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Development and Preclinical Evaluation of the New Pan-Somatostatin PET Imaging Probe ^{68}Ga-DOTA-SOM230 (SOMscan®)

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Background: Imaging of somatostatin receptor (sst)-positive tumors using ^{68}Ga-labeled somatostatin analogs such as the sst2 subtype-specific ^{68}Ga-DOTA-TOC or ^{68}Ga-DOTA-TATE is current clinical standard. Analogs targeting more receptor subtypes, such as ^{68}Ga-DOTA-NOC, may improve detection of heterogeneous tumors. We aim to develop and evaluate a new ^{68}Ga-labeled PET imaging probe based on SOM230 (Pasireotide) highly affine for sst1, 2, 3 and 5.

Methods: SOM230 was conjugated to DOTA and labeled with ^{68}Ga. *In vitro* evaluation included stability studies in human serum, determination of lipophilicity, sst-subtype binding profile and internalization. *In vivo* studies were performed in sst1, 2, 3 and 5 tumor xenografts using small animal PET imaging. ^{68}Ga-DOTA-TATE and ^{68}Ga-DOTA-NOC were used as control.

Results: ^{68}Ga-DOTA-SOM230 was prepared in radiochemical purity >95% and specific activity ~50 MBq/nmol. ^{68}Ga-DOTA-SOM230 had logD = -0.93±0.15 and was highly stable in human serum up to 2 h with no metabolites determined. In *vitro* binding studies revealed high affinity for sst1, 2, 3 and 5 and internalization profiles were observed. **^{68}**Ga-DOTA-SOM230 clearly visualized sst-expressing tumors in PET images within 1 h p.i. Biodistribution studies exhibited relatively high blood pool activity (~4 %IA/g), kidney and liver uptake (~30 and 12 %IA/g, respectively) at 1 h p.i. At 2 h p.i., tumor uptake remained high while tumor-to-background ratios and image contrast were improved. The specificity of the radiotracer was confirmed with blocking experiments, in both biodistribution and PET imaging studies. ^{68}Ga-DOTA-SOM230 compares reasonably well with the control radiotracers. The sst2-tumor uptake is not significantly higher for ^{68}Ga-DOTA-TATE than for ^{68}Ga-DOTA-SOM230 (17.8±2.2 and 14.1±4.5 %IA/g, respectively, $p > 0.05$) while the uptake in sst5 is significantly higher for ^{68}Ga-DOTA-SOM230 than for ^{68}Ga-DOTA-NOC (11.4±1.3 and 7.7±1.5 %IA/g, respectively, $p < 0.05$), 1 h p.i. with similar tumor-to-background contrast.

Conclusion: The preclinical evaluation of ^{68}Ga-DOTA-SOM230 (SOMscan®) reveals its potentiality as PET imaging probe of a broad spectrum of somatostatin receptors.