High resolution and high efficiency multimodal detector for Molecular Breast Imaging

F. Garibaldi – NDIP 2014 – Tours – July 1 – 2014

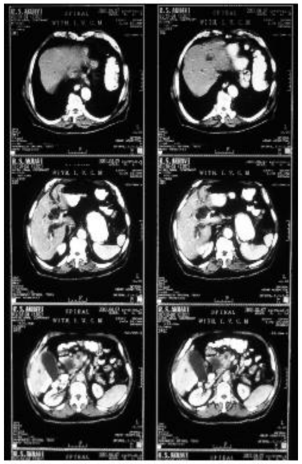
- Molecular Imaging: the role of radionuclides techniques

- Breast cancer diagnosis
  - Detector performance
  - A novel dual detector
  - Multimodality (scintigraphy + tomosinthesys)

- Conclusions and outlook

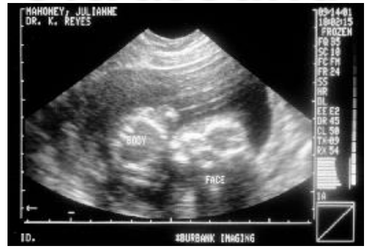
Molecular Imaging Modalities

CT



A Tissue Density, Z
20-50 μm

Ultrasound

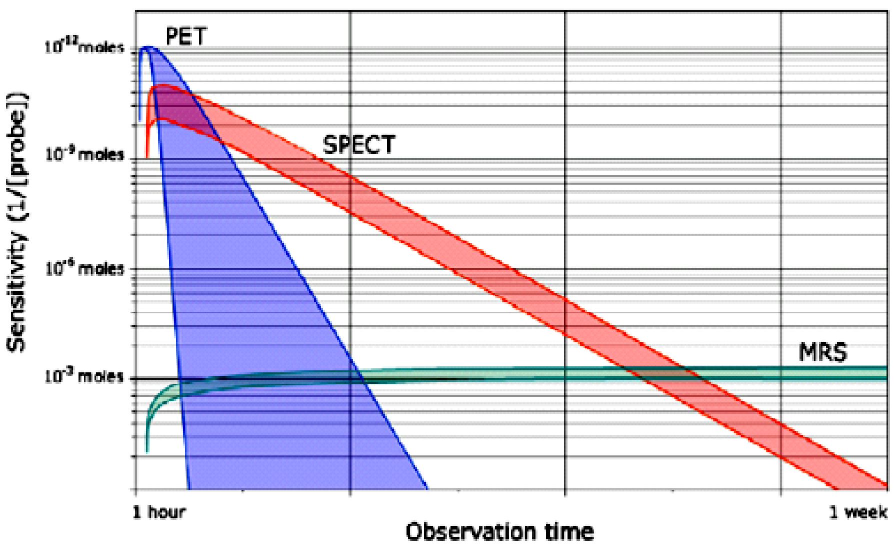


A F
Structure
0.1 mm
Doppler

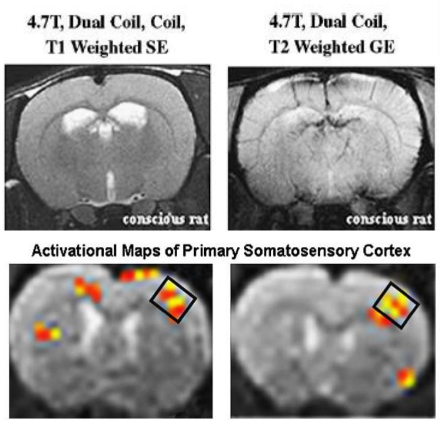
Optical
(Bioluminescence, fluorescence)

A M

Topography
μm to mm
~10^3 cells
quantitative



MRI



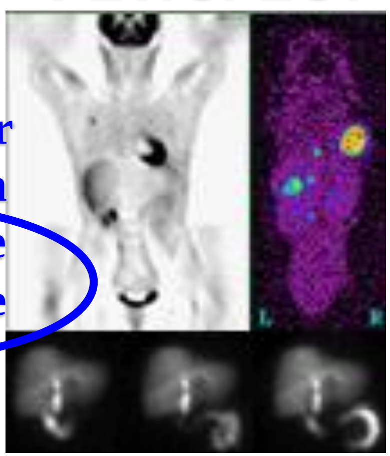
A F M

H Concentration
0.1 mm
BOLD, DCE
β-galactocidase
0.1 μmole H / μmole ^{31}P

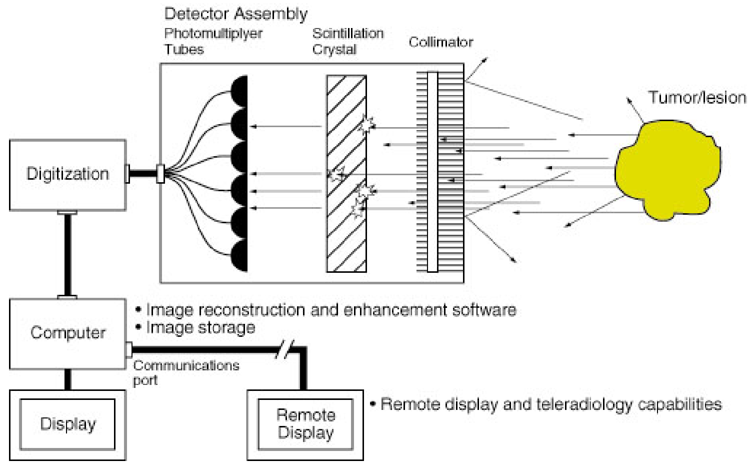
PET/SPECT

F M

Radiotracer
~1-2 mm
<10^{-12} mole
= quantitative

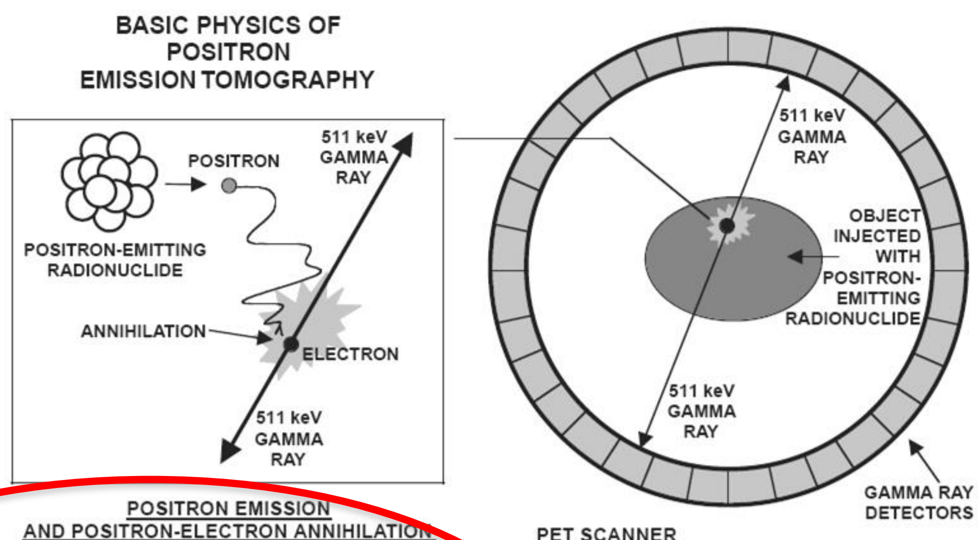


Techniques (scintigraphy)

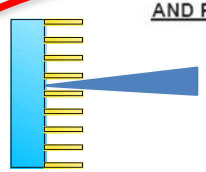


Single Photon Emission Mammography

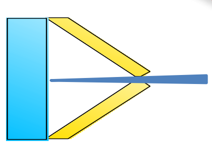
Single Photon Emission Computed Tomography



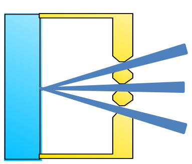
Positron Emission Tomography



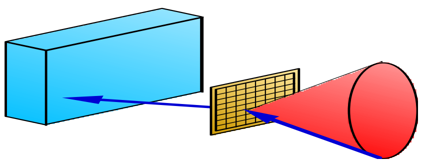
parallel hole



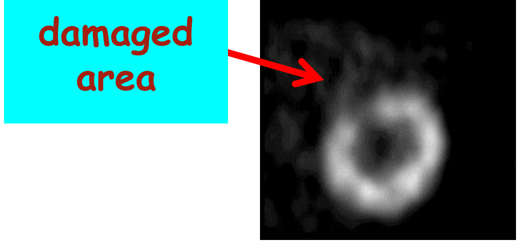
pinhole

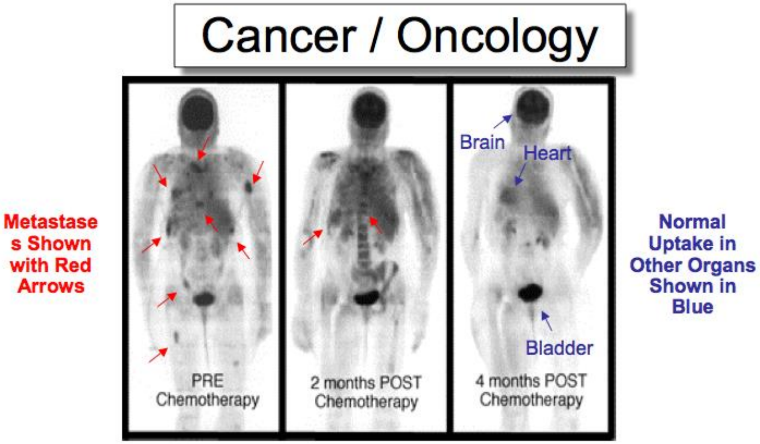


multi-pinhole
coded apperturea

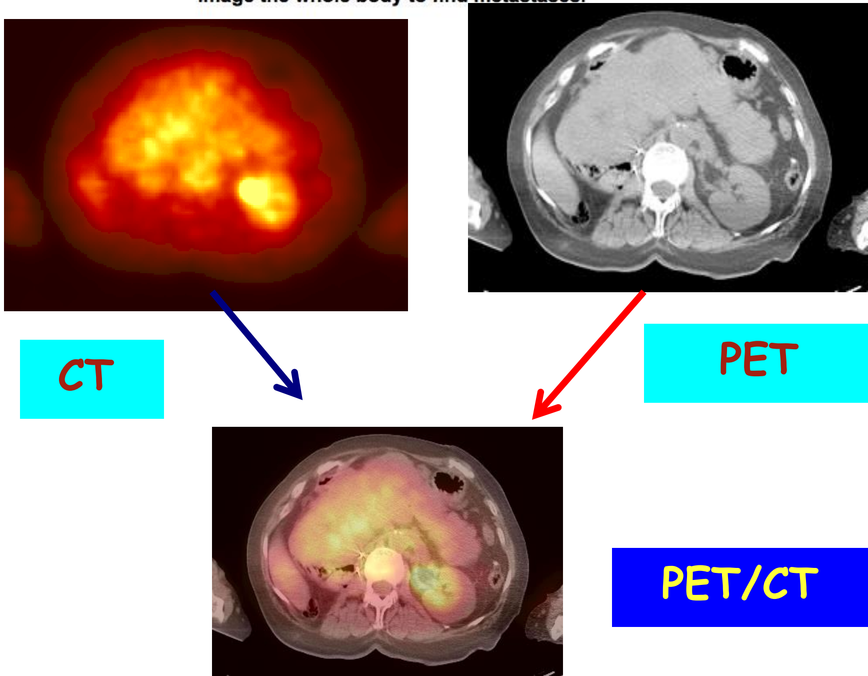


Compton Camera





- Many tumors have higher than normal uptake.
- Image the whole body to find metastases.



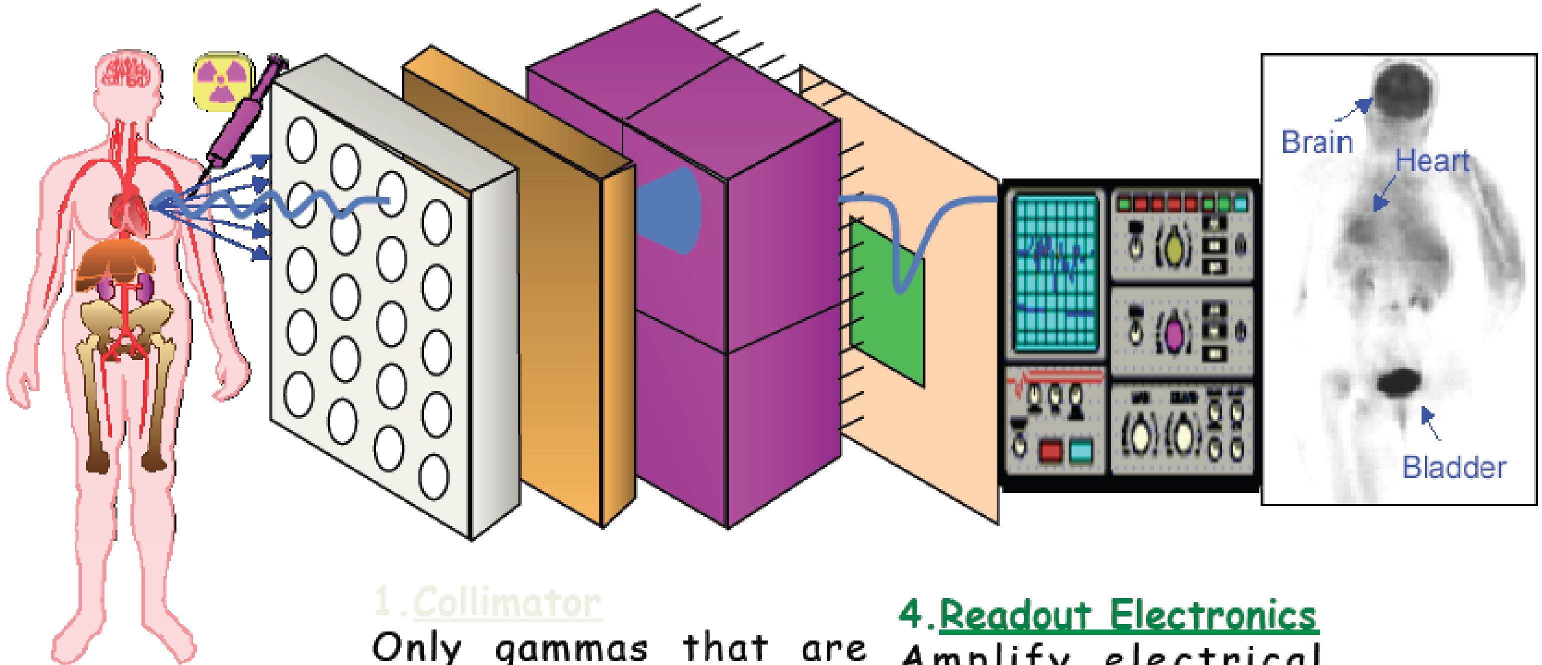
-Not everything can be done with these devices

- Dedicated detectors are needed

- Focusing on small object and imaging at the same time the whole organ (or body)

- Breast cancer

Single Photon Detector Module



Patient injected with radioactive drug.

Drug localizes according to its metabolic properties.

Gamma rays, emitted by radioactive decay, that exit the patient are imaged.

