

From MACACO to AIDER

Gabriela Llosá on behalf of the IRIS group and collaborators.

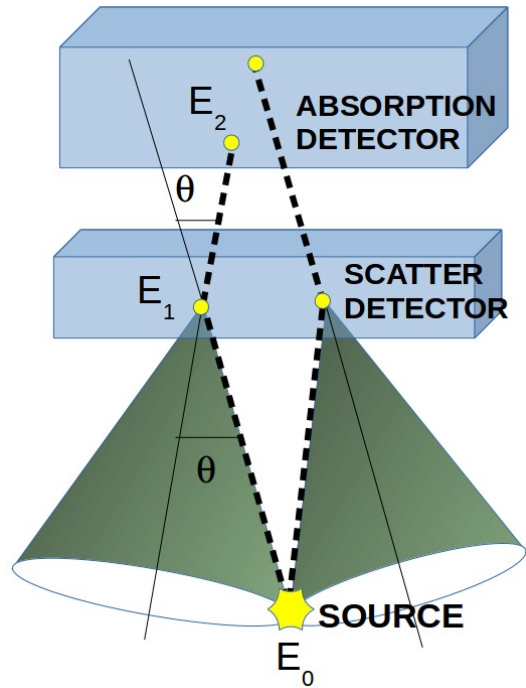
Instituto de Física Corpuscular IFIC (CSIC-UV)
<http://ific.uv.es/iris>

XVII CPAN Days
Valencia, 19-21 November 2025

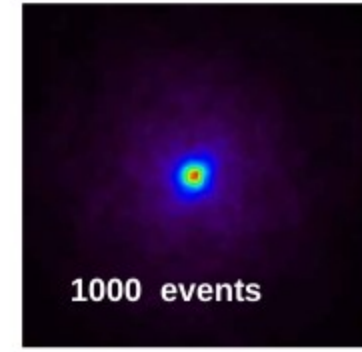
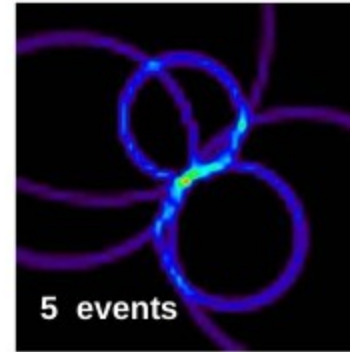
Outline

- MACACO Compton cameras.
- ICOR- CC with silicon
- Application to hadron therapy treatment monitoring.
- Application to treatment verification in targeted radionuclide therapy.
- AIDER project.

Compton camera



Backprojection



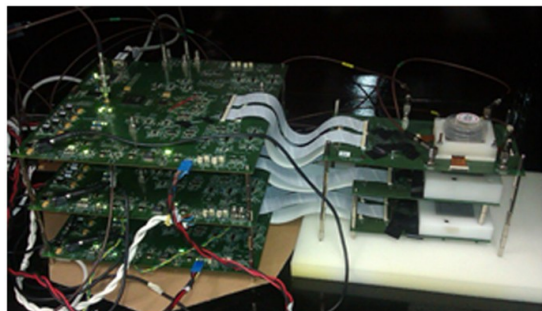
+ Image reconstruction

$$\cos \varphi = 1 - m_0 c^2 \left(\frac{1}{E_{\gamma'}} - \frac{1}{E_{\gamma}} \right)$$
$$E_{\gamma} = E_{e^-} + E_{\gamma'}$$

$$\lambda_j^{n+1} = \frac{\lambda_j^n}{s_j} \sum_{i=0}^N \frac{t_{ij}}{\sum_k t_{ik} \lambda_k^n}$$

List mode ML-EM

MACACO (Medical Applications CompAct COmpton camera)



MACACO I

Llosá et al. Front Oncol 2016

Solevi et al. Phys. Med. Biol. 2017

Muñoz et al. Phys. Med. Biol. 2017

Muñoz et al. JINST 2018

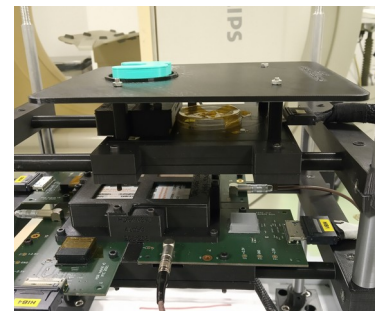
Barrio et al. NIM 2018



MACACO III

Barrientos et al.
Radiat. Phys. Chem. 2023

MACACO III+



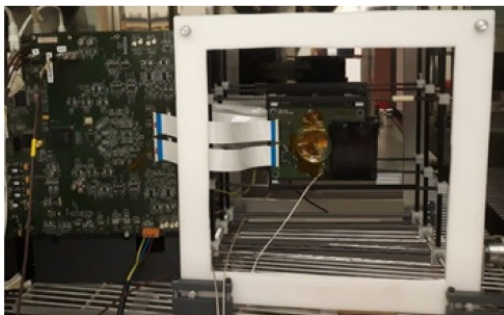
EC FP7

Ros et al. Phys. Med. Biol. 2020

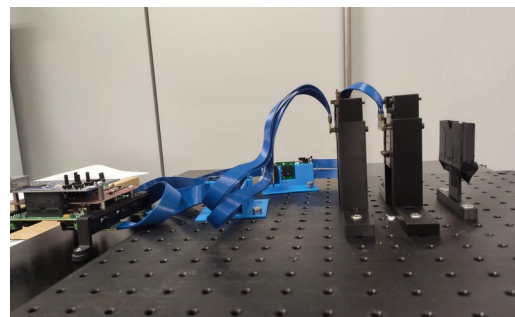
Muñoz et al. Sci. Rep. 2021

Barrientos et al. NIM 2021

MACACO II

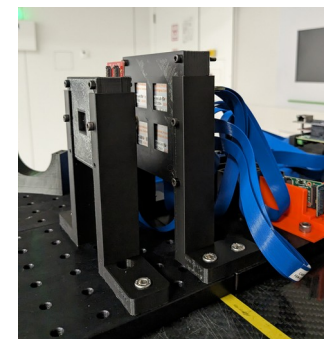


MACACOp



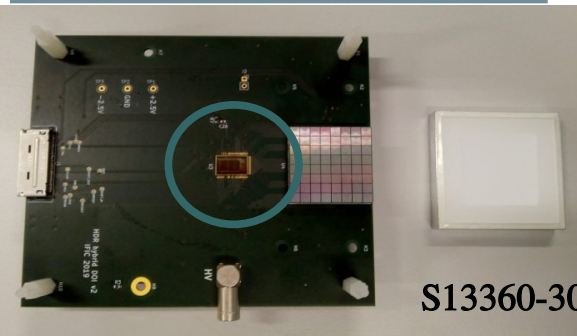
Viegas et al.
Radiat. Phys. Chem. 2022

FALCON



MACACO III

VATA64HDR16 from IDEAS

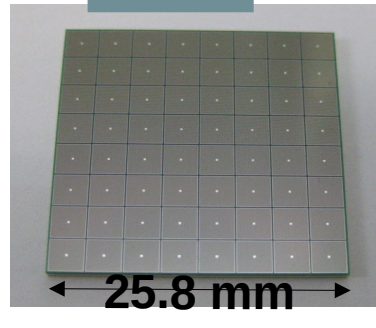


S13360-3025CS

LaBr₃



SiPMs



MACACO_p

TOFPET2 from PETsys

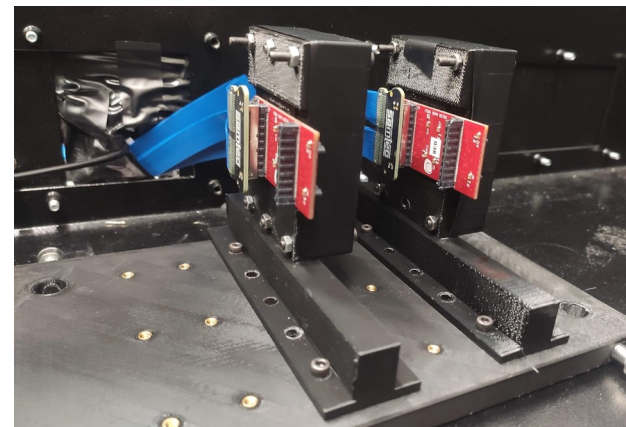


S14161-3050HS-08



AliVATA DAQ board

Now commercialized by
Alibava Systems S. L.



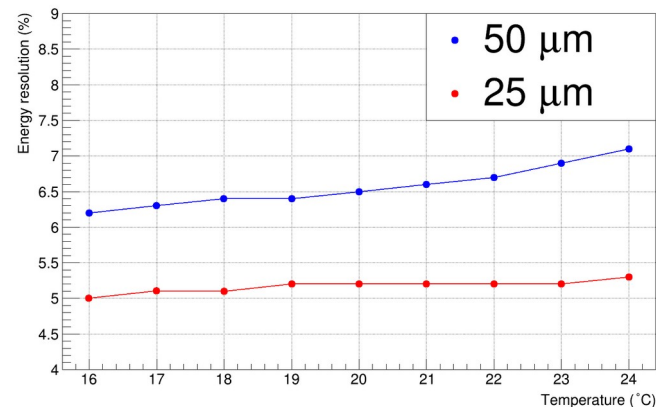
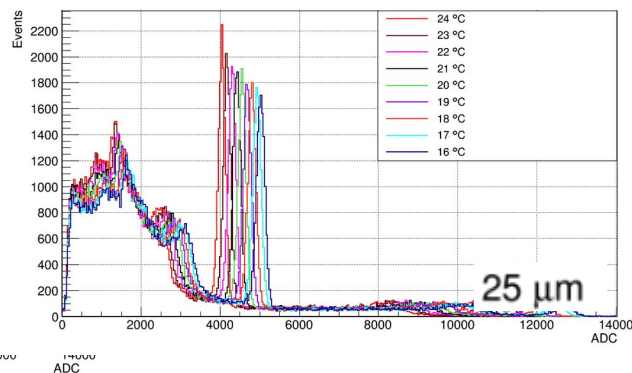
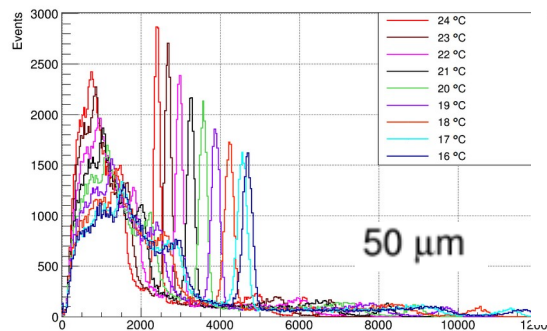
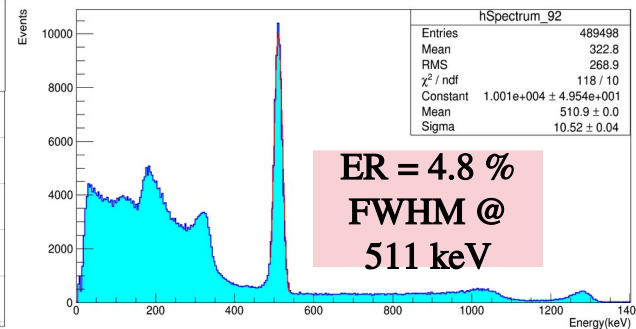
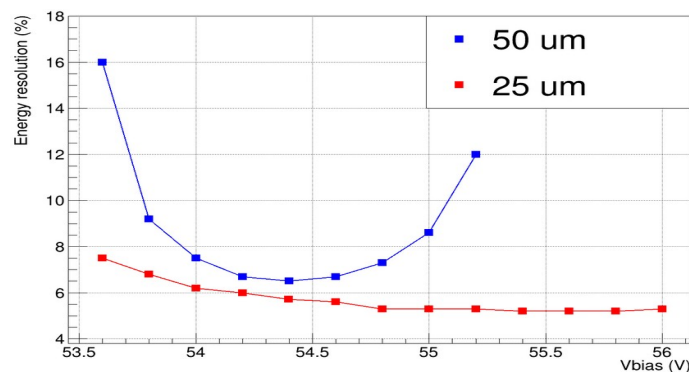
MACACO III characterization

