From MACACO to AIDER

Gabriela Llosá on behalf of the IRIS group and collaborators.

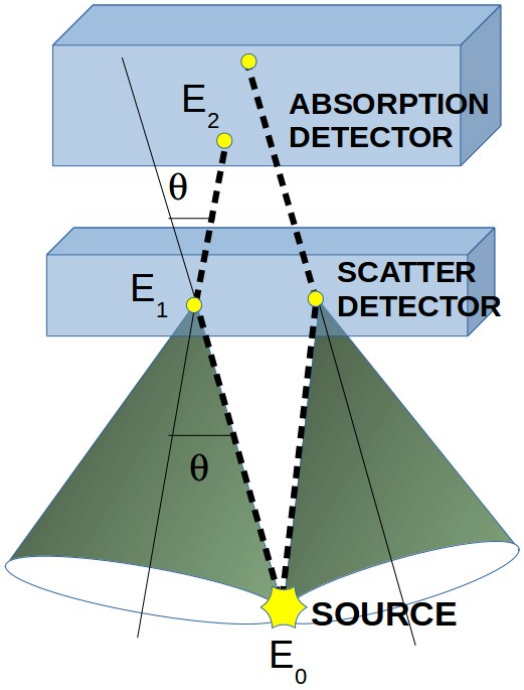
Instituto de Física Corpuscular IFIC (CSIC-UV)
http://ific.uv.es/iris

XVII CPAN Days
Valencia, 19-21 November 2025

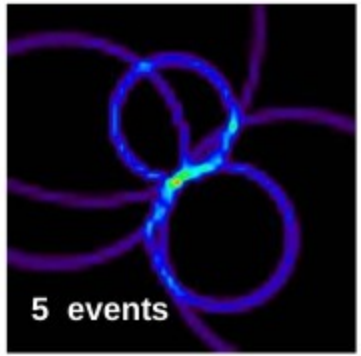
Outline

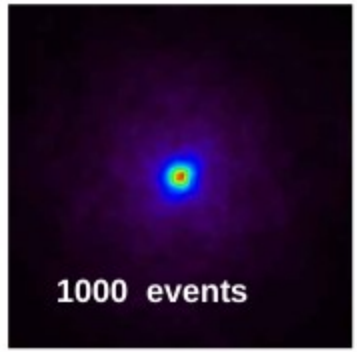
- MACACO Compton cameras.
- ICOR- CC with silicon
- Application to hadron therapy treatment monitoring.
- Application to treatment verification in targeted radionuclide therapy.
- AIDER project.

Compton camera



Backprojection





+ Image reconstruction

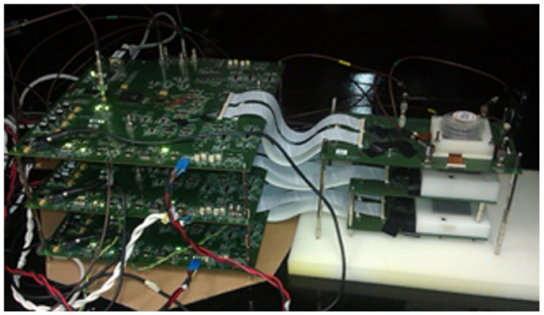
$$\cos\varphi = 1 - m_0 c^2 \left(\frac{1}{E_{\gamma'}} - \frac{1}{E_\gamma} \right)$$

$$E_\gamma = E_{e^-} + E_{\gamma'}$$

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

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

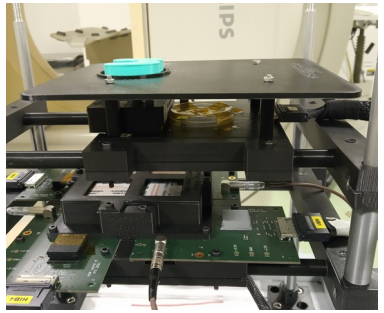
Muñoz et al. JINST 2018

Barrio et al. NIM 2018

MACACO III

Barrientos et al.
Radiat. Phys. Chem. 2023

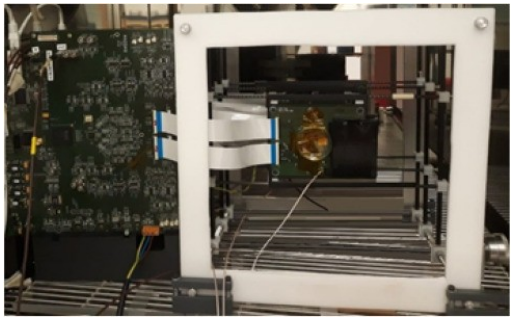
MACACO III+



ENVISION

EC FP7

MACACO II

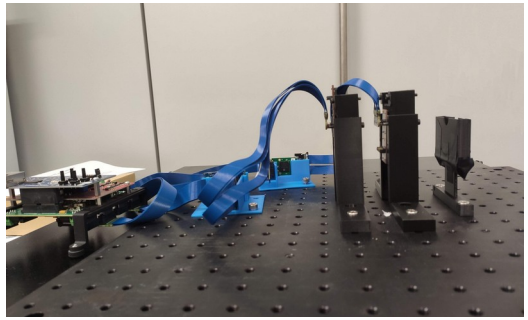


Ros et al. Phys. Med. Biol. 2020

Muñoz et al. Sci. Rep. 2021

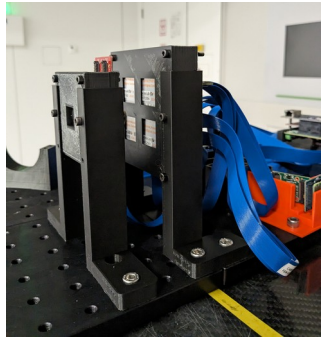
Barrientos et al. NIM 2021

MACACOp



Viegas et al.
Radiat. Phys. Chem. 2022

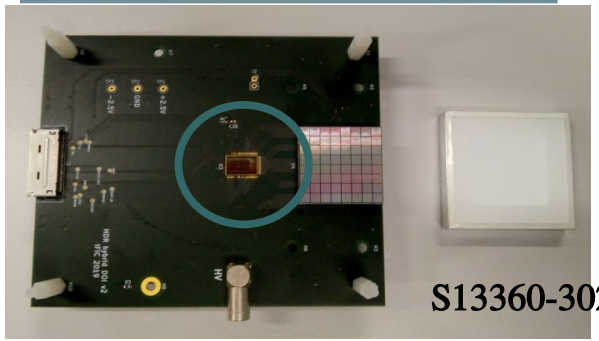
FALCON



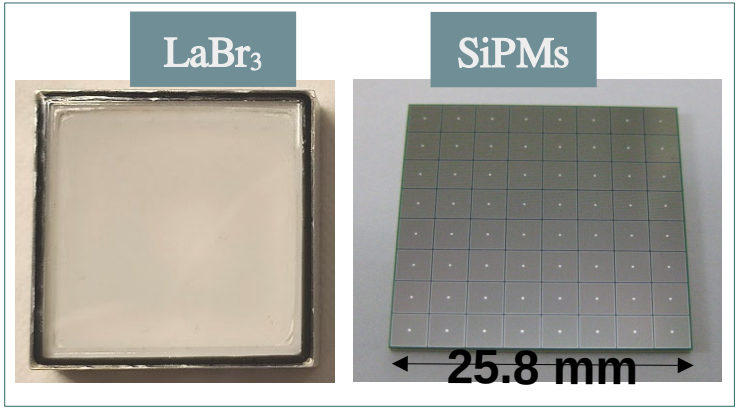
MACACO III

MACACOp

VATA64HDR16 from IDEAS

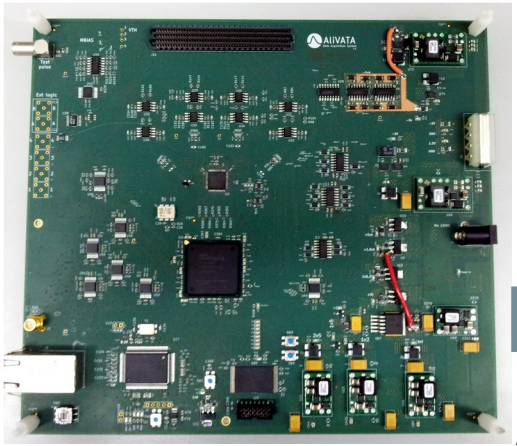


S13360-3025CS



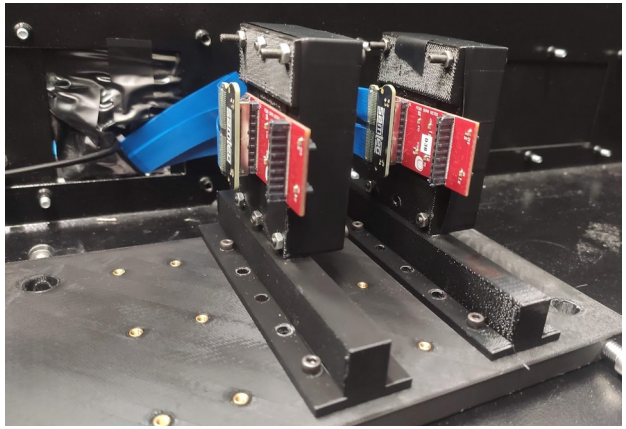
TOFPET2 from PETsys

S14161-3050HS-08



AliVATA DAQ board

Now commercialized by Alibava Systems S. L.



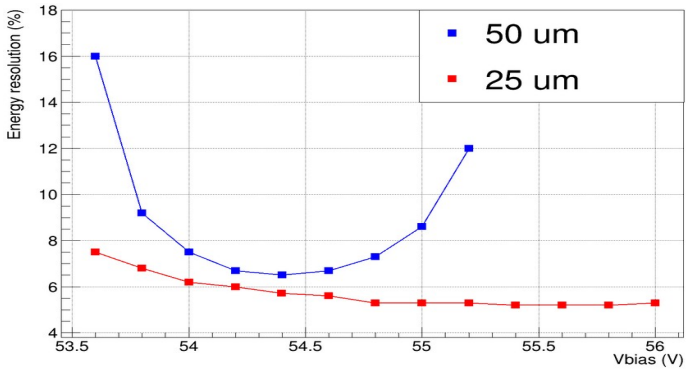
MACACO III characterization

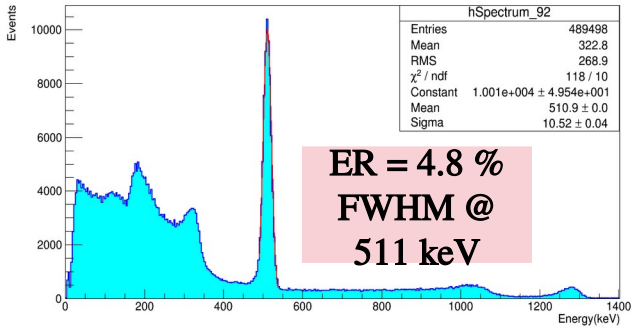
S13360-3025CS (25 µm)

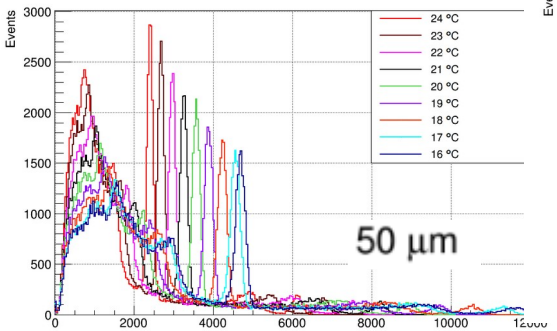
VS

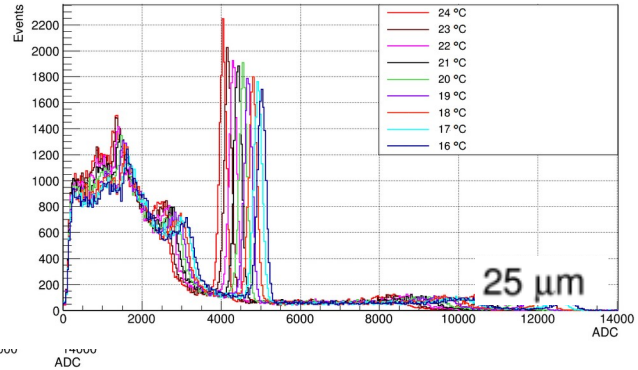
S13361-3050AE-08 (50 µm)