1. Collimator

Only gammas that are perpendicular to imaging plane reach the detector

2. Scintillator

Converts gammas to visible light

3. Photodetector

Convert light to electrical signal

4. Readout Electronics

Amplify electrical signal and interface to computer

5. Computer decoding procedure

Elaborate signal and gives image output

Important parameters for detectability/visibility

they are correlated

$$SNR = \frac{S - BKG}{\sqrt{S}}$$

$$IC = \frac{Max - BKG}{Max}$$

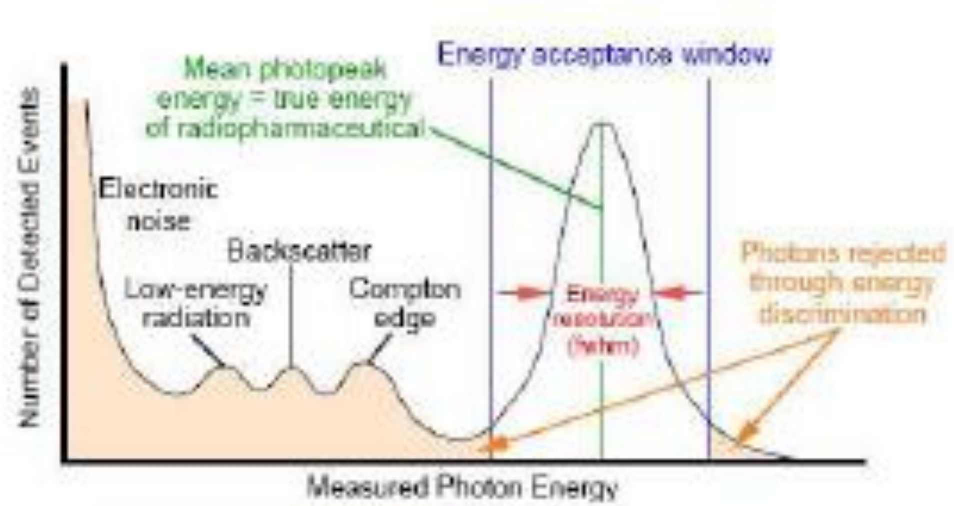
efficiency (collimation)

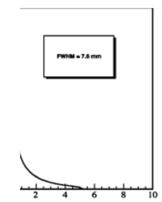
time (and modality)

uptake (radiopharmacy)

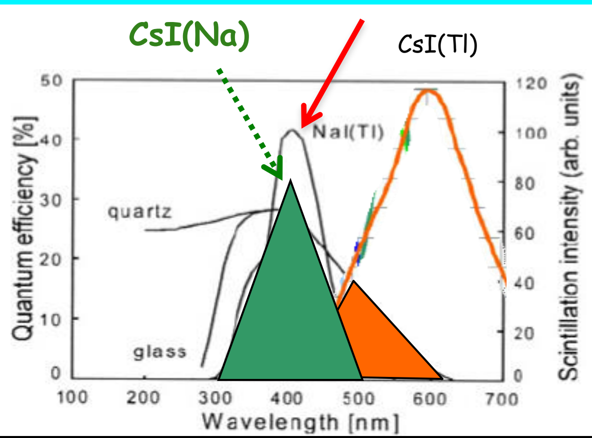
$$X = \frac{\sum_{i=1}^{N_{channel}} c_i X_i}{\sum_{i=1}^{N_{channel}} c_i}$$

tial
tion





energy resolution plays only a secondary additional role when small volumes are involved



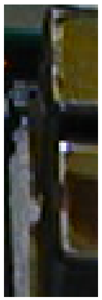
Bialkali PMT

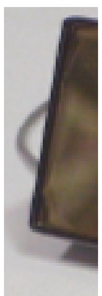
Scintillators

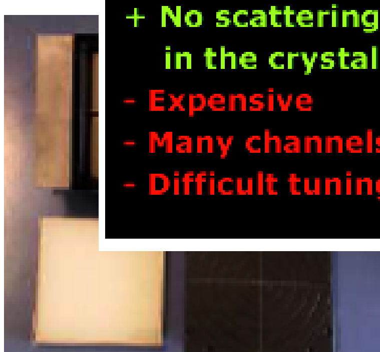
		NaI(Tl)	CsI(Tl)	YAP	$LaBr_3(Ce)$
Density	g/cm^3	3.67	4.51	5.55	5.29
Effective Z		51	54	32	47
Relative Yield	%	100	45	35-40	130
Peak Wavelength	nm	410	550	360	360
$\Delta E/E$ @ 140 keV	%	9	15	20	6
μ @ 140 keV	cm^{-1}	2.7	3.9	1.7	3.0
τ @ 140 keV	cm^{-1}	2.1	3.2	0.9	2.2
Thickness (90% eff)	mm	8.7	6.0	13	7.7

$$\sigma_X \propto \frac{\sigma_{X_i}}{\sqrt{N_{p.e}}} \Rightarrow R \equiv FWHM_X \propto \frac{FWHM_{X_i}}{\sqrt{N_{p.e}}}$$

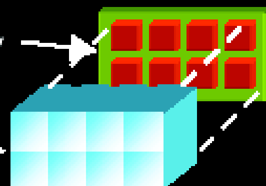
spatial resolution and linearity → ➢number of p.e. ➢light spread ➢light sampling → • scintillator thickness • granularity

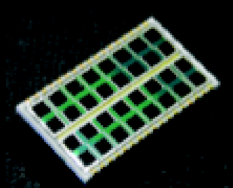




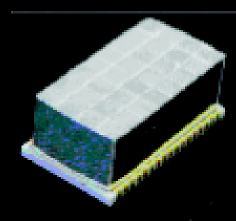


APD





Implemented on MADPET II

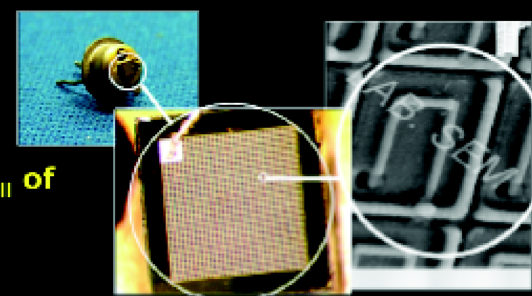


+ High spatial resolution
+ No Pile-up
+ No scattering in the crystals
- Expensive
- Many channels
- Difficult tuning

SiPM

SiPM are p-n diodes operating in **Geiger mode**, which means that the bias voltage is above the diode breakdown voltage.

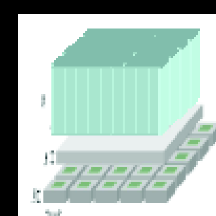
In this way output is independent from input:
⇨ the surface is divided into **m cells** (~1000/m²)



Signal ∝ N_{cell} of hit cells

+ High gain
+ Low noise
+ Good proportionality if $N_{photon} < N_{cell}$

An array of SiPMs can be used for "individual" readout, instead of PSMPT



C8 strips, 4 mm

116 4x4 mm2

164 2x2 mm2

6x6 mm2

3x3 mm2

(Burle)

1.5 mm2

Br$_3$

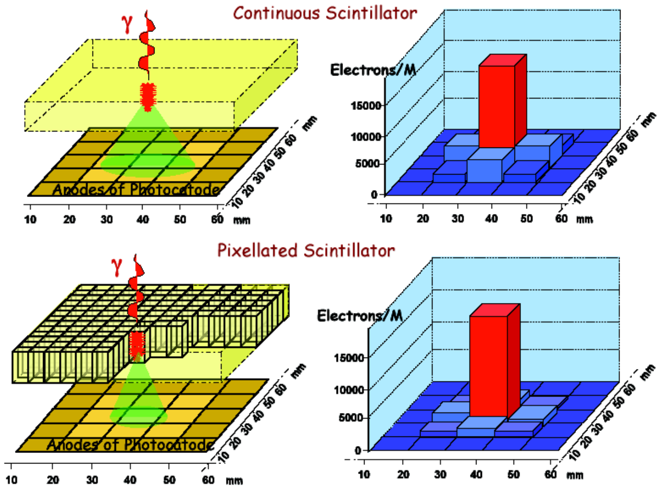
f channels is important

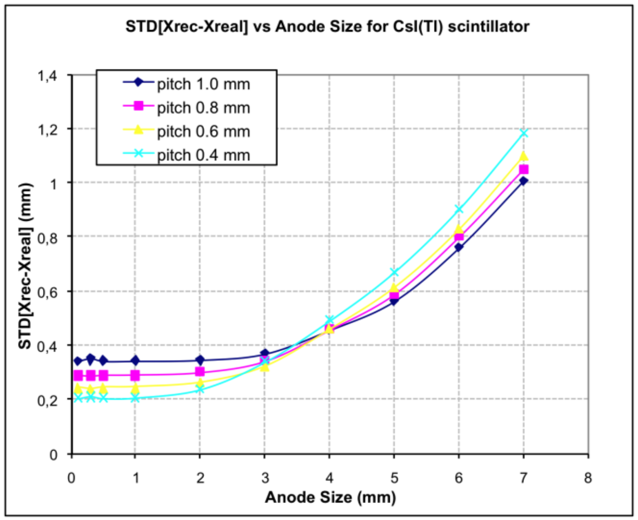
but

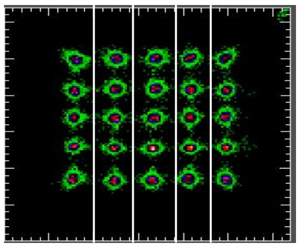
number of channels high

Hamamatsu PSPMT's

Importance of pixel identification

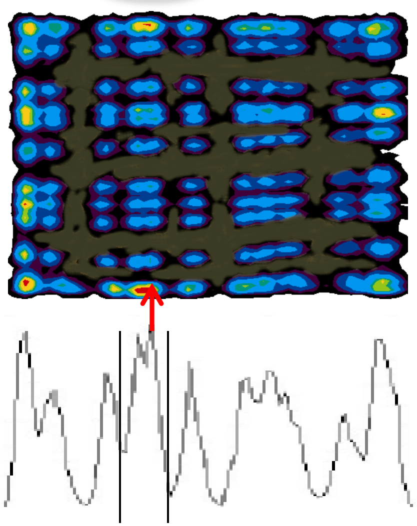






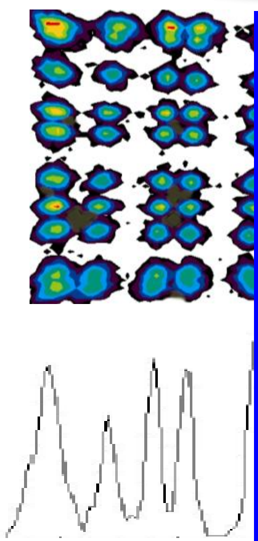
good pixel identification is fundamental for correct digitization affecting spatial resolution and contrast

C8 strips



resitive network

M16 (4 x 4) mm^2



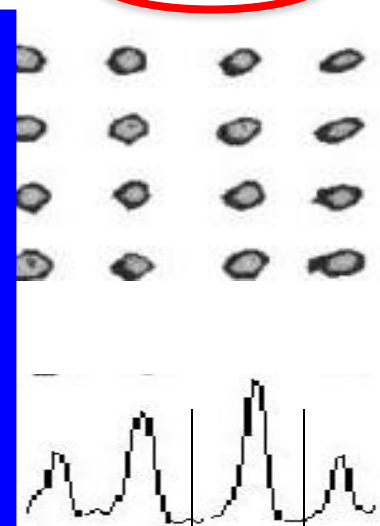
Individual channel readout

Individual readout means better pixel identification

↓

better image

M64 (2 x 2) mm^2



Individual channel readout

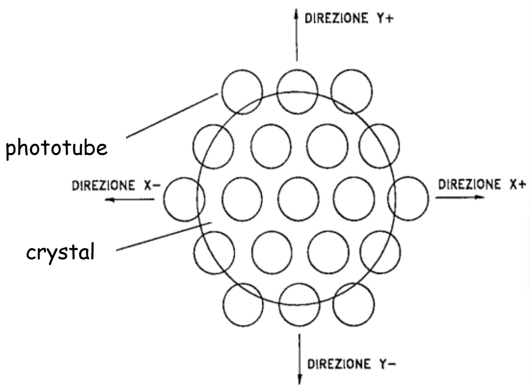
Electronics

Anger L

Resistive C

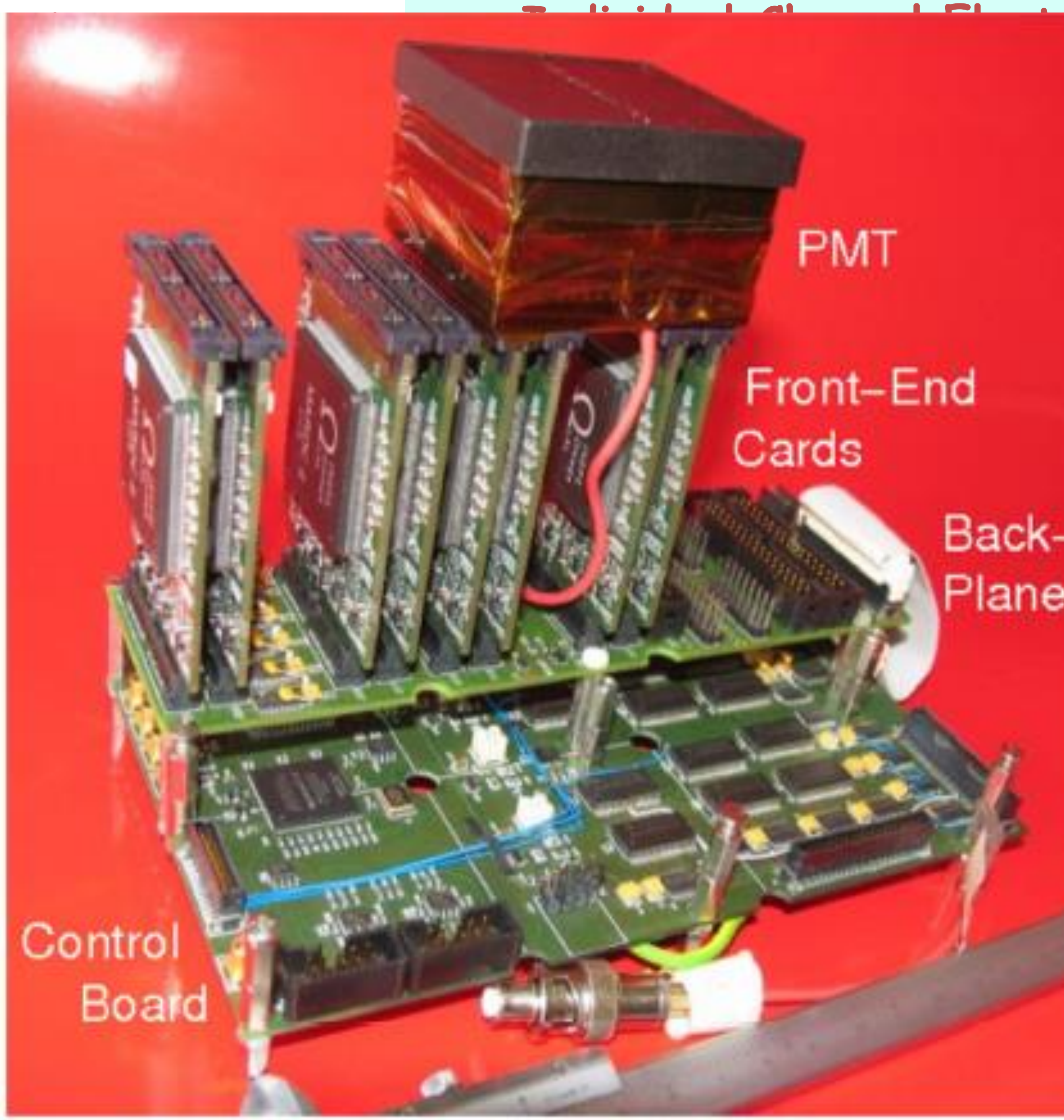
onics:

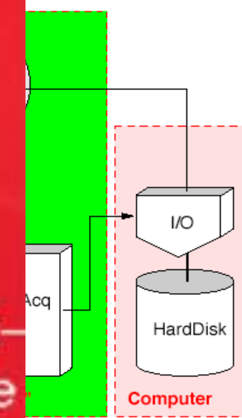
eadout



Cristal and Phototubes,
Planar view

Go





$$X = \frac{X^{+} - X^{-}}{Z}; Y$$

$$Z = X^{+} + X^{-} + $$

$c_i Y_i$

c_i

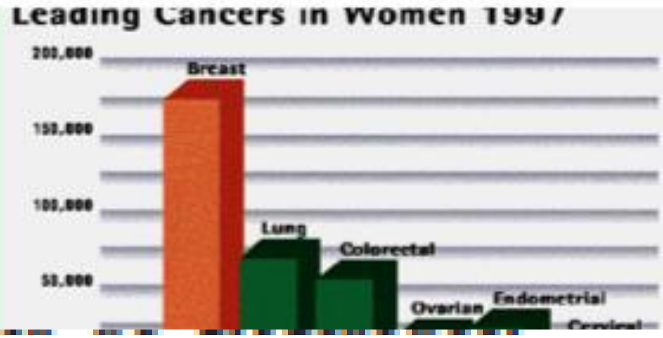
$(X_i, Y_i) = i^{th}$ *channel position*

