KU LEUVEN

# Dedicated phantom measurements to develop and validate quantitative $^{225}Ac$-(micro)SPECT imaging

**Michel Koole**

PRISMAP meeting Lisbon 28 nov 2023

MIRaCLe

MOLECULAR IMAGING RESEARCH AND CLINIC LEUVEN

# Overview

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MOLECULAR IMAGING RESEARCH AND CLINIC LEUVEN

| Source | Activity | Time | Form | site |
|---|---|---|---|---|
| A | 95.8 kBq in 500 µl of 4M $HNO_3$ | 19.06.2023 @ 15h | Liquid | JRC |
| B | 10 MBq | 19.06.2023 @ 15h | Dry | JRC |
| C | 9.26 MBq Ac-225 with 24.2 MBq Ra-225 producing Ac-225 | 20.06.2023 @ 9am | Liquid | MEDICIS |

## Siemens Intevo Bold T16 SPECT/CT system (clinical)

| | |
|---|---|
| Collimator | MEGP & HEGP |
| Crystal thickness | 3/8” |

## Molecubes γ/X-CUBE SPECT/CT system (preclinical)

| | |
|---|---|
| Collimator | LEGP |
| Crystal thickness | 3/8” |

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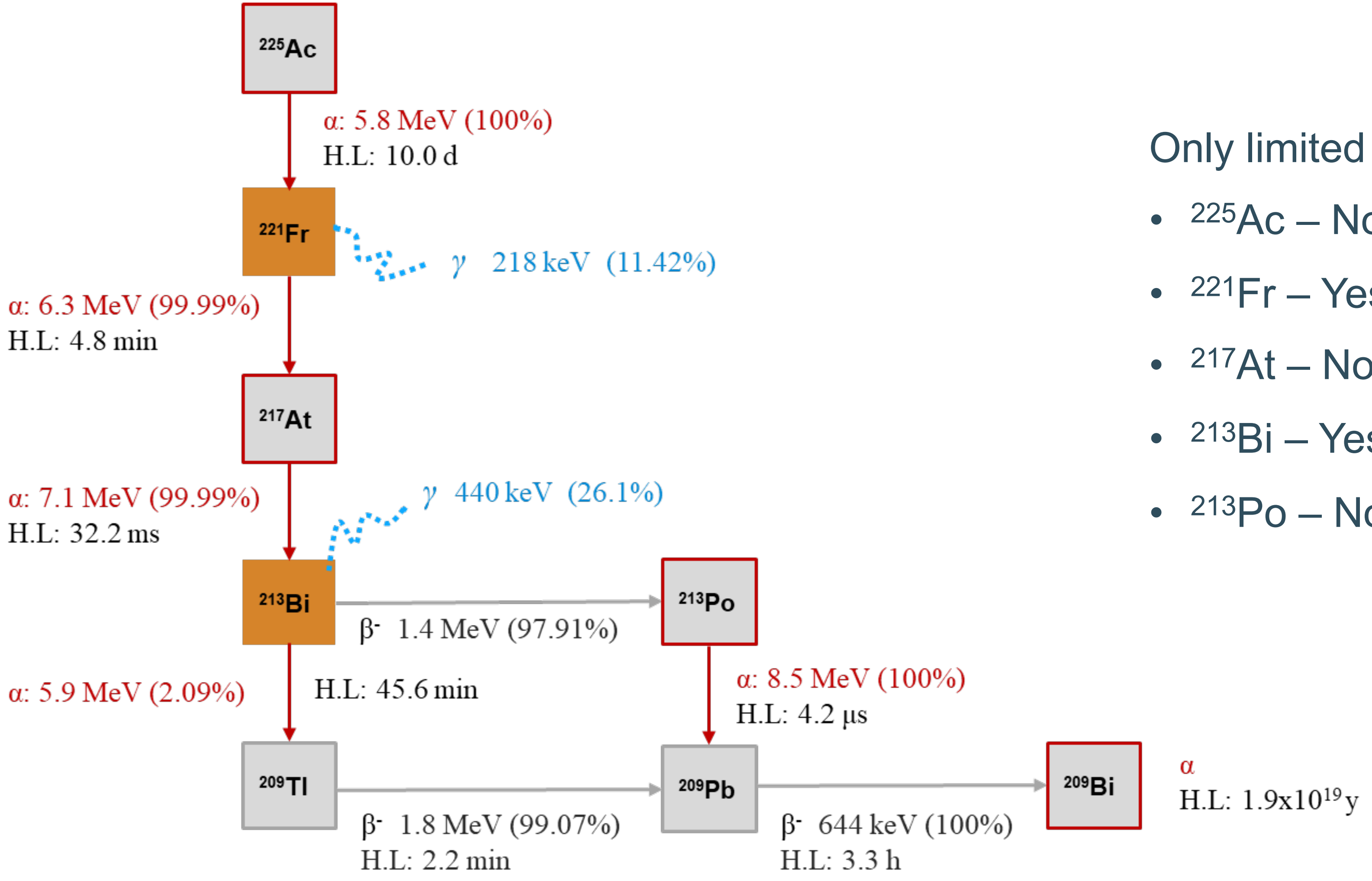


Only limited gamma-emissions in de decay chain

- $^{225}$Ac – No
- $^{221}$Fr – Yes => γ = 218 keV (11.4%)
- $^{217}$At – No
- $^{213}$Bi – Yes => γ = 440 keV (26.1%)
- $^{213}$Po – No

