Breast cancer research with a novel molecular imaging diagnostic system

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CHERNE 2019

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Outline

- Breast Cancer Statistics
- Breast Imaging: techniques, features & issues
- Molecular Breast Imnaging System
- A novel MBI system prototype with two asymmetrical heads

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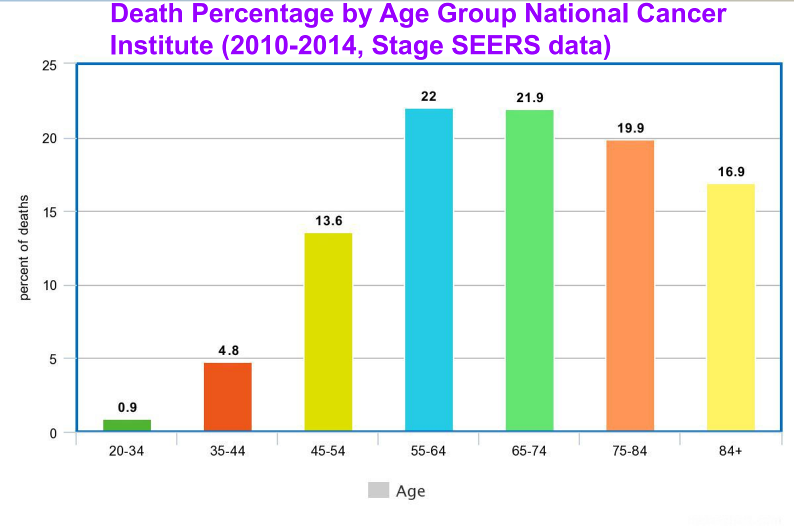
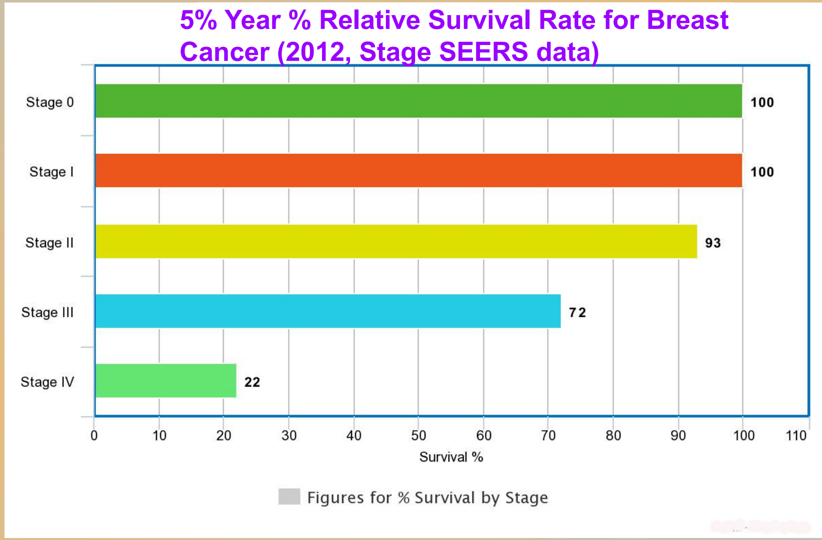
- Breast Imaging: techniques, features & issues
- Molecular Breast Imnaging System
- A novel MBI system prototype with two asymmetrical heads
- Characterization and Calibration Campaigns
- Angular Identification of lesion: LAT configuration
- Simulation tool: GATE software
- Spot-compression configuration: real-simulated data comparison

Breast Cancer Statistics





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- Sites: lympho nodes, ducts, lobules
  BIRADS classes: 0 to 6
  (100% malignancy)

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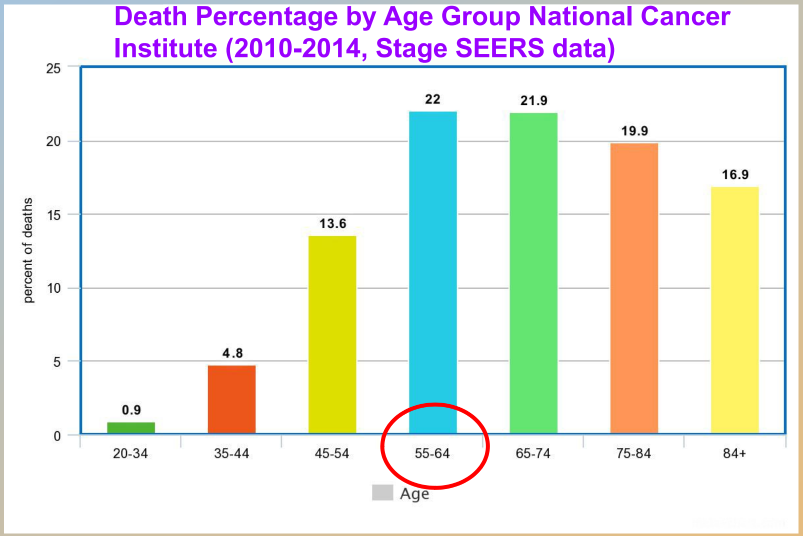

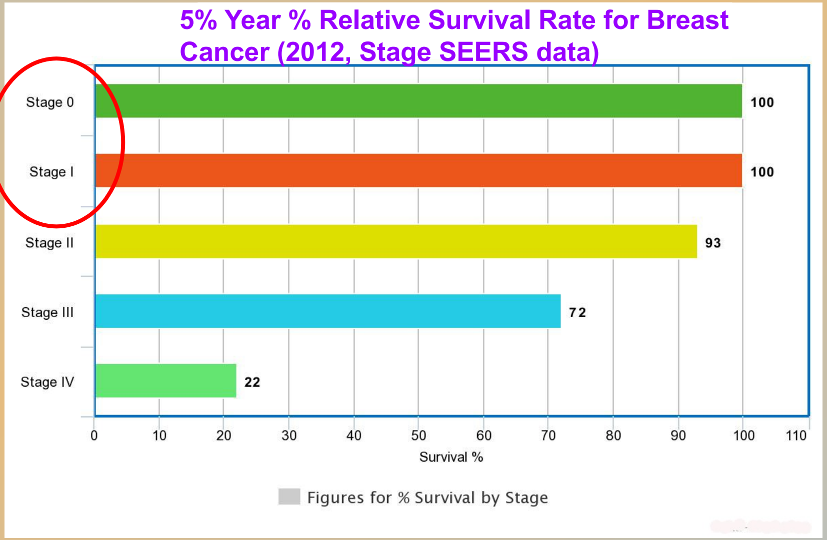

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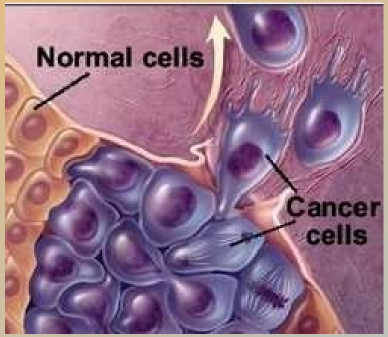

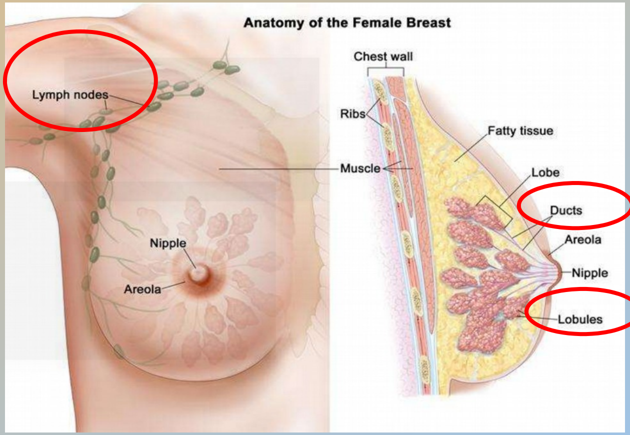

Breast Imaging: features & issues

Three-step Diagnosis

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- **Imaging**
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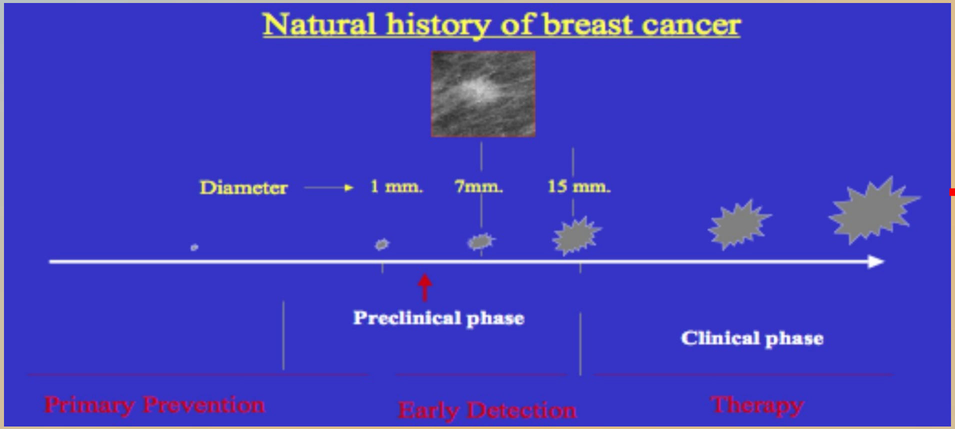

Early diagnosis, in preclinical phase (<10mm, ~5mm)

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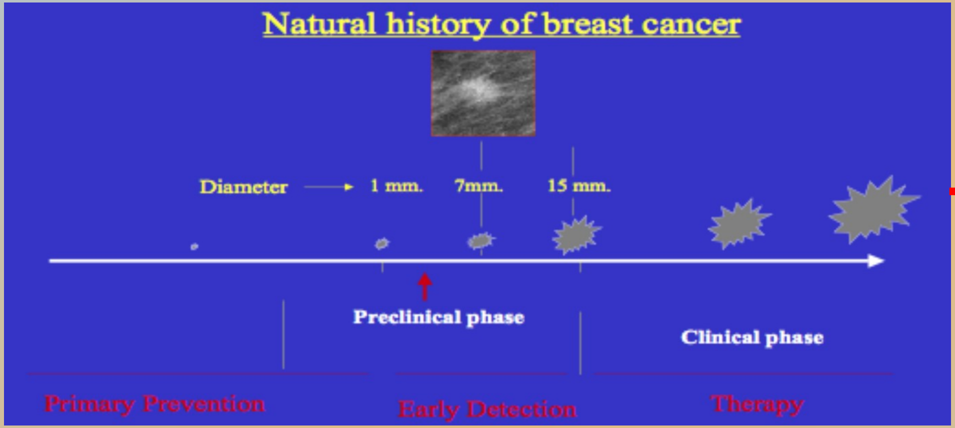
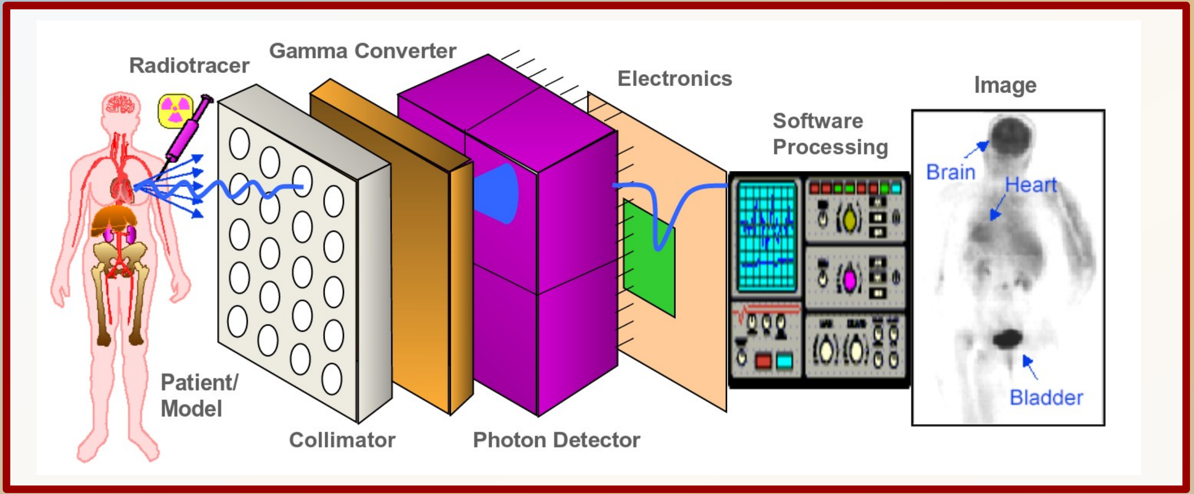


Early diagnosis, in preclinical phase (<10mm, ~5mm)

Param/Techn	MRx	US	MRI	PET	SPECT
Source	X-ray	Sound	e. m. wave	Single-γ	Double-γ
Imaging	Anatomical	Anatomical	Anatomical	Functional	Functional
Sensitivity	Medium	Medium	Medium-high	high	high
Specificity	high	low	Medium-high	high	medium
Limits	Dense Breast, FN rate	Attenuation, FN rate	Artifact, Costs, Time	Lifetime, Resolution	Statistics, Resolution

Molecular Breast Imaging System



Anger Camera scheme: single-head components

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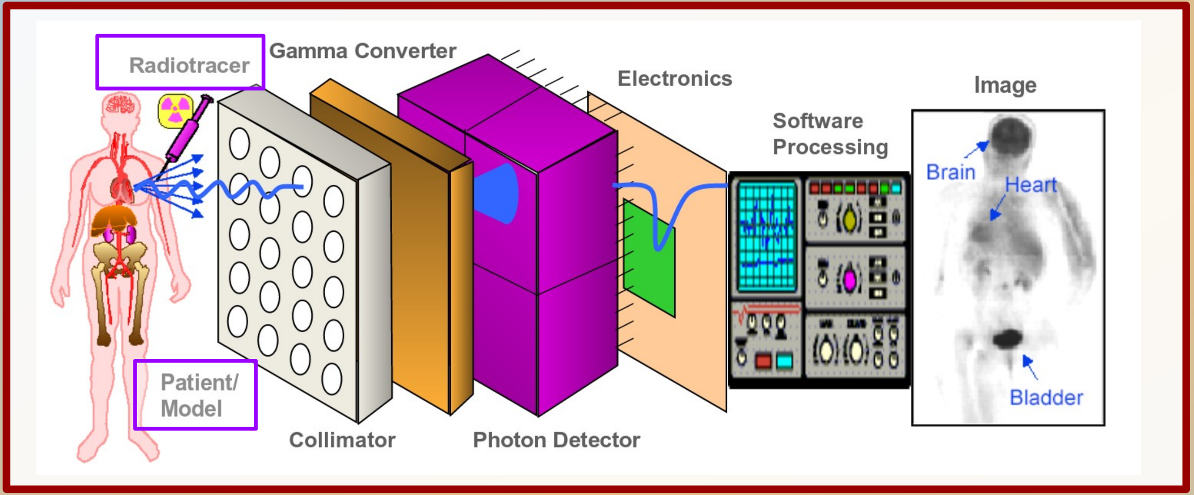

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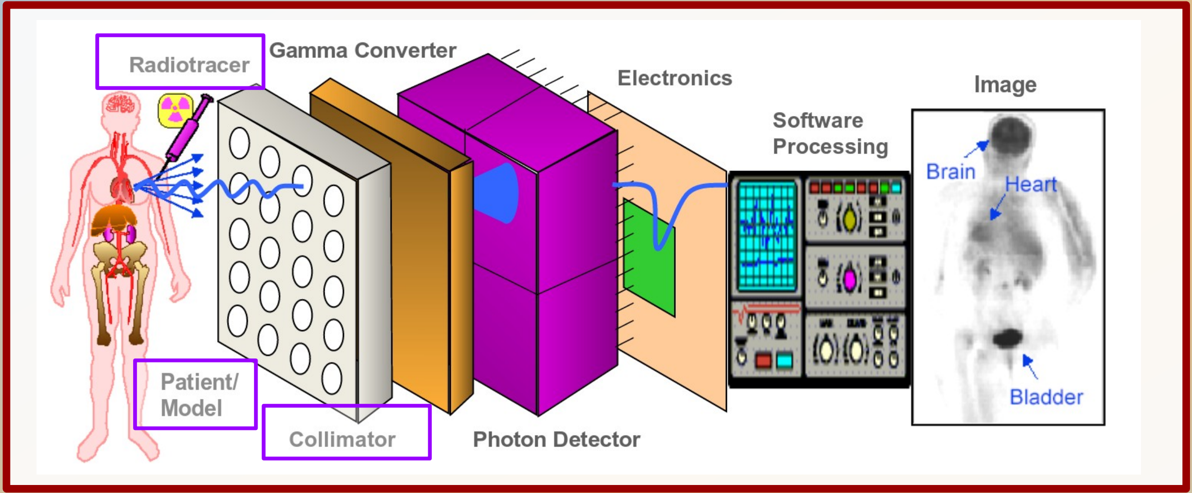