Something you cannot do well with standard systems

Breast cancer

X-ray mammography, the most sensitive method
but
- it shows lesions, not cancers

-15-30% positive



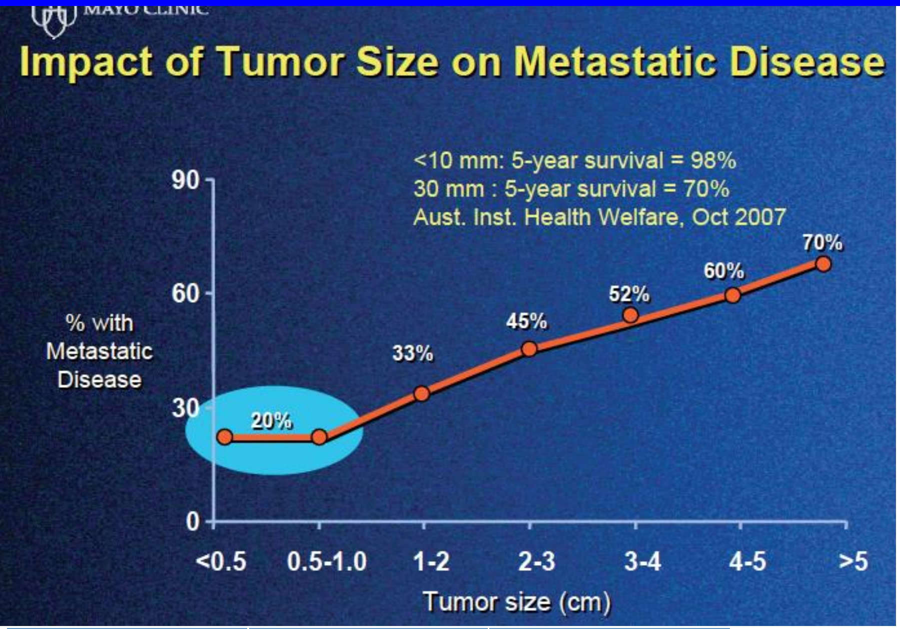
The sensitivity of mammography to the index cancer ranges from 63% to 98% (1–3) and has been reported to be as low as 30%–48% in dense breasts (4,5). Several groups

- false positive (problems in successive mammographic controls)
- false negative (medical problem great, delay in operation)

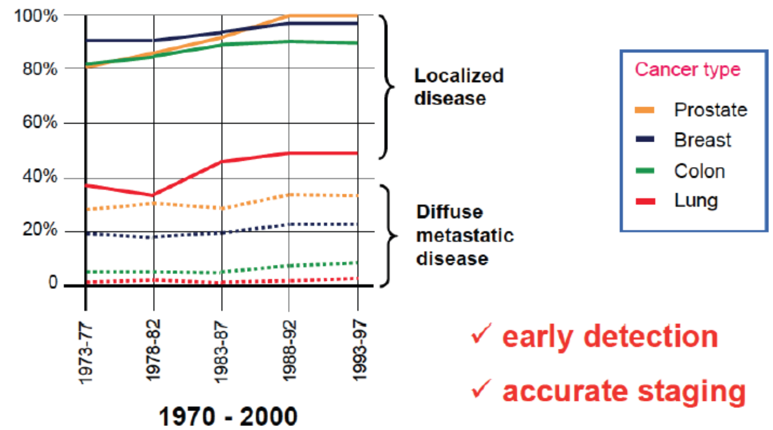
and doesn't work for dense breast

and for invasive lobular carcionoma

Importantce of detection of small lesions



Impact on 5-year cancer survival:



Fortune Magazine, March 2004

✓ **early detection**

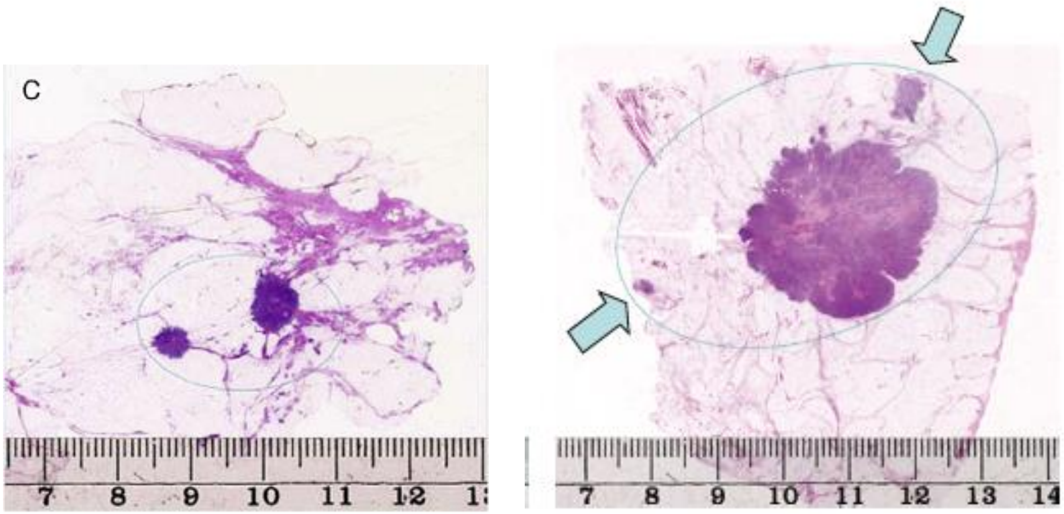
✓ **accurate staging**

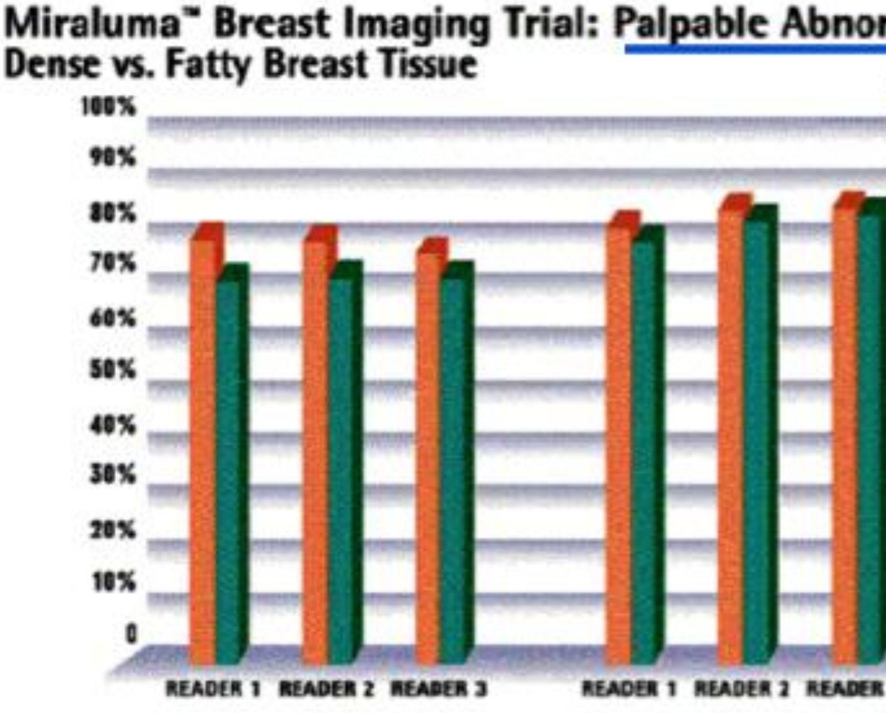
✓ **accurate monitoring**

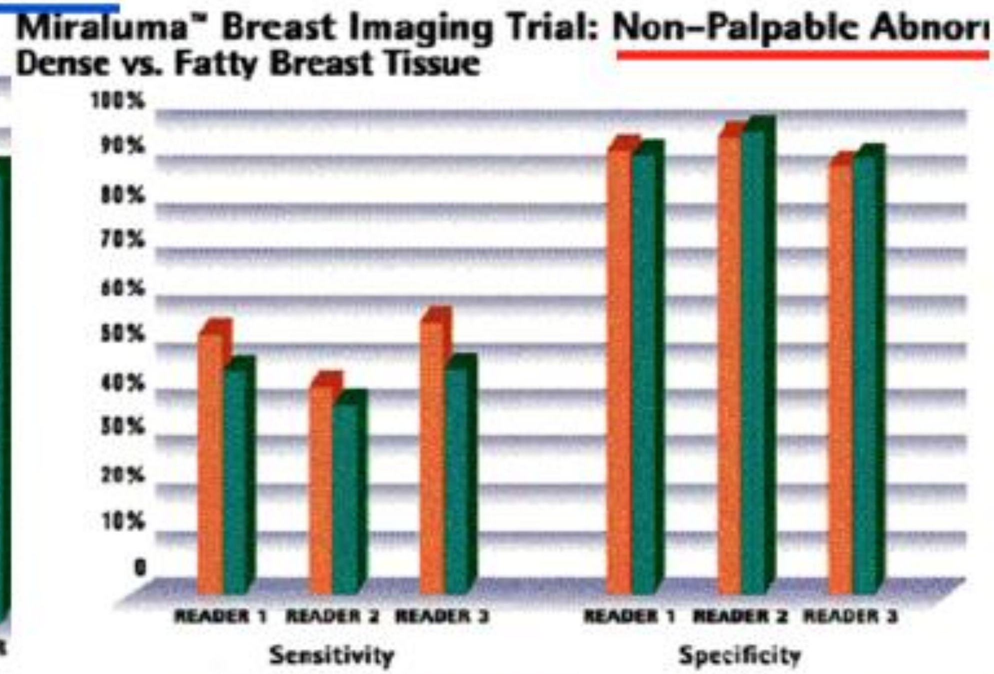
Tumor diameter (mm)		Sensitivity
0 - 5		0.67
6-10		0.87
11-15		0.97
16-20		0.95
> 20		1.00
<10		0.82
all tumors		0.87

Average sensitivity of MBI as a function of tumor size (M. O'Connor et al. Expert Rev. Anticancer, 2009)

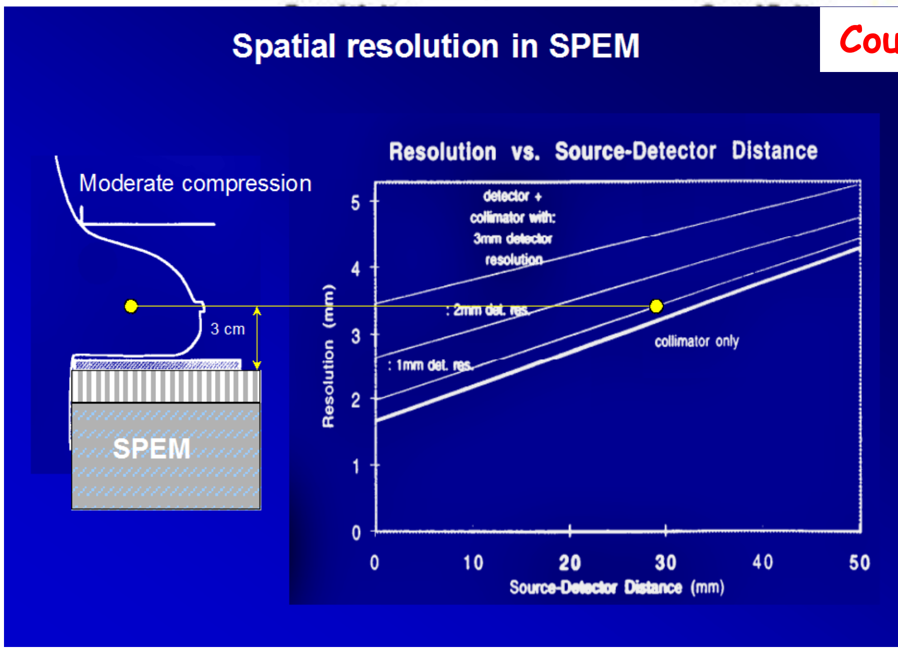
Multifocality

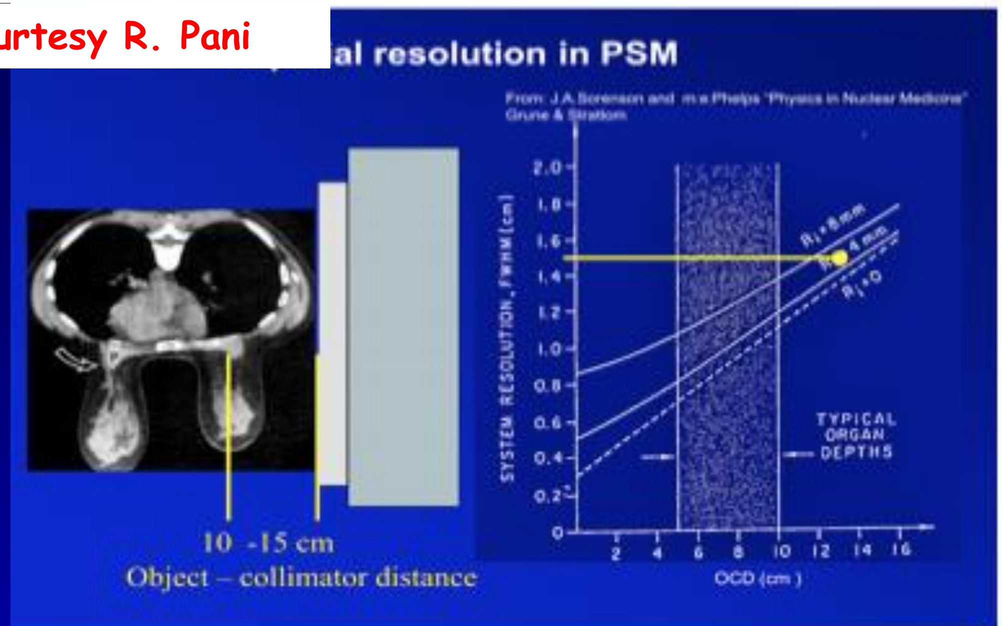






Courtesy R. Pani





Geant4 simulations

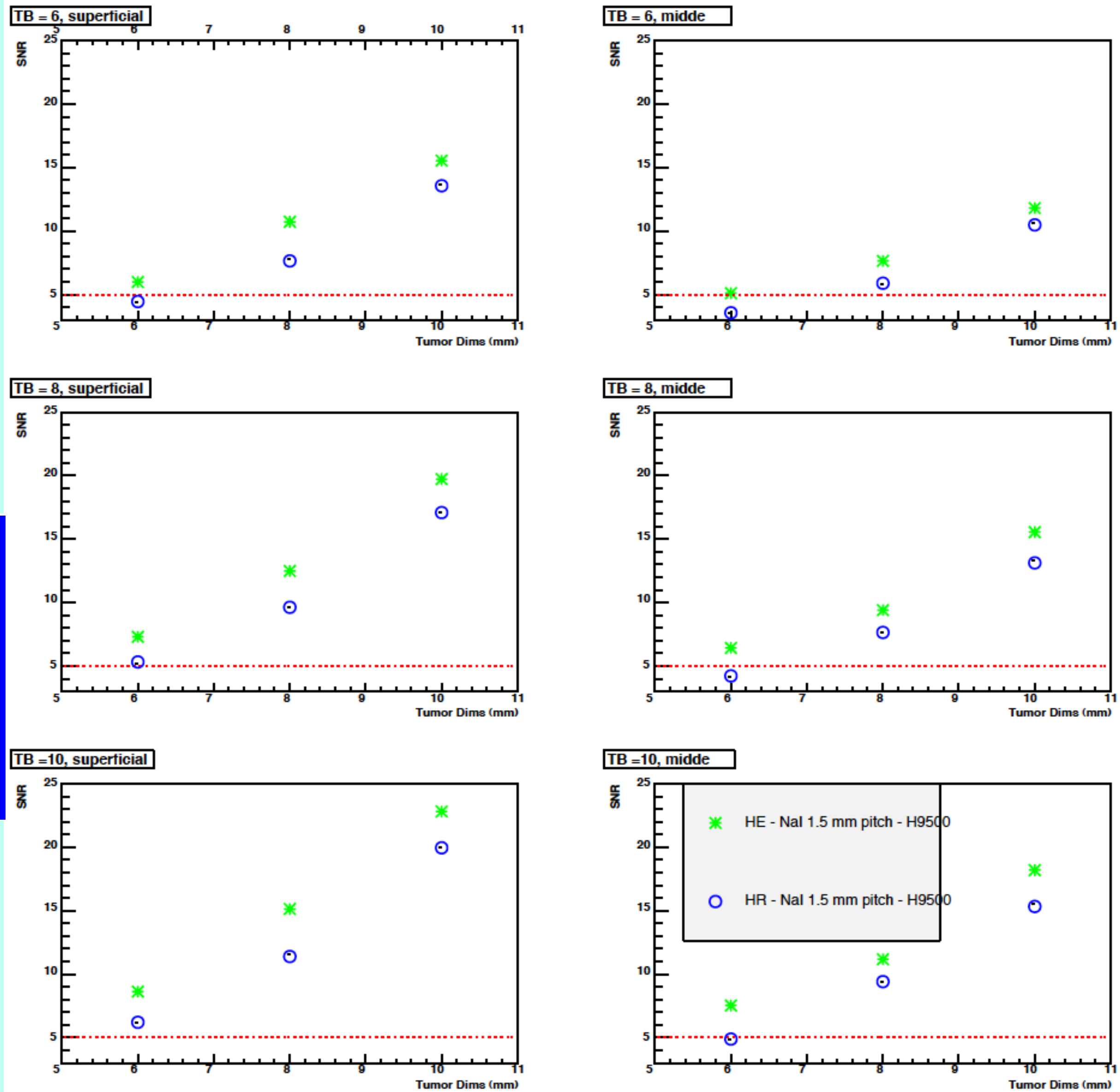
1 detector

- par.hole coll.
- NaI(Tl) 1.5 mm pitch(the smallest pixel in this applications (~13000 pixel in 150 x 200 mm2)
- H8500 (6 x 6) mm2 anode pixel
- Individual channles electronics