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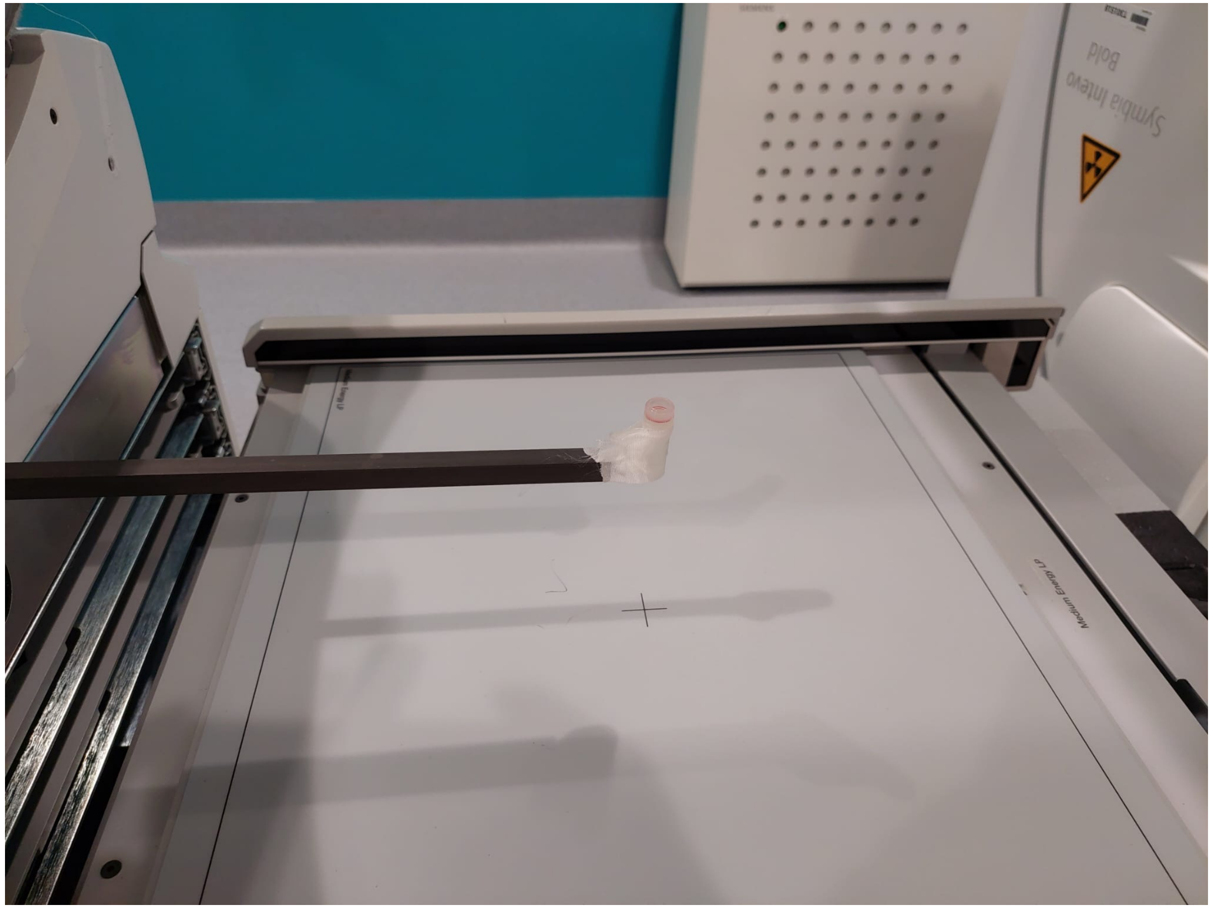
MIRaCLe ) MOLECULAR IMAGING RESEARCH AND CLINIC LEUVEN )



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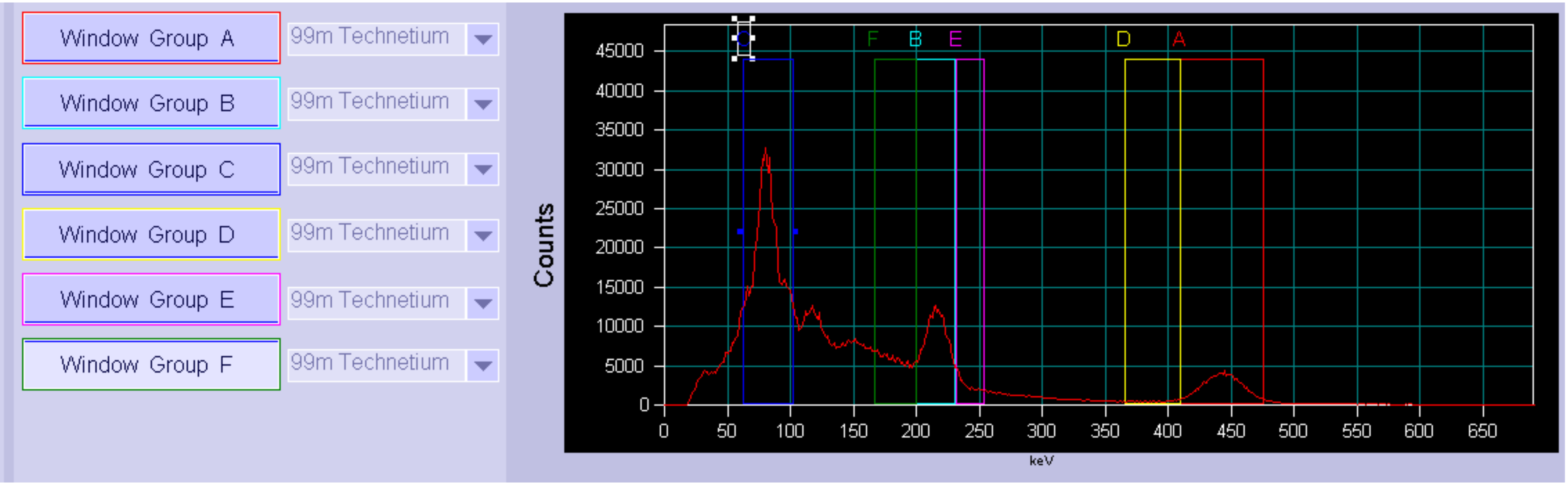


| Window Number | Center (keV) | Width (%) | Shift (%) | Type | Parent |
|---|---|---|---|---|---|
| A1 | 440 | 15 | 0 | Photopeak | |
| B2 | 217 | 15 | 0 | Photopeak | |
| C3 | 80 | 50 | 0 | Photopeak | |
| D4 | | 10 | | Lower Scatter | A1 |
| E5 | | 10 | | Upper Scatter | B2 |
| F6 | | 15 | | Lower Scatter | B2 |

