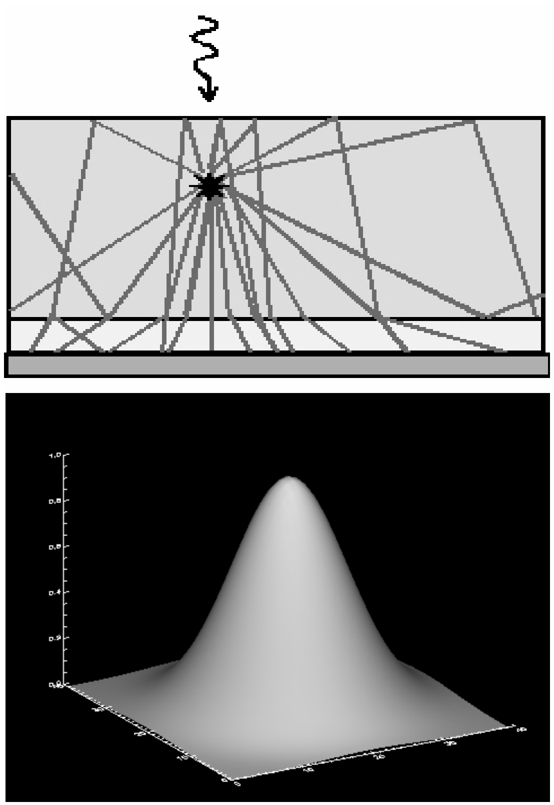


- Array of (semi discrete detectors measured by 4 square PMTs
- Event positioning from light distribution probability map
- Crystal identification by look-up table
- Resolution loss due to
  - photon statistics
  - non linear positioning & distortion
  - pile-up at high rate

Courtesy of Roger Lecomte Sherbrooke University

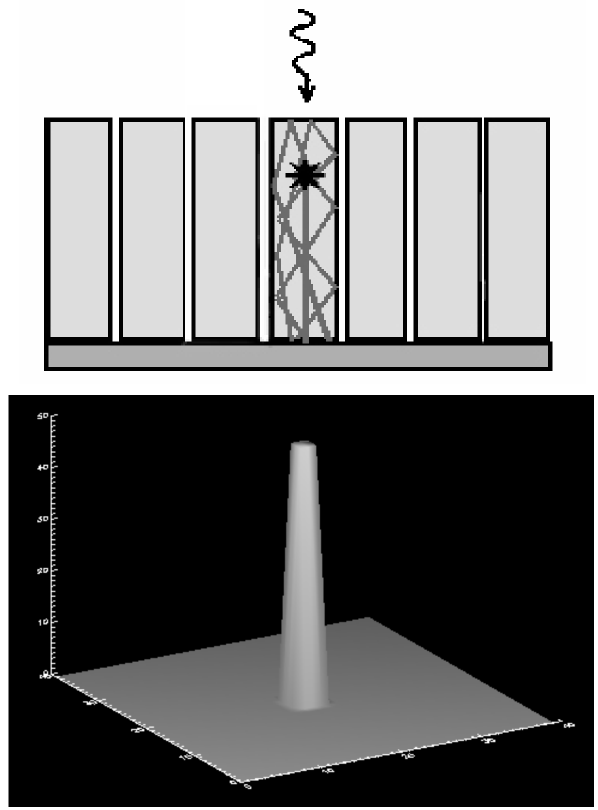
Scintillation crystal read-out technique
Light Point Spread Function and critical angle θ_c

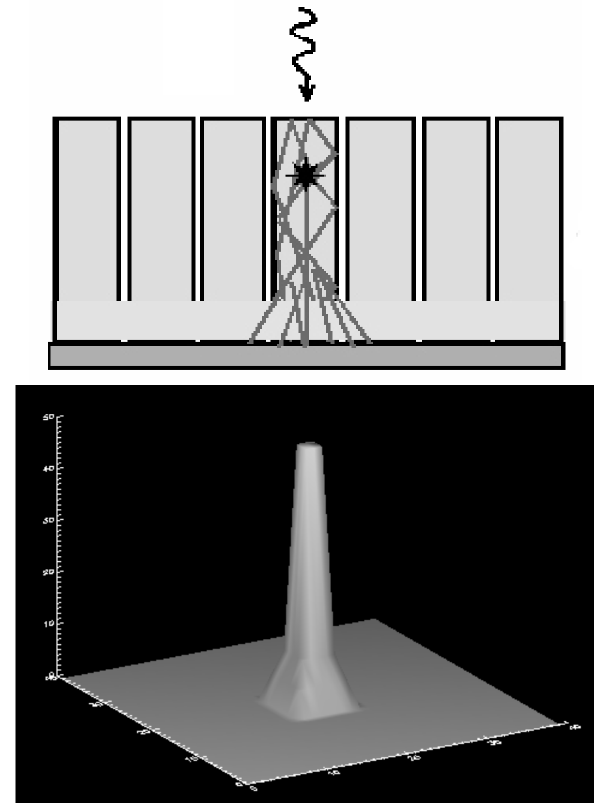
Continuos crystal / PMT glass window



$$\vartheta_c = sen^{-1}\left(\frac{n_2}{n_0}\right) = 52^o$$

Pixellated crystal / PMT glass window



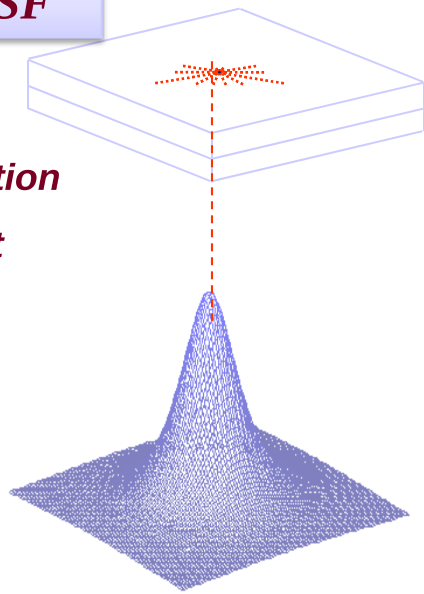


Light output angle < 45°

Position arithmetic and ***intrinsic spatial resolution*** *by light sharing*
Image and scintillation light PSF

Light PSF

Scintillation event



$$X_C = \frac{\sum_j n_j x_j}{\sum_j n_j}$$

where

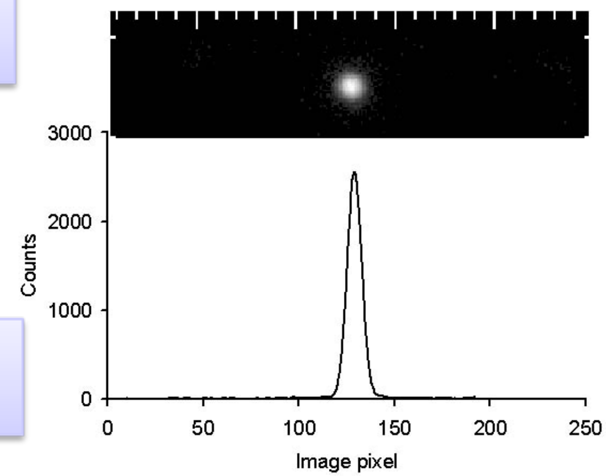
x_j represents the linear weight associated to the anode array

$$n_j = \sum_k n_{k,j}$$

is the projection of the charge collected along the J-th column

Image PSF

$$\sigma_{imm} \cong \frac{\sigma_{PSF}}{\sqrt{n_{phe}}}$$



$$FWHM_{PSFimage} = 2.35 * \sigma_{Xc}$$

$$\sigma^2_{X_c} = \sum_i \left(\frac{\partial X_c}{\partial n_i} \right)^2 \sigma^2_{n_i}$$

Spatial Resolution

$$SR = PSF_{imm} / L \qquad L = \frac{dX_{measured}}{dx_{mech}}$$

L is ideally =1

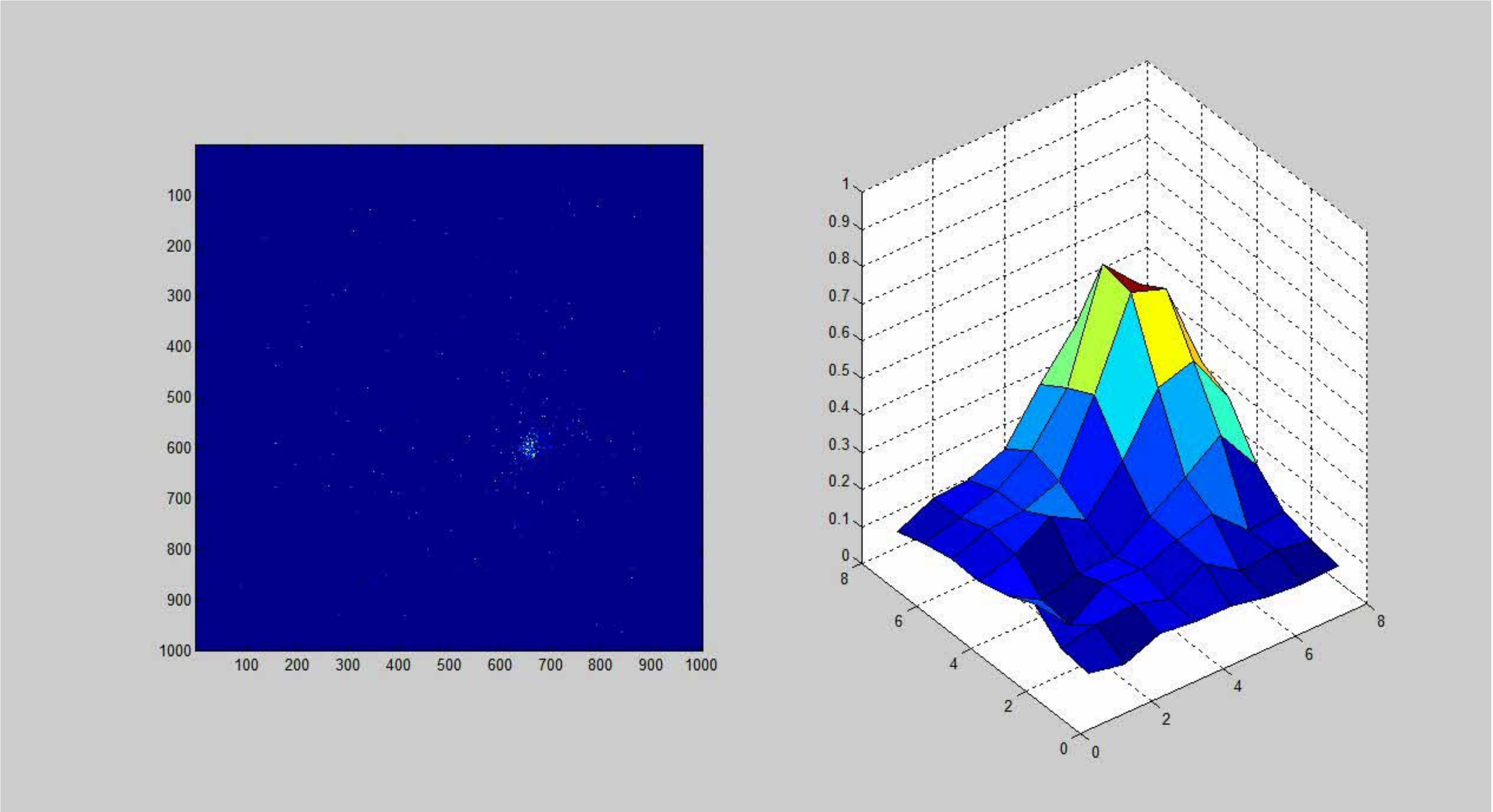


Image reconstruction of an irradiation spot (Tc ^{99m})