Sensitivity dominates the visibility, so we should try to get closer to the lesion and modify collimation and modality

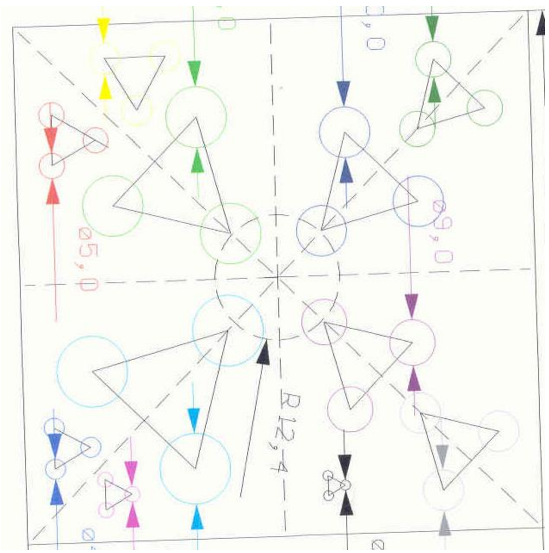
most cancers are in the upper part of the breast

→ 2 detectors



tum: (5, 6, 7, 8,9,10,12)

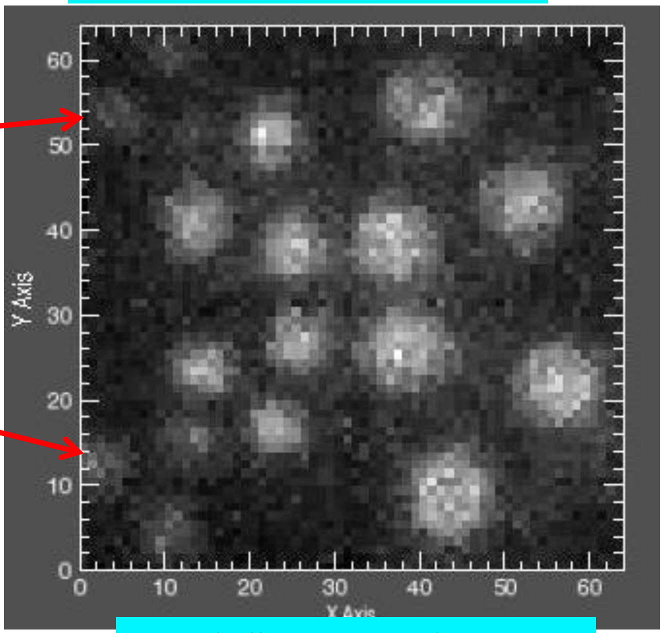
uptake 1:10; breast 6 cm



NaI(Tl) 1.5 pitch;
H8500(6x6 mm2)

6 mm

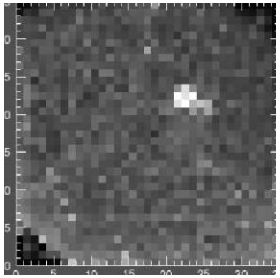
7 mm



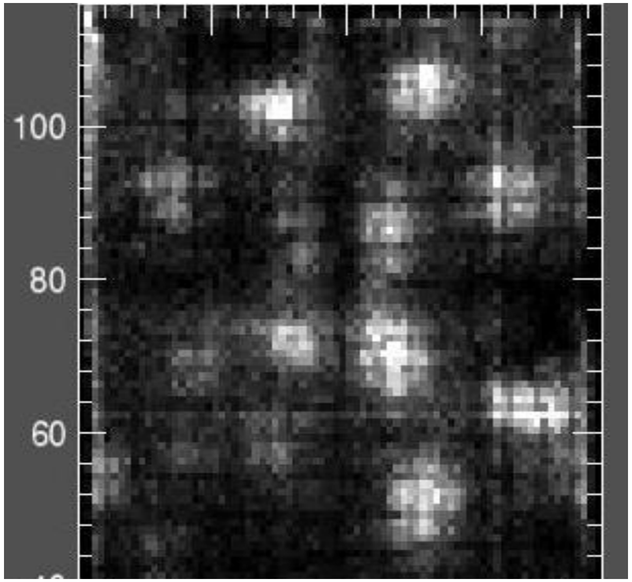
NaI(Tl) 1.3 pitch;
H8500(6x6 mm2)

NaI(Tl) 1.2 pitch

H9500 (3x3 mm2)



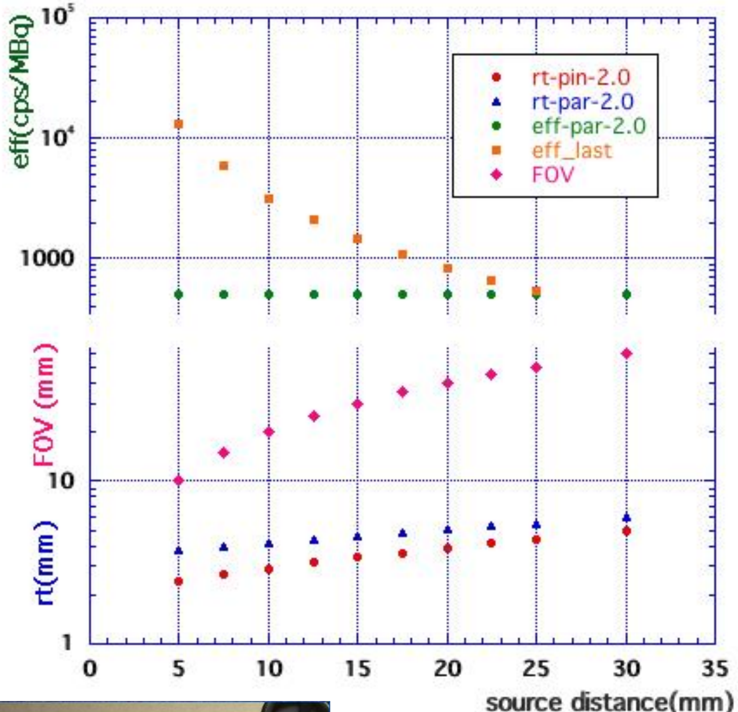
tum 8 mm

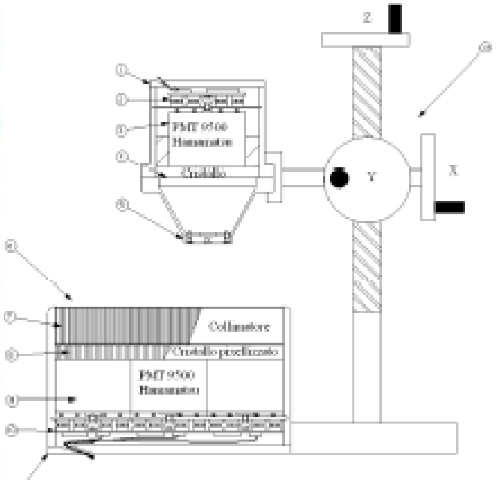


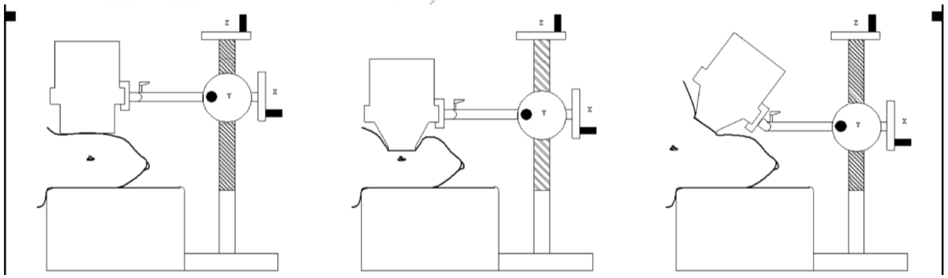
We can do even much better (spot ompression)

(just getting closer to the source and using pinhole collimation)

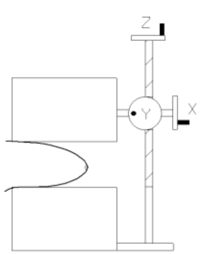
Efficiency-FOV-resolution vs source distance for parallel hole and pinhole collimators

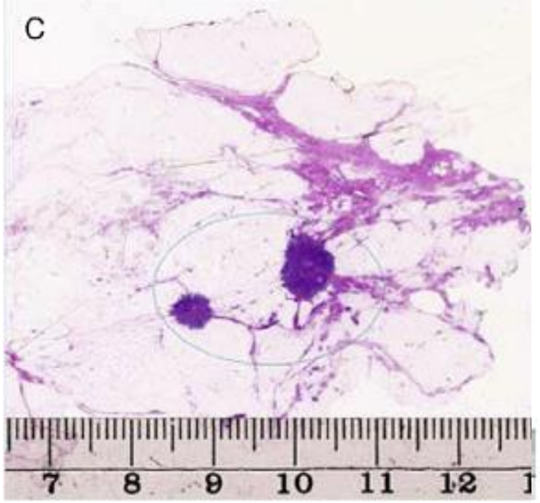


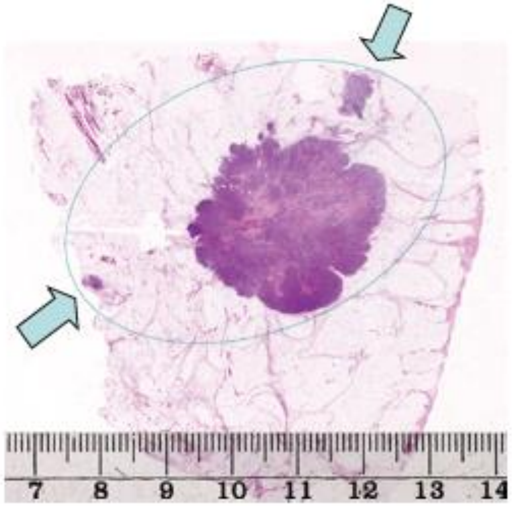




"Italian/European Patent No. RM2008A000541"



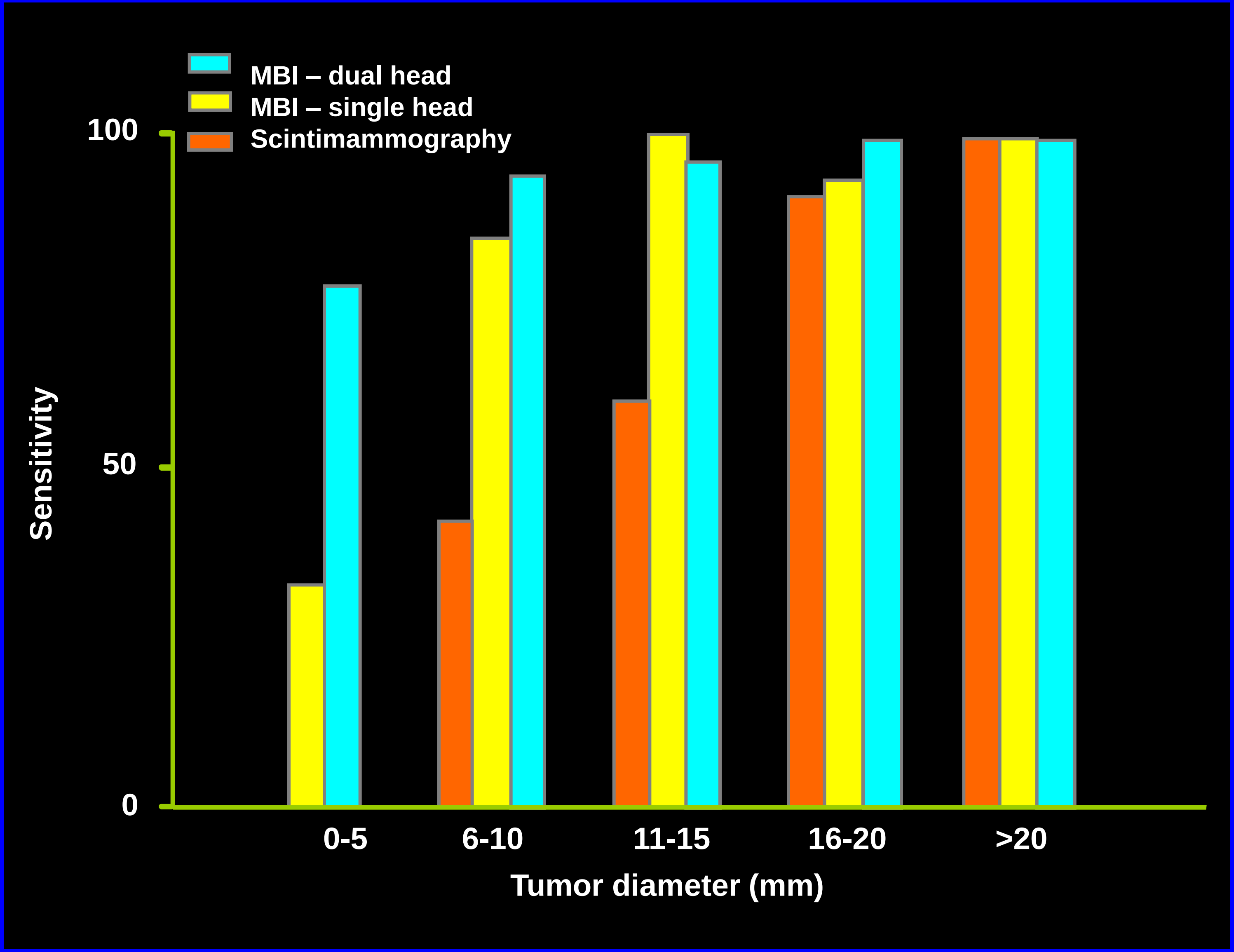


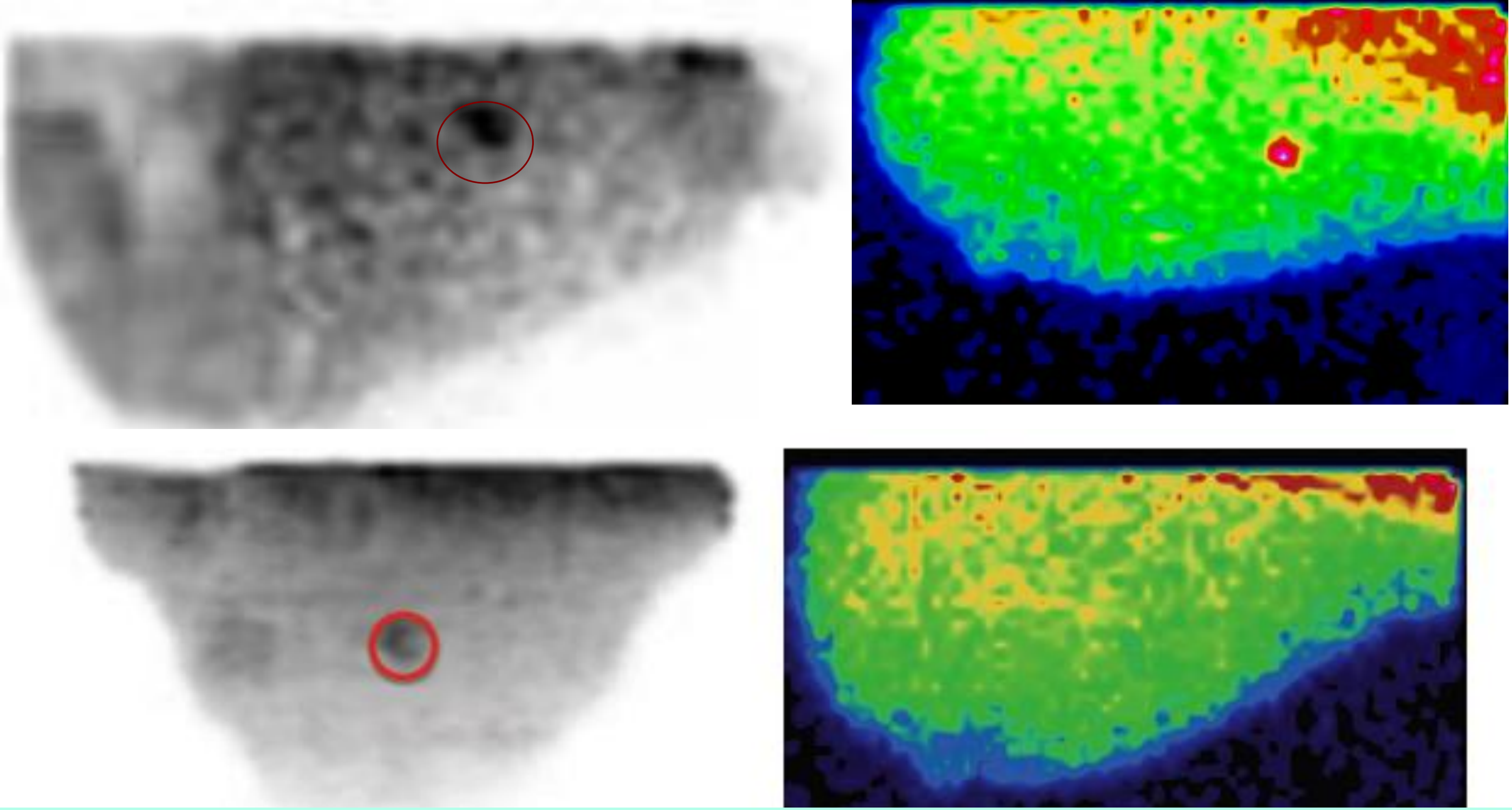


A Monte Carlo study on the collimator and scintillator system for the larger head and the smaller head was performed using the GATE code. Different system configuration were simulated, changing the pitch of the scintillator and of collimator for different source dimensions and for different source-collimator distances. Spatial Resolution, Energy Resolution, Efficiency, were calculated for the different cases. Signal to Noise Ratio (SNR) and Contrast to Noise Ratio (CNR) were obtained. In Tab 1 and 2 SNR and CNR are shown for two different scintillator pixel size for a 11 mm (in diameter) lesion for different source to detector distance. The advantage of smaller scintillator pixel is evident. Tab 1 refers to the larger detector (see later). To calculate the SNR of the whole system one has include the smaller detector having much higher efficiency, combine the counts coming form the two detectors and extract SNR and CNR for the system. This will make possible to detect very small lesions, better that any other dual MBI dual detector (4)

