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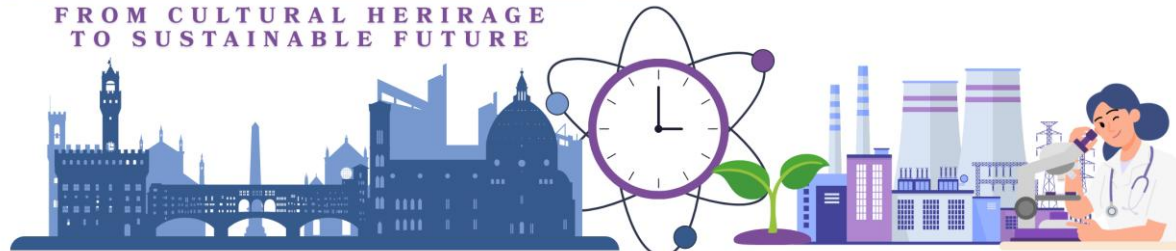


Investigate Quantitative Bremsstrahlung Imaging by ^{90}Y and ^{166}Ho

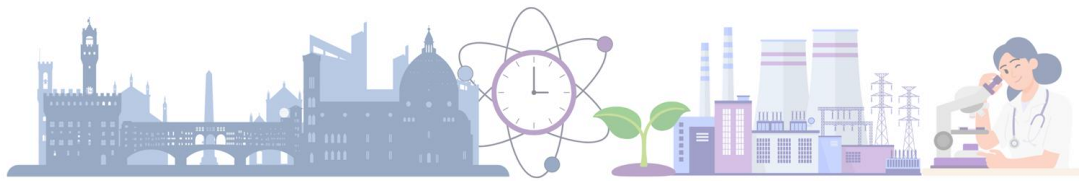
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ISOTOPIC TIME MACHINE
FROM CULTURAL HERITAGE
TO SUSTAINABLE FUTURE



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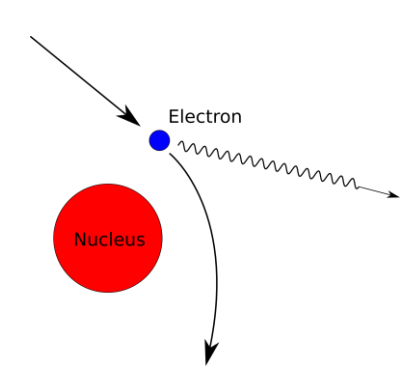
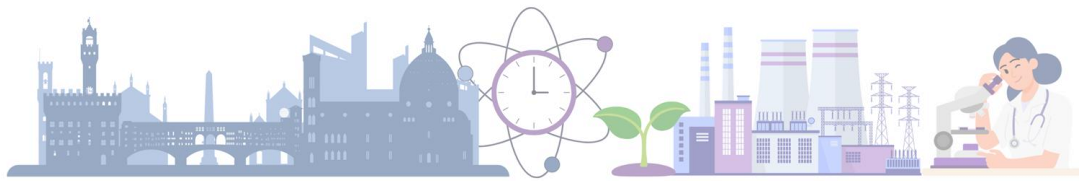


Radiometabolic therapy → Theranostic (therapy & diagnosis)

Use radiopharmaceutical to deliver radiation to diseased (cancer) cells, minimizing harm to healthy tissues

Effectiveness of therapy depends on quantitative knowledge of spatio-temporal biodistribution of the therapeutic agent during treatment (patient specific)

→ **Quantitative imaging** of the emitted radiation fraction escaping from patient body



Aims of the study

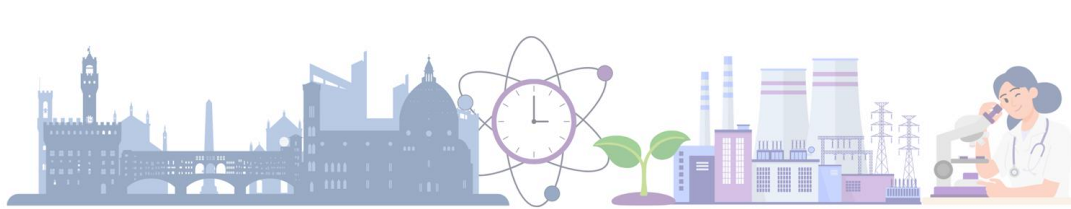
Define and implement **controlled experimental conditions and methodology** to investigate **quantitative Bremsstrahlung Imaging (qBSI) challenging aspects**