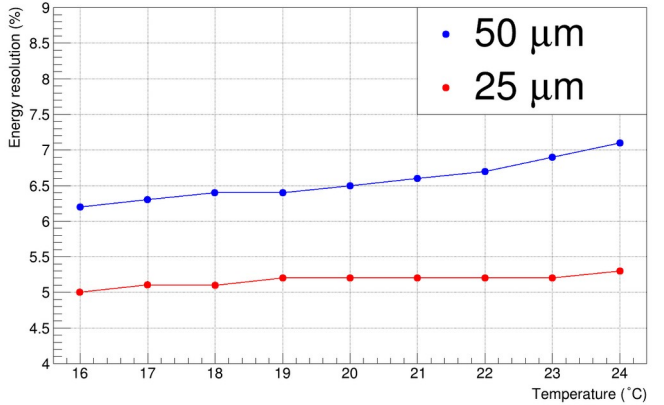
Specific SiPM design - Now commercial product









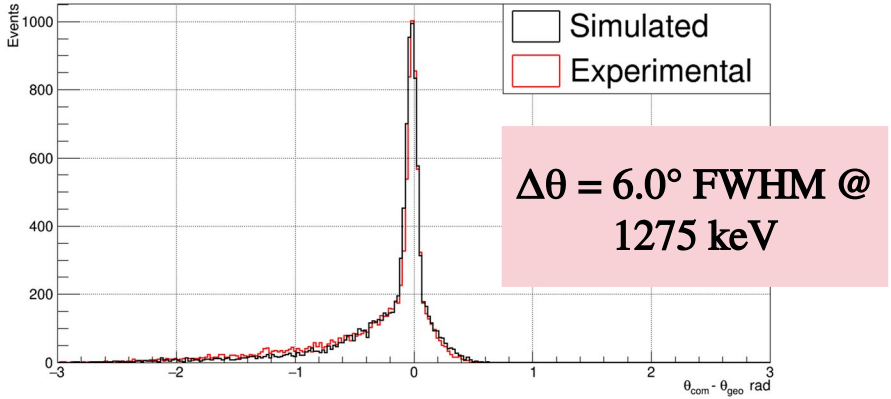


L. Barrientos et al. Rad. Phys. Chem. 2023

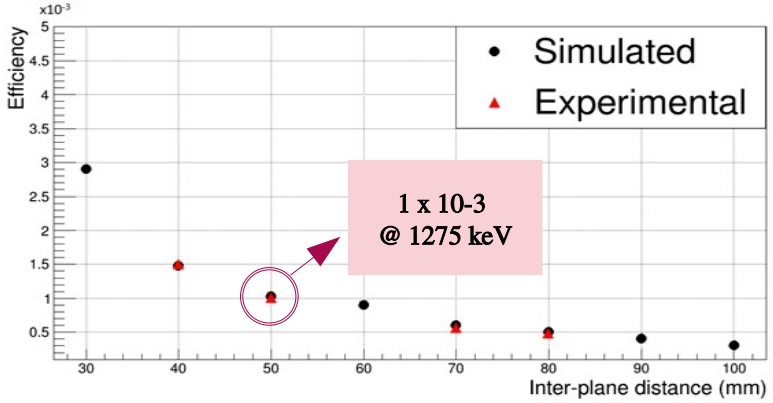
GATE simulations

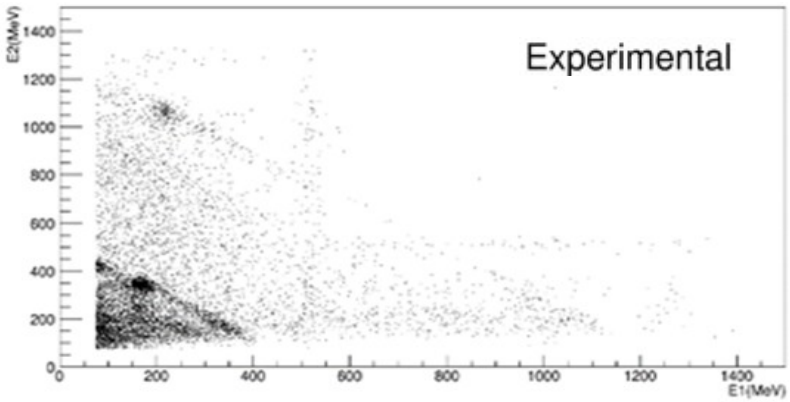
Excellent agreement between experimental results and GATE v8.2 simulations.

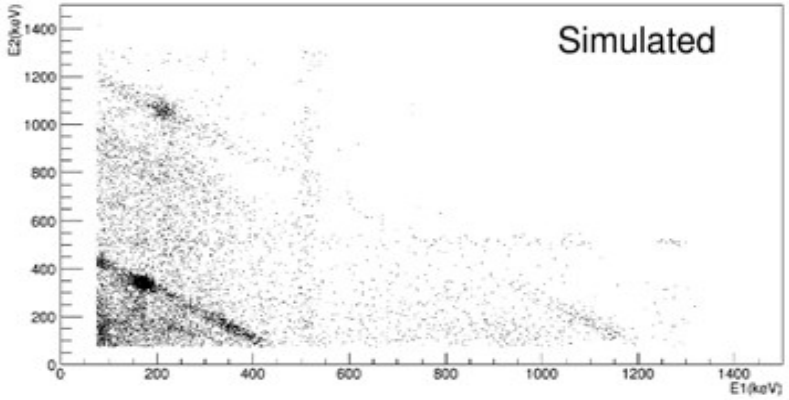
Comparison with MACACO III



$\Delta\theta = 6.0°$ FWHM @ 1275 keV







Prototypes

MACACO III

Readout electronics:
ASIC VATA64HDR1

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

CTR: **24 ns**

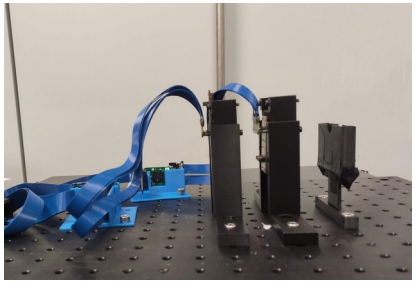
Dynamic range: **−20 pC to 55 pC**

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**

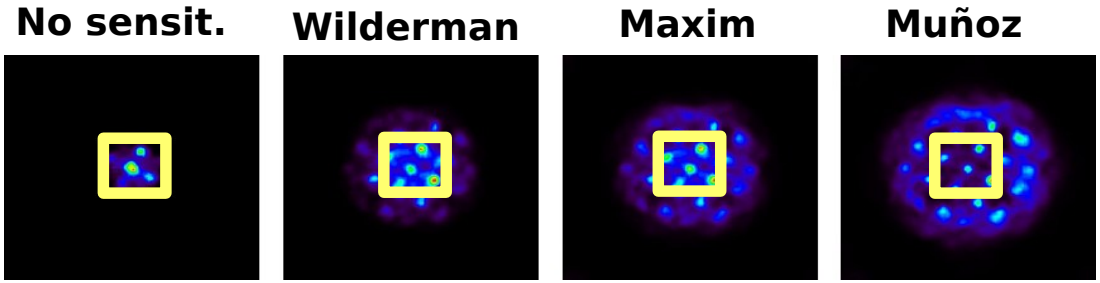
Dynamic range: **up to 1500 pC**

Readout speed: **600 kHz/channel**

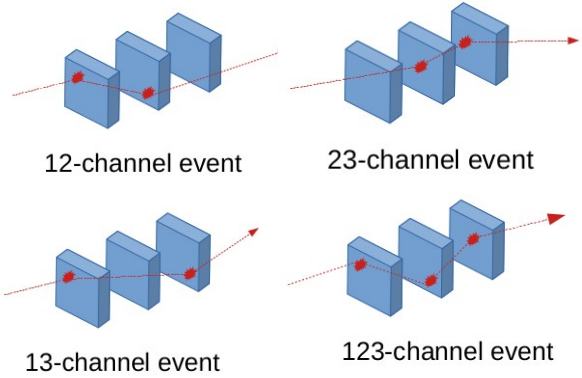
Viegas et al.
Radiat. Phys. Chem. 2022

Image reconstruction: list-mode MLEM

Sensitivity model for 2- and 3- interacion events



Joint reconstruction of all channels

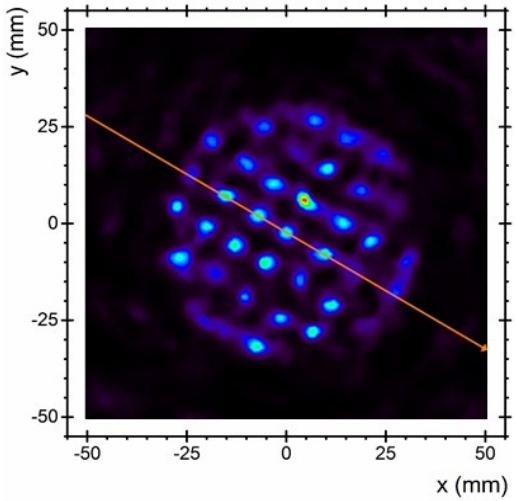


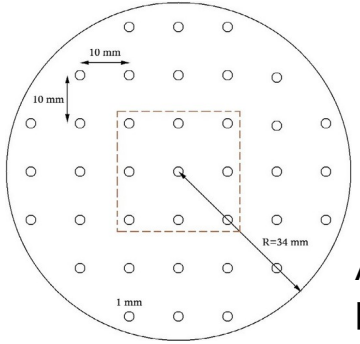
E. Muñoz et al. Phys. Med. Biol. 2018

E. Muñoz et al. Phys. Med. Biol. 2020

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

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





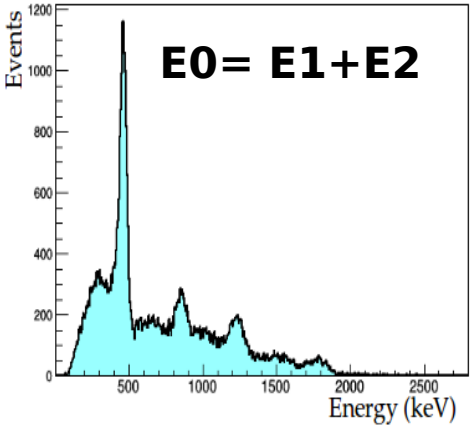
Array of 37 Na-22 point-like sources

Image reconstruction: spectral code

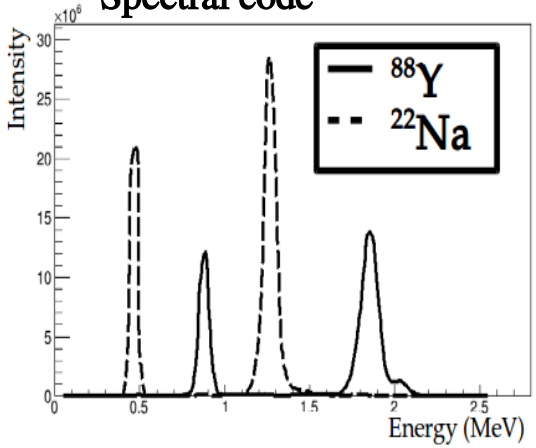
Reconstruction of position and energy distributions