Source-detector distance (mm)	$SNR_{1.5}$	$SNR_{3.0}$	$CNR_{1.5}$	$CNR_{3.0}$
10	33	28	24.2	20.4
15	31	27	22.2	19.8
20	30	25	21.9	19.5
25	28	24	18.5	18.3

Comparative Sensitivity of Scintimammography, single-head MBI and dual-head MBI (M. Oconnor et al. Mayo clinic)





- 10 trials , University of Roma2 (TOV)
  in comparison with standard dedicated detectors (Gammamedica and Dilon)

- 2 big tumors

- 1 small tumor (< 10 mm)

- 7 “negative”, suspicious to mammography, negative (or positive in some case) ultrasound and MRI

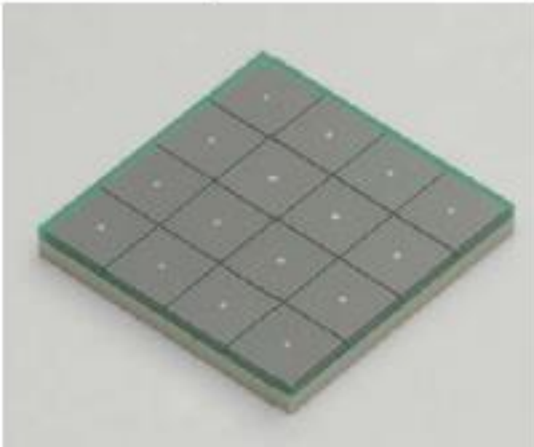
Multimodality

Project funded by FILAS Regione Lazio: collaboratin between Italian National Institute of Health (ISS), Italian National Institute of Nuclear Physicis (INFN) and Metaltronica s.r.l.

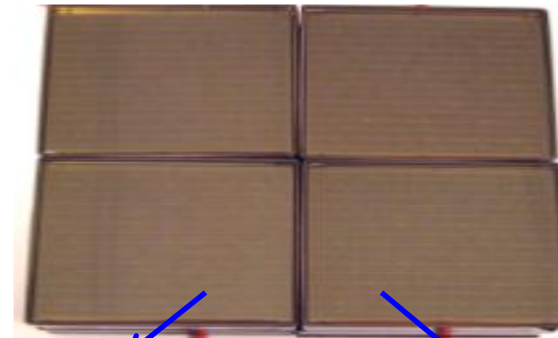
Tomosinthesys + scintigraphy

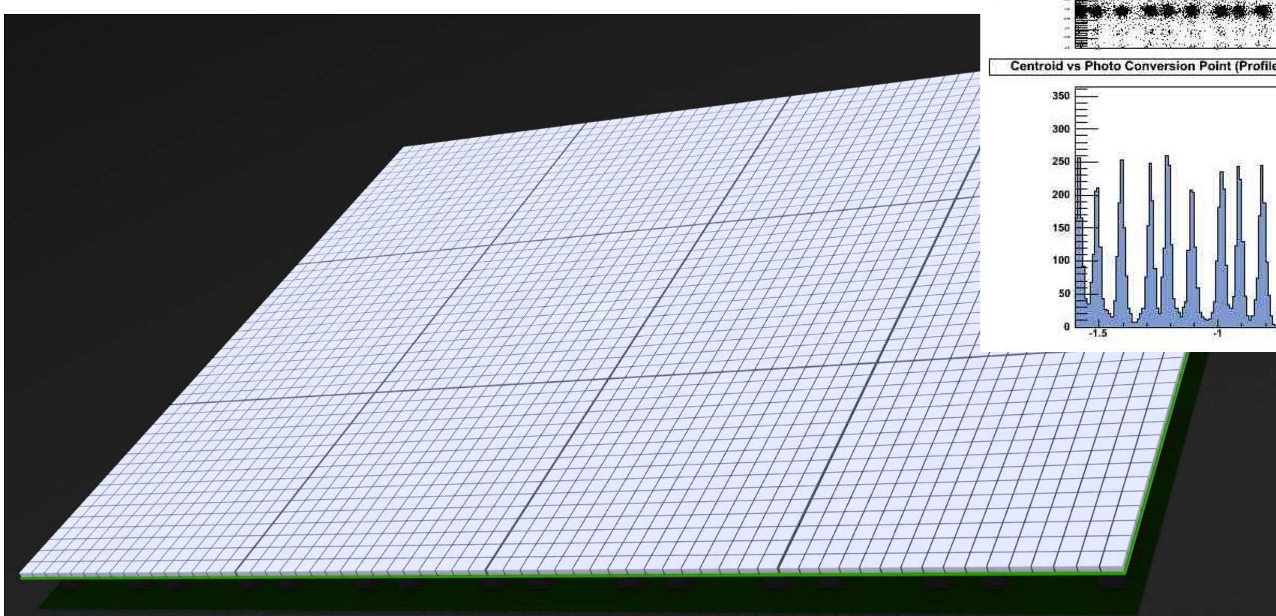
SiPM photodetector

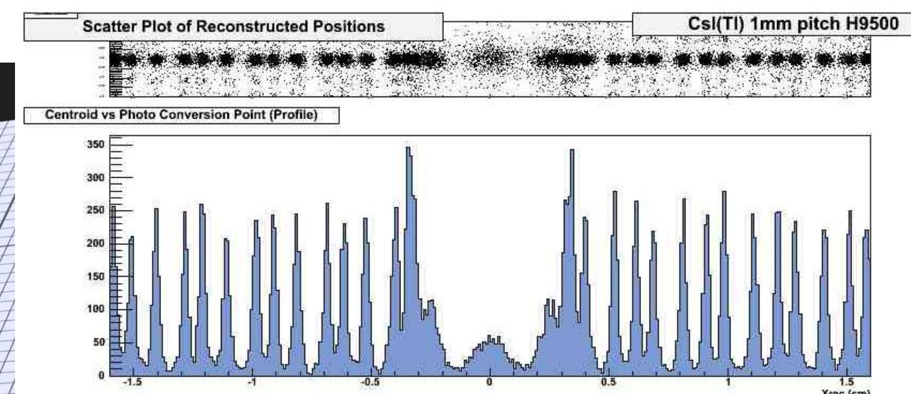
Hamamatsu S12642-1616PA-50: 3x3mm²



3 mm pitch → array 16 x 16

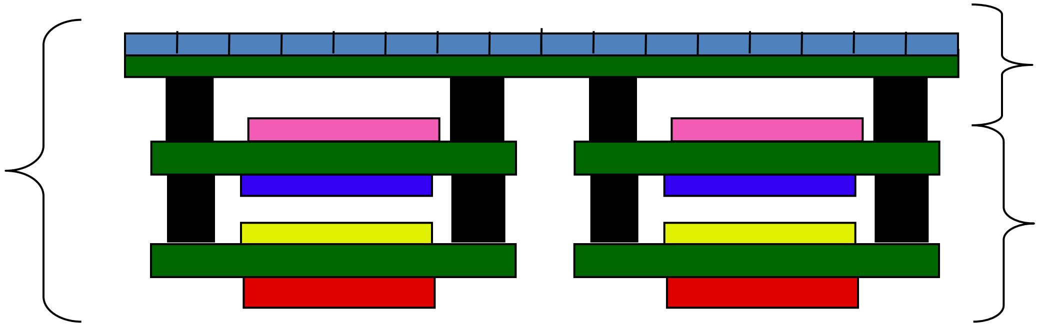






150 x 200 mm2

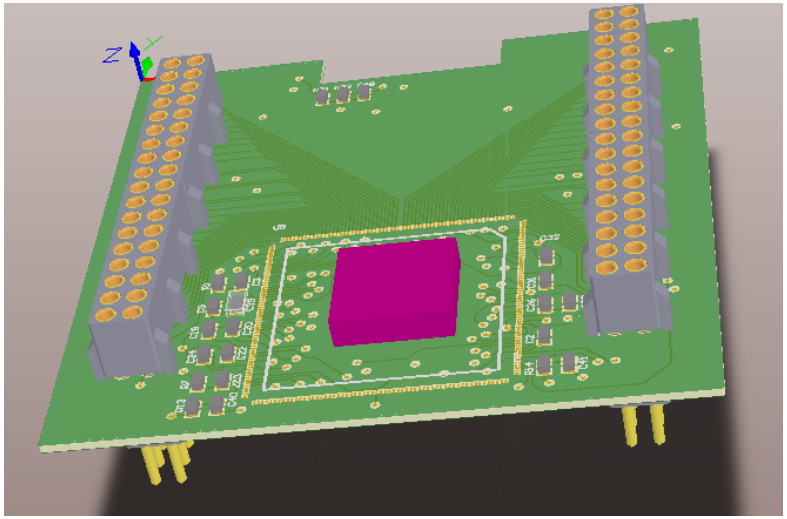
Compact electronic readout



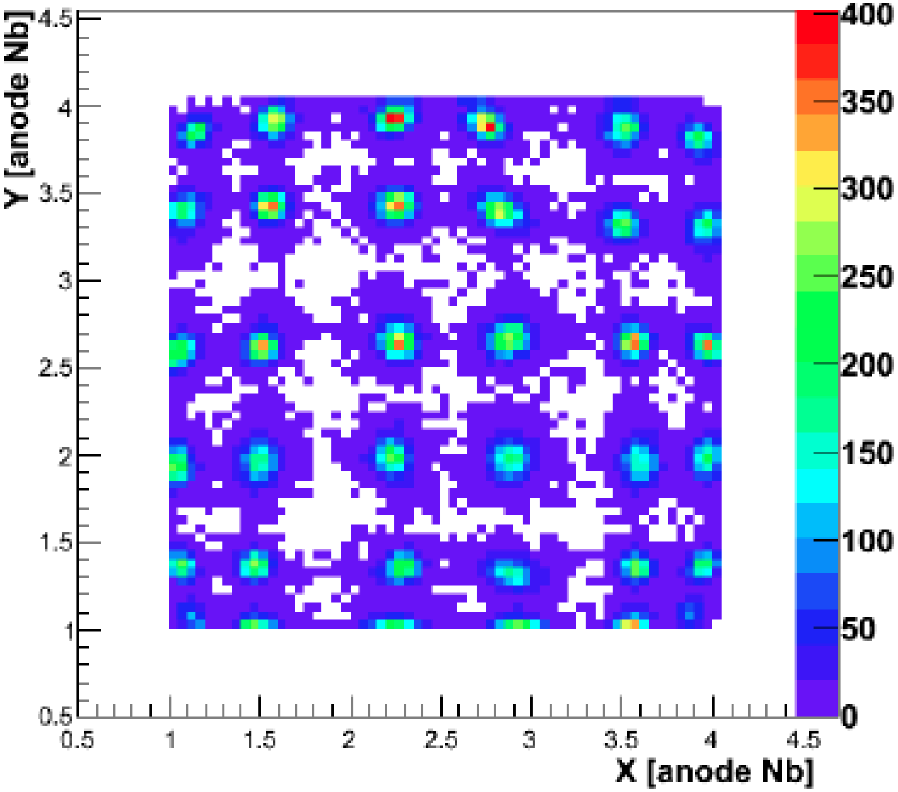
Readout electronics characteristics:

- single channel approach (~3000 channels)
- settable trigger for each channel
- 5 kevent / second throughput
- supply voltage temperature feedback on each MPPC module