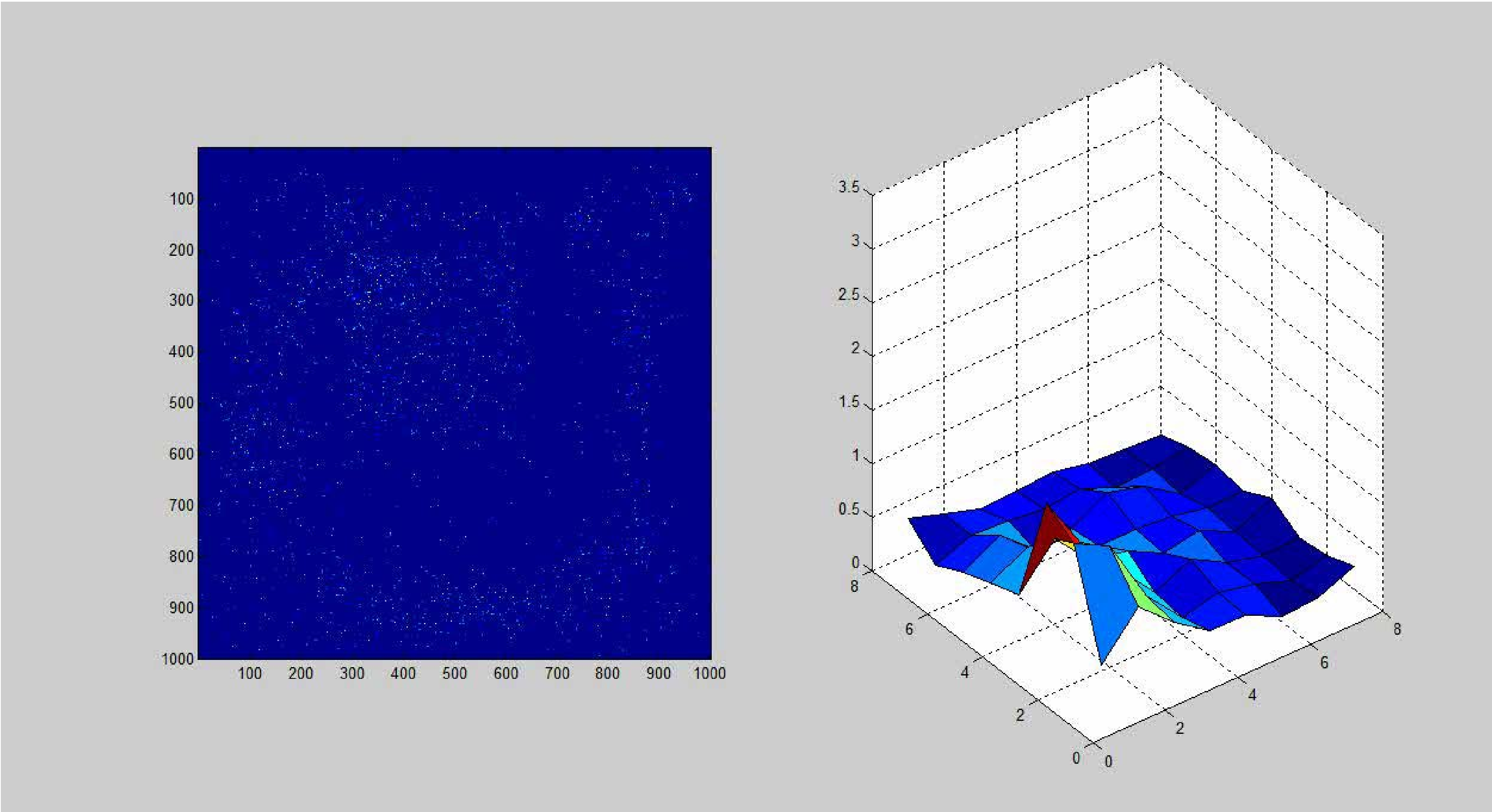
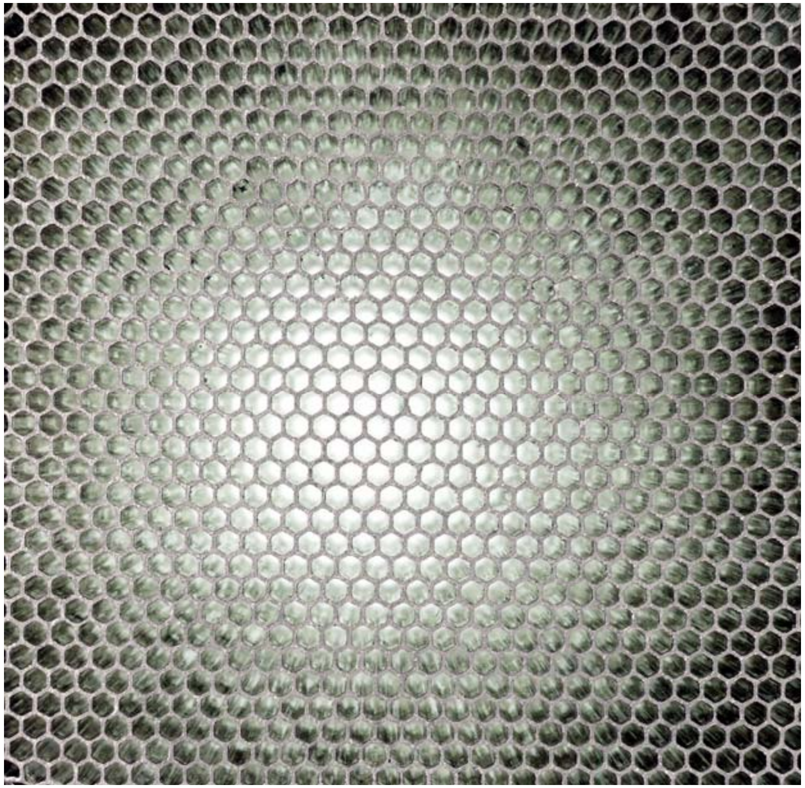


Image reconstruction of a collimator flood irradiation (Tc ^{99m})

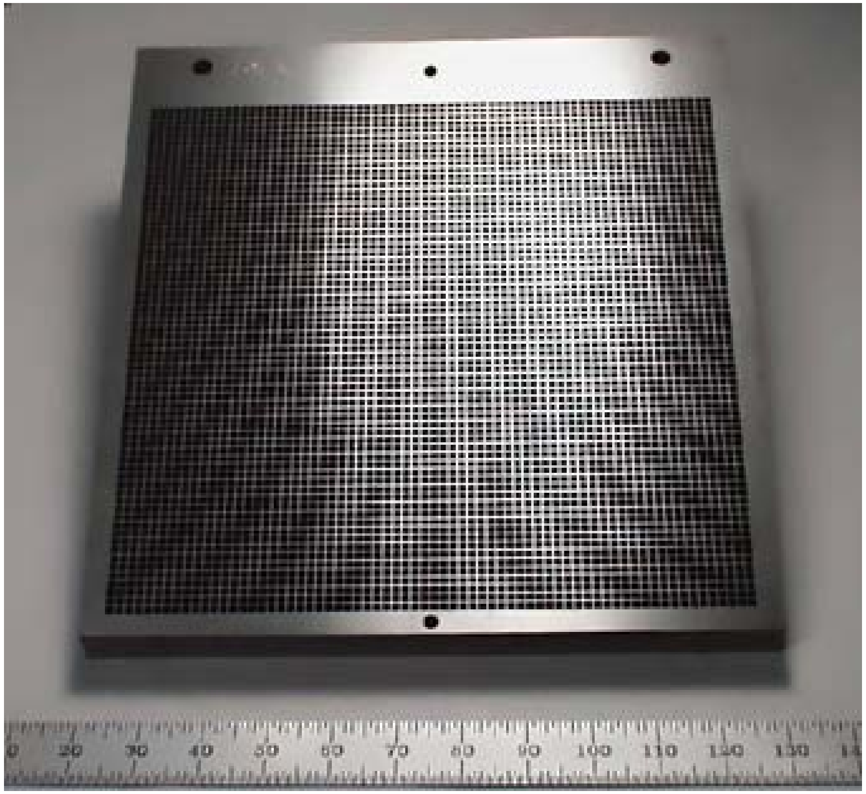
Example of Collimator Designs - Single Photon Imaging

Hexagonal-hole



Courtesy of Lawrence Berkeley Laboratory

Square-hole



Courtesy of Thermo Electron/Tecomet, Inc.

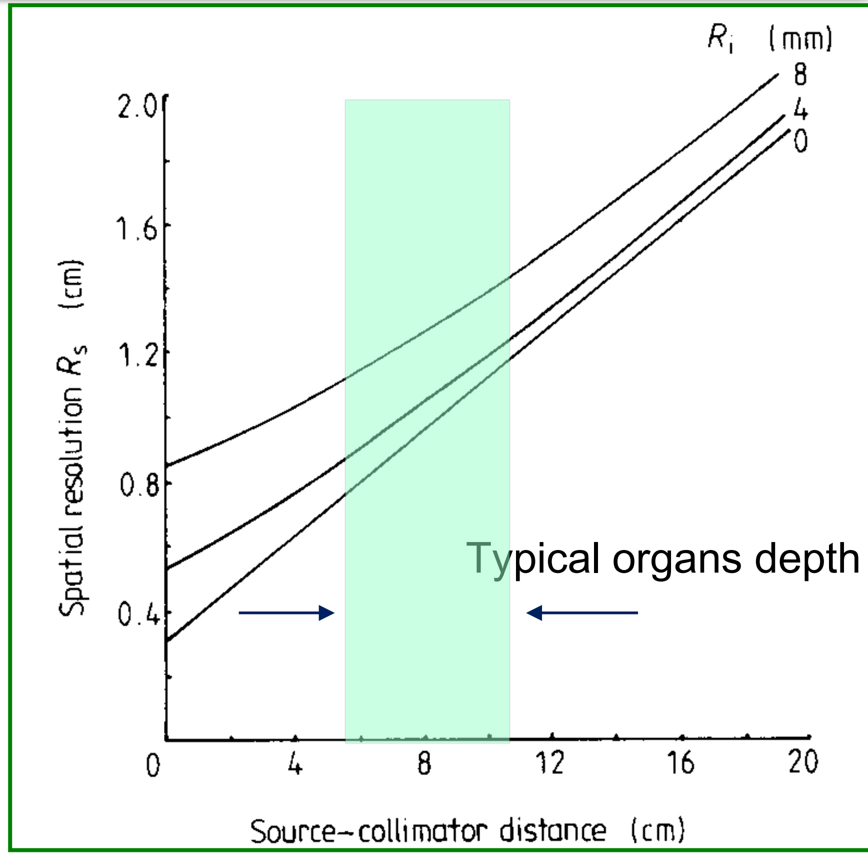
Collimator
The major limitation of Sensitivity and Spatial Resolution

$$R_s = \sqrt{R_i^2 + R_c^2}$$

R_s = overall spatial resolution

R_i = intrinsic spatial resolution

R_c = collimator resolution



Collimation	*Spatial Resolution*	*Geometric Efficiency*
Parallel-hole	degrades with source distance	constant with source distance

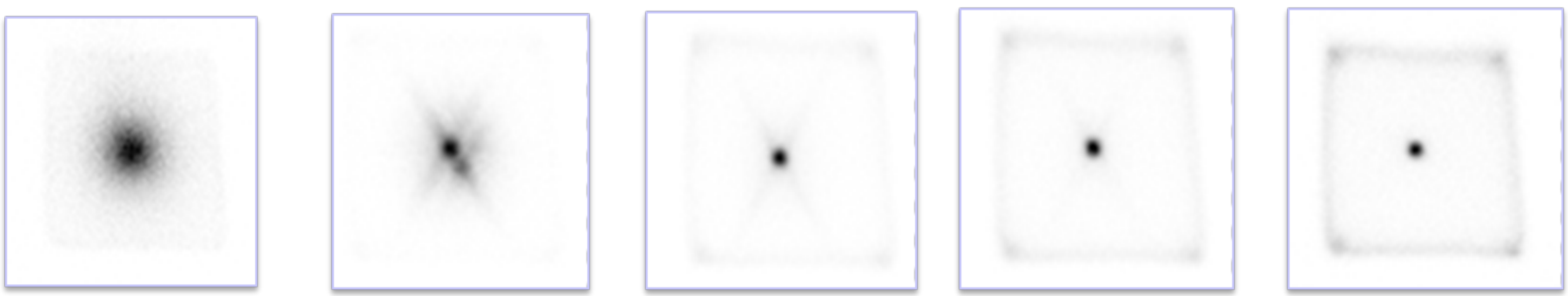
Reducing Collimator Thickness

Example: parallel-hole collimator on NaI(Tl)-PSPMT camera

Co-57 point source 1 cm from collimator

Thickness (cm)

No Collimator	0.5	1.0	1.5	2.0



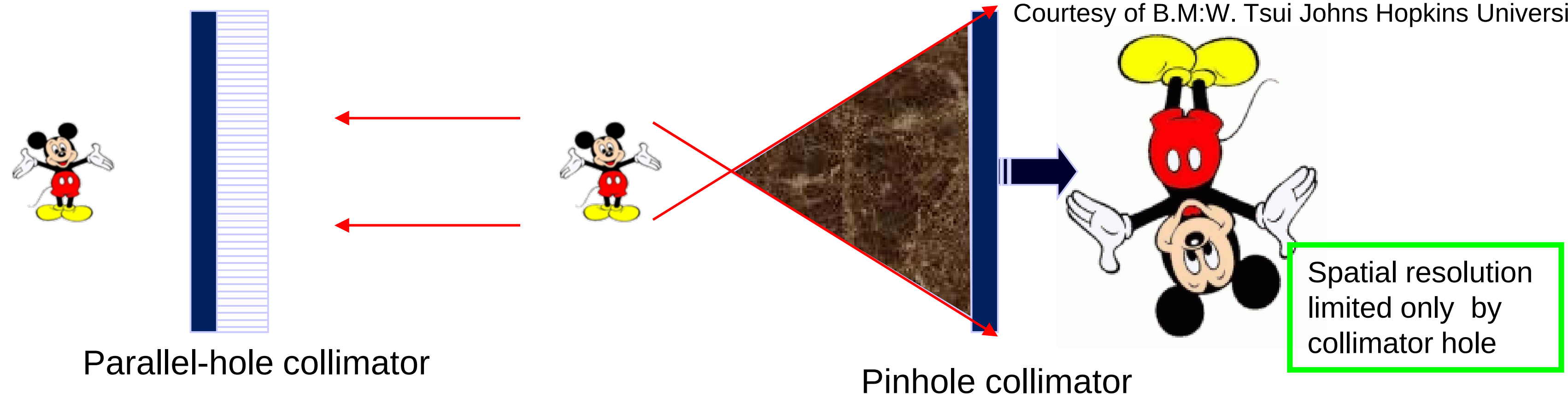
1.0	0.113	0.016	0.011	0.009

Efficiency

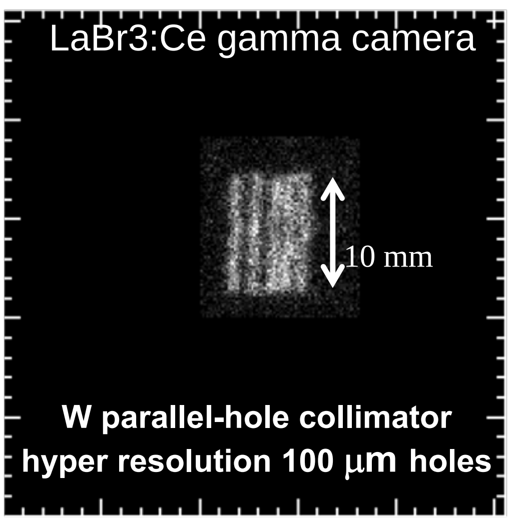
Courtesy of C.S. Levin UCSD school of Medicine USA