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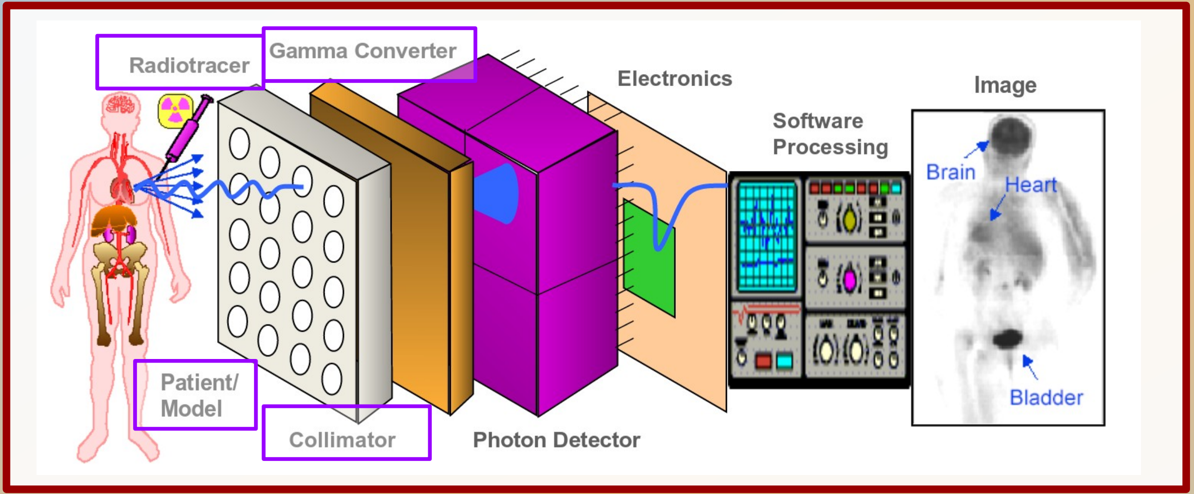

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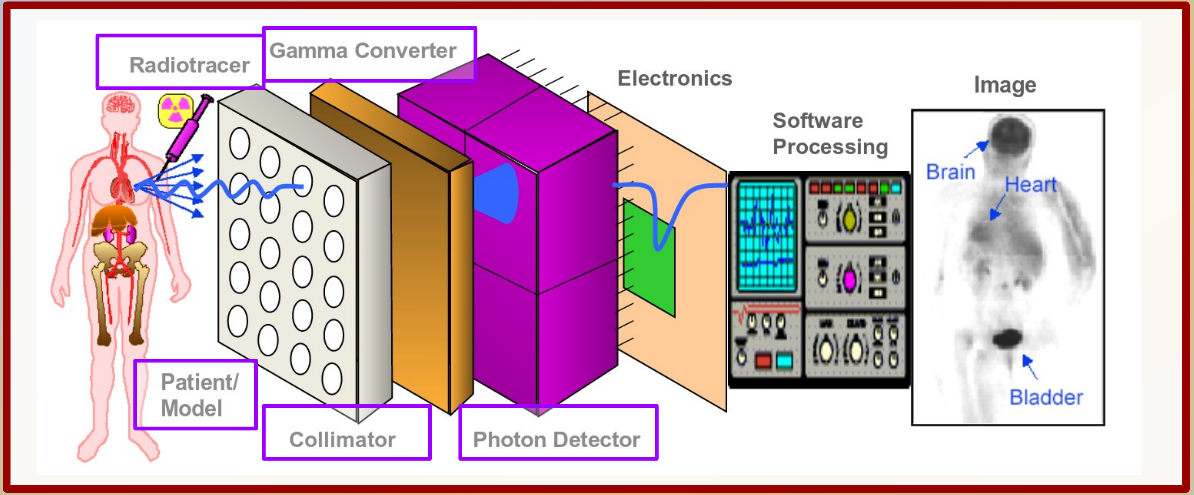

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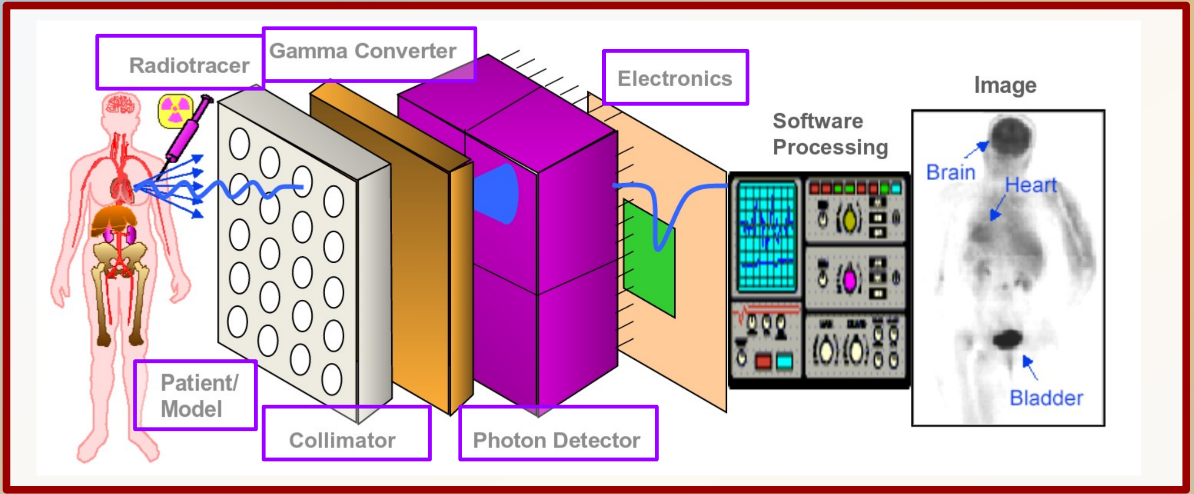

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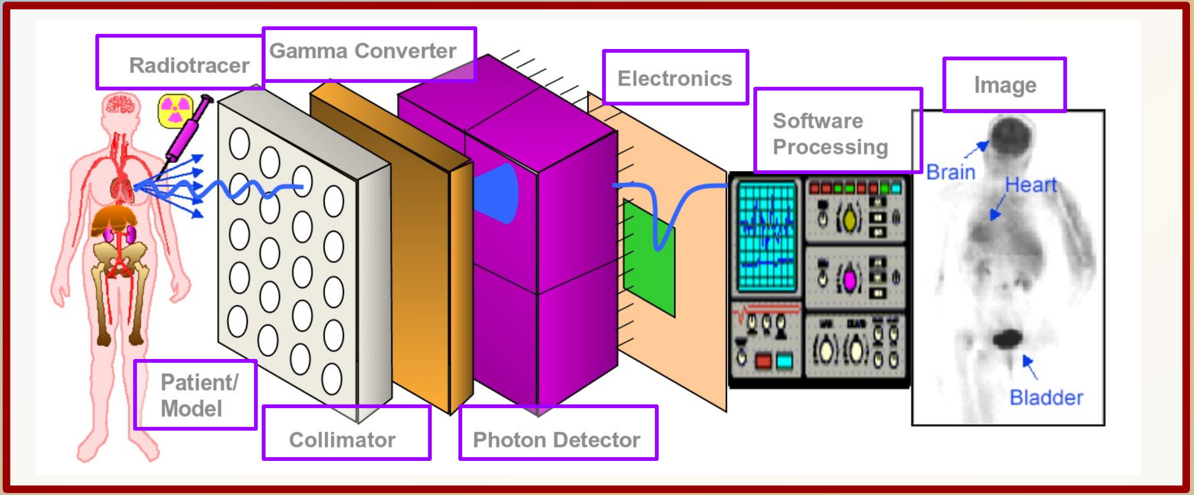

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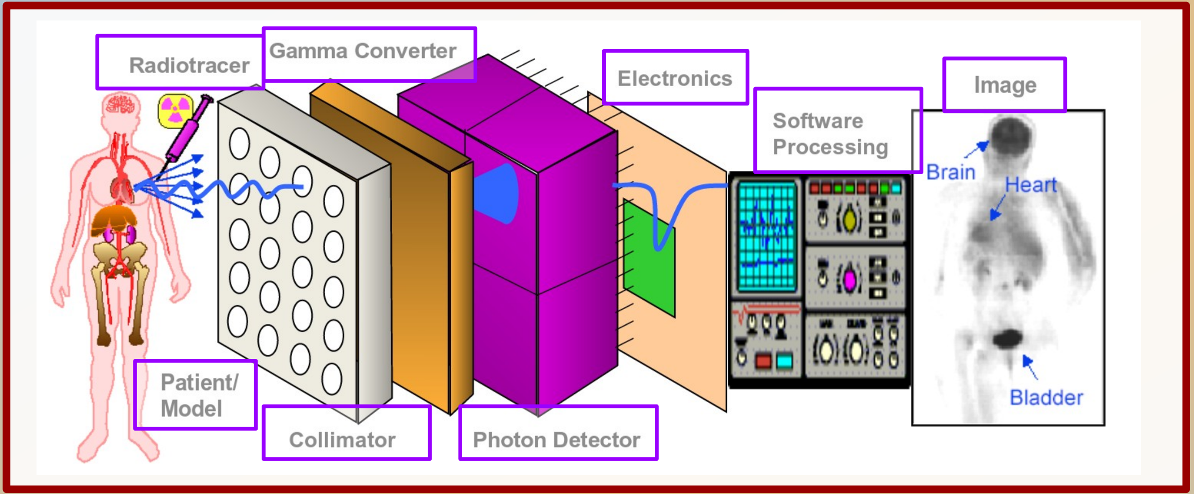

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Standard Gamma Camera Limit: unable to detect tumour < 10 mm

A novel MBI system prototype: two asymmetrical heads

Solution for detection of $\leq$ 5 mm tumour size:

- high-efficiency & high-resolution, high sensibility, good energy resolution
- large head: parallel-holes optics, large field of view (breast support)
- small head points and zooms the lesion: pin-hole optics

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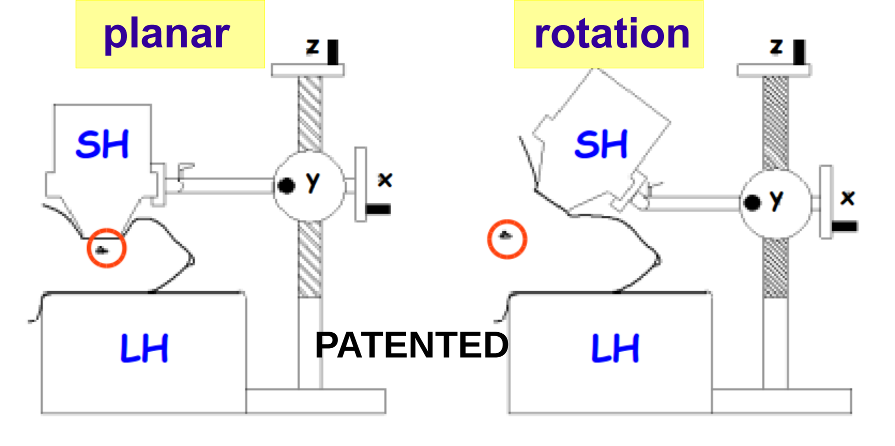
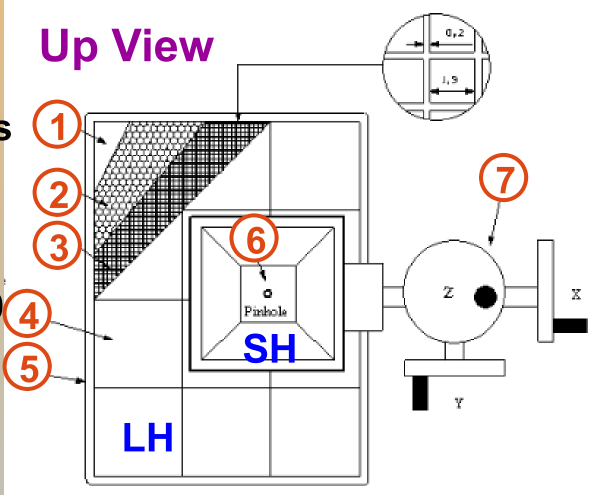
Side View: breast compression



1. Al foil 0.5 mm
2. Parallel&hexagonal holes collimator, Pb
3. 150x200 mm^2 pixellated scintillator
4. PSPMT Hamamatsu 8500
5. External W box
6. Compressor small-head detector & pin-hole optic
7. Handling system



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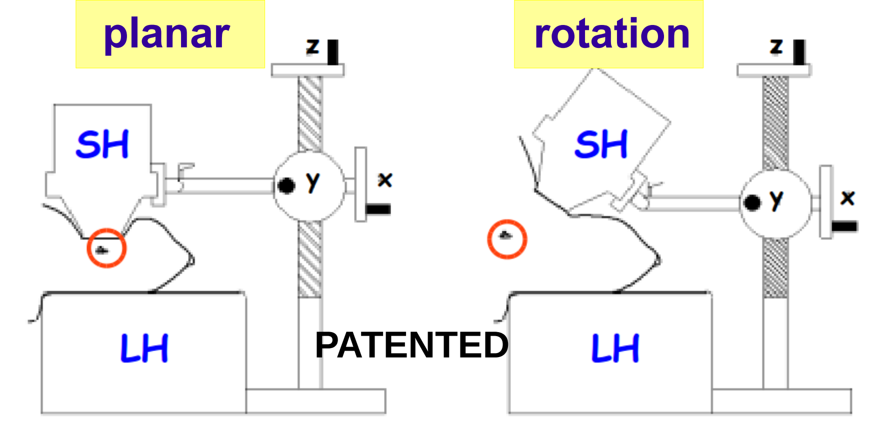

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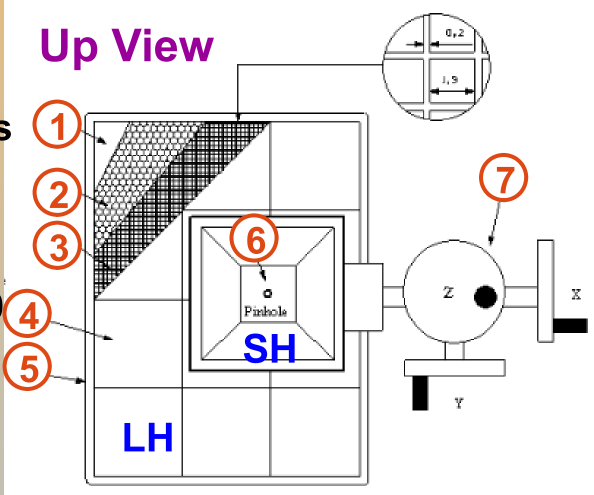
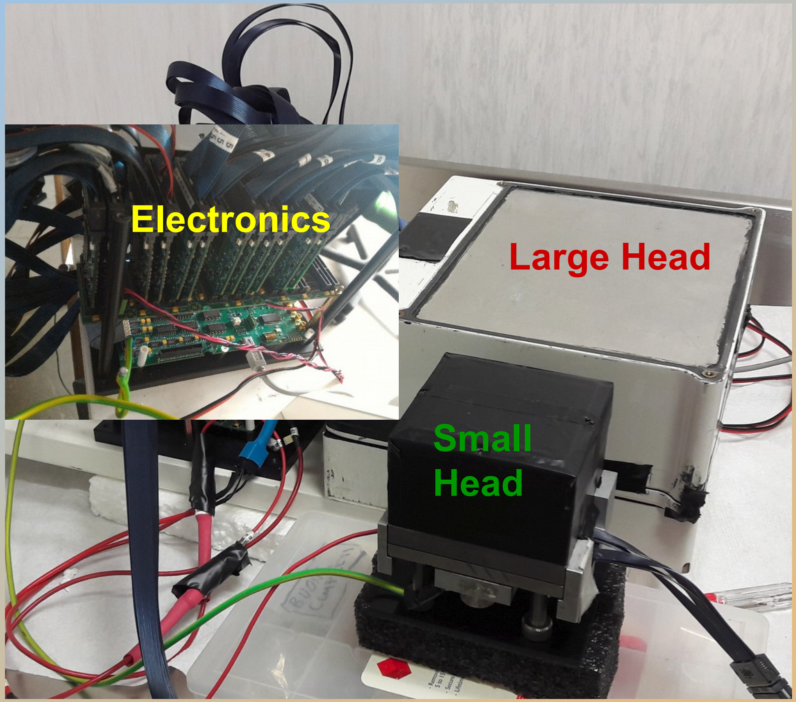