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

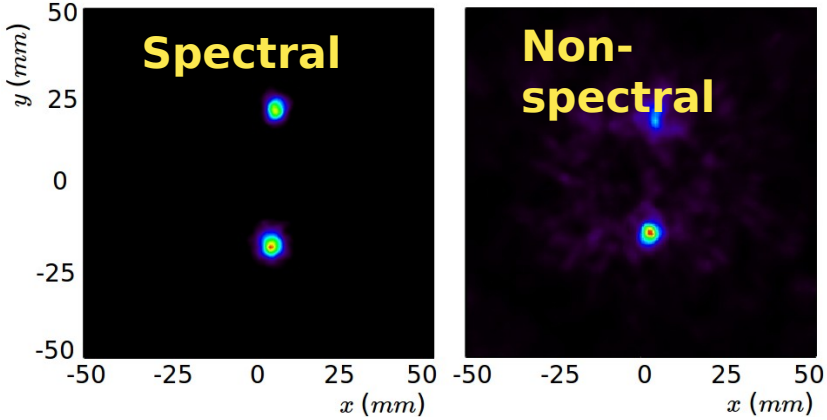
Sum spectrum

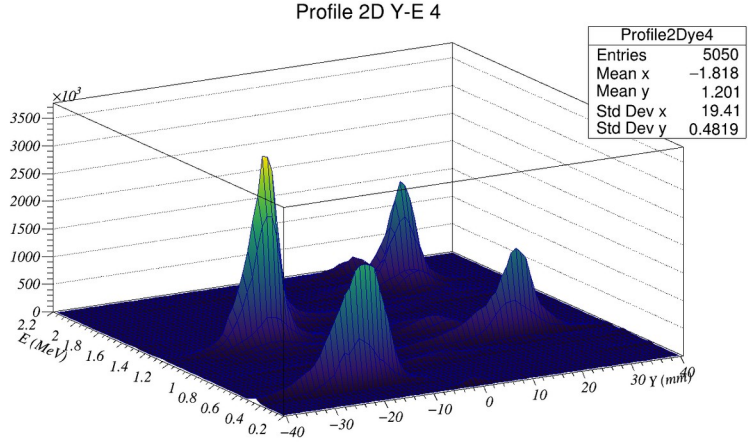


Spectral code



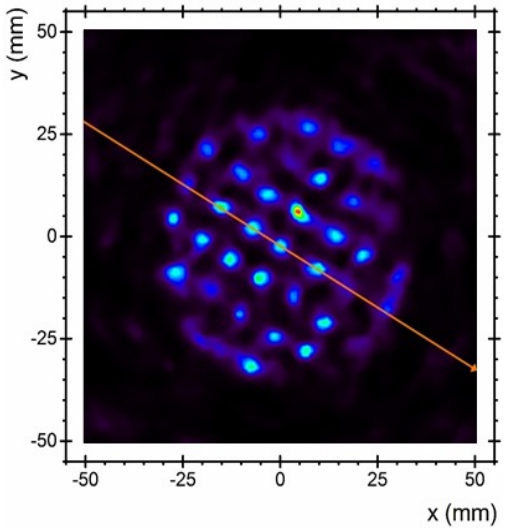
E. Muñoz et al. Phys. Med. Biol. 2020



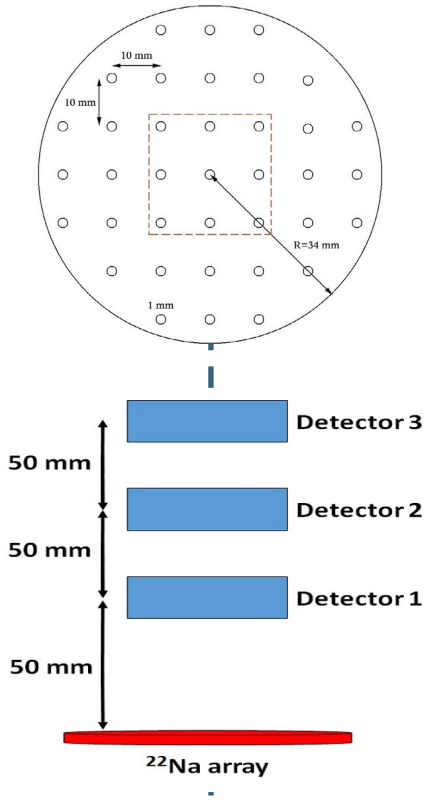


Prototypes

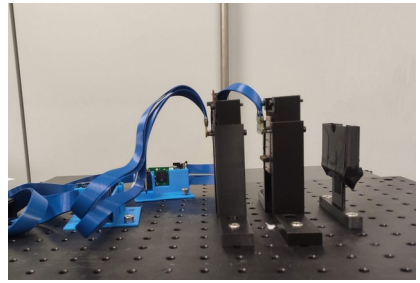
MACACO III

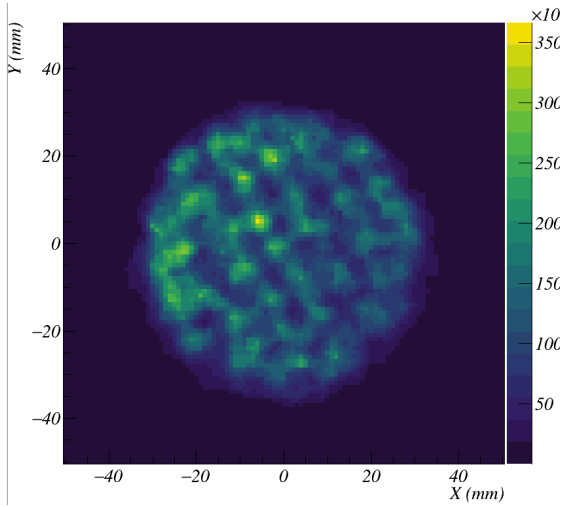


Array of 37 Na-22 point-like sources



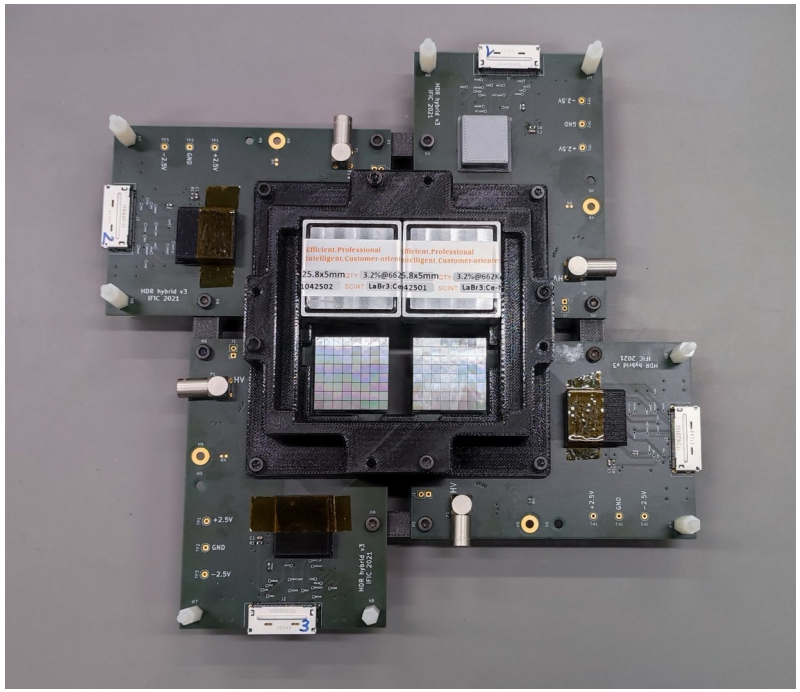
MACACOp



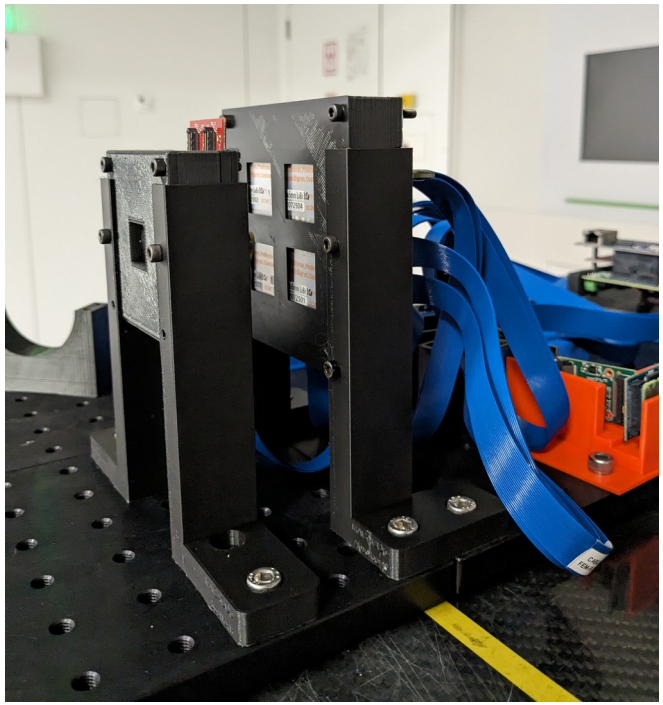


Prototypes

MACACO III+



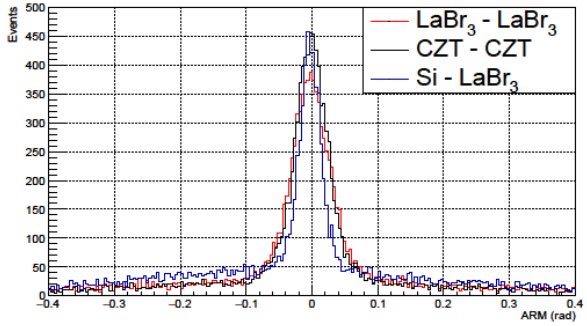
FALCON



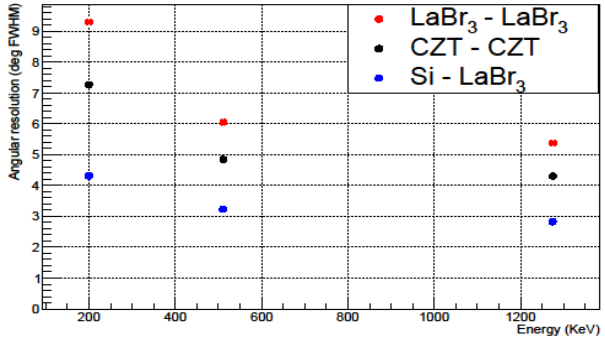
ICOR- CC with a silicon scatterer

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

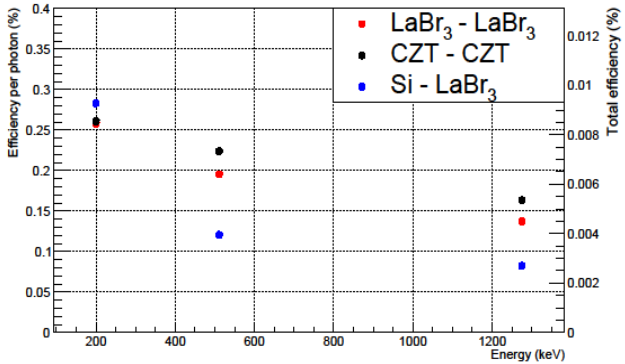
Angular resolution distributions



ARM vs. E

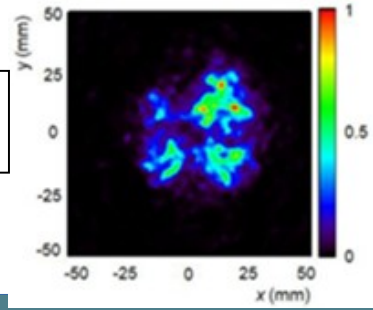


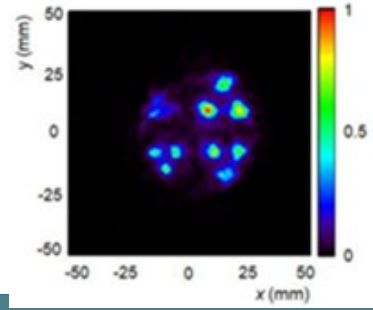
Efficiency vs. E



208 keV

$LaBr_3$



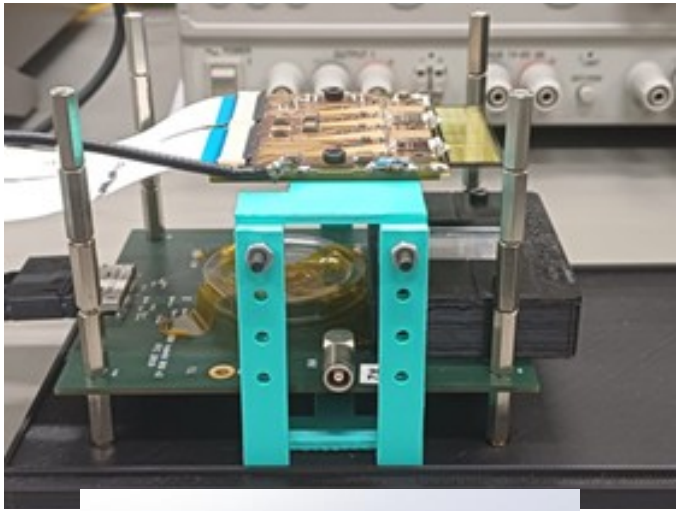


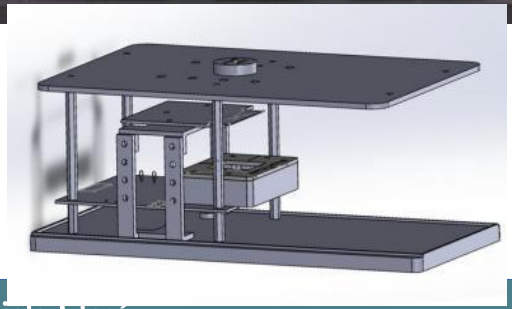
Silicon + $LaBr_3$

ICOR- CC with a silicon scatterer

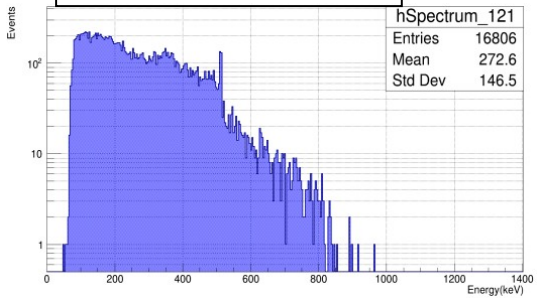
Compact prototype with two AliVATA readout boards
Functionality tests successful. Optimization ongoing