| Source | Activity | Time | Form | site |
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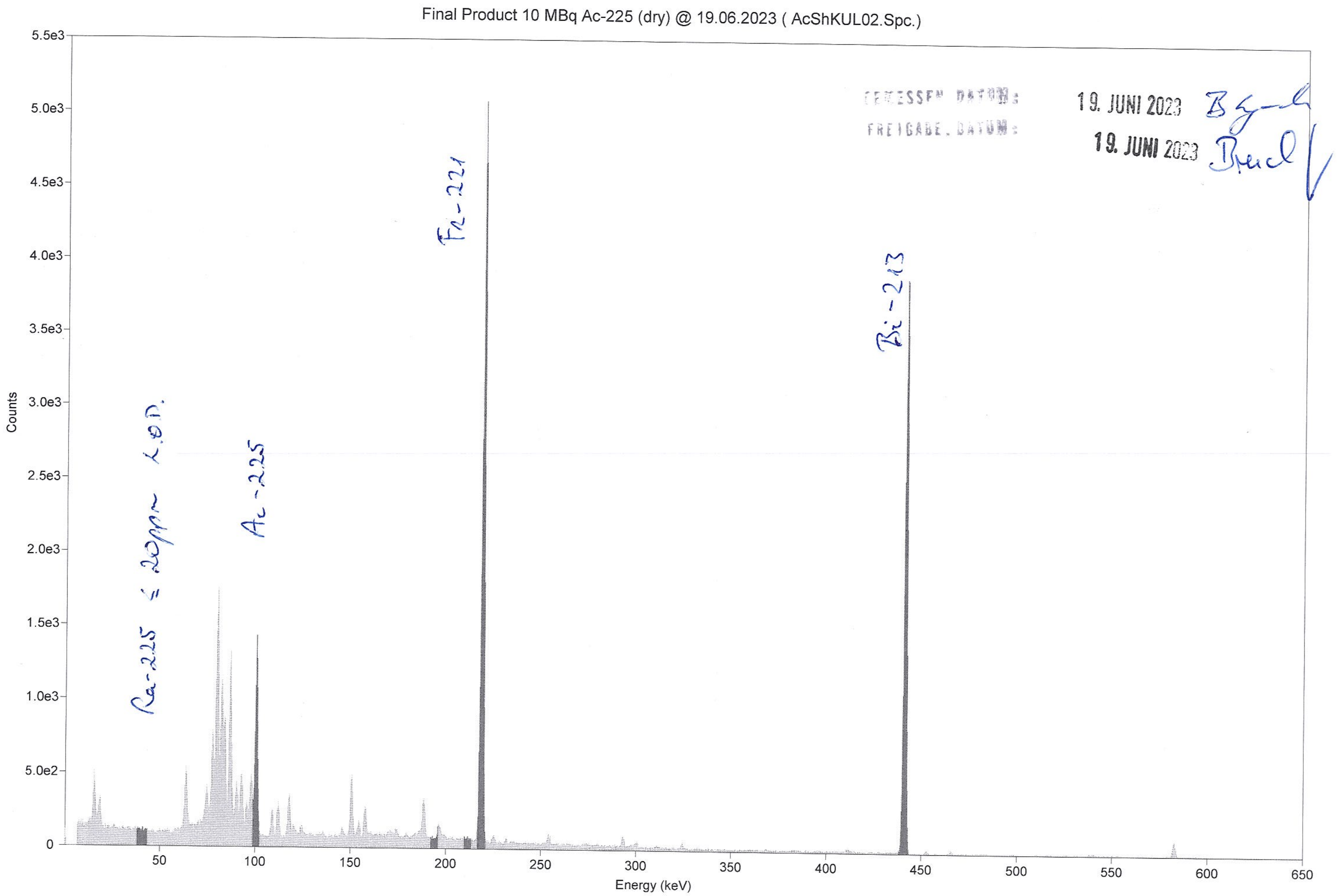

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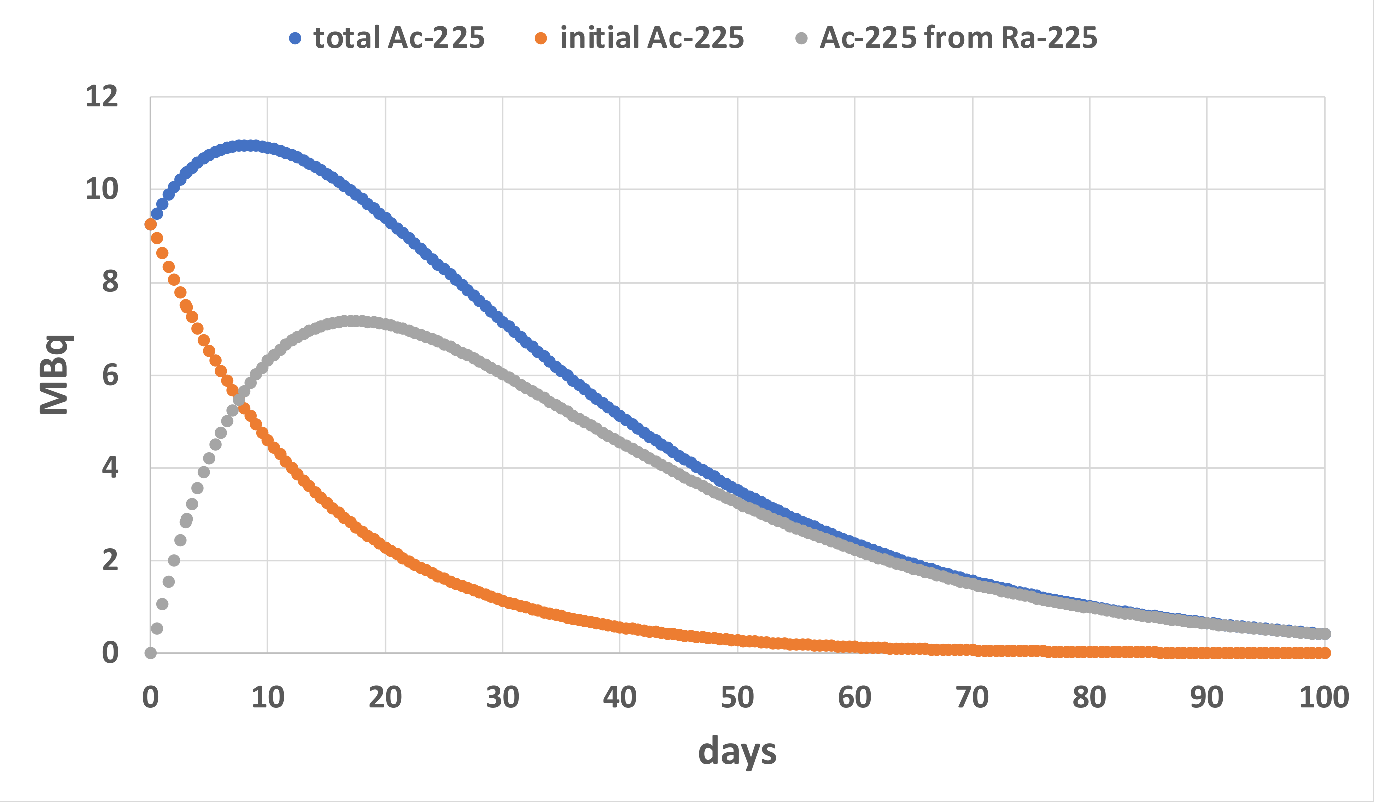



$$N_2 = \frac{\lambda_1}{\lambda_2 - \lambda_1} N_1^{\,0}\left(e^{-\lambda_1 t} - e^{-\lambda_2 t}\right) + N_2^{\,0} e^{-\lambda_2 t}$$

$$\lambda = \frac{\ln 2}{T_{1/2}} = \frac{0.693}{T_{1/2}}$$

# SPECT imaging

Source B: 7.5% residual activity

Source C: 24% residual activity

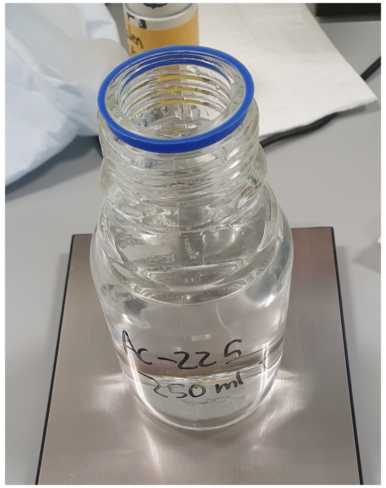
22.06.2023 @ 17h
Source B: 7.33 MBq
Source C: 7.68 MBq