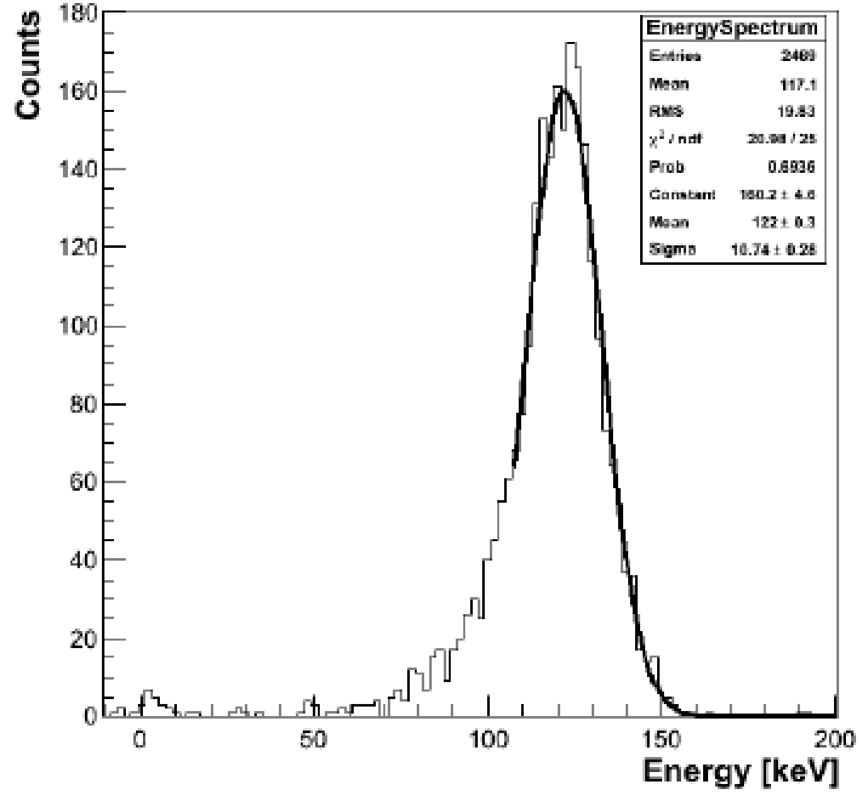
Front-end Board 3D model



NaI(Tl) array, S12642-050 @ 68.4V, Temp ~ 18 deg C

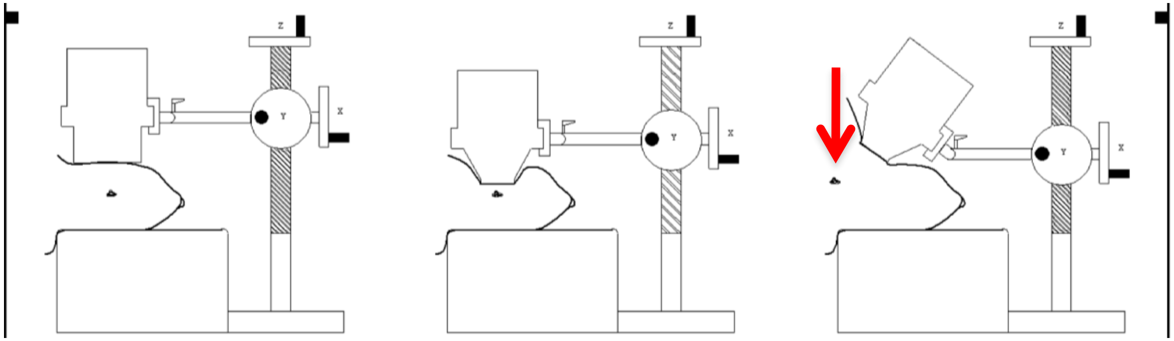


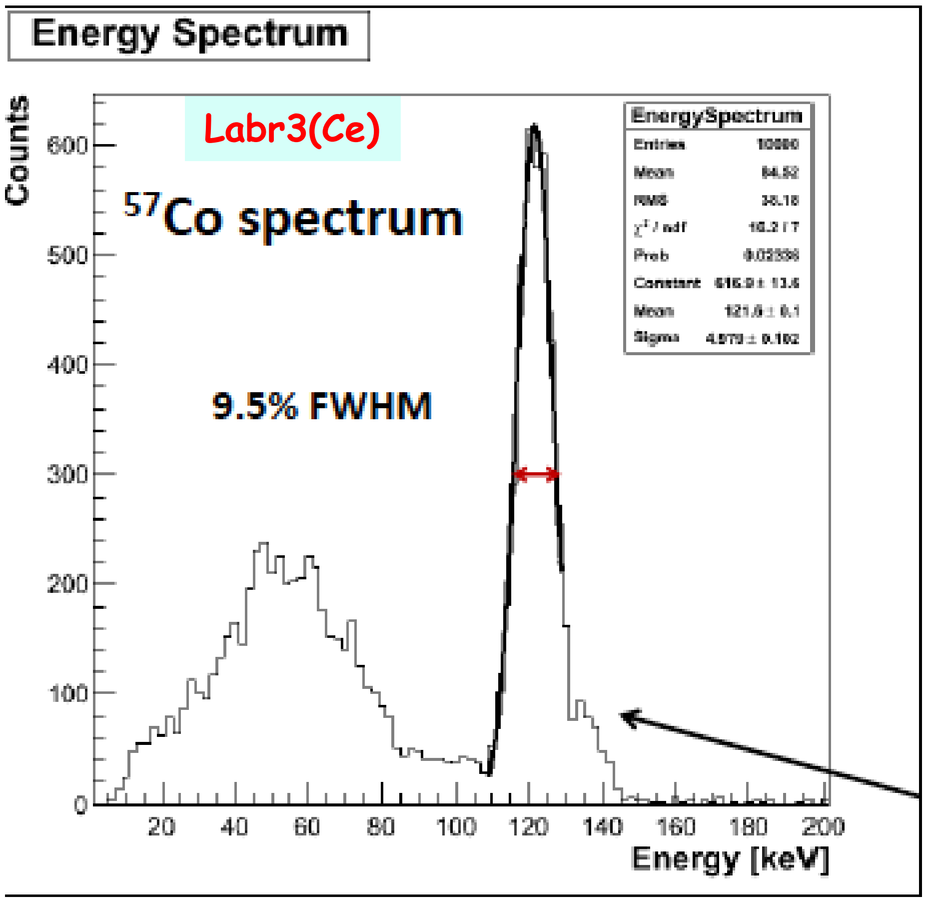
Energy Resolution @ 122 keV: 16-17%

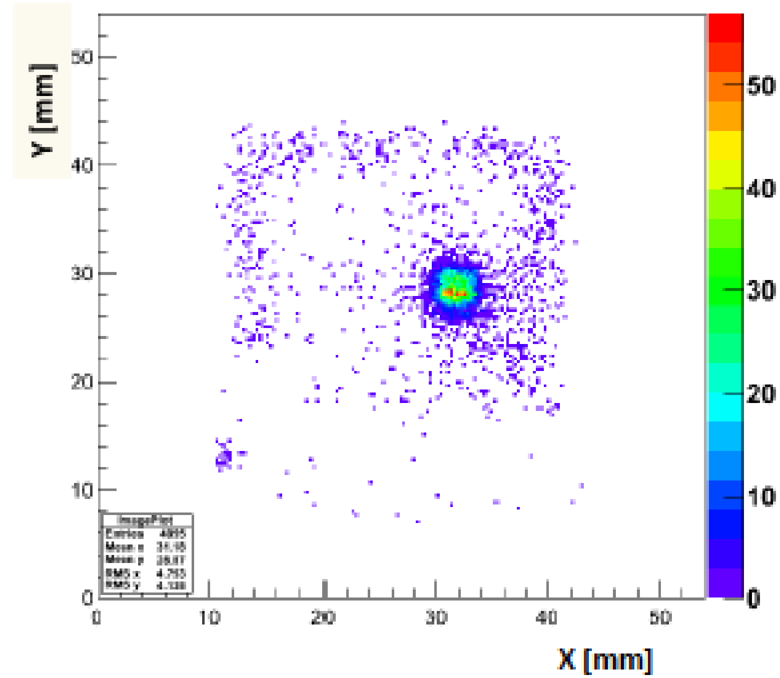


Maroc3 setting: C_buffer = 0.5pF, C_feedback = 2.1pF

ΔE/E might be important for lesion close to the chest (high background)



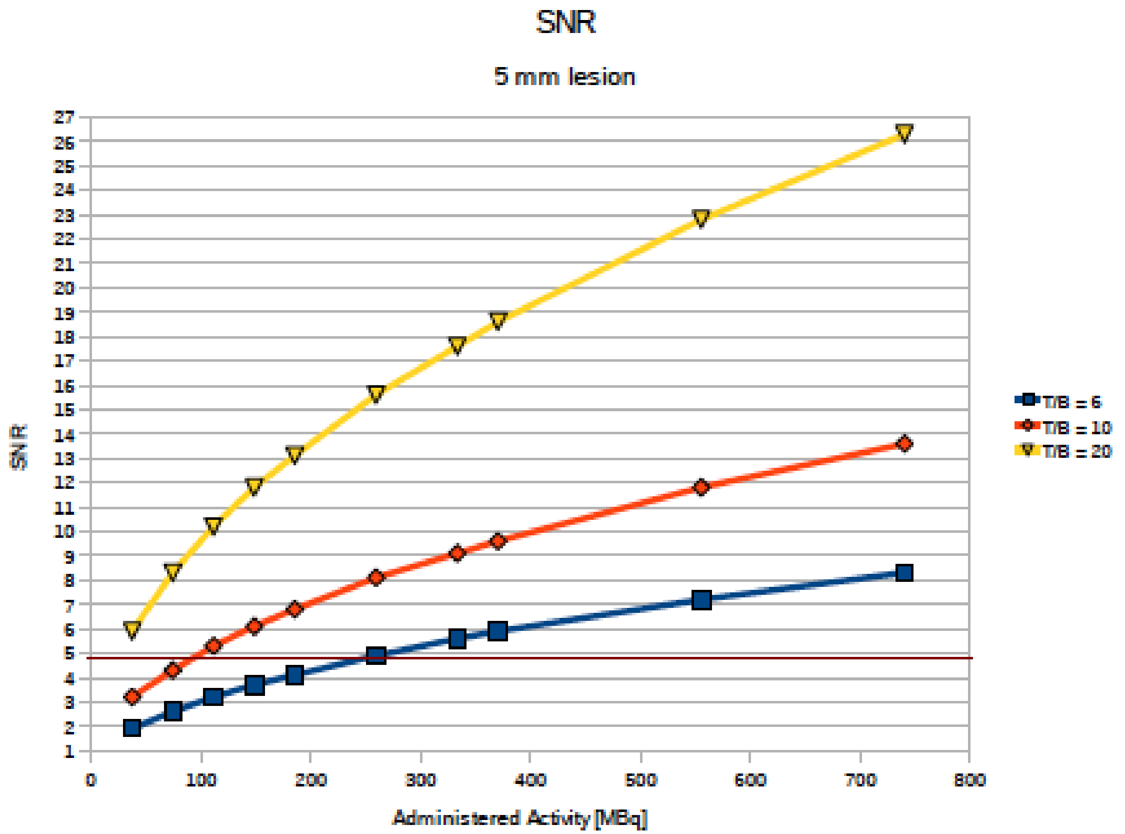




136 keV peak

Screening for women at risk (dense breast)?

The dose has to be much lower ~ the same as for mammography (~ 1/5 (740 MBq))



Summary and conclusions

- Molecular imaging is a powerfull tool for diagnosis and follow up of diseases

- Radioncuclide techniques have a key role

- Dedicated devices are frequently needed

- Focusing on small object and imaging at the same time the whole organ

-Multimodality is mandatory in most cases (practical problems, cost etc)

outlook

-improving reconstruction algorithms to fully profit of multichannel electronics

- optimizing modality and protocol (comparison with MRI)

- new radiotracer ? (Tc99m αVβ3 pepetide)

- Multimodality (tomosinthesys + scintigraphy)

- multicenter trial (international (Italy, USA)) starting early 2015

    - 3 clinics → ~ 10 trials/day → ~ 5000 in 2 years

MEDAMI 2014 - III MEDITERRANEAN THEMATIC WORKSH ADVANCED MOLECULAR IMAGING

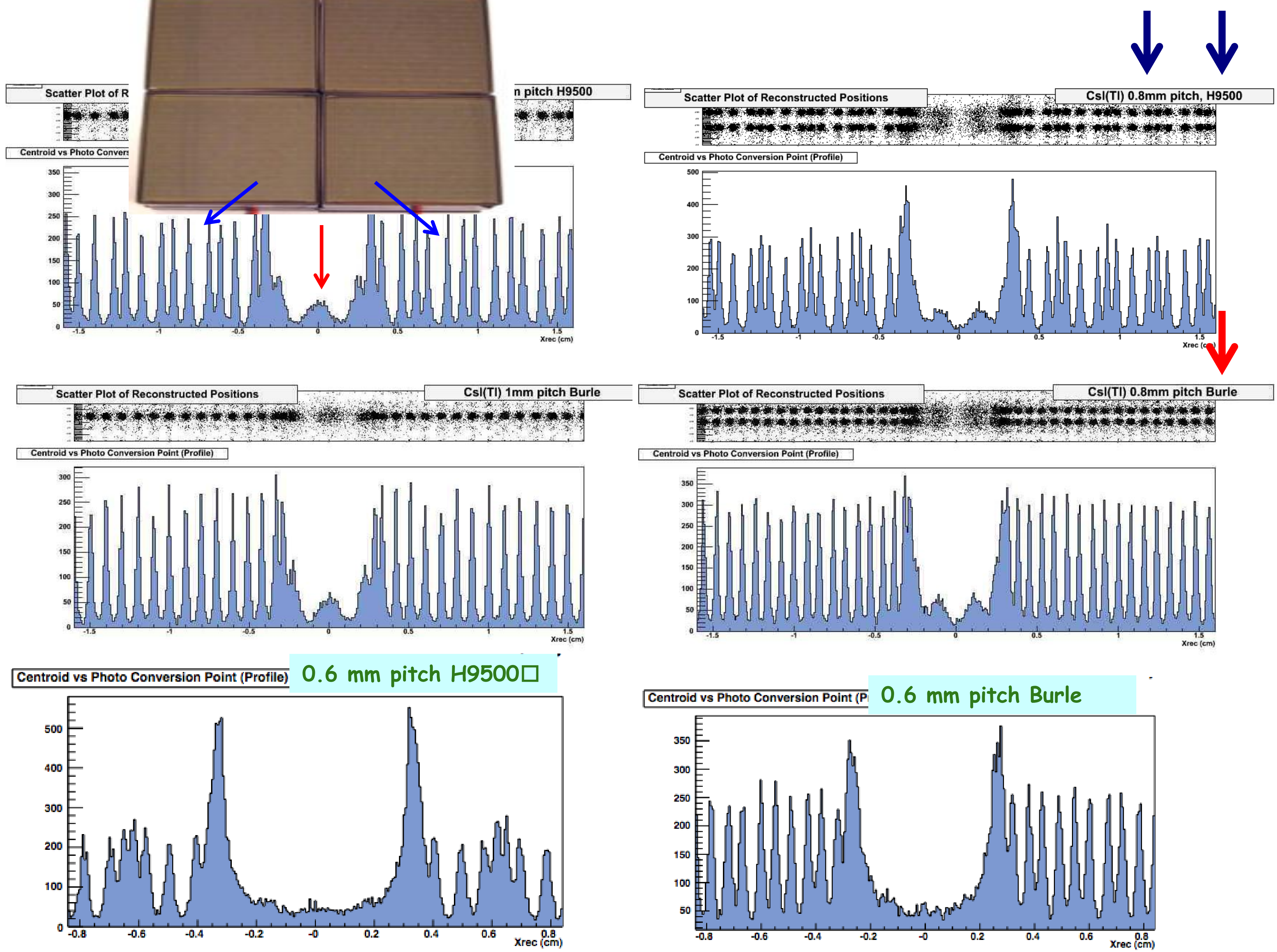
3-7 September 2014
Europe/Rome timezone

Mediterranean
Thematic Workshops
in Advanced Molecular Imaging

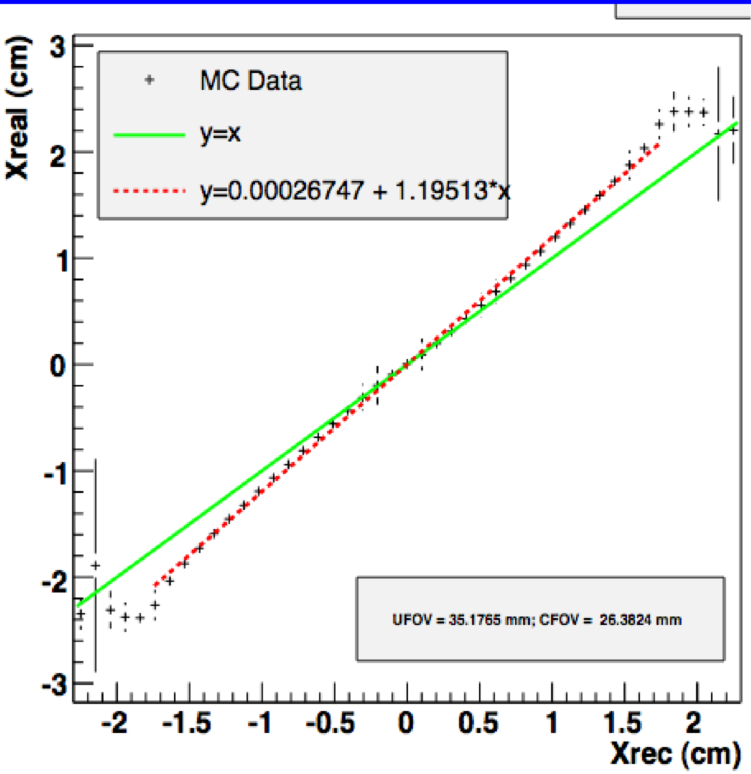
TRANSLATING TECHNOLOGY FROM NUCLEAR AND PARTICLE PHYSICS TO THE CLINIC: ADDRESSING MEDICAL NEEDS BY DETECTOR KNOW-HOW WITH A FOCUS ON ORGAN-SPECIFIC IMAG

Collaboration between the physics-, medical- and industrial communitie

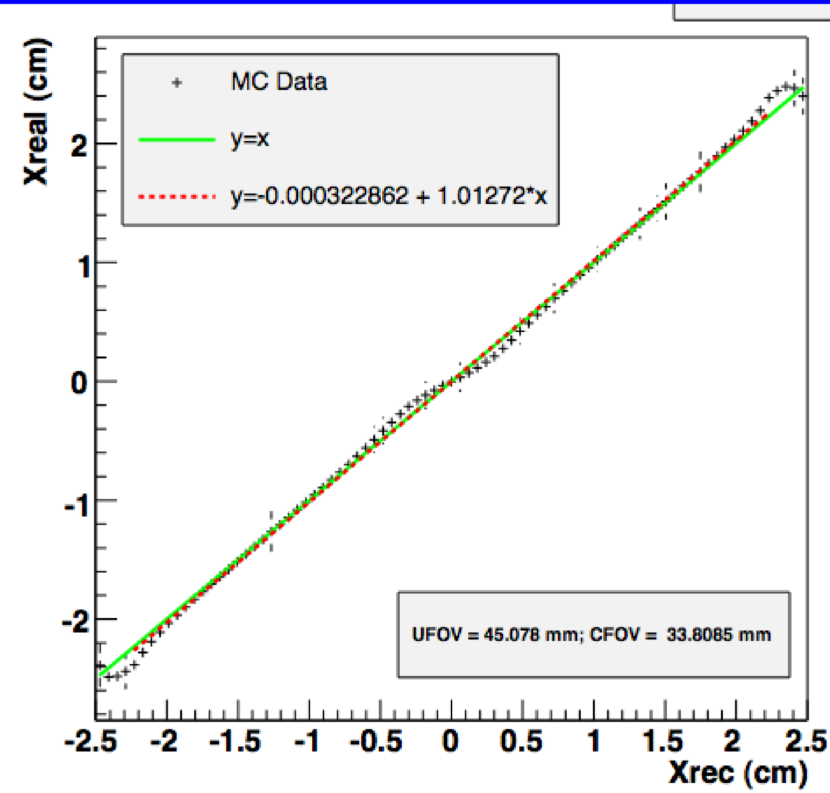
September 3 – 7 – 2014
Alghero (Sardinia - Italy)

