Title: *In vivo* actinium-226 SPECT imaging for preclinical theranostic radiopharmaceutical development

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Introduction:
^{225}Ac-radiopharmaceuticals have tremendous potential for targeted alpha therapy, however, ^{225}Ac ($t_{1/2}$=9.9d) lacks a direct gamma emission for imaging. ^{226}Ac ($t_{1/2}$=29h) is a promising element-equivalent radionuclide for preclinical evaluation of ^{225}Ac-radiopharmaceuticals. ^{226}Ac has two gamma emissions (158keV and 230keV) ideal for SPECT imaging and four alpha emissions from the decay of its progeny ^{226}Th ($t_{1/2}$=30.6m), providing applications as both a diagnostic and therapeutic isotope. This work is the first feasibility study for ^{226}Ac SPECT imaging *in vivo* and validation of preclinical biodistribution and dosimetry estimates for ^{225}Ac-radiopharmaceutical development.

Methods:
^{226}Ac was produced at TRIUMF (Vancouver, Canada) with its Isotope Separator and Accelerator (ISAC) facility. ^{226}Ac-TATE was radiolabelled with TATE from a preclinical radiopharmaceutical developed for ^{225}Ac-therapy targeting neuroendocrine tumours (NET). Mice with AR42J tumour xenografts were injected with 2MBq of ^{226}Ac-TATE and scanned at 1h, 2.5h, 5h, and 24h post injection with the VECTor microSPECT/CT (MILabs, Netherlands) using an extra ultra-high sensitivity collimator. Quantitative SPECT images were reconstructed including attenuation and scatter corrections. Image-based ^{226}Ac activity measurements were assessed from volumes of interest within tumours and organs. Imaging data was compared with *ex vivo* biodistributions via gamma counter measurements. *S*-values for the ^{225}Ac and ^{226}Ac decay chains were derived from Monte Carlo simulations. Dosimetry estimates were calculated from image-based time activity curves (TAC).

Results:
In vivo quantitative SPECT images of ^{226}Ac activity distribution were demonstrated, to the best of our knowledge, for the first time. Image-based activity measurements in the tumours matched with *ex vivo* biodistribution within 8%. Kidney and bladder activity measurements were also in agreement. TACs were fit individually to each animal, allowing personalized dosimetry estimates.

Conclusions:
We have established the ability of ^{226}Ac quantitative SPECT imaging to accurately determine actinium biodistribution with an *in vivo* tumour model. Future work will compare the pharmacokinetics of imageable ^{226}Ac-radiopharmaceuticals with matched therapeutic ^{225}Ac-radiopharmaceuticals.