→ S13360-3025CS (25 μm)

VS

S13361-3050AE-08 (50 μm)

Specific SiPM design - Now commercial product



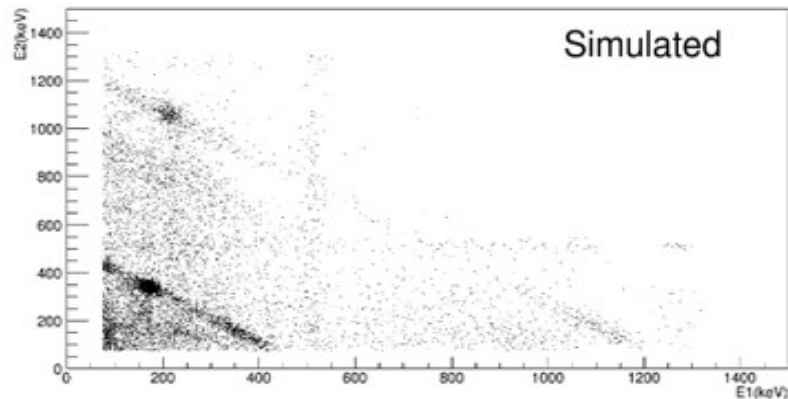
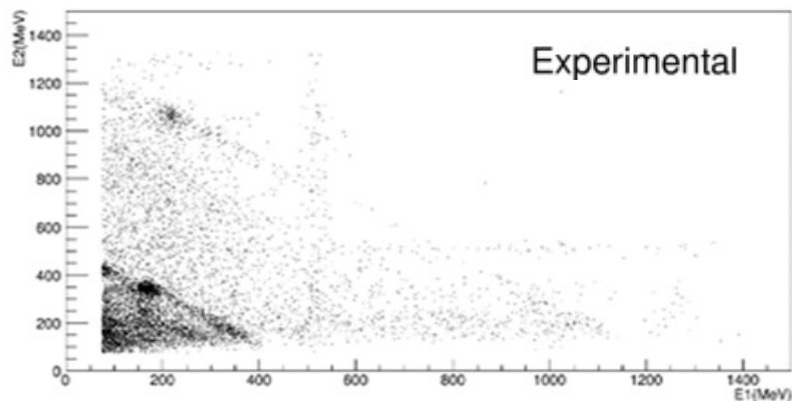
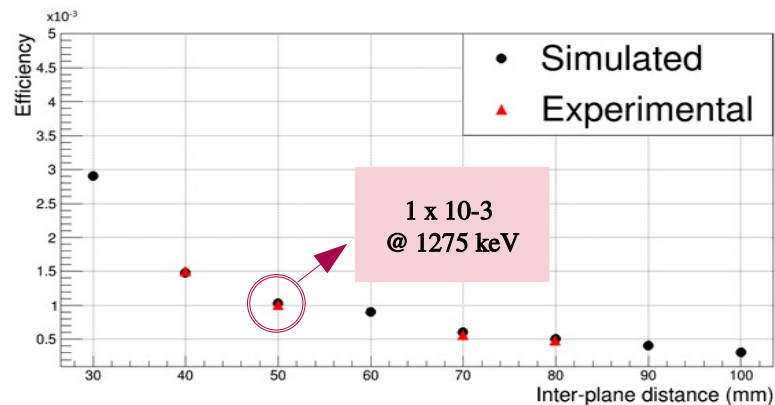
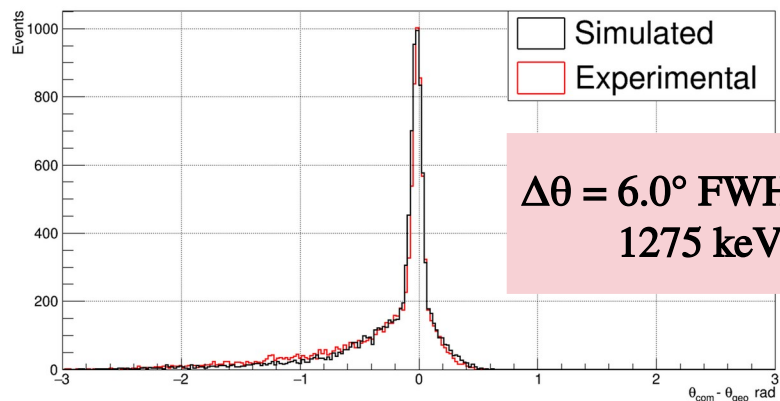
L. Barrientos et al. Rad. Phys. Chem. 2023

GATE simulations

Comparison with MACACO III



Excellent agreement between experimental results and GATE v8.2 simulations.



Prototypes

MACACO III



Readout electronics:
ASIC VATA64HDR1

ER: **5.2 % FWHM @511 keV**

CTR: **24 ns**

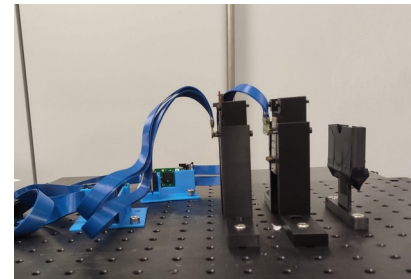
Dynamic range: **-20 pC to 55 pC**

Readout speed: **55 kHz/channel**



Barrientos et al.
Radiat. Phys. Chem. 2023

MACACOp



Readout electronics:
TOFPET2 ASIC

ER: **6.4 % FWHM @511 keV**

CTR: **1.5 ns**

Dynamic range: **up to 1500 pC**

Readout speed: **600 kHz/channel**



Viegas et al.
Radiat. Phys. Chem. 2022

Image reconstruction: list-mode MLEM

Sensitivity model for 2- and 3- interaction events

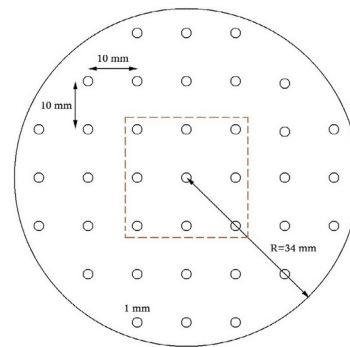
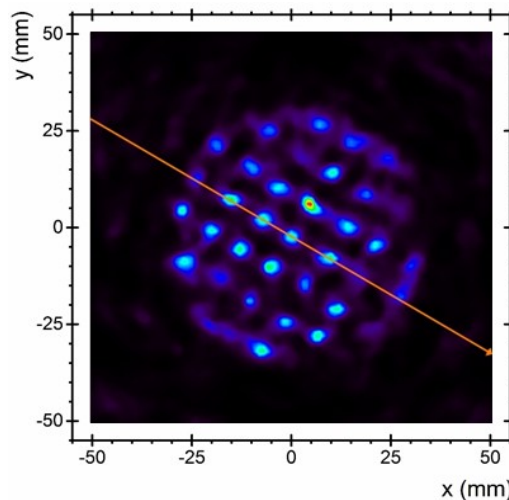
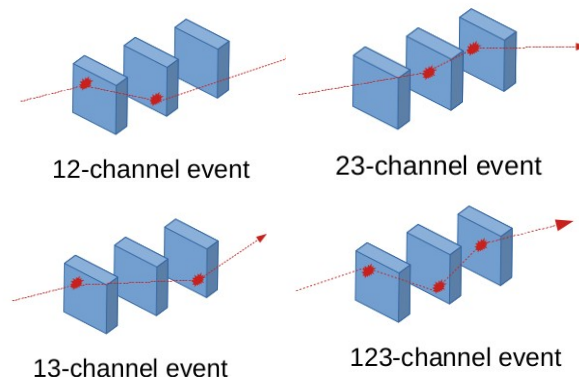
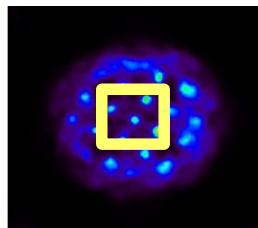
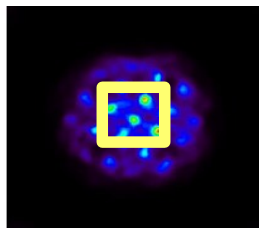
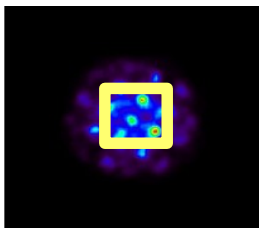
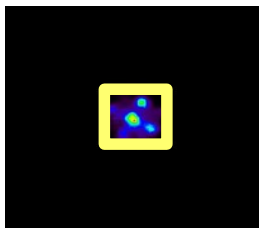
Joint reconstruction of all channels

No sensit.

Wilderman

Maxim

Muñoz



Array of 37 Na-22 point-like sources



E. Muñoz et al. Phys. Med. Biol. 2018

E. Muñoz et al. Phys. Med. Biol. 2020

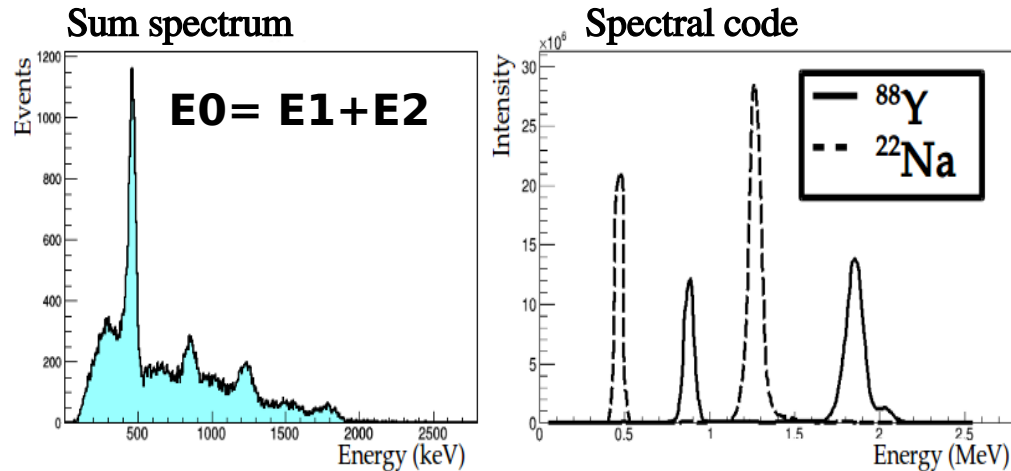
J. Roser et al. Phys. Med. Biol. 2020

J. Roser et al. Phys. Med. Biol. 2022

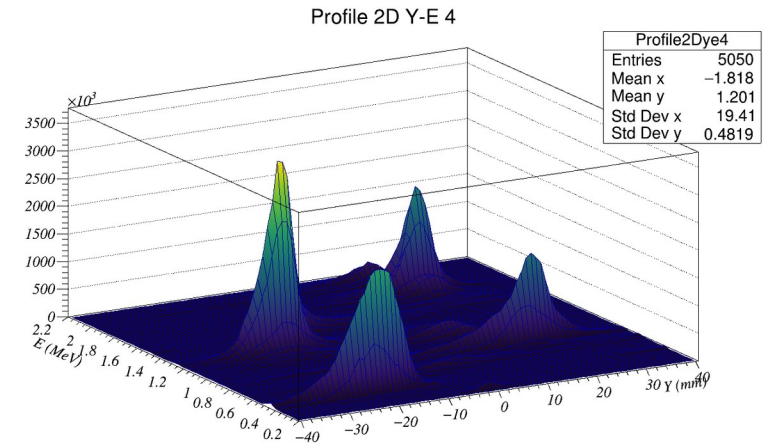
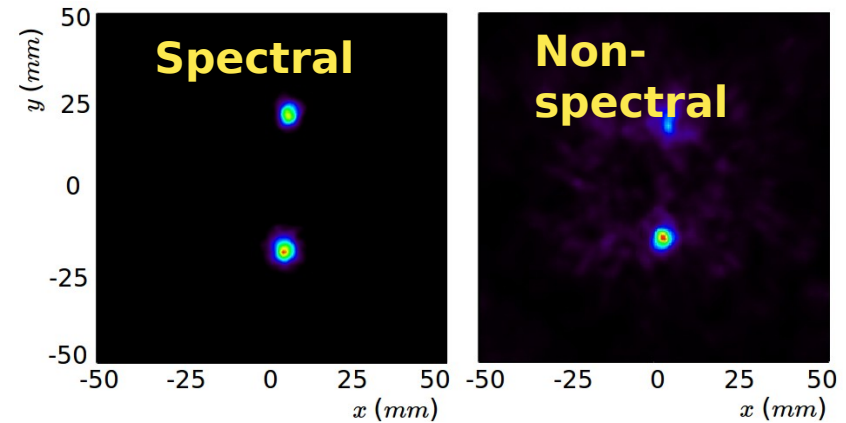
Image reconstruction: spectral code