Parallel-Hole vs. Pinhole Collimation

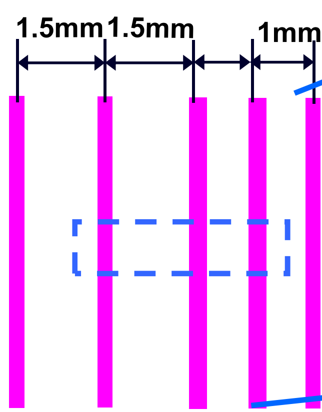
Courtesy of B.M:W. Tsui Johns Hopkins University



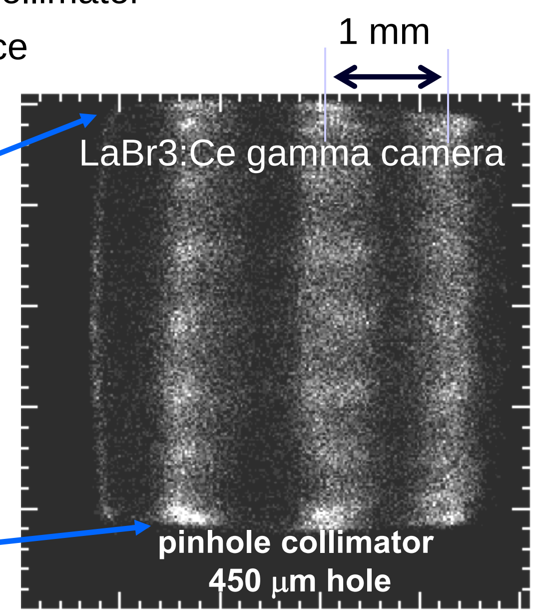
Spatial Resolution and Sensitivity degrades with source distance



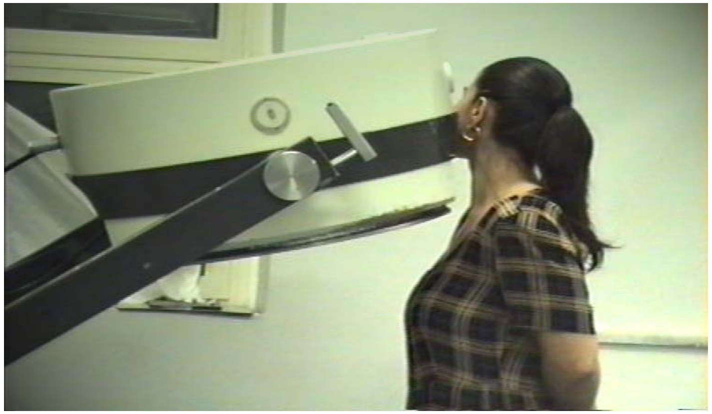
Capillary-setting source Tc[99m]



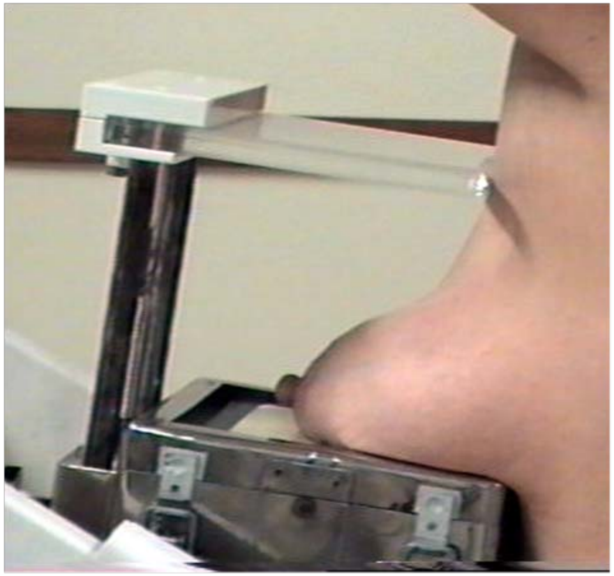
Activity = 30mCi/cc
Capillary size:
ID= 0.45 mm



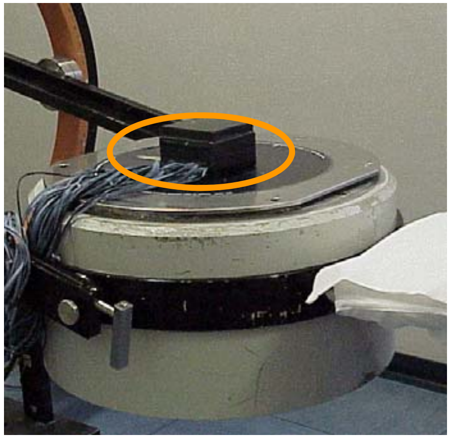
Motivation for the development of new cameras

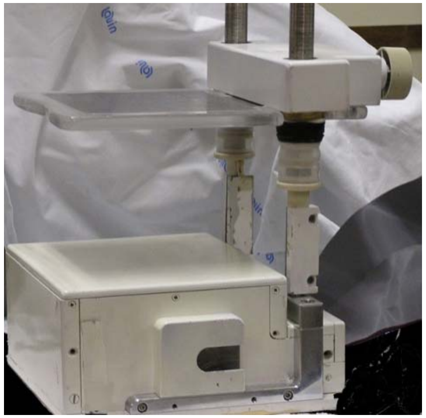


Inability for close-proximity imaging
limited spatial resolution
limited sensitivity



Scintimammography



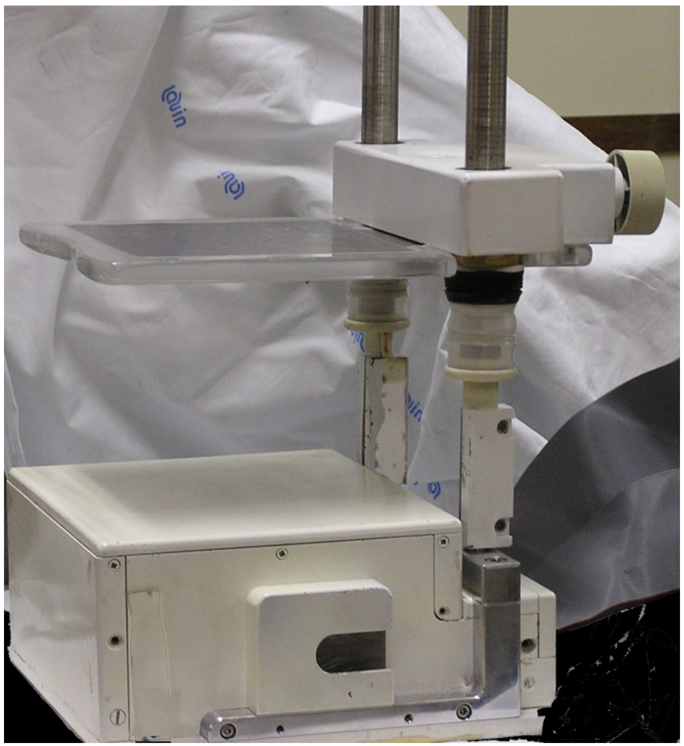


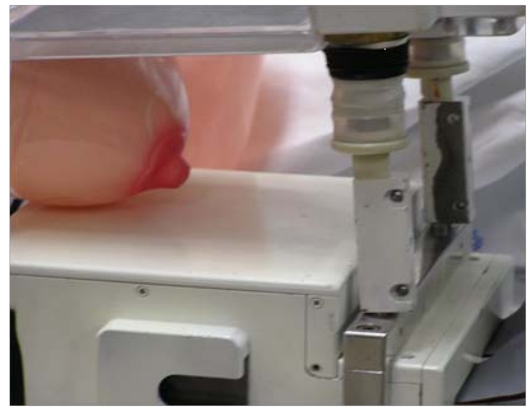
Dedicated gamma camera

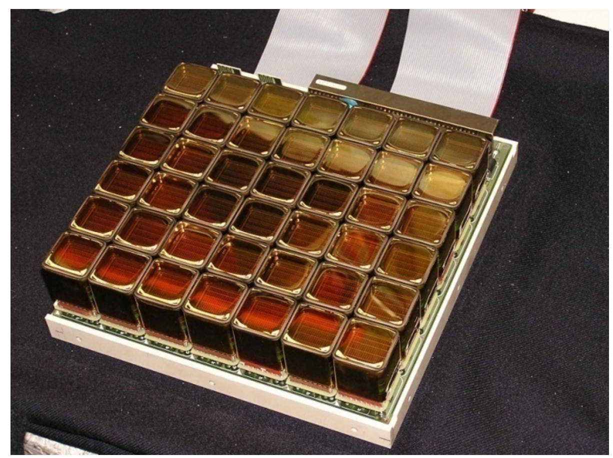
Gamma camera dedicated to scintimammography

- *Detection ability of subcentimeter lesions*
- *Flexibility and accuracy of positioning at multiple orientations*
- *Close-proximity imaging*
- *Positioning at orientations to reduce background organ activity*
- *Incorporate into a mammography unit*
- *Mobile--can be taken into different clinical environments*
- *Design favoring very high spatial resolution at a reasonable cost*

1st Large FOV gamma camera based on INFN-"La Sapienza" Photodetector design (Project IMI L46)



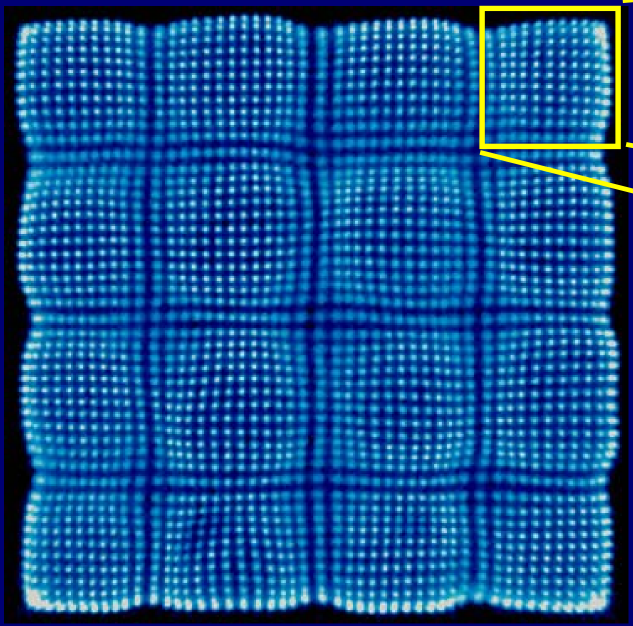


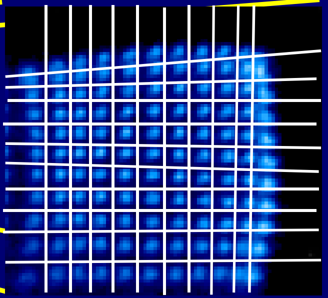


Developed by Pol.Hi.Tech and CAEN

Image reconstruction from pixellated scintillation detector

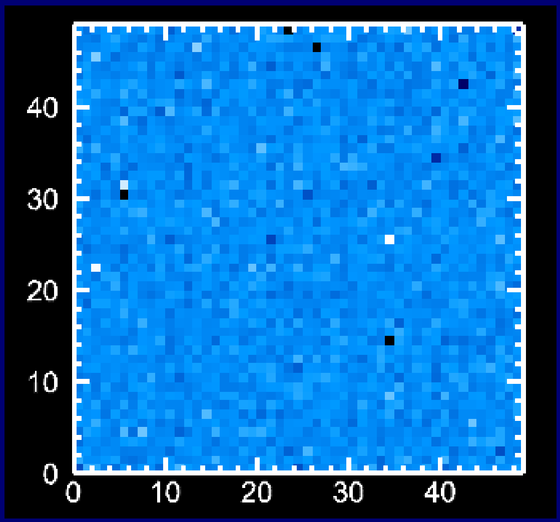
flood field image





LUT pixels spatial identification

LUT Reconstructed image



1.8 mm NaI (Tl) pixel size

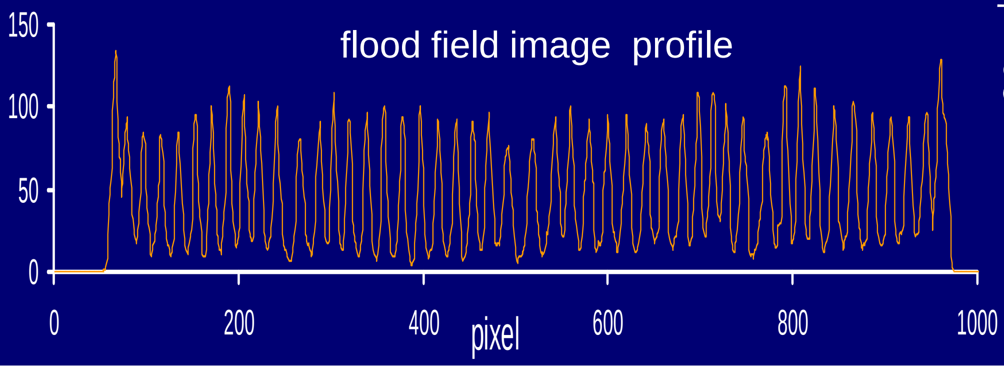
1,54	1,43	1,35	1,07	1,17
1,18	1,21	1,13	0,92	0,90
0,89	0,95	1,05	0,88	0, 90
0,83	0,81	0,87	0,76	0,72
1,08	1,00	1,09	1,18	1,17