Therapeutic radioisotope primarily emits α or β^-

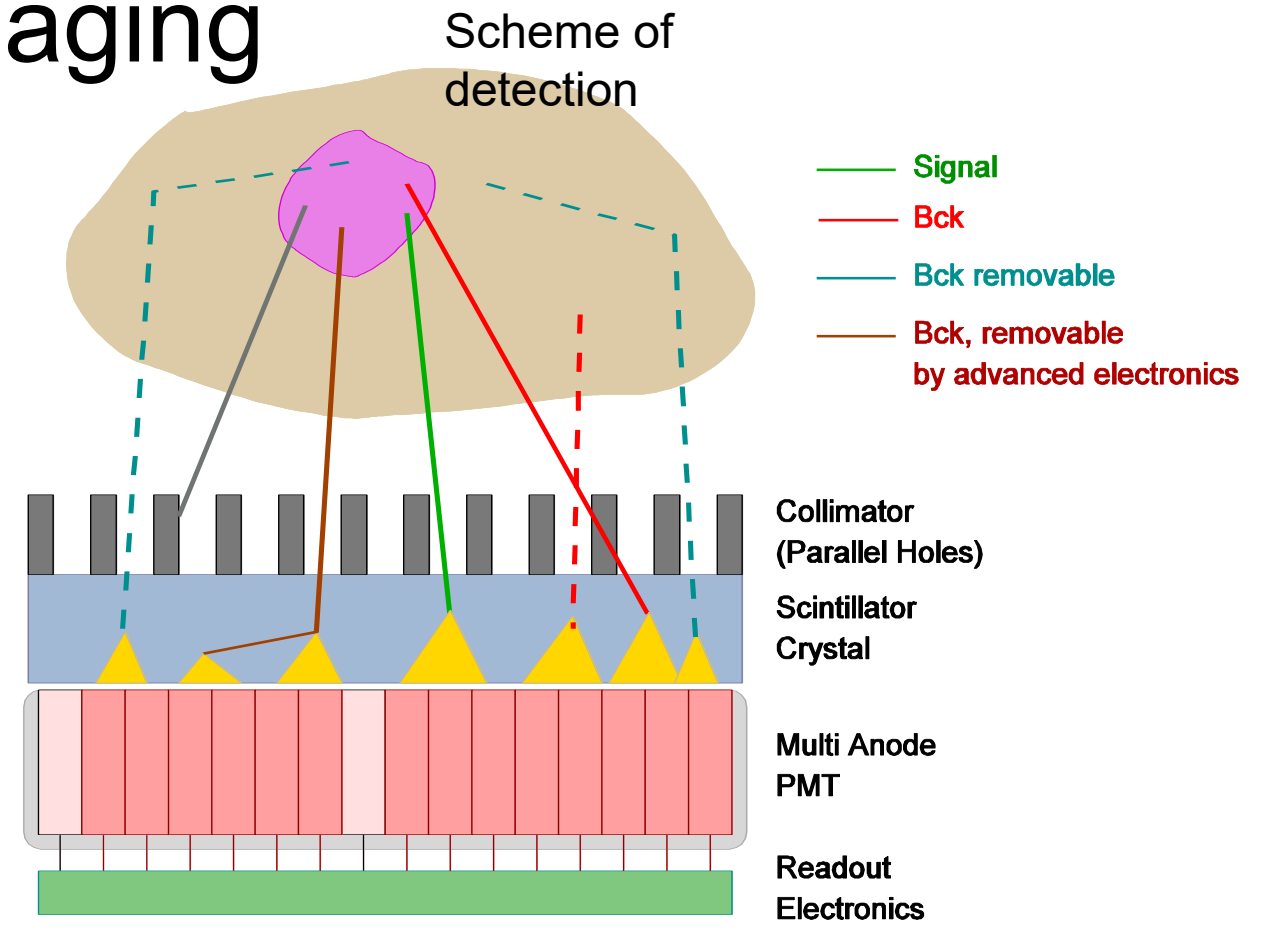
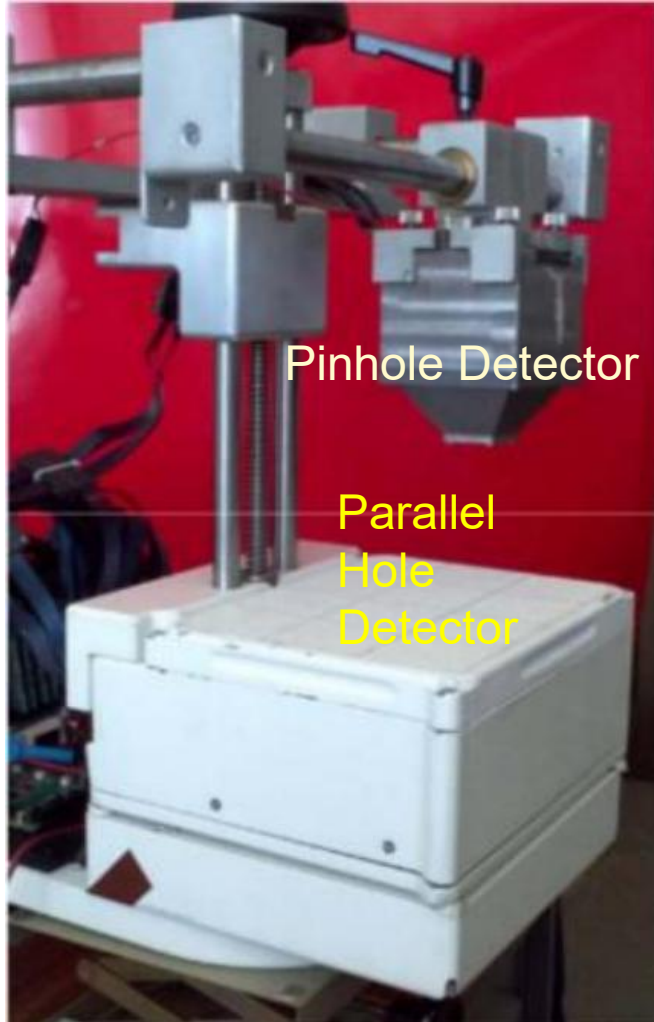
Approved Radioisotope	³² P	⁸⁹ Sr	⁹⁰ Y	¹³¹ I	¹⁵³ Sm	¹⁷⁷ Lu	²²³ Ra
Main emission	β^-	β^-	β^-	β^-	β^-	β^-	α
Secondary emissions			β^+	γ	γ	γ	β^- , γ
Number of diseases	1	1	3	4	1	2	1

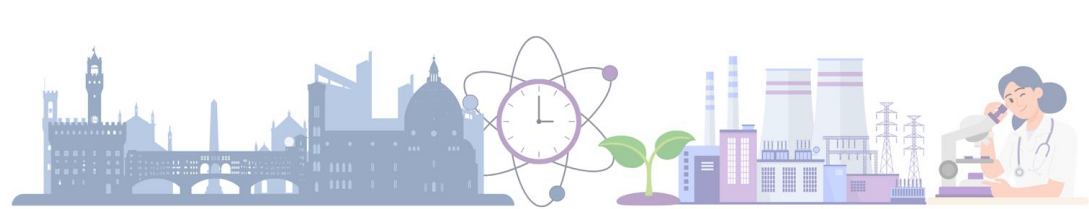
adapted from <https://doi.org/10.1038/s41392-024-02041-6>

qBSI can support adequate determination of delivered dose of β^- emitters (e.g. ⁹⁰Y)

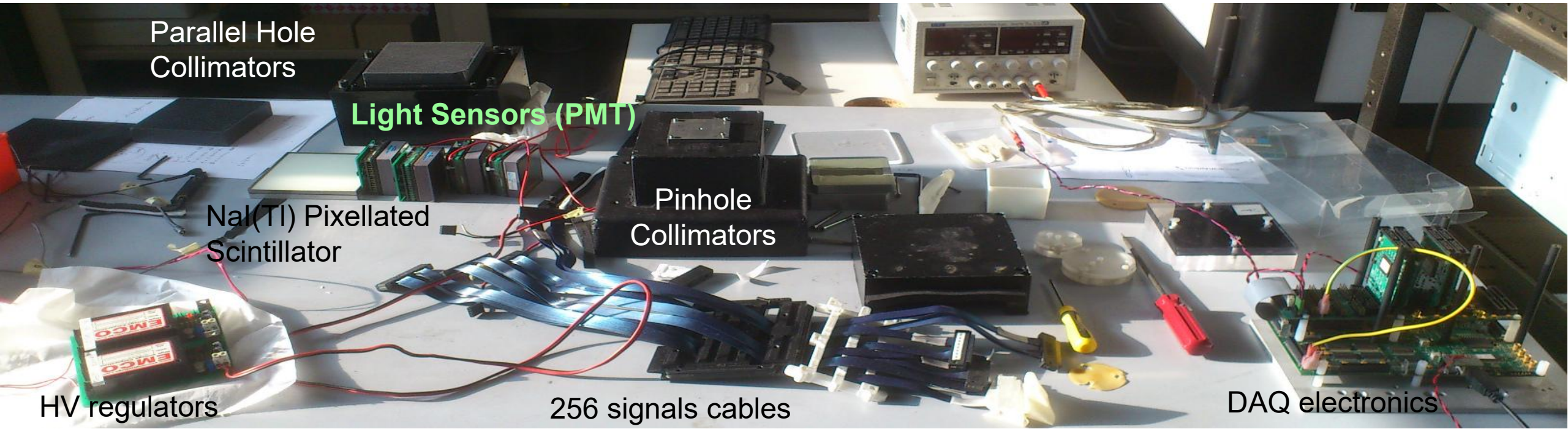


ISS portable and detectors for imaging



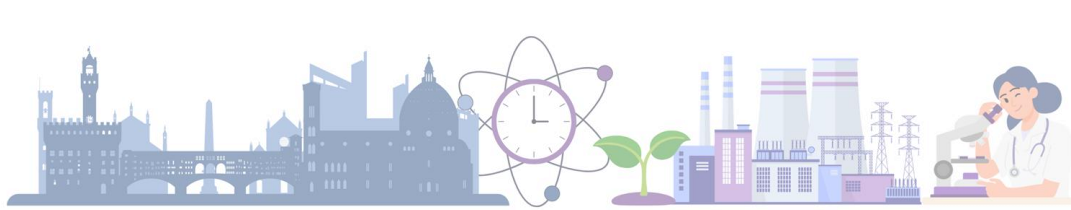


Components of portable and reconfigurable detector



Collimators: pin hole and parallel hole geometries
Scintillators: NaI, pixellated, 5 - 9 mm thick,
PMT: Hamamatsu 64 ch H8500 (and 256 ch H9500)