Reconstruction of position and energy distributions

Simultaneous reconstruction of
Y-88 (898, 1836 keV) + Na-22 (511, 1275 keV)

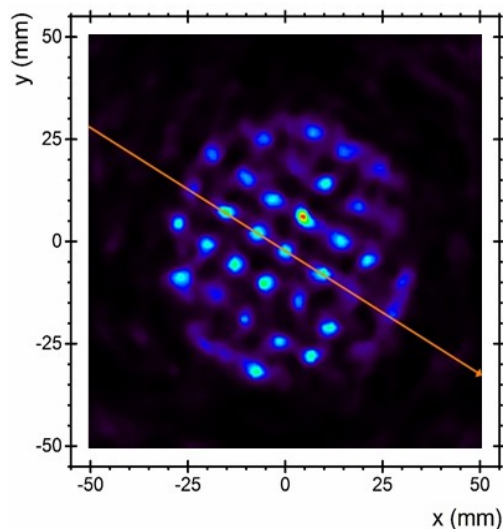


E. Muñoz et al. Phys. Med. Biol. 2020

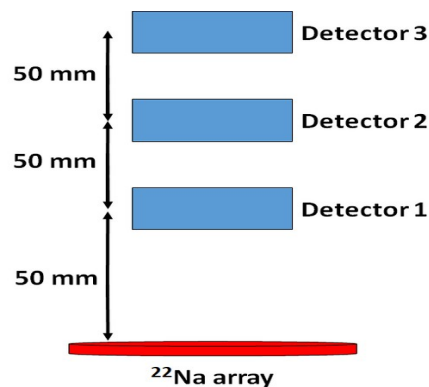
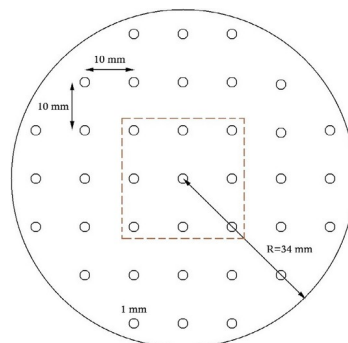


Prototypes

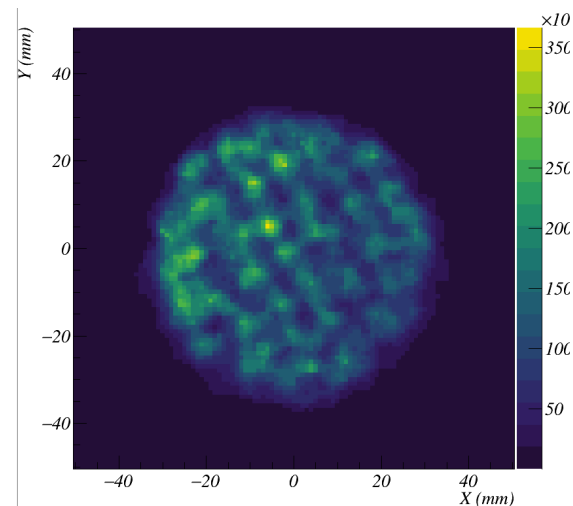
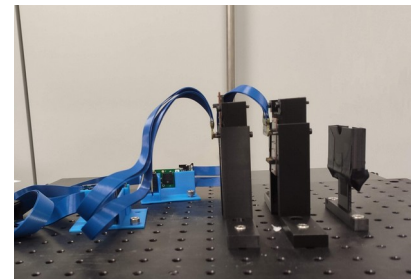
MACACO III



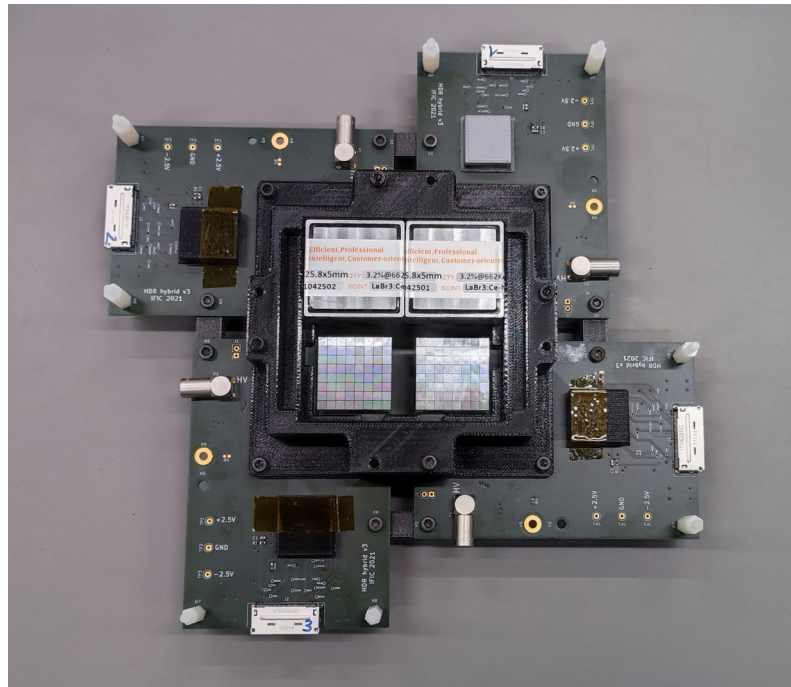
Array of 37 Na-22 point-like sources



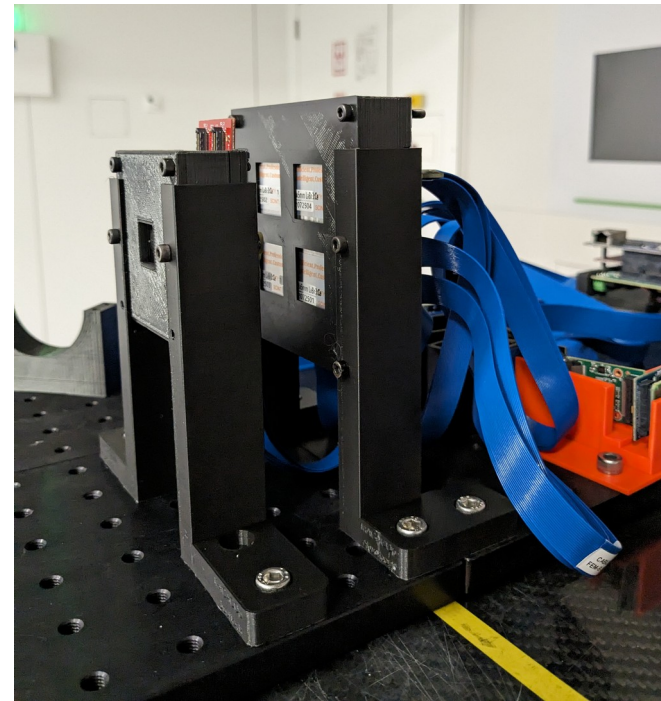
MACACOp



MACACO III+



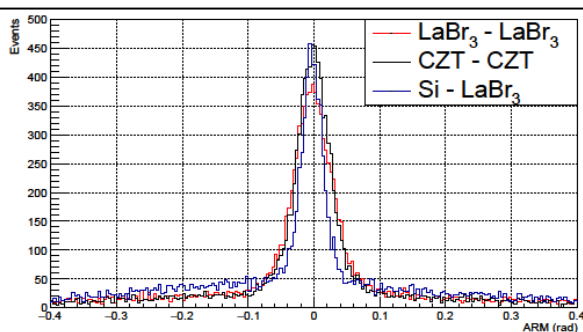
FALCON



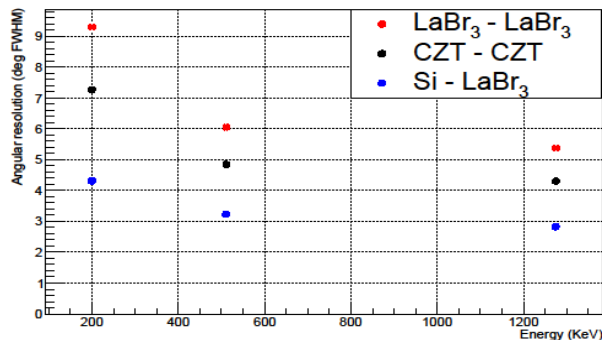
ICOR- CC with a silicon scatterer

Silicon provides better spatial and energy resolution than LaBr_3 .
Lower Z minimizes Doppler broadening for better Compton angle reconstruction.

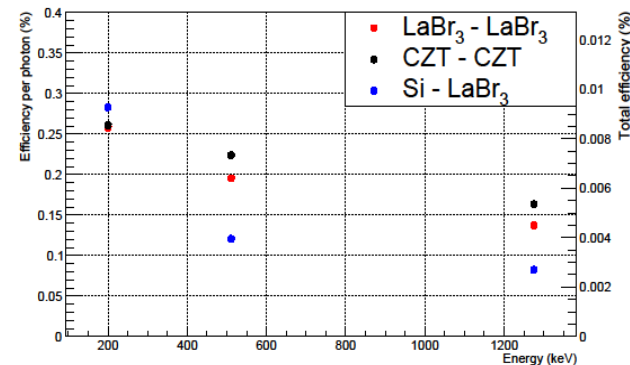
Angular resolution distributions



ARM vs. E

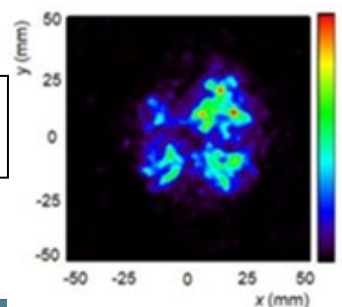


Efficiency vs. E

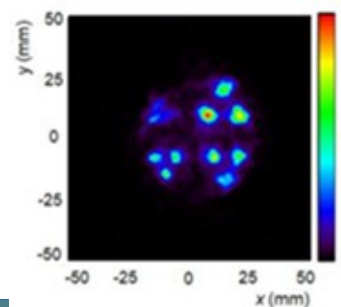


208 keV

LaBr_3



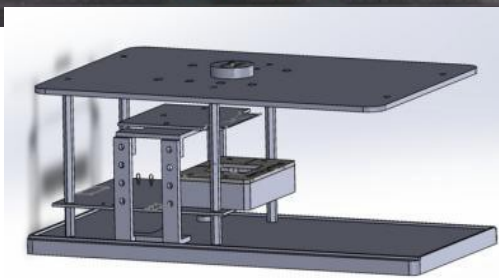
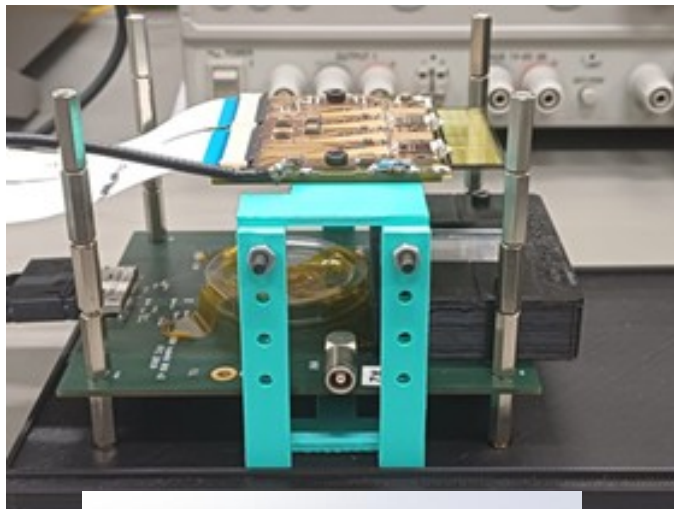
Silicon +
 LaBr_3



