Imaging therapeutic radiopharmaceuticals in mice using the MACACO III+ Compton camera

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Overview

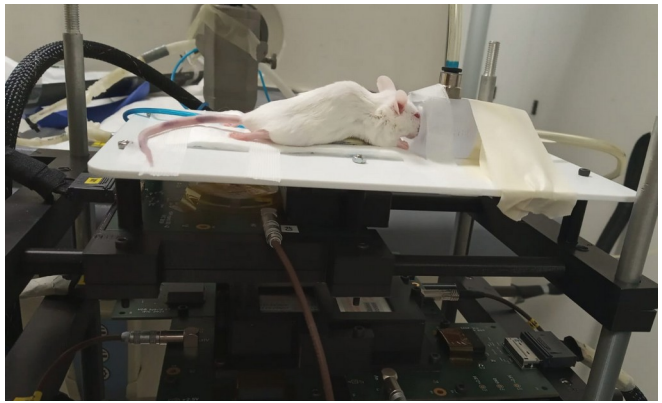
- Preclinical imaging targeted radionuclide therapy (TRT)
- MACACO III+ Compton camera
- Imaging ^{131}I in mice at CIC biomaGUNE
- Prospects for ^{225}Ac imaging in small animals
- Conclusions

Preclinical imaging for TRT

- Development of translational radioisotope therapies in murine models

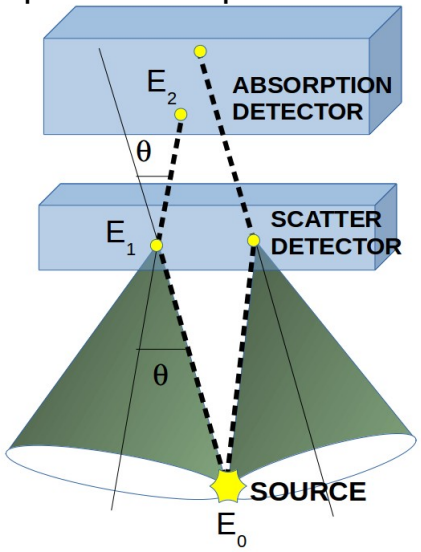
- Dedicated pre-clinical SPECT systems are not optimal (designed for <300 keV)
  - → low efficiency
  - → high energy of the photons emitted by radioisotopes, ex. ^{131}I (364 keV), ^{225}Ac (440 keV)

- Compton camera solution:
  - → Higher efficiency due to electronic collimation
  - → Superior response to high-energy photons
  - → Better suited for multi-gamma imaging



Compton camera

Registration of successive interactions of the incident photons in position-sensitive detectors

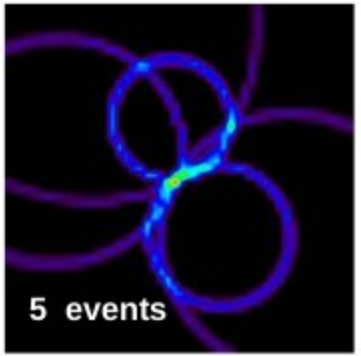


Determination of the Compton scattering angle through Compton kinematics

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

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

Reconstruction of the origin of the incident gamma ray through backprojection of cones of response CoRs:



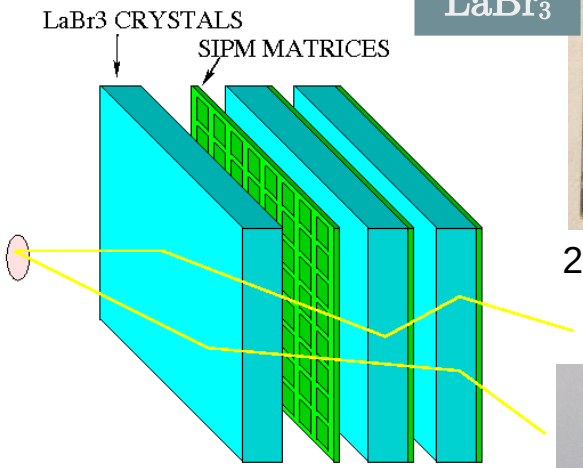
+ Image reconstruction

List mode ML-EM

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

MACACO III (Medical Applications CompAct COmpton camera)