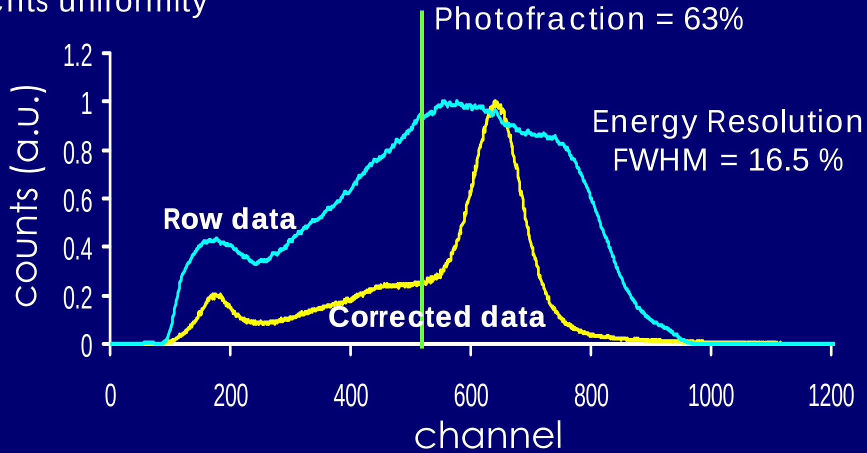
LUT cnts uniformity

Integral uniformity = ± 16.9 %

Differential uniformity = ± 4.5 %

Intrinsic (pixel ID) spatial resolution = 0.9 ± 0.2 mm

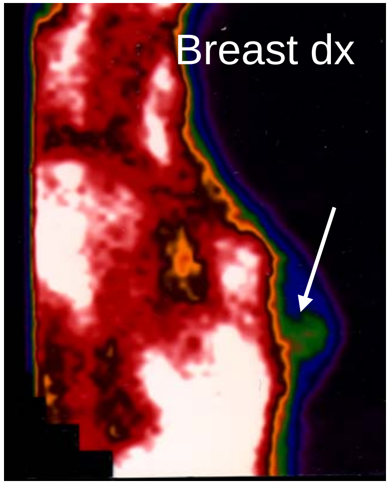


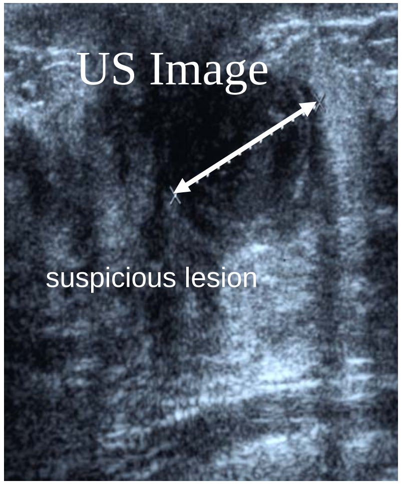


LUT pulse height distribution reconstruction

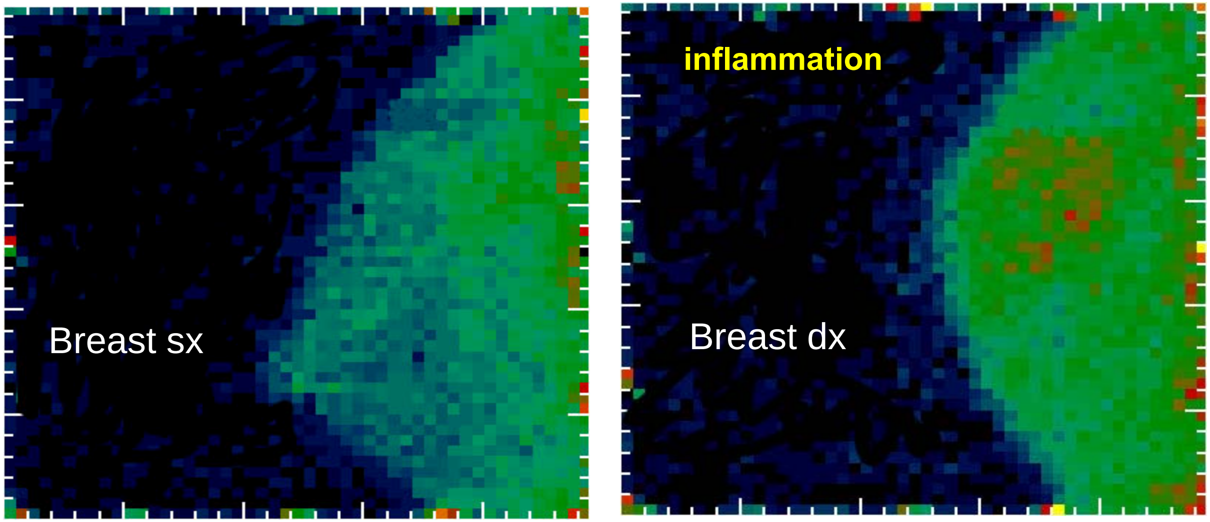
99mTc MIBI Scintimammography

Anger Camera





Dedicated gamma camera

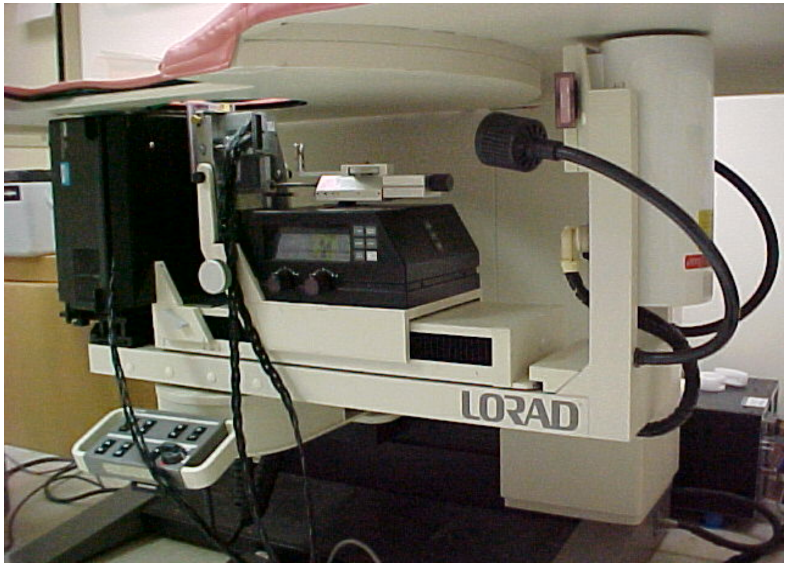


42 PSPMTs camera – NaI(Tl)

High Resolution Scintimammography helps in differentiating benign from malignant finding in scintigraphic hot spot

Application of PEM detectors
Combination Stereotactic Bx - PEM

Collaboration with PEM Technologies MA USA



- LORAD with PEM Detectors

- LORAD with patient and PEM Detectors

New Imaging Devices

Ultra High Resolution Small Animal Imaging

New PET scanners provide excellent sensitivity and spatial solution of the order of 1-2 mm

Advanced SPET and PET scanners are currently under development

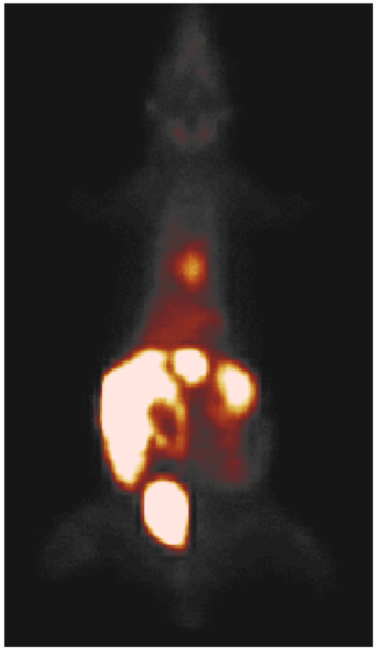
New SPET scanners provide ultra high spatial Resolution (1 mm or better) at the cost of low sensitivity and a reduced field of view.

Assessment of Myocardial Perfusion & Function Using ^{99m}Tc-Sestamibi in Rats & Mice

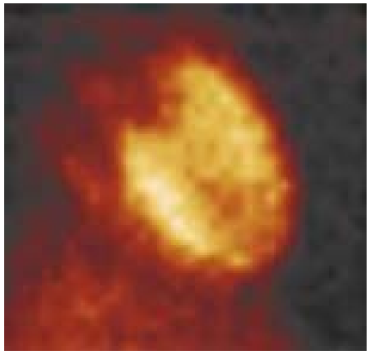
CsI (Tl) Pixellated scintillation crystal

Experimental Animal Protocols:

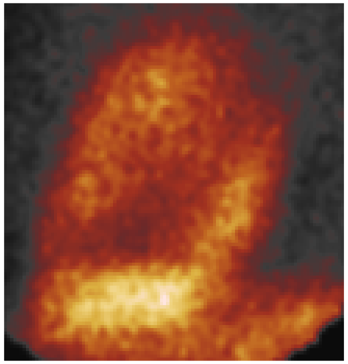
The performance of the prototype planar camera was evaluated for assessing myocardial perfusion and function using ^{99m}Tc- sestamibi (20 mCi) as well as inflammation following ischemia/reperfusion with the neutrophil tracer ^{99m}Tc-RP517 (2-20 mCi). 350 g male Sprague-Dawley rats and 20 g C57BL/6 mice were used in these experiments



Rat Whole Body
Clinical Gamma Camera



Rat Heart: static image



Mouse Heart: static image

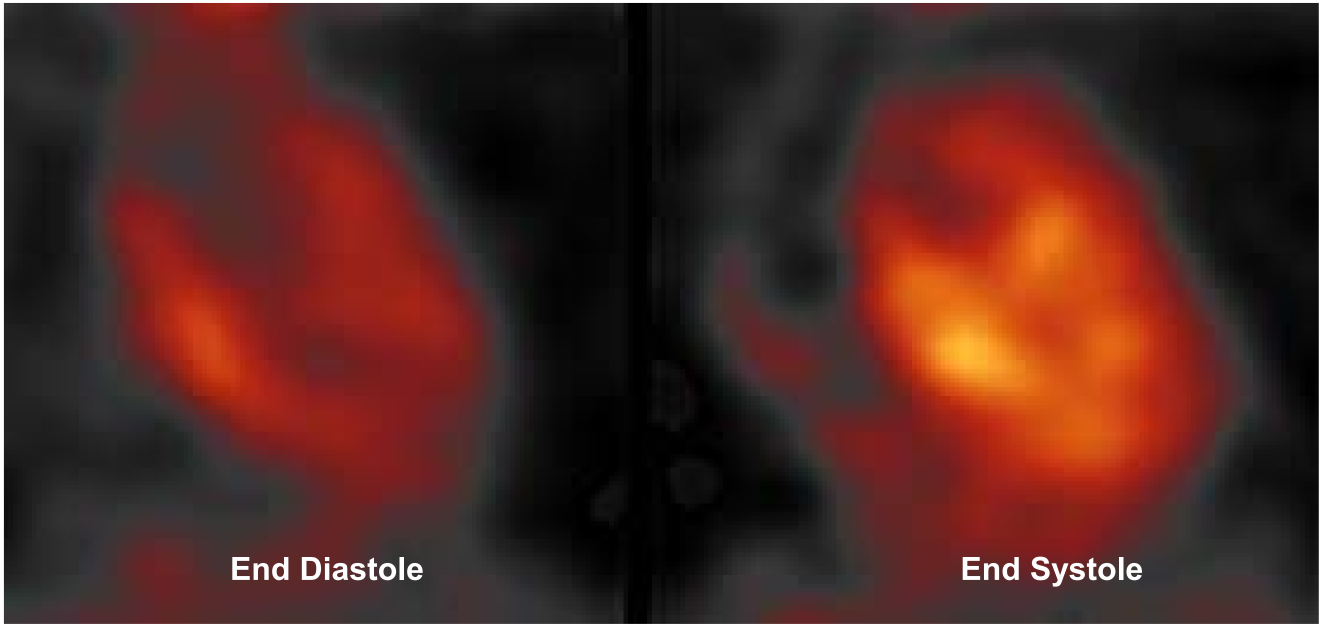
FAR LEFT: *In vivo* parallel hole static planar image of a rat using a standard clinical camera with high resolution, parallel-hole collimator. The resolution of standard clinical cameras is insufficient for imaging structural details in the hearts of small animals. NEAR LEFT: Rat and mouse *in vivo* static pinhole images acquired using the high resolution system. Note that the ventricular chambers and walls can be visualized.

Collaboration with University of Virginia Experimental Nuclear Cardiology Laboratory, and Detector Group, Thomas Jefferson National Accelerator Facility USA

In vivo gated planar image of the heart

Collaboration with University of Virginia Experimental Nuclear Cardiology Laboratory, and Detector Group, Thomas Jefferson National Accelerator Facility USA

Pixellated scintillation crystal
Pinhole collimator



In vivo gated planar image of a rat using a 1 mm pinhole. The left image shows the heart at the end diastolic or filled phase, and the right image shows the heart at the end systolic or empty phase of the cardiac cycle.