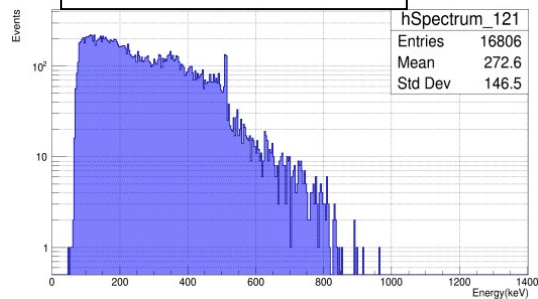
ICOR- CC with a silicon scatterer

Compact prototype with two AliVATA readout boards
Functionality tests successful. Optimization ongoing

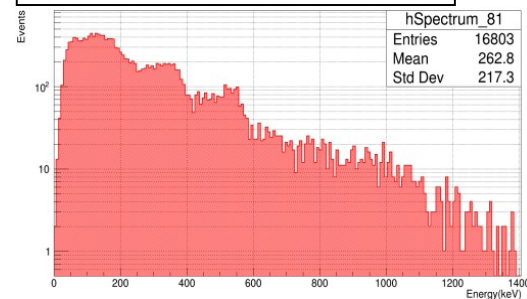
Tests with Na-22
point-like source



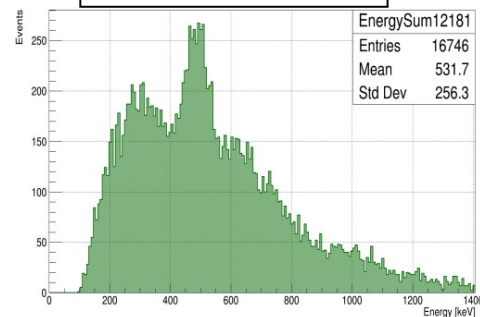
Silicon detector



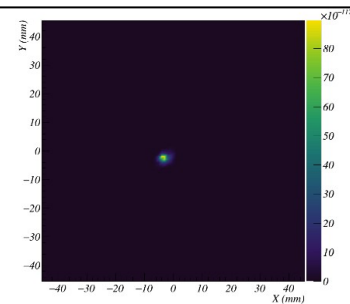
Scintillator detector



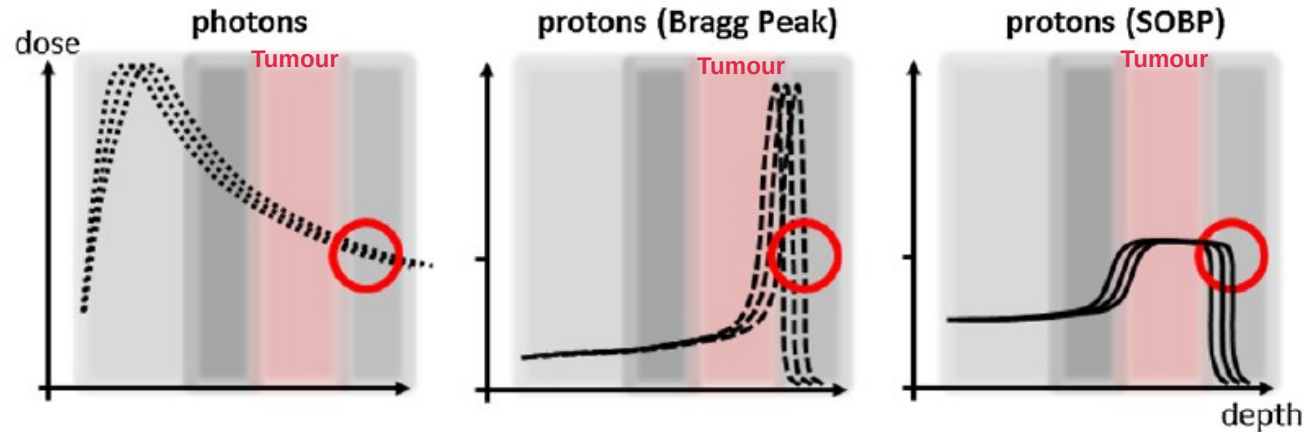
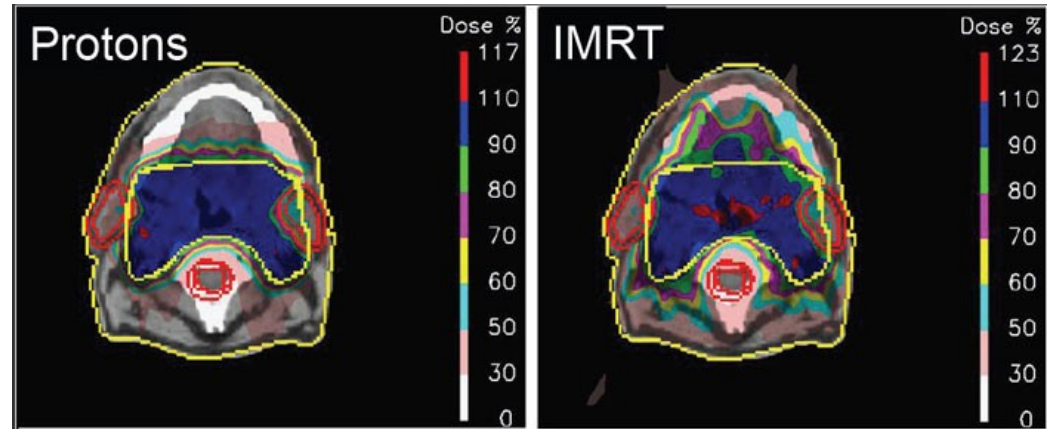
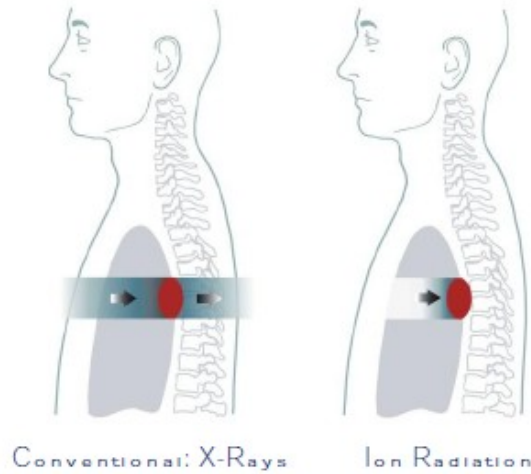
Sum spectrum



Reconstructed image

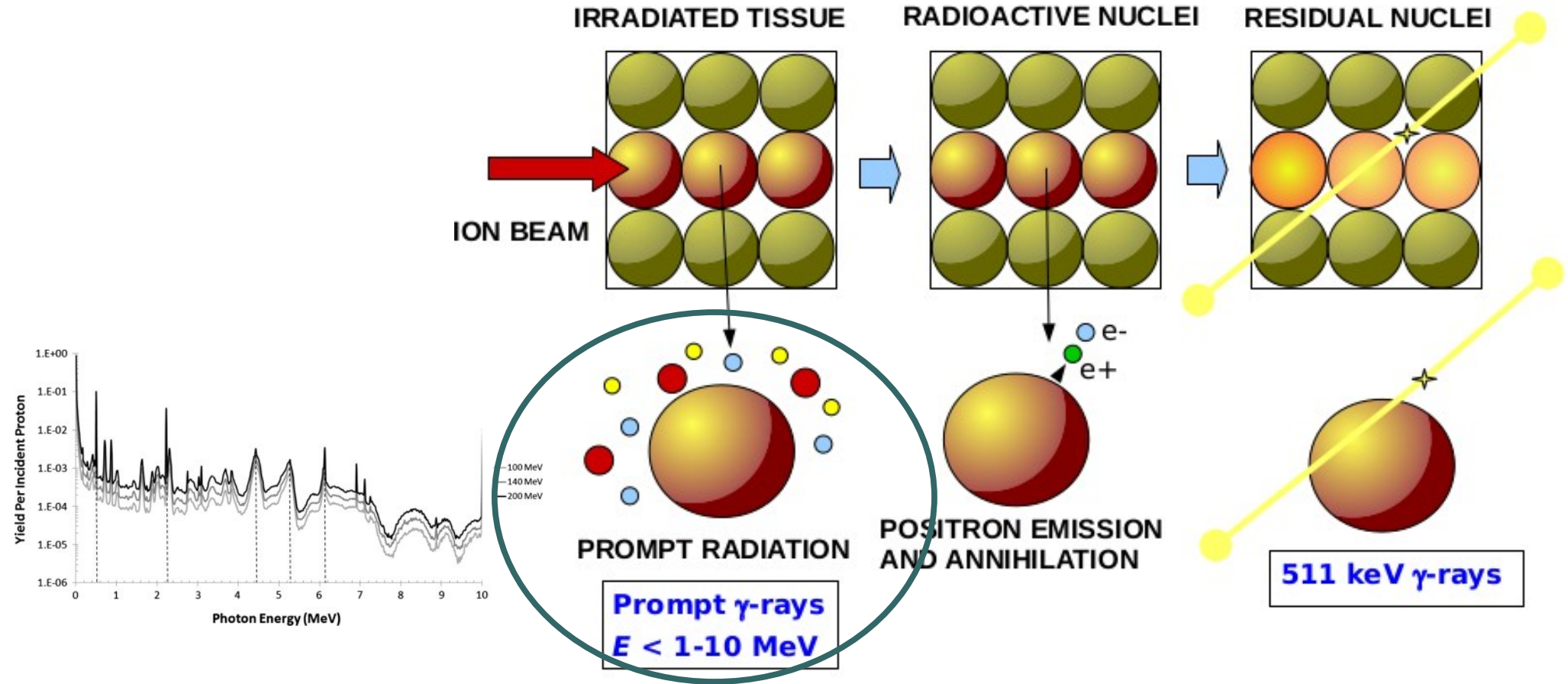


Hadron therapy treatment monitoring



Large safety
margins applied

Hadron therapy treatment monitoring



In-beam experiments

Tests with the current prototypes: Spanish National Accelerator Centre (CNA) and proton therapy centres