Detectors

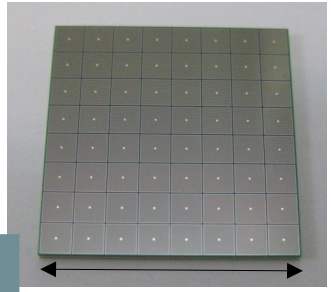


2/3 planes
absorption not required

LaBr$_3$

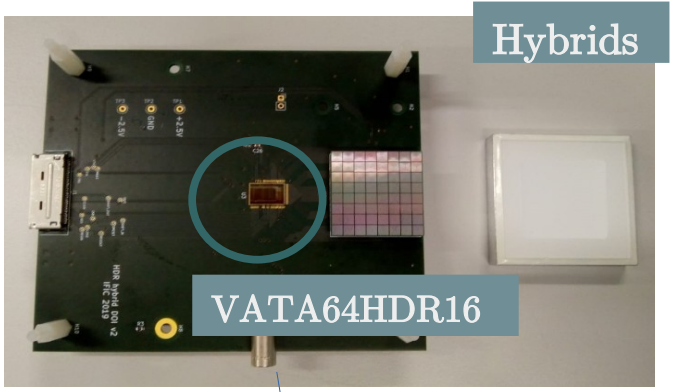
25.8x25.8x5 mm^3

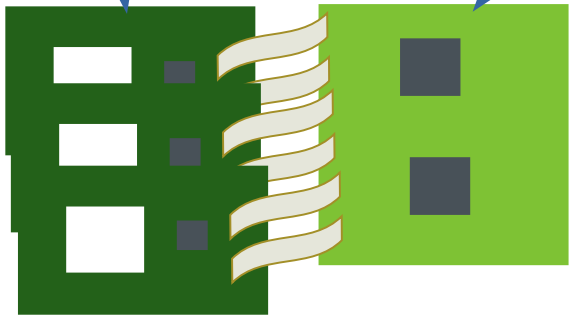
SiPMs



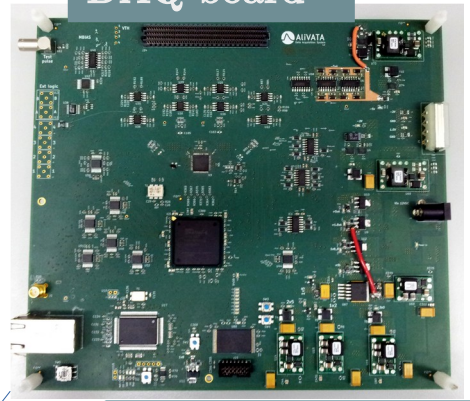
25.8 mm

Readout





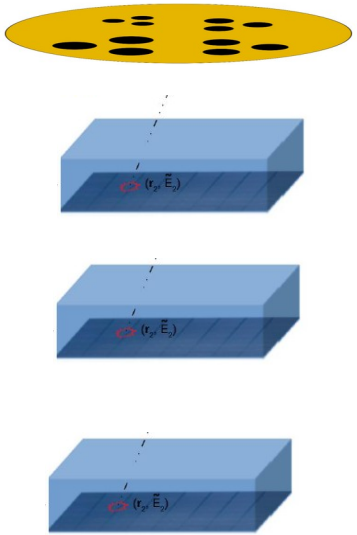
AliVATA
DAQ board



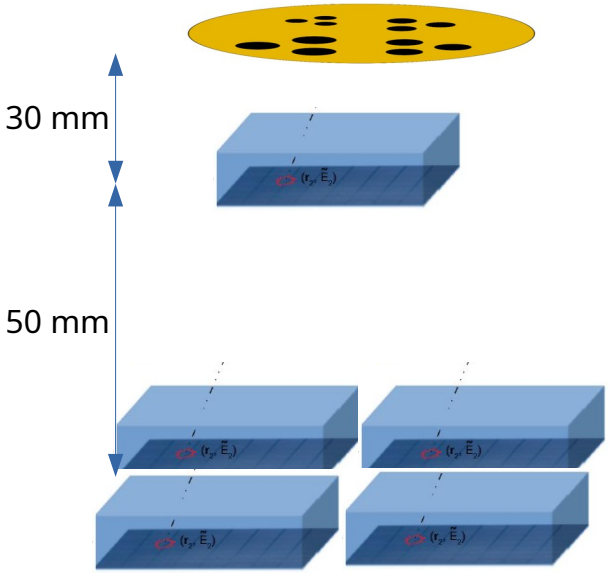
Commercialized by Alibava Systems S. L.