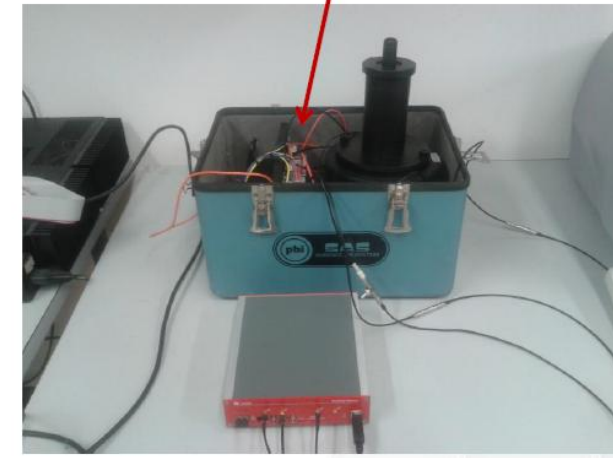
DAQ Electronics: MAROC3 front-end ASICs, up to 4096 independent channels, real-time self trigger (OR&majority) on FPGA



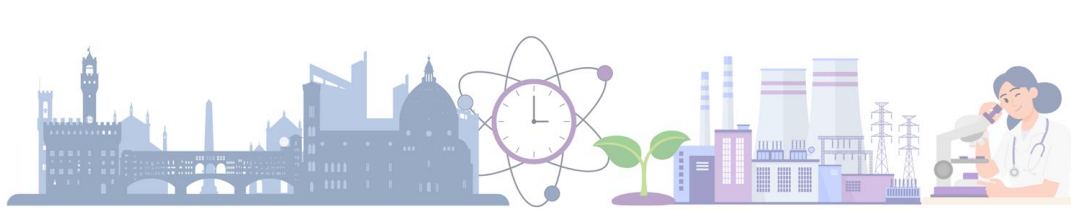
ENEA portable TDCR detector



- Optical chamber made in PTFE with prismatic shape
- Lift for the LS vial and optical shutter (PMT's always powered)
- Compact design (HV modules included in the box)



radioactive liquid source
contained in 20 mL glass vial
filled with 10 ml UG LSC
 β emissions



Main approach

Custom “minimalist” equipment:

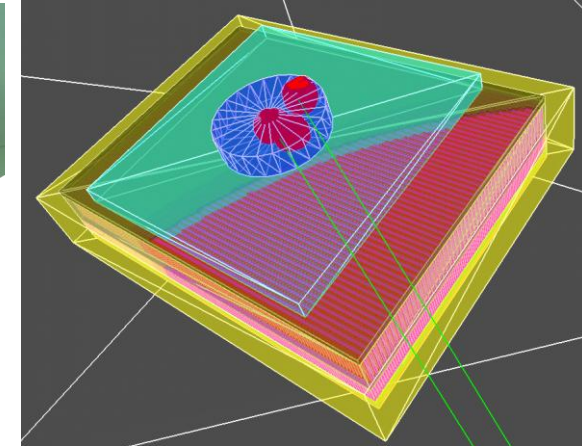
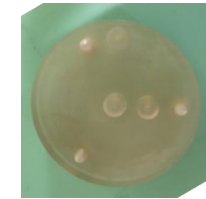
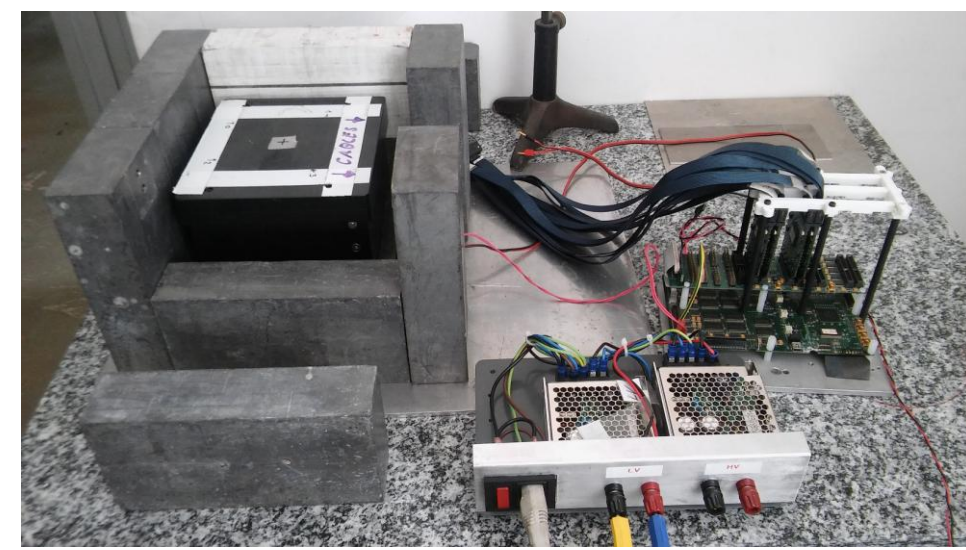
PMMA phantoms, detectors, readout electronics and processing developed “in house”
→ **largely reconfigurable system**

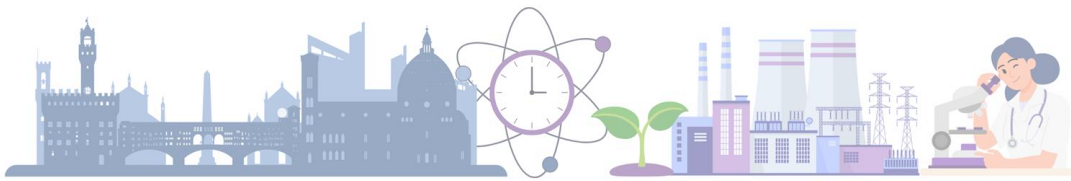
Detailed MonteCarlo modelling: GATE/Geant4

→ identify optimal reconstruction method(s) and provide normalization factors for quantitative activities evaluation

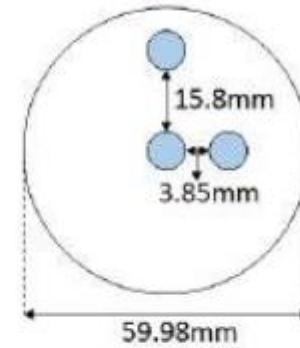
Precise *on site* measurements of the samples activities by portable TDCR (Triple-to-Double Coincidence Ratio) counter

qBSI challenges: production $<10^{-3} \gamma_{BS}/e^-$, continuous energy spectrum up to $E_{e^-}^{max} \sim \text{MeV}$ → no specific photopeak, more involved energy dependent γ interactions with tissue