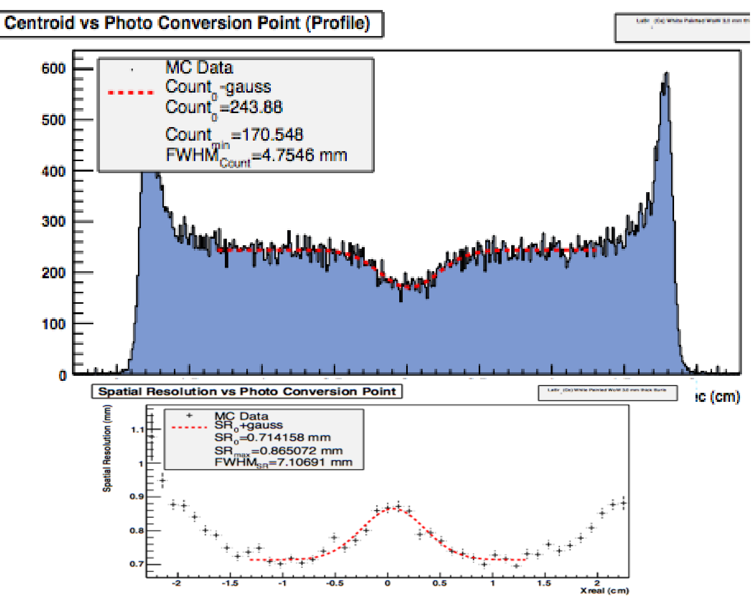

Scatter Plot of R
n pitch H9500
Centroid vs Photo Convers
Xrec (cm)
Scatter Plot of Reconstructed Positions
CsI(Tl) 0.8mm pitch, H9500
Centroid vs Photo Conversion Point (Profile)
Xrec (cm)
Scatter Plot of Reconstructed Positions
CsI(Tl) 1mm pitch Burle
Centroid vs Photo Conversion Point (Profile)
Xrec (cm)
Scatter Plot of Reconstructed Positions
CsI(Tl) 0.8mm pitch Burle
Centroid vs Photo Conversion Point (Profile)
Xrec (cm)
Centroid vs Photo Conversion Point (Profile)
0.6 mm pitch H9500
Xrec (cm)
Centroid vs Photo Conversion Point (P
0.6 mm pitch Burle
Xrec (cm)

Labr3 Continuoum different performances for different window treatment, diffusing (a), absorbing (b)

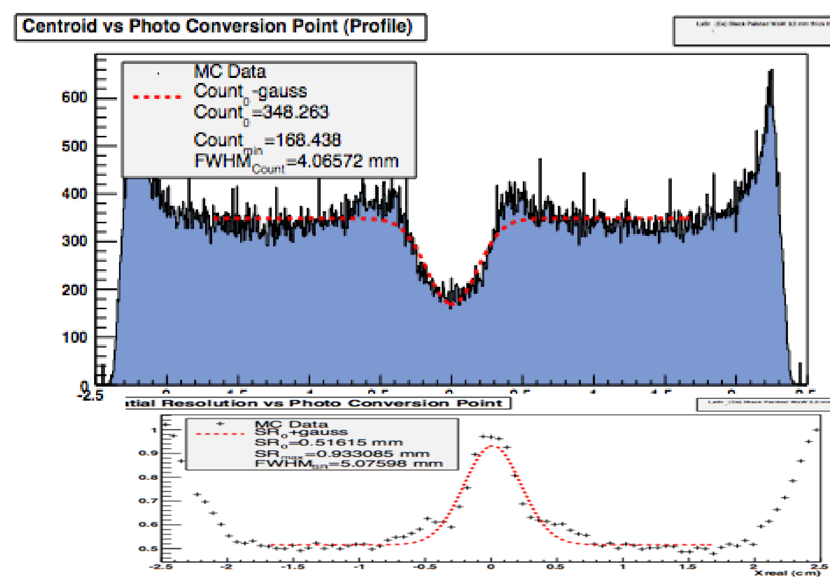


a





b



Molecular Imaging

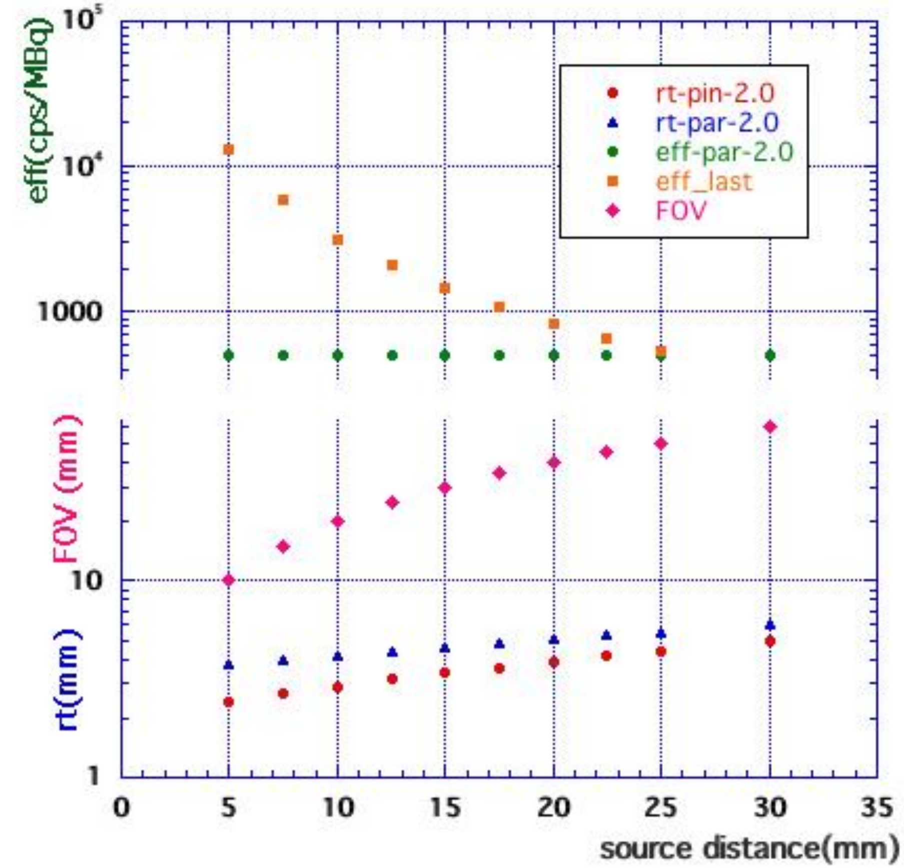
- “… the *in vivo* characterization and measurement

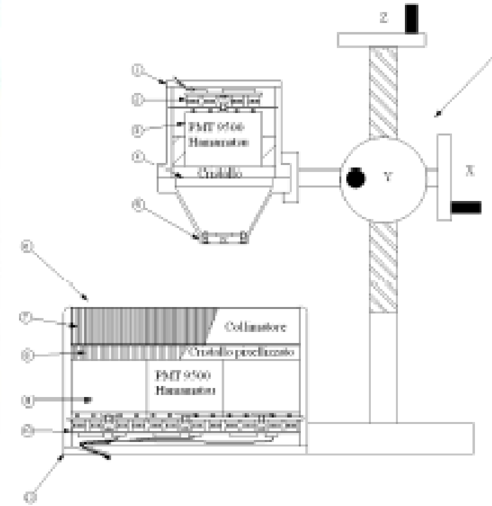
Five Technologies Set to Change the Decade* *(2009 - 2019)*

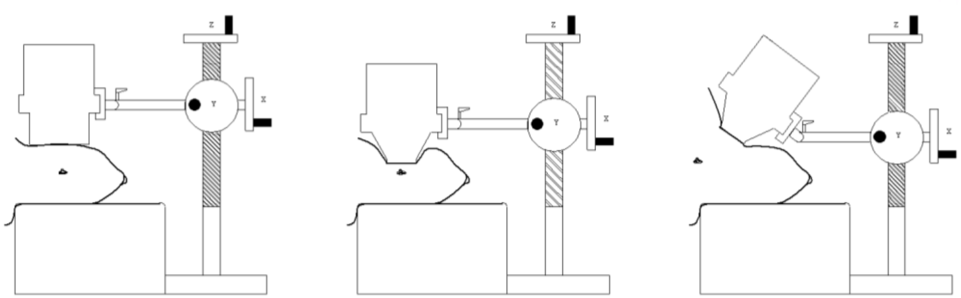
- **Building-Integrated Photovoltaics (BIPV)**
  - ***(solar technology projected to generate 50% of the electrical needs of the developing countries)***
- **Personal Genome Sequencing**
- **Molecular Imaging**
- **Graphene Transistors**
  - ***(nanomaterial graphene to replace silicon flash memory chips)***
- **Multi-touch Displays**

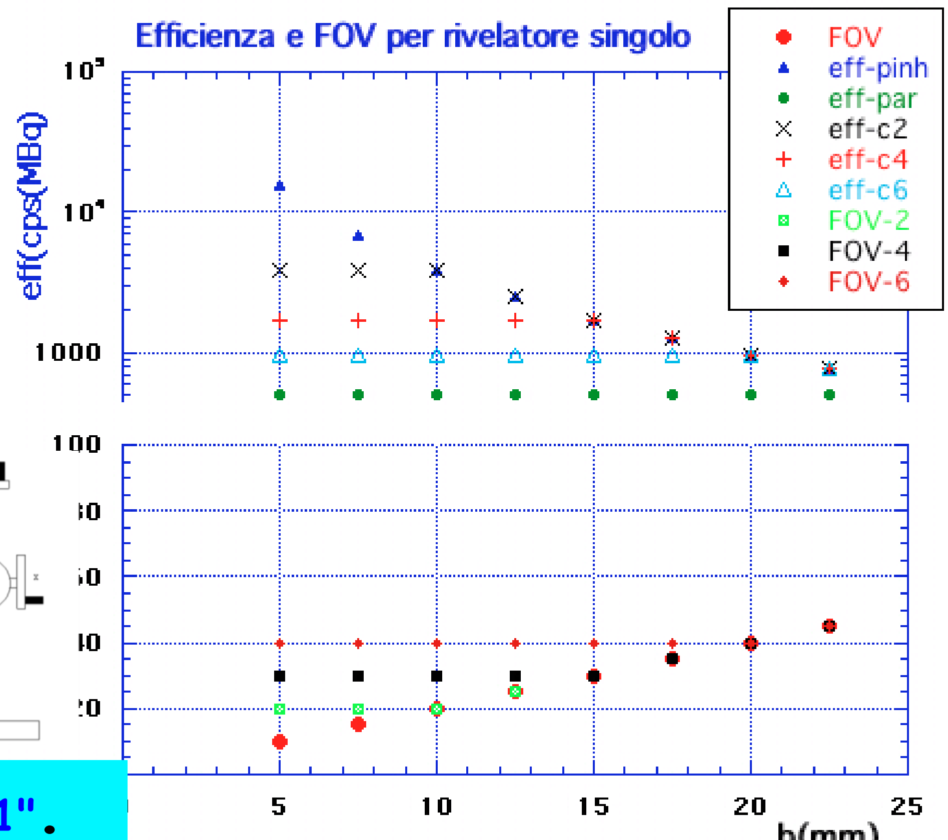
*Wolf, J. Five Technologies Set to Change the Decade. **Forbes.com. Jan. 1, 2009***

Efficiency-FOV-resolution vs source distance for parallel hole and pinhole collimators



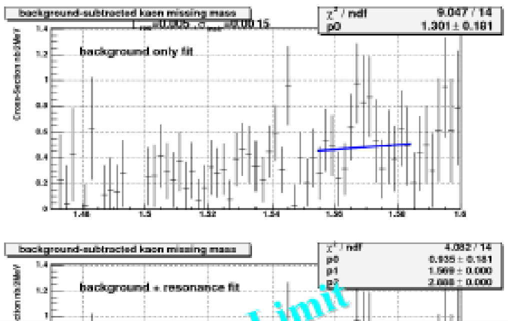




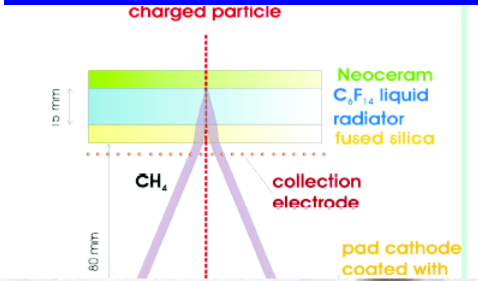


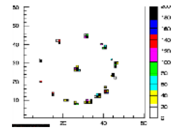
"Italian Patent Pending No. RM2008A000541".

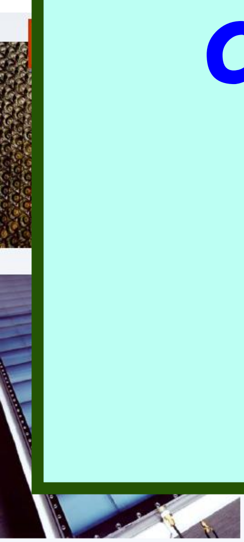
Θ^{++} Search



Freon/CsI RICH detector (like ALICE)







similar is not always the same !

$\langle N_{p.e.}\ (C_4F_{10})\rangle = 12$

E. Nap

Important parameters for detectability/visibility

they are correlated

$$SNR = \frac{S - \ldots}{\sqrt{\ldots}}$$

$$IC = \frac{Max - \ldots}{M\ldots}$$

efficiency (collimation)

$$X = \frac{\sum_{i=1}^{N_{channel}} c_i X_i}{\sum_{i=1}^{N_{channel}} c_i}$$

spatial resolution

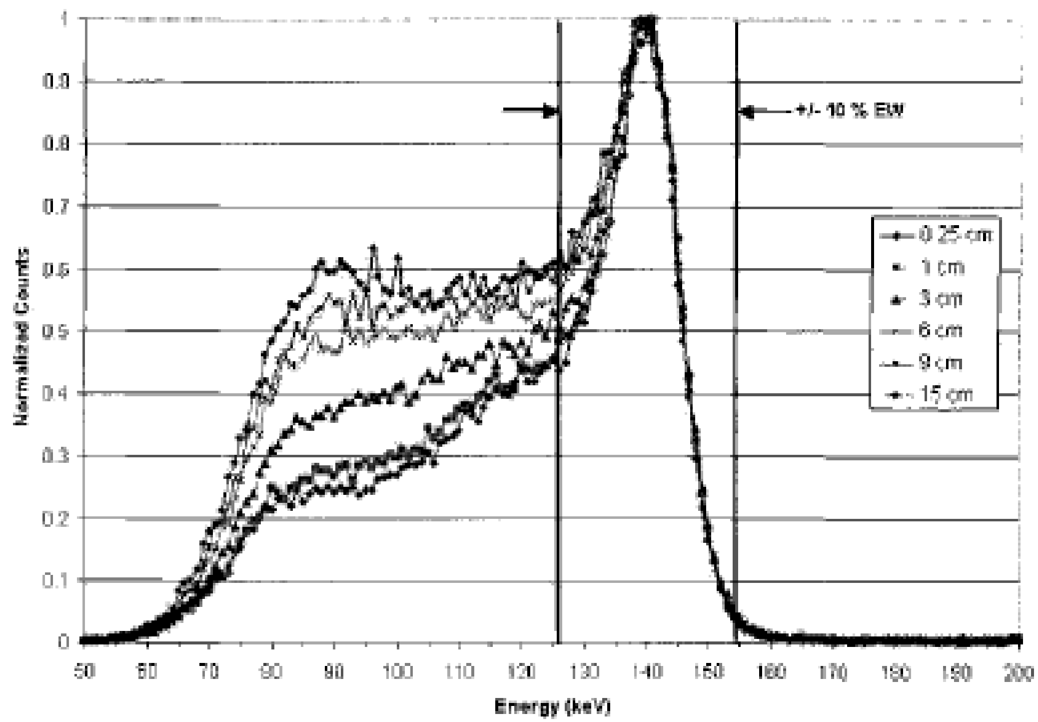
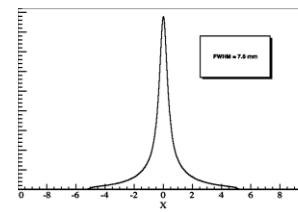
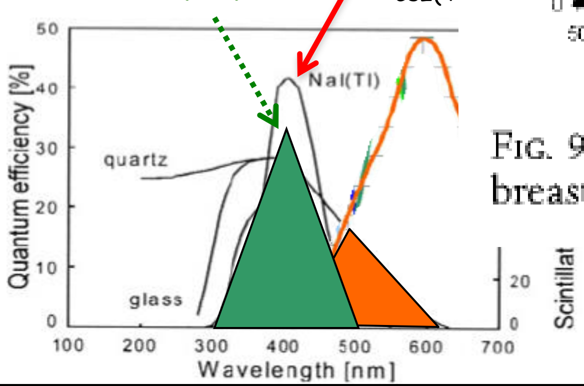


FIG. 9. Energy spectra from breast phantom as a function of breast thickness.



energy resolution pl...
secondary additional ro...
volumes are invol...



