

First in vivo imaging of ^{225}Ac -labelled compounds with the supercluster collimator

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Introduction

Theranostics is an emerging medical field using radiopharmaceuticals for both imaging and targeted radiation therapy. This approach enables personalized treatment, monitoring disease response while minimizing harm to healthy tissues. It holds great promise in oncology by tailoring therapies to individual tumor characteristics ⁽¹⁾.

The success of **LUTATHERA** (^{177}Lu -DOTATATE) and **PSMA-targeting agents** in treating neuroendocrine and prostate tumors has driven new developments and a surge in clinical trials ⁽²⁾. This has increased the demand for radiopharmaceutical production, putting pressure on companies and institutions to deliver effective drugs.

The choice of radiopharmaceutical emissions is crucial for effective imaging and treatment. Gamma and positron emitters (e.g., $^{99\text{m}}\text{Tc}$ for SPECT, ^{18}F for PET) are used for imaging, while beta and alpha emitters are preferred for therapy ⁽³⁾. Alpha emitters offer advantages over beta emitters, with a shorter path length (50-100 μm) and high linear energy transfer (80 keV/ μm), enabling precise tumor targeting while sparing healthy tissue. Many also emit fractional gamma rays, making them ideal for theranostics. However, preclinical doses will be limited.

MILabs' VECTor imaging system offers high sensitivity, spatial, and temporal resolution across a wide energy range. Its ability to image multiple isotopes simultaneously makes

it a leading tool for theranostic applications. Recently, a super-cluster collimator with ultra-high sensitivity (17%) and 1.1 mm resolution (measured with $^{99\text{m}}\text{Tc}$) was introduced.

Actinium-225 (^{225}Ac) is of great interest, but its low administered doses pose challenges for theranostic development, particularly in tracking its biodistribution ⁽⁴⁾. ^{225}Ac has a 9.9-day half-life and decays into six short-lived daughters, including ^{221}Fr (4.8 min, 218 keV gamma) and ^{213}Bi (45.6 min, 411 keV gamma), both suitable for imaging ⁽⁵⁾.

This white paper evaluates the super-cluster collimator's high sensitivity in imaging ^{225}Ac , using phantoms and low-dose in vivo animal scans.

Materials and Methods

Phantom studies were conducted to evaluate collimator resolution. A hot rod phantom (Phantech, Madison, WI, USA) containing rods of variable diameter sizes (1.0, 1.2, 1.4, 1.6, 1.8, and 2.0 mm) was used. The phantom was filled with 270 kBq ^{225}Ac and scanned using the following parameters: spiral scan mode, one frame, and a total scan time of 3 hours. Image reconstruction was performed for the two separate photopeaks representing ^{221}Fr and ^{213}Bi using the SROSEM algorithm (MILabs, Houten, The Netherlands) with 50 iterations, 0.8 mm voxel size and a 1.1 mm Gaussian filter.

All animal studies were conducted under the protocol approved by the University of Wisconsin Institutional Animal Care and Use Committee. *In vivo* imaging was performed using preclinical high-energy SPECT/CT (MILabs, The Netherlands). Tumour-bearing mice (both hind legs) were injected with 74 KBq of ^{225}Ac -labelled targeting ligand and scanned for 50 minutes at 24 hours post-injection. All images were reconstructed using SROSEM algorithm with 25 iterations at 0.8 mm voxel size and a 4 mm Gaussian post-filter. Image visualisation was performed using Pmod software version 4.4 (Pmod Technologies, Bruker).

Results

Figure 1 shows images of the resolution phantom. A resolution of 1.4 and 1.6 mm was achieved for the 218 and 440 keV photopeak, respectively. A schematic drawing of the phantom and the rod sizes is presented below.

In vivo images (Figure 2) demonstrated visible uptake of the ^{225}Ac -labelled compound at the tumour site for both the 218 keV and 440 keV photopeaks observed 24 hours post-injection.

Slight differences are evident between the two images, with the kidneys being the primary distinction for the 218 keV photos and a more pronounced intestinal uptake for the 440 keV.

Conclusion

This is the first *in vivo* imaging report of ^{225}Ac in live animals using a preclinical SPECT scanner, demonstrating its detection at extremely low doses. The enhanced sensitivity of the new high-energy supercluster collimator enables imaging of small injected activities, expanding theranostic possibilities.

Previous phantom studies with the VECTor system and various collimators showed simultaneous imaging of ^{221}Fr and ^{213}Bi from the ^{225}Ac decay chain. However, those studies used higher activities, whereas this study improves visualization of the pharmacokinetics of these challenging isotopes at lower doses.

