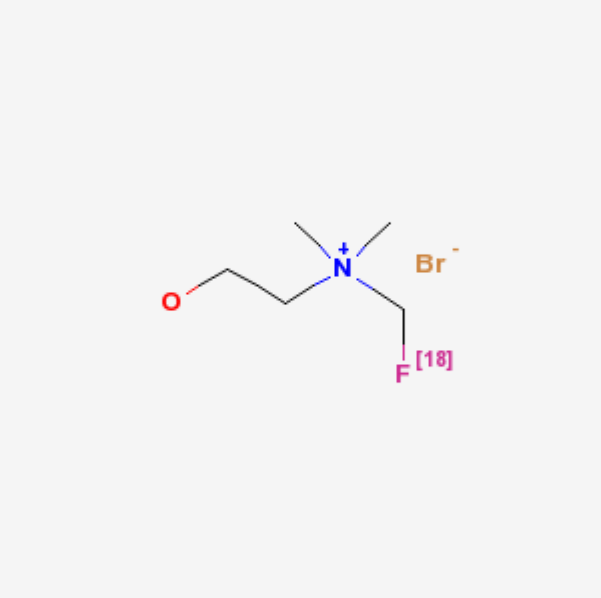
[^{18}F]Fluorocholine

[^{18}F]FCH

Kam Leung, PhD[1]

Created: October 4, 2004; Updated: February 1, 2011.

Chemical name:	[^{18}F]Fluorocholine
Abbreviated name:	[^{18}F]FCH, FCH
Synonym:	[^{18}F]Fluoromethyl-dimethyl-2-hydroxyethylammonium; [^{18}F]fluoromethylcholine
Agent category:	Compound
Target:	Choline kinases
Target category:	Enzyme
Method of detection:	Positron emission tomography (PET)
Source of signal:	^{18}F
Activation:	No
Studies:	• *In vitro* • Rodents • Humans



Click on the above structure for additional information in PubChem.

Background

[PubMed]

[1] National Center for Biotechnology Information, NLM, NIH, Bethesda, MD; Email: MICAD@ncbi.nlm.nih.gov.

Corresponding author.

NLM Citation: Leung K. [^{18}F]Fluorocholine. 2004 Oct 4 [Updated 2011 Feb 1]. In: Molecular Imaging and Contrast Agent Database (MICAD) [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2004-2013.

Choline is an important component of phospholipids in the cell membranes. Tissues with increased metabolism will lead to an increased uptake of choline. Choline is phosphorylated by choline kinases (CHK) to phosphorylcholine within cells, and, after several biosynthetic processes, finally is integrated into phospholipids (1). Because tumor cells have a high metabolic rate, choline uptake is high in order to keep up with the demands with the synthesis of phospholipids in their cellular membranes (2).

Positron emission tomography (PET) with [^{11}C]choline has been reported to be useful for the detection and differential diagnosis of brain tumors, prostate cancer, lung cancer, and esophageal cancer (3). However, [^{11}C]choline has a high uptake in liver, kidney, and spleen. [^{18}F]-labeled choline analog was initially synthesized as [^{18}F]fluoroethylcholine to replace [^{11}C]choline as a PET tracer due to the short physical half-life of ^{11}C (4). Although ^{18}F has a longer half-life (110 min), [^{18}F]fluoroethylcholine showed a rapid accumulation in the urinary bladder, rendering it less desirable for imaging prostate cancer and pelvic lymph nodes. Therefore, [^{18}F]fluorocholine (FCH) was conceived to be a better biological analog than [^{18}F]fluoroethylcholine (5). FCH PET studies showed high uptake in malignancies in patients with prostate cancer, breast carcinoma, and brain tumors (6, 7).

Related Resource Links:

- Chapters in MICAD (Choline)
- Gene information in NCBI (Choline kinase)
- Articles in Online Mendelian Inheritance in Man (OMIM) (Choline kinase)
- Clinical trials (Fluorocholine)
- Drug information in FDA (Fluorocholine)

Synthesis

[PubMed]

[^{18}F]Choline was synthesized from [^{18}F]fluorobromomethane and dimethylethanolamine with a radiochemical purity greater than 98% and a radiochemical yield (not corrected for decay) for the synthesis and purification was approximately 20-40% (5). An automated method of FCH synthesis was achieved by the reaction of [^{18}F]fluoromethyl triflate with dimethylethanolamine on a Sep-Pak column. The total time required for obtaining the finished chemical was 30 min. The radiochemical yield (decay corrected) was 80% with the radiochemical purity and chemical purity of > 98% (8).

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

The radiochemical purity of FCH was found to be stable at room temperature for 7 hours and at 37°C in human whole blood for 2 hours. Both [^{14}C]choline and FCH was phosphorylated by yeast CHK. Cultured PC-3 human prostate cells accumulated FCH at a

slightly lower rate than FDG. The FCH uptake and phosphorylation were inhibited by a CHK inhibitor, HC-3. Approximate 72% of radioactivity was in phosphocholine and 25% of radioactivity was in lipophilic metabolites after two hours of incubation with PC-3 cells (6).