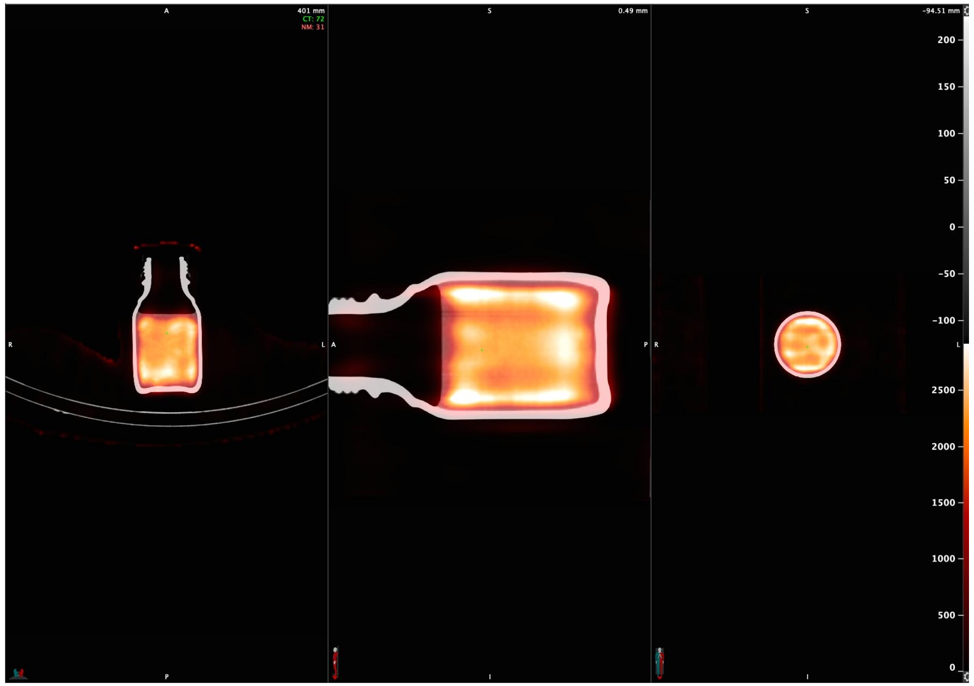
15 MBq in 250 ml volume

=> 60 kBq/ml

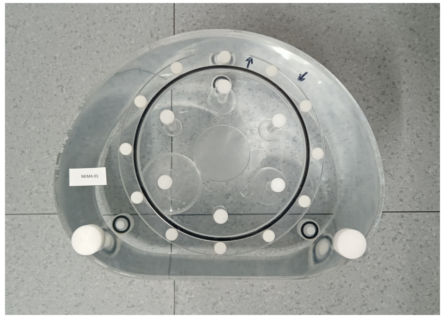
Ac-225 settings for Capintec CRC-55t

Cal # 775 with a multiplication factor of 5



# SPECT imaging



NEMA IEC PET body phantom

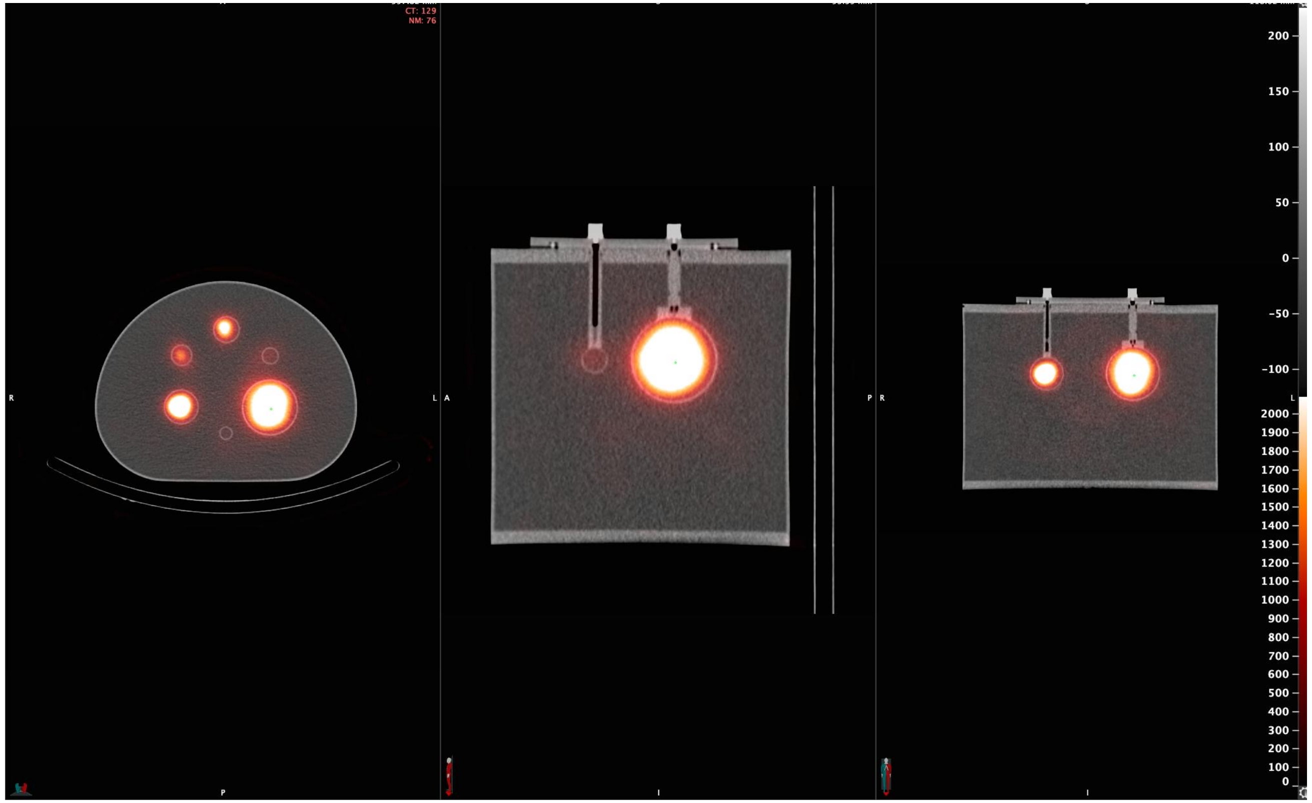
6 spheres (⌀ 13 mm, 17 mm, 22 mm, 28 mm, 37 mm and 60 mm)