				...AP	LaBr$_3$(Ce)
				.55	5.29
Effective Z		51	54	32	47
Relative Yield	%	100	45	35-40	130
Peak Wavelength	nm	410	550	360	360
$\Delta E/E$ @ 140 keV	%	9	15	20	6
μ @ 140 keV	cm^{-1}	2.7	3.9	1.7	3.0
τ @ 140 keV	cm^{-1}	2.1	3.2	0.9	2.2
Thickness (90% eff)	mm	8.7	6.0	13	7.7

$$\sigma_X \propto \frac{\sigma_{X_i}}{\sqrt{N_{p.e}}} \Rightarrow R \equiv FWHM_X \propto \frac{FWHM_{X_i}}{\sqrt{N_{p.e}}}$$

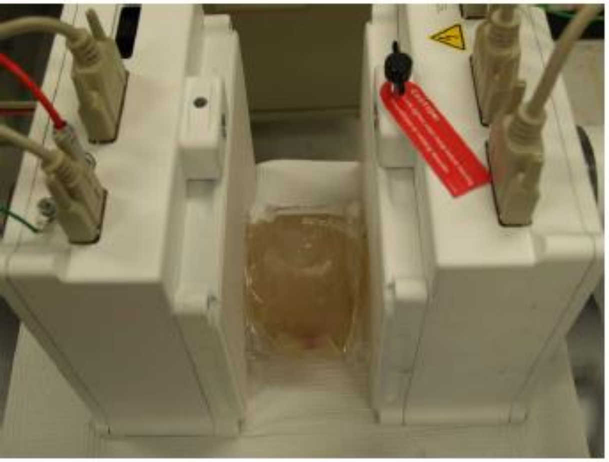
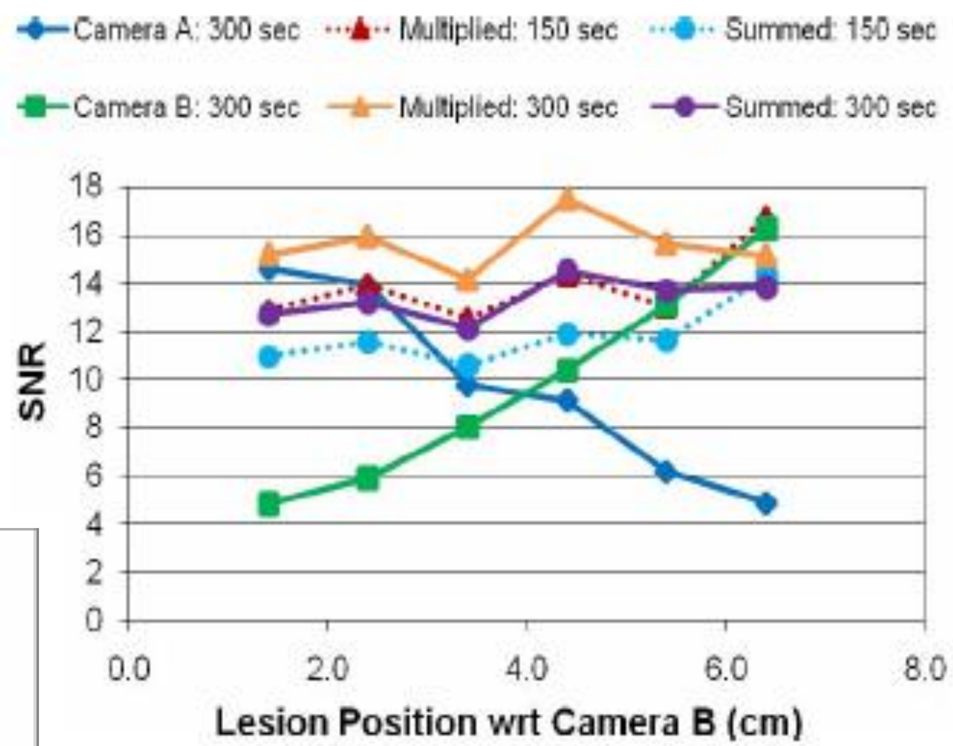


Fig. 4. Photograph of the gelatin phantom experimental set up using two Dilon cameras.



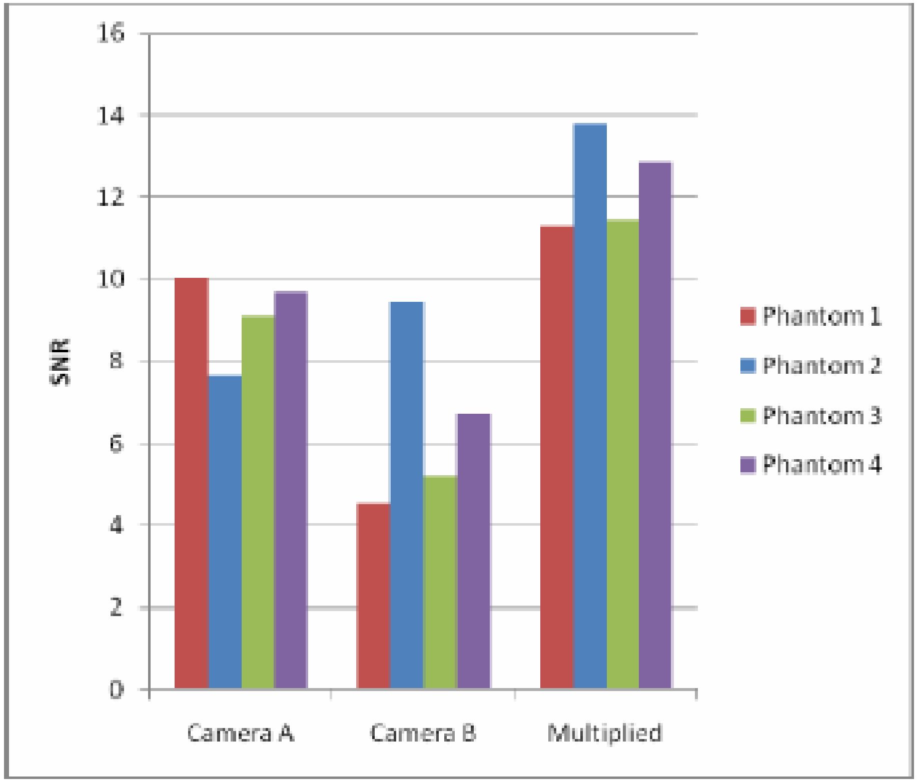
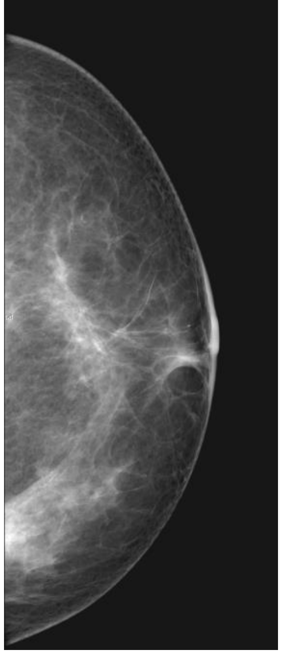
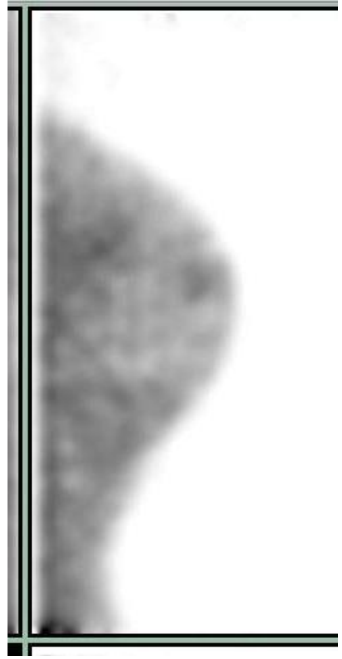
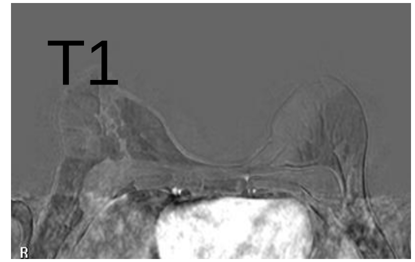


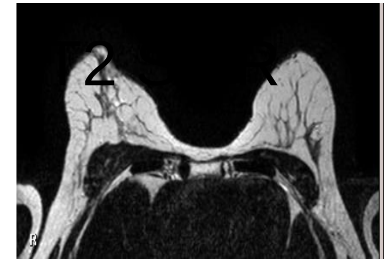
Fig. 10. SNR for four gelatin phantoms, measured using the Dilon cameras.

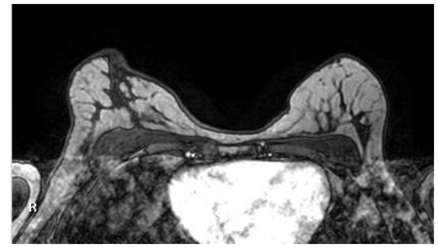
P.Judy, S. Majewski

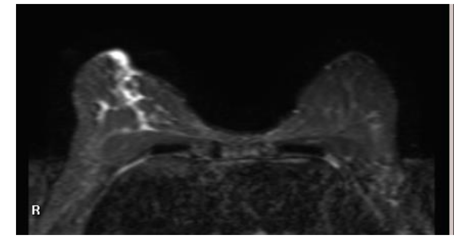


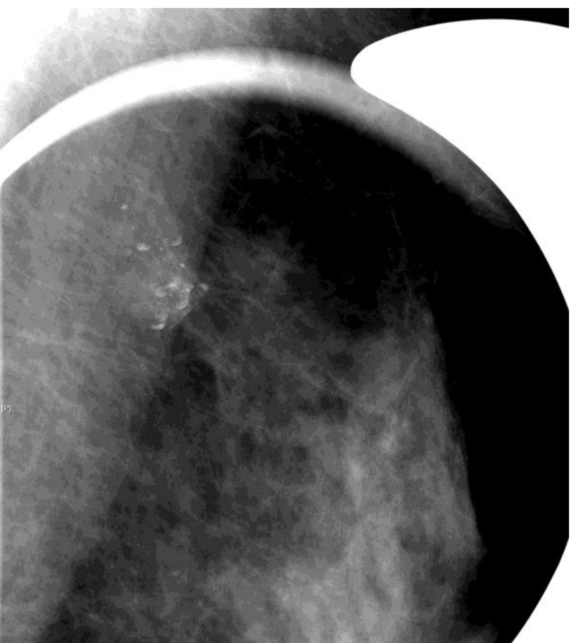


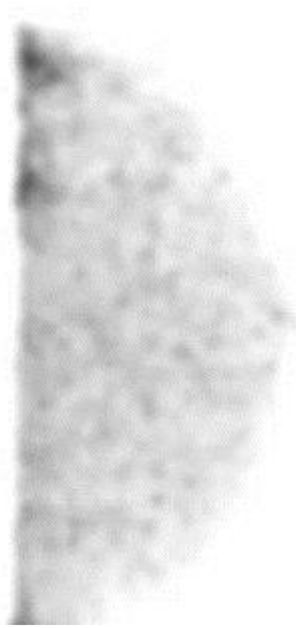

T1
R

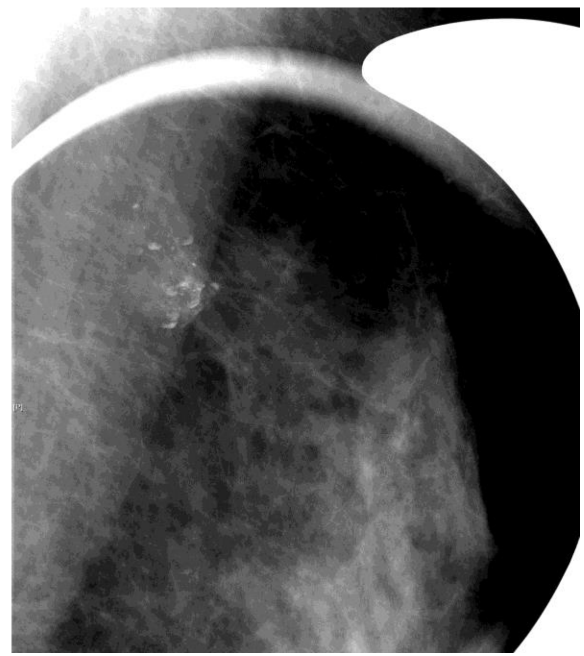

2
R

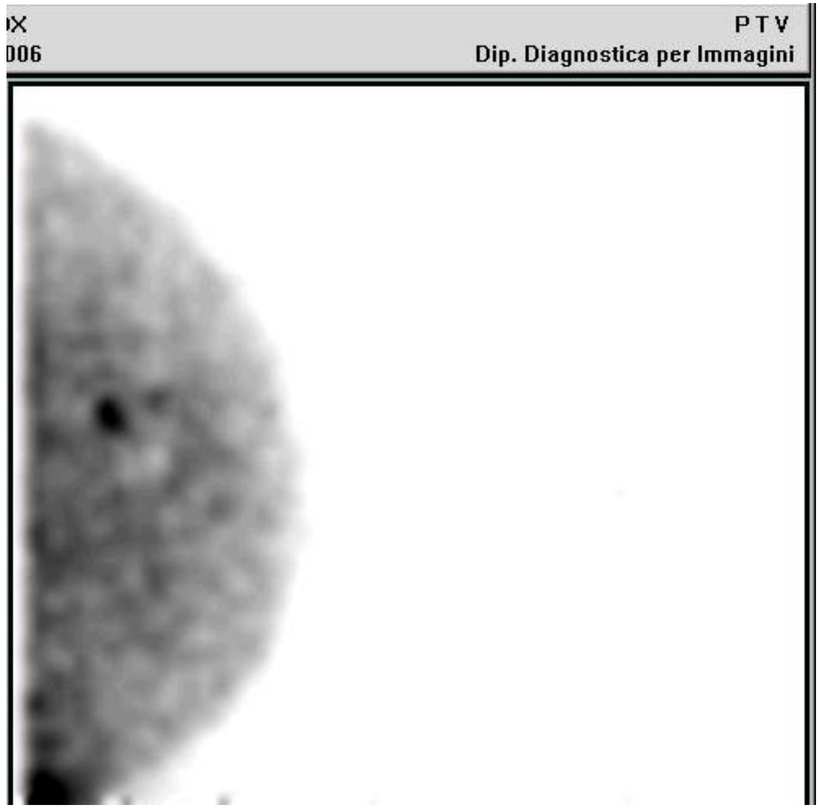

R


R








X
P T V
006
Dip. Diagnostica per Immagini

Geant4 simulations

1 detector

- par.hole coll.
- NaI(Tl) 1.5 mm pitch(the **smallest pixel** in this applications (~13000 pixel in 150 x 200 mm2)
- H8500 (6 x 6) mm2 anode pixel
- Individual channles electronics

Sensitivity dominates the visibility, **so we should try to get** closer to the lesion **and modify collimation and** modality

most cancers are in the upper part of the breast

→ **2 detectors**