Animal Studies

Rodent Studies

[PubMed]

In a murine PC-3 xenograft model, *ex vivo* biodistribution of FDG, [^{14}C]choline and FCH were compared. FCH showed a similar biodistribution to [^{14}C]choline in the tumor-bearing mouse, with prominent uptake in kidney, liver, lung, and heart. No differences were observed in the biodistribution pattern in normal tissues of control and tumor-bearing mice. Tumor uptake of FCH was similar to [^{14}C]choline and FDG in the mouse model, however, tumor-to-blood ratios were moderately higher for FCH (9).

Other Non-Primate Mammal Studies

[PubMed]

No publication is currently available.

Non-Human Primate Studies

[PubMed]

No publication is currently available.

Human Studies

[PubMed]

FCH was cleared from blood in the first 5 min after administration in humans. The radioactivity in the liver increased rapidly in the first 10 min and then gradually thereafter. The FCH PET scan of 12 normal human subjects showed the highest uptake in the kidneys, liver, and spleen. Human dosimetry was estimated based on murine and human biodistribution data. The kidneys received the highest dose of radioactivity, followed by the bladder, liver, and spleen (10). The effective dose equivalent of administration of 4.07 MBq/kg (0.11 mCi/kg) is about 0.03 mSv/MBq (0.1 rad/mCi).

PET imaging studies of cancer patients showed the feasibility of FCH uptake in prostate cancer, breast cancer, and brain tumors. Osseous, soft tissue and lymph node metastases were also detected by FCH uptake foci (5, 6). Two recent prostate cancer studies with a total of 36 patients showed that malignant tumors, recurrent tumors and lymph node metastases could be localized with FCH PET scans (11, 12). However, Schmid et al. (12)

noted that differentiation of benign hyperplasia from malignant prostate lesions was not possible with FCH PET.

References

1. Zeisel S.H., Blusztajn J.K. *Choline and human nutrition.* Annu Rev Nutr. 1994;14:269–96. PubMed PMID: 7946521.
2. Podo F. *Tumour phospholipid metabolism.* NMR Biomed. 1999;12(7):413–39. PubMed PMID: 10654290.
3. Hara T. *11C-choline and 2-deoxy-2-[18F]fluoro-D-glucose in tumor imaging with positron emission tomography.* Mol Imaging Biol. 2002;4(4):267–73. PubMed PMID: 14537115.
4. Hara T., Yuasa M. *Automated synthesis of fluorine-18 labeled choline analogue: 2-fluoroetheyl-dimethyl-2-oxyethylammonium*. J Nucl Med. 1997;38 Supplement:44P. PubMed PMID: 8998148.
5. DeGrado T.R., Coleman R.E., Wang S., Baldwin S.W., Orr M.D., Robertson C.N., Polascik T.J., Price D.T. *Synthesis and evaluation of 18F-labeled choline as an oncologic tracer for positron emission tomography: initial findings in prostate cancer.* Cancer Res. 2001;61(1):110–7. PubMed PMID: 11196147.
6. DeGrado T.R., Baldwin S.W., Wang S., Orr M.D., Liao R.P., Friedman H.S., Reiman R., Price D.T., Coleman R.E. *Synthesis and evaluation of (18)F-labeled choline analogs as oncologic PET tracers.* J Nucl Med. 2001;42(12):1805–14. PubMed PMID: 11752077.
7. Hara T., Kondo T., Hara T., Kosaka N. *Use of 18F-choline and 11C-choline as contrast agents in positron emission tomography imaging-guided stereotactic biopsy sampling of gliomas.* J Neurosurg. 2003;99(3):474–9. PubMed PMID: 12959432.
8. Iwata R., Pascali C., Bogni A., Furumoto S., Terasaki K., Yanai K. *[18F]fluoromethyl triflate, a novel and reactive [18F]fluoromethylating agent: preparation and application to the on-column preparation of [18F]fluorocholine.* Appl Radiat Isot. 2002;57(3):347–52. PubMed PMID: 12201141.
9. Price D.T., Coleman R.E., Liao R.P., Robertson C.N., Polascik T.J., DeGrado T.R. *Comparison of [18 F]fluorocholine and [18 F]fluorodeoxyglucose for positron emission tomography of androgen dependent and androgen independent prostate cancer.* J Urol. 2002;168(1):273–80. PubMed PMID: 12050555.
10. DeGrado T.R., Reiman R.E., Price D.T., Wang S., Coleman R.E. *Pharmacokinetics and radiation dosimetry of 18F-fluorocholine.* J Nucl Med. 2002;43(1):92–6. PubMed PMID: 11801711.
11. Kwee S.A., Coel M.N., Lim J., Ko J.P. *Prostate cancer localization with 18fluorine fluorocholine positron emission tomography.* J Urol. 2005;173(1):252–5. PubMed PMID: 15592091.
12. Schmid D.T., John H., Zweifel R., Cservenyak T., Westera G., Goerres G.W., von Schulthess G.K., Hany T.F. *Fluorocholine PET/CT in patients with prostate cancer: initial experience.* Radiology. 2005;235(2):623–8. PubMed PMID: 15858102.