Tests wit Na-22 point-like source

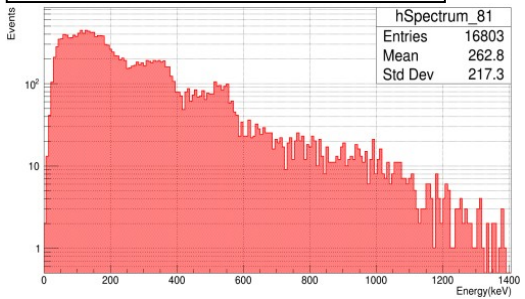




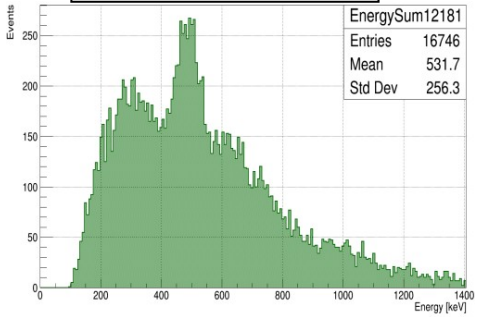
Silicon detector



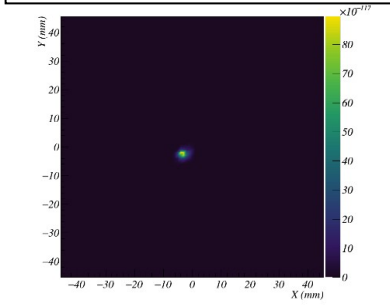
Scintillator detector



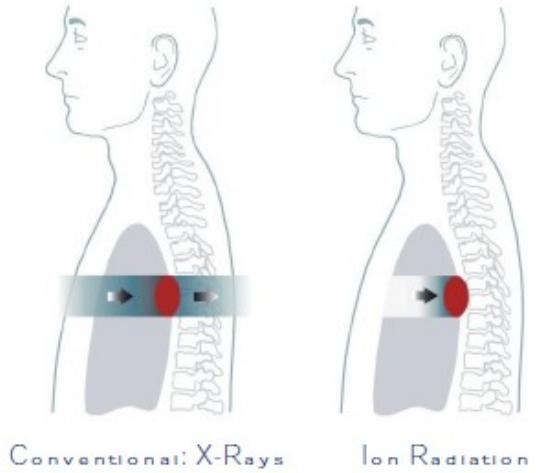
Sum spectrum

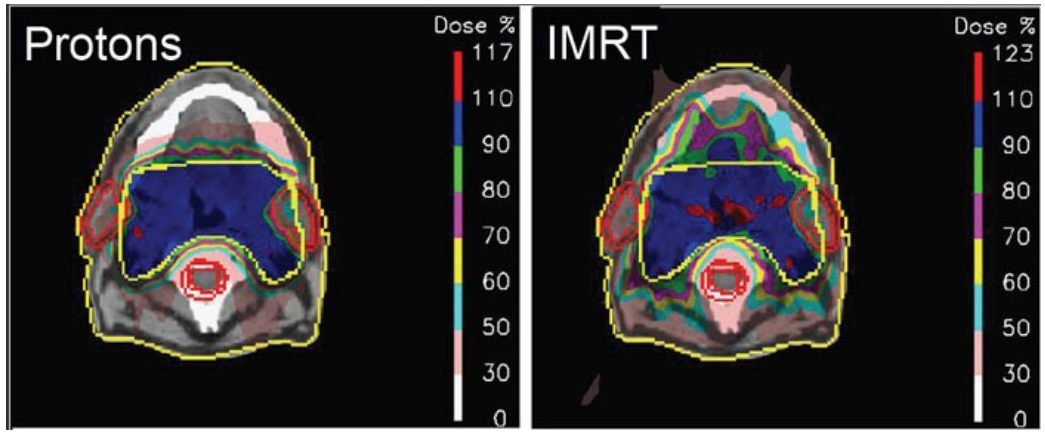


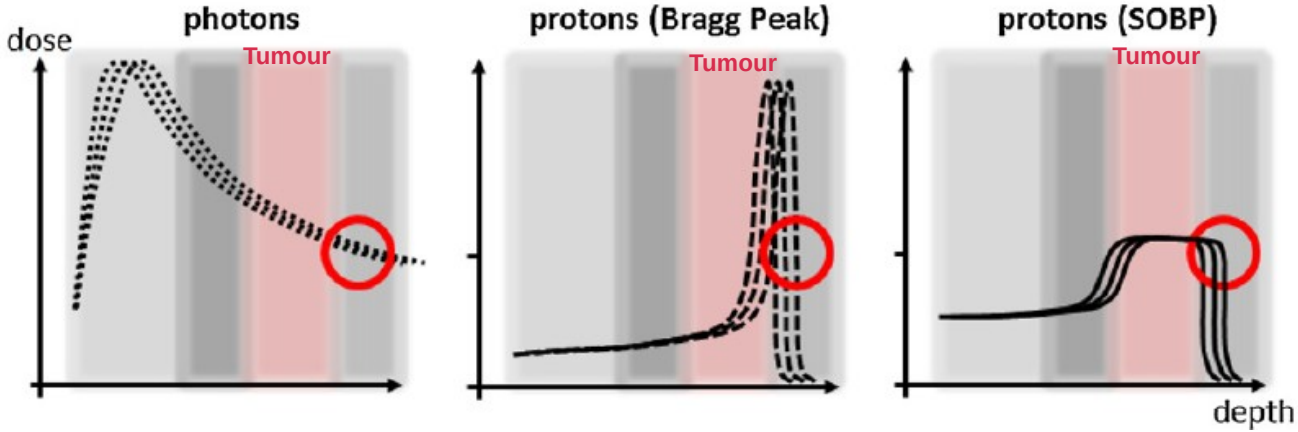
Reconstructed image



Hadron therapy treatment monitoring

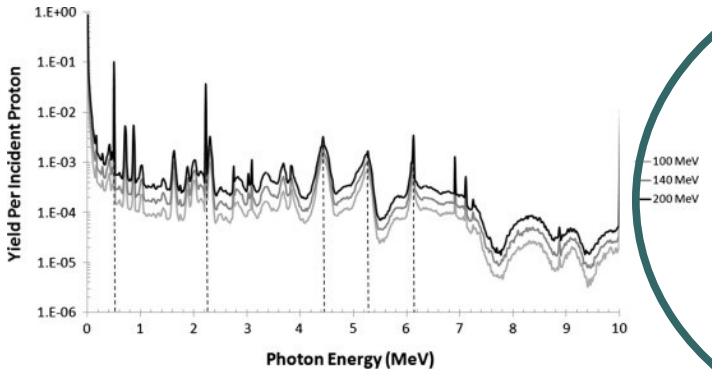


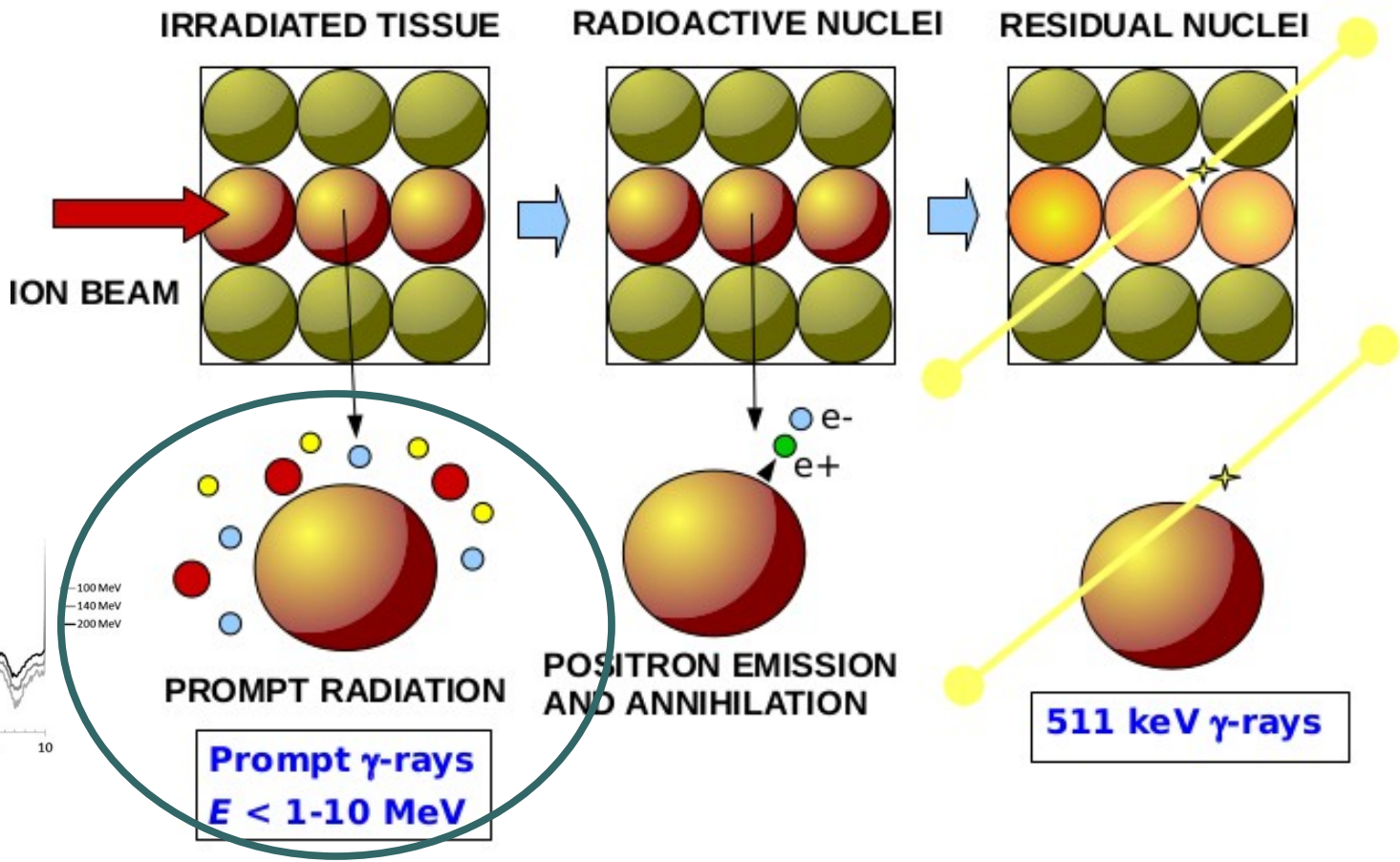




Large safety margins applied

Hadron therapy treatment monitoring





In-beam experiments

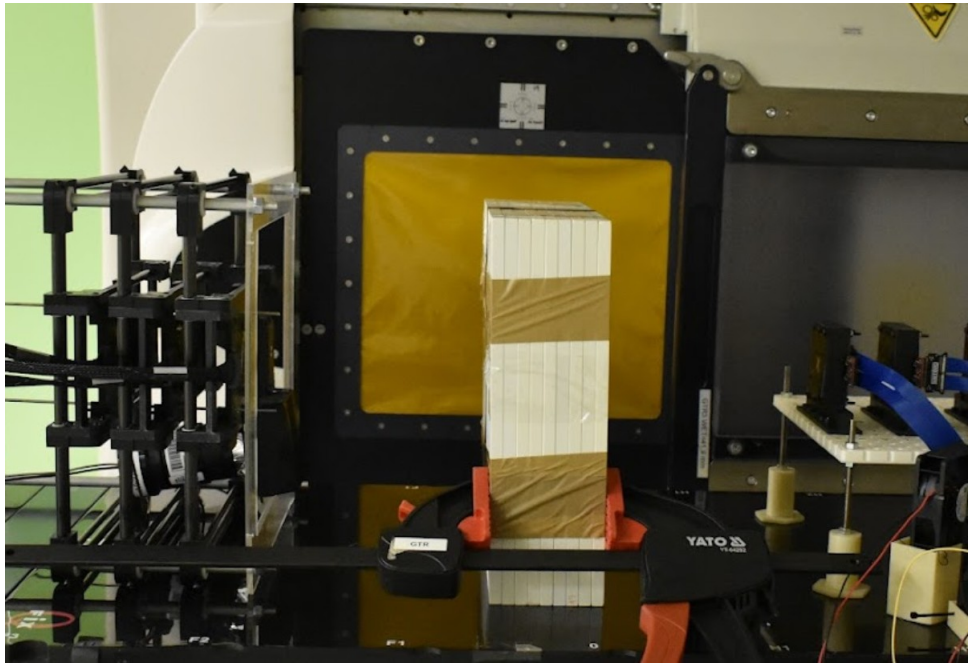
Tests with the current prototypes: Spanish National Accelerator Centre (CNA) and proton therapy centres