Total volume 160 ml

| | Hole diameter (mm) | Septal Thickness (mm) | Hole Length (mm) |
|---|---|---|---|
| ME | 2.94 | 1.14 | 40.64 |
| HE | 3.4 | 3 | 50.8 |

| Acquisition and reconstruction parameters | |
|---|---|
| Orbit | Body contour |
| Matrix | 256 x 256 |
| Pixel size | 2.4 x 2.4 |
| # projections | 60/32 |
| Time per projection | 40 sec |
| Reconstruction | OSEM |
| Iterations/subsets | 50/2 |
| Attenuation map | CT based |
| Scatter correction | scatter windows |
| Filter | No filter |

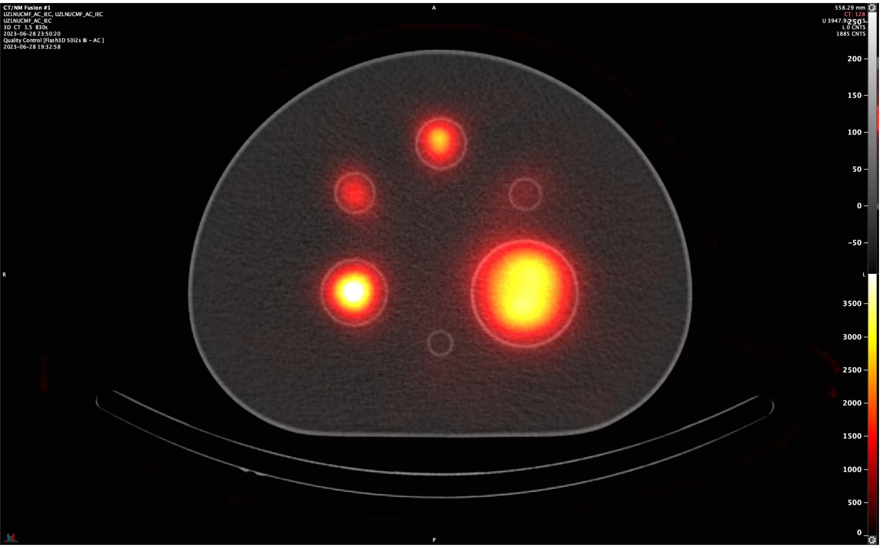
# SPECT imaging



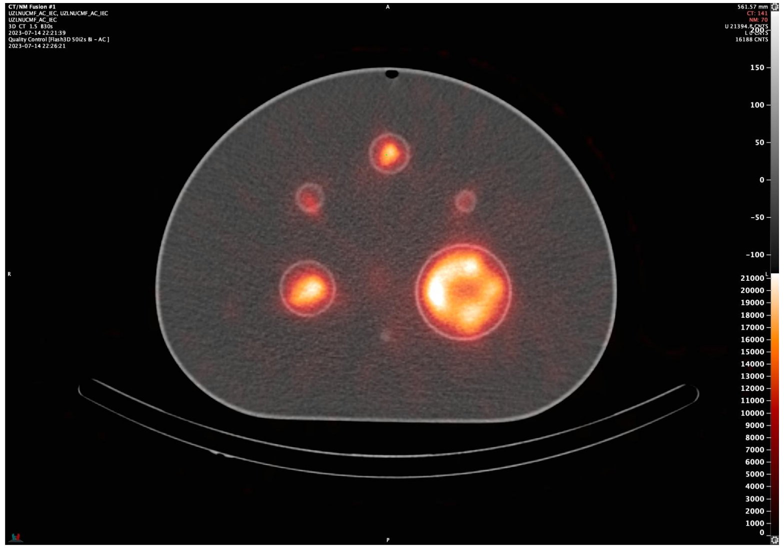

| | collimator | time per projection | # projections per head |
|---|---|---|---|
| 26/06/2023 | calibration measurements | | |
| 28/06/2023 | HE | 40 | 60 |
| 28/06/2023 | HE | 40 | 32 |
| 14/07/2023 | HE | 40 | 60 |
| 14/07/2023 | HE | 40 | 32 |
| 15/07/2023 | ME | 40 | 60 |
| 15/07/2023 | ME | 40 | 32 |
| 15/08/2023 | HE | 40 | 60 |
| 15/08/2023 | HE | 40 | 32 |
| 19/09/2023 | ME | 40 | 60 |
| 19/09/2023 | HE | 40 | 60 |