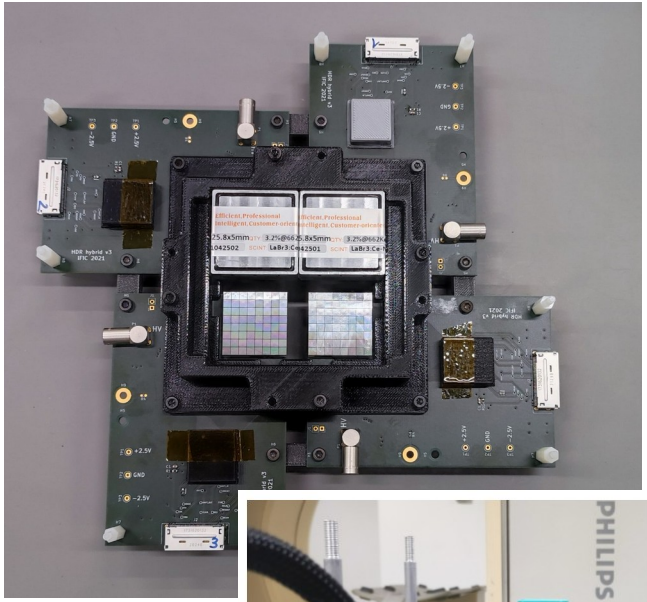
Improved Sensitivity with MACACO III+

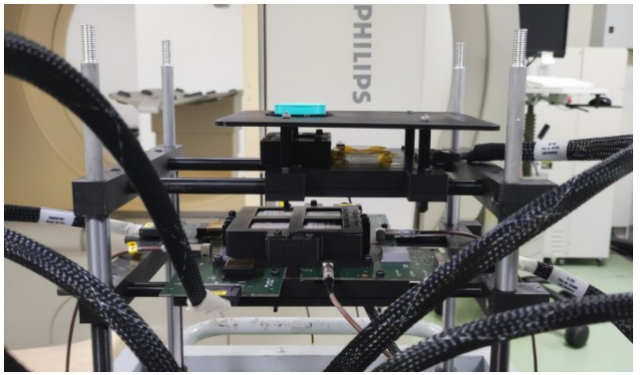
MACACO III



MACACO III+

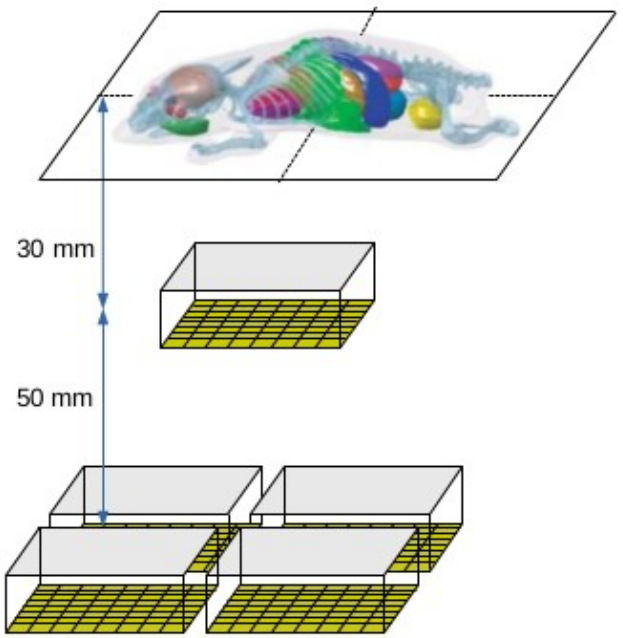


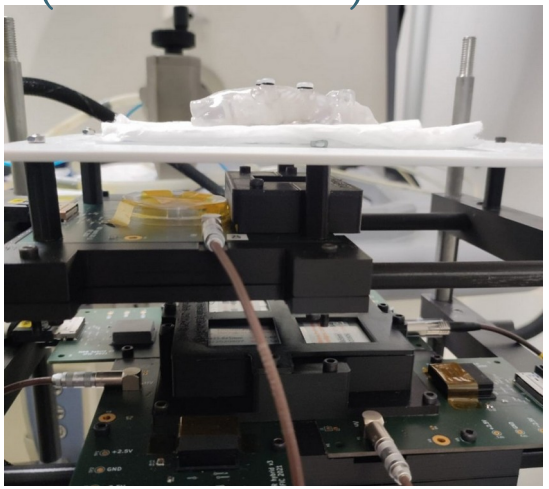


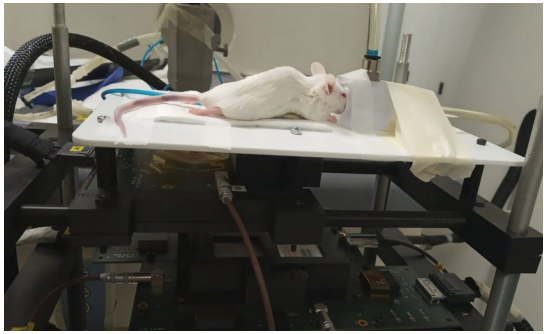


Imaging ^{131}I-NaI in mice

Measurements at CIC biomaGUNE (San Sebastian)







Mouse phantom

Two 45 min measurements

- brain + kidney (2.95 MBq/ml)
- brain+ kidneys + heart + bladder (2.55 MBq/ml) (3.99 MBq/ml)

