In Vivo Study of Total-Body Kinetics of Ac-225 and Its Daughters in Mouse Using a CZT-based Small Animal SPECT-CT System

Xuhan Luo[1], Can Yang[2], Zhonghua Ouyang[2], Anupriya Chhabra[1], Zhi Li[1], Robert Hobbs[1], Ling-Jian Meng[3], and Yong Du[1]

[1]Johns Hopkins University School of Medicine, Baltimore, MD, United States

[2]MH3D Inc, Ann Arbor, MI, United States

[3]University of Illinois Urbana-Champaign, Urbana, IL, United States

Introduction

- Alpha-emitter radiopharmaceutical therapy (αRPT) has shown great promise for targeted cancer treatment but requires accurate in vivo quantification of radionuclide biodistribution.
- Imaging Ac-225 and its daughter radionuclides is challenging because of their multiple photon emissions and low photon abundance.
- Conventional preclinical SPECT systems have limited energy resolution for quantitative imaging of alpha emitters.
- A CZT-based small-animal SPECT-CT system provides improved energy discrimination together with CT anatomical localization for quantitative imaging.

Objectives

- Evaluate a CZT-based small-animal SPECT-CT system for multi-time-point imaging of Ac-225 and its daughter radionuclides.
- Demonstrate the feasibility of quantitative kinetic imaging for preclinical αRPT studies.

Materials and Methods

Dataset:

- Ac-225 labeled antibody (4 μCi) is injected in mouse intravenously.
- SPECT images were acquired for 60 minutes with a projection bin size of 1mm × 1mm and reconstructed using OSEM with 25 iterations and 8 subsets.
- Multi-time-point SPECT-CT acquired at 4 h, 24 h, 48 h, and 72 h post-injection.

Quantitative Analysis:

- Performed VOI-based measurement of organ activity concentration using reconstructed SPECT-CT images.
- Evaluated temporal changes in activity concentration and organ-specific biodistribution across imaging time points (Figures 2 and 3).

Results

Figure 1. Alpha-SPECT-CT Mini system.

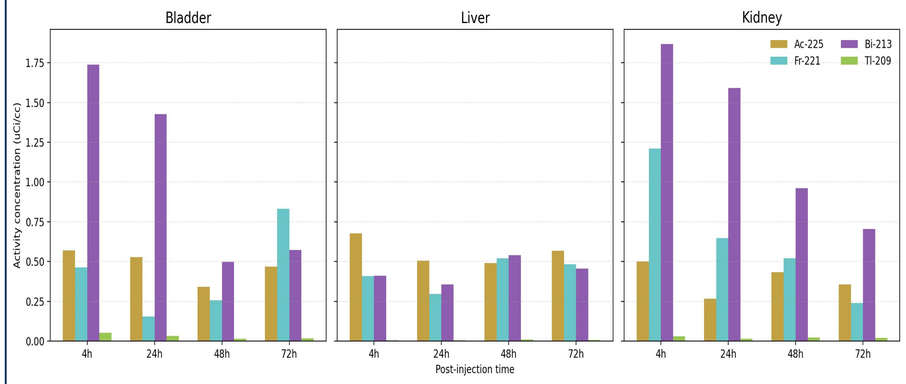

Figure 2. Organ-specific activity concentration of Ac-225 and daughter radionuclides over time

Distinct organ- and radionuclide-dependent biodistribution patterns were observed. Bi-213 showed the highest activity concentrations in the kidneys. In contrast, liver activity concentrations remained relatively stable across all radionuclides and imaging time points.

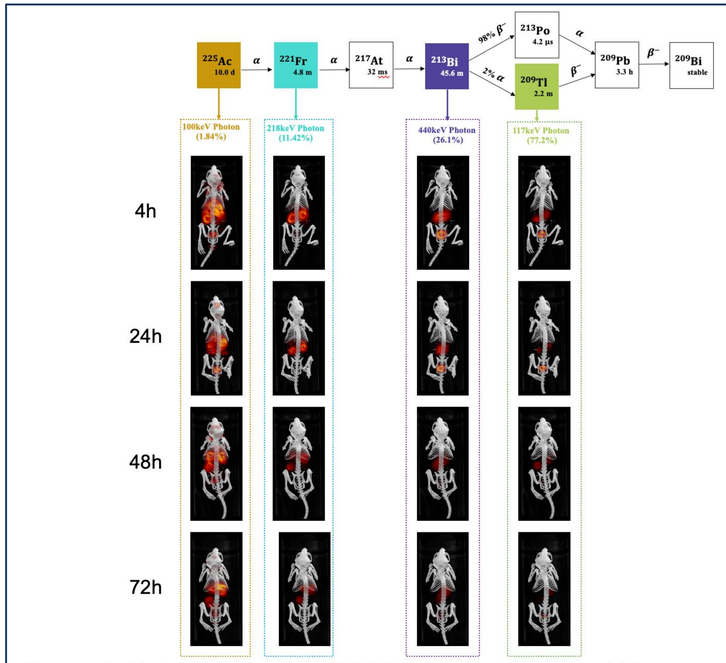

Figure 3. Multi–time-point SPECT-CT imaging of Ac-225 demonstrating organ-specific radionuclide distribution and washout

Serial SPECT-CT images acquired at 4h, 24h, 48h, and 72h post-injection, revealing organ-specific photon distributions arising from Ac-225 and different daughters. CT-based co-registration enabled organ-specific localization of SPECT activity, supporting qualitative evaluation of tracer clearance kinetics over time.

Conclusion

- **The CZT-based small-animal SPECT-CT system enabled quantitative multi-time-point imaging of Ac-225 and its daughter radionuclides.**
- **Bladder activity concentrations exhibited marked radionuclide-dependent differences, with Tl-209 and Bi-213 showing substantially higher early activity concentrations than Ac-225 and Fr-221.**
- **Bi-213 showed the highest activity concentrations in the kidneys**
- **Liver activity concentrations remained relatively similar for all radionuclides with only minor temporal variation.**