Detectability Key Parameters:
- SNR, CNR, spatial resolution
- Radiopharmaceutical Uptake

- Spot compression of SH & pinhole collimator → close to lesion, increasing efficiency & resolution (SNR & CNR)
  → detectability & image reconstruction
  → identification: planar & 3D

A novel MBI system prototype: components & features



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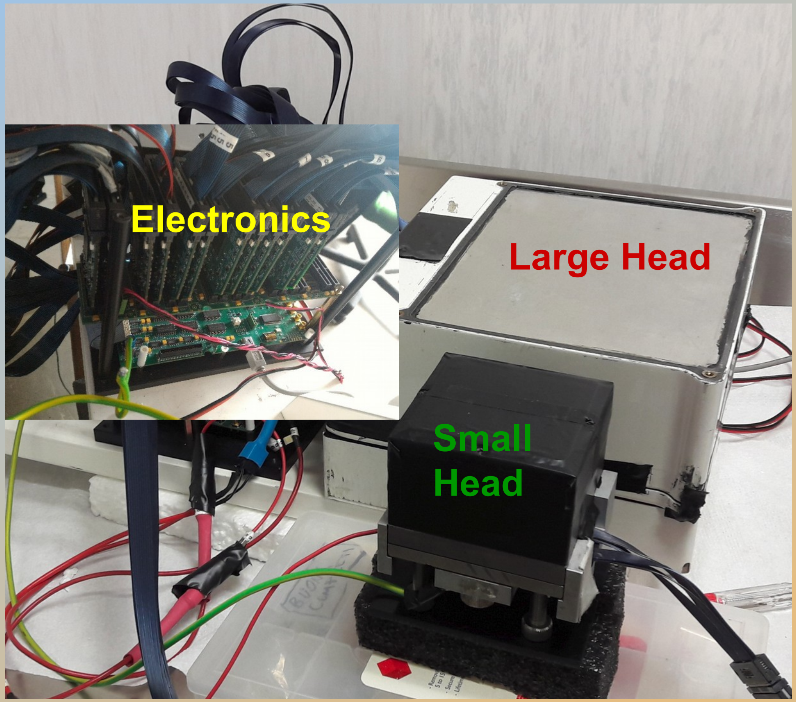

Electronics

- Front End MAROC3 ASICS: up to 4096 indipendent channels
- FPGA based

Scintillators

- Thickness 0.5 mm
- Pixel size 1.3 ± 0.2 mm

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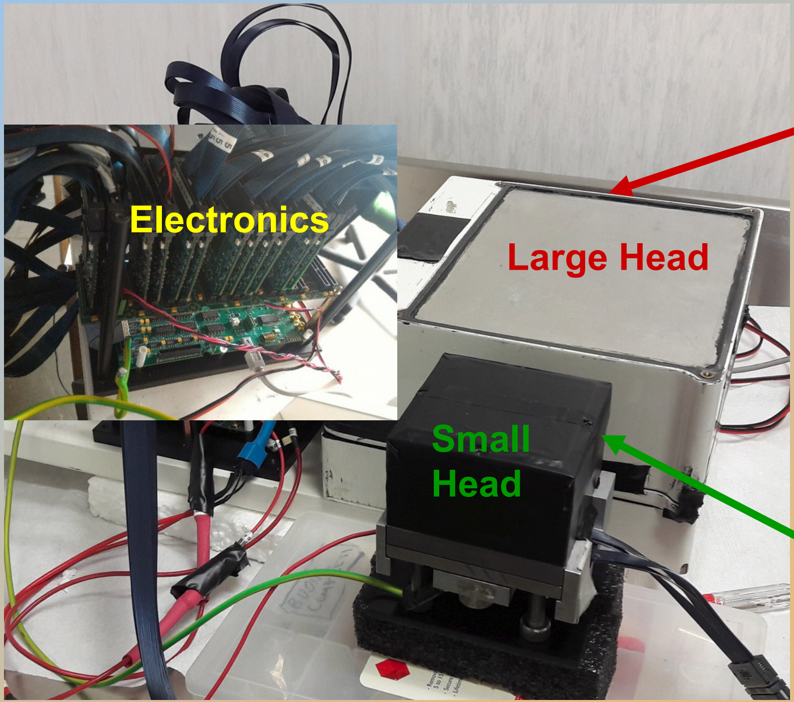

- 15x20 cm^2 size
- 3x4 PSPMT H8500 (6x6 mm^2): 768 chs
- NaI(Tl) pixellated: 15x20 cm^2
- Collimation: pitch 1.5 mm, 19 mm hexagonal septa; ≈ 3000 hole

- 5x5 cm^2 size
- 1 PSPMT H8500 64 chs
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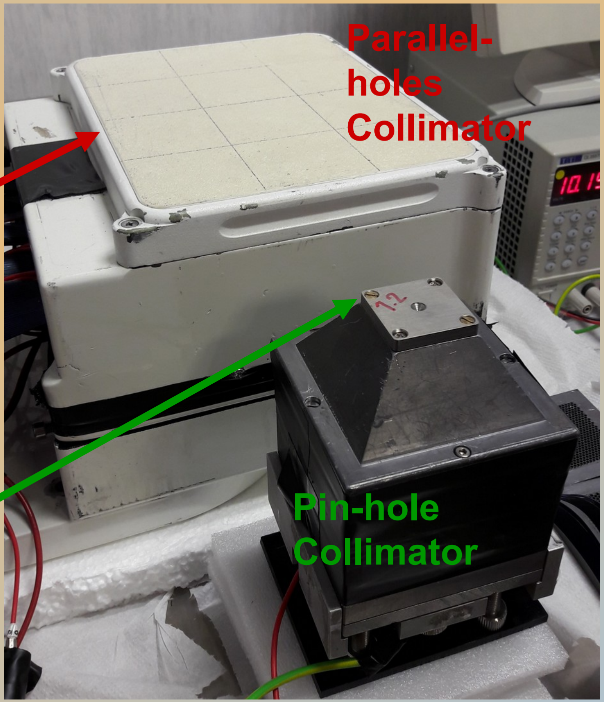
- Collimation: 2 mm diam. size, ≈ 45 mm height



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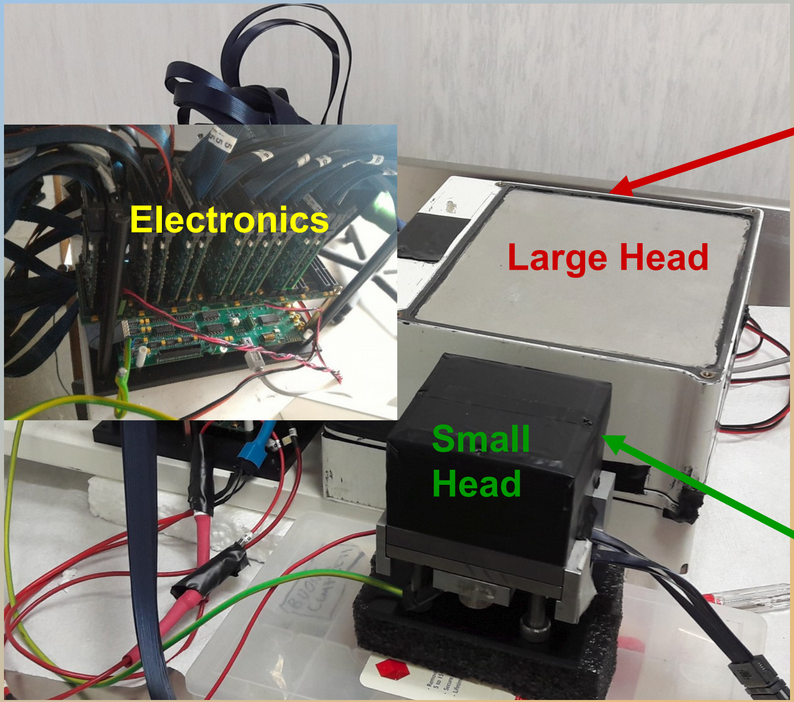

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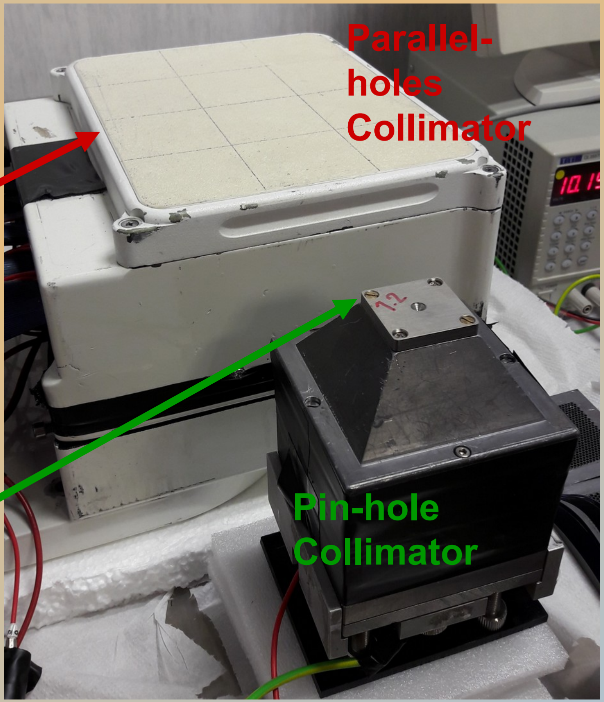

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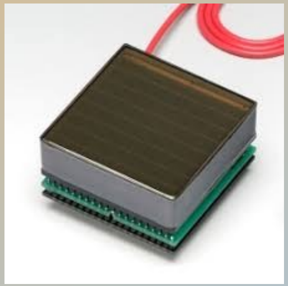

Detectors

- Flat Panel PMT/H8500 64chs
- Anode size/pitch: 5.8x5.8 /6.1 mm
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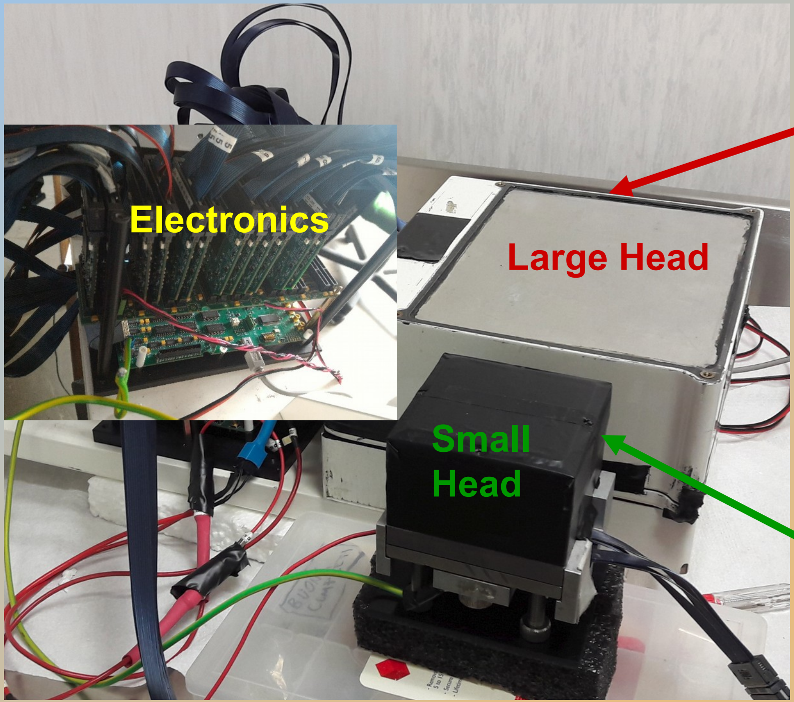

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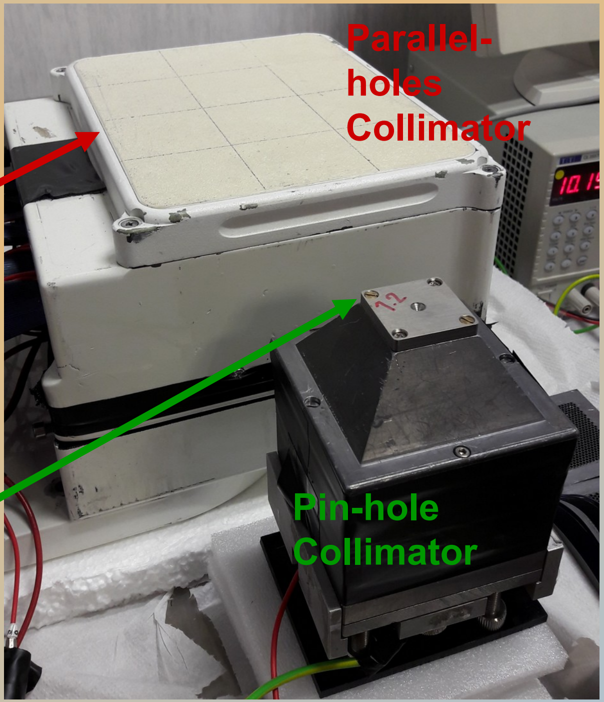

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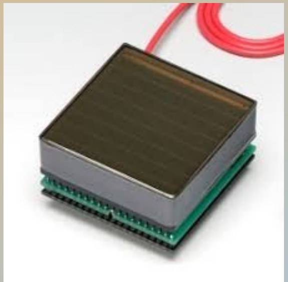

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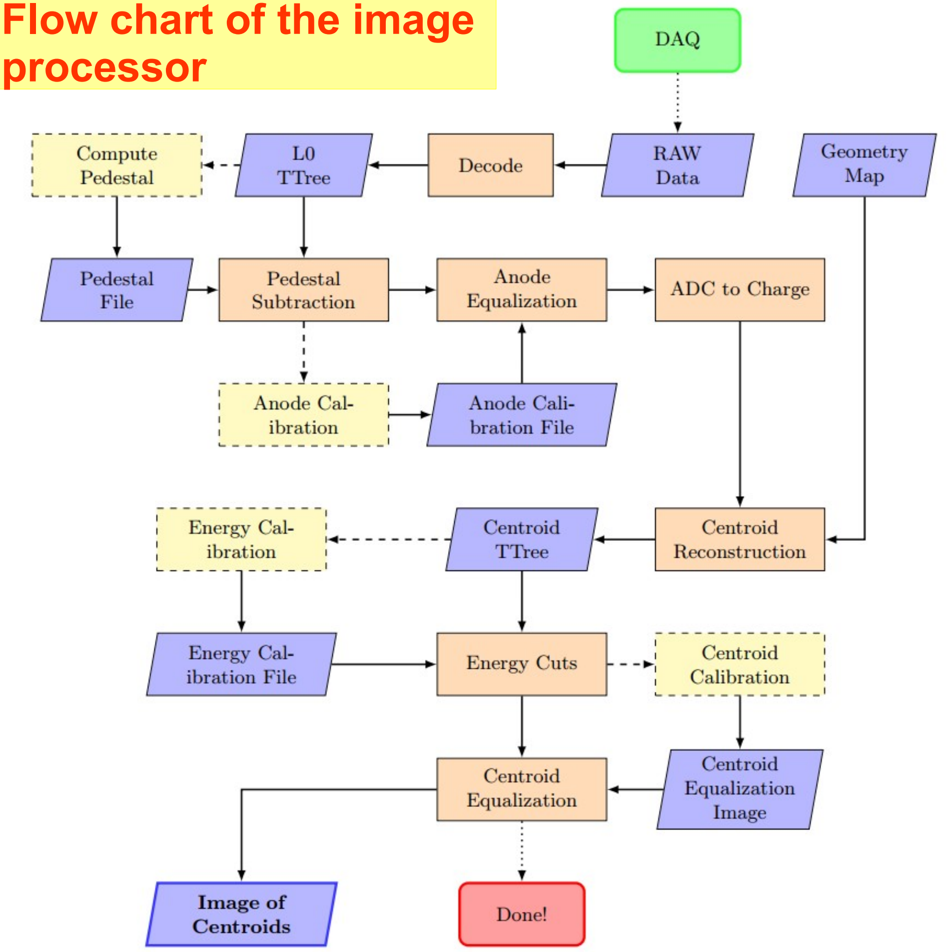
Outlook: SiPM detectors