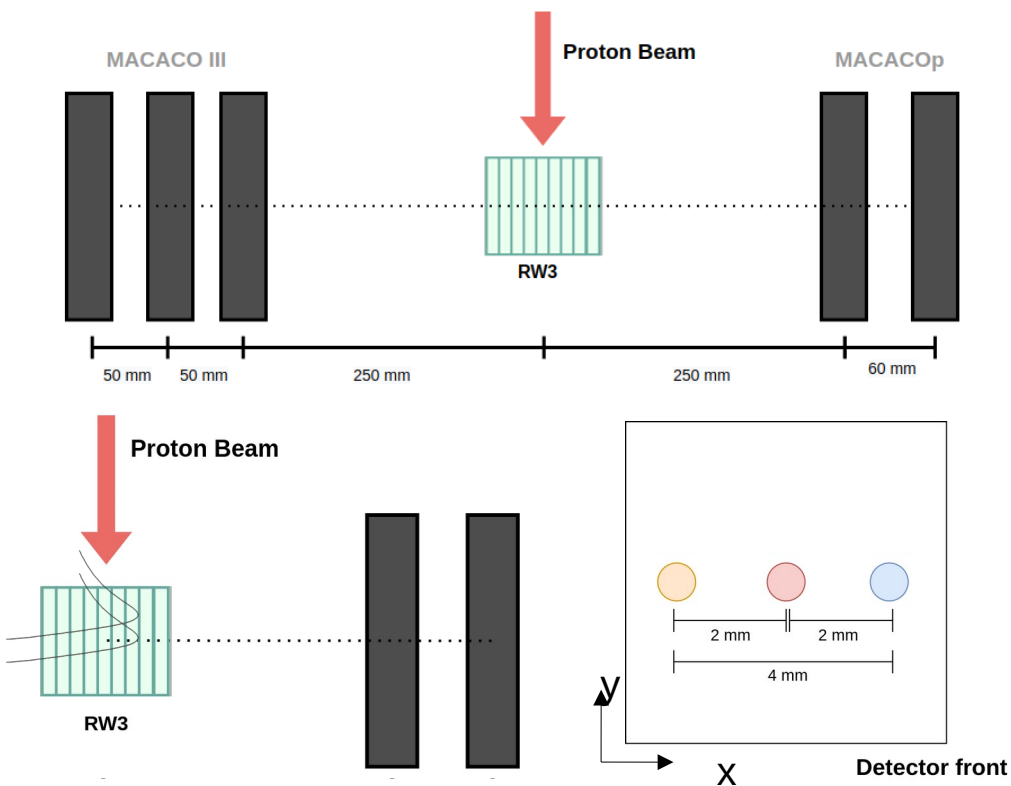
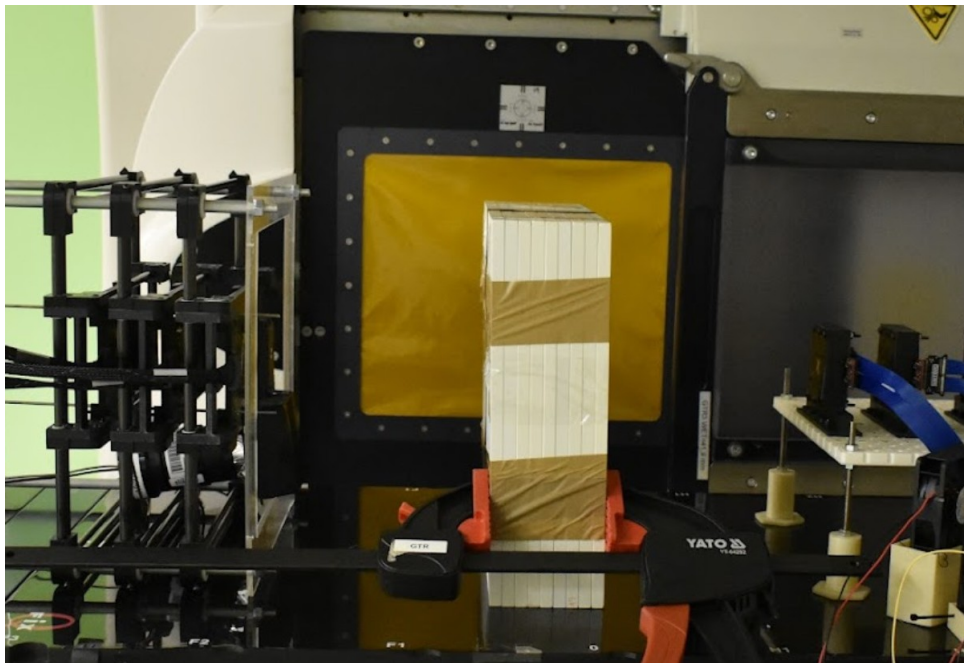
Center	Accelerator	Target	Energy (MeV)
CNA	Cyclotron	Graphite	18
CCB	Cyclotron (Proteus C-235)	RW3	88.38 – 91.62
QuirónSalud	Synchrocyclotron (S2C2)	RW3	70-90
MedAustron	Synchrotron-based particle accelerator	ARDOS	99.6



In-beam experiments

CCB (Krakow, Poland)

Proton beam with different energies on RW3 target
[Cyclotron]



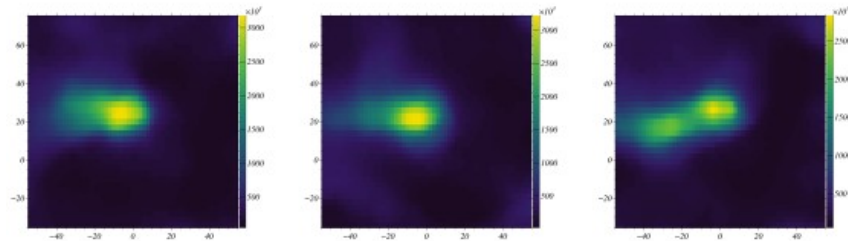
in collaboration with Hubert Jabłoński, Renata Kopeć, Dawid Krzempek and Natalia Mojżeszek, from Institute of Nuclear Physics Polish Academy of Sciences, Krakow, Poland

In-beam experiments

CCB (Krakow, Poland)

90 MeV
 $I = 90 \text{ pA}$

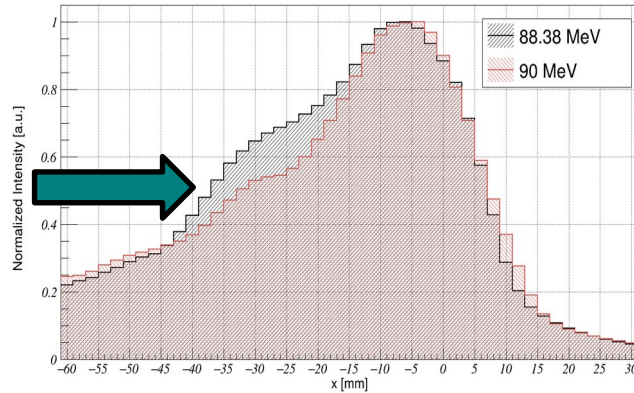
MACACO III



88.38 MeV

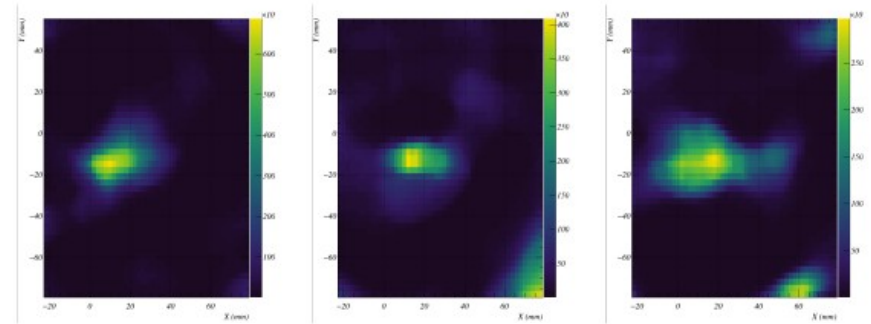
90 MeV

91.62 MeV



2 mm steps detected
with both systems

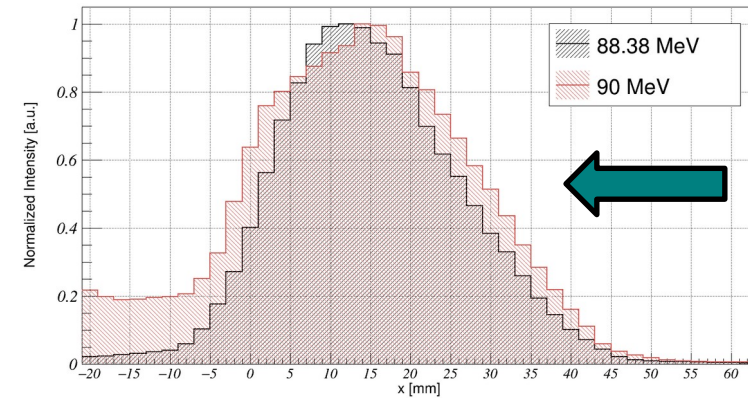
MACACOp



88.38 MeV

90 MeV

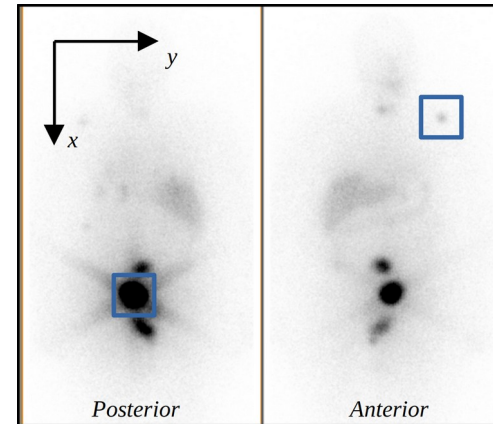
91.62 MeV



Radionuclide imaging

- Imaging can be used to visualize their distribution in the body and carry out dosimetry employing secondary gamma radiation.
- More challenging than diagnostic imaging since photon energies and activities are not optimized for gamma cameras, in particular for alpha emitters.
- Compton cameras can be advantageous in this field.

Gamma camera images of a patient treated with ^{131}I -NaI

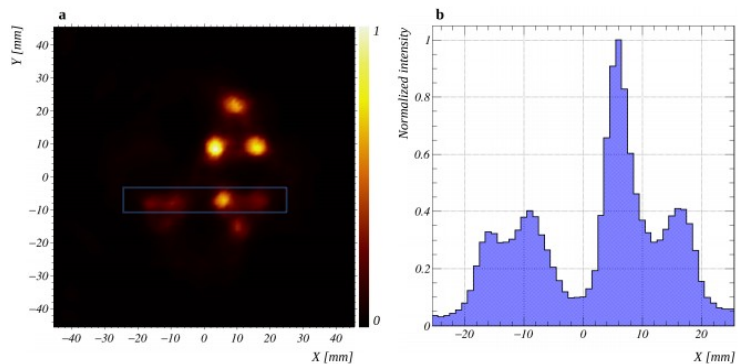


Initial tests in La Fe hospital (Valencia)

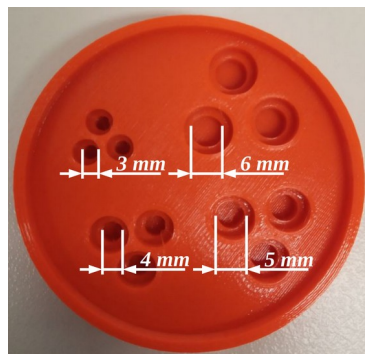
3D printed Derenzo-like phantom

^{18}F -FDG (511 keV)

Compton camera

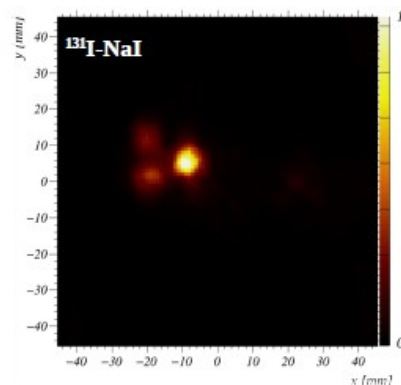


In collaboration with Irene Torres-Espallardo, José Manuel Calatayud, Pilar Bello and Stefan Prado from La Fe hospital.