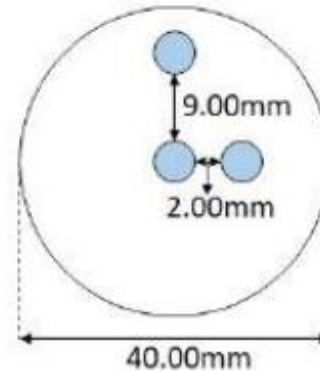
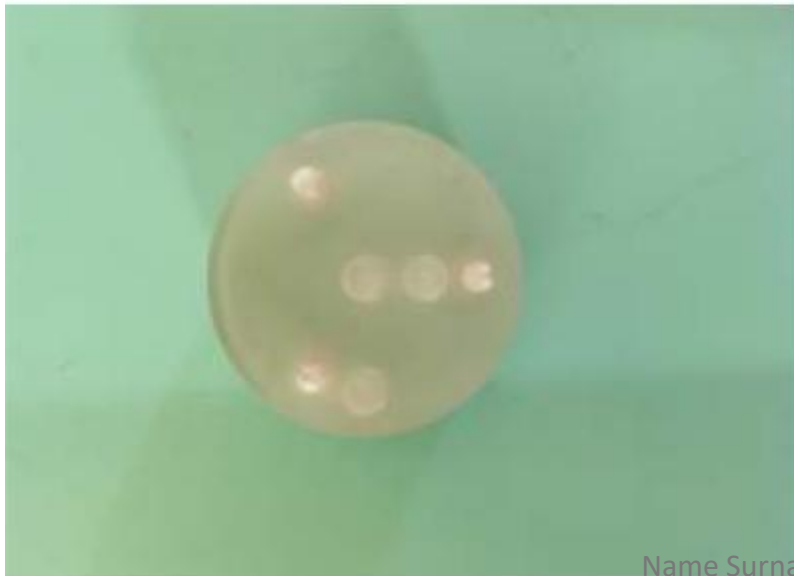


Phantoms



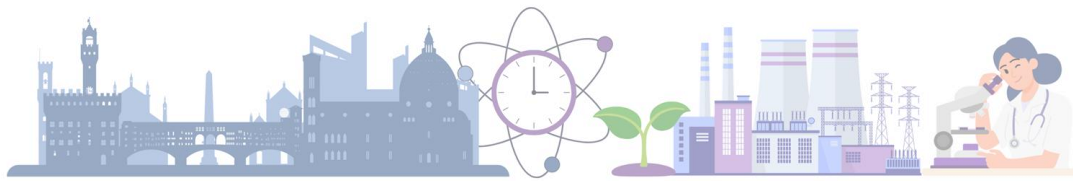
Geometria spot:
 Diametro=7.85mm
 Altezza=5.85mm

Geometria disco:
 Spessore disco=7.92mm
 Spessore coperchio=6.00mm



Geometria spot:
 Diametro=5.85mm
 Altezza=5.80mm

Geometria disco:
 Spessore disco=7.90mm
 Spessore coperchio=5.00mm

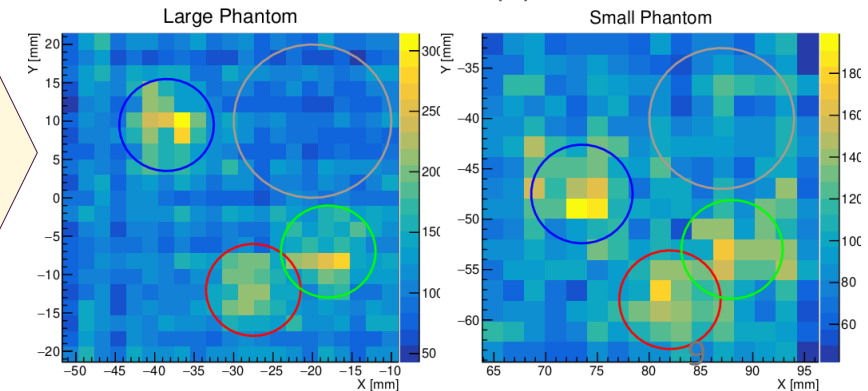
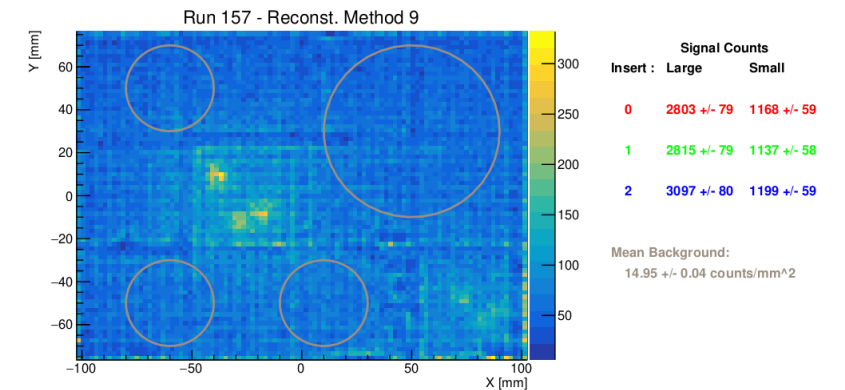
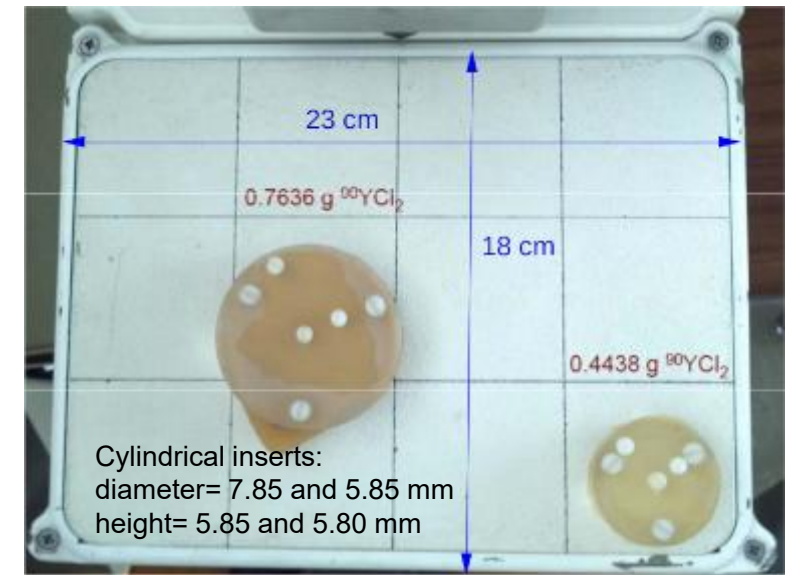


First measurements on ^{90}Y

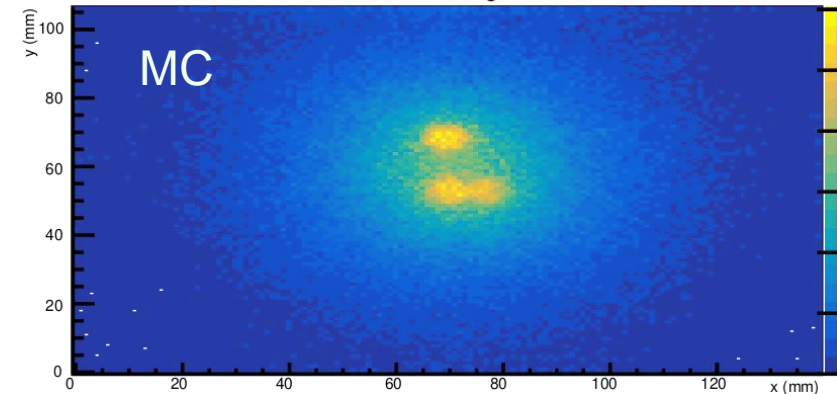
2 phantoms with 3 inserts each filled by ^{90}Y solution of **well known activities**

(TDCR measurement)