Data Processing & Image Reconstruction

Flow chart of the image processor



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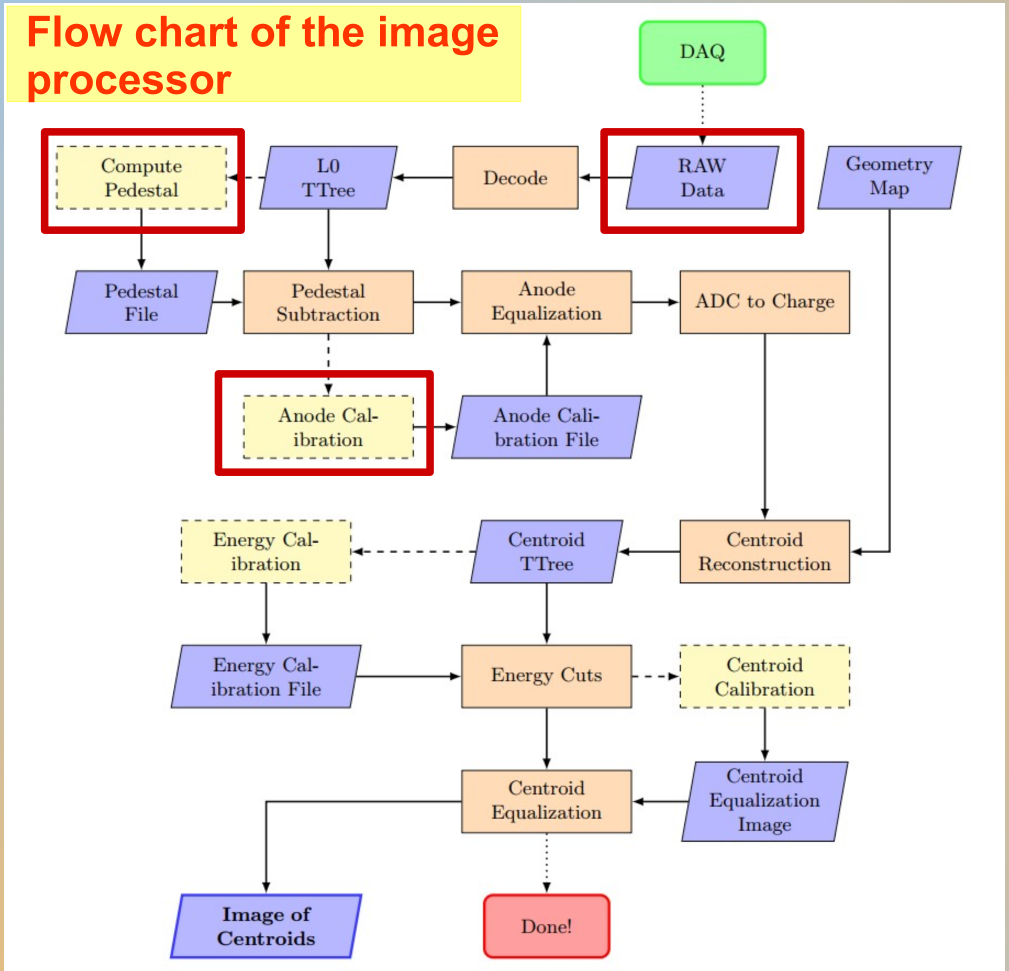

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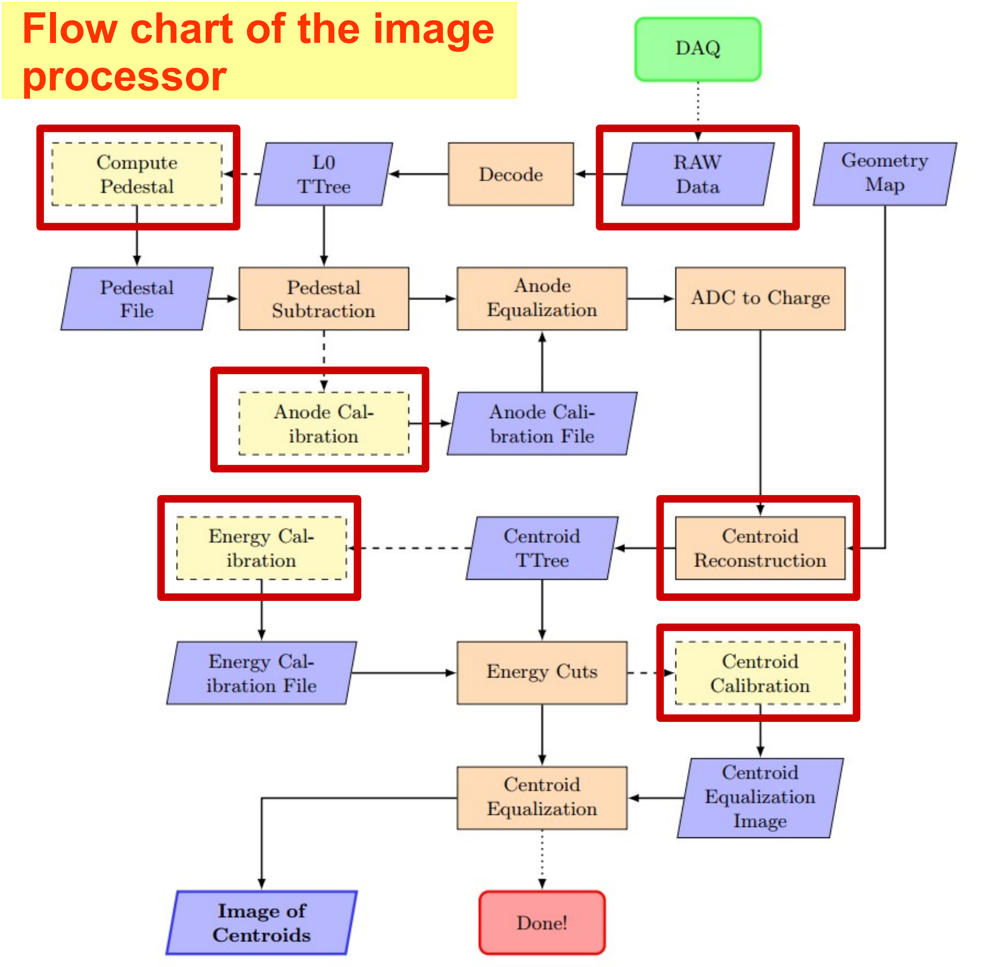

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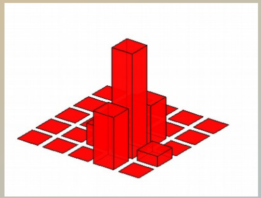

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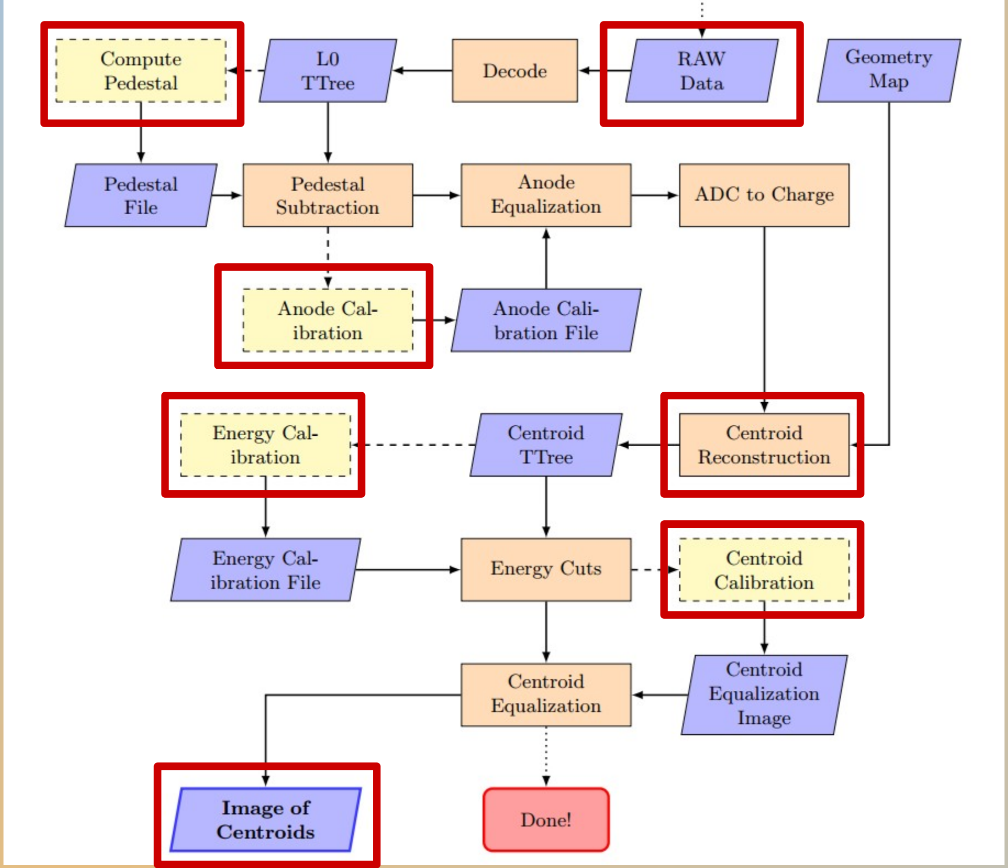

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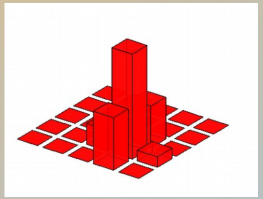

- Final image is the image of the number of centroids in each pixel

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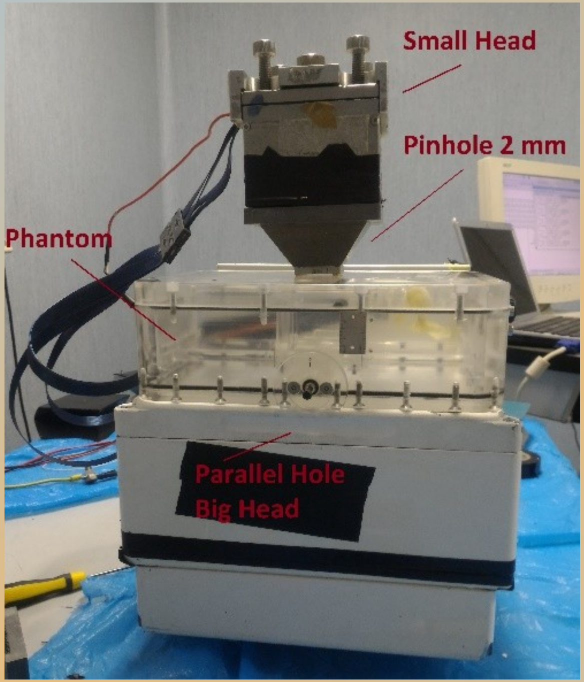
Breast background and Tumour only can runs can be properly combined in offline analysis to get:

- **Tumour uptake scan**
- **Different breast sizes**

by varying the relative acquisition time

First Campaign: Experimental Setup



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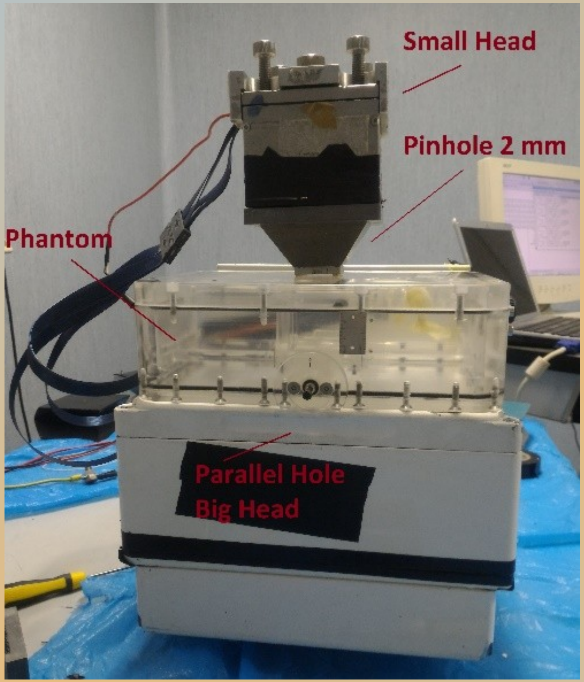
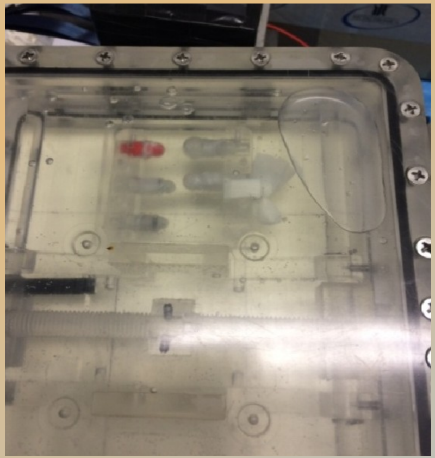
Dedicated Large Breast Phantom

- One perspex box (20x15 cm^2) filled with plain water (2l)
- Plastic support holds 5 hollow perspex spheres (tumours): 3, 4, 5, 6, 8 mm of diameter
- An internal knob allows the tumour movement, simulating different distances from the breast surface → depths inside the breast





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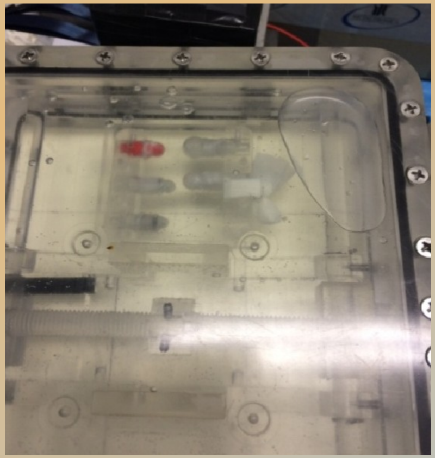

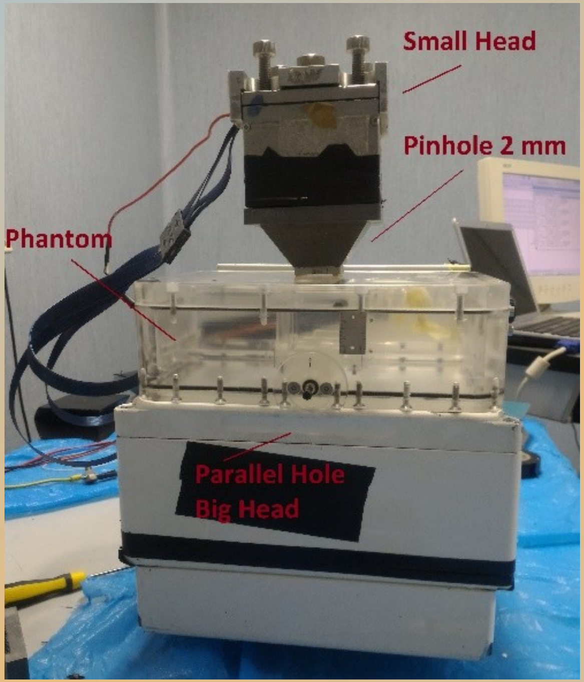

^{99m}Tc Activity and Uptake

- 740 MBq for a typical BSGI → accumulated breast activity ≈ 1% (V=1 l)
- Breast bkg activity concentration ≈ 7 Mbq/l
- Typical Uptake in a breast lesion: 10 → Lesion Activity Concentration: 70 Mbq/l

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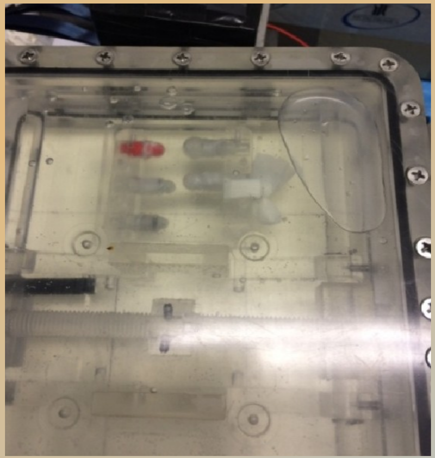
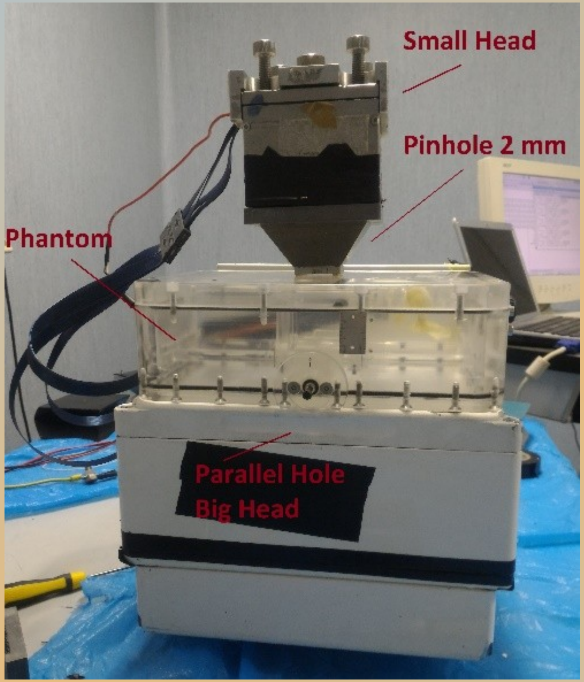