Comparison with comertial SPECT Molecubes γ-CUBE (3 hours)

Live mice

30 min measurements

- Two mice: 30.46 g and 29.06 g
- 1.20 MBq/ml and 2.16 MBq/ml

Mouse Phantom with ^{131}I

γ-CUBE 3 hrs MACACO III+ 45 min

γ-CUBE 3 hrs MACACO III+ 30 min

Mouse Phantom with ^{131}I

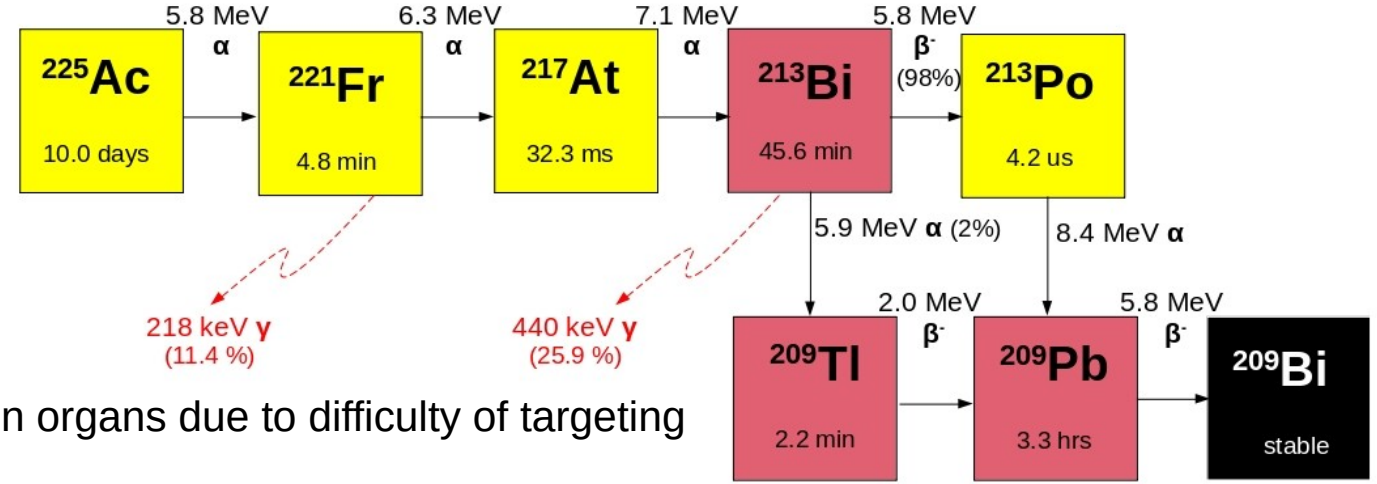
γ-CUBE 3 hrs MACACO III+ 45 min

γ-CUBE 3 hrs MACACO III+ 30 min

Actinium-225 imaging for TAT

TAT: Efficient tumour control, sparing healthy tissue
- high linear energy transfer (LET)
- short range (<100 µm, a few cell diameters)