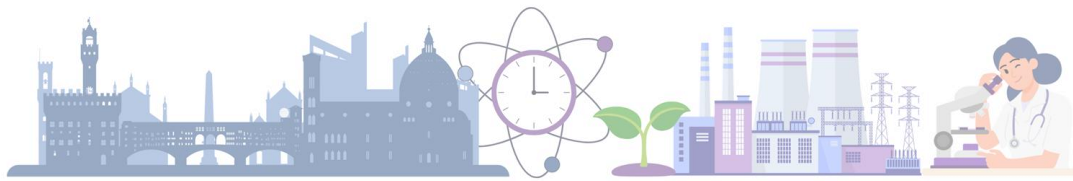
MonteCarlo (Geant4) fine tuning of simulation parameters → optimal cuts in energy and cluster detection (e.g. Compton)



Reconstructed Image with all cuts



Reconstructed image and related counts from each insert
 (proper smearing not applied to enhance pixels structure of the detector system)



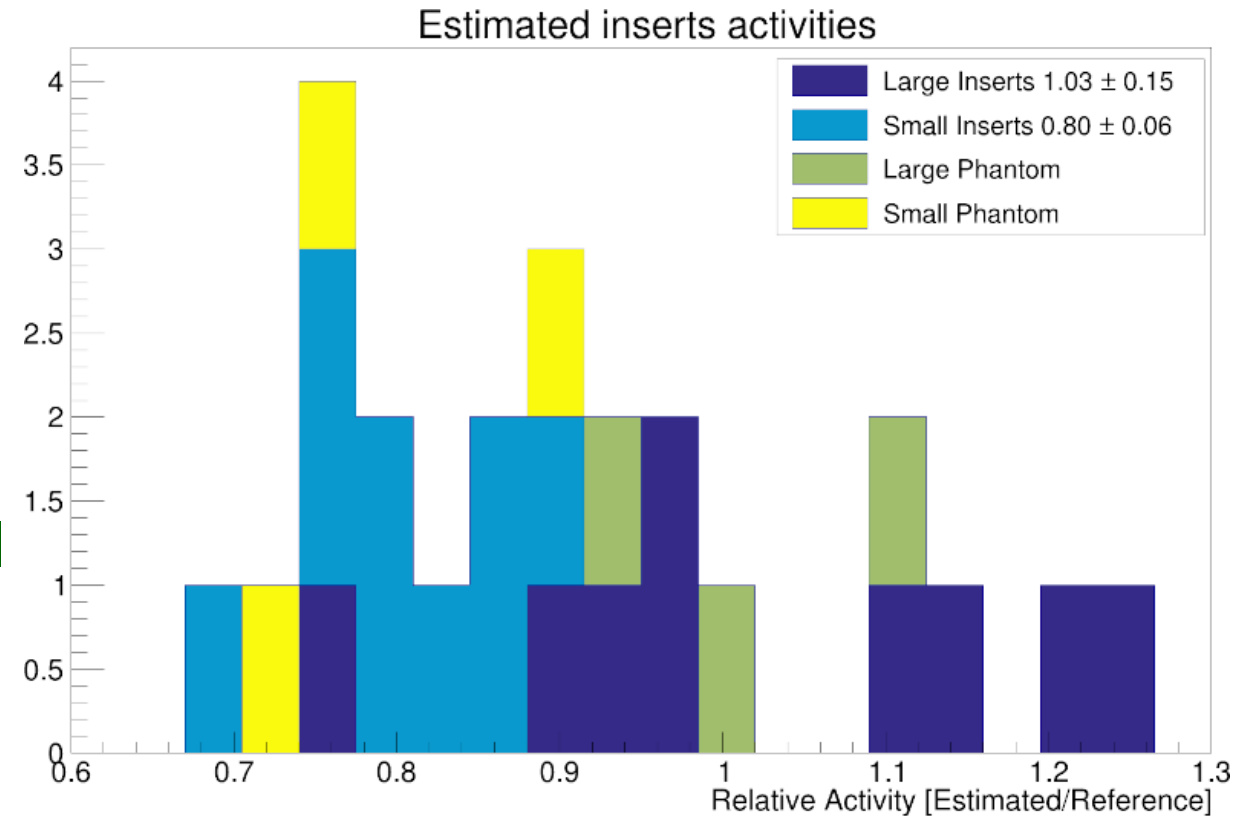
Different PMMA plates interposed between phantom and imaging detector

Example of outcome from ^{90}Y

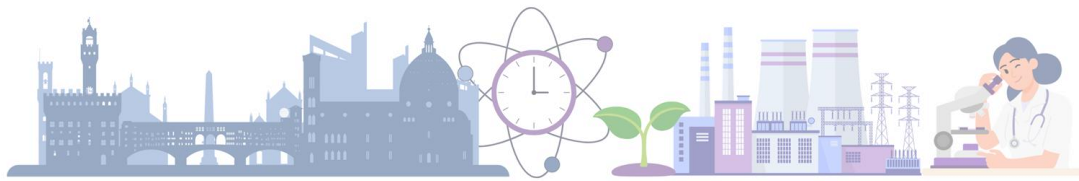
Optimal energy cuts derived from MonteCarlo evaluation of three quality indices: position residual, signal and noise

Reconstructed activities (with parallel hole collimator) of inserts with ^{90}Y deviate from “ground truth” by ~30% in worst case

Pin hole data expected to provide better estimations



Larger RMS (~15%) for large inserts, larger mean bias (~20%) for small inserts

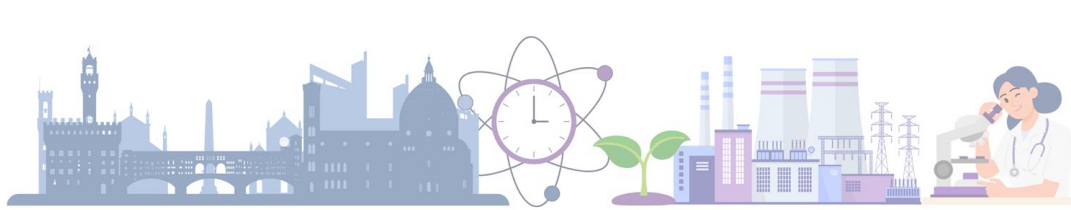


	90Y	166Ho
Half-Life [d]	2.67	1.12
b- E _{max} [MeV]	2.28	1.85, 1.77
secondary radiation abundance [%]	b-b+ 0.0032	g 6.6
energy [MeV]		0.081

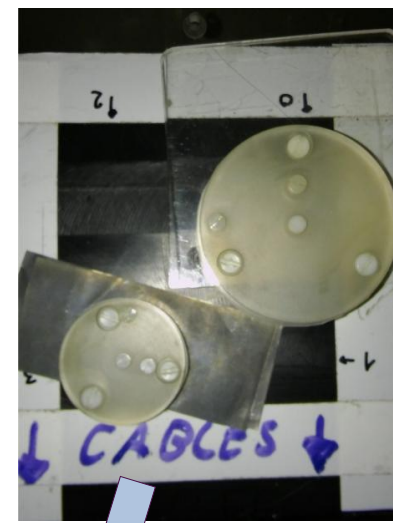
Moving to ¹⁶⁶Ho

⁹⁰Y is routinely used in clinical context; ¹⁶⁶Ho is increasingly investigated as a valid alternative thanks, in particular, to monochromatic γ imaging (and paramagnetic property for MRI)