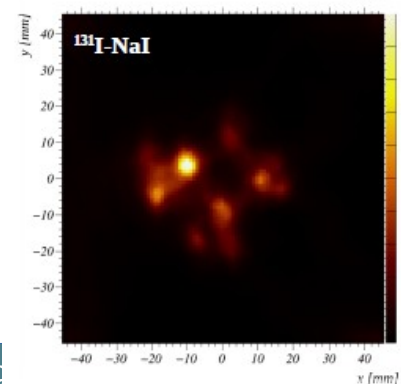


^{131}I -NaI (364 keV)

Compton camera

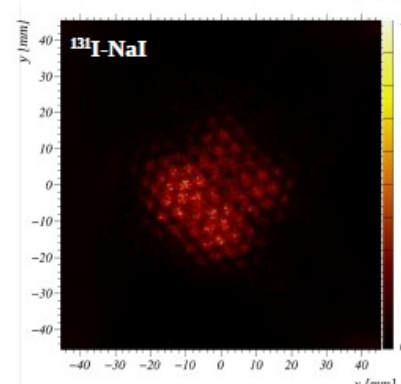
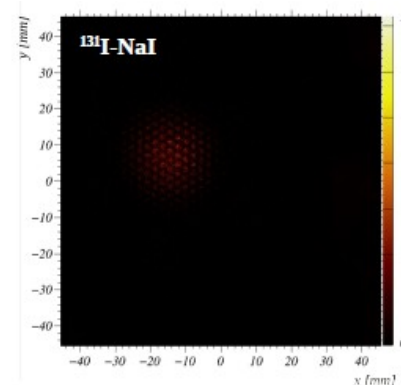


One sector



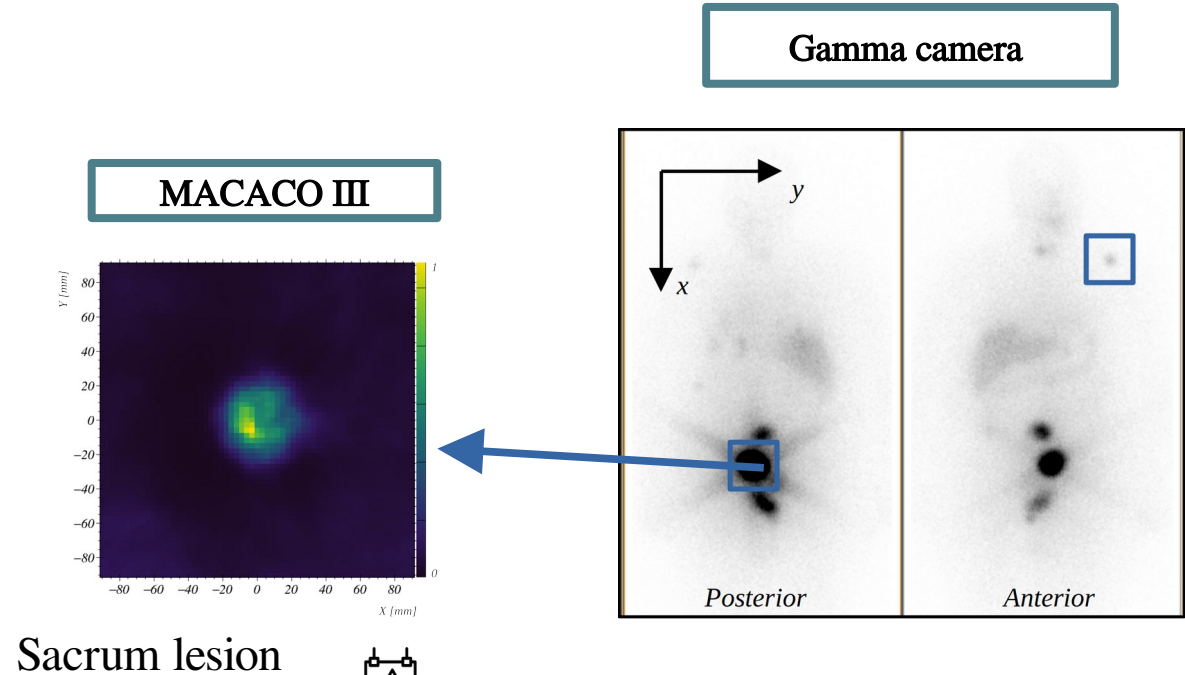
All sectors

Gamma camera
Bright View XCT (Philips)



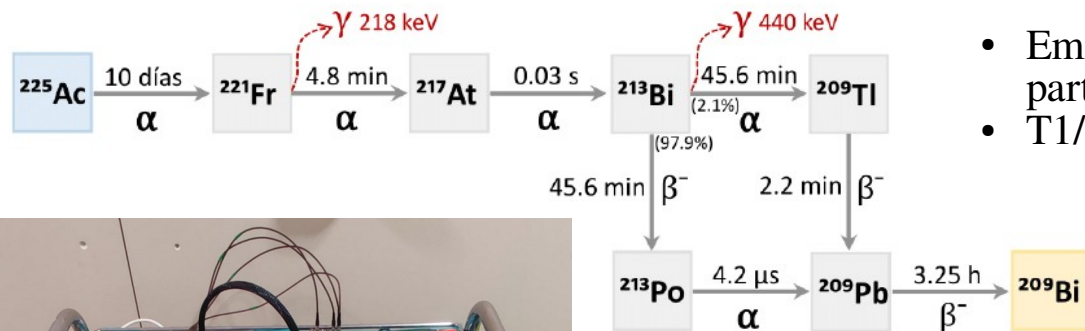
Initial tests in La Fe hospital (Valencia)

- Metastatic lesions from patients treated with ^{131}I -NaI after thyroid gland resection
- Initial activity (total): 150 mCi
- MACACO III @ ~70 mm.



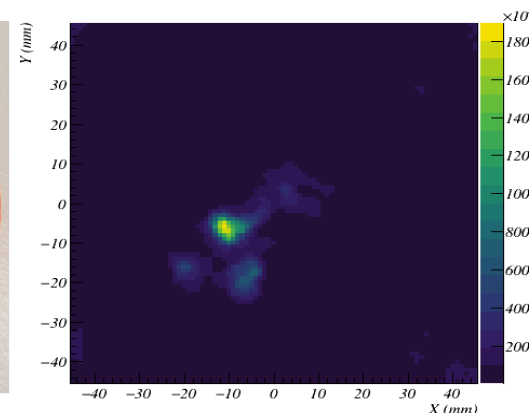
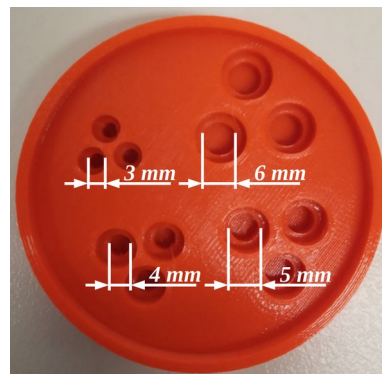
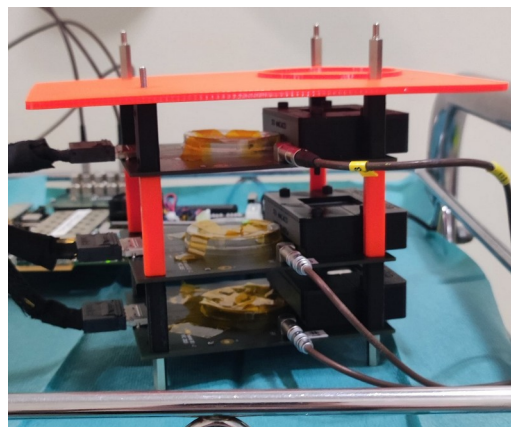
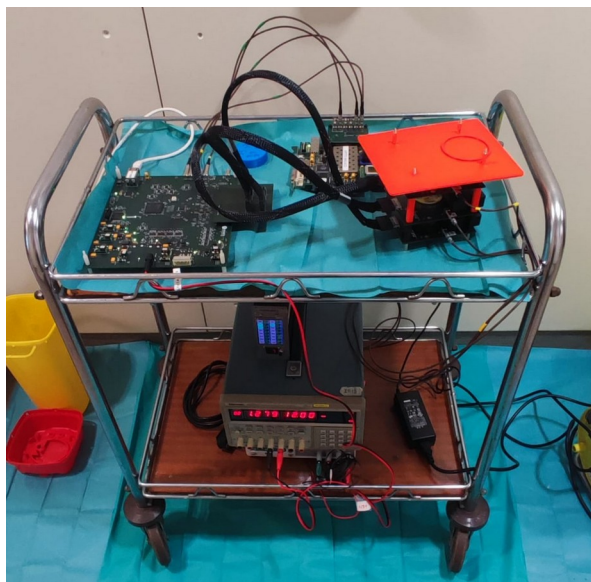
J. Roser et al. Physica Medica 132 (2025) 104928.

Ac-225 Measurements at Léon Bérard hospital (Lyon)



- Emission of 4 alpha particles (5.8-8.4 MeV)
- T1/2= 10 days

6 mm diameter rods reconstructed



In collaboration with Ane Etxebeste, David Sarrut, Jean Noël Badel from Creatis and Léon Bérard hospital (Lyon).

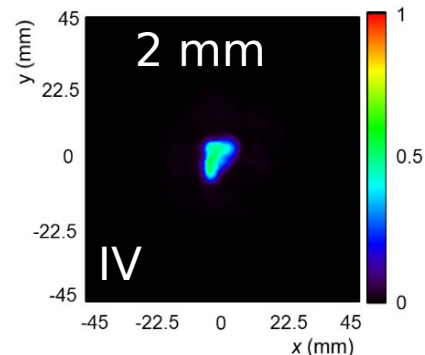
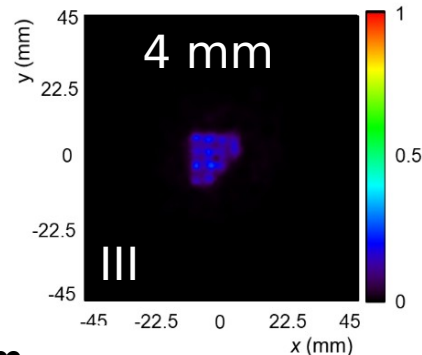
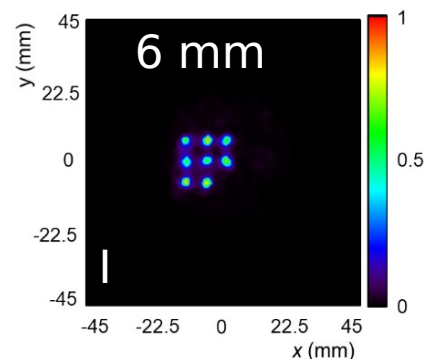
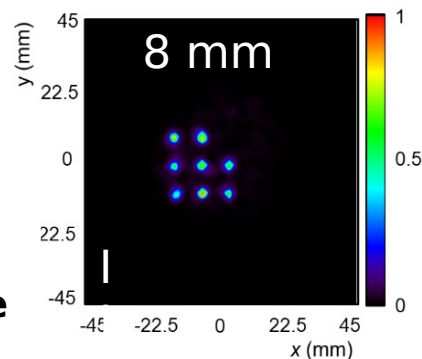
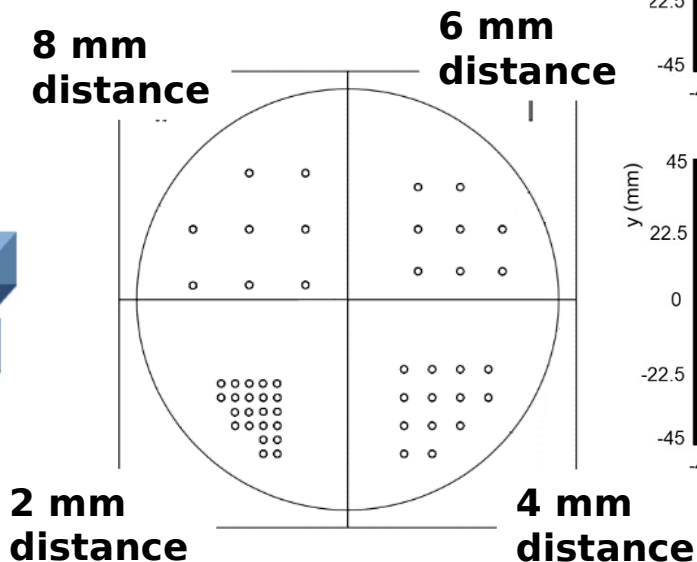
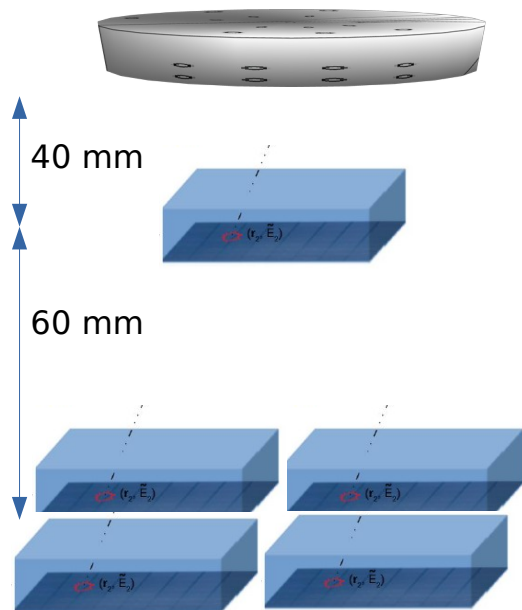
70 kBq /rod