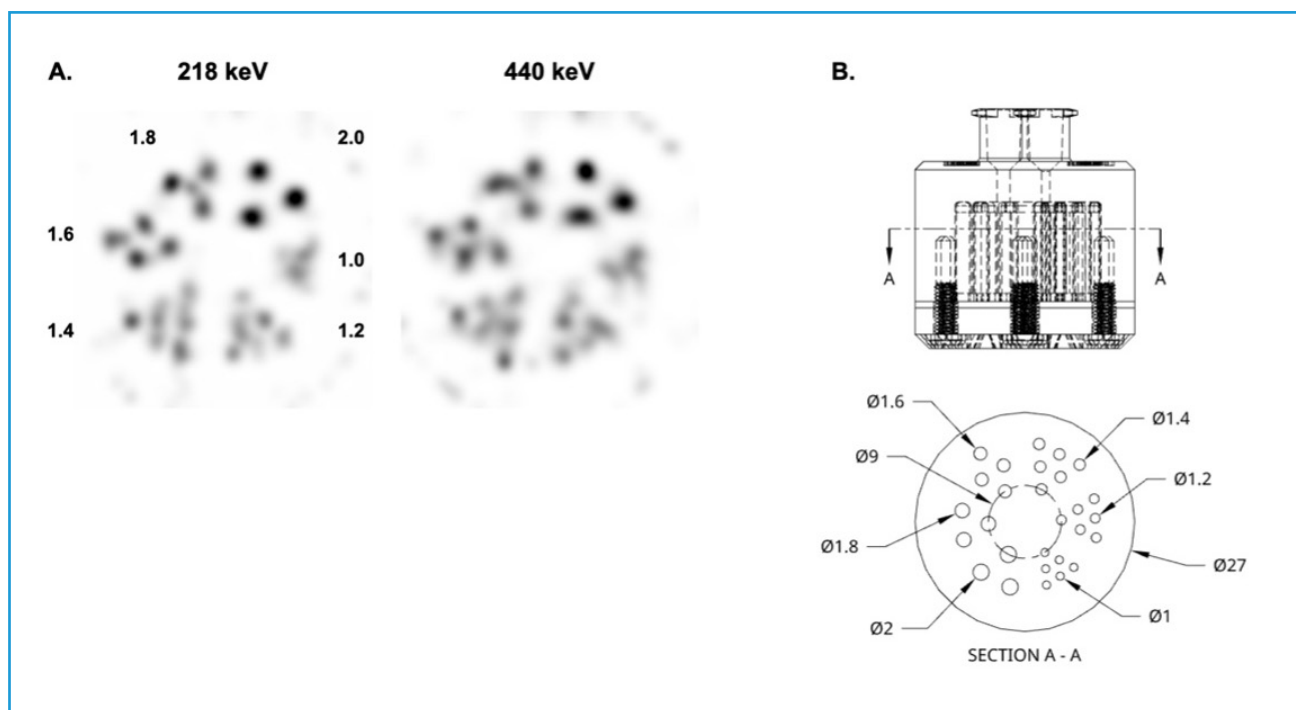


Figure 1. A. Resolution phantom using the 218 keV and 440 keV photopeaks, representing ^{221}Fr and ^{213}Bi , respectively B. Schematic representation of the phantom used.

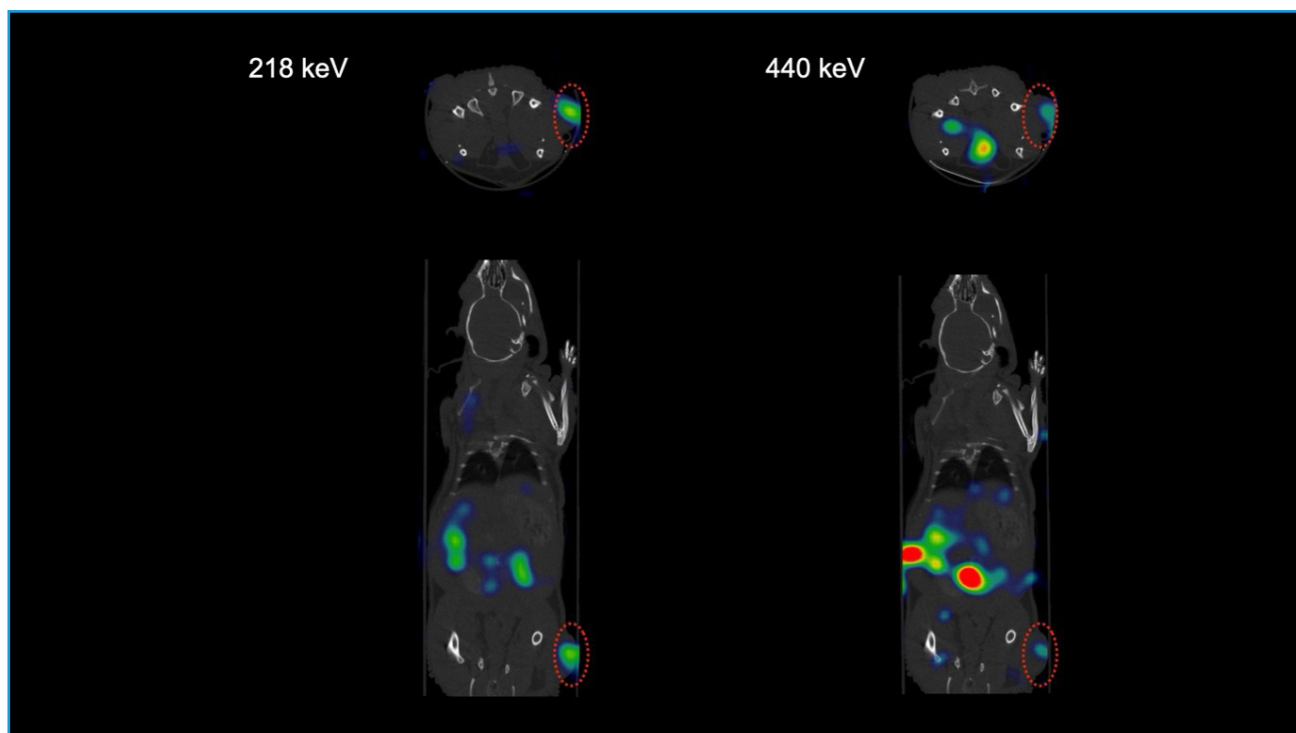


Figure 2. SPECT/CT images of in vivo biodistribution of ^{225}Ac -labelled compounds 24h post-injection.

References

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