In our research the ¹⁶⁶Ho γ emission represents a reference for the investigation of qBSI and permits a simultaneous evaluation of the detector response (in the γ peak region) which facilitates the quantification



Example of setup
with Pb foil and
PMMA slab
between
phantoms and
sensor entrance
window



^{166}Ho Measurements

Performed at Policlinico Gemelli, Medical Physics Unit

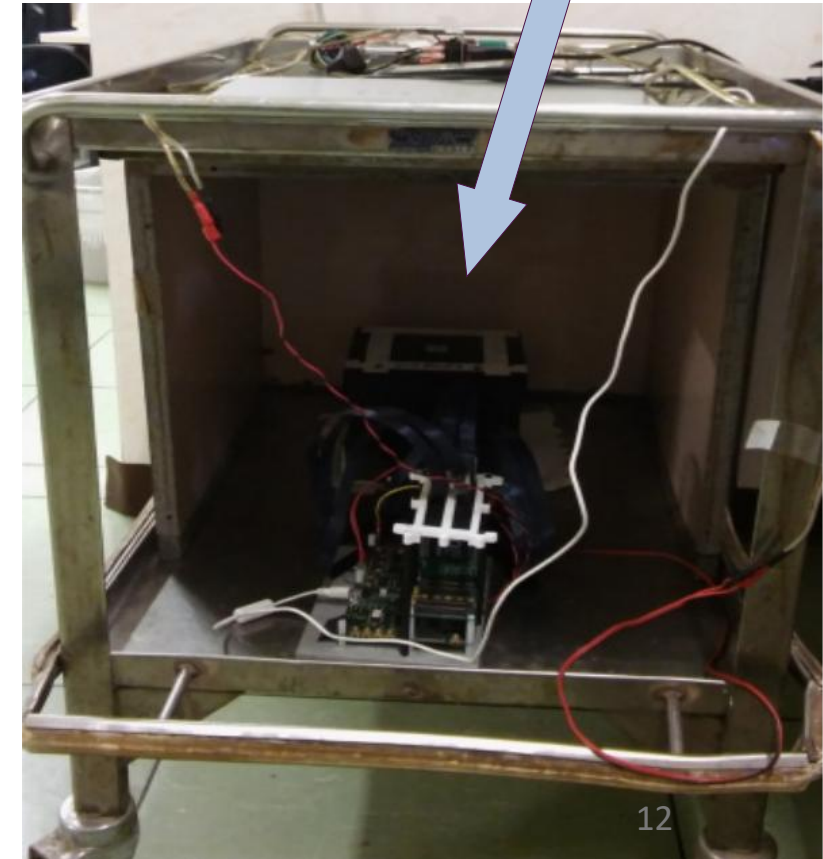
Same phantoms used for ^{90}Y measurements

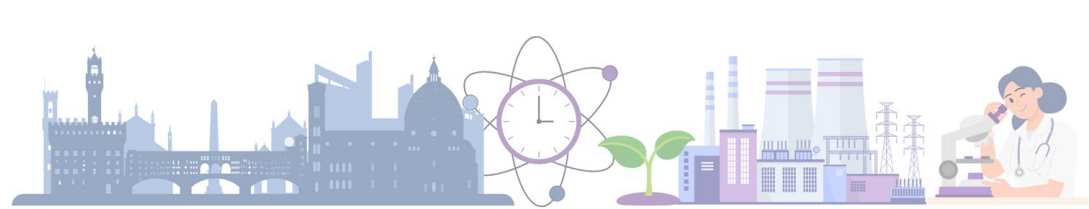
Inserts activities: 6.96 MBq and 13.41 MBq

Different slabs of PMMA, Cd and Pb interposed
between phantom and sensor

Sub-optimal high efficient parallel hole
collimator with exagonal holes (1.5 mm
diameter) and 0.1 mm septa

Single photon detector preliminarily calibrated
and equalized in laboratory with ^{90}Sr and ^{57}Co
sources





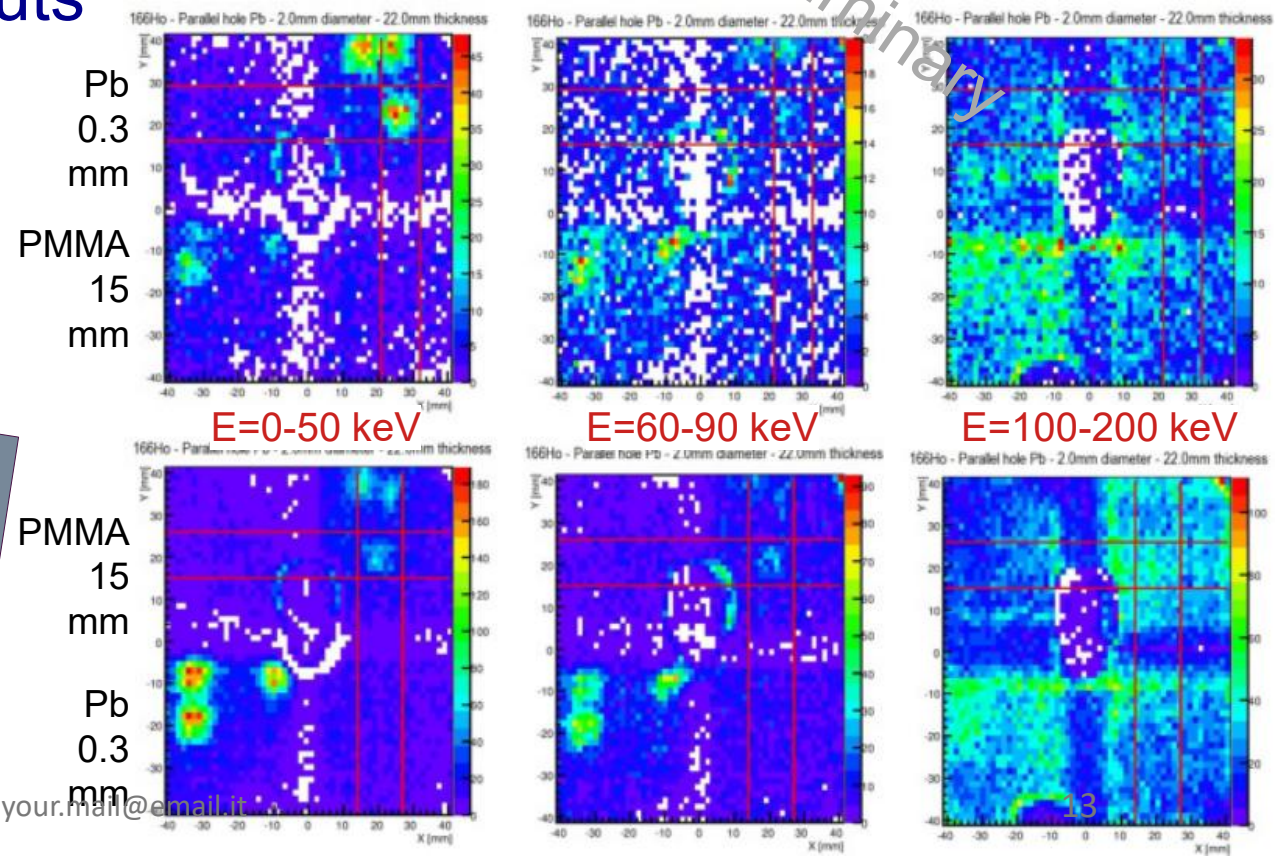
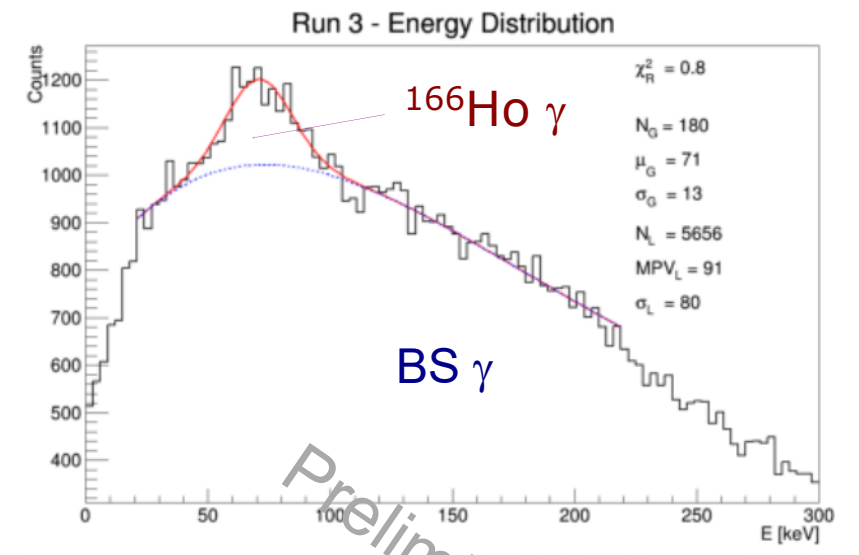
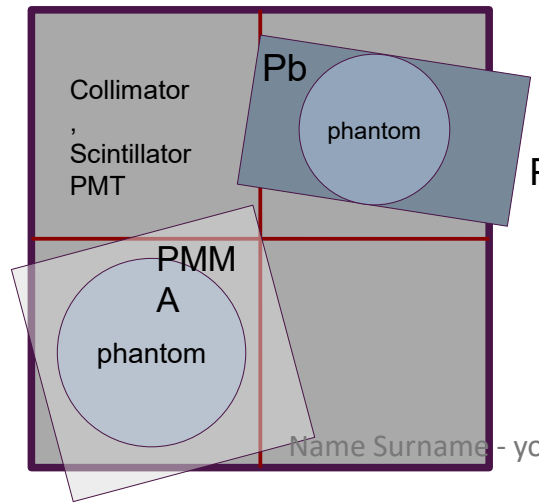
$^{166}\text{Ho}-\gamma$ and BS- γ Imaging