# SPECT imaging

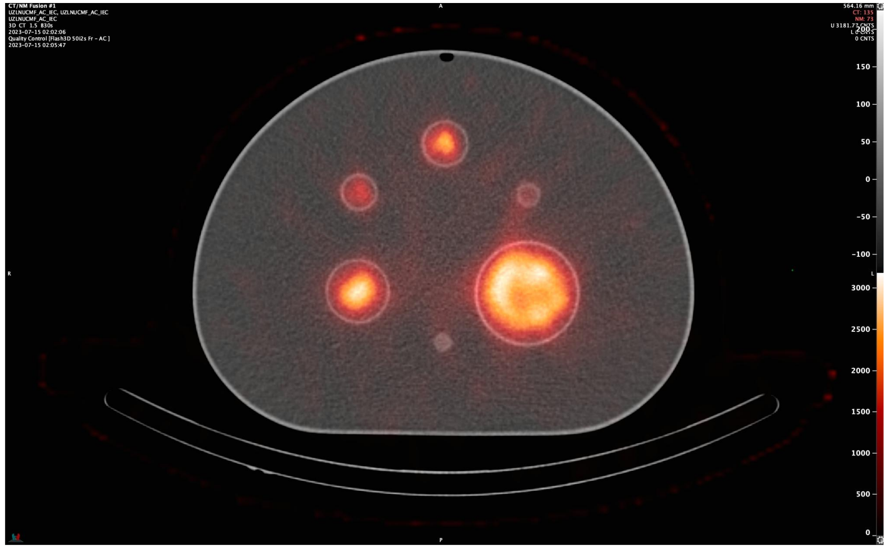
**HE 60** projections per detector head



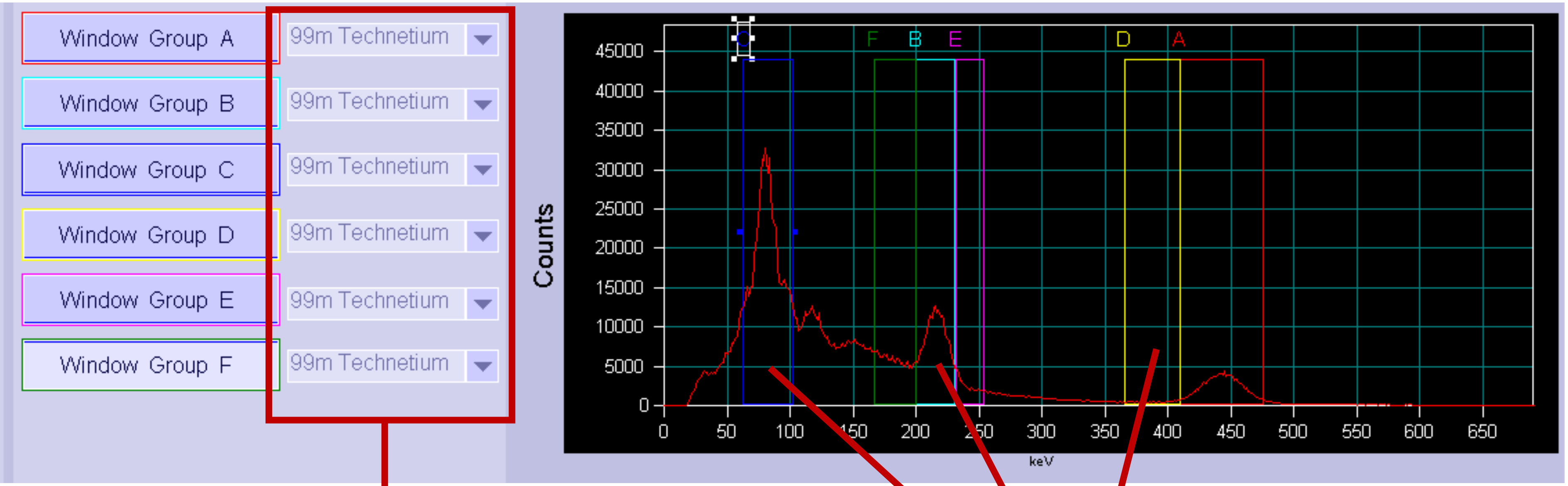
**HE 32** projections per detector head



**ME 60** projections per detector head



# To be solved?




1. Correction maps optimized for Tc-99m (specific maps not available for Bi-213 / Fr-221 / Pb X-rays)

2. Dedicated reconstructions of data acquired with the different photopeak windows (energy dependent attenuation map – scatter correction)

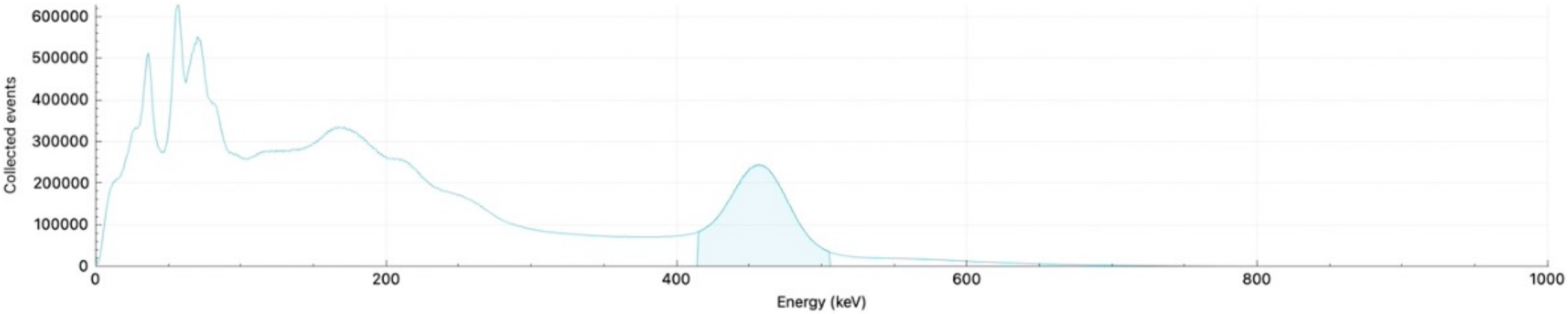
3. Confirm appropriate decay correction

# µSPECT imaging



Molecubes γ/X-CUBE SPECT/CT system

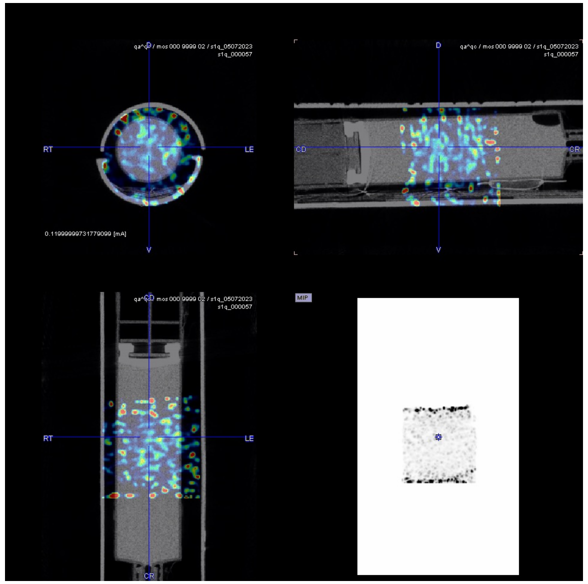
20ml syringe filled with 19.73 ml Ac-225 solution and scanned on the Molecubes γ-cube
Data were reconstructed with a voxel size of 500µm using MLEM/30 iterations with an energy window centred on 460keV ± 10%



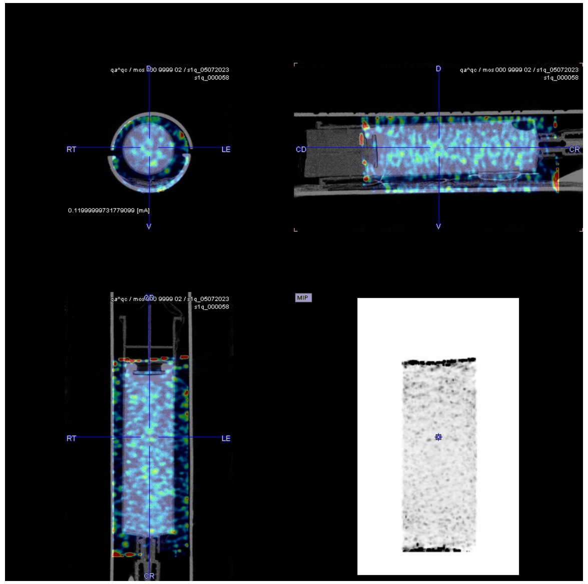
# µSPECT imaging



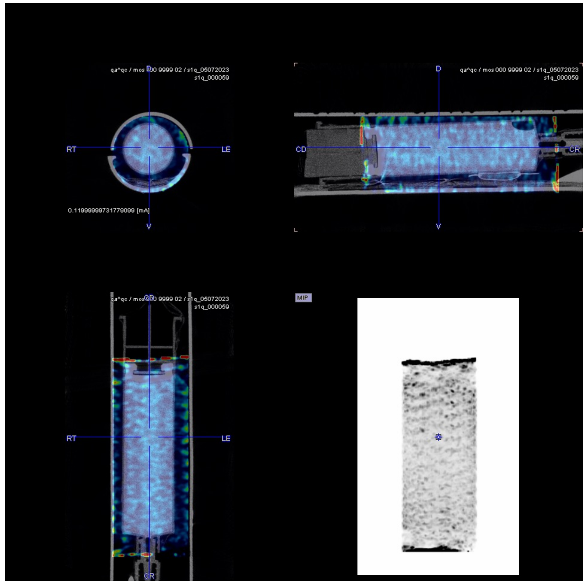
5 min 'test' scan
(short FOV of 1cm)



