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Scandium-43-DOTATATE, a Novel Positron Emission Tomography (PET) Tracer for Neuroendocrine Tumor Imaging

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BACKGROUND

Neuroendocrine tumors (NETs) represent a heterogenous group of neoplasms and their diagnosis can be challenging. In 2019, FDA approved ^{68}Gallium labeled DOTATATE PET tracer for SSTR2 overexpressing NETs, which has been widely adopted since. However, limitations of ^{68}Ga-DOTATATE have led to the development of additional radiotracers for the diagnosis of NETs. Herein we report on a novel PET tracer using 43Sc for DOTATATE labeling. ^{43}Sc provides a longer half-life when compared against ^{68}Ga and its lower positron energy provides better quality of PET imaging and less deposit of radiation into non-tumoral tissues.

METHODS

^{43}Sc production was achieved at the University of Chicago Cyclotron Facility through the ^{42}Ca(d,n)^{43}Sc reaction. The radiolabeling was done on a thermomixer at 450 rpm for 30 min at 95˚C. The crude was passed through a conditioned C18 SPE cartridge where ^{43}Sc-DOTATATE was trapped and eluted in EtOH. Cellular uptake and internalization studies were conducted using the SSTR2 overexpressing pancreatic NET cells, QGP1-SSTR2 and the parental QGP1 cells served as a negative control. *In vivo* PET/CT imaging was conducted on male nude mice bearing QGP1 and QGP1-SSTR2 tumor xenograft on the right and left forelimbs respectively. Dynamic PET acquisition started right before the injection of ^{43}Sc-DOTATATE via a tail vein catheter, and followed by CT imaging for anatomy and attenuation correction. Select tissues were collected post-imaging for biodistribution.

RESULTS

Radiolabeling efficiencies were routinely >97%. Specific activity as high as 660 µCi/nmole was achieved with >99% radiochemical purity. The highest SSTR2-QGP1 uptake of >60%AA/10^5cells was observed at pM level of ^{43}Sc-DOTATATE and ~70% of this activity was internalized. QGP1 cells showed baseline levels of ^{43}Sc-DOTATATE uptake while unlabeled DOTATATE diminished radiotracer uptake in the QGP1-SSTR2 cells. PET imaging revealed that specific uptake of ^{43}Sc-DOTATATE in QGP1-SSTR2 xenografts peaked at 1 hr after IV injection. No signal was observed in QGP1 tumors. The time-activity curve showed a clear separation between surrounding tissues and tumors starting at~30 min post-injection.

Biodistribution analyses post-injection confirmed strong tracer localization, ~30 %ID/g, in QGP1-SSTR2 tumors, with substantially lower uptake seen in both the kidneys and QGP1 tumors, 10 and 4 %ID/g, respectively.

CONCLUSIONS

Cellular uptake and internalization in SSTR2 overexpressing pNET cells are higher than those in SSTR2-deficient cells, demonstrating ^{43}Sc-DOTATATE labeling was successful with high purity and specific activity. High uptake in QGP1-SSTR2 xenografts indicates that this radiotracer is a promising novel diagnostic agent for the clinical diagnosis of NET malignancies.

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