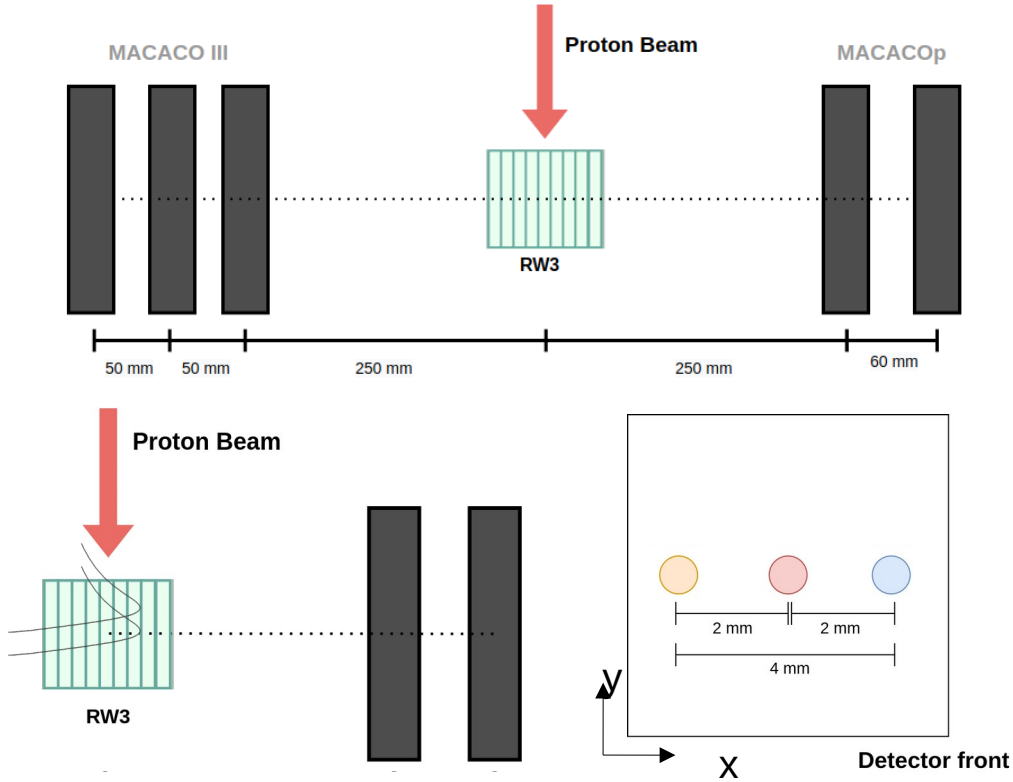
Center	Accelerator	Target	Energy (MeV)
CNA	Cyclotron	Graphite	18
CCB	Cyclotron (Proteus C-235)	RW3	88.38 – 91.62
QuirónSalud	Synchrocyclotron (S2C2)	RW3	70-90
MedAustron	Synchrotron-based particle accelerator	ARDOS	99.6

In-beam experiments

CCB (Krakow, Poland)

Proton beam with different energies on RW3 target [Cyclotron]





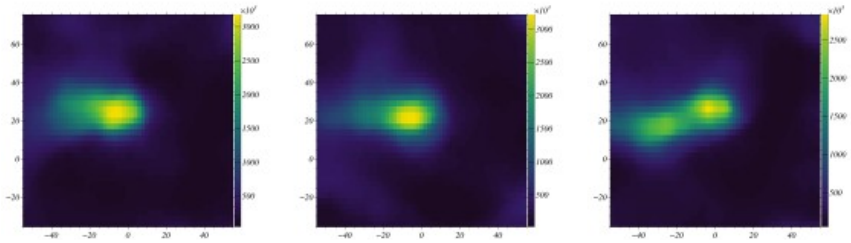
in collaboration with Hubert Jabłoński, Renata Kopeć, Dawid Krzempekand Natalia Mojżeszek, from Institute of Nuclear Physics Polish Academy of Sciences, Krakow, Poland

In-beam experiments

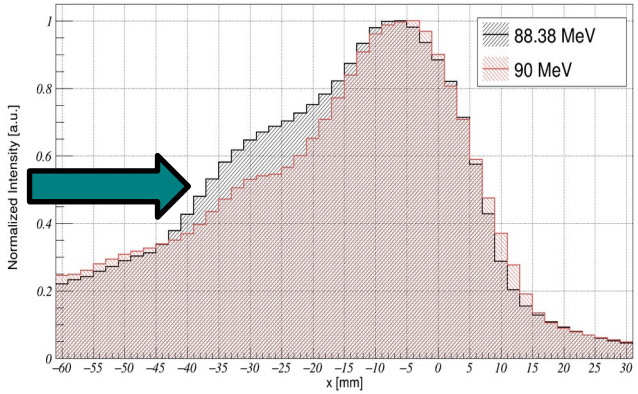
CCB (Krakow, Poland)

90 MeV
I = 90 pA

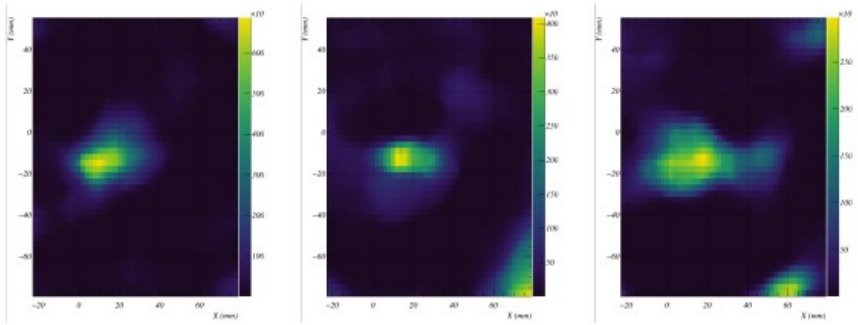
MACACO III



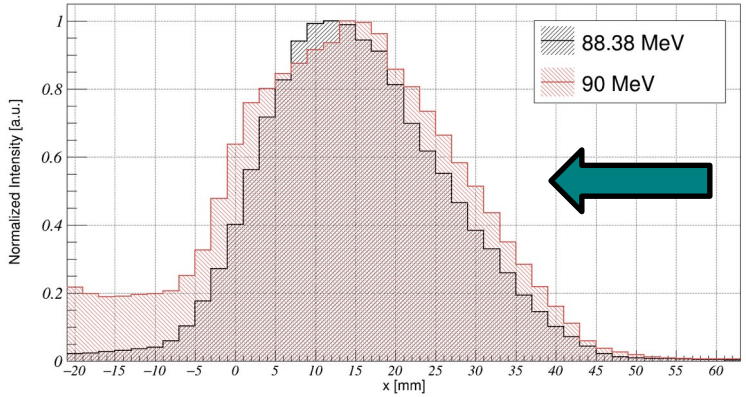
88.38 MeV | 90 MeV | 91.62 MeV



MACACOp



88.38 MeV | 90 MeV | 91.62 MeV



2 mm steps detected with both systems

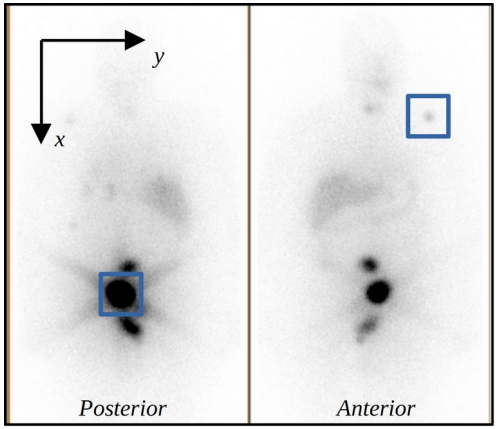
Radionuclide imaging

- 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.

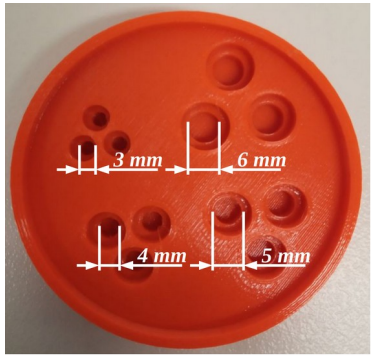
- Compton cameras can be advantageous in this field.

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



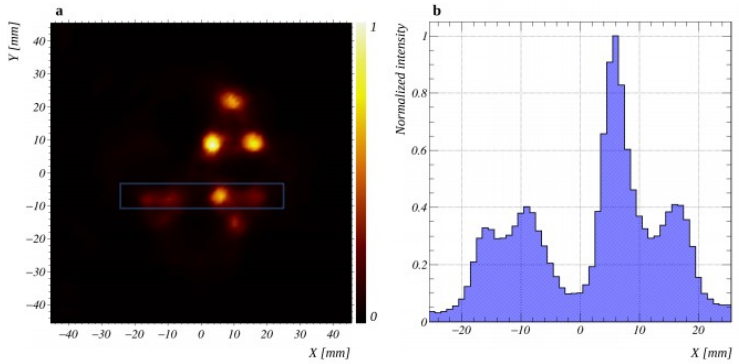
Initial tests in La Fe hospital (Valencia)

3D printed Derenzo-like phantom



^{18}F-FDG (511 keV)

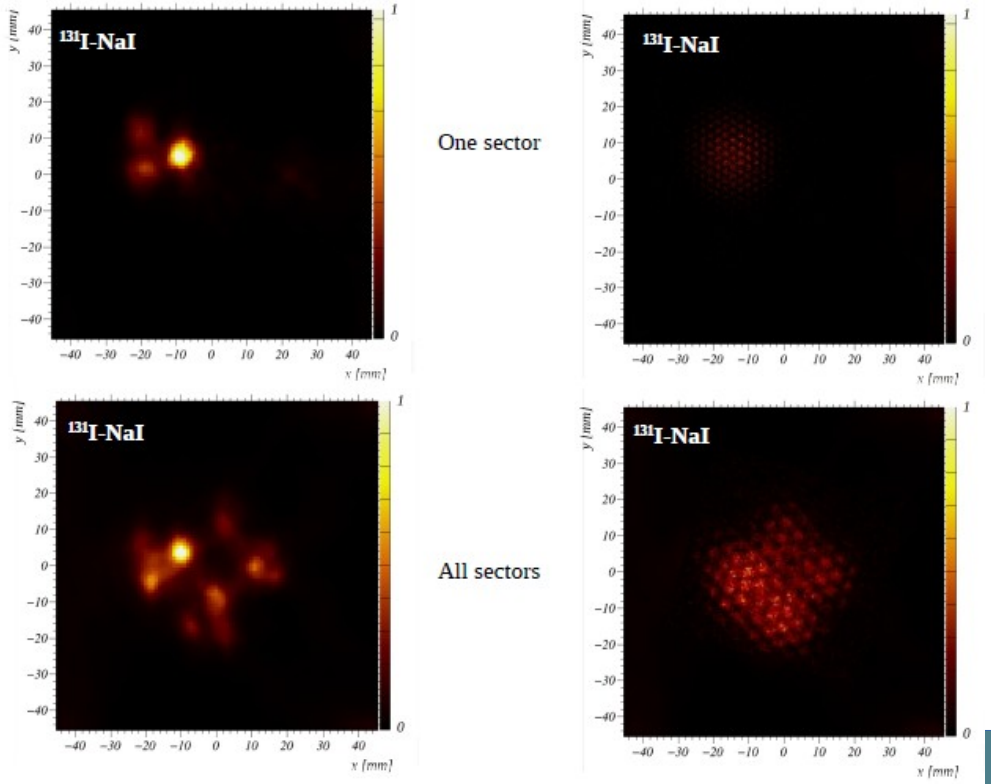
Compton camera



^{131}I-NaI (364 keV)