Measurements with Na-22 arrays

MACACO III+

Array with four sectors
of ^{22}Na point-like
sources at different
distances

1 mm diam. sources



Measurements with ^{131}I with MACACO III+

3D printed thyroid-shaped phantom filled with ^{131}I -MIBG



Background: ~3 ml

Rods:

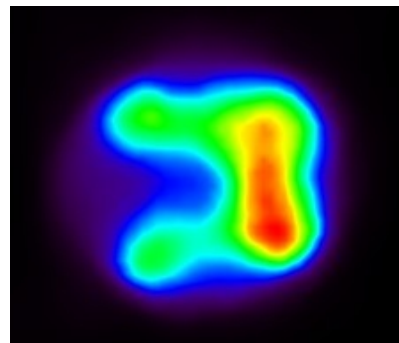
3: 0.021 ml

4: 0.047 ml

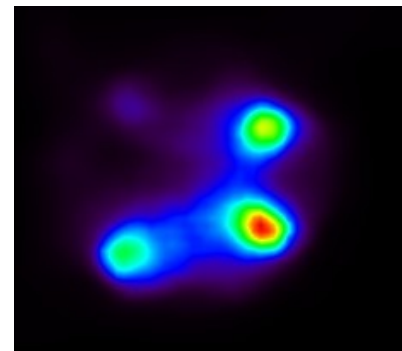
5: 0.084 ml

In collaboration with Irene
Torres-Espallardo et al from La
Fe hospital.

Compton camera images

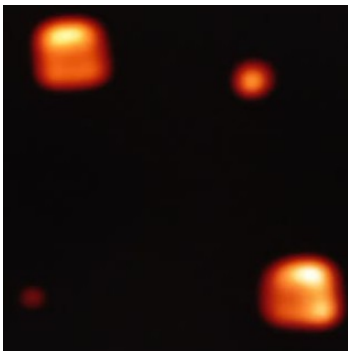


'Uniform' filling
~ 0.5 MB/ml



Background + hot rods at 10:1
activity concentration (0.1 :
0.01 MBq/ml)

Gamma camera images



CT images



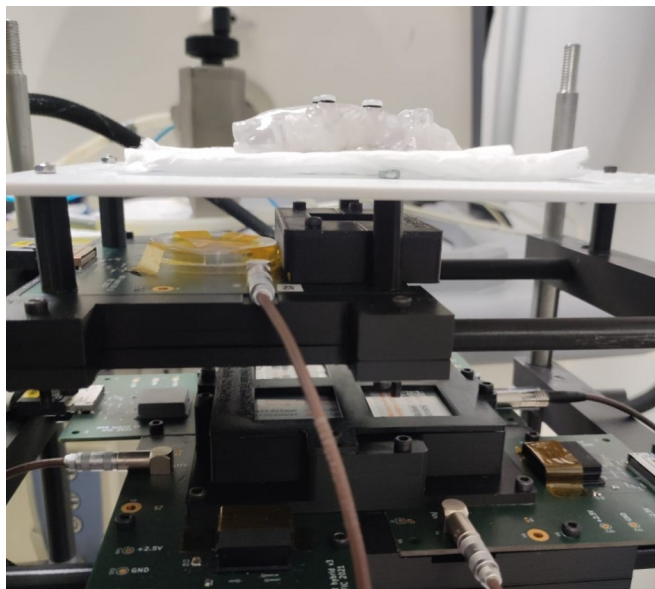
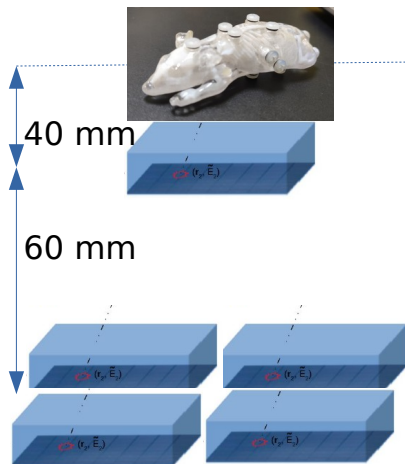
MACACO III+: mouse phantom measurements with ^{131}I



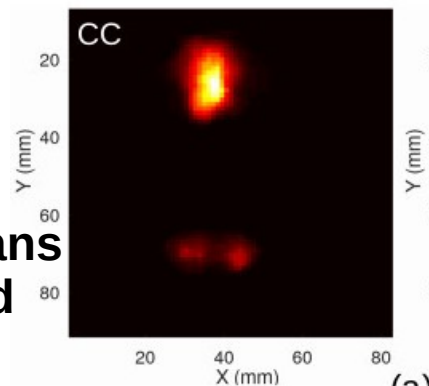
^{131}I (364 keV)

Mouse phantom filling 2/4 organs: brain, heart, bladder and kidneys.

Phantech

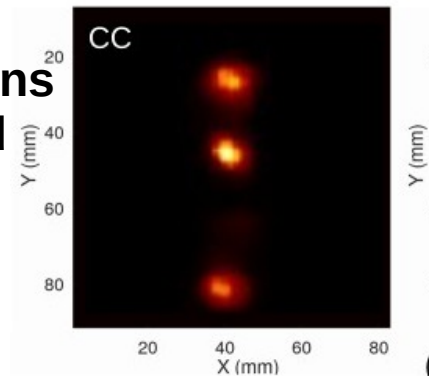


MACACO III+
30 minutes

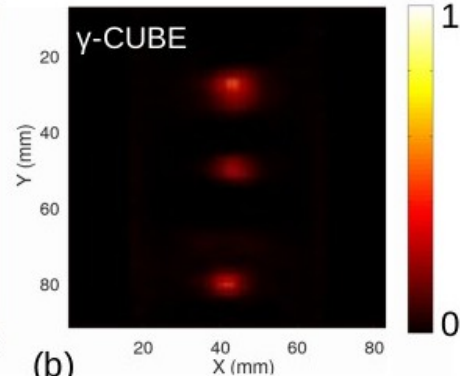
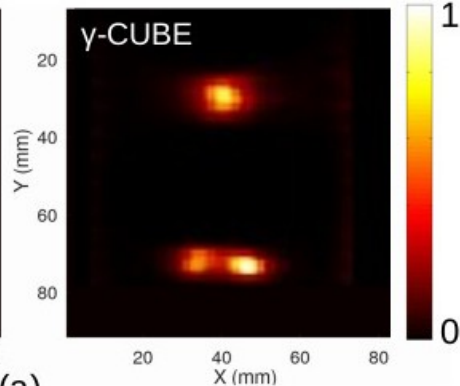


two
organs
filled

four
organs
filled



γ -CUBE SPECT
MOLECUBES
2 hours



MACACO III+: mouse phantom measurements with ^{131}I

^{131}I (364 keV)

Two living mice injected with [^{131}I]NaI:

#1: 30.45g, 1.29 MBq.

#2: 29.06g, 2.22 MBq.

Uptake in thyroid
and stomach.

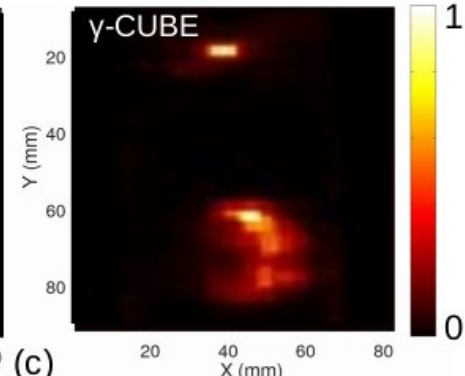
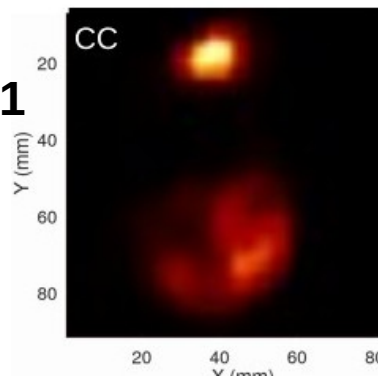
In collaboration with
Jordi Llop, Unai Cossío,
Irati Aiestaran from
CIC biomaGUNE.



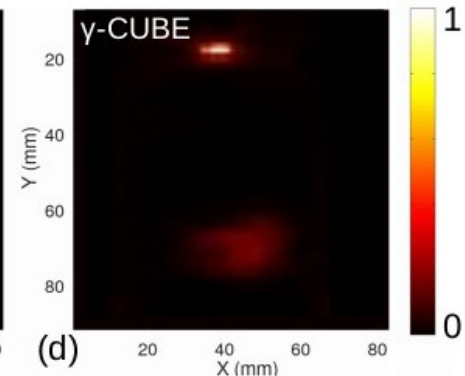
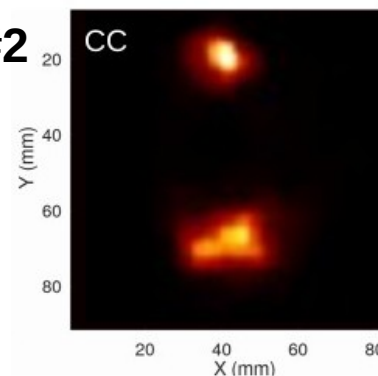
MACACO III+
30 minutes

