Title: Performance assessment of quantitative preclinical SPECT imaging with ^{155}Tb and ^{161}Tb

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Introduction: Element-equivalent matched theranostic pairs provide accurate biodistribution and dosimetry estimates, and this quantitative pharmacokinetic information is essential in optimizing preclinical radiopharmaceuticals. Terbium isotopes have great potential for acting as element-equivalent matched theranostic pairs for many novel radiopharmaceutical applications. ^{155}Tb ($t_{1/2}$=5.32 d, 100% EC) and ^{161}Tb ($t_{1/2}$=6.89 d, 100% beta-decay) have been proposed as a theranostic pair for their applications in single photon emission computed tomography (SPECT) imaging and targeted beta therapy, respectively. We aimed to assess the performance of Tb-based quantitative SPECT imaging for applications in the development of preclinical radiopharmaceuticals.

Methods: ^{155}Tb was produced at TRIUMF (Vancouver, Canada) with its isotope separation on-line (ISOL) facility by a mass-separated ion beam of spallation products resulting from 480 MeV proton irradiation of a tantalum target. ^{161}Tb was produced at SCK CEN (Mol, Belgium) with its BR2 reactor by neutron irradiation of an enriched gadolinium target. A hot rod resolution phantom with thin rod clusters with diameters ranging from 0.85 to 1.70 mm was filled with 20 MBq/mL of either ^{155}Tb or ^{161}Tb. To establish the performance of Tb-based imaging, phantoms were scanned with the VECTor microSPECT/CT (MILabs, Netherlands). Scanning performance was evaluated with two collimators: a high-energy ultra-high resolution (HEUHR) collimator and an extra ultra-high sensitivity (UHS) collimator. A pixel-based ordered subset expectation maximization iterative reconstruction algorithm (16 subsets, 6 iterations) was used to reconstruct the images. Images were reconstructed from photopeaks at 44.0 keV for ^{155}Tb and 48.9 keV for ^{161}Tb. SPECT images were corrected for scatter by the triple energy window method and for attenuation by CT image co-registration. Quantitative SPECT images were obtained via calibration factors determined through activity point source phantoms for each collimator and isotope combination. Quantitative SPECT images of the resolution phantoms were analyzed to report inter-rod contrast, recovery coefficients, and contrast-to-noise metrics.

Results: Quantitative SPECT images of the resolution phantom are presented here. The HEUHR collimator clearly resolved all rods in both the ^{155}Tb and ^{161}Tb images. However, the UHS collimator was only able to resolve rods ≥1.30 mm for ^{155}Tb and ≥1.10 mm for ^{161}Tb. From both the ^{155}Tb and ^{161}Tb SPECT images, quantitative accuracy was better maintained with the HEUHR collimator than the UHS collimator, with recovery coefficients up to 81%. Further, when SPECT images were reconstructed with reduced counts, the HEUHR collimator conserved the resolution of the imaging system. Contrast-to-noise also performed better with the HEUHR collimator.

Conclusions: Overall, both ^{155}Tb and ^{161}Tb show promise as imageable isotopes with quantitative SPECT. ^{155}Tb is a stronger candidate for diagnostic applications due to its decay characteristics while ^{161}Tb could provide treatment verification via SPECT imaging of its gamma emissions. The HEUHR collimator was able to achieve resolution <0.85mm and maintain quantitative accuracy in small objects which is critical for assessing biodistribution and estimating dosimetry in preclinical Tb-radiopharmaceuticals for *in vivo* animal tumour models.

Acknowledgments: This study was financially supported by the NSERC Discovery Grant RGPIN-2021–04093. TRIUMF receives federal funding via a contribution agreement with the National Research Council of Canada.

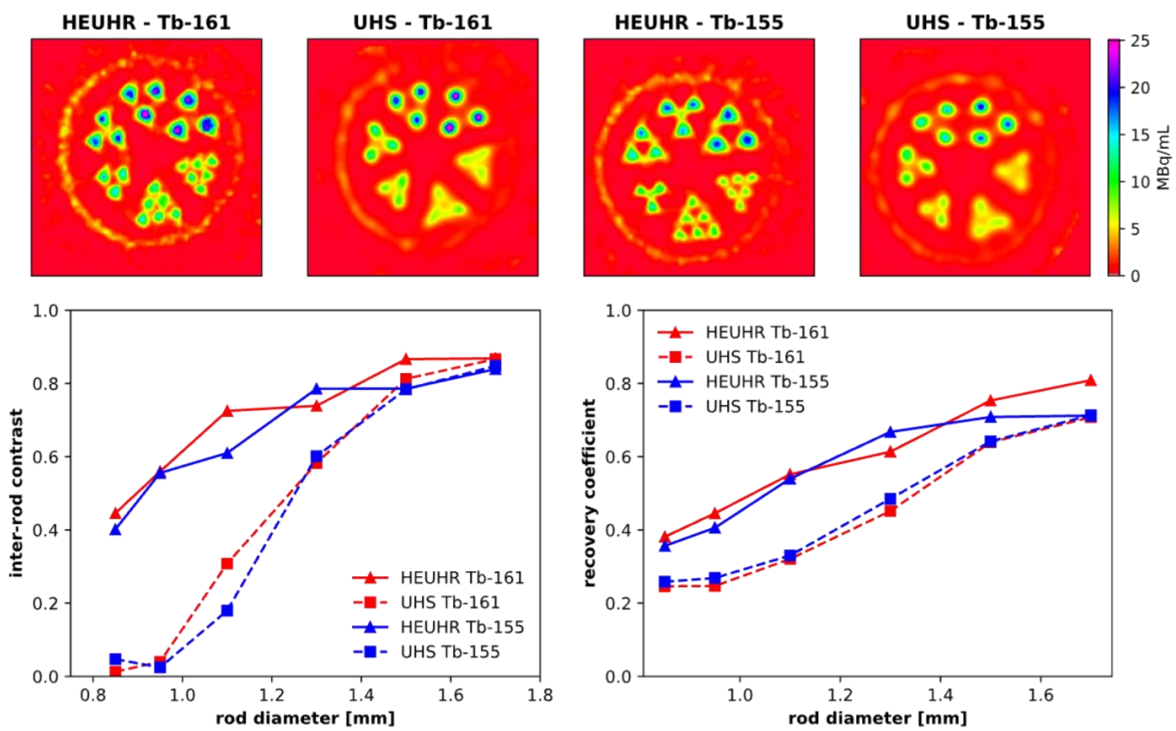

Figure 1: (*top*) Quantitative SPECT images of resolution hot rod phantom filled with ^{155}Tb or ^{161}Tb (20 MBq/mL), scanned with the HEUHR and UHS collimators. (*left*) Inter-rod contrast measurements and (*right*) recovery coefficients for each isotope and collimator combination.