Compton camera

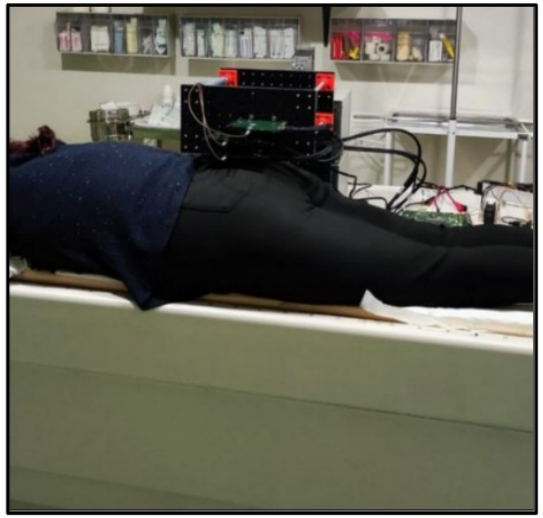
Gamma camera
Bright View XCT (Philips)



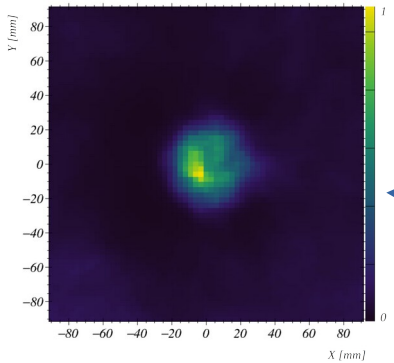
In collaboration with Irene Torres-Espallardo, José Manuel Calatayud, Pilar Bello and Stefan Prado from La Fe hospital.

Initial tests in La Fe hospital (Valencia)

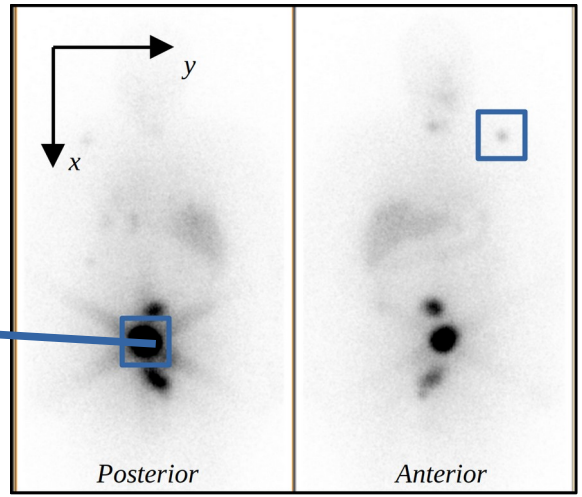
- Metastatic lesions from patients treated with ^{131}I-NaI after thyroid gland resection
- Initial activity (total): 150 mCi
- MACACO III @ ~70 mm.



MACACO III



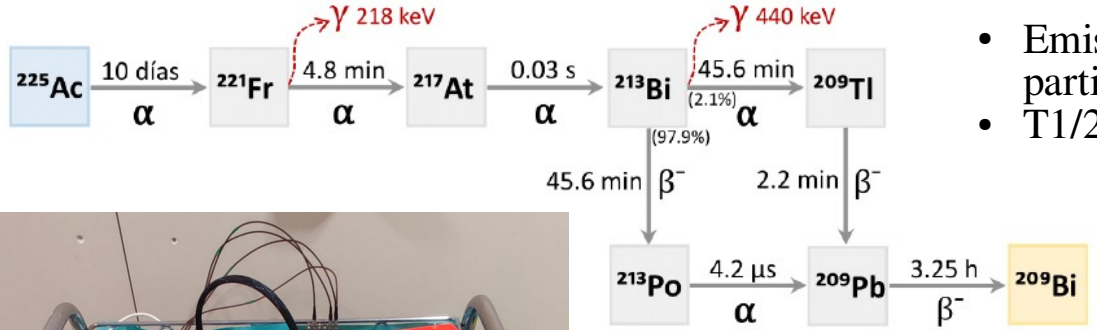
Gamma camera



Sacrum lesion

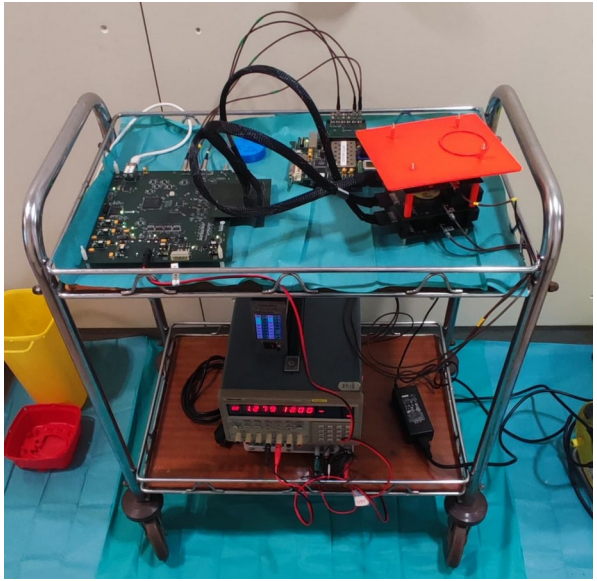
J. Roser et al. Physica Medica 132 (2025) 104928.

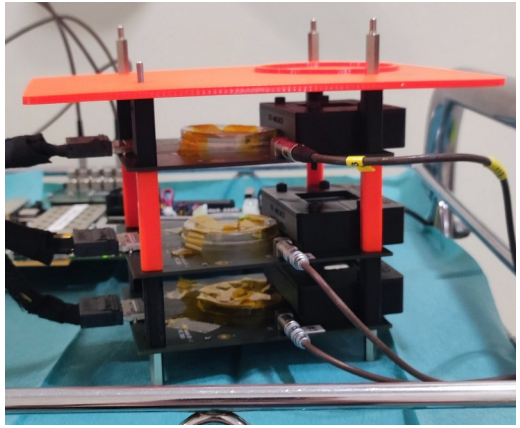
Ac-225 Measurements at Léon Bérard hospital (Lyon)

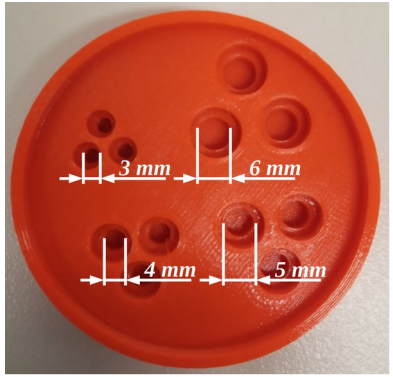


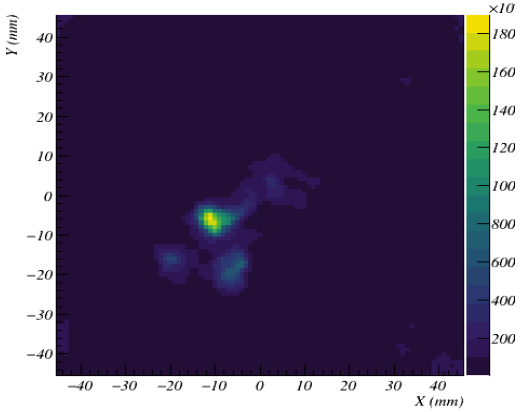
- Emission of 4 alpha particles (5.8-8.4 MeV)
- T1/2= 10 days

6 mm diameter rods reconstructed







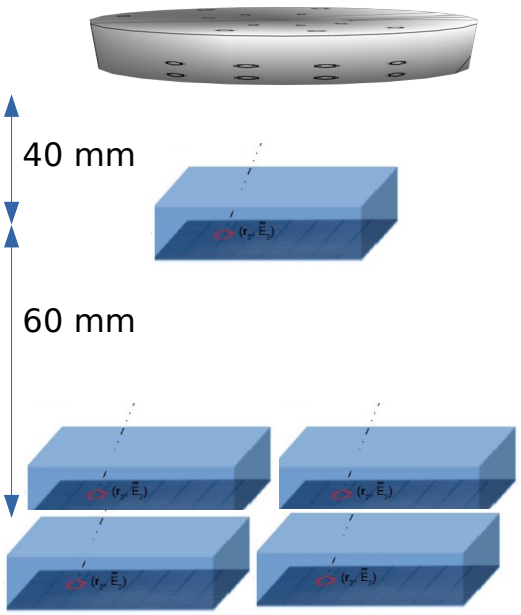


In collaboration with Ane Etxebeste, David Sarrut, Jean Noël Badel from Creatis and Léon Bérard hospital (Lyon).

70 kBq /rod

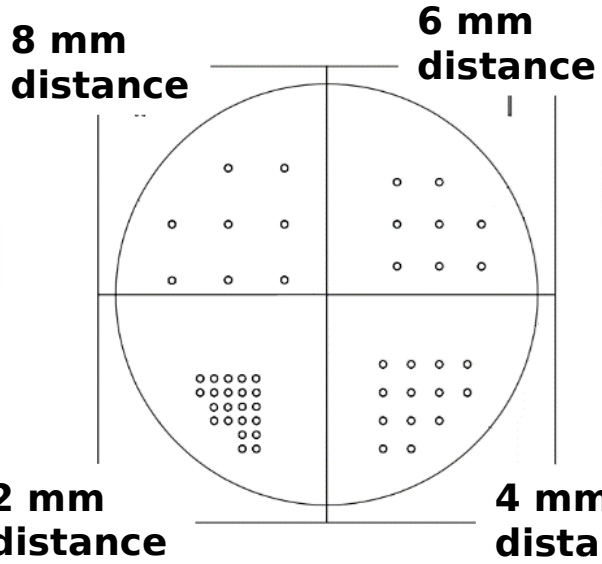
Measurements with Na-22 arrays

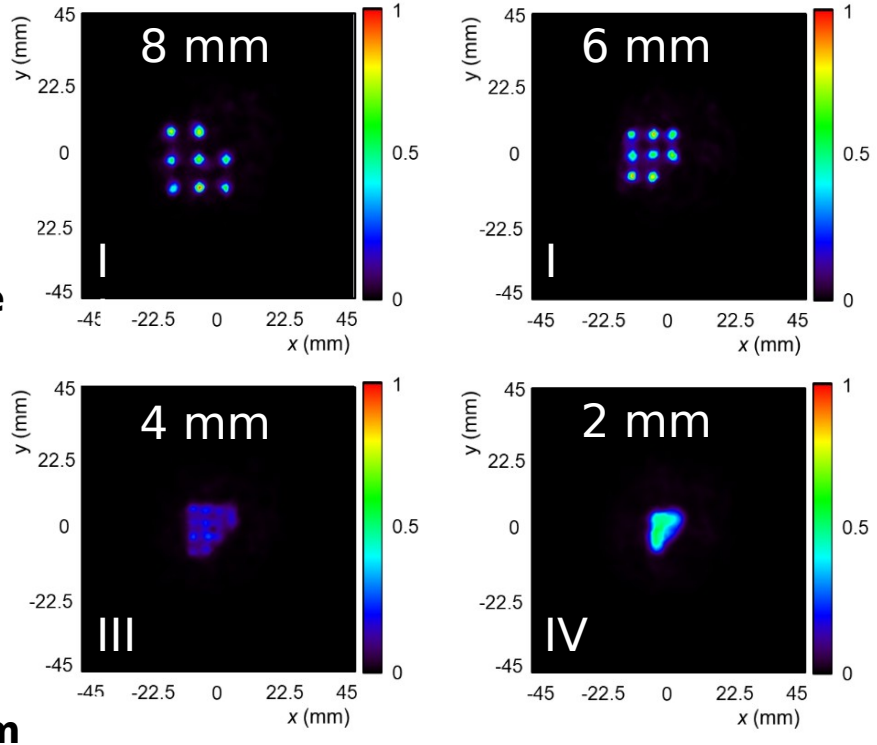
MACACO III+



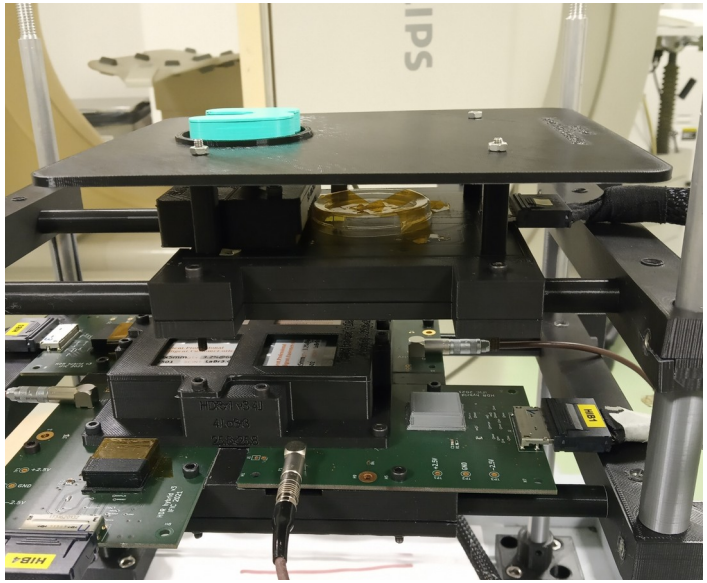
Array with four sectors of ^{22}Na point-like sources at different distances