γ -CUBE SPECT
MOLECUBES
2 hours

#1



#2



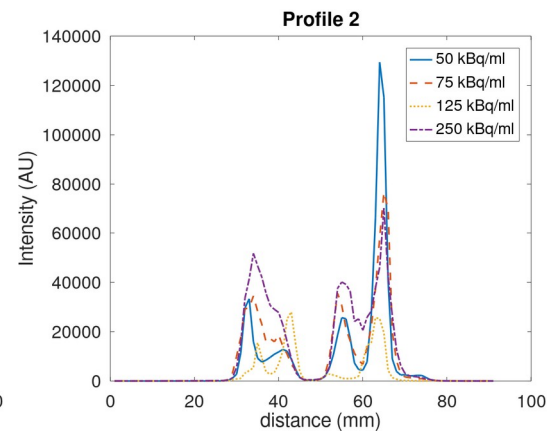
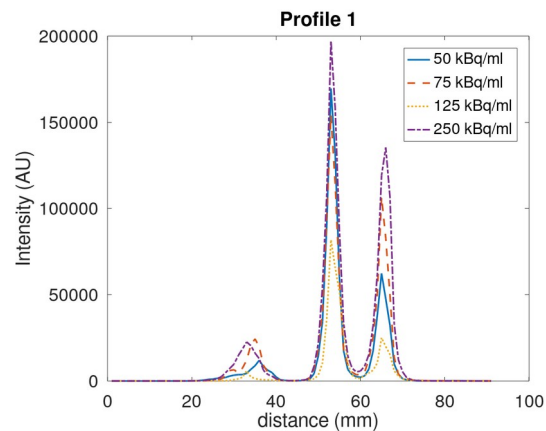
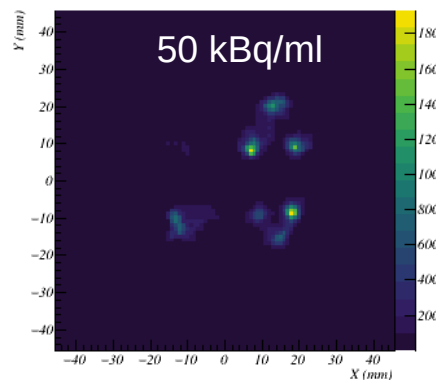
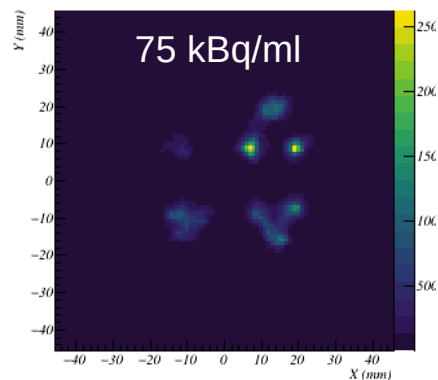
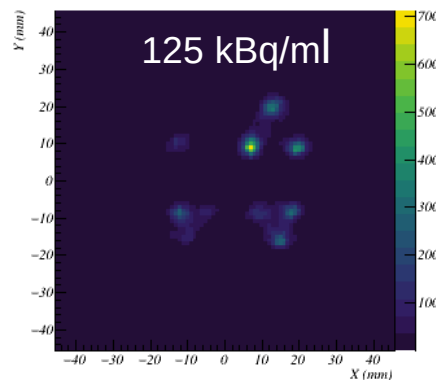
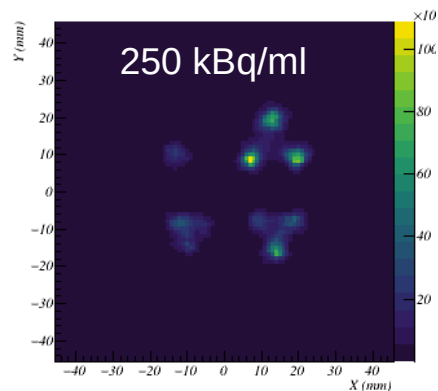
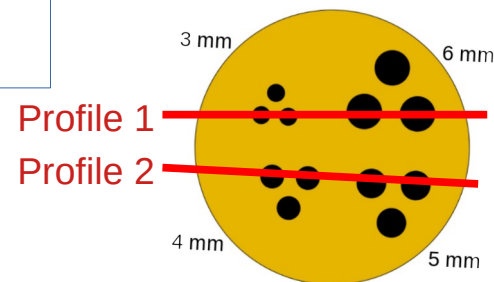
^{225}Ac GATE simulations with MACACO IV geometry

440 keV (^{213}Bi)

Detector:
1 mm FWHM spatial resolution
3.5% @ 511 keV FWHM
Ideal timing

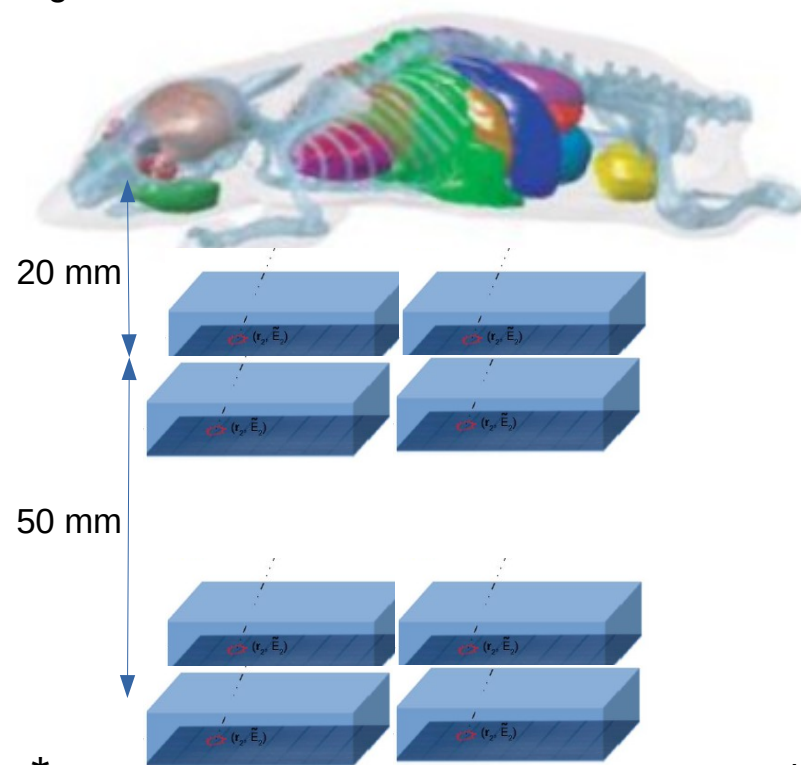
20 min acquisition

50 iterations of ML-EM



^{225}Ac GATE simulations with MACACO IV geometry

Digimouse: 3D Mouse Atlas*



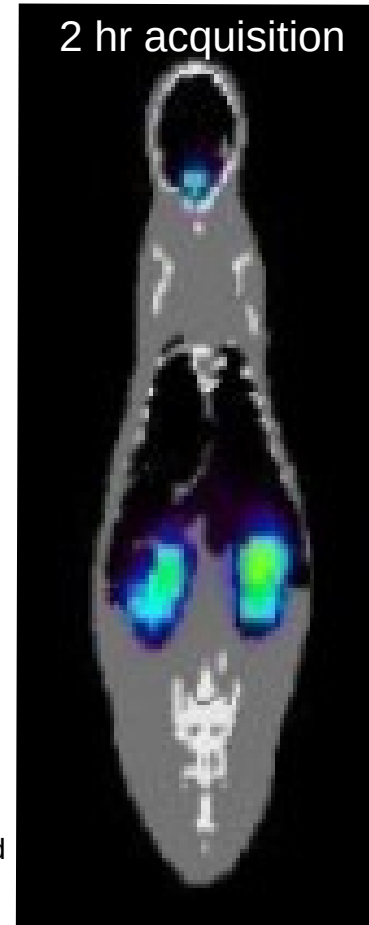
*B. Dogdas, et al. "Digimouse: A 3D Whole Body Mouse Atlas from CT and Cryosection Data", Phys. Med. Bio, 52: 577-587, 2007

From ^{225}Ac biodistributions in live mice**
25 kBq injected activity (IA)

Tissue/organ	mean % IA/g 6 hrs p.i.
Liver	0.32
Spleen	0.17
Lungs	0.05
Heart	0.05
Stomach	0.04
Kidneys	10.31
Pancreas	0.08
Bone	0.09
Tumor (200 mm ³)	9.87

**M. Rodak et al., "Preclinical Evaluation of ^{225}Ac -Labeled Single-Domain Antibody for the Treatment of HER2pos Cancer," Mol Cancer Ther, 21(12), 1835–1845, 2022

2 hr acquisition



Num 101165088.

8 Partners and 2 affiliated entities: 4 academic, 2 hospitals, 1 SME, 1 CSO.

1/9/25-31/8/29



POLITECNICO
MILANO 1863

CREATIS

LaFe
Departament
de Salut

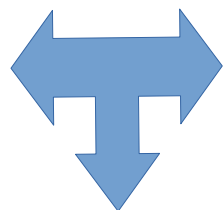


DAMΔVAN
IMAGING

CENTRE
DE LUTTE
CONTRE LE CANCER
LEON
BERARD

Two technological approaches:

CeBr₃ crystal encapsulated
with the photodetector



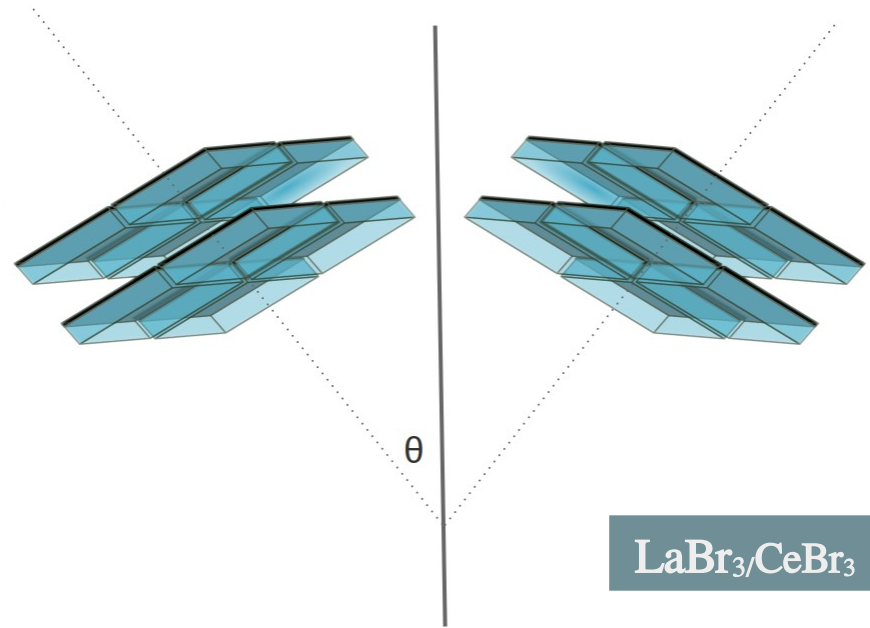
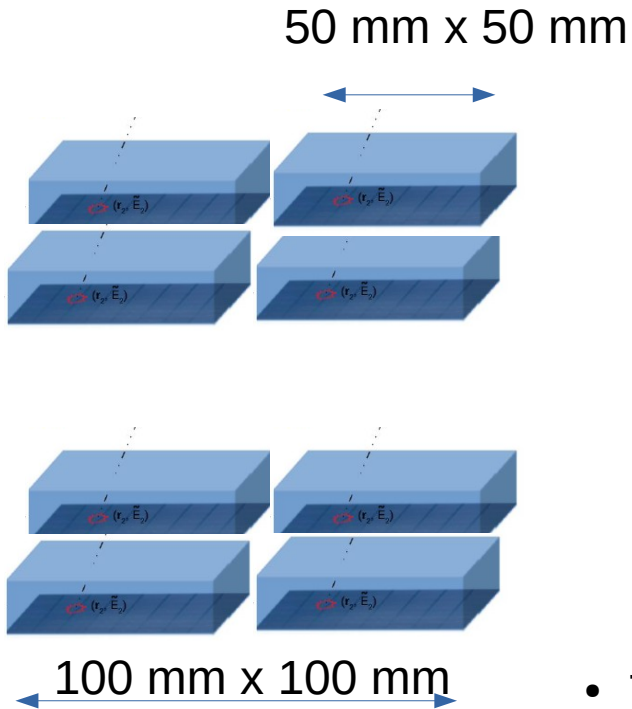
LaBr₃ crystal coupled
to the photodetector

Readout
electronics

MC Simulations

Image
reconstruction

Dosimetric tools



- The IRIS group has developed Compton cameras suitable for photon imaging in the range of 300 keV – 7 Me.

- The IRIS group has developed Compton cameras suitable for photon imaging in the range of 300 keV – 7 MeV.
- Initial results for TRT are very promising.
- Successful tests with I-131 in living mice have been carried out.
- Further tests with Ac-225 planned in collaboration with CLB (Lyon) and CIC biomaGUNE.
- Detector improvements are possible and can lead to better system performance.
- The project AIDER will improve the performance of scintillator-based Compton cameras and evaluate the performance in clinical conditions with patients.



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Brzezinski



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Siddharth
Parashari



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Strugari



Javier
Pérez Curbelo



Declan
Garvey

**+ Nataly
Castellanos
+ Deniel
Rodriguez**

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Thank you

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