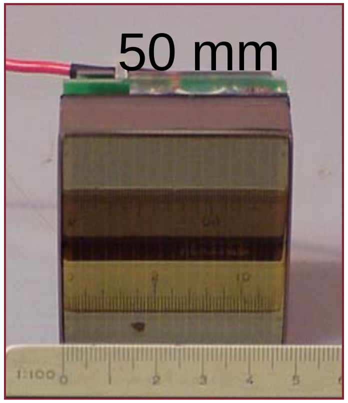
Latest Technological Advances
Hamamatsu H8500 segmented PMT (MAPMT) 38% QE
Gamma Camera Module

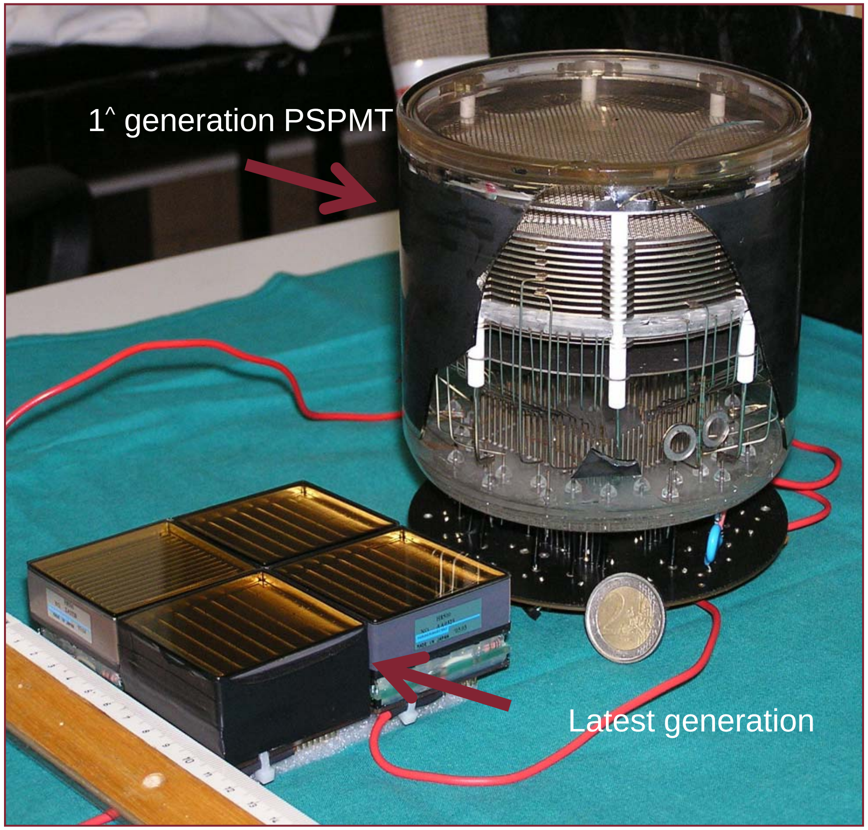
Photodetector: Position sensitive Flat Panel PMT H8500 Hamamatsu

- Extremely compact (15 mm of thickness)
- Ideal for closely packing in array (1.5 mm edge dead zone)
- Intrinsic spatial resolution better than 0.5 mm

It allows large detection area modules for compact SPET system

50 mm

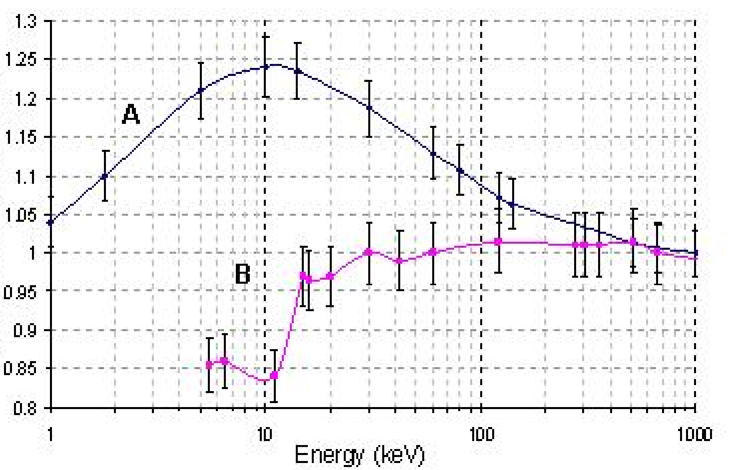




$LaBr_3$:Ce : latest generation of scintillation crystals

	E (keV)	Density (g/cm^3)	Atten.len. (mm)	$Z_{eff.}$	Photo-fraction (%)	Light yield (*ph*/MeV)	Decay time (ns)	Refr. index	ΔE/E (PMT)	Emiss max (nm)
CsI(Tl)	140	4.51	2.55	52.0	86	66,000	630	1.80	14%	565
$LaBr_3$:Ce	140	5.07	3.32	47.4	79	63,000	16 (97%)	1.90	6%	380
NaI:Tl	140	3.67	3.76	51.0	84	38,000	230	1.85	9%	410

Light Yield vs Energy



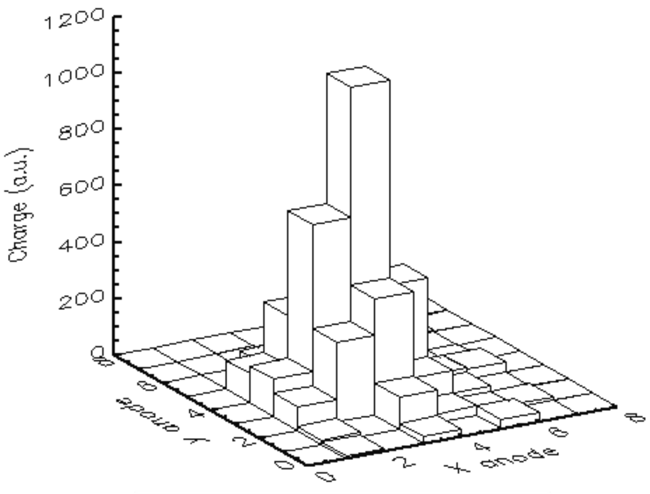
A – *Prescott and Narayan, NIM A, 75 (1969)*
B – *G.Bizarri, IEEE TNS, Vol 53,02 (2006)*

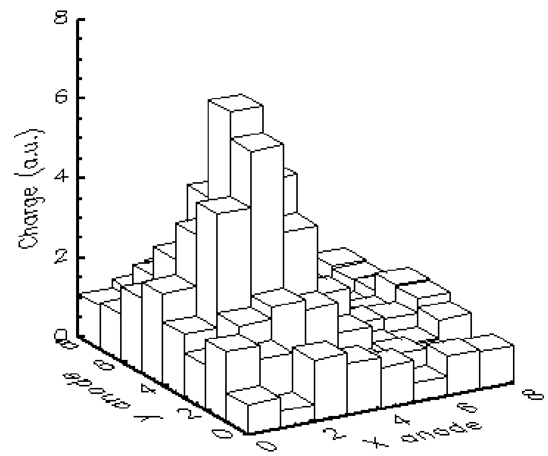
Energy Resolution

$$R^2(E) = R_s^2 + \frac{5.56}{\overline{N}\eta\alpha}\left(\frac{\delta}{\delta - 1}\right)$$

Crystal	ER(%) @ 662 keV	$ER_{scint.}$ (%)	ER_{st} (%)	Ref.
NaI(Tl)	6.7	5.9	3.2	typical
CsI(Tl)	6.6	5.8	3.2	Allier (1998)
$LaBr_3$(Ce)	3.6	2.2	2.5	Moszynski (2006)

Ideal Position linearity of Scintillation array





NaI:Tl *24x24 array*

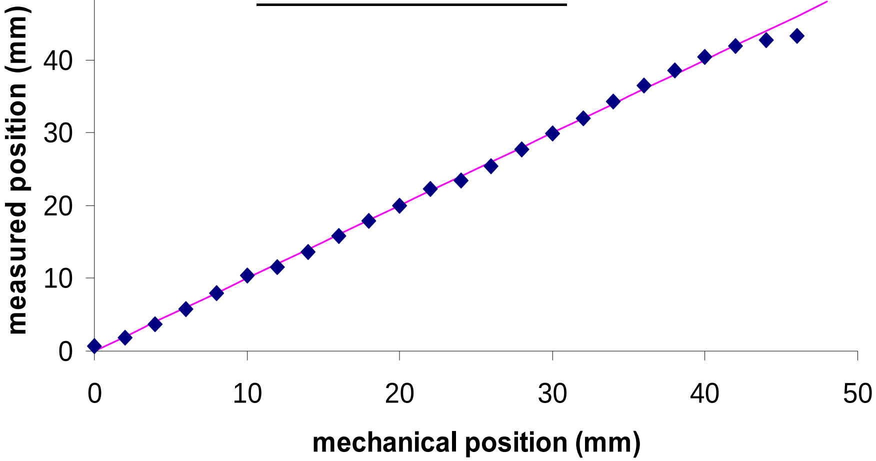
1.8 x 1.8 x 6 mm³ pixel

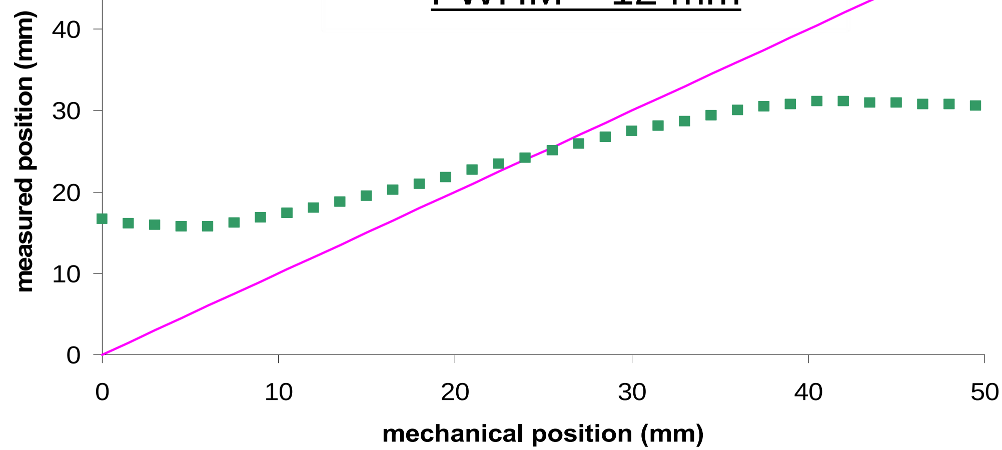
FWHM ~ 10 mm

$LaBr_3:Ce$

Integral assembly 5 mm thick

FWHM ~ 12 mm





New position arithmetic for continuous Scintillators based on floating weights

$$X_C = \frac{\sum_j n_j x_j}{\sum_j n_j}$$

where

x_j represents the linear weight associated to the anode array

$$n_j = \sum_k n_{k,j}$$

is the projection of the charge collected along the J-th column

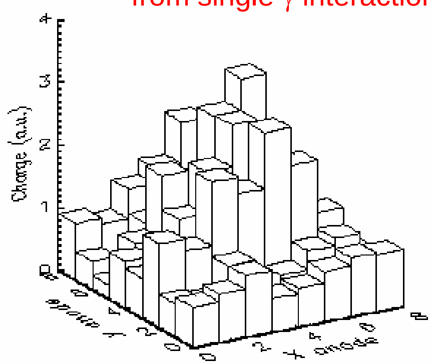
New algorithm:

$$X_C = \frac{\sum_j n'_j x_j}{\sum_j n'_j} \quad \text{where} \quad n'_j = \sum_k \left(n_{k,j} \cdot w_{k,j}\right);$$

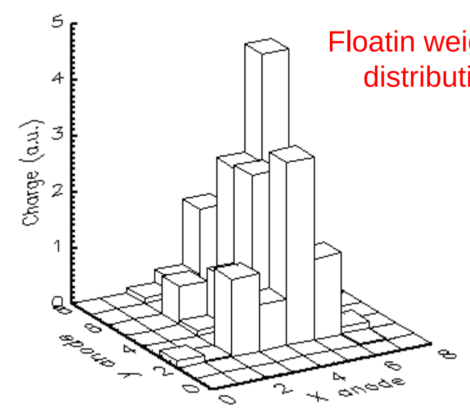
$$w_{k,j} = n_{k,j} \quad \text{is the weight.}$$

In general $w_{k,j}$ is a 2D array of weights strictly related to $n_{k,j}$
In this way the position information related to the anode position x_j is more *enhanced near the interaction point (maximum charge* = maximum weight) and depressed far from interaction location.

Original charge distribution from single γ interaction



Floatin weighted distribution

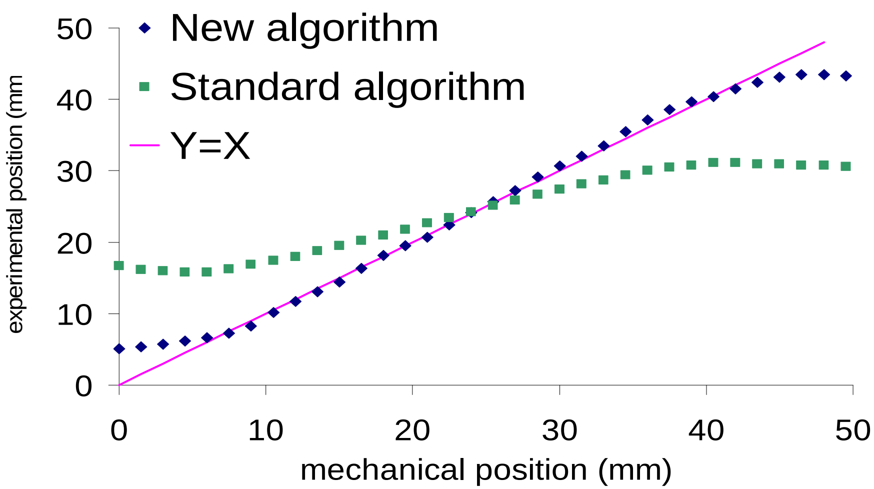


New position arithmetic

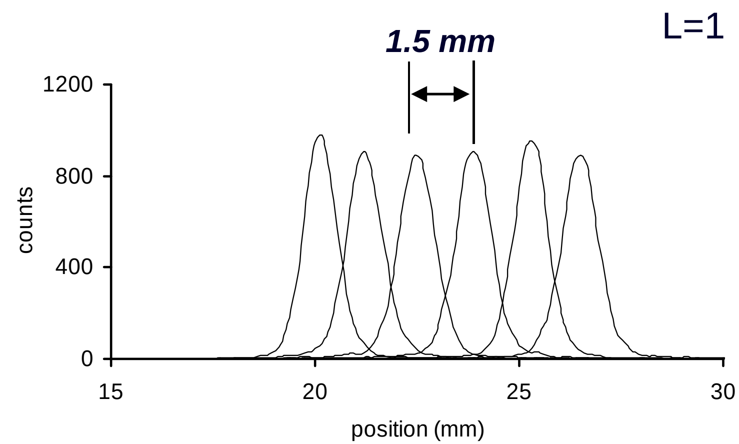
LaBr$_3$:Ce 5 mm thick (integral assembly)