^{225}Ac: Promising alpha-emitters
- high net alpha yield
- high alpha energies
- 10 day half-life



<u>Multi-isotope imaging application</u>
Toxicity to non-target and excretion organs due to difficulty of targeting cells with the entire decay chain
Ex. Renal toxicity due to ^{213}Bi

Challenges for ^{225}Ac Imaging

1) High alpha yield of ^{225}Ac requires small therapeutic doses, limiting signal for gamma imaging
Ex. Comparison of [^{177}Lu]Lu-PSMA-I&T vs. [^{225}Ac]Ac-PSMA-I&T*

2) 440 keV challenging for gamma camera

	[^{177}Lu]Lu-PSMA-I&T	[^{225}Ac]Ac-PSMA-I&T
Therapeutic Activity	7.4 GBq	8 MBq
Photon yield	208 keV (10%) 113 keV (6%)	218 keV (11%) 440 keV (26%)

Activity concentrations

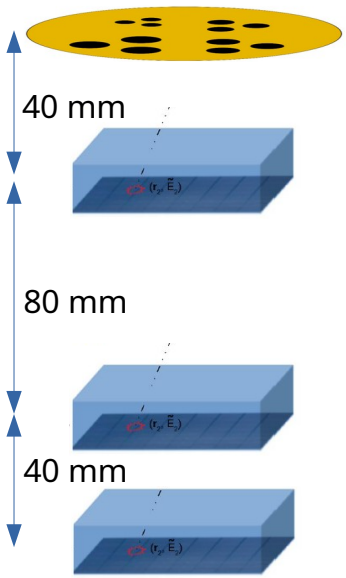
Clinical**:
- Median viable tumour volume: 35.7 mL
- Minimum activity: 10 MBq -> **280 kBq/mL**

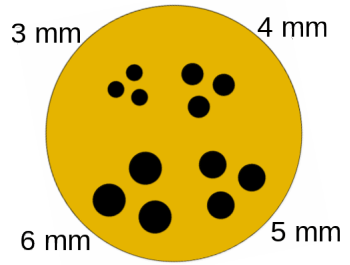
Preclinical***:
- **40 kBq/mL** (EC_{50})

Low activity!

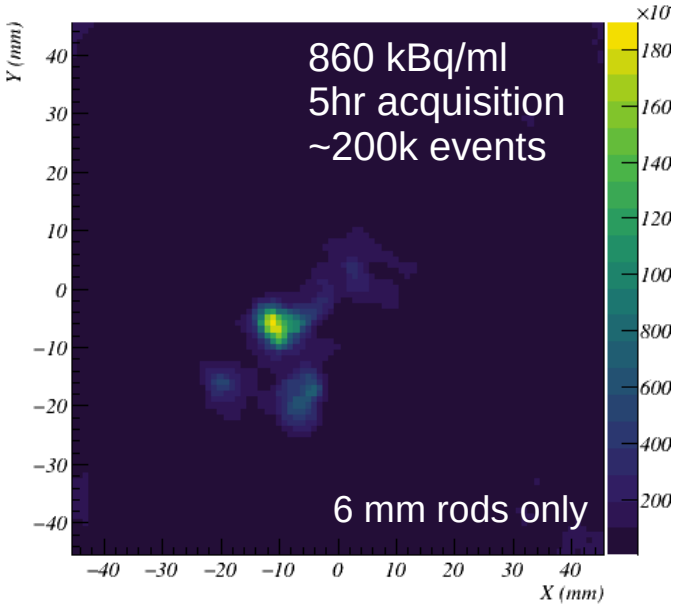
*Dekler et al. EJNMMI (2023) 50:1280–1290
Patients with in glioblastoma treated with [^{225}Ac**] Ac-DOTA-substance P, Tulik et al. EJNMMI Physics (2024) 11:41
**Rodak et al. Mol Cancer Ther. 2022 Sep 21;21(12):1835–184