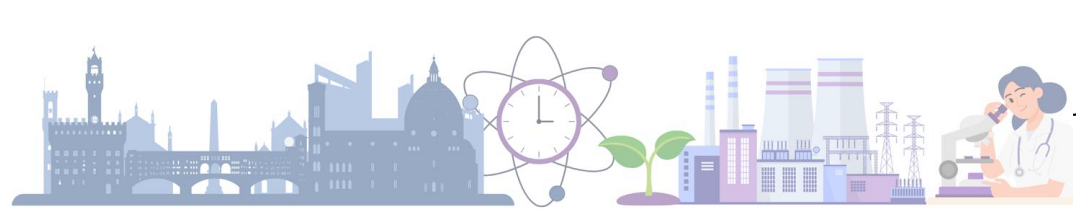
Example of reconstructed images in two configurations at different energy cuts

Reconstruction parameters not yet optimized by MonteCarlo analysis

Optical grease not perfectly distributed on PMT borders (minor impact under the phantoms)

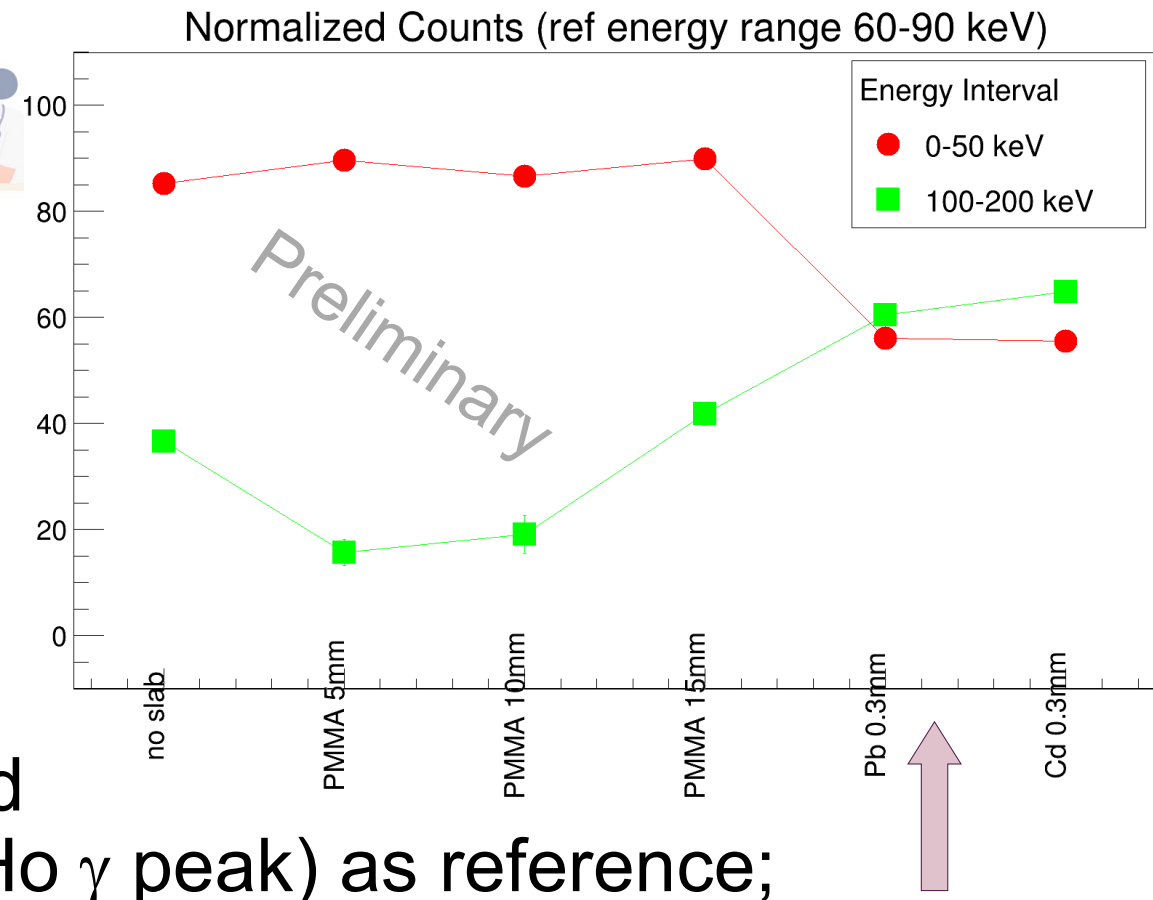
Data in next slides refer to the ROI marked by red lines in images