^{99m}Tc Activity and Uptake

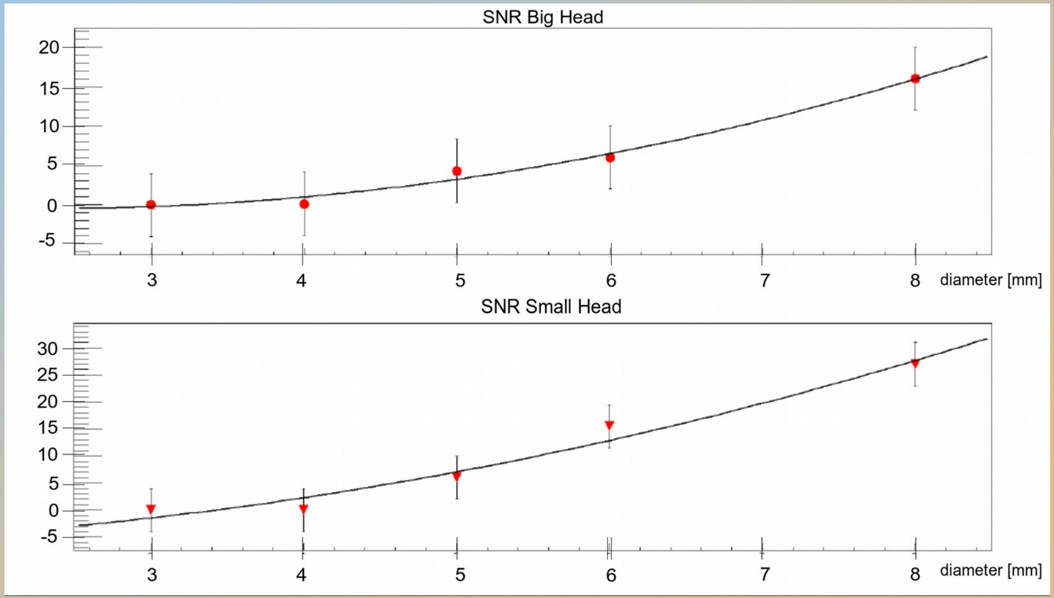
- 740 MBq for a typical BSGI → accumulated breast activity ≈ 1% (V=1 l)
- Breast bkg activity concentration ≈ 7 Mbq/l
- Typical Uptake in a breast lesion: 10 → Lesion Activity Concentration: 70 Mbq/l

Image Reconstruction

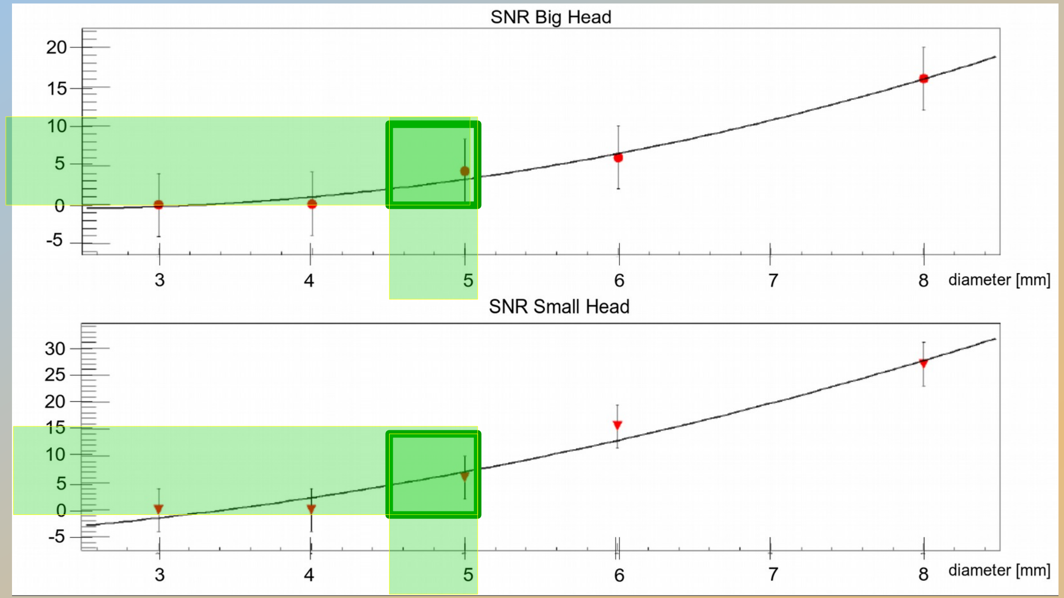
Realistic images of tumour inside breast can be obtained merging by software:

- Environmental bkg (phantom filled with plain water)
- Breast bkg (phantom filled with ^{99m}Tc water)
- Tumors (phantom filled with plain water and spheres with ^{99m}Tc saline)

Detectability and SNR



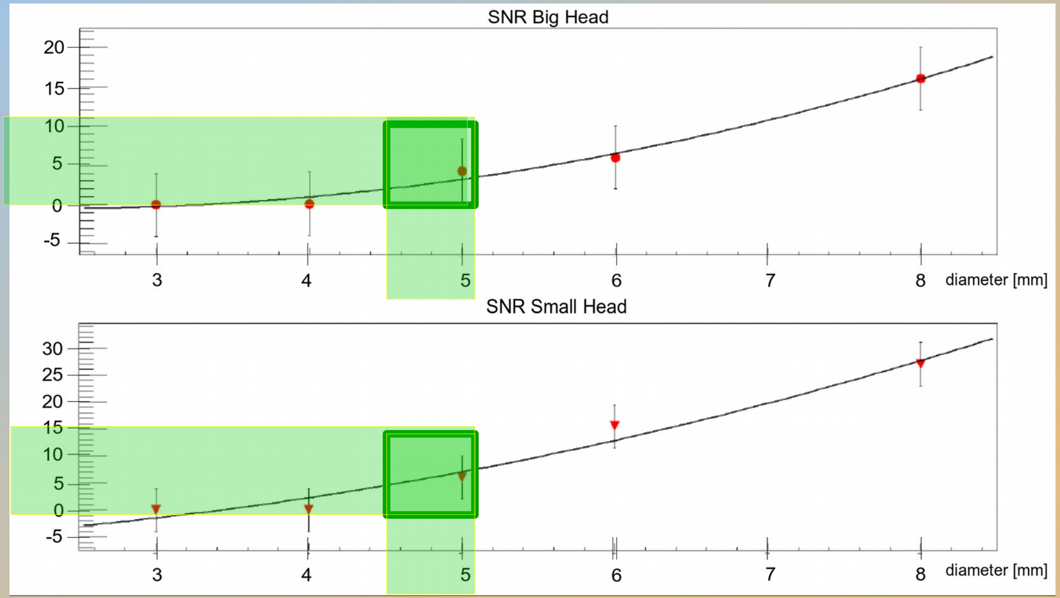
Detectability and SNR

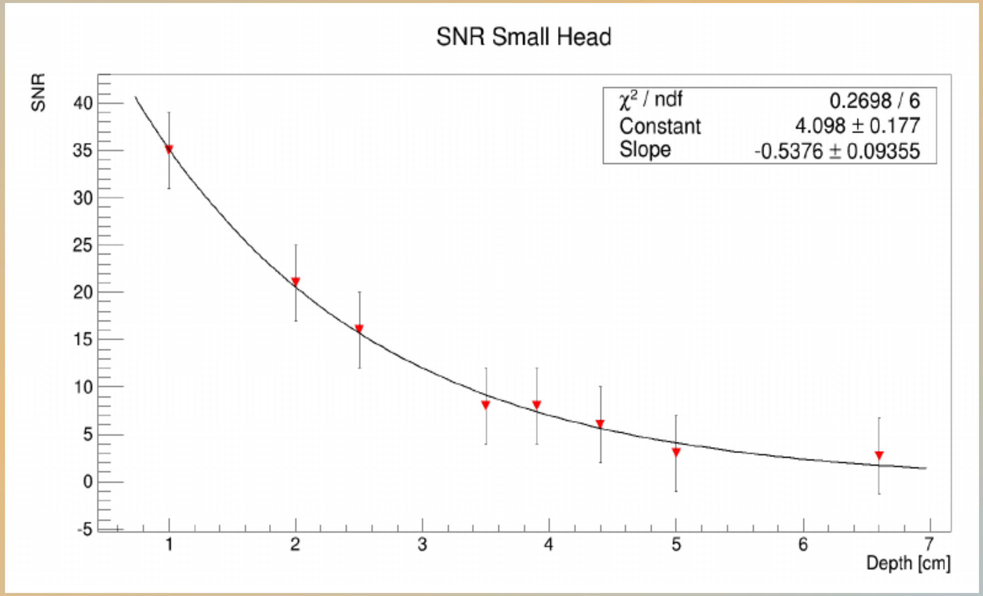


- Uptake U=10
- Parallel Hole collimator for both heads
- Fixed tumour distances of 1 cm from the Big Head and 1 cm from the Small Head

→ **The smallest visible lesion is 5 mm diameter!**

Detectability and SNR





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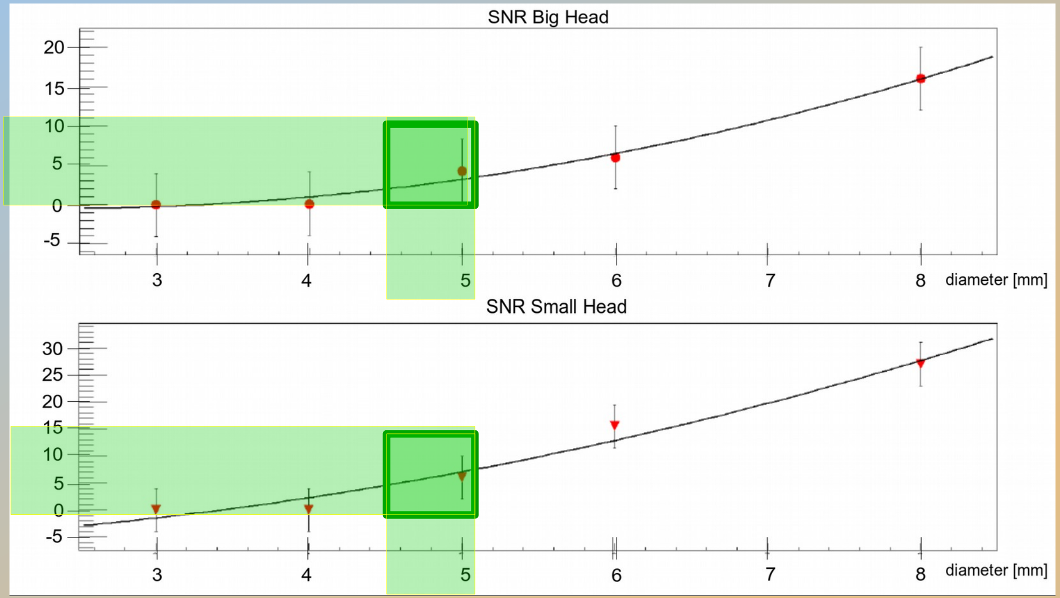
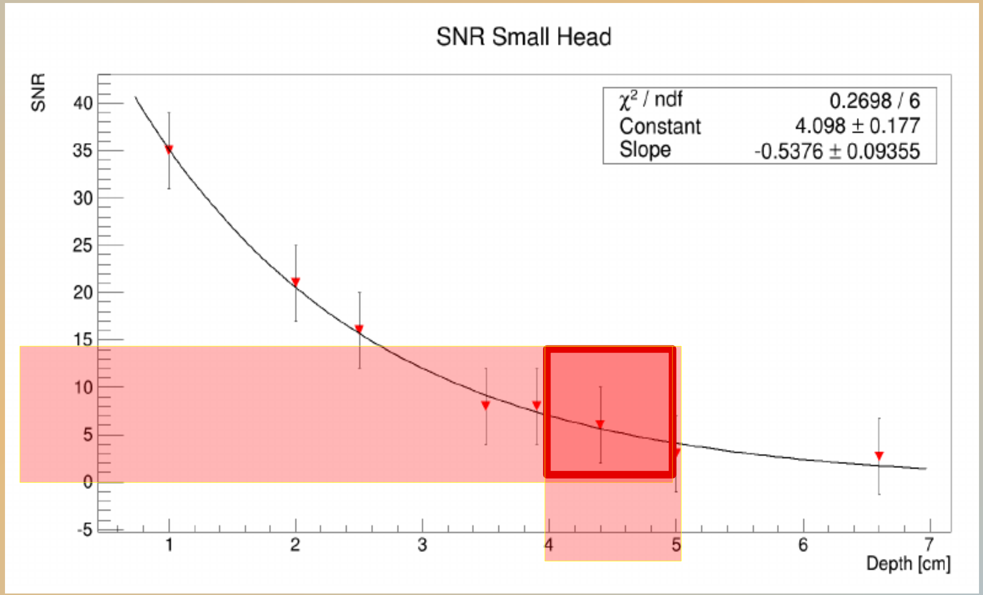
Detectability and SNR





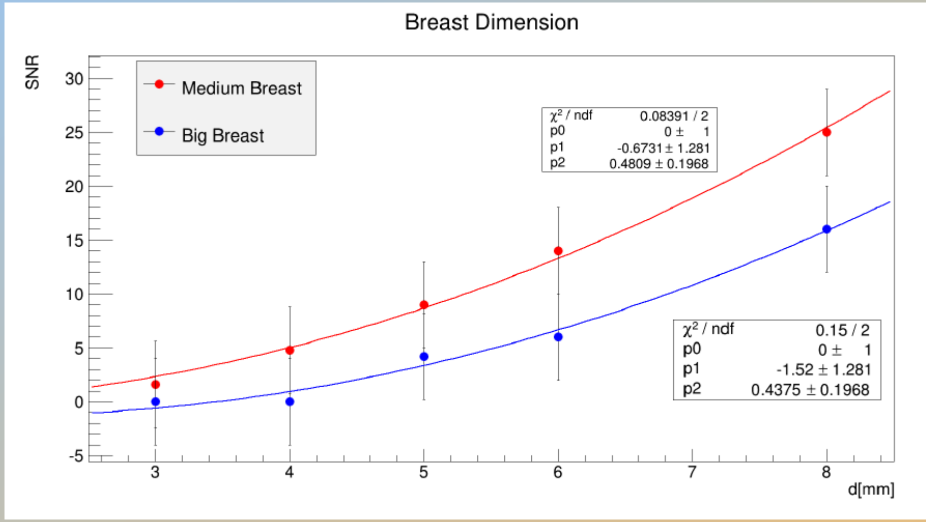
- Uptake U=10
- Parallel Hole collimator for both heads
- Fixed tumour distances of 1 cm from the Big Head and 1 cm from the Small Head

→ **The smallest visible lesion is 5 mm diameter!**

- Uptake U=10
- Pinhole (reduced FOV) has been centered on 6 mm tumour

→ **With the Pinhole SNR is higher then with parallel hole (fixed diameter and depth), but it decreases more rapidly**

Big Head SNR versus Tumour Size & Uptake



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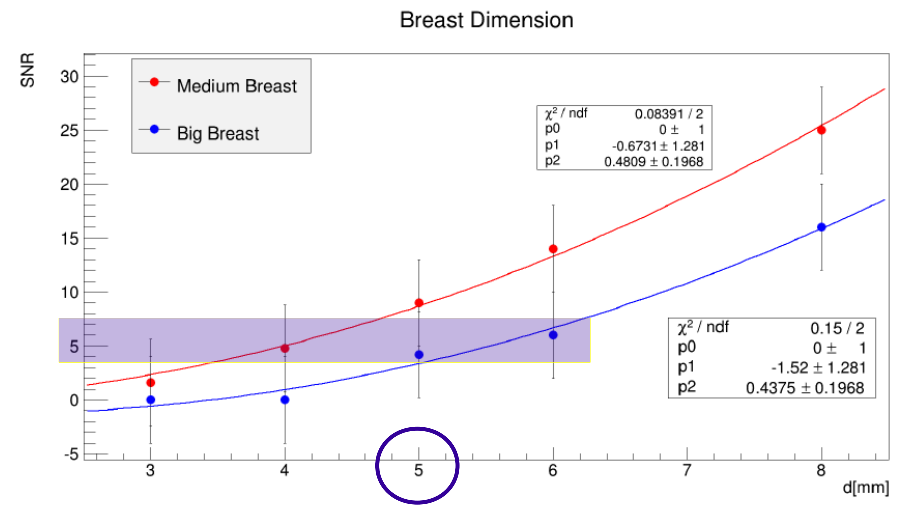
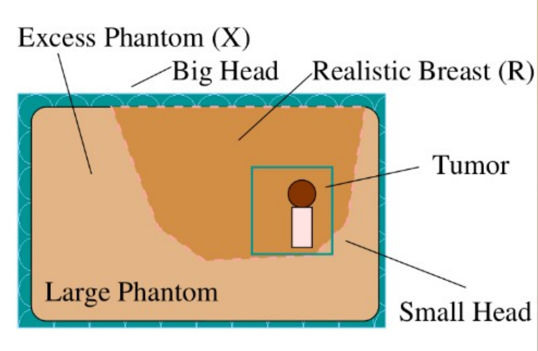