Tc99m scanning 0.4mm coll

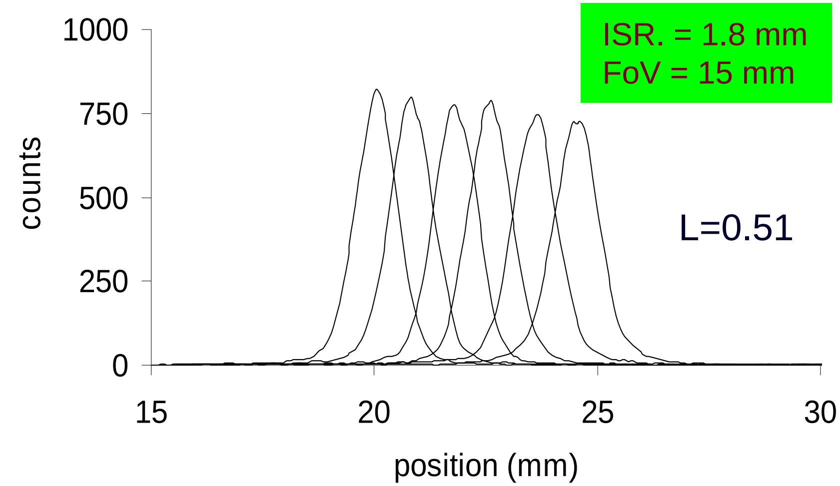
$$L = \frac{dX_{measured}}{dx_{mech}} = 0.51$$



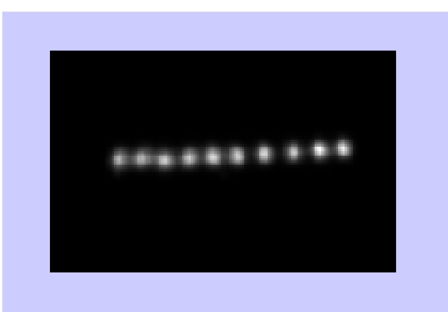
ISR. = 0.9 ÷1.0 mm
FoV = 38 mm



ISR. = 1.8 mm
FoV = 15 mm



Central Spots

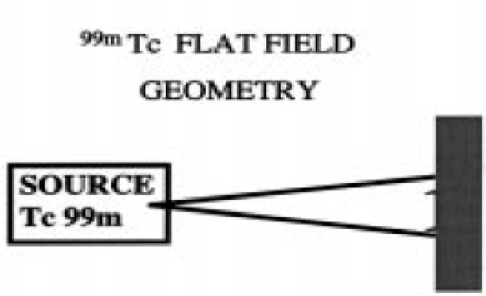


Continuous crystal

can solve limitations offered by segmented detectors

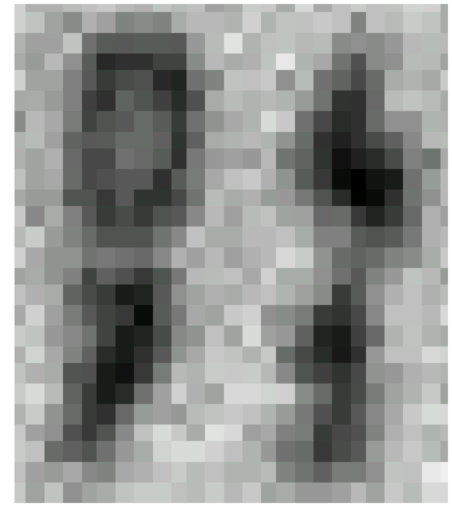
^{99m}Tc Flood Field Absorption image

Lead test object



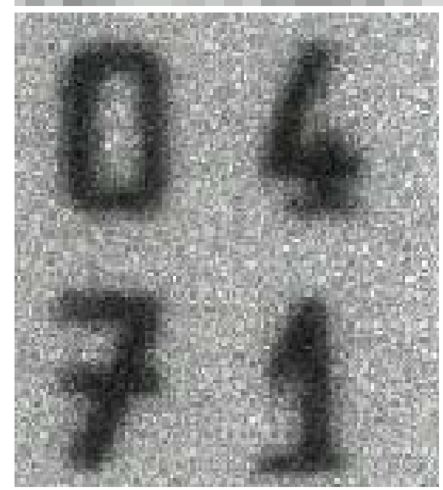
$LaBr_3:Ce$ 5 mm thick

NaI:Tl – Anger camera



CsI(Tl)-R2486

1x1x3 mm^3 pixel size

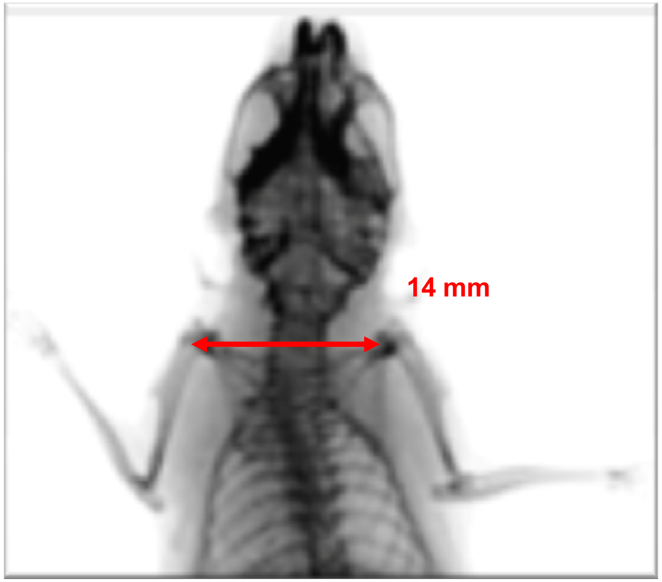


YAP: Ce

0.5x0.5x10 mm^3 pixel size

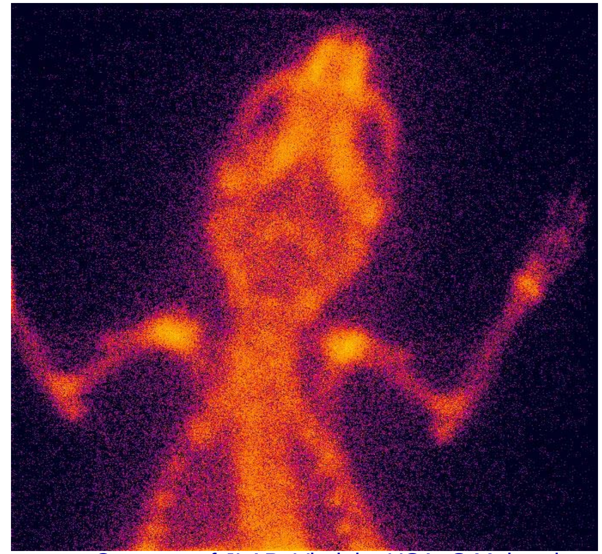
Continuous vs Pixellated crystal
Mouse injected with ^{99m}Tc MDP

X ray image



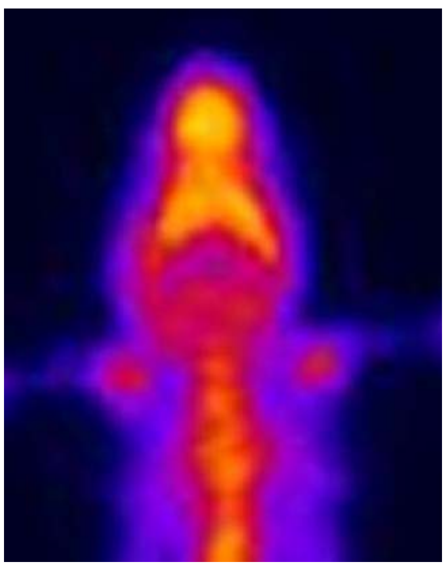
1 mm continuous NaI(Tl)
H9500 MA-PMT

Parallel Hole Collimator (0.364 mm hole, 0.105 mm septa, 10.6 mm length)

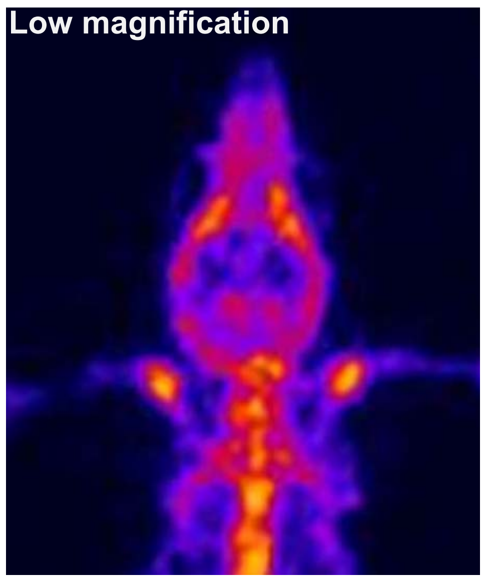


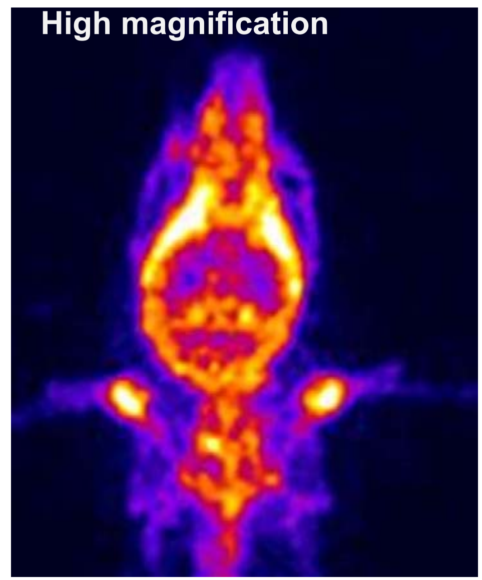
Courtesy of JLAB, Virginia, USA -S.Majewsky

10x20 cm^2 NaI(Tl) 1.2mm pitch pixellated modular detector



Parallel Hole Collimator





Pinhole Collimator

Courtesy of JHU
Maryland, USA
B.M.W.Tsui

INFN Ecorad Collaboration
dual modality imager

- R. Pani, R.Pellegrini, M.N.Cinti, R. Scafé, **INFN -Roma I.**

- V. Orsolini Cencelli, A. Baroncelli, P. Bennati, E. D'Abramo, F. de Notaristefani, A. Fabbri, D. Sacco, **INFN - Roma III** .

- F. Navarria, G. Baldazzi, N. Lanconelli, S Lo Meo, A. Perrotta, **INFN – Bologna.**

- G. Moschini, G. Boccaccio, P. Rossi, M. Bello, **INFN - Laboratori Nazionali di Legnaro.**

❖ The ECORAD collaboration aims to develop a dual compact camera for acquiring ultrasound and scintigraphic images.

❖ It will allow to get both morphological and functional information on the same device. A volumetric image containing the fusion information will be provided to the user

Ecorad Experiment Motivations

•Small FoV gamma cameras improve visual quality by a closer positioning to the object

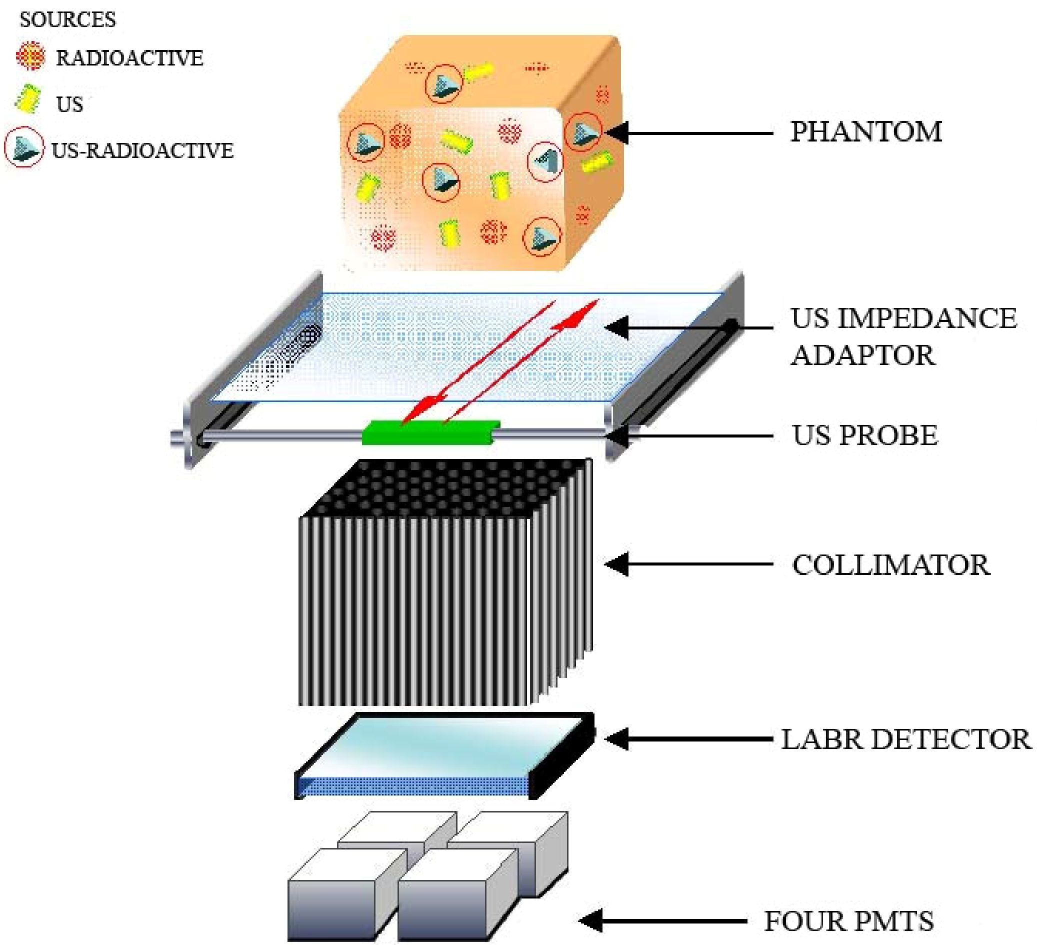
•Radionuclide imaging intrinsically lacks anatomic cues that are needed to localize or stage disease and typically has poorer statistical and spatial characteristics than anatomic imaging methods.