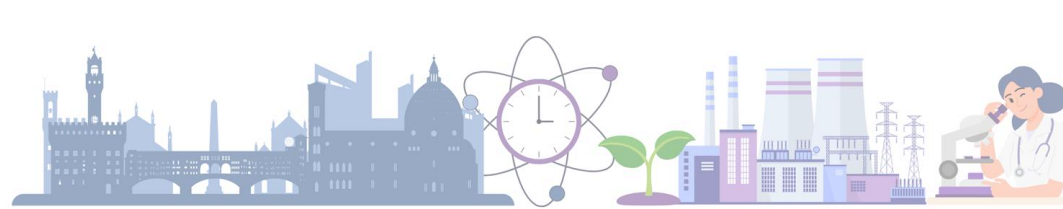


Normalized signal counts

In order to minimize dead time and detector efficiency impact, signal counts in selected insert are normalized using the energy range 60-90 keV (^{166}Ho γ peak) as reference;



The different behavior of the counts in different energy ranges suggests to investigate the potential exploitation of different regions in the continuous energy distribution of the BS radiation

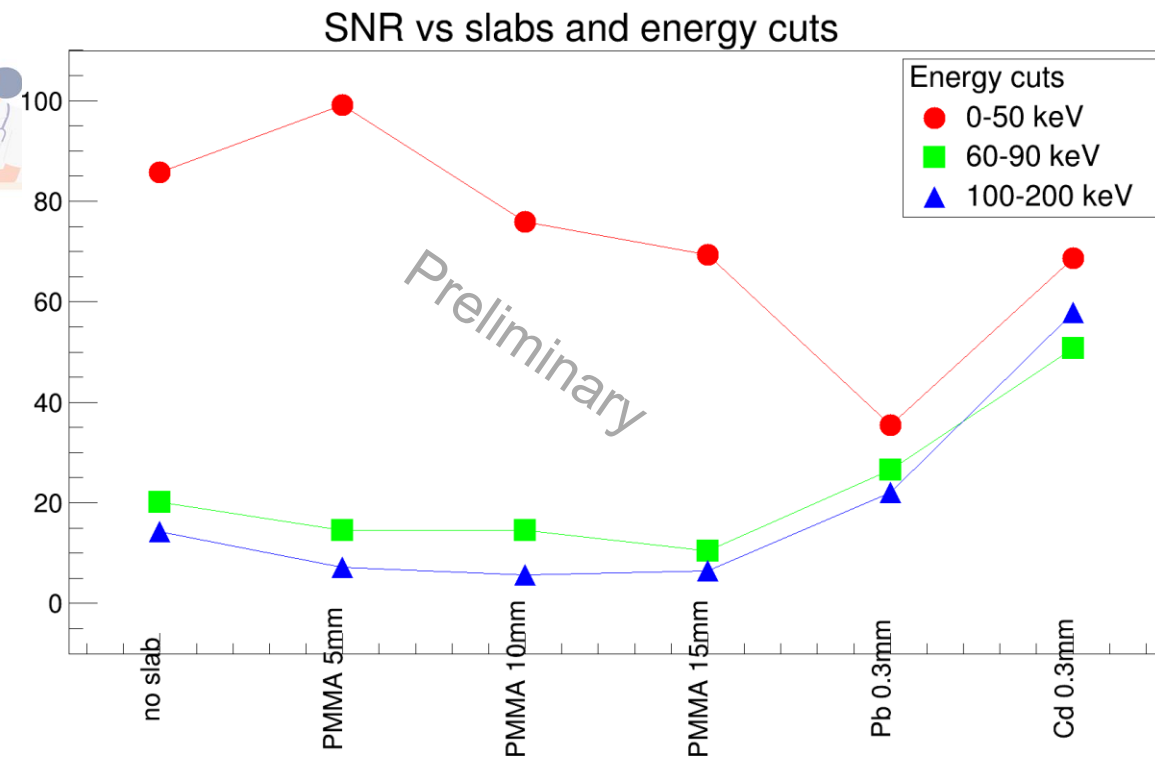


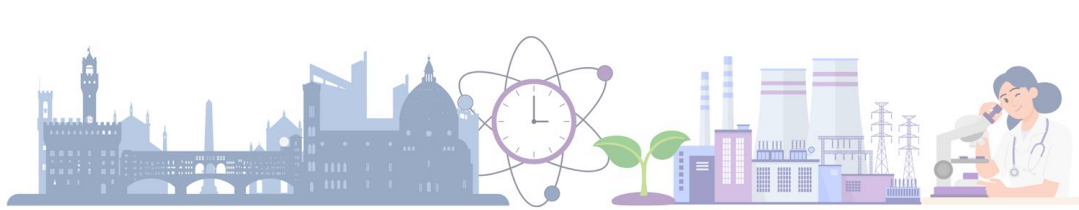
Signal to Noise Ratio

Signal counts in the selected ROI respect to the RMS of the counts around the spot of the considered insert.

At increasing energies SNR decreases for PMMA slabs but stays similar for Pb and Cd foils.

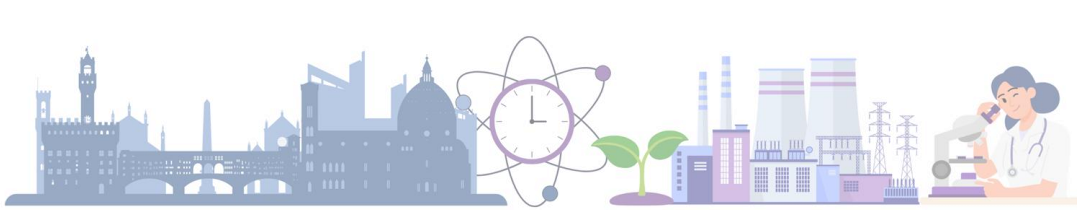
Cd expected to play intermediate role between PMMA and Pb, but SNR tends to be larger → materials can be optimized taking into account experimental setup (by validated MonteCarlo support)





-- Outlook --

- ✓ ^{90}Y activities estimation using sub-optimized detectors for BS g and supported by Monte Carlo simulations within 30% (worst case) from the reference values
- ✓ First analysis of ^{166}Ho encourage the investigation of the possibility to exploit the continuous energy distribution of the BS γ and to optimize, not only the detector components, but also other experimental aspects (e.g. absorbing/irradiation materials) according to the specific imaging task
- ✓ **Work still in progress**



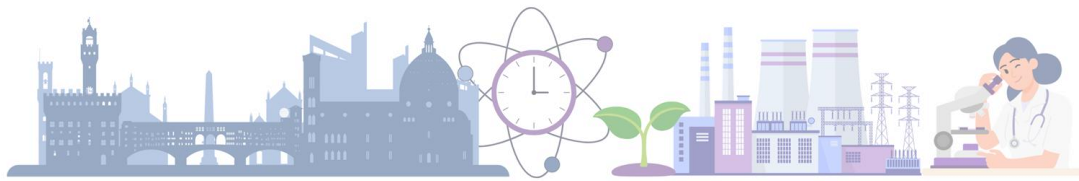
Acknowledgments

The research was carried out thanks also to the support of two EMPIR (European Metrology Programme for Innovation and Research) projects, MetroMRT and MRTDosimetry, in which a metrological approach to internal dosimetry with theranostic (pure β and β - γ) radiopharmaceuticals was studied—starting from the accurate measurement of the radiopharmaceutical's activity, moving to quantitative imaging using SPECT or PET systems, and ultimately leading to dose estimation.

^{90}Y solution was provided by Sirtex Company

^{166}Ho solution was provided by LENA reactor in Pavia by irradiating ^{165}Ho

The impurity check of both provided solutions was performed in the Radioactivity Laboratory of the National Institute of Ionizing Radiation Metrology (INMRI) of ENEA by using high-resolution gamma-ray spectrometry



Thanks for your attention