- Uptake U=10
- Fixed 1 cm from the Big Head
- The SNR increases of about 5, for medium tumours, moving from the full size breast phantom to half size breast



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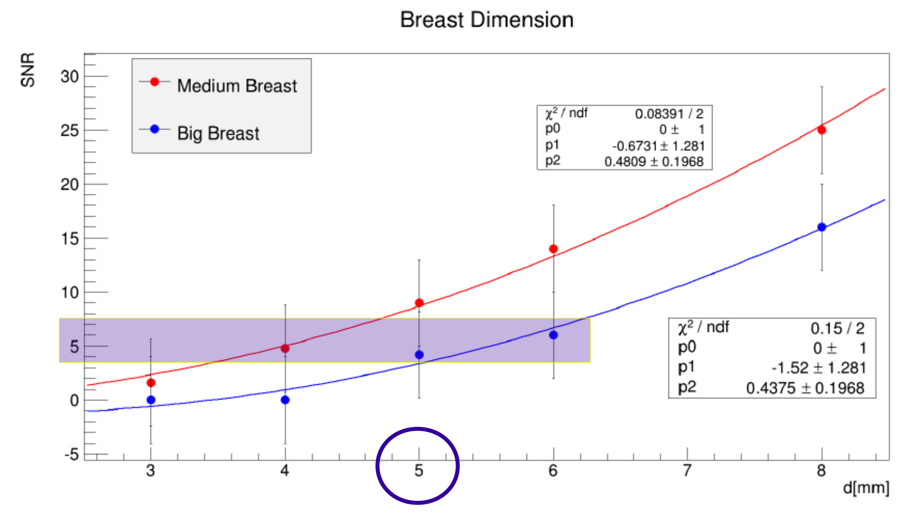

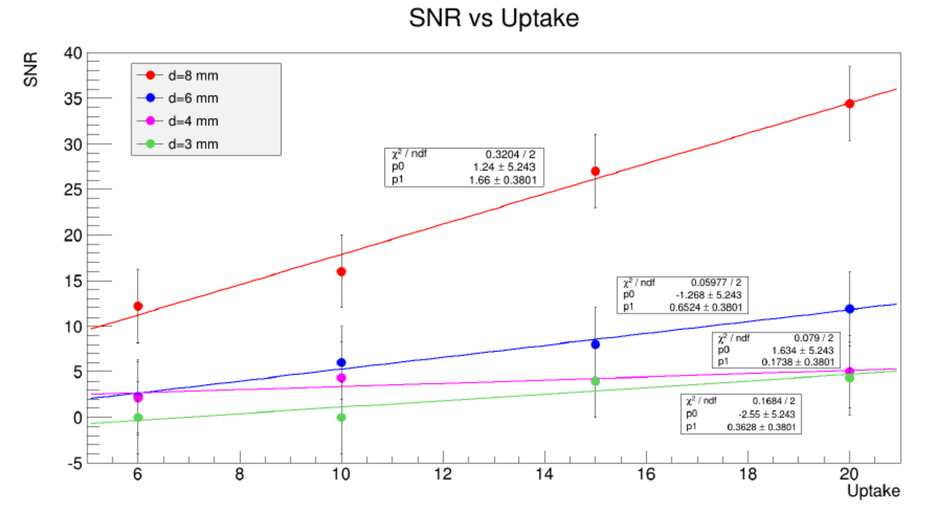

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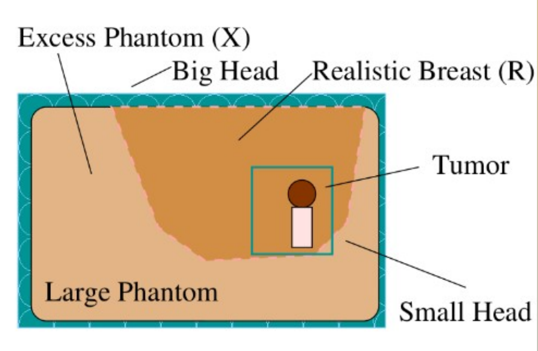

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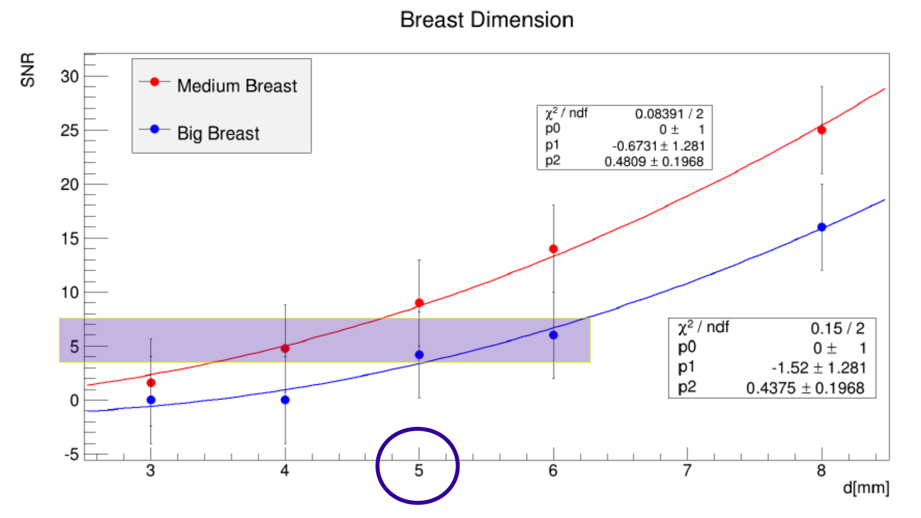

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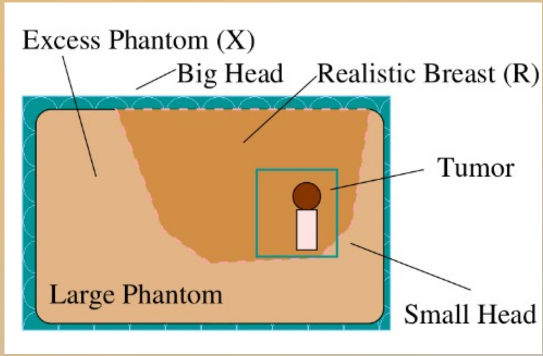
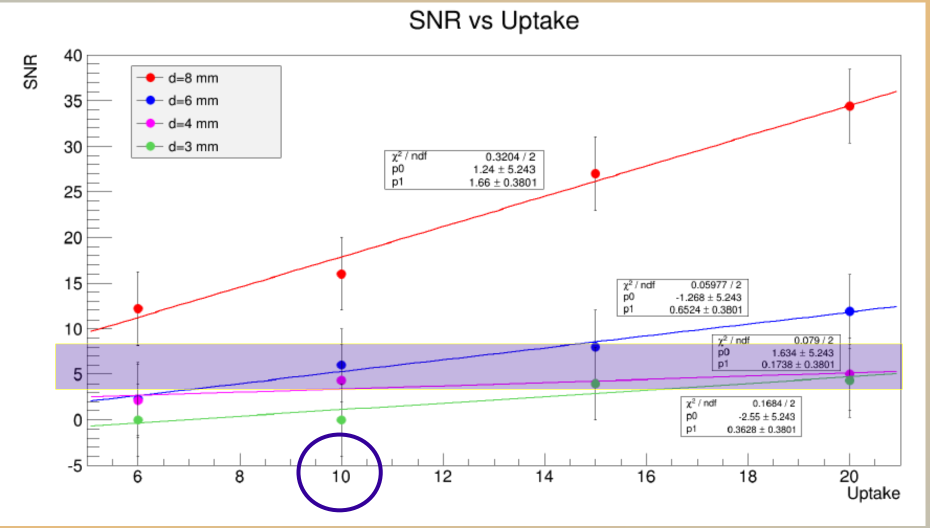
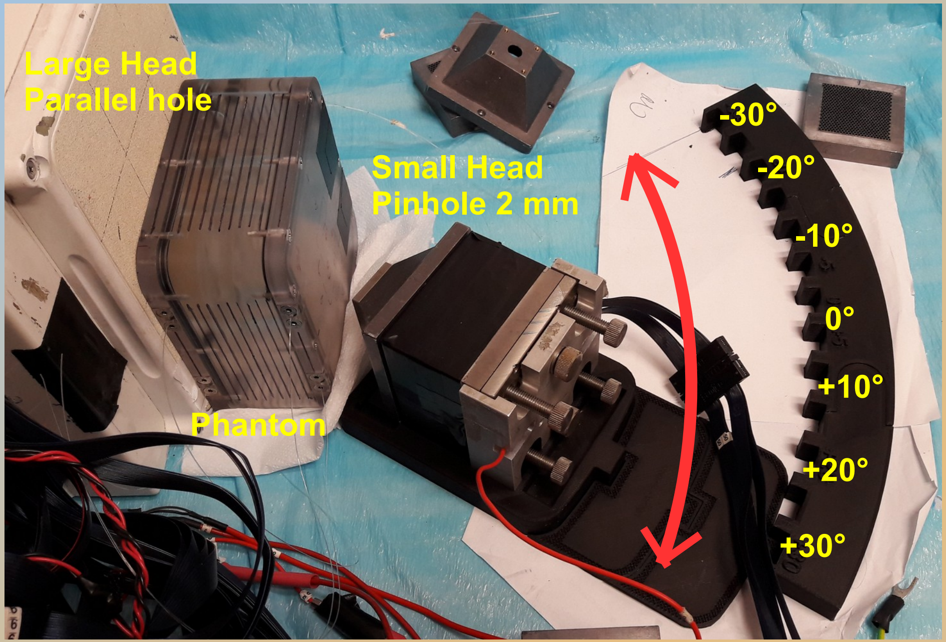
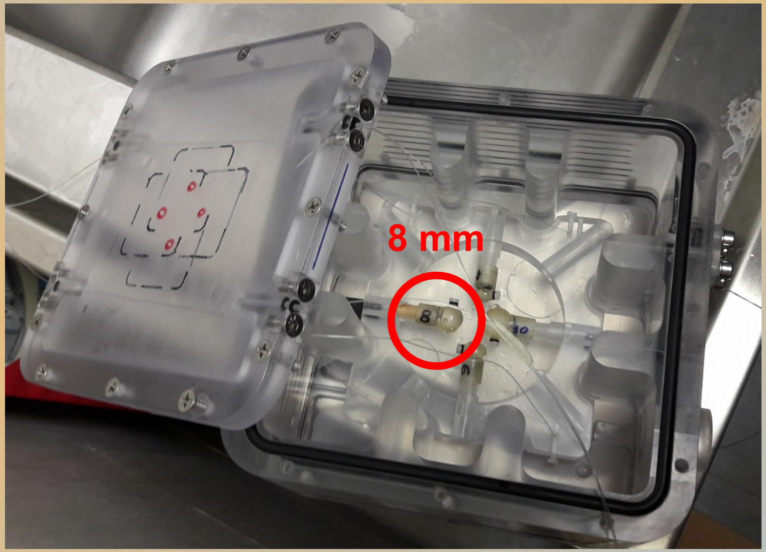




- Fixed 1 cm from the Big Head
- Big Breast
- Smallest tumour (3 mm diameter) becomes visibile for uptake U=15
- At U=10, the SNR=5 for all the tumour sizes less than for 3 mm tumour size

Second Campaign: LAT Experimental Setup

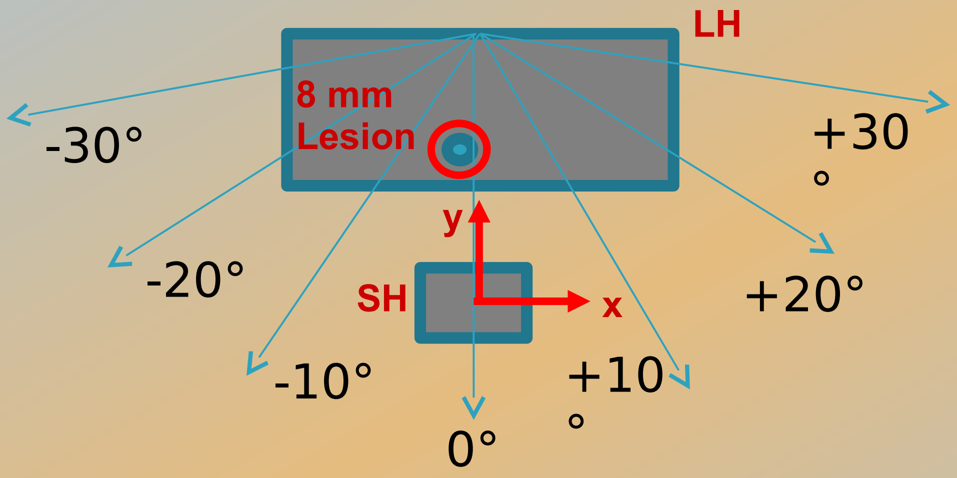




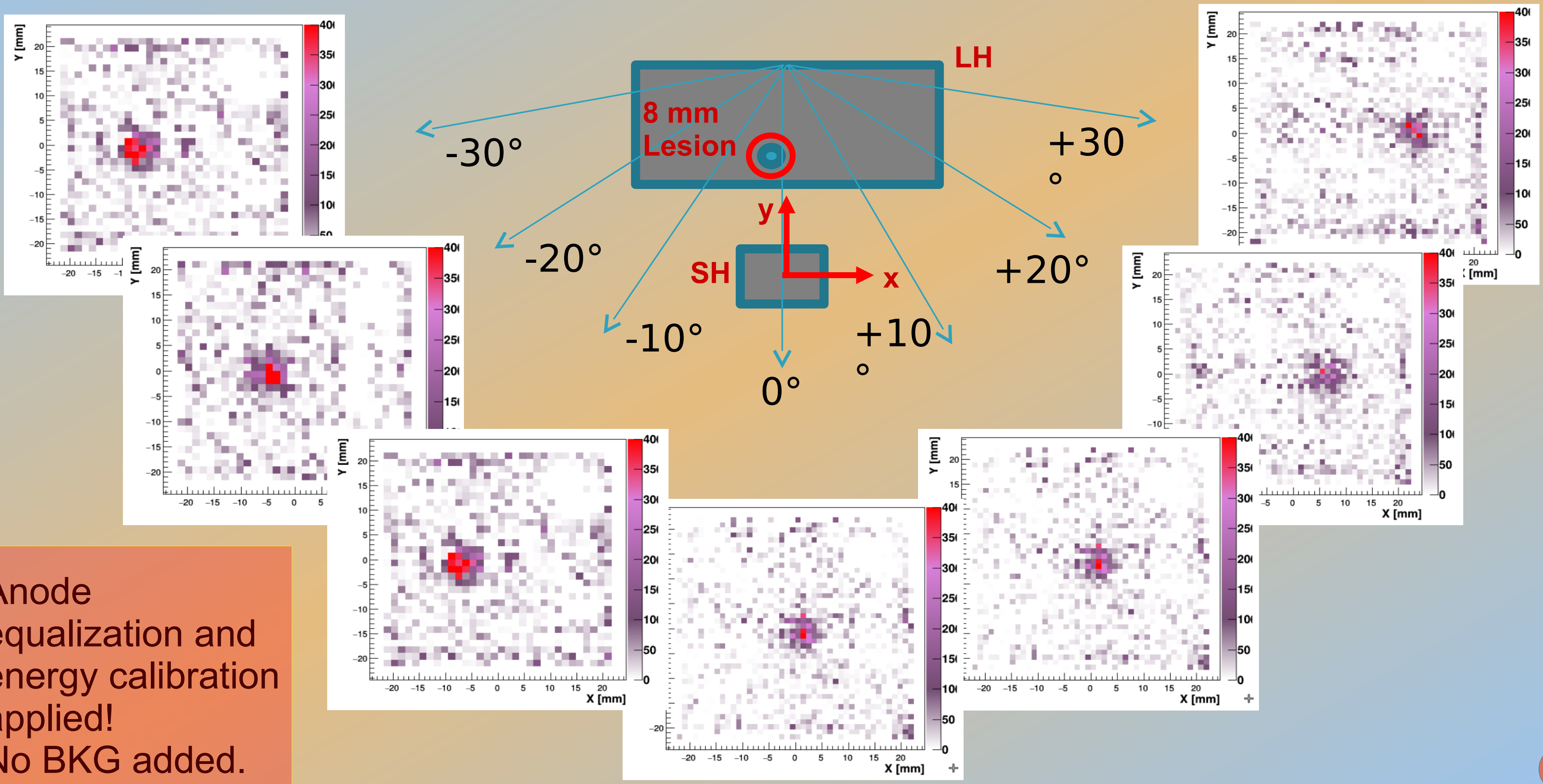
Limited Angle Tomography Configuration

- Same detector heads used in the first campaign
- New breast phantom: 10x10x7 cm^3 (≈1l, smaller than previous campaign)
- PMMA support holds up to 4 hollow perspex spheres (tumours) → **8 mm**
- Ad-hoc wires system permits to shift the tumour along the phantom tickness → **depth scan runs**

Angular Identification of Lesion by Small Head...