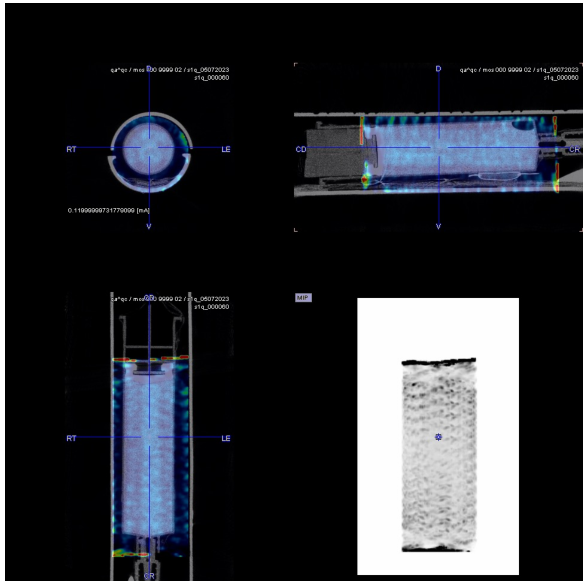
1 hour scan
(3cm FOV)



4 hour scan
(3cm FOV)



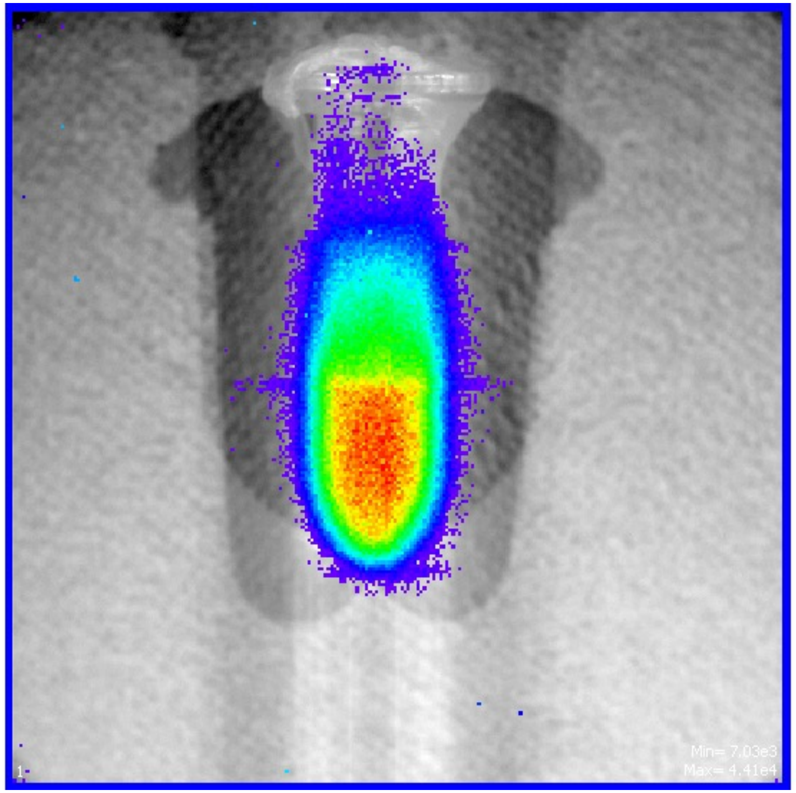
16 hour scan
(3cm FOV)



# µSPECT imaging

## Cerenkov Imaging as alternative

Eppendorf with 5 min exp




## Perkin Elmer IVIS Spectrum

# To conclude

- Radionuclide calibrator settings for Ac-225 confirmed
- Series of image quality measurements with the clinical SPECT system with some reconstruction issues still open (under discussion with Siemens)
- Preclinical SPECT system in current configuration not suitable for Ac-225 imaging <> Cerenkov imaging feasible

<> No protocol yet for gamma counter measurements with Ac-225

<> Hospital environment not very flexible for planning measurements

MEDICIS more flexible to provide Ac-225 <> clinical use of Ac-225 provided by JRC

Ac-225/Ra-225 source manageable but relying on activity measurements MEDICIS

NPL National Physical Laboratory

AlphaMet Metrology for Emerging Targeted Alpha Therapies

# AlphaMet

## A European project on metrology for emerging targeted alpha therapies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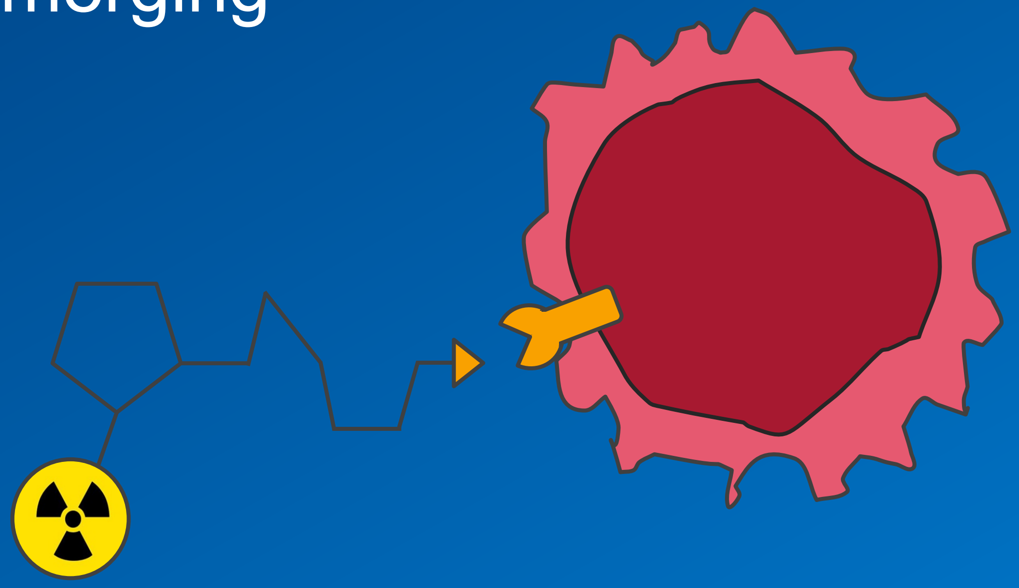
National Physical Laboratory, UK

