Evaluation of the pharmacokinetic properties of ^{18}F-FC119S as an Amyloid-beta targeted PET tracer in normal mice

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To evaluate the efficacy of ^{18}F-FC119S as a positron emission tomography (PET) radiopharmaceutical for the imaging of Alzheimer's disease (AD), we observed the characteristics of drug absorption, distribution of ^{18}F-FC119S in normal mice. ^{18}F-FC119S showed rapid brain uptake and wash-out pattern in normal mice. Most organs, including the brain, ^{18}F-FC119S reached at maximum concentration within 1 min and excreted via intestine. These results indicate that ^{18}F-FC119S could be a suitable candidate for the Aβ *imaging PET tracer.*

I. Introduction

Brain PET imaging can be used for quantitative evaluation of β-amyloid (Aβ), which allows early detection of Alzheimer's disease (AD).[1] ^{18}F-FC119S has recently been developed as an Aβ imaging tracer and has demonstrated the advantages of high binding affinity to Aβ in the previous study.[2] In this study, physical characteristics of ^{18}F-FC119S such as biodistribution at pre-clinical stage were examined using a healthy mouse model.

II. Materials and Methods

II.A.1. PET imaging

PET/CT imaging of ^{18}F-FC119S was performed with normal mice (C57BL/6, n = 5) using a small animal PET scanner (nanoScan®, Mediso). The dynamic PET scanning in 3D mode was performed for 130 min with 28 frames (14 × 30 s, 3 × 60 s, 4 × 300 s, 3 × 600 s, 3 × 1200)

II.A.2. Image analysis

The dynamic PET images were coregistered with the corresponding CT image, and volumes of interest (VOI) were manually drawn over the heart, lung, liver, kidney, bone, blood, gallbladder (GB) and brain. The uptake values were expressed as percent injected dose per gram of tissue (% ID/g). Then, based on the time activity curve for each organ, the pharmacokinetic (PK) parameters was calculated (T_{max}, C_{max}, AUC, $T_{1/2}$).

III. Results and Discussion

The PET images showed that the radioactivity mainly accumulated in the brain and liver at the early phase (Figure 1A), and remained at high concentrations in the gallbladder, intestine and bladder at the late phase (Figure 1B). The $T_{1/2}$ value of ^{18}F-FC119S in the brain region was 8.7 minutes and the brain peak value was observed at approximately 1.6 min (5.4% ID/g) (Figure 1C). In literature precedents, the ideal amyloid imaging drug should have a half-life of less than 30 min in the brain area, and the peak uptake value in the brain area should be 4 % ID/g or more.[3] These findings indicated that ^{18}F-FC119S pass the brain efficiently and it showed rapid clearance property of nonspecific binding from the brain.

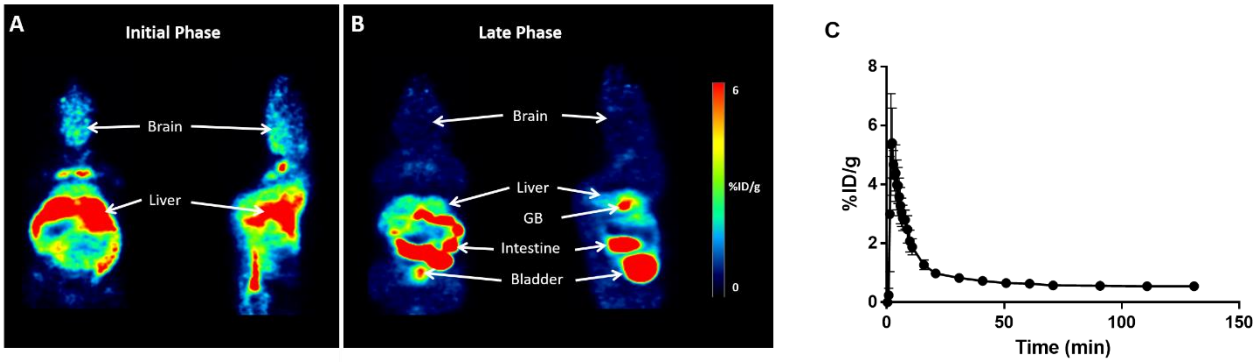

Figure 1. Whole body ^{18}F-FC119S PET images in the coronal and sagittal planes of normal mice at initial phase (0 ~ 4 min, A) and late phase (110 ~ 130 min, B). The time activity curves of ^{18}F-FC119S in whole brain for the entire 130 min PET scan (C).

II. CONCLUSIONS

Our findings showed that the advantageous pharmacokinetic characteristics and low nonspecific binding make ^{18}F-FC119S a promising PET tracer for imaging of Aβ in the mouse brain.

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REFERENCES

1. Jack, C. R. Alzheimer Disease: New Concepts on Its Neurobiology and the Clinical Role Imaging Will Play. Radiology **2012**, 263 (2), 344–361.

2. Lee, B. S.; Chu, S. Y.; Kwon, H. R.; Park, C.; Sirion, U.; Brockschnieder, D.; Dyrks, T.; Oh, S. J.; Kim, J. S.; Chi, D.Y. Synthesis and Evaluation of 6-(3-[18F]fluoro-2-Hydroxypropyl)-Substituted 2-Pyridylbenzothiophenes and 2-Pyridylbenzothiazoles as Potential PET Tracers for Imaging Abeta Plaques. Bioorganic Med. Chem. **2016**, 24 (9), 2043–2052.
3. Rominger, a; Brendel, M.; Burgold, S.; Keppler, K.; Baumann, K.; Xiong, G.; Mille, E.; Gildehaus, F. J.; Carlsen, J.; Schlichtiger, J.; Niedermoser, S.; Wangler, B.; Cumming, P.; Steiner, H.; Herms, J.; Haass, C.; Bartenstein, P. Longitudinal Assessment of Cerebral Beta-Amyloid Deposition in Mice Overexpressing Swedish Mutant Beta-Amyloid Precursor Protein Using 18F-Florbetaben PET. J Nucl Med **2013**, 54 (7), 1127–1134.