PhD Thesis title: 'Imaging neutron activated Sm-153 oral dose forms in the gastrointestinal tract'

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ABSTRACT:

Samarium-153 (^{153}Sm) is a radionuclide that decays with a physical half-life of 46.3 h by emitting several beta [E_{max} = 632 (34%), 702 (44%), 805 (21%) keV] and gamma radiations [E_{max} = 70 (5%), 97 (1%), 103 (28%) keV]. In the last two decades, ^{153}Sm has been used as both a radiotracer for pharmacoscintigraphic studies and a therapeutic radionuclide in bone metastasis. This thesis investigated the use of ^{153}Sm as a tracer for imaging in oral drug delivery and clinical diagnostics of the gastrointestinal (GI) transit.

The physical and imaging characteristics as well as the production of ^{153}Sm were initially investigated. A protocol for the production of ^{153}Sm by thermal neutron activation in a nuclear research reactor (TRIGA Mark II) was established, and the factors affecting the activity produced were identified. The imaging quality of ^{153}Sm was compared to the commonly used radionuclides ^{99m}Tc and ^{111}In demonstrating comparable image quality.

A clinical trial of oral drug delivery to validate the use of imaging as a surrogate method of drug release and as a mean of assessing the *in vivo* imaging characteristics of ^{153}Sm was carried out. This followed *in vitro* validation of the drug dissolution and ^{153}Sm release, where healthy volunteers were studied using six different targeted release formulations. 62 courses of imaging completed by 23 healthy volunteers (11

females, 12 males, aged 55 ± 8 years) showed that ^{153}Sm was an excellent radiotracer for visualization of the behavior of oral dose forms in the GI tract.

For whole GI transit investigation, enteric-coated gelatine capsules filled with neutron activated Amberlite^{TM} IR120 (H^+) cation-exchange resins labeled with $^{152}Sm_2O_3$ were subsequently developed. After *in vitro* validation, the first human studies carried out in 10 healthy volunteers (6 females, 4 males, aged 33 ± 13 years). Additional MR imaging for SPECT-MR image fusion was also performed to verify diagnostic outcomes. Blood and urine samples were collected during the study to ensure non-absorption of free ^{153}Sm into the body fluid and plasma.

Finally, internal radiation dosimetry of ^{153}Sm was assessed theoretically using the MIRD methods and the standard ICRP 30 GI model. The effective dose from 5 MBq administered ^{153}Sm (1.060 mSv for female; 0.986 mSv for male) was about 2.5 times higher than that from the ^{111}In. This compared favourably to an estimated total dose of 20 mSv for the use of radio-opaque markers with multiple X-ray exposures.

In conclusion, due to the greater global availability, minimal radiation exposure to radiopharmacy personnel and possibility of batch manufacture and storage prior to neutron activation, ^{153}Sm appears to be a valuable alternative radionuclide to ^{111}In for the assessment of GI motility and transit.

References to author publications that relate specifically to the dissertation:

1. C. H. Yeong, B. J. J. Abdullah, K. H. Ng, L. Y. Chung, K. L. Goh, S. A. Sarji, A. C. Perkins, "Production and first use of $^{153}SmCl_3$-ion-exchange resin capsule formulation for assessing gastrointestinal motility," Appl Radiat Isot **70**, 450–455 (2012).
2. C. H. Yeong, B. J. J. Abdullah, , K. H. Ng, L. Y. Chung, K. L. Goh, S. A. Sarji, A. C. Perkins, "Neutron activated ^{153}Sm-ion-exchange resin as a tracer for gastrointestinal scintigraphy," Nucl Med Comm **32**(12), 1256-1260 (2011).
3. C. H. Yeong, P. E. Blackshaw, K. H. Ng, B. J. J. Abdullah, M. Blaauw, R. J. Dansereau, A. C. Perkins, "Reproducibility of neutron activated Sm-153 oral dose formulations intended for human administration," Appl Radiat Isot **69**(9), 1181-1184 (2011).