Development of novel 18F-labeled tyrosine derivatives, O-(3-[18F]fluoro-2-hydroxypropyl)-L-tyrosines for PET imaging of tumor

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Objectives.
Compared with [^{11}C]MET and [^{18}F]FDOPA, tyrosine derivatives are more specific PET imaging agent to tumor [1]. As novel ^{18}F-labeled tyrosine derivatives, *O*-(3-[^{18}F]fluoro-2-hydroxypropyl)-L-tyrosines were synthesized and evaluated in the tumor-bearing mouse.

Methods.
(R)- and (S)-[^{18}F]FHPT were synthesized by the nucleophilic [^{18}F]fluorination of the corresponding nosylate precursors, and subsequent deprotection with 2 N HCl solution. MicroPET and biodistribution study were conducted using the inflammation-induced and concurrent glioma-baring mouse. [^{18}F]FDG and [^{18}F]FET were also examined for comparison.

Results
Two diastereomeric (R)- and (S)-[^{18}F]FHPT were prepared within 60 min including HPLC purification in 42% radiochemical yield (decay-corrected) with high specific activities. During preparation, no epimerization were observed. In vitro cellular uptake experiment, the amount of tumor cell uptake was (R)-[^{18}F]FHPT>(S)-[^{18}F]FHPT>[^{18}F]FET. MicroPET image revealed that while the inflammatory tissue uptake of new tracers was observed to be much lower than [^{18}F]FDG, the accumulation of new tracers into tumor was similar to [^{18}F]FET. In biodistribution study, (S)-[^{18}F]FHPT showed about 2~3 times faster clearance in most organs, e.g. muscle, heart, lung, liver, spleen, stomach, intestine, brain and blood than (R)-[^{18}F]FHPT.

Conclusion
Two [^{18}F]FHPT diastereomers have proved to be tumor-specific PET tracer in the presence of inflammatory lesion. (R)-[^{18}F]FHPT showed similar tumor uptake level (SUV = 1.73 at 60 min) and renal clearance to [^{18}F]FET. Whereas (S)-[^{18}F]FHPT was found to have better pharmacokinetics property although tumor uptake level (SUV and %ID/g) was lower than [^{18}F]FET and (R)-[^{18}F]FHPT.

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