Imaging ^{225}Ac with MACACO III





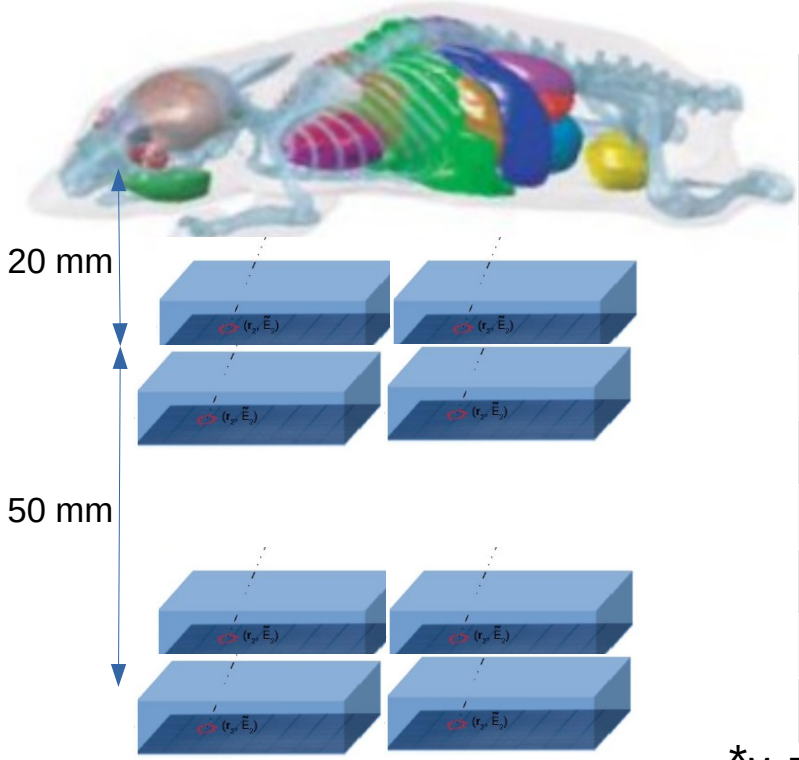
^{225}Ac (440 keV)



Measurements at Léon Bérard hospital in Lyon

Imaging ^{225}Ac in mice (simulations)

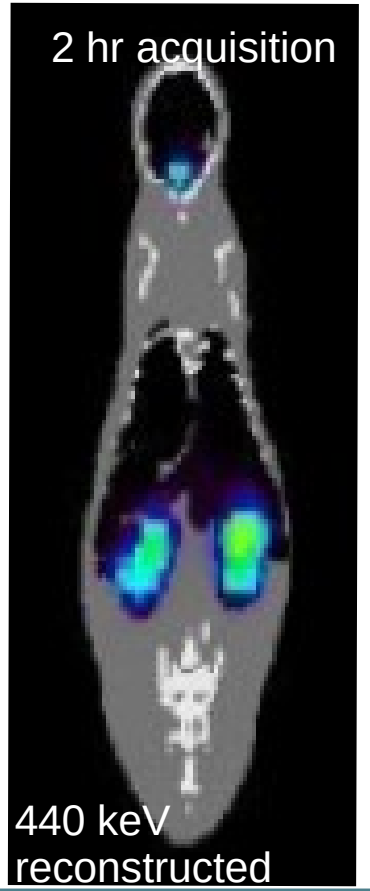
Digimouse: 3D Mouse Atlas*



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., Mol Cancer Ther, 21(12), 1835–1845, 2022



Conclusions

- $LaBr_3$-based Compton camera proposed for preclinical imaging for TRT.
- Images of ^{131}I in mice obtained with MACACO III+ are comparable to those obtained using a commertial preclinical SPECT system, in less time.
- Encouraging initial results for ^{225}Ac imaging at Léon Bérard hospital in Lyon.
- Simulations show possibilities of imaging ^{225}Ac decay products mice, with low activities.
- Optimization for preclinical conditions are under way.

Acknowledgements

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Thank you

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