•Functional and anatomic information need to be considered together if one wants to give meaning to a small photon emission image and obtain a more reliable diagnosis.

•Ultrasounds are a cost-effective and reliable method.

•Ultrasound probes are one of the most common ways to assemble portable devices.

ECORAD dual modality imager



Application field:
- **Core biopsy**
- **Lymphnode scintigraphy**
- **Breast scintigraphy**
- **Intraoperative probe**

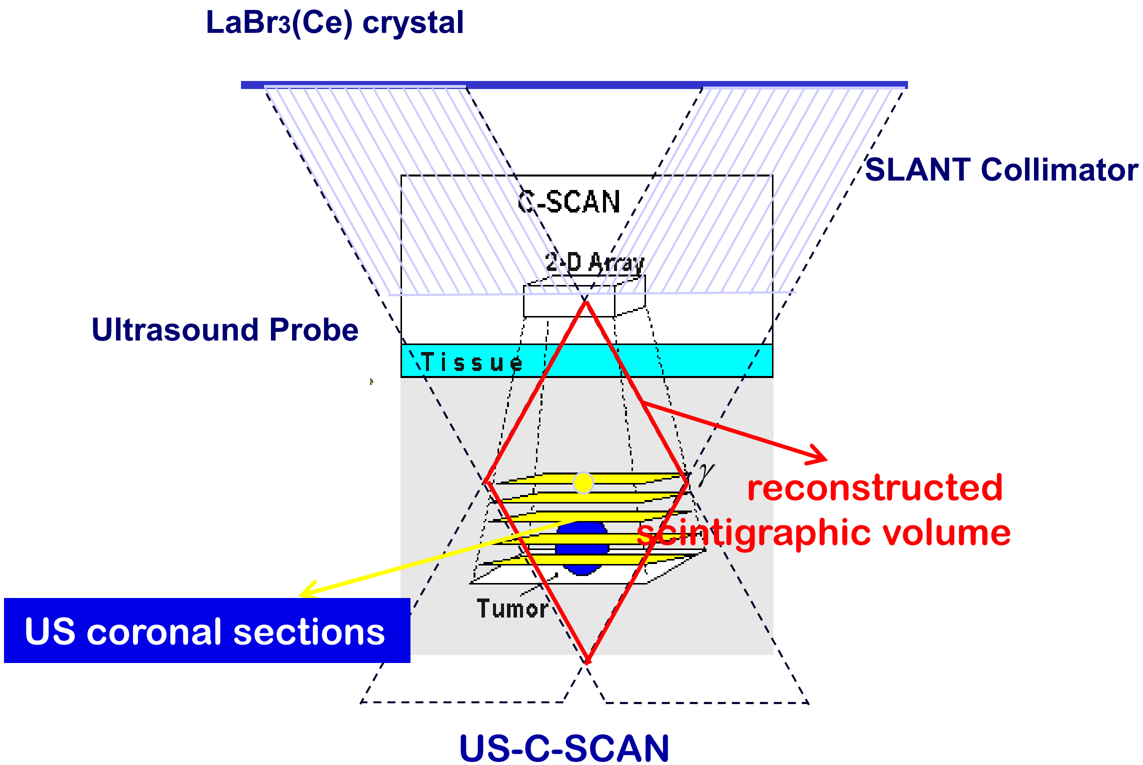
Dual modality system for functional and morphological imaging

Gamma camera based on $LaBr_3$:Ce scintillator integrated with US linear transducer

ECORAD dual modality imager

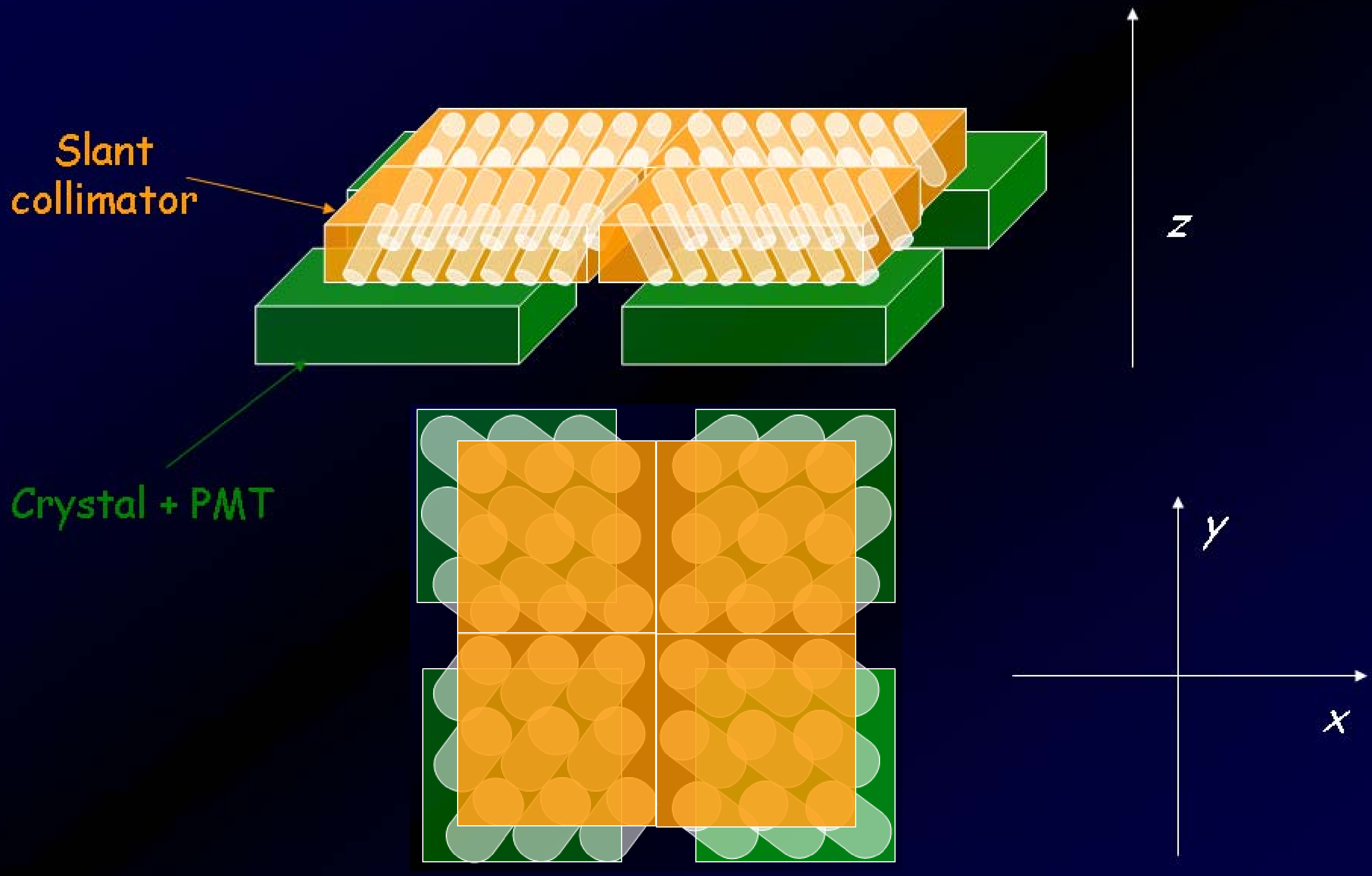
Integrated system for morphological and functional imaging

Images reconstruction geometry gamma and 3D US

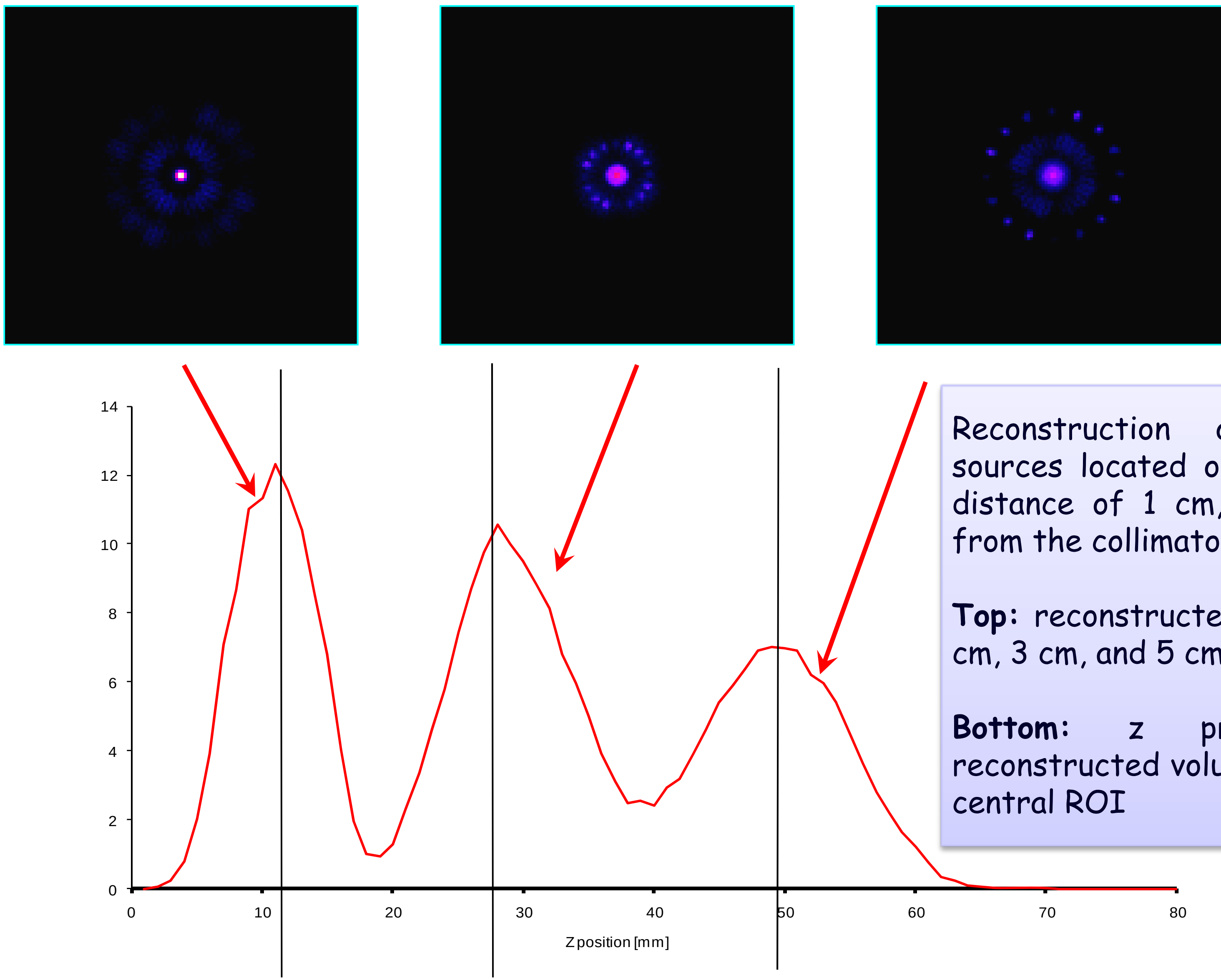


Four slants collimators rotating around the object with stationary gamma camera

Sketch of the slant collimators



Point Sources



Reconstruction of three point sources located on the z axis at a distance of 1 cm, 3 cm, and 5 cm from the collimator.

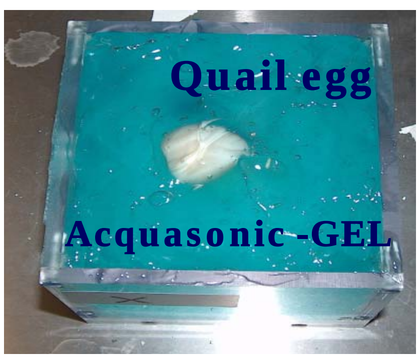
Top: reconstructed slices at depth 1 cm, 3 cm, and 5 cm.