1 mm diam. sources





Measurements with ^{131}I with MACACO III+

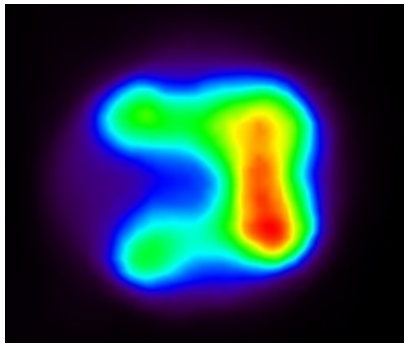


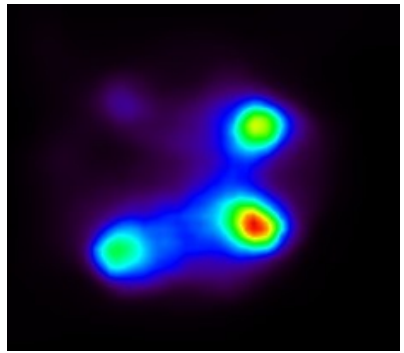
3D printed thyroid-shaped phantom filled with ^{131}I-MIBG

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

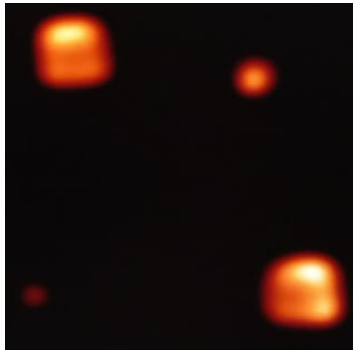




‘Uniform’ filling
~ 0.5 MB/ml

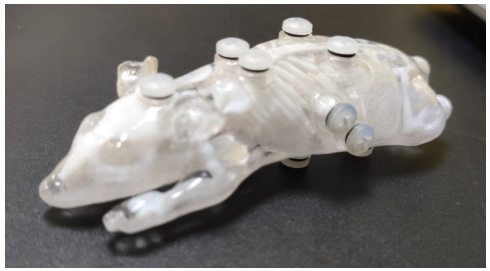
Background + hot rods at 10:1 activity concentration (0.1 : 0.01 MBq/ml)

Gamma camera images

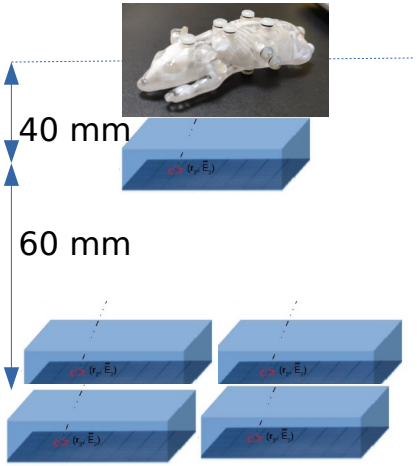


CT images

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

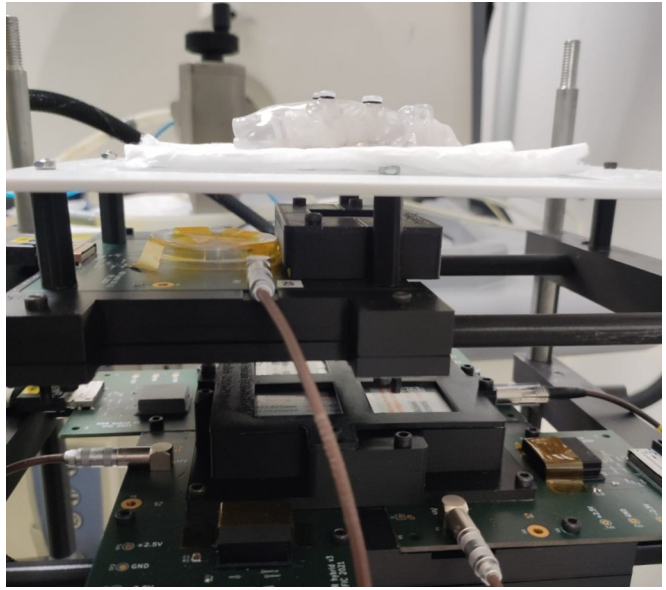


Phantech



^{131}I (364 keV)

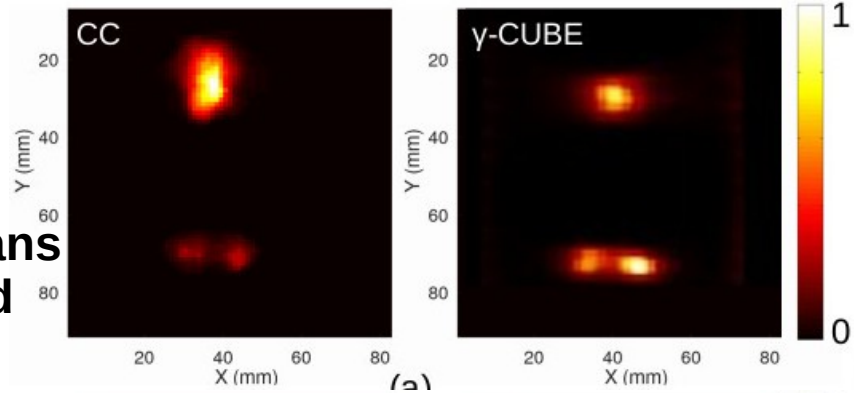
Mouse phantom filling 2/4 organs: brain, heart, bladder and kidneys.



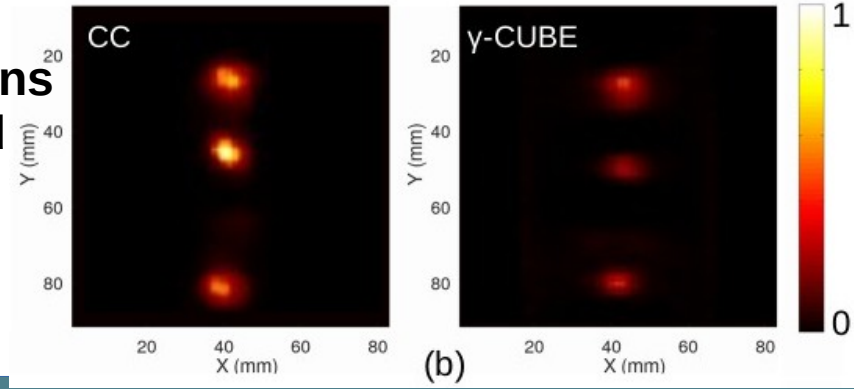
MACACO III+ 30 minutes

γ-CUBE SPECT MOLECUBES 2 hours

two organs filled



four organs filled

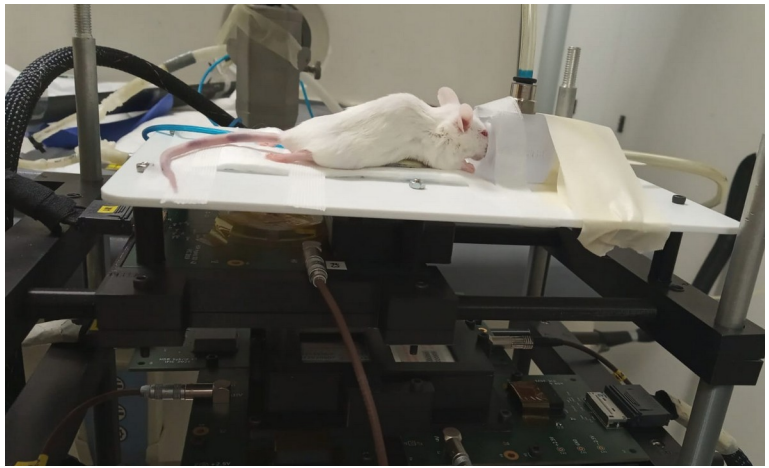


MACACO III+: mouse phantom measurements with ^{131}I

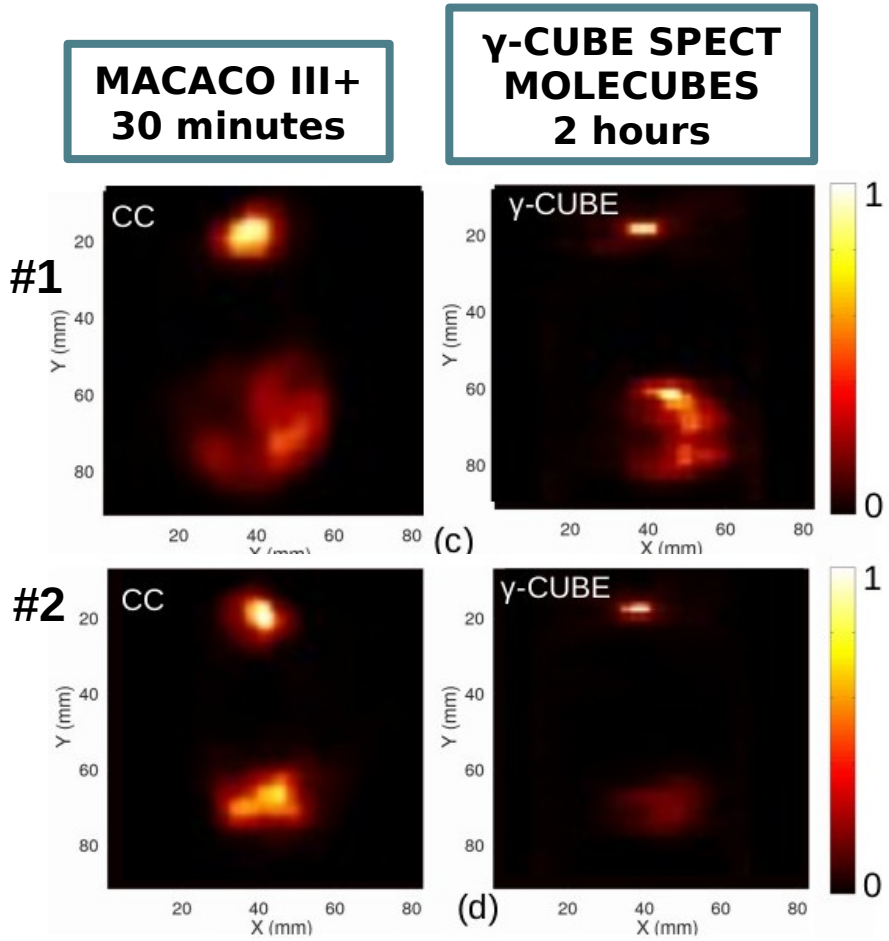
^{131}I (364 keV)

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.

