[68Ga]Ga-THP-Pam: A PET radiotracer for imaging vascular calcification

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**Introduction**

[68Ga]Ga-THP-Pam was previously demonstrated to have high affinity towards a number of calcium salts while [18F]NaF, the most used PET radiotracer for bone imaging has high affinity only for hydroxyapatite (the main component of bone mineral).1 We hypothesised that the broad calcium mineral affinity of [68Ga]Ga-THP-Pam may be advantageous in detection of vascular calcification (VC), where the composition of solid calcium mineral may be more varied than the composition of bone.2 We report a direct comparison of [68Ga]Ga-THP-Pam and [18F]NaF in a rat model of VC.

**Methods**

We used a model of VC in which rats were fed a diet containing warfarin and vitamin K1 along with subcutaneous administration of vitamin D3 to induce severe VC.3 Anaesthetised rats were injected with [68Ga]Ga-THP-Pam and scanned using preclinical PET/CT 60–120 min post-injection. The rats were imaged using [18F]NaF the following day. As a control study, animals fed a healthy diet were imaged using the same procedure.

**Results**

Imaging showed high uptake of [68Ga]Ga-THP-Pam and [18F]NaF (3.44 ± 0.69 and 0.91 ± 0.24 %ID respectively, p = 0.002) in a region of tissue around the stomach, with severe calcification as identified by CT. Additionally, [68Ga]Ga-THP-Pam demonstrated increased uptake in the VC group *vs.* the healthy group across several major organs, most notably in the kidneys (2.21 ± 0.76 *vs.* 0.25 ± 0.13 %ID, p = 0.002). *Ex vivo* biodistribution data confirmed the increased uptake of [68Ga]Ga-THP-Pam seen in the imaging data. The presence of calcification in the kidneys, stomach and other organs of interest was confirmed by microCT-based 3D X-ray histology and conventional histology. To visualise small areas of interest such as the aorta, we present preliminary results highlighting the potential utility of a post-reconstruction method to improve the spatial resolution of preclinical PET with gallium-68. Analysis of the mineral composition of the calcifications is ongoing.

**Conclusions**

These results demonstrate that [68Ga]Ga-THP-Pam may offer improved detection of VC in comparison to [18F]NaF, including microcalcifications undetectable by preclinical CT.

**References**

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