*EFOMP Symposium on Molecular Radiotherapy Dosimetry 2023*

**AlphaMet** aims to address the unique and unmet metrological challenges of alpha emitters and support the implementation of end-to-end traceability for alpha therapies before wide routine adoption

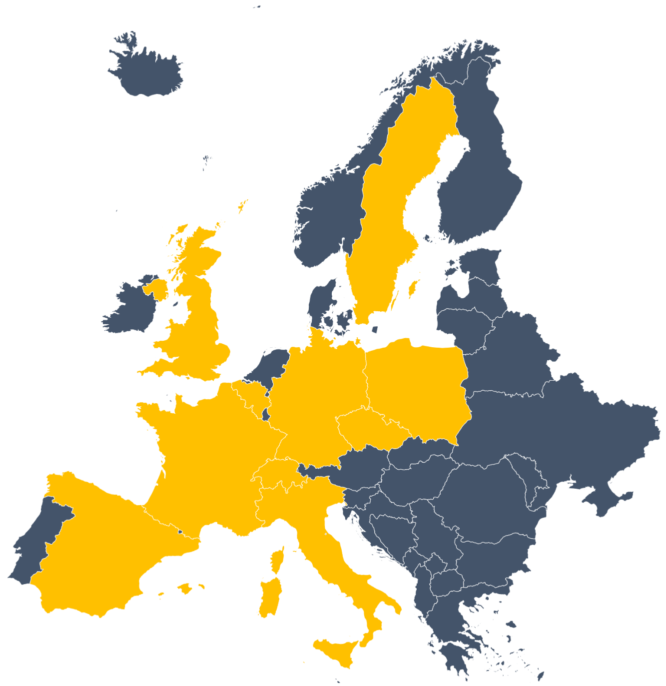
EUROPEAN PARTNERSHIP

Co-funded by the European Union

METROLOGY PARTNERSHIP

EURAMET

## Consortium



2.3M€, Sep 2023 – Aug 2026

### Eight metrology institutes (NMI/DI)

- CZECH METROLOGY INSTITUTE
- cea
- GOBIERNO DE ESPAÑA – MINISTERIO DE CIENCIA E INNOVACIÓN – Ciemat, Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas
- NPL National Physical Laboratory
- ENEA – AGENZIA NAZIONALE PER LE NUOVE TECNOLOGIE, L'ENERGIA E LO SVILUPPO ECONOMICO SOSTENIBILE
- CHUV Centre hospitalier universitaire vaudois
- SCK CEN – STUDIECENTRUM VOOR KERNENERGIE, CENTRE D'ETUDE DE L'ENERGIE NUCLEAIRE
- NATIONAL CENTRE FOR NUCLEAR RESEARCH ŚWIERK

### Eight clinical and research partners, and one affiliated entity

- LMU KLINIKUM
- BfS Bundesamt für Strahlenschutz
- KU LEUVEN
- UNIVERSITY OF GOTHENBURG
- Osakidetza
- biocruces bizkaia – osasun ikerketa institutua, instituto de investigación sanitaria
- UK Universitätsklinikum Würzburg
- NHS Royal Surrey NHS Foundation Trust
- Arronax Nantes

# WP1: Radioactivity standards

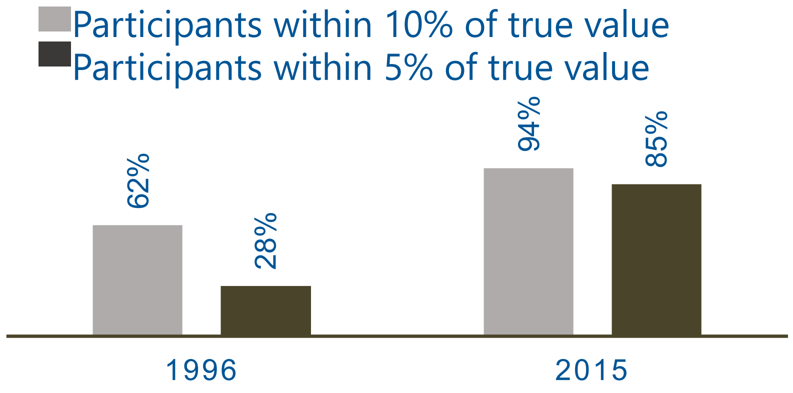
## Current State of the Art

- Revision of $^{223}Ra$ standards found that patients were being injected with 9% more activity than intended
- No fully validated standards available for other α-emitters
- Recommended administered activity accuracies < ±5%, however, how well can user measure alpha emitters?

## Beyond State of the Art

- Development and dissemination of standards for $^{225}Ac$, $^{212}Pb$ and $^{211}At$ at multiple institutes
- Intercomparison of activity measurement capabilities in preclinical centres and hospitals to assess user needs ($^{225}Ac$)

Potential improvements in activity measurement capabilities (e.g. $^{123}I$)




Ferreira *et al*, *ARI* (2016)

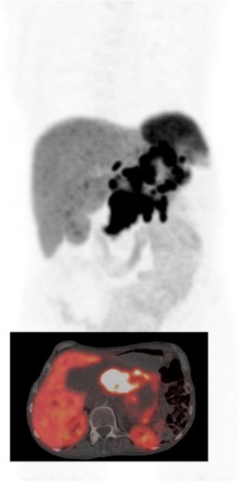
# WP2: In-vivo activity quantification

NPL
National Physical Laboratory

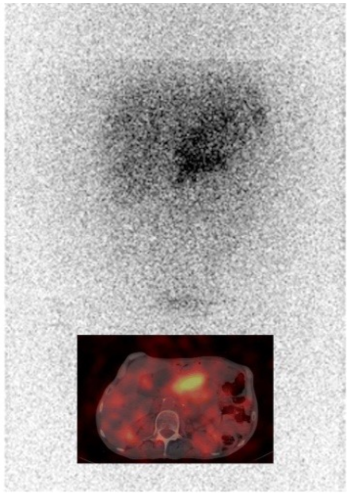
## Current State of the Art

- 3D quantitative SPECT (QSPECT) imaging is not well established for α-emitters, but is essential for post-treatment verification (BSS)
- Progeny in-growth, low activities ➔ low counts, poor resolution
- Unknown accuracy, reproducibility and uncertainties

SPECT



$^{68}$Ga-DOTATATE



$^{225}$Ac-DOTATATE

## Beyond State of the Art

- Assess feasibility/practicality of QSPECT for α-emitters (calibration, limits of detectability, quality control)
- Improve QSPECT with advanced processing techniques:
  - *In-silico models for optimisation and generation of ground truth reference data*
  - *Reconstruction algorithms*
- Harmonisation of α-QSPECT imaging ➔ international multi-centre comparison exercise