Bottom: z profile of the reconstructed volume estimated on a central ROI

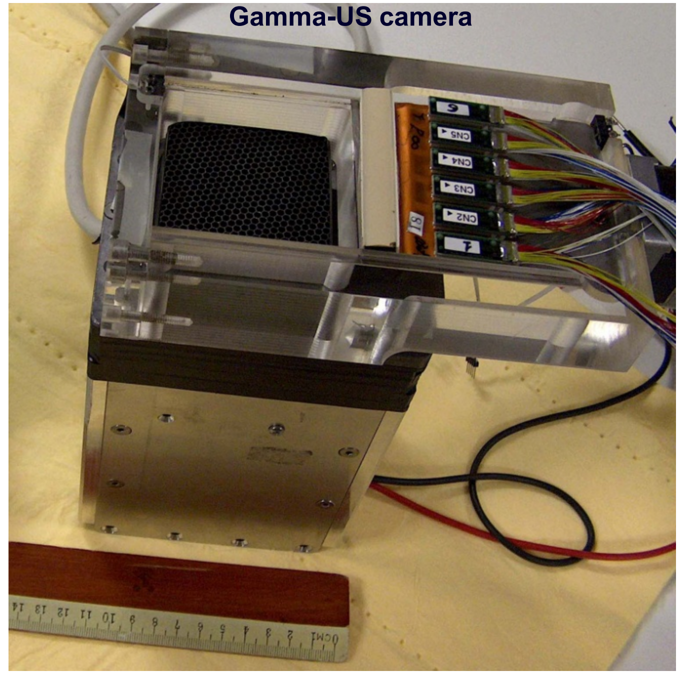
“Biological” Experiment

Quail egg

Phantom



Front view

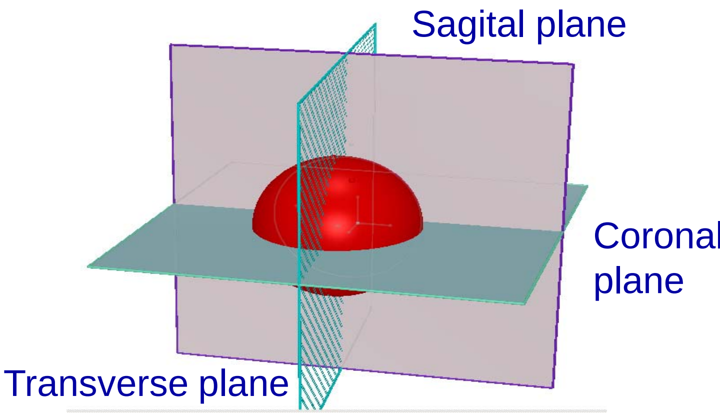


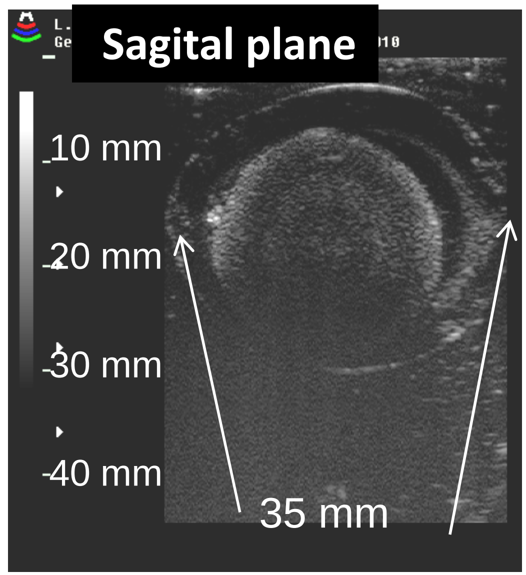
Small FoV gamma camera

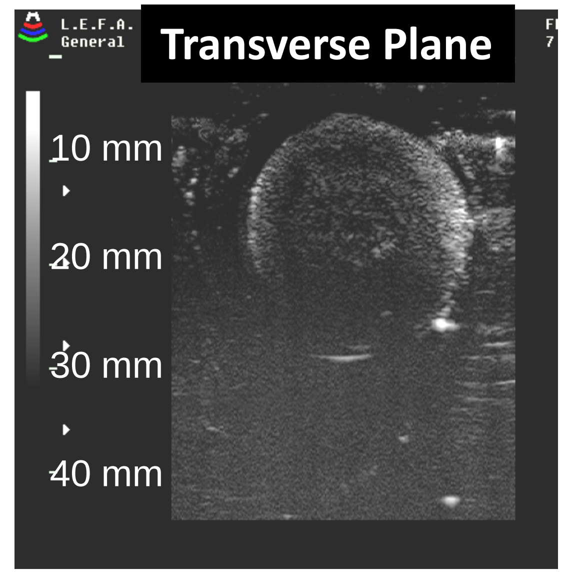
US probe

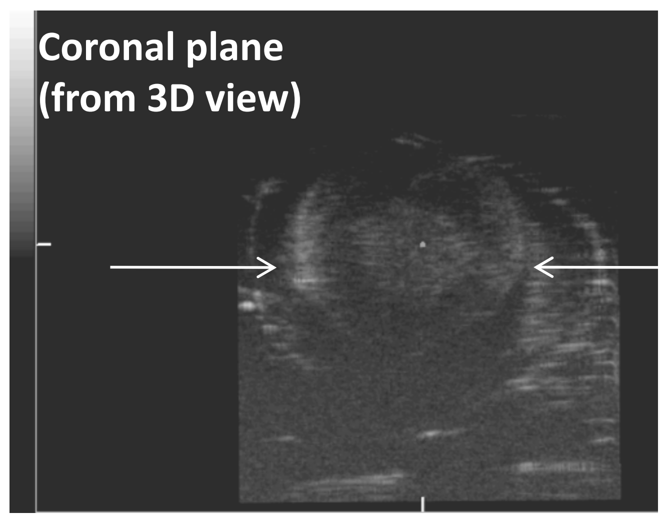
3D Ultrasound – imaging

(35 mm probe – 10MHz)





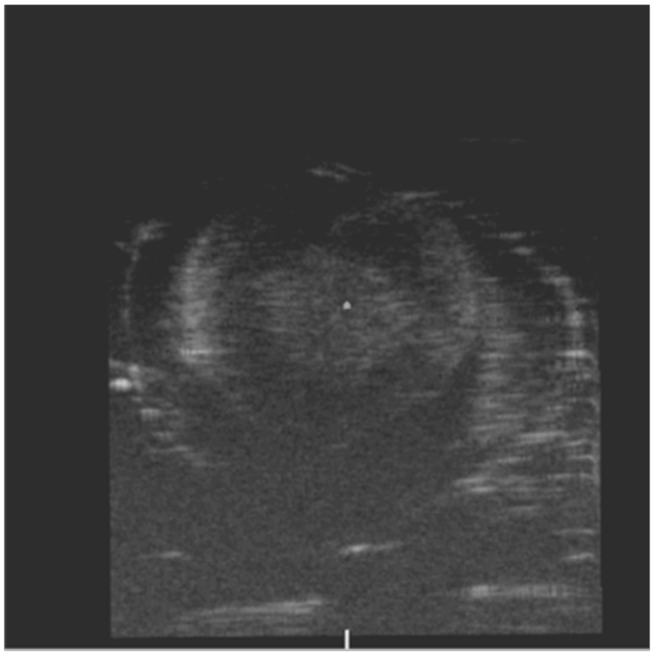




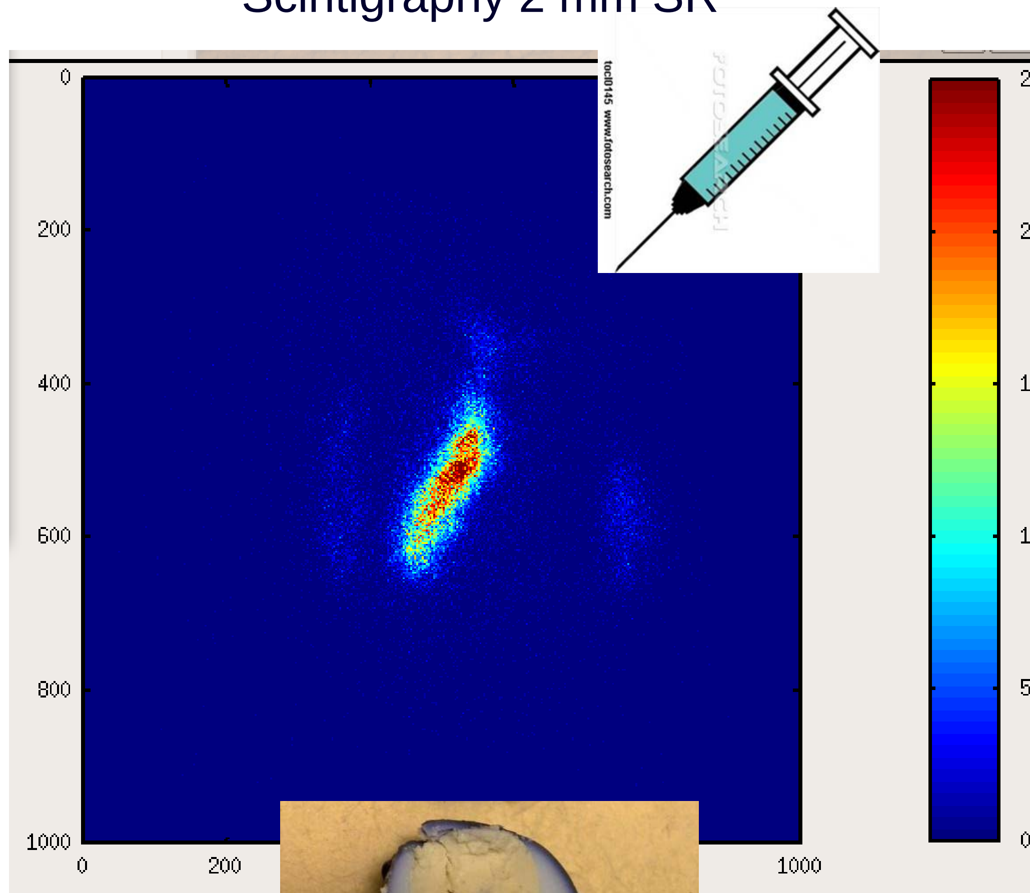
18 mm

US and Scintigraphic images :
3D US & 2D Gamma

US Image 1mm SR

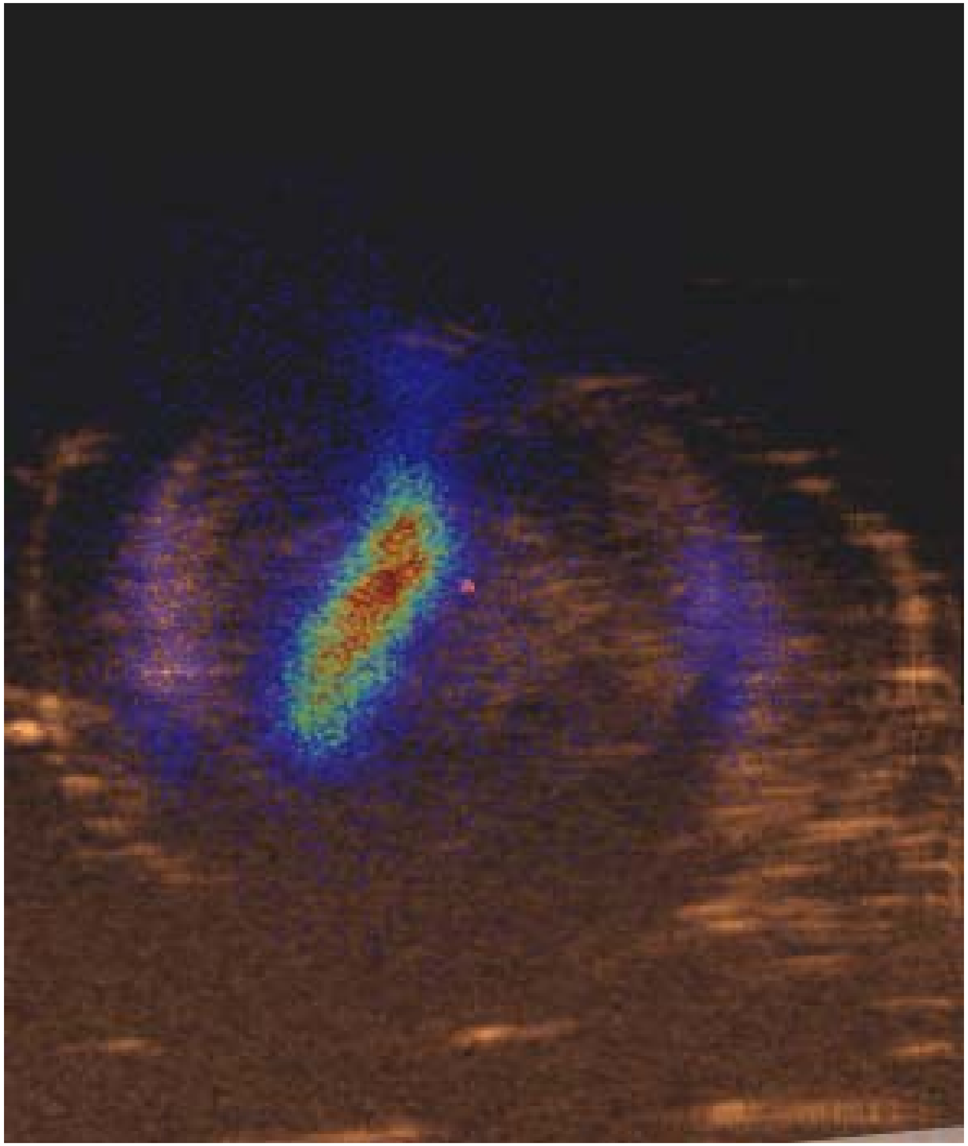


Scintigraphy 2 mm SR



Egg after injection
(20 μl Tc99m + methylene blue

US-Scintigraphy dual image: 3D US & 2D Gamma



Conclusioni

Sfide future in SPET

- ✓ Cristalli continui e nuova matematica della posizione : alta risoluzione spaziale, alta risoluzione energetica, minimo numero di catene elettroniche di lettura ,basso costo.
- ✓ Camere ad alta risoluzione spaziale intrinseca con acquisizioni combinate con collimatori paralleli e pinhole per esperimenti biologici
- ✓ Gamma Camere di piccolo campo combinate con sistemi di imaging anatomico (dual imaging)
- ✓ Gamma camere o rivelatori da utilizzare con sonde intracavitarie e/o laparoscopiche
- ✓ Nuovi metodi di ricostruzione tomografica basati su camere statiche e collimatori paralleli obliqui ad angolo variabile