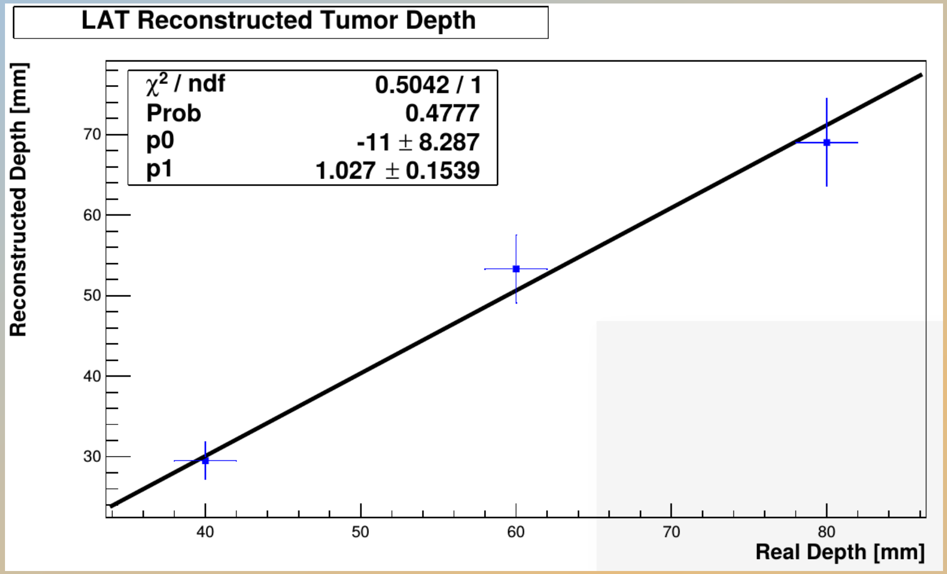


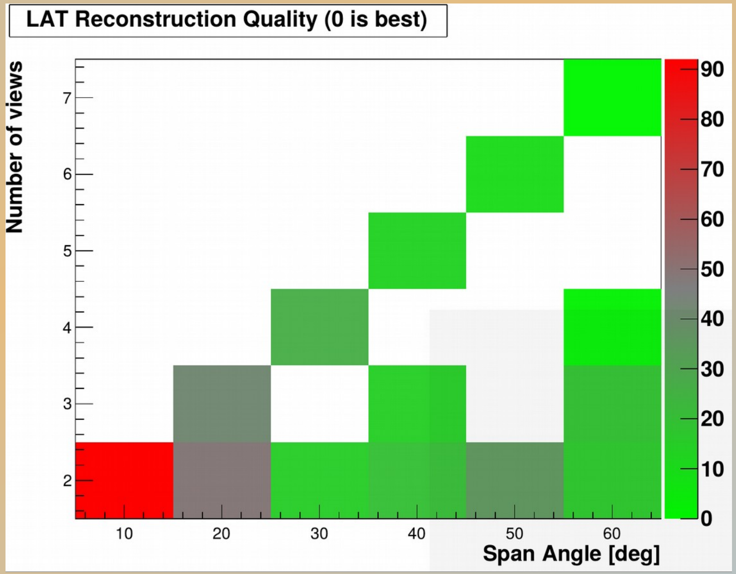
Angular Identification of Lesion by Small Head...



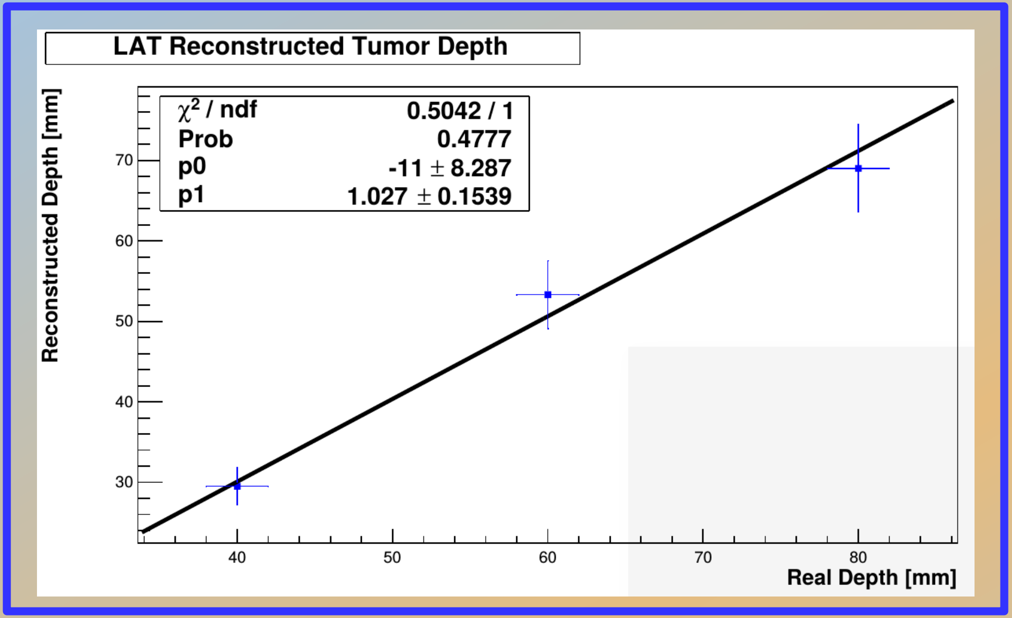
Anode equalization and energy calibration applied!
No BKG added.

Deep Localization of Lesion



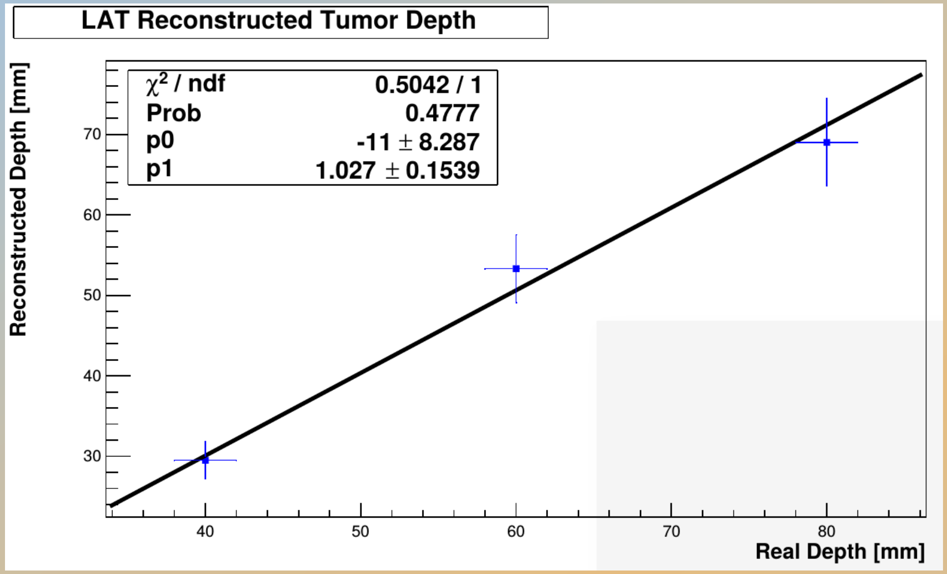


Deep Localization of Lesion



- Reconstructed versus Real Depth: span angle 60° and 7 measures for each depth (40, 60, 80 mm)
- **Result**: LAT maximum reconstruction accuracy of deep lesion ⟷ **fit slope = 1!**

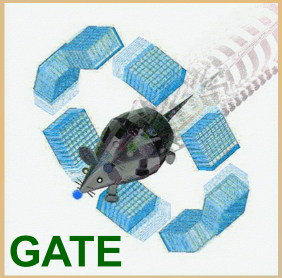
Deep Localization of Lesion



- Reconstructed versus Real Depth: span angle 60° and 7 measures for each depth (40, 60, 80 mm)
- **Result**: LAT maximum reconstruction accuracy of deep lesion ⟷ **fit slope = 1!**
- Number Of Views versus Span Angle: 7 experimental views and 60° span angle
- **Result**: LAT reconstruction quality of lesion grows with **N_{VIEWS} & Span Angle**

Simulation Tool

In order to improve the system performances & images optimization, a Monte Carlo simulator has been implemented in Geant4 environment,
using GATE (Geant4 Application for Tomographic Emission)

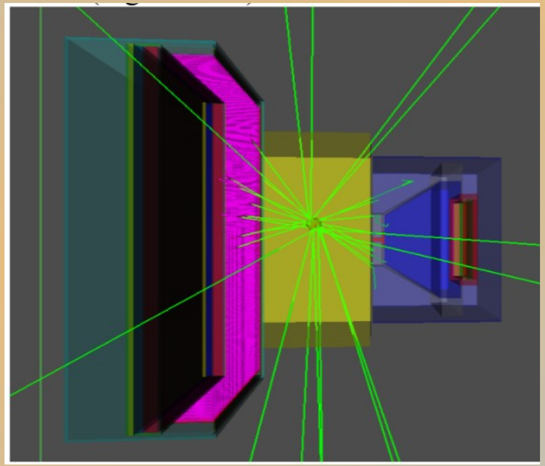


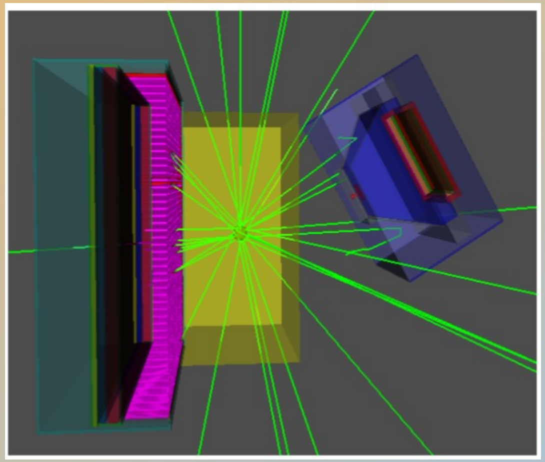
Simulation Tool

In order to improve the system performances & images optimization, a Monte Carlo simulator has been implemented in Geant4 environment,
using GATE (Geant4 Application for Tomographic Emission)

SIMULATOR

- modelisation of detectors, sources, patient
- movement (detector, patient)
- time-dependent processes (radioactive decay, movement management, biological kinetics)

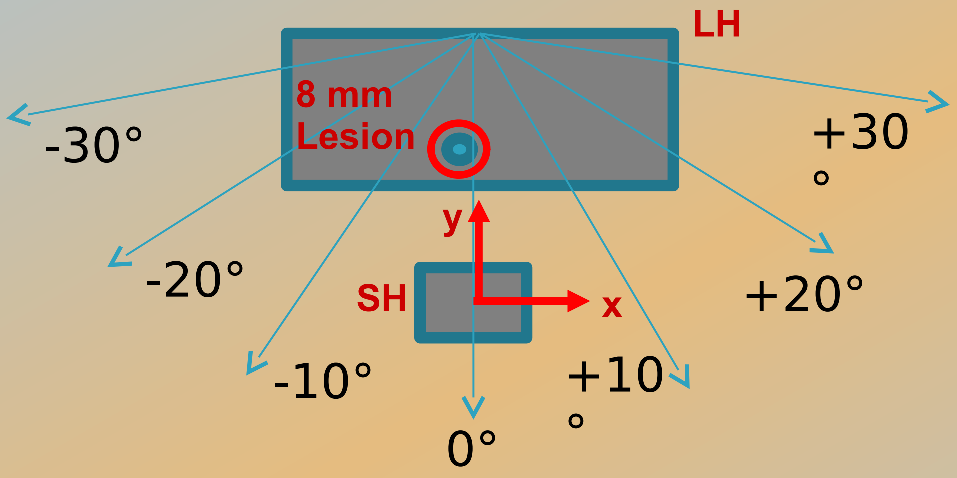




OUTLOOK

- Accurate offline analysis tool of raw data in output from the Monte Carlo simulation
- Optimization of reconstruction alghoritms
- Definition of acquisition protocols
- System configuration evaluation to improve the lesion detectability & quantification, Image corrections

...Angular Identification: GATE simulations



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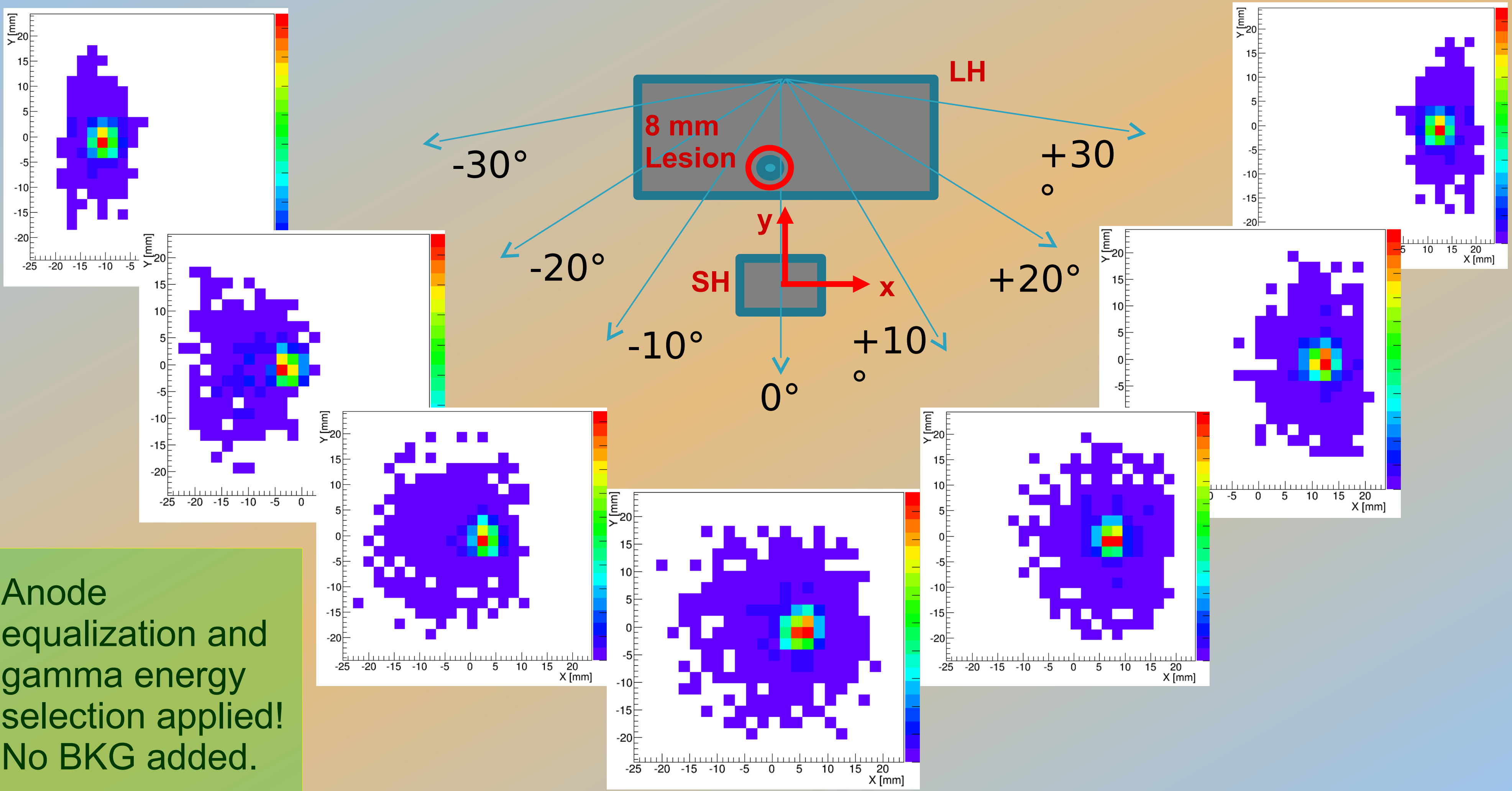
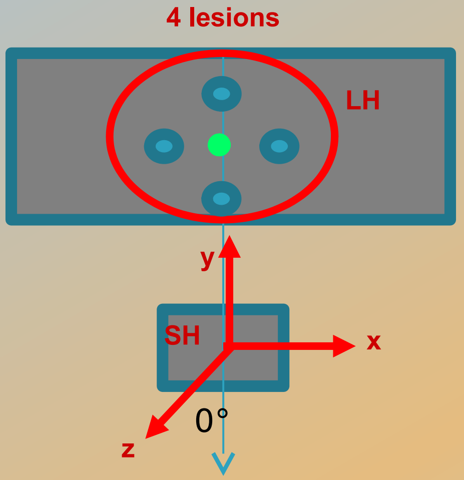
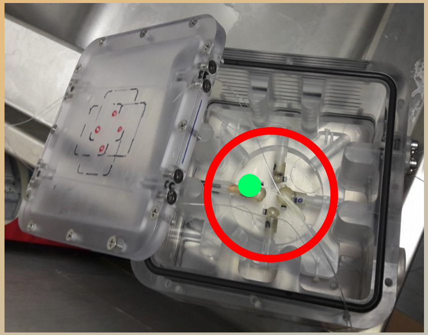


Anode equalization and gamma energy selection applied! No BKG added.

