O-(3-[^{18}F]Fluoropropyl)-L-tyrosine

[^{18}F]FPT

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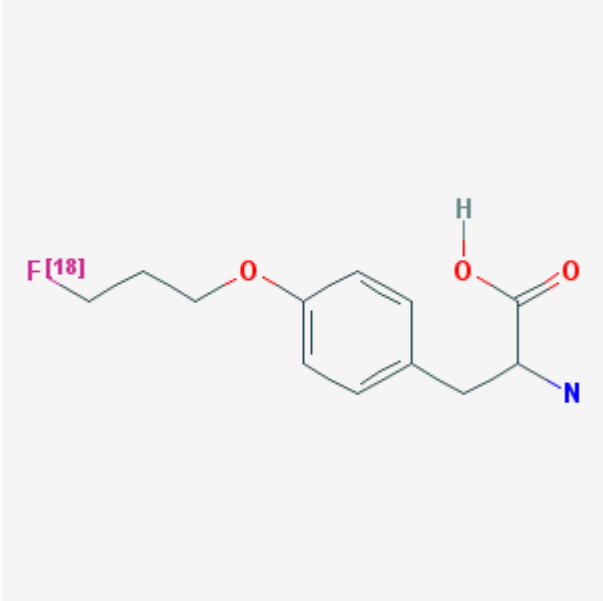
Created: February 18, 2005; Updated: December 5, 2011.

Chemical name:	*O*-(3-[^{18}F]Fluoropropyl)-L-tyrosine
Abbreviated name:	FPT, [^{18}F]FPT
Synonym:	
Agent category:	Compound
Target:	L-type amino acid transporter system and Na^+-dependent system B^0
Target category:	Transporter
Method of detection:	Positron emission tomography (PET)
Source of signal:	^{18}F
Activation:	No
Studies:	• *In vitro* • Rodents • Humans



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Background

[PubMed]

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NLM Citation: Leung K. *O*-(3-[^{18}F]Fluoropropyl)-L-tyrosine. 2005 Feb 18 [Updated 2011 Dec 5]. In: Molecular Imaging and Contrast Agent Database (MICAD) [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2004-2013.

A variety of [^{11}C] and [^{18}F] labeled amino acids have been studied for potential use in positron emission tomography (PET) oncology (1, 2). Most brain tumors show an increased uptake of amino acids as compared with normal brain (3). These amino acids are composed of naturally occurring amino acids such as, L-[^{11}C]leucine, L-[^{11}C]methionine (MET), and L-[^{11}C]tyrosine and non-natural amino acids such as [^{11}C]aminoisobutyric acid, [^{11}C]1-aminocyclopentane-1-carboxylic acid, and [^{11}C]1-aminocyclobutane-1-carboxylic acid. There are also ^{123}I-labeled amino acids used in imaging in oncology (1, 4, 5).

Some 20 amino acid transporter systems have been identified (1). Most of the amino acids are taken up by tumor cells through an energy-independent L-type amino acid transporter system and a sodium-dependent transporter system A but also a Na^+-dependent system B^0 (6). They are retained in tumor cells due to their higher metabolic activities including incorporation into proteins than most normal cells (1). Malignant transformation increases the use of amino acids for energy, protein synthesis and cell division. Tumor cells were found to have over-expressed transporter systems (7). L-[^{11}C]MET, [^{18}F]fluorotyrosine, L-[^{11}C]leucine, and [^{18}F]fluoro-α-methyl tyrosine have been widely used in detection of tumors (2, 6) but are not approved by the FDA. They are moved into cells by various amino acid transporters and are incorporated into proteins. The fraction of radiolabeled amino acid that is incorporated into protein is usually small compared to the total amount taken up into the cell. These natural amino acid images are based on amino acid transport and protein incorporation.

All of the non-natural amino acids are not incorporated into proteins (2, 8). These amino acids are rapidly transported into cells. Recently, a new L-tyrosine analog, *O*-(3-[^{18}F]Fluoropropyl)-L-tyrosine (FPT), was synthesized and evaluated as an amino acid PET tracer for detection of tumors with a higher specificity as compared to FDG (9-11). Therefore, FPT could be a promising tracer in PET tumor imaging based solely on amino acid transport.

Related Resource Links:

- Chapters in MICAD (Amino acid transporters)
- Gene information in NCBI (L-type amino acid transporter, A-type amino acid transporter)
- Articles in Online Mendelian Inheritance in Man (OMIM) (Amino acid transporters)
- Clinical trials (Amino acid transporters)
- Drug information in FDA (Amino acid transporters)

Synthesis

[PubMed]

FPT was prepared by [^{18}F]fluoropropylation of L-tyrosine in a two-step procedure (9). [^{18}F] fluorination (K[^{18}F]F/Kryptofix 2.2.2.) of 1,3-ditosyloxypropane led to a yield of

40-50% with no decay correction. The radiochemical purity of 1-[^{18}F]fluoro-3-tosyloxypropane was about 100%. Subsequently, fluoropropylation with unprotected L-tyrosine by 1-[^{18}F]fluoro-3-tosyloxypropane were performed to give FPT in 60% yield with a chemical purity of >95%. The overall radiochemical yield was about 25-30% in 60 min. This method was automated to give a radiochemical yield of 12% (not decay corrected) in 52 min and a radiochemical purity of >95% (10)

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

O-(2-[^{18}F]Fluoroethyl)-L-tyrosine (FET), a close analog to FPT, was shown to be transported mainly (80%) by the L-type amino acid transporter system and not incorporated into proteins in human SW 707 colon carcinoma cells (12). FET was also found to be transported into F98 rat gliomas (30%) by the Na^+-dependent system B^0 (6).

Animal Studies

Rodents

[PubMed]

Biodistribution of FPT was determined in normal mice with FPT, FET, and [^{18}F]fluoro-2-deoxy-2-D-glucose (FDG) uptake studies in mice bearing S18 fibrosarcoma and *Staphylococcus aureus*-inoculated mice (9). Mice were injected with 0.74-1.48 MBq (20-40 μCi) of the tracers. In addition, S18-bearing mice and *S. aureus*-inoculated mice were imaged using FPT PET compared with FET and FDG PET imaging. High uptake and long retention time of FPT and FET in most organs, such as kidneys, liver, lung, blood, and heart, and low uptake in brain were found. Furthermore, high FPT, FET, and FDG uptake in tumor, and almost no FPT and FET uptake in inflammatory tissue, were observed. In contrast, FDG uptake in inflammatory tissue was high. FPT seems to be a potential amino acid tracer similar to FET for tumor imaging with PET.

Other Non-Primate Mammals

[PubMed]

No publication is currently available.

Non-Human Primates

[PubMed]

No publication is currently available.

Human Studies

[PubMed]

Internal dosimetry data for FPT in humans have not yet been available in the literature. The human dosimetry resulting from the intravenous administration of FPT were estimated using biodistribution data from normal mice (11). The highest uptake of FPT was found in the urinary bladder and pancreas, followed by the liver and kidneys. The urinary bladder wall received the highest absorbed dose of 101.0 μGy/MBq (373.7 mrad/mCi) for a 70-kg standard man. The brain received the lowest dose, 6.5 μGy/MBq or 24.1 mrad/mCi. Other organs received doses in the range of 6.5–37.5 μGy/MBq (24.1-138.8 mrad/mCi). The effective dose was 18.2 μSv/MBq (67.3 mrem/mCi). The data show that a 370-MBq (10 mCi) injection of FPT would lead to an estimated effective dose of 6.7 mSv (24.8 rem), which is in the accepted range of routine nuclear medicine investigations.

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