A Phase 0 Study for Brain Tumor Imaging Using D-[^{18}F]FMT PET in Human Brains

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Objectives

The aim of the present phase 0 study was to obtain information about distribution, toxicity, pharmacokinetics, and optimal scan time of *O*-([^{18}F]fluoromethyl)-D-tyrosine (D-[^{18}F]FMT) [1][2].

Methods

Six control subjects (median age = 23.0 y) and 3 patients (median age = 55.0 y) with primary or metastatic brain tumor were enrolled (M: F = 4: 5). We acquired 5 times of whole-body PET images during 4 hours (4 control subjects) after injection of 370 MBq of D-[^{18}F]FMT or a 60 min dynamic brain PET image (2 control subjects and 3 patients). The distribution of D-[^{18}F]FMT in each organ was assessed on whole-body PET dataset and the standardized uptake value (SUV) of brain tumor was measured on each dynamic brain PET dataset and. All adverse effects during the clinical trial periods were collected.

Results

D-[^{18}F]FMT was synthesized by the nucleophilic [^{18}F]fluorination of triazolium salt leaving group-tethered precursor [3] and the subsequent deprotection under acid condition in 40% radiochemical yield (non-decay corrected). After injection, the highest uptake of D-[^{18}F]FMT was observed in the kidney and urinary bladder. The brain showed little uptake and the liver showed mild uptake, which decreased over time. In patients with a meningioma (n = 1) metastatic brain tumor from rectal cancer (n = 1), the maximum SUV of brain tumor was 3.5 and 2.0, respectively. In these patients, the SUV of brain tumor reached a peak before 15 min after injection of D-[^{18}F]FMT then continuously decreased over 60 min. In a patient with glioblastoma multiforme (highly malignant primary brain tumor), however, the SUV of brain tumor continuously increased during the first 25 min after injection of D-[^{18}F]FMT and showed little change over 60 min. The maximum SUV of brain tumor was 2.5 in this patient. No adverse event was observed.

Conclusion: D-[^{18}F]FMT is safe and its kinetic behavior is suitable for amino acid imaging in the brain. Further clinical investigations are needed to determine the optimal scan time according to the type of brain tumor.

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References

[1] Tsukada, H. et al., *J. Nucl. Med.* **2006**, *47*, 679-688.
[2] Burger, I. A. et al., *J Nucl. Med.* **2014**, *56*, 1778-1785.
[3] Park, C. et al., *Org. Lett.* **2013**, *15*, 4346-4349.