Second Campaign: Spot-Compression Experimental Setup



BREAST PHANTOM: 4 lesions



Spot-Compression Configuration

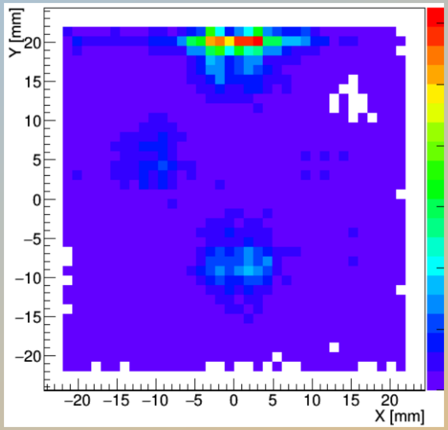
- Same detector heads and breast phantom used in the LAT experimental setup, 3 lesion depths investigated
- SH head with parallel-holes (pinhole) collimator → centered to the center of 4 lesions (8 mm lesion)

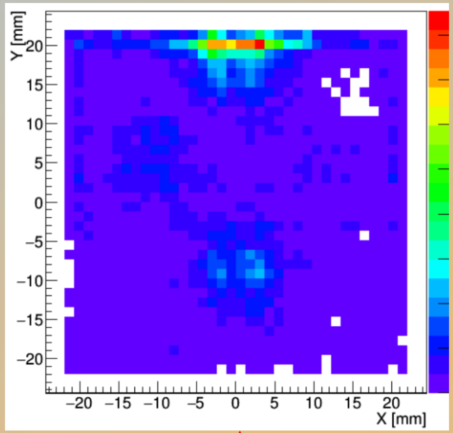
^{99m}Tc Activity and Uptake

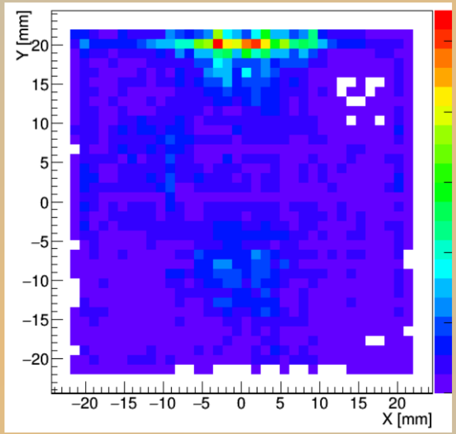
- Breast bkg activity concentration ≈ 5 Mbq/l
- Typical Uptake in a breast lesion: 6 (10) → Lesion Activity Concentration: 30 (50) KBq/ml

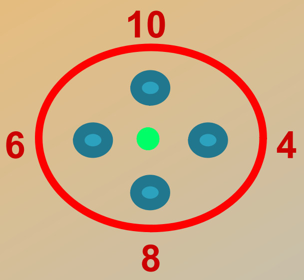
Spot Compression Configuration: Parallel-holes Collimator

Real Data







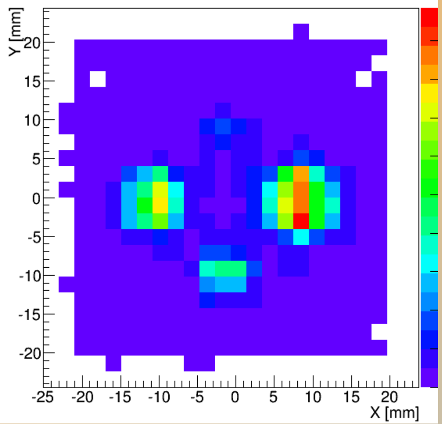


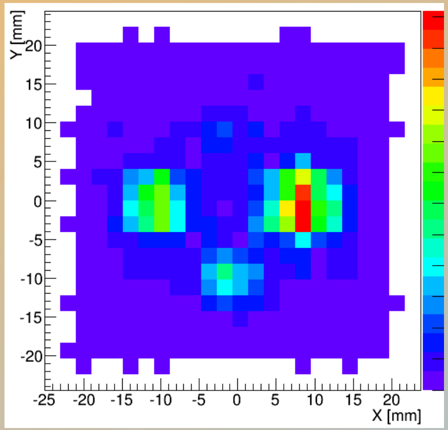
Lesions close to SH

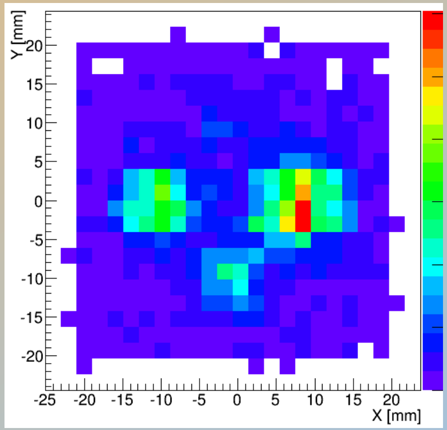
Lesions in middle

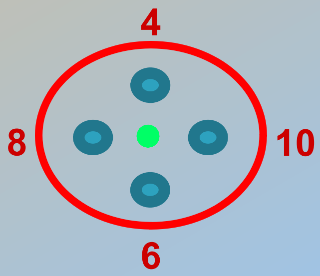
Lesions close to LH

Simulated Data





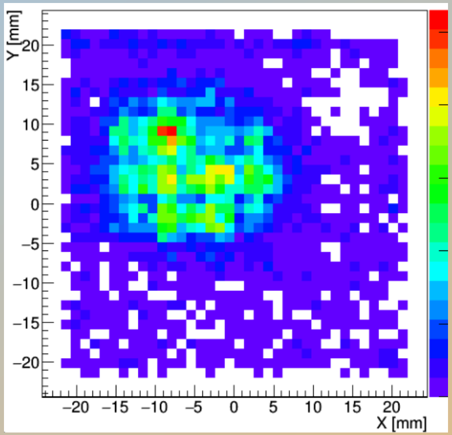


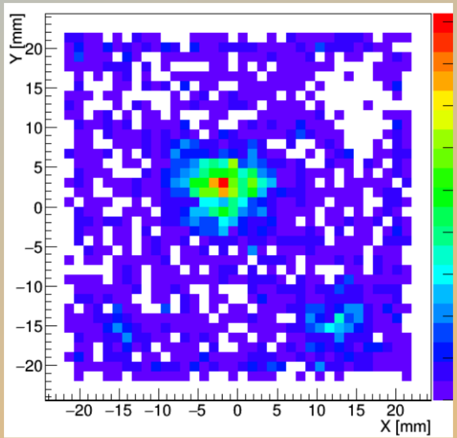


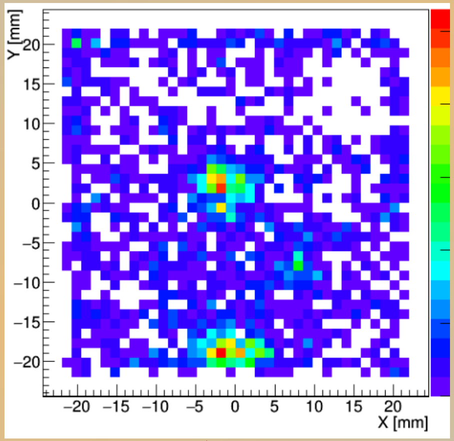
Spot Compression Configuration: Pin-hole Collimator

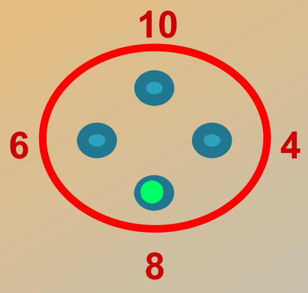
Real Data

→ 8 mm









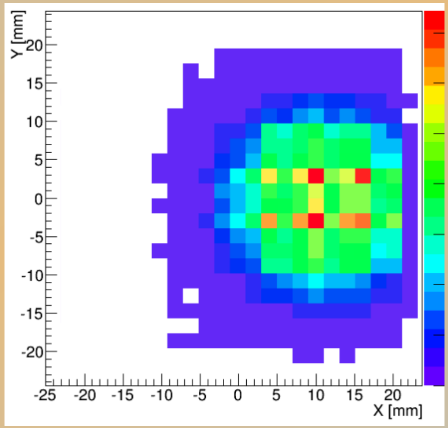
Lesions close to SH

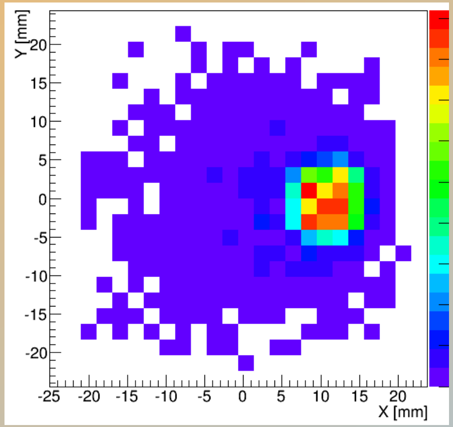
Lesions in middle

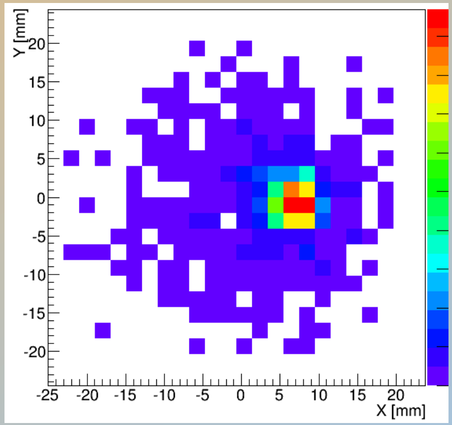
Lesions close to LH

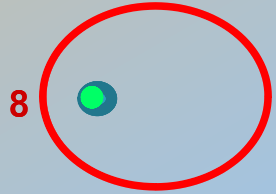
Simulated Data

→ 8 mm









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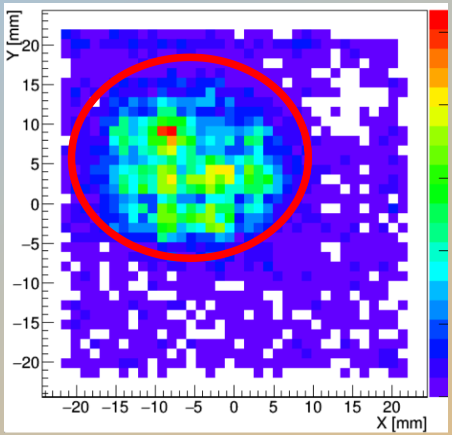
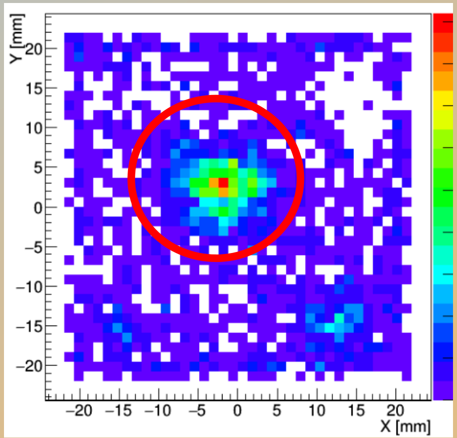
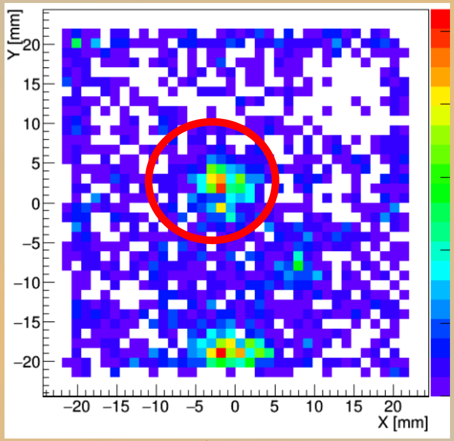
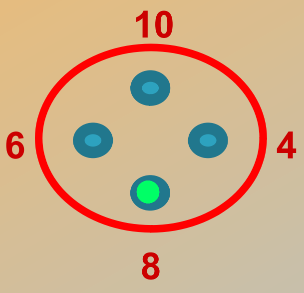








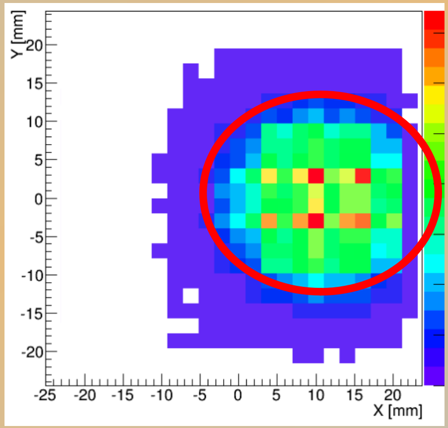
Lesions close to SH

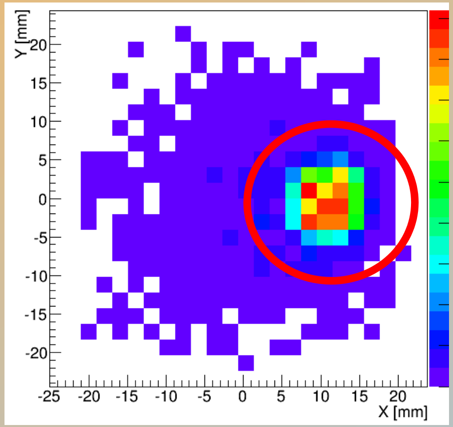
Lesions in middle

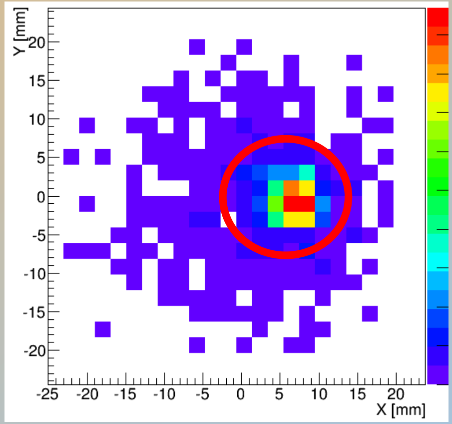
Lesions close to LH

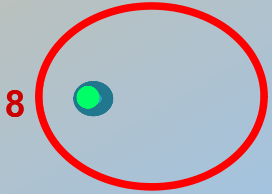
Simulated Data

→ 8 mm









Conclusion & Outlook

- Development of new dedicated dual-asymmetrical head compact Gamma Camera is under calibration and characterization to improve the detection sensitivity for sub cm lesions
- The quality of reconstructed images has been optimized with deep calibration and characterization, and accurate data processing
- First results on lesion detectability shows approx. 5 mm diameter as lower limit (with nominal Uptake = 10)
- Preliminary analysis on limited angle tomography:
  - good correspondence of reconstructed and real tumour depth (in optimal conditions)
  - reconstruction improves with larger span angle and number of views (as expected); but trade off between them and clinical session time and complexity need to be evaluated
- Reliability of GATE simulations and the fusion of BKG and lesion images will allow to find the best configuration to detect the cancers lesions smaller than 5 mm using an Uptake < 10
- Analysis will be continued and integrated by simulations: images fusion in 2D and 3D
- New measurements on LAT will overcome current limitations on mechanical accuracy of the heads positioning

THANKS FOR YOUR ATTENTION

Email: **elio.poma@ct.infn.it**