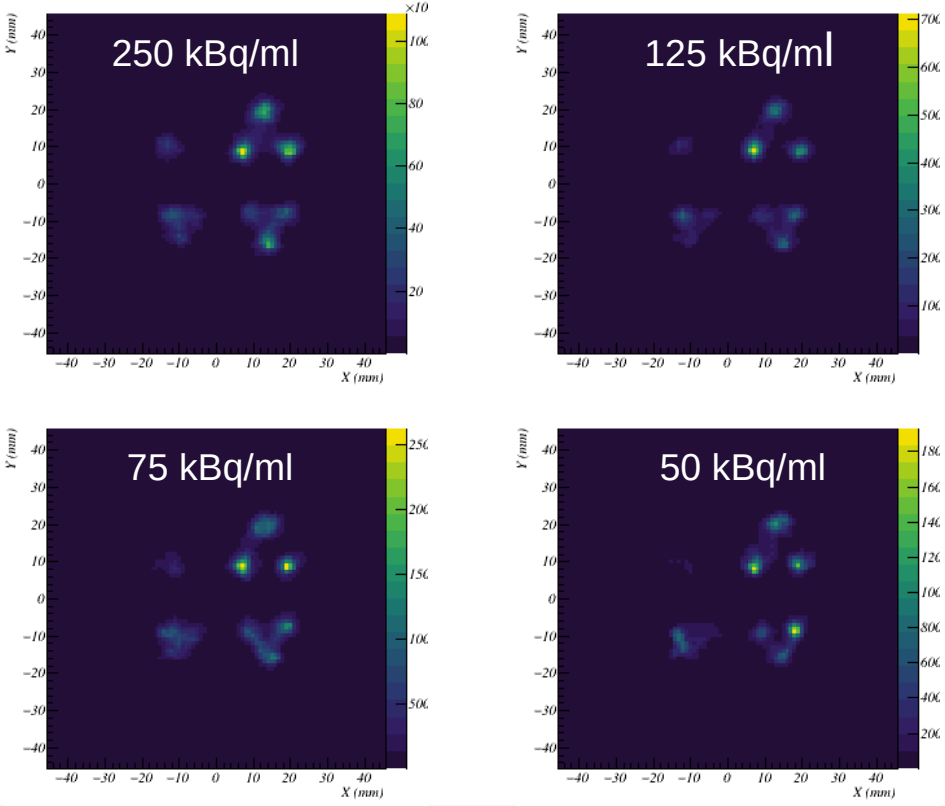


In collaboration with Jordi Llop, Unai Cossío, Irati Aiestaran from CIC biomaGUNE.



^{225}Ac GATE simulations with MACACO IV geometry

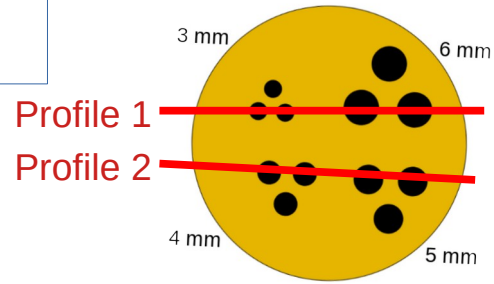
440 keV (^{213}Bi)

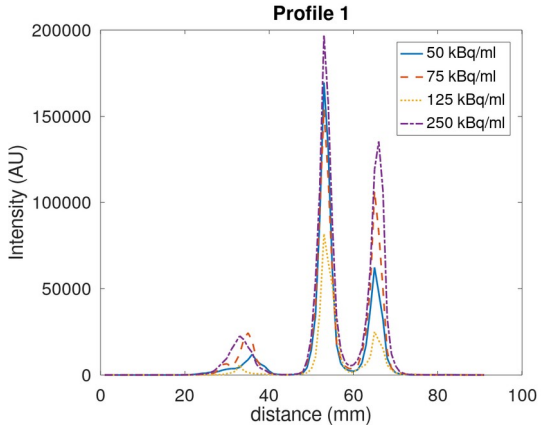


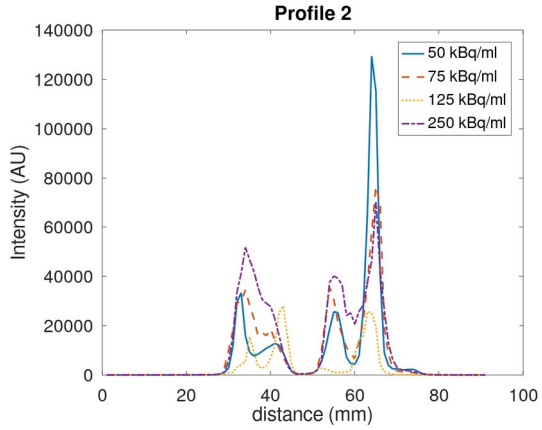
Detector:
1 mm FWHM spatial resolution
3.5% @ 511 keV FWHM
Ideal timing

20 min acquisition

50 iterations of ML-EM

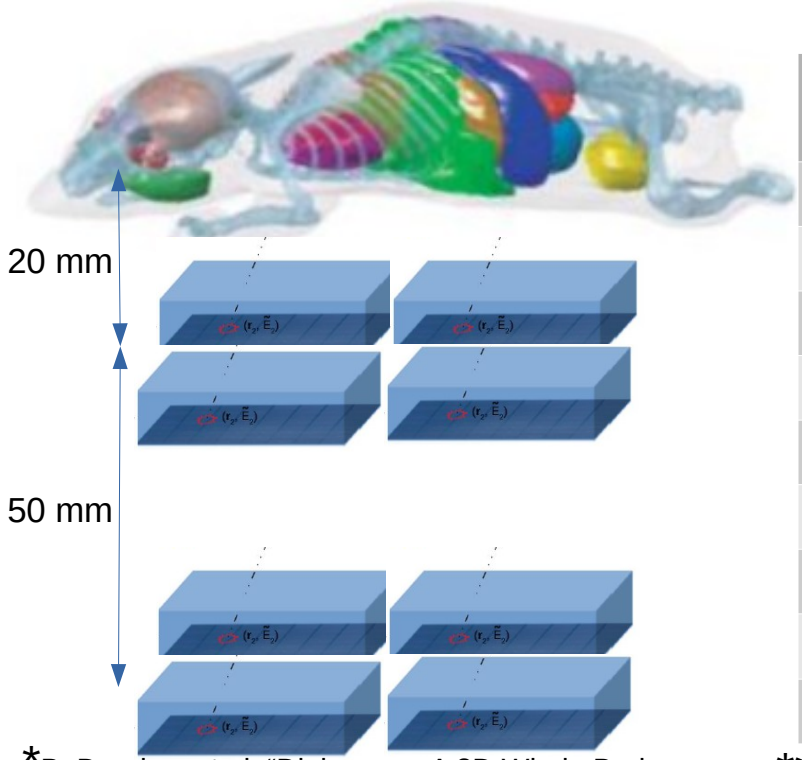






^{225}Ac GATE simulations with MACACO IV geometry

Digimouse: 3D Mouse Atlas*

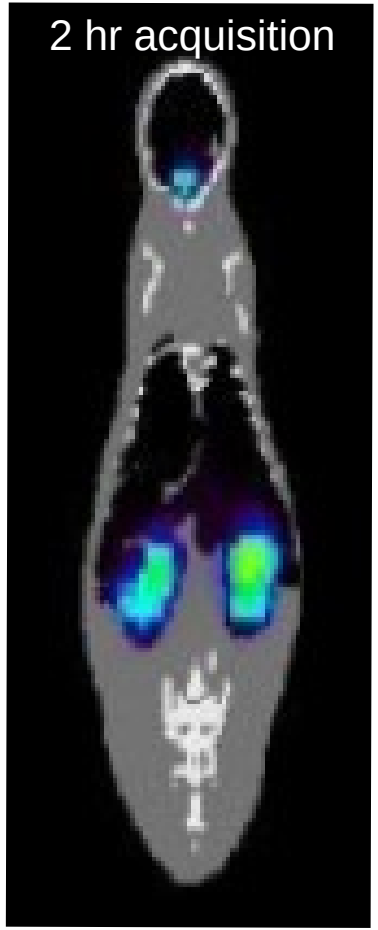


*B. Dogdas, et al. “Digimouse: A 3D Whole Body Mouse Atlas from CT and Cryosection Data”, Phys. Med. Bio, 52: 577-587, 2007

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 225Ac-Labeled Single-Domain Antibody for the Treatment of HER2pos Cancer,” Mol Cancer Ther, 21(12), 1835–1845, 2022



AIDER

European Commission

Num 101165088.
8 Partners and 2 affiliated entities: 4 academic, 2 hospitals, 1 SME, 1 CSO.
1/9/25-31/8/29

AIDER

European Commission

Two tecnological approaches:

$CeBr_3$ crystal encapsulated with the photodetector

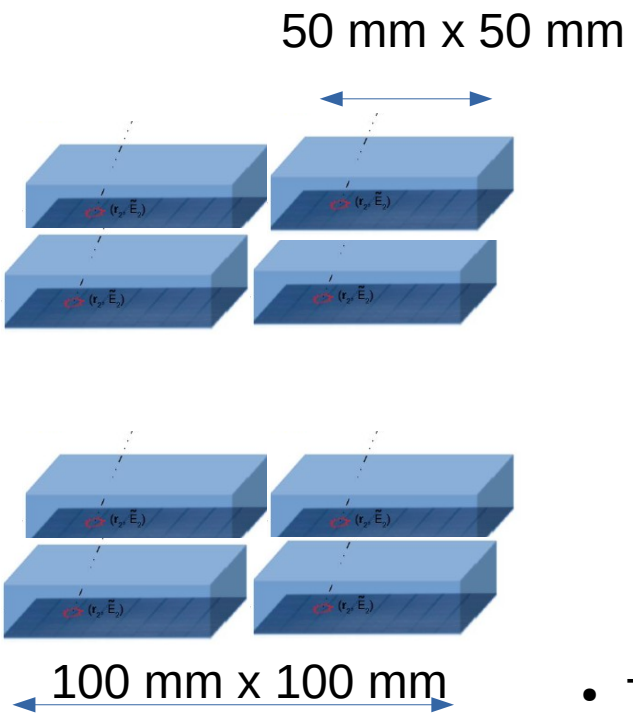
$LaBr_3$ crystal coupled to the photodetector

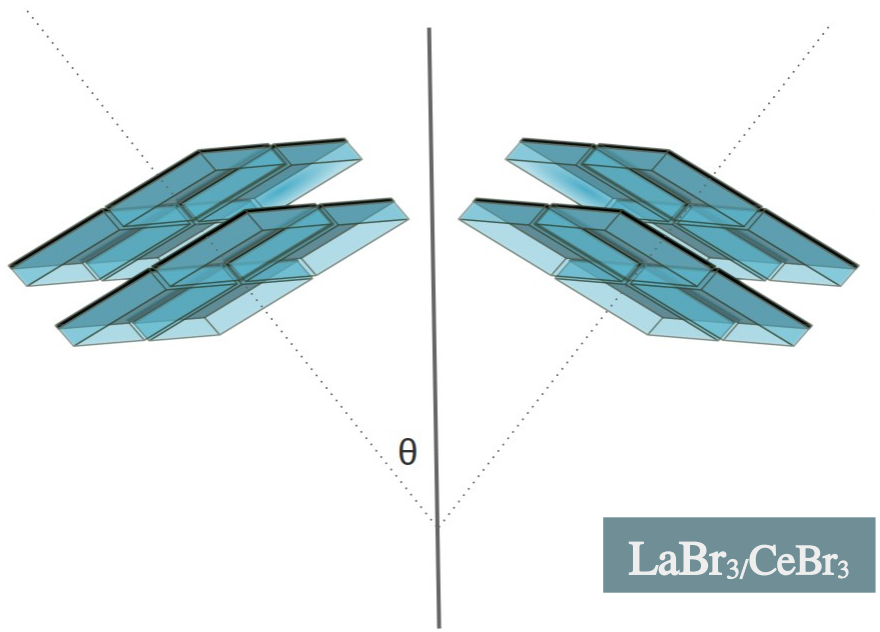
Readout electronics

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.

Conclusions

- 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.

Gabriela Llosá

Ana Ros

Fernando Hueso-Gonzalez

Karol Brzezinski

Luis Barrientos

Siddharth Parashari

Matthew Strugari

Javier Pérez Curbelo

Declan Garvey

+ Nataly Castellanos
+ Deniel Rodriguez

Acknowledgements

This work was supported by:

- MCIN /AEI (PID2019-110657RB-I00, PID2022-143246OB-I00).
- MCIN /AEI 10.13039/501100011033 (PDC2021-121839-I00).
- Support from the MCIN with funding from theEuropean Union NextGenerationEU and Generalitat Valenciana in the call Programa de Planes Complementarios de I+D+i (PRTR 2022). Project ICOR, reference ASFAE/2022/019.

Group members are supported by GVA Excellence programmes, UVEG Atracció de Talent, GVA Grisolía and FPU contracts.

Thank you

Gabriela.llosa@ific.uv.es

http://ific.uv.es/iris